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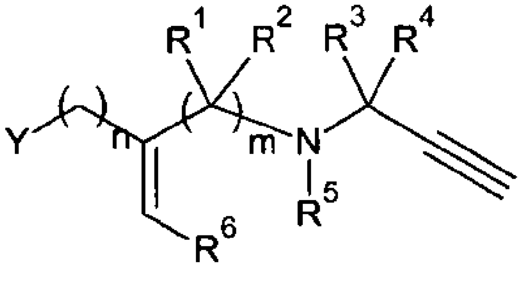
(54) **Title**: NEW ARYLALKENYLPROPARGYLAMINE DERIVATIVES EXHIBITING NEUROPROTECTIVE ACTION FOR THE TREATMENT OF NEURODEGENERATIVE DISEASES



(I)

(57) **Abstract**: The invention relates to novel arylalkenylpropargylamine derivatives of general formula (I) or enantiomers or diastereomers thereof or salts, optionally pharmaceutically acceptable salts, or solvates of any of these. The compounds can be used in treating or preventing a disease or condition in a mammal related to monoamine oxidase dysfunction, especially in neurodegenerative diseases, e.g. Parkinson's disease, Alzheimer's disease or Huntington's disease.

New arylalkenylpropargylamine derivatives exhibiting neuroprotective action for the treatment of neurodegenerative diseases

Field of the invention

The invention relates to novel (hetero)aryl propargylamines and compositions containing thereof. The compounds can be used in treating or preventing a disease or condition in a mammal related to monoamine oxidase dysfunction, especially in neurodegenerative diseases, e.g. Parkinson's disease, Alzheimer's disease or Huntington's disease.

Background of the invention

Brain diseases represent a considerable economic and social burden all over the world. According to the WHO, they are responsible for 35% of total disease burden. Neurodegenerative diseases (Parkinson disease, Alzheimer's disease, stroke, etc.) are characterized by the progressive loss of neurons and typically occur in the elderly population, therefore, their incidence is continuously rising in industrialized countries. Parkinson's disease (PD) is a chronic neurodegenerative disease, which is characterized by the progressive degeneration of nigrostriatal dopaminergic pathway of the brain. The disease is manifested in various motor symptoms such as bradykinesia, postural instability, resting tremor and muscle rigidity, appearing only at an advanced (70%) stage of degeneration. The disease primarily affects the elderly population and during the progress of pathology, the degeneration extends to other cortical and subcortical non-dopaminergic pathways, which are responsible for non–motor symptoms such as depression, delusions and cognitive decline.

The current treatment of PD relies on the replacement of the precursor of dopamine by L-DOPA substitution or dopaminergic agonists (Poewe L et al, Curr. Opin. Neurol., 2012, 25, 448-459; Jankovic J et al, Curr. Opin. Neurol., 2012, 25, 433-447). However, a necessary prerequisite of these approaches are functioning dopaminergic nerve terminals in the striatum, therefore, in parallel with the progression of the disease they become ineffective. Moreover, they have untoward side effects and complications, e.g. dyskinesias or motor fluctuations, which cannot be easily tolerated during a life-long treatment. Another mainstream approach used in existing therapies is to inhibit the enzymes involved in the metabolic degradation of dopamine (MAO, COMT) and thereby elevate dopamine bioavailability, which is primarily used as an add-on therapy (Youdim MB et al, Neurology, 2004, 63, S32-35). Selective mono-aminooxidase-B (MAO-B) inhibitors inhibit the enzyme, responsible for the intracellular degradation of dopamine and thereby increase dopamine availability of the nigrostriatal pathway and they also prolong the action of L-DOPA replacement therapy. In addition, certain MAO-B inhibitors, such as selegiline or rasagiline, were thought to be neuroprotective against dopaminergic cell death. In fact, rasagiline, which is a selective and irreversible inhibitor of the MAO-B, increases cell survival in cell culture and animal models of PD (Zheng H et al, J. Neurochem., 2005, 95, 68-78;

Bar-Am O et al, J. Neurochem., 2007, 103, 500-508); however, this protective effect is not translated to a clinically convincing neuroprotective action (Ahlskog JE et al, Neurology, 2010, 74, 1143-1148; Olanow CW et al, Neurology, 2010, 74, 1149-1150). In the recent ADAGIO (Attenuation of Disease Progression with Azilect Given Once-Daily) trial, a delayed start study design was applied to separate symptomatic benefit from disease-modifying effect, however, the results failed to define a clear, neuroprotective action of rasagiline (Ahlskog JE et al, Neurology, 2010, 74, 1143-1148).

Accordingly, FDA rejected expanded indication for rasagiline as a disease-modifying agent for Parkinson disease (October, 2011, http://www.medscape.com-/viewarticle/751680). Neurodegeneration – depending on the size and function of the affected brain area – can be manifested in sensory, motor, associative or cognitive dysfunction, all of them having tremendous impact on the quality of life. Despite the intensive effort in the recent years directed at understanding the biological basis of neuronal death and survival, treatments for neurodegenerative diseases have, unfortunately, not yet been found. As a rule, neurons are *ab ovo* unable to divide and thus dead neurons are neither replaced nor regenerated in the adult CNS. On the other hand, the process leading to neuronal death is remarkably complex and involves different self-amplifying mechanisms on subcellular, cellular and system levels, which provides numerous individual target sites for pharmacological intervention. However, those drugs that act on a single target site are not likely to have significant influence on the final outcome. Conversely, those drugs or drug-candidates that have some neuroprotective action usually have serious CNS side effects and so far the majority of these compounds have failed at different steps of the drug development process (Dunkel P et al, Expert Opin. Investig. Drugs, 2012, 21, 1267-1308). Therefore, despite of considerable efforts, at present, there is no single therapeutic agent, which is clinically neuroprotective in PD, i.e., which is able to halt or slow down the progression of the neurodegeneration in clinical settings (Seidl SE et al, Front. Neurol., 2011, 2, 68; Meissner WG et al, Nat. Rev. Drug Discov., 2011, 10, 377-393), and there is an urgent need to find new and innovative strategies to interrupt neurodegeneration.

As referred above, MAO inhibitors (MAOI) are used in the treatment of Parkinson's disease and depression, and these inhibitors provide symptomatic relief in patients as a result of higher concentrations of the neurotransmitters due to reduced metabolism. Monoamine oxidases A and B are mitochondrial enzymes that metabolise neurotransmitters in the CNS. MAO B has long been relevant drug target for neurodegenerative and neurological diseases.

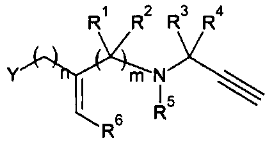
The development of neurodegeneration is also linked closely to mitochondrial dysfunction caused by oxidative stress (Schapira AH et al, JAMA, 2004, 291, 358-364; Fahn S et al, NeuroRx, 2004, 1, 139-154). In dopaminergic neurons, monoamines and their metabolites provide an additional source of highly reactive free radicals during their breakdown by monoamine oxidase or auto-oxidation, thereby potentially reinforcing the harmful effects of oxidative stress. Moreover, mitochondrial dysfunction and oxidative stress have a supraaddditive impact on the pathological, cytoplasmic accumulation of dopamine and subsequent release (Milusheva E et al, Free Radic. Biol.

Med., 2005, 39, 133-142; Baranyi M et al, J. Chromatogr. A., 2006, 1120, 13-20). Thus, even a minimal mitochondrial deficit could predispose neurons to the harmful effect of subsequent oxidative stress and thereby aggravate the generation of the toxic dopamine metabolites and hence the process leading to neuronal death. This information suggests that those drugs which simultaneously target mitochondrial dysfunction, oxidative stress and pathological dopamine release may have disease-modifying potential in addition to symptomatic improvement.

This invention outlines the synthesis, biological activities and potential applications of a novel series of compounds that demonstrates highly potent MAO-B inhibitory activity with remarkable selectivity over other types of monoamine oxidase enzymes as well as exhibits unexpectedly excellent neuroprotection properties. Based on our studies described below, the compounds of the invention may represent a real therapeutic breakthrough for neurodegenerative diseases, having the potential to provide both symptomatic relief and disease-modifying action such that further degeneration is prevented. Undoubtedly, one possible application area of the compounds described herein is the treatment of Parkinson's disease. In addition, as most neurodegenerative mechanisms are shared in many CNS disorders, the compounds could be used to treat other neurodegenerative diseases.

Summary of the invention

1. The invention relates to a compound of general formula (I)



wherein:

R^1 and R^2 are independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl and optionally substituted C_{6-10} aryl;

R^3 and R^4 are independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl and optionally substituted C_{6-10} aryl;

R^5 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl and optionally substituted C_{6-10} aryl;

R^6 is hydrogen or halogen;

Y is C_{6-10}aryl or heteroaryl, optionally substituted with one or more substituents selected from the group consisting of

- C_{1-6}alkyl or C_{2-6}alkenyl which is optionally substituted with one or more halogen, C_{6-10}aryl, aminoC_{6-10}aryl, C_{6-10}aryloxy or C_{5-14}heteroaryloxy,
- halogen,
- nitro,
- cyano,

- C_{1-6}alkoxy which is optionally substituted with one or more halogen, C_{6-10}aryl or amino, which amino is optionally substituted with one or more C_{1-6}alkyl,

- C_{1-6}alkoxycarbonyl,
- C_{1-6}alkylsulfanyl,
- C_{1-6}alkylsulfonyl,
- amino which is optionally substituted with one or more C_{1-6}alkyl, C_{6-10}arylsulfonyl, C_{1-6}alkylsulfonyl, C_{6-10}arylC_{1-6}alkyl or C_{1-6}alkoxy substituted with C_{6-10}aryl,
- C_{3-7}cycloalkoxy,
- C_{3-7}cycloalkyl,
- C_{6-10}aryl,
- C_{5-14}heteroaryl;
- saturated C_{5-12}heterocyclyl;
- hydroxyC_{1-6}alkyl
- hydroxyl,
- carbamate which is optionally substituted with one or more C_{1-6}alkyl
- all the aryl given as substituent of Y is optionally further substituted with halogen, C_{1-6}alkyl, C_{1-6}alkoxy or cyano;

n is an integer of 0 to 2
m is an integer of 1 to 5;

or an enantiomer or diastereomer thereof or a salt, optionally a pharmaceutically acceptable salt, or a solvate of any of these.

2. The compounds of general formula (I) according to above point 1, wherein
R^1 and R^2 is independently selected from hydrogen and C_{1-4}alkyl;
R^3 and R^4 is independently selected from hydrogen and C_{1-4}alkyl;
R^5 is selected from the group consisting of hydrogen and C_{1-6}alkyl optionally substituted with phenyl or with 1 to 3 halogen;
R^6 is hydrogen or halogen;
n has the value of 0 or 1;
m has the value of 1 to 4.

3. The compounds of general formula (I) according to above point 2, wherein
R^1 and R^2 is independently selected from hydrogen and methyl;
R^3 and R^4 is independently selected from hydrogen and methyl;
R^5 is selected from the group consisting of hydrogen, methyl optionally substituted with phenyl, and ethyl optionally substituted with 1 to 3 halogen(s);
R^6 is hydrogen or halogen.

4. The compounds of general formula (I) according to above points 1 to 3, wherein

Y is selected from the group consisting of phenyl, naphthyl, indenyl, dihydrobenzodioxinyl, dihydrobenzofuranyl, benzodioxolyl, pyrrolyl, thienyl, thiazolyl, imidazolyl, furanyl, indolyl, isoindolyl, dioxolo-indolyl, oxazolyl, isoxazolyl, benzothiazolyl, benzoimidazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiophenyl, benzo[b]thiophenyl, indazolyl, pyrazolyl, benzofuranyl, naphtofuranyl, triazolyl, tetrazolyl and imidazolyl, optionally substituted with one or more substituents selected from the group consisting of

- C_{1-4}alkyl which is optionally substituted with one or more halogen, C_{6-10}aryl, aminoC_{6-10}aryl, C_{6-10}aryloxy or C_{5-13}heteroaryloxy,
- C_{2-4}alkenyl,
- halogen,
- nitro,
- cyano,
- C_{1-4}alkoxy which is optionally substituted with one or more halogen, C_{6-10}aryl or amino, which amino is optionally substituted with one or more C_{1-6}alkyl,
- C_{1-4}alkoxycarbonyl,
- C_{1-4}alkylsulfanyl,
- C_{1-4}alkylsulfonyl,
- amino which is optionally substituted with one or more C_{1-4}alkyl, C_{6-10}arylsulfonyl, C_{1-4}alkylsulfonyl, C_{6-10}arylC_{1-4}alkyl or C_{1-4}alkoxy substituted with C_{6-10}aryl,
- C_{3-5}cycloalkoxy,
- C_{3-5}cycloalkyl,
- C_{6-10}aryl,
- C_{5-13}heteroaryl;
- saturated C_{5-12}heterocyclyl;
- hydroxyC_{1-4}alkyl
- hydroxyl,
- carbamate which is optionally substituted with one or more C_{1-4}alkyl
- all the aryl given as substituent of Y is optionally further substituted with halogen, C_{1-4}alkyl, C_{1-4}alkoxy or cyano.

5. The compounds of general formula (I) according to above point 4, wherein

Y is selected from the group consisting of phenyl, naphthyl, indenyl, pyrrolyl, thiazolyl, furanyl, indolyl, dioxolo-indolyl, isoxazolyl, benzothiazolyl, pyridinyl, thiophenyl, benzo[b]thiophenyl, indazolyl, pyrazolyl, benzofuranyl, naphtofuranyl, dihydrobenzofuranyl and benzodioxolyl, optionally substituted with one or more substituents selected from the group consisting of

- C_{1-4}alkyl which is optionally substituted with one or more halogen, phenyl, aminophenyl, phenoxy or indolyloxy,
- C_{2-4}alkenyl,
- halogen,
- nitro,
- cyano,
- C_{1-4}alkoxy which is optionally substituted with one or more halogen, phenyl or amino, which amino is optionally substituted with one or more C_{1-6}alkyl,
- C_{1-4}alkoxycarbonyl,
- C_{1-4}alkylsulfanyl,
- C_{1-4}alkylsulfonyl,
- amino which is optionally substituted with one or more C_{1-4}alkyl, tosyl, mesyl, benzyl or benzyloxy,
- C_{3-5}cycloalkoxy,
- C_{3-5}cycloalkyl,
- phenyl,
- benzofuranyl
- morpholinyl
- hydroxyC_{1-4}alkyl
- hydroxyl,
- carbamate which is optionally substituted with one or more C_{1-4}alkyl;
- all the phenyl given as substituent of Y is optionally further substituted with halogen, C_{1-4}alkyl, C_{1-4}alkoxy or cyano.

6. The compounds of general formula (I) according to above point 5, wherein

Y is selected from phenyl optionally substituted with one or more substituents selected the group consisting of halogen, nitro, cyano, benzyloxy, methoxy, 5-indolyloxymethyl, methyl optionally substituted with 1 to 3 halogen, benzyloxy optionally substituted with methylsulfanyl, halogen and methoxy, phenoxymethyl optionally substituted with methoxy or with 1 to 3 halogen, and

tiophen-2-yl optionally substituted with chloro,
furan-2-yl,
furan-3-yl,
benzofuran-2-yl optionally substituted with chloro, methoxy or fluoro,
methyl-pyrazol-4-yl,
1-methylene-2,3-dihydro-1H-inden-2-yl.

7. The compounds of general formula (I) according to above point 6 comprising

N-Methyl-2-phenyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine

2-Phenyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(4-Chlorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Fluorobenzyl)oxy)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Fluorobenzyl)oxy)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3,4-Difluorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3,4-Difluorophenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
N-Methyl-2-(3-(phenoxymethyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-(Phenoxymethyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
N-methyl-N-(prop-2-yn-1-yl)-2-(thiophen-2-yl)prop-2-en-1-amine
2-(Furan-3-yl)-N-methyl-N-(prop-2-ynyl)prop-2-en-1-amine
2-(3-(Benzyloxy)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(5-Chlorothiophen-2-yl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Methoxybenzyl)oxy)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-(((1H-indol-5-yl)oxy)methyl)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((4-Fluorophenoxy)methyl)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Chlorobenzyl)oxy)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((4-Fluorobenzyl)oxy)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Fluorophenoxy)methyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3,5-Difluorophenoxy)methyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(4-Fluorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine

or an enantiomer or diastereomer thereof or a salt, optionally a pharmaceutically acceptable salt, or solvate of any of these.

8. A pharmaceutical composition comprising a compound of general formula (I) or an enantiomer or diastereomer thereof or a salt, optionally a pharmaceutically acceptable salt or solvate according to any of above points 1 to 7 admixed with a pharmaceutically acceptable carrier, excipient or diluent.

9. A compound according to any of above points 1 to 7 for use in treating or preventing a disease or condition in a mammal related to monoamine oxidase dysfunction.

10. The compound for use according to above point 9 wherein the disease or condition is selected from the group consisting of neurodegenerative diseases.

11. The compound for use according to above point 9 wherein the condition is Parkinson's disease.

12. The compound for use according to above point 9 wherein the compound is administered at a dose range of 0,1-10 mg/kg in animals and 0.1-10 mg in human.

In a second aspect of the invention there is provided use of a compound according to the first aspect for the manufacture of a medicament for the treatment of neurodegenerative diseases. In a third aspect of the invention there is provided use of a compound according to the first aspect in therapy. In particular there is provided use of a compound according to the first aspect for the treatment of neurodegenerative diseases. In a fourth aspect of the invention there is provided a composition, in particular a pharmaceutical composition, comprising a compound according to the first aspect, or an enantiomer, diastereomer or pharmaceutically acceptable salt thereof, together with one or more pharmaceutically acceptable carriers, diluents, excipients or adjuvants. The composition may be suitable for the treatment of cancer. In a fifth aspect of the invention there is provided a method of treating neurodegenerative diseases comprising administering to a patient in need thereof a clinically effective amount of a compound according to the first aspect, or an enantiomer, diastereomer or pharmaceutically acceptable salt thereof, or of a composition according to the fourth aspect. The present invention also encompasses enantiomers and diastereomers of the compounds described above. It also encompasses solvates, e.g. hydrates, of the compounds and of their enantiomers and diastereomers. It also encompasses salts of the compounds and of their enantiomers and diastereomers. The salts may be clinically acceptable salts. They may pharmaceutically acceptable.

Brief description of drawings

Figure 1: Effect of test compounds (10 nM) on oxidative stress induced pathological dopamine release in rat striatum slices.

Figure 2: Effect of test compounds (10 nM) on oxidative stress induced pathological dopamine release in rat striatum slices.

Figure 3 A and B: Effect of test compounds (10 nM) on ischemic-like conditions induced pathological dopamine release in rat striatum slices. [^{3}H]dopamine release is expressed as fractional release (%) i.e. as percentage of the actual tritium content of the slices. N=4-8 independent experiment/group. Test compounds or their vehicle (CTRL) were administered (A) 15 min before the start of the ischemic-like conditions (B) 18 min before the second stimulation period (EFS2) and onwards.

Figure 4: Effect compounds of the invention (10 mg/kg i.p.) on endogenous dopamine content in the striatum and on the survival of animals after *in vivo* MPTP treatment. Symbols represent significant changes from saline treated ($^{+++}P<0.001$), MPTP treated ($^*P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$) and rasagiline (20 mg/kg) treated animals, ($^{\#}P<0.05$, $^{\#\#\#}P<0.001$), respectively. Statistical analysis: one-way ANOVA followed by the Tukey test (dopamine content) and log rank test (survival). Number of independent experiments: 5-8/group.

Figure 5: Effect of compounds of the invention (10 mg/kg i.p.) on endogenous dopamine content in the striatum and on the survival of animals after *in vivo* MPTP treatment. Statistical analysis: one-way ANOVA followed by the Tukey test (dopamine content) and log rank test (survival). Number of independent experiments: 5-8/group.

Figure 6 A: Effect of compounds of the invention (10 mg/kg i.p.) on the basal locomotor activity, measured in the open field test . Symbols represent significant changes from saline ($^{+++}$P<0.001) and MPTP treated (***P<0.001) animals, respectively. Statistical analysis: one-way ANOVA followed by the Tukey test.

Figure 6 B: Effect of compounds of the invention (10 mg/kg i.p.) on the basal locomotor activity, measured in the rotarod test. Symbols represent significant changes from respective pretreatment values (**P<0.01). Statistical analysis: one-way ANOVA followed by the Dunnett test. The time elapsed until the falling of the mice was expressed in sec.

Figure 7: Dose-dependent effect of compound SZV-1902 (0.1-10 mg/kg i.p.) on endogenous dopamine content in the striatum after *in vivo* MPTP (4x20 mg/kg) treatment. Dopamine content is expressed as pmol/mg protein. Symbols represent significant changes from saline treated ($^{+++}$P<0.001), MPTP treated (**P<0.01, ***P<0.001) treated animals, respectively. Statistical analysis: one-way ANOVA followed by the Tukey test. Number of independent experiments: 5-8/group.

Figure 8 A and B: Effect of compounds of the invention (10 mg/kg i.p.) on endogenous dopamine metabolite (DOPAC, HVA) levels in mouse striatum 72 h after after *in vivo* MPTP treatment. Metabolite levels are expressed as pmol/mg protein. Symbols represent significant changes from saline treated ($^{+}$P<0.05), MPTP treated (*P<0.01, ***P<0.001) and rasagiline (20 mg/kg) treated animals, ($^{\#}$P<0.05, $^{\#\#\#}$P<0.001), respectively. Statistical analysis: one-way ANOVA followed by the Tukey test. Number of independent experiments: 7-12/group.

Figure 9: The duration of action of compound SZV-1902 (10 mg/kg) i.p. and the effect on endogenous dopamine content in the striatum and on the survival of animals after *in vivo* MPTP treatment.

Figure 10: The effect of SZV-1902, SZV-2220 and rasagiline (10 mg/kg i.p for 21 days each) on MPTP depleted endogenous dopamine content in the mice striatum using the Tatton-Kish model. Symbols represent significant changes from saline treated ($^{+++}$P<0.001), MPTP treated (***P<0.001) and rasagiline treated animals, ($^{\#}$P<0.05), respectively. Statistical analysis: one-way ANOVA followed by the Tukey test. Number of independent experiments: 8-12/group.

Figure 11 A-F: Hematoxylin-eosin staining on striatal sections of mice undergone subacute MPTP treatment according to the Tatton-Kish model.

(A) The control tissue show typical staining and round shape morphology of nuclei (black arrow). Damaged structure of striatal section in case of MPTP treatment (B). Similar morphology and nuclear staining in rasagiline (C), SZV-1902 (D) and SZV-2220 (E) treated mouse striatal sections. Among healthy, typically stained nuclei, white arrowhead shows a damaged one. Its shape is not spherical, nucleoli cannot be distinguished. This type of staining is abundantly found in C-E pictures and only few in control sections. (F) Statistical analysis of nuclei number in the different sections. Nuclei were counted in five-five parallel sections, one-way ANOVA, with Tukey's post-test was used. *P<0.05, ***P<0.0001. Bars: 50 μmeter

The representative pictures were taken at 40X original magnification (Figure 11A-E). The difference among the appearance of striatal sections originated from control, rasagiline+MPTP, SZV-1902 +MPTP, SZV-2220+MPTP and MPTP treated mouse brain is obvious.

In case of MPTP treatment the tissue is highly damaged, it is full with defects, holes and, compared with the control section, only few healthy, impeccable nuclei can be seen. On the contrary, there are no defects in the sections derived from control, SZV-1902 +MPTP and SZV-2220+MPTP treated mouse brain. Counting of nuclei on the same area of the different sections and statistical analysis resulted significant difference between the number of nuclei found in control and MPTP sections and between MPTP and SZV-1902, SZV-2220 and rasagiline sections (Figure 11F).

Figure 12: Electron microscopic analyses of cell damage after striatal sections of mice undergone subacute MPTP treatment according to the Tatton-Kish model.

Figure 13: Effect of compounds of the invention (10 μM) on the survival of PC12 cells 24 h after 6-OHDA (200 μM) treatment. Survival data are expressed as percentage of 6-OHDA treated cells. Symbols represent significant changes from 6-OHDA treated (**P<0.01, ***P<0.001) cells. Statistical analysis: one-way ANOVA followed by the Tukey test. Each data are the average of at least 8 values measured in 2 independent plates

Detailed description of the invention

Unless otherwise stated, the following terms used in the specification and claims are defined for the purposes of this Application and have the following meaning:

As used herein the term "aryl" means a monovalent mono- or bicyclic aromatic hydrocarbon moiety of 6 to 10 ring atoms ("C_{6-10}aryl") e.g., phenyl or naphthyl. In a preferred embodiment aryl is phenyl.

The phrase "aryl" embraces such bicyclic rings where a linear hydrocarbon moiety of 3 to 4 carbon atoms is fused to a monocyclic aryl forming bicyclic ring system having an aromatic ring and a saturated or partially unsaturated ring, see e.g. dihydronaphtyl, tetrahydronaphtyl and indenyl. In a preferred embodiment the bicyclic ring comprising a saturated or partially unsaturated ring-forming moiety, see e.g. in indenyl.

The phrase "aryl" also embraces such bicyclic rings where one of the rings is monocyclic aromatic ring and a saturated or partially unsaturated heterocyclyl is fused to said aromatic ring comprising one or more heteroatoms selected from N, O, or S and the remaining ring atoms are carbon. In a preferred embodiment the saturated or partially unsaturated ring-forming moiety comprises one or two heteroatoms selected from N or O, preferably said ring is of 5 or 6 ring atoms and comprises one or two O. In a more preferred embodiment the bicyclic ring system comprising a heterocyclic ring is benzodioxolyl, 2,3-dihydro-1,4-benzodioxinyl or 2,3-dihidro-benzofuranyl.

Those substituted aryl groups are also within the scope which contain one or more substituent(s) usually applied in the organic chemistry for substitution of aryl groups. So, the substituted aryl groups carry one or more, preferably 1 to 4, e.g. 1 to 3 or 1 to 2 substituent(s), independently selected from the group of halogen, optionally substituted alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, aralkyl, aryloxy, heteroaryloxy, hydroxyl, hydroxyalkyl, optionally substituted saturated heterocyclyls, optionally substituted carbamate, optionally substituted alkoxy, cycloalkoxy, carboxyl, alkoxycarbonyl, cyano, nitro, optionally substituted amino, aminoaryl, alkylsulfanyl, cycloalkylsulfanyl and alkylsulfonyl.

As used herein the term "heteroaryl" means a monovalent mono-, bi- or tricyclic aromatic hydrocarbon moiety of 5 to 14 ring atoms (“C_{5-14}heteroaryl”) , preferably of 5 to 13 (“C_{5-13}heteroaryl”) ring atoms where one or more, preferably one, two, or three, ring atom(s) is/are heteroatom(s) selected from N, O, or S, the remaining ring atoms being carbon. Non-limiting examples are pyrrolyl, thienyl, thiazolyl, imidazolyl, furanyl, indolyl, isoindolyl, oxazolyl, isoxazolyl, benzothiazolyl, benzoimidazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiophenyl, benzo[b]thiophenyl, indazolyl, pyrazolyl, benzofuranyl, triazolyl, tetrazolyl, imidazolyl and naphtofuranyl, wherein pyrrolyl, thiazolyl, furanyl, indolyl, isoindolyl, oxazolyl, isoxazolyl, benzothiazolyl, benzoxazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiophenyl, benzo[b]thiophenyl, indazolyl, pyrazolyl, naphtofuranyl and benzofuranyl are preferred. In a more preferred embodiment heteroaryl is tiophenyl, furanyl, benzofuranyl, pyrazolyl or indenyl.

The phrase "heteroaryl" also embraces such bi- or tricyclic rings where at least one of the rings is aromatic, with the proviso that the aromatic ring is the one that comprises the heteroatom(s), such as 6,7-dihidro-benzofuranyl and dioxolo-indolyl.

Those substituted heteroaryl groups are also within the scope which contain one or more substituent(s) usually applied in the organic chemistry for substitution of heteroaryl groups. So, the substituted heteroaryl groups carry one or more, preferably 1 to 4 substituent(s), e.g. 1 to 3 or 1 to 2 substituent(s), independently selected from the group of halogen, alkyl, hydroxyl, hydroxyalkyl, carboxyl, alkoxy, nitro, amino, alkylsulfinyl, alkylsulfonyl and cyano, where alkyl (more preferably methyl), optionally substituted with halogen, alkoxy and halogen are preferred.

As used herein the term “heterocyclyl” are saturated or partially unsaturated mono- or bicyclic groups of 5 to 12 ring atoms (“C_{5-12}heterocyclyl”) where one or more, preferably one, two, or three, ring atom(s) is/are heteroatom(s) selected from N, O, or S, the remaining ring atoms being carbon, such as pyrollidinyl, piperidinyl, piperazinyl, morpholinyl, dioxanyl. In a preferred embodiment heterocyclyl is morpholinyl.

The term "halogen” means fluorine, chlorine, bromine or iodine atoms.

The term "alkyl" means a linear or branched saturated monovalent hydrocarbon moiety of one to six carbon atoms ("C_{1-6}alkyl"), e.g., methyl, ethyl, propyl, 2-propyl, butyl (including all isomeric forms), pentyl (including all isomeric forms), and the like. In a preferred embodiment alkyl ("C_{1-4}alkyl") is methyl, ethyl, *i*-propyl or *t*-butyl. In addition, the term is intended to include both unsubstituted and substituted alkyl groups, the latter referring to alkyl moieties having one or more hydrogen atoms replaced by usual substituents of alkyl groups, preferably selected from the following group: halogen, optionally substituted amino, aryl, optionally substituted aryloxy and heteroaryloxy. In a preferred embodiment the alkyl which is substituted is methyl or ethyl.

The term "alkenyl" means monovalent hydrocarbon chains of either linear or branched configuration comprising 2 to 6 carbon atoms and further comprising one or more carbon-carbon double bonds ("C_{2-6}alkenyl"), preferably comprising 2 to 4 carbon atoms and one carbon-carbon double bond ("C_{2-4}alkenyl"), more preferably alkenyl is ethenyl.

The term "cycloalkyl" means a non-aromatic monocyclic ring system of about 3 to about 7 carbon atoms ("C_{3-7}cycloalkyl"), preferably monocyclic ring having 3 to 5 carbon atoms ("C_{3-5}cycloalkyl"), most preferably cyclopropyl.

The term "C_{6-10}arylC_{1-6}alkyl" means a C_{6-10}aryl group coupling via alkyl group of 1 to 6 carbon atoms. In a preferred embodiment C_{6-10}arylC_{1-6}alkyl is benzyl.

The term "aryloxy" means a C_{6-10}aryl group coupling via oxygen ("C_{6-10}aryloxy"). In addition, the term is intended to include both unsubstituted and substituted aryloxy groups, the latter referring to aryloxy moieties having one or more hydrogen atoms replaced by usual substituents of aryl groups, preferably selected from the following group: halogen, cyano and alkoxy. In a preferred embodiment C_{6-10}aryloxy is phenoxy optionally substituted with halogen cyano or methoxy.

The term "heteroaryloxy" means a heteroaryl group coupling via oxygen ("C_{5-14}heteroaryloxy"). In a preferred embodiment heteroaryloxy is indolyloxy.

The term "hydroxyalkyl" means a C_{1-6}alkyl group substituted with one or two hydroxyl groups ("hydroxyC_{1-6}alkyl"), provided that if two hydroxyl groups are present they are not both on the same carbon atom. Examples include, but are not limited to hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl and 3-hydroxypropyl, wherein hydroxymethyl is preferred.

The term "alkoxy" is intended to mean an alkyl group coupling via oxygen ("C_{1-6}alkoxy"). In addition, the term is intended to include both unsubstituted and substituted alkoxy groups, the latter referring to alkoxy moieties having one or more hydrogen atoms replaced by usual substituents of the alkyl groups, preferably selected from the following group: halogen, aryl, cycloalkyl and optionally substituted amino. In a preferred embodiment alkoxy is methoxy optionally substituted with 1 to 3 halogen, ethoxy optionally substituted with 1 to 3 halogen, dimethylamino-ethoxy, *i*-propyloxy, cyclopropyl-methoxy and benzyloxy.

The term "cycloalkoxy" is intended to mean a cycloalkyl group coupling via oxygen ("C_{3-7}cycloalkoxy"). In a preferred embodiment cycloalkoxy is cyclopropyloxy.

The term "carbonyl" means a functional group composed of a carbon atom double-bonded to an oxygen atom: C=O.

The term "carboxyl" means a hydroxyl group coupling via carbonyl.

The term "alkoxycarbonyl" means an alkoxy group coupling via carbonyl ("C_{1-6}alkoxycarbonyl"). In a preferred embodiment alkoxycarbonyl is methoxicarbonyl.

The term "amino" means the monovalent group $-NH_2$. In addition, the term is intended to include both unsubstituted and substituted amino groups, the latter referring to amino moieties having one or more hydrogen atoms replaced by usual substituents preferably selected from the following group: alkyl, aryl, arylsulfonil, and alkylsulfonyl, more preferably methyl, ethyl, phenyl, tosyl and mesyl. In a preferred embodiment amino is dimethylamino, diethylamino, phenylamino, methylphenylsulfonamido or methanesulfonamido.

The term "alkylsulfanyl" means an alkyl group coupling via sulphur ("C_{1-6}alkylsulfanyl"). In a preferred embodiment alkylsulfanyl is methylthio, ethylthio or *i*-propylthio.

The term "alkylsulfonyl" means an alkyl group coupling via $-SO_2-$ ("C_{1-6}alkylsulfonyl"). In a preferred embodiment alkylsulfonyl is methylsulfonyl or ethylsulfonyl.

The term "arylsulfonyl" means an aryl group coupling via $-SO_2-$ ("C_{6-10}arylsulfonyl"), preferably methylphenylsulfonyl.

The term "benzyloxy" means a methoxy group monosubstituted with phenyl.

In the context of the present invention, general formula (I) includes all stereoisomeric forms of the compounds of the present invention. The term "stereoisomer" as used herein includes all possible stereoisomeric forms, including all chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure, unless the specific stereochemistry or isomer form is specifically indicated. Where the compounds of the present invention contain one or more chiral centers, all possible enantiomeric and diastereomeric forms, as well as the racemate, are included. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. All processes used to prepare compounds of the present invention and intermediates made therein are considered to be part of the present invention.

In the context of the present invention, it is intended to include all crystalline and polymorph forms of the compounds of the present invention.

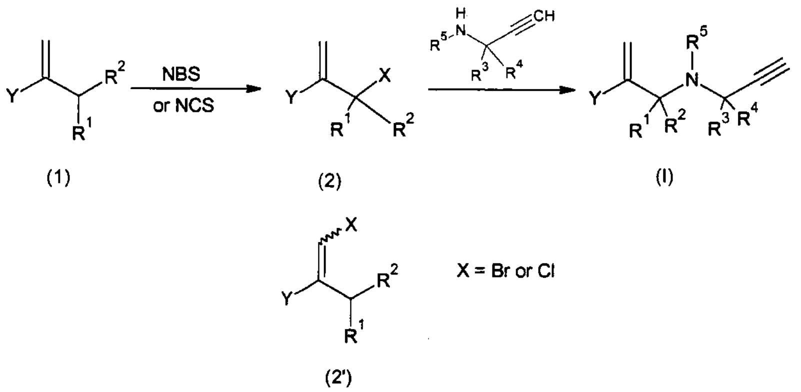
The term "salt" means any ionic compound formed between one of the embodiments of the present invention and an acidic or basic molecule that can donate or accept ionic particle to/from its partner. The quaternary amine salts are also included.

Pharmaceutically acceptable (i.e., non-toxic, physiologically acceptable) salts are preferred, although other salts are also useful. Salts of the compounds of the formula (I) may be formed, for example, by reacting a compound of formula (I) with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates. Exemplary acid addition salts include acetates, adipates, alginates, ascorbates, aspartates, benzoates, benzenesulfonates, bisulfates, borates, butyrates, citrates, camphorates, camphorsulfonates, cyclopentanepropionates, digluconates, dodecylsulfates, ethanesulfonates, fumarates, glucoheptanoates, glycerophosphates, hemisulfates, heptanoates, hexanoates, hydrochlorides, hydrobromides, hydroiodides, 2-hydroxyethanesulfonates, lactates, maleates, methanesulfonates, 2-naphthalenesulfonates, nicotinates, nitrates, oxalates, pectinates, persulfates, 3-phenylpropionates, phosphates, picrates, pivalates, propionates, salicylates, succinates, sulfates, sulfonates (such as those mentioned herein), tartarates, thiocyanates, toluenesulfonates (also known as tosylates) undecanoates, and the like. More preferred pharmaceutically acceptable salt is oxalate or hydrochloride.

Neurodegenerative diseases (Parkinson disease, Alzheimer's disease, Huntington's disease, stroke, etc.) are characterized by the progressive loss of neurons and typically occur in the elderly population, therefore, their incidence is continuously rising in industrialized countries. Parkinson's disease (PD) is a chronic neurodegenerative disease, which is characterized by the progressive degeneration of nigrostriatal dopaminergic pathway of the brain.

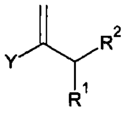
Preparation of the compounds of general formula (I) and their salts, solvates, enantiomers and diastereoisomers can be accomplished in a number ways using methods known in synthetic organic chemistry. Preferred methods include, but not limited to, those described below.

One of the methods for the preparation of the compounds of the general formula (I) is presented on **Process A.**, where Y has the same meaning as above, R^1 and R^2 are hydrogen, R^3 and/or R^4 are hydrogen or optionally substituted alkyl, R^5 is hydrogen, optionally substituted alkyl and optionally substituted aryl, n is 0, and m is 1.



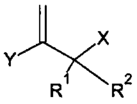
Process A.

According to the this version propenes of general formula (1)



(1)

- where the meanings of Y, R^1, R^2 are defined above - are reacted with *N*-bromosuccinimide, or *N*-chlorosuccinimide to afford allyl bromides, or allyl chlorides of general formula (2)

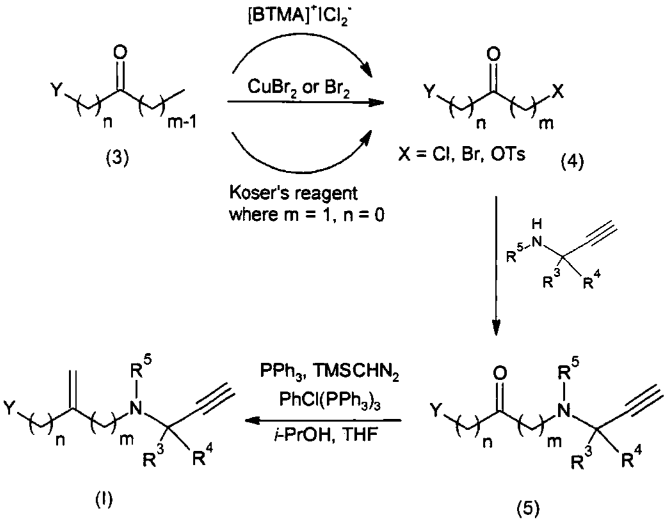


(2)

- where the meanings of, Y, R^1 and R^2 are defined above and X represents bromo or chloro atom.

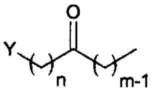
Propenes of general formula (1) can be halogenated at the allylic position using *N*-bromo- or *N*-chlorosuccinimide under usual conditions to afford allyl halogenides of general formula (2). The reaction can be carried out in an inert solvent such as chlorobenzene at reflux temperature, or by using a microwave method. This reaction may yield a mixture of the desired allyl bromide (2) and a vinyl bromide side product (2'), which could be conveniently separated by column chromatography. Alternatively, an allylic chlorination reaction could be carried out using *N*-chlorosuccinimide, using diphenyl-diselenid, as a catalyst, in an inert solvent, such as dichloromethane, at temperature 20-30 °C for longer reaction time. Nucleophilic substitution of the general formula (2) with a propargylamine affords the corresponding compounds of general formula (I). The reaction can be conveniently carried out in a solvent, e.g. dichoromethane, acetonitrile, diethylether, preferably in an alcohol such as 2-propanol with one or two equivalents of propargylamine, in case of one equivalent of the amine in the presence of an acid acceptor, such as DIPEA, at room temperature or elevated temperature during 1-24 h reaction time, or using microwave conditions.

The compounds of the general formula (I) - where the meaning of Y is shown above, R^1 and/or R^2 is hydrogen or optionally substituted alkyl, R^3, R^4 are hydrogen, R^5 is hydrogen or optionally substituted alkyl, n is 0 or 1 and m is 0 or 3, according to the invention can be also prepared by the method demonstrated in **Process B.**



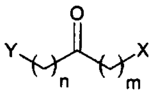
Process B.

In this version a (hetero)aryl methyl ketone of the general formula (3),



(3)

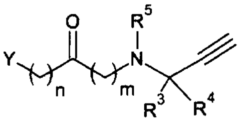
- where the meaning of Y, n and m have the same meaning as above, after α-functionalisation in the first step, results in the compounds of general formula (4)



(4)

- where the meanings of Y, n and m, are defined above, X represents halogen atom or a leaving group if m is 1 and n is 0.

Reactions of compounds of general formula (4) with a propargylamine afford the corresponding amino ketone compounds of the general formula (5)



(5)

-where the meanings of Y, R^3, R^4, R^5, n and m are defined above.

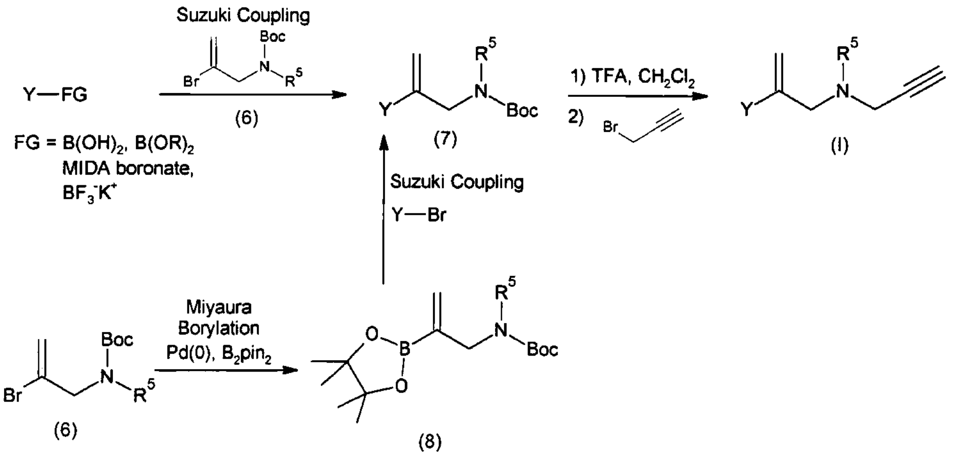
The compounds of general formula (5) can be converted to the target compounds of general formula (I).

The key difference in this approach is the use of a mild α-functionalisation of a (hetero)aryl methyl ketone of general formula (3) and installation of the alkene moiety in the final step. Functionalisation of the (hetero)aryl methyl ketone with a leaving group at the α-carbon position is carried out in the first step. Chlorination of benzofuranyl, indolyl, furanyl and aryl methyl ketones are achieved using benzyltrimethylammonium dichloroiodate, in inert solvent, preferably tetrahydrofurane, at room temperature in 24-72 hours. Alternatively, oxytosylation could be carried out (e.g. for thiophenyl substrates) using hydroxy(tosyloxy)iodobenzene (Koser's reagent), in inert solvent, such as acetonitrile, at reflux temperature. In the case of pyridyl ketones, α-bromination is achieved using bromine in toluene-acetic acid mixture, between 0 °C -rt or using copper(II) bromide. A number of the compounds of general formula (4) are commercially available and hence were purchased wherever possible.

Nucleophilic subustitution reaction of compounds of general formula (4) with a propargylamine affords the corresponding amino ketone compounds of the general formula (5). These compounds can be converted to the requisite allylic amine target compounds of general formula (I) under mild conditions using a modified Wittig olefination reaction in dioxane, THF-2-propanol mixture using $RhCl(Ph_3)_3$ and Ph_3P and trimethylsilyldiazomethan, at 60 °C.

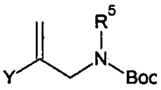
Both of the aforementioned approaches involve either an allylic functionalisation step or α-functionalisation of a ketone to install a leaving group. Subsequent approaches were aimed at avoiding these functionalisation steps by direct formation of an allylic amine derivative or allylic alcohol.

The third approach of the synthesis of compounds of the general formula (I) is shown in **Process C.**



Process C.

In this version compounds of general formula (I) - where R^1, R^2, R^3, R^4 represent hydrogen, R^5 is an optionally substituted alkyl group, n is 0 and m is 1, Y has the same meaning as above, can be prepared from the aryl/heteroaryl-boronic acids, esters or salts with a vinyl bromide derivative, to give the coupling product of the general formula (7)



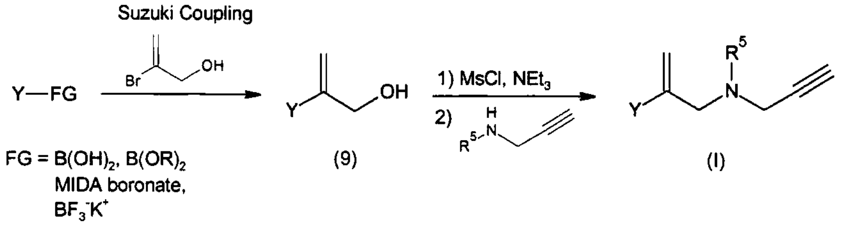
(7)

- where the meanings of Y and R^5 are defined above. Then the carbamate group can be cleaved, and the amine thus obtained can be readily alkylated with propargyl bromide to afford the compound of the general formula (I). The Suzuki coupling reaction is a key transformation that allows a multitude of commercially available boronic acids (or derivatives thereof) to be coupled with vinyl bromide (6).

The using (2-bromoallyl)methylcarbamate (6) is prepared from 2,3-dibromopropene with with methylamine solution followed by reaction with Boc_2O. The coupling reaction is carried out in microwave condition, using the catalyst of Palladium-acetate-XPhos or SPhos, and potassium triphosphate monohydrate as basis component, in alcohol-water solvent mixture. The cleavage of the Boc group can be carried out using trifluoroacetic acid in dichloromethane and, upon neutralization. The alkylation of the resulting amino compound with propargylbromide can be performed in the presence of a base, such as Na_2CO_3 in an inert solvent, preferably DCM, at room temperature, for longer reaction time.

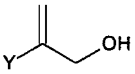
This approach is deployed in the synthesis of a large number of substituted aryl targets. In cases where the requisite boronic acids (or derivatives thereof) are not readily accessible, an alternative method is used to access intermediates of compounds of the general formula (7). The vinyl bromide is converted to the corresponding vinyl boronic ester of the general formula (8) using a Miyaura borylation protocol. Intermediate of general formula (8) is then coupled with a (hetero)arylbromide to afford the compounds of general formula (7) which is converted to the compounds of the general formula (I). However, the approach shown in **Process C.** was not suitable for all target compounds. During the attempted acidic deprotection of the Boc group from intermediates of type of compounds of general formula (7) bearing *p*-electron donating substituents, oxazolidinones are formed rather than the desired amine. So a complementary Suzuki coupling methodology was developed to circumvent this complication in relevant cases.

The synthesis of compounds of the general formula (I) is presented in **Process D.** - where the meanings of R^1, R^2, R^3, R^4 are hydrogen, R^5 is optionally substituted alkyl, n is 0 and m is 1, Y is defined above.



Process D.

The compounds of the general formula (I) can be obtained in the first step by reaction of boronic acids (or derivatives thereof) with 2-bromoallyl alcohol resulted in the compounds of the general formula (9)

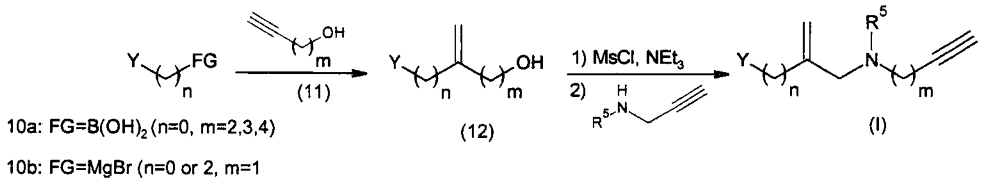


(9)

- where Y is defined above. This intermediate can be used for the synthesis of compounds of general formula (I) by reaction with MsCl, followed by reaction with the appropriately substituted propargyalmine. This approach is advantageous for several reasons. First, both the coupling partners, boronic acids (or derivatives thereof) and the 2-bromoallyl alcohol are commercially available. Second, it can be used for the synthesis of compounds of general formula (I) bearing electron donating moieties at the *para* position of the aryl ring. The reaction of the boronic acid with 2-bromoallyl alcohol can be carried out in microwave condition, using the catalyst of XPhos-[2-(2'-amino-1,1'-biphenyl)]-palladium II adduct, or Xphos-2,2-aminoethylphenyl-palladium II methyl-*t*-butylether adduct, or $Pd_2(dba)_3$ and PPh_3 and using potassium triphosphate monohydrate as a base component, in inert solvent, preferably THF, at 40-80 °C, for shorter or longer reaction time, depending on the substrate. In many cases instead of the boronic acid, the dioxaborolan derivative of the aryl/heteroaryl derivatives is used as starting material. It may be prepared from the aryl/hetaroaryl-bromide with pinacolborane, usig as catalyst $PdCl_2(dppf)$, or tris(dibenzylideneaceton) palladium-XPhos adduct, in the presence of triethyamine, as base in inert solvent such as dioxane.

The compounds of general formula (9) are readily converted to mesylate derivatives with MsCl, in an inert solvent, such as DCM, in the presence of a base. Its nucleophilic substitution with a propargylamine, affords the compounds of general formula (I).

Another possible route for preparation of the compounds of general formula (I) is presented in **Process E.** - where the meanings of Y are defined above, R^5 is optionally substituted alkyl, R^1, R^2, R^3, R^4 are hydrogen, n can be 0, 1 or 2, the meanings of m can be 1,2,3 or 4.

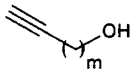


10a: FG=B(OH)$_2$ (n=0, m=2,3,4)

10b: FG=MgBr (n=0 or 2, m=1

Process E.

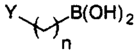
In this version, an alcohol of general formula (11)



(11)

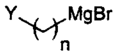
- where m can be 1 or 2, 3, 4, is reacted with compounds of general formula (10).

When m means 2, 3 or 4, compounds (11) are reacted with boronic acids of general formula (10a),



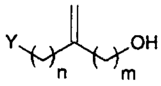
(10a)

- where the meanings of Y are as defined above, n is 0. When m means 1, the compounds of general formula (11) are reacted with arylmagnesium bromides of general formula (10b)



(10b)

- where the meanings of Y are given above, meaning of n can be 0 or 2, to afford compounds of general formula (12)



(12)

- where Y, n, and m have the above meanings.

Suzuki coupling methodologies may have limitations in certain cases (e.g. where the boronic acid coupling partners are unstable), therefore, a complementary method may be also used to access alcohols of general formula (12). Thus, using copper catalysis, arylmagnesium bromides can add regioselectively to propargylic alcohols to afford allylic alcohols of compounds of general structure (12). Alternatively, a palladium catalysed regioselective addition of boronic acids to alkynylols (i.e. m ≥ 2) can be used to access alkenylols of type (12). The Suzuki reaction can be carried out in microwave vial, using $Pd(PPh_3)_4$ as a catalyst in inert solvent, such as 1,4-dioxane, in presence of acetic acid. Some alcohol intermediates of general formula (12) can be converted into the mesylate derivatives, in which the mesyloxy group can be substituted with propargylamines to afford the target compounds of general formula (I).

Another reaction route for preparation of compounds of general formula (I), where n is 0, m means 2, 3 or 4, is based on a reductive amination process. It starts from an alcohol of general formula (11), which is oxidized, using Dess-Martin periodinane (DMP) at room temperature, in inert solvent, such as DCM, then using $NaBH(OAc)_3$ for the reduction step. This method can be performed at room temperature, in an inert solvent, e.g. DCM as well.

Other aspects of the invention will be apparent in the following part of examples provided to illustrate biological activities of compounds of the invention.

General Experimental Details. All reaction solvents were dried by PureSolv MD 7 Solvent Purification System (Innovative Technology, USA) prior to use. All reagents were used as purchased without further purification. All reactions were conducted under a slight positive pressure of argon using oven-dried (110 °C) glassware. Room temperature corresponds to a temperature interval from 20 to 25 °C. The solvents were removed under reduced pressure using standard rotary evaporators.

Analytical thin layer chromatography (TLC) separations were performed on Merck's silica gel 60 F254-precoated aluminum sheets. Visualization was accomplished with UV light (254 or 365 nm) and/or ninhydrin (200.0 mmol in ethanol) stain followed by heating. Solvent mixtures used for chromatography are always given in a vol/vol ratio. Flash column chromatography was generally performed using Silica Gel 60 (spherical, 40-100 μm or 40-63 μm) purchased from Sigma- Aldrich, or Biotage SP1™ purification system by gradient. Melting points were determined on a Büchi-540 capillary melting point apparatus and are uncorrected. Fourier-transform infra-red spectroscopy was conducted using Spectrum 100 software (Perkin Elmer). High-resolution mass spectrometry was run by the electrospray ionization time-of-flight (ESI-TOF) mode on an Agilent 6210 mass spectrometer.

Tandem Liquid Chromatography Mass Spectrometry (LCMS) was performed on a Waters 2996 separations module and 3100 mass detector using a reverse phase analytical column Luna®-5u-C18(2) (150 x 4.6 mm) at flow rate of 1.0 ml/min. The eluting system, consisting of A (water) and B (acetonitrile), was used under a linear gradient. The performance was monitored by Photodiode array detection with wavelength of 254 nm. Generally, the eluting program started from 80% of A and 20% of B for the first two minutes, followed by changing the concentration of B from 20% to 80% in 20 minutes. This condition was maintained for another 5 minutes.

Elemental analyses were performed on an Elementar VarioEL III apparatus. MW irradiation experiments were carried out in a monomode CEM-Discover MW reactor, using the standard configuration as delivered, including proprietary software. The experiments were executed in open vessel mode with control of the temperature by infrared detection. After completion of the reaction, the vial was cooled to 50 °C by air jet cooling.

^{1}H nuclear magnetic resonance (NMR) spectra was recorded at ambient temperature (if not indicated otherwise), in the solvent indicated, on a Bruker 400 Ultra Shield Spectrometer operating at 400 MHz and 101 MHz respectively or Varian Mercury Plus 400 spectrometer at frequency of 400 and 100 MHz or on a Varian Unity 600 spectrometer at frequency at 600 and 150 MHz or on a Bruker Avance III 500 spectrometer at frequency of 500 or 125 MHz respectively. Chemical shifts for ^{1}H NMR were recorded in parts per million (ppm) downfield from tetramethylsilane or proton signal of residual non-deuterated solvent (δ 7.26 ppm for $CHCl_3$ or δ 4.87 ppm for CH_3OH) as the internal signal. Coupling constants are indicated in Hertz (Hz). Chemical shifts are given using the δ-scale relative to tetramethylsilane or the residual solvent signal as an internal reference. The following abbreviations are used for spin multiplicity: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad, dd = doublet doublet, dm = doublet multiplet and tm = triplet multiplet.

General procedure for the α-bromination of ketones (method A) To a solution of the appropriate ketone (5.0 mmol) in toluene (10.0 ml) and acetic acid (2.5 ml) at 0 °C was added a solution of bromine (0.3 ml, 1.1 eq) in toluene (5.0 ml) in a drop-wise manner. The resulting solution was allowed to stir at rt for 1 hour. A saturated solution of Na_2CO_3 was added until pH≈9 followed by a saturated solution of sodium thiosulfate (5.0 ml). The aqueous phase was extracted in ether (3x25.0 ml), the organic layers were combined and dried over $MgSO_4$. Subsequently, the solvent was reduced *in vacuo* to 30.0 ml and the resulting solution used without further purification in the next step (nucleophilic halogen substitution) in which no further solvent was added.

General procedure for the α-oxytosylation of ketones (method B) To the appropriate ketone in acetonitrile (400.0 mmol) was added hydroxy(oxytosyl)iodobenzene (1.5 eq). The reaction was stirred for 1.5 h at 100 °C under microwave irradiation. The solvent was then removed under reduced pressure. The residue was purified via the Biotage SP1 silica-packed 25+S column with eluent of EtOAc:Hexane (12-40%, quick flush to remove top spot of iodobenzene and bottom spot of starting material HTIB) to afford white solid compound. The product thus obtained was used for the next step without further purification.

General procedure for the α-chlorination of ketones (method C)

(method C1) To a solution of the appropriate ketone (5.0 mmol) in abs. THF (15.0 ml) under argon atmosphere it was added a solution of benzyltrimethyl ammonium dichloroiodate (3.5 g, 2 eq) in abs. THF (15.0 ml). The resulting solution was allowed to stir at room temperature for 24 hours. Then the solvent was reduced *in vacuo* to ≈10.0 ml and ether (20.0 ml) was added followed by an aqueous solution of sodium thiosulfate (15 ml.0). The aqueous phase was extracted in ether (3x25.0 ml), the organic layers were combined and dried over $MgSO_4$. Subsequently, the solvent was reduced *in vacuo* to 30.0 ml and the resulting solution used without further purification in the next step (nucleophilic halogen substitution) in which no further solvent was.

(method C2) To the appropriate ketone in tetrahydrofuran (200.0 mmol) was added benzyltrimethylammonium dichloroiodate (3 eq). The reaction was stirred for 72 h at room temperature. The solvent was then removed under reduced pressure. Adding 90.0 ml of ethyl acetate, the organic product was washed with aqueous sodium thiosulphate (5% w/w, 3x30.0 ml) and de-ionized water (30.0 ml), dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was used for the next step without further purification.

(method C3) To the appropriate ketone in THF (200.0 mmol) was added benzyltrimethylammoniumdichloroiodate (2 eq). The reaction was stirred for 72 h at room temperature. The solvent was then removed under reduced pressure. Adding ethyl acetate, the organic product was washed with aqueous sodium thiosulphate (5% w/w) and de-ionized water, dried over anhydrous $MgSO_4$, and concentrated in vacuo. If necessary, the residue was purified via the Biotage SP1 silica-packed 25+S column with eluent of Dichloromethane:Hexane (5-50%) to afford desired product. Some of these products may not be very stable and hence were used for the next step without further delay.

(method C4) To the acetophenone derivatives in dry THF was added benzyltrimethyl ammonium dichloroiodate (2 eq). The mixture was left to stir under argon at room temperature for 72 h. When the reaction was completed, the solvent from the reaction mixture was evaporated *in vacuo* before the residue was partitioned between ethyl acetate and 5% sodium thiosulphate solution. The organic layer was washed twice with 5% sodium thiosulphate solution and dried over magnesium sulphate. The solvent was removed *in vacuo* to afford the crude compound which was used for the amination reaction without further purification.

General procedure for introduction of amino substituent by a nucleophilic substitution reaction (method D)

(method D1) To a solution of the appropriate α-halogenated ketone (5.0 mmol) in ether (20.0 ml) it was added diisopropyl ethyl amine (0.9 ml, 2 eq) and *N*-methylpropargyl amine (0.4 ml). The resulting solution was allowed to stir at rt for 24 hours. The solvent was evaporated *in vacuo* and the residue purified by column chromatography.

(method D2) To the appropriate α-chlorinated or α-oxytosylated compounds in ACN (200.0 mmol) was added *N*-methylpropargylamine (2 eq). The reaction was stirred for 10-60 seconds at 100 °C under microwave irradiation. The solvent was then removed under reduced pressure. The residue was purified via the Biotage SP1 silica- packed 25+S column with eluent of EtOAc:Hexane (5-35%) to afford desired products as yellow to orange oil. The product thus obtained degraded in days and was therefore used for the next step immediately after column purification.

(method D3) To the appropriate halogenated keton in ACN (200.0 mmol) was added *N*-methylpropargylamine (2 eq). The reaction was stirred for 1.5 h at 100 °C. The solvent was then removed under reduced pressure. The residue was purified via the Biotage SP1 silica- packed 40+M column with eluent of EtOAc:Hexane (12-50%) to afford desired compound as yellow oil. This reaction only reaches 50% (at most) conversion. Un-reacted starting material was recovered from column purification.

(method D4) To the appropriate α-chlorinated compounds in DCM (150.0 mmol) was added *N*-methylpropargylamine (2 eq) with or without K_2CO_3 (1 eq). The reaction was stirred for 0.5 to 1.5 h at rt depending on the stability of product. Adding 12.0 ml of de-ionized water, the organic product was extracted with dichloromethane, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified via the Biotage SP1 silica-packed 25+S column.

(method D5) To the appropriate α-chlorinated compounds in ACN (100.0 mmol) was added *N*-methylpropargylamine (2 eq). The reaction was stirred for 16 h at 40 °C. The solvent was then removed under reduced pressure. The residue was purified via the Biotage SP1 silica- packed 25+S column with eluent of EtOAc:Hexane (5-40%) to afford the following procucts.

(method D6) *N*-methylpropargylamine (2.0 eq) was added dropwise to the α-chlorinated or α-brominated compounds in dry ACN. The mixture was left to stir under argon at room temperature for 16 h. When the reaction was completed, the solvent from the reaction mixture was evaporated *in vacuo* before the residue was partitioned between DCM and deionised water. The organic layer was washed twice with deionised water and dried over magnesium sulphate. After filtration, the solvent was removed *in vacuo* to afford the crude compound which was purified by column chromatography.

(method D7) To a solution of the appropriate 2-aryl-3-haloprop-1-en (1 eq) in anhydrous 2-propanol (10.0 ml), a solution of the appropriate amine (3 eq) in anhydrous 2-propanol (10.0 ml) was added at room temperature under argon. The reaction mixture was stirred at 25 °C-reflux for 1-24 h under argon. After evaporation to dryness, the residue was purified by column chromatography on silica gel.

(method D8) To a solution of bromide or chloride in DCM was added *N*-methylpropargylamine (2 eq). The mixture was left to stir under argon at rt for 16 h. When the reaction was completed, the solvent from the reaction mixture was evaporated *in vacuo* before the residue was partitioned between DCM and deionised water. The organic layer was washed twice with deionised water and dried over magnesium sulphate. After filtration, the solvent was removed *in vacuo* to afford the crude compound which was further purified by column chromatography.

One pot mesylation and amination (method D9) To a solution of the arylallyl alcohol in DCM was added triethylamine (1.2 eq) and mesyl chloride (1.1 eq) at 0 °C. The reaction mixture was stirred at 0 °C for 15 mins before warming to rt. The extent of the reaction was monitored by NMR. When the mesylation reaction was completed, *N*-methylpropargyl amine (or propargyl amine) (2.2 eq) was added to the stirred solution. The reaction mixture was further stirred at rt for 16 h. After 16 h of reaction, the DCM organic layer was washed twice with H_2O, dried with $MgSO_4$, filtered and the solvent removed *in vacuo* to afford a yellow crude residue. The crude product was further purified by column chromatography.

(method D10) Propargylamine (2.2 eq) was added to a solution of mesylate or bromide (1.0 eq) in dichloromethane (120.0 mmol). The reaction mixture was allowed to stir at room temperature overnight. TLC and NMR analysis indicated starting material has been consumed. The reaction was quenched with water. Aqueous later was washed with DCM twice, combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude mixture was purified using flash column chromatography.

General procedure for the modified Wittig reaction (method E)

(method E1) (Lebel H et al, Org. Lett., 2004, 6, 3047-3050; Paquet V et al, Synthesis, 2005, 11, 1901-1905) To a solution of $RhCl(PPh_3)_3$ (0.025 eq), triphenylphosphine (1.5 eq) and anhydrous 2-propanol (15 eq) in abs. 1,4-dioxane (10.0 ml) it was added a solution of the appropriate ketone (1.7 mmol) and a 2M solution of trimethylsilyldiazo methane (2 eq). The resulting solution was heated at 60 °C under an argon atmosphere for 4 hours. The solvent was evaporated *in vacuo* and the residue purified by column chromatography.

(method E2) To a mixture of triphenylphosphine (1.1 eq) and $RhCl(PPh_3)_3$ (0.025 eq) in 1,4-dioxane was added appropriate keton (200.0 mmol), 2-propanol (15 eq) and (trimethylsily)diazomethane (2.0 M solution in hexane, 2.4 eq). The reaction was stirred for overnight at 60 °C. The solvent was then removed under reduced pressure. Purification of the crude by the Biotage SP1 silica-packed 40+M column.

(method E3) $RhCl(PPh_3)_3$ and PPh_3 were weighed into a flame-dried 2-necked round-bottom flask before 1,4-dioxane was added under argon condition. To the stirred mixture at 60 °C was added dry isopropanol. The starting α-amino ketones were dissolved in 1,4-dioxane (10.0 ml) and introduced as a solution into the mixture before trimethylsilyldiazomethane (2.4 eq) was added dropwise to start the reaction. The reaction mixture was left to stir under argon at 60 °C for 16 h. When the reaction was completed, the solvent from the reaction mixture was evaporated *in vacuo* before a filtration through a pad of silica gel was carried out to remove the decomposed material. After filtration, the solvent was removed *in vacuo* to afford the crude compound which was purified by column chromatography.

General procedure for the chlorination of α-methylstyrenes (method F) A mixture of the appropriate α-methylstyrenes (4.8 mmol), diphenyl diselenide (0.2 mmol) (Hori T et al, J. Org. Chem., 1979, 44, 4208-4210; Hori T et al, J. Org. Chem., 1979, 44, 4204-4208) and *N*-chlorosuccinimide (5.3 mmol) in anhydrous DCM (25.0 ml) was stirred at 30 °C under argon for 24 h. The mixture was evaporated to dryness and the residue was triturated with *n*-hexane (30.0 ml). The precipitated crystals (succinimide) were filtered off and washed with *n*-hexane, the filtrate was evaporated to dryness. The residue obtained was purified by flash chromatography on silica gel.

General procedure for the bromination of α-methylstyrenes (method G) i) In an oven-dried two-neck flask, prop-1-en-2-ylbenzene (88.8 mmol) and *N*-bromosuccinimide (263.0 mmol) were added to chlorobenzene (30.0 ml). The flask was placed in an oil bath preheated to 160-170 °C upon stirring for 15 min (!: strongly effervescent, exothermic reaction), then the mixture was cooled down with an ice-water bath. The succinimide precipitated upon cooling was filtered off and washed with chlorobenzene, the solvent was evaporated *in vacuo*. The crude product was purified by vacuum distillation (2 Hgmm, main fraction: 106-110 °C) and subsequent flash chromatography on silica gel (*n*-hexane) to afford compound **(SZV-1907/2) (Scheme 50)**. In case of compound **(SZV-2030/2) (Scheme 50)** the crude product was purified by flash chromatography on silica gel (*n*-hexane) and besides the product, a mixture of unreacted starting material and 1-[1-bromoprop-1-en-2-yl]-4-fluorobenzene were isolated. **ii)** In an oven-dried two-neck flask equipped with a condenser, 1-chloro-4-(prop-1-en-2-yl)benzene (25.0 g, 147.0 mmol) and *N*-bromosuccinimide (58.1 g, 323.0 mmol) were added to chlorobenzene (60.0 ml). The flask was placed in an oil bath preheated to 160-170 °C upon stirring for 45 min (!: strongly effervescent, exothermic reaction), then the mixture was cooled down with an ice-water bath. The succinimide precipitated upon cooling was filtered off and washed with chlorobenzene, the solvent was evaporated *in vacuo*. The crude product was purified by vacuum distillation (1 Hgmm, main fraction: 103-106 °C) and subsequent flash chromatography on silica gel (*n*-hexane). Only traces of the expected 1-chloro-4-[(*Z*)-1,2-dibromoethenyl]benzene were observed, 1-(3-bromoprop-1-en-2-yl)-4-chlorobenzene and 1-[(1*E*)-1-bromoprop-1-en-2-yl]-4-chlorobenzene could be isolated (~2:1 mixture).

In an oven-dried two-neck flask equipped with a condenser, a ~2:1 mixture (22.00 g) of 1-(3-bromoprop-1-en-2-yl)-4-chlorobenzene (~14.7 g, 63.4 mmol) and 1-[(1*E*)-1-bromoprop-1-en-2-yl]-4-chlorobenzene (~7.33 g, 31.67 mmol) and *N*-bromosuccinimide (80.0 g, 449.0 mmol) were added to chlorobenzene (60.0 ml). The flask was placed in an oil bath preheated to 160-170 °C upon stirring for 15 min (!: strongly effervescent, exothermic reaction), then the mixture was cooled down with an ice-water bath. The succinimide precipitated upon cooling was filtered off and washed with chlorobenzene, the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (*n*-hexane). Three products, 1-chloro-4-(1,1,2,3-tetrabromopropan-2-yl)benzene, 1-chloro-4-[(1*E*)-1,3,3-tribromoprop-1-en-2-yl]benzene and 1-chloro-4-[(1*Z*)-1,3-dibromoprop-1-en-2-yl]benzene were isolated.

1-chloro-4-(1,1,2,3-tetrabromopropan-2-yl)benzene: recrystallized from anhydrous EtOH.

A suspension of 1-chloro-4-(1,1,2,3-tetrabromopropan-2-yl)benzene (2.0 g, 4.3 mmol) and silica gel (20 mg) in CCl_4 (20.0 ml) was heated to reflux, while protected from light (tinfoil wrapping) (Suarez AR et al, J. Org. Chem., 1987, 52, 1145-1147). The mixture was evaporated to dryness, the residue was purified by flash chromatography on silica gel (*n*-hexane) to afford compound **(SZV-1919/2) (Scheme 50)**. **iii)** A mixture of 1-chloro-4-(prop-1-en-2-yl)benzene (10.0 g, 65.5 mmol) and *N*-bromosuccinimide (9.3 g, 52.4 mmol) in chlorobenzene (30.0 ml) was subjected to 1 h heating at 180 °C in MW reactor. The solvent was removed *in vacuo*, the residue obtained was purified by vacuum distillation. The main fraction (1 Hgmm, bp 74-76 °C) was purified by column chromatography on silica gel (*n*-hexane) to afford compound **(SZV-1294/2) (Scheme 50)**.

General procedure for the salt formation (method H)

(method H1) A stock solution of oxalic acid (2.6 mmol, Fw = 126.07, oxalic acid dihydrate) in abs. *i*-PrOH (5.0 ml) was prepared. This solution was used straight after. Stock solutions should not be kept since ester formation has previously been observed. To a solution of the appropriate base (0.9 mmol) in abs. *i*-PrOH (0.5 ml) it was added a 0.512 M solution of oxalic acid dihydrate in *i*-PrOH (1.8 ml, 0.9 mmol). The resulting solution was allowed to stir at rt for 30 min, then it was kept at -18 °C for 16 hours. Then, the precipitate was filtered and washed with ether (2.0 ml) to afford the products. Note: poor precipitation is observed with wet solvents.

(method H2) To a solution of the appropriate base in 96% EtOH or dioxane or EtOAc, 37% HCl was added dropwise or HCl gas was bubbled into an ice-cooled solution of the amine in ether until pH < 3. After 30 min stirring at room temperature, the residue was filtered or the mixture was evaporated to dryness. The residue obtained was recrystallized to afford the salt.

General procedure for benzofuran synthesis (method I) To the appropriate 2-hydroxybenzaldehyde in tetrahydrofuran (200.0 mmol) was added potassium carbonate (1.2 eq), followed by chloroacetone (1.2 eq). The reaction was stirred for 16 h at refluxing temperature. The solvent was then removed under reduced pressure. Adding 90.0 ml of dichloromethane, the organic product was washed with de-ionized water (3x30.0 ml), dried over anhydrous sodium sulphate, concentrated in vacuo, and purified via the Biotage SP1 silica-packed 40+M column.

General procedure for the modified Cadogan indole synthesis (method J) To the appropriate *o*-nitrobenzylideneacetone in dry toluene (100.0 mmol) was added triphenylphosphine (2 eq) and $MoO_2Cl_2(DMF)_2$ (0.1 eq) under nitrogen atmosphere. The reaction was heated under microwave irradiation 30 min at 200 °C. The completion of the reductive cyclization was monitored by TLC. The solvent was then removed under reduced pressure and the residue was purified via the Biotage SP1 silica-packed 40+M column.

General procedure for Boc-protection (method K) To a solution of the substrate (0.5 mmol) in DCM (10.0 ml) was added triethylamine (134.7 µl, 2.0 eq), Boc-anhydride (212.0 mg, 2 eq) and DMAP (11.9 mg, 0.2 eq). The mixture was left to stir under argon at room temperature for 16 h. When the reaction was completed, the solvent from the reaction mixture was evaporated *in vacuo* before the residue was purified by column chromatography.

General procedure for Boc-deprotection (method L) To a solution of arylallyl carbamate in DCM was added trifluoroacetic acid (20-50 eq). The extent of the reaction was monitored by TLC. When the reaction was completed, saturated sodium bicarbonate solution and solid sodium bicarbonate was added until the aqueous layer was basic on pH paper. The organic layer was removed and the aqueous layer was extracted twice with DCM. The combined organic layer was dried over magnesium sulphate. After filtration, the solvent was removed *in vacuo* to afford the crude amines which was used for the next step of without further purification.

General Procedure for substitution reaction between Boc-protected amine and propargyl bromide

(method M1) To a solution of arylallyl carbamate in DCM was added trifluoroacetic acid (20 eq). The extent of the reaction was monitored by TLC. When the reaction was completed, saturated sodium bicarbonate solution and solid sodium bicarbonate was added until the aqueous layer was basic on pH paper. The organic layer was removed and the aqueous layer was extracted twice with DCM. The combined organic layer was dried over magnesium sulphate. After filtration, the solvent was removed *in vacuo* to afford the crude amines which was used for the next step of without further purification. To a solution of the crude amine in DCM was added solid Na_2CO_3 (1.5 eq) and propargyl bromide (1.1 eq). The reaction mixture was allowed to stir under argon at rt for 16 h. When the reaction was completed, the mixture was partitioned between DCM and H_2O. The organic layer was washed twice with H_2O and dried with $MgSO_4$. After filtration, the solvent was removed *in vacuo* to afford the crude product which was further purified by column chromatography.

(method M2) To a solution of the appropriate amine (1.0 eq) in anhydrous DMF (250.0 mmol) under Ar atmosphere, was added NaH (1.5 eq) slowly at 0 °C. Efferverscence was observed. Reaction mixture was allowed to stir for 1 h before the addition of propargyl bromide (1.5 eq). The reaction mixture was allowed to stir at 60 °C overnight before the addition of H_2O. Organic layer was separated and aqueous layer was washed with EtOAc twice. Combined organic layer was washed with water, dried over $MgSO_4$, and concentrated in vacuo. Crude mixture was purified using flash column chromatography.

Regioselective addition of Grignard reagent to propargyl alcohol (method N)

To a dry 2 neck flask, magnesium (2.65 eq) was added followed by dry ether (0.045 l/g). A solution of the appropriate halide (2.60 eq) in ether (1800.0 mmol to 4500.0 mmol) was prepared. A few crystals of iodine were added into the reaction followed by one quarter of the prepared halide solution. The flask was warmed gently until the color of the iodine faded. The remaining portion of the halide was added and the reaction was stirred at rt for 1 h or until all the magnesium had been consumed. To the freshly prepared Grignard reagent was added CuI (0.15 eq) and the black suspension was stirred for 15 mins. Then, a solution of propargyl alcohol (1 eq) in ether (1 l/g) was added and the reaction was refluxed overnight. The next day, ether and H_2O were added. The aqueous layer was extracted with ether (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. Purification by flash chromatography.

Appel reaction (method O) To a solution of alcohol (0.6 mmol) in DCM (7.0 ml) was added CBr_4 (2 eq) and triphenylphosphine (1.5 eq). The reaction mixture was stirred under an argon atmosphere for 16 h. After 16 h of reaction, the solvent was removed *in vacuo* to afford the crude compound which was further purified by column chromatography.

General Procedure for Suzuki Coupling reactions (method P)

(method P1) To a dry microwave vial containing the boronic acid or boron pinacol ester (1.0 eq), XPhos (0.06 eq) and potassium triphosphate monohydrate (2.0 eq) under argon atmosphere, was added a solution of *tert*-butyl (2-bromoallyl)(methyl)carbamate (0.9 eq) in ethanol. H_2O was added and the mixture was degassed using nitrogen gas for 10 mins. Palladium (II) acetate catalyst (2 mol%) was subsequently added and the mixture was further degassed for 5 mins before the sealed reaction mixture was heated under microwave condition at 70 °C for 1 h. When the reaction was completed, the solvents were removed *in vacuo* and the residue was partitioned between ethyl acetate and H_2O. The organic layer was washed twice with H_2O and dried with $MgSO_4$. After filtration, the solvent was removed *in vacuo* to afford the crude product which was further purified by column chromatography.

(method P2) To a dry microwave vial containing the aryl boronic acid and potassium triphosphate monohydrate (3.0 eq) under argon atmosphere, was added a solution of 2-bromo-allyl alcohol/bromide (1.0 eq) in THF. H_2O was added and the mixture was degassed using nitrogen gas for 10 mins. The *Buchwald pre-catalyst (Gen I or Gen II) (2 mol%) was added and the mixture was further degassed for 5 mins before the sealed reaction mixture was heated at the optimized temperature (60 – 80 °C) for each compound for 16 h. When the reaction was completed, the solvents were removed in vacuo and the residue was partitioned between ethyl acetate and H_2O. The organic layer was washed twice with H_2O and dried with $MgSO_4$. After filtration, the solvent was removed in vacuo to afford the crude product which was further purified by column chromatography. *$Pd_2(dba)_3$ (2mol%) and PPh_3 (4 mol%) were used instead of the precatalyst when R group contains chlorine.

General Procedure for the Miyaura borylation of aryl bromide (method Q)

(method Q1) Aryl bromide (1.8 mmol), tris(dibenzylideneacetone)dipalladium (1 mol%) and 2- dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (4 mol%) were placed in a pre-dried 2-neck round-bottom flask fitted with a condenser. The flask was degassed before adding anhydrous triethylamine (3 eq), pinacolborane (3 eq) and anhydrous dioxane (20.0 ml). The reaction mixture was then stirred at 100 °C for 4 h under argon. After cooling to room temperature, the reaction mixture was filtered with filter paper and residue washed with diethyl ether. The combined filtrate was concentrated under reduced pressure and then purified by flash column chromatography on silica gel.

(method Q2) To a solution of the aryl bromide (1 eq) in anhydrous THF (150.0 mmol) was added KOAc (3 eq) and B_2pin_2 (1.15 eq). The solution was degassed under Ar for 2 mins before the addition of $PdCl_2(dppf)$ (0.1 g, 0.2 mmol, 0.02 eq). The reaction mixture was further degassed again for 2 mins and stir at 60 °C under Ar atmosphere overnight. TLC showed the starting material has been consumed. The reaction mixture was quenched with water and organic layer was separated. Aqueous layer was washed with EtOAc twice. Combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. Crude mixture was purified using flash column chromatography to afford the desired biaryl boronate esters.

General procedure for microwave-assisted Miyaura borylation of 2 followed by Suzuki-Miyaura coupling reactions with arylbromides (method R1) In a 20.0 ml-microwave vial, a mixture of **2** (600.0 mg, 2.4 mmol), B_2pin_2 (731.0 mg, 2.9 mmol), PPh_3 (38.0 mg, 0.1 mmol) and potassium phenoxide (539.0 mg, 4.8 mmol) in toluene (10.0 ml) was degassed with argon for 5 min and $PdCl_2(PPh_3)_2$ (50.5 mmol, 0.1 mmol) was added. The mixture was continuously degassed for another 5 min and then sealed with a cap. The reaction was performed in microwave irradiation at 65 °C for 85 min, which included the time for the temperature to reach 65 °C (~ 2-3 min). After cooling to room temperature, the mixture was filtered using filter paper and the solid kept on the paper was washed several times with Et_2O. The combined organic layers were concentrated to dryness, and re-dissolved in $CHCl_3$ (3.0 ml). To the solution was added CH_2Br_2 (0.1 ml, 1.4 mmol) and a small amount of the resulted solution was taken for ^{1}H-NMR to estimate the yield of the borylated product **3**. After estimating the reaction yield (from 82-90%), the solution was concentrated to dryness and crude **3** was used directly in the next step without purification.

To a 0.3 M solution of crude **3** (1 eq) in EtOH/ H_2O (2:1, v/v) in a size-corresponding microwave vial were added arylbromide (1.5 eq), K_3PO_4 (3 eq) and SPhos or XPhos (0.1 eq). The mixture was degassed with argon for 5 min following which $Pd(OAc)_2$ or $PdCl_2$ (0.05 eq) was added. The mixture was continuously degassed for another 3 min then sealed with a cap. The reaction was performed under microwave irradiation at 65 °C for 2 h in order to prevent the formation of the deboronated product. After cooling to room temperature, saturated aqueous NaCl solution and CH_2Cl_2 were added and two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 times). The organic layers were combined and dried on $MgSO_4$. After concentration under reduced pressure, flash chromatographic purification on silica gel afforded coupling product.

(method R2) A mixture of bromoallyl carbamate (2.4 mmol), bis(pinacolato)diboron (1.2 eq) and triphenylphosphine (6 mol%) in anhydrous toluene (10.0 ml) was degassed for 10 min in a 20.0 ml microwave vial. Potassium phenoxide (2 eq) was then added and reaction mixture further degassed for 5 min. Trans-dichlorobis(triphenylphosphine)palladium (3 mol%) was added and reaction mixture further degassed for 5 min. Microwave vial was then sealed with a cap. The reaction was performed in microwave at 65 °C for 85 min. After cooling to room temperature, the reaction mixture was filtered using a filter paper and residue washed with diethyl ether. The combined filtrate was then concentrated under reduced pressure to afford the desired crude product. The crude product was used in the next step without further purification. A mixture of allyl boronic ester (2.4 mmol), 2-dicyclohexylphosphino-2',6'- dimethoxybiphenyl (10 mol%), aryl bromide (1.5 eq) and potassium phosphate tribasic monohydrate (3 eq) in ethanol/water (6.0 ml/3.0 ml) was degassed for 10 min in a 20.0 ml microwave vial. Palladium acetate* (5 mol%) was added and reaction mixture further degassed for 5 min. Microwave vial was then sealed with a cap. The reaction mixture was stirred under argon at 60 °C overnight. After cooling to room temperature, saturated aqueous sodium chloride (10.0 ml) and dichloromethane (10.0 ml) were added and two layers separated. The aqueous layer was extracted with dichloromethane (3x20.0 ml). The organic layers were then combined, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel.

*$Pd_2(dba)_3$ and PPh_3 were used in replace of $Pd(OAc)_2$ and SPhos for the coupling reaction when R-group contains chlorine

General Procedure for Alkylation Reaction between Phenol Derivatives and Bromobenzylbromide derivatives (method S)

(method S1) A solution of bromobenzylbromide derivative (8.0 mmol), phenol derivative (1 eq) and potassium carbonate (1.1 eq) in anhydrous dimethylformamide (50.0 ml) was stirred at room temperature under argon overnight. The reaction mixture was filtered and the filtrate concentrated under reduced pressure. The filtrate was purified by flash column chromatography on silica gel.

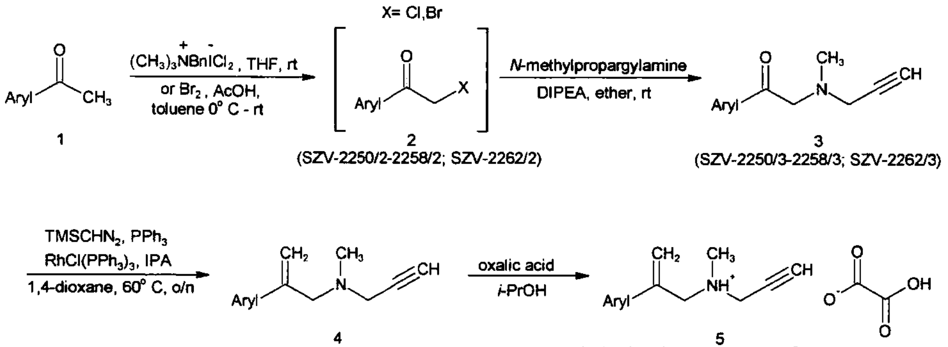
(method S2) To a solution of phenol derivative (1.2 eq) in DMF (400.0 mmol) was added 3-bromobenzylbromide (1.0 eq) followed by K_2CO_3 (1.5 eq). The reaction mixture was allowed to stir at room temperature for 3 h. TLC showed the starting material, 3-bromobenzylbromide was consumed. The reaction was quenched with water, and the aqueous layer was washed with EtOAc thrice. Combined organic layer was washed with water twice, dried over $MgSO_4$ and concentrated in vacuo. Crude mixture was purified using flash column chromatography to afford the desired aryl bromide.

General procedure for synthesis of mesylate and reaction between mesylate and *tert*-butyl (3-(*tert*-butyldimethylsilyl)prop-2-yn-1-yl)carbamate

Formation of mesylate starting from aryl allyl alcohol (method T1) To a solution of the appropriate alcohol in dichloromethane (120.0 mmol) was added MsCl (1.0 eq) and Et_3N (1.2 eq) at 0 °C. The reaction mixture was allowed to stir at 0 °C under Ar atmosphere. Progression of the reaction was monitored by NMR analysis which indicated the complete consumption of the alcohol after 10 mins. The reaction was quenched with water and aqueous layer was washed with DCM thrice. Combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude was purified using flash column chromatography to afford the desired mesylate product.

(**method T2**) To a solution of *tert*-butyl (3-(*tert*-butyldimethylsilyl)prop-2-yn-1-yl)carbamate (1.5 eq) in DMF (300.0 mmol) was added NaH (1.5 eq) at 0 °C under Ar atmosphere. Efferverscence was observed. Reaction mixture was allowed to stir at room temperature for 1h. A solution of mesylate in DMF (180.0 mmol) was added subsequently and the reaction mixture was allowed to stir at room temperature under Ar overnight. The reaction was quenched with water and the organic layer was separated. Aqueous layer was washed with EtOAc twice. Combined organic layer was washed with water, dried over $MgSO_4$ and concentrated in vacuo. Crude mixture was purified using flash column chromatography (EtOAc : Petroleum Ether = 10 : 90) to give a mixture of products with and without TBS group. The mixture was dissolved in dichloromethane (120.0 mmol) and TFA (10 eq) was added dropwise. Reaction mixture was allowed to stir at room temperature for 3 h before it was neutralized with $NaHCO_3$ to pH 7. Aqueous layer was washed with DCM twice. Combined organic layer was dried over $MgSO_4$ and concentrated in vacuo to afford the desired amine.

Scheme 1



Aryl = 2-pyridyl (SZV-2250)
Aryl = 3-pyridyl (SZV-2251)
Aryl = 4-pyridyl (SZV-2252)
Aryl = 3-furanyl (SZV-2253)
Aryl = 2-furanyl (SZV-2254)
Aryl = 2-benzo[b]thiophenyl (SZV-2255)
Aryl = 3-benzo[b]thiophenyl (SZV-2256)
Aryl = 3-thiophenyl (SZV-2257)
Aryl = 2-thiazolyl (SZV-2258)
Aryl = 2-benzo[b]furanyl (SZV-2262)

2-(Methyl(prop-2-ynyl)amino)-1-(pyridin-2-yl)ethanone (SZV-2250/3) Following the **method A** and **D1**, the crude was purified by Silica gel column chromatography (6 : 4, pet. ether : ethyl acetate, R_f = 0.23) to afford the title compound as a red oil (84%). ^1H NMR (400 MHz, Chloroform-*d*) δ 8.66-8.67 (m, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.83-7.87 (m, 1H), 4.30 (s, 2H), 7.47-7.51 (m, 1H), 3.61 (d, *J* = 2.4 Hz, 2H), 2.51 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(Methyl(prop-2-ynyl)amino)-1-(pyridin-3-yl)ethanone (SZV-2251/3) Following the **method A** and **D1**, the crude was purified by Silica gel column chromatography (pet. ether : ethyl acetate 5:5, R_f = 0.26) to afford the title compound as a red oil (64%). ^1H NMR (400 MHz, Chloroform-*d*): δ 9.24 (s, 1H), 8.80-8.78 (m, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.45-7.41 (m, 1H), 3.99 (s, 2H), 3.59 (d, *J* = 2.4 Hz, 2H), 2.49 (s, 3H), 2.34 (t, *J* = 2.4 Hz, 1H).

