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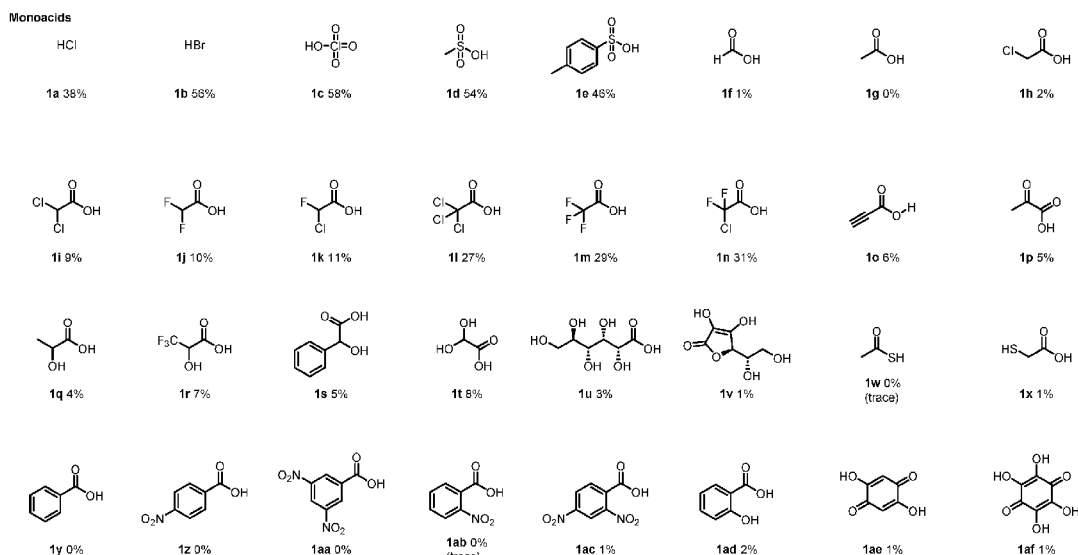


FIGURE 1

(57) Abstract: The present invention relates to processes for preparing fluorochemicals. The present invention also relates to the fluorochemicals resulting from the processes of the present invention. The processes of the present invention can avoid the need to use hydrofluoric acid as an intermediate for fluorochemical production.

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FLUOROCHEMICAL PREPARATION

INTRODUCTION

[0001] The present invention relates to processes for preparing fluorochemicals, as well as the fluorochemicals resulting therefrom. The processes of the present invention can avoid the need to use hydrofluoric acid as an intermediate for fluorochemical production.

BACKGROUND OF THE INVENTION

[0002] Fluorochemicals play a crucial role in modern society, and their use is highly important for a wide range of industrial, commercial, and consumer applications. They are found in everything from non-stick cookware to refrigerants, from firefighting foams to medical imaging agents, as well as pharmaceuticals and agrochemicals. The incorporation of fluorine into pharmaceutical molecules has been shown to improve their efficacy, bioavailability, and metabolic stability. As a result, many modern drugs, including several blockbuster drugs, contain fluorine, most commonly in form of fluoroarenes.

[0003] Due to the lack of biologically produced fluorine-containing molecules, essentially all fluorochemicals originate from mineral fluorine sources, such as fluorspar (CaF_2). To harvest the fluorine, CaF_2 is heated with concentrated sulfuric acid which releases gaseous hydrofluoric acid (HF), a highly toxic and corrosive substance known to cause severe harm to human health and the environment. In spite of this, HF remains a key intermediate in the synthesis of many fluorochemicals. To minimize the risks associated with HF, strict safety protocols must be followed in its handling and disposal. However, accidents involving HF remain a problem in industry and frequently have severe consequences.

[0004] Efforts to avoid the use of HF altogether have been limited. The direct use of CaF_2 from the mineral as a fluorochemical would be an ideal way to avoid HF, as well as having economic and ecologic advantages. However, the high lattice energy of CaF_2 compared to other alkali metal fluorides used in organic synthesis means that its use as a fluorochemical is limited. Furthermore, its prohibitively low solubility in water and complete insolubility in solvents suitable for organic fluorination make this an unviable option.

[0005] Thus, there remains a need for safer and more environmentally-friendly processes for the preparation of fluorochemicals which avoid the generation of gaseous HF. The present invention was devised with the foregoing in mind.

SUMMARY OF THE INVENTION

[0006] According to a first aspect of the present invention there is provided a process for the preparation of a fluorochemical, the process comprising the step of:

- a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein
- the activator is an organic compound having a pK_a of -4 to 4.2 in water, and a water solubility of greater than 0.05 mol/L; and
 - the fluoride acceptor is a hydroxide, an oxide, an alkoxide, a halide or a pseudohalide of B, Si, Ge, Al, P, Sb, Ti, S or Sn.

[0007] According to a second aspect of the present invention there is provided a process for the preparation of a fluorochemical, the process comprising the step of:

- a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein
- the activator is selected from any one of compounds 1-55 defined herein, or a salt thereof; and
 - the fluoride acceptor is a hydroxide, an oxide, an alkoxide, a halide or a pseudohalide of B, Si, Ge, Al, P, Sb, Ti, S or Sn.

[0008] According to a third aspect of the present invention there is provided a process for the preparation of a fluorochemical, the process comprising the step of:

- a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein
- the activator is an organic compound having a pK_a of -4 to 4.2 in water, and a water solubility of greater than 0.05 mol/L; and
 - the fluoride acceptor is selected from $B(OH)_3$, $B(OH)_2R$, R_3SiCl , $SiCl_4$, RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), $(BOH)_3O_3$, $H_2B_4O_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , Sb_2O_5 or $SbCl_5$.

[0009] According to a fourth aspect of the present invention there is provided a process for the preparation of a fluorochemical, the process comprising the step of:

- a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein
- the activator is selected from any one of compounds 1-55 defined herein, or a salt thereof; and
 - the fluoride acceptor is selected from $B(OH)_3$, $B(OH)_2R$, R_3SiCl , $SiCl_4$, RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), $(BOH)_3O_3$, $H_2B_4O_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , Sb_2O_5 or $SbCl_5$.

[0010] According to a fifth aspect of the present invention there is provided a process for the preparation of a fluorochemical, the process comprising the step of:

- a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein

the activator is selected from any one of compounds 1-56 defined herein, or a salt thereof; and

the fluoride acceptor is a hydroxide, an oxide, an alkoxide, a halide or a pseudohalide of B, Si, Ge, Al, P, Sb, Ti, S or Sn.

[0011] According to a sixth aspect of the present invention there is provided a process for the preparation of a fluorochemical, the process comprising the step of:

a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein the activator is selected from any one of compounds 1-56 defined herein, or a salt thereof; and

the fluoride acceptor is selected from B(OH)_3 , $\text{B(OH)}_2\text{R}$, R_3SiCl , SiCl_4 , RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), $(\text{BOH})_3\text{O}_3$, $\text{H}_2\text{B}_4\text{O}_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , Sb_2O_5 or SbCl_5 .

[0012] Suitably in any one of the first, second, third, fourth, fifth or sixth aspects of the present invention, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51 or 53 defined herein, or salt thereof. More suitably, the activator is selected from any one of compounds 1, 24 or 51 defined herein, or a salt thereof. Most suitably, the activator is compound 24 defined herein (i.e., oxalic acid), or a salt thereof.

[0013] Suitably in any one of the first, second, third, fourth, fifth or sixth aspects of the present invention, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51, 53 or 56 defined herein, or salt thereof. More suitably, the activator is selected from any one of compounds 1, 24, 51 or 56 defined herein, or a salt thereof. Most suitably, the activator is compound 24 defined herein (i.e., oxalic acid), or a salt thereof.

[0014] Suitably in any one of the first, second, third, fourth, fifth or sixth aspects of the present invention, the fluoride acceptor is selected from B(OH)_3 , 4-fluorophenyl- B(OH)_2 , B_2O_3 , SiO_2 , Ph_3SiCl , SiCl_4 , *p*- ToISO_2Cl , GeO_2 or Al_2O_3 . More suitably, the fluoride acceptor is selected from B(OH)_3 , SiO_2 , SiCl_4 or *p*- ToISO_2Cl . Most suitably, the fluoride acceptor is B(OH)_3 .

[0015] Suitably in any one of the first, second, third, fourth, fifth or sixth aspects of the present invention, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51 or 53 defined herein, or a salt thereof, and the fluoride acceptor is selected from B(OH)_3 , 4-fluorophenyl- B(OH)_2 , B_2O_3 , SiO_2 , Ph_3SiCl , SiCl_4 , *p*- ToISO_2Cl , GeO_2 or Al_2O_3 . More suitably, the activator is selected from any one of the compounds 1, 24 or 51 defined herein, or a salt thereof, and the fluoride acceptor is selected from B(OH)_3 , SiO_2 , SiCl_4 or *p*- ToISO_2Cl . Most suitably, the activator is compound 24 defined herein (i.e., oxalic acid), or a salt thereof, and the fluoride acceptor is B(OH)_3 .

[0016] Suitably in any one of the first, second, third, fourth, fifth or sixth aspects of the present invention, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51, 53 or 56

defined herein, or a salt thereof, and the fluoride acceptor is selected from B(OH)_3 , 4-fluorophenyl- B(OH)_2 , B_2O_3 , SiO_2 , Ph_3SiCl , SiCl_4 , *p*- ToISO_2Cl , GeO_2 or Al_2O_3 . More suitably, the activator is selected from any one of the compounds 1, 24, 51 or 56 defined herein, or a salt thereof, and the fluoride acceptor is selected from B(OH)_3 , SiO_2 , SiCl_4 or *p*- ToISO_2Cl . Most suitably, the activator is compound 24 defined herein (i.e., oxalic acid), or a salt thereof, and the fluoride acceptor is B(OH)_3 .

[0017] Most suitably, the inorganic fluoride source in any one of the first, second, third, fourth, fifth or sixth aspects of the present invention is CaF_2 . The CaF_2 may be in its naturally occurring form (i.e., fluorspar) or may be a synthetic, industrially produced material having fewer impurities (e.g., acidspar or metspar). Alternatively, the CaF_2 may be present within a waste product (e.g., the CaF_2 may be CaF_2 sludge) or may have been obtained (e.g., purified) from such a waste product. The MgF_2 may be derived from waste fluorochemicals.

[0018] According to a seventh aspect of the present invention there is provided a fluorochemical obtained, directly obtained or obtainable by the process of any one of the first, second, third, fourth, fifth or sixth aspects of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0019] The term "(m-nC)" or "(m-nC) group" used alone or as a prefix, refers to any group having m to n carbon atoms.

[0020] The term "alkyl" as used herein refers to straight or branched chain alkyl moieties, typically having 1, 2, 3, 4, 5 or 6 carbon atoms. This term includes reference to groups such as methyl, ethyl, propyl (n-propyl or isopropyl), butyl (n-butyl, sec-butyl or tert-butyl), pentyl, hexyl and the like. In particular, an alkyl may have 1, 2 or 3 carbon atoms.

[0021] The term "aryl" or "aromatic" as used herein means an aromatic ring system comprising 6, 7, 8, 9 or 10 ring carbon atoms. Aryl is often phenyl but may be a polycyclic ring system, having two or more rings, at least one of which is aromatic. This term includes reference to groups such as phenyl, naphthyl and the like. A particularly suitable aryl group is phenyl.

[0022] The term "heteroaryl" or "heteroaromatic" means an aromatic mono-, bi-, or polycyclic ring incorporating one or more (for example 1-4, particularly 1, 2 or 3) heteroatoms selected from nitrogen, oxygen or sulfur. Examples of heteroaryl groups are monocyclic and bicyclic groups containing from five to twelve ring members, and more usually from five to ten ring members. The heteroaryl group can be, for example, a 5- or 6-membered monocyclic ring or a 9- or 10- membered bicyclic ring, for example a bicyclic structure formed from fused five and

six membered rings or two fused six membered rings. Each ring may contain up to about four heteroatoms typically selected from nitrogen, sulfur and oxygen.

[0023] The term “substituted” as used herein in reference to a moiety means that one or more, especially 1, 2 or 3, of the hydrogen atoms in said moiety are replaced independently of each other by the corresponding number of the described substituents. The term “optionally substituted” as used herein means substituted or unsubstituted.

[0024] It will, of course, be understood that substituents are only at positions where they are chemically possible, the person skilled in the art being able to decide (either experimentally or theoretically) without inappropriate effort whether a particular substitution is possible.

[0025] Throughout the entirety of the description and claims of this specification, where subject matter is described herein using the term “comprise” (or “comprises” or “comprising”), the same subject matter instead described using the term “consist of” (or “consists of” or “consisting of”) or “consist essentially of” (or “consists essentially of” or “consisting essentially of”) is also contemplated.

[0026] Throughout the description and claims of this specification, the singular encompasses the plural unless the context otherwise requires. In particular, where the indefinite article is used, the specification is to be understood as contemplating plurality as well as singularity, unless the context requires otherwise.

[0027] Features described in conjunction with a particular aspect (e.g., the first, second, third, fourth, fifth, sixth or seventh aspect of the present invention), embodiment or example of the invention are to be understood to be applicable to any other aspect (e.g., the first, second, third, fourth, fifth, sixth or seventh aspect of the present invention), embodiment or example described herein unless incompatible therewith. All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive. The invention is not restricted to the details of any of the specific embodiments recited herein. The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any accompanying claims, abstract and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

[0028] As described hereinbefore, the first, second, third, fourth, fifth and sixth aspects of the present invention provide a process for the preparation of a fluorochemical. Through rigorous investigations, the inventors have arrived at a solution to the long-standing problem described hereinbefore by devising a process that allows fluoride sources, such as CaF_2 and

others, to be directly converted into fluorochemicals without the need for converting them into HF using sulfuric acid. This is achieved by reacting an inorganic fluoride source with an activator and a fluoride acceptor. The process of the invention therefore allows for the preparation of value-added fluorochemicals using safer and environmentally friendly techniques.

[0029] The processes of the present invention require the use of an inorganic fluoride source as one of the starting reagents. As described hereinbefore, the use of mineral fluoride sources is preferred, the majority of which have high lattice energies (determined by the Born-Haber cycle). The inorganic fluoride source may have a lattice energy of 1500 kJ/mol or greater. Suitably, the inorganic fluoride source has a lattice energy of 2000 kJ/mol or greater. More suitably, the inorganic fluoride source has a lattice energy of 2300 kJ/mol or greater.

[0030] The inorganic fluoride source may be an ionic compound. Suitably, the inorganic fluoride source is an ionic compound comprising M^{2+} and F^- , wherein M^{2+} is an alkaline earth metal cation (i.e., a group II metal cation). For example M^{2+} may be Be^{2+} , Mg^{2+} , Ca^{2+} , Sr^{2+} or Ba^{2+} . Suitably, M^{2+} is Mg^{2+} , Ca^{2+} , Sr^{2+} or Ba^{2+} . Most suitably, M^{2+} is Ca^{2+} .

[0031] In embodiments wherein the inorganic fluoride source is an ionic compound comprising M^{2+} and F^- , the activator may be an M^{2+} -sequestering agent. Without wishing to be bound by theory, it is believed that the activator promotes the formation of the fluorochemical by sequestering the alkaline earth metal species that is formed when the inorganic fluoride source reacts with the fluoride acceptor. Suitably, the M^{2+} -sequestering agent comprises one or more M^{2+} -coordinating groups. More suitably, the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups.