2-(Methyl(prop-2-ynyl)amino)-1-(pyridin-4-yl)ethanone (SZV-2252/3) Following the **method A** and **D1**, the crude was purified by Silica gel column chromatography (5 : 5, pet. ether : ethyl acetate, $R_f = 0.30$) to afford the title compound as a red oil (37%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.81 (d, *J* = 6.0 Hz, 1H), 7.79 (d, *J* = 6.0 Hz, 1H), 3.93 (s, 2H), 3.54 (d, *J* = 2.4 Hz, 2H), 2.44 (s, 3H), 2.31 (t, *J* = 2.4 Hz, 1H).

1-(Furan-3-yl)-2-(methyl(prop-2-ynyl)amino)ethanone (SZV-2253/3) Following the **method A** and **D1**, the crude was purified by Silica gel column chromatography (8 : 2, pet. ether : ethyl acetate, $R_f = 0.19$) to afford the title compound as a red oil (68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (s, 1H), 7.44 (d, *J* = 1.6 Hz, 1H), 6.82 (d, *J* = 1.6 Hz, 1H), 3.65 (s, 2H), 3.48 (d, *J* = 2.4 Hz, 2H), 2.41 (s, 3H), 2.29 (t, *J* = 2.4 Hz, 1H).

1-(Furan-2-yl)-2-(methyl(prop-2-ynyl)amino)ethanone (SZV-2254/3) Following the **method A** and **D1**, the crude was purified by Silica gel column chromatography (6 : 4, pet. ether : ether, $R_f = 0.27$) to afford the title compound as a red oil (56%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 1.6 Hz, 1H), 7.32 (d, *J* = 3.6 Hz, 1H), 6.55 (dd, *J* = 3.6, 1.6 Hz, 1H), 3.81 (s, 2H), 3.54 (d, *J* = 2.4 Hz, 2H); 2.45 (s, 3H), 2.29 (t, *J* = 2.4 Hz, 1H).

1-Benzo[b]thiophen-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2255/3) Following the **method C1** and **D1**, the reaction was refluxed for 1 h in chloroform to give the title compound (43%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.40 (d, *J* = 0.4 Hz, 1H), 8.03 – 7.99 (m, 2H), 7.42 – 7.31 (m, 2H), 3.93 (s, 2H), 3.55 (d, *J* = 2.4 Hz, 1H), 2.79 (t, *J* = 2.4 Hz, 1H), 2.43 (s, 3H).

1-(Benzo[b]thiophen-3-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2256/3) Following the **method C1** and **D1**, the reaction was refluxed for 1 h in chloroform to give the title compound (57%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 9.01 (s, 1H), 8.71 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.53 – 7.44 (m, 2H), 3.89 (s, 2H), 3.54 (d, *J* = 2.4 Hz, 1H), 2.78 (t, *J* = 2.4 Hz, 1H), 2.41 (s, 3H).

2-(Methyl(prop-2-ynyl)amino)-1-thiophen-3-yl)ethanone (SZV-2257/3) Following the **method A** and **D1**, the crude was purified by Silica gel column chromatography (6 : 4, pet. ether : ethyl acetate, $R_f = 0.23$) to afford the title compound as a red oil (69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 (dd, *J* = 2.8, 1.2 Hz, 1H), 7.60 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.32 (dd, *J* = 5.2, 2.8 Hz, 1H), 3.83 (s, 2H), 3.53 (d, *J* = 2.4 Hz, 2H) , 2.44 (s, 3H) , 2.29 (t, *J* = 2.4 Hz, 1H).

2-(Methyl(prop-2-ynyl)amino)-1-(thiazol-4-yl)ethanone (SZV-2258/3) Following the **method C1** and **D1**, the crude was purified by Silica gel column chromatography (8 : 2, pet. ether : ethyl acetate, $R_f = 0.28$) to afford the title compound as a red oil (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 2.8 Hz, 1H), 7.70 (d, *J* = 2.8, 1H), 4.22 (s, 2H), 3.60 (d, *J* = 2.4 Hz, 2H) , 2.51 (s, 3H) , 2.28 (t, *J* = 2.4 Hz, 1H).

1-(Benzofuran-2-yl)-2-(methyl(prop-2-ynyl)amino)ethanone (SZV-2262/3) Following the **method C1** and **D1**, the crude product was purified by column chromatography (9:1, *n*-hexane : ethyl acetate) to afford the title compound as an off-white solid (42%). ^{1}H NMR (400 MHz, Acetone-d_6) δ

7.84 – 7.82 (m, 2H), 7.64 – 7.62 (m, 1H), 7.56 – 7.51 (m, 1H), 7.38 – 7.33 (m, 1H), 3.90 (s, 2H), 3.55 (d, $J = 2.0$ Hz, 2H), 2.79 (t, $J = 2.0$ Hz, 1H), 2.43 (s, 3H).

***N*-Methyl-*N*-(prop-2-ynyl)-2-(pyridin-2-yl)prop-2-en-1-amine (SZV-2250/4)** Following the **method E1**, the crude was purified by Silica gel column chromatography (50 : 50, pet. ether:ethyl acetate, $R_f = 0.25$) to afford the title compound as an orange oil (27%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59-8.57 (m, 1H), 7.68-7.63 (m, 1H), 7.56 (d, $J = 8.0$ Hz, 1H), 7.19-7.15 (m, 1H), 6.02 (s, $J = 1.6$ Hz), 3.58 (s, 2H), 5.50 (s, $J = 1.6$ Hz, 1H), 3.39 (d, $J = 2.4$ Hz, 2H), 2.36 (s, 3H), 2.26 (t, $J = 2.4$ Hz, 1H).

***N*-Methyl-*N*-(prop-2-ynyl)-2-(pyridin-3-yl)prop-2-en-1-amine (SZV-2251/4)** Following the **method E1**, the crude was purified by Silica gel column chromatography (pet. ether : ethyl acetate 50:50, $R_f = 0.23$) to afford the title compound as an orange oil (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.76 (d, $J = 1.6$, 1H), 8.51-8.49 (m, 1H), 7.82 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.28-7.23 (m, 1H), 5.54 (s, 1H), 5.37 (s, 1H), 3.45 (s, 2H), 3.34 (d, $J = 2.4$ Hz, 2H), 2.31 (s, 3H), 2.27 (t, $J = 2.4$ Hz, 1H).

***N*-Methyl-*N*-(prop-2-ynyl)-2-(pyridine-4-yl)prop-2-en-1-amine (SZV-2252/4)** Following the **method E1**, the crude was purified by Silica gel column chromatography (80 : 20, pet. ether : ethyl acetate, $R_f = 0.14$) to afford the title compound as an orange oil (30%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.55 (d, $J = 6.0$ Hz, 1H), 7.41 (d, $J = 6.0$ Hz, 1H), 5.68 (s, 1H), 5.45 (s, 1H), 3.45 (s, 2H), 3.35 (d, $J = 2.4$ Hz, 2H), 2.32 (s, 3H), 2.28 (t, $J = 2.4$ Hz, 1H).

2-(Furan-3-yl)-*N*-methyl-*N*-(prop-2-ynyl)prop-2-en-1-amine (SZV-2253/4) Following the **method E1**, the crude was purified by Silica gel column chromatography (95 : 5, pet. ether : EtOAc, $R_f = 0.38$) to afford the title compound as a colourless oil (43%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (s, 1H), 7.35 (t, $J = 1.6$ Hz, 1H), 6.55 (dd, $J = 1.6$, 0.8 Hz, 1H), 5.36 (s, $J = 1.2$ Hz, 1H), 5.15 (d, $J = 1.2$ Hz, 1H), 3.35 (d, $J = 2.4$ Hz, 2H), 3.29 (s, 2H), 2.32 (s, 3H), 2.25 (t, $J = 2.4$ Hz, 1H).

2-(Furan-2-yl)-*N*-methyl-*N*-(prop-2-ynyl)prop-2-en-1-amine (SZV-2254/4) Following the **method E1**, the crude was purified by Silica gel column chromatography (90 : 10, pet. ether : ether, $R_f = 0.33$) to afford the title compound as a colourless oil (64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (d, $J = 1.2$ Hz, 1H), 6.48 (d, $J = 3.2$ Hz, 1H), 6.37 (dd, $J = 3.2$, 1.2 Hz, 1H), 5.66 (s, $J = 1.6$ Hz, 1H), 5.18 (d, $J = 1.6$ Hz, 1H), 3.38 (d, $J = 2.4$ Hz, 2H), 3.32 (s, 2H), 2.34 (s, 3H), 2.26 (t, $J = 2.4$ Hz, 1H).

2-(Benzo[*b*]thiophen-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2255/4) Following the **method E1**, the reaction was heated at 50 °C for 16 h to give the title compound (33%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.84 (m, 1H), 7.76 (m, 1H), 7.62 (s, 1H), 7.32 (m, 2H), 5.64 (d, $J = 1.2$ Hz, 1H), 5.35 (d, $J = 1.2$ Hz, 1H), 3.49 (s, 2H), 3.42 (d, $J = 2.4$ Hz, 1H), 2.76 (t, $J = 2.4$ Hz, 1H), 2.35 (s, 3H).

2-(Benzo[*b*]thiophen-3-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2256/4) Following the **method E1**, the reaction was heated at 50 °C for 16 h to give the title compound (31%).

^{1}H NMR (400 MHz, Acetone-d_6) δ 8.01(d, $J = 8.0$ Hz, 1H), 7.95 (d, $J = 8.0$ Hz, 1H), 7.75 (s, 1H), 7.44-7.36 (m, 2H), 5.57 (s, 1H), 5.51 (d, $J = 2.0$ Hz, 1H), 3.48 (d, $J = 0.8$ Hz, 2H), 3.38 (d, $J = 2.4$ Hz, 2H), 2.71 (t, $J = 2.4$ Hz, 1H), 2.31 (s, 3H).

***N*-Methyl-*N*-(prop-2-ynyl)-2-(thiophen-3-yl)prop-2-en-1-amine (SZV-2257/4)** Following the **method E1**, the crude was purified by Silica gel column chromatography (90 : 10, pet. ether : ether, $R_f = 0.29$) to afford the title compound as a colourless oil (71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (dd, $J = 3.2$, 1.2 Hz, 1H), 7.29-7.27 (m, 1H), 7.25-7.25 (m, 1H), 5.50 (d, $J = 1.2$ Hz, 1H), 5.22 (d, $J = 1.2$ Hz, 1H), 3.40-3.37 (m, 4H), 2.34 (s, 3H), 2.26 (t, $J = 2.4$ Hz, 1H).

***N*-Methyl-*N*-(prop-2-ynyl)-2-(thiazol-2-yl)prop-2-en-1-amine (SZV-2258/4)** Following the **method E1**, the crude was purified by Silica gel column chromatography (80 : 20, pet. ether : EtOAc, $R_f = 0.31$) to afford the title compound as a yellow oil (42%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, $J = 3.2$, 1H), 7.26 (d, $J = 3.2$ Hz, 1H), 6.10 (s, 1H), 5.49 (d, $J = 0.8$ Hz, 1H), 3.53 (s, 2H), 3.43 (d, $J = 2.4$ Hz, 2H), 2.39 (s, 3H), 2.27 (t, $J = 2.4$ Hz, 1H).

2-(Benzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2262/4) Following the **method E1**, the crude was purified by Silica gel column chromatography (80:20, pet. ether : EtOAc) to afford the title compound as a yellow oil (52%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.60 – 7.58 (m, 1H), 7.48 (dd, $J = 8.0$, 0.8 Hz, 1H), 7.30 (td, $J = 7.6$, 1.2 Hz, 1H), 7.21 (td, $J = 7.6$, 1.2 Hz, 1H), 7.02 (s, 1H), 5.92 (d, $J = 1.2$ Hz, 1H), 5.42 (d, $J = 1.2$ Hz, 1H), 3.44 (d, $J = 0.4$ Hz, 2H), 3.40 (d, $J = 2.4$ Hz, 2H), 2.76 (t, $J = 2.4$ Hz, 1H), 2.33 (s, 3H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(pyridin-2-yl)prop-2-en-1-aminium carboxyformate (SZV-2250)** Following the **method H1**, the title compound was isolated. Mp 112.8-113.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 8.55 (ddd, $J = 4.8$, 1.6, 0.8 Hz, 1H), 7.78 (td, $J = 8.0$, 1.6 Hz, 1H), 7.69 (dt, $J = 8.0$, 0.8 Hz, 1H), 7.30 (ddd, $J = 8.0$, 4.8, 1.2 Hz, 1H), 3.35 (t, $J = 2.0$ Hz, 1H), 3.47 (d, $J = 2.0$ Hz, 2H), 3.67 (s, 2H), 5.50 (d, $J = 0.4$ Hz, 1H), 6.09 (d, $J = 1.6$ Hz, 1H), 2.32 (s, 3H). Anal. calcd. for $C_{12}H_{14}N_2x(COOH)_2$ (276.29): C, 60.86%; H, 5.84%; N, 10.14%. Found: C, 59.90%; H, 5.88%; N, 10.10%.

3-(3-(Methyl(prop-2-yn-1-yl)ammonio)prop-1-en-2-yl)pyridin-1-ium carboxyformate (SZV-2251) Following the **method H1**, the title compound was isolated. Mp 144.9-145.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 8.74 (dd, $J = 2.0$, 0.4 Hz, 1H), 8.48 (dd, $J = 4.8$, 1.6 Hz, 1H), 7.93 (ddd, $J = 8.0$, 2.0, 1.6 Hz, 1H), 7.37 (ddd, $J = 8.0$, 4.8, 0.8 Hz, 1H), 5.69 (d, 1H, $J = 0.8$ Hz), 5.40 (d, 1H, $J = 0.8$ Hz), 3.55 (s, 2H), 3.39 (d, 2H, $J = 2.4$ Hz), 3.29 (t, 1H, $J = 2.4$ Hz), 2.25 (s, 3H). Anal. calcd. for $C_{12}H_{14}N_2x2(COOH)_2$ (366.32): C, 52.46%; H, 4.95%; N, 7.65%. Found: C, 51.86%; H, 5.04%; N, 7.64%.

4-(3-(Methyl(prop-2-yn-1-yl)ammonio)prop-1-en-2-yl)pyridin-1-ium carboxyformate (SZV-2252) Following the **method H1**, the title compound was isolated. Mp 152.5 – 153.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 8.53 (d, $J = 6.0$ Hz, 1H), 7.54 (d, $J = 6.0$ Hz, 1H) 5.80 (s, 1H), 5.45 (s, 1H), 3.46 (s, 2H), 3.32 (d, $J = 2.4$ Hz, 2H), 3.23 (t, $J = 2.4$ Hz, 1H), 2.19 (s, 3H). Anal.

calcd. for $C_{12}H_{14}N_2x2(COOH)_2$ (366.32): C, 52.46%; H, 4.95%; N, 7.65%. Found: C, 51.18%; H, 5.13%; N, 7.68%.

2-(Furan-3-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2253) Following the **method H1**, the title compound was isolated. Mp 115.3 – 116.1 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.84 (s, 1H), 7.61 (t, *J* = 1.6 Hz, 1H), 6.74 (dd, *J* = 1.6, 0.8 Hz, 1H), 5.46 (s, 1H), 5.12 (s, 1H), 3.38 (s, 2H), 3.30 (s, 2H), 3.25 (s, 1H), 2.26 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{11}H_{14}NO^+$ $[M+H]^+$ 176.1070, found 176.1072.

2-(Furan-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2254) Following the **method H1**, the title compound was isolated. Mp 118.0 – 119.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.63 (dd, *J* = 2.0, 0.8 Hz, 1H), 6.59 (dd, *J* = 3.2, 0.8 Hz, 1H), 5.60 (d, *J* = 1.2 Hz, 1H), 6.49 (dd, *J* = 3.2, 2.0 Hz, 1H), 5.18 (d, *J* = 1.2 Hz, 1H), 3.42 (d, *J* = 2.4 Hz, 2H), 3.35 (s, 2H), 3.27 (t, *J* = 2.4 Hz, 1H), 2.28 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{11}H_{14}NO^+$ $[M+H]^+$ 176.1070, found 176.1077.

2-(Benzo[b]thiophen-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2255) Following the **method H1**, the title compound was isolated. Mp 145.3 – 148.5 °C.^{1}H NMR (400 MHz, Acetone-d_6) δ 7.86 – 7.84 (m, 1H), 7.78 – 7.76 (m, 1H), 7.63 (s, 1H), 7.36 – 7.32 (m, 2H), 5.68 (s, 1H), 5.40 (d, *J* = 1.2 Hz, 1H), 3.59 (d, *J* = 1.2 Hz, 2H), 3.50 (d, *J* = 2.4 Hz, 2H), 2.83 (t, *J* = 2.4 Hz, 1H), 2.42 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{16}NS^+$ $[M+H]^+$ 242.0998, found 242.1002.

2-(Benzo[b]thiophen-3-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2256) Following the **method H1**, the title compound was isolated. Mp 118.8 – 120.6 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.02 – 7.96 (m, 2H), 7.78 (s, 1H), 7.45 – 7.37 (m, 2H), 5.69 (s, 1H), 5.60 (s, 1H), 3.72 (s, 2H), 3.56 (d, *J* = 2.4 Hz, 2H), 2.86 (t, *J* = 2.4 Hz, 1H), 2.46 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{16}NS^+$ $[M+H]^+$ 242.0998, found 242.1005.

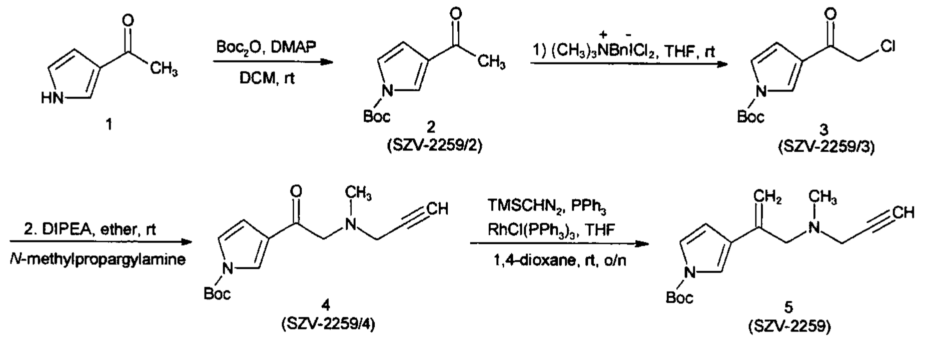
***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(thiophen-3-yl)prop-2-en-1-aminium carboxyformate (SZV-2257)** Following the **method H1**, the title compound was isolated. Mp 121.6 – 122.8 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6): δ 7.78 (dd, *J* = 2.8, 1.2 Hz, 1H), 7.64 (dd, *J* = 4.8, 2.8 Hz, 1H), 7.52 (dd, *J* = 4.8, 1.2 Hz, 1H), 5.74 (s, 1H), 5.34 (s, 1H), 3.55 (bs, 4H), 3.40 (s, 1H), 2.41 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{11}H_{14}NS^+$ $[M+H]^+$ 192.0841, found 192.0844.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(thiazol-2-yl)prop-2-en-1-aminium carboxyformate (SZV-2258)** Following the **method H1,** the title compound was isolated. Mp 123.4 – 124.0 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6): δ 7.82 (d, 1H, *J* = 3.2 Hz), 7.69 (d, 1H, *J* = 3.2 Hz), 6.04 (s, 1H), 5.47 (s, 1H), 3.49 (s, 2H), 3.41 (d, 2H, *J* = 2.4 Hz), 3.25 (t, 1H, *J* = 2.4 Hz), 2.28 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{10}H_{13}N_2S^+$ $[M+H]^+$ 193.0794, found 193.0795.

2-(Benzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2262) Following the **method H1,** the title compound was isolated. Mp 134.1 – 135.4 °C (dec). ^{1}H NMR (400 MHz, Methanol-d_4, 400 MHz) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.33

(m, 1H), 7.24 (m, 1H), 7.10 (s, 1H), 6.24 (s, 1H) and 5.71 (s, 1H), 4.12 (s, 2H), 3.99 (d, *J* = 2.0 Hz, 2H), 3.27 (t, *J* = 2.0 Hz, 1H), 2.84 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{16}NO^+$ $[M+H]^+$ 226.1226, found 226.1232.

Scheme 2

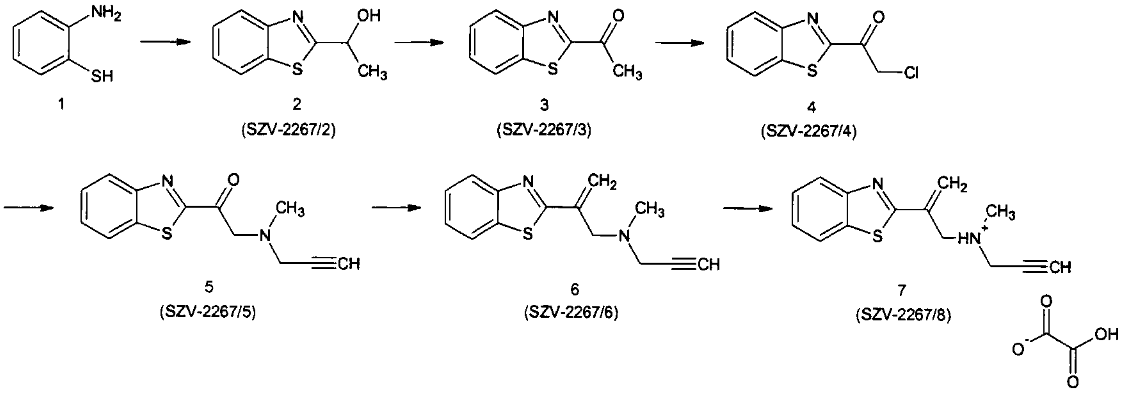


***tert*-Butyl 3-acetyl-1-*H*-pyrrole-1-carboxylate (SZV-2259/2)** Following **method K**, the title compound was isolated as a colourless oil (85%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.80 (t, *J* = 1.6 Hz, 1H), 7.21 (dd, *J* = 3.2, 1.6 Hz, 1H), 6.62 (d, *J* = 3.2, 1.6 Hz, 1H), 2.44 (s, 3H), 1.62 (s, 9H).

***tert*-Butyl 3-(2-methyl(prop-2-ynyl)amino)acetyl)-1*H*-pyrrole-1-carboxylate (SZV-2259/4)** Following the **method C1 and D1**, the crude was purified by basic alumina column chromatography (7 : 3, pet. ether : EtOAc, R_f = 0.20) to afford the title compound as a colourless oil in 30% yield. ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.98 (t, *J* = 2.0 Hz, 1H), 7.21 (dd, *J* = 3.2, 2.0 Hz, 1H), 6.67 (d, *J* = 3.2, 2.0 Hz, 1H), 3.71 (s, 2H), 3.51 (d, *J* = 2.4 Hz, 2H), 2.42 (s, 3H), 2.28 (t, *J* = 2.4 Hz, 1H), 1.62 (s, 9H).

***tert*-Butyl 3-(3-(methyl(prop-2-ynyl)amino)prop-1-en-2-yl)-1*H*-pyrrole-1-carboxylate (SZV-2259)** Following the **method E1**, the crude was purified by basic alumina column chromatography (95 : 05, pet. ether : DCM, R_f = 0.28) to afford the title compound as a colourless oil in 46% yield. ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.41 (s, 1H), 7.16 (t, *J* = 2.0 Hz, 1H), 6.39 (dd, *J* = 3.6, 1.6 Hz, 1H), 5.38 (d, *J* = 1.2 Hz, 1H), 5.11 (s, 1H), 3.37 (d, *J* = 2.4 Hz, 2H), 3.30 (s, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H), 1.58 (s, 9H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{23}N_2O_2^+$ $[M+H]^+$ 275.1754, found 275.1757.

Scheme 3



1-(Benzo[*d*]thiazol-2-yl)ethanol (SZV-2267/2) (Florio S et al, Tetrahedron, 1997, 53, 5839-5846) D, l-lactic acid (7.0 ml, 95.9 mmol) was added to 2-amino thiophenol (8.6 ml, 79.9 mmol) in a round-bottomed flask. The mixture was then heated to reflux with a Dean-Stark trap at 150 °C for 96 h. After 96 h, the reaction mixture was cooled to room temperature before dichloromethane (DCM, 30.0 ml) was added to it. The organic layer was then washed with water three times. The organic layer was dried over magnesium sulphate and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (4:1 *n*-hexane: ethyl acetate). The resulting mixture of the desired product and its ester with lactic acid was isolated as a yellow solid. This solid was then dissolved in methanol (50.0 ml). Lithium hydroxide (0.1 g, 10 mol%) was added to the solution which was stirred for 1 hour. The solvent was removed *in vacuo* before HCl solution (10%, 50.0 ml) was added to it. The resulting mixture was extracted with ethyl acetate three times before the organic layer was dried over magnesium sulphate. The solvent was removed *in vacuo* to obtain the title product as a yellow solid (42%). Mp 52.3-58.0 °C (lit. Mp 54-56 °C). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.96 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.46 – 7.44 (m, 1H), 7.38 – 7.36 (m, 1H), 5.25 (m, 1H), 3.69 (bs, 1H), 1.69 (s, 3H).

1-(benzo[*d*]thiazol-2-yl)ethanone (SZV-2267/3) (Minisci F et al, J. Chem. Soc. C, 1971, 1747-1750) 1-(benzo[*d*]thiazol-2-yl)ethanol (3.1 g, 17.2 mmol) was dissolved in DCM (50.0 ml). Manganese dioxide (7.5 g, 860.0 mmol) was added to the mixture one equivalent (1.5 g) a day. The mixture was left to stir at room temperature for 5 days, after which the mixture was filtered (through filter paper) and the solvent of the filtrate was removed *in vacuo*. The crude product was purified by column chromatography (9:1, *n*-hexane: ethyl acetate) to afford the title compound as a yellow solid (80%). Mp 109-110.5 °C (lit. Mp 108-109 °C). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.19 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.58 – 7.53 (m, 2H), 2.82 (s, 3H).

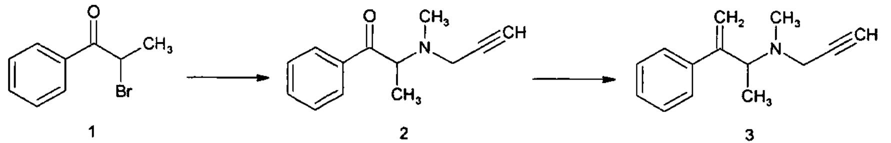
1-(Benzo[*d*]thiazol-2-yl)-2-chloroethanone (SZV-2267/4) Following the **method C1** the crude product was purified by column chromatography (9:1, *n*-hexane : ethyl acetate) to afford the title compound as a solid (87%). Mp 86.5-96.9 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.25 – 8.24 (m, 2H), 7.69 – 7.68 (m, 2H), 5.29 (s, 2H).

1-(Benzo[*d*]thiazol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2267/5) Following the **method D1**, however, after column chromatography (9:1, *n*-hexane : ethyl acetate), a mixture of the title compound and *N*-methylpropargylamine was isolated. This mixture was used in the next step without additional purification.

2-(Benzo[*d*]thiazol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2267/6) Following the **method E1** (using an impure mixture of **(SZV-2267/5)** and *N*-methylpropargylamine) the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.02 (ddd, J = 8.0, 1.2, 0.8 Hz, 1H), 7.98 (ddd, J = 8.0, 1.2, 0.8 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.45 – 7.41 (m, 1H), 6.24 (d, J = 1.2 Hz, 1H), 5.70 (q, J = 1.2 Hz, 1H), 3.62 (s, 2H), 3.46 (d, J = 2.4 Hz, 2H), 2.76 (t, J = 2.4 Hz, 1H), 2.39 (s, 3H).

2-(Benzo[*d*]thiazol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2267) Following the **method H1,** the title compound was isolated. Mp 131.1 – 134.5 °C (dec). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.03 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.53 – 7.41 (m, 2H), 6.27 (d, J = 1.2 Hz, 1H), 5.77 (d, J = 1.2 Hz, 1H), 3.73 (s, 2H), 3.55 (d, J = 2.4 Hz, 2H), 2.84 (t, J = 2.4 Hz, 1H), 2.46 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{15}N_2S^+$ $[M+H]^+$ 243.0950, found 243.0955.

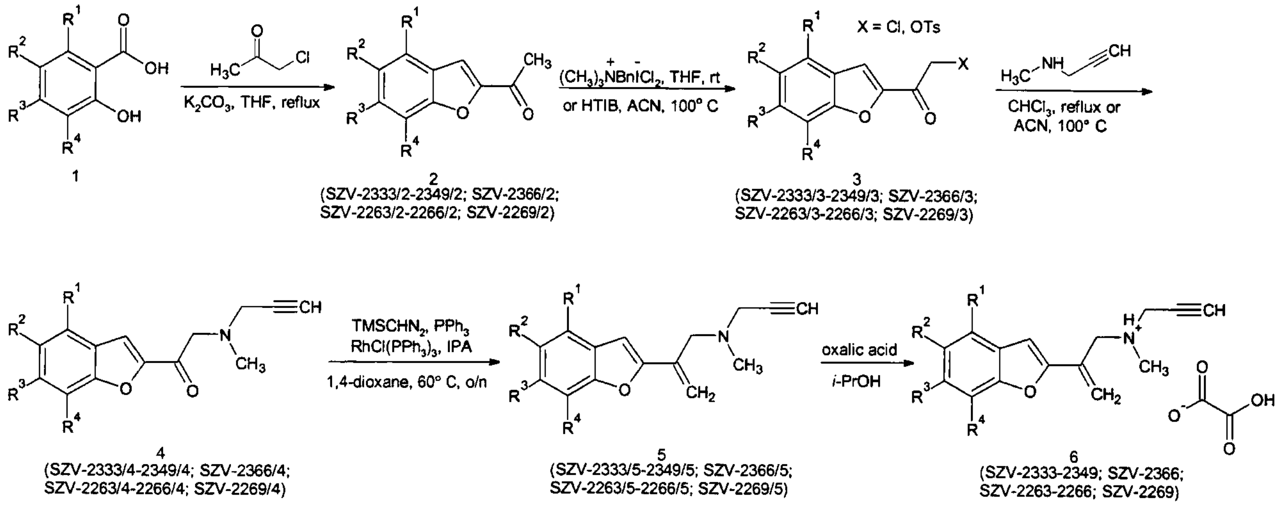
Scheme 4



(*rac*)-2-(Methyl(prop-2-ynyl)amino-1-phenylpropan-1-one (SZV-2268/2) (Warawa EJ et al, US3577461) Following the **method D1**, the crude was purified by Silica gel column chromatography (9 : 1, pet. ether : ethyl acetate, R_f = 0.21) to afford the title compound as a yellow oil in 51% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.11-8.08 (m, 2H), 7.58-7.54 (m, 1H), 7.48-7.44 (m, 2H), 4.39 (q, J = 6.8 Hz, 1H), 2.35 (s, 3H), 3.49 (dd, J = 16.8, 2.4 Hz, 2H), 2.29 (t, J = 2.4 Hz, 1H), 1.32 (d, J = 6.8 Hz, 2H).

(*rac*)-*N*-Methyl-3-phenyl-*N*-(prop-2-ynyl)but-3-en-2-amine (SZV-2268) Following the **method E1**, the crude was purified by Silica gel column chromatography (97 : 03, pet. ether : ethyl acetate, R_f = 0.25) to afford the title compound as a colourless oil in 60% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.37-7.35 (m, 2H), 7.17-7.10 (m, 3H), 5.29 – 5.24 (m, 2H), 3.46 (q, J = 6.8 Hz, 1H), 3.42 (t, J = 2.4 Hz, 2H), 2.30 (s, 3H), 2.16 (t, J = 2.4 Hz, 1H), 1.12 (d, J = 6.8 Hz, 3H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{17}N^+$ $[M+H]^+$ 200.1434, found 200.1428.

Scheme 5



R_1	**R_2**	**R_3**	**R_4**	**SZV #**
H	H	**Cl**	H	**2333**
H	H	H	**OEt**	**2334**
H	**Cl**	H	**Cl**	**2335**
H	H	H	**Me**	**2336**
H	**I**	H	**I**	**2337**
H	**F**	H	H	**2338**
Naphtha-C_4H_4		H	H	**2339**
H	H	**OBn**	H	**2340**
H	**Br**	H	**Br**	**2341**
H	H	**Me**	H	**2342**
H	**Br**	H	H	**2343**
F	H	H	H	**2344**
H	H	**F**	H	**2345**
H	H	H	**F**	**2346**
H	H	H	**Br**	**2347**
H	H	H	**Cl**	**2348**
H	H	**Br**	H	**2349**
H	H	H	**OMe**	**2366**
H	**Me**	H	H	**2263**
H	**OMe**	H	H	**2264**
H	H	**OMe**	H	**2265**
Br	H	H	**OMe**	**2266**
H	**Cl**	H	H	**2269**

1-(6-Chlorobenzofuran-2-yl)ethanone (SZV-2333/2) (Sapkal SB et al, Chin. Chem. Lett., 2010, 21, 1439-1442) Following **method I,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.84 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 1.6 Hz, 1H), 7.75 (s, 1H), 7.40 (dd, J = 8.4, 1.6 Hz, 1H), 2.57 (s, 3H).

1-(7-Ethoxybenzofuran-2-yl)ethanone (SZV-2334/2) Following **method I,** the title compound was isolated. Mp 61.7-65.0 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.69 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 4.29 (q, J = 6.8 Hz, 2H), 2.57 (s, 3H), 1.47 (t, J = 6.8 Hz, 3H).

1-(5,7-Dichlorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2335/2) (Khodarahmi GA et al, J. Pharm. Pharmacol. 1998, 50, 1321-1330) Following **method I,** the title compound was isolated. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 2.0 Hz, 1H), 7.48 (d, *J* = 2.0 Hz, 1H), 7.45 (s, 1H), 2.65 (s, 3H).

1-(7-Methylbenzofuran-2-yl)-ethanone (SZV-2336/2) (Sapkal SB et al, Chin. Chem. Lett., 2010, 21, 1439-1442) Following **method I**, 1.59 g of the title compound was isolated (70%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.69 (s, 1H), 7.61 (ddd, *J* = 8.0, 1.2, 0.8 Hz, 1H), 7.33 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 2.57 (s, 3H), 2.53 (s, 3H).

1-(5,7-Diiodobenzofuran-2-yl)ethanone (SZV-2337/2) Following **method I,** the title compound was isolated. Mp 187-189 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 1.6 Hz, 1H), 7.98 (d, *J* = 1.6 Hz, 1H), 7.47 (s, 1H), 2.63 (s, 3H).

1-(5-Fluorobenzofuran-2-yl)ethanone (SZV-2338/2) (Wempe MF et al, WO2012048058) Following **method I**, 4.69 g of the title compound was isolated (92%). Mp 91-92 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.70 (d, *J* = 0.8 Hz, 1H), 7.66 (dd, *J* = 9.2, 4.0 Hz, 1H), 7.54 (ddd, *J* = 8.4, 2.8, 0.8 Hz, 1H), 7.33 (td, *J* = 9.2, 2.8 Hz, 1H), 2.57 (s, 3H).

1-(Naphtho[2,1-b]furan-2-yl)ethanone (SZV-2339/2) (El-Wahab AHFA et al, Molecules, 2011, 16, 307-318) Following **method I**, 5.86 g of the title compound was isolated (96%). Mp 115-116 °C (lit. Mp 108-110 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.35 (ddd, *J* = 8.0, 1.2, 0.8 Hz, 1H), 8.29 (d, *J* = 1.2 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.75 (dd, *J* = 9.2, 0.8 Hz, 1H), 7.69 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.59 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 2.62 (s, 3H).

1-(6-(Benzyloxy)benzofuran-2-yl)ethanone (SZV-2340/2) (Mackenzie JBD et al, J. Chem. Soc., 1949, 2057-2061) Following **method I**, 4.90 g of the title compound was isolated (84%). Mp 100-101 °C (lit. Mp 98 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.71 (dd, *J* = 8.8, 0.4 Hz, 1H), 7.66 (d, *J* = 0.8 Hz, 1H), 7.54 – 7.52 (m, 2H), 7.44 – 7.28 (m, 3H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.07 (dd, *J* = 8.8, 2.0 Hz, 1H), 5.25 (s, 2H), 2.52 (s, 3H).

1-(5,7-Dibromobenzofuran-2-yl)ethanone (SZV-2341/2) (Khodarahmi GA et al, J. Pharm. Pharmacol. 1998, 50, 1321-1330) Following **method I**, 4.30 g of the title compound was isolated (76%). Mp 151-153 °C (lit. Mp 152-153 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.04 (d, *J* = 1.6 Hz, 1H), 7.90 (d, *J* = 1.6 Hz, 1H), 7.80 (s, 1H), 2.62 (s, 3H).

1-(6-Methylbenzofuran-2-yl)ethanone (SZV-2342/2) (Reddy YT et al, Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem., 2005, 44B, 1079-1083) Following **method I**, 5.13 g of the title compound was isolated as yellow solid (80%). Mp 78-80 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.69 – 7.67 (m, 2H), 7.45 (d, *J* = 0.4 Hz, 1H), 7.24 – 7.16 (ddd, *J* = 8.0, 2.0, 0.4 Hz 1H), 2.54 (s, 3H), 2.49 (s, 3H).

1-(5-Bromobenzofuran-2-yl)ethanone (SZV-2343/2) (Paizs C et al, Tetrahedron: Asymmetry, 2003, 14, 1495-1501) Following **method I**, 5.42 g of the title compound was isolated as yellow solid (91%). Mp 112-113 °C (lit. Mp 110 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.01 (dd, *J* = 2.0, 0.8 Hz, 1H), 7.70 (d, *J* = 0.8 Hz, 1H), 7.70 – 7.61 (m, 2H), 2.58 (s, 3H).

1-(4-Fluorobenzofuran-2-yl)ethanone (SZV-2344/2) Following **method I**, 2.19 g of the title compound was isolated (88%). Mp 90-92 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.76 (d, J = 0.8 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.10 (ddd, J = 9.6, 8.0, 0.8 Hz, 1H), 2.59 (s, 3H).

1-(6-Fluorobenzofuran-2-yl)ethanone (SZV-2345/2) Following **method I**, 2.34 g of the title compound was isolated (92%). Mp 98-99 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.81 (dd, J = 8.8, 5.6 Hz, 1H), 7.69 (d, J = 0.8 Hz, 1H), 7.66 (ddd, J = 9.2, 1.2, 0.8 Hz, 1H), 7.17 (ddd, J = 9.6, 8.8, 2.4 Hz, 1H), 2.55 (s, 3H).

1-(7-Fluorobenzofuran-2-yl)ethanone (SZV-2346/2) (Wempe MF et al, WO2012048058) Following **method I**, 4.69 g of the title compound was isolated (83%). Mp 88-90 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.76 (d, J = 2.8 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.34 – 7.31 (m, 2H), 2.59 (s, 3H).

1-(7-Bromobenzofuran-2-yl)ethanone (SZV-2347/2) (Gardinier KMG et al, WO2002071827) Following **method I**, 1.92 g of the title compound was isolated (85%). Mp 74-76 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.75 (dd, J = 8.0, 1.2 Hz, 1H), 7.74 (s, 1H), 7.66 (dd, J = 8.0, 1.2 Hz, 1H), 7.25 (t, J = 8.0 Hz, 1H), 2.59 (s, 3H).

1-(7-Chlorobenzofuran-2-yl)ethanone (SZV-2348/2) Following **method I**, 2.24 g of the title compound was isolated (90%). Mp 80-82 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.72 (s, 1H), 7.72 (dd, J = 8.0, 1.2 Hz, 1H), 7.52 (dd, J = 8.0, 1.2 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 2.59 (s, 3H).

1-(6-Bromobenzofuran-2-yl)ethanone (SZV-2349/2) (Sapkal SB et al, Chin. Chem. Lett., 2010, 21, 1439-1442) Following **method I**, 2.04 g of the title compound was isolated (91%). Mp 108-110 °C (lit. Mp 148-150 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.87 (ddd, J = 1.2, 0.8, 0.4 Hz, 1H), 7.75 (dd, J = 8.0, 0.4 Hz, 1H), 7.70 (d, J = 1.2 Hz, 1H), 7.50 (dd, J = 8.4, 1.2 Hz, 1H), 2.57 (s, 3H).

1-(7-Methoxybenzofuran-2-yl)ethanone (SZV-2366/2) (Wempe MF et al, WO2012048058) Compound (**SZV-2366/2**) was purchased from Alfa Aesar and was used without further purification. Mp 144-145 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.67 (s, 1H), 7.35 (dd, J = 7.9, 1.0 Hz, 1H), 7.27 (t, J = 7.9 Hz, 1H), 7.10 (dd, J = 7.9, 0.8 Hz, 1H), 4.02 (s, 3H), 2.57 (s, 3H).

1-(5-Methylbenzofuran-2-yl)ethanone (SZV-2263/2) (Nordmann J et al, DE2307535) Following **method I,** the title compound was isolated. Mp 79-80 °C (lit. Mp 72 °C). ^{1}H NMR (400 MHz, Acetone) δ 7.63 (d, J = 0.8 Hz, 1H), 7.57 (s, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.35 (dd, J = 8.4, 0.8 Hz, 1H), 2.55 (s, 3H), 2.43 (s, 3H).

1-(5-Methoxybenzofuran-2-yl)ethanone (SZV-2264/2) (Nordmann J et al, DE2307535) Following **method I,** the title compound was isolated. Mp 84-85 °C (lit. Mp 85 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.63 (s, 1H), 7.53 (d, J = 9.2 Hz, 1H), 7.27 (d, J = 2.8 Hz, 1H), 7.13 (dd, J = 9.2, 2.8 Hz, 1H), 3.85 (s, 3H), 2.54 (s, 3H).

1-(6-Methoxybenzofuran-2-yl)ethanone (SZV-2265/2) (Sapkal SB et al, Chin. Chem. Lett., 2010, 21, 1439-1442) Following **method I,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.67 (d, J = 8.4 Hz, 1H), 7.66 (s, 1H), 7.18 (d, J = 2.0 Hz, 1H), 6.98 (dd, J = 8.4, 2.0 Hz, 1H), 3.90 (s, 3H), 2.51 (s, 3H).

1-(4-Bromo-7-methoxybenzofuran-2-yl)ethanone (SZV-2266/2) (Ando K et al, Org. Biomol. Chem., 2007, 5, 655-663) Following **method I,** the title compound was isolated. Mp 144-145 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.62 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 4.03 (s, 3H), 2.62 (s, 3H).

1-(5-Chlorobenzofuran-2-yl)ethanone (SZV- 2269/2) (Nordmann J et al, DE2307535) Following **method I,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.86 (d, J = 2.0 Hz, 1H), 7.70 (s, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.53 (dd, J = 8.8, 2.0 Hz, 1H), 2.58 (s, 3H).

1-(6-Chlorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2333/4) Following **method B** and **method D2,** the title compound was isolated. Mp 116-117.5 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.88 (s,1H), 7.84 (d, J = 8.4 Hz, 1H), 7.75 (s, 1H), 7.39 (d, J = 8.4 Hz, 1H), 3.88 (s, 2H), 3.54 (d, J = 2.4 Hz, 2H), 2.79 (t, J = 2.4 Hz, 1H), 2.42 (s, 3H).

1-(7-Ethoxybenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2334/4) Following **method C2** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.62 (s, 1H), 7.26 (dd, J = 8.0, 1.2 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 6.92 (dd, J = 8.0, 1.2 Hz, 1H), 4.28 (q, J = 6.8 Hz, 2H), 3.98 (s, 2H), 3.58 (d, J = 2.4 Hz, 2H), 2.49 (s, 3H), 2.29 (t, J = 2.4 Hz, 1H), 1.53 (t, J = 6.8 Hz, 3H).

1-(5,7-Dichlorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2335/4) Following **method C2** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.57 (s, 1H), 7.56 (d, J = 2.0 Hz, 1H), 7.44 (d, J = 2.0 Hz, 1H), 3.94 (s, 2H), 3.55 (d, J = 2.4 Hz, 2H), 2.47 (s, 3H), 2.30 (t, J = 2.4 Hz, 1H).

2-(Methyl(prop-2-yn-1-yl)amino)-1-(7-methylbenzofuran-2-yl)ethanone (SZV-2336/4) Following **method B** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.84 (s, 1H), 7.63 (ddd, J = 8.0, 1.2, 0.8 Hz, 1H), 7.34 (dt, J = 8.0, 1.2 Hz, 1H), 7.25 (t, J = 8.0 Hz, 1H), 3.90 (s, 2H), 3.55 (d, J = 2.4 Hz, 2H), 2.78 (t, J = 2.4 Hz, 1H), 2.54 (s, 3H), 2.43 (s, 3H).

1-(5,7-Diiodobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2337/4) Following **method B** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.12 (d, J = 1.6 Hz, 1H), 8.00 (d, J = 1.6 Hz, 1H), 7.63 (s, 1H), 3.95 (s, 2H), 3.58 (d, J = 2.4 Hz, 2H), 2.50 (s, 3H), 2.30 (t, J = 2.4 Hz, 1H).

1-(5-Fluorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2338/4) Following **method B** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.87 (d, J = 0.8 Hz, 1H), 7.70 (dd, J = 9.2, 4.0 Hz, 1H), 7.58 (dd, J = 8.4, 2.4 Hz, 1H), 7.36 (td, $J = 9.2$, 2.8 Hz, 1H), 3.91 (s, 2H), 3.56 (d, $J = 2.4$ Hz, 2H),2.79 (t, $J = 2.4$ Hz, 1H), 2.45 (s, 3H).

2-(Methyl(prop-2-yn-1-yl)amino)-1-(naphtho[2,1-b]furan-2-yl)ethanone (SZV-2339/4) Following **method C2** and **method D2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.47 (d, $J = 0.8$ Hz, 1H), 8.39 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.06 (d, $J = 8.4$ Hz, 1H), 7.79 (dd, $J = 8.4$, 0.8 Hz, 1H), 7.71 (ddd, $J = 8.0$, 7.2, 1.2 Hz, 1H), 7.60 (ddd, $J = 8.2$, 7.2, 1.2 Hz, 1H), 3.96 (s, 2H), 3.59 (d, $J = 2.4$ Hz, 2H), 2.79 (t, $J = 2.4$ Hz, 1H), 2.47 (s, 3H).

1-(6-(Benzyloxy)benzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2340/4) Following **method C2** and **method D2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.79 (d, $J = 1.2$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 7.53 (d, $J = 7.2$ Hz, 2H), 7.45 – 7.31 (m, 3H), 7.28 (d, $J = 2.0$ Hz, 1H), 7.07 (dd, $J = 8.4$, 2.0 Hz, 1H), 5.25 (s, 2H), 3.83 (s, 2H), 3.53 (d, $J = 2.4$ Hz, 2H), 2.76 (t, $J = 2.4$ Hz, 1H), 2.41(s, 3H).

1-(5,7-Dibromobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2341/4) Following **method B** and **method D2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.04 (d, $J = 2.0$ Hz, 1H), 7.93 (s, 1H), 7.89 (d, $J = 2.0$ Hz, 1H), 3.91 (s, 2H), 3.55 (d, $J = 2.4$ Hz, 2H), 2.78 (t, $J = 2.4$ Hz, 1H), 2.44 (s, 3H).

2-(Methyl(prop-2-yn-1-yl)amino)-1-(6-methylbenzofuran-2-yl)ethanone (SZV-2342/4) Following **method B** and **method D2**, 0.659 g of the title compound was isolated (90%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.77 (d, $J = 0.8$ Hz, 1H), 7.66 (d, $J = 8.0$ Hz, 1H), 7.41 (dd, $J = 1.2$, 0.8 Hz, 1H), 7.17 (ddd, $J = 8.0$, 1.6, 0.8 Hz, 1H), 3.86 (s, 2H), 3.54 (d, $J = 2.4$ Hz, 2H), 2.78 (t, $J = 2.4$ Hz, 1H), 2.47 (s, 3H), 2.42 (s, 3H).

1-(5-Bromobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2343/4) Following **method B** and **method D2**, 0.322 g of the title compound was isolated (80%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.03 (dd, $J = 2.0$, 0.8 Hz, 1H), 7.83 (d, $J = 0.8$ Hz, 1H), 7.69 – 7.62 (m, 2H), 3.90 (s, 2H), 3.54 (d, $J = 2.4$ Hz, 2H), 2.77 (t, $J = 2.4$ Hz, 1H), 2.43 (s, 3H).

1-(4-Fluorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2344/4) Following **method B** and **method D2**, 0.961 g of the title compound was isolated (85%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.90 (d, $J = 0.8$ Hz, 1H), 7.57 – 7.52 (m, 1H), 7.48 (d, $J = 7.6$ Hz, 1H), 7.10 (ddd, $J = 9.2$, 8.0, 0.8 Hz, 1H), 3.91 (s, 2H), 3.56 (d, $J = 2.4$ Hz, 2H), 2.77 (t, $J = 2.4$ Hz, 1H), 2.44 (s, 3H).

1-(6-Fluorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2345/4) Following **method B** and **method D2**, 1.18 g of the title compound was isolated (90%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.90 – 7.82 (m, 2H), 7.51 – 7.43 (m, 1H), 7.20 (ddd, $J = 9.6$, 8.8, 2.4 Hz, 1H), 3.87 (s, 2H), 3.54 (d, $J = 2.4$ Hz, 2H), 2.77 (t, $J = 2.4$ Hz, 1H), 2.43 (s, 3H).

1-(7-Fluorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2346/4) Following **method B** and **method D2**, 1.12 g of the title compound was isolated as yellow oil (93%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.93 (d, $J = 2.8$ Hz, 1H), 7.66 – 7.64 (m, 1H), 7.37 – 7.34 (m, 2H), 3.92 (s, 2H), 3.55 (d, J = 2.4 Hz, 2H), 2.77 (t, J = 2.4 Hz, 1H), 2.44 (s, 3H).

1-(7-Bromobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2347/4) Following **method B** and **method D2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.96 (s, 1H), 7.84 (dd, J = 8.0, 1.2 Hz, 1H), 7.74 (dd, J = 8.0, 1.2 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 3.91 (s, 2H), 3.56 (d, J = 2.4 Hz, 2H), 2.76 (t, J = 2.4 Hz, 1H), 2.45 (s, 3H).

1-(7-Chlorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2348/4) Following **method B** and **method D2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.94 (s, 1H), 7.81 (dd, J = 8.0, 1.2 Hz, 1H), 7.59 (dd, J = 8.0, 1.2 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 3.91 (s, 2H), 3.56 (d, J = 2.4 Hz, 2H), 2.76 (t, J = 2.4 Hz, 1H), 2.44 (s, 3H).

1-(6-Bromobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2349/4) Following **method B** and **method D2**, 0.696 g of the title compound was isolated (86%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.90 (brs, 1H), 7.86 (d, J = 0.8 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.52 (dd, J = 8.4, 1.6 Hz, 1H), 3.88 (s, 2H), 3.54 (d, J = 2.4 Hz, 2H), 2.76 (t, J = 2.4 Hz, 1H), 2.43 (s, 3H).

1-(7-Methoxybenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2366/4) Following **method C2** and **method D2**, impure 0.617 g of the title compound was isolated (86%). It was deduced that heating at 100 °C caused the formation of side product which has similar Rf value to that of the desired product. Impure compound **(SZV-2366/4)** was used for the next step without further purification.

2-(Methyl(prop-2-yn-1-yl)amino)-1-(5-methylbenzofuran-2-yl)ethanone (SZV-2263/4) Following **method C1** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.74 (d, J = 1.2 Hz, 1H), 7.56 (s, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.34 (dd, J = 8.8, 1.2 Hz, 1H), 3.88 (s, 2H), 3.55 (d, J = 2.4 Hz, 3H), 2.78 (t, J = 2.4 Hz, 1H), 2.42 (s, 6H).

1-(5-Methoxybenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2264/4) Following **method C1** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.77 (s, 1H), 7.54 (d, J = 9.2 Hz, 1H), 7.28 (d, J = 2.8 Hz, 1H), 7.14 (dd, J = 9.2, 2.8 Hz, 1H), 3.88 (s, 2H), 3.85 (s, 3H), 3.54 (d, J = 2.4 Hz, 2H), 2.77 (t, J = 2.4 Hz, 1H), 2.42 (s, 3H).

1-(6-Methoxybenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2265/4) Following **method C1** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.78 (s, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.17 (d, J = 2.0 Hz, 1H), 6.97 (dd, J = 8.8, 2.0 Hz, 1H), 3.90 (s, 3H), 3.83 (s, 2H), 3.54 (d, J = 2.4 Hz, 2H), 2.78 (t, J = 2.4 Hz, 1H), 2.42 (s, 3H).

1-(4-Bromo-7-methoxybenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2266/4) Following **method C1** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.76 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 4.03 (s, 3H), 3.94 (s, 2H), 3.56 (d, J = 2.4 Hz, 2H), 2.79 (t, J = 2.4 Hz, 1H), 2.44 (s, 3H)

1-(5-Chlorobenzofuran-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2269/4) Following **method C1** and **method D2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.87 (d, J = 2.0, 1H), 7.84 (s, 1H), 7.68 (d, J = 8.8, 1H), 7.55 (dd, J = 8.8, 2.0 Hz, 1H), 3.90 (s, 2H), 3.54 (d, J = 2.4 Hz, 2H), 2.78 (t, J = 2.4 Hz, 1H), 2.42 (s, 3H).

2-(6-Chlorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2333/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.60 (d, J = 8.4 Hz, 1H), 7.57 (d, J = 1.6 Hz, 1H), 7.25 (dd, J = 8.4, 1.6 Hz, 1H), 7.05 (s, 1H), 5.91 (d, J = 1.2 Hz, 1H), 5.46 (d, J = 1.2 Hz, 1H), 3.44 (s, 2H), 3.40 (d, J = 2.4 Hz, 2H), 2.77 (t, J = 2.4 Hz, 1H), 2.33 (s, 3H).

2-(7-Ethoxybenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2334/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 – 7.04 (m, 2H), 6.86 (s, 1H), 6.78 (dd, J = 7.2, 1.6 Hz, 1H), 6.03 (d, J = 1.2 Hz, 1H), 5.41 (d, J = 1.2 Hz, 1H), 4.28 (q, J = 6.8 Hz, 2H), 3.46 – 3.33 (m, 4H), 2.37 (s, 3H), 2.29 (t, J = 2.4 Hz, 1H), 1.51 (t, J = 6.8 Hz, 3H).

2-(5,7-Dichlorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2335/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, J = 2.0 Hz, 1H), 7.25 (d, J = 2.0 Hz, 1H), 6.86 (s, 1H), 6.07 (d, J = 0.8 Hz, 1H), 5.49 (d, J = 0.8 Hz, 1H), 3.40 (s, 2H), 3.40 (d, J = 2.4 Hz, 2H), 2.36 (s, 3H), 2.29 (t, J = 2.4 Hz, 1H).

***N*-Methyl-2-(7-methylbenzofuran-2-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2336/5)** Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.43 – 7.37 (m, 1H), 7.12 – 7.08 (m, 2H), 7.01 (s, 1H), 5.95 (d, J = 1.2 Hz, 1H), 5.42 (d, J = 1.2 Hz, 1H), 3.44 (d, J = 0.8 Hz, 1H), 3.41 (d, J = 2.4 Hz, 1H), 2.77 (t, J = 2.4 Hz, 1H), 2.50 (s, 3H), 2.34 (s, 3H).

2-(5,7-Diiodobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2337/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.98 (d, J = 1.6 Hz, 2H), 7.96 (d, J = 1.6 Hz, 1H), 7.15 (s, 1H), 6.01 (d, J = 0.8 Hz, 1H), 5.54 (d, J = 0.8 Hz, 1H), 3.45 (s, 2H), 3.40 (d, J = 2.4 Hz, 2H), 2.78 (s, 1H), 2.33 (s, 3H).

2-(5-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2338/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.49 (dd, J = 8.8, 4.0 Hz, 1H), 7.33 (dd, J = 8.8, 2.4 Hz, 1H), 7.07 (td, J = 9.2, 2.8 Hz, 1H), 7.04 (s, 1H), 5.93 (d, J = 1.6 Hz, 1H), 5.46 (d, J = 1.6 Hz, 1H), 3.44 (s, 1H), 3.40 (d, J = 2.4 Hz, 1H), 2.75 (t, J = 2.4 Hz, 1H), 2.33 (s, 3H).

***N*-Methyl-2-(naphtho[2,1-b]furan-2-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2339/5)** Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.23 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.50 (ddd, J = 8.0, 7.2, 1.2 Hz, 1H), 5.95 (d, J = 1.2 Hz, 1H), 5.43 (d, J = 1.2 Hz, 1H), 3.52 (s, 2H), 3.46 (d, J = 2.4 Hz, 2H), 2.78 (t, J = 2.4 Hz, 1H), 2.38 (s, 3H).

2-(6-(Benzyloxy)benzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2340/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ

7.53 – 7.45 (m, 3H), 7.42 – 7.31 (m, 3H), 7.17 (d, *J* = 1.6 Hz, 1H), 6.98 – 6.90 (m, 2H), 5.81 (d, *J* = 1.2 Hz, 1H), 5.34 (d, *J* = 1.2 Hz, 1H), 5.19 (s, 2H), 3.41 (s, 2H), 3.39 (d, *J* = 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 1H), 2.32 (s, 3H).

2-(5,7-Dibromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2341/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.81 (d, *J* = 2.0 Hz, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.14 (s, 1H), 6.01 (d, *J* = 0.8 Hz, 1H), 5.54 (d, *J* = 0.8 Hz, 1H), 3.46 (s, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 1H), 2.33 (s, 3H).

***N*-Methyl-2-(6-methylbenzofuran-2-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2342/5)** Following **method E2,** 0.193 g of the title compound was isolated (34%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.45 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 0.8 Hz, 1H), 7.04 (ddd, *J* = 8.0, 1.6, 0.8 Hz, 1H), 6.95 (s, 1H), 5.87 (d, *J* = 1.2 Hz, 1H), 5.38 (d, *J* = 1.2 Hz, 1H), 3.42 (d, *J* = 0.8 Hz, 2H), 3.39 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.43 (s, 3H), 2.33 (s, 3H).

2-(5-Bromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2343/5) Following **method E2,** 0.380 g of the title compound was isolated (40%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.74 (d, *J* = 1.2 Hz, 1H), 7.44 – 7.39 (m, 2H), 6.99 (s, 1H), 5.93 (d, *J* = 1.2 Hz, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 3.42 (s, 2H), 3.39 (d, *J* = 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 1H), 2.32 (s, 3H).

2-(4-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2344/5) Following **method E2,** 0.538 g of the title compound was isolated (44%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.36 – 7.28 (m, 2H), 7.10 (s, 1H), 6.98 (ddd, *J* = 9.6, 8.0, 0.4 Hz, 1H), 5.94 (d, *J* = 1.2 Hz, 1H), 5.48 (d, *J* = 1.2 Hz, 1H), 3.46 (d, *J* = 0.8 Hz, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.34 (s, 3H).

2-(6-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2345/5) Following **method E2,** 0.535 g of the title compound was isolated (46%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.60 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.32 (ddd, *J* = 9.2, 2.4, 0.8 Hz, 1H), 7.07 – 7.02 (m, 2H), 5.88 (d, *J* = 1.2 Hz, 1H), 5.42 (d, *J* = 1.2 Hz, 1H), 3.43 (s, 2H), 3.40 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.33 (s, 3H).

2-(7-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2346/5) Following **method E2,** 0.404 g of the title compound was isolated as colourless oil (36%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.42 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.20 (td, *J* = 8.0, 4.4 Hz, 1H), 7.13 – 7.08 (m, 2H), 5.97 (d, *J* = 1.2 Hz, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 3.46 (d, *J* = 0.8 Hz, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 1H), 2.34 (s, 3H).

2-(7-Bromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2347/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.61 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.49 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 7.14 (s, 1H), 5.99 (d, *J* = 1.2 Hz, 1H), 5.50 (d, *J* = 1.2 Hz, 1H), 3.46 (s, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 1H), 2.34 (s, 3H).

2-(7-Chlorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2348/5) Following **method E2,** the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.35 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.12 (s, 1H), 5.99 (d, *J* = 1.2 Hz, 1H), 5.50 (d, *J* = 1.2 Hz, 1H), 3.46 (s, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.34 (s, 3H).

2-(6-Bromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2349/5) Following **method E2**, 0.248 g of the title compound was isolated (36%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.72 (s, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.38 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.05 (s, 1H), 5.92 (d, *J* = 1.2 Hz, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 3.44 (s, 2H), 3.40 (d, *J* = 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 1H), 2.33 (s, 3H).

2-(7-Methoxybenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2366/5) Following **method E2**, 89.5 mg of the title compound was isolated (29%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.17 – 7.10 (m, 2H), 7.00 (s, 1H), 6.89 (dd, *J* = 7.2, 1.2 Hz, 1H), 5.92 (d, *J* = 1.2 Hz, 1H), 5.42 (d, *J* = 1.2 Hz, 1H), 3.99 (s, 3H), 3.44 (s, 2H), 3.40 (d, *J* = 2.4 Hz, 2H), 2.73 (t, *J* = 2.4 Hz, 1H), 2.34 (s, 3H).

***N*-Methyl-2-(5-methylbenzofuran-2-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2263/5)** Following **method E2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.38 – 7.34 (m, 2H), 7.11 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.94 (s, 1H), 5.88 (d, *J* = 1.2 Hz, 1H), 5.40 (d, *J* = 1.2 Hz, 1H), 3.43 (d, *J* = 0.8 Hz, 2H), 3.40 (d, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 1H), 2.39 (s, 3H), 2.33 (s, 3H).

2-(5-Methoxybenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2264/5) Following **method E2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.37 (d, *J* = 8.8 Hz, 1H), 7.10 (d, *J* = 2.4 Hz, 1H), 6.96 (s, 1H), 6.89 (dd, *J* = 8.8, 2.4 Hz, 1H), 5.87 (d, *J* = 1.2 Hz, 1H), 5.39 (d, *J* = 1.2 Hz, 1H), 3.81 (s, 3H), 3.42 (d, *J* = 0.8 Hz, 2H), 3.39 (d, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 1H), 2.33 (s, 3H).

2-(6-Methoxybenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2265/5) Following **method E2**, the title compound was isolated ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.46 (d, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 2.0 Hz, 1H), 6.94 (s, 1H), 6.85 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.82 (d, *J* = 1.2 Hz, 1H), 5.35 (d, *J* = 1.2 Hz, H), 3.85 (s, 3H), 3.43 (s, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.77 (t, *J* = 2.4 Hz, 1H), 2.34 (s, 3H).

2-(4-Bromo-7-methoxybenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2266/5) Following **method E2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.30 (d, *J* = 8.4 Hz, 1H), 6.98 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 5.97 (d, *J* = 1.2 Hz, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 3.99 (s, 3H), 3.47 (s, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.77 (t, *J* = 2.4 Hz, 1H), 2.34 (s, 3H).

2-(5-Chlorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2269/5) Following **method E2**, the title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6)

δ 7.62 (d, J = 2.0 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.30 (dd, J = 8.8, 2.0 Hz, 1H), 7.03 (s, 1H), 5.89 (d, J = 1.2 Hz, 1H), 5.42 (d, J = 1.2 Hz, 1H), 3.39 (d, J = 0.8 Hz, 2H), 3.35 (d, J = 2.4 Hz, 2H), 2.71 (t, J = 2.4 Hz, 1H), 2.28 (s, 3H).

2-(6-Chlorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2333) Following **method H1**, the title compound was isolated. Mp 122 – 126 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.72 (s, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.28 (dd, J = 8.4, 1.6 Hz, 1H), 7.09 (s, 1H), 5.89 (d, J = 0.8 Hz, 1H), 5.45 (s, 1H), 3.43 (brs, 4H), 3.28 (t, J = 2.4 Hz, 1H), 2.29 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}ClNO^+$ $[M+H]^+$ 260.0837, found 260.0849.

2-(7-Ethoxybenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2334) Following **method H1**, the title compound was isolated. Mp 133 – 134 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.17 (dd, J = 8.0, 0.8 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 7.02 (s, 1H), 6.91 (dd, J = 8.0, 0.8 Hz, 1H), 5.87 (s, 1H), 5.41 (s, 1H), 4.23 (q, J = 6.8 Hz, 2H), 3.42 (brs, 4H), 3.27 (t, J = 2.4 Hz, 1H), 2.29 (s, 3H), 1.40 (t, J = 6.8 Hz, 3H). HRMS (ESI+) *m/z* calcd. for $C_{17}H_{20}NO_2^+$ $[M+H]^+$ 270.1489, found 270.1499.

2-(5,7-Dichlorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2335) Following **method H1**, the title compound was isolated. Mp 146 – 150 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.73 (d, J = 2.0 Hz, 1H), 7.56 (d, J = 2.0 Hz, 1H), 7.14 (s, 1H), 5.95 (s, 1H), 5.52 (s, 1H), 3.48 – 3.33 (m, 4H), 3.26 (t, J = 2.4 Hz, 1H), 2.27 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{14}Cl_2NO^+$ $[M+H]^+$ 294.0447, found 294.0456.

***N*-Methyl-2-(7-methylbenzofuran-2-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2336)** Following **method H1**, the title compound was isolated. Mp 108 – 109 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.42 (t, J = 4.8 Hz, 1H), 7.12 (d, J = 4.8 Hz, 2H), 7.03 (s, 1H), 5.93 (s, 1H), 5.43 (s, 1H), 3.45 (s, 4H), 3.26 (s, 1H), 2.47 (s, 3H), 2.31 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{18}NO^+$ $[M+H]^+$ 240.1383, found 240.1393.

2-(5,7-Diiodobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2337) Following **method H1**, the title compound was isolated. Mp 85 – 86 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.99 (d, J = 1.6 Hz, 1H), 7.94 (d, J = 1.6 Hz, 1H), 7.14 (s, 1H), 5.92 (s, 1H), 5.50 (s, 1H), 4.00 – 2.84 (brs, 5H), 2.27 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{14}I_2NO^+$ $[M+H]^+$ 477.9159, found 477.9167.

2-(5-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2338) Following **method H1**, the title compound was isolated. Mp 137 – 138 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.57 (dd, J = 8.8, 4.0 Hz, 1H), 7.43 (dd, J = 8.8, 2.4 Hz, 1H), 7.13 (td, J = 9.2, 2.8 Hz, 1H), 7.05 (s, 1H), 5.90 (d, J = 0.8 Hz, 1H), 5.45 (d, , J = 0.8 Hz, 1H), 3.41 (brs, 4H), 3.23 (t, J = 2.4 Hz, 1H), 2.28 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}FNO^+$ $[M+H]^+$ 244.1132, found 244.1173.

***N*-Methyl-2-(naphtho[2,1-b]furan-2-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2339)** Following **method H1**, the title compound was isolated. Mp 170 –

172 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 8.27 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 9.2 Hz, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.67 (s, 1H), 7.62 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 7.52 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 5.93 (s, 1H), 5.42 (s, 1H), 3.50 (s, 2H), 3.48 (d, J = 2.4 Hz, 2H), 3.27 (t, J = 2.4 Hz, 1H), 2.35 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{19}H_{18}NO^+$ $[M+H]^+$ 276.1383, found 276.1395.

2-(6-(Benzyloxy)benzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2340) Following **method H1**, the title compound was isolated. Mp 103 – 105 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.50 – 7.31 (m, 6H), 7.24 (d, J = 2.0 Hz, 1H), 6.96 (s, 1H), 6.93 (dd, J = 8.4, 2.0 Hz, 1H), 5.78 (s, 1H), 5.33 (s, 1H), 5.16 (s, 2H), 3.40 – 3.38 (m, 4H), 3.22 (t, J = 2.4 Hz, 1H), 2.27 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{22}H_{22}NO_2^+$ $[M+H]^+$ 332.1645, found 332.1654.

2-(5,7-Dibromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2341) Following **method H1**, the title compound was isolated. Mp 159 – 162 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.88 (d, J = 1.6 Hz, 1H), 7.74 (d, J = 1.6 Hz, 1H), 7.15 (s, 1H), 5.94 (s, 1H), 5.52 (s, 1H), 3.41 – 3.39 (m, 4H), 3.22 (t, J = 2.4 Hz, 1H), 2.27 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{14}Br_2NO^+$ $[M+H]^+$ 381.9437, found 381.9442.

***N*-Methyl-2-(6-methylbenzofuran-2-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2342)** Following **method H1**, 183 mg of the title compound was isolated (81%). Mp 130.3 – 132.9 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.46 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 0.8 Hz, 1H), 7.05 (dd, J = 8.0, 0.8 Hz, 1H), 6.99 (s, 1H), 5.91 (d, J = 1.2 Hz, 1H), 5.44 (d, J = 1.2 Hz, 1H), 3.54 (d, J = 0.4 Hz, 2H), 3.50 (d, J = 2.4 Hz, 2H), 2.84 (t, J = 2.4 Hz, 1H), 2.44 (s, 3H), 2.41 (s, 3H). Anal. calcd. for $C_{16}H_{17}NOx(COOH)_2$ (329.35): C, 65.64%; H, 5.81%; N, 4.25%. Found: C, 65.36%; H, 5.82%; N, 4.34%.

2-(5-Bromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2343) Following **method H1**, 431 mg of the title compound was isolated (88%). Mp 151.0 – 152.6 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.79 (d, J = 1.6 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.05 (s, 1H), 5.98 (s, 1H), 5.52 (s, 1H), 3.53 (s, 2H), 3.48 (d, J = 2.4 Hz, 2H), 2.81 (t, J = 2.4 Hz, 1H), 2.39 (s, 3H). Anal. calcd. for $C_{15}H_{14}BrNOx(COOH)_2$ (394.22): C, 51.79%; H, 4.09%; N, 3.55%. Found: C, 51.97%; H, 4.13%; N, 3.63%.

2-(4-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2344) Following **method H1**, 572 mg of the title compound was isolated (85%). Mp 99.0 – 101.3 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.38 – 7.32 (m, 2H), 7.16 (s, 1H), 7.05 – 6.94 (ddd, J = 9.6, 8.0, 0.8 Hz, 1H), 6.03 (s, 1H), 5.59 (s, 1H), 3.66 (s, 2H), 3.59 (d, J = 2.4 Hz, 2H), 2.88 (t, J = 2.4 Hz, 1H), 2.49 (s, 3H). Anal. calcd. for $C_{15}H_{14}FNOx(COOH)_2$ (333.31): C, 61.26%; H, 4.84%; N, 4.20%. Found: C, 61.25%; H, 5.01%; N, 4.32%.

2-(6-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium

carboxyformate (SZV-2345) Following **method H1**, 629 mg of the title compound was isolated (87%). Mp 117.8 – 118.8 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.60 (dd, J = 8.8, 5.6 Hz, 1H), 7.31 (ddd, J = 9.2, 2.4, 0.8 Hz, 1H), 7.12 – 7.00 (m, 2H), 5.92 (d, J = 1.2 Hz, 1H), 5.47 (d, J = 1.2 Hz, 1H), 3.52 (d, J = 0.8 Hz, 2H), 3.48 (d, J = 2.4 Hz, 2H), 2.80 (t, J = 2.4 Hz, 1H), 2.40 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}FNO^+$ $[M+H]^+$ 244.1138, found 244.1136.

2-(7-Fluorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2346) Following **method H1**, 477 mg of the title compound was isolated (88%). Mp 137.4 – 138.6 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.42 (dd, J = 6.8, 0.8 Hz, 1H), 7.21 (td, J = 8.0, 4.4 Hz, 1H), 7.15 – 7.09 (m, 2H), 6.04 (s, 1H), 5.57 (d, J = 0.8 Hz, 1H), 3.61 (d, J = 0.8 Hz, 2H), 3.54 (d, J = 2.4 Hz, 2H), 2.85 (t, J = 2.4 Hz, 1H), 2.45 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}FNO^+$ $[M+H]^+$ 244.1138, found 244.1129.

2-(7-Bromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2347) Following **method H1**, title compound was isolated. Mp 98 – 100 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.64 (dd, J = 8.0, 1.2 Hz, 1H), 7.53 (dd, J = 8.0, 1.2 Hz, 1H), 7.20 – 7.16 (m, 2H), 5.92 (s, 1H), 5.48 (s, 1H), 3.42 – 3.41 (m, 4H), 3.23 (t, J = 2.4 Hz, 1H), 2.29 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}BrNO^+$ $[M+H]^+$ 304.0332, found 304.0346.

2-(7-Chlorobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2348) Following **method H1**, title compound was isolated. Mp 106 – 107 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.61 (dd, J = 7.6, 1.2 Hz, 1H), 7.40 (dd, J = 7.6, 1.2 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.15 (s, 1H), 5.93 (s, 1H), 5.48 (s, 1H), 3.42 (s, 2H), 3.41 (d, J = 2.4 Hz, 2H), 3.23 (t, J = 2.4 Hz, 1H), 2.28 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}ClNO^+$ $[M+H]^+$ 260.0837, found 260.0847.

2-(6-Bromobenzofuran-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2349) Following **method H1**, 254 mg of the title compound was isolated (79%). Mp 130.2 – 131.2 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.72 (s, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.38 (dd, J = 8.4, 2.4 Hz, 1H), 7.06 (s, 1H), 5.94 (d, J = 0.8 Hz, 1H), 5.48 (d, J = 0.8 Hz, 1H), 3.47 (s, 2H), 3.43 (d, J = 2.4 Hz, 2H), 2.76 (t, J = 2.4 Hz, 1H), 2.35 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}BrNO^+$ $[M+H]^+$ 306.0337, found

***N*-(2-(7-Methoxybenzofuran-2-yl)-2-oxoethyl)-*N*-methylprop-2-yn-1-aminium carboxyformate (SZV-2366)** Following **method H1**, 99.5 mg of the title compound was isolated (82%). Mp 134.9 – 135.6 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.17 – 7.11 (m, 2H), 7.04 (s, 1H), 6.90 (dd, J = 7.6, 1.2 Hz, 1H), 5.99 (d, J = 1.2 Hz, 1H), 5.50 (d, J = 1.2 Hz, 1H), 3.99 (s, 3H), 3.59 (d, J = 0.8 Hz, 2H), 3.54 (d, J = 2.4 Hz, 2H), 2.84 (t, J = 2.4 Hz, 1H), 2.45 (s, 3H). Anal. calcd. for $C_{16}H_{17}NO_2x(COOH)_2$ (345.35): C, 62.60%; H, 5.55%; N, 4.06%; O, 27.80%. Found: C, 62.23%; H, 5.32%; N, 3.99%; O, 27.72%.

N-Methyl-2-(5-methylbenzofuran-2-yl)-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2263) Following **method H1**, the title compound was isolated. Mp 118.3 – 121.7 °C. ^{1}H NMR (Methanol-d_4, 600 MHz) δ 7.39 (d, J = 1.2 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.15 (dd, J = 8.4, 1.2 Hz), 7.01 (s, 1H), 6.19 (s, 1H), 5.65 (s, 1H), 4.05 (s, 2H), 3.94 (d, J = 2.0 Hz, 2H), 3.24 (t, J = 2.0 Hz, 1H), 2.80 (s, 3H), 2.42 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{18}NO^+$ $[M+H]^+$ 240.1383, found 240.1392.

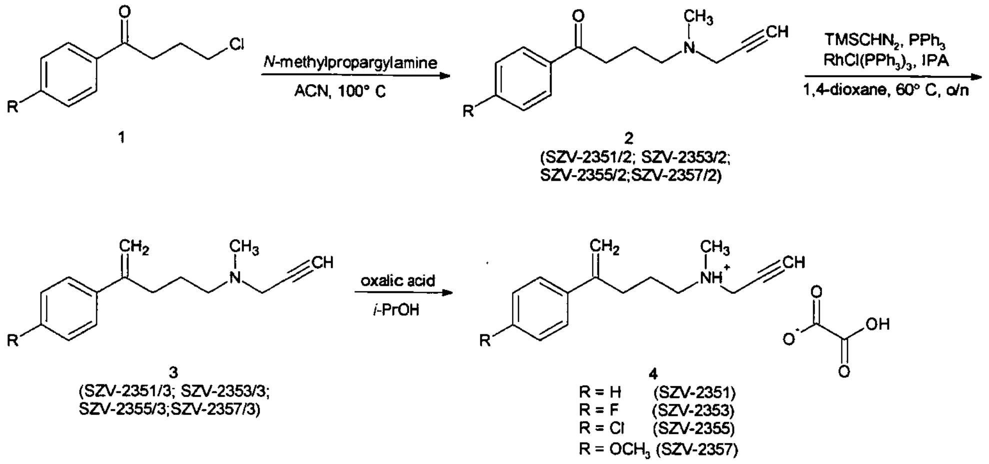
2-(5-Methoxybenzofuran-2-yl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2264) Following **method H1**, title compound was isolated. Mp 128.0 – 131.0 °C (dec). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.38 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 2.8 Hz, 1H), 7.01 (s, 1H), 6.90 (dd, J = 8.8, 2.8 Hz, 1H), 5.96 (d, J = 1.2 Hz, 1H), 5.50 (d, J = 1.2 Hz, 1H), 3.81 (s, 3H), 3.64 (s, 2H), 3.58 (d, J = 2.4 Hz, 2H), 2.91 (t, J = 2.4 Hz, 1H), 2.48 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{18}NO_2^+$ $[M+H]^+$ 256.1332, found 256.1335.

2-(6-Methoxybenzofuran-2-yl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2265) Following **method H1**, title compound was isolated. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.45 (d, J = 8.8 Hz, 1H), 7.08 (d, J = 2.0 Hz, 1H), 6.94 (s, 1H), 6.85 (dd, J = 8.8, 2.0 Hz, 1H), 5.82 (s, 1H), 5.35 (s, 1H), 3.85 (s, 3H), 3.43 (s, 2H), 3.41 (d, J = 2.4 Hz, 2H), 2.77 (t, J = 2.4 Hz, 1H), 2.33 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{18}NO_2^+$ $[M+H]^+$ 256.1332, found 256.1339.

2-(4-Bromo-7-methoxybenzofuran-2-yl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2266) Following **method H1**, title compound was isolated. Mp 119 – 128 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.32 (d, J = 8.8 Hz, 1H), 7.00 (s, 1H), 6.89 (d, J = 8.8 Hz, 1H), 5.98 (d, J = 1.2 Hz, 1H), 5.50 (d, J = 1.2 Hz, 1H), 4.00 (s, 3H), 3.49 (d, J = 0.8 Hz, 2H), 3.42 (d, J = 2.4 Hz, 2H), 2.78 (t, J = 2.4 Hz, 1H), 2.35 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{17}BrNO_2^+$ $[M+H]^+$ 334.0437, found 334.0451.

2-(5-Chlorobenzofuran-2-yl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2269) Following **method H1**, title compound was isolated. Mp 146.5 – 148.8 °C (dec). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.64 (d, J = 2.0 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.30 (dd, J = 8.4, 2.0 Hz, 1H), 7.06 (s, 1H), 5.99 (d, J = 1.2 Hz, 1H), 5.53 (d, J = 1.2 Hz, 1H), 3.56 (d, J = 0.8 Hz, 2H), 3.50 (d, J = 2.4 Hz, 2H), 2.84 (t, J = 2.4 Hz, 1H), 2.41 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{15}ClNO^+$ $[M+H]^+$ 260.0837, found 260.0842.

Scheme 6



4-(Methyl(prop-2-yn-1-yl)amino)-1-phenylbutan-1-one (SZV-2351/2) Following **method D3**, 0.516 g of the title compound was isolated (44%), 40% of starting material was recovered. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.01-7.98 (m, 2H), 7.62-7.58 (m, 1H), 7.53-7.49 (m, 2H), 3.31 (d, J = 2.4 Hz, 2H), 3.07 (t, J = 7.0 Hz, 2H), 2.62 (t, J = 2.4 Hz, 1H), 2.48 (t, J = 7.0 Hz, 2H), 2.25 (s, 3H), 1.85 (p, J = 7.0 Hz, 2H).

1-(4-Fluorophenyl)-4-(methyl(prop-2-yn-1-yl)amino)butan-1-one (SZV-2353/2) Following **method D3**, 0.918 g of the title compound was isolated (39%), 57% of starting material was recovered. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.10-8.06 (m, 2H), 7.26 (app. t, 2H), 3.30 (d, J = 2.4 Hz, 2H), 3.06 (t, J = 7.0 Hz, 2H), 2.62 (t, J = 2.4 Hz, 1H), 2.48 (t, J = 7.0 Hz , 2H), 2.24 (s, 3H), 1.85 (p, J = 7.0 Hz, 2H).

(4-Chlorophenyl)-4-(methyl(prop-2-yn-1-yl)amino)butan-1-one (SZV-2355/2) Following **method D3**, 1.00 g of the title compound was isolated (36%), 58% of starting material was recovered. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.02-7.99 (m, 2H), 7.56-7.52 (m, 2H), 3.29 (d, J = 2.4 Hz, 2H), 3.06 (t, J = 7.0 Hz, 2H), 2.62 (t, J = 2.4 Hz, 1H), 2.47 (t, J = 7.0 Hz, 2H), 2.23 (s, 3H), 1.85 (p, J = 7.0 Hz, 2H).

1-(4-Methoxyphenyl)-4-(methyl(prop-2-yn-1-yl)amino)butan-1-one (SZV-2357/2) Following **method D3**, 1.79 g of the title compound was isolated (41%), 53% of starting material was recovered. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.00-7.96 (m, 2H), 7.03-7.00 (m, 2H), 3.88 (s, 3H), 3.31 (d, J = 2.4 Hz, 2H), 2.99 (t, J = 7.0 Hz, 2H), 2.61 (t, J = 2.4 Hz, 1H), 2.47 (t, J = 7.0 Hz, 2H), 2.25 (s, 3H), 1.83 (p, J = 7.0 Hz, 2H).

***N*-Methyl-4-phenyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-amine (SZV-2351/3)** Following **method E2**, 0.160 g of the title compound was isolated (51%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.49 – 7.38 (m, 2H), 7.38 – 7.20 (m, 3H), 5.28 (d, J = 1.2 Hz, 1H), 5.09 (q, J = 1.2 Hz, 1H), 3.28 (d, J = 2.4

Hz, 2H), 2.61 (t, $J = 2.4$ Hz, 1H), 2.57 (td, $J = 7.2$, 1.2 Hz, 2H), 2.42 (t, $J = 7.2$ Hz, 2H), 2.22 (s, 3H), 1.57 (p, $J = 7.2$ Hz, 2H).

4-(4-Fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-amine (SZV-2353/3) Following **method E2**, 0.303 g of the title compound was isolated (44%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.51-7.48 (m, 2H), 7.12-7.08 (m, 2H), 5.26 (d, $J = 1.2$ Hz, 1H), 5.09 (d, $J = 1.2$ Hz, 1H), 3.28 (d, $J = 2.4$ Hz, 2H), 2.61 (t, $J = 2.4$ Hz, 1H), 2.56 (t, $J = 7.2$ Hz, 2H), 2.42 (t, $J = 7.2$ Hz, 2H), 2.22 (s, 3H), 1.57 (p, $J = 7.2$ Hz, 2H).

4-(4-Chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-amine (SZV-2355/3) Following **method E2**, 0.269 g of the title compound was isolated (38%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.50-7.46 (m, 2H), 7.38-7.35 (m, 2H), 5.32 (d, $J = 1.2$ Hz, 1H), 5.13 (dd, $J = 2.5$, 1.2 Hz, 1H), 3.28 (d, $J = 2.4$ Hz, 2H), 2.61 (t, $J = 2.4$ Hz, 1H), 2.59 – 2.53 (m, 2H), 2.42 (t, $J = 7.0$ Hz, 2H), 2.22 (s, 3H), 1.57 (p, $J = 7.2$ Hz, 2H).

4-(4-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-amine (SZV-2357/3) Following **method E2**, 0.354 g of the title compound was isolated (32%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.42-7.38 (m, 2H), 6.92-6.88 (m, 2H), 5.21 (d, $J = 2.0$ Hz, 1H), 4.99 (dd, $J = 2.0$, 1.2 Hz, 1H), 3.80 (s, 3H), 3.29 (d, $J = 2.4$ Hz, 2H), 2.61 (t, $J = 2.4$ Hz, 1H), 2.53 (td, $J = 7.2$, 1.2 Hz, 2H), 2.42 (t, $J = 7.2$ Hz, 2H), 2.22 (s, 3H), 1.57 (p, $J = 7.2$ Hz, 2H).

***N*-Methyl-4-phenyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-aminium carboxyformate (SZV-2351)** Following **method H1**, 0.166 g of the title compound was isolated (77%). Mp 96.6 – 97.3 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.48-7.45 (m, 2H), 7.36-7.26 (m, 3H), 5.33 (d, $J = 1.2$ Hz, 1H), 5.14 (d, $J = 1.2$ Hz, 1H), 3.83 (d, $J = 2.4$ Hz, 2H), 3.04 (t, $J = 2.4$ Hz, 1H), 3.00 (t, $J = 7.6$ Hz, 2H), 2.67 (s, 3H), 2.63 (t, $J = 7.6$ Hz, 2H), 1.83 (p, $J = 7.6$ Hz, 2H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{20}N^+$ $[M+H]^+$ 214.1590, found 214.1596.

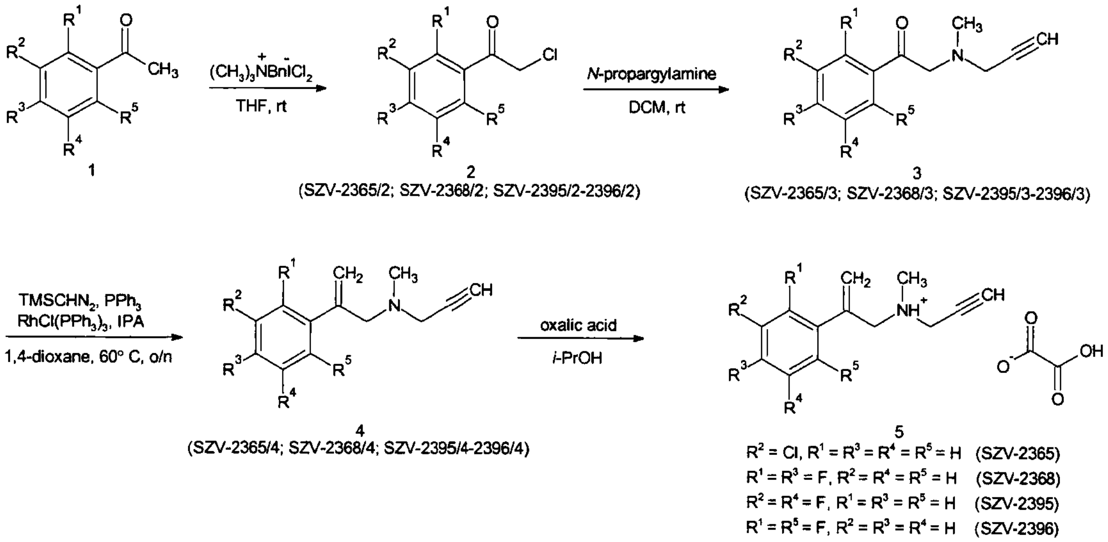
4-(4-Fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-aminium carboxyformate (SZV-2353) Following **method H1**, 0.321 g of the title compound was isolated (80%). Mp 102.2 – 103.1 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.53-7.49 (m, 2H), 7.12-7.07 (m, 2H), 5.32 (s, 1H), 5.16 (s, 1H), 3.99 (d, $J = 2.4$ Hz, 2H), 3.18-3.14 (m, 3H), 2.80 (s, 3H), 2.64 (t, $J = 7.4$ Hz, 2H), 1.90 (p, $J = 7.4$ Hz, 2H). Anal. calcd. for $C_{15}H_{18}FNx(COOH)_2$ (321.34): C, 63.54%; H, 6.27%; N, 4.36%; O 19.92%. Found: C, 63.74%; H, 6.29%; N, 4.32%; O, 22.44%.