[0032] In particular embodiments, M^{2+} is Ca and the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups.

[0033] Each M^{2+} coordinating group may independently be an oxygen-containing M^{2+} -coordinating group, a nitrogen-containing M^{2+} -coordinating group or a sulfur-containing M^{2+} -coordinating group. Suitably, each M^{2+} coordinating group is an oxygen-containing M^{2+} -coordinating group.

[0034] Oxygen-containing M^{2+} coordinating groups may be hydroxy groups or oxo groups.

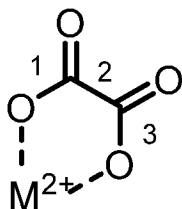
[0035] Nitrogen-containing M^{2+} coordinating groups may be amino groups.

[0036] Sulfur-containing M^{2+} coordinating groups may be thiol groups.

[0037] In particular embodiments, the M^{2+} -sequestering agent comprises two hydroxy M^{2+} -coordinating groups (i.e., the M^{2+} -sequestering agent is a bidentate ligand). In particular

embodiments, M^{2+} is Ca and the M^{2+} -sequestering agent comprises two hydroxy M^{2+} -coordinating groups (i.e., the M^{2+} -sequestering agent is a bidentate ligand).

[0038] The M^{2+} -coordinating group may be capable of binding to M^{2+} , thereby coordinating the M^{2+} -sequestering agent (i.e., the activator) to M^{2+} . When the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups, the M^{2+} -sequestering agent may form a chelate with M^{2+} . Suitably, the M^{2+} -sequestering agent forms a 5-, 6- or 7-membered chelate with M^{2+} . More suitably, the M^{2+} -sequestering agent forms a 5- or 6-membered chelate with M^{2+} . Most suitably, the M^{2+} -sequestering agent forms a 5-membered chelate with M^{2+} . Thus, it may be that the M^{2+} -sequestering agent comprises a first M^{2+} -coordinating group and a second M^{2+} -coordinating group, wherein the first M^{2+} -coordinating group is separated from the second M^{2+} -coordinating group by 3, 4 or 5 bond lengths. More suitably, the M^{2+} -sequestering agent comprises a first M^{2+} -coordinating group and a second M^{2+} -coordinating group, wherein the first M^{2+} -coordinating group is separated from the second M^{2+} -coordinating group by 3 or 4 bond lengths. Most suitably, the M^{2+} -sequestering agent comprises a first M^{2+} -coordinating group and a second M^{2+} -coordinating group, wherein the first M^{2+} -coordinating group is separated from the second M^{2+} -coordinating group by 3 bond lengths. This particular embodiment is outlined below, using compound 24 (i.e., oxalic acid) as an exemplary M^{2+} -sequestering agent (i.e., activator).



Highlighting the separation of a first and second M^{2+} -coordinating group within a M^{2+} sequestering agent by 3 bond lengths

[0039] The activator may have a pK_a of -3 to 3 in water. Suitably, the activator has a pK_a of -3 to 2 in water. Most suitably, the activator has a pK_a of -2.8 to 1.5 in water. It will be understood that the pK_a values described herein refer to the dissociation of a first proton in the activator (i.e., pK_{a1}).

[0040] The activator may be a mono-carboxylic acid, a di-carboxylic acid, a tri-carboxylic acid, a tetra-carboxylic acid, a penta-carboxylic acid, a hexa-carboxylic acid, a dione compound comprising 2-6 carbon atoms, or an SO_3 -Lewis base adduct. Suitably, the activator is a mono-carboxylic acid, a di-carboxylic acid, a tetra-carboxylic acid, a dione-dihydroxy compound comprising 3-5 carbon atoms, a nitrogen-containing SO_3 -Lewis base adduct, or an oxygen-containing SO_3 -Lewis base adduct.

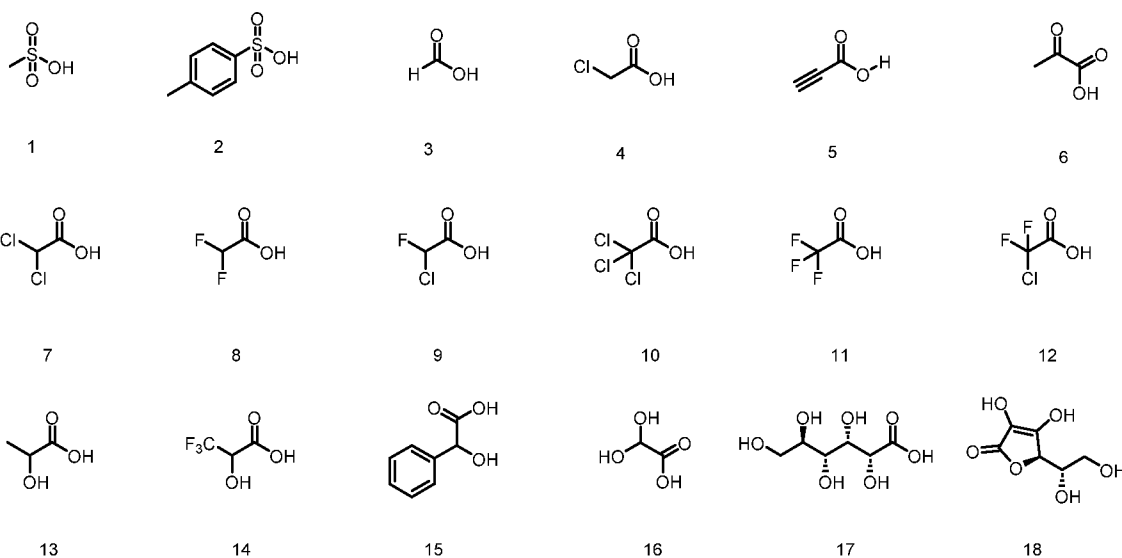
[0041] In particular embodiments, the activator has a pK_a of -3 to 3 in water and the activator is a mono-carboxylic acid, a di-carboxylic acid, a tetra-carboxylic acid, a dione-dihydroxy compound comprising 3-5 carbon atoms, a nitrogen-containing SO_3 -Lewis base adduct, or an oxygen-containing SO_3 -Lewis base adduct.

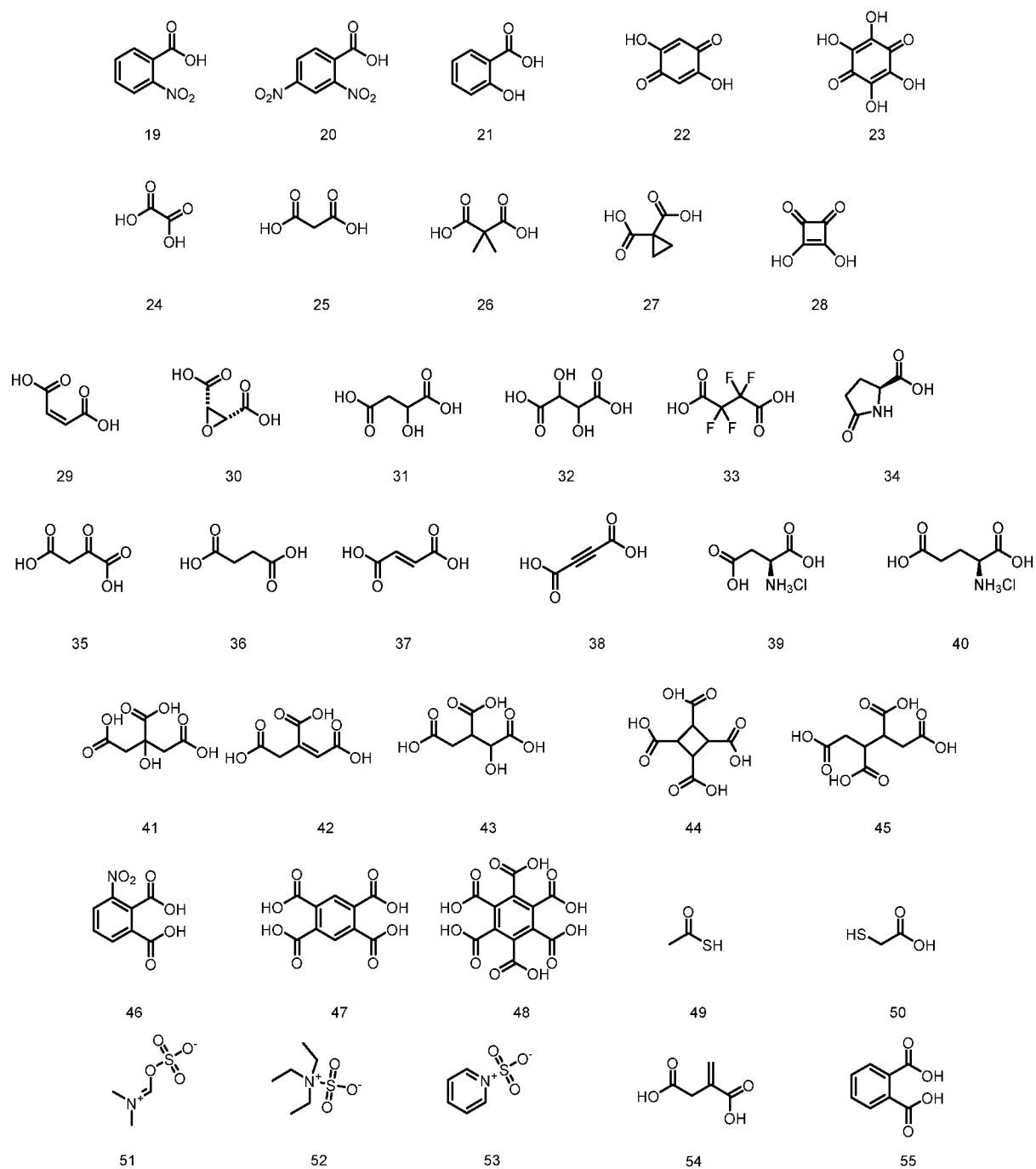
[0042] The inventors have found that activators with water solubilities of 0.05 mol/L or less are unable to form a fluorochemical according to the processes defined herein. Suitably, the activator has a water solubility of greater than 0.10 mol/L. More suitably, the activator has a water solubility of greater than 0.15 mol/L. More suitably, the activator has a water solubility of greater than 0.19 mol/L. Even more suitably, the activator has a water solubility of greater than 0.50 mol/L. Yet still more suitably, the activator has a water solubility of greater than 0.75 mol/L. Yet still even more suitably, the activator has a water solubility of greater than 1.00 mol/L. Most suitably, the activator has a water solubility of greater than 1.25 mol/L. The water solubility values described herein are determined by mixing (at 1000 rpm) a molar quantity of the activator in 1 mL distilled water for 1h at 20 °C. Following mixing, the molar quantity of the activator remaining (i.e., not dissolved) is determined and the solubility in water of the activator is calculated accordingly.

[0043] In particular embodiments, the activator has a pK_a of -3 to 3 in water and a water solubility of greater than 0.10 mol/L. In particular embodiments, the activator has a pK_a of -3 to 2 in water and a water solubility of greater than 0.19 mol/L.

[0044] In particular embodiments, the activator has a pK_a of -3 to 3 in water and a water solubility of greater than 1.00 mol/L. In particular embodiments, the activator has a pK_a of -3 to 2 in water and a water solubility of greater than 1.25 mol/L.

[0045] The activator may be selected from any one of the following compounds 1-55:



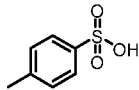


or a salt thereof.

[0046] The activator may be selected from any one of the following compounds 1-56:



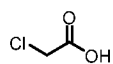
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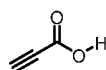
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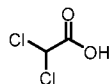
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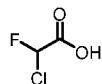
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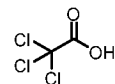
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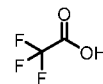
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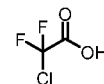
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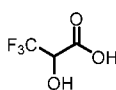
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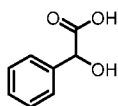
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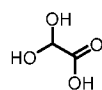
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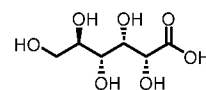
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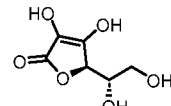
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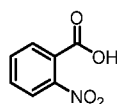
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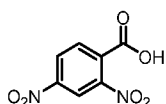
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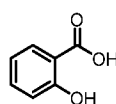
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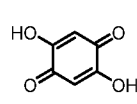
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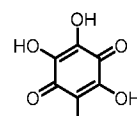
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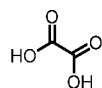
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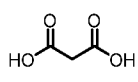
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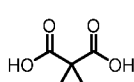
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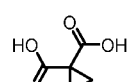
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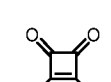
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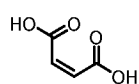
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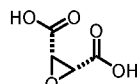
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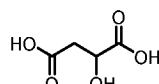
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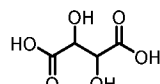
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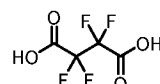
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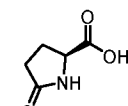
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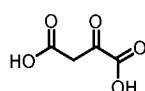
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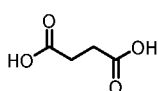
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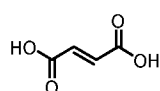
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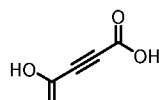
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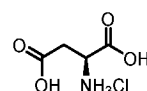
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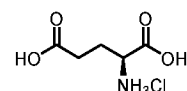
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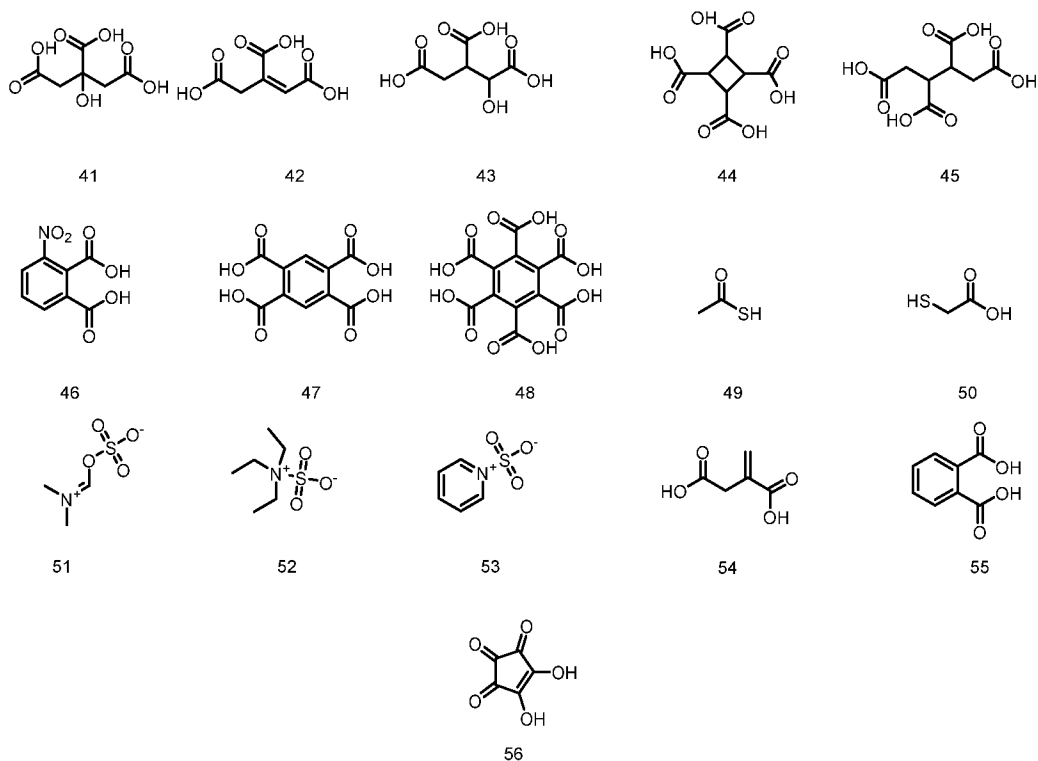
38