4-(4-Chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-aminium carboxyformate (SZV-2355) Following **method H1**, 0.304 g of the title compound was isolated (83%). Mp 118.4 – 119.5 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.49 (d, $J = 8.8$ Hz, 2H), 7.36 (d, $J = 8.8$ Hz, 2H), 5.38 (s, 1H), 5.20 (s, 1H), 3.99 (d, $J = 2.4$ Hz, 2H), 3.18-3.14 (m, 3H), 2.80 (s, 3H), 2.64 (t, $J = 7.6$ Hz, 2H), 1.90 (p, $J = 7.6$ Hz, 2H). Anal. calcd. for $C_{15}H_{18}ClNx(COOH)_2$ (337.80): C 60.44, H 5.97, N 4.15, O 18.95. Found: C, 60.39%; H, 5.92%; N, 4.08%; O, 18.98%.

4-(4-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)pent-4-en-1-aminium carboxyformate (SZV-2357) Following **method H1**, 0.404 g of the title compound was isolated (86%). Mp 95.2

– 97.1 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.41 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 5.26 (d, J = 1.2 Hz, 1H), 5.05 (d, J = 1.2 Hz, 1H), 3.97 (d, J = 2.4 Hz, 2H), 3.80 (s, 3H), 3.16-3.11 (m, 3H), 2.78 (s, 3H), 2.61 (t, J = 7.6 Hz, 2H), 1.89 (p, J = 7.6 Hz, 2H). Anal. calcd. for $C_{16}H_{21}NOx(COOH)_2$ (333.78): C, 64.85%; H, 6.95%; N, 4.20%; O, 24.00%. Found: C, 64.95%; H, 6.91%; N, 4.18%; O, 24.03%.

Scheme 7



2-chloro-1-(3-chlorophenyl)ethanone (SZV-2365/2) Following **method C3** without column purification, 0.360 g of crude product was isolated (quantitative). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.94 (app. t, 1H), 7.85-7.82 (m, 1H), 7.61-7.58 (m, 1H), 7.45 (app. t, 1H), 4.66 (s, 2H).

2-Chloro-1-(2,4-difluorophenyl)-ethanone (SZV-2368/2) Following **method C3** without column purification, 1.35 g of crude product was isolated (quantitative). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.08-8.02 (m, 1H), 7.28 – 7.15 (m, 2H), 4.91 (d, J = 2.4 Hz, 2H).

2-Chloro-1-(2,5-difluorophenyl)ethanone (SZV-2395/2) Following **method C3** with column purification, 1.33 g of the title compound was isolated (97%) as white crystal. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.66-7.62 (m, 1H), 7.54-7.48 (m, 1H), 7.43-7.38 (m, 1H), 4.95 (d, J = 2.4 Hz, 2H).

2-Chloro-1-(2,6-difluorophenyl)ethanone (SZV-2396/2) Following **method C3** with column purification, 1.08 g of the title compound was isolated (91%) as pale yellow liquid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.51-7.44 (m, 1H), 7.03-6.97 (m, 2H), 4.54 (t, J = 0.8 Hz, 2H).

1-(3-Chlorophenyl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2365/3)

Following **method D4** without using K_2CO_3 as base, yellow crystal formed in the reaction mixture after 30 min. The reaction was stirred for 15 h (overnight) and 0.447 g of the title compound was isolated (75%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.06 – 7.96 (m, 2H), 7.66-7.63 (m, 1H), 7.54 (app. t, 1H), 3.91 (s, 2H), 3.50 (d, J = 2.4 Hz, 2H), 2.75 (t, J = 2.4 Hz, 1H), 2.36 (s, 3H).

1-(2,4-Difluorophenyl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2368/3) Following **method D4** without using K_2CO_3 as base, yellow crystal formed in the reaction mixture after 1 h. The reaction was stirred for 16 h (overnight) and 0.866 g of the title compound was isolated (53%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.99-7.93 (m, 1H), 7.17-7.12 (m, 2H), 3.82 (d, J = 2.8 Hz, 2H), 3.48 (d, J = 2.4 Hz, 2H), 2.71 (t, J = 2.4 Hz, 1H), 2.37 (s, 3H).

1-(2,5-Difluorophenyl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2395/3) Following **method D4** without using K_2CO_3 as base, yellow crystal formed in the reaction mixture after 0.5 h. The reaction was stirred for 15 h (overnight) and 1.06 g of the title compound was isolated (84%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.57-7.53 (m, 1H), 7.45-7.39 (m, 1H), 7.36-7.30 (m, 1H), 3.85 (d, J = 2.4 Hz, 2H), 3.48 (d, J = 2.4 Hz, 2H), 2.72 (t, J = 2.4 Hz, 1H), 2.37 (s, 3H).

1-(2,6-Difluorophenyl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2396/3) Following **method D4** using K_2CO_3 as base, no yellow crystal formed during the reaction. The reaction was worked-up after 2 h without full consumption of starting material (recovered 26%). 0.661 g of impure product was isolated (49%) and was used for the next step without further purification.

2-(3-Chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2365/4) Following **method E2**, 0.311 g of the title compound was isolated (47%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.61 (t, J = 1.6 Hz, 1H), 7.53 (dt, J = 7.2, 1.6 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.31-7.28 (m, 1H), 5.57 (d, J= 1.2 Hz, 1H), 5.34 (q, J = 1.2 Hz, 1H), 3.46 (d, J = 1.2 Hz, 2H), 3.33 (d, J = 2.4 Hz, 2H), 2.71 (t, J = 2.4 Hz, 1H), 2.27 (s, 3H).

2-(2,4-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2368/4) Following **method E2**, 0.327 g of the title compound was isolated (39%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.53-7.46 (m, 1H), 7.00-6.94 (m, 2H), 5.47 (s, 1H), 5.35 (s, 1H), 3.42 (s, 2H), 3.29 (d, J = 2.4 Hz, 2H), 2.67 (t, J = 2.4 Hz, 1H), 2.24 (s, 3H).

2-(2,5-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2395/4) Following **method E2**, 0.433 g of the title compound was isolated (41%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.27-7.23 (m, 1H), 7.17-7.11 (m, 2H), 5.53 (s, 1H), 5.44 (s, 1H), 3.43 (s, 2H), 3.31 (d, J = 2.4 Hz, 2H), 2.68 (t, J = 2.4 Hz, 1H), 2.25 (s, 3H).

2-(2,6-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2396/4) Following **method E2**, 0.174 g of the title compound was isolated (27%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.38-7.31 (m, 1H), 7.03-6.96 (m, 2H), 5.67 (d, J = 2.0 Hz, 1H), 5.28 (d, J = 2.0 Hz, 1H), 3.37 (s, 2H), 3.32 (d, J = 2.4 Hz, 2H), 2.65 (t, J = 2.4 Hz, 1H), 2.25 (s, 3H).

2-(3-Chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2365) Following **method H1**, 0.341 g of the title compound was isolated (78%). Mp 142.4 – 144.4 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.58 (t, J = 2.0 Hz, 1H), 7.50 (dt, J = 6.8, 2.0 Hz, 1H), 7.39-7.33 (m, 2H), 5.60 (d, J = 1.2 Hz, 1H), 5.31 (d, J = 1.2 Hz, 1H), 3.45 (s, 2H), 3.33 (d,

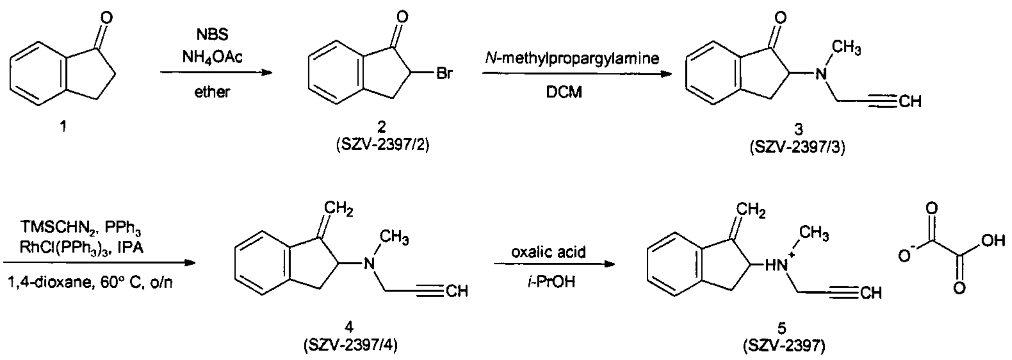
$J = 2.0$ Hz, 2H), 3.21 (t, $J = 2.0$ Hz, 1H), 2.21 (s, 3H). Anal. calcd. for $C_{13}H_{14}ClNx(COOH)_2$ (309.74): C, 58.16%; H, 5.21%; N, 4.52%; O, 20.66%; Found: C, 57.88%; H, 5.15%; N, 4.43%; O, 21.10%.

2-(2,4-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2368) Following **method H1**, 0.295 g of the title compound was isolated (69%). Mp 129.1 - 130.3 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.53-7.49 (m, 1H), 7.01-6.96 (m, 2H), 5.64 (s, 1H), 5.48 (s, 1H), 3.72 (s, 2H), 3.57 (d, $J = 2.4$ Hz, 2H), 2.89 (t, $J = 2.4$ Hz, 1H), 2.47 (s, 3H). Anal. calcd. for $C_{13}H_{13}F_2Nx(COOH)_2$ (311.28): C, 57.88%; H, 4.86%; N, 4.50%; O, 20.56%. Found: C, 57.64%; H, 5.01%; N, 4.45%; O, 22.20%.

2-(2,5-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2395) Following **method H1**, 0.428 g of the title compound was isolated (72%). Mp 131.9 – 132.6 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.28-7.24 (m, 1H), 7.18-7.05 (m, 2H), 5.65 (s, 1H), 5.53 (s, 1H), 3.65 (s, 2H), 3.51 (d, $J = 2.4$ Hz, 2H), 2.84 (t, $J = 2.4$ Hz, 1H), 2.42 (s, 3H). Anal. calcd. for $C_{13}H_{13}F_2Nx(COOH)_2$ (311.28): C, 57.88%; H, 4.86%; N, 4.50%. Found: C, 57.90%; H, 4.90%; N, 4.34%.

2-(2,6-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2396) Following **method H1**, 0.187 g of the title compound was isolated (78%). Mp 138.5 – 139.0 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.40-7.32 (m, 1H), 7.03-6.96 (m, 2H), 5.81 (d, $J = 1.2$ Hz, 1H), 5.42 (d, $J = 1.2$ Hz, 1H), 3.63 (s, 2H), 3.55 (d, $J = 2.4$ Hz, 2H), 2.85 (t, $J = 2.4$ Hz, 1H), 2.46 (s, 3H). Anal. calcd. for $C_{13}H_{13}F_2Nx(COOH)_2$ (311.28): C, 57.88%; H, 4.86%; N, 4.50%. Found: C, 57.82%; H, 4.92%; N, 4.32%.

Scheme 8



2-Bromo-2,3-dihydro-1*H*-inden-1-one (SZV-2397/2) To a mixture of compound **1** (1.0 g, 7.8 mmol) and *N*-bromosuccinimide (1.5 g, 8.2 mmol) in anhydrous diethyl ether (8.0 ml) was added ammonium acetate (60.2 mg, 0.8 mmol) at 0 °C. The reaction was warmed up to room temperature and stirred for 6 h. The mixture was then filtered, and the filtrate was washed with water (3x12.0 ml), dried over anhydrous $MgSO_4$, and concentrated in vacuo. The residue was purified via the Biotage SP1 silica-packed 25+S column with eluent of Dichloromethane:Hexane (20-80%) to afford 1.33 g of the title compound (81%) as a yellow liquid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.76 (t,

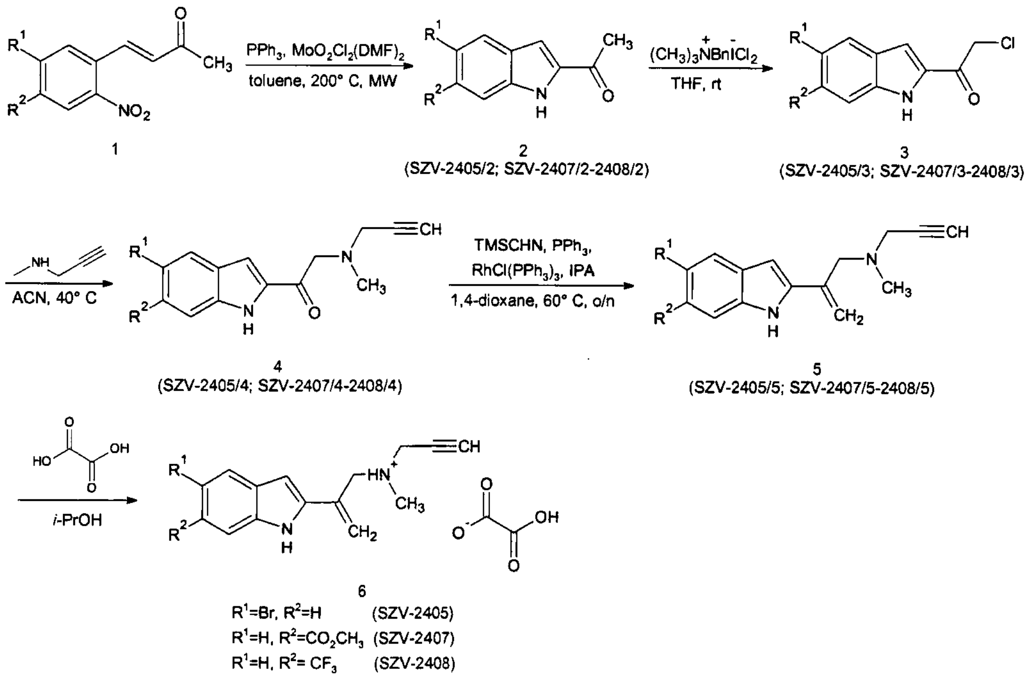
$J = 7.6$ Hz, 2H), 7.59 (d, $J = 7.6$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 1H), 4.88 (dd, $J = 7.4$, 3.0 Hz, 1H), 3.97 (dd, $J = 18.0$, 7.4 Hz, 1H), 3.39 (dd, $J = 18.0$, 3.0 Hz, 1H).

2-(Methyl(prop-2-yn-1-yl)amino)-2,3-dihydro-1*H*-inden-1-one (SZV-2397/3) Following **method D4** using K_2CO_3 (1 eq), the crude was purified by flash chromatography with eluent of EtOAc:Hexane (5-20%) to isolate 0.203 g of starting material (24%) and 0.534 g of the title compound (68%) as a dark brown oil. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.69-7.63 (m, 2H), 7.56-7.54 (m, 1H), 7.44-7.40 (m, 1H), 3.84 (dd, $J = 7.6$, 5.2 Hz, 1H), 3.70 (dd, $J = 16.8$, 2.4 Hz, 1H), 3.57 (dd, $J = 16.8$, 2.4 Hz, 1H), 3.35 (dd, $J = 17.2$, 7.6 Hz, 1H), 3.17 (dd, $J = 17.2$, 5.2 Hz, 1H), 2.69 (t, $J = 2.4$ Hz, 1H), 2.38 (s, 3H).

***N*-Methyl-1-methylene-*N*-(prop-2-yn-1-yl)-2,3-dihydro-1*H*-inden-2-amine (SZV-2397/4)** Following **method E2**, the title compound was isolated as light brown liquid (0.191 g, 33%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.58 – 7.51 (m, 1H), 7.31 – 7.14 (m, 3H), 5.71 (d, $J = 2.0$ Hz, 1H), 5.23 (d, $J = 2.0$ Hz, 1H), 4.28-4.24 (m, 1H), 3.44 (dd, $J = 16.6$, 2.4 Hz, 1H), 3.35 (dd, $J = 16.6$, 2.4 Hz, 1H), 3.09 (dd, $J = 16.8$, 5.2 Hz, 1H), 2.93 (dd, $J = 16.8$, 8.2 Hz, 1H), 2.66 (t, $J = 2.4$ Hz, 1H), 2.27 (s, 3H).

***N*-Methyl-1-methylene-*N*-(prop-2-yn-1-yl)-2,3-dihydro-*1H*-inden-2-aminium carboxyformate (SZV-2397)** Following **method H1**, the title compound was isolated as white powder (92%). Mp 120.9 – 122.7 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.59 (d, $J = 6.8$ Hz, 1H), 7.32-7.24 (m, 3H), 5.85 (d, $J = 2.0$ Hz, 1H), 5.46 (d, $J = 2.0$ Hz, 1H), 4.58-4.55 (m, 1H), 3.69 (qd, $J = 16.6$, 2.5 Hz, 2H), 3.26 (dd, $J = 17.3$, 4.1 Hz, 1H), 3.14 (dd, $J = 17.3$, 8.2 Hz, 1H), 2.88 (t, $J = 2.5$ Hz, 1H), 2.45 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{16}N\,[M+H]^+$ 198.1277, found, 198.1274.

Scheme 9



R^1=Br, R^2=H (SZV-2405)
R^1=H, R^2=CO_2CH_3 (SZV-2407)
R^1=H, R^2= CF_3 (SZV-2408)

1-(5-Bromo-1*H*-indol-2-yl)ethanone (SZV-2405/2) Following **method J**, 1.21 g of the title compound was isolated (65%). Mp 225-228 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.94 (brs, 1H), 7.92 (br. d, 1H), 7.54-7.51 (m, 1H), 7.45-7.40 (m, 1H), 7.32-7.30 (m, 1H), 2.57 (s, 3H).

Methyl 2-acetyl-1*H*-indole-6-carboxylate (SZV-2407/2) Following **method J**, the title compound was isolated as yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.16 (br, 1H), 8.17 (brs. d, 1H), 7.83 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.76-7.74 (m, 1H), 7.21 (dd, *J* = 1.6, 1.6 Hz, 1H), 3.96 (s, 3H), 2.62 (s, 3H).

1-(6-(Trifluoromethyl)-1*H*-indol-2-yl)ethan-1-one LRS-2-127-1SM (SZV-2408/2) Following **method J**, the title compound was isolated as yellow solid. Mp 173-175 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.25 (brs, 1H), 7.83-7.81 (m, 1H), 7.73-7.72 (m, 1H), 7.40-7.37 (m, 1H), 7.24-7.23 (m, 1H), 2.63 (s, 3H).

1-(5-Bromo-1*H*-indol-2-yl)-2-chloroethanone (SZV-2405/3) Following **method C3** after column purification, 1.08 g of the title compound was isolated (99%) as orange-brown solid. Mp 198-199 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.15 (brs, 1H), 7.94 (d, *J* = 2.0 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.47-7.46 (m, 1H), 7.45 (d, *J* = 2.0 Hz, 1H), 4.93 (s, 2H).

Methyl 2-(2-chloroacetyl)-1*H*-indole-6-carboxylate (SZV-2407/3) Following **method C3** without column purification, 0.705 g of the title compound was isolated (98%) as light brown solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.30 (brs, 1H), 8.31 (br, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.79 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.57 (brs. d, 1H), 4.99 (s, 2H), 3.93 (s, 3H).

2-Chloro-1-(6-(trifluoromethyl)-1*H*-indol-2-yl)ethanone (SZV-2408/3) Following **method C3** after column purification, 0.650 g of the title compound was isolated (97%) as orange-yellow solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.39 (brs, 1H), 8.00 (brs. d, 1H), 7.96-7.95 (m, 1H), 7.61 (brs, 1H), 7.44 (dd, *J* = 8.5, 1.6 Hz, 1H), 5.00 (s, 2H).

1-(5-Bromo-1*H*-indol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2405/4) Following **method D5**, 0.843 g of the title compound was isolated (81%) as brown solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.02 (brs, 1H), 7.91 (brs. d, 1H), 7.52 (brs. d, 1H), 7.47 – 7.38 (m, 2H), 3.87 (s, 2H), 3.53 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.42 (s, 3H).

Methyl 2-(2-(methyl(prop-2-yn-1-yl)amino)acetyl)-1*H*-indole-6-carboxylate (SZV-2407/4) Following **method D5**, 0.670 g of the title compound was isolated (84%) as brown solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.17 (brs, 1H), 8.29-8.28 (m, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.75 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.53 (brs. d, 1H), 3.90 (s, 5H), 3.55 (d, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 1H), 2.43 (s, 3H).

2-(Methyl(prop-2-yn-1-yl)amino)-1-(6-(trifluoromethyl)-1*H*-indol-2-yl)ethanone (SZV-2408/4) Following **method D5**, 0.701 g of the title compound was isolated (98%) as red-orange oil. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.26 (brs, 1H), 7.95-7.92 (m, 2H), 7.60 – 7.55 (m, 1H), 7.39 (dd, *J* = 8.4, 1.2 Hz, 1H), 3.91 (s, 2H), 3.55 (d, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 1H), 2.43 (s, 3H).

2-(5-Bromo-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2405/5) Following **method E2**, 0.264 g of the title compound was isolated (32%) as orange-yellow oil. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.65 (brs, 1H), 7.67 (d, J = 1.9 Hz, 1H), 7.30 (d, J = 8.6 Hz, 1H), 7.17 (dd, J = 8.6, 1.9 Hz, 1H), 6.71 (s, 1H), 5.76 (d, J = 1.2 Hz, 1H), 5.33 (d, J = 1.2 Hz, 1H), 3.48 (s, 2H), 3.43 (d, J = 2.4 Hz, 2H), 2.75 (t, J = 2.4 Hz, 1H), 2.36 (s, 3H).

Methyl 2-(3-(methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)-1*H*-indole-6-carboxylate (SZV-2407/5) Following **method E2**, 0.252 g of the title compound was isolated (38%) as yellow solid. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.86 (brs, 1H), 8.09-8.08 (m, 1H), 7.68 (dd, J = 8.4, 1.5 Hz, 1H), 7.59-7.56 (m, 1H), 6.81-6.80 (m, 1H), 5.82 (d, J = 0.8 Hz, 1H), 5.38 (d, J = 0.8 Hz, 1H), 3.86 (s, 3H), 3.52 (s, 2H), 3.46 (d, J = 2.4 Hz, 2H), 2.76 (d, J = 2.4 Hz, 1H), 2.38 (s, 3H).

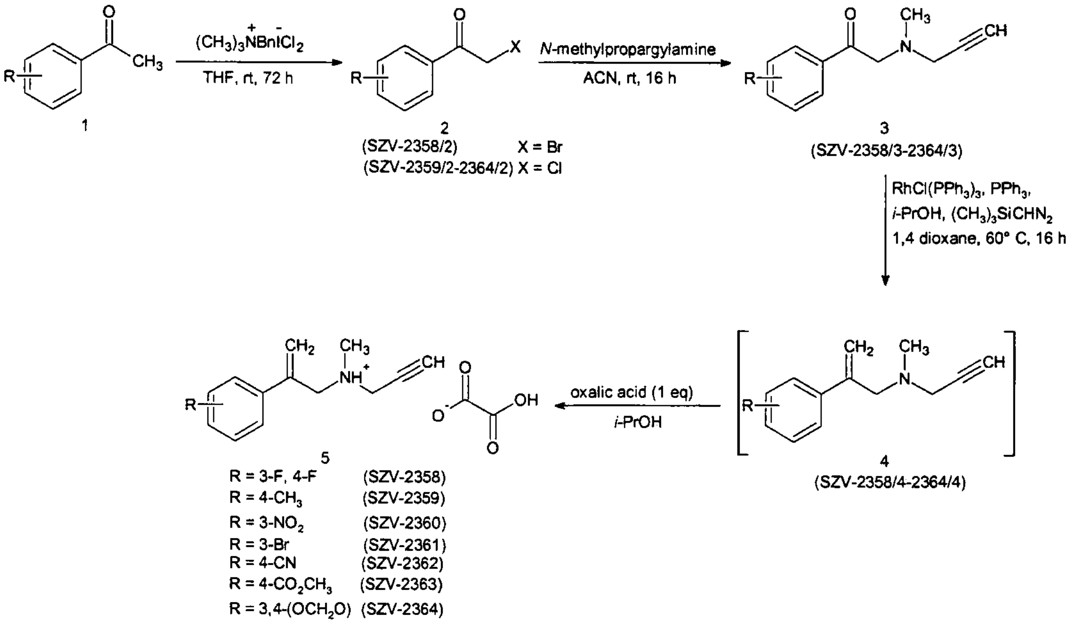
***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(6-(trifluoromethyl)-1*H*-indol-2-yl)prop-2-en-1-amine (SZV-2408/5)** Following **method E2**, 0.275 g of the title compound was isolated (40%) as yellow oil. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.94 (brs, 1H), 7.71-7.69 (m, 2H), 7.27 (dd, J = 8.3, 1.2 Hz, 1H), 6.84 (d, J = 1.2 Hz, 1H), 5.83 (s, 1H), 5.39 (d, J = 0.8 Hz, 1H), 3.52 (d, J = 0.8 Hz, 2H), 3.45 (d, J = 2.4 Hz, 2H), 2.77 (t, J = 2.4 Hz, 1H), 2.38 (s, 3H).

2-(5-Bromo-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2405) Following **method H1**, 0.267 g of the title compound was isolated (78%) as light yellow solid. Mp 138.0 – 141.5 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.70 (brs, 1H), 7.68 (d, J = 1.9 Hz, 1H), 7.31 (d, J = 8.6 Hz, 1H), 7.19 (dd, J = 8.6, 1.9 Hz, 1H), 6.73 (s, 1H), 5.83 (s, 1H), 5.42 (d, J = 0.8 Hz, 1H), 3.64 (d, J = 0.8 Hz, 2H), 3.57 (d, J = 2.4 Hz, 2H), 2.86 (t, J = 2.4 Hz, 1H), 2.47 (s, 3H). Anal. calcd. for $C_{15}H_{15}BrN_2x(COOH)_2$ (393.23): C, 51.92%; H, 4.36%; N, 7.12%; O, 16.27%. Found: C, 52.23%; H, 4.30%; N, 7.04%; O, 16.55%.

2-(6-(Methoxycarbonyl)-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2407) Following **method H1**, 0.286 g of the title compound was isolated (86%) as white solid. Mp 130.7 – 132.3 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.09-8.08 (m, 1H), 7.68 (dd, J = 8.4, 1.6 Hz, 1H), 7.58 (dd, J = 8.4, 0.4 Hz, 1H), 6.87 (d, J = 0.4 Hz, 1H), 5.88 (s, 1H), 5.46 (d, J = 0.4 Hz, 1H), 3.65 (d, J = 0.4 Hz, 2H), 3.57 (d, J = 2.4 Hz, 2H), 2.85 (t, J = 2.4 Hz, 1H), 2.47 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{17}H_{19}N_2O_2^+$ $[M+H]^+$ 283.1441, found 283.1440.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(6-(trifluoromethyl)-1*H*-indol-2-yl)prop-2-en-1-aminium carboxyformate (SZV-2408)** Following **method H1**, 0.321 g of the title compound was isolated (89%) as yellow solid. Mp 82.6 – 83.1 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.73 (brs, 1H), 7.71 (brs, 1H), 7.30 (dd, J = 8.3, 1.3 Hz, 1H), 6.87 (s, 1H), 5.89 (s, 1H), 5.47 (s, 1H), 3.64 (s, 1H), 3.56 (d, J = 2.4 Hz, 2H), 2.85 (t, J = 2.4 Hz, 1H), 2.47 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{16}H_{16}$ $F_3N_2^+$ $[M+H]^+$ 293.1260, found 293.1264.

Scheme 10



(SZV-2358/2) is commercially available.

2-Chloro-1-(p-tolyl)ethanone (SZV-2359/2) (Giboulot S et al, Chem. Commun., 2012, 48, 5889-5891) Following **method C4**, the crude product was used directly for the next step.

2-Chloro-1-(3-nitrophenyl)ethanone (SZV-2360/2) (El-Ahl AAS et al, Synth. Commun., 2011, 41, 1508-1513) Following **method C4**, the title compound was isolated as a pale solid (90%). Mp 98 – 100 °C (lit. Mp 96-98 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.79 (app. t, 1H), 8.54-8.51 (m, 1H), 8.47-8.45 (m, 1H), 7.90 (app. t, 1H), 5.18 (s, 2H).

1-(3-Bromophenyl)-2-chloroethanone (SZV-2361/2) (Kajigaeshi S et al, Synthesis, 1988, 7, 545-546) Following **method C4**, the title compound was isolated as a white solid (99%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.16 (app. t, 1H), 8.03 (m, 1H), 7.86 (m, 1H), 7.54 (app. t, 1H), 5.07 (s, 2H).

4-(2-Chloroacetyl)benzonitrile (SZV-2362/2) (Russell GA et al, J. Am. Chem. Soc., 1985, 107, 2506-2511) Following **method C4**, the title compound was isolated as a pale yellow solid (99%). Mp 142 – 143 °C (lit. Mp 91-95 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.21 (d, J = 8.2 Hz, 2H), 7.99 (d, J = 8.2 Hz, 2H), 5.12 (s, 2H).

Methyl 4-(2-chloroacetyl)benzoate (SZV-2363/2) (Anderson JC et al, Tetrahedron Lett., 1962, 1-4) Following **method C4**, the title compound was isolated as a pale yellow solid (99%). Mp 148 – 149 °C (lit. Mp 148-150 °C). ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.15 (s, 4H), 5.09 (s, 2H), 3.94 (s, 3H).

1-(Benzo[*d*][1,3]dioxol-5-yl)-2-chloroethanone (SZV-2364/2) Following **method C4**, the title compound was isolated as a brown solid (99%). Mp 88 – 90 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.68 (dd, J = 2.0, 8.2 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H), 6.99 (d, J = 8.2 Hz, 1H), 6.15 (s, 2H), 4.92 (s, 2H).

1-(3,4-Difluorophenyl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2358/3) Following **method D6**, the title compound was isolated as a yellow oil (82%). ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 8.05 – 7.94 (m, 2H), 7.51 – 7.42 (m, 1H), 3.89 (s, 2H), 3.49 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.36 (s, 3H).

2-(Methyl(prop-2-yn-1-yl)amino)-1-(p-tolyl)ethanone (SZV-2359/3) Following **method D6**, the title compound was isolated as a yellow oil (82%). ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 3.87 (s, 2H), 3.49 (d, *J* = 2.4 Hz, 2H), 2.72 (t, *J* = 2.4 Hz, 1H), 2.39 (s, 3H), 2.36 (s, 3H).

2-(Methyl(prop-2-yn-1-yl)amino)-1-(3-nitrophenyl)ethanone (SZV-2360/3) Following **method D6**, the title compound was isolated as a yellow oil (74%). ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 8.84 (app. t, 1H), 8.51 – 8.44 (m, 2H), 7.84 (app. t, 1H), 4.00 (s, 2H), 3.52 (d, *J* = 2.4 Hz, 2H), 2.77 (t, *J* = 2.4 Hz, 1H), 2.38 (s, 3H).

1-(3-Bromophenyl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2361/3) Following **method D6**, the title compound was isolated as a yellow oil (57%). ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 8.18 (app. t, 1H), 8.07 – 8.02 (m, 1H), 7.80 (m, 1H), 7.48 (app. t, 1H), 3.91 (s, 2H), 3.50 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.37 (s, 3H).

4-(2-(Methyl(prop-2-yn-1-yl)amino)acetyl)benzonitrile (SZV-2362/3) Following **method D6**, the title compound was isolated as a yellow oil (59%). ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 8.22 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 2H), 3.95 (s, 2H), 3.50 (d, *J* = 2.0 Hz, 2H), 2.76 (t, *J* = 2.0 Hz, 1H), 2.37 (s, 3H).

Methyl 4-(2-(methyl(prop-2-yn-1-yl)amino)acetyl)benzoate (SZV-2363/3) Following **method D6**, the title compound was isolated as a yellow oil (47%). ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 8.18 – 8.08 (m, 4H), 3.95 (s, 2H), 3.93 (s, 3H), 3.51 (d, *J* = 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 1H), 2.38 (s, 3H).

1-(Benzo[*d*][1,3]dioxol-5-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2364/3) Following **method D6**, the title compound was isolated as a yellow oil (68%). ^{1}H NMR (400 MHz, Acetone-*d*$_6$) δ 7.72 (dd, *J* = 1.6, 8.2 Hz, 1H), 7.49 (d, *J* = 1.6 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.11 (s, 2H), 3.81 (s, 2H), 3.48 (d, *J* = 2.4 Hz, 2H), 2.73 (t, *J* = 2.4 Hz, 1H), 2.35 (s, 3H).

2-(3,4-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2358) Following **method E3** and **H1**, the title compound was isolated as a white solid (60%). Mp 144.2 – 144.6 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.66 – 7.56 (m, 1H), 7.38 (m, 2H), 5.59 (s, 1H), 5.30 (s, 1H), 3.44 (s, 2H), 3.34 (d, *J* = 2.1 Hz, 2H), 3.21 (t, *J* = 2.1 Hz, 1H), 2.21 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{13}H_{13}F_2NNa^+$ $[M+Na]^+$ 244.0908, found 244.0913.

***N*-methyl-*N*-(prop-2-yn-1-yl)-2-(p-tolyl)prop-2-en-1-aminium carboxyformate (SZV-2359)** Following **method E3** and **H1**, the title compound was isolated as a white solid (60%). Mp 134.8 – 136.0 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.21 (s, 1H), 3.47 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 3.23 (t,

J = 2.4 Hz, 1H), 2.29 (s, 3H), 2.24 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{14}H_{18}N^+$ $[M+H]^+$ 200.1434, found 200.1431

N-Methyl-2-(3-nitrophenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2360) Following **method E3** and **H1**, the title compound was isolated as a white solid (58%). Mp 146.5 – 146.9 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 8.35 (app. t, 1H), 8.17 – 8.12 (m, 1H), 8.02 – 7.98 (m, 1H), 7.64 (app. t, 1H), 5.73 (s, 1H), 5.42 (s, 1H), 3.52 (s, 2H), 3.34 (d, J = 2.3 Hz, 2H), 3.21 (t, J = 2.3 Hz, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{13}H_{14}N_2O_2x(COOH)_2$ (320.30): C, 56.25%; H, 5.04%; N, 8.75%; O, 29.97%. Found: C, 55.99%; H, 5.00%; N, 8.59%; O, 29.71%.

2-(3-Bromophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2361) Following **method E3** and **H1**, the title compound was isolated as a white solid (56%). Mp 130 – 132 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.71 (s, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 5.59 (s, 1H), 5.31 (s, 1H), 3.45 (s, 2H), 3.34 (d, J = 2.0 Hz, 2H), 3.21 (t, J = 2.0 Hz, 1H), 2.22 (brs, 3H). Anal. calcd. for $C_{13}H_{14}BrNx(COOH)_2$ (354.20): C, 50.86%; H, 4.55%; N, 3.95%; O, 18.07%. Found: C, 50.48%; H, 4.51%; N, 3.90%; O, 18.33%.

2-(4-Cyanophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2362) Following **method E3** and **H1**, the title compound was isolated as a white solid (65%). Mp 144.6 – 145.4 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.79 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 5.70 (s, 1H), 5.42 (s, 1H), 3.48 (s, 2H), 3.32 (d, J = 2.1 Hz, 2H), 3.20 (t, J = 2.1 Hz, 1H), 2.20 (s, 3H). Anal. calcd. for $C_{14}H_{14}N_2x(COOH)_2$ (300.31): C, 63.99%; H, 5.37%; N, 9.33%; O, 21.31%. Found: C, 63.55%; H, 5.34%; N, 9.06%; O, 21.28%.

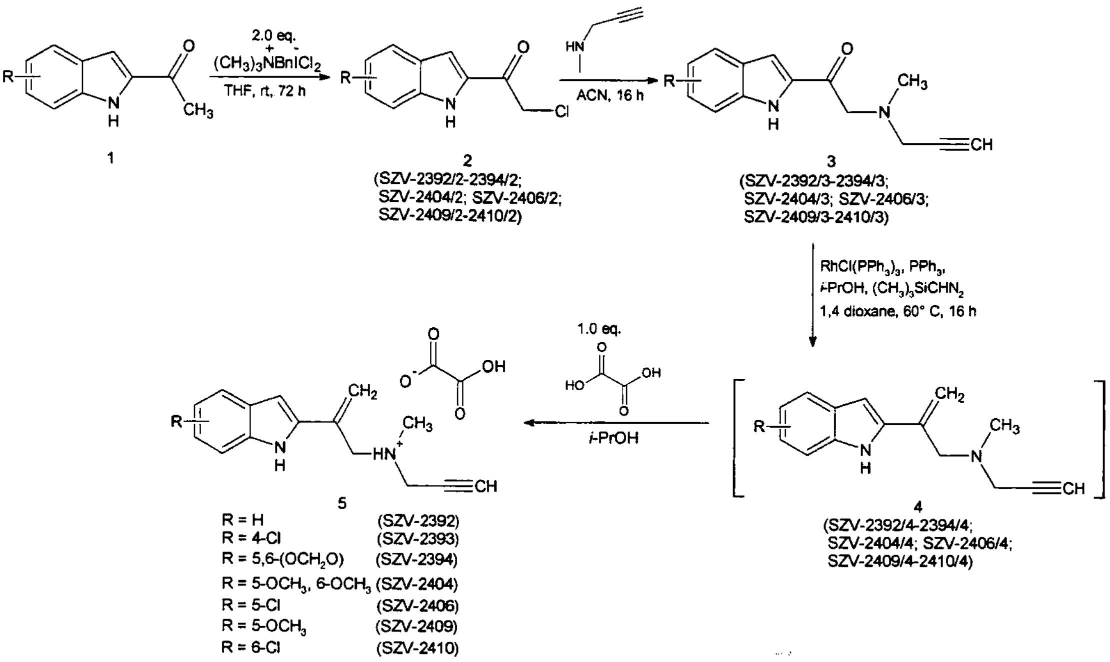
2-(4-(Methoxycarbonyl)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate

(SZV-2363) Following **method E3** and **H1**, the title compound was isolated as a white solid (56%). Mp 144.4 – 145.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.92 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 5.67 (s, 1H), 5.39 (s, 1H), 3.85 (s, 3H), 3.50 (s, 2H), 3.35 (d, J = 2.2 Hz, 2H), 3.22 (t, J = 2.2 Hz, 1H), 2.23 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{15}H_{18}NO_2^+$ $[M+H]^+$ 244.1332, found 244.1327.

2-(Benzo[d][1,3]dioxol-5-yl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate

(SZV-2364) Following **method E3** and **H1**, the title compound was isolated as a white solid (68%). Mp 124.2 – 125.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.12 (s, 1H), 7.03 (d, J = 8.1 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.00 (s, 2H), 5.46 (s, 1H), 5.19 (s, 1H), 3.48 (s, 2H), 3.39 (d, J = 2.4 Hz, 2H), 3.26 (t, J = 2.4 Hz, 1H), 2.26 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{14}H_{16}NO_2^+$ $[M+H]^+$ 230.1176, found 230.1182.

Scheme 11



2-Chloro-1-(1*H*-indol-2-yl)ethanone (SZV-2392/2) Following **method C4**, the title compound was isolated as pale yellow solid (97%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.97 (s, 1H), 7.75 (t, J = 7.85 Hz, 1H), 7.68 – 7.42 (m, 2H), 7.35 (dd, J = 7.44, 15.43 Hz, 1H), 7.14 (dd, J = 7.81, 14.91 Hz, 1H), 4.91 (dd, J = 3.50, 4.97 Hz, 2H).

2-Chloro-1-(4-chloro-1*H*-indol-2-yl)ethanone (SZV-2393/2) Following **method C4**, the title compound was isolated as pale yellow solid (98%). Mp 163 – 164 °C. ^{1}H NMR (400 MHz, Chloroform-d) δ 9.30 (s, 1H), 7.31-7.28 (m, 2H), 7.23 (t, J = 8.0 Hz, 1H), 7.12 (dd, J = 8.0, 1.2 Hz, 1H), 4.62 (s, 2H).

1-(5*H*-[1,3]Dioxolo[4,5-f]indol-6-yl)-2-chloroethanone (SZV-2394/2) Following **method C4**, the title compound was isolated as yellow solid (99%). Mp 187 – 190 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.83 (s, 1H), 7.34 (brs, 1H), 7.06 (s, 1H), 6.97 (s, 1H), 6.01 (s, 2H), 4.78 (s, 2H).

2-Chloro-1-(5,6-dimethoxy-1*H*-indol-2-yl)ethanone (SZV-2404/2) Following **method C4**, the title compound was isolated as yellow solid (98%). Mp 191 – 194 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.66 (s, 1H), 7.35 – 7.32 (m, 1H), 7.14 (s, 1H), 7.03 (s, 1H), 4.78 (s, 2H), 3.87 (s, 3H), 3.83 (s, 3H).

2-Chloro-1-(5-chloro-1*H*-indol-2-yl)ethanone (SZV-2406/2) Following **method C4**, the title compound was isolated as brown solid (99%). Mp 187 – 189 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.14 (s, 1H), 7.77 (d, J = 2.0 Hz, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.33 (dd, J = 2.0, 8.8 Hz, 1H), 4.92 (s, 2H).

2-Chloro-1-(5-methoxy-1*H*-indol-2-yl)ethanone (SZV-2409/2) Following **method C4**, the title compound was isolated as dark green solid (98%). Mp 157 – 159 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.84 (s, 1H), 7.47 (d, *J* = 8.8 Hz, 1H), 7.37 (m, 1H), 7.17 (d, *J* = 2.4 Hz, 1H), 7.02 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.86 (s, 2H), 3.82 (s, 3H).

2-Chloro-1-(6-chloro-1*H*-indol-2-yl)ethanone (SZV-2410/2) Following **method C4**, the title compound was isolated as green solid (99%). Mp 139 – 140 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.10 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.50 (dd, *J* = 0.8, 1.6 Hz, 1H), 7.14 (dd, *J* = 1.6, 8.4 Hz, 1H), 4.91 (s, 2H). HRMS (ESI +) *m/z* calcd. for $C_{10}H_8Cl_2NO^+$ $[M+H]^+$ 227.9977, found 227.9981.

1-(1*H*-Indol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2392/3) Following **method D6,** the title compound was isolated as yellowish brown solid (52%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.81 (s, 1H), 7.71 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.49 – 7.43 (m, 1H), 7.31 (td, *J* = 7.6, 0.8 Hz, 1H), 7.10 (td, *J* = 7.6, 0.8 Hz, 1H), 3.87 (s, 2H), 3.54 (d, *J* = 2.39 Hz, 2H), 2.75 (t, *J* = 1.06 Hz, 1H), 2.42 (s, 3H).

1-(4-Chloro-1*H*-indol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2393/3) Following **method D6,** the title compound was isolated as light brown solid (67%). Mp 128 – 129 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.14 (s, 1H), 7.53 – 7.51 (m, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 3.92 (s, 2H), 3.55 (d, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.40 Hz, 1H), 2.44 (s, 3H).

1-(5*H*-[1,3]Dioxolo[4,5-f]indol-6-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2394/3) Following **method D6,** the title compound was isolated as brown solid (54%). Mp 116 – 117 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.69 (s, 1H), 7.33 (brs, 1H), 7.04 (s, 1H), 6.95 (s, 1H), 5.99 (s, 2H), 3.77 (s, 2H), 3.52 (d, *J* = 2.4 Hz, 2H), 2.73 (t, *J* = 2.4 Hz, 1H), 2.40 (s, 3H).

1-(5,6-Dimethoxy-1*H*-indol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2404/3) Following **method D6,** the title compound was isolated as brown solid (44%). Mp 140 – 142 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.54 (s, 1H), 7.32 (m, 1H), 7.12 (s, 1H), 7.02 (s, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.78 (s, 2H), 3.52 (d, *J* = 2.4 Hz, 2H), 2.74 (t, *J* = 2.4 Hz, 1H), 2.41 (s, 3H).

1-(5-Chloro-1*H*-indol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2406/3) Following **method D6,** stirring at 40 °C the title compound was isolated as brown solid (77%). Mp 108 – 110 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 11.01 (s, 1H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.44 (m, 1H), 7.29 (dd, *J* = 8.8, 2.0 Hz, 1H), 3.87 (s, 2H), 3.54 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.42 (s, 3H).

1-(5-Methoxy-1*H*-indol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2409/3) Following **method D6,** stirring at 40 °C the title compound was isolated as brown solid (78%). Mp 110 – 112 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.71 (s, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.36 (m, 1H), 7.15 (d, *J* = 2.4 Hz, 1H), 6.97 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.84 (s, 2H), 3.81 (s, 3H), 3.53 (d, *J* = 2.4 Hz, 2H), 2.75 (t, *J* = 2.4 Hz, 1H), 2.42 (s, 3H). HRMS (ESI +) *m/z* calcd. for $C_{15}H_{17}N_2O_2^+$ $[M+H]^+$ 257.1285, found 257.1293.

1-(6-Chloro-1*H*-indol-2-yl)-2-(methyl(prop-2-yn-1-yl)amino)ethanone (SZV-2410/3) Following **method D6,** stirring at 40 °C the title compound was isolated as brown solid (30%). Mp

113 – 114 °C. ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.98 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.60 – 7.56 (m, 1H), 7.50 – 7.46 (m, 1H), 7.11 (dd, J = 8.4, 1.6 Hz, 1H), 3.86 (s, 2H), 3.53 (d, J = 2.4 Hz, 2H), 2.75 (t, J = 2.4 Hz, 1H), 2.42 (s, 3H).

2-(1*H*-Indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2392) Following **method E3** and **method H1**, the title compound was isolated (64%). Mp 101.7 – 106.9 °C .^{1}H NMR (400 MHz, Methanol-d_4) δ 7.55 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.74 (s, 1H), 6.01 (s, 1H), 5.60 (s, 1H), 4.21 (s, 2H), 4.04 (d, J = 2.4 Hz, 2H), 3.37 (s, 1H), 2.88 (s, 3H). Anal. calcd. for $C_{15}H_{16}N_2x(COOH)_2$ (314.36): C, 64.96%; H, 5.77%; N, 8.91%; O, 20.36%. Found: C, 61.98%; H, 5.57%; N, 8.45%; O, 20.65%.

2-(4-Chloro-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2393) Following **method E3** and **method H1**, the title compound was isolated as brown solid (23%). Mp 109.3 – 110.0 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.31 (d, J = 7.6 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 7.6 Hz, 1H), 6.84 (s, 1H), 6.05 (s, 1H), 5.67 (s, 1H), 4.24 (s, 2H), 4.05 (s, 2H), 3.33 (s, 1H), 2.88 (s, 3H). Anal. calcd. for $C_{15}H_{15}ClN_2x(COOH)_2$ (348.78): C, 58.54%; H, 4.91%; N, 8.03%; O, 18.35%. Found: C, 55.75%; H, 4.73%; N, 7.36%; O, 19.86%.

2-(5*H*-[1,3]Dioxolo[4,5-f]indol-6-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2394) Following **method E3** and **method H1**, the title compound was isolated as brown solid (39%). Mp 128.4 – 130.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 6.90 (s, 1H), 6.81 (s, 1H), 6.59 (s, 1H), 5.88 (s, 2H), 5.86 (s, 1H), 5.49 (s, 1H), 4.20 (s, 2H), 4.07 (d, J = 2.0 Hz, 2H), 3.36 (s, 1H), 2.90 (s, 3H). Anal. calcd. for $C_{16}H_{16}N_2O_2x(COOH)_2$ (358.35): C, 60.33%; H, 5.06%; N, 7.82%; O, 26.79%. Found: C, 59.49%; H, 5.07%; N, 7.37%; O, 27.16%.

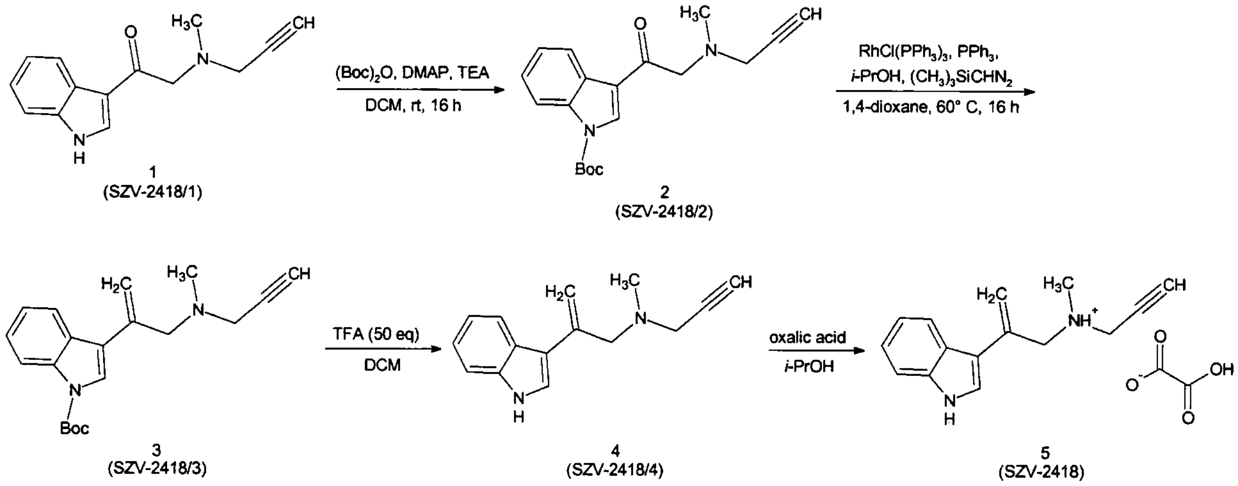
2-(5,6-Dimethoxy-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2404) Following **method E3** and **method H1**, the title compound was isolated as brown solid (43%). Mp 101.4 – 102.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 10.83 (s, 1H), 6.99 (s, 1H), 6.85 (s, 1H), 6.51 (s, 1H), 5.63 (s, 1H), 5.17 (s, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.44 (s, 4H), 3.26 (s, 1H), 2.32 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{17}H_{21}N_2O_2^+$ $[M+H]^+$ 285.1598, found 285.1603.

2-(5-Chloro-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2406) Following **method E3** and **method H1**, the title compound was isolated as brown solid (56%). Mp 136.7 – 137.6 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 11.32 (s, 1H), 7.53 (d, J = 2.0 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.07 (dd, J = 8.4, 2.0 Hz, 1H), 6.64 (d, J = 1.2 Hz, 1H), 5.80 (s, 1H), 5.33 (s, 1H), 3.46 (s, 2H), 3.44 (d, J = 2.0 Hz, 2H), 3.25 (t, J = 2.0 Hz , 1H), 2.31 (s, 3H). Anal. calcd. for $C_{15}H_{15}ClN_2x(COOH)_2$ (348.78): C, 58.54%; H, 4.91%; N, 8.03%; O, 18.35%. Found: C, 58.67%; H, 4.88%; N, 7.98%; O, 17.65%.

2-(5-Methoxy-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2409) Following **method E3** and **method H1**, the title compound was isolated as yellow solid (80%). Mp 83.8 – 84.0 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 10.99 (s, 1H), 7.24 (d, $J = 8.0$ Hz, 1H), 6.99 (s, 1H), 6.74 (d, $J = 8.0$ Hz, 1H), 6.58 (s, 1H), 5.77 (s, 1H), 5.29 (s, 1H), 3.73 (s, 3H), 3.53 (s, 2H), 3.52 (s, 2H), 3.31 (s, 1H), 2.37 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{16}H_{19}N_2O^+$ $[M+H]^+$ 255.1492, found 255.1484.

2-(6-Chloro-1*H*-indol-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2410) Following **method E3** and **method H1**, the title compound was isolated as yellow solid (99%). Mp 84.0 – 85.7 °C. 90 ^1H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 11.30 (s, 1H), 7.50 (d, $J = 8.4$ Hz, 1H), 7.35 (s, 1H), 6.97 (dd, $J = 1.6$, 8.4 Hz, 1H), 6.67 (s, 1H), 5.78 (s, 1H), 5.33 (s, 1H), 3.48 (s, 2H), 3.46 (d, $J = 2.0$ Hz, 2H), 3.26 (s, 1H), 2.32 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{15}H_{16}ClN_2^+$ $[M+H]^+$ 259.0997, found 259.1002.

Scheme 12



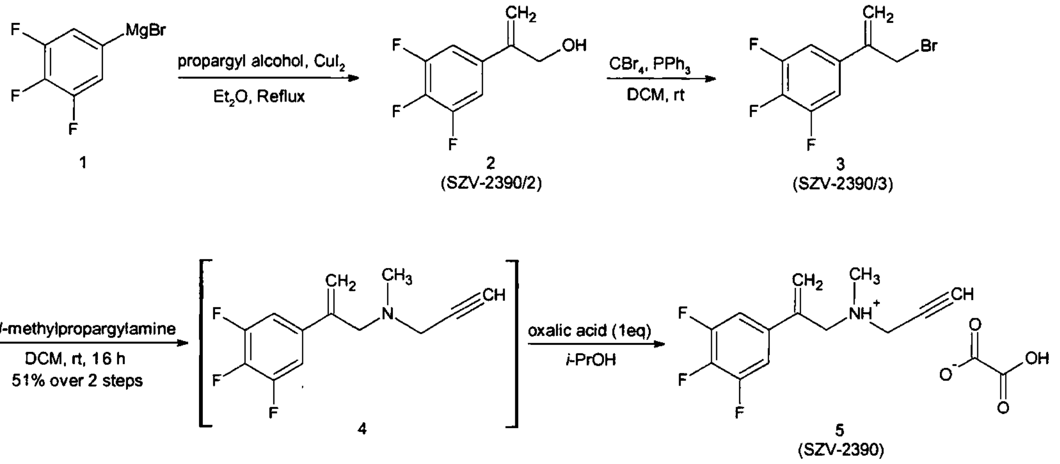
***tert*-Butyl 3-(2-(methyl(prop-2-yn-1-yl)amino)acetyl)-1*H*-indole-1-carboxylate (SZV-2418/2)** Following **method K**, the title compound was isolated as white solid (97%). ^1H NMR (400 MHz, Acetone-d_6) δ 8.76 (s, 1H), 8.33 (m, 1H), 8.20 – 8.13 (m, 1H), 7.43 – 7.31 (m, 2H), 3.77 (s, 2H), 3.52 (d, $J = 2.4$ Hz, 2H), 2.77 (brs, 1H), 2.40 (s, 3H), 1.72 (s, 9H).

***tert*-Butyl 3-(3-(methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)-1*H*-indole-1-carboxylate (SZV-2418/3)** Following **method E3**, the title compound was isolated as colourless oil (41%). ^1H NMR (400 MHz, Acetone-d_6) δ 8.20 (d, $J = 8.0$ Hz, 1H), 7.96 (s, 1H), 7.86 (d, $J = 8.0$ Hz, 1H), 7.37 – 7.25 (m, 2H), 5.68 (d, $J = 1.6$ Hz, 1H), 5.45 (d, $J = 1.6$ Hz, 1H), 3.45 (d, $J = 0.8$ Hz, 2H), 3.38 (d, $J = 2.4$ Hz, 2H), 2.72 (t, $J = 2.4$ Hz, 1H), 2.33 (s, 3H), 1.69 (s, 9H).

2-(1*H*-Indol-3-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2418/4) Following **method L**, the title compound was isolated yellowish white solid (67%). ^1H NMR (400 MHz, Acetone-d_6) δ 7.88 (d, $J = 7.6$ Hz, 1H), 7.69 (d, $J = 2.8$ Hz, 1H), 7.43 (d, $J = 7.6$ Hz, 1H), 7.10 (m, 2H), 5.61 (d, $J = 2.0$ Hz, 1H), 5.28 – 5.20 (m, 1H), 3.45 (s, 2H), 3.38 (d, $J = 2.4$ Hz, 2H), 2.69 (t, $J = 2.4$ Hz, 1H), 2.33 (s, 3H).

2-(1*H*-Indol-3-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2418) Following **method H1**, the title compound was isolated as beige solid (84%). Mp 125.5 – 126.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.53 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.14 (m, 2H), 5.83 (s, 1H), 5.54 (s, 1H), 4.23 (s, 2H), 3.31 (s, 1H), 3.98 (s, 2H), 2.83 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{17}N_2^+$ $[M+H]^+$ 225.1386, found 225.1394.

Scheme 13



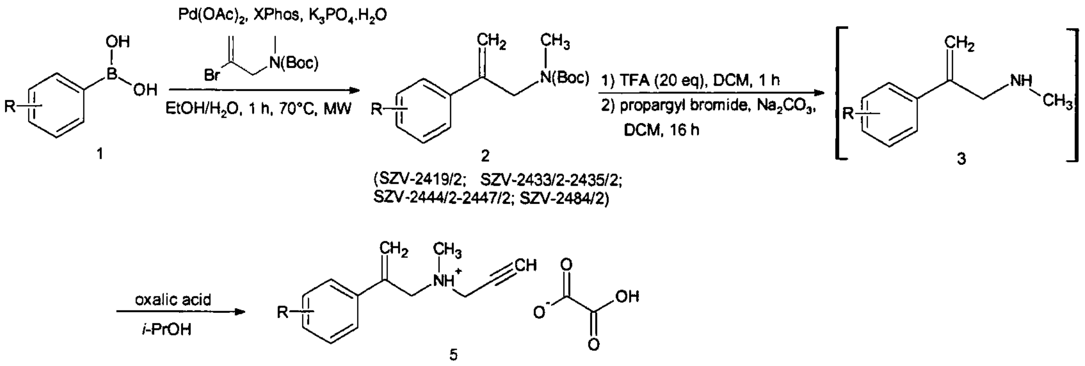
2-(3,4,5-Trifluorophenyl)prop-2-en-1-ol (SZV-2390/2) Following **method N**, the title compound was isolated as white solid (70%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.37 – 7.30 (m, 2H), 5.57 (s, 1H), 5.46 (s, 1H), 4.46 (d, *J* = 5.6 Hz, 2H).

5-(3-Bromoprop-1-en-2-yl)-1,2,3-trifluorobenzene (SZV-2390/3) Following **method O**, the title compound was isolated as colourless oil (50%). ^{1}H NMR (400 MHz, Acetone) δ 7.56 – 7.37 (m, 2H), 5.73 (s, 1H), 5.70 (s, 1H), 4.59 (s, 2H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(3,4,5-trifluorophenyl)prop-2-en-1-aminium carboxyformate**

(SZV-2390) Following **method D8 and method H1**, the title compound was isolated as white solid (68%). Mp 153.3 – 153.7 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.43 – 7.34 (m, 2H), 5.80 (s, 1H), 5.66 (s, 1H), 4.05 (s, 2H), 3.84 (d, *J* = 2.4 Hz, 2H), 3.17 (t, *J* = 2.4 Hz, 1H), 2.71 (s, 3H). Anal. calcd. for $C_{13}H_{12}F_3Nx(COOH)_2$ (329.27): C, 54.71%; H, 4.29%; N, 4.25%. Found: C, 54.66%; H, 4.44%; N, 4.28%.

Scheme 14



R = 3-F (SZV-2419)
R = 3-SCH$_3$ (SZV-2433)
R = 4-CF$_3$ (SZV-2434)
R = 3-Me, 4-F (SZV-2435)
R = 3-OCH$_2$-CH(CH$_2$CH$_2$) (SZV-2444)
R = 4-SO$_2$CH$_3$ (SZV-2245)
R = 3-NHTs (SZV-2446)
R = 4-SO$_2$Et (SZV-2447)
R = 3-CH$_2$OH (SZV-2484)

***tert*-Butyl (2-(3-fluorophenyl)allyl)(methyl)carbamate (SZV-2419/2)** Following **method P1**, but it was used n-BuOH, SPhos, conventional heating for 16 h at 60 °C, the title compound was isolated (86%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.52 – 7.13 (m, 3H), 7.09-7.05 (m, 1H), 5.53 (brs. d, 1H), 5.23 (s, 1H), 4.33 (s, 2H), 2.74 (s, 3H), 1.42 (s, 9H).

***tert*-Butyl methyl(2-(3-(methylthio)phenyl)allyl)carbamate (SZV-2433/2)** Following **method P1**, the title compound was isolated as a colourless oil (84%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.38-7.22 (m, 4H), 5.45 (brs. d, 1H), 5.18 (s, 1H), 4.32 (s, 2H), 2.73 (br, 3H), 2.51 (s, 3H), 1.42 (s, 9H).

***tert*-Butyl methyl(2-(4-(trifluoromethyl)phenyl)allyl)carbamate (SZV-2434/2)** Following **method P1**, the title compound was isolated as a colourless oil (83%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.70 (s, 4H), 5.61 (brs. d, 1H), 5.30 (s, 1H), 4.37 (s, 2H), 2.75 (s, 3H), 1.41 (s, 9H).

***tert*-Butyl (2-(4-fluoro-3-methylphenyl)allyl)(methyl)carbamate (SZV-2435/2)** Following **method P1**, the title compound was isolated as a colourless oil (90%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.34 (brs, 2H), 7.02 (app. t, 1H), 5.40 (br. d, 1H), 5.13 (s, 1H), 4.30 (s, 2H), 2.72 (s, 3H), 2.26 (s, 3H), 1.42 (s, 9H).

***tert*-Butyl methyl(2-(4-(methylsulfonyl)phenyl)allyl)carbamate (SZV-2445/2)** Following **method P1**, the title compound was isolated as a colourless oil (89%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 8.1 Hz, 2H), 7.57 (brs, 2H), 5.49 (brs, 1H), 5.25 (s, 1H), 4.26 (brs, 2H), 2.98 (s, 3H), 2.66 (brs, 3H), 1.35 (s, 9H).

***tert*-Butyl methyl(2-(3-(4-methylphenylsulfonamido)phenyl)allyl)carbamate (SZV-2446/2)** Following **method P1**, the title compound was isolated as a colourless oil (80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.50 (s, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.16-6.84 (m, 4H), 5.29 (brs. d, 1H), 5.07 (s, 1H), 4.18 (brs. d, 2H), 2.71 (brs. d, 3H), 2.34 (s, 3H), 1.41 (s, 9H).

***tert*-Butyl (2-(3-(cyclopropylmethoxy)phenyl)allyl)(methyl)carbamate (SZV-2444/2)** Following **method P1**, the title compound was isolated as a colourless oil (95%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (app. t, 1H), 6.97 (brs, 2H), 6.83-6.80 (m, 1H), 5.40 (brs. d, 1H), 5.09 (s, 1H), 4.26 (brs. d, 2H), 3.80 (d, J = 6.9 Hz, 2H), 2.76 (brs. d, 3H), 1.44 (s, 9H), 1.31 – 1.19 (m, 1H), 0.65-0.60 (m, 2H), 0.36-0.32 (m, 2H).

***tert*-Butyl (2-(4-(ethylsulfonyl)phenyl)allyl)(methyl)carbamate (SZV-2447/2)** Following **method P1**, the title compound was isolated as a yellow oil (96%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (d, J = 8.25 Hz, 2H), 7.61-7.58 (m, 2H), 5.53 (brs, 1H), 5.28 (s, 1H), 4.31 (brs, 2H), 3.10 (q, J = 7.4 Hz, 2H), 2.85 – 2.62 (m, 3H), 1.41 (s, 9H), 1.26 (t, J = 7.4 Hz, 3H).

***tert*-Butyl (2-(3-(hydroxymethyl)phenyl)allyl)(methyl)carbamate (SZV-2484/2)** Following **method P1**, the title compound was isolated as a colourless oil (96%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42-7.26 (m, 4H), 5.40 (brs. d, 1H), 5.10 (s, 1H), 4.65 (s, 2H), 4.26 (brs. d, 2H), 2.77-2.71 (m, 3H), 1.41 (s, 9H).

2-(3-Fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2419) Following **method M1** and **method H1**, the title compound was isolated. Mp 142.2 - 142.9 °C. ^{1}H NMR (400 MHz, Methanol-d4) δ 7.45-7.40 (m, 1H), 7.37-7.30 (m, 2H), 7.14-7.09 (m, 1H), 5.81 (s, 1H), 5.68 (s, 1H), 4.22 (s, 2H), 3.94 (d, J = 2.5 Hz, 2H), 3.26 (t, J = 2.5 Hz, 1H), 2.79 (s, 3H). Anal. calcd. for $C_{13}H_{14}FNx(COOH)_2$ (293.29): C, 61.43%; H, 5.50%; N, 4.78%. Found: C, 61.42%; H, 5.43%; N, 4.64%.

***N*-Methyl-2-(3-(methylthio)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2433)** Following **method M1** and **method H1**, the title compound was isolated as a white solid (73%). Mp 128.0 – 129.6 °C ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.44-7.30 (m, 4H), 5.78 (s, 1H), 5.64 (s, 1H), 4.22 (s, 2H), 3.92 (s, 2H), 3.28 (s, 1H), 2.78 (s, 3H), 2.53 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{14}H_{18}NS^+$ $[M+H]^+$ 232.1154, found 232.1155.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(4-(trifluoromethyl)phenyl)prop-2-en-1-aminium carboxyformate (SZV-2434)** Following **method M1** and **method H1**, the title compound was isolated as a white solid (76%). Mp 154.2 – 155.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.71 (s, 4H), 5.88 (s, 1H), 5.77 (s, 1H), 4.28 (s, 2H), 3.95 (s, 2H), 3.25 (s, 1H), 2.80 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{14}H_{15}F_3N^+$ $[M+H]^+$ 254.1151, found 254.1155.

2-(4-Fluoro-3-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2435) Following **method M1** and **method H1**, the title compound was isolated as a white solid (76%). Mp 156.2 – 157.9 °C ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.51 – 7.28 (m, 2H), 7.05 (app. t, 1H), 5.71 (s, 1H), 5.60 (s, 1H), 4.23 (s, 2H), 3.96 (s, 2H), 3.28 (s, 1H), 2.81 (s, 3H), 2.29 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{20}H_{22}NO^+$ $[M+H]^+$ 292.1696, found 292.1701.

2-(3-(Cyclopropylmethoxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2444) Following **method M1** and **method H1**, the title compound was isolated as a white solid (79%). Mp 138.9 – 139.3 °C ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.32 (app. t, 1H), 7.11 – 7.04 (m, 2H), 6.95-6.92 (m, 1H), 5.76 (s, 1H), 5.61 (s, 1H), 4.24 (s, 2H), 3.94 (d, *J* = 2.5 Hz, 2H), 3.86 (d, *J* = 6.9 Hz, 2H), 3.28 (t, *J* = 2.5 Hz, 1H), 2.79 (s, 3H), 1.30-1.20 (m, 1H), 0.65 – 0.58 (m, 2H), 0.37-0.33 (m, 2H). HRMS (ESI+) *m/z* calc for $C_{17}H_{21}NNaO^+$ $[M+H]^+$ 278.1515, found 278.1521.

***N*-Methyl-2-(4-(methylsulfonyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate**

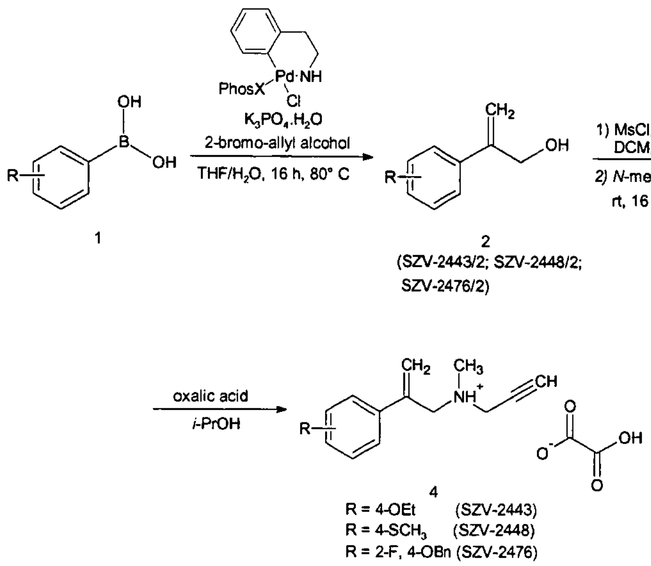
(SZV-2445) Following **method M1** and **method H1**, the title compound was isolated as an off-white solid (75%). Mp 173.4 – 175.4 °C. ^1H NMR (400 MHz, Methanol-d_4) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H), 5.89 (s, 1H), 5.76 (s, 1H), 4.19 (s, 2H), 3.88 (d, *J* = 2.5 Hz, 2H), 3.19 (t, *J* = 2.5 Hz, 1H), 3.13 (s, 3H), 2.74 (s, 3H). Anal. calcd. for $C_{14}H_{17}NO_2Sx(COOH)_2$ (353.39): C, 54.38%; H, 5.42%; N, 3.96%; O, 27.16%; S, 9.07%. Found: C, 54.44%; H, 5.42%; N, 3.68%; O, 27.15%; S, 8.89%.

***N*-Methyl-2-(3-(4-methylphenylsulfonamido)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2446)** Following **method M1** and **method H1**, the title compound was isolated as a yellow sticky solid (68%). ^1H NMR (400 MHz, Methanol-d_4) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.26-7.20 (m, 3H), 7.12-7.10 (m, 1H), 5.67 (s, 1H), 5.64 (s, 1H), 4.22 (s, 2H), 3.93 (d, *J* = 2.4 Hz, 2H), 3.28 (t, *J* = 2.4 Hz, 1H), 2.76 (s, 3H), 2.35 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{20}H_{23}N_2O_2S^+$ $[M+H]^+$ 355.1475, found 355.1490.

2-(4-(Ethylsulfonyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2447) Following **method M1** and **method H1**, the title compound was isolated as a white solid (65%). Mp 150.5 – 154.3 °C. ^1H NMR (400 MHz, Methanol-d_4) δ 7.92 (d, *J* = 8.6 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H), 5.90 (s, 1H), 5.76 (s, 1H), 4.19 (s, 2H), 3.87 (d, *J* = 2.5 Hz, 2H), 3.23 (q, *J* = 7.4 Hz, 2H), 3.19 (t, *J* = 2.5 Hz, 1H), 2.74 (s, 3H), 1.24 (t, *J* = 7.4 Hz, 3H). HRMS (ESI+) *m/z* calc for $C_{15}H_{20}NO_2S^+$ $[M+H]^+$ 278.1209, found 278.1204.

2-(3-(Hydroxymethyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2484) Following **method M1** and **method H1**, the title compound was isolated as a white solid (76%). Mp 104.6 – 106.6 °C. ^1H NMR (400 MHz, Methanol-d_4) δ 7.52 (s, 1H), 7.46-7.37 (m, 3H), 5.77 (d, *J* = 0.55 Hz, 1H), 5.61 (s, 1H), 4.65 (s, 2H), 4.23 (s, 2H), 3.92 (d, *J* = 2.5 Hz, 2H), 3.26 (t, *J* = 2.5 Hz, 1H), 2.78 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{18}NO^+$ $[M+H]^+$ 216.1383, found 216.1374.

Scheme 15



2-(4-Ethoxyphenyl)prop-2-en-1-ol (SZV-2443/2) Following **method P2**, the title compound was isolated as a flake-like solid (56%). Mp 52 – 54 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.35 (m, 2H), 6.91 – 6.84 (m, 2H), 5.39 (d, *J* = 0.9 Hz, 1H), 5.26-5.25 (m, 1H), 4.52 (d, *J* = 4.7 Hz, 2H), 4.05 (q, *J* = 6.9 Hz, 2H), 1.42 (t, *J* = 6.9 Hz, 3H).

2-(4-(Methylthio)phenyl)prop-2-en-1-ol (SZV-2448/2) Following **method P2**, the title compound was isolated as a pale yellow solid (57%). Mp 88 – 89 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.36 (m, 2H), 7.26 – 7.22 (m, 2H), 5.46 (d, *J* = 0.8 Hz, 1H), 5.33-5.32 (m, 1H), 4.52 (d, *J* = 5.9 Hz, 2H), 2.49 (s, 3H).

2-(4-(Benzyloxy)-2-fluorophenyl)prop-2-en-1-ol (SZV-2476/2) Following **method P2**, the title compound was isolated as a yellow solid (72%). Mp 46 – 49 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.31 (m, 5H), 6.76 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.70 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.45 (d, *J* = 1.2 Hz, 1H), 5.34 (d, *J* = 1.2 Hz, 1H), 5.06 (s, 2H), 4.46 (s, 2H).

2-(4-Ethoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2443/3) Following **method D9**, the title compound was isolated as a colourless oil (72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47-7.43 (m, 2H), 6.87-6.83 (m, 2H), 5.40 (d, *J* = 1.2 Hz, 1H), 5.19 (d, *J* = 1.2 Hz, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 3.42 (s, 2H), 3.36 (d, *J* = 2.3 Hz, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.3 Hz, 1H), 1.41 (t, *J* = 7.1 Hz, 3H).

***N*-Methyl-2-(4-(methylthio)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2448/3)** Following **method D9**, the title compound was isolated as a colourless oil (68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.42 (m, 2H), 7.24 – 7.18 (m, 2H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.25 (d, *J* = 1.2 Hz, 1H), 3.43 (s, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.48 (s, 3H), 2.31 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(4-(Benzyloxy)-2-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2476/3) Following **method D9**, the title compound was isolated as a white solid (86%). Mp 35 –

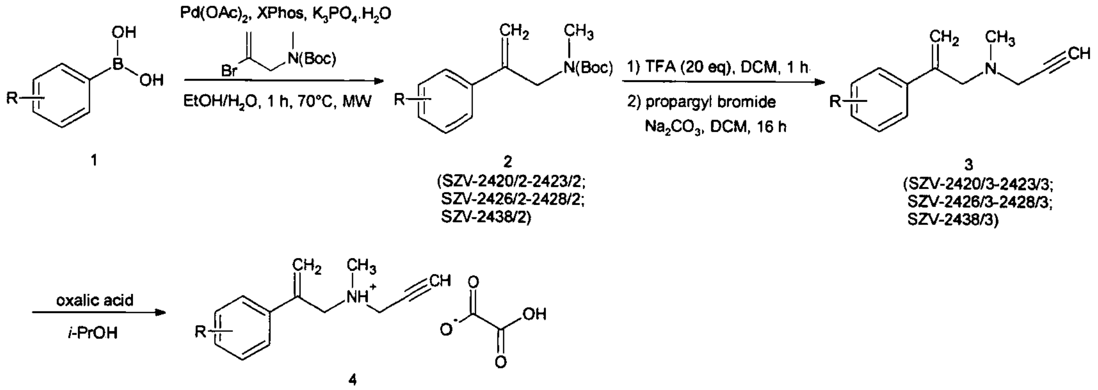
36 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43-7.29 (m, 5H), 7.26 (app. t, 1H), 6.73 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.68 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.39 (s, 1H), 5.33 (s, 1H), 5.04 (s, 2H), 3.42 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 2.29 (s, 3H), 2.23 (t, *J* = 2.4 Hz, 1H).

2-(4-Ethoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2443) Following **method H1**, the title compound was isolated as a white solid (73%). Mp 126.4 – 126.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.47-7.44 (m, 2H), 6.97-6.93 (m, 2H), 5.67 (s, 1H), 5.51 (s, 1H), 4.23 (s, 2H), 4.06 (q, *J* = 6.9 Hz, 2H), 3.96 (d, *J* = 2.4 Hz, 2H), 3.30 (t, *J* = 2.4 Hz, 1H), 2.81 (s, 3H), 1.39 (t, *J* = 6.9 Hz, 3H). Anal. calcd. for $C_{15}H_{19}NOx(COOH)_2$ (319.35): C, 63.94%; H, 6.63%; N, 4.39%; O, 25.05%. Found: C, 63.66%; H, 6.54%; N, 4.38%; O, 25.07%.

***N*-Methyl-2-(4-(methylthio)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2448)** Following **method H1**, the title compound was isolated as a white solid (71%). Mp 138.1 – 138.7 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 5.75 (s, 1H), 5.58 (s, 1H), 4.23 (s, 2H), 3.94 (d, *J* = 2.4 Hz, 2H), 3.28 (t, *J* = 2.4 Hz, 1H), 2.79 (s, 3H), 2.49 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{14}H_{18}NS^+$ $[M+H]^+$ 232.1154, found 232.1159.

2-(4-(Benzyloxy)-2-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2476) Following **method H1**, the title compound was isolated as a white solid (66%). Mp 122.5 – 124.9°C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.50 – 7.27 (m, 6H), 6.89-6.81 (m, 2H), 5.71 (s, 1H), 5.63 (s, 1H), 5.13 (s, 2H), 4.15 (s, 2H), 3.92 (d, *J* = 2.5 Hz, 2H), 3.24 (t, *J* = 2.5 Hz, 1H), 2.78 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{21}FNO^+$ $[M+H]^+$ 310.1602, found 310.1603.

Scheme 16



1

2
(SZV-2420/2-2423/2;
SZV-2426/2-2428/2;
SZV-2438/2)

3
(SZV-2420/3-2423/3;
SZV-2426/3-2428/3;
SZV-2438/3)

4

R = 3-OEt (SZV-2420)
R = 4-C(CH$_3$)$_3$ (SZV-2421)
R = 3-OCH$_3$, 4-CH$_3$ (SZV-2422)
R = 3-CH$_3$, 4-CH$_3$ (SZV-2423)
R = 3-OCF$_3$ (SZV-2426)
R = 3-OBn (SZV-2427)
R = 3-F, 4-CH$_3$ (SZV-2428)
R = 3-CN (SZV-2438)

***tert*-Butyl (2-(3-ethoxyphenyl)allyl)(methyl)carbamate (SZV-2420/2)** Following **method P1**, the title compound was isolated (88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 7.8 Hz, 1H), 7.00 (brs, 2H), 6.82 (d, $J = 8.0$ Hz, 1H), 5.41 (brd, 1H), 5.10 (s, 1H), 4.27 (brd, 2H), 4.04 (q, $J = 6.8$ Hz, 2H), 2.77 (brd, 3H), 1.44 (s, 9H), 1.41 (t, $J = 6.8$ Hz, 1H).

***tert*-Butyl (2-(4-(*tert*-butyl)phenyl)allyl)(methyl)carbamate (SZV-2421/2)** Following **method P1**, the title compound was isolated (80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.13 (m, 4H), 5.39 (brd, 1H), 5.06 (s, 1H), 4.27 (brd, 2H), 2.78 (brd, 3H), 1.44 (s, 9H), 1.32 (s, 9H).

***tert*-Butyl methyl(2-(3-(trifluoromethoxy)phenyl)allyl)carbamate (SZV-2426/2)** Following **method P1**, the title compound was isolated as colourless oil (82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.27 (m, 3H), 7.15 – 7.13 (m, 1H), 5.46 (brd, 1H), 5.19 (s, 1H), 4.28 (brd, 2H), 2.76 (brd, 3H), 1.44 (s, 9H).

***tert*-Butyl (2-(3-fluoro-4-methylphenyl)allyl)(methyl)carbamate (SZV-2428/2)** Following **method P1**, the title compound was isolated as colourless oil (81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.11 (d, $J = 7.0$ Hz, 3H), 5.39 (s, 1H), 5.11 (s, 1H), 4.25 (d, $J = 24.8$ Hz, 2H), 2.75 (d, $J = 17.0$ Hz, 3H), 2.26 (d, $J = 1.7$ Hz, 3H), 1.45 (s, 9H).

***tert*-Butyl (2-(3-methoxy-4-methylphenyl)allyl)(methyl)carbamate (SZV-2422/2)** Following **method P1**, the title compound was isolated (78%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.07 (d, $J = 7.6$ Hz, 1H), 7.05 – 6.79 (m, 2H), 5.40 (brd, 1H), 5.08 (s, 1H), 4.27 (brd, 2H), 3.85 (s, 3H), 2.78 (brd, 3H), 2.21 (s, 3H), 1.44 (s, 9H).

***tert*-Butyl (2-(3,4-dimethylphenyl)allyl)(methyl)carbamate (SZV-2423/2)** Following **method P1**, the title compound was isolated (81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24-7.07 (m, 3H), 5.38 (brd, 1H), 5.04 (s, 1H), 4.27 (brd, 2H), 2.76 (brd, 3H), 2.26 (s, 3H), 2.25 (s, 3H), 1.45 (s, 9H).

***tert*-Butyl (2-(3-(benzyloxy)phenyl)allyl)(methyl)carbamate (SZV-2427/2)** Following **method P1**, the title compound was isolated (78%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.31 (m, 5H), 7.23 (d, $J = 8.4$ Hz, 1H), 7.11-7.00 (m, 2H), 6.91 (ddd, $J = 8.4, 2.4, 0.8$ Hz, 1H), 5.42 (brd, 1H), 5.11 (s, 1H), 5.07 (s, 2H), 4.27 (brd, 2H), 2.77 (brd, 3H), 1.45 (s, 9H).

***tert*-Butyl (2-(3-cyanophenyl)allyl)(methyl)carbamate (SZV-2438/2)** Following **method P1**, the title compound was isolated (59%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (brs, 2H), 7.57 (d, $J = 7.6$ Hz, 1H), 7.43 (t, $J = 7.6$ Hz, 1H), 5.47 (brs, 1H), 5.25 (s, 1H), 4.29 (brd, 2H), 2.74 (brd, 3H), 1.44 (s, 9H).

2-(3-Ethoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2420/3) Following **method M1**, the title compound was isolated as colourless oil (66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (t, $J = 8.0$ Hz, 1H), 7.09 – 7.06 (m, 2H), 6.82 – 6.79 (m, 1H), 5.47 (s, 1H), 5.28 (s, 1H), 4.05 (q, $J = 6.8$ Hz, 2H), 3.43 (s, 2H), 3.37 (d, $J = 2.4$ Hz, 2H), 2.32 (s, 3H), 2.24 (t, $J = 2.4$ Hz, 1H), 1.41 (t, $J = 6.8$ Hz, 3H).

2-(4-(*tert*-Butyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2421/3) Following **method M1**, the title compound was isolated as colourless oil (57%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (d, $J = 8.4$ Hz, 2H), 7.35 (d, $J = 8.4$ Hz, 2H), 5.48 (d, $J = 1.2$ Hz, 1H), 5.25 (d,

J = 1.2 Hz, 1H), 3.45 (d, J = 0.8 Hz, 2H), 3.38 (d, J = 2.4 Hz, 2H), 2.33 (s, 3H), 2.25 (t, J = 2.4 Hz,1H), 1.32 (s, 9H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(3-(trifluoromethoxy)phenyl)prop-2-en-1-amine (SZV-2426/3)** Following **method M1**, the title compound was isolated as colourless oil (46%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.43 (m, 1H), 7.39 (s, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.14 – 7.10 (m, 1H), 5.52 (d, J = 1.2 Hz, 1H), 5.35 (d, J = 1.2 Hz, 1H), 3.43 (d, J = 1.2 Hz, 2H), 3.36 (d, J = 2.4 Hz, 2H), 2.32 (s, 3H), 2.26 (t, J = 2.4 Hz, 1H).

2-(3-Fluoro-4-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2428/3) Following **method M1**, the title compound was isolated as colourless oil (69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 – 7.16 (m, 2H), 7.14 – 7.10 (m, 1H), 5.47 (d, J = 1.2 Hz, 1H), 5.27 (d, J = 1.2 Hz, 1H), 3.41 (d, J = 0.8 Hz, 2H), 3.35 (d, J = 2.0 Hz, 2H), 2.31 (s, 3H), 2.25 (m, 4H).

2-(3-Methoxy-4-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2422/3) Following **method M1**, the title compound was isolated (34%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.08 (d, J = 8.1 Hz, 1H), 7.01 – 7.00 (m, 2H), 5.45 (s, 1H), 5.25 (s, 1H), 3.85 (s, 3H), 3.44 (s, 2H), 3.37 (d, J = 2.4 Hz, 2H), 2.33 (s, 3H), 2.25 (t, J = 2.4 Hz, 1H), 2.21 (s, 3H).

2-(3,4-Dimethylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2423/3) Following **method M1**, the title compound was isolated (30%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.21 (m, 2H), 7.09 (d, J = 8.0 Hz, 1H), 5.47 (d, J = 1.2 Hz, 1H), 5.28 (d, J = 1.2 Hz, 1H), 3.43 (s, 2H), 3.36 (d, J = 2.4 Hz, 2H), 2.32 (s, 3H), 2.27 (s, 3H), 2.24-2.25 (m, 4H).

2-(3-(Benzyloxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2427/3) Following **method M1**, the title compound was isolated (48%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.30 (m, 5H), 7.23 (d, J = 8.0 Hz, 1H), 7.12 – 7.10 (m, 1H), 6.90 (ddd, J = 8.0, 2.4, 0.8 Hz, 1H), 5.47 (d, J = 1.6 Hz, 1H), 5.28 (d, J = 1.6 Hz, 1H), 5.08 (s, 2H), 3.42 (s, 2H), 3.36 (d, J = 2.4 Hz, 2H), 2.32 (s, 3H), 2.24 (t, J = 2.4 Hz, 1H).

3-(3-(Methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)benzonitrile (SZV-2438/3) Following **method M1**, the title compound was isolated (21%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83-7.84 (m, 1H), 7.76 – 7.73 (m, 1H), 7.55 (dt, J = 7.8, 1.6 Hz, 1H), 7.42 (td, J = 7.8 Hz, 0.8 Hz, 1H), 5.54 (d, J = 1.2 Hz, 1H), 5.38 (d, J = 1.2 Hz, 1H), 3.44 (d, J = 0.8 Hz, 2H), 3.34 (d, J = 2.4 Hz, 2H), 2.30 (s, 3H), 2.27 (t, J = 2.4 Hz, 1H).

2-(3-Ethoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2420) Following **method H1**, the title compound was isolated (67%). Mp 103.0 – 103.4 °C ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.23 (t, J = 8.0Hz, 1H), 7.09 – 7.04 (m, 2H), 6.85 (ddd, J = 8.0, 2.8, 0.8 Hz, 1H), 5.53 (d, J = 1.2 Hz, 1H), 5.26 (d, J = 1.2 Hz, 1H), 4.03 (q, J = 6.8 Hz, 2H), 3.47 (s, 2H), 3.37 (d, J = 2.4 Hz, 2H), 3.24 (t, J = 2.4 Hz, 1H), 2.24 (s, 3H), 1.32 (t, J = 6.8 Hz, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{20}NO^+$ $[M+H]^+$ 230.1539, found 230.1532.

2-(4-(*tert*-Butyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2421) Following **method H1**, the title compound was isolated (79%). Mp

164.4 – 165.5 °C ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.45 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.8 Hz, 2H), 5.49 (d, J = 1.2 Hz, 1H), 5.22 (d, J = 1.2 Hz, 1H), 3.48 (s, 2H), 3.36 (d, J = 2.4 Hz, 2H), 3.23 (t, J = 2.4 Hz, 1H), 2.24 (s, 3H), 1.28 (s, 9H). HRMS (ESI+) *m/z* calc for $C_{17}H_{24}N^+$ $[M+H]^+$ 242.1903, found 242.1908.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(3-(trifluoromethoxy)phenyl)prop-2-en-1-aminium carboxyformate (SZV-2426)** Following **method H1**, the title compound was isolated (81%). Mp 111.8 – 112.3 °C ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.59 – 7.56 (m, 1H), 7.51 (s, 1H), 7.47 (t, J = 8.0 Hz, 1H), 7.30 – 7.25 (m, 1H), 5.63 (d, J = 1.2 Hz, 1H), 5.34 (d, J = 1.2 Hz, 1H), 3.47 (s, 2H), 3.34 (d, J = 2.4 Hz, 2H), 3.21 (t, J = 2.4 Hz, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{14}H_{14}F_3NOx(COOH)_2$ (359.30): C, 53.49%; H, 4.49%; N, 3.90%. Found: C, 53.60%; H, 4.41%; N, 3.88%.

2-(3-Fluoro-4-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2428) Following **method H1**, the title compound was isolated (70%). Mp 135.6 – 136.7 °C ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.33 – 7.20 (m, 3H), 5.57 (d, J = 1.2 Hz, 1H), 5.26 (d, J = 1.2 Hz, 1H), 3.45 (s, 2H), 3.35 (d, J = 2.4 Hz, 2H), 3.22 (t, J = 2.4 Hz, 1H), 2.22 (s, 6H). HRMS (ESI+) *m/z* calc for $C_{14}H_{17}N^+$ $[M+H]^+$ 218.1340, found 218.1350.

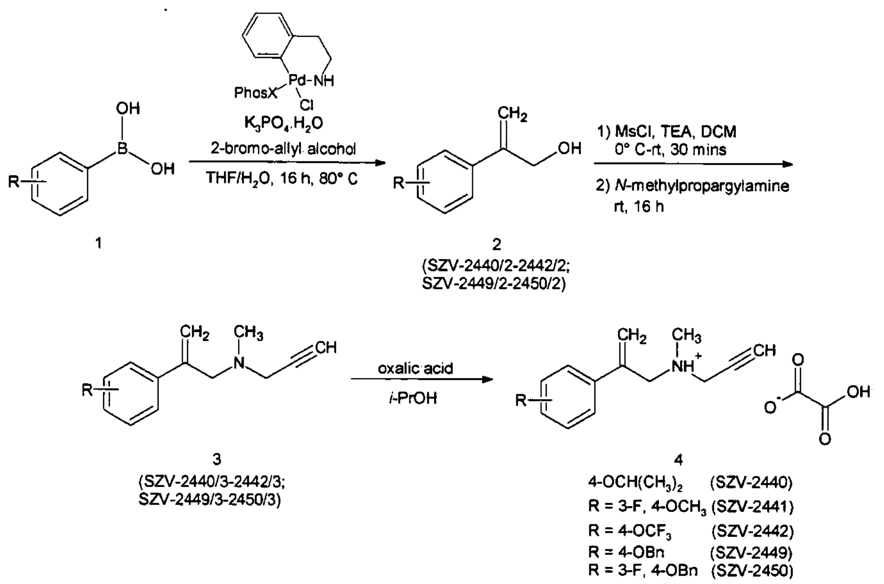
2-(3-Methoxy-4-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2422) Following **method H1**, the title compound was isolated (71%). Mp 127 – 128 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.16 (d, J = 8.0 Hz, 1H), 7.05 – 6.97 (m, 2H), 5.75 (d, J = 0.4 Hz, 1H), 5.58 (d, J = 0.4 Hz, 1H), 4.26 (s, 2H), 3.96 (d, J = 2.4 Hz, 2H), 3.88 (s, 3H), 2.80 (s, 3H), 2.19 (s, 3H). Anal. calcd. for $C_{15}H_{19}NOx(COOH)_2$ (319.35): C, 63.94%; H, 6.63%; N, 4.39%; O, 25.05%. Found: C, 64.06%; H, 6.56%; N, 4.30%; O, 25.11%.

2-(3,4-Dimethylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2423) Following **method H1**, the title compound was isolated (71%). Mp 136 – 137 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.30 (s, 1H), 7.24 (dd, J = 7.6, 2.0 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 5.71 (d, J = 0.4 Hz, 1H), 5.55 (d, J = 0.4 Hz, 1H), 4.24 (s, 2H), 3.94 (d, J = 2.4 Hz, 2H), 2.80 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H). Anal. calcd. for $C_{15}H_{19}Nx(COOH)_2$ (303.35): C, 67.31%; H, 6.98%; N, 4.62%; O, 21.10%. Found: C, 67.32%; H, 6.93%; N, 4.30%; O, 21.19%.

2-(3-(Benzyloxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2427) Following **method H1**, the title compound was isolated (73%). Mp 112 – 113 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.48 – 7.31 (m, 6H), 7.16 – 7.15 (m, 1H), 7.12 – 7.09 (m, 1H), 7.03 (ddd, J = 8.0, 2.4, 0.8 Hz, 1H), 5.75 (d, J = 0.8 Hz, 1H), 5.61 (d, J = 0.8 Hz, 1H), 5.13 (s, 2H), 4.22 (s, 2H), 3.92 (d, J = 2.4 Hz, 2H), 3.27 (t, J = 2.4 Hz, 1H), 2.77 (s, 3H). Anal. calcd. for $C_{20}H_{21}NOx(COOH)_2$ (381.42): C, 69.28%; H, 6.08%; N, 3.67%; O, 20.97%. Found: C, 69.25%; H, 6.07%; N, 3.52%; O, 20.84%.

2-(3-Cyanophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2438) Following **method H1**, the title compound was isolated (75%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.94 (s, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 5.82 (s, 1H), 5.67 (s, 1H), 4.08 (s, 2H), 3.80 (d, J = 2.4 Hz, 2H), 3.13 (t, J = 2.4 Hz, 1H), 2.68 (s, 3H). HRMS (ESI +) m/z calcd. for $C_{14}H_{15}N_2^+$ $[M+H]^+$ 211.1230, found 211.1233.

Scheme 17



2-(4-Isopropoxyphenyl)prop-2-en-1-ol (SZV-2440/2) Following **method P2**, the title compound was isolated as yellow oil (47%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.38 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 5.39 (s, 1H), 5.25 (d, J = 1.2 Hz, 1H), 4.58 - 4.51 (m, 3H), 1.34 (d, J = 6.0 Hz, 1H).

2-(3-Fluoro-4-methoxyphenyl)prop-2-en-1-ol (SZV-2441/2) Following **method P2**, the title compound was isolated as colourless oil (56%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.24 – 7.16 (m, 2H), 6.93 (t, J = 8.8 Hz, 1H), 5.41 (d, J = 0.8 Hz, 1H), 5.30 (d, J = 0.8 Hz, 1H), 4.49 (s, 2H), 3.90 (s, 3H).

2-(4-(Trifluoromethoxy)phenyl)prop-2-en-1-ol (SZV-2442/2) Following **method P2**, the title compound was isolated as yellow oil (38%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.48 (d, J = 8.8 Hz, 2H), 7.20 (dd, J = 8.8, 0.8 Hz, 2H), 5.47 (d, J = 0.8 Hz, 1H), 5.39 (d, J = 0.8 Hz, 1H), 4.53 (d, J = 6.0 Hz, 2H), 1.59 (d, J = 6.0 Hz, 1H).

2-(4-(Benzyloxy)phenyl)prop-2-en-1-ol (SZV-2449/2) (Honda T et al, Tetrahedron Lett., 2003, 44, 3035-3038) Following **method P2**, the title compound was isolated as yellow oil (36%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.45 – 7.31 (m, 7H), 6.97 (d, J = 8.8 Hz, 2H), 5.40 (s, 1H), 5.26 (d, J = 1.2 Hz, 1H), 5.08 (s, 2H), 4.52 (s, 2H).

2-(4-(Benzyloxy)-3-fluorophenyl)prop-2-en-1-ol (SZV-2450/2) Following **method P2**, the title compound was isolated as colourless oil (56%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.45 – 7.32 (m, 5H), 7.23 (dd, J = 12.8, 2.4 Hz, 1H), 7.14 (ddd, J = 8.4, 2.4, 1.2 Hz, 1H), 6.96 (t, J = 8.4 Hz, 1H), 5.41 (s, 1H), 5.30 (d, J = 0.8 Hz, 1H), 5.16 (s, 2H), 4.48 (d, J = 5.6 Hz, 2H), 1.54 (d, J = 5.6 Hz, 1H).

2-(4-Isopropoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2440/3) Following **method D9**, the title compound was isolated as colourless oil (80%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.44 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.40 (d, *J* = 1.2 Hz, 1H), 5.18 (d, *J* = 1.2 Hz, 1H), 4.54 (sept, *J* = 6.0 Hz, 1H), 3.42 (d, *J* = 0.8 Hz, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H), 1.34 (d, *J* = 6.0 Hz, 1H).

2-(3-Fluoro-4-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2441/3) Following **method D9**, the title compound was isolated as colourless oil (74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.24 (m, 2H), 6.91 (t, *J* = 8.8 Hz, 1H), 5.42 (d, *J* = 1.2 Hz, 1H), 5.23 (d, *J* = 1.2 Hz, 1H), 3.89 (s, 3H), 3.39 (d, *J* = 0.8 Hz, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.31 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(4-(trifluoromethoxy)phenyl)prop-2-en-1-amine (SZV-2442/3)** Following **method D9**, the title compound was isolated as colourless oil (61%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.8 Hz, 2H), 7.16 (dd, *J* = 8.8, 1.2 Hz, 2H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.31 (d, *J* = 1.2 Hz, 1H), 3.43 (d, *J* = 0.8 Hz, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(4-(Benzyloxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2449/3) Following **method D9**, the title compound was isolated as colourless oil (71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.30 (m, 7H), 6.94 (d, *J* = 8.8 Hz, 2H), 5.41 (d, *J* = 1.2 Hz, 1H), 5.20 (d, *J* = 1.2 Hz, 1H), 5.07 (s, 2H), 3.43 (d, *J* = 0.8 Hz, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(4-(Benzyloxy)-3-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2450/3) Following **method D9**, the title compound was isolated as colourless oil (54%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.29 (m, 6H), 7.21 (ddd, *J* = 8.8, 2.0, 1.2 Hz, 1H), 6.94 (t, *J* = 8.8 Hz, 1H), 5.42 (d, *J* = 1.2 Hz, 1H), 5.23 (d, *J* = 1.2 Hz, 1H), 5.14 (s, 2H), 3.39 (s, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.31 (s, 3H), 2.25 (s, 1H).

2-(4-Isopropoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2440) Following **method H1**, the title compound was isolated (92%). Mp 137.8 – 138.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.44 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.44 (d, *J* = 1.6 Hz, 1H), 5.16 (d, *J* = 0.8 Hz, 1H), 4.60 (sept, *J* = 6.0 Hz, 1H), 3.46 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.24 (t, *J* = 2.4 Hz, 1H), 2.25 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 1H). Anal. calcd. for $C_{16}H_{21}NOx(COOH)_2$ (333.38): C, 64.85%; H, 6.95%; N, 4.20%; O, 24.00%. Found: C, 64.80%; H, 6.88%; N, 4.25%; O, 24.38%.

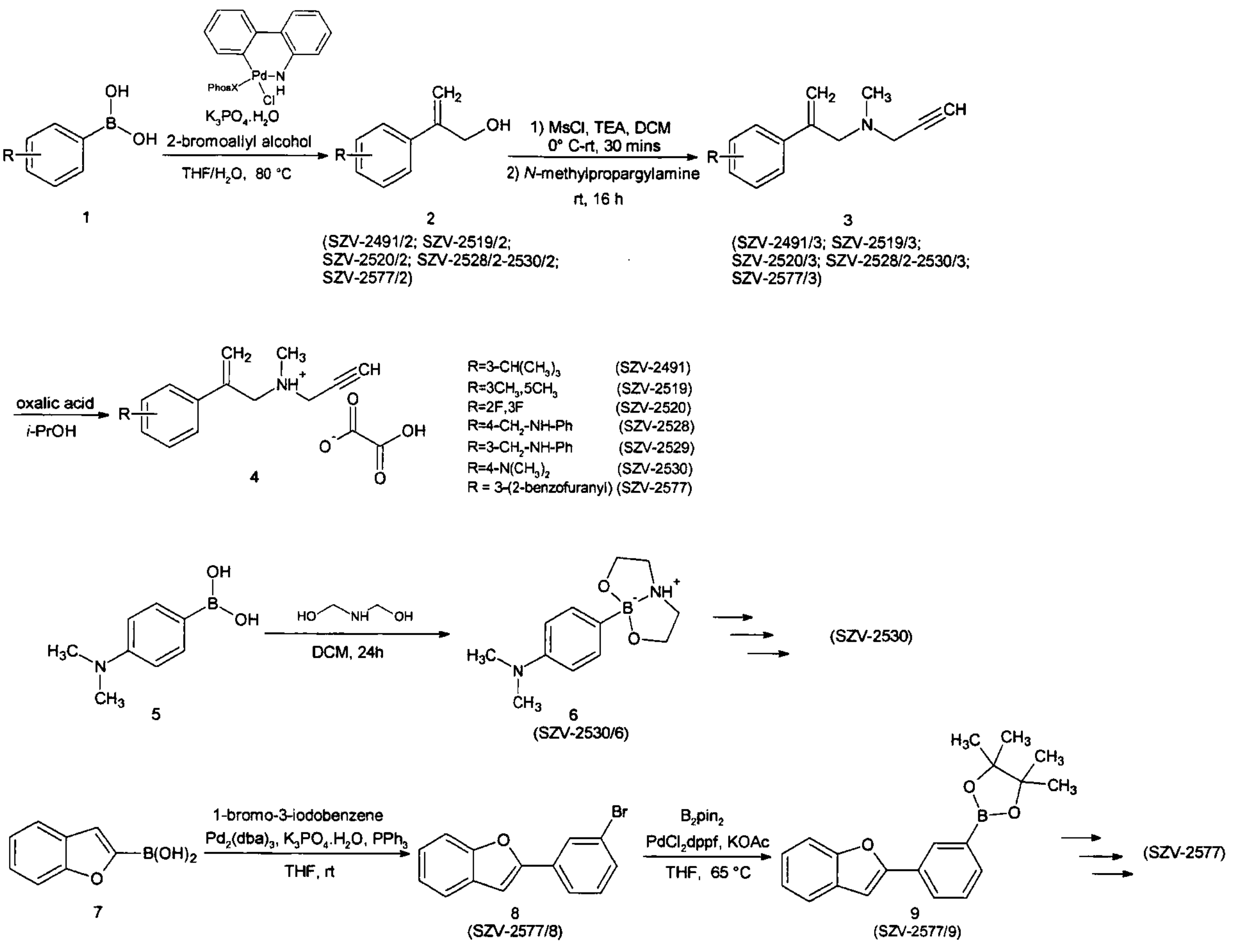
2-(3-Fluoro-4-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2441) Following **method H1**, the title compound was isolated (58%). Mp 129.6 – 130.4 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.41 (dd, *J* = 13.2, 2.4 Hz, 1H), 7.33 (ddd, *J* = 8.8, 2.4, 1.2 Hz, 1H), 7.11 (t, *J* = 8.8 Hz, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.22 (d, *J* = 0.4 Hz, 1H), 3.84 (s, 3H), 3.46 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 3.24 (t, *J* = 2.4 Hz, 1H), 2.24 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{14}H_{17}NO^+$ $[M+H]^+$ 234.1289, found 234.1294.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(4-(trifluoromethoxy)phenyl)prop-2-en-1-aminium carboxyformate (SZV-2442)** Following **method H1**, the title compound was isolated (68%). Mp 145.0 – 145.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.58 (d, *J* = 1.2 Hz, 1H), 5.32 (d, *J* = 1.2 Hz, 1H), 3.48 (s, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H), 2.23 (s, 3H). Anal. calcd. for $C_{14}H_{14}F_3NOx(COOH)_2$ (359.30): C, 53.49%; H, 4.49%; N, 3.90%. Found: C, 53.66%; H, 4.57%; N, 3.89%.

2-(4-(Benzyloxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2449) Following **method H1**, the title compound was isolated (66%). Mp 137.8 – 138.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.49 – 7.30 (m, 7H), 6.97 (d, *J* = 8.8 Hz, 2H), 5.45 (d, *J* = 1.2 Hz, 1H), 5.16 (d, *J* = 0.4 Hz, 1H), 5.11 (s, 2H), 3.46 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 3.24 (t, *J* = 2.4 Hz, 1H), 2.24 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{20}H_{22}NO^+$ $[M+H]^+$ 292.1696, found 292.1697.

2-(4-(Benzyloxy)-3-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2450) Following **method H1**, the title compound was isolated (78%). Mp 137.2 – 138.6 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.47 – 7.29 (m, 7H), 7.18 (t, *J* = 8.8 Hz, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.21 (s, 1H), 5.19 (s, 2H), 3.44 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 3.23 (t, *J* = 2.4 Hz, 1H), 2.23 (s, 3H). Anal. calcd. for $C_{20}H_{20}FNOx(COOH)_2$ (399.41): C, 66.16%; H, 5.55%; N, 3.51%. Found: C, 66.13%; H, 5.52%; N, 3.49%.

Scheme 18



***N,N*-Dimethyl-4-(tetrahydro-8λ^4-[1,3,2]oxazaborolo[2,3-b][1,3,2]oxazaborol-8-yl)aniline (SZV-2530/6)** Boronic acid **(SZV-2530/5)** (462.0 mg, 2.8 mmol) in dichloromethane (12.0 ml) was added diethanolamine (295.0 mg, 1 eq). The reaction mixture was allowed to stir at room temperature under air atmosphere for 24 h. The resulting suspension was filtered and triturated using EtOAc for 5 mins to remove excess diethanolamine. **(SZV-2530/6)** was isolated as white solid (130 mg, 45%). Mp 167-170 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.58 (brs, 1H), 7.39 (d, J = 7.6 Hz, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.70 (d, J = 7.6 Hz, 1H), 4.06 – 3.95 (m, 2H), 3.68 (s, 2H), 2.83 (brd, 6H).

2-(3-Bromophenyl)benzofuran (SZV-2577/8) Following **method P2** and the reaction was stirred at rt under argon for 16 h, the title compound was isolated as a white solid (116 mg, 85%). Mp 84 – 85 °C ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.09 (t, J = 1.6 Hz, 1H), 7.92 (ddd, J = 8.0, 1.6, 1.2 Hz, 1H), 7.66 (ddd, J = 8.0, 1.6, 1.2 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.44 (t, J = 8.0 Hz, 1H), 7.39 (d, J = 0.8 Hz, 1H), 7.35 (ddd, J = 8.0, 7.2, 1.2 Hz, 1H), 7.27 (td, J = 8.0, 0.8 Hz, 1H).

2-(3-(Benzofuran-2-yl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SZV-2577/9) Following **method Q2** using **(SZV-2577/8)** and the reaction was stirred at 65 °C for 4 h, the title compound was isolated as a white solid (284 mg, 69%). Mp 124 – 125 °C ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.31 (brs, 1H), 8.05 (ddd, J = 8.0, 1.6, 1.2 Hz, 1H), 7.71 (dd, J = 7.2, 1.2 Hz, 1H), 7.66

(ddd, *J* = 7.6, 1.2, 0.4 Hz, 1H), 7.61 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.35 – 7.31 (m, 2H), 7.26 (td, *J* = 8.0, 0.8 Hz, 1H), 1.38 (s, 12H).

2-(3-(*tert*-Butyl)phenyl)prop-2-en-1-ol (SZV-2491/2) Following **method P2**, the title compound was isolated as colourless oil (20%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (t, *J* = 1.6 Hz, 1H), 7.35 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.23 (m, 1H), 5.45 (d, *J* = 0.8 Hz, 1H), 5.35 (q, *J* = 1.2 Hz, 1H), 4.56 (dd, *J* = 1.2, 0.8 Hz, 2H), 1.34 (s, 9H).

2-(3,5-Dimethylphenyl)prop-2-en-1-ol (SZV-2519/2) Following **method P2**, the title compound was isolated as pale yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.06 (s, 2H), 6.96 (s, 1H), 5.43 (s, 1H), 5.31 (s, 1H), 4.52 (s, 2H), 2.33 (s, 6H).

2-(2,3-Difluorophenyl)prop-2-en-1-ol (SZV-2520/2) Following **method P2**, the title compound was isolated. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.13 – 7.02 (m, 3H), 5.57 (d, *J* = 0.8 Hz, 1H), 5.41 (d, *J* = 0.8 Hz, 1H), 4.47 (s, 2H).

2-(4-((Phenylamino)methyl)phenyl)prop-2-en-1-ol (SZV-2528/2) Following **method P2**, the title compound was isolated as pale yellow oil (45%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.18 (dd, *J* = 8.0, 7.2 Hz, 1H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 2H), 5.47 (s, 1H), 5.34 (d, *J* = 1.2 Hz, 1H), 4.54 (s, 2H), 4.34 (s, 2H).

2-(3-((Phenylamino)methyl)phenyl)prop-2-en-1-ol (SZV-2529/2) Following **method P2** (heating at 40 °C), the title compound was isolated as pale yellow oil (67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (s, 1H), 7.41 – 7.30 (m, 3H), 7.21 (dd, *J* = 8.8, 7.6 Hz, 1H), 6.75 (tt, *J* = 7.6, 0.4 Hz, 1H), 6.66 (dd, *J* = 8.8, 0.4 Hz, 2H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.36 (d, *J* = 1.2 Hz, 1H), 4.52 (s, 2H), 4.34 (s, 2H).

2-(4-(Dimethylamino)phenyl)prop-2-en-1-ol (SZV-2530/2) Following **method P2**, the title compound was isolated as yellow oil (50-64% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 9.2 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 2H), 5.36 (s, 1H), 5.17 (d, *J* = 1.2 Hz, 1H), 4.52 (d, *J* = 6.0 Hz, 2H), 2.97 (s, 6H), 1.49 (t, *J* = 6.0 Hz, 1H),

2-(3-(Benzofuran-2-yl)phenyl)prop-2-en-1-ol (SZV-2577/2) Following **method P2** (heating at 40 °C), the title compound was isolated as colourless oil (40%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (dd, *J* = 2.4, 1.6 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.59 (ddd, *J* = 8.0, 1.2, 0.4 Hz, 1H), 7.54 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.45 – 7.43 (m, 2H), 7.30 (td, *J* = 7.2, 1.2 Hz, 1H), 7.24 (td, *J* = 7.2, 1.2 Hz, 1H), 7.06 (d, *J* = 0.8 Hz, 1H), 5.57 (d, *J* = 1.2 Hz, 1H), 5.44 (q, *J* = 1.2 Hz, 1H), 4.61 (q, *J* = 1.2 Hz, 2H).

2-(3-(*tert*-Butyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2491/3) Following **method D9**, the title compound was isolated as colourless oil (82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (t, *J* = 1.6 Hz, 1H), 7.35 – 7.27 (m, 3H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.31 (s, 1H), 3.49 (s, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.36 (s, 3H), 2.28 (t, *J* = 2.4 Hz, 1H), 1.36 (s, 9H).

2-(3,5-Dimethylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2519/3) Following **method D9**, the title compound was isolated as colourless oil (78%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 (s, 2H), 6.92 (s, 1H), 5.42 (d, *J* = 1.6 Hz, 1H), 5.26 (s, 1H), 3.43 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 2.33 (s, 3H), 2.32 (s, 6H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(2,3-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2520/3) Following **method D9**, the title compound was isolated as colourless oil (73%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 – 6.97 (m, 3H), 5.51 (s, 1H), 5.41 (s, 1H), 3.45 (s, 2H), 3.34 (d, *J* = 2.0 Hz, 2H), 2.30 (s, 3H), 2.24 (t, *J* = 2.0 Hz, 1H).

***N*-(4-(3-(Methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)benzyl)aniline (SZV-2528/3)** Following **method D9**, the title compound was isolated as crystalline solid (71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.18 (dd, *J* = 8.0, 7.2 Hz, 2H), 6.72 (tt, *J* = 7.2, 0.8 Hz, 1H), 6.64 (dd, *J* = 8.0, 0.8 Hz, 2H), 5.49 (d, *J* = 1.6 Hz, 1H), 5.29 (d, *J* = 0.8 Hz, 1H), 4.32 (s, 2H), 4.01 (s, 1H), 3.46 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 2.33 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

***N*-(3-(3-(Methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)benzyl)aniline (SZV-2529/3)** Following **method D9**, the title compound was isolated as crystalline solid (75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (s, 1H), 7.42 (dt, *J* = 6.8, 2.4 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.18 (dd, *J* = 8.8, 7.6 Hz, 2H), 6.72 (tt, *J* = 7.6, 1.2 Hz, 1H), 6.66 (dd, *J* = 8.8, 1.2 Hz, 2H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.30 (d, *J* = 1.2 Hz, 1H), 4.33 (s, 2H), 4.02 (s, 1H), 3.45 (s, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.31 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

***N*,*N*-Dimethyl-4-(3-(methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)aniline (SZV-2530/3)** Following **method D9**, the title compound was isolated as white solid (88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 9.2 Hz, 2H), 6.69 (d, *J* = 9.2 Hz, 2H), 5.37 (d, *J* = 1.2 Hz, 1H), 5.12 (d, *J* = 1.2 Hz, 1H), 3.43 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 2.95 (s, 6H), 2.33 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-[3-(1-Benzofuran-2-yl)phenyl]-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2577/3) Following **method D9**, the title compound was isolated as colourless oil (82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 (t, *J* = 1.2 Hz, 1H), 7.79 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.60(ddd, *J* = 8.0, 1.2, 0.8 Hz, 1H), 7.56 – 7.48 (m, 2H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.24 (td, *J* = 8.0, 1.2 Hz, 1H), 7.05 (d, *J* = 1.2 Hz, 1H), 5.61 (d, *J* = 1.2 Hz, 1H), 5.40 (d, *J* = 1.2 Hz, 1H), 3.55 (s, 2H), 3.43 (d, *J* = 2.4 Hz, 2H), 2.38 (s, 3H), 2.30 (t, *J* = 2.4 Hz, 1H).

2-(3-(*tert*-Butyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2491) Following **method H1**, the title compound was isolated (63%). Mp 100.9 -102.0 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.55 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.38 – 7.33 (m, 2H), 5.73 (s, 1H), 5.61 (s, 1H), 4.25 (s, 2H), 3.93 (d, *J* = 2.4 Hz, 2H), 3.29 (t, *J* = 2.4 Hz, 1H), 2.78 (s, 3H), 1.35 (s, 9H). Anal. calcd. for $C_{17}H_{23}Nx(COOH)_2$ (331.41): C, 68.86%; H, 7.60%; N, 4.23%; O, 19.31%. Found: C, 68.77%; H, 7.55%; N, 4.25%; O, 19.05%.

2-(3,5-Dimethylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2519) Following **method H1**, the title compound was isolated (79%). Mp

146.5 – 147.8 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.14 (s, 2H), 7.04 (s, 1H), 5.72 (d, $J = 0.4$ Hz, 1H), 5.58 (d, $J = 0.4$ Hz, 1H), 4.24 (s, 2H), 3.94 (d, $J = 2.8$ Hz, 2H), 2.80 (s, 3H), 2.33 (s, 6H). ^{13}C NMR (101 MHz, Methanol-d4) δ 165.96, 140.99, 139.92, 138.48, 131.64, 125.41, 123.14, 80.87, 73.56, 59.67, 45.90, 40.71, 21.36. Anal. calcd. for $C_{15}H_{19}Nx(COOH)_2$ (303.35): C, 67.31%; H, 6.98%; N, 4.62%; O, 21.10%. Found: C, 67.07%; H, 6.91%; N, 4.54%; O, 21.10%.

2-(2,3-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium (SZV-2520) Following **method H1**, the title compound was isolated (78%). Mp 120.6 – 121.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.32 – 7.16 (m, 3H), 5.83 (s, 1H), 5.72 (s, 1H), 4.10 (s, 2H), 3.86 (d, $J = 2.8$ Hz, 2H), 3.17 (t, $J = 2.8$ Hz, 1H), 2.73 (s, 3H). Anal. calcd. for $C_{13}H_{13}FNx(COOH)_2$ (311.28): C, 57.88%; H, 4.86%; N, 4.50%; O, 20.56%. Found: C, 58.01%; H, 5.07%; N, 4.21%; O, 20.83%.

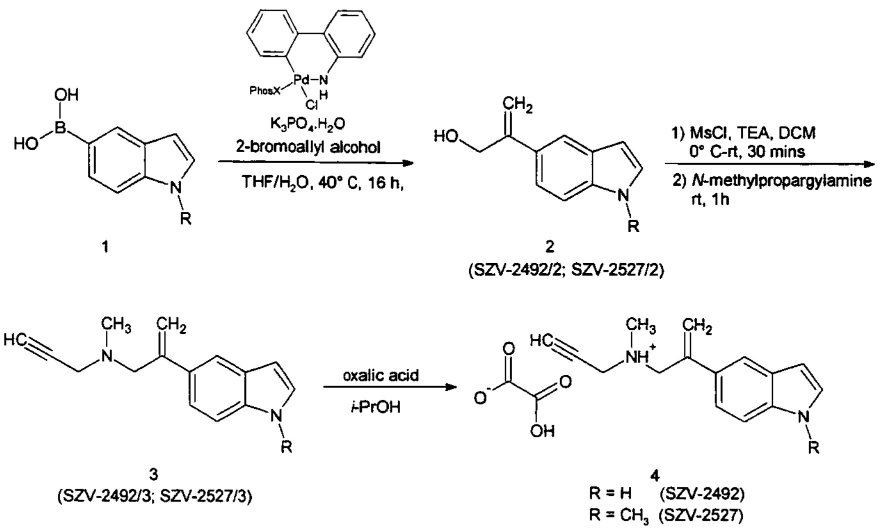
***N*-Methyl-2-(4-((phenylamino)methyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2528)** Following **method H1**, the title compound was isolated (85%). Mp 139.6 - 140.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.49 (d, $J = 8.4$ Hz, 2H), 7.43 (d, $J = 8.4$ Hz, 2H), 7.06 (dd, $J = 8.8$, 7.2 Hz, 2H), 6.64 – 6.55 (m, 3H), 5.74 (s, 1H), 5.58 (s, 1H), 4.35 (s, 2H), 4.21 (s, 2H), 3.91 (d, $J = 2.4$ Hz, 2H), 3.26 (t, $J = 2.4$ Hz, 1H), 2.76 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{23}N_2^+$ $[M+H]^+$ 291.1856, found 291.1856.

***N*-Methyl-2-(3-((phenylamino)methyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2529)** Following **method H1**, the title compound was isolated (80%). Mp 142.6 - 146.8 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.54 (s, 1H), 7.45 – 7.33 (m, 3H), 7.09 (dd, $J = 8.4$, 7.6 Hz, 2H), 6.73 – 6.59 (m, 3H), 5.77 (s, 1H), 5.63 (s, 1H), 4.38 (s, 2H), 4.28 (s, 2H), 3.94 (d, $J = 2.4$ Hz, 2H), 3.29 (t, $J = 2.4$ Hz, 1H), 2.78 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{23}N_2^+$ $[M+H]^+$ 291.1856, found 291.1861.

2-(4-(Dimethylamino)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2530) Following **method H1**, the title compound was isolated as white solid (77%). Mp 129.9 – 130.6 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.39 (d, $J = 8.0$ Hz, 2H), 6.79 (d, $J = 8.0$ Hz, 2H), 5.62 (s, 1H), 5.41 (s, 1H), 4.23 (s, 2H), 3.97 (s, 2H), 3.31 (s, 1H), 2.97 (s, 6H), 2.82 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{21}N_2^+$ $[M+H]^+$ 229.1699, found 229.1708.

2-(3-(Benzofuran-2-yl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2577) Following **method H1**, the title compound was isolated as white solid (70%). Mp 162.4 – 163.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.09 (d, $J = 0.8$ Hz, 1H), 7.96 – 7.93 (m, 1H), 7.67 – 7.62 (m, 1H), 7.59 – 7.52 (m, 3H), 7.36 – 7.30 (m, 2H), 7.26 (td, $J = 8.0$, 0.8 Hz, 1H) 5.89 (s, 1H), 5.72 (s, 1H), 4.31 (s, 2H), 3.97 (d, $J = 2.4$ Hz, 2H), 3.29 (t, $J = 2.4$ Hz, 1H), 2.82 (s, 3H Anal. calcd. for $C_{21}H_{19}NOx(COOH)_2$ (391.42): C, 70.58%; H, 5.41%; N, 3.58%; O, 20.44%. Found: C, 70.27%; H, 5.36%; N, 3.47%; O, 20.92%.

Scheme 19



2-(1*H*-Indol-5-yl)prop-2-en-1-ol (SZV-2492/2) Following **method P2**, the title compound was isolated as white crystalline solid (61%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.2 (brs, 1H), 7.67 – 7.66 (m, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.31 – 7.29 (m, 1H), 6.28 (dd, *J* = 8.8, 1.6 Hz, 1H), 6.47 – 6.45 (m, 1H), 5.36 (dt, *J* = 2.0, 0.8 Hz, 1H), 5.29 (q, *J* = 1.6 Hz, 1H), 4.53 – 4.51 (m, 3H), 3.91 (t, *J* = 6.0 Hz, 1H).

2-(1-Methyl-1*H*-indol-5-yl)prop-2-en-1-ol (SZV-2527/2) Following **method P2**, the title compound was isolated as yellow solid (74%). Mp 60-63 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 0.8 Hz, 1H), 7.36 (dd, *J* = 8.8, 2.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 3.2 Hz, 1H), 6.49 (dd, *J* = 3.2, 0.8 Hz, 1H), 5.45 (s, 1H), 5.30 (d, *J* = 1.2 Hz, 1H), 4.62 (s, 2H), 3.80 (s, 3H).

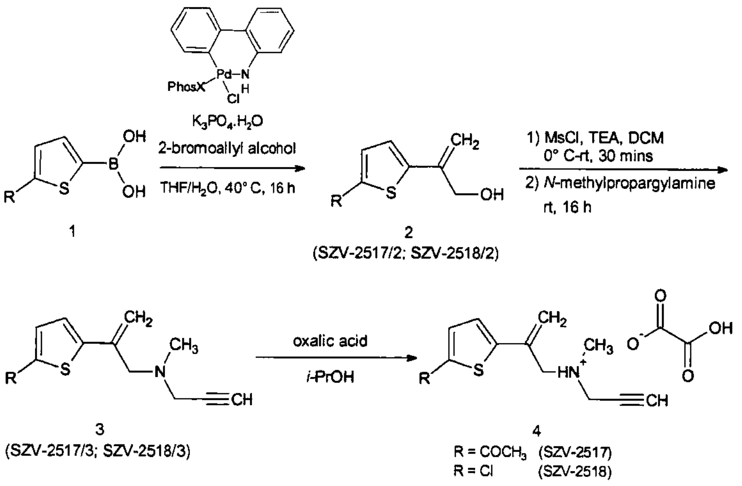
2-(1*H*-Indol-5-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2492/3) Following **method D9**, the title compound was isolated as white solid (53%). Mp 75-77 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (s, 1H), 7.79 (t, *J* = 0.8 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.19 (dd, *J* = 3.2, 2.4 Hz, 1H), 6.54 (ddd, *J* = 2.8, 2.0, 0.8 Hz, 1H), 5.48 (d, *J* = 2.0 Hz, 1H), 5.27 (s, 1H), 3.55 (s, 2H), 3.42 (d, *J* = 2.4 Hz, 2H), 2.37 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

***N*-Methyl-2-(1-methyl-1*H*-indol-5-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2527/3)** Following **method D9**, the title compound was isolated as oil (80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 0.4 Hz, 1H), 7.40 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.02 (d, *J* = 2.8 Hz, 1H), 6.47 (dd, *J* = 8.8, 0.4 Hz, 1H), 5.46 (d, *J* = 2.0 Hz, 1H), 5.25 (s, 1H), 3.78 (s, 3H), 3.53 (s, 2H), 3.40 (d, *J* = 2.4 Hz, 2H), 2.35 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(1*H*-Indol-5-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2492) Following **method H1**, the title compound was isolated as white solid (83%). Mp 71.5 - 72.6 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.74 (d, *J* = 1.2 Hz, 1H), 7.44 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.30 – 7.28 (m, 2H), 6.49 (dd, *J* = 3.2, 0.8 Hz, 1H), 5.69 (d, *J* = 1.2 Hz, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 4.31 (s, 2H), 3.94 (d, *J* = 2.4 Hz, 2H), 3.29 (t, *J* = 2.4 Hz, 1H), 2.79 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{17}N_2^+$ $[M+H]^+$ 225.1386, found 225.1395.

***N*-Methyl-2-(1-methyl-1*H*-indol-5-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2527)** Following **method H1**, the title compound was isolated as white solid (80%). Mp 114.4 – 115.3 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.74 (d, *J* = 1.2 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.21 (d, *J* = 2.8 Hz, 1H), 6.48 (dd, *J* = 3.2, 0.4 Hz, 1H), 5.70 (d, *J* = 0.8 Hz, 1H), 5.53 (d, *J* = 0.8 Hz, 1H), 4.31 (s, 2H), 3.94 (d, *J* = 2.4 Hz, 2H), 3.82 (s, 3H), 3.29 (t, *J* = 2.4 Hz, 1H), 2.80 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{19}N_2^+$ $[M+H]^+$ 239.1543, found 239.1545.

Scheme 20



1-(5-(3-Hydroxyprop-1-en-2-yl)thiophen-2-yl)ethanone (SZV-2517/2) Following **method P2**, the title compound was isolated as yellow solid (60%). Mp 113-116 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 4.0 Hz, 1H), 7.12 (d, *J* = 4.0 Hz, 1H), 5.66 (s, 1H), 5.42 (s, 1H), 4.49 (s, 2H), 2.52 (s, 3H).

2-(5-Chlorothiophen-2-yl)prop-2-en-1-ol (SZV-2518/2) Following **method P2**, the title compound was isolated as yellow oil (64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.88 (d, *J* = 4.0 Hz, 1H), 6.80 (d, *J* = 4.0 Hz, 1H), 5.40 (s, 1H), 5.24 (d, *J* = 1.2 Hz, 1H), 4.45 (s, 2H).

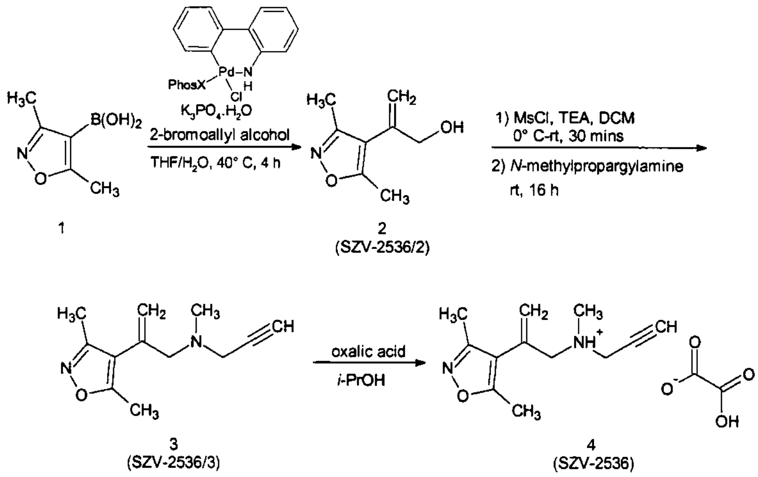
1-(5-(3-(Methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)thiophen-2-yl)ethanone (SZV-2517/3) Following **method D9**, the title compound was isolated as colourless oil (82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 4.0 Hz, 1H), 7.24 (d, *J* = 4.0 Hz, 1H), 5.68 (s, 1H), 5.32 (s, 1H), 3.39 (m, 4H), 2.52 (s, 3H), 2.35 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(5-Chlorothiophen-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2518/3) Following **method D9**, the title compound was isolated as pale yellow oil (85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.00 (d, *J* = 4.0 Hz, 1H), 6.77 (d, *J* = 4.0 Hz, 1H), 5.43 (s, 1H), 5.13 (d, *J* = 0.8 Hz, 1H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.31 (brs, 2H), 2.35 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(5-Acetylthiophen-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium (SZV-2517) Following **method H1**, the title compound was isolated as white solid (67%). Mp 130.3 – 131.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.78 (d, *J* = 4.0 Hz, 1H), 7.37 (d, *J* = 4.0 Hz, 1H), 5.95 (s, 1H), 5.59 (s, 1H), 3.96 (s, 2H), 3.82 (d, *J* = 2.4 Hz, 2H), 3.11 (t, *J* = 2.4 Hz, 1H), 2.70 (s, 3H), 2.55 (s, 3H). Anal. calcd. for $C_{13}H_{15}NOSx(COOH)_2$ (323.36): C, 55.71%; H, 5.30%; N, 4.33%; S, 9.92%; O, 24.74%. Found: C, 55.39%; H, 5.25%; N, 4.28%; S, 9.71%; O, 24.62%.

2-(5-Chlorothiophen-2-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2518) Following **method H1**, the title compound was isolated as white solid (54%). Mp 126.6 – 127.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.12 (d, *J* = 4.0 Hz, 1H), 6.93 (d, *J* = 4.0 Hz, 1H), 5.70 (s, 1H), 5.43 (s, 1H), 3.95 (s, 2H), 3.86 (d, *J* = 2.4 Hz, 2H), 3.14 (t, *J* = 2.4 Hz, 1H), 2.73 (s, 3H). Anal. calcd. for $C_{11}H_{12}ClNSx(COOH)_2$ (315.77): C, 49.45%; H, 4.47%; N, 4.44%; S, 10.15%; O, 20.27%. Found: C, 49.30%; H, 4.43%; N, 4.38%; S, 10.08%; O, 19.89%.

Scheme 21

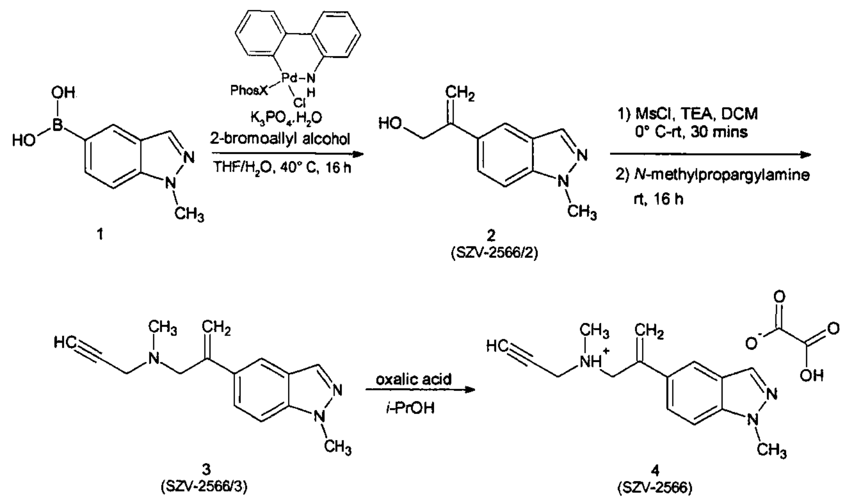


2-(3,5-Dimethylisoxazol-4-yl)prop-2-en-1-ol (SZV-2536/2) Following **method P2**, the title compound was isolated as yellow oil (64-71%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.54 (d, *J* = 1.2 Hz, 1H), 5.10 (d, *J* = 1.2 Hz, 1H), 4.25 (s, 2H), 2.36 (s, 3H), 2.22 (s, 3H).

2-(3,5-Dimethylisoxazol-4-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2536/3) Following **method D9**, the title compound was isolated as white solid (40%). Mp 43-45 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.45 (d, *J* = 1.2 Hz, 1H), 5.10 (d, *J* = 1.2 Hz, 1H), 3.28 (d, *J* = 2.4 Hz, 2H), 3.23 (s, 2H), 2.36 (s, 3H), 2.25 (s, 3H), 2.24 (s, 3H), 2.22 (t, *J* = 2.4 Hz, 1H).

2-(3,5-Dimethylisoxazol-4-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2536) Following **method H1**, the title compound was isolated as white solid (70%). Mp 120.5 – 121.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 5.78 (d, *J* = 0.8 Hz, 1H), 5.48 (d, *J* = 0.8 Hz, 1H), 3.88 (s, 2H), 3.83 (d, *J* = 2.4 Hz, 2H), 3.17 (t, *J* = 2.4 Hz, 1H), 2.70 (s, 3H), 2.43 (s, 3H), 2.27 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{12}H_{17}N_2O^+$ $[M+H]^+$ 205.1335, found 205.1343.

Scheme 22

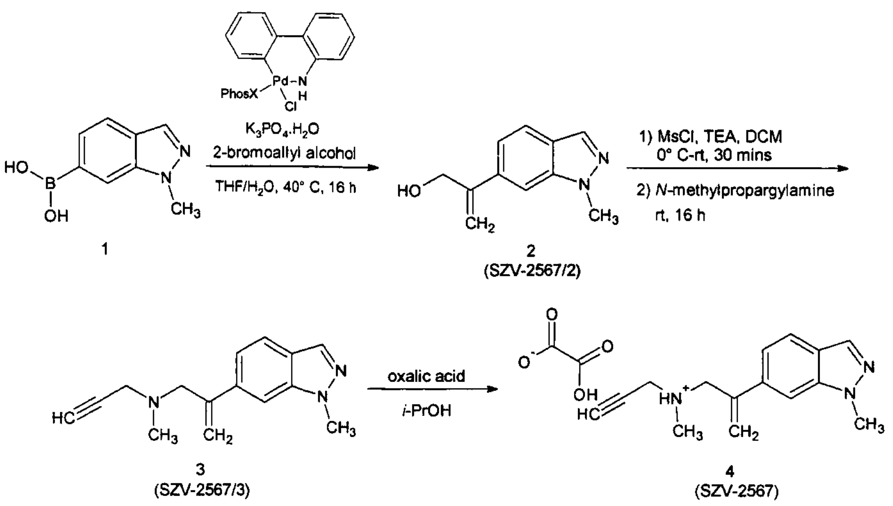


2-(1-Methyl-1*H*-indazol-5-yl)prop-2-en-1-ol (SZV-2566/2) Following **method P2**, the title compound isolated was not pure by ^{1}H NMR analysis, however, it was used directly without additional purification for the subsequent step.

***N*-Methyl-2-(1-methyl-1*H*-indazol-5-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2566/3)** Following **method D9**, the title compound was isolated as white solid (23% over two steps). Mp 70-72 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (s, 1H), 7.88 (d, *J* = 1.6 Hz, 1H), 7.58 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.30 (d, *J* = 1.2 Hz, 1H), 4.05 (s, 3H), 3.52 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.34 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

***N*-Methyl-2-(1-methyl-1*H*-indazol-5-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2566)** Following **method H1**, the title compound was isolated as white solid (71%). Mp 143.8 -146.4 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.04 (d, *J* = 0.8 Hz, 1H), 7.94 (dd, *J* = 1.6, 1.2 Hz, 1H), 7.66 – 7.57 (m, 2H), 5.79 (s, 1H), 5.63 (s, 1H), 4.32 (s, 2H), 4.08 (s, 3H), 3.95 (d, *J* = 2.4 Hz, 2H), 3.28 (t, *J* = 2.4 Hz, 1H), 2.81 (s, 3H). Anal. calcd. for $C_{15}H_{17}N_3x(COOH)_2$ (329.35): C, 62.00%; H, 5.81%; N, 12.76%; O, 19.43%. Found: C, 61.81%; H, 5.75%; N, 12.61%; O, 19.78%.

Scheme 23

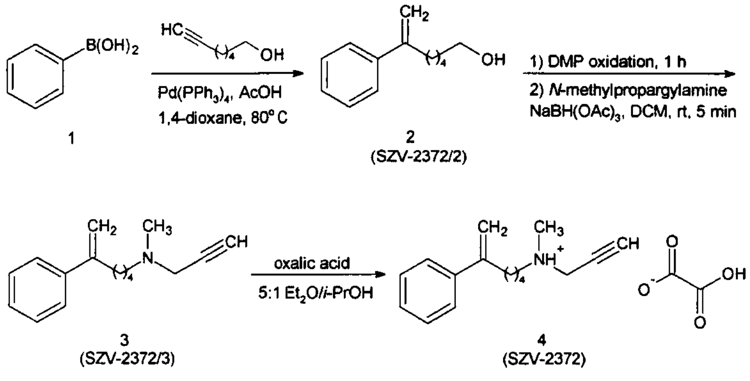


2-(1-Methyl-1*H*-indazol-6-yl)prop-2-en-1-ol (SZV-2567/2) Following **method P2**, the title compound isolated was not pure by ^{1}H NMR analysis, however, it was used directly without additional purification for the subsequent step.

***N*-Methyl-2-(1-methyl-1*H*-indazol-6-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2567/3)** Following **method D9**, the title compound was isolated as colourless oil (27% over two steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 (d, J = 0.8 Hz, 1H), 7.66 (dd, J = 8.8, 0.8 Hz, 1H), 7.55 (brs, 1H), 7.31 (dd, J = 8.8, 1.2 Hz, 1H), 5.58 (s, 1H), 5.39 (s, 1H), 4.08 (s, 3H), 3.56 (s, 2H), 3.40 (d, J = 2.4 Hz, 2H), 2.36 (s, 3H), 2.29 (t, J = 2.4 Hz, 1H).

***N*-Methyl-2-(1-methyl-1*H*-indazol-6-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2567)** Following **method H1**, the title compound was isolated white solid (71%). Mp 157.9 – 158.3 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.01 (d, J = 1.2 Hz, 1H), 7.80 (dd, J = 8.4, 0.8 Hz, 1H), 7.73 (brs, 1H), 7.35 (dd, J = 8.4, 1.2 Hz, 1H), 5.89 (s, 1H), 5.72 (s, 1H), 4.33 (s, 2H), 4.10 (s, 3H), 3.94 (d, J = 2.4 Hz, 2H), 3.29 (t, J = 2.4 Hz, 1H), 2.80 (s, 3H). Anal. calcd. for $C_{15}H_{17}N_3x(COOH)_2$ (329.35): C, 62.00%; H, 5.81%; N, 12.76%; O, 19.43%. Found: C, 61.65%; H, 5.74%; N, 12.67%; O, 19.65%.

Scheme 24

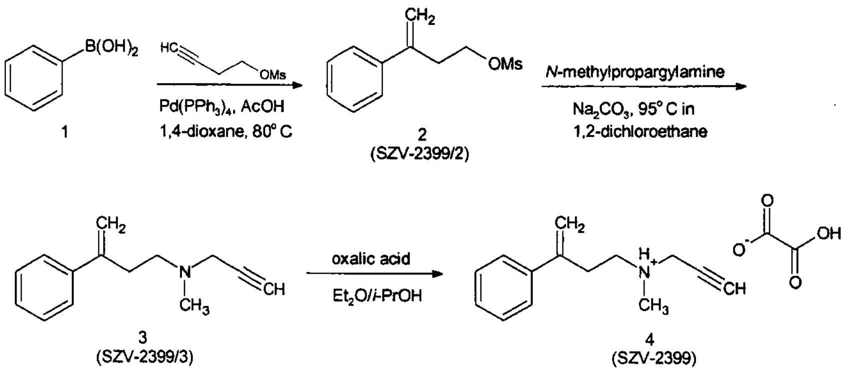


5-Phenylhex-5-en-1-ol (SZV-2372/2) (Oh CH et al, Angew. Chem., Int. Ed., 2003, 42, 805-808) In a 20-ml microwave vial were added phenylboronic acid (750 mg, 6.2 mmol), 5-hexyn-1-ol (500.0 mg, 5.1 mmol), AcOH (30 µl, 0.5 mmol) in 1,4-dioxane (15.0 ml). The mixture was degassed with argon for 5 min and $Pd(PPh_3)_4$ (178.0 mg, 0.2 mmol) was rapidly added. The mixture was continuously degassed for another 3 min and sealed with a cap. The reaction was performed at 80 °C overnight and then concentrated to dryness under reduced pressure. Flash chromatographic purification (hexane/ethyl acetate 90:10, v/v) afforded the title compound (685.0 mg, 79%) as a colorless oil. All ^{1}H- and ^{13}C-NMR data were identical to those reported in the literature.

***N*-Methyl-5-phenyl-*N*-(prop-2-yn-1-yl)hex-5-en-1-amine (SZV-2372/3)** To a solution of **(SZV-2372/2)** (150.0 mg, 0.9 mmol) in CH_2Cl_2 (5.0 ml) was added Dess-Martin periodinane (DMP) (433.0 mg, 1.0 mmol). The reaction was stirred at room temperature and monitored by TLC. After 30 min, the reaction was completed. A saturated aqueous $NaHCO_3$ (5.0 ml) solution and a saturated aqueous $Na_2S_2O_3$ solution (5.0 ml) were subsequently added. The mixture was kept under strong stirring for 10 min, following which CH_2Cl_2 was added. After separation of two layers, the aqueous phase was extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford the corresponding crude aldehyde. The crude was re-dissolved in CH_2Cl_2 (5.0 ml) and *N*-methylpropargylamine (137 µl, 1.6 mmol) was added. After stirring at room temperature for 5 min, the solution was cooled down to 0 °C and $NaBH(OAc)_3$ (361.0 mg, 1.7 mmol) was added slowly. The reaction mixture was stirred at room temperature for another 5 min then quenched with saturated aqueous $NaHCO_3$ solution. Two layers were separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatographic purification afforded the title compound (135 mg, 70%) as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41-7.26 (m, 5H), 5.26 (d, J = 1.2 Hz, 1H), 5.06 (d, J = 1.2 Hz, 1H), 3.37 (d, J = 2.4 Hz, 1H), 3.33 (d, J = 2.4 Hz, 2H), 2.53 (t, J = 6.8 Hz, 2H), 2.42 (t, J = 7.2 Hz, 2H), 2.30 (s, 3H), 2.21 (t, J = 2.4 Hz, 1H), 1.64 – 1.35 (m, 4H).

***N*-Methyl-5-phenyl-*N*-(prop-2-yn-1-yl)hex-5-en-1-aminium carboxyformate (SZV-2372)** Following the **method H1**, the title compound was isolated as a white solid (66 mg, 80%). Mp 100.1-102.3°C. ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.42 (d, J = 7.2 Hz, 2H), 7.36 – 7.23 (m, 3H), 5.29 (s, 1H), 5.11 (s, 1H), 4.03 (d, J = 1.6 Hz, 2H), 3.21 – 3.05 (m, 2H), 2.87 (s, 3H), 2.62 (t, J = 7.2 Hz, 2H), 1.73 – 1.71 (m, 2H), 1.65 – 1.41 (m, 2H). HRMS (ESI+) *m/z* calc for $C_{16}H_{22}N^+$ $[M+H]^+$ 228.1747, found 228.1746.

Scheme 25

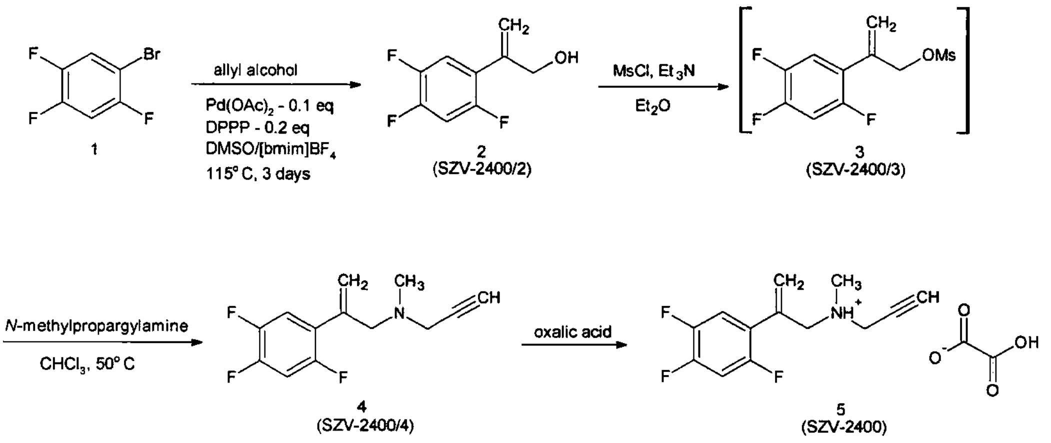


3-Phenylbut-3-en-1-yl methanesulfonate (SZV-2399/2) (Brodney MA et al, Tetrahedron Lett., 2007, 48, 1939-1943) In a 5-ml microwave vial were added phenylboronic acid (1234 mg, 10.1 mmol), but-3-yn-1-yl methanesulfonate (1000.0 mg, 6.8 mmol), AcOH (120 µl, 2.0 mmol) in 1,4-dioxane (10.0 ml). The mixture was degassed with argon for 5 min and $Pd(PPh_3)_4$ (780.0 mg, 0.68 mmol) was rapidly added. The mixture was continuously degassed for another 3 min and sealed with a cap. The reaction was performed at 80 °C overnight. The crude was then concentrated to dryness and purified by flash chromatography on silica gel (hexane/ethyl acetate 95:5, v/v) to afford the title compound (340.0 mg, 22%) as a colorless oil. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.27 (m, 5H), 5.43 (s, 1H), 5.20 (d, J = 1.2 Hz, 1H), 4.30 (t, J = 6.8 Hz, 2H), 2.98 (td, J = 6.8, 1.2 Hz, 2H), 2.90 (s, 3H).

***N*-Methyl-3-phenyl-*N*-(prop-2-yn-1-yl)but-3-en-1-amine (SZV-2399/3)** To a solution of **(SZV-2399/2)** (320.0 mg, 1.4 mmol) in 1,2-dichloroethane (5.0 ml) were added solid Na_2CO_3 (600.0 mg, 5.7 mmol) and *N*-methylpropargylamine (132 µl, 2.8 mmol). The stirred mixture was heated at 90 °C overnight. After cooling to room temperature and filtration, the solution was concentrated under reduced pressure. Flash chromatographic purification gave the title compound (70.5 mg, 25%) and undesired (4-chlorobut-1-en-2-yl)benzene. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.18 (m, 5H), 5.33 (s, 1H), 5.12 (d, J = 0.8 Hz, 1H), 3.39 (d, J = 2.4 Hz, 2H), 2.80 – 2.66 (m, 2H), 2.66 – 2.52 (m, 2H), 2.36 (s, 3H), 2.21 (t, J = 2.4 Hz, 1H).

***N*-Methyl-3-phenyl-*N*-(prop-2-yn-1-yl)but-3-en-1-aminium carboxyformate (SZV-2399)** Following the **method H1**, the title compound was isolated as a white solid (75 mg, 76%). Mp 117.7-119.6° C. ^1H NMR (400 MHz, Methanol-d_4) δ 7.49 (d, J = 7.2 Hz, 2H), 7.46 – 7.25 (m, 3H), 5.49 (s, 1H), 5.28 (s, 1H), 4.13 (brs, 2H), 3.28 (s, 2H), 3.09 – 2.96 (m, 6H); HRMS (ESI+) *m/z* calcd. for $C_{14}H_{17}N^+$ $[M+H]^+$ 200.1434, found 200.1436.

Scheme 26

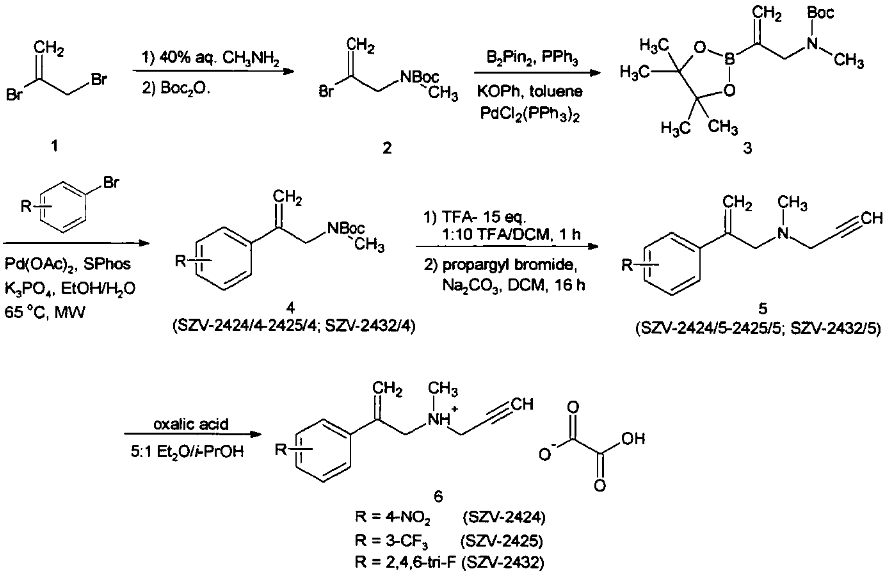


2-(2,4,5-Trifluorophenyl)prop-2-en-1-ol (SZV-2400/2) To a flame-dried two necked round-bottom flask were added 1-bromo-2,4,5-trifluorobenzene (422.0 mg, 2.0 mmol), $Pd(OAc)_2$ (90.0 mg, 0.4 mmol) and DPPP (330.0 mg, 0.8 mmol). The mixture was purged and refilled with argon three times using Schlenk technique, and Dimethyl sulfoxide-d6 (2.0 ml) and $[bmim][BF_4]$ (2.0 ml) were added under argon. Allyl alcohol (0.3 ml, 4.0 mmol) and Et_3N (0.4 ml, 3.0 mmol) were sequentially injected. The flask was placed in an oil bath, stirred and heated at 115 °C for 3 days. After cooling to room temperature, the product was extracted with CH_2Cl_2 (3x40.0 ml). The combined organic layer was washed with H_2O (2x20.0 ml) then dried over $MgSO_4$. After concentration to dryness under reduced pressure, flash chromatographic purification (petroleum ether/ethyl acetate 85:15, v/v) gave the title compound as a colorless oil (95 mg, 25%). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.22 – 7.15 (m, 1H), 6.96 – 6.89 (m, 1H), 5.55 (s, 1H), 5.39 (s, 1H), 4.44 (d, J = 1.0 Hz, 2H), 1.59 (s, 1H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(2,4,5-trifluorophenyl)prop-2-en-1-amine (SZV-2400/4).** To a solution of **(SZV-2400/2)** (95.0 mg, 0.5 mmol) in Et_2O (5.0 ml) was added dropwise MsCl (43 µl, 0.6 mmol) at 0 °C and the reaction mixture was stirred at this temperature for 1 h, following which H_2O (5.0 ml) was added. The product was extracted with Et_2O (3x10.0 ml). The combined organic layer was washed with $MgSO_4$ and concentrated under reduced pressure to give crude mesylate **(SZV-2400/3)** (133.0 mg, quant.), which was used directly in the following step without purification. To a solution of mesylate **(SZV-2400/3)** (169.8 mg, 0.6 mmol) in $CHCl_3$ were added *N*-methylpropargylamine (108 µl, 1.3 mmol) and solid Na_2CO_3 (329.0 mg, 1.6 mmol) and the stirred reaction mixture was heated at 50 °C overnight. After filtration and evaporation of the crude mixture, flash chromatographic purification (petroleum ether/ethyl acetate 90:10, v/v) afforded the title compound as a colorless oil (104 mg, 68% over 2 steps). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.14 (m, 1H), 6.93 – 6.80 (m, 1H), 5.49 (s, 1H), 5.40 (s, 1H), 3.39 (s, 2H), 3.33 (d, J = 2.0 Hz, 2H), 2.29 (s, 3H), 2.24 (t, J = 2.0 Hz, 1H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(2,4,5-trifluorophenyl)prop-2-en-1-aminium carboxyformate (SZV-2400).** Following the **method H1**, the title compound was isolated as a white solid (215.0 mg, 97%). Mp 138.9 - 139.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.49 – 7.42 (m, 1H), 7.25 – 7.18 (m, 1H), 5.82 (s, 1H), 5.70 (s, 1H), 4.07 (s, 2H), 3.88 (d, J = 2.4 Hz, 2H), 3.18 (t, J = 2.4 Hz, 1H), 2.75 (s, 3H). HRMS (ESI+) m/z calcd. for $C_{13}H_{12}F_3^+$ $[M+H]^+$ 240.0995, found 240.1005.

Scheme 27



tert-Butyl (2-bromoallyl)(methyl)carbamate (2). To a biphasic mixture of 40% aqueous solution of CH_3NH_2 (0.5 ml, 5.2 mmol) and chloroform (5.0 ml) was added Na_2CO_3 (369.0 mg, 3.5 mmol). 2,3-dibromopropene (0.2 ml, 1.7 mmol) was added slowly at room temperature and the reaction mixture was stirred at 50 °C overnight. After cooling down to room temperature was added dropwise a solution of di-*tert*-butyl dicarbonate (380.0 mg, 1.7 mmol) in CH_2Cl_2 (2.0 ml) and the reaction mixture was stirred for another 2 h at room temperature. H_2O (10 ml) was added to quench the reaction and the crude was extracted with CH_2Cl_2 (3x10.0 ml). The organic layers were combined and dried on $MgSO_4$. After concentration under reduced pressure, flash chromatographic purification on silica gel (petroleum ether/ethyl acetate 95:5, v/v) afforded **2** as a colorless oil (350 mg, 80%). ^{1}H NMR (400 MHz, Chloroform-d) δ 5.69 (s, 1H), 5.56 (s, 1H), 4.06 (brd, 2H), 2.87 (brd, 3H), 1.46 (s, 9H).

tert-Butyl methyl(2-(4-nitrophenyl)allyl)carbamate (SZV-2424/4). Following **method R1**, the first borylation was carried out on the same scale as described. The yield of **3** was estimated to be 82% (2.0 mmol). A small amount of crude **3** (estimated 0.114 mmol) was taken for the Suzuki reaction with 1-bromo-4-nitrobenzene (34.5 mg, 0.2 mmol), $Pd(OAc)_2$ (1.3 mg, 0.006 mmol), SPhos (4.9 mg, 0.012 mmol) and K_3PO_4 (38.4 mg, 0.4 mmol) to yield the title product as a colorless oil (20.5 mg, 50% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-d) δ 8.17 (d, J = 8.8 Hz, 2H), 7.57 (brs, 2H), 5.57 (brs, 1H), 5.32 (s, 1H), 4.35 (brs, 2H), 2.72 (brs, 3H), 1.43 (s, 9H).

***tert*-Butyl methyl(2-(3-(trifluoromethyl)phenyl)allyl)carbamate (SZV-2425/4)**. Following **method R1**, the first borylation was carried out on the same scale as described. The yield of **3** was estimated to be 92% (2.2 mmol) using CH_2Br_2 as the internal standard. Crude **3** was used for the Suzuki reaction with 1-bromo-3-(trifluoromethyl)benzene (742.5 mg, 3.3 mmol), $Pd(OAc)_2$ (24.7 mg, 0.1 mmol), SPhos (90.3 mg, 0.1 mmol) and K_3PO_4 (934 mg, 4.4 mmol) to yield the title product as a colorless oil (431.6 mg, 71% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (m, 4H), 5.50 (brd, 1H), 5.22 (brs, 1H), 4.31 (brd, 2H), 2.76 (brd, 3H), 1.43 (s, 9H).

***tert*-Butyl methyl(2-(2,4,6-trifluorophenyl)allyl)carbamate (SZV-2432/4)** Following **method R1**, the first borylation was carried out on the same scale as described. The yield of **3** was estimated to be 82% (2.0 mmol) using CH_2Br_2 as the internal standard. In the second step, 1-bromo-2,4,6-trifluorobenzene (622.0 mg, 2.9 mmol), $Pd(OAc)_2$ (22.1 mg, 0.1 mmol), SPhos (80.0 mg, 0.2 mmol) and K_3PO_4 (836.0 mg, 3.9 mmol) were used to yield the title product as a colorless oil (362.0 mg, 1.2 mmol, 50% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.65 (t, J = 8.0 Hz, 2H), 5.47 (brs, 1H), 5.23 (s, 1H), 4.08 (brs, 2H), 2.84 (brs, 3H), 1.34 (s, 9H).

***N*-Methyl-2-(4-nitrophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2424/5).** Following the **method M1,** title compound was isolated (83 mg, 45%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, J = 8.8 Hz, 2H), 7.68 (d, J = 8.8 Hz, 2H), 5.63 (d, J = 1.2 Hz, 1H), 5.47 (d, J = 1.2 Hz, 1H), 3.48 (d, J = 0.8 Hz, 2H), 3.34 (d, J = 2.4 Hz, 2H), 2.31 (s, 3H), 2.27 (t, J = 2.4 Hz, 1H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(3-(trifluoromethyl)phenyl)prop-2-en-1-amine (SZV-2425/5)** Following the **method M1,** title compound was isolated (143.8 mg, 51%) as a white solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (brs, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.44 (t, J = 7.8 Hz, 1H), 5.54 (d, J = 1.2 Hz, 1H), 5.37 (d, J = 1.2 Hz, 1H), 3.46 (d, J = 0.8 Hz, 2H), 3.36 (d, J = 2.4 Hz, 2H), 2.32 (s, 3H), 2.26 (t, J = 2.4 Hz, 1H).

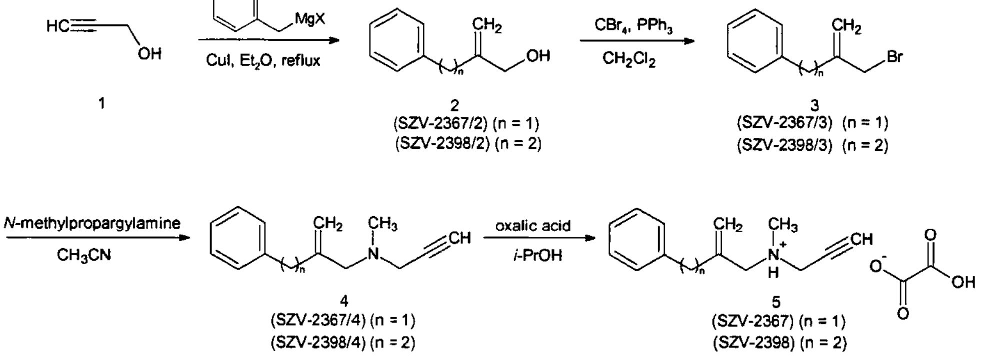
***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(2,4,6-trifluorophenyl)prop-2-en-1-amine (SZV-2432/5).** Following the **method M1,** the title compound was isolated (83 mg, 42%) as a yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.71 – 6.54 (m, 2H), 5.64 (s, 1H), 5.28 (brs, 1H), 3.35 (s 2H), 3.34 (d, J = 2.4 Hz, 2H), 2.28 (s, 3H), 2.21 (t, J = 2.4 Hz, 1H).

***N*-Methyl-2-(4-nitrophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate SZV-2424**. Following the **method H1**, the title compound was isolated as a white solid (114 mg, quant.). Mp 169.5-171.2°C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (d, J = 8.8 Hz, 2H), 7.68 (d, J = 8.8 Hz, 2H), 5.80 (s, 1H), 5.64 (s, 1H), 4.01 (s, 2H), 3.71 (d, J = 2.4 Hz, 2H), 3.03 (t, J = 2.4 Hz, 1H), 2.59 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{13}H_{14}N_2O_2^+$ $[M+H]^+$ 231.1128, found 231.1138.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(3-(trifluoromethyl)phenyl)prop-2-en-1-aminium carboxyformate) (SZV-2425)**. Following the **method H1**, the title compound was isolated as a white solid (194 mg, quant.) Mp 129.3 -129.8 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.85 (s, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 5.83 (s, 1H), 5.70 (s, 1H), 4.20 (s, 2H), 3.88 (d, *J* = 2.4 Hz, 2H), 3.19 (t, *J* = 2.4 Hz, 1H), 2.75 (s, 3H); Anal. calcd. for $C_{14}H_{14}F_3Nx(COOH)_2$ (343.30): C, 55.98%; H, 4.70%; N, 4.08%. Found: C, 55.84%; H, 4.98%; N, 3.81%.

_N_-Methyl-_N_-(prop-2-yn-1-yl)-2-(2,4,6-trifluorophenyl)prop-2-en-1-aminium carboxyformate (SZV-2432). Following the **method H1**, the title compound was isolated as a white solid (71 mg, 62%). Mp 129.1 -130.3 °C. ^{1}H NMR (400 MHz, Methanol-*d*$_4$) *δ* 6.92 (t, *J* = 8.8 Hz, 2H), 6.12 (s, 1H), 5.77 (s, 1H), 4.21 (s, 2H), 4.08 (d, *J* = 2.4 Hz, 2H), 2.94 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{13}H_{12}F_3N^+$ $[M+H]^+$ 240.0995, found 240.1002.

Scheme 28



2-Benzylprop-2-en-1-ol (SZV-2367/2) (Nielsen L et al, J. Am. Chem. Soc., 2008, 130, 13145-13151) Following the **method N**, the title compound was isolated as a colorless oil (28%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.28 (m, 2H), 7.23 – 7.20 (m, 3H), 5.13 (s, 1H), 4.91 (s, 1H), 4.05 (s, 2H), 3.42 (s, 2H).

2-Methylene-4-phenylbutan-1-ol (SZV-2398/2) (Clark JS et al, J. Org. Chem., 2004, 69, 3886-3898) Following the **method N**, the title compound was isolated as a colorless oil (67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.26 (m, 2H), 7.24 – 7.15 (m, 3H), 5.07 (s, 1H), 4.93 (s, 1H), 4.10 (s, 2H), 2.80 (t, *J* = 8.0 Hz, 2H), 2.39 (t, *J* = 8.0 Hz, 2H).

(2-(Bromomethyl)allyl)benzene (SZV-2367/3) (Kozyrkov YYK et al, Synlett, 2002, 3, 443-446) Following the **method O**, the title compound was isolated as a colorless oil (57%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.29 (m, 2H), 7.25 – 7.21 (m, 3H), 5.24 (brs, 1H), 4.98 (q, *J* = 1.2 Hz, 1H), 3.89 (d, *J* = 0.4 Hz, 2H), 3.56 (s, 2H).

(3-(Bromomethyl)but-3-en-1-yl)benzene (SZV-2398/3) Following the **method O**, the title compound was isolated as a colorless oil (86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.26 (m, 2H), 7.24 – 7.16 (m, 3H), 5.21 (s, 1H), 5.00 (d, *J* = 1.2 Hz, 1H), 3.98 (d, *J* = 0.4 Hz, 2H), 2.81 (t, *J* = 8.0 Hz, 2H), 2.55 (t, *J* = 8.0 Hz, 2H).

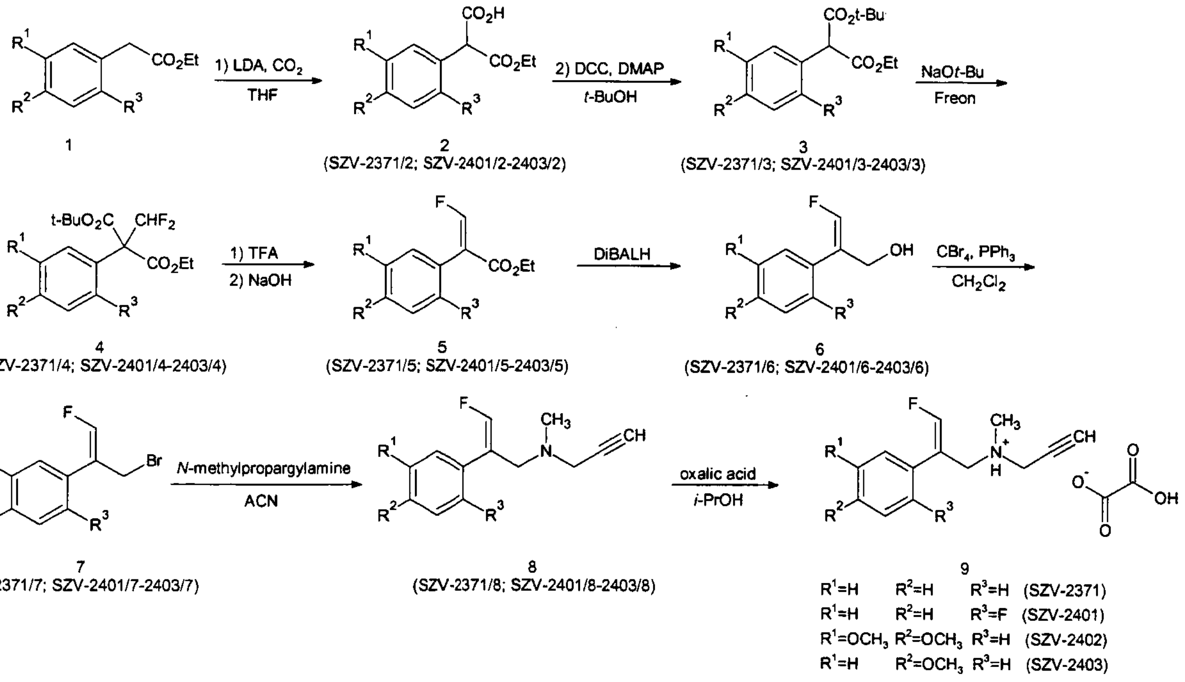
2-Benzyl-_N_-methyl-_N_-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2367/4) Following the **method D8**, the compound was isolated as a colorless oil (80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.18 (m, 5H), 5.03 (s, 1H), 4.86 (s, 1H), 3.39 (s, 2H), 3.31 (d, *J* = 2.4 Hz, 2H), 2.90 (s, 2H), 2.28 (s, 3H), 2.19 (t, *J* = 2.4 Hz, 1H).

N-methyl-2-methylene-4-phenyl-N-(prop-2-yn-1-yl)butan-1-amine (SZV-2398/4) Following the **method D8**, the title compound was isolated as a colorless oil (55%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.27 (m, 2H), 7.22 – 7.15 (m, 3H), 5.00 (s, 1H), 4.92 (s, 1H), 3.31 (d, *J* = 0.4 Hz, 2H), 3.00 (s, 2H), 2.78 (t, *J* = 8.0 Hz, 2H), 2.40 (t, *J* = 8.0 Hz, 2H), 2.28 (s, 3H), 2.22 (t, *J* = 2.4 Hz, 1H).

2-Benzyl-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2367) Following the **method H1**, the title compound was isolated as a white solid (58%). Mp 115.8 – 118.2 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.36 – 7.25 (m, 2H), 7.22 – 7.18 (m, 3H), 5.03 (s, 1H), 4.87 (s, 1H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.34 (s, 2H), 3.20 (t, *J* = 2.4 Hz, 1H), 2.95 (s, 2H), 2.25 (s, 3H). Anal. calcd. for $C_{14}H_{17}N$x$(COOH)_2$ (289.33): C, 66.42%; H, 6.62%; N, 4.84%. Found: C, 66.23%; H, 6.41%; N, 4.78%.

N-Methyl-2-methylene-4-phenyl-N-(prop-2-yn-1-yl)butan-1-aminium carboxyformate (SZV-2398) Following the **method H1**, the title compound was isolated as a white solid (38%). Mp 116.9 -118.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.29 – 7.25 (m, 2H), 7.22 – 7.14 (m, 3H), 4.96 (s, 1H), 4.93 (s, 1H), 3.36 (s, 2H), 3.23 (s, 1H), 3.05 (s, 2H), 2.72 (t, *J* = 8.0 Hz, 2H), 2.32 (t, *J* = 8.0 Hz, 2H), 2.24 (s, 3H). Anal. calcd. for $C_{15}H_{19}N$x$(COOH)_2$ (303.35): C, 67.31%; H, 6.98%; N, 4.62%. Found: C, 67.38%; H, 6.80%; N, 4.59%.

Scheme 29



To a solution of DIPA (1.4 eq) in THF (0.7 M) at – 78 °C, was added ^{n}BuLi (1.3 eq) dropwise. The reaction was stirred for 5 mins then at 0 °C for 10 mins before being cooled to – 78 °C. A solution of the ester (1 eq) in THF (0.8 M) was added dropwise. The anion was stirred for 1 h at – 78 °C before the addition of a few pieces of dry ice. Reaction was allowed to warm to rt over 1 h before the addition of EtOAc and H_2O. The aqueous layer was collected, acidified to pH 1, and extracted with EtOAc. The organic extracts were combined, dried ($MgSO_4$) and concentrated to afford the acid **2** which was used for the next step without further purification.

3-Ethoxy-3-oxo-2-phenylpropanoic acid (SZV-2371/2) (Niwayama S J. Org. Chem., 2000, 65, 5834-5836) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.34 (m, 5H), 4.64 (s, 1H), 4.29 – 4.19 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H).

3-Ethoxy-2-(2-fluorophenyl)-3-oxopropanoic acid (SZV-2401/2) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (td, *J* = 7.6, 1.6 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.17 (td, *J* = 7.6, 1.2 Hz, 1H), 7.09 (ddd, *J* = 9.6, 8.4, 1.2 Hz, 1H), 5.00 (s, 1H), 4.30 – 4.20 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H).

2-(3,4-Dimethoxyphenyl)-3-ethoxy-3-oxopropanoic acid (SZV-2402/2) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.95 (d, *J* = 2.0 Hz, 1H), 6.93 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 4.57 (s, 1H), 4.29 – 4.17 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).

3-Ethoxy-2-(4-methoxyphenyl)-3-oxopropanoic acid (SZV-2403/2) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.58 (s, 1H), 4.30 – 4.18 (m, 2H), 3.80 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).

To the acid **2** (1 eq) in CH_2Cl_2 (170.0 mmol) at 0 °C, was added DMAP (0.03 eq), ^{t}BuOH (1.7 eq) followed by DCC (1.3 eq). The reaction was stirred at rt overnight. The next day, the white solid was filtered and the filtrate was purified by column chromatography eluting with 10% EtOAc/petrol to give the diester **3**.

1-*tert*-Butyl 3-ethyl 2-phenylmalonate (SZV-2371/3) (McDonald IA et al, J. Med. Chem., 1985, 28, 186-193) The title compound was isolated as a colorless oil (81% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.30 (m, 5H), 4.52 (s, 1H), 4.26 – 4.17 (m, 2H), 1.46 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H).

1-*tert*-Butyl 3-ethyl 2-(2-fluorophenyl)malonate (SZV-2401/3) The title compound was isolated as a colorless oil (84% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (td, *J* = 7.6, 1.6 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.15 (td, *J* = 7.6, 1.2 Hz, 1H), 7.07 (ddd, *J* = 9.6, 8.4, 1.2 Hz, 1H), 4.89 (s, 1H), 4.28 – 4.19 (m, 2H), 1.47 (s, 9H), 1.28 (t, *J* = 7.2 Hz, 3H).

1-*tert*-Butyl 3-ethyl 2-(3,4-dimethoxyphenyl)malonate (SZV-2402/3) (McDonald IA et al, J. Med. Chem., 1985, 28, 186-193) The title compound was isolated as a colorless oil (85% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.97 (d, *J* = 2.0 Hz, 1H), 6.91 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 4.45 (s, 1H), 4.26 – 4.16 (m, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 1.46 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H).

1-*tert*-Butyl 3-ethyl 2-(4-methoxyphenyl)malonate (SZV-2403/3) The title compound was isolated as a colorless oil (78% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 4.46 (s, 1H), 4.28 – 4.11 (m, 2H), 3.80 (s, 3H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H).

NaO^{t}Bu (2.7 to 2.9 eq) was added to a solution of ester **3** (1 eq) in THF (0.11 l/g) in a reactor. The reactor was pressurized to 9 bar with Freon gas overnight. The next day, the pressure was released slowly and most of the THF was removed in vacuo before the addition of EtOAc and H_2O. The aqueous layer was extracted with EtOAc (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. Purification by flash chromatography with 10% EtOAc/petrol as eluent gave **4** as an oil.

1-*tert*-Butyl 3-ethyl 2-(difluoromethyl)-2-phenylmalonate (SZV-2371/4) (McDonald IA et al, J. Med. Chem., 1985, 28, 186-193) The title compound was isolated as a colorless oil (86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.33 (m, 5H), 6.48 (t, *J* = 54.8 Hz, 1H), 4.39 – 4.31 (m, 2H), 1.51 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H).

1-*tert*-Butyl 3-ethyl 2-(difluoromethyl)-2-(2-fluorophenyl)malonate (SZV-2401/4) The title compound was isolated as a colorless oil (44%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (t, *J* = 7.6 Hz, 1H), 7.42 – 7.32 (m, 1H), 7.18 (td, *J* = 7.6, 1.2 Hz, 1H), 7.11 – 7.05 (m, 1H), 6.62 (t, *J* = 55.2 Hz, 1H), 4.38 – 4.29 (m, 2H), 1.50 (s, 8H), 1.30 (t, *J* = 7.2 Hz, 3H).

1-*tert*-Butyl 3-ethyl 2-(difluoromethyl)-2-(3,4-dimethoxyphenyl)malonate (SZV-2402/4) (McDonald IA et al, J. Med. Chem., 1985, 28, 186-193) The title compound was isolated as a colorless oil (76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.93 – 6.85 (m, 3H), 6.44 (t, *J* = 55.2 Hz, 1H), 4.33(q, *J* = 7.2 Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 1.51 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H).

1-*tert*-Butyl 3-ethyl 2-(difluoromethyl)-2-(4-methoxyphenyl)malonate (SZV-2403/4) The title compound was isolated as a colorless oil (75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (d, *J* = 9.2 Hz, 2H), 6.91 (d, *J* = 9.2 Hz, 2H), 6.45 (t, *J* = 55.2 Hz, 1H), 4.37 – 4.29 (m, 2H), 3.81 (s, 3H), 1.51 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H).

TFA (11 eq) was added to the difluoro compound **4** (1 eq) and the reaction mixture was stirred for 40 mins. The reagent was removed in vacuo, then azeotroped with MeOH and dried on pump to afford the crude acid. To the acid (1 eq) was added THF (2000.0 mmol) and NaOH (2000.0 mmol, 1 eq) and the mixture was stirred for 15 mins before the addition of EtOAc and H_2O. The aqueous layer was extracted with EtOAc (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. Purification by flash chromatography with 10% EtOAc/petrol as eluent gave **5** as an oil.

(*E*)-Ethyl 3-fluoro-2-phenylacrylate (SZV-2371/5) The title compound was isolated as a colorless oil (68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 80.8 Hz, 1H), 7.44 - 7.30 (m, 5H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H).

(*E*)-Ethyl 3-fluoro-2-(2-fluorophenyl)acrylate (SZV-2401/5) The title compound was isolated as a colorless oil (88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 79.6 Hz, 1H), 7.40 – 7.33 (m, 1H), 7.28 (td, *J* = 7.6, 1.2 Hz, 1H), 7.17 (td, *J* = 7.6, 1.2 Hz, 1H), 7.11 (ddd, *J* = 9.6, 8.4, 1.2 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H).

(*E*)-Ethyl 2-(3,4-dimethoxyphenyl)-3-fluoroacrylate (SZV-2402/5) (McDonald IA et al, J. Med. Chem., 1985, 28, 186-193) The title compound was isolated as a colorless oil (81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 80.8 Hz, 1H), 6.96 – 6.87 (m, 3H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H).

(*E*)-Ethyl 3-fluoro-2-(4-methoxyphenyl)acrylate (SZV-2403/5) The title compound was isolated as a colorless oil (86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 81.2 Hz, 1H), 7.30 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H).

To a solution of ester **5** (1 eq) in THF (22 g/L) was added DiBALH (1.0 M, 2.6 eq) at 0 °C. The reaction was stirred for 1 h at 0 °C. The progress of the reaction was monitored by TLC. When TLC indicated complete consumption of the starting material, EtOAc and H_2O were added. The aqueous layer was extracted with EtOAc (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. Purification by flash chromatography with 20% EtOAc/petrol as eluent gave **6** as an oil.

(*E*)-3-Fluoro-2-phenylprop-2-en-1-ol (SZV-2371/6) (McDonald IA et al, J. Med. Chem., 1985, 28, 186-193) The title compound was isolated as a colorless oil (68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.35 – 7.29 (m, 1H), 6.89 (d, *J* = 82.4 Hz, 1H), 4.40 (t, *J* = 4.4 Hz, 2H), 1.47 (brs, 1H).

(*E*)-3-Fluoro-2-(2-fluorophenyl)prop-2-en-1-ol (SZV-2401/6) The title compound was isolated as a colorless oil (74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.29 (m, 2H), 7.17 (td, *J* = 7.6, 0.8 Hz, 1H), 7.14 – 7.09 (m, 1H), 6.90 (d, *J* = 82.4 Hz, 1H), 4.37 (d, *J* = 4.4 Hz, 2H).