39

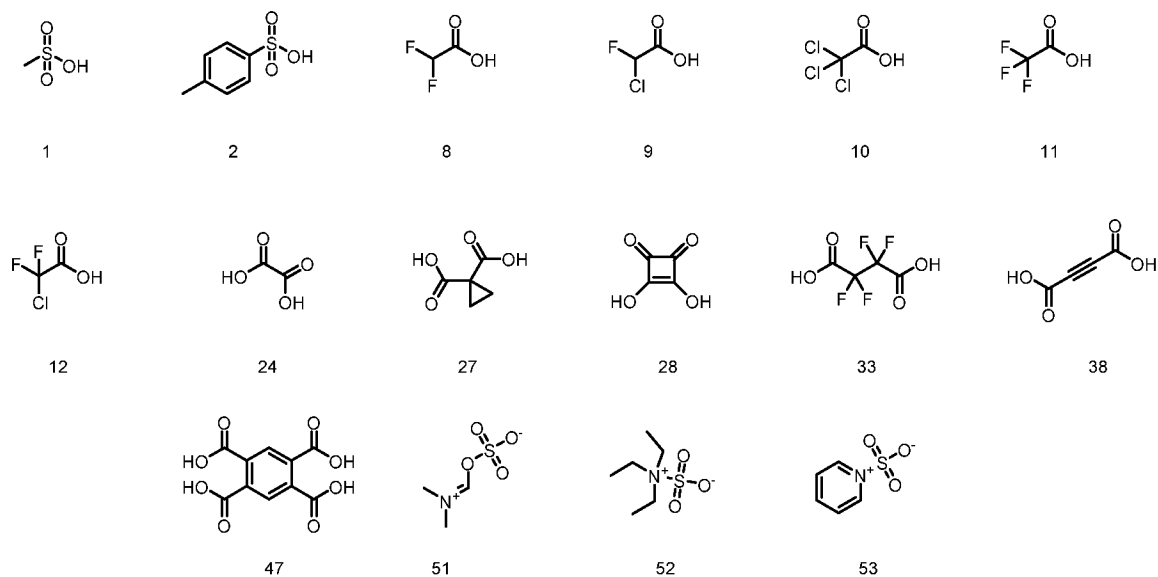


40



or a salt thereof.

[0047] Suitably, the activator is selected from any one of the following compounds 1, 2, 8-12, 24, 27, 28, 33, 38, 47 or 51-53:

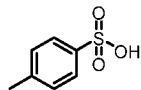


or a salt thereof.

[0048] Suitably, the activator is selected from any one of the following compounds 1, 2, 8-12, 24, 27, 28, 33, 38, 47, 51-53 or 56:



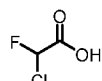
1



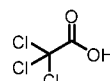
2



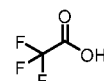
8



9



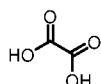
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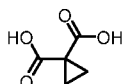
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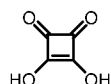
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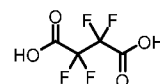
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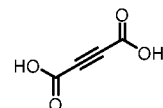
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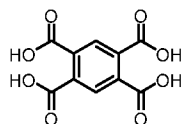
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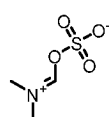
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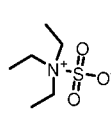
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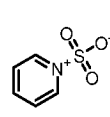
47



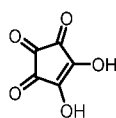
51



52



53



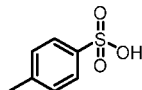
56

or a salt thereof.

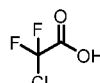
[0049] More suitably, the activator is selected from any one of the following compounds 1, 2, 12, 24, 28, 51 or 53:



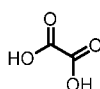
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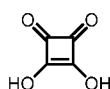
2



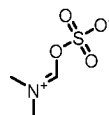
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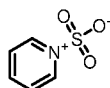
24



28



51



53

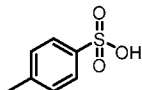
or a salt thereof.

[0050] More suitably, the activator is selected from any one of the following compounds 1, 2, 12, 24, 28, 51, 53 or 56:

13



1



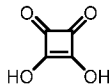
2



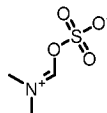
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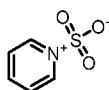
24



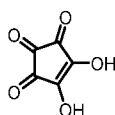
28



51



53



56

or a salt thereof.

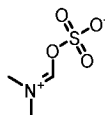
[0051] Even more suitably, the activator is selected from any one of the following compounds 1, 24 or 51:



1



24



51

or a salt thereof.

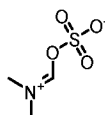
[0052] Even more suitably, the activator is selected from any one of the following compounds 1, 24, 51 or 56:



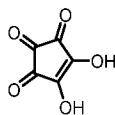
1



24



51



56

or a salt thereof.

[0053] Most suitably, the activator is compound 24 (i.e., oxalic acid):



or a salt thereof.

[0054] It will be understood that salts of activators mentioned herein are also embraced by the invention, and may include ammonium salts (e.g., NH_4^+ or TBA^+), group 1 salts (e.g., Li^+ , K^+ , Na^+ or Cs^+) and hydrates (e.g., dihydrates). The activator may therefore be oxalic acid, ammonium oxalate, tetra butyl ammonium oxalate, lithium oxalate, potassium oxalate, sodium oxalate, cesium oxalate or oxalic acid dihydrate, for example.

[0055] Suitably, the activator is oxalic acid dihydrate.

[0056] The inorganic fluoride source may be CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$. Suitably, the inorganic fluoride source is CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$. Most suitably, the inorganic fluoride source is CaF_2 (e.g., CaF_2 sludge, fluor spar, metspar or acidspar, of which acidspar is typically used).

[0057] In particular embodiments, the activator is selected from any one of compounds 1-55 described herein, or a salt thereof, and the inorganic fluoride source is CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$. In particular embodiments, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51 or 53 described herein, or a salt thereof, and the inorganic fluoride source is CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0058] In particular embodiments, the activator is selected from any one of compounds 1-56 described herein, or a salt thereof, and the inorganic fluoride source is CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$. In particular embodiments, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51, 53 or 56 described herein, or a salt thereof, and the inorganic fluoride source is CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0059] The fluoride acceptor can bind to fluoride (i.e., F^-) from the inorganic fluoride source, thereby forming a fluorochemical. As used herein, the term fluorochemical denotes a fluorine-containing compound that is not the inorganic fluoride source. The fluorochemical may be used in a variety of industrial applications. For example, it may be that the fluorochemicals formed as part of the present invention are used directly as a fluorinating reagent to introduce fluorine into organic molecules, or further transformed to afford alternative types of fluorine-containing compounds, some of which may also be useful as fluorinating reagents (e.g., for the Halex reaction). The fluorochemicals may alternatively be used as ionic liquids.

[0060] The fluoride acceptor may be:

a hydroxide of B, Si, Ge, Al, Sb, Ti;

an oxide of B, Si, Ge, Al, P, Sb, Ti;

an alkoxide of B, Si, Ge, Al, Sb, Ti; or

a halide or pseudohalide of B, Si, S, Ge, Al, Sb, Ti, Sn.

[0061] Suitably, the fluoride acceptor is:

a hydroxide of B;

an oxide of B, Si, Ge, Al, P, Sb, Ti; or

a halide or pseudohalide of Si, S or Sb.

[0062] In particular embodiments, the fluoride acceptor is a hydroxide of B, Si, Ge, Al, Sb, Ti; an oxide of B, Si, Ge, Al, P, Sb, Ti; an alkoxide of B, Si, Ge, Al, Sb, Ti; or a halide or pseudohalide of B, Si, S, Ge, Al, Sb, Ti, Sn and the inorganic fluoride source is CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0063] In particular embodiments, the fluoride acceptor is: a hydroxide of B; an oxide of B, Si, Ge, Al, P, Sb, Ti; or a halide or pseudohalide of Si, S or Sb and the inorganic fluoride source is CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0064] In particular embodiments, the activator is selected from any one of compounds 1-55 described herein, or a salt thereof, and the fluoride acceptor is a hydroxide of B, Si, Ge, Al, Sb, Ti; an oxide of B, Si, Ge, Al, P, Sb, Ti; an alkoxide of B, Si, Ge, Al, Sb, Ti; or a halide or pseudohalide of B, Si, S, Ge, Al, Sb, Ti, Sn. In this embodiment, the inorganic fluoride source may be CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0065] In particular embodiments, the activator is selected from any one of compounds 1-56 described herein, or a salt thereof, and the fluoride acceptor is a hydroxide of B, Si, Ge, Al, Sb, Ti; an oxide of B, Si, Ge, Al, P, Sb, Ti; an alkoxide of B, Si, Ge, Al, Sb, Ti; or a halide or pseudohalide of B, Si, S, Ge, Al, Sb, Ti, Sn. In this embodiment, the inorganic fluoride source may be CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0066] In particular embodiments, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51 or 53 described herein, or a salt thereof, and the fluoride acceptor is: a hydroxide of B; an oxide of B, Si, Ge, Al, P, Sb, Ti; or a halide or pseudohalide of Si, S or Sb. In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0067] In particular embodiments, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51, 53 or 56 described herein, or a salt thereof, and the fluoride acceptor is: a hydroxide of B; an oxide of B, Si, Ge, Al, P, Sb, Ti; or a halide or pseudohalide of Si, S or Sb. In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0068] The fluoride acceptor may be a hydroxide of B. In this context, the fluoride acceptor may be $B(OH)_3$ (i.e., orthoboric acid), $B(OH)_2R$, $B(OH)R_2$ (wherein each R is independently (1-6C)alkyl, aryl or heteroaryl, wherein any alkyl is optionally substituted with one or more halo, hydroxide, oxo, amino, amido, thiol or phosphate groups, and wherein any aryl or heteroaryl is optionally substituted with one or more (1-3C)alkyl, halo, hydroxide, oxo, amino, amido, thiol or phosphate groups), $(BOH)_3O_3$ (i.e., metaboric acid) or $H_2B_4O_7$ (i.e., tetraboric acid). Suitably, the fluoride acceptor is $B(OH)_3$, $B(OH)_2R$, $B(OH)R_2$ (wherein each R is independently (1-4C)alkyl, aryl or heteroaryl, wherein any aryl or heteroaryl is optionally substituted with one or more halo or hydroxide groups), $(BOH)_3O_3$ or $H_2B_4O_7$. More suitably, the fluoride acceptor is selected from $B(OH)_3$, $B(OH)_2R$ (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), $(BOH)_3O_3$ or $H_2B_4O_7$. Even more suitably, the fluoride acceptor is selected from $B(OH)_3$, $B(OH)_2R$ (wherein each R is independently phenyl optionally substituted with one or more fluoro) or $H_2B_4O_7$. Most suitably, the fluoride acceptor is $B(OH)_3$ or 4-fluorophenyl- $B(OH)_2$.

[0069] The fluoride acceptor may be an oxide of B, Si, Ge, Al, P, Sb, Ti. In this context, the fluoride acceptor may be selected from B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , P_2O_5 , Sb_2O_5 , TiO_2 , Ti_2O_3 , TiO , SnO_2 or Sb_2O_3 . Suitably, the fluoride acceptor is selected from B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 or Sb_2O_5 .

[0070] The fluoride acceptor may be a halide or pseudohalide of Si, S or Sb. In this context, the fluoride acceptor may be selected from R_3SiX , R_2SiX_2 , $RSiX_3$, SiX_4 , RSO_2Cl (wherein each X is independently Cl, Br, I, OH, OR or $OSiR_3$; and wherein each R is independently (1-6C)alkyl, aryl or heteroaryl, wherein any alkyl is optionally substituted with one or more halo, hydroxide, oxo, amino, amido, thiol or phosphate groups, and wherein any aryl or heteroaryl is optionally substituted with one or more (1-3C)alkyl, halo, hydroxide, oxo, amino, amido, thiol or phosphate groups), $SbCl_5$, or $SbCl_3$. Suitably, the fluoride acceptor is selected from R_3SiX , R_2SiX_2 , $RSiX_3$, SiX_4 , RSO_2Cl (wherein each X is independently Cl, Br or OH; and wherein each R is independently (1-4C)alkyl, aryl or heteroaryl, wherein any aryl or heteroaryl is optionally substituted with one or more methyl, ethyl, halo or hydroxide groups), $SbCl_5$, or $SbCl_3$. More suitably, the fluoride acceptor is selected from R_3SiCl , $SiCl_4$, RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), $SbCl_5$ or $SbCl_3$. Even more suitably, the fluoride acceptor is selected from R_3SiCl , $SiCl_4$, RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more fluoro groups) or $SbCl_5$. Most suitably, the fluoride acceptor is selected from Ph_3SiCl , $SiCl_4$ or *p*- $TolSO_2Cl$.

[0071] Thus, the fluoride acceptor may be $B(OH)_3$, $B(OH)_2R$, $B(OH)R_2$, R_3SiX , R_2SiX_2 , $RSiX_3$, SiX_4 , RSO_2X (wherein each X is independently Cl, Br, I, OH, OR or $OSiR_3$; and wherein

each R is independently (1-6C)alkyl, aryl or heteroaryl, wherein any alkyl is optionally substituted with one or more halo, hydroxide, oxo, amino, amido, thiol or phosphate groups, and wherein any aryl or heteroaryl is optionally substituted with one or more (1-3C)alkyl, halo, hydroxide, oxo, amino, amido, thiol or phosphate groups groups), (BOH)₃O₃, H₂B₄O₇, B₂O₃, SiO₂, GeO₂, Al₂O₃, P₂O₅, Sb₂O₅, TiO₂, Ti₂O₃, TiO, SnO₂, Sb₂O₃, SbCl₅ or SbCl₃. Suitably, the fluoride acceptor is B(OH)₃, B(OH)₂R, B(OH)R₂, R₃SiX, R₂SiX₂, RSiX₃, SiX₄, RSO₂X (wherein each X is independently Cl, Br or OH; and wherein each R is independently (1-4C)alkyl, aryl or heteroaryl, wherein any aryl or heteroaryl is optionally substituted with one or more methyl, ethyl, halo or hydroxide groups), (BOH)₃O₃, H₂B₄O₇, B₂O₃, SiO₂, GeO₂, Al₂O₃, P₂O₅, Sb₂O₅, TiO₂, Ti₂O₃, TiO, SnO₂, Sb₂O₃, SbCl₅ or SbCl₃. More suitably, the fluoride acceptor is B(OH)₃, B(OH)₂R, R₃SiCl, SiCl₄, RSO₂Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), (BOH)₃O₃, H₂B₄O₇, B₂O₃, SiO₂, GeO₂, Al₂O₃, Sb₂O₅ or SbCl₅. Even more suitably, the fluoride acceptor is B(OH)₃, B(OH)₂R, R₃SiCl, SiCl₄, RSO₂Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more fluoro), H₂B₄O₇, B₂O₃, SiO₂, GeO₂, Al₂O₃, Sb₂O₅ or SbCl₅. Yet even more suitably, the fluoride acceptor is selected from B(OH)₃, 4-fluorophenyl-B(OH)₂, B₂O₃, SiO₂, Ph₃SiCl, SiCl₄, *p*-TolSO₂Cl, GeO₂ or Al₂O₃. Yet still even more suitably, the fluoride acceptor is selected from B(OH)₃, SiO₂, SiCl₄ or *p*-TolSO₂Cl. Most suitably, the fluoride acceptor is B(OH)₃.