(*E*)-2-(3,4-Dimethoxyphenyl)-3-fluoroprop-2-en-1-ol (SZV-2402/6) (McDonald IA et al, J. Med. Chem., 1985, 28, 186-193) The title compound was isolated as a colorless oil (86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (d, *J* = 2.0 Hz, 1H), 7.10 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 82.4 Hz, 1H), 4.37 (dd, *J* = 4.4, 1.2 Hz, 2H), 3.89 (s, 6H).

(*E*)-3-Fluoro-2-(4-methoxyphenyl)prop-2-en-1-ol (SZV-2403/6) The title compound was isolated as a colorless oil (83%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 82.8 Hz, 1H), 4.37 (dd, *J* = 4.4, 1.2 Hz, 2H), 3.83 (s, 3H).

(*E*)-(3-Bromo-1-fluoroprop-1-en-2-yl)benzene (SZV-2371/7) Following the **method O**, the title compound was isolated as a colorless oil (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.37 – 7.33 (m, 1H), 7.01 (d, *J* = 80.8 Hz, 1H), 4.24 (dd, *J* = 4.0, 0.4 Hz, 2H).

(*E*)-1-(3-Bromo-1-fluoroprop-1-en-2-yl)-2-fluorobenzene (SZV-2401/7) Following the **method O**, the title compound was isolated as a colorless oil (88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.33 (m, 2H), 7.19 (td, *J* = 7.6, 1.2 Hz, 1H), 7.15 – 7.09 (m, 1H), 6.99 (d, *J* = 80.4, 1H), 4.24 (dd, *J* = 3.6, 0.8 Hz, 2H).

(*E*)-4-(3-Bromo-1-fluoroprop-1-en-2-yl)-1,2-dimethoxybenzene (SZV-2402/7) Following the **method O**, the title compound was isolated as a colorless oil (89%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.11 – 7.07 (m, 2.5H), 6.92 – 6.88 (m, 1.5H), 4.23 (d, *J* = 4.0 Hz, 2H), 3.91 (s, 6H).

(*E*)-1-(3-Bromo-1-fluoroprop-1-en-2-yl)-4-methoxybenzene (SZV-2403/7) Following the **method O**, the title compound was isolated as a colorless oil (76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 81.2 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 4.22 (d, *J* = 4.0 Hz, 2H), 3.84 (s, 3H).

(*E*)-3-Fluoro-*N*-methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2371/8) Following the **method D8**, the title compound was isolated as a colorless oil (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.29 – 7.26 (m, 1H), 6.80 (d, *J* = 83.6 Hz, 1H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.26 (dd, *J* = 3.6, 0.8 Hz, 2H), 2.31 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

(*E*)-3-Fluoro-2-(2-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2401/8) Following the **method D8**, the title compound was isolated as a colorless oil (97%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.27 (m, 2H), 7.14 (td, *J* = 7.6, 1.2 Hz, 1H), 7.08 (ddd, *J* = 9.6, 8.4, 1.2 Hz, 1H), 6.82 (d, *J* = 82.8 Hz, 1H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.30 (d, *J* = 1.2 Hz, 2H), 2.30 (s, 3H), 2.24 (t, *J* = 2.4 Hz, 1H).

(*E*)-2-(3,4-Dimethoxyphenyl)-3-fluoro-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2402/8)

Following the **method D8**, the title compound was isolated as a colorless oil (73%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (d, *J* = 2.0 Hz, 1H), 7.14 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 82.4 Hz, 1H), 3.880 (s, 3H), 3.881 (s, 3H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.24 (d, *J* = 3.6 Hz, 2H), 2.32 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

(*E*)-3-Fluoro-2-(4-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2403/8) Following the **method D8**, the title compound was isolated as a colorless oil (87%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 84.0 Hz, 1H), 3.81 (s, 3H), 3.37 (d, *J* = 2.4 Hz, 2H), 3.24 (d, *J* = 3.6 Hz, 2H), 2.31 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

(E)-3-Fluoro-*N*-methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2371) Following the **method H1**, the title compound was isolated as a colorless oil (67%). Mp 153-155 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 84.0 Hz, 1H), 3.32 (d, *J* = 2.0

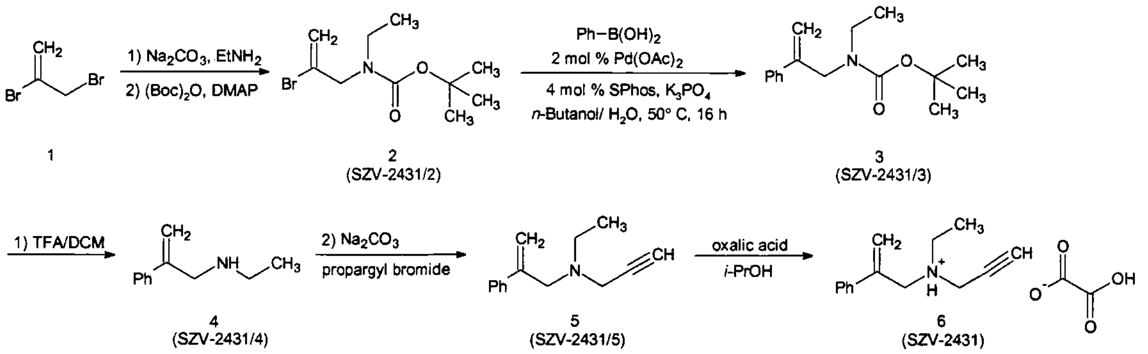
Hz, 2H), 3.28 (d, $J = 3.2$ Hz, 2H), 3.20 (brs, 1H), 2.19 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{13}H_{15}FN^+$ $[M+H]^+$ 204.1183, found 204.1184.

(E)-3-Fluoro-2-(2-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2401) Following the **method H1**, the title compound was isolated as a white solid (77%). Mp 149.4 – 151.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.46 – 7.32 (m, 2H), 7.23 – 7.17 (m, 2.5H), 7.00 (s, 0.5H), 3.34 (d, $J = 2.4$ Hz, 2H), 3.32 (d, $J = 2.4$ Hz, 2H), 3.21 (t, $J = 2.4$ Hz, 1H), 2.21 (s, 3H). Anal. calcd. for $C_{13}H_{13}F_2N$x$(COOH)_2$ (311.28): C, 57.88%; H, 4.86%; N, 4.50%. Found: C, 57.81%; H, 4.85%; N, 4.51%.

(E)-2-(3,4-Dimethoxyphenyl)-3-fluoro-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2402) Following the **method H1**, the title compound was isolated as a white solid (70%). Mp 122.7 - 124.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.13 – 7.02 (m, 2.5H), 6.94 (d, $J = 8.4$ Hz, 1H), 6.89 (s, 0.5H), 3.76 (s, 3H), 3.74 (s, 3H), 3.38 (brs, 2H), 3.33 (brs, 2H), 3.25 (brs, 1H), 2.24 (brs, 3H). Anal. calcd. for $C_{15}H_{18}FNO_2$x$(COOH)_2$ (353.34): C, 57.79%; H, 5.71%; N, 3.96%. Found: C, 57.32%; H, 5.61%; N 3.92%.

(E)-3-Fluoro-2-(4-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2403) Following the **method H1**, the title compound was isolated as a white solid (80%). Mp 144.0 -147.7 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.44 (d, $J = 8.8$ Hz, 2H), 6.99 (d, $J = 84.0$ Hz, 1H), 6.93 (d, $J = 8.8$ Hz, 2H), 3.76 (s, 3H), 3.36 (brs, 2H), 3.30 (brs, 2H), 3.24 (brs, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{14}H_{16}FNO$x$(COOH)_2$ (323.32): C, 59.44%; H, 5.61%; N, 4.33%. Found: C, 59.52%; H, 5.71%; N, 4.37%.

Scheme 30



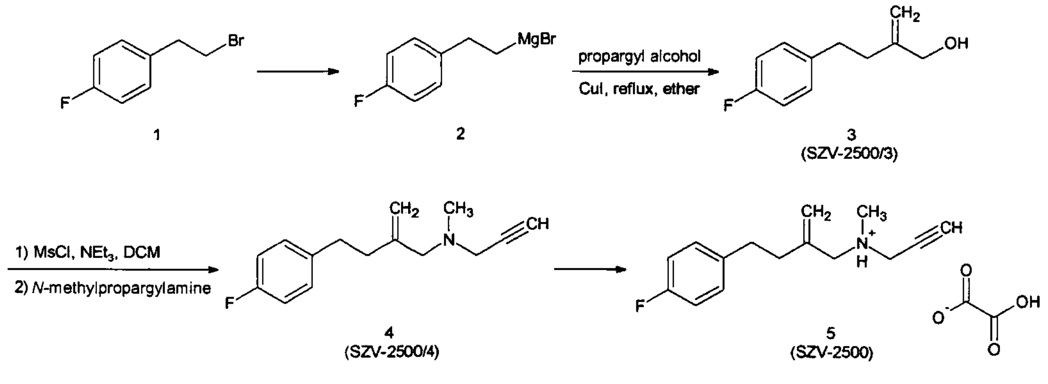
***tert*-Butyl (2-bromoallyl)(ethyl)carbamate (SZV-2431/2)** 2, 3-dibromopropene (2.0 ml, 8.5 mmol) was dissolved in $CHCl_3$ (21.0 ml) and ethyl amine (79% in H_2O, 3.4 ml, 42.5 mmol) followed by Na_2CO_3 (1.8 g, 17.0 mmol) were added. The reaction was heated to 50 °C overnight. The reaction mixture was filtered and the organic phase collected and concentrated at 500 mbar. Because the product is volatile, the mixture need not be evaporated to dryness. CH_2Cl_2 (10.0 ml) was added to the solution containing the crude product, followed by DMAP (31.2 mg, 0.26 mmol), di-*tert*-butyl-dicarbonate (2.3 ml, 10.0 mmol) were added at 0° C. The reaction was allowed to warm to rt overnight. Most of the solvent was removed in vacuo to give a crude which was purified by flash chromatography using 5% EtOAc/petrol as eluent to give the title compound (251.0 mg, 46%) as an oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.70 (s, 1H), 5.54 (brs, 1H), 4.04 (brd, 2H), 3.28 (brs, 2H), 1.46 (s, 9H), 1.11 (t, *J* = 7.2 Hz, 3H).

***tert*-Butyl ethyl(2-phenylallyl)carbamate (SZV-2431/3)** Following **method P1**, but it was used tert-butyl (2-bromoallyl) (ethyl)carbamate, n-BuOH, SPhos, conventional heating for 16 h at 60 °C, the title compound was isolated (470.4 mg, 92%) as an oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.39 (brs, 2H), 7.34 – 7.27 (m, 3H), 5.40 (brd, 1H), 5.12 (s, 1H), 4.28 (brd, 2H), 3.20 (brd, 2H), 1.45 (s, 9H), 1.06 (brs, 3H).

***N*-Ethyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2431/4)** Following **method M1**, using Na_2CO_3 (2 eq) and propargyl bromide (2 eq) and heating at 40 °C for 30 mins, the title compound was isolated as a colorless oil. (56% over 2 steps) as ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 – 7.46 (m, 2H), 7.37 – 7.23 (m, 3H), 5.48 (d, *J* = 2.0 Hz, 1H), 5.32 (dd, *J* = 2.8, 1.2 Hz, 1H), 3.50 (d, *J* = 1.2 Hz, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 2.61 (q, *J* = 7.2 Hz, 2H), 2.19 (t, *J* = 2.4 Hz, 1H), 1.08 (t, *J* = 7.2 Hz, 3H).

***N*-Ethyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2431)** To the amine (89.6 mg, 0.5 mmol) in *i*-PrOH (0.4 ml) was added a solution of oxalic acid (40.4 mg, 0.5 mmol) in ^{i}PrOH (0.4 ml). White solid did not form even after the reaction was left at 0° C overnight. The oil was left stirring in ether for 3 d. Eventually, the white solid which formed was filtered, washed with cold ether and dried to give the title compound (86.8 mg, 67%). Mp 84.4 – 86.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.53 – 7.51 (m, 2H), 7.35 – 7.26 (m, 3H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.29 (d, *J* = 1.2 Hz, 1H), 3.53 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.17 (t, *J* = 2.4 Hz, 1H), 2.57 (q, *J* = 7.2 Hz, 2H), 1.00 (t, *J* = 7.2 Hz, 3H). HRMS (ESI+) *m/z* calcd. for $C_{16}H_{19}NNaO_4^+$ $[M+Na]^+$ 312.1206, found 312.1202.

Scheme 31

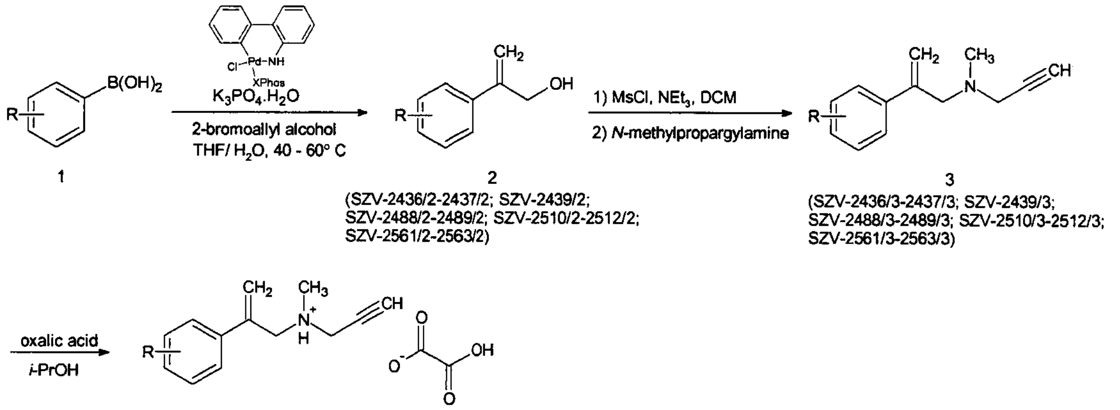


4-(4-Fluorophenyl)-2-methylenebutan-1-ol (SZV-2500/3) Following **method N**, purification by flash chromatography using 5% to 20% EtOAc/petrol as eluent gave the desired alcohol (32 mg, 6%) as a colorless oil and the Wurtz coupled product (15%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 – 7.12 (m, 2H), 6.96 (t, *J* = 8.8 Hz, 2H), 5.06 (d, *J* = 0.4 Hz, 1H), 4.90 (q, *J* = 1.2 Hz, 1H), 4.09 (s, 2H), 2.76 (t, *J* = 8.4 Hz, 2H), 2.36 (t, *J* = 8.4 Hz, 2H).

4-(4-Fluorophenyl)-*N*-methyl-2-methylene-*N*-(prop-2-yn-1-yl)butan-1-amine (SZV-2500/4) Following **method D9**, the title compound was isolated (51%) as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (dd, *J* = 8.8, 5.6 Hz, 2H), 6.95 (t, *J* = 8.8 Hz, 2H), 4.99 (s, 1H), 4.89 (s, 1H), 3.30 (d, *J* = 2.4 Hz, 2H), 2.99 (s, 2H), 2.74 (t, *J* = 7.6 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 2.27 (s, 3H), 2.22 (t, *J* = 2.4 Hz, 1H).

4-(4-Fluorophenyl)-*N*-methyl-2-methylene-*N*-(prop-2-yn-1-yl)butan-1-aminium carboxyformate (SZV-2500) Following **method H1**, the title compound was isolated (32.7 mg, 61%) as a white solid. Mp 118.4 - 119.1 °C. ^{1}H NMR (600 MHz, Methanol-d_4) δ 7.23 (dd, *J* = 8.4, 5.4 Hz, 2H), 6.99 (t, *J* = 8.4 Hz, 2H), 5.34 (s, 2H), 3.99 (d, *J* = 2.4 Hz, 2H), 3.75 (s, 2H), 2.85 (s, 3H), 2.81 (t, *J* = 7.8 Hz, 2H), 2.45 (t, *J* = 7.8 Hz, 2H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{19}FN$ [M+H]$^+$ 232.1496, found 232.1502.

Scheme 32



1

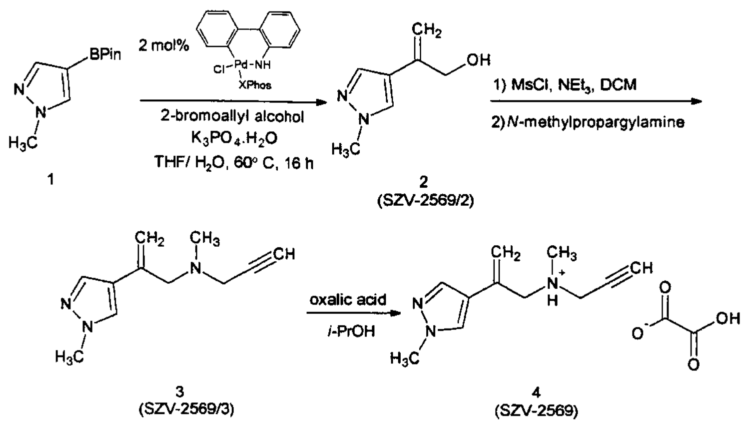
2
(SZV-2436/2-2437/2; SZV-2439/2; SZV-2488/2-2489/2; SZV-2510/2-2512/2; SZV-2561/2-2563/2)

3
(SZV-2436/3-2437/3; SZV-2439/3; SZV-2488/3-2489/3; SZV-2510/3-2512/3; SZV-2561/3-2563/3)

4

R = 3-CH_3, 4-OCH_3	(SZV-2436)
R = 3-OCH_3, 4-OCH_3	(SZV-2437)
R = 3,4-ethylenedioxy	(SZV-2439)
R = 3-CH_3	(SZV-2488)
R = 3-OCH_3	(SZV-2489)
R = 3-Ph	(SZV-2510)
R = 3-F, 4-Cl	(SZV-2511)
R = 3-N(CH_3)$_2$	(SZV-2512)
R = 2-F, 3-OCH_3	(SZV-2561)
R = 2-F, 5-OCH_3	(SZV-2562)
R = 4-F, 3-OCH_3	(SZV-2563)

Scheme 33



2-(4-Methoxy-3-methylphenyl)prop-2-en-1-ol (SZV-2436/2) Following the **method P2**, the title compound was isolated (66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.23 (m, 2H), 6.80 (d, *J* = 8.8 Hz, 1H), 5.38 – 5.37 (m, 1H), 5.24 (q, *J* = 1.2 Hz, 1H), 4.51 (d, *J* = 5.2 Hz, 2H), 3.84 (s, 3H), 2.23 (s, 3H), 1.54 (t, *J* = 5.2 Hz, 1H).

2-(3,4-Dimethoxyphenyl)prop-2-en-1-ol (Gong W et al, Chem. Lett., 2012, 41, 1597-1599) **(SZV-2437/2)**Following the **method P2**, the title compound was isolated (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.02 – 6.99 (m, 2H), 6.85 (d, *J* = 8.8 Hz, 1H), 5.45 – 5.36 (m, 1H), 5.28 (q, *J* = 1.2 Hz, 1H), 4.51 (s, 2H), 3.90 (s, 3H), 3.88 (s, 3H).

2-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)prop-2-en-1-ol (SZV-2439/2) Following the **method P2**, the title compound was isolated (68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.98 (d, *J* = 2.4 Hz, 1H), 6.95 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 5.38 (d, *J* = 0.8 Hz, 1H), 5.25 (q, *J* = 1.2 Hz, 1H), 4.48 (d, *J* = 4.0 Hz, 2H), 4.26 (s, 4H), 1.57 (t, *J* = 4.0 Hz, 1H).

2-(m-tolyl)prop-2-en-1-ol (SZV-2488/2) Following the **method P2**, the title compound was isolated (54%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.26 (m, 3H), 7.16 – 7.13 (m, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.35 (d, *J* = 1.2 Hz, 1H), 4.55 (s, 2H), 2.39 (s, 3H).

2-(3-Methoxyphenyl)prop-2-en-1-ol (SZV-2489/2) Following the **method P2**, the title compound was isolated (52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (t, *J* = 8.0 Hz, 1H), 7.05 – 7.03 (m, 1H), 6.99 (t, *J* = 2.4 Hz, 1H), 6.86 (ddd, *J* = 8.4, 2.8, 0.8 Hz, 1H), 5.47 (d, *J* = 0.8 Hz, 1H), 5.35 (q, *J* = 1.2 Hz, 1H), 4.53 (d, *J* = 5.6 Hz, 2H), 3.83 (s, 3H), 1.58 (t, *J* = 5.6 Hz, 1H).

2-([1,1'-Biphenyl]-3-yl)prop-2-en-1-ol (SZV-2510/2) Following the **method P2**, subsequent purification by column chromatography using 10% - 30% EtOAc/petrol afforded the title compound as a colorless oil (170 mg, 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.65 (m, 1H), 7.62 – 7.58 (m, 2H), 7.56 – 7.50 (m, 1H), 7.49 – 7.41 (m, 4H), 7.36 (tt, *J* = 7.6, 1.2 Hz, 1H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.40 (d, *J* = 1.2 Hz, 1H), 4.60 (s, 2H).

2-(4-Chloro-3-fluorophenyl)prop-2-en-1-ol (SZV-2511/2) Following the **method P2**, subsequent, purification by column chromatography using 10% - 30% EtOAc/petrol afforded the title compound as a colorless oil (125 mg, 47%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (t, *J* = 8.0, 1H), 7.26 (dd, *J* = 10.4, 2.0 Hz, 1H), 7.19 (ddd, *J* = 8.0, 2.0, 0.8 Hz, 1H), 5.50 (s, 1H), 5.42 (s, 1H), 4.50 (s, 2H).

2-(3-(Dimethylamino)phenyl)prop-2-en-1-ol (SZV-2512/2) Following the **method P2**, subsequent purification by column chromatography using 30% EtOAc/petrol afforded the title compound as a colorless oil (137 mg, 68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (t, *J* = 7.6 Hz, 1H), 6.83 – 6.76 (m, 2H), 6.74 – 6.69 (m, 1H), 5.43 (d, *J* = 1.2 Hz, 1H), 5.32 (q, *J* = 1.2 Hz, 2H), 4.53 (s, 2H), 2.97 (s, 6H).

2-(2-Fluoro-3-methoxyphenyl)prop-2-en-1-ol (SZV-2561/2) Following the **method P2**, subsequent, purification by column chromatography using 5% - 20% EtOAc/petrol afforded the title compound as a colorless oil (224 mg, 92%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.05 (td, *J* = 7.6, 1.6 Hz, 1H), 6.94 – 6.87 (m, 2H), 5.53 (d, *J* = 1.2 Hz, 1H), 5.38 (s, 1H), 4.48 (d, *J* = 1.2 Hz, 2H), 3.89 (s, 3H).

2-(3-Fluoro-5-methoxyphenyl)prop-2-en-1-ol (SZV-2562/2) Following the **method P2**, subsequent purification by column chromatography using 5% - 20% EtOAc/petrol afforded the title compound as a colorless oil (126 mg, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.79 – 6.74 (m, 2H), 6.57 (dt, *J* = 10.4, 2.4 Hz, 1H), 5.48 (d, *J* = 0.8 Hz, 1H), 5.39 (d, *J* = 0.8 Hz, 1H),4.49 (s, 2H), 3.81 (s, 3H).

2-(4-Fluoro-3-methoxyphenyl)prop-2-en-1-ol (SZV-2563/2) Following the **method P2**, subsequent purification by column chromatography using 5% - 20% EtOAc/petrol afforded the title compound as a colorless oil (157 mg, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 – 7.01 (m, 2H), 6.99 – 6.95 (m, 1H), 5.41 (s, 1H), 5.34 (d, *J* = 0.8 Hz, 1H), 4.51 (d, *J* = 0.8 Hz, 2H), 3.91 (s, 3H).

2-(1-Methyl-1*H*-pyrazol-4-yl)prop-2-en-1-ol (SZV-2569/2) Following the **method P2**, subsequent purification by column chromatography using 50% - 80% EtOAc/petrol afforded the title compound as a colorless oil (93 mg, 54%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (s, 1H), 7.46 (s, 1H), 5.30 (s, 1H), 5.11 (d, *J* = 1.2 Hz, 1H), 4.35 (brs, 2H), 3.86 (s, 3H).

2-(4-Methoxy-3-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2436/3) Following the **method D9**, the title compound was isolated (75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 5.38 (d, *J* = 2.0 Hz, 1H), 5.18 (q, *J* = 1.2 Hz, 1H), 3.82 (s, 3H), 3.42 (d, *J* = 1.2 Hz, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H), 2.22 (s, 3H).

2-(3,4-Dimethoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2437/3) Following the **method D9**, the title compound was isolated (75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.10 – 7.08 (m, 2H), 6.83 (d, *J* = 8.8 Hz, 1H), 5.41 (d, *J* = 1.6 Hz, 1H), 5.21 (d, *J* = 1.6 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.43 (d, *J* = 0.8 Hz, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2439/3) Following the **method D9**, the title compound was isolated (65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.06 (d, *J* = 2.0 Hz, 1H), 7.01 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 5.39 (d, *J* = 1.6 Hz, 1H), 5.19 (d, *J* = 1.6 Hz, 1H), 4.25 (s, 4H), 3.39 (d, *J* = 0.8 Hz, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 2.31 (s, 3H), 2.24 (t, *J* = 2.4 Hz, 1H).

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(m-tolyl)prop-2-en-1-amine (SZV-2488/2)** Following the **method D9**, the title compound was isolated (78%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.30 – 7.29 (m, 2H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.28 (s, 1H), 3.45 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.36 (s, 3H), 2.33 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(3-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2489/3) Following the **method D9**, the title compound was isolated (84%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.25 (t, *J* = 7.8 Hz, 1H), 7.10 – 7.08 (m, 1H), 7.07 (t, *J* = 2.4 Hz, 1H), 6.83 (ddd, *J* = 7.8, 3.0, 0.4 Hz, 1H), 5.49 (s, 1H), 5.30 (s, 1H), 3.82 (s, 3H), 3.45 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.33 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-([1,1'-Biphenyl]-3-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2510/3) Following **method D9**, subsequently purification by column chromatography using 20% EtOAc/petrol afforded the title compound as a colorless oil (147 mg, 69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (brs, 1H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.53 – 7.48 (m, 2H), 7.48 – 7.33 (m, 4H), 5.56 (s, 1H), 5.35 (s, 1H), 3.52 (s, 2H), 3.40 (d, *J* = 2.0 Hz, 2H), 2.36 (s, 3H), 2.27 (t, *J* = 2.0 Hz, 1H).

2-(4-Chloro-3-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2511/3) Following **method D9**, subsequently purification by column chromatography using 10% EtOAc/petrol afforded the title compound as a colorless oil (76 mg, 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.31 (m, 2H), 7.26 – 7.24 (m, 1H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.33 (d, *J* = 1.2 Hz, 1H), 3.41 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 2.31 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

***N*,*N*-Dimethyl-3-(3-(methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)aniline (SZV-2512/3)** Following **method D9**, subsequently purification by column chromatography using 30% EtOAc/petrol afforded the title compound as a colorless oil (125 mg, 69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (t, *J* = 8.0 Hz, 1H), 6.91 (t, *J* = 2.0 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.70 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.28 (s, 1H), 3.46 (s, 2H), 3.40 (d, *J* = 2.4 Hz, 2H), 2.97 (s, 6H), 2.35 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(2-Fluoro-3-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2561/3) Following **method D9**, subsequently purification by column chromatography using ether/petrol (1:8) afforded the title compound as a colorless oil (159 mg, 65%). ^{1}H NMR (400 MHz, Acetone) δ 7.08 – 7.01 (m, 2H), 6.96 – 6.92 (m, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.32 (d, *J* = 1.2 Hz, 1H), 3.87 (s, 3H), 3.42 (s, 2H), 3.30 (d, *J* = 2.4 Hz, 2H), 2.66 (t, *J* = 2.4 Hz, 1H), 2.24 (s, 3H).

2-(3-Fluoro-5-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2562/3) Following **method D9**, subsequently purification by column chromatography using ether/petrol (1:6) afforded the title compound as a colorless oil (105 mg, 65%). ^{1}H NMR (400 MHz, Acetone) δ 6.99 (t, *J* = 2.0 Hz, 1H), 6.93 (ddd, *J* = 10.8, 2.0, 1.2 Hz, 1H), 6.63 (dt, *J* = 10.8, 2.0 Hz, 1H), 5.57 (d, *J* = 1.2 Hz, 1H), 5.32 (d, *J* = 1.2 Hz, 1H), 3.83 (s, 3H), 3.43 (d, *J* = 0.8 Hz, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 2.70 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

2-(4-Fluoro-3-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2563/3) Following **method D9**, subsequently purification by column chromatography using ether/petrol (1:10) afforded the title compound as a colorless oil (109 mg, 60%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.37 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.14 (ddd, *J* = 8.4, 4.4, 2.0 Hz, 1H), 7.05 (dd, *J* = 11.6, 8.4 Hz, 1H), 5.50 (d, *J* = 1.2 Hz, 1H), 5.25 (d, *J* = 0.8 Hz, 1H), 3.90 (s, 3H), 3.44 (d, *J* = 1.2 Hz, 2H), 3.33 (d, *J* = 2.4 Hz, 2H), 2.71 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

***N*-Methyl-2-(1-methyl-1*H*-pyrazol-4-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2569/3)** Following **method D9**, subsequently purification by column chromatography using 50% - 80% EtOAc /petrol afforded the title compound as a colorless oil (78 mg, 62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (s, 1H), 7.57 (s, 1H), 5.35 (d, *J* = 1.2 Hz, 1H), 5.05 (d, *J* = 1.2 Hz, 1H), 3.87 (s, 3H), 3.36 (d, *J* = 2.4 Hz, 2H), 3.27 (s, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(4-Methoxy-3-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2436) Following **method H1**, the title compound was isolated as a white solid (74%). Mp 135 – 136 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.42 – 7.25 (m, 2H), 6.93 (d, *J* = 8.0 Hz, 1H), 5.66 (d, *J* = 0.8 Hz, 1H), 5.50 (d, *J* = 0.8 Hz, 1H), 4.25 (s, 2H), 3.97 (d, *J* = 2.4 Hz, 2H), 3.84 (s, 3H), 2.82 (s, 3H), 2.21 (s, 3H). Anal. calcd. for $C_{15}H_{19}NOx(COOH)_2$ (319.35): C, 63.94%; H, 6.63%; N, 4.39%; O, 25.01%. Found: C, 64.00%; H, 6.64%; N, 4.23%; O, 25.01%.

2-(3,4-Dimethoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2437) Following **method H1**, the title compound was isolated as a white solid (72%). Mp 122 – 123 °C

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.12 – 7.08 (m, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 5.71 (d, *J* = 0.4 Hz, 1H), 5.54 (d, *J* = 0.4 Hz, 1H), 4.23 (s, 2H), 3.95 (d, *J* = 2.4 Hz, 2H), 3.88 (s, 3H), 3.85 (s, 3H), 2.80 (s, 3H). Anal. calcd. for $C_{15}H_{19}NO_2x(COOH)_2$ (335.35): C, 60.89%; H, 6.31%; N 4.18%; O 28.63%. Found: C, 60.74%; H, 6.24%; N, 3.87%; O, 28.58%.

2-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2439) Following **method H1**, the title compound was isolated as a white solid (71%). Mp 130 – 132 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.02 (d, *J* = 2.0 Hz, 1H), 6.99 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 5.67 (s, 1H), 5.53 (s, 1H), 4.25 (s, 4H), 4.23 (s, 2H), 3.98 (d, *J* = 2.4 Hz, 2H), 2.82 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{18}NO_2^+$ $[M+H]^+$ 244.1332, found 244.1337.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(m-tolyl)prop-2-en-1-aminium carboxyformate (SZV-2488)** Following **method H1**, the title compound was isolated as a white solid (86%). Mp 142–144 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.34 – 7.28 (m, 2H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.10 (d, $J = 7.6$ Hz, 1H), 5.52 (d, $J = 1.2$ Hz, 1H), 5.28 (d, $J = 1.2$ Hz, 1H), 3.54 (s, 2H), 3.42 (d, $J = 2.4$ Hz, 2H), 3.27 (t, $J = 2.4$ Hz, 1H), 2.31 (s, 3H), 2.28 (s, 3H). Anal. calcd. for $C_{14}H_{17}Nx(COOH)_2$ (289.33): C, 66.42%; H, 6.62%; N, 4.84%; O, 22.12%. Found: C, 66.27%; H, 6.45%; N, 4.78%; O, 22.39%.

2-(3-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2489) Following **method H1,** the title compound was isolated as a white solid (86%). Mp 106–107 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.25 (t, $J = 8.0$ Hz, 1H), 7.12 – 7.08 (m, 1H), 7.06 (t, $J = 2.4$ Hz, 1H), 6.87 (ddd, $J = 8.0, 2.4, 0.4$ Hz, 1H), 5.56 (d, $J = 1.2$ Hz, 1H), 5.29 (d, $J = 1.2$ Hz, 1H), 3.76 (s, 3H), 3.53 (s, 2H), 3.41 (d, $J = 2.4$ Hz, 2H), 3.27 (t, $J = 2.4$ Hz, 1H), 2.28 (s, 3H). Anal. calcd. for $C_{14}H_{17}NOx(COOH)_2$ (305.33): C, 62.94%; H, 6.27%; N, 4.59%; O, 26.20%. Found: C, 62.87%; H, 6.14%; N, 4.56%; O, 26.47%.

2-([1,1'-Biphenyl]-3-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2510) Following **method H1,** the title compound was isolated as a white solid (68%). Mp 131.5 – 132.4 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.77 (brs, 1H), 7.67 – 7.64 (m, 3H), 7.53 – 7.42 (m, 4H), 7.36 (tt, $J = 7.6, 1.6$ Hz, 1H), 5.83 (s, 1H), 5.66 (s, 1H), 4.28 (s, 2H), 3.94 (s, 2H), 3.26 (s, 1H), 2.79 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{19}H_{20}N^+$ $[M+H]^+$ 262.1590, found 262.1594.

2-(4-Chloro-3-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2511) Following **method H1,** the title compound was isolated as a white solid (60%). Mp 155.5 – 157.3 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.53 – 7.45 (m, 2H), 7.37 (ddd, $J = 8.4, 2.8, 0.8$ Hz, 1H), 5.80 (s, 1H), 5.62 (s, 1H), 4.05 (s, 2H), 3.81 (s, 2H), 3.15 (s, 1H), 2.68 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{13}H_{14}ClFN^+$ $[M+H]^+$ 238.0793, found 238.0797.

2-(3-(Dimethylamino)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2512) Following **method H1,** the title compound was isolated as a white solid (71%). Mp 127.7 – 128.7 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.26 (t, $J = 8.0$ Hz, 1H), 6.88 – 6.80 (m, 3H), 5.72 (d, $J = 0.8$ Hz, 1H), 5.56 (d, $J = 0.8$ Hz, 1H), 4.23 (s, 2H), 3.92 (d, $J = 2.4$ Hz, 2H), 3.30 (t, $J = 2.4$ Hz, 1H), 2.98 (s, 6H), 2.77 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{21}N_2^+$ $[M+H]^+$ 229.1699, found 229.1704.

2-(2-Fluoro-3-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2561) Following **method H1,** the title compound was isolated as a white solid (77%). Mp 106.8 – 107.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.17– 7.10 (m, 2H), 7.02 – 6.95 (m, 1H), 5.77 (d, $J = 0.8$ Hz, 1H), 5.67 (brs, 1H), 4.13 (s, 2H), 3.89 (s, 2H), 3.89 (s, 3H), 3.21 (t, $J = 2.4$ Hz, 1H), 2.75 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{17}FNO^+$ $[M+H]^+$ 234.1289, found 234.1295.

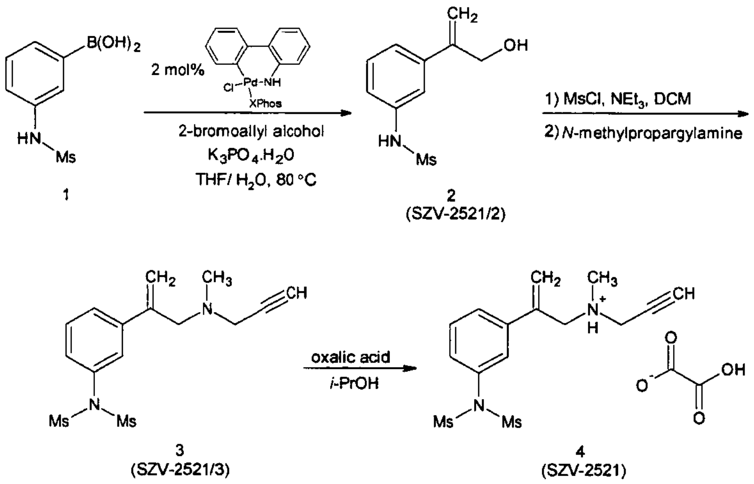
2-(3-Fluoro-5-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2562) Following **method H1,** the title compound was isolated as a white solid (76%). Mp 117.2 – 119.2 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 6.94 (t, $J = 2.0$ Hz, 1H), 6.91 (ddd, $J = 10.8, 2.0, 1.6$ Hz, 1H), 6.74 (dt, $J = 10.8, 2.0$ Hz, 1H), 5.80 (d, $J = 0.4$ Hz, 1H), 5.63 (s, 1H), 4.13 (s, 2H), 3.88 (d, $J = 2.4$ Hz, 3H), 3.85 (s, 3H), 3.24 (t, $J = 2.4$ Hz, 1H), 2.74 (s, 3H). Anal. calcd. for

$C_{14}H_{16}FNOx(COOH)_2$ (323.32): C, 59.44%; H, 5.61%; N, 4.33%; O, 24.74%. Found: C, 59.06%; H, 5.55%; N, 4.15%; O, 24.54%.

2-(4-Fluoro-3-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2563) Following **method H1,** the title compound was isolated as a white solid (74%). Mp 120.9 – 122.2 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.25 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.15 – 7.06 (m, 2H), 5.73 (s, 1H), 5.59 (s, 1H), 4.18 (s, 2H), 3.92 (s, 3H), 3.91 (d, *J* = 2.4 Hz, 2H), 3.26 (t, *J* = 2.4 Hz, 1H), 2.76 (s, 3H). Anal. calcd. for $C_{14}H_{16}FNOx(COOH)_2$ (323.32): C, 59.44%; H, 5.61%; N, 4.33%; O, 24.74%. Found: C, 58. 97%; H, 5.62%; N, 4.15%; O, 24.48%.

***N*-Methyl-2-(1-methyl-1*H*-pyrazol-4-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2569)** Following **method H1,** the title compound was isolated as a white solid (47%). Mp 105.6 – 106.7 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.84 (s, 1H), 7.70 (s, 1H), 5.68 (s, 1H), 5.34 (s, 1H), 3.96 (s, 2H), 3.91 (s, 2H), 3.89 (s, 3H), 3.24 (s, 1H), 2.78 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{11}H_{16}N_3^+$ $[M+H]^+$ 190.1339, found 190.1341.

Scheme 34

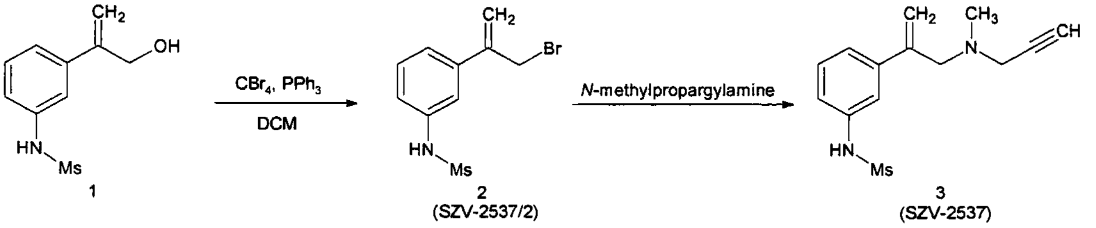


***N*-(3-(3-Hydroxyprop-1-en-2-yl)phenyl)methanesulfonamide (SZV-2521/2)** Following **method P2,** the title compound was isolated (35%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.28 (m, 3H), 7.21 – 7.15 (m, 1H), 5.50 (d, *J* = 0.8 Hz, 1H), 5.41 (d, *J* = 0.8 Hz, 1H), 4.53 (s, 2H), 3.03 (s, 3H).

***N*-(3-(3-(Methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)phenyl)-*N*-methylsulfonyl)methanesulfon amide (SZV-2521/3)** Following **method D9,** the title compound was isolated in 19% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (ddd, *J* = 8.0, 1.6, 1.2 Hz, 1H), 7.55 (t, *J* = 1.6 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.27-7.24 (m, 1H), 5.57 (s, 1H), 5.36 (s, 1H), 3.45 (s, 2H), 3.41 (s, 6H), 3.32 (d, *J* = 2.4 Hz, 2H), 2.30 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

***N*-Methyl-2-(3-(*N*-(methylsulfonyl)methylsulfonamido)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2521)** Following **method H1,** the title compound was isolated as a white solid (76%). Mp 175.0 - 177.7 °C. ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.65 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.63 (t, *J* = 2.0 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.49 - 7.44 (m, 1H), 5.82 (s, 1H), 5.65 (s, 1H), 4.12 (s, 2H), 3.83 (s, 2H), 3.47 (s, 6H), 3.16 (s, 1H), 2.69 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{21}N_2O_4S_2^+$ [M+H]$^+$ 357.0937, found 357.0950.

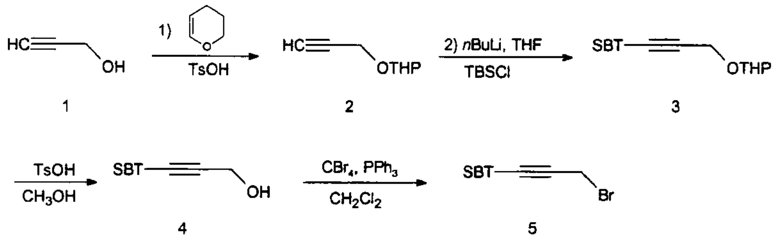
Scheme 35



***N*-(3-(3-Bromoprop-1-en-2-yl)phenyl)methanesulfonamide (SZV-2537/2)** Following **method O**, the title compound was isolated as an oil (32%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.30 (m, 3H), 7.20 (ddd, *J* = 7.6, 2.4, 1.2 Hz, 1H), 6.74 (s, 1H), 5.58 (s, 1H), 5.53 (s, 1H), 4.36 (s, 2H), 3.04 (s, 3H).

***N*-(3-(3-(Methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)phenyl)methanesulfonamide (SZV-2537)** Following **method D8**, the title compound isolated was initially an oil (42%) which solidifies into off-white crystals upon standing. Mp 100.5 – 103.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.28 (m, 3H), 7.16 (dt, *J* = 7.2, 2.0 Hz, 1H), 5.53 (d, *J* = 0.8 Hz, 1H), 5.34 (d, *J* = 0.8 Hz, 1H), 3.47 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 3.02 (s, 3H), 2.34 (s, 3H), 2.28 (t, *J* = 2.4 Hz, 1H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{19}N_2O_2S^+$ [M+H]$^+$ 279.1162, found 279.1162.

Scheme 36



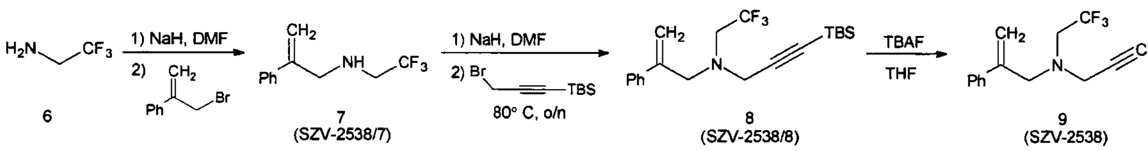
***tert*-Butyldimethyl(3-((tetrahydro-2*H*-pyran-2-yl)oxy)prop-1-yn-1-yl)silane** (Sharma A et al, J. Org. Chem., 1998, 63, 6128-6131) **(SZV2538/3)** To a solution of propargyl alcohol (0.5 ml, 8.6 mmol) in CH_2Cl_2 (5.0 ml) was added 3, 4-dihydro-2*H*-pyran (1.0 ml, 11.9 mmol) and TsOH (49 mg, 0.3 mmol). The reaction was stirred at rt for 2 h. Then, sat $NaHCO_3$ and CH_2Cl_2 were added. The aqueous layer was extracted with CH_2Cl_2 (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated to give the desired product which was pure by ^{1}H NMR analysis, and this was used in the next step without further purification. ^{1}H NMR (400 MHz, Chloroform-*d*) δ

4.82 (t, *J* = 3.6 Hz, 1H), 4.26 (qd, *J* = 15.6, 2.4 Hz, 2H), 3.87 – 3.81 (m, 1H), 3.56 – 3.51 (m, 1H), 2.40 (t, *J* = 2.4 Hz, 1H), 1.91 – 1.48 (m, 6H). To a solution of the protected alcohol (1.4 g) in THF (15.0 ml) at 0 °C, was added ^{n}BuLi (5.4 ml, 2390.0 mmol, 12.9 mmol) dropwise. The reaction was stirred for 20 mins before the dropwise addition of a solution of TBSCl (1.9 g, 12.9 mmol) in THF (8.0 ml). The reaction was stirred at rt for 2 h. Then, water and EtOAc were added. The aqueous layer was extracted with EtOAc (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. The crude residue was purified by column chromatography eluting with petrol to 2% ether/petrol to give the title compound (1.27 g, 58% over 2 steps) as a dark brown oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.85 (t, *J* = 3.6 Hz, 1H), 4.28 (d, *J* = 0.8 Hz, 2H), 3.85 (ddd, *J* = 11.6, 8.8, 2.8 Hz, 1H), 3.55 – 3.49 (m, 1H), 1.84 – 1.52 (m, 6H), 0.94 (s, 9H), 0.11 (s, 6H).

3-(*tert*-Butyldimethylsilyl)prop-2-yn-1-ol (SZV-2538/4) (Danheiser RL et al, J. Am. Chem. Soc., 1989, 111, 4407-4413) To a solution of the THP ether (523.0 mg, 2.1 mmol) in AR MeOH (10.0 ml) was added TsOH (11.7 mg, 0.1 mmol) and the reaction was stirred at rt for 16 h. The next day, the solvent was removed in vacuo and the crude was purified by column chromatography eluting with 5% - 10% EtOAc/petrol to give the title compound (312.0 mg, 89%) as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.28 (d, *J* = 5.6 Hz, 2H), 1.51 (t, *J* = 5.6 Hz, 1H), 0.94 (s, 9H), 0.12 (s, 6H).

(3-Bromoprop-1-yn-1-yl)(*tert*-butyl)dimethylsilane (SZV-2538/5) (Owada Y et al, Tetrahedron, 1997, 53, 11069-11086) Following **method O**, and purification by column chromatography eluting with 1% EtOAc/petrol, the title compound was isolated as a colorless oil (393 mg, 92%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.92 (s, 2H), 0.94 (s, 9H), 0.12 (s, 6H).

Scheme 37



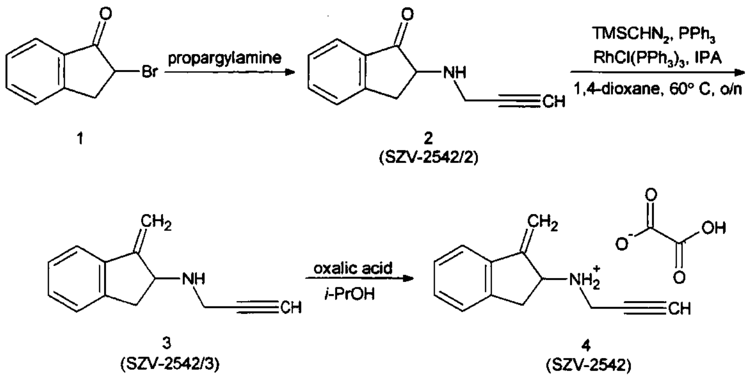
2-Phenyl-*N*-(2,2,2-trifluoroethyl)prop-2-en-1-amine (SZV-2538/7) (Niwayama S J. Org. Chem., 2000, 65, 5834-5836) To a stirring solution of trifluoroethylamine (293.0 ml, 3.7 mmol) in DMF (12.0 ml) at 0 °C, was added 60% NaH dispersion in mineral oil (149.0 mg, 3.7 mmol) and the white suspension was stirred for 1 h. Still at 0 °C, a solution of (3-bromoprop-1-en-2-yl)benzene (736.0 mg, 3.7 mmol) in DMF (12.0 ml) was added dropwise. The yellow suspension was allowed to warm to rt and stirred for 16 h. The next day, water and ether were added to the brown solution. The aqueous layer was extracted with ether (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. The crude residue was purified by column chromatography eluting with 10% ether/petrol to give the title compound (342 mg, 43%) as a colorless oil (this compound is quite volatile, therefore do not leave on the rotavap for too long). Bromide (214 mg, 29%) was recovered from the column chromatography. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 –

7.40 (m, 2H), 7.37 – 7.28 (m, 3H), 5.45 (s, 1H), 5.27 (d, *J* = 1.2 Hz, 1H), 3.79 (s, 2H), 3.18 (q, *J* = 9.6 Hz, 1H).

***N*-(3-(*tert*-Butyldimethylsilyl)prop-2-yn-1-yl)-2-phenyl-*N*-(2,2,2-trifluoroethyl)prop-2-en-1-amine (SZV-2583/8)** To a stirring solution of the amine (57.1 mg, 0.3 mmol) in DMF (2.0 ml) at 0 °C, was added 60% NaH dispersion in mineral oil (18.0 mg, 0.5 mmol) and the milky brown suspension was stirred for 1 h. Still at 0 °C, a solution of **(SZV-2538/5)** (114.0 mg, 0.5 mmol) in DMF (1.5 ml) was added dropwise. The color of the mixture turned from dark brown to black. The reaction was heated at 100 °C for 16 h. The extent of the reaction was monitored by TLC and ^{1}H NMR analysis. Then, water and ether were added to the black mixture. The aqueous layer was extracted with ether (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. The crude residue was purified by column chromatography eluting with petrol to give the title compound (45 mg, 46%) as a light yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 – 7.50 (m, 2H), 7.36 – 7.27 (m, 3H), 5.55 (d, *J* = 1.2 Hz, 1H), 5.34 (d, *J* = 1.2 Hz, 1H), 3.70 (s, 2H), 3.50 (s, 2H), 3.16 (q, *J* = 9.6 Hz, 1H), 0.98 (s, 9H), 0.15 (s, 6H).

2-Phenyl-*N*-(prop-2-yn-1-yl)-*N*-(2,2,2-trifluoroethyl)prop-2-en-1-amine (SZV-2538) To a stirring solution of the TBS ether (51 mg, 0.1 mmol) in THF (2.0 ml) at 0 °C, was added TBAF (1000.0 mmol in THF, 0.2 ml, 0.2 mmol). The color of the reaction mixture turned from yellow brown to dark purple. The reaction was stirred at 0 °C for 20 min. The extent of the reaction was monitored by TLC analysis. Then, water and ether were added to the black mixture. The aqueous layer was extracted with ether (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. The crude residue was purified by column chromatography eluting with 5% - 10% ether/petrol to give the title compound (30.4 mg, 87%) as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 – 7.47 (m, 2H), 7.39 – 7.27 (m, 3H), 5.55 (d, *J* = 1.2 Hz, 1H), 5.36 (d, *J* = 1.2 Hz, 1H), 3.70 (s, 2H), 3.49 (d, *J* = 2.4 Hz, 2H), 3.17 (q, *J* = 9.6 Hz, 2H), 2.27 (t, *J* = 2.4 Hz, 1H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{15}F_3N^+$ $[M+H]^+$ 254.1151, found 254.1143.

Scheme 38

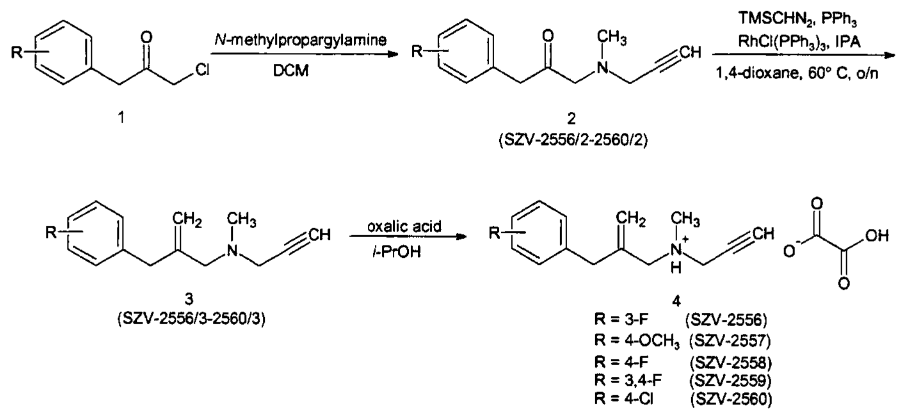


2-(Prop-2-yn-1-ylamino)-2,3-dihydro-1*H*-inden-1-one (SZV-2542/2) Following **method D10**, purification by column chromatography using 5% - 50% EtOAc/petrol afforded the title compound (638 mg, 30%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.61 (td, *J* = 7.6, 1.2 Hz, 1H), 7.46 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 3.88 (dd, *J* = 7.6, 4.4 Hz, 1H), 3.73 (dd, *J* = 17.2, 2.4 Hz, 1H), 3.53 (dd, *J* = 17.2, 2.4 Hz, 1H), 3.48 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.91 (dd, *J* = 16.8, 4.4 Hz, 1H), 2.27 (t, *J* = 2.4 Hz, 1H).

1-Methylene-*N*-(prop-2-yn-1-yl)-2,3-dihydro-1*H*-inden-2-amine (SZV-2542/3) Following **method E3**, subsequently purification by column chromatography using 15% - 25% ether/petrol afforded the title compound as a dark brown oil (80 mg, 16%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.59 – 7.45 (m, 1H), 7.34 – 7.14 (m, 3H), 5.65 (d, *J* = 2.0 Hz, 1H), 5.24 (d, *J* = 2.0 Hz, 1H), 4.22 – 4.18 (m, 1H), 3.54 (dd, *J* = 16.8, 2.4 Hz, 1H), 3.44 (dd, *J* = 16.8, 2.4 Hz, 1H), 3.23 (dd, *J* = 16.4, 7.2 Hz, 1H), 2.79 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.63 (t, *J* = 2.4 Hz, 1H).

1-Methylene-*N*-(prop-2-yn-1-yl)-2,3-dihydro-1*H*-inden-2-aminium carboxyformate (SZV-2542) Following **method H1**, the title compound was isolated as a light yellow solid (62%). Mp 173.2 – 173.8 °C (dec). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.62 (d, *J* = 6.8 Hz, 1H), 7.37 – 7.29 (m, 3H), 5.98 (s, 1H), 5.59 (s, 1H), 4.66 (d, *J* = 6.8 Hz, 1H), 4.02 (t, *J* = 2.4 Hz, 2H), 3.49 (dd, *J* = 17.6, 7.6 Hz, 1H), 3.22 (t, *J* = 2.4 Hz, 1H), 3.17 (d, *J* = 17.6 Hz, 1H). HRMS (ESI+) *m/z* calcd. for $C_{13}H_{14}N^+$ $[M+H]^+$ 184.1121, found 184.1129.

Scheme 39



1-(3-Fluorophenyl)-3-(methyl(prop-2-yn-1-yl)amino)propan-2-one (SZV-2556/2) Following **method D8**, and subsequent purification by column chromatography using 10% - 40% EtOAc/petrol afforded the title compound as a yellow oil (568 mg, 89%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 1H), 7.01 – 6.94 (m, 3H), 3.75 (s, 2H), 3.44 (d, *J* = 2.4 Hz, 2H), 3.38 (s, 2H), 2.37 (s, 3H), 2.24 (t, *J* = 2.4 Hz, 1H).

1-(4-Methoxyphenyl)-3-(methyl(prop-2-yn-1-yl)amino)propan-2-one (SZV-2557/2) Following **method D8**, and subsequent purification by column chromatography using 5% - 50% EtOAc/petrol afforded the title compound as a yellow oil (520 mg, 83%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.67 (s, 2H), 3.42 (d, *J* = 2.4, 2H), 3.35 (s, 2H), 2.34 (s, 3H), 2.22 (t, *J* = 2.4 Hz, 1H).

1-(4-Fluorophenyl)-3-(methyl(prop-2-yn-1-yl)amino)propan-2-one (SZV-2558/2) Following **method D8**, and subsequent purification by column chromatography using 5% - 30% EtOAc/petrol afforded the title compound as a yellow oil (531 mg, 87%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (dd, *J* = 8.4, 5.2 Hz, 2H), 7.01 (t, *J* = 8.4 Hz, 2H), 3.72 (s, 2H), 3.41 (d, *J* = 2.4 Hz, 2H), 3.35 (s, 2H), 2.34 (s, 3H), 2.22 (t, *J* = 2.4 Hz, 1H).

1-(3,4-Difluorophenyl)-3-(methyl(prop-2-yn-1-yl)amino)propan-2-one (SZV-2559/2) Following **method D8**, and subsequent purification by column chromatography using 5% - 30% EtOAc/petrol afforded the title compound as a orange oil (522 mg, 85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 – 7.04 (m, 2H), 6.96 – 6.92 (m, 1H), 3.72 (s, 2H), 3.43 (d, *J* = 2.4 Hz, 2H), 3.36 (s, 2H), 2.36 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

1-(4-Chlorophenyl)-3-(methyl(prop-2-yn-1-yl)amino)propan-2-one (SZV-2560/2) Following **method D8**, and subsequent purification by column chromatography using 5% - 30% EtOAc/petrol afforded the title compound as a yellow oil (528 mg, 86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 3.72 (s, 2H), 3.42 (d, *J* = 2.4 Hz, 2H), 3.35 (s, 2H), 2.34 (s, 3H), 2.23 (t, *J* = 2.4 Hz, 1H).

2-(3-Fluorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2556/3) Following **method E3**, and subsequent purification by column chromatography using pure hexane afforded the title compound as a colorless oil (206 mg, 37%). The eluent was changed to 10% ether/petrol to provide unreacted starting material (142 mg, 25%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.32 (td, *J* = 7.6, 6.4 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.02 – 6.93 (m, 2H), 5.04 – 5.03 (m, 1H), 4.90 – 4.89 (m, 1H), 3.42 (s, 2H), 3.29 (d, *J* = 2.4 Hz, 2H), 2.90 (s, 2H), 2.64 (t, *J* = 2.4 Hz, 1H), 2.23 (s, 3H).

2-(4-Methoxybenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2557/3) Following **method E3**, and subsequent purification by column chromatography using 5% - 10% ether/petrol afforded the title compound as a colorless oil (155 mg, 30%). The eluent was changed to 40% EtOAc/petrol to provide unreacted starting material (50 mg, 10%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.12 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.97 – 4.96 (m, 1H), 4.84 – 4.83 (m, 1H), 3.76 (s, 3H), 3.32 (s, 2H), 3.29 (d, *J* = 2.4 Hz, 2H), 2.88 (s, 2H), 2.63 (t, *J* = 2.4 Hz, 1H), 2.23 (s, 3H).

2-(4-Fluorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2558/3) Following **method E3**, and subsequent purification by column chromatography using 5% - 10% ether/petrol afforded the title compound as a colorless oil (195 mg, 37%). The eluent was changed to 40% EtOAc/petrol to provide unreacted starting material (98 mg, 18%). ^{1}H NMR (400 MHz, Acetone-

d_6) δ 7.24 (dd, *J* = 8.8, 5.2 Hz, 2H), 7.04 (t, *J* = 8.8 Hz, 2H), 5.01 – 5.00 (m, 1H), 4.86 – 4.85 (m, 1H), 3.39 (s, 2H), 3.28 (d, *J* = 2.4 Hz, 2H), 2.88 (s, 2H), 2.64 (t, *J* = 2.4 Hz, 1H), 2.23 (s, 3H).

2-(3,4-Difluorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2559/3) Following **method E3**, and subsequent purification by column chromatography using 5% - 10% ether/petrol afforded the title compound as a colorless oil (205 mg, 40%). The eluent was changed to 40% EtOAc/petrol to provide unreacted starting material (82 mg, 16%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.29 – 7.13 (m, 2H), 7.07 – 7.03 (m, 1H), 5.04 – 5.03 (m, 1H), 4.90 – 4.89 (m, 1H), 3.40 (s, 2H), 3.28 (d, *J* = 2.4 Hz, 2H), 2.90 (s, 2H), 2.64 (t, *J* = 2.4 Hz, 1H), 2.22 (s, 3H).

2-(4-Chlorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2560/3) Following **method E3**, and subsequent purification by column chromatography using 5% - 10% ether/petrol afforded the title compound as a colorless oil (155 mg, 30%). The eluent was changed to 40% EtOAc/petrol to provide unreacted starting material (50 mg, 10%). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.31 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 5.02 – 5.01 (m, 1H), 4.88 – 4.87 (m, 1H), 3.39 (s, 2H), 3.28 (d, *J* = 2.4 Hz, 2H), 2.89 (s, 2H), 2.64 (t, *J* = 2.4 Hz, 1H), 2.22 (s, 3H).

2-(3-Fluorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2556) Following **method H1**, the title compound was isolated as a white solid (83%). Mp 108.2 - 109.2 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.36 – 7.30 (m, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.02 – 6.95 (m, 2H), 5.38 – 5.37 (m, 1H), 5.24 – 5.23 (m, 1H), 3.94 (d, *J* = 2.4 Hz, 2H), 3.60 (s, 2H), 3.50 (s, 2H), 3.20 (t, *J* = 2.4 Hz, 1H), 2.80 (s, 3H). Anal. calcd. for $C_{14}H_{16}FNx(COOH)_2$ (307.32): C, 62.53%; H, 5.90%; N, 4.56%; O, 20.82%. Found: C, 62.34%; H, 5.78%; N, 4.32%; O, 20.68%.

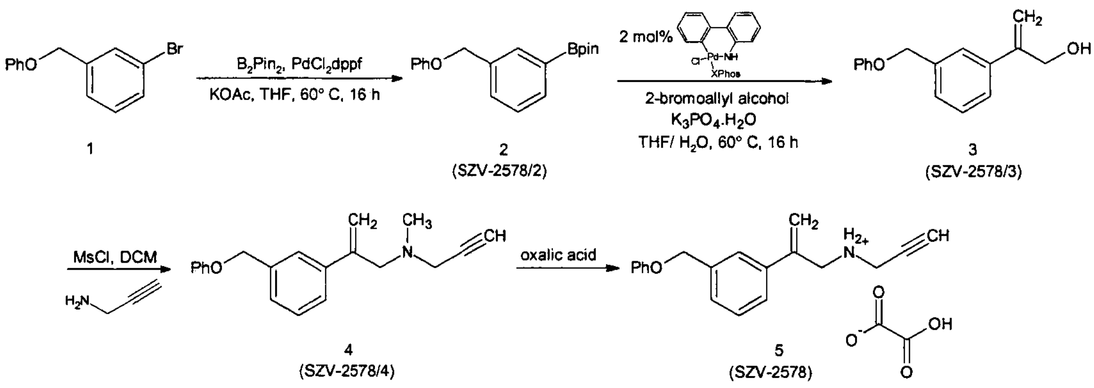
2-(4-Methoxybenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2557) Following **method H1**, the title compound was isolated as a white solid (63%). Mp 103.2 – 105.6 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.14 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 5.32 (s, 1H), 5.22 (s, 1H), 3.93 (s, 2H), 3.78 (s, 3H), 3.58 (s, 2H), 3.41 (s, 2H), 3.21 (s, 1H), 2.79 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{15}H_{20}NO^+$ $[M+H]^+$ 230.1539, found 230.1540.

2-(4-Fluorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2558) Following **method H1,** the title compound was isolated as a white solid (83%). Mp 97.5 – 98.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.24 (dd, *J* = 8.4, 5.2 Hz, 2H), 7.04 (t, *J* = 8.4 Hz, 2H), 5.34 (s, 1H), 5.20 (s, 1H), 3.91 (d, *J* = 2.4 Hz, 2H), 3.57 (s, 2H), 3.46 (s, 2H), 3.18 (t, *J* = 2.4 Hz, 1H), 2.77 (s, 3H). Anal. calcd. for $C_{14}H_{16}FNx(COOH)_2$ (307.32): C, 62.53%; H, 5.90%; N, 4.56%; O, 20.82%. Found: C, 62.43%; H, 5.89%; N, 4.34%; O, 20.85%.

2-(3,4-Difluorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2559) Following **method H1**, the title compound was isolated as a white solid (78%). Mp 97.3 – 99.0 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.23 – 7.12 (m, 2H), 7.05 – 7.01 (m, 1H), 5.35 (d, *J* = 1.2 Hz, 1H), 5.19 (d, *J* = 1.2 Hz, 1H), 3.86 (d, *J* = 2.4 Hz, 2H), 3.51 (s, 2H), 3.46 (s, 2H), 3.12 (t, *J* = 2.4 Hz, 1H), 2.73 (s, 3H). Anal. calcd. for $C_{14}H_{15}F_2Nx(COOH)_2$ (325.31): C, 59.07%; H, 5.27%; F, 11.68%; N, 4.31%; O, 19.67%. Found: C, 59.02%; H, 5.31%; N, 4.15%; O, 20.35%.

2-(4-Chlorobenzyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2560) Following **method H1**, the title compound was isolated as a white solid (78%). Mp 99.2 - 101.5 °C. ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.32 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 5.36 (d, *J* = 0.8 Hz, 1H), 5.21 (d, *J* = 0.8 Hz, 1H), 3.92 (d, *J* = 2.4 Hz, 2H), 3.58 (s, 2H), 3.47 (s, 2H), 3.19 (t, *J* = 2.4 Hz, 1H), 2.78 (s, 3H). Anal. calcd. for $C_{14}H_{16}ClNx(COOH)_2$ (323.77): C, 59.35%; H, 5.60%; N, 4.33%; O, 19.77%. Found: C, 59.19%; H, 5.52%; N, 4.14%; O, 19.48%.

Scheme 40



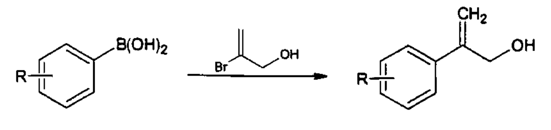
4,4,5,5-Tetramethyl-2-(3-(phenoxymethyl)phenyl)-1,3,2-dioxaborolane (SZV-2578/2) (Spencer J et al, ACS Combi. Sci., 2011, 13, 24-31) Following **method Q2**, the title compound was isolated (85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (s, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.34 – 7.26 (m, 2H), 6.99 – 6.94 (m, 3H), 5.07 (s, 2H), 1.36 (s, 12H).

2-(3-(Phenoxymethyl)phenyl)prop-2-en-1-ol (SZV-2578/3) Following **method P2,** the title compound was isolated (48-53%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (s, 1H), 7.42 – 7.37 (m, 3H), 7.32 – 7.28 (m, 2H), 7.00 – 6.95 (m, 3H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.38 (d, *J* = 1.2 Hz, 1H), 5.08 (s, 2H), 4.56 (s, 2H).

2-(3-(Phenoxymethyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2578/4) Following **method D9**, the title compound was isolated (49%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (s, 1H), 7.43 – 7.40 (m, 1H), 7.38 – 7.36 (m, 2H), 7.30 (dd, *J* = 8.8, 7.2 Hz, 2H), 7.00 – 6.94 (m, 3H), 5.49 (d, *J* = 0.8 Hz, 1H), 5.35 (s, 1H), 5.08 (s, 2H), 3.81 (s, 2H), 3.48 (d, *J* = 2.4 Hz, 2H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(3-(Phenoxymethyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2578) Following **method H1**, the title compound was isolated as a white solid (81%). Mp 184.7 - 186.9 °C (dec) . ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.60 (s, 1H), 7.50 – 7.43 (m, 3H), 7.27 (dd, *J* = 8.8, 7.6 Hz, 2H), 6.99 (dd, *J* = 8.8, 0.8 Hz, 2H), 6.94 (tt, *J* = 7.6, 0.8 Hz, 1H), 5.75 (s, 1H), 5.55 (s, 1H), 5.13 (s, 2H), 4.23 (d, *J* = 0.4 Hz, 2H), 3.91 (d, *J* = 2.4 Hz, 2H), 3.21 (t, *J* = 2.4 Hz, 1H). HRMS (ESI+) *m/z* calcd. for $C_{19}H_{20}NO^+$ $[M+H]^+$ 278.1539, found 278.1542.

Scheme 41



1 2

R=3-OCH_3, 4-OBn	(SZV-2462/2)	R=3-Cl, 4-CH_3	(SZV-2468/2)	R=4-CH_2-CH_3	(SZV-2482/2)	R=3-OCH_2CHF_2	(SZV-2497/2)
R=3-CH_3, 4-Cl	(SZV-2463/2)	R=3-Cl, 4-F	(SZV-2469/2)	R=3,5-di-OCH_3	(SZV-2483/2)	R=3-$OCH(CH_3)_2$	(SZV-2498/2)
R=4-Ph	(SZV-2464/2)	R=4-$OCHF_2$	(SZV-2478/2)	R=3-F, 4-$OCHF_2$	(SZV-2493/2)	R=3-Cl, 4-$OCH(CH_3)_2$	(SZV-2499/2)
R=3-$OCHF_2$	(SZV-2465/2)	R=4-CHF_2	(SZV-2479/2)	R=CHF_2	(SZV-2494/2)	R=4-$SCH(CH_3)_2$	(SZV-2514/2)
R=3-CF_3, 4-Cl	(SZV-2466/2)	R=4-CH=CH_2	(SZV-2480/2)	R=3-$OCHF_2$, 4-F	(SZV-2495/2)	R=3,4-(OCH_2CH_2)	(SZV-2515/2)
R=3,4-di-Cl	(SZV-2467/2)	R=3,5-di-F	(SZV-2481/2)	R=4-cyclopropyl	(SZV-2496/2)	R=4-N($CH_2CH_2OCH_2CH_2$)	(SZV-2516/2)
						R=3-Bn	(SZV-2531/2)
						R=3,4-(CHCHNH)	(SZV-2532/2)

2-(4-(Benzyloxy)-3-methoxyphenyl)prop-2-en-1-ol (SZV-2462/2) Following **method P2**, the title compound was isolated as a white solid (57%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45-7.43 (m, 2H), 7.39 – 7.35 (m, 2H), 7.32-7.28 (m, 1H), 7.03 (d, *J* = 2.1 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 5.39 (d, *J* = 1.2 Hz, 1H), 5.28 (d, *J* = 1.2 Hz, 1H), 5.17 (s, 2H), 4.51 (d, *J* = 6.0 Hz, 2H), 3.91 (s, 3H), 1.55 (t, *J* = 6.0 Hz, 1H).

2-(4-Chloro-3-methylphenyl)prop-2-en-1-ol (SZV-2463/2) Following **method P2**, the title compound was isolated as a yellow oil (23%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32-7.30 (m, 2H), 7.23-7.20 (m, 1H), 5.44 (s, 1H), 5.35 (s, 1H), 4.51 (d, *J* = 5.6 Hz, 2H), 2.39 (s, 3H) 1.54 (t, *J* = 5.6 Hz, 1H).

2-([1,1'-Biphenyl]-4-yl)prop-2-en-1-ol (SZV-2464/2) (Garzan A et al, Chem. - Euro. J., 2013, 19, 9015-9021) Following **method P2**, the title compound was isolated as a light yellow solid (31%). Mp 132-135 °C (lit. Mp 115-118 °C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62-7.58 (m, 4H), 7.55-7.53 (m, 2H), 7.47-7.43 (m, 2H), 7.37-7.33 (m, 1H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.39 (d, *J* = 1.2 Hz, 1H), 4.60 (s, 2H).

2-(3-Chloro-4-fluorophenyl)prop-2-en-1-ol (SZV-2469/2) Following **method P2**, the title compound was isolated as a light yellow oil (33%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (dd, *J* = 7.0, 2.2 Hz, 1H), 7.35-7.31 (m, 1H), 7.11 (app. t, 1H), 5.44 (s, 1H), 5.38 (s, 1H), 4.49 (d, *J* = 6.0 Hz, 2H), 1.56 (t, *J* = 6.0 Hz, 1H).

2-(4-Chloro-3-(trifluoromethyl)phenyl)prop-2-en-1-ol (SZV-2466/2) Following **method P2**, the title compound was isolated as a light yellow oil (36%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 2.1 Hz, 1H), 7.57 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 5.53 (d, *J* = 0.8 Hz, 1H), 5.46 (q, *J* = 0.8 Hz, 1H), 4.53 (dd, *J* = 6.0, 0.4 Hz, 2H), 1.58 (t, *J* = 6.0 Hz, 1H).

2-(3-Chloro-4-methylphenyl)prop-2-en-1-ol (SZV-2468/2) Following **method P2**, the title compound was isolated as a yellow oil (36%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 1.6 Hz, 1H), 7.25 – 7.19 (m, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 5.46 (d, *J* = 0.6 Hz, 1H), 5.35 (d, *J* = 0.6 Hz, 1H), 4.50 (d, *J* = 5.6 Hz, 2H), 2.37 (s, 3H), 1.56 (t, *J* = 5.6 Hz).

2-(3,4-Dichlorophenyl)prop-2-en-1-ol (SZV-2467/2) Following **method P2**, the title compound was isolated as a yellow oil (38%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, J = 2.1 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.29 (dd, J = 8.4, 2.1 Hz, 1H), 5.49 (d, J = 0.8 Hz, 1H), 5.41 (d, J = 0.8 Hz, 1H), 4.50 (s, 2H).

2-(3-(Difluoromethoxy)phenyl)prop-2-en-1-ol (SZV-2465/2) Following **method P2**, the title compound was isolated as a yellow oil (52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (t, J = 7.6 Hz, 1H), 7.30 (td, J = 7.6, 1.6 Hz, 1H), 7.21 (t, J = 1.6 Hz, 1H), 7.08-7.05 (m, 1H), 6.52 (t, J = 73.8 Hz, 1H), 5.50 (d, J = 0.8 Hz, 1H), 5.41 (d, J = 0.8 Hz, 1H), 4.53 (d, J = 4.0 Hz, 2H), 1.60 (t, J = 4.0 Hz, 1H).

2-(4-(Difluoromethyl)phenyl)prop-2-en-1-ol (SZV-2479/2) Following **method P2**, the title compound was isolated as a yellow oil (47%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 6.65 (t, J = 56.6 Hz, 1H), 5.53 (d, J = 1.2 Hz, 1H), 5.43 (d, J = 1.2 Hz, 1H), 4.56 (d, J = 4.4 Hz, 2H), 1.60 (t, J = 4.4 Hz, 1H).

2-(4-(Difluoromethoxy)phenyl)prop-2-en-1-ol (SZV-2478/2) Following **method P2**, the title compound was isolated as a yellow oil (40%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47-7.44 (m, 2H), 7.13-7.10 (m, 2H), 6.51 (t, J = 74.0 Hz, 1H), 5.45 (d, J = 0.8 Hz, 1H), 5.36 (d, J = 0.8 Hz, 1H), 4.53 (d, J = 5.6 Hz, 2H), 1.54 (t, J = 5.6 Hz, 1H).

2-(4-Vinylphenyl)prop-2-en-1-ol (SZV-2480/2) Following **method P2**, the title compound was isolated as a creamy white solid (61%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.44 – 7.39 (m, 4H), 6.72 (dd, J = 17.6, 10.9 Hz, 1H), 5.76 (dd, J = 17.6, 0.8 Hz, 1H), 5.50 (d, J = 0.4 Hz, 1H), 5.35 (d, J = 0.4 Hz, 1H), 5.26 (dd, J = 10.9, 0.8 Hz, 1H), 4.55 (s, 2H).

2-(3,5-Difluorophenyl)prop-2-en-1-ol (SZV-2481/2) Following **method P2**, the title compound was isolated as a brown oil (60%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.00-6.97 (m, 2H), 6.75 (tt, J = 8.8, 2.3 Hz, 1H), 5.52 (d, J = 0.4 Hz, 1H), 5.44 (s, 1H), 4.49 (d, J = 0.4 Hz, 2H).

2-(4-Ethylphenyl)prop-2-en-1-ol (SZV-2482/2) Following **method P2**, the title compound was isolated as a dark yellow oil (65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.37 (m, 2H), 7.21-7.18 (m, 2H), 5.44 (d, J = 0.8 Hz, 1H), 5.31 (d, J = 0.8 Hz, 1H), 4.54 (s, 2H), 2.66 (q, J = 7.6 Hz, 2H), 1.24 (t, J = 7.6 Hz, 3H).

2-(3,5-Dimethoxyphenyl)prop-2-en-1-ol (SZV-2483/2) Following **method P2**, the title compound was isolated as a dark yellow oil (49%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.59 (d, J = 2.0 Hz, 2H), 6.43 (t, J = 2.0 Hz, 1H), 5.45 (d, J = 0.8 Hz, 1H), 5.35 (d, J = 0.8 Hz, 1H), 4.50 (s, 2H), 3.81 (s, 6H).

2-(3-(Difluoromethyl)phenyl)prop-2-en-1-ol (SZV-2494/2) Following **method P2**, the title compound was isolated as a yellow oil (53%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60-7.56 (m, 2H), 7.46-7.44 (m, 2H), 6.65 (t, J = 56.4 Hz, 1H), 5.52 (dd, J = 1.6, 0.8 Hz, 1H), 5.43 (dd, J = 1.6, 1.3 Hz, 1H), 4.56 (dd, J = 1.3, 0.8 Hz, 2H).

2-(3-(2,2-Difluoroethoxy)phenyl)prop-2-en-1-ol (SZV-2497/2) Following **method P2**, the title compound was isolated as a dark yellow oil (42%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (app. t, 1H), 7.12-7.10 (m, 1H), 7.03-7.02 (m, 1H), 6.88-6.85 (m, 1H), 6.09 (tt, *J* = 55.2, 4.1 Hz, 1H), 5.48 (dd, *J* = 2.4, 0.8 Hz, 1H), 5.38 (dd, *J* = 2.4, 1.6 Hz, 1H), 4.53 (dd, *J* = 1.6, 0.8 Hz, 2H), 4.20 (td, *J* = 13.1, 4.1 Hz, 2H).

2-(3-(Difluoromethoxy)-4-fluorophenyl)prop-2-en-1-ol (SZV-2495/2) Following **method P2**, the title compound was isolated as a dark yellow oil (64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36-7.33 (m, 1H), 7.32-7.28 (m, 1H), 7.17-7.12 (m, 1H), 6.66 (d, *J* = 73.6 Hz, 1H), 5.45 (d, *J* = 0.8 Hz, 1H), 5.39 (q, *J* = 0.8 Hz, 1H), 4.50 (d, *J* = 0.8 Hz, 2H).

2-(4-Cyclopropylphenyl)prop-2-en-1-ol (SZV-2496/2) Following **method P2**, the title compound was isolated as a dark brown solid (64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36-7.33 (m, 2H), 7.08 – 7.04 (m, 2H), 5.43 (d, *J* = 0.8 Hz, 1H), 5.29 (d, *J* = 0.8 Hz, 1H), 4.53 (s, 2H), 1.92-1.86 (m, 1H), 0.99-0.94 (m, 2H), 0.72-0.68 (m, 2H).

2-(4-(Difluoromethoxy)-3-fluorophenyl)prop-2-en-1-ol (SZV-2493/2) Following **method P2**, the title compound was isolated as a yellow oil (74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31-7.27 (m, 1H), 7.22-7.21 (m, 2H), 6.55 (t, *J* = 73.5 Hz, 1H), 5.48 (d, *J* = 0.5 Hz, 1H), 5.41 (s, 1H), 4.50 (d, *J* = 0.5 Hz, 2H).

2-(3-Isopropoxyphenyl)prop-2-en-1-ol (SZV-2498/2) Following **method P2**, the title compound was isolated as a dark brown oil (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26-7.23 (m, 1H), 7.02-6.97 (m, 2H), 6.85-6.82 (m, 1H), 5.46 (d, *J* = 0.8 Hz, 1H), 5.34 (d, *J* = 0.8 Hz, 1H), 4.61-4.52 (m, 1H), 4.52 (s, 2H), 1.34 (d, *J* = 6.0 Hz, 6H).

2-(3-Chloro-4-isopropoxyphenyl)prop-2-en-1-ol (SZV-2499/2) Following **method P2**, the title compound was isolated as a yellow oil (33%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 2.3 Hz, 1H), 7.29 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.92 (d, *J* = 8.6 Hz, 1H), 5.41 (s, 1H), 5.30 (s, 2H), 4.60-4.51 (m, 1H), 4.49 (s, 2H), 1.38 (d, *J* = 6.1 Hz, 6H).

2-(4-Morpholinophenyl)prop-2-en-1-ol (SZV-2516/2) Following **method P2**, the title compound was isolated as a yellow solid (70%). 1H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.37 (m, 2H), 6.91-6.89 (m, 2H), 5.40 (d, *J* = 0.4 Hz, 1H), 5.24 (d, *J* = 0.4 Hz, 1H), 4.52 (s, 2H), 3.89 – 3.83 (m, 4H), 3.20 – 3.15 (m, 4H).

2-(4-(Isopropylthio)phenyl)prop-2-en-1-ol (SZV-2514/2) Following **method P2**, the title compound was isolated as a yellow oil (62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40-7.35 (m, 4H), 5.48 (dd, *J* = 2.0, 0.8 Hz, 1H), 5.35 (dd, *J* = 2.0, 1.2 Hz, 1H), 4.53 (dd, *J* = 1.2, 0.8 Hz, 2H), 3.44-3.34 (m, 1H), 1.31 (d, *J* = 6.7 Hz, 6H).

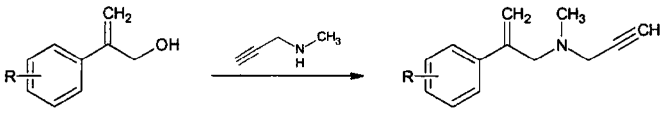
2-(2,3-Dihydrobenzofuran-5-yl)prop-2-en-1-ol (SZV-2515/2) Following **method P2**, the title compound was isolated as a yellow oil (80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (br, 1H), 7.24 – 7.20 (m, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 5.35 (d, *J* = 1.2 Hz, 1H), 5.23 (d, *J* = 1.2 Hz, 1H), 4.58 (t, *J* = 8.7 Hz, 2H), 4.51 (s, 2H), 3.22 (t, *J* = 8.7 Hz, 2H).

2-(1*H*-Indol-6-yl)prop-2-en-1-ol (SZV-2532/2) Following **method P2**, the title compound was isolated as a white solid (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (br, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.51 (s, 1H), 7.25-7.22 (m, 1H), 6.55-6.54 (m, 1H), 5.49 (d, J = 1.2 Hz, 1H), 5.33 (d, J = 1.2 Hz, 1H), 4.62 (s, 2H).

2-(3-Benzylphenyl)prop-2-en-1-ol (SZV-2531/2) Following **method P2**, the title compound was isolated as a yellow oil (43%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 5H), 7.22-7.18 (m, 3H), 7.14 – 7.12 (m, 1H), 5.44 (d, J = 0.8 Hz, 1H), 5.33 (d, J = 0.8 Hz, 1H), 4.52 (s, 2H), 4.00 (s, 2H).

2-(4-(ethylthio)phenyl)prop-2-en-1-ol (SZV2513/2) Following **method P2**, the title compound was isolated white solid (72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.36 (m, 2H), 7.35 – 7.27 (m, 2H), 5.47 (d, J = 0.8 Hz, 1H), 5.33 (d, J = 0.8 Hz, 1H), 4.53 (s, 2H), 2.96 (q, J = 7.4 Hz, 2H), 1.33 (t, J = 7.4 Hz, 3H).

Scheme 42



2 3

R=3-OCH$_3$, 4-OBn	(SZV-2462/3)	R=3-Cl, 4-CH$_3$	(SZV-2468/3)	R=4-CH$_2$-CH$_3$	(SZV-2482/3)	R=3-OCH$_2$CHF$_2$	(SZV-2497/3)
R=3-CH$_3$, 4-Cl	(SZV-2463/3)	R=3-Cl, 4-F	(SZV-2469/3)	R=3,5-di-OCH$_3$	(SZV-2483/3)	R=3-OCH(CH$_3$)$_2$	(SZV-2498/3)
R=4-Ph	(SZV-2464/3)	R=4-OCHF$_2$	(SZV-2478/3)	R=3-F, 4-OCHF$_2$	(SZV-2493/3)	R=3-Cl, 4-OCH(CH$_3$)$_2$	(SZV-2499/3)
R=3-OCHF$_2$	(SZV-2465/3)	R=4-CHF$_2$	(SZV-2479/3)	R=CHF$_2$	(SZV-2494/3)	R=4-SCH(CH$_3$)$_2$	(SZV-2514/3)
R=3-CF$_3$, 4-Cl	(SZV-2466/3)	R=4-CH=CH$_2$	(SZV-2480/3)	R=3-OCHF$_2$, 4-F	(SZV-2495/3)	R=3,4-(OCH$_2$CH$_2$)	(SZV-2515/3)
R=3,4-di-Cl	(SZV-2467/3)	R=3,5-di-F	(SZV-2481/3)	R=4-cyclopropyl	(SZV-2496/3)	R=4-N(CH$_2$CH$_2$OCH$_2$CH$_2$)	(SZV-2516/3)
						R=3-Bn	(SZV-2531/3)
						R=3,4-(CHCHNH)	(SZV-2532)

2-(4-(Benzyloxy)-3-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2462/3) Following **method D9**, the title compound was isolated as a colourless oil (68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45-7.43 (m, 2H), 7.38-7.34 (m, 2H), 7.32-7.29 (m, 1H), 7.12 (d, J = 2.0 Hz, 1H), 7.02 (dd, J = 8.3, 2.1 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 5.41 (d, J = 1.2 Hz, 1H), 5.21 (d, J = 1.2 Hz, 1H), 5.16 (s, 2H), 3.91 (s, 3H), 3.41 (s, 2H), 3.36 (d, J = 2.4 Hz, 2H), 2.32 (s, 3H), 2.25 (t, J = 2.4 Hz, 1H).

2-(4-Fluoro-3-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2463/3) Following **method D9**, the title compound was isolated as a light yellow oil (59%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.35 (m, 1H), 7.27-7.26 (m, 2H), 5.44 (d, J = 1.2 Hz, 1H), 5.27 (d, J = 1.2 Hz, 1H), 3.41 (s, 2H), 3.34 (d, J = 2.4 Hz, 2H), 2.37 (s, 3H), 2.30 (s, 3H), 2.25 (t, J = 2.4 Hz, 1H).