[0072] In particular embodiments, the activator has a pK_a of -3 to 3 in water and a water solubility of greater than 0.10 mol/L, and the fluoride acceptor is selected from B(OH)₃, 4-fluorophenyl-B(OH)₂, B₂O₃, SiO₂, Ph₃SiCl, SiCl₄, *p*-TolSO₂Cl, GeO₂ or Al₂O₃. Suitably, the water solubility is greater than 0.19 mol/L.

[0073] In particular embodiments, the activator has a pK_a of -3 to 3 in water and a water solubility of greater than 0.75 mol/L, and the fluoride acceptor is selected from B(OH)₃, 4-fluorophenyl-B(OH)₂, B₂O₃, SiO₂, Ph₃SiCl, SiCl₄, *p*-TolSO₂Cl, GeO₂ or Al₂O₃. Suitably, the water solubility is greater than 1.0 mol/L.

[0074] In particular embodiments, the activator is selected from any one of compounds 1-55 described herein, or a salt thereof, and the fluoride acceptor is selected from B(OH)₃, 4-fluorophenyl-B(OH)₂, B₂O₃, SiO₂, Ph₃SiCl, SiCl₄, *p*-TolSO₂Cl, GeO₂ or Al₂O₃. In this embodiment, the inorganic fluoride source may be CaF₂, MgF₂, BaF₂, SrF₂ or Ca₅(PO₄)₃F.

[0075] In particular embodiments, the activator is selected from any one of compounds 1-56 described herein, or a salt thereof, and the fluoride acceptor is selected from B(OH)₃, 4-fluorophenyl-B(OH)₂, B₂O₃, SiO₂, Ph₃SiCl, SiCl₄, *p*-TolSO₂Cl, GeO₂ or Al₂O₃. In this embodiment, the inorganic fluoride source may be CaF₂, MgF₂, BaF₂, SrF₂ or Ca₅(PO₄)₃F.

[0076] In particular embodiments, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51 or 53 described herein, or a salt thereof, and the fluoride acceptor is B(OH)_3 , SiO_2 , SiCl_4 or $p\text{-TolSO}_2\text{Cl}$. In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0077] In particular embodiments, the activator is selected from any one of compounds 1, 2, 12, 24, 28, 51, 53 or 56 described herein, or a salt thereof, and the fluoride acceptor is B(OH)_3 , SiO_2 , SiCl_4 or $p\text{-TolSO}_2\text{Cl}$. In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0078] In particular embodiments, the activator is selected from any one of compounds 1, 24 or 51 described herein, or a salt thereof, and the fluoride acceptor is B(OH)_3 . In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0079] In particular embodiments, the activator is selected from any one of compounds 1, 24, 51 or 56 described herein, or a salt thereof, and the fluoride acceptor is B(OH)_3 . In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0080] In particular embodiments, the activator is compound 24 (i.e., oxalic acid) described herein, or a salt thereof, and the fluoride acceptor is selected from B(OH)_3 , 4-fluorophenyl- B(OH)_2 , B_2O_3 , SiO_2 , Ph_3SiCl , SiCl_4 , $p\text{-TolSO}_2\text{Cl}$, GeO_2 or Al_2O_3 . In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0081] In particular embodiments, the activator is compound 24 (i.e., oxalic acid) described herein, or a salt thereof, and the fluoride acceptor is B(OH)_3 . In this embodiment, the inorganic fluoride source may be CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

[0082] Step a) of the present invention involves mixing together an inorganic fluoride source, an activator and a fluoride acceptor. The reagents in this step may be added at any time and in any order during mixing. For example, it may be that the reagents are added at the same time (e.g., concurrently). Alternatively, it may be that the reagents are added separately (e.g., consecutively). For example, the activator and fluoride acceptor may be mixed together before addition of the inorganic fluoride source. In such instances, it may be that the activator and the fluoride acceptor form an activator-acceptor complex before addition of the inorganic fluoride source. By way of illustration, compound 24 (i.e., oxalic acid) as activator and B(OH)_3 as fluoride acceptor may be mixed together to form bis(oxalate)boric acid prior to addition of the inorganic fluoride source. The activator-acceptor complex may be isolated before being mixed with the inorganic fluoride source.

[0083] It will be understood that the term fluoride acceptor will include salts thereof. Salts of the fluoride acceptor may include group 1 salts (e.g., Li^+ , K^+ , Na^+ or Cs^+). For example, tetraboric acid may be present as potassium tetraborate or borax ($\text{Na}_2[\text{B}_4\text{O}_5(\text{OH})_4] \cdot 8\text{H}_2\text{O}$).

[0084] As discussed hereinbefore, the fluoride acceptor can bind to fluoride from the inorganic fluoride source, thereby forming a fluorochemical. Therefore, in embodiments wherein the inorganic fluoride source is an ionic compound comprising M^{2+} and F^- , the fluoride acceptor binds to F^- , forming a fluorochemical. The fluorochemical may have a solvent (discussed herein) solubility greater than the inorganic fluoride source.

[0085] In embodiments wherein the inorganic fluoride source is an ionic compound comprising M^{2+} and F^- , the activator can be an M^{2+} -sequestering agent and can bind to M^{2+} from the inorganic fluoride source, thereby forming an activator- M^{2+} complex.

[0086] Suitably, the fluorochemical has a solvent solubility greater than the activator- M^{2+} complex.

[0087] Suitably, the activator- M^{2+} complex is insoluble in solvents that dissolve the fluorochemical, thereby allowing the latter to be readily purified, if required, by solvent extraction and/or filtration. Thus, the process of the present invention may comprise step b) isolating the fluorochemical resulting from step a) by solvent extraction and/or filtration.

[0088] Step a) may be conducted in the presence of a solvent (e.g., an organic solvent). Suitably, the solvent comprises water (e.g., H_2O or D_2O), ethylene glycol, dimethylformamide, dimethylsulfoxide, acetonitrile, acetone, pentane, hexane, toluene, xylene, methanol, ethanol, propanol and/or butanol. More suitably, the solvent comprises water, methanol and/or ethanol. Even more suitably, the solvent comprises water, a water:methanol mixture (e.g., 1:1) or a water:ethanol mixture (e.g., 1:1). Yet still even more suitably, the solvent comprises water. Most suitably, the solvent consists of / consists essentially of water.

[0089] Step a) may be conducted at a temperature of 0 °C to 100 °C. Suitably, step a) is conducted at a temperature of 20 °C to 90 °C. More suitably, step a) is conducted at a temperature of 23 °C to 80 °C. Yet more suitably, step a) is conducted at a temperature of 50 °C to 80 °C.

[0090] The ratio of equivalents of inorganic fluoride source : activator : fluoride acceptor may be from 1 : 1 : 4 to 4 : 4 : 1. Suitably, the ratio of equivalents of inorganic fluoride source : activator : fluoride acceptor is from 1 : 1 : 3 to 3 : 3 : 1. Suitably, the ratio of equivalents of inorganic fluoride source : activator : fluoride acceptor is from 1 : 1 : 2 to 2.5 : 2.5 : 1.

[0091] As described hereinbefore, in a seventh aspect of the present invention there is provided a fluorochemical obtained, directly obtained or obtainable by the process of any one of the first, second, third, fourth, fifth or sixth aspects of the present invention.

[0092] The following numbered statements 1 to 70 are not claims, but instead describe particular aspects and embodiments of the invention:

1. A process for the preparation of a fluorochemical, the process comprising the step of:
a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein the activator is an organic compound having a pK_a of -4 to 4.2 in water, and a water solubility of greater than 0.05 mol/L; and the fluoride acceptor is a hydroxide, an oxide, an alkoxide, a halide or a pseudohalide of B, Si, Ge, Al, P, Sb, Ti, S or Sn.
2. The process of statement 1, wherein the inorganic fluoride source has a lattice energy of 1500 kJ/mol or greater.
3. The process of statement 1 or 2, wherein the inorganic fluoride source has a lattice energy of 2000 kJ/mol or greater.
4. The process of statement 1, 2 or 3, wherein the inorganic fluoride source has a lattice energy of 2300 kJ/mol or greater.
5. The process of any one of the preceding statements, wherein the inorganic fluoride source is an ionic compound.
6. The process of any one of the preceding statements, wherein the inorganic fluoride source is an ionic compound comprising M^{2+} and F^- , wherein M^{2+} is an alkaline earth metal cation (i.e., a group II metal cation).
7. The process of statement 6, wherein M^{2+} is Be^{2+} , Mg^{2+} , Ca^{2+} , Sr^{2+} or Ba^{2+} .
8. The process of any one of statements 6 or 7, wherein M^{2+} is Mg^{2+} , Ca^{2+} , Sr^{2+} or Ba^{2+} .
9. The process of any one of statements 6, 7 or 8, wherein M^{2+} is Ca^{2+} .

10. The process of any one of statements 6-9, wherein the activator is an M^{2+} -sequestering agent.
11. The process of statement 10, wherein the M^{2+} -sequestering agent comprises one or more M^{2+} -coordinating groups.
12. The process of any one of statements 10 or 11, wherein the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups.
13. The process of any one of statements 11 or 12, wherein each M^{2+} coordinating group is independently an oxygen-containing M^{2+} -coordinating group, a nitrogen-containing M^{2+} -coordinating group or a sulfur-containing M^{2+} -coordinating group.
14. The process of any one of statements 11, 12 or 13, wherein each M^{2+} coordinating group is an oxygen-containing M^{2+} -coordinating group.
15. The process of any one of statements 13 or 14, wherein the oxygen-containing M^{2+} coordinating group is a hydroxy group or an oxo group.
16. The process of any one of statements 10-14, wherein the M^{2+} -sequestering agent comprises two hydroxy M^{2+} -coordinating groups.
17. The process of statement 13, wherein the nitrogen-containing M^{2+} coordinating group is an amino group.
18. The process of statement 13, wherein the sulfur-containing M^{2+} coordinating group is a thiol group.
19. The process of any one of statements 10-18, wherein the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups and the M^{2+} -sequestering agent forms a chelate with M^{2+} .

20. The process of any one of statements 10-19, wherein the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups and the M^{2+} -sequestering agent forms a 5-, 6- or 7-membered chelate with M^{2+} .
21. The process of any one of statements 10-20, wherein the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups and the M^{2+} -sequestering agent forms a 5- or 6-membered chelate with M^{2+} .
22. The process of any one of statements 10-21, wherein the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups and the M^{2+} -sequestering agent forms a 5-membered chelate with M^{2+} .
23. The process of any one of the preceding statements, wherein the activator has a pK_a of -3 to 3 in water.
24. The process of any one of the preceding statements, wherein the activator has a pK_a of -3 to 2 in water.
25. The process of any one of the preceding statements, wherein the activator has a pK_a of -2.8 to 1.5 in water.
26. The process of any one of the preceding statements, wherein the activator is a mono-carboxylic acid, a di-carboxylic acid, a tri-carboxylic acid, a tetra-carboxylic acid, a penta-carboxylic acid, a hexa-carboxylic acid, a dione compound comprising 2-6 carbon atoms, or an SO_3 -Lewis base adduct.
27. The process of any one of the preceding statements, wherein the activator is a mono-carboxylic acid, a di-carboxylic acid, a tetra-carboxylic acid, a dione-dihydroxy compound comprising 3-5 carbon atoms, a nitrogen-containing SO_3 -Lewis base adduct, or an oxygen-containing SO_3 -Lewis base adduct.

28. The process of any one of the preceding statements, wherein the activator has a water solubility of greater than 0.10 mol/L.
29. The process of any one of the preceding statements, wherein the activator has a water solubility of greater than 0.15 mol/L.
30. The process of any one of the preceding statements, wherein the activator has a water solubility of greater than 0.19 mol/L.
31. The process of any one of the preceding statements, wherein the activator has a water solubility of greater than 0.50 mol/L.
32. The process of any one of the preceding statements, wherein the activator has a water solubility of greater than 0.75 mol/L.
33. The process of any one of the preceding statements, wherein the activator has a water solubility of greater than 1.00 mol/L.
34. The process of any one of the preceding statements, wherein the activator has a water solubility of greater than 1.25 mol/L.
35. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1-55 described herein, or a salt thereof.
36. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1, 2, 8-12, 24, 27, 28, 33, 38, 47 or 51-53 described herein, or a salt thereof.
37. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1, 2, 12, 24, 28, 51 or 53 described herein, or a salt thereof.

38. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1, 24 or 51 described herein, or a salt thereof.

39. The process of any one of the preceding statements, wherein the activator is compound 24 (i.e., oxalic acid) described herein, or a salt thereof.

40. The process of any one of the preceding statements, wherein the inorganic fluoride source is CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

41. The process of any one of the preceding statements, wherein the inorganic fluoride source is CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

42. The process of any one of the preceding statements, wherein the inorganic fluoride source is CaF_2 .

43. The process of any one of the preceding statements, wherein the fluoride acceptor is:

a hydroxide of B, Si, Ge, Al, Sb, Ti;

an oxide of B, Si, Ge, Al, P, Sb, Ti;

an alkoxide of B, Si, Ge, Al, Sb, Ti; or

a halide or pseudohalide of B, Si, S, Ge, Al, Sb, Ti, Sn.

44. The process of any one of the preceding statements, wherein the fluoride acceptor is:

a hydroxide of B;

an oxide of B, Si, Ge, Al, P, Sb, Ti; or

a halide or pseudohalide of Si, S or Sb.

45. The process of any one of the preceding statements, wherein the fluoride acceptor is $\text{B}(\text{OH})_3$, $\text{B}(\text{OH})_2\text{R}$, $\text{B}(\text{OH})\text{R}_2$, R_3SiX , R_2SiX_2 , RSiX_3 , SiX_4 , RSO_2X (wherein each X is

independently Cl, Br, I, OH, OR or OsiR_3 ; and wherein each R is independently (1-6C)alkyl, aryl or heteroaryl, wherein any alkyl is optionally substituted with one or more halo, hydroxide, oxo, amino, amido, thiol or phosphate groups, and wherein any aryl or heteroaryl is optionally substituted with one or more (1-3C)alkyl, halo, hydroxide, oxo, amino, amido, thiol or phosphate groups groups), $(\text{BOH})_3\text{O}_3$, $\text{H}_2\text{B}_4\text{O}_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , P_2O_5 , Sb_2O_5 , TiO_2 , Ti_2O_3 , TiO , SnO_2 , Sb_2O_3 , SbCl_5 or SbCl_3 .

46. The process of any one of the preceding statements, wherein the fluoride acceptor is $\text{B}(\text{OH})_3$, $\text{B}(\text{OH})_2\text{R}$, $\text{B}(\text{OH})\text{R}_2$, R_3SiX , R_2SiX_2 , RSiX_3 , SiX_4 , RSO_2X (wherein each X is independently Cl, Br or OH; and wherein each R is independently (1-4C)alkyl, aryl or heteroaryl, wherein any aryl or heteroaryl is optionally substituted with one or more methyl, ethyl, halo or hydroxide groups), $(\text{BOH})_3\text{O}_3$, $\text{H}_2\text{B}_4\text{O}_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , P_2O_5 , Sb_2O_5 , TiO_2 , Ti_2O_3 , TiO , SnO_2 , Sb_2O_3 , SbCl_5 or SbCl_3 .

47. The process of any one of the preceding statements, wherein the fluoride acceptor is $\text{B}(\text{OH})_3$, $\text{B}(\text{OH})_2\text{R}$, R_3SiCl , SiCl_4 , RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), $(\text{BOH})_3\text{O}_3$, $\text{H}_2\text{B}_4\text{O}_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , Sb_2O_5 or SbCl_5 .

48. The process of any one of the preceding statements, wherein the fluoride acceptor is $\text{B}(\text{OH})_3$, $\text{B}(\text{OH})_2\text{R}$, R_3SiCl , SiCl_4 , RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more fluoro), $\text{H}_2\text{B}_4\text{O}_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , Sb_2O_5 or SbCl_5 .

49. The process of any one of the preceding statements, wherein the fluoride acceptor is selected from $\text{B}(\text{OH})_3$, 4-fluorophenyl- $\text{B}(\text{OH})_2$, B_2O_3 , SiO_2 , Ph_3SiCl , SiCl_4 , *p*- ToISO_2Cl , GeO_2 or Al_2O_3 .

50. The process of any one of the preceding statements, wherein the fluoride acceptor is selected from $\text{B}(\text{OH})_3$, SiO_2 , SiCl_4 or *p*- ToISO_2Cl .

51. The process of any one of the preceding statements, wherein the fluoride acceptor is $\text{B}(\text{OH})_3$.

52. The process of any one of the preceding statements further comprising step b) isolating the fluorochemical resulting from step a) by solvent extraction and/or filtration.

53. The process of any one of the preceding statements, wherein step a) is conducted in the presence of a solvent (e.g., an organic solvent).

54. The process of statement 53, wherein the solvent comprises water, ethylene glycol, dimethylformamide, dimethylsulfoxide, acetonitrile, acetone, pentane, hexane, toluene, xylene, methanol, ethanol, propanol and/or butanol.

55. The process of any one of statements 53 or 54, wherein the solvent comprises water (e.g., H₂O or D₂O), methanol and/or ethanol.

56. The process of any one of statements 53, 54 or 55, wherein the solvent comprises water, a water:methanol mixture (e.g., 1:1) or a water:ethanol mixture (e.g., 1:1).

57. The process of any one of statements 53-56, wherein the solvent comprises water.

58. The process of any one of statements 53-57, wherein the solvent consists of / consists essentially of water.

59. The process of any one of the preceding statements, wherein step a) is conducted at a temperature of 0 °C to 100 °C.

60. The process of any one of the preceding statements, wherein step a) is conducted at a temperature of 20 °C to 90 °C.

61. The process of any one of the preceding statements, wherein step a) is conducted at a temperature of 23 °C to 80 °C.

62. The process of any one of the preceding statements, wherein step a) is conducted at a temperature of 50 °C to 80 °C.
63. The process of any one of the preceding statements, wherein the ratio of equivalents of inorganic fluoride source : activator : fluoride acceptor is from 1 : 1 : 4 to 4 : 4 : 1.
64. The process of any one of the preceding statements, wherein the ratio of equivalents of inorganic fluoride source : activator : fluoride acceptor is from 1 : 1 : 3 to 3 : 3 : 1.
65. The process of any one of the preceding statements, wherein the ratio of equivalents of inorganic fluoride source : activator : fluoride acceptor is from 1 : 1 : 2 to 2.5 : 2.5 : 1.
66. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1-56 described herein, or a salt thereof.
67. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1, 2, 8-12, 24, 27, 28, 33, 38, 47, 51-53 or 56 described herein, or a salt thereof.
68. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1, 2, 12, 24, 28, 51, 53 or 56 described herein, or a salt thereof.
69. The process of any one of the preceding statements, wherein the activator is selected from any one of the compounds 1, 24, 51 or 56 described herein, or a salt thereof.
70. A fluorochemical obtained, directly obtained or obtainable by the process of any one of the preceding statements.

[0093] It will be understood that any one of numbered statements 2-70 may be applied *mutatis mutandis* to the second, third, fourth, fifth or sixth aspects of the present invention.

EXAMPLES

[0094] One or more examples of the invention will now be described, for the purpose of illustration only, with reference to the accompanying figures:

Fig. 1: tested activators in the activator screening;

Fig. 2: tested fluoride acceptors in the acceptor screening;

Fig. 3: applications of BF-containing compounds in organic chemistry;

Fig. 4: fluorine transfer to boronic acid with different activators;

Fig. 5: isolation of potassium tetrafluoroborate and fluoroarenes via tetrafluoroboric acid;

Fig. 6: fluorination with CaF_2 using a boronic acid (4-fluorophenyl-B(OH)₂);

Fig. 7: use of KF derived from CaF_2 in the Halex reaction;

Fig. 8: overview of accessible reagents via *in-situ* formation of H_2SiF_6 ;

Fig. 9: transfer of fluorine to organic silicon species;

Fig. 10: investigation of other inorganic fluoride sources as well as reaction conditions;

Fig. 11. **a.** Screening of Brønsted acids for cooperative activation of acid grade fluorspar (AGF) with B(OH)_3 (2.0 mmol) at 50 °C in water; yields of HBF_4 and HBF_3OH determined by ^{19}F NMR spectroscopy. Yields for HCl and H_2SO_4 slightly differ from fig. 4 due to minor adjustments in reaction conditions. **b.** Preparation of HBF_4 from AGF, B(OH)_3 and $\text{H}_2\text{Ox}\cdot 2\text{H}_2\text{O}$ with ^{19}F NMR (D_2O) spectra of reaction mixture containing [B-F] products HBF_4 , HBF_3OH and HOxBF_2 . **c.** Preparation of KF, Me_4NF and $^n\text{Bu}_4\text{NF}$ from AGF, SiO_2 and $\text{H}_2\text{Ox}\cdot 2\text{H}_2\text{O}$ with ^{19}F NMR (D_2O) spectra of reaction mixture containing [Si-F] products H_2SiF_6 , $\text{H}_2\text{SiF}_5\text{OH}$ and H_2OxSiF_4 ; yields of H_2SiF_6 , $\text{H}_2\text{SiF}_5\text{OH}$ and H_2OxSiF_4 determined by ^{19}F NMR spectroscopy. **d.** Monitoring the reaction of AGF (0.5 mmol) with anhydrous H_2Ox with and without B(OH)_3 by ^{19}F NMR spectroscopy in D_2O (HF, HBF_4 and HBF_3OH % quantified by ^{19}F NMR spectroscopy);

Fig. 12. Powder X-ray diffraction patterns of insoluble by-product formed in the reaction of acid grade fluorspar (CaF_2) with H_2Ox and B(OH)_3 after 15 h at 50 °C (top), $\text{CaOx}\cdot\text{H}_2\text{O}$ (middle) and acid grade fluorspar (CaF_2) (bottom). All powder X-ray diffraction patterns recorded at room temperature;

Fig. 13. Powder X-ray diffraction patterns of K_2SiF_6 prepared via acid grade fluorspar and commercial K_2SiF_6 collected at room temperature;

Fig. 14. Reaction of acid grade fluorspar (CaF_2) with H_2Ox in D_2O at 50 °C monitored by ^{19}F NMR. Singlet diagnostic of HF observed at -166.0 ppm. Sodium triflate internal standard at -78.0 ppm;

Fig. 15. **a.** Fluoroarenes prepared via Balz-Schiemann reaction using AGF-derived HBF_4 or metspar-derived HBF_4 (yield of diazotization/dediazotization). Diazotization reactions were carried out with 5.0 mmol of aryl amine. Dediazotization reactions were carried out on 1.0 mmol scale unless otherwise stated. All yields are for isolated products (unless otherwise stated). **b.** Fluoroarenes prepared via halogen exchange ($\text{S}_{\text{N}}\text{Ar}$) of chloroarenes using AGF-derived $\text{KF} [\text{KF}]^{\text{AGF}}$ or metspar-derived $\text{KF} [\text{KF}]^{\text{M}}$ or fluorodenitration reactions of nitroarenes using AGF-derived $\text{Me}_4\text{NF} \cdot t\text{AmOH}$. All yields are for isolated products (1.0 mmol scale unless otherwise stated). **c.** Fluoroarenes prepared using AGF-derived HBF_4 for Balz-Schiemann reaction and AGF-derived $\text{Me}_4\text{NF} \cdot t\text{AmOH}$ for $\text{S}_{\text{N}}\text{Ar}$ reactions. AGF, acid grade fluorspar; M, metspar; MK, MAP-activated protein kinase. ^{19}F NMR yields using 4-fluoroanisole as internal standard.

Part A

Activator screening

[0095] In a 3.5 mL glass vial, acid grade fluorspar (97%, 33 mg, 0.42 mmol, 1.1 equiv.), a stock solution of $\text{B}(\text{OH})_3$ (11.9 mg in 0.5 mL H_2O , 0.19 mmol, 0.5 equiv.) and the activator (0.82 mmol, 2.0 equiv. for 'mono-acids', 0.41 mmol, 1.0 equiv. for 'di- and oligo-acids') were added. The mixture was stirred in a sand bath at 50 °C for 15 h. The suspension was allowed to settle and the total amount of solubilised fluoride was determined by ^1H NMR using NaOTf (1.0 mg, 5.9 μmol) as internal standard.

[0096] Data from the activator screening are found in figure 1, with fluoride yield expressed as a percentage.

[0097] The activators screened in figure 1 were assessed for their water solubility and pK_{a} . The water solubility of the activators was determined by mixing (at 1000 rpm) a molar quantity of the activator in 1 mL distilled water for 1h at 20 °C. Following mixing, the molar quantity of the activator remaining (i.e., not dissolved) is determined and the solubility in water of the activator is calculated accordingly. Activators which afforded at least a trace quantity of fluoride had a water solubility of greater than 0.05 mol/L and a pK_{a} value of -4 to 4.2. Activators which did not have a water solubility of greater than 0.05 mol/L and/or a pK_{a} value of -4 to 4.2 did not afford any fluoride.

Fluoride acceptor screening

[0098] In a 15 mL PP tube, acid grade fluorspar (97%, 33 mg, 0.42 mmol, 1.1 equiv.), a stock solution of oxalic acid (for oxides or alkoxides: 34.6 mg in 1.0 mL H₂O, 0.38 mmol, 1.0 equiv.) or ammonium oxalate (for halides or pseudohalides: 47.7 mg in 1.0 mL H₂O, 0.38 mmol, 1.0 equiv.) and the fluoride acceptor (0.05 – 0.38 mmol, 0.13 to 1.0 equiv.) were added. The mixture was stirred in a sand bath at 50 °C for 15 h. The suspension was allowed to settle and the total amount of solubilised fluoride was determined by ¹H NMR using NaOTf (1.0 mg, 5.9 μmol) as internal standard.

[0099] Data from the fluoride acceptor screening are found in figure 2, with fluoride yield expressed as a percentage.

[00100] From the data in figure 2, it was determined that hydroxides, oxides, alkoxides, halides and pseudohalides of B, Si, Ge, Al, P, Sb, Ti, S or Sn were the best performing fluoride acceptors.

Activator-Fluoride acceptor cross screening

[00101] In a 1.5 mL PP centrifuge tube, acid grade fluorspar (97%, 33 mg, 0.42 mmol, 1.1 equiv.), the activator (0.39 mmol, 1.0 equiv), the fluoride acceptor (0.5 equiv for B(OH)₃ and SiO₂, 0.4 equiv for Al₂O₃) and water (0.5 mL) were added. The mixture was stirred at 50 °C for 17 h, the precipitate was settled by centrifugation and the aqueous phase analysed by NMR using an internal standard (NaOTf, 1.0 mg).

[00102] Data from the activator-fluoride acceptor cross screening are found in table 1, with fluoride yield expressed as a percentage.

Table 1 activator-fluoride acceptor cross screening

Fluorspar (CaF ₂) + activator + acceptor $\xrightarrow{\text{H}_2\text{O}, 50\text{ }^\circ\text{C}, 15\text{ h}}$ Ca-activator acceptor-F			
acceptor activator	B(OH) ₃	SiO ₂	Al ₂ O ₃
oxalic acid	85%	quant.	50%
sulfuric acid	75%	85%	67%
squaric acid	32%	14%	29%
tartaric acid	7%	1%	16%
formic acid	1%	1%	20%

quant. refers to a yield of greater than or equal to 99%

[00103] Following determination of the best performing activators and fluoride acceptors, their uses in preparing a fluorochemical was investigated.

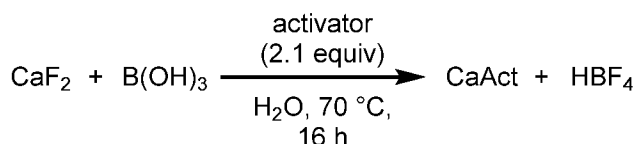
Boron-fluorine bond formation

[00104] The boron-fluorine bond plays a significant part in organic synthesis (see figure 3), *i.e.* as coupling partners (Molander salts), Lewis acids (BF_3), non-coordinating anions (BF_4^- for a large number of complexes or ionic liquids) or even as reagents for C-F bond forming reactions (AgBF_4 , Balz-Schiemann reaction). To date, these species rely either directly or indirectly on the hydrofluoric acid supply chain.

[00105] The solubility of calcium salts using several activators was tested to promote the fluorination of boric acid to the tetrafluoroborate anion (table 2). Oxalic acid was found to achieve the highest yields under the reaction conditions surpassing sulfuric acid and hydrochloric acid in NMR yield (figure 4).

Table 2 solubilities in water of selected calcium salts. OX – oxalate, TA – tartrate, CIT – citrate.

Calcium salts	solubility /100 g H_2O	Calcium salts	solubility /100 g H_2O
CaF_2	1.6 mg	CaMoO_4	1.1 mg
$\text{Ca}_3(\text{PO}_4)_2$	0.12 mg	CaTA	40 mg
CaOX	0.61 mg	CaCIT	96 mg
CaCO_3	0.66 mg	CaSO_4	205 mg



[00106] The *in situ* formed fluoroboric acid solution can be filtered to remove the calcium precipitate and used directly for further reactions. Addition of a potassium salt and cooling the solution led to precipitation of potassium tetrafluoroborate which could be isolated in 69% from CaF_2 (figure 5a). Alternatively, its use in the Balz-Schiemann reaction was demonstrated in the synthesis of 2-fluorobiphenyl (figure 5b). Therein, the fluoroboric acid solution was treated with sodium nitrite and 2-aminobiphenyl at 0°C to precipitate the respective diazonium salt. Drying the salt and heat-promoted decomposition afforded the desired fluoroarene in 42% yield from 2-aminobiphenyl.