2-([1,1'-Biphenyl]-4-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2464/3) Following **method D9**, the title compound was isolated as a white solid (74%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.55 (m, 6H), 7.45-7.42 (m, 2H), 7.36-7.32 (m, 1H), 5.55 (d, *J* = 1.6 Hz, 1H), 5.32 (d, *J* = 1.6 Hz, 1H), 3.50 (s, 2H), 3.40 (d, *J* = 2.4 Hz, 2H), 2.35 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(4-Fluoro-3-(trifluoromethyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2469/3) Following **method D9**, the title compound was isolated as a colourless oil (64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.38 (ddd, *J* = 8.6, 4.6, 2.0 Hz, 1H), 7.08 (app. t, 1H), 5.44 (d, *J* = 0.8 Hz, 1H), 5.30 (d, *J* = 0.8 Hz, 1H), 3.40 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 2.30 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(4-Chloro-3-(trifluoromethyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2466/3) Following **method D9**, the title compound was isolated as a light yellow oil (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 2.0 Hz, 1H), 7.62 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 5.53 (d, *J* = 1.2 Hz, 1H), 5.37 (d, *J* = 1.2 Hz, 1H), 3.44 (s, 2H), 3.33 (d, *J* = 2.4 Hz, 2H), 2.30 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(3-Chloro-4-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2468/3) Following **method D9**, the title compound was isolated as a yellow oil (52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 1.8 Hz, 1H), 7.29 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 5.45 (d, *J* = 1.2 Hz, 1H), 5.27 (d, *J* = 1.2 Hz, 1H), 3.41 (s, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.35 (s, 3H), 2.31 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(3,4-Dichlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2467/3) Following **method D9**, the title compound was isolated as a colourless oil (69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 2.0 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.35 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.33 (d, *J* = 1.2 Hz, 1H), 3.40 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 2.30 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(3-(Difluoromethoxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2465/3) Following **method D9**, the title compound was isolated as a colourless oil (76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.29 (m, 3H), 7.04-7.01 (m, 1H), 6.52 (t, *J* = 74.2 Hz, 1H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.33 (q, *J* = 1.2 Hz, 1H), 3.43 (d, *J* = 1.2 Hz, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(4-(Difluoromethyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2479/3) Following **method D9,** the title compound was isolated as a yellow oil (72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 2H), 6.63 (t, *J* = 56.5 Hz, 1H), 5.53 (d, *J* = 1.2 Hz, 1H), 5.36 (q, *J* = 1.2 Hz, 1H), 3.46 (d, *J* = 1.2 Hz, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.31 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(4-(Difluoromethoxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2478/3) Following **method D9**, the title compound was isolated as a pale yellow oil (82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54-7.50 (m, 2H), 7.09-7.05 (m, 2H), 6.50 (t, *J* = 74.1 Hz, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.28 (q, *J* = 1.2 Hz, 1H), 3.43 (d, *J* = 1.2 Hz, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 2.31 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

N-Methyl-N-(prop-2-yn-1-yl)-2-(4-vinylphenyl)prop-2-en-1-amine (SZV-2480/3) Following **method D9,** the title compound was isolated as a colourless oil (78%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 – 7.47 (m, 2H), 7.39-7.36 (m, 2H), 6.71 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.74 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.51 (d, *J* = 1.1 Hz, 1H), 5.30 (br, 1H), 5.23 (dd, *J* = 10.9, 0.9 Hz, 1H), 3.47 (s, 2H), 3.37 (d, *J* = 2.0 Hz, 2H), 2.33 (s, 3H), 2.26 (t, *J* = 2.0 Hz, 1H).

2-(3,5-Difluorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2481/3) Following **method D9,** the title compound was isolated as a colourless oil (86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09-7.04 (m, 2H), 6.71 (tt, *J* = 8.8, 2.3 Hz, 1H), 5.53 (s, 1H), 5.36 (s, 1H), 3.40 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(4-Ethylphenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2482/3) Following **method D9**, the title compound was isolated as a colourless oil (42%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45-7.42 (m, 2H), 7.18-7.15 (m, 2H), 5.46 (d, *J* = 1.5 Hz, 1H), 5.25 (br, 1H), 3.45 (s, 2H), 3.37 (d, *J* = 2.3 Hz, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 2.25 (t, *J* = 2.3 Hz, 1H), 1.24 (t, *J* = 7.6 Hz, 3H).

2-(3,5-Dimethoxyphenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2483/3) Following **method D9**, the title compound was isolated as a light yellow oil (69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.67 (d, *J* = 2.3 Hz, 2H), 6.40 (t, *J* = 2.3 Hz, 1H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.30 (br, 1H), 3.80 (s, 6H), 3.43 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.33 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(3-(Difluoromethyl)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2494/3) Following **method D9**, the title compound was isolated as a light yellow oil (75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65-7.61 (m, 2H), 7.43-7.41 (m, 2H), 6.65 (t, *J* = 56.5 Hz, 1H), 5.54 (s, 1H), 5.38 (s, 1H), 3.49 (s, 2H), 3.38 (s, 2H), 2.34 (s, 3H), 2.28 (s, 1H).

2-(3-(2,2-Difluoroethoxy)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2497/3) Following **method D9**, the title compound was isolated as a light yellow oil (82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29-7.25 (m, 1H), 7.38-7.34 (m, 1H), 7.11-7.10 (m, 1H), 6.85-6.82 (m, 1H), 6.09 (tt, *J* = 55.2, 4.1 Hz, 1H), 5.50 (s, 1H), 5.33 (s, 1H), 4.20 (td, *J* = 13.1, 4.1 Hz, 2H), 3.45 (s, 2H), 3.38 (d, *J* = 2.0 Hz, 2H), 2.33 (s, 3H), 2.27 (t, *J* = 2.0 Hz, 1H).

2-(3-(Difluoromethoxy)-4-fluorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2495/3) Following **method D9**, the title compound was isolated as a yellow oil (84%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44-7.41 (m, 1H), 7.38-7.34 (m, 1H), 7.14-7.09 (m, 1H), 6.56 (t, *J* = 73.7 Hz, 1H), 5.47 (s, 1H), 5.33 (s, 1H), 3.42 (s, 2H), 3.36 (s, 2H), 2.32 (s, 3H), 2.28 (s, 1H).

2-(4-Cyclopropylphenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2496/3) Following **method D9**, the title compound was isolated as a yellow oil (70%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.38 (m, 2H), 7.05 – 7.01 (m, 2H), 5.45 (d, *J* = 1.0 Hz, 1H), 5.25 (br, 1H), 3.45 (s, 2H), 3.37 (d, *J* = 2.0 Hz, 2H), 2.33 (s, 3H), 2.26 (t, *J* = 2.0 Hz, 1H), 1.91-1.85 (m, 1H), 0.97-0.92 (m, 2H), 0.71-0.67 (m, 2H).

2-(4-(Difluoromethoxy)-3-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2493/3) Following **method D9,** the title compound was isolated as a yellow oil (79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (dd, *J* = 12.0, 2.1 Hz, 1H), 7.29 (ddd, *J* = 8.4, 2.1, 1.1 Hz, 1H), 7.17 (t, *J* = 8.4 Hz, 1H), 6.53 (t, *J* = 73.7 Hz, 1H), 5.50 (s, 1H), 5.34 (s, 1H), 3.42 (s, 2H), 3.36 (s, 2H), 2.32 (s, 3H), 2.27 (s, 1H).

2-(3-Isopropoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2498/3) Following **method D9**, the title compound was isolated as a colourless oil (79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26-7.20 (m, 1H), 7.07-7.05 (m, 2H), 6.82-6.79 (m, 1H), 5.47 (d, *J* = 1.5 Hz, 1H), 5.28 (br, 1H), 4.60-4.51 (m, 1H), 3.43 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.33 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H), 1.34 (d, *J* = 6.0 Hz, 6H).

2-(3-Chloro-4-isopropoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2499/3) Following **method D9**, the title compound was isolated as pale yellow oil (69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 2.3 Hz, 1H), 7.35 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 1H), 5.42 (d, *J* = 1.2 Hz, 1H), 5.23 (d, *J* = 1.2 Hz, 1H), 4.58-4.49 (m, 1H), 3.40 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 2.32 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H), 1.38 (d, *J* = 6.0 Hz, 6H).

***N*-Methyl-2-(4-morpholinophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2516/3)** Following **method D9**, the title compound was isolated as a yellow oil (73%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 8.9 Hz, 2H), 6.87 (d, *J* = 8.9 Hz, 2H), 5.45 (s, 1H), 5.23 (s, 1H), 3.85 (t, *J* = 4.8 Hz, 4H), 3.49 (s, 2H), 3.41 (s, 2H), 3.17 (t, *J* = 4.8 Hz, 4H), 2.36 (s, 3H), 2.29 (s, 1H).

2-(4-(Isopropylthio)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2514/3) Following **method D9**, the title compound was isolated as a colourless oil (75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46-7.43 (m, 2H), 7.36-7.33 (m, 2H), 5.52 (s, 1H), 5.32 (s, 1H), 3.47 (s, 2H), 3.41-3.34 (m, 3H), 2.35 (s, 3H), 2.27 (s, 1H), 1.31 (d, *J* = 6.4 Hz, 6H).

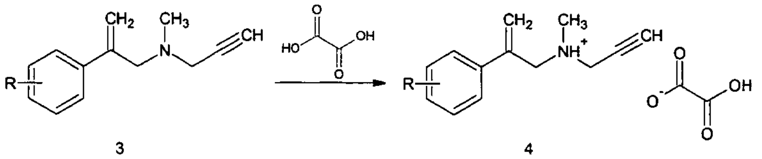
2-(2,3-Dihydrobenzofuran-5-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2515/3) Following **method D9**, the title compound was isolated as a light yellow oil (77%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 1.2 Hz, 1H), 7.28 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.36 (d, *J* = 1.6 Hz, 1H), 5.18 (br, 1H), 4.56 (t, *J* = 8.7 Hz, 2H), 3.42 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 3.21 (t, *J* = 8.7 Hz, 2H), 2.32 (s, 3H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(1*H*-Indol-6-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2532) Following **method D9,** the title compound was isolated as a yellow solid (79%). Mp 45.3 – 45.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.55 (br, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 2.8 Hz, 1H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.40 (dd, *J* = 2.8, 0.8 Hz, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.23 (q, *J* = 1.2 Hz, 1H), 3.56 (d, *J* = 1.2 Hz, 2H), 3.33 (d, *J* = 2.4 Hz, 2H), 2.64 (t, *J* = 2.4 Hz, 1H), 2.30 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{13}H_{14}FClN^+$ $[M+H]^+$ 225.1386, found 225.1396.

2-(3-Benzylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2531/3) Following **method D9,** the title compound was isolated as a yellow oil (68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35-7.28 (m, 3H), 7.24-7.19 (m, 3H), 7.09 (d, *J* = 7.6 Hz, 1H), 5.47 (s, 1H), 5.30 (s, 1H), 3.99 (s, 2H), 3.46 (s, 2H), 3.37 (s, 2H), 2.33 (s, 3H), 2.25 (s, 1H).

2-(4-(Ethylthio)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2513/3) Following **method D9**, the title compound was isolated as colourless oil (80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46-7.42 (m, 2H), 7.29-7.26 (m, 2H), 5.49 (d, *J* = 0.8 Hz, 1H), 5.29 (br, 1H), 3.46 (s, 2H), 3.38 (d, *J* = 2.0 Hz, 2H), 2.94 (q, *J* = 7.4 Hz, 2H), 2.34 (s, 3H), 2.27 (t, *J* = 2.0 Hz, 1H), 1.32 (t, *J* = 7.4 Hz, 3H).

Scheme 43



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R=3-OCH$_3$, 4-OBn	(SZV-2462)
R=3-CH$_3$, 4-Cl	(SZV-2463)
R=4-Ph	(SZV-2464)
R=3-OCHF$_2$	(SZV-2465)
R=3-CF$_3$, 4-Cl	(SZV-2466)
R=3,4-di-Cl	(SZV-2467)
R=3-Cl, 4-CH$_3$	(SZV-2468)
R=3-Cl, 4-F	(SZV-2469)
R=4-OCHF$_2$	(SZV-2478)
R=4-CHF$_2$	(SZV-2479)
R=4-CH=CH$_2$	(SZV-2480)
R=3,5-di-F	(SZV-2481)
R=4-CH$_2$-CH$_3$	(SZV-2482)
R=3,5-di-OCH$_3$	(SZV-2483)
R=3-F, 4-OCHF$_2$	(SZV-2493)
R=CHF$_2$	(SZV-2494)
R=3-OCHF$_2$, 4-F	(SZV-2495)
R=4-cyclopropyl	(SZV-2496)
R=3-OCH$_2$CHF$_2$	(SZV-2497)
R=3-OCH(CH$_3$)$_2$	(SZV-2498)
R=3-Cl, 4-OCH(CH$_3$)$_2$	(SZV-2499)
R=4-SCH(CH$_3$)$_2$	(SZV-2514)
R=3,4-(OCH$_2$CH$_2$)	(SZV-2515)
R=4-N(CH$_2$CH$_2$OCH$_2$CH$_2$)	(SZV-2516)
R=3-Bn	(SZV-2531)

2-(4-(Benzyloxy)-3-methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2462) Following **method H1**, the title compound was isolated as a white solid (63%). Mp 147.6 -149.4 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.46 – 7.36 (m, 4H), 7.35-7.31 (m, 1H), 7.14 (d, *J* = 2.0 Hz, 1H), 7.05 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.18 (d, *J* = 1.5 Hz, 1H), 5.09 (s, 2H), 3.79 (s, 3H), 3.47 (s, 2H), 3.38 (d, *J* = 2.2 Hz, 2H), 3.25 (d, *J* = 2.2 Hz, 1H), 2.25 (s, 3H). Anal. calcd. for $C_{21}H_{23}NO_2x(COOH)_2$ (411.45): C, 67.14%; H, 6.12%; N, 3.40%; O 23.33%. Found: C, 66.98%; H, 6.02%; N, 3.37%; O, 23.86%.

2-(4-Chloro-3-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2463) Following **method H1**, the title compound was isolated as a white solid (73%). Mp 156.8 – 158.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.50 (br, 1H), 7.36 (br, 2H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.27 (d, *J* = 1.2 Hz, 1H), 3.45 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H), 2.33 (s, 3H), 2.22 (s, 3H). Anal. calcd. for $C_{14}H_{16}ClNx(COOH)_2$ (323.77): C, 59.35%; H, 5.60%; N, 4.33%; O 19.77%. Found: C, 60.07%; H, 5.60%; N, 4.25%; O, 20.20%.

2-([1,1'-Biphenyl]-4-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2464) Following **method H1**, the title compound was isolated as a white solid (81%). Mp 168.6 -169.9 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.69-7.67 (m, 2H), 7.63 (s, 4H), 7.49-7.45 (m, 2H), 7.36 (app. t, 1H), 5.61 (d, *J* = 1.6 Hz, 1H), 5.30 (d, *J* = 1.6 Hz, 1H), 3.53 (s, 2H), 3.39 (d, *J* = 2.4 Hz, 2H), 3.24 (t, *J* = 2.4 Hz, 1H), 2.26 (s, 3H). Anal. calcd. for $C_{19}H_{19}Nx(COOH)_2$ (351.40): C, 71.78%; H, 6.02%; N, 3.99%; O, 18.21%. Found: C, 72.52%; H, 6.01%; N, 3.93%; O, 18.49%.

2-(3-Chloro-4-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2469) Following **method H1**, the title compound was isolated as a white solid (77%). Mp 145.2 – 146.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.75 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.57-7.53 (m, 1H), 7.37 (app. t, 1H), 5.59 (d, *J* = 0.6 Hz, 1H), 5.30 (d, *J* = 0.6 Hz, 1H), 3.45 (s, 2H), 3.34 (d, *J* = 2.3 Hz, 2H), 3.22 (t, *J* = 2.3 Hz, 1H), 2.21 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{13}H_{14}FClN^+$ $[M+H]^+$ 238.0793, found 238.0803.

2-(4-Chloro-3-(trifluoromethyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2466) Following **method H1**, the title compound was isolated as a white solid (87%). Mp 160.6 – 162.2 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.96 (d, *J* = 2.0 Hz, 1H), 7.85 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 5.70 (d, *J* = 1.2 Hz, 1H), 5.39 (d, *J* = 1.2 Hz, 1H), 3.49 (s, 2H), 3.33 (d, *J* = 2.3 Hz, 2H), 3.21 (t, *J* = 2.3 Hz, 1H), 2.20 (s, 3H). Anal. calcd. for $C_{14}H_{13}ClF_3N$x$(COOH)_2$ (377.74): C, 50.87%; H, 4.00%; N, 3.71%; O, 16.94%. Found: C, 51.46%; H, 4.32%; N, 3.65%; O, 21.18%.

2-(3-Chloro-4-methylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2468) Following **method H1**, the title compound was isolated as a white solid (78%). Mp 139.3 -140.2 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.56 (d, *J* = 1.7 Hz, 1H), 7.40 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 5.56 (d, *J* = 1.2 Hz, 1H), 5.27 (d, *J* = 1.2 Hz, 1H), 3.45 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H), 2.31 (s, 3H), 2.22 (s, 3H). Anal. calcd. for $C_{14}H_{16}ClN$x$(COOH)_2$ (323.77): C, 59.35%; H, 5.60%; N, 4.33%; O, 19.77%. Found: C, 60.07%; H, 5.74%; N, 4.32%; O, 19.88%.

2-(3,4-Dichlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate

(SZV-2467) Following **method H1**, the title compound was isolated as a white solid (81%). Mp 153.3 – 156.0 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.79 (d, *J* = 2.0 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.53 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.65 (d, *J* = 0.8 Hz, 1H), 5.34 (d, *J* = 0.8 Hz, 1H), 3.45 (s, 2H), 3.33 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H), 2.21 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{13}H_{14}Cl_2N^+$ $[M+H]^+$ 254.0498, found 254.0503.

2-(3-(difluoromethoxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2465) Following **method H1**, the title compound was isolated as a white solid (81%). Mp 104.4 – 104.9 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.43-7.38 (m, 2H), 7.32 (br, 1H), 7.24 (s, 1H), 7.11-7.06 (m, 1H), 5.60 (d, *J* = 1.2 Hz, 1H), 5.32 (d, *J* = 1.2 Hz, 1H), 3.48 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H), 2.24 (s, 3H). Anal. calcd. fo: $C_{14}H_{15}F_2NO$x$(COOH)_2$ (341.31): C, 56.30%; H, 5.02%; N, 4.10%; O, 23.44%. Found: C, 56.93%; H, 5.27%; N, 4.13%; O, 26.01%.

2-(4-(Difluoromethyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2479) Following **method H1**, the title compound was isolated as a white solid (81%). Mp 139.0 -140.1 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.01 (app. t, 1H), 5.61 (s, 1H), 5.35 (s, 1H), 3.50 (s, 2H), 3.35 (d, J = 2.4 Hz, 2H), 3.22 (t, J = 2.4 Hz, 1H), 2.23 (s, 3H). Anal. calcd. for $C_{14}H_{15}F_2Nx(COOH)_2$ (325.31): C, 59.07%; H, 5.27%; N, 4.31%; O, 19.67%. Found: C, 59.01%; H, 5.13%; N, 4.23%; O, 21.06%.

2-(4-(Difluoromethoxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2478) Following **method H1**, the title compound was isolated as a white solid (77%). Mp 131.9 – 133.1 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.60-7.57 (m, 2H), 7.23 (t, J = 74.0 Hz, 1H), 7.15-7.11 (m, 2H), 5.52 (d, J = 1.2 Hz, 1H), 5.26 (d, J = 1.2 Hz, 1H), 3.46 (s, 2H), 3.34 (d, J = 2.4 Hz, 2H), 3.21 (t, J = 2.4 Hz, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{14}H_{15}F_2NOx(COOH)_2$ (341.31): C, 56.30%; H, 5.02%; N, 4.10%; O, 23.44%. Found: C, 56.06%; H, 4.98%; N, 3.99%; O, 24.95%.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(4-vinylphenyl)prop-2-en-1-aminium carboxyformate (SZV-2480)** Following **method H1**, the title compound was isolated as a white solid (94%). Mp 144.6 -145.4 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.51 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 6.73 (dd, J = 17.8, 10.8 Hz, 1H), 5.83 (dd, J = 17.8, 1.2 Hz, 1H), 5.57 (d, J = 1.2 Hz, 1H), 5.28 (d, J = 1.2 Hz, 1H), 5.26 (dd, J = 10.8, 1.2 Hz, 1H), 3.52 (s, 2H), 3.39 (d, J = 2.4 Hz, 2H), 3.25 (t, J = 2.4 Hz, 1H), 2.26 (s, 3H). Anal. calcd. for $C_{15}H_{17}Nx(COOH)_2$ (301.34): C, 67.76%; H, 6.36%; N, 4.65%; O, 21.24%. Found: C, 67.31%; H, 6.31%; N, 4.52%; O, 20.95%.

2-(3,5-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2481) Following **method H1**, the title compound was isolated as a white solid (89%). Mp 160.0 – 161.0 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.31-7.26 (m, 2H), 7.13 (tt, J = 9.2, 2.4 Hz, 1H), 5.70 (s, 1H), 5.37 (s, 1H), 3.46 (s, 2H), 3.36 (d, J = 2.4 Hz, 2H), 3.23 (t, J = 2.4 Hz, 1H), 2.23 (s, 3H). Anal. calcd. for $C_{13}H_{13}F_2Nx(COOH)_2$ (311.28): C, 57.88%; H, 4.86%; N, 4.50%; O, 20.56%. Found: C, 57.69%; H, 5.10%; N, 4.46%; O, 22.43%.

2-(4-ethylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2482) Following **method H1**, the title compound was isolated as a white solid (85%). Mp 123.2 -125.7 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.43 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 5.50 (d, J = 1.2 Hz, 1H), 5.24 (d, J = 1.2 Hz, 1H), 3.51 (s, 2H), 3.39 (d, J = 2.4 Hz, 2H), 3.26 (t, J = 2.4 Hz, 1H), 2.59 (q, J = 7.6 Hz, 2H), 2.26 (s, 3H), 1.17 (t, J = 7.6 Hz, 3H). HRMS (ESI+) *m/z* calc for $C_{15}H_{20}N^+$ $[M+H]^+$ 214.1590, found 214.1600.

2-(3,5-Dimethoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2483) Following **method H1**, the title compound was isolated as a white solid (88%). Mp 144.8 -145.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 6.66 (d, J = 2.4 Hz, 2H), 6.44 (t, J = 2.4 Hz, 1H), 5.55 (d, J = 1.2 Hz, 1H), 5.27 (d, J = 1.2 Hz, 1H), 3.75 (s, 6H), 3.48 (s, 2H), 3.39 (d, J = 2.4 Hz, 2H), 3.26 (t, J = 2.4 Hz, 1H), 2.26 (s, 3H). Anal. calcd. for $C_{15}H_{19}NO_2x(COOH)_2$ (335.35): C, 60.89%; H, 6.31%; N, 4.18%; O, 28.63%. Found: C, 60.87%; H, 6.32%; N, 4.10%; O, 28.10%.

2-(3-(Difluoromethyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2494) Following **method H1**, the title compound was isolated as a white solid (79%). Mp 119.4 -120.2 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.71-7.69 (m, 2H), 7.50-7.48 (m, 2H), 7.02 (t, J = 55.8 Hz, 1H), 5.60 (d, J = 1.2 Hz, 1H), 5.34 (d, J = 1.2 Hz, 1H), 3.50 (s, 2H), 3.36 (d, J = 2.4 Hz, 2H), 3.22 (t, J = 2.4 Hz, 1H), 2.24 (s, 3H). Anal. calcd. for $C_{14}H_{15}F_2Nx(COOH)_2$ (325.31): C, 59.07%; H, 5.27%; N, 4.31%; O, 19.67%. Found: C, 58.99%; H, 5.29%; N, 4.19%; O, 21.39%.

2-(3-(2,2-Difluoroethoxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2497) Following **method H1**, the title compound was isolated as a white solid (87%). Mp 118.1 -119.2 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.28 (app. t, 1H), 7.17-7.14 (m, 2H), 6.94 (dd, J = 7.8, 2.4 Hz, 1H), 6.38 (tt, J = 54.4, 3.6 Hz, 2H), 5.57 (d, J = 1.6 Hz, 1H), 5.29 (d, J = 1.6 Hz, 1H), 4.32 (td, J = 14.8, 3.6 Hz, 2H), 3.50 (s, 2H), 3.38 (d, J = 2.4 Hz, 2H), 3.24 (t, J = 2.4 Hz, 1H), 2.25 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{15}H_{18}F_2NO^+$ $[M+H]^+$ 266.1351, found 266.1358.

2-(3-(Difluoromethoxy)-4-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2495) Following **method H1**, the title compound was isolated as a white solid (86%). Mp 140.2 -140.8 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.54-7.51 (m, 1H), 7.49-7.45 (m, 1H), 7.38-7.33 (m, 1H), 5.57 (s, 1H), 5.30 (s, 1H), 3.45 (s, 2H), 3.35 (d, J = 2.4 Hz, 2H), 3.21 (t, J = 2.4 Hz, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{14}H_{14}F_3NOx(COOH)_2$ (359.30): C, 53.49%; H, 4.49%; N, 3.90%. Found: C, 53.54%; H, 4.18%; N, 3.85%.

2-(4-Cyclopropylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2496) Following **method H1**, the title compound was isolated as a white solid (78%). Mp 142.8 -143.8 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.40 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 5.48 (d, J = 1.2 Hz, 1H), 5.21 (d, J = 1.2 Hz, 1H), 3.47 (s, 2H), 3.36 (d, J = 2.4 Hz, 2H), 3.23 (t, J = 2.4 Hz, 1H), 2.24 (s, 3H), 1.93-1.87 (m, 1H), 0.96-0.92 (m, 2H), 0.68-0.64 (m, 2H). Anal. calcd. for $C_{16}H_{19}Nx(COOH)_2$ (315.36): C, 68.55%; H, 6.71%; N, 4.44%. Found: C, 68.48%; H, 6.34%; N, 4.47%.

2-(4-(Difluoromethoxy)-3-fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2493) Following **method H1**, the title compound was isolated as a white solid (64%). Mp 125.0 -125.9 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.58 (dd, J = 12.6, 2.2 Hz, 1H), 7.43-7.41 (m, 1H), 7.32 (t, J = 8.4 Hz, 1H), 7.23 (t, J = 73.6 Hz, 1H), 5.61 (d, J = 1.2 Hz, 1H), 5.32 (d, J = 1.2 Hz, 1H), 3.46 (s, 2H), 3.35 (d, J = 2.4 Hz, 2H), 3.22 (t, J = 2.4 Hz, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{14}H_{14}F_3NOx(COOH)_2$ (359.30): C, 53.49%; H, 4.49%; N, 3.90%. Found: C, 53.52%; H, 4.21%; N, 3.89%.

2-(3-Isopropoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2498) Following **method H1**, the title compound was isolated as a white solid (80%). Mp 106.2 -106.9 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.22 (app. t, 1H), 7.07 –

7.03 (m, 2H), 6.85 – 6.82 (m, 1H), 5.53 (d, *J* = 1.2 Hz, 1H), 5.27 (d, *J* = 1.2 Hz, 1H), 4.65-4.59 (m, 1H), 3.50 (s, 2H), 3.39 (d, *J* = 2.4 Hz, 2H), 3.25 (t, *J* = 2.4 Hz, 1H), 2.26 (s, 3H), 1.26 (d, *J* = 6.0 Hz, 6H). Anal. calcd. for $C_{16}H_{21}NOx(COOH)_2$ (333.38): C, 64.85%; H, 6.95%;N, 4.20%. Found: C, 64.74%; H, 6.64%; N, 4.26%.

2-(3-Chloro-4-isopropoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2499) Following **method H1**, the title compound was isolated as a white solid (77%). Mp 154.2 – 155.8 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.59 (d, *J* = 2.2 Hz, 1H), 7.45 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.21 (d, *J* = 1.2 Hz, 1H), 4.70-4.64 (m, 1H), 3.45 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 3.26 (d, *J* = 2.4 Hz, 1H), 2.23 (s, 3H), 1.29 (d, *J* = 6.0 Hz, 6H). Anal. calcd. for $C_{16}H_{20}ClNOx(COOH)_2$ (367.82): C, 58.78%; H, 6.03%; N, 3.81%. Found: C, 58.84%; H, 5.76%; N, 3.83%.

***N*-methyl-2-(4-morpholinophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2516)** Following **method H1**, the title compound was isolated as a white solid (79%). Mp 148.8 – 149.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.41 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.42 (d, *J* = 1.6 Hz, 1H), 5.11 (d, *J* = 1.6 Hz, 1H), 3.74-3.72 (m, 4H), 3.45 (s, 2H), 3.36 (d, *J* = 2.0 Hz, 2H), 3.23 (t, *J* = 2.0 Hz, 1H), 3.12-3.10 (m, 4H), 2.24 (s, 3H). Anal. calcd. for $C_{17}H_{22}N_2Ox(COOH)_2$ (360.40): C, 63.32%; H, 6.71%; N, 7.77%. Found: C, 63.13%; H, 6.35%; N, 7.75%.

2-(4-(Isopropylthio)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2514) Following **method H1**, the title compound was isolated as a white solid (82%). Mp 140.3 – 140.9 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.56 (d, *J* = 1.2 Hz, 1H), 5.26 (d, *J* = 1.2 Hz, 1H), 3.53-3.48 (m, 1H), 3.47 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 3.23 (t, *J* = 2.4 Hz, 1H), 2.24 (s, 3H), 1.24 (d, *J* = 6.8 Hz, 6H). Anal. calcd. for $C_{16}H_{21}NSx(COOH)_2$ (349.44): C, 61.87%; H, 6.63%; N, 4.01%. Found: C, 61.84%; H, 6.40%; N, 4.15%.

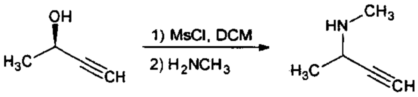
2-(2,3-Dihydrobenzofuran-5-yl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2515) Following **method H1**, the title compound was isolated as a white solid (83%). Mp 147.4 – 148.4 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.41 (d, *J* = 2.0 Hz, 1H), 7.26 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 5.41 (d, *J* = 1.6 Hz, 1H), 5.14 (d, *J* = 1.6 Hz, 1H), 4.52 (t, *J* = 8.8 Hz, 2H), 3.46 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 3.25 (t, *J* = 2.4 Hz, 1H), 3.17 (t, *J* = 8.8 Hz, 2H), 2.26 (s, 3H). Anal. calcd. for $C_{15}H_{17}NOx(COOH)_2$ (317.34): C, 64.34%; H, 6.03%; N, 4.41%. Found: C, 64.25%; H, 5.72%; N, 4.48%.

2-(4-(Ethylthio)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2513) Following **method H1**, the title compound was isolated as a white solid (83%). Mp 125.6 – 126.1 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.50-7.47 (m, 2H), 7.2-7.25 (m, 2H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.24 (d, *J* = 1.2 Hz, 1H), 3.47 (s, 2H), 3.36 (d, *J* = 2.4 Hz, 2H), 3.23 (t, *J* = 2.4 Hz, 1H), 2.98 (q, *J* = 7.2 Hz, 2H), 2.24 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H). Anal. calcd.

for $C_{15}H_{19}NSx(COOH)_2$ (335.42): C, 60.87%; H, 6.31%; N, 4.18%. Found: C, 60.85%; H, 6.03%; N, 4.27%.

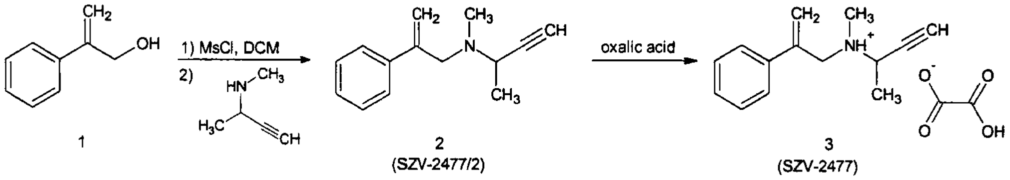
2-(3-Benzylphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2531) Following **method H1**, the title compound was isolated as a white solid (70%). Mp 127.7 – 128.1 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.41 (br, 1H), 7.35-7.12 (m, 8H), 5.49 (d, *J* = 1.6 Hz, 1H), 5.24 (d, *J* = 1.6 Hz, 1H), 3.94 (s, 2H), 3.45 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 3.22 (d, *J* = 2.4 Hz, 1H), 2.22 (s, 3H). HRMS (ESI+) *m/z* calc for $C_{20}H_{22}N^+$ $[M+H]^+$ 276.1717, found 276.1749.

Scheme 44



To a solution of (*R*)-but-3-yn-2-ol (3.7 mmol) in dichloromethane (20.0 ml) at 0 °C was added triethylamine (1.2 eq) followed by methanesulfonyl chloride (1eq). The reaction mixture was then stirred at 0 °C for 30 min before warming up to room temperature. After stirring at room temperature for another 30 min, methylamine (40% w/w in H_2O) (10 eq) was added and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was then extracted with diethyl ether (4x15.0 ml). The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure (40 °C and 400 mbar) to afford the desired crude product. The crude product was used in the next step without further purification.

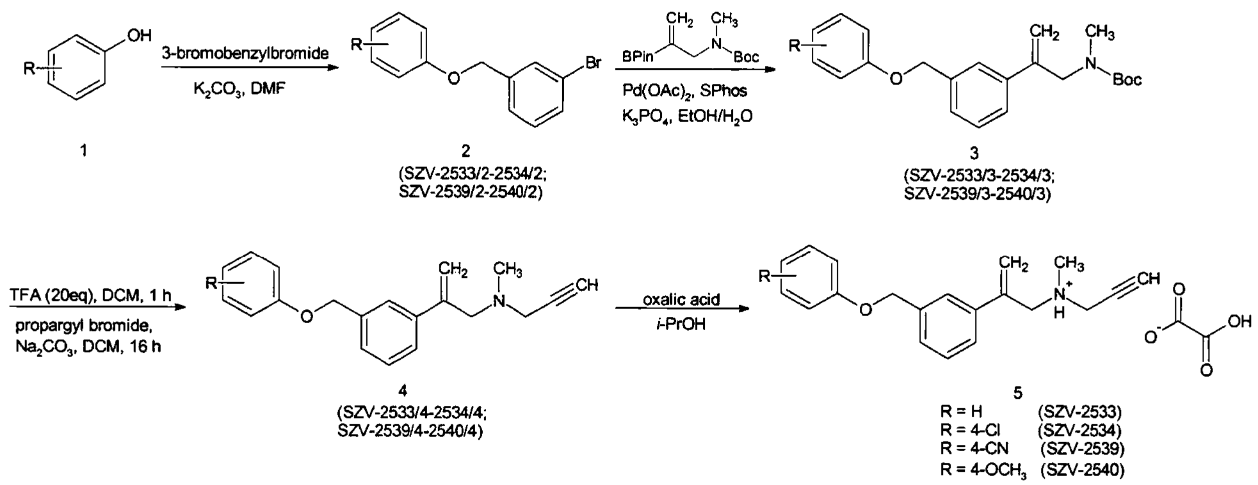
Scheme 45



***N*-Methyl-*N*-(2-phenylallyl)but-3-yn-2-amine (SZV-2477/2)** To a solution of 2-phenylprop-2-en-1-ol (0.8 mmol) in dichloromethane (17.0 ml) at 0 °C was added triethylamine (1.2 eq) followed by methanesulfonyl chloride (1 eq). The reaction mixture was then stirred at 0 °C for 30 min before warming up to room temperature. After stirring at room temperature for another 30 min, crude *N*-methylbut- 3-yn-2-amine (4 eq) was added and the reaction mixture was stirred at room temperature overnight. The organic layer was then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (typical eluent: 5% ethyl acetate in petroleum ether, Rf = 0.3) to afford the the title compound as a yellow oil (33% over two steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52-7.49 (m, 2H), 7.34-7.26 (m, 3H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.29 (d, *J* = 1.2 Hz, 1H), 3.65 (qd, $J = 7.1$, 2.2 Hz, 1H), 3.54 (d, $J = 13.6$ Hz, 1H), 3.32 (d, $J = 13.6$ Hz, 1H), 2.28 (d, $J = 2.2$ Hz, 1H), 2.23 (s, 3H), 1.32 (d, $J = 7.1$ Hz, 3H).

***N*-Methyl-*N*-(2-phenylallyl)but-3-yn-2-aminium carboxyformate (SZV-2477)** Following **method H1**, the title compound was isolated as a white solid (63%). Mp 108.5 -110.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.52-7.50 (m, 2H), 7.35-7.28 (m, 3H), 5.50 (d, $J = 1.2$ Hz, 1H), 5.26 (d, $J = 1.2$ Hz, 1H), 3.67 (qd, $J = 6.8$, 2.0 Hz, 1H), 3.55 (d, $J = 13.6$ Hz, 1H), 3.35 (d, $J = 13.6$ Hz, 1H), 3.23 (d, $J = 2.0$ Hz, 1H), 2.14 (s, 3H), 1.23 (d, $J = 6.8$ Hz, 3H). HRMS (ESI+) *m/z* calcd. for $C_{14}H_{18}N^+$ $[M+H]^+$ 200.1434, found 200.1430.

Scheme 46



1-Bromo-3-(phenoxymethyl)benzene (SZV-2533/2) (Mann FG et al, J. Chem. Soc., 1954, 2819-2826) Following **method S1**, the title compound was isolated as a colourless oil (82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (s, 1H), 7.47-7.44 (m, 1H), 7.37-7.35 (m, 1H), 7.32-7.23 (m, 4H), 7.00-6.96 (m, 3H), 5.04 (s, 2H).

1-Bromo-3-((4-chlorophenoxy)methyl)benzene (SZV-2534/2) Following **method S1**, the title compound was isolated as a colourless oil (85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (br, 1H), 7.48 – 7.45 (m, 1H), 7.35-7.32 (m, 1H), 7.27-7.23 (m, 4H), 6.91-6.87 (m, 2H), 5.01 (s, 2H).

4-((3-Bromobenzyl)oxy)benzonitrile (SZV-2539/2) Following **method S1** the title compound was isolated as a white solid (70%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62-7.57 (m, 3H), 7.50-7.47 (m, 1H), 7.35-7.32 (m, 1H), 7.29-7.25 (m, 2H), 7.03-6.99 (m, 2H), 5.08 (s, 2H).

1-Bromo-3-((4-methoxyphenoxy)methyl)benzene (SZV-2540/2) Following **method S1**, the title compound was isolated as a colourless crystals (90%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (br, 1H), 7.46-7.43 (m, 1H), 7.36-7.33 (m, 1H), 7.26-7.22 (m, 1H), 6.91-6.88 (m, 2H), 6.86 – 6.83 (m, 2H), 4.98 (s, 2H), 3.77 (s, 3H).

***tert*-Butyl methyl(2-(3-(phenoxymethyl)phenyl)allyl)carbamate (SZV-2533/3)** Following **method R2**, the title compound was isolated as a colourless oil (54% over two steps). ^{1}H NMR (400

MHz, Chloroform-*d*) δ 7.52-7.36 (m, 4H), 7.32-7.27 (m, 2H), 7.00-6.95 (m, 3H), 5.43 (br. d, 1H), 5.13 (s, 1H), 5.06 (s, 2H), 4.30 (br. d, 2H), 2.78 (br. d, 3H), 1.44 (s, 9H).

***tert*-Butyl (2-(3-((4-chlorophenoxy)methyl)phenyl)allyl)(methyl)carbamate (SZV-2534/3)** Following **method R2**, the title compound was isolated as a yellow solid (55% over two steps). Mp 101-102 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52-7.34 (m, 4H), 7.26-7.23 (m, 2H), 6.91-6.89 (m, 2H), 5.43 (br. d, 1H), 5.14 (s, 1H), 5.02 (s, 2H), 4.29 (d, J = 31.0 Hz, 2H), 2.77 (br. d, 3H), 1.43 (s, 9H).

***tert*-Butyl (2-(3-((4-cyanophenoxy)methyl)phenyl)allyl)(methyl)carbamate (SZV-2539/3)** Following **method R2**, the title compound was isolated as a yellow solid (63% over two steps). Mp 99-101 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61-7.58 (m, 2H), 7.52-7.32 (m, 4H), 7.04-7.00 (m, 2H), 5.43 (br. d, 1H), 5.15 (s, 1H), 5.10 (s, 2H), 4.29 (br. d, 2H), 2.77 (br. d, 3H), 1.43 (s, 9H).

***tert*-Butyl (2-(3-((4-methoxyphenoxy)methyl)phenyl)allyl)(methyl)carbamate (SZV-2540/3)** Following **method R2**, the title compound isolated was not pure, however, it was used directly for the subsequent step.

***N*-Methyl-2-(3-(phenoxymethyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2533/4)** Following **method M1,** the title compound was isolated as a colourless oil (52% over two steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (br, 1H), 7.48-7.46 (m, 1H), 7.36-7.34 (m, 2H), 7.31 – 7.27 (m, 2H), 7.00-6.94 (m, 3H), 5.51 (s, 1H), 5.32 (s, 1H), 5.07 (s, 2H), 3.47 (s, 2H), 3.37 (d, J = 2.0 Hz, 2H), 2.33 (s, 3H), 2.25 (t, J = 2.0 Hz, 1H).

2-(3-((4-Chlorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2534/4) Following **method M1**, the title compound was isolated as a yellow oil (25% over two steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (br, 1H), 7.48-7.46 (m, 1H), 7.37-7.33 (m, 2H), 7.25 – 7.22 (m, 2H), 6.92-6.90 (m, 2H), 5.51 (s, 1H), 5.33 (s, 1H), 5.04 (s, 2H), 3.47 (s, 2H), 3.37 (s, 2H), 2.33 (s, 3H), 2.26 (s, 1H).

4-((3-(3-(Methyl(prop-2-yn-1-yl)amino)prop-1-en-2-yl)benzyl)oxy)benzonitrile (SZV-2539/4) Following **method M1**, the title compound was isolated as a yellow oil (49% over two steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.56 (m, 2H), 7.55 (s, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.35 (dt, J = 15.1, 7.5 Hz, 2H), 7.06 – 7.00 (m, 2H), 5.51 (br, 1H), 5.34 (br, 1H), 5.12 (s, 2H), 3.47 (br, 2H), 3.37 (br, 2H), 2.27 (br, 1H).

2-(3-((4-Methoxyphenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2540/4) Following **method M1**, the title compound was isolated was not pure but was converted to the corresponding oxalate salt in the next step.

***N*-Methyl-2-(3-(phenoxymethyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2533)** Following **method H1**, the title compound was isolated as a white solid (85%). Mp 125.6 – 126.9 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.60 (br, 1H), 7.50-7.47 (m, 1H), 7.37-7.35 (m, 2H), 7.31-7.27 (m, 2H), 7.03-7.00 (m, 2H), 6.96-6.92 (m, 1H), 5.55 (d, J = 1.2 Hz, 1H), 5.29 (d, J = 1.2 Hz, 1H), 5.10 (s, 2H), 3.50 (s, 2H), 3.37 (d, J = 2.3 Hz, 2H), 3.23 (t, J = 2.3

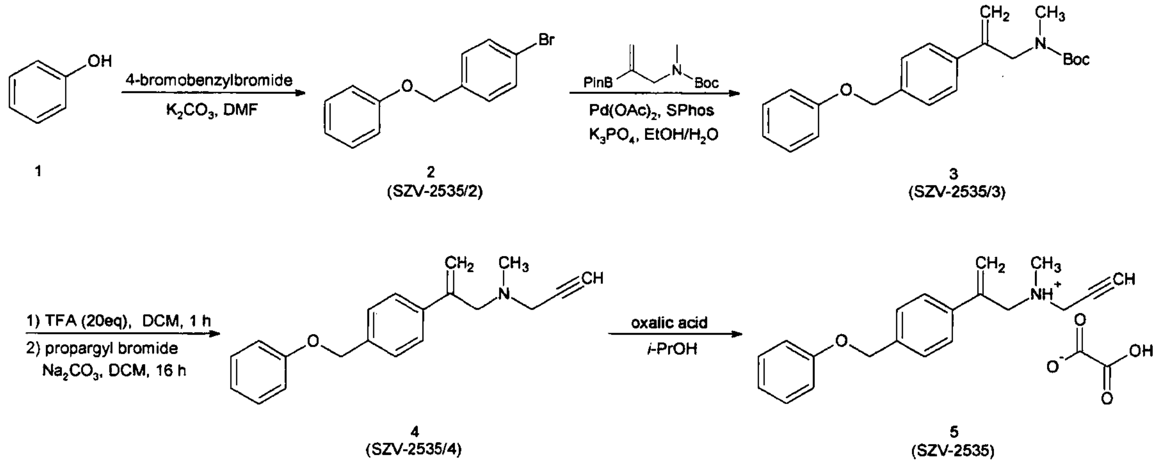
Hz, 1H), 2.25 (s, 3H). Anal. calcd. for $C_{20}H_{21}NOx(COOH)_2$ (381.42): C, 69.28%; H, 6.08%; N, 3.67%. Found: C, 69.21%; H, 5.72%; N, 3.74%.

2-(3-((4-Chlorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2534) Following **method H1**, the title compound was isolated as a white solid (82%). Mp 122.5 – 123.6 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.59 (br, 1H), 7.50-7.48 (m, 1H), 7.36-7.31 (m, 4H), 7.06-7.03 (m, 2H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.28 (d, *J* = 1.2 Hz, 1H), 5.10 (s, 2H), 3.47 (s, 2H), 3.34 (d, *J* = 2.3 Hz, 2H), 3.21 (t, *J* = 2.3 Hz, 1H), 2.23 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{21}ClNO^+$ $[M+H]^+$ 326.1306, found 326.1302.

2-(3-((4-Cyanophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2539) Following **method H1**, the title compound was isolated as a white solid (97%). Mp 149.1 – 150.8 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.81 – 7.75 (m, 2H), 7.61 (s, 1H), 7.53 – 7.47 (m, 1H), 7.37 (dd, *J* = 4.0, 1.2 Hz, 2H), 7.23 – 7.17 (m, 2H), 5.55 (d, *J* = 1.6 Hz, 1H), 5.29 (d, *J* = 1.6 Hz, 1H), 5.21 (s, 2H), 3.47 (s, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 3.21 (t, *J* = 2.4 Hz, 1H), 2.23 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{21}H_{21}N_2O^+$ $[M+H]^+$ 317.1648, found 317.1659.

2-(3-((4-Methoxyphenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2540) Following **method H1**, the title compound was isolated as a white solid (47%). Mp 117.8 – 119.6 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.58 (br, 1H), 7.49-7.46 (m, 1H), 7.35-7.34 (m, 2H), 6.97-6.93 (m, 2H), 6.88-6.83 (m, 2H), 5.53 (d, *J* = 1.2 Hz, 1H), 5.28 (d, *J* = 1.2 Hz, 1H), 5.03 (s, 2H), 3.69 (s, 6H), 3.47 (s, 2H), 3.35 (d, *J* = 2.4 Hz, 2H), 3.21 (t, *J* = 2.4 Hz, 1H), 2.23 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{21}H_{24}NO_2^+$ $[M+H]^+$ 322.1802, found 322.1804.

Scheme 47



1-Bromo-4-(phenoxymethyl)benzene (SZV-2535/2) (Quach TD et al, Org. Lett., 2003, 5, 1381-1384) Following **method S1**, the title compound was isolated as a white crystals (85%). Mp 97-

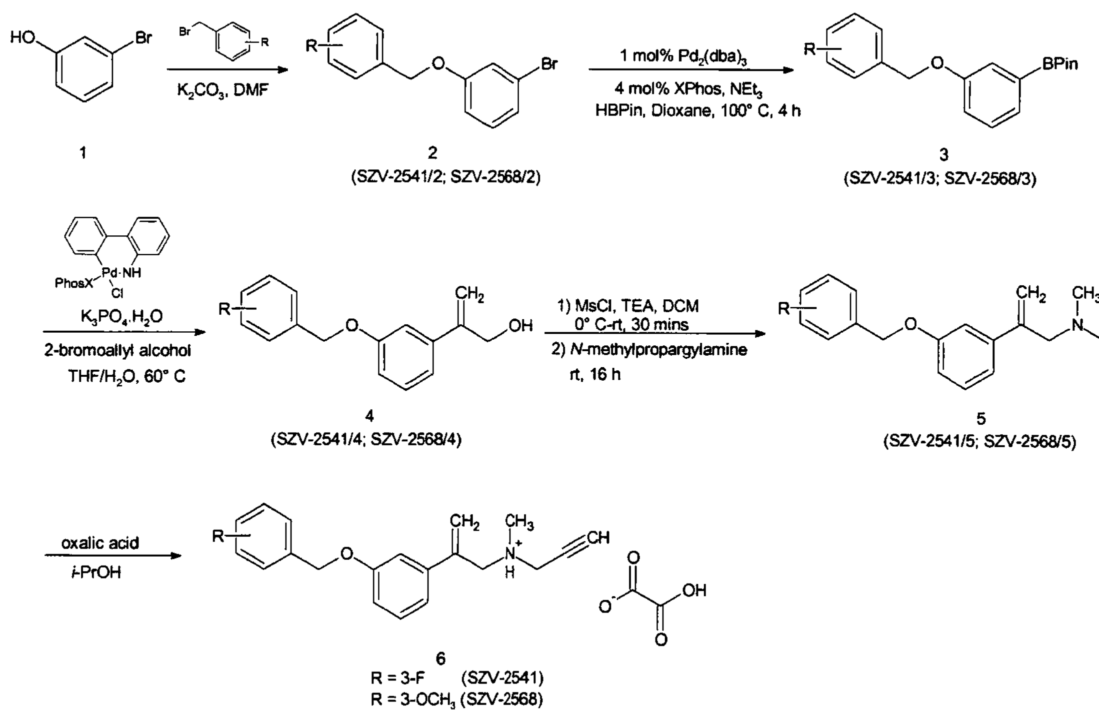
99 °C (lit. Mp 91-92 °C). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 – 7.54 (m, 2H), 7.36 – 7.29 (m, 4H), 7.03 – 6.98 (m, 3H), 5.06 (s, 2H).

***tert*-Butyl methyl(2-(4-(phenoxymethyl)phenyl)allyl)carbamate (SZV-2535/3)** Following **method R2**, the title compound was isolated as a colourless oil (51%). 1H NMR (400 MHz, Chloroform-*d*) δ 7.44-7.38 (m, 4H), 7.31-7.26 (m, 2H), 6.99-6.94 (m, 3H), 5.43 (br. d, 1H), 5.12 (s, 1H), 5.06 (s, 2H), 4.29 (br. d, 2H), 2.77 (br. d, 3H), 1.45 (s, 9H).

***N*-Methyl-2-(4-(phenoxymethyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2535/4)** Following **method M1** the title compound was isolated as a colourless solid (46%). Mp 44-46 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54-7.52 (m, 2H), 7.41-7.39 (m, 2H), 7.31-7.26 (m, 2H), 6.99-6.94 (m, 3H), 5.51 (s, 1H), 5.32 (s, 1H), 5.06 (s, 2H), 3.48 (s, 2H), 3.38 (s, 2H), 2.34 (s, 3H), 2.26 (s, 1H).

***N*-methyl-2-(4-(phenoxymethyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2535)** Following **method H1**, the title compound was isolated as a white solid (75%). Mp 147.3 – 150.1 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.54 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.32 – 7.26 (m, 2H), 7.00 (dd, J = 8.7, 0.9 Hz, 2H), 6.93 (t, J = 7.3 Hz, 1H), 5.55 (d, J = 1.6 Hz, 1H), 5.27 (d, J = 1.6 Hz, 1H), 5.09 (s, 2H), 3.49 (s, 2H), 3.36 (d, J = 2.3 Hz, 2H), 3.23 (t, J = 2.3 Hz, 1H), 2.24 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{20}H_{22}NO^+$ $[M+H]^+$ 292.1696, found 292.1701.

Scheme 48



1-Bromo-3-((3-fluorobenzyl)oxy)benzene (SZV-2541/2) Following **method S1**, the title compound was isolated as a colourless oil (75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38-7.33 (m, 1H), 7.20-7.10 (m, 5H), 7.05-7.00 (m, 1H), 6.91-6.88 (m, 1H), 5.04 (s, 2H).

1-Bromo-3-((3-methoxybenzyl)oxy)benzene (SZV-2568/2) Following **method S1,** the title compound was isolated as a colourless oil (80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (app. t, 1H), 7.16 – 7.08 (m, 3H), 7.00-6.97 (m, 2H), 6.92 – 6.86 (m, 2H), 5.02 (s, 2H), 3.82 (s, 3H).

2-(3-((3-Fluorobenzyl)oxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SZV-2541/3) Following **method Q1,** the title compound was isolated as a colourless oil (30%) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44-7.43 (m, 2H), 7.37-7.29 (m, 2H), 7.21-7.16 (m, 2H), 7.08-7.05 (m, 1H), 7.03-6.98 (m, 1H), 5.09 (s, 2H), 1.35 (s, 12H).

2-(3-((3-Methoxybenzyl)oxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SZV-2568/3) Following **method Q1,** the title compound was isolated as a yellow solid (39%). Mp 59-61 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45-7.41 (m, 2H), 7.32-7.27 (m, 2H), 7.09-7.06 (m, 1H), 7.03-7.01 (m, 2H), 6.87-6.85 (m, 1H), 5.07 (s, 2H), 3.82 (s, 3H), 1.35 (s, 12H).

2-(3-((3-Fluorobenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2541/4) Following **method P2,** the title compound was isolated as a colourless oil (47%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 2H), 7.22 – 7.14 (m, 2H), 7.10 – 6.98 (m, 3H), 6.91 (ddd, *J* = 8.2, 2.4, 1.0 Hz, 1H), 5.46 (dd, *J* = 1.8, 0.8 Hz, 1H), 5.36 (dd, *J* = 1.8, 1.2 Hz, 1H), 5.08 (s, 2H), 4.52 (dd, *J* = 1.2, 0.8 Hz, 2H), 3.49 (s, 1H).

2-(3-((3-Methoxybenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2568/4) Following **method P2,** the title compound was isolated as a brown oil (50%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32-7.25 (m, 2H), 7.08-7.00 (m, 4H), 6.94-6.91 (m, 1H), 6.88-6.86 (m, 1H), 5.46 (dd, *J* = 2.0, 0.8 Hz, 1H), 5.35 (dd, *J* = 2.0, 1.2 Hz, 1H), 5.06 (s, 2H), 4.52 (dd, *J* = 1.2, 0.8 Hz, 2H), 3.82 (s, 3H).

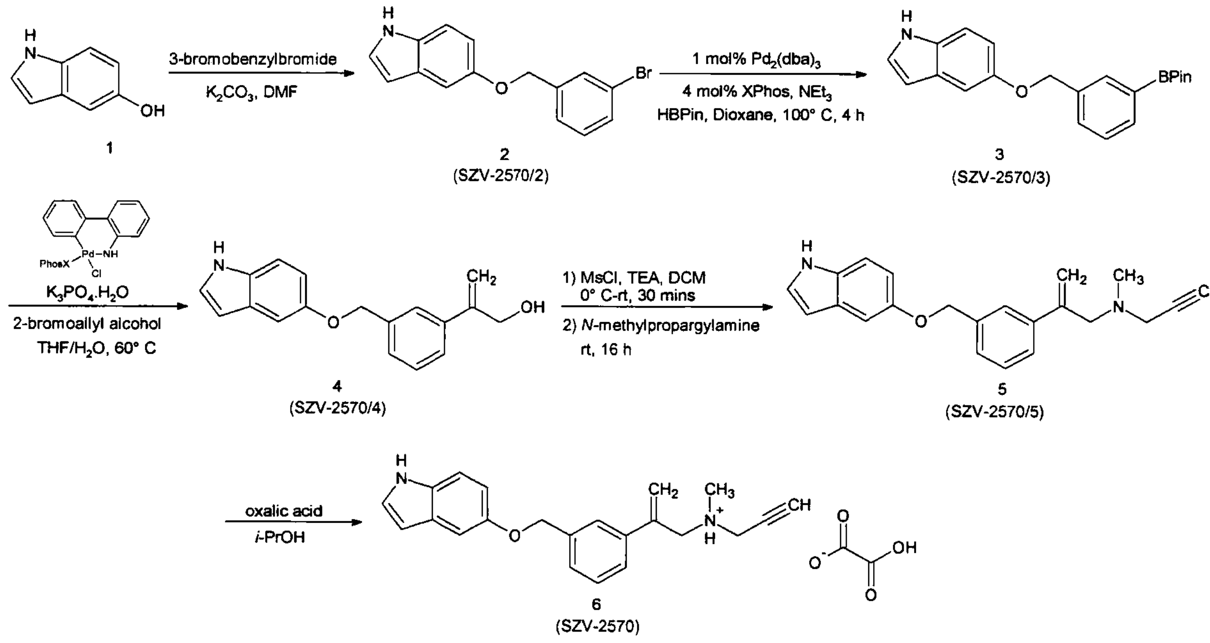
2-(3-((3-Fluorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2541/5) Following **method D9,** the title compound was isolated as a colourless oil (56%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37-7.32 (m, 1H), 7.27-7.11 (m, 5H), 7.03-6.99 (m, 1H), 6.89-6.87 (m, 1H), 5.49 (brs, 1H), 5.31 (brs, 1H), 5.07 (s, 2H), 3.45 (s, 2H), 3.38 (s, 2H), 2.33 (s, 3H), 2.26 (s, 1H).

2-(3-((3-Methoxybenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2568/5) Following **method D9,** the title compound was isolated as a yellow oil (64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32-7.22 (m, 2H), 7.15-7.09 (m, 2H), 7.03-7.00 (m, 2H), 6.91-6.85 (m, 2H), 5.50 (brs, 1H), 5.33 (brs, 1H), 5.05 (s, 2H), 3.82 (s, 3H), 3.47 (s, 2H), 3.39 (s, 2H), 2.34 (s, 3H), 2.27 (s, 1H).

2-(3-((3-Fluorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2541) Following **method H1,** the title compound was isolated as a white solid (87%). Mp 100.1 – 102.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.47-7.41 (m, 1H), 7.31-7.23 (m, 3H), 7.18-7.10 (m, 3H), 6.95-6.93 (m, 1H), 5.53 (d, *J* = 1.6 Hz, 1H), 5.26 (d, *J* = 1.6 Hz, 1H), 5.14 (s, 2H), 3.45 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{20}H_{20}FNOx(COOH)_2$ (399.41): C, 66.16%; H, 5.55%; N, 3.51%. Found: C, 65.97%; H, 5.21%; N, 3.59%.

2-(3-((3-Methoxybenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2568) Following **method H1,** the title compound was isolated as a white solid (68%). Mp 113.9 - 114.3 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.30 (app. t, 1H), 7.24 (app. t, 1H), 7.16 – 7.15 (m, 1H), 7.11-7.09 (m, 1H), 7.03-7.01 (m, 2H), 6.94-6.92 (m, 1H), 6.90-6.88 (m, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.25 (d, *J* = 1.2 Hz, 1H), 5.08 (s, 2H), 3.76 (s, 3H), 3.44 (s, 2H), 3.34 (d, *J* = 2.4 Hz, 2H), 3.21 (t, *J* = 2.4 Hz, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{21}H_{23}NO_2x(COOH)_2$ (411.45): C, 67.14%; H, 6.12%; N, 3.40%. Found: C, 66.98%; H, 6.21%; N, 3.07%.

Scheme 49



5-((3-Bromophenoxy)methyl)-1*H*-indole (SZV-2570/2) Following **method S1**, the title compound was isolated as a colourless oil (67%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.64 (brs, 1H), 7.46-7.42 (m, 2H), 7.30-7.27 (m, 2H), 7.18 (d, *J* = 3.1 Hz, 1H), 7.12 (d, *J* = 2.4 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.35 (dd, *J* = 3.1, 0.8 Hz, 1H), 5.07 (s, 2H).

5-((3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)methyl)-1*H*-indole (SZV-2570/3) Following **method Q1,** the title compound was isolated as a yellow oil (43%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.85 (br, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.18 (d, *J* = 3.2 Hz, 1H), 7.14 (d, *J* = 2.4 Hz, 1H), 6.85 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.35 (dd, *J* = 3.2, 0.8 Hz, 1H), 5.08 (s, 2H), 1.36 (s, 12H).

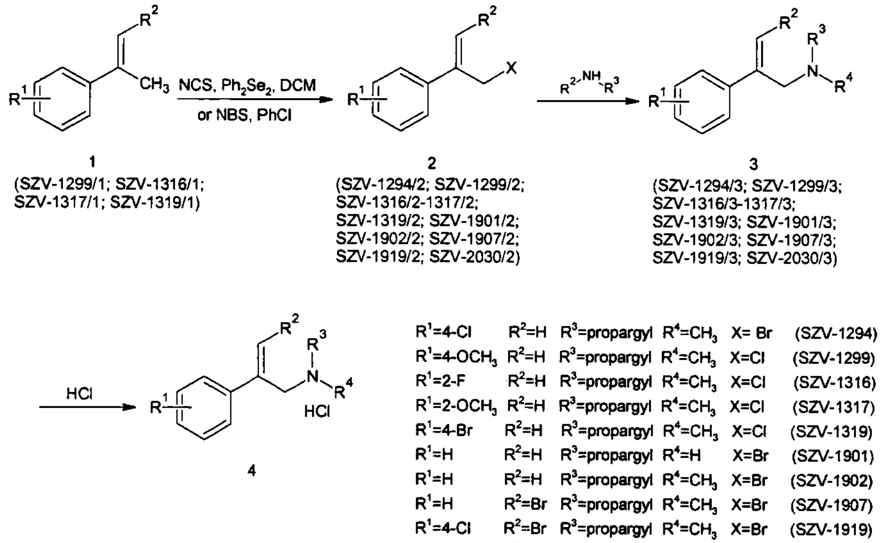
2-(3-((1*H*-Indol-5-yl)oxy)methyl)phenyl)prop-2-en-1-ol (SZV-2570/4) Following **method P2,** the title compound was isolated as a yellow gel (41%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.56

(br, 1H), 7.42 – 7.35 (m, 3H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.18 (d, *J* = 3.2 Hz, 1H), 7.14 (d, *J* = 2.4 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.35 (dd, *J* = 3.2, 0.8 Hz, 1H), 5.46 (dd, *J* = 2.4, 0.8 Hz, 1H), 5.36 (dd, *J* = 2.4, 1.6 Hz, 1H), 5.09 (s, 2H), 4.47 (dd, *J* = 1.6, 0.8 Hz, 2H).

2-(3-((1*H*-Indol-5-yl)oxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2570/5) Following **method D9**, the title compound was isolated as a colourless gel (91%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.60 (brs, 1H), 7.46-7.44 (m, 1H), 7.39-7.31 (m, 2H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.17 (d, *J* = 2.8 Hz, 1H), 7.13 (d, *J* = 2.4 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.34 (dd, *J* = 2.8, 0.8 Hz, 1H), 5.49 (d, *J* = 1.6 Hz, 1H), 5.29 (dd, *J* = 1.6, 0.8 Hz, 1H), 5.09 (s, 2H), 3.50 (d, *J* = 0.8 Hz, 2H), 3.29 (d, *J* = 2.4 Hz, 2H), 2.61 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

2-(3-(((1*H*-Indol-5-yl)oxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2570) Following **method H1**, the title compound was isolated as a white solid (80%). Mp 106.2 - 109.7 °C (dec). ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 10.89 (s, 1H), 7.61 (brs, 1H), 7.48-7.46 (m, 1H), 7.39-7.33 (m, 2H), 7.29-7.26 (m, 2H), 7.13 (d, *J* = 2.4 Hz, 1H), 6.81 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.32-6.31 (m, 1H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.28 (d, *J* = 1.2 Hz, 1H), 5.08 (s, 2H), 3.49 (s, 2H), 3.36 (d, *J* = 2.0 Hz, 2H), 3.22 (t, *J* = 2.0 Hz, 1H), 2.24 (s, 3H). HRMS (ESI+) *m/z* calcd. for $C_{22}H_{23}N_2O^+$ $[M+H]^+$ 331.1805, found 331.1812.

Scheme 50



R^1=4-Cl	R^2=H	R^3=propargyl	R^4=CH_3	X= Br	(SZV-1294)
R^1=4-OCH_3	R^2=H	R^3=propargyl	R^4=CH_3	X=Cl	(SZV-1299)
R^1=2-F	R^2=H	R^3=propargyl	R^4=CH_3	X=Cl	(SZV-1316)
R^1=2-OCH_3	R^2=H	R^3=propargyl	R^4=CH_3	X=Cl	(SZV-1317)
R^1=4-Br	R^2=H	R^3=propargyl	R^4=CH_3	X=Cl	(SZV-1319)
R^1=H	R^2=H	R^3=propargyl	R^4=H	X=Br	(SZV-1901)
R^1=H	R^2=H	R^3=propargyl	R^4=CH_3	X=Br	(SZV-1902)
R^1=H	R^2=Br	R^3=propargyl	R^4=CH_3	X=Br	(SZV-1907)
R^1=4-Cl	R^2=Br	R^3=propargyl	R^4=CH_3	X=Br	(SZV-1919)
R^1=4-F	R^2=H	R^3=propargyl	R^4=CH_3	X=Br	(SZV-2030)

1-(3-Bromoprop-1-en-2-yl)-4-chlorobenzene (SZV-1294/2) (Allerheiligen S et al, DE102004061751) Following **method G/iii)**, 7.01 g of the title compound was isolated (46%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (m, 2H, Ar-H), 7.34 (m, 2H, Ar-H), 5.54 (m, 1H, =CH_2), 5.50 (q, *J*=0.6 Hz, 1H, =CH_2), 4.34 (d, *J*=0.6 Hz, 2H, CH_2).

1-(3-Chloroprop-1-en-2-yl)-4-methoxybenzene (SZV1299/2) (Bodrikov IV et al, Zh. Org. Khim., 1976, 12, 1864-1871) Following **method F**, the residue isolated was purified by flash chromatography on silica gel (*n*-hexane:EtOAc 95:5), to afford a 1:1 mixture of 1-[1-chloroprop-1-en-2-yl]-4-methoxybenzene and 1-(3-chloroprop-1-en-2-yl)-4-methoxybenzene, that was used without further purification for the next reaction step. Pale yellow oil. 1-(3-chloroprop-1-en-2-yl)-4-methoxybenzene: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (m, 2H, Ar-H), 6.89 (m, 2H, Ar-H), 5.48 (d, *J*=0.8 Hz, 1H, =CH_2), 5.35 (q, *J*=0.9 Hz, 1H, =CH_2), 4.44 (d, *J*=0.9 Hz, 2H, CH_2), 3.81 (s, 3H, OCH_3).

1-(3-Chloroprop-1-en-2-yl)-2-fluorobenzene (SZV-1316/2) Following **method F**, the residue isolated was purified by flash chromatography (*n*-hexane), to afford a ~1:1 mixture of 1-(3-chloroprop-1-en-2-yl)-2-fluorobenzene and 1-[1-chloroprop-1-en-2-yl]-2-fluorobenzene, that was used without further purification for the next reaction step. Pale yellow oil. 1-(3-chloroprop-1-en-2-yl)-2-fluorobenzene: ^{1}H NMR (Chloroform-*d*, 400 MHz) δ 7.38-7.01 (m, 4H, Ar-H), 6.26 (m, 1H, =CH-), 2.17 (m, 3H, CH_3).

1-(3-Chloroprop-1-en-2-yl)-2-methoxybenzene (SZV-1317/2) Following **method F,** the residue isolated was purified by flash chromatography on silica gel (*n*-hexane:EtOAc 50:1), to afford a ~1:1 mixture of 1-(3-chloroprop-1-en-2-yl)-2-methoxybenzene and 1-[1-chloroprop-1-en-2-yl]-2-methoxybenzene, that was used without further purification for the next reaction step. Pale yellow oil. 1-(3-chloroprop-1-en-2-yl)-2-methoxybenzene: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33-6.83 (m, 4H, Ar-H), 5.49 (m, 1H, =CH_2), 5.26 (m, 1H, =CH_2), 4.50 (m, 2H, CH_2), 3.83 (s, 3H, OCH_3).

1-Bromo-4-(3-chloroprop-1-en-2-yl)benzene (SZV-1319/2) Following **method F**, the residue isolated was purified by flash chromatography on silica gel (DCM), to afford a 1:1 mixture of 1-bromo-4-(3-chloroprop-1-en-2-yl)benzene and 1-bromo-4-[1-chloroprop-1-en-2-yl]benzene, that was used without further purification and characterization for the next reaction step. Pale yellow oil.

(3-Bromoprop-1-en-2-yl)benzene (SZV-1901/2, SZV-1902/2) (Wen Y et al, Org. Lett., 2009, 11, 2365-2368; Salter-Cid LM et al, WO2006094201)

The title compound was synthetised by Yamanaka M et al, Tetrahedron Lett., 2002.43.2403-2406, 2.77 g of compound was isolated (yield:70%, purity: 88%), pale yellow oil, that was used without further purification and characterization for the next reaction step. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59-7.56 (m, 2H), 7.45-7.42 (m, 3H), 5.63 (s, 1H), 5.56 (s, 1H), 4.45 (s, 2H).

[(1*Z*)-1,3-Dibromoprop-1-en-2-yl]benzene (SZV-1907/2) (Vaccher C et al, Synth. Commun., 1993, 23, 671-679) Following method **method G/i),** 19.3 g of the title compound was isolated (79%), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44-7.35 (m, 5H, Ar-H), 6.66 (s, 1H, =CH-), 4.48 (s, 2H, CH_2).

1-Chloro-4-[(1*Z*)-1,3-dibromoprop-1-en-2-yl]benzene (SZV-1919/2) (Vaccher C et al, Synth. Commun., 1993, 23, 671-679) Following method **method G/ii),** 1.07 g of the title compound was isolated (81%), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35- (s, 4H, Ar-H), 6.66 (m, 1H, =CH-), 4.44 (s, 2H, CH_2).

1-(3-Bromoprop-1-en-2-yl)-4-fluorobenzene (SZV-2030/2) (Chakravarty S et al, WO2011103485) Following method **method G/i),** 27.40 g of the title compound was isolated (72%), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (m, 2H, Ar-H), 7.06 (m, 2H, Ar-H), 5.49 (br.s, 1H, =CH_2), 5.47 (m, 1H, =CH_2), 4.35 (d, *J*=0.6 Hz, 2H, CH_2).

Synthesis of amino substitued compounds

2-(4-Chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1294/3) Following **method D7**, 345 mg of the title compound was isolated (80%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (m, 2H, Ar-H), 7.28 (m, 2H, Ar-H), 5.46 (d, *J*=1.5 Hz, 1H, =CH_2), 5.29 (dt, *J*=1.5 and 1.0 Hz, 1H, =CH_2), 3.42 (d, *J*=1Hz, 2H, CH_2), 3.33 (d, J=2.4 Hz, 2H, CH_2), 2.30 (s, 3H, CH_3), 2.26-2.25 (t, *J*=2.4 Hz, 1H, ≡CH).

2-(4-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1299/3) Following **method D7**, 218 mg of the title compound was isolated (71%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (m, 2H, Ar-H), 6.86 (m, 2H, Ar-H), 5.40 (d, *J*=1.6 Hz, 1H, =CH_2), 5.19 (dt, *J*=1.6 and 1.0 Hz, 1H, =CH_2), 3.80 (s, 3H, OCH_3), 3.42 (d, *J*=1.0 Hz, 2H, CH_2), 3.35 (d, J=2.3 Hz, 2H, CH_2), 2.31 (s, 3H, CH_3), 2.25 (t, J=2.3 Hz, 1H, ≡CH).

2-(2-Fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1316/3) Following **method D7**, 358 mg of the title compound was isolated (70%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (td, J=7.6, 1.8 Hz, 1H, Ar-H), 7.26-7.20 (m, 1H, Ar-H), 7.09 (td, J=7.6, 1.2 Hz, 1H, Ar-H), 7.02 (ddd, J=11.2, 8.0, 1.2 Hz, 1H, Ar-H), 5.46 (m, 1H, =CH_2), 5.37 (m, 1H, =CH_2), 3.45 (m, 2H, CH_2), 3.34 (d, *J*=2.4 Hz, 2H, CH_2), 2.29 (s, 3H, CH_3), 2.23 (t, J=2.4 Hz, 1H, ≡CH).

2-(2-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1317/3) Following **method D7**, 597 mg of the title compound was isolated (63%), pale yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 (ddd, J=8.0, 7.2, 1.7 Hz, 1H, Ar-H), 7.18 (dd, J=7.2, 1.7 Hz, 1H, Ar-H), 6.91 (ddd, J=7.6, 7.6 and 1.1 Hz, 1H, Ar-H), 6.86 (dd, J=8.0, 1.1 Hz, 1H, Ar-H), 5.40 (m, 1H, =CH_2), 5.22 (m, 1H, Ar-H), 3.81 (s, 3H, OCH_3), 3.49 (m, 2H, CH_2), 3.36 (d, J=2.4 Hz, 2H, CH_2), 2.30 (s, 3H, CH_3), 2.22 (t, J=2.4 Hz, 1H, ≡CH).

2-(4-Bromophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1319/3) Following **method D7**, 594 mg of the title compound was isolated (93%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50-7.32 (m, 4H, Ar-H), 5.47 (d, *J*=1.4 Hz, 1H, =CH_2), 5.29 (dt, *J*=1.4 and 1.0 Hz, 1H, =CH_2), 3.41 (d, J=1.0 Hz, 2H, CH_2), 3.33 (d, *J*=2.4 Hz, 2H, CH_2), 2.29 (s, 3H, CH_3), 2.25 (t, *J*=2.4 Hz, 1H, ≡CH).

2-Phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1901/3) Following **method D7**, 1.03 g of the title compound was isolated (59%), colourless oil. Used for salt formation without further characterization.

(2*Z*)-3-Bromo-*N*-methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1907/3) Following **method D7**, 3.02 g of the title compound was isolated (80%), colourless oil. Used for salt formation without further characterization.

(2*Z*)-3-Bromo-2-(4-chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1919/3) Following **method D7**, 194 mg of the title compound was isolated (93%), colourless oil. Used for salt formation without further characterization.

2-(4-Fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2030/3) Following **method D7**, 2.05 g of the title compound was isolated (61%), colourless oil. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.64-7.59 (m, 2H, Ar-H), 7.28-7.20 (m, 2H, Ar-H), 5.78 (br.s, 1H, =CH_2), 5.72 (br.s, 1H, =CH_2), 4.41-4.14 (m, 2H, CH_2), 4.04 (br.s, 2H, CH_2), 3.88 (s, 1H, ≡CH), 2.70 (s, 3H, CH_3).

Synthesis of hydro chloride salts

2-(4-Chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1294) Following **method H2,** 287 mg of the title compound was isolated (77%), white crystals, mp 182 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 11.0 (br.s, 1H NH), 7.60 (m, 2H, Ar-H), 7.45 (m, 2H, Ar-H), 5.84 (br.s, 1H, =CH_2), 5.78 (br.s, 1H, =CH_2), 4.27 (br.s, 2H, CH_2), 4.04 (br.s, 2H, CH_2), 3.86 (br.s, 1H, ≡CH), 2.70 (s, 3H, CH_3). Anal. calcd. for $C_{13}H_{14}ClNxHCl$ (256.17): C, 60.95%; H, 5.90%; N, 5.47%. Found: C, 60.82%; H, 5.6%; N, 5.43%.

Oxalic salt of SZV-1294

2-(4-Chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine ethanedioate (SZV-2220) Following **method H1,** 2.02 g of the title compound was isolated (88%), white crystals, mp 160-161 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.55 (m, 2H, Ar-H), 7.38 (m, 2H, Ar-H), 5.57 (d, *J*=1.1 Hz, 1H, =CH_2), 5.31 (q, *J*=0.9 Hz, 1H, =CH_2), 3.50 (br.s, 2H, CH_2), 3.37 (d, *J*=2.4 Hz, 2H, CH_2), 3.25 (t, J=2.4 Hz, 1H, ≡CH), 2.24 (s, 3H, CH_3). Anal. calcd. for $C_{13}H_{14}ClNx(COOH)_2$ (309.74): C, 58.16%; H, 5.21%; N, 4.52%. Found: C, 58.04%; H, 5.13%; N, 4.46%.

2-(4-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1299) Following **method H2,** 206 mg of the title compound was isolated (93%), white crystals, mp 148-149 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.50 (m, 2H, Ar-H), 6.96 (m, 2H, Ar-H), 5.71 (br.s, 1H, =CH_2), 5.62 (br.s, 1H, =CH_2), 4.23 (br.s, 2H, CH_2), 4.04 (br.s, 2H, CH_2), 88 (br.s, 1H, ≡CH), 3.77 (s, 3H, OCH_3), 2.70 (s, 3H, CH_3). Anal. calcd. for $C_{14}H_{17}NOxHCl$ (251.75): C, 66.79%; H, 7.21%; N, 5.56%. Found: C, 66.36%; H, 7.09%; N, 5.51%.

2-(2-Fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1316) Following **method H2,** 264 mg of the title compound was isolated (73%), white crystals, mp 140 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.50 (m, 1H, Ar-H), 7.42 (m, 1H, Ar-H), 7.27-7.21 (m, 2H, Ar-H), 6.00 (br.s, 1H, =CH_2), 5.72 (br.s, 1H, =CH_2), 4.22 (br.s, 2H, CH_2), 4.15 (br.s, 2H, CH_2), 3.84 (br.s, 1H, ≡CH), 2.70 (br.s, 3H, CH_3). Anal. calcd. for $C_{13}H_{14}FNxHCl$ (239.71): C, 65.13%; H, 6.31%; N, 5.84%. Found: C, 65.09%; H, 6.18%; N, 5.78%.

2-(2-Methoxyphenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1317) Following **method H2,** 262 mg of the title compound was isolated (44%), white crystals, mp 135 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 11.03 (br.s, 1H, NH), 7.36 (ddd, J=8.0, 7.6, 1.8 Hz, 1H, Ar-H), 7.27 (dd, J=7.6, 1.8 Hz, 1H, Ar-H), 7.04 (dm, J=8.0 Hz, 1H, Ar-H), 6.97 (td, J=7.2, 1.0 Hz, 1H, Ar-H), 5.82 (br.s, 1H, =CH$_2$), 5.52 (br.s, 1H, =CH$_2$), 4.36-4.05 (m, 2H, CH$_2$), 4.00 (br.s, 2H, CH$_2$), 3.85 (br.s, 1H, ≡CH), 3.81 (s, 3H, OCH$_3$), 2.68 (s, 3H, CH$_3$). Anal. calcd. for $C_{14}H_{17}NOxHCl$ (251.75): C, 66.79%; H, 7.21%; N, 5.56%. Found: C, 66.70%; H, 7.11%; N, 5.49%.

2-(4-Bromophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1319) Following method **method H2,** 302 mg of the title compound was isolated (49%), white crystals, mp 176-177 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 11.10 (br.s, 1H, NH), 7.61-7.51 (m, 4H, Ar-H), 5.85 (br.s, 1H, =CH$_2$), 5.78 (br.s, 1H, =CH$_2$), 4.24 (br.s, 2H, CH$_2$), 4.03 (br.s, 2H, CH$_2$), 3.86 (br.s, 1H, ≡CH), 2.69 (s, 3H, CH$_3$). Anal. calcd. for $C_{13}H_{14}BrNxHCl$ (300.62): C, 51.94%; H, 5.03%; N, 4.66%. Found: C, 51.84%; H, 5.11%; N, 4.52%.

2-Phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1901) Following method **method H2,** 169 mg of the title compound was isolated (14%), white crystals, mp 135 °C. ^{1}H NMR (400 MHz, Deuterium oxide) δ 7.56-7.43 (m, 5H, Ar-H), 5.77 (br.s, 1H, =CH$_2$), 5.59 (br.s, 1H, =CH$_2$), 4.29 (br.s, 2H, CH$_2$), 3.93 (d, J=2.6 Hz, 2H, CH$_2$), 3.03 (t, J=2.6 Hz, 1H, ≡CH). Anal. calcd. for $C_{12}H_{13}NxHCl$ (207.70): C, 69.39%; H, 6.97%; N, 6.74%. Found: C, 69.10%; H, 6.80%; N, 6.73%.

(2*Z*)-3-Bromo-*N*-methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1907) Following **method H2,** 1.72 g of the title compound was isolated (50%), white crystals, mp 177-179 °C. ^{1}H NMR (400 MHz, Deuterium oxide) δ 7.55-7.48 (m, 5H, Ar-H), 7.11 (s, 1H, =CH-), 4.63 (br.s, 2H, CH$_2$), 4.06 (d, J=2.5 Hz, 2H, CH$_2$), 3.18 (t, J=2.5 Hz, 1H, ≡CH), 2.92 (s, 3H, CH$_3$). Anal. calcd. for $C_{13}H_{14}BrNxHCl$ (300.62): C, 51.94%; H, 5.03%; N, 4.66%. Found: C, 52.00%; H, 4.91%; N, 4.77%.

(2*Z*)-3-Bromo-2-(4-chlorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1919) Following **method H2,** 191 mg of the title compound was isolated (90%), white crystals, mp 166-167 °C. ^{1}H NMR (400 MHz, Deuterium oxide) δ 7.39-7.31 (m, 4H, Ar-H), 7.02 (br.s, 1H, =CH-), 4.49 (br.s, 2H, CH$_2$), 3.93 (d, J=2.5 Hz, 2H, CH$_2$), 3.04 (t, J=2.5 Hz, 1H, ≡CH), 2.80 (s, 3H, CH$_3$). Anal. calcd. for $C_{13}H_{13}BrClNxHCl$ (335.07): C, 46.60%; H, 4.21%; N, 4.18%. Found: C, 46.14%; H, 4.11%; N, 4.06%.

2-(4-Fluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-2030) Following method **method H2,** 1.45 g of the title compound was isolated (62%), white crystals, mp 182-183 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 11.20 (br.s, 1H, NH), 7.60 (m, 2H, Ar-H), 7.21 (m, 2H, Ar-H), 5.77 (br.s, 1H, =CH$_2$), 5.74 (br.s, 1H, =CH$_2$), 4.36-4.16 (br m, 2H, CH$_2$), 4.02 (br.s, 2H, CH$_2$), 3.85 (br.s, 1H, ≡CH), 2.68 (s, 3H, CH$_3$). Anal. calcd. for $C_{13}H_{14}FNxHCl$ (239.72): C, 65.13%; H, 6.31%; N, 5.84%. Found: C, 65.26%; H, 6.11%; N, 5.84%.

***N*-Methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1902)**

The title compound was prepared two different way i) and ii).

i) *N*-Methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1902/3) Following **method D7**, 2.05 g of the title compound was isolated (62%), colourless oil. Used for salt formation without further characterization.

***N*-Methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1902)** Following **method H2,** 2.15 g of the title compound was isolated (87%), white crystals, mp 166-167 °C. ^{1}H NMR (400 MHz, Deuterium oxide) δ 7.58-7.44 (m, 5H, Ar-H), 5.84 (s, 1H, =CH$_2$), 5.70 (br.s, 1H, =CH$_2$), 4.42 (br.s, 2H, CH$_2$), 4.01 (d, J=2.4 Hz, 2H, CH$_2$), 3.17 (t, J=2.4 Hz, 1H, ≡CH), 2.90 (s, 3H, CH$_3$). Anal. calcd. for $C_{12}H_{15}NxHCl$ (221.73): C, 70.42%; H, 7.27%; N, 6.32%. Found: C, 70.50%; H, 7.51%; N, 6.30%.

Oxalic salt of SZV-1902

***N*-Methyl-2-phenyl -*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2221)** Following **method H1,** 1.40 g of the title compound was isolated (82%), white crystals, mp 142-143 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.52 (m, 2H, Ar-H), 7.37-7.26 (m, 3H, Ar-H), 5.54 (d, J=1.4 Hz, =CH$_2$), 5.29 (dt, J=1.4 and 1.4 Hz, 1H, =CH$_2$), 3.53 (br.s, 2H, CH$_2$), 3.40 (d, J=2.4 Hz, 2H, CH$_2$), 3.27 (t, J=2.4 Hz, 1H, ≡CH), 2.27 (s, 3H, CH$_3$). Anal. calcd. for $C_{13}H_{15}Nx(COOH)_2$ (275.30): C, 65.44%; H, 6.22%; N, 5.09%. Found: C, 64.93%; H, 6.16%; N, 4.97%.

ii) 2-[Methyl(prop-2-yn-1-yl)amino]-1-phenylethanone Following **method D1**, 11.17 g of the title compound was isolated (95%), yellow oil. ^{1}H NMR (Chloroform-*d*, 400 MHz) δ 8.00 (m, 2H, Ar-H), 7.57 (m, 1H, Ar-H), 7.46 (m, 2H, Ar-H), 3.96 (s, 2H, CH$_2$), 3.56 (d, J=2.2 Hz, 2H, CH$_2$), 2.46 (s, 3H, CH$_3$), 2.30-2.27 (t, J=2.2 Hz, 1H, ≡CH).

***N*-Methyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1902/3)** Following **method E1**, 1.78 g of the title compound was isolated (45%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (m, 2H, Ar-H), 7.36-7.23 (m, 3H, Ar-H), 5.48 (br.s, 1H, =CH$_2$), 5.29 (br.s, 1H, =CH$_2$), 3.45 (s, 2H, CH$_2$), 3.36 (d, J=2.2 Hz, 2H, CH$_2$), 2.23 (s, 3H, CH$_3$), 2.25 (t, J=2.2 Hz, 1H, ≡CH).

The preparation of substituted α-methylstyrenes

A) A solution of 1-(4-methoxyphenyl)ethanone (7.5 g, 50.0 mmol) in anhydrous diethyl ether (50.0 ml) was added dropwise under argon (within 1.5 h) to a solution of CH_3MgBr in diethyl ether (30.0 ml 2M solution, 60.0 mmol), upon stirring the mixture in an ice bath (keeping the temperature below 30 °C by controlling the rate of addition). The mixture was allowed to warm to room temperature for 1 h, then was cooled down again in an ice bath and saturated $NaHCO_3$ solution (10.0 ml) was added carefully. The isolated mixture was dissolved in H_2O (130.0 ml) and the aqueous phase was extracted with diethyl ether (2x50.0 ml). The combined organic layers were washed with saturated NaCl solution (50.0 ml), dried (K_2CO_3), filtered and evaporated to dryness (at max. 25 °C). To the crude alcohol $KHSO_4$ (100.0 mg) and 4-*tert*-butylbenzene-1,2-diol (10.0 mg) were added and the mixture was placed in a 110 °C oil bath under air for 15 min. After cooling, the mixture was partitioned between diethyl ether (100.0 ml) and H_2O (40.0 ml) and the organic layer was extracted with H_2O (1x40.0 ml) and saturated NaCl solution (1x40.0 ml), dried (K_2CO_3), filtered and evaporated to dryness (at max. 25 °C). The crude product was purified by flash chromatography on silica gel (*n*-hexane) to afford compound **(SZV-1299/1)** (Serra S Tetrahedron: Asymmetry, 2011, 22, 619-628). Colourless oil (4.52 g, 61%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 (m, 2H, Ar-H), 6.87 (m, 2H, Ar-H), 5.28 (m, 1H, $=CH_2$), 4.98 (m, 1H, $=CH_2$), 3.81 (s, 3H, CH_3), 2.13 (s, 3H, CH_3).