[00107] Moving beyond boric acid as activator, the use of boronic acids, such as 4-fluorophenyl-B(OH)₂, as fluoride acceptor was investigated. An unexpected product was formed containing only one fluorine bond that was identified as potassium fluorooxalateborate. At elevated temperature, both the fluorooxalateborate as well as the trifluoroborate were observed (figure 6).

Silicon-fluorine bond formation

[00108] While silicon-fluorine bonds themselves do not play a large role in organic synthesis, with the exception of the nucleophilic fluorinating reagent tetrabutylammonium difluorotriphenylsilicate (TBAT), their pH-dependant liability makes them ideal precursors to form fluorinating agents of everyday use such as KF, CsF, tetra-n-butylammonium fluoride (TBAF) and others. When investigating the formation of silicon fluorides in water with different activators, sulfuric acid afforded the highest yield, followed by oxalic acid. Following optimisation of concentration and stoichiometry, the conversion could be increased up to 99% as determined by ¹⁹F-NMR using oxalic acid as activator.

[00109] After filtration, alkaline hydrolysis successfully released the fluoride back into solution with the concomitant formation of silica. It was found that direct hydrolysis was also feasible. The resulting suspension of aqueous KF and insoluble silica was further filtered and dried to afford a source of potassium fluoride in yields ranging between 74 and 92% and a purity between 75% and 95% (table 3). Alternatively, direct evaporation of water led to a mixture of KF and silica which could also be used directly for several applications.

Table 3 Overview of yields and purities obtained from different stoichiometries

$$\text{CaF}_2 + \text{H}_2\text{Ox} \xrightarrow[\text{H}_2\text{O}, 80^\circ\text{C}, 7-15\text{ h}]{\text{SiO}_2} \left[\text{H}_2\text{SiF}_6 \right] \xrightarrow[\text{H}_2\text{O}, 60^\circ\text{C}, 7\text{ h}]{\text{KOH}} \text{KF}$$

entry	stoichiometry			limiting reagent	scale (CaF ₂)	yield (%)	purity (%)
	CaF ₂	H ₂ Ox	SiO ₂				
1	2.1	2.3	1	CaF ₂	500 mg	75	80
2	2.1	2.3	1	CaF ₂	10 g	92	75
3	1.6	1.4	1	H ₂ Ox	623 mg	74	95
4	2.4	2.2	1	H ₂ Ox	935 mg	89	91

[00110] The formed KF can be used as fluorinating agent for various reactions such as the synthesis of aryl fluorides using the Halex-reaction which was chosen as model reaction

(figure 7). Due to its requirement for rigorously dry conditions, the KF was heated with methanol, toluene and sulfolane to remove residual water. The subsequent Halex reaction afforded the product in a good yield 76% (NMR yield).

[00111] In addition to the conversion to KF, other fluorinating agents are also readily accessible *via* the hexafluorosilicate route. When cesium hydroxide was used for basic hydrolysis, cesium fluoride was obtained. Due to its lower lattice energy and higher solubility, cesium fluoride is often a preferred fluorine source especially for aryl fluorides.

[00112] Similarly, the highly versatile fluoride TBAF could be prepared upon reacting *in situ* formed H_2SiF_6 with a tetrabutylammonium hydroxide solution. Filtration and concentration gave a viscous liquid which could be purified by crystallisation as an alcohol complex (e.g., $\text{TBAF} \cdot 4t\text{BuOH}$). Alternatively, the TBAF-containing mixture could be used to prepare TBAT, another common non-hygroscopic fluoride source (figure 8).

[00113] Fluorine bonds could also be forged with organic silicon species as demonstrated with triphenylsilyl chloride (figure 9). The corresponding triphenylsilyl fluoride is the other component of the reagent TBAT which can therefore be prepared with both fluorides stemming directly from fluorspar.

Other inorganic fluoride sources and generality of reaction conditions

[00114] Apart from fluorspar, MgF_2 and BaF_2 can also be used. Fluorapatite is also a competent fluoride source (see figure 10).

[00115] Various reaction conditions were also investigated (see figure 10).

Synthetic procedures and analysis

Potassium fluoride KF_{CaF_2}

[00116] Fluorspar (acid grade 97%, 623.0 mg, 8.0 mmol, 0.6 equiv), silica gel (300.0 mg, 4.9 mmol, 0.37 equiv) and oxalic acid (628.6 mg, 7.0 mmol, 0.52 equiv) were weighed into a 50 mL Conical Sterile Polypropylene Centrifuge Tube. A stir bar and water (1.5 mL) were added and the mixture was heated under stirring in a sand bath at 70 °C for 15 h. The resulting suspension was cooled to ambient temperature, diluted with water (10 mL) and filtered with a Büchner funnel into a 50 mL PP tube. The solid and reaction tube were washed with water (2x 5 mL).

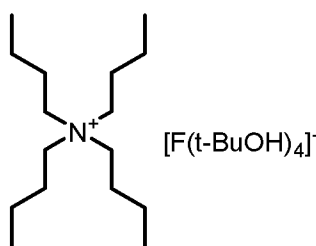
[00117] Subsequently, the filtrate was equipped with a stir bar and KOH was added portion-wise over 5 min (750.0 mg total, 13.4 mmol, 1.0 equiv). After the addition is complete, the tube

was heated in a sand bath at 70 °C for 6 h. The resulting suspension was filtered using a Büchner funnel to separate insoluble silica from the solution and washed with water (2 x 5 mL). The filtrate was concentrated under reduced pressure (50 mbar, 60 °C), then methanol was added (30 mL) and the suspension was concentrated to dryness. The solid was transferred into a glass vial and further dried under vacuum while being heated with a heatgun to provide a white solid (637.7 mg, 82%, 776.6 mg theory). An aliquot of the solid was dissolved in H₂O and the purity determined by NMR using an internal standard (NaOTf) to be 97% resulting in a purity corrected yield of 80%.

[00118] Performing the initial reaction at ambient temperature (23 °C) afforded a yield of 74% KF in a 90% purity resulting in a purity corrected yield of 67%.

[00119] The reaction on a 10 g scale of acid grade fluorspar (97%) afforded 11.3 g KF in a 93% purity resulting in a purity corrected yield of 85%.

Tetrabutylammonium fluoride – tert-butylalcohol complex



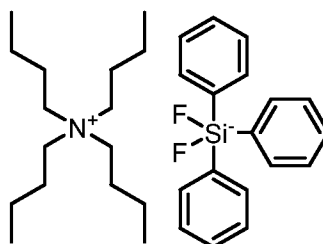
[00120] Fluorspar (acid grade 97%, 500.0 mg, 6.4 mmol, 1.0 equiv), silica gel (180.0 mg, 3.0 mmol, 0.47 equiv) and oxalic acid (634.2 mg, 7.0 mmol, 1.1 equiv) were weighed into a 15 mL PP tube. A stir bar and water (2.0 mL) were added and the mixture was heated under stirring in a sand bath at 70 °C for 17 h. The resulting suspension was cooled to ambient temperature, diluted with water (10 mL) and filtered with a Büchner funnel into a 50 mL PP tube. The resulting solid and reaction tube were washed with water (2x 5 mL).

[00121] Subsequently, the filtrate was equipped with a stir bar and solution of TBAOH hydrate (1M in methanol, 14.1 mL, 14.1 mmol, 2.2 equiv) was added. After the addition is complete, the tube was heated in a sand bath at 70 °C for 6 h. The mixture was concentrated at reduced pressure (150 mbar, 40 °C) to an approximate volume of 20 mL. Acetonitrile (50 mL) was added and the resulting suspension was filtered through celite and concentrated at reduced pressure to afford a light orange liquid that was used directly for the next step. Analysis by ¹⁹F NMR revealed a yield of 42% of TBAF based on an internal standard (4-Fluoroanisole).

[00122] The crude TBAF mixture (purity 84% by NMR, 1.02 g, 3.3 mmol) was mixed with t-butanol (70 mL) and hexane (30 mL) and the solution was concentrated under reduced

pressure to afford a white precipitate. Pentane (30 mL) and t-butanol (5 mL) were added and the ensuing solution was cooled to 4 °C over 15 h. The formed crystals were collected as long needles affording the desired complex in 66% yield (1.2 g).

Tetrabutylammonium difluorotriphenylsilicate(IV)



[00123] Fluorotriphenylsilane (278.4 mg, 1.0 mmol, 1.0 equiv) was dissolved in dichloromethane (1.0 mL), 50.0 mg MgSO₄ and a solution of crude TBAF mixture (prepared directly from fluorspar as described above, purity 84% by NMR, 0.322 g, 1.03 equiv) in THF (1.0 mL). The suspension was filtered and concentrated under reduced pressure. The residue was treated with ethyl acetate (15 mL) and the suspension was heated to reflux until the solution became clear. The solution was allowed to cool to ambient temperature and before further cooling to -20 °C over 15 h, the crystals were collected to afford the desired compound (344.7 mg, 73%).

[00124] ¹H NMR (400 MHz, CD₃CN) δ 7.96 – 7.89 (m, 2H), 7.22 – 7.16 (m, 3H), 7.09 – 6.97 (m, 5H), 6.95 – 6.85 (m, 5H), 3.11 – 2.98 (m, 8H), 1.66 – 1.48 (m, 8H), 1.41 – 1.25 (m, 8H), 0.96 (t, *J* = 7.3 Hz, 12H).

Aqueous hexafluorosilicic acid solution

[00125] Fluorspar (acid grade 97%, 500 mg, 6.4 mmol, 2.1 equiv), silica gel (180 mg, 3.0 mmol, 1.0 equiv) and oxalic acid (634.2 mg, 7.0 mmol, 2.35 equiv) were weighed into a 50 mL Conical Sterile Polypropylene Centrifuge Tube. A stir bar and water (2 mL) were added and the mixture was heated in a sand bath to 70 °C for 15 h. The resulting suspension was cooled to ambient temperature and filtered with a Büchner funnel into a 50 mL PP tube. The solid and reaction tube were washed with water (2x 16 mL) to give a filtrate containing a fluorosilicate anions. Aliquot analysis by ¹⁹F NMR using NaOTf as internal standard revealed a yield of 99%.

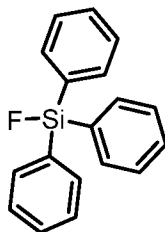
[00126] Performing the initial reaction at ambient temperature (23 °C) afforded a yield of 82% determined by ¹⁹F NMR using NaOTf as internal standard.

[00127] Performing the initial reaction at ambient temperature (23 °C) and using celite instead of silica gel afforded a yield of 20% determined by ¹⁹F NMR using NaOTf as internal standard.

[00128] Performing the initial reaction at ambient temperature (23 °C) and using sea sand instead of silica gel afforded a yield of 2% determined by ^{19}F NMR using NaOTf as internal standard.

Fluorotriphenylsilane

From chlorotriphenylsilane:



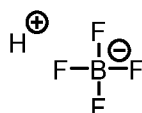
[00129] Fluorspar (acid grade 97%, 39.7 mg, 0.5 mmol, 0.6 equiv), chlorotriphenylsilane (250 mg, 0.85 mmol, 1 equiv), and oxalic acid (45.8 mg, 0.5 mmol, 0.6 equiv) were weighed into a 15 mL PP tube. A stir bar and water (4 mL) were added and the mixture was heated in a sand bath to 60 °C for 15 h. The resulting suspension was cooled to ambient temperature and extracted with dichloromethane (2 x 2 mL). The combined organic phases were dried over MgSO_4 and the crude mixture was analysed by NMR showing a 48% yield of the desired product based on the internal standard (NaOTf).

From bis(triphenylsilyl) oxalate:

[00130] Fluorspar (acid grade 97%, 33.0 mg, 0.42 mmol, 1.1 equiv) and bis(triphenylsilyl) oxalate (233.1 mg, 0.38 mmol, 1 equiv) were weighed into a 15 mL PP tube. A stir bar and water (4 mL) were added and the mixture was heated in a sand bath to 60 °C for 15 h. The resulting suspension was cooled to ambient temperature and extracted with dichloromethane (2 x 2 mL). The combined organic phases were dried over MgSO_4 and the crude mixture was analysed by NMR showing a 32% yield of the desired product based on the internal standard (NaOTf).

Aqueous tetrafluoroboric acid solution

From Boric acid:



[00131] Fluorspar (acid grade 97%, 10.0 g, 128.1 mmol, 2.3 equiv), boric acid (3.4 mg, 55.7 mmol, 1.0 equiv) and oxalic acid (10.0 g, 111.4 mmol, 2.0 equiv) were weighed into a 50 mL Conical Sterile Polypropylene Centrifuge Tube. A stir bar and water (20 mL) were added and the mixture was heated in a sand bath to 60 °C for 22 h. The resulting suspension was cooled to ambient temperature and filtered with a Büchner funnel and washed with water (2 x 5 mL) to give a solution of aqueous tetrafluoroboric acid. Aliquot analysis by ^{19}F NMR using NaOTf as internal standard revealed a yield of >95%.

[00132] Performing the initial reaction at ambient temperature (23 °C) for 16h afforded a yield of 94% as determined by ^{19}F NMR using NaOTf as internal standard.

[00133] The reaction using a 1:1 mixture of water and ethanol at 80 °C for 16 h afforded a yield of 66% as determined by ^{19}F NMR using NaOTf as internal standard.

[00134] The reaction in methanol at 60 °C for 16 h afforded a yield of 8% as determined by ^{19}F NMR using NaOTf as internal standard.

From Boron oxide:

[00135] Fluorspar (acid grade 97%, 312.3 mg, 4.0 mmol, 4.0 equiv), boron oxide (69.6 mg, 1.0 mmol, 1.0 equiv) and oxalic acid (360.2 mg, 4.0 mmol, 4.0 equiv) were weighed into a 15 mL Conical Sterile Polypropylene Centrifuge Tube. A stir bar and water (2 mL) were added and the mixture was heated in a sand bath to 60 °C for 17 h. The resulting suspension was cooled to ambient temperature and filtered with a Büchner funnel and washed with water (2 x 5 mL) to give a solution of aqueous tetrafluoroboric acid solution. Aliquot analysis by ^{19}F NMR using NaOTf as internal standard revealed a yield of >95%.

From Bis(oxalate)boric acid:

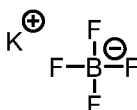
[00136] Fluorspar (acid grade 97%, 30.0 mg, 0.38 mmol, 2.0 equiv) and bis(oxalate)boric acid (36.1 mg, 0.19 mmol, 1.0 equiv) were weighed into a 15 mL Conical Sterile Polypropylene Centrifuge Tube. A stir bar and water (3 mL) were added and the mixture was heated in a sand bath to 80 °C for 17 h. The resulting suspension was cooled to ambient temperature, filtered with a Büchner funnel and washed with water (2 x 5 mL) to give a solution of aqueous tetrafluoroboric acid. Aliquot analysis by ^{19}F NMR using NaOTf as internal standard revealed a yield of 77%.

From a boronic acid:

[00137] Fluorspar (acid grade 97%, 30.0 mg, 0.38 mmol, 1.0 equiv), 4-fluorophenyl-B(OH)₂ acid (107.7 mg, 2.0 mmol, 2.0 equiv), oxalic acid (103.9.0 mg, 1.2 mmol, 3.0 equiv) and potassium carbonate (53.2, 0.38 mmol, 1 equiv) were weighed into a 7 mL glass vial. A stir bar and water (3 mL) were added and the mixture was heated in a sand bath to 70 °C for 12 h. The resulting suspension was cooled to ambient temperature and the supernatant was analysed by ¹⁹F NMR using NaOTf as internal standard. The yield of fluorine in solution was determined to be 86% spread over species such as tetrafluoroborate and the trifluoroborate ion.

Potassium tetrafluoroborate

From Boric acid:



[00138] Fluorspar (acid grade 97%, 1.2 g, 15.3 mmol, 2.0 equiv), boric acid (475.2 mg, 7.7 mmol, 1.0 equiv) and oxalic acid (1.45 g, 16.1 mmol, 2.1 equiv) were weighed into a 15 mL Conical Sterile Polypropylene Centrifuge Tube. A stir bar and water (2 mL) were added and the mixture was heated in a sand bath to 70 °C for 15 h. The resulting suspension was cooled to ambient temperature and filtered with a Büchner funnel into a 15 mL PP tube. The solid and reaction tube were washed with methanol (2x 5 mL). The filtrate was concentrated under reduced pressure to a volume of 1 mL and an aqueous solution of K₂HPO₄ (1.0 g, 5.75 mmol, 0.75 equiv) in 1 mL of H₂O was added. The resulting precipitate was collected by filtration, washed with cold water (1 mL) and dried in an oven (80 °C) then under high vacuum to give the title compound as white crystalline solid (664.2 mg, 69%).

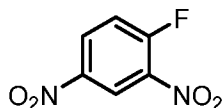
[00139] ¹⁹F NMR (377 MHz, D₂O) δ -150.1, -150.2.

From Potassium tetraborate tetrahydrate:

[00140] Fluorspar (acid grade 97%, 168.0 mg, 2.2 mmol, 8.8 equiv), Potassium tetraborate tetrahydrate (74.7 mg, 0.24 mmol, 1.0 equiv), oxalic acid (154.1 mg, 1.7 mmol, 7.0 equiv) and potassium oxalate hydrate (45.1 mg, 0.24 mmol, 1 equiv) were weighed into a 15 mL Conical Sterile Polypropylene Centrifuge Tube. A stir bar and water (7.5 mL) were added and the mixture was heated in a sand bath to 50 °C for 60 h. The suspension was filtrated hot and concentrated under reduced pressure to a volume of approx. 2 mL. The mixture was cooled

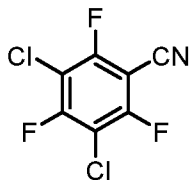
in an ice bath for 1 h, then filtered to afford the title compound after drying as white solid (28.3 mg, 21%).

1-fluoro-2,4-dinitrobenzene



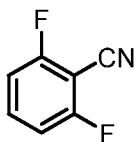
[00141] In a 10 mL Schlenk flask, KF_{CaF_2} (62.5 mg, 80% purity, 0.86 mmol, 2.0 equiv) was stirred in MeOH (0.2 mL) for 1 min before sulfolane (100.0 mg) and toluene (2.5 mL) were added. The Schlenk flask is equipped with a Distilling link according to Claisen and placed in a sand bath at 150 °C for 1 h. The Schlenk was cooled to ambient temperature, flushed with N_2 and 1-chloro-2,4-dinitrobenzene (87.1 mg, 0.43 mmol, 1.0 equiv) and anhydrous DMSO (1 mL) were added and the mixture was stirred in an 80 °C sand bath for 30 min. Addition of an internal standard and NMR analysis of an aliquot showed 98% conversion and 76% yield of the desired product as well as 17% of 2,4-dinitrophenolderivative.

3,5-dichloro-2,4,6-trifluorobenzonitrile



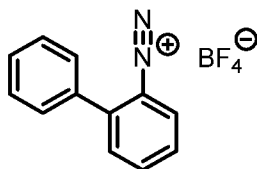
[00142] In a 7 mL glass vial, KF_{CaF_2} (130.7 mg, 93% purity, 2.25 mmol, 4.5 equiv = 1.5 equiv/F) was stirred open to air in methanol (2 mL) in a sand bath heated to 180 °C for 15 min. Another 2 mL of methanol was added and stirring was continued for 15 min. To the dried KF was added pentachlorobenzonitrile (137.7 mg, 0.5 mmol) and a stock solution of sulfolane (2.5 mL containing 2.74 mg of TMAC (5 mol%) and 6.61 mg 18-crown-6 (5 mol%). The vial was sealed with a screw cap and heated at 170 °C for 15 h. After cooling, water (3 mL) was added and the mixture was extracted with ether (3 x 3 mL). The combined organic phases were dried over MgSO_4 and concentrated. Purification by column chromatography (pentane:ether 0 to 20%) afforded the desired product (73.3 mg, 65%) as colourless oil.

[00143] ^{19}F NMR (377 MHz, CDCl_3) δ -98.68 (t, J = 5.7 Hz), -104.13 (d, J = 5.7 Hz).

2,6-difluorobenzonitrile

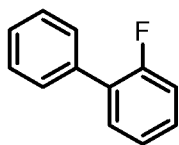
[00144] In a 7 mL glass vial, KF_{CaF_2} (87.1 mg, 93% purity, 2.25 mmol, 3.0 equiv = 1.5 equiv/F) was stirred open to air in methanol (2 mL) in a sand bath heated to 180 °C for 15 min. Another 2 mL of methanol was added and stirring was continued for 15 min. To the dried KF was added 2,6-dichlorobenzonitrile (86.0 mg, 0.5 mmol) and a stock solution of sulfolane (2.5 mL containing 2.74 mg of TMAC (5 mol%) and 6.61 mg 18-crown-6 (5 mol%). The vial was sealed with a screw cap and heated at 180 °C for 60 h. After cooling, water (3 mL) was added and the mixture was extracted with ether (3 x 3 mL). The combined organic phases were dried over MgSO_4 and concentrated. Purification by column chromatography (pentane:ether 0 to 20%) afforded the desired product (39.1 mg, 56%) as colourless oil.

[00145] ^1H NMR (400 MHz, CDCl_3) δ 7.61 (tt, J = 8.6, 6.3 Hz, 1H), 7.10 – 7.03 (m, 2H); ^{19}F NMR (377 MHz, CDCl_3) δ -103.46 – -103.55 (m).

[1,1'-biphenyl]-2-diazonium tetrafluoroborate

[00146] In a 50 mL round-bottom flask, [1,1'-biphenyl]-2-amine (423.1 mg, 2.5 mmol, 1.0 equiv) was suspended with tetrafluoroboric acid solution (1.5 mL, 2.9 equiv based on the amount of CaF_2) and cooled to 0 °C in an ice bath. An aqueous solution of (340.0 mg, 4.9 mmol, 2.0 equiv) in 0.5 mL was added dropwise over 2 min. The reaction was stirred at 0 °C for 30 minutes before being filtered and washed with cold water (0.5 mL), EtOH (0.5 mL) and Et_2O (1.5 mL). The resulting residue was dried with high vacuum for 10 minutes to give the title compound (481.0 mg, 72%) which was stored in the freezer. The compound was used as such for the next step.

2-fluoro-1,1'-biphenyl



[00147] Under an air atmosphere, a 7mL-vial was charged with aryldiazonium tetrafluoroborate (134.0 mg, 0.5 mmol) and solvent (2 mL hexane). The mixture was heated to 80 °C for 2 h after which time, the lid was unscrewed and white smoke emerged the vial. Water was added (4 drops using a Pasteur pipette) and after further stirring for 5 min at ambient temperature, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica using pentane as eluent to afford the title compound as a white crystalline solid (49.9 mg, 58%).

[00148] ^1H NMR (400 MHz, CDCl_3) δ 7.58 – 7.53 (m, 2H), 7.48 – 7.42 (m, 3H), 7.40 – 7.35 (m, 1H), 7.32 (dddd, J = 8.1, 7.4, 5.0, 1.9 Hz, 1H), 7.21 (td, J = 7.5, 1.3 Hz, 1H), 7.16 (ddd, J = 10.8, 8.2, 1.3 Hz, 1H).

[00149] ^{19}F NMR (377 MHz, CDCl_3) δ -118.07 – -118.16 (m).

Part B

[00150] Fluoride capture from acid grade fluorspar (AGF) with $\text{B}(\text{OH})_3$ was found to be highly effective in the presence of H_2Ox when the reaction was carried out in water for 15 h at 50 °C (Fig. 11a). The [B–F] products were identified by ^{19}F and ^{11}B nuclear magnetic resonance (NMR) spectroscopy in D_2O (Fig. 11b). By ^{19}F NMR, HBF_4 (quartet, δ = 150.3 ppm, $^1J_{\text{B-F}}$ = 1.1 Hz) and HBF_3OH (quartet, δ = -145.3 ppm, $^1J_{\text{B-F}}$ = 10.7 Hz) were identified as major products. Additionally, a broad singlet (δ = 152.3 ppm) characteristic of difluoro(oxalate)borate species HOxBF_2 was observed in trace amount (<1%). Notably, H_2Ox afforded a higher yield (96%) of [B–F] products than tartaric acid (2%), sulfuric acid (69%) or hydrochloric acid (60%) under these reaction conditions (Fig. 11a). An investigation on fluorspar activation with a range of Brønsted acids gave insight on the interplay between acidity, denticity and solubility of the Ca^{2+} salt by-product. For monoacids (2 equiv. versus CaF_2), it was noted that there was a correlation between acidity and fluoride release in the $\text{p}K_{\text{a}}$ value range between 4.2 to –0.5. Multifunctional activators (1 equiv. versus CaF_2) were also investigated. Organic acids leading to five-membered Ca^{2+} chelates stood out with H_2Ox ($\text{p}K_{\text{a}}$ = 1.3 and 4.1) being the most effective activator followed by croconic acid ($\text{p}K_{\text{a}}$ = 0.8 and 2.2) and squaric acid ($\text{p}K_{\text{a}}$ = 1.5 and 3.4). Oxalic acid dihydrate ($\text{H}_2\text{Ox} \cdot 2\text{H}_2\text{O}$) which is more cost effective than H_2Ox gave the [B–F] products HBF_4 and HBF_3OH with efficacy similar to H_2Ox (total yield of 98%) upon

treatment of AGF with $B(OH)_3$ at 50 °C for 15 h (Table 4). Subsequent studies were therefore performed with $H_2Ox \cdot 2H_2O$.

Table 4 Replacement of anhydrous oxalic acid for oxalic acid dihydrate for B-F product formation

Entry	Oxalic acid	HBF_4	HBF_3OH	H_2OxBF_2 (%)
1	anhydrous	81	16	<1%
2	dihydrate	82	16	<1%

[00151] $H_2Ox \cdot 2H_2O$ was found to be a suitable activator for AGF when combined with silica (SiO_2) in water at 50 °C for 15 h, with fluoride release as $[Si-F]$ products (total 97%). The formation of H_2SiF_6 (broad singlet, $\delta = -129.6$ ppm), which in water exists in equilibrium with $H_2SiF_5(OH)$ (broad singlet, $\delta = -128.8$ ppm), was evidenced by ^{19}F NMR spectroscopy of the reaction mixture. Two triplets were also observed ($\delta = -124.5$ ppm and -135.9 ppm, $^2J_{F-F} = 8.9$ Hz) and assigned to H_2OxSiF_4 (supported by ^{29}Si NMR spectroscopy).

[00152] Subsequent studies focused on the synthesis of commonly used fluorinating reagents from these $[Si-F]$ products (Fig. 11c). For this purpose, AGF (1.1 equiv) was reacted with $H_2Ox \cdot 2H_2O$ (1 equiv) and SiO_2 (0.4 equiv) in water at 50 °C for 15 h. The reaction mixture was filtered and treated with KOH. The insoluble by-product of this filtration was unambiguously characterized as $CaOx \cdot H_2O$ by powder X-ray diffraction (PXRD) (Fig. 12). Neutralization with KOH (2 equiv) led to the formation of K_2SiF_6 (Fig. 13), whilst treatment with excess KOH (6 equiv) afforded KF^{AGF} (85% yield, calculated from AGF). Alternatively, treatment of the filtered reaction mixture with tetramethylammonium hydroxide (6 equiv) afforded tetramethylammonium fluoride hydrate which was converted to tetramethylammonium *tert*-amyl alcohol fluoride ($Me_4NF \cdot ^tAmOH$) (88% yield), a fluorinating reagent well documented for nucleophilic aromatic fluorination (S_NAr). This strategy also enabled the preparation of tetrabutylammonium fluoride hydrate, which was converted to the bench stable reagent tetrabutylammonium tetra(*tert*-butyl alcohol) fluoride [$Bu_4NF \cdot (^tBuOH)_4$] (71% yield calculated from AGF).

[00153] Mechanistic investigations by ^{19}F NMR in D_2O established whether HF is formed upon dissolution of CaF_2 with H_2Ox (Fig. 14). In the absence of fluorophilic Lewis acid, HF is observed (singlet, $\delta = -166.0$ ppm), and an equilibrium is established with the amount of HF plateauing after 3 h at approximately 10% (Fig. 11d). In the presence of either $B(OH)_3$ or SiO_2 , the equilibrium is displaced *via* the precipitation of highly insoluble $CaOx$ and immediate HF capture by the Lewis acid. Under these conditions, the singlet diagnostic of HF was not detected by ^{19}F NMR during the entire course of the reaction. As anticipated, the reaction of

AGF with fluorophilic Lewis acid in the absence of H₂Ox resulted in no fluoride release. These data highlight how Brønsted and Lewis acid cooperativity allows for Fluorspar activation under mild conditions, prevents HF from building up, and enables access to commonly used fluorinating reagents for synthesis, directly from fluorspar.

[00154] With an effective strategy to convert AGF into HBF₄ (aqueous), KF, Me₄NF·^tBuOH and ⁿBu₄NF·(^tBuOH)₄, it was investigated whether these AGF-derived reagents react as expected, with the synthesis of industrially valuable fluoroarenes and a focus on those not accessible *via* mechanochemical activation of AGF using a phosphate salt. For Balz-Schiemann chemistry, a two-step procedure followed the preparation of HBF₄ (aqueous); addition of *tert*-butyl nitrite to a solution of aryl amine and aqueous HBF₄ led to the precipitation of the corresponding aryl diazonium tetrafluoroborate salt which was isolated and subsequently heated to liberate the desired fluoroarene (Fig. 15a). The protocol was validated firstly with 4-bromoaniline, AGF-derived HBF₄ (HBF₄^{AGF}) (1.1 equiv) and *tert*-butyl nitrite (2 equiv). Heating the resulting diazonium salt at 90 °C in PhCl gave 4-bromofluorobenzene in 98% yield (as measured by ¹⁹F NMR spectroscopy), a key intermediate featured in the synthesis of the antidepressant citalopram. This chemistry was subsequently applied to prepare multiple fluoroarenes commonly used as building blocks in the synthesis of various organo-fluorine containing drugs in up to 87% yield (dediazotization yield). Examples include the precursors of Lipitor (cholesterol-lowering), norfloxacin (antibiotic), raltegravir (HIV), eravacycline (antibiotic), rosuvastatin (cardiovascular disease), flurbiprofen (anti-inflammatory), flunarizine (vertigo), and ezetimibe (cholesterol-lowering drug).