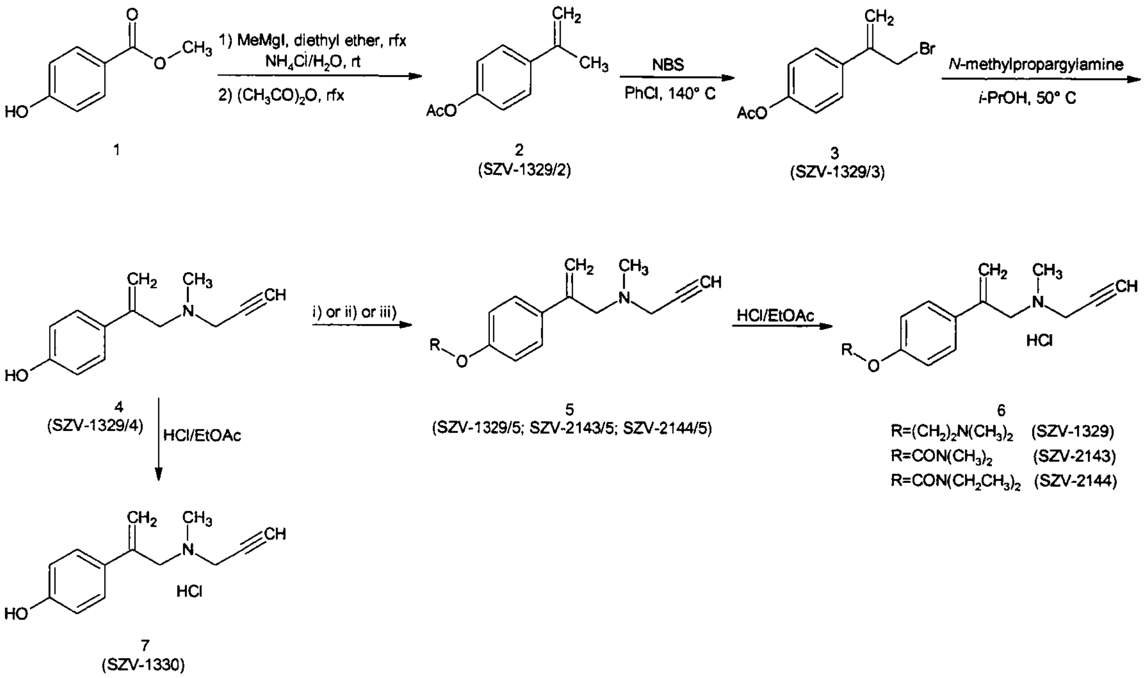
B) To a suspension of triphenylmethylphosphonium iodide (4.9 g, 12.0 mmol) in anhydrous diethyl ether (15.0 ml), *n*-BuLi in *n*-hexane (4.8 ml 2M solution, 12.0 mmol) was added dropwise under argon at 18 °C upon stirring (Ali HM et al, J. Labelled Compd. Radiopharm., 1985, 22, 559-563). The resulting suspension was stirred at 18 °C for 4 h, then a solution of the appropiate acetophenon (1.7 g, 12.0 mmol) in anhydrous diethyl ether (3.0 ml) was added. The reaction mixture was stirred for a further 1 h at 18 °C. Then a solution of potassium *tert*-butoxide (3.5 g, 31.0 mmol) in anhydrous *tert*-butanol (2.8 ml) was added and the mixture was stirred overnight at 18 °C. The precipitated triphenylphosphine oxide was filtered off and washed with anhydrous diethyl ether. The filtrate was washed with H_2O (2x50.0 ml), saturated $Na_2S_2O_3$ solution (1x50.0 ml), dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure (at max. 19-20 °C/20 Hgmm). The residue was purified by flash chromatography on silica gel (*n*-hexane) to afford the following compounds:

1-Fluoro-2-(prop-1-en-2-yl)benzene (SZV-1316/1) (Ali HM et al, J. Labelled Compd. Radiopharm., 1985, 22, 559-563) Colourless oil (1.02 g, 63%). ^{1}H NMR (400 MHz, Chloroform-*d*) 7.29 (tm, J=7.6 Hz, 1H, Ar-H), 7.7.21 (m, 1H, Ar-H), 7.08 (tm, J=7.6 Hz, 1H, Ar-H), 7.02 (ddd, J=11.2, 8.0, 1.3 Hz, 1H, Ar-H), 5.23-5.21 (ovl.m, 2H, $=CH_2$), 2.14 (ddd, *J*=1.3, 1.3 and 1.3 Hz, 3H, CH_3).

1-Methoxy-2-(prop-1-en-2-yl)benzene (SZV-1317/1) (Fryszkowska A et al, J. Org. Chem., 2008, 73, 4295-4298) Colourless oil (2.43 g, 68%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26-7.17 (m, 2H, Ar-H), 6.93-6.86 (m, 2H, Ar-H), 5.14 (m, 1H, $=CH_2$), 5.06-5.05 (m, 1H, $=CH_2$), 3.83 (s, 3H, OCH_3), 2.12 (dd, J=1.5, 0.9 Hz, 3H, CH_3).

1-Bromo-4-(prop-1-en-2-yl)benzene (SZV-1319/1) (Fryszkowska A et al, J. Org. Chem., 2008, 73, 4295-4298) Colourless oil (2.10 g, 69%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (m, 2H, Ar-H), 7.32 (m, 2H, Ar-H), 5.35 (dq, *J*=1.4 and 0.9 Hz, 1H, $=CH_2$), 5.10 (dq, *J*=1.4 and 1.4 Hz, 1H, $=CH_2$), 2.12 (dd, *J*=1.4 and 0.9 Hz, 3H, CH_3).

Scheme 51



4-(Prop-1-en-2-yl)phenyl acetate (SZV-1329/2) (Krimm H et al, DE1193031) A solution of methyl 4-hydroxybenzoate (7.9 g, 52.0 mmol) in diethyl ether (90.0 ml) was added dropwise to a ~1M solution of methyl iodide (25.4 g, 179.0 mmol) and magnesium (4.2 g, 173.2 mmol) in diethyl ether (100.0 ml) under argon, upon intensive stirring and heating to reflux (within ~15 min) (Gilman H et al, J. Org. Chem., 1954, 19, 1067-1079). The reaction mixture was heated to reflux for 2 h, then was allowed to cool down to room temperature. A solution of NH_4Cl (20.3 g, 378.8 mmol) in H_2O (63.0 ml) was carefully added dropwise upon intensive stirring. The two layers formed were separated, the aqueous layer was extracted with diethyl ether (2x40.0 ml). The combined organic layers were washed with saturated NaCl solution, dried ($MgSO_4$), filtered and evaporated to dryness to afford pale yellow solid (72%). The crude product (32.8 mmol) thus isolated was dissolved in acetic anhydride (11.8 ml) and the solution was heated to reflux for 10 h under argon. The reaction mixture was evaporated to dryness under reduced pressure (at max. 48-50 °C), the residue isolated was purified by flash chromatography on silica gel (*n*-hexane: EtOAc 9:1). Pale yellow oil (5.0 g, 76%). ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.53 (m, 2H, Ar-H), 7.10 (m, 2H, Ar-H), 5.41 (dq, *J*=1.4 and 0.8 Hz, 1H, =CH_2), 5.10 (dq, *J*=1.4 and 1.4 Hz, 1H, =CH_2), 2.27 (s, 3H, $COCH_3$), 2.11 (dd, J=1.4, 0.8 Hz, 1H, =CH_2).

4-(3-Bromoprop-1-en-2-yl)phenyl acetate (SZV-1329/3) (Perera RP et al, J. Med. Chem., 2003, 46, 2599-2605) A mixture of 4-(prop-1-en-2-yl)phenyl acetate (5.0 g, 28.4 mmol) and *N*-bromosuccinimide (5.1 g, 28.4 mmol) in anhydrous chlorobenzene (5.0 ml) was placed in an oil bath preheated to 140 °C. After 15 min stirring at 140 °C, the mixture was cooled down (ice-water bath), the precipitated succinimide was filtered off and washed with *n*-hexane. The filtrate was evaporated to dryness to afford a ~3:2 mixture of 4-(3-bromoprop-1-en-2-yl)phenyl acetate and 4-[(1*E*)-1-bromoprop-1-en-2-yl]phenyl acetate, that was used without further purification for the next reaction step. Pale yellow solid (6.19 g, ~3:2 mixture of the two brominated products). 4-(3-bromoprop-1-en-2-yl)phenyl acetate (~3.7 g, 51%): ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (m, 2H, Ar-H), 7.09 (m, 2H, Ar-H), 5.52 (dt, *J*=0.7 and 0.4 Hz, 1H, =CH$_2$), 5.47 (dt *J*=0.7 and 0.7 Hz, 1H, =CH$_2$), 4.33 (dd, *J*=0.7 and 0.4 Hz, 2H, CH$_2$), 2.28 (s, 3H, COCH$_3$).

4-{3-[Methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenol (SZV-1329/4) To a solution of a ~3:2 mixture of 4-(3-bromoprop-1-en-2-yl)phenyl acetate and 4-[1-bromoprop-1-en-2-yl]phenyl acetate (recovered as 4-[(1*E*)-1-bromoprop-1-en-2-yl]phenol after the reaction) (6.2 g, ~14.6 mmol/4-(3-bromoprop-1-en-2-yl)phenyl acetate) in anhydrous propan-2-ol (30.0 ml), a solution of *N*-methylprop-2-yn-1-amine (4.0 g, 57.4 mmol) in anhydrous propan-2-ol (30.0 ml) was added at room temperature under argon. The reaction mixture was stirred at 40 °C for 24 h. After evaporation to dryness, the residue was triturated with *n*-hexane and DCM and the liquid was decanted from the solid (repeated three times). The liquid phases were evaporated to dryness and the crude product thus isolated was purified by column chromatography on silica gel (1. column: CHCl$_3$, 2. column: *n*-hexane:EtOAc 1:1). Pale yellow crystals (922.0 mg, 31%), mp 69-70 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.18 (m, 2H, Ar-H), 6.43 (m, 2H, Ar-H), 5.32 (d, *J*=1.6 Hz, 1H, =CH$_2$), 5.19 (dt, *J*=1.6 and 0.7 Hz, 1H, =CH$_2$), 3.48 (d, *J*=0.7 Hz, 2H, CH$_2$), 3.40 (d, *J*=2.4 Hz, 2H, CH$_2$), 2.37 (s, 3H, CH$_3$), 2.31 (t, *J*=2.4 Hz, 1H, ≡CH).

2-{4-[2-(Dimethylamino)ethoxy]phenyl}-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1329/5)

i) A mixture of 4-{3-[methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenol (500.0 mg, 2.5 mmol), 2-chloro-*N*,*N*-dimethylethanamine hydrochloride (394.0 mg, 2.7 mmol) and K$_2$CO$_3$ (755.0 mg, 5.5 mmol) in anhydrous acetone was heated to reflux for 20 h. The precipitated KCl was filtered off and washed with acetone, the filtrate was evaporated to dryness. The residue was purified by column chromatography on silica gel (CH$_3$OH). Colourless oil (549.0 mg, 81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (m, 2H, Ar-H), 6.87 (m, 2H, Ar-H), 5.39 (d, *J*=1.6 Hz, 1H, =CH$_2$), 5.18 (dt, *J*=1.6 and 0.8 Hz, 1H, =CH$_2$), 4.06 (t, J=5.6 Hz, 2H, CH$_2$), 3.41 (d, *J*=0.8 Hz, 2H, CH$_2$), 3.35 (d, *J*=2.4 Hz, 2H, CH$_2$), 2.71 (t, *J*=5.6 Hz, 2H, CH$_2$), 2.32 (s, 6H, N(CH$_3$)$_2$), 2.31 (s, 3H, NCH$_3$), 2.25-2.24 (t, *J*=2.4 Hz, 1H, ≡CH).

4-{3-[Methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenyl dimethylcarbamate (SZV-2143/5)

ii) 4-{3-[methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenol (201.0 mg, 1.0 mmol) was dissolved in anhydrous ACN (1.0 ml) under argon, to the solution dimethylcarbamic chloride (0.2 ml, 1.7 mmol) was added (Chorev M et al, WO199827055). Upon cooling (ice-water bath), sodium hydride (31.0 mg 60% dispersion in mineral oil, 1.3 mmol) and anhydrous ACN (2.0 ml) were added. The mixture was stirred at room temperature for 5 h. After evaporation to dryness, ice was added to the residue and it was extracted with DCM and $CHCl_3$ (1x40.0 ml). The organic phase was washed with 0.67 M NaOH solution (30.0 ml), dried (Na_2SO_4), filtered and evaporated to dryness. The residue was purified by column chromatography on silica gel ($CHCl_3$:EtOAc 10:1). Pale yellow oil (245 mg, 90%). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.50 (m, 2H, Ar-H), 7.06 (m, 2H, Ar-H), 5.45 (d, *J*=1.6 Hz, 1H, $=CH_2$), 5.26 (dt, J=1.6 and 0.7 Hz, 1H, $=CH_2$), 3.42 (d, *J*=0.7 Hz, 1H, CH_2), 3.35 (d, *J*=2.4 Hz, 1H, CH_2), 3.09 (br.s, 3H, *N*-CH_3), 3.01 (br.s, 3H, N-CH_3), 2.31 (s, 3H, CH_3), 2.24 (t, *J*=2.4 Hz, 1H, ≡CH).

4-{3-[Methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenyl diethylcarbamate (SZV-2144/5)

iii) 4-{3-[methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenol (201.0 mg, 1.0 mmol) was dissolved in anhydrous ACN (1.0 ml) under argon, to the solution diethylcarbamic chloride (0.2 ml, 1.7 mmol) was added[57]. Upon cooling (ice-water bath), sodium hydride (31.0 mg 60% dispersion in mineral oil, 1.3 mmol) and anhydrous ACN (2.0 ml) were added. The mixture was stirred at room temperature for 2 h, then additional sodium hydride (10.0 mg 60% dispersion in mineral oil, 0.4 mmol) was added and the mixture was stirred at room temperature for a further 3 h. After evaporation to dryness, ice was added to the residue and it was extracted with DCM and $CHCl_3$ (1x30.0 ml). The organic phase was washed with 0.67 M NaOH solution, dried (Na_2SO_4), filtered and evaporated to dryness. The residue was purified by column chromatography on silica gel ($CHCl_3$:EtOAc 10:1). Pale yellow oil (170 mg, 57%). ^1H NMR (Chloroform-*d*, 400 MHz) δ 7.50 (m, 2H, Ar-H), 7.07 (m, 2H, Ar-H), 5.44 (d, *J*=1.6 Hz, 1H, $=CH_2$), 5.26 (dt, *J*=1.6 and 1.0 Hz, 1H, $=CH_2$), 3.46-3.36 (m, 6H, 3xCH_2), 3.35 (d, *J*=2.4 Hz, 2H, CH_2), 2.31 (s, 3H, CH_3), 2.25 (t, *J*=2.4 Hz, 1H, ≡CH), 1.28-1.16 (m, 6H, 2xCH_3).

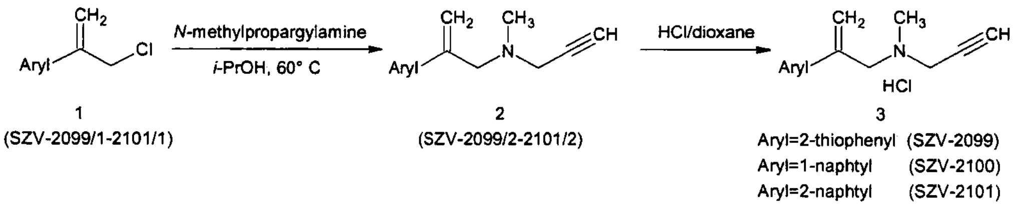
2-{4-[2-(Dimethylamino)ethoxy]phenyl}-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1329) Following **method H2,** 394 mg of the title compound was isolated (68%), white crystals, mp. 156-157 °C (dec). ^1H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 7.49 (m, 2H, Ar-H), 6.95 (m, 2H, Ar-H), 5.43 (br.s, 1H, $=CH_2$), 5.15 (br.s, 1H, $=CH_2$), 4.37 (m, 2H, CH_2), 3.48 (m, 2H, CH_2), 3.39 (br.s, 2H, CH_2), 3.29 (br.s, 2H, CH_2, 3.19 (br.s, 1H, ≡CH), 2.81 (s, 6H, $N(CH_3)_2$), 2.18 (s, 3H, CH_3). Anal. calcd. for $C_{17}H_{24}N_2O$xHCl (308.85): C, 65.38%; H, 8.03%; N, 8.96%. Found: C, 65.01%; H, 8.12%; N, 8.78%.

4-{3-[Methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenol hydrochloride (SZV-1330) Following **method H2,** 179 mg of the title compound was isolated (64%), white crystals, mp 154 °C (dec). ^1H NMR (400 MHz, Dimethyl sulfoxide-*d*$_6$) δ 10.70 (br.s, 1H, NH), 9.90 (br.s, 1H, OH), 7.38 (m, 2H, Ar-H), 6.82 (m, 2H, Ar-H), 5.65 (br.s, 1H, $=CH_2$), 5.55 (br.s, 1H, $=CH_2$), 4.21 (br.s, 2H, CH_2), 4.04 (br.s, 2H, CH_2), 3.88 (br.s, 1H, ≡CH). Anal. calcd. for $C_{13}H_{15}NO$xHCl (237.73): C, 65.68%; H, 6.78%; N, 5.89%. Found: C, 65.04%; H, 6.65%; N, 5.76%.

4-{3-[Methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenyl dimethylcarbamate hydrochloride (SZV-2143) Following **method H2,** 229 mg of the title compound was isolated (88%), white crystals, mp 166-167 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.26 (br.s, 1H, NH), 7.42 (m, 2H, Ar-H), 7.17 (m, 2H, Ar-H), 6.01 (s, 1H, =CH$_2$), 5.87 (s, 1H, =CH$_2$), 4.20-4.10 (m, 2H, CH$_2$), 3.96-3.83 (m, 2H, CH$_2$), 3.11 (s, 3H) and 3.02 (s, 3H) (N(CH$_3$)$_2$), 2.79 (br.s, 3H, CH$_3$), 2.67 (t, *J*=2.4 Hz, 1H, ≡CH). Anal. calcd. for $C_{16}H_{20}N_2O_2$x1.2 HCl (316.10): C, 60.79%; H, 7.03%; N, 8.86%. Found: C, 60.28%; H, 6.48%; N, 8.72%.

4-{3-[Methyl(prop-2-yn-1-yl)amino]prop-1-en-2-yl}phenyl diethylcarbamate hydrochloride (SZV-2144) Following **method H2,** 150 mg of the title compound was isolated (88%), white crystals, mp 164-165 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.16 (br.s, 1H, NH), 7.42 (m, 2H, Ar-H), 7.18 (m, 2H, Ar-H), 6.00 (br.s, 1H, =CH$_2$), 5.86 (br.s, 1H, =CH$_2$), 4.23-4.09 (m, 2H, CH$_2$), 3.99-3.82 (m, 2H, CH$_2$), 3.50-3.30 (m, 4H, 2xCH$_2$), 2.79 (br.s, 3H, CH$_3$), 2.68 (t, *J*=2.4 Hz, 1H, ≡CH), 1.26 (t, *J*=7.2 Hz, 3H, CH$_3$), 1.21 (t, *J*=7.2 Hz, 3H, CH$_3$). Anal. calcd. for $C_{18}H_{24}N_2O_2$x1.1HCl (340.51): C, 63.49%; H, 7.43%; N, 8.23%. Found: C, 63.42%; H, 7.49%; N, 8.19%.

Scheme 52



2-(3-chloroprop-1-en-2-yl)thiophene (SZV-2099/1) The title compound was prepared by Bargar TM et al, J. Med. Chem., 1986, 29, 315-317, which was used without further purification in the next step.

1-(3-chloroprop-1-en-2-yl)naphthalene (SZV-2100/1) The title compound was prepared by Matsumoto K et al, Polym. J., 2000, 32, 1022-1029, which was used without further purification in the next step.

2-(3-chloroprop-1-en-2-yl)naphthalene (SZV-2101/1) The title compound was prepared by analogue reaction of SZV-2100/1.

***N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(thiophen-2-yl)prop-2-en-1-amine (SZV-2099/2)** Following **method D7**, 260 mg of the title compound was isolated (59%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (m, 1H, Ar-H), 7.16 (m, 1H, Ar-H), 6.96 (dd, *J*=5.0 and 3.6 Hz, 1H, Ar-H), 5.52 (br.s, 1H, =CH$_2$), 5.16 (br.s, 1H, =CH$_2$), 3.40 (d, 2H, *J*=2.3 Hz, 2H, CH$_2$), 3.38 (s, 2H, CH$_2$), 2.35 (s, 3H, CH$_3$), 2.25 (t, *J*=2.3 Hz, 1H, ≡CH).

***N*-Methyl-2-(naphthalen-1-yl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2100/2)** Following **method D7**, 253 mg of the title compound was isolated (49%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (m, 1H, Ar-H), 7.85 (m, 1H, Ar-H), 7.76 (d, *J*=8.0 Hz, 1H, Ar-H), 7.49-7.40 (m, 3H, Ar-H), 7.33 (dm, *J*=7.2 Hz, 1H, Ar-H), 5.68 (br.s, 1H, =CH$_2$), 5.30 (br.s, 1H,

=CH_2), 3.46 (br.s, 2H, CH_2), 3.44 (d, *J*=2.2 Hz, 2H, CH_2), 2.38 (s, 3H, CH_3), 2.23 (t, *J*=2.2 Hz, 1H, ≡CH).

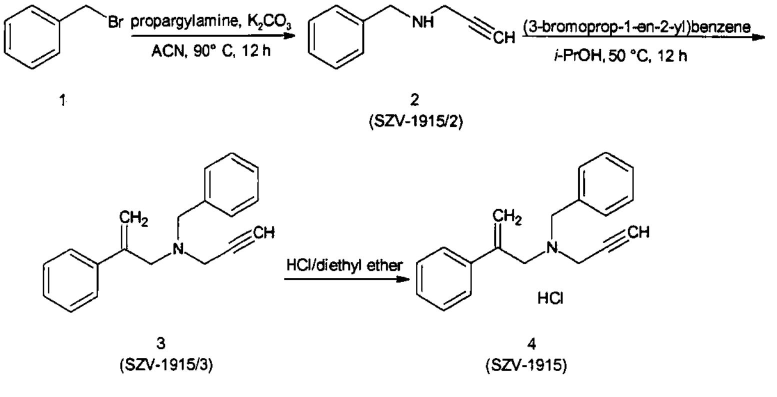
N-Methyl-2-(naphthalen-2-yl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2101/2) Following **method D7**, 380 mg of the title compound was isolated (89%), colourless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (m, 1H, Ar-H), 7.85-7.77 (m, 3H, Ar-H), 7.64 (dd, J=8.8, 1.6 Hz, 1H, Ar-H), 7.48-7.40 (m, 2H, Ar-H), 5.62 (br.s, 1H, =CH_2), 5.39 (br.s, 1H, =CH_2), 3.56 (s, 2H, CH_2), 3.40 (d, J=2.2 Hz, 2H, CH_2), 2.36 (s, 3H, CH_3), 2.28 (t, J=2.2 Hz, 1H, ≡CH).

N-Methyl-N-(prop-2-yn-1-yl)-2-(thiophen-2-yl)prop-2-en-1-amine hydrochloride (SZV-2099) Following **method H2,** 110 mg of the title compound was isolated (36%), white crystals, mp 155 °C (dec). ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 10.85 (br.s, 1H, NH), 7.55 (m, 1H, Ar-H), 7.39 (m, 1H, Ar-H), 7.10 (dd, *J*=5.1 and 3.6 Hz, 1H, Ar-H), 5.80 (br.s, 1H, =CH_2), 5.60 (br.s, 1H, =CH_2), 4.16 (br.s, 2H, CH_2), 4.08 (br.s, 2H, CH_2), 3.87 (br.s, 1H, ≡CH), 2.75 (s, 3H, CH_3). Anal. calcd. for $C_{11}H_{13}NSxHCl$ (227.75): C, 58.01%; H, 6.20%; N, 6.15%. Found: C, 57.98%; H, 6.22%; N, 5.97%.

N-Methyl-2-(naphthalen-1-yl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-2100) Following **method H2,** 124 mg of the title compound was isolated (44%), white crystals, mp 163 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 11.11 (br.s, 1H, NH), 8.02-7.92 (m, 3H, Ar-H), 7.61-7.51 (m, 4H, Ar-H), 6.15 (br.s, 1H, =CH_2), 5.65 (br.s, 1H, =CH_2), 4.43-4.17 (m, 2H, CH_2), 4.07 (br.s, 2H, CH_2), 3.81 (br.s, 1H, ≡CH), 2.75 (s, 3H, CH_3). Anal. calcd. for $C_{17}H_{17}Nx1.1HCl$ (275.43): C, 74.17%; H, 6.57%; N, 5.08%. Found: C, 74.12%; H, 6.40%; N, 5.00%.

N-Methyl-2-(naphthalen-2-yl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-2101) Following **method H2,** 254 mg of the title compound was isolated (58%), white crystals, mp 141 °C. ^{1}H NMR (600 MHz, Dimethyl sulfoxide-d_6) δ 11.10 (br.s, 1H, NH), 8.16 (d, *J*=1.2 Hz, 1H, Ar-H), 7.94-7.90 (m, 3H, Ar-H), 7.74 (dd, *J*=8.4, 1.8 Hz, 1H, Ar-H), 7.58-7.52 (m, 2H, Ar-H), 6.01 (br.s, 1H, =CH_2), 5.87 (br.s, 1H, =CH_2), 4.48 (br.s, 1H, CH_2), 4.37 (br.s, 1H, CH_2), 4.10 (br.s, 2H, CH_2), 3.91 (br.s, 1H, ≡CH), 2.75 (s, 3H, CH_3). Anal. calcd. for $C_{17}H_{17}Nx1.1HCl$ (275.43): C, 74.17%; H, 6.57%; N, 5.08%. Found: C, 73.96%; H, 6.32%; N, 5.04%.

Scheme 53

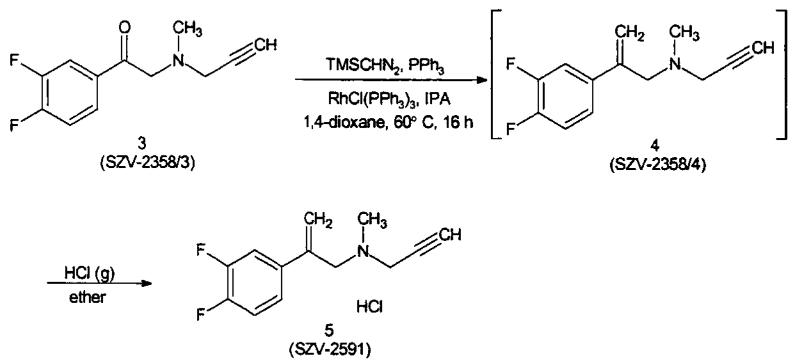


***N*-Benzylprop-2-yn-1-amine (SZV-1915/2)** (Gruit M et al, Org. Biomol. Chem., 2011, 9, 1148-1159) A suspension of (bromomethyl)benzene (5.8 ml, 48.6 mmol), prop-2-yn-1-amine (10.0 ml, 145.0 mmol) and K_2CO_3 (8.0 g, 58.3 mmol) in anhydrous CH_3CN (150.0 ml) was stirred at 90 °C under argon for 12 h. After filtration, the solvent was removed *in vacuo*. The residue was purified by flash chromatography on silica gel (*n*-hexane:EtOAc 10:1). Pale yellow oil (6.50 g, 94%). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.37-7.23 (m, 5H, Ar-H), 3.88 (s, 2H, CH_2), 3.42 (d, *J*=2.4 Hz, 2H, CH_2), 2.26 (t, *J*=2.4 Hz, 1H, ≡CH).

***N*-Benzyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-1915/3)** To a solution of (3-bromoprop-1-en-2-yl)benzene (5.3 g, 26.9 mmol) in anhydrous propan-2-ol (60.0 ml), a solution of *N*-benzylprop-2-yn-1-amine (6.0 g, 41.3 mmol) in anhydrous propan-2-ol (60.0 ml) was added at room temperature under argon. The reaction mixture was stirred at 50 °C for 12 h. After evaporation to dryness, DCM (50.0 ml) was added to the residue solidifying upon cooling. The precipitated crystals were filtered off and washed with DCM, to afford *N*-benzylprop-2-yn-1-amine hydrobromide. The filtrate was evaporated to dryness and purified by flash chromatography on silica gel (1) *n*-hexane, 2) $CHCl_3$). Besides *N*-benzyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine and *N*-benzylprop-2-yn-1-amine hydrobromide, unreacted starting material ((3-bromoprop-1-en-2-yl)benzene – 1.48 g, 28%) was isolated. Colourless oil (3.91 g, 56%). ^1H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.7.48 (m, 2H, Ar-H), 7.37-7.20 (m, 6H, Ar-H), 7.17 (m, 2H, Ar-H), 5.54 (d, J=1.6 Hz, 1H, =CH_2), 5.32 (m, 1H, =CH_2), 3.60 (s, 2H, CH_2), 3.53 (br.s, 2H, CH_2), 3.21 (t, *J*=2.4 Hz, 1H, ≡CH), 3.19 (d, *J*=2.4 Hz, 2H, CH_2).

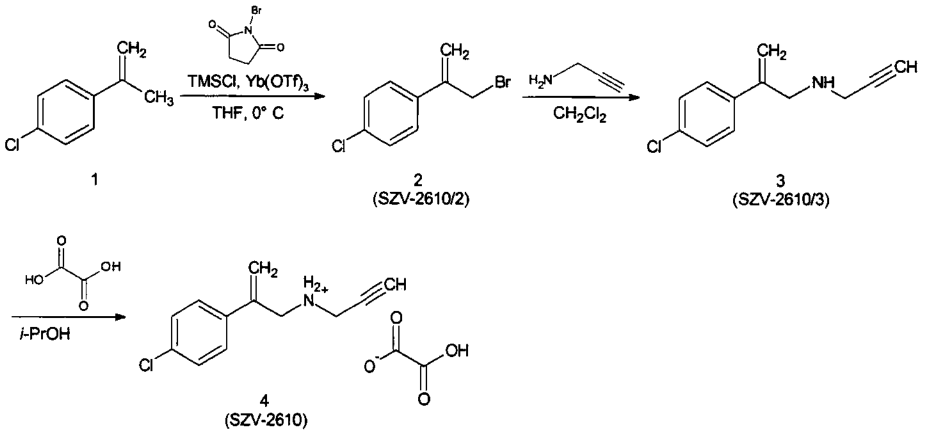
***N*-Benzyl-2-phenyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-1915)** Following **method H2,** the title compound was isolated (38%), white crystals, mp 141-142 °C. Due to the extreme signal broadening at lower temperatures, ^1H NMR was recorded at 90 °C. ^1H NMR (400 MHz, 90 °C, Dimethyl sulfoxide-d_6) δ 7.49-7.42 (m, 4H, Ar-H), 7.39-7.29 (m, 6H, Ar-H), 5.67 (br.s, 1H, =CH_2), 5.64 (br.s, 1H, =CH_2), 4.04 (s, 2H, CH_2), 3.93 (s, 2H, CH_2), 3.61 (s, 2H, CH_2), 3.41 (br.s, 1H, ≡CH). Anal. calcd. for $C_{19}H_{19}NxHCl$ (297.82): C, 76.62%; H, 6.77%; N, 4.70%. Found: C, 76.04%; H, 6.81%; N, 4.63%.

Scheme 54



2-(3,4-Difluorophenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine hydrochloride (SZV-2591) Following **method E3** and **H2**, the title compound was isolated a white powder (60%). Mp 169-171 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.58 – 7.52 (m, 1H), 7.41 – 7.32 (m, 2H), 5.87 (s, 1H), 5.75 (s, 1H), 4.38 (brs, 2H), 4.09 (d, $J = 2.4$ Hz, 2H), 3.45 (t, $J = 2.4$ Hz, 1H), 2.91 (s, 3H). Anal. calcd. for $C_{13}H_{13}F_2NxHCl$ (257.71): C, 60.59%; H, 5.48%; N, 5.44%. Found: C, 60.33%; H, 5.17%; N, 5.54%.

Scheme 55

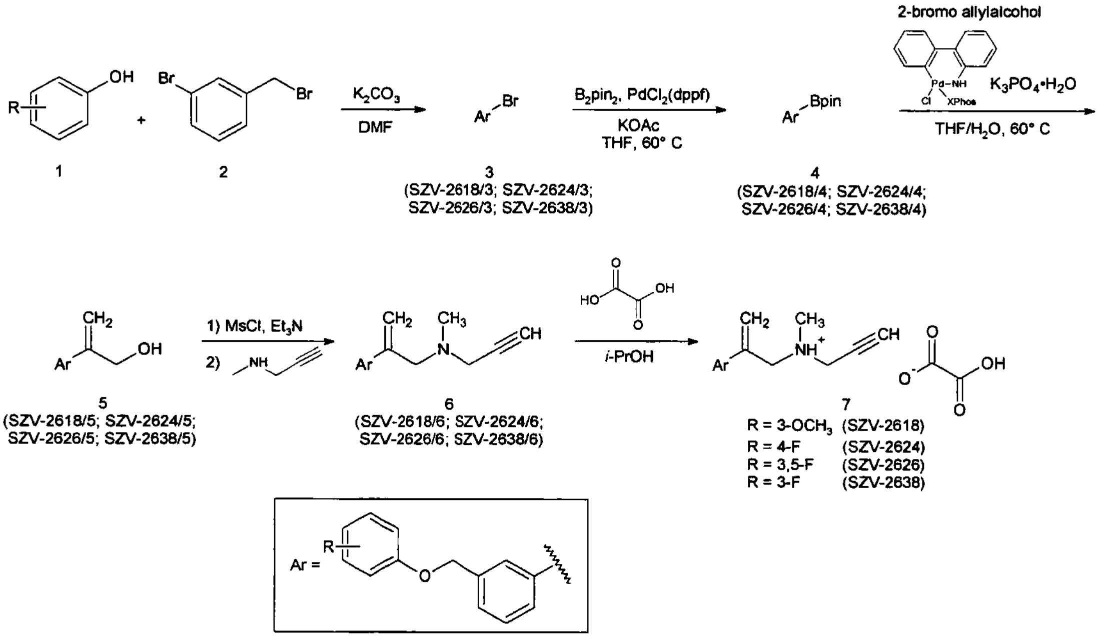


1-(3-Bromoprop-1-en-2-yl)-4-chlorobenzene (SZV-2610/2) A solution of p-Cl-α-methyl styrene (1.0 ml, 7.0 mmol) in THF (5.0 ml) and DCM (20.0 ml) was cooled to 0 °C. To the mixture were added TMSCl (8.8 µl, 0.1 mmol) and $Yb(OTf)_3$ (43.3 mg, 0.1 mol) followed by NBS (1.4 g, 7.7 mmol). The reaction was stirred for 2 h at 0 °C before the addition of water and DCM. The aqueous layer was extracted with DCM (2x). The organic extract was washed with brine and dried ($MgSO_4$), filtered and concentrated. The crude was purified by column chromatography using 5% Et_2O/Hexane as eluent to give the title compound (61%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (d, $J = 8.8$ Hz, 2H), 7.34 (d, $J = 8.8$ Hz, 2H), 5.54 (s, 1H), 5.50 (d, $J = 0.4$ Hz, 1H), 4.35 (d, $J = 0.4$ Hz, 2H).

2-(4-Chlorophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2610/3) Following **method D10**, and purification using flash column chromatography (5 : 95 = MeOH : DCM), the title compound was isolated as a as yellow oil (37%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42-7.39 (m, 2H), 7.34-7.29 (m, 2H), 5.45 (s, 1H), 5.34 (d, *J* = 0.8 Hz, 1H), 3.76 (d, *J* = 0.8 Hz, 2H), 3.47 (d, *J* = 2.4 Hz, 2H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(4-Chlorophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2610) Following **method H1**, the title compound was isolated as white solid (61%). Mp 184.9 – 185.3 °C. ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.53-7.49 (m, 2H), 7.49-7.41 (m, 2H), 5.75 (s, 1H), 5.56 (t, *J* = 1.2 Hz, 1H), 4.19 (d, *J* = 1.2 Hz, 2H), 3.92 (d, *J* = 2.6 Hz, 2H), 3.21 (t, *J* = 2.6 Hz, 1H). HRMS (ESI+) *m/z* calcd. for $C_{12}H_{13}ClN^+$ $[M+H]^+$ 206.0731, found 206.0736.

Scheme 56



1-Bromo-3-((3-methoxyphenoxy)methyl)benzene (SZV-2618/3) Following **method S2**, the crude was purified by flash column chromatography using 5% EtOAc/pet ether as eluent to give the title compound (93%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (t, *J* = 1.2 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.36 – 7.34 (m, 1H), 7.27 – 7.17 (m, 2H), 6.58 – 6.53 (m, 3H), 5.02 (s, 2H), 3.79 (s, 3H).

1-Bromo-3-((4-fluorophenoxy)methyl)benzene (SZV-2624/3) Following **method S2**, the crude was purified by flash column chromatography using 5% EtOAc/pet ether as eluent to give the title compound (99%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.00 – 6.88 (m, 4H), 5.00 (s, 2H).

1-((3-Bromobenzyl)oxy)-3,5-difluorobenzene (SZV-2626/3) Following **method S2**, the crude was purified by flash column chromatography using 5% EtOAc/pet ether as eluent to give the title compound (94%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (brs, 1H), 7.49 – 7.47 (m, 1H), 7.34 – 7.31 (m, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 6.52 – 6.42 (m, 3H), 5.00 (s, 2H).

1-Bromo-3-((3-fluorophenoxy)methyl)benzene (SZV-2638/3) Following **method S2**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (91%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (brs, 1H), 7.48-7.46 (m, 1H), 7.36-7.33 (m, 1H), 7.28-7.20 (m, 2H), 6.76-6.73 (m, 1H), 6.72-6.66 (m, 2H), 5.02 (s, 2H).

2-(3-((3-Methoxyphenoxy)methyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SZV-2618/4) Following **method Q2**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (brs, 1H), 7.78 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.56 – 7.53 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.18 (td, *J* = 8.0, 0.4 Hz, 1H), 6.59 – 6.51 (m, 3H), 5.04 (s, 2H), 3.78 (s, 3H), 1.35 (s, 12H).

2-(3-((4-Fluorophenoxy)methyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SZV-2624/4) Following **method Q2**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (brs, 1H), 7.78 (dt, *J* = 8.8, 0.8 Hz, 1H), 7.54 – 7.52 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.00 – 6.89 (m, 4H), 5.02 (s, 2H), 1.35 (s, 12H).

2-(3-((3,5-Difluorophenoxy)methyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SZV-2626/4) Following **method Q2**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (95%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (brs, 1H), 7.80 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.52 – 7.50 (m, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 6.53 – 6.47 (m, 2H), 6.42 (tt, *J* = 8.8, 2.4 Hz, 1H), 5.02 (s, 2H), 1.36 (s, 12H).

2-(3-((3-Fluorophenoxy)methyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SZV-2638/4) Following **method Q2**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound as a white solid (81%). Mp 56-57 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (brs, 1H), 7.80-7.78 (m, 1H), 7.55-7.52 (m, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.26-7.19 (m, 1H), 6.77-6.75 (m, 1H), 6.71 (t, *J* = 2.4 Hz, 1H), 6.69 – 6.64 (m, 1H), 5.04 (s, 2H), 1.36 (s, 12H).

2-(3-((3-Methoxyphenoxy)methyl)phenyl)prop-2-en-1-ol (SZV-2618/5) Following **method P2**, the crude was purified by flash column chromatography using 10% to 30% EtOAc/pet ether as eluent to give the title compound (60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (brs, 1H), 7.42 – 7.36 (m, 3H), 7.19 (td, *J* = 8.0, 0.4 Hz, 1H), 6.60 – 6.52 (m, 3H), 5.49 (q, *J* = 0.8 Hz, 1H), 5.38 (q, *J* = 1.2 Hz, 1H), 5.05 (s, 2H), 4.55 (dd, *J* = 1.2, 0.8 Hz, 2H), 3.79 (s, 3H).

2-(3-((4-Fluorophenoxy)methyl)phenyl)prop-2-en-1-ol (SZV-2624/5) Following **method P2**, the crude was purified by flash column chromatography using 10% to 30% EtOAc/pet ether as eluent to give the title compound (56%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.49 (m, 1H), 7.43 – 7.35 (m, 3H), 7.00 – 6.90 (m, 4H), 5.49 (q, *J* = 0.8 Hz, 1H), 5.38 (q, *J* = 1.2 Hz, 1H), 5.03 (s, 2H), 4.55 (q, *J* = 0.8 Hz, 2H).

2-(3-((3,5-Difluorophenoxy)methyl)phenyl)prop-2-en-1-ol (SZV-2626/5) Following **method P2**, the crude was purified by flash column chromatography using 10% to 20% EtOAc/pet ether as eluent to give the title compound (32%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (s, 1H), 7.44 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.35 (dt, *J* = 7.6, 1.6 Hz, 1H), 6.54 – 6.48 (m, 2H), 6.43 (tt, *J* = 8.8, 2.4 Hz, 1H), 5.50 (d, *J* = 0.8 Hz, 1H), 5.39 (q, *J* = 1.2 Hz, 1H), 5.03 (s, 2H), 4.56 (dd, *J* = 1.2, 0.8 Hz, 2H).

2-(3-((3-Fluorophenoxy)methyl)phenyl)prop-2-en-1-ol (SZV-2638/5) Following **method P2**, the crude was purified by flash column chromatography using 10% to 30% EtOAc/pet ether as eluent to give the title compound (48%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (brs, 1H), 7.33-7.29 (m, 1H), 7.28-7.25 (m, 2H), 7.15-7.09 (m, 1H), 6.67-6.65 (m, 1H), 6.61-6.55 (m, 2H), 5.38 (d, *J* = 0.8 Hz, 1H), 5.27 (q, *J* = 1.2 Hz, 1H), 4.94 (s, 2H), 4.44 (s, 2H), 1.71 (br, 1H).

2-(3-((3-Methoxyphenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2618/6) Following **method D9**, the crude was purified by flash column chromatography using 10% Et$_2$O/pet ether as eluent to give the title compound (52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (brs, 1H), 7.46 (td, *J* = 4.8, 2.0 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.19 (td, *J* = 8.0, 0.4 Hz, 1H), 6.61 – 6.51 (m, 3H), 5.54 (s, 1H), 5.37 (s, 1H), 5.05 (s, 2H), 3.79 (s, 3H), 3.52 (s, 2H), 3.40 (s, 2H), 2.36 (s, 3H), 2.28 (t, *J* = 2.0 Hz, 1H).

2-(3-((4-Fluorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2624/6) Following **method D9**, the crude was purified using flash column chromatography using 10% Et$_2$O/pet ether as eluent to give the title compound (67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (brs, 1H), 7.47 (dt, *J* = 6.8, 2.4 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.00 – 6.90 (m, 4H), 5.51 (s, 1H), 5.33 (s, 1H), 5.03 (s, 2H), 3.47 (s, 2H), 3.37 (s, 2H), 2.33 (s, 3H), 2.26 (s, 1H).

2-(3-((3,5-Difluorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2626/6) Following **method D9**, the crude was purified by flash column chromatography using 10% Et$_2$O/pet ether as eluent to give the title compound (54%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 – 7.54 (m, 1H), 7.49 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.31 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.53 – 6.47 (m, 2H), 6.42 (tt, *J* = 8.8, 2.4 Hz, 1H), 5.52 (s, 1H), 5.34 (s, 1H), 5.03 (s, 2H), 3.48 (s, 2H), 3.37 (d, *J* = 2.0 Hz, 2H), 2.33 (s, 3H), 2.26 (t, *J* = 2.0 Hz, 1H).

2-(3-((3-Fluorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2638/6) Following **method D9**, the crude was purified by flash column chromatography using 10% Et$_2$O/pet ether as eluent to give the title compound (64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (brs, 1H), 7.48 (dt, *J* = 7.0, 2.0 Hz, 1H), 7.38-7.34 (m, 2H), 7.26-7.20 (m, 1H), 6.78-6.76 (m, 1H), 6.72 (t, *J* = 2.4 Hz, 1H), 6.70-6.65 (m, 1H), 5.52 (d, *J* = 1.6 Hz, 1H), 5.34 (s, 1H), 5.05 (s, 2H), 3.48 (d, *J* = 1.6 Hz, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.34 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

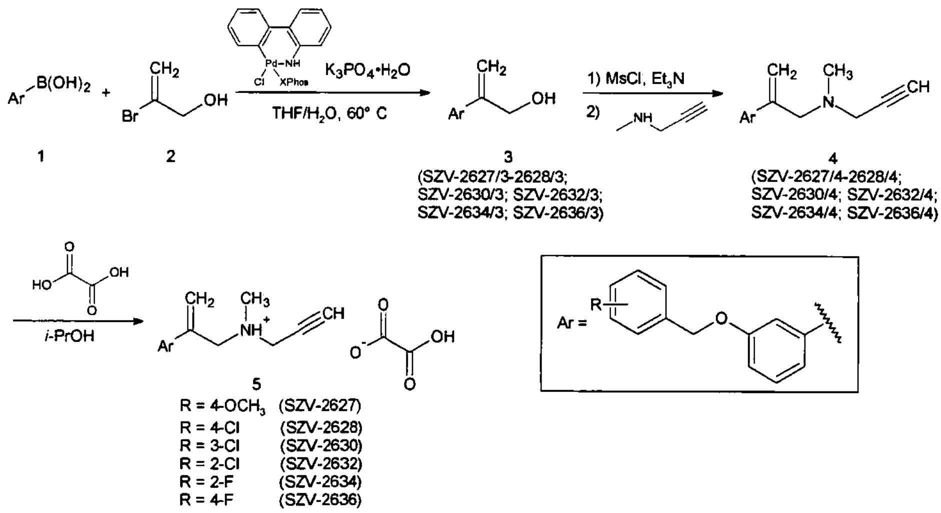
2-(3-((3-Methoxyphenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2618) Following **method H1**, the title compound was isolated as white solid (55%). Mp 114.7 – 116.0 °C. ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.62 (s, 1H), 7.52 – 7.41 (m, 3H), 7.16 (t, *J* = 8.0 Hz, 1H), 6.60 – 6.51 (m, 3H), 5.77 (s, 1H), 5.62 (s, 1H), 5.11 (s, 2H), 4.21 (s, 2H), 3.89 (s, 2H), 3.76 (s, 3H), 3.23 (s, 1H), 2.75 (s, 3H). Anal. calcd. for $C_{21}H_{23}NO_2x(COOH)_2$ (411.45): C, 67.14%; H, 6.12%; N, 3.40%. Found: C, 67.16%; H, 5.90%; N, 3.53%.

2-(3-((4-Fluorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2624) Following **method H1**, the title compound was isolated as white solid (59%). Mp 111.0 – 112.2 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.61 (brs, 1H), 7.51 – 7.42 (m, 3H), 7.02 – 6.97 (m, 4H), 5.76 (s, 1H), 5.61 (s, 1H), 5.10 (s, 2H), 4.19 (s, 2H), 3.88 (s, 2H), 3.22 (s, 1H), 2.74 (s, 3H). Anal. calcd. for $C_{20}H_{20}NOx(COOH)_2$ (399.41): C, 66.16%; H, 5.55%; N, 3.51%. Found: C, 65.66%; H, 5.59%; N, 3.56%.

2-(3-((3,5-Difluorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2626) Following **method H1**, the title compound was isolated as white solid (63%). Mp 127 – 128 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.62 (brs, 1H), 7.52 (dt, J = 6.4, 2.0 Hz, 1H), 7.50 – 7.42 (m, 2H), 5.67 – 5.61 (m, 2H), 6.52 (tt, J = 9.2, 2.4 Hz, 1H), 5.78 (s, 1H), 5.64 (s, 1H), 5.13 (s, 2H), 4.23 (s, 2H), 3.91 (s, 2H), 3.25 (s, 1H), 2.77 (s, 3H). Anal. calcd. for $C_{20}H_{19}F_2NOx(COOH)_2$ (417.40): C, 63.30%; H, 5.07%; N, 3.36%. Found: C, 63.12%; H, 4.77%; N, 3.30%.

2-(3-((3-Fluorophenoxy)methyl)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2638) Following **method H1**, the title compound was isolated as white solid (65%). Mp 126.1 – 127.0 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.62 (brs, 1H), 7.52-7.43 (m, 3H), 7.30-7.24 (m, 1H), 6.84-6.81 (m, 1H), 6.77 (dt, J = 11.1, 2.4 Hz, 1H), 6.70-6.65 (m, 1H), 5.78 (d, J = 0.8 Hz, 1H), 5.63 (d, J = 0.8 Hz, 1H), 5.13 (s, 2H), 4.23 (s, 2H), 3.91 (d, J = 2.8 Hz, 2H), 3.24 (t, J = 2.8 Hz, 1H), 2.77 (s, 3H). Anal. calcd. for $C_{20}H_{20}FNOx(COOH)_2$ (399.41): C, 66.16%; H, 5.55%; N, 3.51%. Found: C, 66.05%; H, 5.35%; N, 3.61%.

Scheme 57



2-(3-((4-Methoxybenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2627/3) Following **method P2**, the crude was purified by flash column chromatography using 20% EtOAc/pet ether as eluent to give the title compound (37%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 8.6 Hz, 2H), 7.29-7.25 (m, 1H), 7.08-7.04 (m, 2H), 6.93-6.91 (m, 3H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.35 (d, *J* = 1.2 Hz, 1H), 5.01 (s, 2H), 4.52 (s, 2H), 3.82 (s, 3H).

2-(3-((4-Chlorobenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2628/3) Following **method P2**, the crude was purified by flash column chromatography using 5% to 20% EtOAc/pet ether as eluent to give the title compound (51%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40-7.35 (m, 4H), 7.30-7.26 (m, 1H), 7.08-7.06 (m, 2H), 6.90 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.36 (d, *J* = 1.2 Hz, 1H), 5.05 (s, 2H), 4.52 (s, 2H).

2-(3-((3-Chlorobenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2630/3) Following **method P2** the crude was purified by flash column chromatography using 5% to 30% EtOAc/pet ether as eluent to give the title compound (39%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43-7.42 (m, 1H), 7.29-7.22 (m, 4H), 7.05-7.02 (m, 2H), 6.89-6.86 (m, 1H), 5.44 (d, *J* = 0.8 Hz, 1H), 5.33 (q, *J* = 1.2 Hz, 1H), 5.01 (s, 2H), 4.48 (q, *J* = 1.2 Hz, 2H), 1.81 (br, 1H).

2-(3-((2-Chlorobenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2632/3) Following **method P2**, the crude was purified by flash column chromatography using 10% to 20% EtOAc/pet ether as eluent to give the title compound (47%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.56 (m, 1H), 7.42-7.40 (m, 1H), 7.32 – 7.24 (m, 4H), 7.10 – 7.06 (m, 2H), 6.95-6.92 (m, 1H), 5.47 (d, *J* = 0.8 Hz, 1H), 5.36 (q, *J* = 1.2 Hz, 1H), 5.19 (s, 2H), 4.53 (q, *J* = 0.8 Hz, 2H).

2-(3-((2-Fluorobenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2634/3) Following **method P2**, the crude was purified by flash column chromatography using 10% to 20% EtOAc/pet ether as eluent to give the title compound (45%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54-7.50 (m, 1H), 7.35-7.26 (m, 2H), 7.17 (td, *J* = 7.5, 1.2 Hz, 1H), 7.12-7.05 (m, 3H), 6.95-6.92 (m, 1H), 5.47 (d, *J* = 0.8 Hz, 1H), 5.36 (q, *J* = 1.2 Hz, 1H), 5.15 (s, 2H), 4.52 (q, *J* = 0.8 Hz, 2H).

2-(3-((4-Fluorobenzyl)oxy)phenyl)prop-2-en-1-ol (SZV-2636/3) Following **method P2**, the crude was purified by flash column chromatography using 5% to 30% EtOAc/pet ether as eluent to give the title compound (38%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43-7.40 (m, 2H), 7.30-7.26 (m, 2H), 7.10-7.05 (m, 4H), 6.92-6.89 (m, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.35 (d, *J* = 1.2 Hz, 1H), 5.04 (s, 2H), 4.52 (s, 2H).

2-(3-((4-Methoxybenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2627/4) Following **method D9**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (86%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 8.6 Hz, 2H), 7.28-7.24 (m, 1H), 7.17 (t, *J* = 2.0 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.95-6.89 (m, 3H), 5.49 (d, *J* = 1.2 Hz, 3H), 5.31 (d, *J* = 1.2 Hz, 1H), 5.01 (s, 2H), 3.83 (s, 3H), 3.45 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.34 (s, 3H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(3-((4-chlorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2628/4) Following **method D9**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39-7.34 (m, 4H), 7.27-7.23 (m , 1H), 7.15-7.11 (m, 2H), 6.87 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 5.48 (d, *J* = 1.6 Hz, 1H), 5.30 (d, *J* = 1.6 Hz, 1H), 5.04 (s, 2H), 3.44 (s, 2H), 3.37 (d, *J* = 2.4 Hz, 2H), 2.33 (s, 3H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(3-((3-Chlorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2630/4) Following **method D9**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (49%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.47 (brs, 1H), 7.38-7.29 (m, 3H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.15 (t, *J* = 2.0 Hz, 1H), 7.11-7.09 (m, 1H), 6.91 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.47 (d, *J* = 1.6 Hz, 1H), 5.27 (d, *J* = 1.6 Hz, 1H), 5.10 (s, 2H), 3.47 (s, 2H), 3.30 (d, *J* = 2.4 Hz, 1H), 2.63 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

2-(3-((2-chlorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2632/4) Following **method D9**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (52%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.58-7.55 (m, 1H), 7.45 – 7.42 (m, 1H), 7.33 – 7.30 (m, 2H), 7.24 (t, *J* = 7.9 Hz, 1H), 7.15 (t, *J* = 2.0 Hz, 1H), 7.13-7.10 (m, 1H), 6.92 (dd, *J* = 8.0, 2.4 Hz, 1H), 5.47 (d, *J* = 1.6 Hz, 1H), 5.27 (d, *J* = 1.6 Hz, 1H), 5.19 (s, 2H), 3.46 (s, 2H), 3.29 (t, *J* = 2.4 Hz, 2H), 2.62 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

2-(3-((2-Fluorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2634/4) Following general **method D9**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (73%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.52 (t, *J* = 7.6 Hz, 1H), 7.38-7.33 (m, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.20-7.10 (m, 4H), 5.47 (d, *J* = 1.6 Hz, 1H), 5.27 (q, *J* = 1.2 Hz, 1H), 5.15 (s, 2H), 3.47 (d, *J* = 1.3 Hz, 2H), 3.29 (d, *J* = 2.4 Hz, 2H), 2.62 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

2-(3-((4-Fluorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2636/4) Following **method D9**, the crude was purified by flash column chromatography using 10% Et_2O/pet ether as eluent to give the title compound (65%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.48-7.44 (m, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.13 (t, *J* = 2.0 Hz, 1H), 7.11-7.07 (m, 3H), 6.91 (dd, *J* = 8.0, 2.4 Hz, 1H), 5.46 (d, *J* = 1.6 Hz, 1H), 5.27 (d, *J* = 1.6 Hz. 1H), 5.07 (s, 2H), 3.46 (s, 2H), 3.30 (d, *J* = 2.4 Hz, 2H), 2.63 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

2-(3-((4-Methoxybenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2627) Following **method H1**, the title compound was isolated as white solid (57%). Mp 104 – 105 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.38-7.31 (m, 3H), 7.13 (s, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.02 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.94-6.91 (m, 2H), 5.74 (s, 1H), 5.60 (brs. d, 1H), 5.05 (s, 2H), 4.19 (br, 2H), 3.90 (br, 2H), 3.26 (t, *J* = 2.4 Hz, 1H), 2.75 (s, 3H). Anal. calcd. for $C_{21}H_{23}NO_2x(COOH)_2$ (411.45): C, 67.14%; H, 6.12%; N, 3.40%. Found: C, 66.96%; H, 5.89%; N, 3.39%.

2-(3-((4-Chlorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2628) Following **method H1**, the title compound was isolated as white solid (59%). Mp 122 – 123 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.50-7.44 (m, 4H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 2.0 Hz, 1H), 7.11 (dt, *J* = 7.8, 1.2 Hz, 1H), 6.93 (ddd, *J* = 8.3, 2.0, 1.2 Hz, 1H), 5.52 (s, 1H), 5.26 (s, 1H), 5.11 (s, 2H), 3.45 (s, 2H), 3.34 (s, 2H), 3.22 (s, 1H), 2.22 (s, 3H). Anal. calcd. for $C_{20}H_{20}ClNOx(COOH)_2$ (415.87): C, 63.54%; H, 5.33%; N, 3.37%. Found: C, 63.37% H, 5.10%; N, 3.35%.

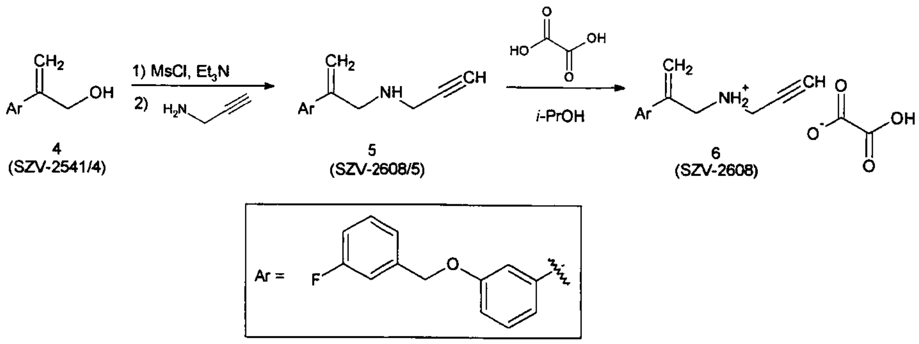
2-(3-((3-Chlorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2630) Following **method H1**, the title compound was isolated as white solid (49%). Mp 119.8 – 120.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.48 (br, 1H), 7.39-7.31 (m, 4H), 7.17 (brs, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 7.03 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.75 (s, 1H), 5.60 (s, 1H), 5.14 (s, 2H), 4.18 (s, 2H), 3.89 (s, 2H), 3.25 (s, 1H), 2.75 (s, 3H). HRMS (ESI +) *m/z* calcd. for $C_{20}H_{21}ClNO^+$ $[M+H]^+$ 326.1306, found 326.1318.

2-(3-((2-Chlorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2632) Following **method H1**, the title compound was isolated as white solid (49%). Mp 116.2 – 116.4 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.60 – 7.56 (m, 1H), 7.47 – 7.42 (m, 1H), 7.38-7.31 (m, 3H), 7.19 – 7.13 (m, 2H), 7.06-7.03 (m, 1H), 5.76 (s, 1H), 5.61 (s, 1H), 5.23 (s, 2H), 4.19 (s, 2H), 3.90 (d, *J* = 2.4 Hz, 2H), 3.25 (t, *J* = 2.4 Hz, 1H), 2.75 (s, 3H). Anal. calcd. for $C_{20}H_{20}ClNOx(COOH)_2$ (415.87): C, 63.54%; H, 5.33%; N, 3.37%. Found: C, 63.68%; H, 5.10%; N, 3.42%.

2-(3-((2-Fluorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2634) Following **method H1**, the title compound was isolated as white solid (33%). Mp 107.2 – 108.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.53 (td, *J* = 7.5, 1.8 Hz, 1H), 7.38-7.33 (m, 2H), 7.22-7.11 (m, 4H), 7.06-7.03 (m, 1H), 5.76 (s, 1H), 5.62 (s, 1H), 5.19 (s, 2H), 4.22 (s, 2H), 3.92 (d, *J* = 2.4 Hz, 2H), 3.26 (t, *J* = 2.4 Hz, 1H), 2.77 (s, 3H). Anal. calcd. for $C_{20}H_{20}FNOx(COOH)_2$ (399.41): C, 66.16%; H, 5.55%; N, 3.51%. Found: C, 66.39%; H, 5.25%; N, 3.59%.

2-(3-((4-Fluorobenzyl)oxy)phenyl)-*N*-methyl-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2636) Following **method H1**, the title compound was isolated as white solid (68%). Mp 117.6 – 118.9 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.50 – 7.45 (m, 2H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 1.8 Hz, 1H), 7.13 – 7.07 (m, 3H), 7.04-7.01 (m, 1H), 5.75 (s, 1H), 5.61 (s, 1H), 5.11 (s, 2H), 4.20 (s, 2H), 3.91 (d, *J* = 2.8 Hz, 2H), 3.27 (t, *J* = 2.8 Hz, 1H), 2.76 (s, 3H). Anal. calcd. for $C_{20}H_{20}FNOx(COOH)_2$ (399.41): C, 66.16%; H, 5.55%; N, 3.76%. Found: C, 66.16%; H, 5.31%; N, 3.61%.

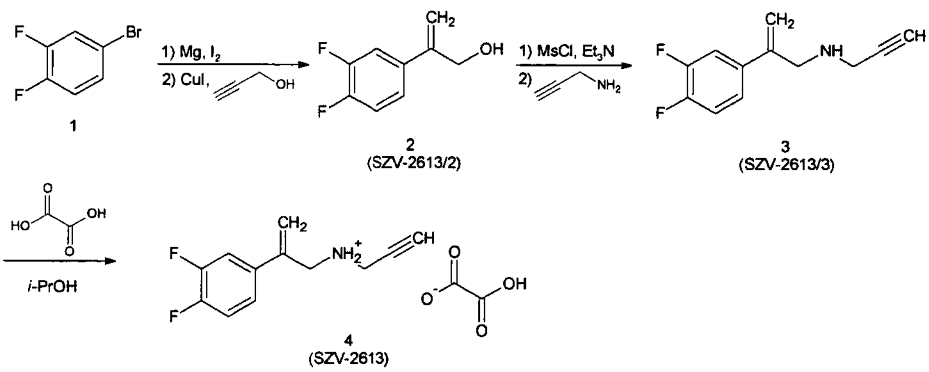
Scheme 58



2-(3-((3-Fluorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2608/5) Following **method D9**, the crude was purified by flash column chromatography using 1% MeOH/DCM as eluent to give the title compound (52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40-7.35 (m, 1H), 7.31-7.27 (m, 1H), 7.24-7.19 (m, 2H), 7.12-7.10 (m, 2H), 7.06-7.02 (m, 1H), 6.93-6.91 (m, 1H), 5.46 (s, 1H), 5.32 (s, 1H), 5.10 (s, 2H), 3.77 (s, 2H), 3.47 (d, *J* = 2.4 Hz, 2H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(3-((3-Fluorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2608) Following **method H1**, the title compound was isolated as white solid (84%). Mp 182 - 184 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.42-7.33 (m, 2H), 7.27-7.25 (m, 1H), 7.22-7.19 (m, 1H), 7.14-7.13 (m, 1H), 7.12-7.09 (m, 1H), 7.07-7.02 (m, 2H), 5.72 (s, 1H), 5.53 (s, 1H), 5.16 (s, 2H), 4.19 (s, 2H), 3.90 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H). Anal. calcd. for $C_{19}H_{18}FNOx(COOH)_2$ (385.39): C, 65.45%; H, 5.23%; N, 3.63%. Found: C, 65.21%; H, 5.06%; N, 3.82%.

Scheme 59

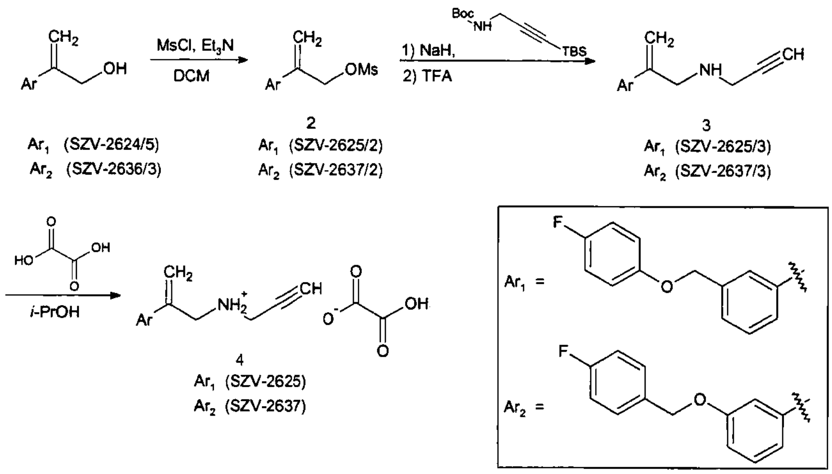


2-(3,4-Difluorophenyl)prop-2-en-1-ol (SZV-2613/2) Following **method N**, the title compound was isolated (97%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31-7.28 (m, 1H), 7.21-7.16 (m, 1H), 7.14-7.10 (m, 1H), 5.45 (s, 1H), 5.38 (s, 1H), 4.49 (dd, *J* = 1.5, 0.7 Hz, 2H).

2-(3,4-Difluorophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2613/3) Following **method D9**, the crude was purified by flash column chromatography using 1% to 2.5% MeOH/DCM as eluent to give the title compound (38%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34-7.29 (m, 1H), 7.22-7.18 (m, 1H), 7.15-7.08 (m, 1H), 5.42 (s, 1H), 5.33 (s, 1H), 3.72 (d, *J* = 1.2 Hz, 2H), 3.46 (d, *J* = 2.4 Hz, 2H), 2.26 (t, *J* = 2.4 Hz, 1H).

2-(3,4-Difluorophenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2613) Following **method H1**, the title compound was isolated as white solid (84%). Mp 188.4 – 189.5 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.50-7.45 (m, 1H), 7.34-7.27 (m, 1H), 5.75 (s, 1H), 5.58 (s, 1H), 4.18 (d, *J* = 1.2 Hz, 2H), 3.92 (d, *J* = 2.4 Hz, 1H), 3.21 (t, *J* = 2.4 Hz, 1H). Anal. calcd. for $C_{12}H_{11}F_2Nx(COOH)_2$ (297.25): C, 56.57%; H, 4.41%; N, 4.71%. Found: C, 56.76%; H, 4.38%; N, 4.59%.

Scheme 60



2-(3-((4-Fluorophenoxy)methyl)phenyl)allyl methanesulfonate (SZV-2625/2) Following **method T1** using SZV-1624/5, the title compound was isolated (87%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (brs, 1H), 7.44-7.39 (m, 3H), 7.02-6.95 (m, 2H), 6.94 – 6.89 (m, 2H), 5.70 (s, 1H), 5.53 (d, *J* = 0.8 Hz, 1H), 5.13 (d, *J* = 1.1 Hz, 2H), 5.04 (d, *J* = 1.2 Hz, 2H), 2.94 (s, 3H).

2-(3-((4-Fluorobenzyl)oxy)phenyl)allyl methanesulfonate (SZV-2637/2) Following **method T1** using SZV-2638/3, the crude was purified by flash column chromatography using 10% EtOAc/pet ether as eluent to give the title compound was isolated (62%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44-7.39 (m, 2H), 7.32-7.28 (m, 1H), 7.11-7.05 (m, 4H), 6.96-6.93 (m, 1H), 5.68 (s, 1H), 5.51 (d, *J* = 0.8 Hz, 1H), 5.09 (d, *J* = 0.8 Hz, 2H), 5.05 (s, 2H), 2.94 (s, 3H).

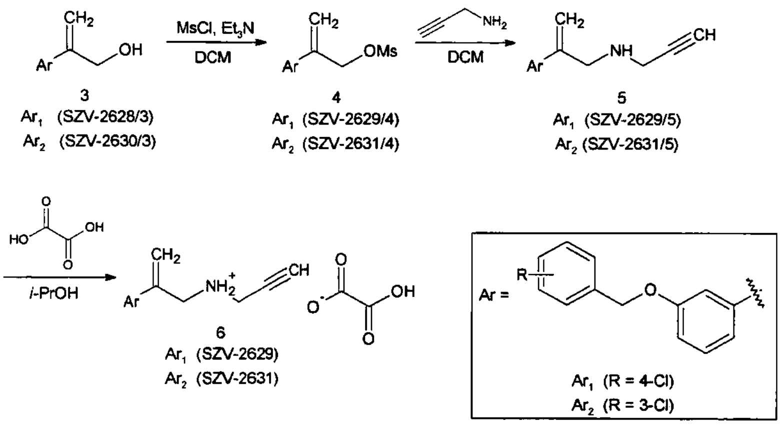
2-(3-((4-Fluorophenoxy)methyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2625/3) Following **method T2**, the title compound was isolated (43% over 2 steps). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (br, 1H), 7.44 (dt, *J* = 6.8, 2.2 Hz, 1H), 7.39-7.34 (m, 2H), 7.00-6.90 (m, 4H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.32 (d, *J* = 1.2 Hz, 1H), 5.03 (s, 2H), 3.77 (s, 2H), 3.45 (d, *J* = 2.4 Hz, 2H), 2.25 (t, *J* = 2.4 Hz, 1H).

2-(3-((4-Fluorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2637/3) Following **method T2**, the title compound was isolated (46% over 2 steps). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.48-7.45 (m, 2H), 7.26 (t, *J* = 7.9 Hz, 1H), 7.12-7.04 (m, 4H), 6.94-6.92 (m, 1H), 5.43 (d, *J* = 1.2 Hz, 1H), 5.26 (d, *J* = 1.2 Hz, 1H), 5.08 (s, 2H), 3.71 (s, 2H), 3.38 (d, *J* = 2.4 Hz, 2H), 2.61 (t, *J* = 2.4 Hz, 1H).

2-(3-((4-Fluorophenoxy)methyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2625) Following **method H1**, the title compound was isolated as white solid (75%). Mp 189.8 - 191.1 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.59 (br, 1H), 7.49 – 7.42 (m, 3H), 7.03-6.96 (m, 4H), 5.74 (s, 2H), 5.54 (t, *J* = 1.2 Hz, 1H), 5.10 (s, 2H), 4.21 (d, *J* = 1.2 Hz, 2H), 3.90 (d, *J* = 2.4 Hz, 2H), 3.20 (t, *J* = 2.4 Hz, 1H). Anal. calcd. for $C_{19}H_{18}FNOx(COOH)_2$ (385.39): C, 65.45%; H, 5.23%; N, 4.93%. Found: C, 65.48%; H, 4.93%; N, 3.62%.

2-(3-((4-Fluorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2637) Following **method H1**, the title compound was isolated as white solid (73%). Mp 186.7 – 187.8 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.49-7.46 (m, 2H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.13 – 7.08 (m, 4H), 7.05-7.02 (m, 1H), 5.72 (s, 1H), 5.53 (s, 1H), 5.11 (s, 2H), 4.19 (s, 2H), 3.90 (d, *J* = 2.4 Hz, 2H), 3.21 (t, *J* = 2.4 Hz, 1H). Anal. calcd. for $C_{19}H_{18}FNOx(COOH)_2$ (385.39): C, 65.45%; H, 5.23%; N, 3.63%. Found: C, 65.35%; H, 5.00%; N, 3.7%.

Scheme 61



2-(3-((4-Chlorobenzyl)oxy)phenyl)allyl methanesulfonate (SZV-2629/4) Following **method T1**, the crude was purified by flash column chromatography using 10% EtOAc/pet ether as eluent to give the title compound (88%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39-7.35 (m, 4H), 7.31-7.27 (m, 1H), 7.08-7.04 (m, 2H), 6.95-6.92 (m, 1H), 5.67 (s, 1H), 5.51 (d, *J* = 1.0 Hz, 1H), 5.09 (d, *J* = 1.0 Hz, 2H), 5.06 (s, 2H), 2.94 (s, 3H).

2-(3-((3-Chlorobenzyl)oxy)phenyl)allyl methanesulfonate (SZV-2631/4) Following **method T1**, the crude was purified by flash column chromatography using 40% Et_2O/pet ether as eluent to give the title compound (53%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (s, 1H), 7.28-7.22 (m, 4H), 7.05-7.02 (m, 2H), 6.92-6.89 (m, 1H), 5.64 (s, 1H), 5.48 (s, 1H), 5.06 (s, 2H), 5.03 (s, 2H), 2.91 (s, 3H).

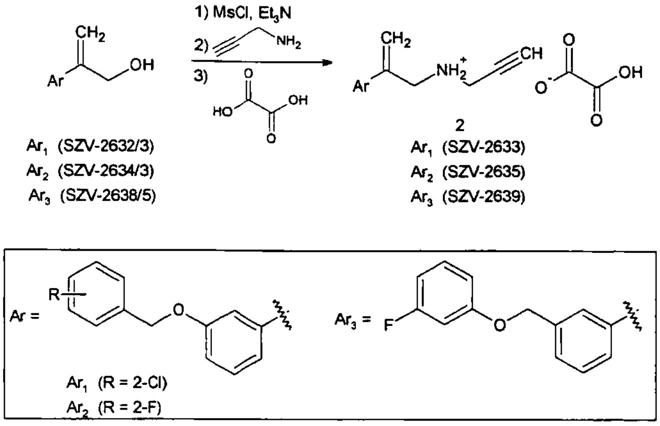
2-(3-((4-Chlorobenzyl)oxy)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2629/5) Following **method D10**, the crude was purified by flash column chromatography using 1% to 2.5% MeOH/DCM as eluent to give the title compound (61%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41-7.35 (m, 4H), 7.30-7.26 (m, 1H), 7.11-7.08 (m, 2H), 6.92-6.89 (m, 1H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.32 (q, *J* = 1.2 Hz, 1H), 5.06 (s, 2H), 3.77 (d, *J* = 0.8 Hz, 2H), 3.48 (d, *J* = 2.4 Hz, 2H), 2.27 (t, *J* = 2.4 Hz, 1H).

2-(3-((3-Chlorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2631/5) Following **method D10**, the crude was purified by flash column chromatography using 1% MeOH/DCM as eluent to give the title compound (58%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (brs, 1H), 7.33-7.25 (m, 5H), 7.08-7.06 (m, 2H), 6.91-6.88 (m, 1H), 5.49 (s, 1H), 5.38 (s, 1H), 5.06 (s, 2H), 3.82 (s, 2H), 3.51 (d, *J* = 2.4 Hz, 2H), 2.30 (t, *J* = 2.4 Hz, 1H).

2-(3-((4-Chlorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2629) Following **method H1**, the title compound was isolated as white solid (66%). Mp 198 – 200 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.45-7.33 (m, 5H), 7.13-7.09 (m, 2H), 7.05-7.02 (m, 1H), 5.72 (s, 1H), 5.52 (t, *J* = 1.2 Hz, 1H), 5.12 (s, 2H), 4.19 (d, *J* = 1.2 Hz, 2H), 3.90 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H). Anal. calcd. for $C_{19}H_{18}ClNOx(COOH)_2$ (401.84): C, 62.77%; H, 5.02%; N, 3.49%. Found: C, 62.48%; H, 4.76%; N, 3.47%.

2-(3-((3-Chlorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2631) Following **method H1**, the title compound was isolated as white solid (71%). Mp 189.2 – 190.7 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.48 (brs, 1H), 7.39-7.30 (m, 4H), 7.14-7.10 (m, 2H), 7.05-7.02 (m, 1H), 5.72 (s, 1H), 5.53 (s, 1H), 5.14 (s, 2H), 4.19 (s, 2H), 3.89 (d, *J* = 2.4 Hz, 2H), 3.20 (t, *J* = 2.4 Hz, 1H). HRMS (ESI +) *m/z* calcd. for $C_{19}H_{19}ClNO^+$ $[M+H]^+$ 312.1150, found 312.1155.

Scheme 62

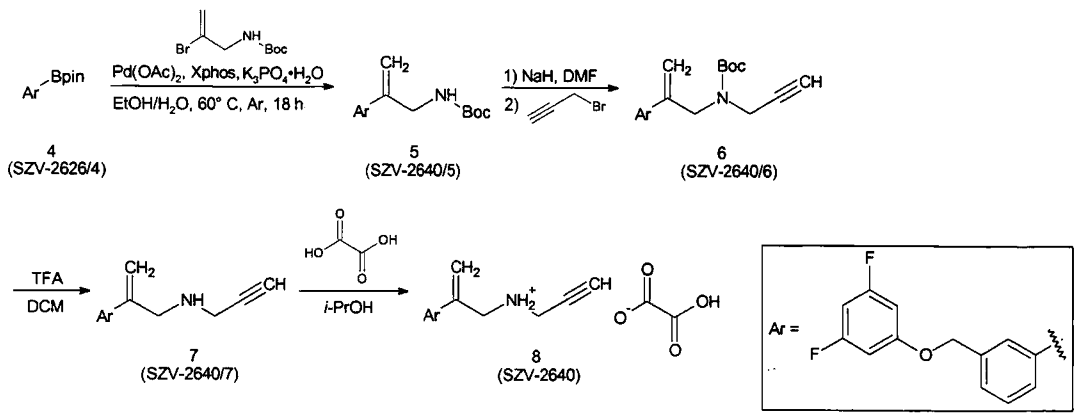


2-(3-((2-Chlorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2633) Following **method D9** and **method H1** using SZV-2632/3, the title compound was isolated as white solid (15% over 3 steps). Mp 204.7 – 205.8 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.63-7.60 (m, 1H), 7.53-7.51 (m, 1H), 7.42-7.39 (m, 2H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.16-7.10 (m, 2H), 7.02 (dd, *J* = 8.0, 2.4 Hz, 1H), 5.64 (s, 1H), 5.40 (s, 1H), 5.19 (s, 2H), 3.90 (s, 2H), 3.68 (d, *J* = 2.4 Hz, 2H), 3.46 (t, *J* = 2.4 Hz, 1H). Anal. calcd. for $C_{19}H_{18}ClNOx(COOH)_2$ (401.84): C, 62.77%; H, 5.02%; N, 3.49%. Found: C, 62.54%; H, 4.81%; N, 3.64%.

2-(3-((2-Fluorobenzyl)oxy)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2635) Following **method D9** and **method H1** using SZV-2634/3, the title compound was isolated as white solid (13% over 3 steps). Mp 183.5 – 185.5 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.53 (td, *J* = 7.5, 1.8 Hz, 1H), 7.40-7.34 (m, 2H), 7.22-7.10 (m, 4H), 7.06 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.73 (s, 1H), 5.53 (s, 1H), 5.19 (s, 2H), 4.20 (s, 2H), 3.91 (d, *J* = 2.4 Hz, 2H), 3.22 (t, *J* = 2.4 Hz, 1H). HRMS (ESI +) *m/z* calcd. for $C_{19}H_{19}FNO^+$ $[M+H]^+$ 296.1445, found 296.1437.

2-(3-((3-Fluorophenoxy)methyl)phenyl)-*N*-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2639) Following **method D9** and **method H1** SZV-2638/5, the title compound was isolated as white solid (26% over 3 steps). Mp 190.4 – 193.3 °C. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.60 (brs, 1H), 7.50-7.43 (m, 3H), 7.30-7.24 (m, 1H), 6.83 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.76 (dt, *J* = 11.1, 2.4 Hz, 1H), 6.71-6.66 (m, 1H), 5.75 (s, 1H), 5.55 (s, 1H), 5.13 (s, 2H), 4.22 (s, 2H), 3.91 (d, *J* = 2.8 Hz, 2H), 3.20 (t, *J* = 2.8 Hz, 1H). Anal. calcd. for $C_{19}H_{18}FNOx(COOH)_2$ (385.39): C, 65.45%; H, 5.23%; N, 3.63%. Found: C, 65.19%; H, 5.09%; N, 3.80%.

Scheme 63



tert-Butyl (2-(3-((3,5-difluorophenoxy)methyl)phenyl)allyl)carbamate (SZV-2640/5) Following **method P1**, but it was used tert-butyl (2-bromoallyl)carbamate, and conventional heating for 16 h at 60 °C, the crude was purified by flash column chromatography using 10% EtOAc/pet ether as eluent to give the title compound (75%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.51 (brs, 1H), 7.42-7.41 (m, 1H), 7.37-7.35 (m, 2H), 6.63 (dd, J = 9.2, 2.0 Hz, 2H), 6.50 (tt, J = 9.2, 2.0 Hz, 1H), 5.41 (d, J = 1.2 Hz, 1H), 5.22 (d, J = 1.2 Hz, 1H), 5.09 (s, 2H), 4.09 (s, 2H), 1.42 (s, 9H).

tert-Butyl (2-(3-((3,5-difluorophenoxy)methyl)phenyl)allyl)(prop-2-yn-1-yl)carbamate (SZV-2640/6) Following **method M2**, the crude was purified by flash column chromatography using 5% EtOAc/pet ether as eluent to give the title compound (37%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.52 (brs, 1H), 7.42-7.34 (m, 3H), 6.62 (dd, J = 9.3, 2.0 Hz, 2H), 6.51 (tt, J = 9.3, 2.0 Hz, 1H), 5.49 (br. d, 1H), 5.25 (s, 1H), 5.09 (s, 2H), 4.43 (s, 2H), 3.92 (br. d, 2H), 2.60 (t, J = 2.5 Hz, 1H), 1.43 (s, 9H).

2-(3-((3,5-Difluorophenoxy)methyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine (SZV-2640/7) Following **method L**, the crude was purified by flash column chromatography using DCM as eluent to give the title compound (57%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.54 (br, 1H), 7.46-7.43 (m, 1H), 7.40-7.37 (m, 2H), 6.63 (dd, J = 9.2, 2.0 Hz, 2H), 6.50 (tt, J = 9.2, 2.0 Hz, 1H), 5.47 (d, J = 1.6 Hz, 1H), 5.30 (d, J = 1.6 Hz, 1H), 5.10 (s, 2H), 3.75 (s, 2H), 3.39 (d, J = 2.8 Hz, 2H), 2.61 (t, J = 2.8 Hz, 1H).

2-(3-((3,5-Difluorophenoxy)methyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-aminium carboxyformate (SZV-2640) Following **method H1**, the title compound was isolated as a white solid (69%). Mp 190.4 – 191.7 °C. ^{1}H NMR (400 MHz, Dimethyl sulfoxide-d_6) δ 7.59 (brs, 1H), 7.50-7.47 (m, 1H), 7.44-7.41 (m, 2H), 6.93 – 6.72 (m, 3H), 5.64 (s, 1H), 5.41 (s, 1H), 5.14 (s, 2H), 3.90 (s, 2H), 3.66 (s, 2H), 3.43 (t, J = 2.6 Hz, 1H). Anal. calcd. for $C_{19}H_{17}NOx(COOH)_2$ (403.38): C, 62.53%; H, 4.75%; N, 3.47%. Found: C, 62.03%; H, 4.78%; N, 3.09%.

Biological examples

The compounds of the invention and some international reference compounds were investigated in MAO A and MAO B enzyme assays as well as in *in vitro* and *in vivo* experiments.

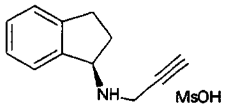
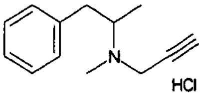
A) Monoamine oxidase B and A enzyme assays

MAO-A and MAO-B enzyme inhibitory activities were determined on brain human recombinant MAO A and MAO-B enzyme and results are summarized in Table 1A (international reference compounds) and Table 1B (examples of compounds of the invention).

Experimental protocol

Human recombinant MAO A and MAO B were purchased in the form of Supersomes (BD Biosciences) expressed in Sf9. The enzymatic activity was measured in a fluorescent coupled reaction. MAO-A and MAO-B oxidize their substrates (5-hydroxytryptamine and phenylethylamine respecitively) to produce hydrogenperoxide which produces the oxidized form of Amplex® UltraRed (invitrogen) that can be readily measured in a fluorimetric plate reader at Ex/Em 540/590 nm. Measurements were conducted in a 384-well format in the final volume of 40 μl. The enzymes were preincubated on ice for 1 hour prior to tests. The drug candidates were incubated 10 minutes at room temperature with the enzyme, and then substrate was added to initialize the reaction at 30 °C. Fluorescence was read at one hour of reaction and corrected with the value read before substrate addition. Dose response curves were measured using at least 7 dilution points with 5-fold dilution steps. Duplicate points were determined for each concentration. IC_{50} values were calculated from the remaining activity, the graphs were fitted using Origin 5.0 software.

Results are given in Tables 1A and 1B, where hMAO and hIC_{50} mean human MAO enzyme, and human IC_{50} (50% inhibition, mole concentration) on the same enzyme, respectively; selectivity of a compound in respect to the MAO B vs MAO A enzyme is expressed by HS values as the ratio of the IC_{50} values).

Number	**Structure**	**hMAO-B hIC_{50} (M)**	**hMAO-A hIC_{50} (M)**	**HS h(A/B)**
Rasagiline mesylate		8.0±2.2 x 10^{-8}	6.3±0.5 x 10^{-6}	**78**
Deprenyl (selegiline)		2.5±1.0 x 10^{-8}	6.9±0.5 x 10^{-6}	**276**

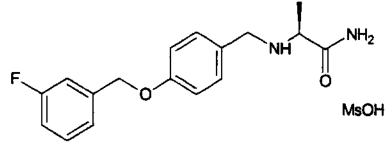
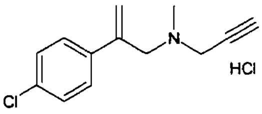
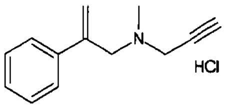
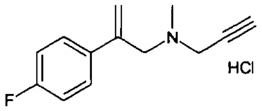
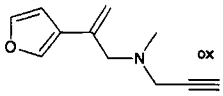
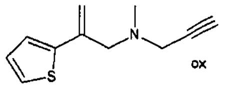
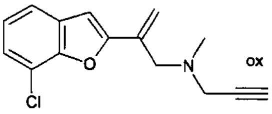
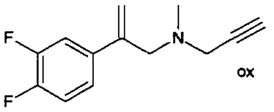
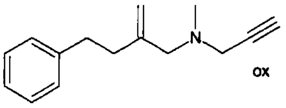
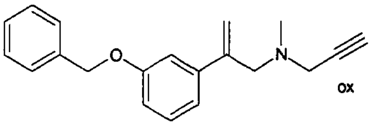
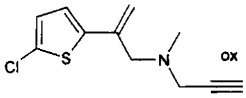
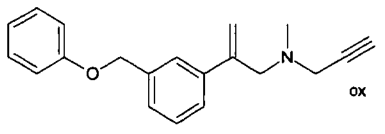
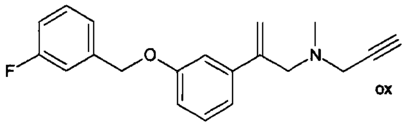
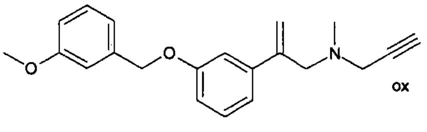
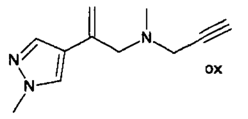
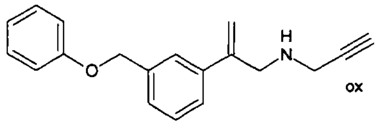
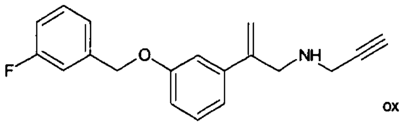
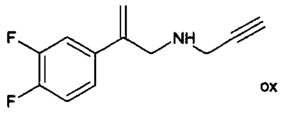
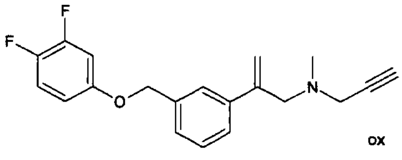
Safinamide mesylate		5.0±1.2 x 10^{-8}	>10^{-4}	**>2000**

Table 1A. MAO inhibitory data of reference compounds of the invention

Number	**Structure**	**hMAO-B hIC$_{50}$ (M)**	**hMAO-A hIC$_{50}$ (M)**	**HS h(A/B)**
SZV-1294*		3.9±0.6 x 10^{-9}	1.2±0.2 x 10^{-7}	**31**
SZV-1902**		6.0±0.5 x 10^{-8}	3.5±0.4 x 10^{-6}	**58**
SZV-2030		3.7±0.3 x 10^{-9}	2.8±0.7 x 10^{-7}	**74**
SZV-2253		7.2±3.1 x 10^{-10}	1.9±0.1 x 10^{-6}	**2638**
SZV-2270***		3.4±0.8 x 10^{-9}	2.5±0.2 x 10^{-6}	**735**
SZV-2348		4.5±0.7 x 10^{-8}	5.4±0.2 x 10^{-8}	**1**
SZV-2358****		2.3±0.3 x 10^{-9}	3.1±0.1 x 10^{-6}	**1347**
SZV-2398		1.4±0.2 x 10^{-7}	3.9±0.7 x 10^{-8}	**0**
SZV-2427		6.0±0.2 x 10^{-9}	2.1±0.1 x 10^{-6}	**350**
SZV-2518		4.6±0.3 x 10^{-9}	1.1±0.0 x 10^{-7}	**23**

Number	Structure	hMAO-B hIC_{50} (M)	hMAO-A hIC_{50} (M)	HS h(A/B)
SZV-2533		$2.0 \pm 0.3 \times 10^{-8}$	$4.0 \pm 0.3 \times 10^{-7}$	**20**
SZV-2541		$5.0 \pm 1.2 \times 10^{-8}$	$1.2 \pm 0.2 \times 10^{-6}$	**24**
SZV-2568		$6.6 \pm 1.7 \times 10^{-9}$	$5.9 \pm 0.2 \times 10^{-7}$	**88**
SZV-2569		$4.5 \pm 0.5 \times 10^{-7}$	$2.6 \pm 0.3 \times 10^{-5}$	**57**
SZV-2578		$6.3 \pm 1.5 \times 10^{-9}$	$2.5 \pm 1.3 \times 10^{-7}$	**40**
SZV-2608		$1.9 \pm 0.2 \times 10^{-9}$	$4.2 \pm 0.5 \times 10^{-6}$	**2211**
SZV-2613		$1.0 \pm 0.0 \times 10^{-7}$	$2.6 \pm 0.1 \times 10^{-6}$	**26**
SZV-2640		$4.9 \pm 0.1 \times 10^{-9}$	$5.6 \pm 0.2 \times 10^{-7}$	**114**

*The corresponding oxalate salt is SZV-2220. **The corresponding oxalate salt is SZV-2221.

***The corresponding hydrogen chloride salt is SZV- 2099. ****The corresponding hydrogen chloride salt is SZV-2591.

Table 1B. MAO inhibitory data of compounds of the invention

B) In vitro and in vivo experiments. neuroprotection study

The putative anti-parkinsonian compounds were tested in four different experimental models of Parkinson's disease, induced by three different toxins (rotenone, MPTP, 6-OHDA) in two different rodent species (rat and mouse) and a catecholaminergic cell culture (PC12 cells). The protective effects of the compounds were studied

i) *in vitro* via oxidative stress induced pathological dopamine release in the rat striatum after rotenone treatment

ii) *in vivo* against MPTP-induced nigrostriatal damage in mice using two different experimental protocols

iii) *in vitro* against 6-OHDA induced cell death in PC12 cells.

Example 1. Effect on rotenone-induced mitochondrial dysfunction and subsequent pathological dopamine release in the in vitro rodent striatum.

Coincidence of mitochondrial dysfunction and oxidative stress and the consequent dysregulation of neuronal DA pools are believed to play a determinant role in the development of neurodegeneration (Fahn S et al, NeuroRx, 2004, 1, 139-154) and recent studies pointed to the etiopathogenetic role of environmental toxins causing mitochondrial dysfunction in PD. Such an environmental toxin, the irreversible complex I inhibitor rotenone was shown to reproduce the major anatomical, neurochemical and behavioral features of PD in rats (Betarbet R et al, Nat. Neurosci., 2000, 3, 1301-1306; Sherer TB et al, Exp. Neurol., 2003, 179, 9-16; Milusheva E et al, Free Radic. Biol. Med., 2005, 39, 133-142). These include the degeneration of dopaminergic neurons in the substantia nigra pars compacta and their terminals projecting to the striatum, progressive depletion of striatal dopamine content, motor symptoms, such as hypokinesia and rigidity. In addition uniquely among toxin-induced PD models, the rotenone model reproduces systemic complex I deficit, and the deposition of Lewy body-like cytoplasmic inclusions in *substantia nigra* neurons containing ubiquitin and α-synuclein (Betarbet R et al, Nat. Neurosci., 2000, 3, 1301-1306).Inhibition of mitochondrial complex I by rotenone leads to energy depletion and serves as a source of reactive species, causing oxidative damage at multiple target sites (lipid peroxidation, protein and DNA damage, etc.). As a result, DA is redistributed from vesicles and accumulates in the cytosol, where it provides an additional source of highly reactive free radicals due to its breakdown by MAO or auto-oxidation. Thus, DA might be oxidized to dopamine quinone (DAQ) (Graham DG et al, Mol. Pharmacol., 1978, 14, 633-643). DAQ can be adducted by cysteine, and thereby involved in aberrant metabolism and ubiquitination pathways, Lewy body's formation or mediate the synthesis of hydroxyl radical and oxyradical species (Sulzer D et al, Neurotox. Res., 2000, 1, 181-195). In addition, DAQ stabilizes protofibrils resulting from synuclein aggregation (Conway KA et al, Science, 2001, 294, 1346-1349) and inhibits the DA transporter (Whitehead RE et al, J. Neurochem., 2001, 76, 1242-1251). In striatal slices of rats, undergone *in vivo* subchronic rotenone pretreatment, DAQ is generated from released DA, but only under conditions of coincident oxidative stress (Milusheva E et al, Free Radic. Biol. Med., 2005, 39, 133-142; Baranyi M et al, J. Chromatogr. A., 2006, 1120, 13-20). Moreover, rotenone-induced mitochondrial dysfunction and oxidative stress had supra-additive impact on the pathological, presumably cytoplasmic release of DA (Milusheva E et al, Free Radic. Biol. Med., 2005, 39, 133-142; Baranyi M et al, J. Chromatogr. A., 2006, 1120, 13-20). More recently, it was confirmed that the same neurochemical alterations could be reproduced by *in vitro* pretreatment of striatal slices with rotenone and thereby the weak reproducibility of the *in vivo* rotenone model could also be overcome (Milusheva E et al, J. Neurochem., 2008, 105, 360-368; Milusheva E et al, Neuropharmacology, 2010, 58, 816-825). Therefore the rotenone-induced *in vitro* and *in vivo* PD models, although laborious, represents higher degree of construct validity than other toxin-induced PD models and is regarded well accepted models of PD, suitable for testing therapeutic interventions aimed at counteracting PD-related cell death (Cicchetti F et al, Trends Pharmacol. Sci., 2009, 30, 475-483; Blandini F et al, FEBS J., 2012, 279, 1156-1166).

Experimental protocol

The [^{3}H]dopamine ([^{3}H]DA) release experiments were performed as described in (Milusheva E et al, J. Neurochem., 2008, 105, 360-368; Milusheva E et al, Neuropharmacology, 2010, 58, 816-825): Male Wistar rats (180-220 g) were decapitated and the brain was quickly removed into ice-cold Krebs' solution. Then the striatum was dissected out and sliced into 400 µm-thick sections with a McIlwain tissue chopper.

Striatum slices then were pretreated with rotenone (10 µM) for 60 min, and subsequently they were incubated in 1 ml of Krebs' solution containing 5 µCi [^{3}H]DA for 45 min continuously gassed with a mixture of 95% O_2 and 5% CO_2 at 37 °C.

After incubation the slices were transferred to tissue chambers and perfused continuously with modified Krebs solution at a rate of 0.5 ml/min. After a 60-min pre-perfusion 3-min samples were collected and assayed for [^{3}H]DA. Oxidative stress was mimicked by addition of H_2O_2 (250 µM) to the Krebs solution starting at the 9th min of collection. Compounds were added to the perfusion fluid 18 min before H_2O_2 application.

The release of tritium was calculated in Bq/g and expressed as percentage of the amount of radioactivity in the tissue at the time of sample collection (fractional release, FR %). The effect of drugs on H_2O_2 - evoked release of [^{3}H]DA was expressed as the net release evoked by treatment and was calculated by the area-under-the-curve (AUC) method, i.e. subtracting the resting release calculated from the prestimulation period, from the release measured during H_2O_2.

Results

Whereas a switch to an identical medium does not elicit change in [^{3}H]DA efflux (CTRL), as expected, oxidative stress, simulated by H_2O_2 (250 µM) perfusion elicited a remarkable increase in the release of [^{3}H]DA (Figures 1, 2 and Table 2). In line with literature data (Milusheva E et al, Neuropharmacology, 2010, 58, 816-825), selective MAO-B inhibitors, like rasagiline (10 nM) did not decrease oxidative stress induced pathological [^{3}H]DA release. **Surprisingly,** however, **SZV-2220, SZV-1902, SZV-2358, SZV-2541, SZV-2270, SZV-2533, SZV-2578, and SZV-2591 had a**

profound inhibitory effect on the oxidative stress induced pathological dopamine release in rat striatum slices in nanomolar concentrations (Figures 1 and 2, Table 2), which illustrates the **qualitatively superior actions of the compounds over rasagiline**.

The above conditions, i.e., the simultaneous exposure of striatal dopaminergic nerve terminals to mitochondrial dysfunction by the complex I inhibitor rotenone and subsequent oxidative stress, simulated by H_2O_2 represent core pathological features of PD, which lead to pathological dopamine release in the degenerating nerve terminals. In contrast to normal, physiological dopamine release, this pathological dopamine release serves as further source of toxic dopamine metabolites, such as dopamine (DAQ) and thereby leads to further generation of free radicals and oxidative damage of the neurons (Milusheva E et al, Free Radic. Biol. Med., 2005, 39, 133-142; Baranyi M et al, J. Chromatogr. A., 2006, 1120, 13-20). Therefore, a better protective effect could be expected in PD from those compounds, which are able to inhibit this pathological, abnormal dopamine release and subsequent cellular pathways. Consequently, only compounds of the invention, but not rasagiline have been proved to be neuroprotective in this experimental model of Parkinson disease.

Treatment	**[^{3}H]dopamine (%)**
Control	-2.72 ± 0.86
H_2O_2	$104.5 \pm 10.05^{+++}$
H_2O_2 + rasagiline 10 nM	$142.16 \pm 9.49^{+++}$
H_2O_2 + SZV-2220 1 nM	72.99 ± 15.23
10 nM	$36.09 \pm 6.83^{***}$
100 nM	$33.26 \pm 5.10^{***}$
H_2O_2 + SZV-1902 10 nM	$45.51 \pm 0.648^{***}$
100 nM	$46.27 \pm 4.37^{**}$
H_2O_2 + SZV-2358 10 nM	$54.89 \pm 2.20^{*}$
100 nM	$45.94 \pm 13.51^{***}$
H_2O_2 + SZV-2541 10 nM	$41.47 \pm 4.24^{***}$
H_2O_2 + SZV-2220 100 nM	$39.46 \pm 5.53^{***}$
H_2O_2 + SZV-2533 100 nM	$32.77 \pm 4.42^{***}$
H_2O_2 + SZV-2578 100 nM	$50.44 \pm 4.78^{***}$
H_2O_2 + SZV-2591 100 nM	$41.67 \pm 8.32^{***}$

Table 2. Effect of test compounds (10 nM) on oxidative stress induced pathological dopamine release in rat striatum slices after rotenone (10 μM) treatment.

In Figures 1, 2 and Table 2, [^{3}H]dopamine release is expressed as fractional release (%) i.e. as percentage of the actual tritium content of the slices. When the effects of drugs were compared, the net release evoked by H_2O_2, calculated by the area-under-the-curve method was taken into account. N=4-8 independent experiment/group. Symbols represent significant changes from control slices ($^{+++}$P<0.001), and H_2O_2 treated slices (*P<0.05, **P<0.01, ***P<0.001), respectively. Statistical analysis: one-way ANOVA followed by the Tukey test. Control slices were perfused with Krebs' solution without H_2O_2.

Example 2. The differential effect of compounds on pathological and physiological dopamine release

Oxidative stress plays a central role in the pathogenesis of not only Parkinson's disease, but also other neurodegenerative diseases, such as ischemia-reperfusion injury (Hall ED et al, J. Neurosci. Res., 1993, 34, 107-112). Whereas the core pathological feature of ischemia is the lack of oxygen and glucose, which compromise energy-dependent neuronal functions, oxidative free radicals are generated from the monoamine transmitters in the reperfusion phase, such as dopamine and noradrenaline by autooxidation and by the action of monoamino-oxidases (Cadet JL et al, Neurochem. Int., 1998, 32, 117-131). Moreover, ischemia also leads to excess, pathological release of monoamines by the insufficient supply of Na^+/K^+ pump, subsequent intracellular Na^+ accumulation and sodium dependent reversal of monoamine transporters (Milusheva E et al, J. Neurochem., 1992, 59, 946-952; Milusheva E et al, Neuroscience, 2003, 120, 771-781).

Opposite from physiological neuronal activity-evoked transmitter release, this ischemia-induced transmitter release is pathological, similar to oxidative stress-induced dopamine release. Example 2 shows the differential effect of SZV-1902 on pathological, ischemia-like conditions induced and physiological, electrical stimulation-induced [^{3}H]DA release in rat striatum slices.

Experimental protocol

Rat striatum slices were prepared and incubated with [^{3}H]dopamine, as described above, and then superfused with Krebs solution. In the first set of experiments, slices were subjected to ischemia-like conditions, i.e. oxygen and glucose was withdrawn from the superfusing medium. Test compounds or their vehicle (CTRL) were administered 15 min before the start of the ischemic-like conditions. In the second set of experiments, slices were subjected to electrical field stimulation (EFS1, EFSS2) twice, during the 3rd and 13th sample of the collection period, using platinum ring electrodes attached to the top and bottom of tissue chambers and a Grass S88 stimulator, with the following parameters: 25 V, 1 msec, 2 Hz, 240 shocks and drugs were administered 18 min before the second stimulation period (EFS2) and onwards. Analysis of radioactivity and processing the data was as described above.

Results

As expected ischemia-like conditions elicited a massive release of [^{3}H]DA to the extracellular fluid (Figure 3A). Compound SZV-1902 (10 nM) significantly decreased this pathological [^{3}H]DA efflux (evoked release: 24.43±3.56%, SZV-1902+ischemia: 10.84±1.47%, n=8, P<0.01).

Effect of test compounds (10 nM) on ischemic-like conditions induced pathological dopamine release in rat striatum slices is shown on Figure 3. [^{3}H]dopamine release is expressed as fractional release (%) i.e. as percentage of the actual tritium content of the slices. N=4-8 independent experiment/group. Test compounds or their vehicle (CTRL) were administered (Figure 3 A) 15 min before the start of the ischemic-like conditions (Figure 3 B) 18 min before the second stimulation period (EFS2) and onwards.

However, compound SZV-1902 was able to preserve physiological dopamine release, which is important feature required from putative neuroprotective drugs. There was detected no significant change in the amount of [^{3}H]DA released by EFS after application of compound SZV-1902 (Figure 3B).

Example 3. The protective effect of compounds in an *in vivo* acute MPTP model

Example 3 illustrates the results obtained in an *in vivo* animal model of PD. This model is used widely for preclinical *in vivo* assessment of anti-parkinsonian effects, due to its high reproducibility and disease-related pathological features (Mori A et al, Neurosci. Res., 2005, 51, 265-274; Melrose HL et al, Exp. Brain Res., 2006, 173, 196-204; Hracskó Z et al, Mol. Neurodegener., 2011, 6, 28.; Blandini F et al, FEBS J., 2012, 279, 1156-1166). In contrast to rotenone, which is a highly lipophilic and well diffusible and penetrating toxin, MPTP is first taken up by astrocytes and converted there to the toxic metabolite MPP+ by the MAO enzyme.

MPP+ is then released and selectively taken up to the dopaminergic nerve terminals by the dopamine transporters and causes the oxidative damage of dopaminergic neurons in the aforementioned way (Cicchetti F et al, Trends Pharmacol. Sci., 2009, 30, 475-483). The MPTP PD model is routinely used on mice, and occasionally on primates. The relevance of this model to human PD is exemplified by the accidental discovery of the “frozen addict syndrome”, a drug-induced PD syndrome observed in meperidine addicts, after consumption of meperidine contaminated with MPTP (Langston JW et al, Science, 1983, 219, 979-980).

In this *in vivo* model the compounds of the invention possess significant protective actions. It is also remarkable that their effect is well superior over rasagiline both quantitatively and qualitatively.

Experimental protocol

In this set of experiments, the most commonly used acute MPTP protocol was used, established by numerous previous studies (cf. Jackson-Lewis V et al, Nat. Protoc., 2007, 2, 141-151). Briefly, adult (2-3 month old, 30 g) C57/Bl6 mice were used. MPTP was applied in a 4x20 mg/kg i.p.

dose 2h apart, and the survival of the animals and the biogenic amine content of the striatum analyzed 72h after the last MPTP dose by HPLC-EC analysis. The motor function was evaluated 2h and 1 day after the last MPTP treatment by the open field and rotarod tests. Test compounds in these experiments were applied in a single, 0.1-20 mg/kg dose i.p. 18h prior to the MPTP treatment, or by *per os* using a 20 mg/kg dose using a gavage. In all experiments animals were daily monitored for general health and overt side effects. In all experiments rasagiline was used as a reference compound. Results are given below (Table 3, Figures 4 and 5).

HPLC analysis

The tissue slices were immediately frozen in liquid nitrogen after termination of the experiment. The weighed frozen tissue was homogenized in an appropriate volume of ice-cold 0.1 M PCA that contained theophylline (as an internal standard) at 10 nmol/ml concentration and 0.5 mM sodium metabisulphite (antioxidant for biogenic amines). The suspension was centrifuged at 300 g for 10 min at 0–4 °C. The perchloric anion was precipitated by addition of 10 μl of 1 M KOH to 190 μl of the supernatant. The precipitate was then removed by centrifugation. The supernatant was kept at -20 °C until analysis. The pellet was saved for protein measurement according to (Lowry et al, J. Biol. Chem., 1951, 193, 265-275). For the analysis 545-μl sample volumes were diluted with 5 μl of 10-5 mol/l dihydroxybenzyl amine as an internal standard and 500 μl were injected. A liquid–liquid two-dimensional reversed-phase and ion pair-reversed-phase chromatographic separation was applied, as described earlier (Baranyi M et al, J. Chromatogr. A., 2006, 1120, 13-20). Briefly, a Gilson liquid chromatographic system with 715-operation software (Gilson Medical Electronics Inc., Middletown, and WI USA) was used. For the enrichment a "trap-column" (15-25 μm Nucleosil C-18 (20 × 4.0) was inserted into a loop position. The separation of neurotransmitters was performed on a 3 μm Discovery C18 HS F5 (150 × 4.0 mm) analytical column. The separation of catecholamines was accomplished with ion pair-reversed-phase buffer at constant flow rate of 1.0 ml/min. The effluents were monitored by UV, electrochemical and radiochemical detectors. The detectors were connected in a cascade line. Tissue contents of DA, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanilic acid (HVA) were expressed in pmol/mg protein.

Behavioral analyses

Open field test

The open field test is the most commonly used method to measure alterations of behavioral activity after MPTP treatment (Sedelis M et al, Behav. Brain Res., 2001, 125, 109-125).

In the example shown C57/Bl6 mice were placed 2 h after the last MPTP injection for 30 min to the open field arena, following a protocol used for the test of putative antiparkinsonian drugs on locomotion (Hu SC et al, J. Pharmacol. Exp. Ther., 1991, 259, 1379-1387; Shiozaki S et al, Psychopharmacology, 1999, 147, 90-95). Experiments were performed in the light phase under dimmed lights (~3 lux). At least 3 days before the tests animals were transferred to the experimental room. Each animal was placed in the center of a nontransparent plexiglas arena (dimensions: 40x40x40 cm) for a habituation period of 30 minutes, and the locomotor activity of the animals was recorded for 30 minutes using a video camera positioned above the arena. To measure locomotor activity video files were analyzed offline by converting them into single frames (25 frames/second) and a custom-written motion tracking algorithm was applied within the image processing software ImageJ. The total distance in meters was provided for the 30 minutes of the experiment.

Rotarod test

Motor coordination was tested on the IITC (Woodland Hills, CA, USA) Rotarod Apparatus, which enables the simultaneous examination of five mice or rats. Because mice with striatal dopamine depletion show only mild or no deficit on the typical accelerating rotarod test, the modified protocol of (Shiotsuki H et al, J. Neurosci. Methods, 2010, 189, 180-185) was followed. In this version mice are tested on a larger drum with fixed speed to obtain a steep learning curve and therefore this test is more selective to motor skill learning rather than maximal gait performance. The apparatus consists of five compartments separated by 8 cm diameter rotating rod, which is equipped 25 cm above the base of the apparatus. Motor coordination of animals was tested for 180 seconds with a fix speed of 10 rpm. Mice were acclimatized to the rotarod in two trials (180 sec) per days for 2 consecutive days before the start of the experiment. On the test day 1h before drug administration baseline latencies to fall were determined. Then the animals were treated with sterile saline or with test compounds, and then with MPTP as described above. 6 and 24 h after the last MPTP treatment the falling latency was measured again in the 180 sec test period. The latency time to fall off the rod was expressed in seconds.

Results

MPTP treatment on mice pretreated with saline, elicited a progressive and high depletion of endogenous dopamine content in the striatum, which was accompanied with a substantial increase in the mortality of the animals, showing the toxicity of MPTP (Table 3, Figures 4 and 5).

Treatment	**dopamine content (pmol/mg protein)**	**Survival (%)**
Saline	602.05±31.86	100%
MPTP	$88.56 \pm 24.89^{+++}$	$50\%^{+++}$
MPTP + rasagiline 10 mg/kg	$319.25 \pm 67.05^{*\#}$	$100\%^{**}$
MPTP + SZV-2220 10 mg/kg	$527.17 \pm 37.02^{***}$	$100\%^{**}$
MPTP + SZV-1902 10 mg/kg	$385.64 \pm 35.99^{**}$	$100\%^{**}$

MPTP + SZV-2358 10 mg/kg	$425.97\pm31.95^{***}$	$100\%^{**}$
MPTP + SZV-2541 10 mg/kg	$477.32\pm22.29^{***}$	$100\%^{**}$
MPTP + rasagiline 20 mg/kg	$363.91\pm21.90^{**}$	$100\%^{**}$
MPTP + SZV-1902 20 mg/kg per os	$1021.27\pm87.23^{+++***\#\#\#}$	$100\%^{**}$

Table 3. Effect of compounds of the invention (10 mg/kg i.p.) on endogenous dopamine content in the striatum and on the survival of animals after *in vivo* MPTP treatment.

In Figures 4 and 5, and Table 3, dopamine content is expressed as pmol/mg protein. Symbols represent significant changes from saline treated ($^{+++}$P<0.001), MPTP treated (*P<0.05, **P<0.01, ***P<0.001) and rasagiline (20 mg/kg) treated animals, ($^{\#}$P<0.05, $^{\#\#\#}$P<0.001), respectively. Statistical analysis: one-way ANOVA followed by the Tukey test (dopamine content) and log rank test (survival). Number of independent experiments: 5-8/group.

The deteriorated motor function of the MPTP-treated animals was also substantially restored by compounds SZV-2220 and SZV-1902. The motor performance of the animals was monitored by two widely used tests, the open field and the rotarod test. Whereas the former determines basal locomotor activity, the latter is indicative for motor coordination and both tests are adjusted to the evaluation of motor impairment in parkinsonian animal models (Sedelis M et al, Behav. Brain Res., 2001, 125, 109-125; Shiotsuki H et al, J. Neurosci. Methods, 2010, 189, 180-185).

As expected, 2 hrs after the last MPTP treatment the basal locomotor activity of mice was minimal, i.e. they displayed akinesia. In contrast, those mice, which were pretreated with SZV-1902 and SZV-2220 (10 mg/kg i.p. each) showed a profound increase in basal locomotor activity even at this early time point (Table 4. Figure 6A).

In the rotarod test, mice treated with MPTP displayed a time-dependent decrease in the motor performance, when compared to values measured before MPTP treatment, according to literature data (Shiotsuki H et al, J. Neurosci. Methods, 2010, 189, 180-185). This progressive decline in performance was almost completely prevented by both compounds SZV-1902 and compounds SZV-2220 and was maintained up to 24 h after drug injection (Table 5, Figure 6B)

Thus MPTP treatment elicited an 85% loss of endogenous dopamine and 50% decrease in the survival of the animals. The motor function of the surviving animals was seriously compromised, quantified in the open field and rotarod tests, according to what is described in the literature (Table 4, Figure 6).

Treatment	**Distance traveled (m)**
Saline	67.23 ± 8.04
MPTP	$3.48\pm3.30^{+++}$

MPTP + rasagiline	62.22±6.31***
MPTP + SZV-2220	71.29±5.43***
MPTP + SZV-1902	77.97±6.87***

Table 4. Effect of compounds of the invention (10 mg/kg i.p.) on the basal locomotor activity, measured in the open field test. In the open field test (Figure 6A and Table 4), locomotion is expressed as the distance traveled during the whole 30 min test period. Symbols represent significant changes from saline ($^{+++}$P<0.001) and MPTP treated (***P<0.001) animals, respectively. Statistical analysis: one-way ANOVA followed by the Tukey test.

Treatment	**Falling latency (sec)**
Saline pretreatment value	159.08±13.49
Saline 6 h	124.33±13.00
Saline 24 h	131.5±18.82
MPTP pretreatment value	139.50±20.76
MPTP 6 h	47.63±21.38**
MPTP 24 h	16.25±8.20**
MPTP + rasagiline pretreatment value	164.57±10.02
MPTP + rasagiline 6 h	161.14±10.51
MPTP + rasagiline 24 h	149.57±12.71
MPTP + SZV-2220 pretreatment value	156.50±10.87
MPTP + SZV-2220 6 h	129.67±21.80
MPTP + SZV-2220 24 h	104.67±31.10
MPTP + SZV-1902 pretreatment value	147.86±11.84
MPTP + SZV-1902 6 h	119.36±24.80
MPTP + SZV-1902 24 h	129.93±25.01

Table 5. Effect of compounds of the invention (10 mg/kg i.p.) on the basal locomotor activity, measured in the rotarod test.

In the rotarod test (Figure 6B and Table 5), symbols represent significant changes from respective pretreatment values (**P<0.01). Statistical analysis: one-way ANOVA followed by the Dunnett test. The time elapsed until the falling of the mice was expressed in sec.

In contrast, mice pretreated with compounds of the invention, such as compounds SZV-2220, SZV-1902, SZV-2358, and SZV-2541, were in overall good health conditions after MPTP treatment, and none of the compounds produced any obvious untoward behavioral alteration at the used dose levels.

Moreover, the test compounds were able to significantly protect *in vivo* against the effect of MPTP treatment on the depletion of striatal dopamine content and the i.e. against hallmark feature of PD and also completely prevented premature death of animals during the course of the experiment. The majority of the test compounds elicited a more remarkable elevation of endogenous dopamine level than rasagiline did.

The data indicate **a quantitative superiority of the compounds of the invention over rasagiline.**

The effect of SZV-1902 was dose-dependent (Figure 7), it was also active using p.o. application (20 mg/kg), and was able to completely restore the dopamine content of the striatum above the level of mice treated only with saline but not with MPTP (Table 3, Figure 4). At this dose SZV-1902 was significantly more effective than rasagiline ($P<0.001$). All test compounds elicited 100% survival in contrast to mice, which were treated with MPTP only.

Surprisingly, SZV-2220, SZV-2358 and SZV-2533 had a preferable effect on the striatal level of dopamine metabolites after *in vivo* MPTP treatment, which was qualitatively superior over rasagiline: whereas the above three compounds preserved DOPAC and HVA levels, rasagiline did not (Table 6, Figure 8). In line with literature data (Ugrumov MV et al, Neuroscience, 2011, 181, 175-188), MPTP treatment caused a change in the level of dopamine metabolites, i.e. it decreased the level of DOPAC and HVA. Rasagiline, however, was not able to restore the level of metabolites in the presence of MPTP, but further decreased the level of DOPAC and HVA, which was probably due to its inhibition by both MAO-A and MAO-B at this dose (Kupsch A et al, J. Neural Transm., 2001, 108, 985-1009).

In contrast, compounds of the invention, in particular SZV-2220 and SZV-2533 were able to preserve both DOPAC and HVA levels (Table 6, Figure 8 A and B respectively).

Treatment	**DOPAC (pmol/mg protein)**	**HVA (pmol/mg protein)**
Saline	36.31±4.44	129.07±40.05
MPTP	21.36± 4.83	35.83±7.03^{+}
MPTP + rasagiline	6.95±2.39	11.91±5.59**
MPTP +SZV-2220	59.79±12.47$^{***\#\#\#}$	141.26±13.34$^{\#\#\#}$
MPTP +SZV-2541	17.01±2.69	70.89±9.45
MPTP +SZV-2533	82.41±10.95$^{***\#\#\#}$	60.86±9.66

Table 6. Effect compounds of the invention (10 mg/kg i.p.) on endogenous dopamine metabolite (DOPAC, HVA) levels in mouse striatum 72 h after after *in vivo* MPTP treatment.

In Figure 8 and Table 6, metabolite levels are expressed as pmol/mg protein. Symbols represent significant changes from saline treated ($^{+}P<0.05$), MPTP treated ($^{*}P<0.01$, $^{***}P<0.001$) and rasagiline (20 mg/kg) treated animals, ($^{\#}P<0.05$, $^{\#\#\#}P<0.001$), respectively. Statistical analysis: one-way ANOVA followed by the Tukey test. Number of independent experiments: 7-12/group.

Example 4. Duration of action and metabolic activity of SZV-1902 in the in vivo MPTP model

Example 4 illustrates the duration of action of compound SZV-1902.

Experimental protocol

In these experiments MPTP was applied in a 4x20 mg/kg i.p. dose 2h apart to adult C57/Bl6 mice and the survival of the animals and the biogenic amine content of the striatum analyzed 72h after the last MPTP dose by HPLC-EC analysis as described above. Test compound in these experiments were applied in a single, 10 mg/kg dose i.p. 2 h, 18 h or 42 h before the first dose of MPTP.

Results

A significant protective effect against dopamine depletion elicited by MPTP was already detected 1 h after a single i.p. injection of SZV-1902 (Table 6, Figure 8). The peak of the effect of SZV-1902 was obtained 18 h after the application. The effect of SZV-1902 was then declined; however a significant protection was still observed 42 h after SZV-1902 detection (Table 7, Figure 9). These data may indicate an irreversible inhibition of the MAO-B enzyme by SZV-1902; in case of rasagiline, which is also an irreversible inhibitor of the MAO-B enzyme, it was observed a similar duration of action. Therefore, a long duration of action can be expected from the compounds of the invention and it is irrespective from their potential metabolism in the liver.

Treatment	**dopamine content (pmol/mg protein)**	**Survival (%)**
Saline	602.05±31,86	100%
MPTP	88.56±24,89	50%
SZV-1902 1 h	205.76±13.98	100%
SZV-1902 18 h	385.63±35.99	100%
SZV-1902 42 h	183.82±35.53	100%
rasagiline 18 h	319.25±67.05	100%
rasagiline 42 h	114.79±4.20	100%

Table 7. The duration of action of SZV-1902 (10 mg/kg) i.p. and the effect on endogenous dopamine content in the striatum and on the survival of animals after *in vivo* MPTP treatment.

In above experiments (Figure 9 and Table 7) test compounds were added 1h, 18h or 42h before the first dose of MPTP, respectively, as shown on the horizontal axis. Dopamine content is expressed as pmol/mg protein. Number of independent experiments: 5-8/group.

Example 5. In vivo antiapoptotic effect of compounds SZV-1902 and SZV-2220 in a subacute MPTP model

The acute MPTP model used in the example 4 represents a fast and reliable experimental method to elicit non-apoptotic degeneration of the nigrostriatal dopaminergic pathway affected in PD. However, the progress of the neurodegeneration human PD patients is initially slow and gradual and take place in both apoptotic and non-apoptotic way. Moreover, in MPTP-induced rodent PD models, MPTP is converted to the toxic metabolite MPP^+ by the MAO-B enzyme therefore the protective effect of the compounds could be simply due to their potent MAO-B inhibitory property. However, as example 5 shows, this is not the case.

To clarify this issue, two test compounds SZV-1902 and SZV-2220 were examined in another rodent model resulting in a prolonged, apoptotic degeneration of *substantia nigra pars compacta* (Snc) neurons lasting about 3 weeks after a short course of daily MPTP administration.

The model, called **Tatton-Kish model** (Tatton NA et al, Neuroscience, 1997, 77, 1037-1048); Jackson-Lewis V et al, Nat. Protoc., 2007, 2, 141-151), has an additional advantage, namely a protective effect that is independent from the disruption of MPTP uptake and metabolism (as a consequence of MAO-B inhibition) could also be revealed.

Experimental protocol

Mice are treated with MPTP in a daily 30 mg/kg i.p. dose for 5 days and the test compounds are delivered for 21 days only after then, when the injected MPTP is already converted to MPP^+ and taken up by the dopaminergic nerve terminals (Jackson-Lewis V et al, Nat. Protoc., 2007, 2, 141-151;

De Jesús-Cortés H et al, Proc. Natl. Acad. Sci. USA., 2012, 109, 17010-17015).

In contrast to the acute MPTP model, using this protocol, dopaminergic neurons degenerate in a delayed, apoptotic manner (De Jesús-Cortés H et al, Proc. Natl. Acad. Sci. USA., 2012, 109, 17010-17015). After the experiments, the endogenous dopamine content of the striatum was analyzed HPLC method as described above. In addition, neurodegeneration of the striatal nerve terminals were also analyzed histologically.

Histological analysis

Briefly, control, MPTP treated as well as MPTP + rasagiline, MPTP + SZV-1902 and MPTP + SZV-2220 treated C57/Bl6 mice were decapitated after a short ether stress and the brain was quickly removed. The cortex were carefully taken off and one of each pair striatum was immersed in 4% paraformaldehyde, 0.5% glutaraldehyde, and 15% saturated picric acid in 0.1 M phosphate buffer (PB), pH 7.4, for 6 h. The fixative was changed every half hour then the tissue block was washed in 0.1 M PB overnight at 4 °C. Forty-micrometer sections were cut by vibratome (Leica) in the same buffer. Parallel striatum sections were stained with hematoxylin-eosin, dehydrated in xylene, and mounted in Canada balsam. Virtual slides were made with Panoramic 250 scanner (3DHISTECH, Budapest, Hungary). Pictures were taken at five representative areas in each of samples at 20x–40x magnifications by means of Panoramic Viewer 1.15.2 software provided by 3DHISTECH, Budapest, Hungary. Nuclei were scored and then statistically analyzed using Prism-3 software (version 3.00, Graph Pad, San Diego, CA): one-way ANOVA, with Tukey's post-test was used. Differences with p values of 0.05 or less are considered significant, *P<0.05, **P<0.001, ***P<0.0001.

Results

Application of MPTP treatment using this method resulted in an approx. 60% reduction of endogenous dopamine content in the striatum, when compared to saline treatment, which is equivalent to literature data (Table 8, Figure 10). SZV-1902, but not the reference compound rasagiline (10 mg/kg/day i.p. each, for 21 days), significantly restored the endogenous dopamine content. These findings directly implicate that compound SZV-1902 has, in addition to MAO-B inhibition, another neuroprotective effect. **Therefore, it fulfills the criteria of a 'multitarget anti-PD' compound.**

Treatment	**dopamine content (pmol/mg protein)**
Saline	616.62±30.27
MPTP	$258.13 \pm 12.94^{+++}$
SZV-1902	$410.03 \pm 21.96^{***}$
SZV-2220	208.05±22.83
rasagiline	$297.61 \pm 33.95^{\#}$

Table 8. The effect of SZV-1902, SZV-2220 and rasagiline (10 mg/kg i.p for 21 days each) on MPTP depleted endogenous dopamine content in the mice striatum using the Tatton-Kish model.

In Figure 10 and Table 8, dopamine content is expressed as pmol/mg protein. Symbols represent significant changes from saline treated (${}^{+++}$P<0.001), MPTP treated (***P<0.001) and rasagiline treated animals, (${}^{\#}$P<0.05), respectively. Statistical analysis: one-way ANOVA followed by the Tukey test. Number of independent experiments: 8-12/group.

The histological analyses confirmed the above findings. The classical hematoxilin-eosin staining, the primary diagnostic technique in the histopathology, was used to reveal the morphologic changes in the structure of striatum due to the different treatments. In a typical, properly fixed and well conserved tissue, nuclei are stained blue-purple and show intranuclear details, while the cytoplasm, extracellular matrix and nucleoli are stained by eosin and show varying degrees of pink.

Hematoxylin-eosin staining on striatal sections of mice undergone subacute MPTP treatment according to the Tatton-Kish model as shown in Figure 11 A-E.

(A) The control tissue show typical staining and round shape morphology of nuclei (black arrow). Damaged structure of striatal section are shown in case of MPTP treatment on Figure 11 B. Similar morphology and nuclear staining can be observed in rasagiline (Figure 11 C), SZV-1902 (Figure 11 D) and SZV-2220 (Figure 11 E) treated mouse striatal sections. Among healthy, typically stained nuclei, white arrowhead shows a damaged one. Its shape is not spherical, nucleoli cannot be distinguished. This type of staining is abundantly found in C-E pictures and only few in control sections. Figure 11 F depicts statistical analysis of nuclei number in the different sections. Nuclei were counted in five-five parallel sections, one-way ANOVA, with Tukey's post-test was used. $^{*}P<0.05$, $^{***}P<0.0001$. Bars: 50 µmeter

The representative pictures were taken at 40X original magnification (Figure 11A-E). The difference among the appearance of striatal sections originated from control, rasagiline+MPTP, SZV-1902 +MPTP, SZV-2220+MPTP and MPTP treated mouse brain is obvious.

In case of MPTP treatment the tissue is highly damaged, it is full with defects, holes and, compared with the control section, only few healthy, impeccable nuclei can be seen. On the contrary, there are no defects in the sections derived from control, SZV-1902 +MPTP and SZV-2220+MPTP treated mouse brain. Counting of nuclei on the same area of the different sections and statistical analysis resulted significant difference between the number of nuclei found in control and MPTP sections and between MPTP and SZV-1902, SZV-2220 and rasagiline sections (Figure 11F).

In line with the DA content results, the highest score was obtained in case of SZV-1902, which was nearly equal to control. Electron microscopic investigation revealed more details about the effect of the different treatments on striatal structure (Figure 12). In control section, nuclei of the nerve cells are typically light and spherical shaped (one of them is labeled with "N"). Due to MPTP treatment, many cells are perished (stars) and activated macrophages (white arrow) are taken them up. Presence of higher number of lymphocytes (black arrows) was typical in the striatal structure of SZV-1902 and SZV-2220 treated mice. Rarely, but dead nerve cells can also be found (rasagiline, star) as severely damaged capillaries (SZV-1902, arrow) or dying nerve cells with microglia or lymphocyte in their vicinity (SZV-2220, arrow).

Example 6. Inhibition of 6-OHDA induced cell death in vitro

Although cell-based cell survival assays have limited predictive value for clinical neuroprotection, they are relatively simplified systems, and therefore widely used for *in vitro* high throughput screening of potential anti-PD drugs (Tischler AS et al, Ann. NY Acad. Sci., 2002, 971, 366-370); Bar-Am O et al, J. Neurochem., 2007, 103, 500-508).

In this example, PC12 cells are chosen, as they are catecholaminergic in origin, similar to dopaminergic neurons, and 6-hydroxidopamine (6-OHDA), a catecholaminergic neurotoxin was used to elicit the death of the cells. Similar to MPTP, the effect of 6-OHDA is also selective to catecholaminergic cells. In these experiments, the procedures described in (Zheng H et al, J. Neurochem., 2005, 95, 68-78) were followed, with slight modification, and rasagiline, and aminoindan were used as reference compounds. Cells were incubated with 6-OHDA (200 μM) for 24h and test compounds and rasagiline were applied in a single 10^{-5} M concentration for 1h prior 6-OHDA application. The MTT assay was used to assess cell death.

Experimental protocol

Cell culture

PC12 cells were grown in Dulbecco's Modified Eagle's Medium (DMEM 4500) supplemented with 10% horse serum, 5% fetal bovine serum (FBS) and L-glutamine. The cultures were maintained in a humidified atmosphere containing 5% CO_2 at 37 °C. For experiments assessing the effect of drugs on 6-OHDA-induced cell death, PC12 cells were seeded on 96-well plates in a density of 10000 cells/well. The data are expressed as percentage of the survival of MPTP treated cells of the same plate. Every measurement was performed at least in n=8 number, and repeated on at least 2 independent plates.

MTT assay

Cell viability was assessed using the colorimetric reagent, 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT). A stock solution of the dye was prepared, filter-sterilized and stored at -20 °C. After 6-OHDA treatment in 96-well plates, 5 mg/ml MTT was added to each well, and the incubation was continued for another 4 h. The converted dye was solubilized with acidic isopropyl alcohol (0.04 M HCl in anhydrous isopropyl alcohol). Reduced MTT was measured at a wavelength of 570 nm.

Results

In line with literature data (Zheng H et al, J. Neurochem., 2005, 95, 68-78; Bar-Am O et al, J. Neurochem., 2007, 103, 500-508), rasagiline exerted significant, 48% protective effect in 10 μM concentration, and aminoindan has been proven to be even more effective (Table 9, Figure 13). The test compounds, including SZV-1902, SZV-2220, SZV-2358, SZV-2533 were also protective against 6-OHDA induced cell death and among them SZV-2358, SZV-2533 displayed the highest increase in the survival of the cells (Table 9, Figure 13). These compounds elicited an approx. 74 % increase in the survival of 6-OHDA treated cells.

Treatment	**Concentration (μM)**	**Survival (%)**
6-OHDA 200 μM		100±10.62
6-OHDA + rasagiline	10	147.82±7.23**
6-OHDA + aminoindane	0.1	165.02±18.04**
6-OHDA + SZV-2220	10	147.17±6.76**
6-OHDA + SZV-1902	10	166.71±7.17***
6-OHDA + SZV-2358	10	174.46±14.07***
6-OHDA + SZV-2533	10	174.24±6.27***

Table 9. Effect of compounds of the invention (10 μM) on the survival of PC12 cells 24 h after 6-OHDA (200 μM) treatment.

In Figure 13 and Table 9, survival data are expressed as percentage of 6-OHDA treated cells. Symbols represent significant changes from 6-OHDA treated (**$P<0.01$, ***$P<0.001$) cells. Statistical analysis: one-way ANOVA followed by the Tukey test. Each data are the average of at least 8 values measured in 2 independent plates

C) Acute toxicity in rats.

To provide some further information of biological profile of the compounds of the invention, toxicity of some compounds were also determined. In the following part, experiments carried out with three compounds of the invention are described.

Briefly, rats were treated with a compound of the invention in doses of 150 mg/kg, in p.o. and subcutan (s.c.) routes, i.e., in much higher doses than their therapeutic doses. Experiments were carried out on male Wistar rats (Charles River) weighing 160-180 g. The animals were kept in a 12-hour light/dark cycle and under condition of controlled temperature. They were maintained on standard rat laboratory chow and tap water ad libitum. The test compounds were given either orally (po) after 12 h starvation, or subcutaneously (sc).

Animals were observed for 72 h. Body weights were also measured before and after the treatment. After 72 h animals were euthanized by inhalation of CO_2 and the entire gastrointestinal tract was examined for mucosal lesion macroscopically.

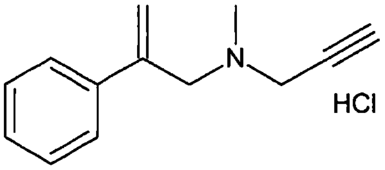
For sc. administration the compounds were dissolved in distilled water or mixture of DMSO and distilled water. For oral administration the compounds were suspended in 1 % methylcellulose.

In these experiments, compounds SZV-1902, SZV-2541, SZV-2591 did not exert any significant sign of toxic symptoms, indicating, besides their anti-PD effects, another particularly advantageous feature.

Compound SZV-1902

Animals: rat; general condition is good, stomach, no lesions in gastrointestinal tract.

Treatment: 150 mg/kg (sc) or oral (po); observation for 72 h.



Treatment, sc				
	Bw, initial (g)	**Solution vol (ml)**	**Bw, final (g)**	**Bw, gain (g)**
1.	160	0.80	180	20
2.	180	0.90	190	10
3.	180	0.90	190	10
4.	170	0.85	190	20
5.	180	0.90	190	10
Mean	**174**		**188**	**14**
S.E.M.	**4.0**		**2.0**	**2.4**

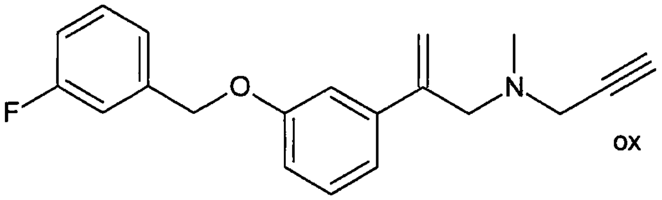
Treatment, po				
	Bw, initial (g)	**Solution vol (ml)**	**Bw, final (g)**	**Bw, gain (g)**
1.	170	0.85	195	25
2.	175	0.90	185	10
3.	170	0.85	180	10
4.	175	0.90	195	20
5.	175	0.90	185	10
Mean	**173**		**188**	**15**
S.E.M.	**1.2**		**3.0**	**3.2**

Volume of injection: 0.5 ml/100 g, the compounds were dissolved in distilled water (sc) or suspended in 1% methylcellulose (for oral).

Good general condition, no lesions in gastrointestinal tract in 72 h.

Compound SZV-2541

Animals: rat; general condition is good, stomach, no lesions in gastrointestinal tract.
Treatment: 150 mg/kg sc or oral po; observation for 72 h.



Treatment, sc				
	Bw, initial (g)	**Solution vol (ml)**	**Bw, final (g)**	**Bw, gain (g)**
1.	170	0.85	195	25
2.	160	0.80	175	15
3.	170	0.85	180	10
4.	180	0.90	195	15
5.	170	0.85	180	10
Mean	**170**		**185**	**15**
S.E.M.	**3.2**		**4.2**	**2.7**

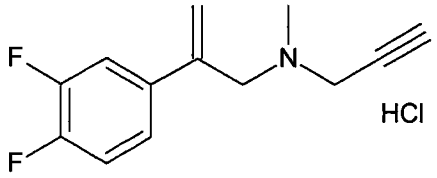
Treatment, po				
	Bw, initial (g)	**Solution vol (ml)**	**Bw, final (g)**	**Bw, gain (g)**
1.	170	0.85	190	20
2.	180	0.90	195	15
3.	175	0.90	200	25
4.	165	0.80	185	20
5.	170	0.85	195	25
Mean	**172**		**193**	**21**
S.E.M.	**2.5**		**2.5**	**1.9**

For sc treatment the compound was dissolved in the mixture of DMSO and distilled water.

For oral administration the compound was suspended in 1% metylcellulose. Good general condition, no any macroscopic lesions in gastrointestinal tract in 72 h.

Compound SZV-2591

Animals: rat; general condition is good, stomach, no lesions in gastrointestinal tract.
Treatment: 150 mg/kg sc or oral po; observation for 72 h.



Treatment, sc				
	Bw, initial (g)	**Solution vol (ml)**	**Bw, final (g)**	**Bw, gain (g)**
1.	135	0.70	145	10
2.	160	0.80	170	10
3.	150	0.75	165	15
4.	140	0.70	150	10
5.	165	0.85	175	10
Mean	**150**		**161**	**11**
S.E.M.	**5.7**		**5.8**	**1.0**

Treatment, po				
	Bw, initial (g)	**Solution vol (ml)**	**Bw, final (g)**	**Bw, gain (g)**
1.	170	0.90	190	20
2.	140	0.70	150	10
3.	145	0.75	160	15
4.	150	0.75	160	10
5.	155	0.80	165	10
Mean	**152**		**165**	**13**
S.E.M.	**5.1**		**6.7**	**2.0**

Volume of injection: 0.5 ml/100 g, the compounds were dissolved in mixture of DMSO and distilled water or suspended in 1% methylcellulose (for po).

Good general condition, no lesions in gastrointestinal tract in 72 h.

Significance of the results

Parkinson's disease (PD) is a devastating condition, characterized by motor and non-motor symptoms, which progressively deteriorate the ability of work, the quality of life and end up in permanent disability. Although these symptoms can be improved using currently available dopamine replacement strategies, there is still a need to improve current strategies for treating these symptoms, together with a need to alleviate non-motor symptoms of the disease. Moreover, treatments that provide neuroprotection and/or disease-modifying effects remain an urgent unmet clinical need

(Meissner WG et al, Nat. Rev. Drug Discov., 2011, 10, 377-393). Selective MAO-B inhibitors are important supplementation of the dopamine replacement therapy; however, without a clearly defined and profound neuroprotective action they are unable to exert a clinically detectable disease-modifying effect. In addition, although the available MAO-B inhibitors are relatively safe drugs, adverse effects, such as headache, arthalgia, depression and hallucinations are reported in up to 2-5% of the patients. Very recently, the appearance of impulse control disorder induced by rasagiline has also been reported in a case study (Vitale C et al, Parkinsonism. Relat. Disord., 2013, 19, 483-484).

In vivo animal models of PD have been widely used by the academic research to investigate the pathogenesis of neurodegeneration as well as by drug industry for the preclinical assessment of novel anti-parkinsonian drugs. Among them, toxin-induced animal models (e.g. MPTP, rotenone, 6-OHDA) elicit substantial and reproducible nigrostriatal lesion therefore they are especially suitable for testing neuroprotective therapeutic interventions (Blandini F et al, FEBS J., 2012, 279, 1156-1166). Available transgenic models (e.g. α-synuclein, LRRK2, PINK1 mutants) so far, on the other hand, although etiologically more relevant in genetic forms of PD (corresponding to less than 5% of all PD cases (Langston JW et al, Ann. Neurol., 1998, 44, S45-52), in general, are not associated with either significant nigrostriatal degeneration or behavioral phenotype, therefore are less appropriate for preclinical assessment of novel compounds.

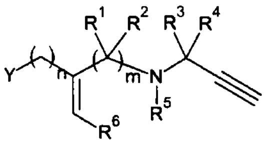
The effects of compounds of the present invention and, as a reference compound, rasagiline were evaluated in four different toxin-induced PD models, including two rodent species and a cell culture model. In cases of compounds of the invention, a consistent protective effect was detected in all models, which was qualitatively and quantitatively superior over rasagiline. Moreover, the protective effect was manifested in various forms of indicators from cell survival to animal behavior, without the appearance of any visible unwanted side effects.

Also importantly, the compounds of the invention elicited several, therapeutically relevant beneficial effects, whereas no such effects could be detected with rasagiline, which, on the contrary, elicited an opposite, i.e. worsening effect. The most outstanding features of the compounds of the invention include selective inhibition of oxidative stress induced a pathological dopamine release in the rotenone treated striatum slices, the preservation of dopamine metabolite level in the striatum after MPTP treatment, and a MAO-B inhibition –independent antiapoptotic effect in the Tatton-Kish model, each of which is relevant to neuroprotection. In addition, in models of PD, the test compounds not only retained all beneficial effects of selective MAO-B inhibitors, but, in comparison to the clinically used best MAO-B inhibitor rasagiline, they are more potent in terms of both the inhibition of MAO-B and the protection against cell death. It is also remarkable that duration of action of the compounds of the invention was as long as 42 h, as a consequence of the potent and irreversible inhibition of the

MAO-B enzyme, also indicating a particularly favorable pharmacodynamic half life. Therefore, taking into account that rasagiline devoid of significant efficacy in the above models, was not proven to be neuroprotective in clinical settings, while the compounds of our invention exerted significant effects, their disease-modifying effect could be well expected in PD.

Claims

1. A compound of general formula (I)



wherein:

R^1 and R^2 are independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl and optionally substituted C_{6-10} aryl;

R^3 and R^4 are independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl and optionally substituted C_{6-10} aryl;

R^5 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl and optionally substituted C_{6-10} aryl;

R^6 is hydrogen or halogen;

Y is C_{6-10}aryl or heteroaryl, optionally substituted with one or more substituents selected from the group consisting of

- C_{1-6}alkyl or C_{2-6}alkenyl which is optionally substituted with one or more halogen, C_{6-10}aryl, aminoC_{6-10}aryl, C_{6-10}aryloxy or C_{5-14}heteroaryloxy,
- halogen,
- nitro,
- cyano,
- C_{1-6}alkoxy which is optionally substituted with one or more halogen, C_{6-10}aryl or amino, which amino is optionally substituted with one or more C_{1-6}alkyl,
- C_{1-6}alkoxycarbonyl,
- C_{1-6}alkylsulfanyl,
- C_{1-6}alkylsulfonyl,
- amino which is optionally substituted with one or more C_{1-6}alkyl, C_{6-10}arylsulfonyl, C_{1-6}alkylsulfonyl, C_{6-10}arylC_{1-6}alkyl or C_{1-6}alkoxy substituted with C_{6-10}aryl,
- C_{3-7}cycloalkoxy,
- C_{3-7}cycloalkyl,
- C_{6-10}aryl,
- C_{5-14}heteroaryl;
- saturated C_{5-12}heterocyclyl;
- hydroxyC_{1-6}alkyl
- hydroxyl,
- carbamate which is optionally substituted with one or more C_{1-6}alkyl

- all the aryl given as substituent of Y is optionally further substituted with halogen, C_{1-6}alkyl, C_{1-6}alkoxy or cyano;

n is an integer of 0 to 2;

m is an integer of 1 to 5;

or an enantiomer or diastereomer thereof or a salt, optionally a pharmaceutically acceptable salt, or a solvate of any of these.

2. The compounds of general formula (I) according to claim 1, wherein

R^1 and R^2 is independently selected from hydrogen and C_{1-4}alkyl;

R^3 and R^4 is independently selected from hydrogen and C_{1-4}alkyl;

R^5 is selected from the group consisting of hydrogen and C_{1-6}alkyl optionally substituted with phenyl or with 1 to 3 halogen;

R^6 is hydrogen or halogen;

n has the value of 0 or 1;

m has the value of 1 to 4.

3. The compounds of general formula (I) according to claim 2, wherein

R^1 and R^2 is independently selected from hydrogen and methyl;

R^3 and R^4 is independently selected from hydrogen and methyl;

R^5 is selected from the group consisting of hydrogen, methyl optionally substituted with phenyl, and ethyl optionally substituted with 1 to 3 halogen(s);

R^6 is hydrogen or halogen.

4. The compounds of general formula (I) according to claim 1 to 3, wherein

Y is selected from the group consisting of phenyl, naphthyl, indenyl, dihydrobenzodioxinyl, dihydrobenzofuranyl, benzodioxolyl, pyrrolyl, thienyl, thiazolyl, imidazolyl, furanyl, indolyl, isoindolyl, dioxolo-indolyl, oxazolyl, isoxazolyl, benzothiazolyl, benzoimidazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiophenyl, benzo[b]thiophenyl, indazolyl, pyrazolyl, benzofuranyl, naphtofuranyl, triazolyl, tetrazolyl and imidazolyl, optionally substituted with one or more substituents selected from the group consisting of

- C_{1-4}alkyl which is optionally substituted with one or more halogen, C_{6-10}aryl, aminoC_{6-10}aryl, C_{6-10}aryloxy or C_{5-13}heteroaryloxy,
- C_{2-4}alkenyl,
- halogen,
- nitro,
- cyano,

- C_{1-4}alkoxy which is optionally substituted with one or more halogen, C_{6-10}aryl or amino, which amino is optionally substituted with one or more C_{1-4}alkyl,
- C_{1-4}alkoxycarbonyl,
- C_{1-4}alkylsulfanyl,
- C_{1-4}alkylsulfonyl,
- amino which is optionally substituted with one or more C_{1-4}alkyl, C_{6-10}arylsulfonyl, C_{1-4}alkylsulfonyl, C_{6-10}arylC_{1-4}alkyl or C_{1-4}alkoxy substituted with C_{6-10}aryl,
- C_{3-5}cycloalkoxy,
- C_{3-5}cycloalkyl,
- C_{6-10}aryl,
- C_{5-13}heteroaryl;
- saturated C_{5-12}heterocyclyl;
- hydroxyC_{1-4}alkyl
- hydroxyl,
- carbamate which is optionally substituted with one or more C_{1-4}alkyl
- all the aryl given as substituent of Y is optionally further substituted with halogen, C_{1-4}alkyl, C_{1-4}alkoxy or cyano.

5. The compounds of general formula (I) according to claim 4, wherein

Y is selected from the group consisting of phenyl, naphthyl, indenyl, pyrrolyl, thiazolyl, furanyl, indolyl, dioxolo-indolyl, isoxazolyl, benzothiazolyl, pyridinyl, thiophenyl, benzo[b]thiophenyl, indazolyl, pyrazolyl, benzofuranyl, naphtofuranyl, dihydrobenzofuranyl and benzodioxolyl, optionally substituted with one or more substituents selected from the group consisting of

- C_{1-4}alkyl which is optionally substituted with one or more halogen, phenyl, aminophenyl, phenoxy or indolyloxy,
- C_{2-4}alkenyl,
- halogen,
- nitro,
- cyano,
- C_{1-4}alkoxy which is optionally substituted with one or more halogen, phenyl or amino, which amino is optionally substituted with one or more C_{1-4}alkyl,
- C_{1-4}alkoxycarbonyl,
- C_{1-4}alkylsulfanyl,
- C_{1-4}alkylsulfonyl,
- amino which is optionally substituted with one or more C_{1-4}alkyl, tosyl, mesyl, benzyl or benzyloxy,

- C_{3-5}cycloalkoxy,
- C_{3-5}cycloalkyl,
- phenyl,
- benzofuranyl
- morpholinyl
- hydroxyC_{1-4}alkyl
- hydroxyl,
- carbamate which is optionally substituted with one or more C_{1-4}alkyl;
- all the phenyl given as substituent of Y is optionally further substituted with halogen, C_{1-4}alkyl, C_{1-4}alkoxy or cyano.

6. The compounds of general formula (I) according to claim 5, wherein

Y is selected from phenyl optionally substituted with one or more substituents selected the group consisting of halogen, nitro, cyano, benzyloxy, methoxy, 5-indolyloxymethyl, methyl optionally substituted with 1 to 3 halogen, benzyloxy optionally substituted with methylsulfanyl, halogen and methoxy, phenoxymethyl optionally substituted with methoxy or with 1 to 3 halogen, and
tiophen-2-yl optionally substituted with chloro,
furan-2-yl,
furan-3-yl,
benzofuran-2-yl optionally substituted with chloro, methoxy or fluoro,
methyl-pyrazol-4-yl,
1-methylene-2,3-dihydro-1H-inden-2-yl.

7. The compounds of general formula (I) according to claim 6 comprising

N-Methyl-2-phenyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-Phenyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(4-Chlorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Fluorobenzyl)oxy)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Fluorobenzyl)oxy)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3,4-Difluorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3,4-Difluorophenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
N-Methyl-2-(3-(phenoxymethyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-(Phenoxymethyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
N-methyl-N-(prop-2-yn-1-yl)-2-(thiophen-2-yl)prop-2-en-1-amine
2-(Furan-3-yl)-N-methyl-N-(prop-2-ynyl)prop-2-en-1-amine
2-(3-(Benzyloxy)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine

2-(5-Chlorothiophen-2-yl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Methoxybenzyl)oxy)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-(((1H-indol-5-yl)oxy)methyl)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((4-Fluorophenoxy)methyl)phenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Chlorobenzyl)oxy)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((4-Fluorobenzyl)oxy)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3-Fluorophenoxy)methyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(3-((3,5-Difluorophenoxy)methyl)phenyl)-N-(prop-2-yn-1-yl)prop-2-en-1-amine
2-(4-Fluorophenyl)-N-methyl-N-(prop-2-yn-1-yl)prop-2-en-1-amine

or an enantiomer or diastereomer thereof or a salt, optionally a pharmaceutically acceptable salt, or solvate of any of these.

8. A pharmaceutical composition comprising a compound of general formula (I) or an enantiomer or diastereomer thereof or a salt, optionally a pharmaceutically acceptable salt or solvate according to any of claims 1 to 7 admixed with a pharmaceutically acceptable carrier, excipient or diluent.

9. A compound according to any of claims 1 to 7 for use in treating or preventing a disease or condition in a mammal related to monoamine oxidase dysfunction.

10. The compound for use according to claim 9 wherein the disease or condition is selected from the group consisting of neurodegenerative diseases.

11. The compound for use according to claim 9 wherein the condition is Parkinson’s disease.

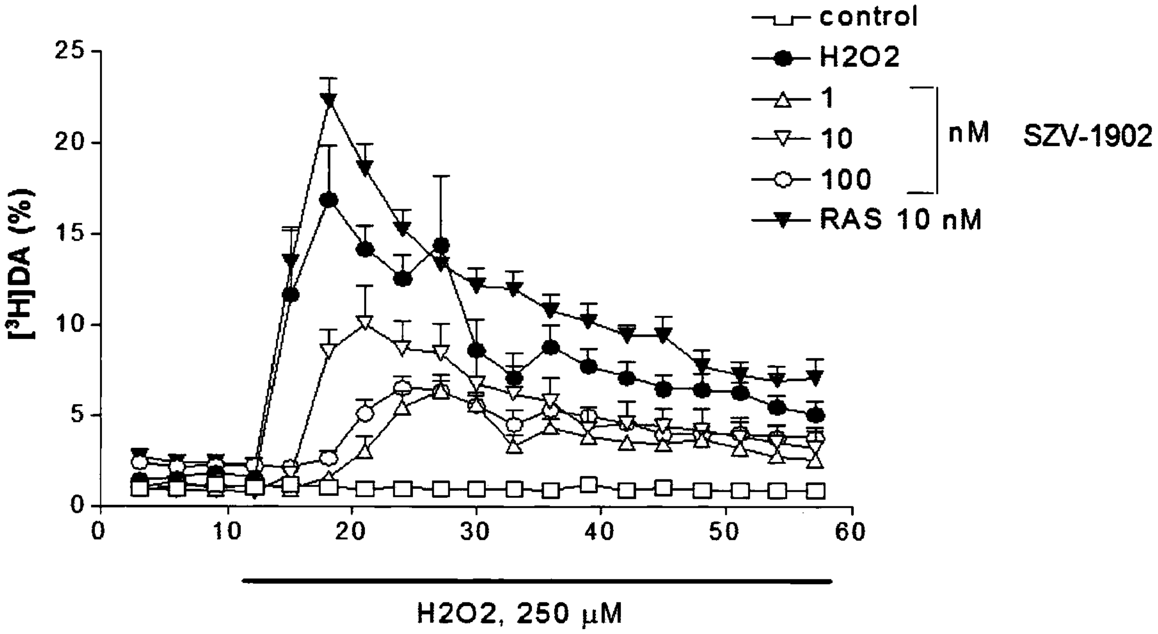


Figure 1

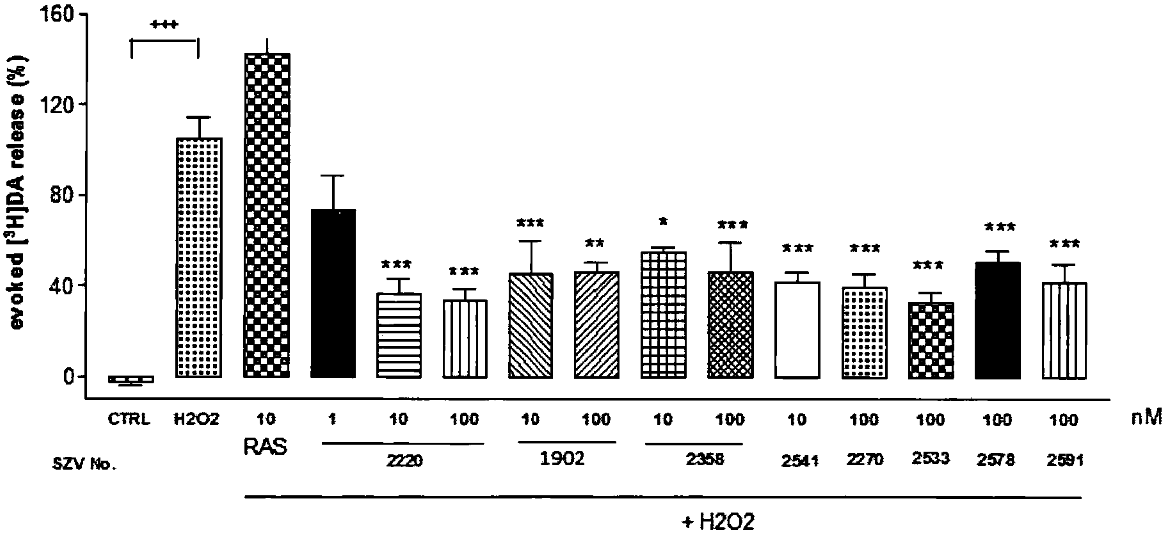


Figure 2

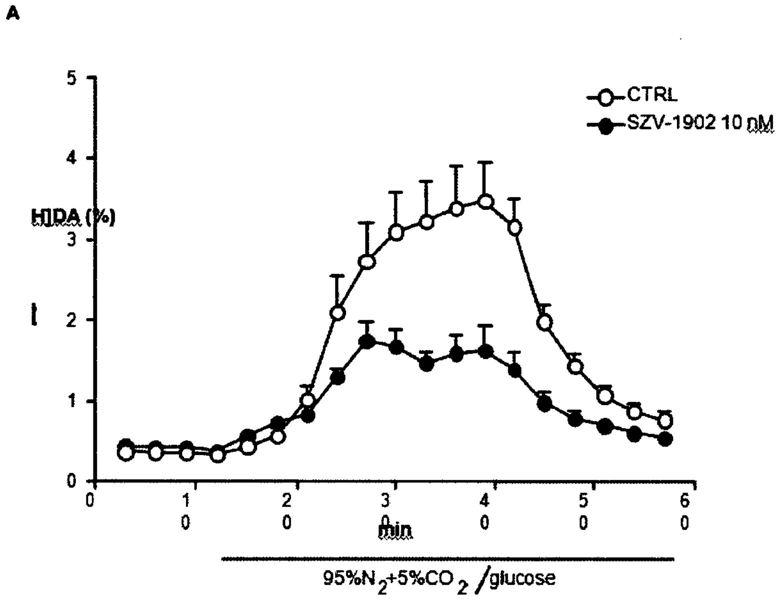


Figure 3 A

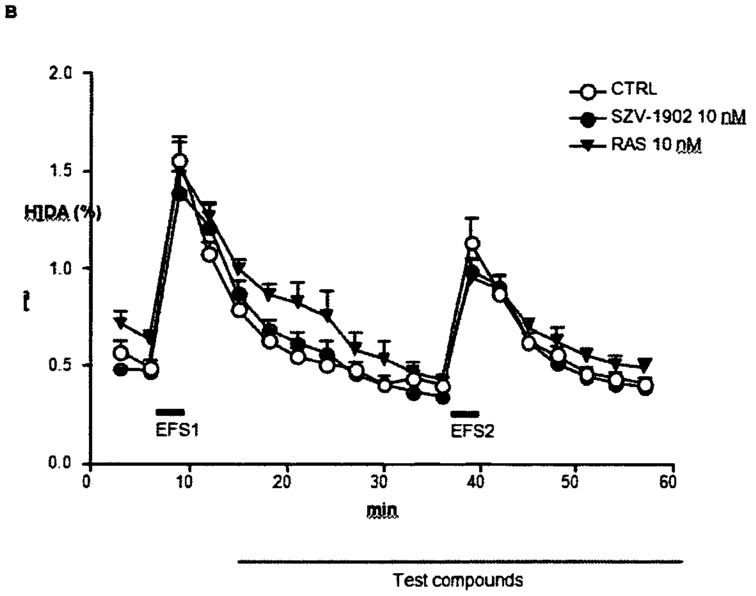


Figure 3 B

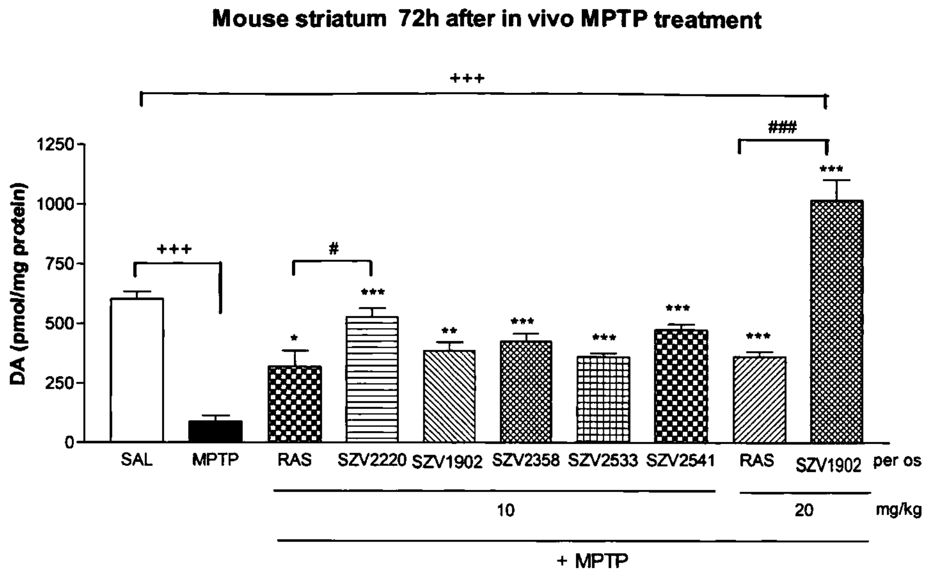


Figure 4

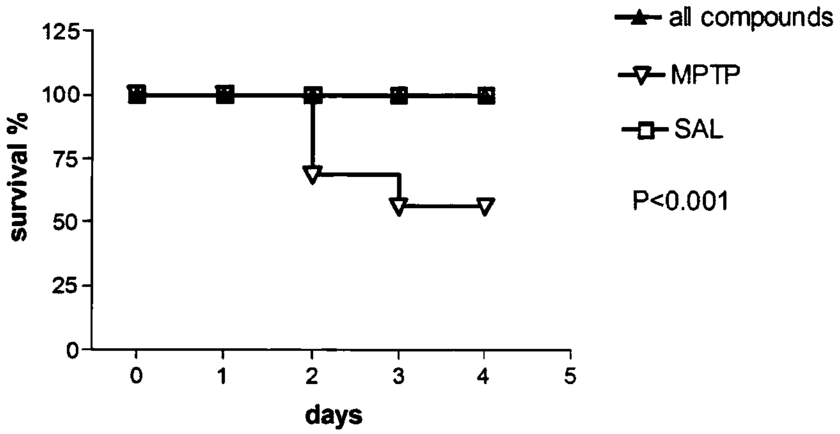


Figure 5

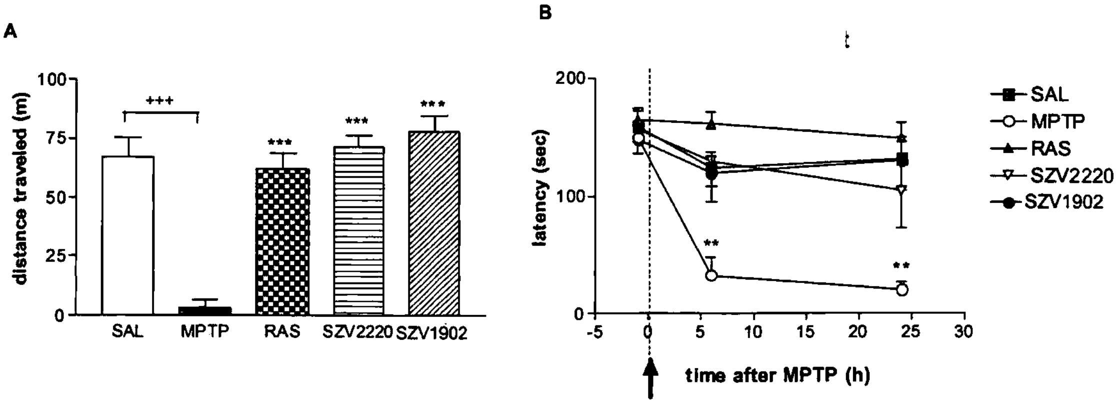


Figure 6 A and B

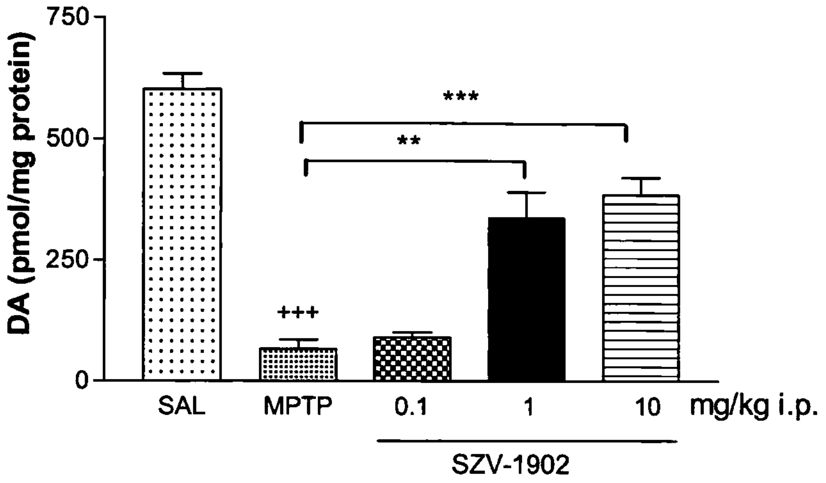


Figure 7

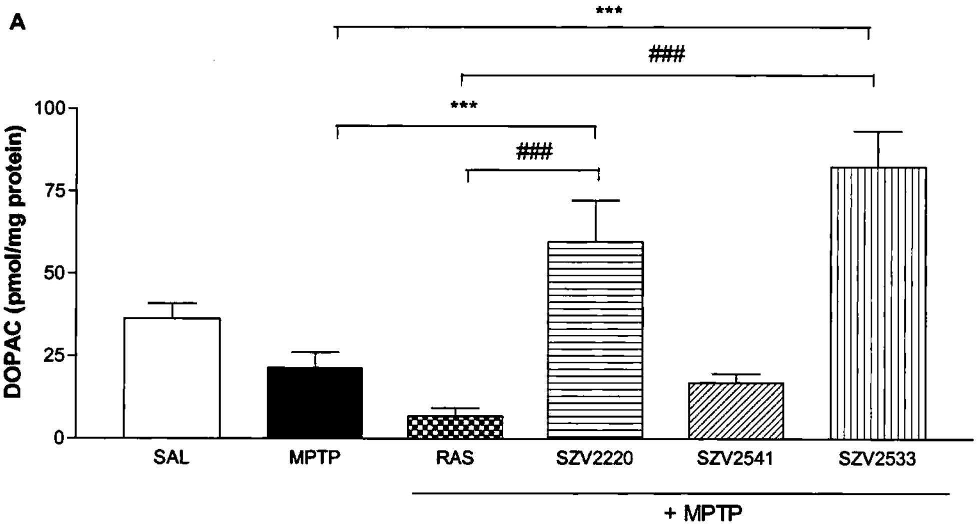


Figure 8 A

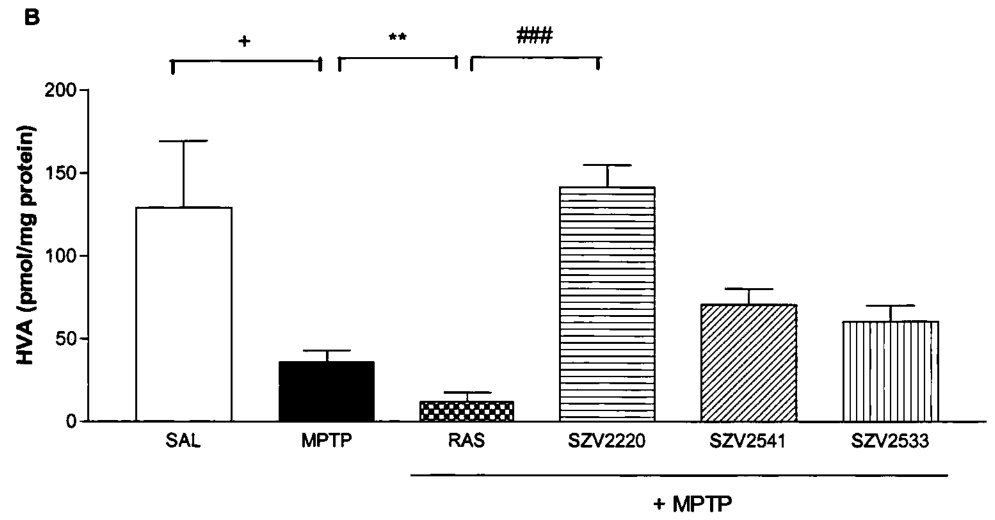


Figure 8 B

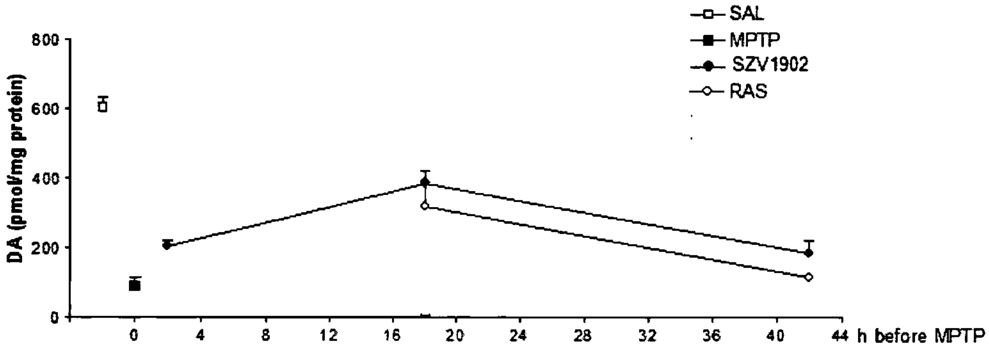


Figure 9

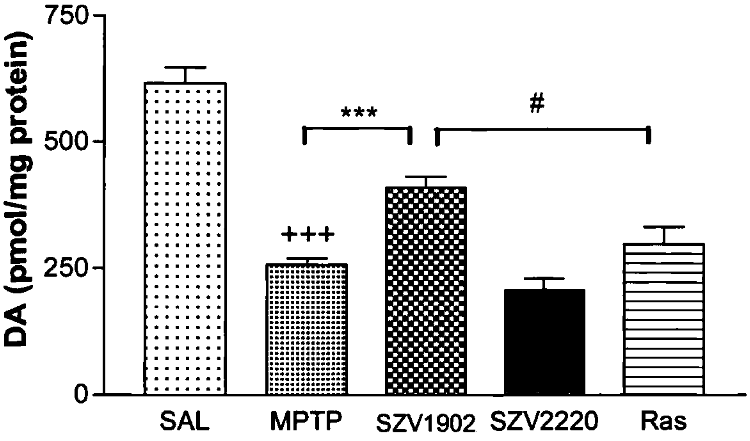


Figure 10

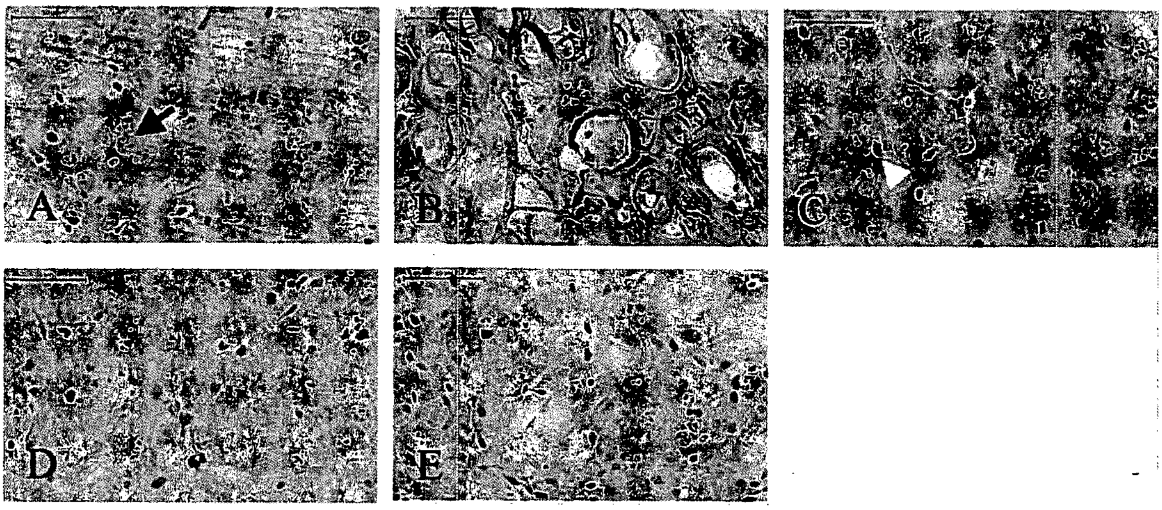


Figure 11 A – E

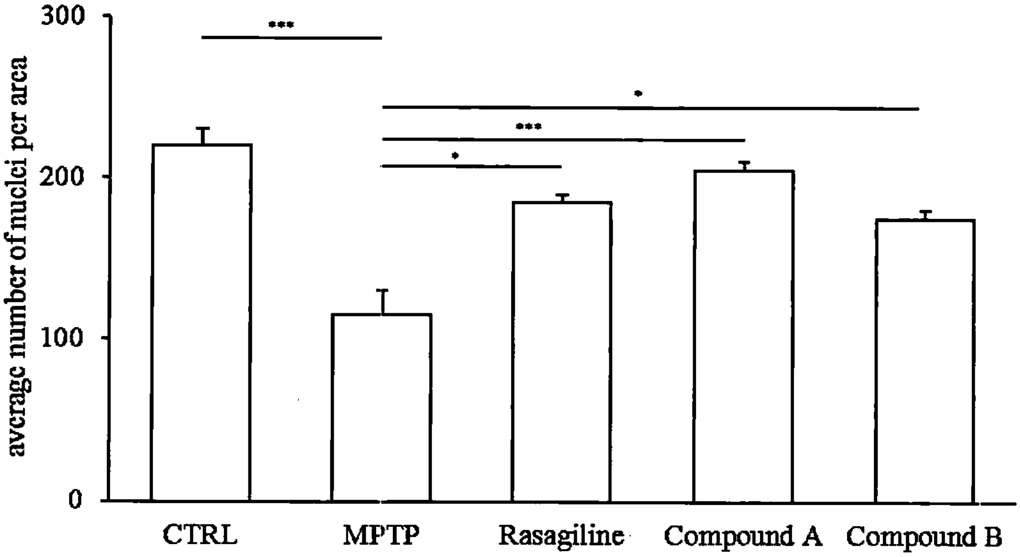


Figure 11 F

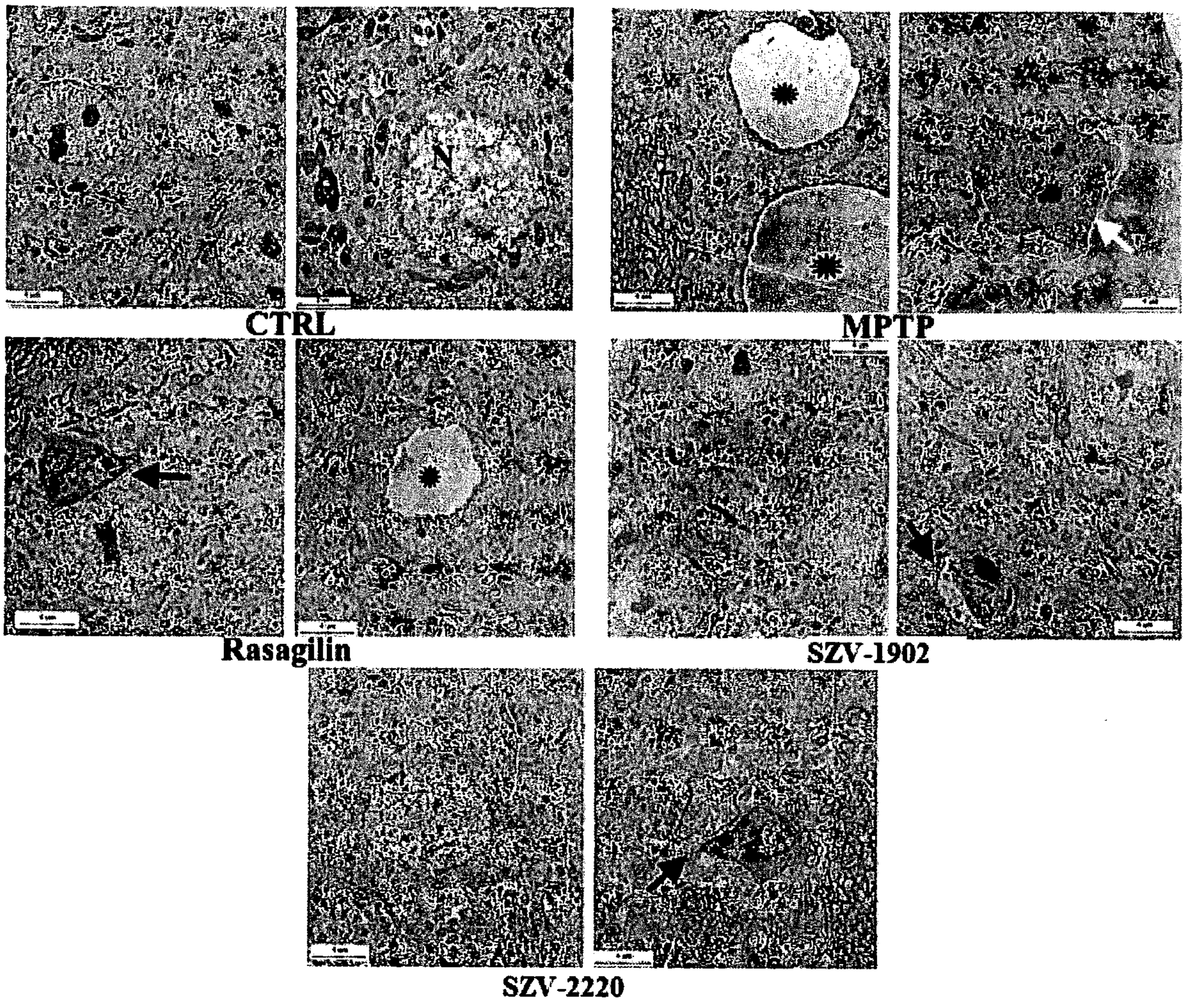


Figure 12

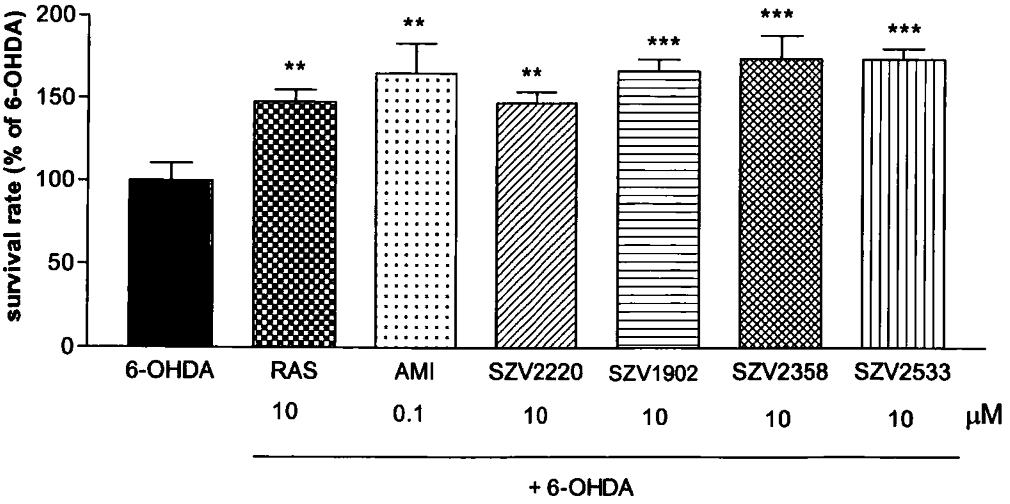


Figure 13

INTERNATIONAL SEARCH REPORT

International application No
PCT/HU2013/000122

A. CLASSIFICATION OF SUBJECT MATTER

INV.	C07C211/28	C07C211/29	C07D231/12	C07D333/20	C07D231/56
	C07D261/08	C07D207/323	C07D209/08	C07D277/64	C07D307/79
	A61K31/135	A61K31/341	A61K31/381	A61K31/40	A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 85/05617 A1 (CHINOIN GYOGYSZER ES VEGYESZET [HU]) 19 December 1985 (1985-12-19) claims; examples	1-11
Y	US 4 454 158 A (BEY PHILIPPE [FR] PHILIPPE BEY [FR]) 12 June 1984 (1984-06-12) claims; examples	1-11

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search 10 April 2014	Date of mailing of the international search report 22/04/2014
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Bosma, Peter

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/HU2013/000122

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