[00155] The methodology was also suitable for the preparation of diverse fluoropyridines (**4,8** and **13**) that are building blocks for drugs such as MK2 inhibitors (autoimmune diseases), vericiguat (heart failure), and agrochemicals including the herbicide clodinafop. Next, AGF-derived KF (KF^{AGF}) (90% purity) was found to achieve high yielding fluorination of chloroarene substrates using Me₄NCl (5 mol%) in DMSO as solvent. It was noted that the performance of KF^{AGF} was comparable to commercial KF (see Table 5).

Table 5. Performance of KF^{AGF} and KF^M

Entry	KF	source	ArF (%)
1	KF ^C	commercial	95%
2	KF ^{AGF}	this work	90%
3	KF ^M	this work	92%

[00156] The method was applied to the synthesis of 1-fluoro-2,4-dinitrobenzene (**14**), 2-chloro-1-fluoro-4-nitrobenzene (**15**), 2-fluoro-5-nitrobenzonitrile (**16**) and 3-chloro-4-

fluorobenzonitrile (**17**). Aromatic fluorodenitration using AGF-derived $\text{Me}_4\text{NF} \cdot t\text{AmOH}$ proceeded at 70 °C in DMSO to access 2,6-difluorobenzonitrile (**18**), 4-fluoronitrobenzene (**19**) and 2-fluorobenzonitrile (**20**) in high yield. The successful cooperative activation of AGF in water and its application to the synthesis of fluoroarenes encouraged an investigation on the reactivity of lower grade metallurgical fluorspar (metspar, ~ 85% CaF_2). Metspar yielded the [B–F] products HBF_4 and HBF_3OH with an overall yield of 83%, upon activation with B(OH)_3 and $\text{H}_2\text{Ox} \cdot 2\text{H}_2\text{O}$ at 50 °C for 15 hours. The reaction of metspar with $\text{H}_2\text{Ox} \cdot 2\text{H}_2\text{O}$ and SiO_2 also enabled the preparation of metspar-derived KF (KF^{M}) (53% yield, calculated from metspar). Fluoroarenes **1**, **14** and **16** were prepared in good yield using HBF_4^{M} or KF^{M} despite the reduced purity of metspar.

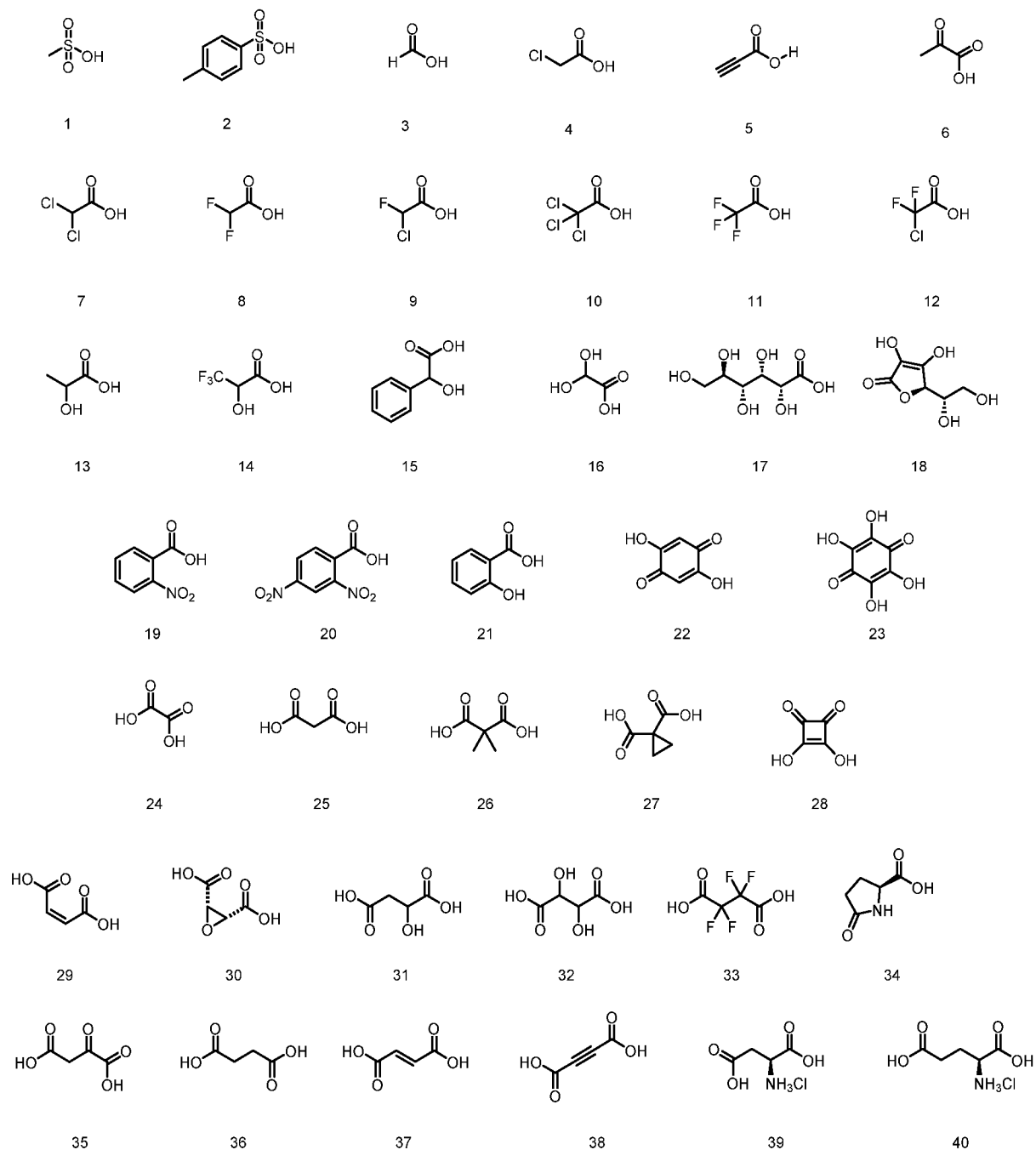
[00157] While specific embodiments of the invention have been described herein for the purpose of reference and illustration, various modifications will be apparent to a person skilled in the art without departing from the scope of the invention as defined by the appended claims.

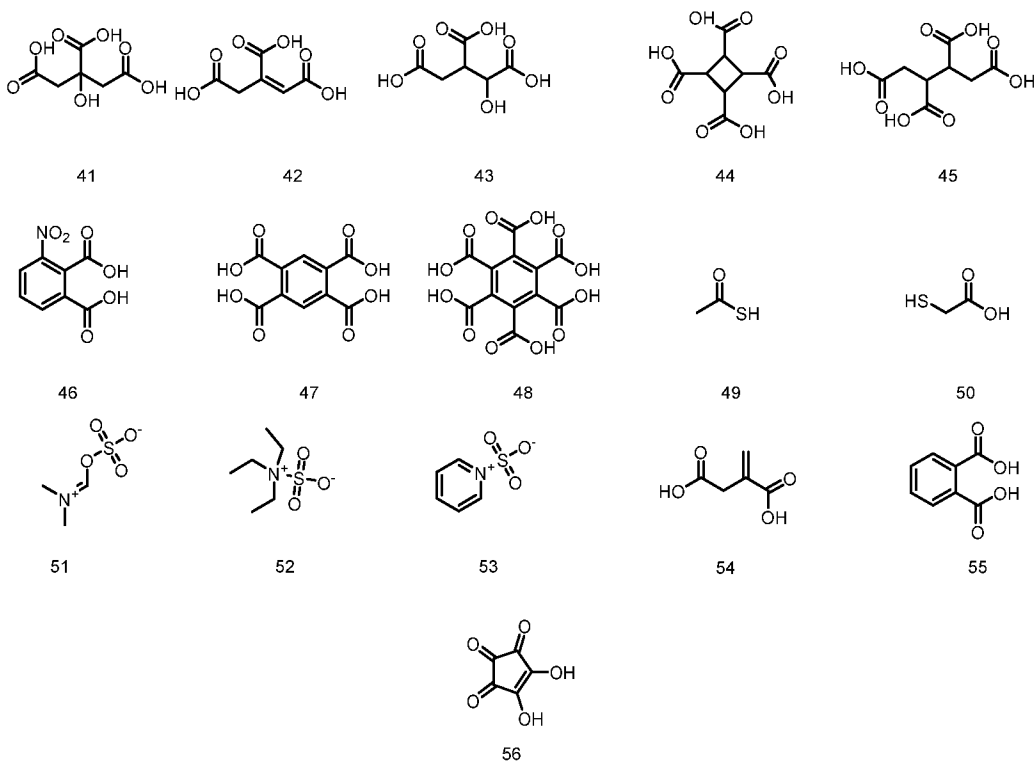
CLAIMS

1. A process for the preparation of a fluorochemical, the process comprising the step of:
a) mixing together an inorganic fluoride source, an activator and a fluoride acceptor, wherein the activator is an organic compound having a pK_a of -4 to 4.2 in water, and a water solubility of greater than 0.05 mol/L; and the fluoride acceptor is a hydroxide, an oxide, an alkoxide, a halide or a pseudohalide of B, Si, Ge, Al, P, Sb, Ti, S or Sn.
2. The process of claim 1, wherein the inorganic fluoride source is an ionic compound comprising M^{2+} and F^- , wherein M^{2+} is an alkaline earth metal cation (i.e., a group II metal cation).
3. The process of claim 2, wherein M^{2+} is Mg^{2+} , Ca^{2+} , Sr^{2+} or Ba^{2+} .
4. The process of any one of claims 2 or 3, wherein the activator is an M^{2+} -sequestering agent.
5. The process of claim 4, wherein the M^{2+} -sequestering agent comprises one or more M^{2+} -coordinating groups.
6. The process of claim 4, wherein the M^{2+} -sequestering agent comprises two or more M^{2+} -coordinating groups and the M^{2+} -sequestering agent forms a 5-, 6- or 7-membered chelate with M^{2+} .
7. The process of any one of the preceding claims, wherein the activator has a pK_a of -3 to 2 in water.
8. The process of any one of the preceding claims, wherein the activator is a mono-carboxylic acid, a di-carboxylic acid, a tetra-carboxylic acid, a dione-dihydroxy compound comprising 3-5 carbon atoms, a nitrogen-containing SO_3 -Lewis base adduct, or an oxygen-containing SO_3 -Lewis base adduct.
9. The process of any one of the preceding claims, wherein the activator has a water solubility of greater than 0.15 mol/L.

10. The process of any one of the preceding claims, wherein the activator has a water solubility of greater than 0.19 mol/L.

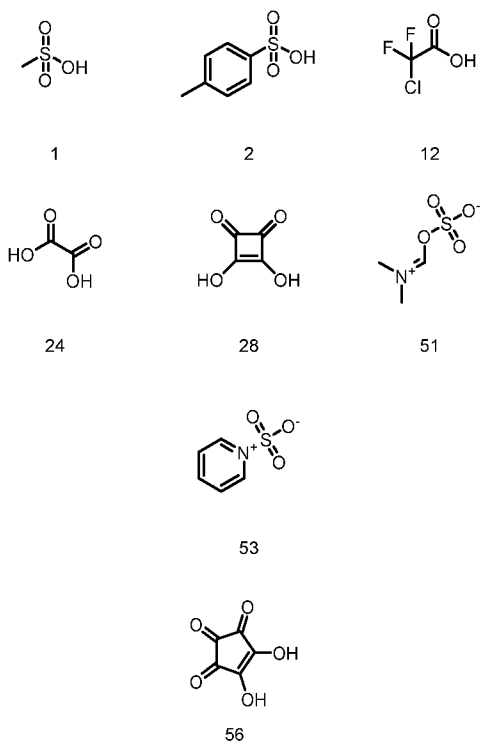
11. The process of any one of the preceding claims, wherein the activator is selected from any one of the following compounds 1-56:





or a salt thereof.

12. The process of any one of the preceding claims, wherein the activator is selected from any one of the following compounds 1, 2, 12, 24, 28, 51, 53 or 56:



or a salt thereof.

13. The process of any one of the preceding claims, wherein the activator is compound 24 (i.e., oxalic acid):



24

or a salt thereof.

14. The process of any one of the preceding claims, wherein the inorganic fluoride source is CaF_2 , MgF_2 , BaF_2 , SrF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

15. The process of any one of the preceding claims, wherein the inorganic fluoride source is CaF_2 or $\text{Ca}_5(\text{PO}_4)_3\text{F}$.

16. The process of any one of the preceding claims, wherein the fluoride acceptor is:
a hydroxide of B, Si, Ge, Al, Sb, Ti;
an oxide of B, Si, Ge, Al, P, Sb, Ti;
an alkoxide of B, Si, Ge, Al, Sb, Ti; or
a halide or pseudohalide of B, Si, S, Ge, Al, Sb, Ti, Sn.

17. The process of any one of the preceding claims, wherein the fluoride acceptor is $\text{B}(\text{OH})_3$, $\text{B}(\text{OH})_2\text{R}$, $\text{B}(\text{OH})\text{R}_2$, R_3SiX , R_2SiX_2 , RSiX_3 , SiX_4 , RSO_2X (wherein each X is independently Cl, Br or OH; and wherein each R is independently (1-4C)alkyl, aryl or heteroaryl, wherein any aryl or heteroaryl is optionally substituted with one or more methyl, ethyl, halo or hydroxide groups), $(\text{BOH})_3\text{O}_3$, $\text{H}_2\text{B}_4\text{O}_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , P_2O_5 , Sb_2O_5 , TiO_2 , Ti_2O_3 , TiO , SnO_2 , Sb_2O_3 , SbCl_5 or SbCl_3 .

18. The process of any one of the preceding claims, wherein the fluoride acceptor is $\text{B}(\text{OH})_3$, $\text{B}(\text{OH})_2\text{R}$, R_3SiCl , SiCl_4 , RSO_2Cl (wherein each R is independently (1-2C)alkyl, phenyl or tolyl, any of which are optionally substituted with one or more halo groups), $(\text{BOH})_3\text{O}_3$, $\text{H}_2\text{B}_4\text{O}_7$, B_2O_3 , SiO_2 , GeO_2 , Al_2O_3 , Sb_2O_5 or SbCl_5 .

19. The process of any one of the preceding claims, wherein the fluoride acceptor is selected from B(OH)_3 , 4-fluorophenyl- B(OH)_2 , B_2O_3 , SiO_2 , Ph_3SiCl , SiCl_4 , *p*-TolSO₂Cl, GeO_2 or Al_2O_3 .

20. The process of any one of the preceding claims, wherein the fluoride acceptor is B(OH)_3 .

21. The process of any one of the preceding claims, wherein step a) is conducted in the presence of a solvent (e.g., an organic solvent).

22. The process of claim 21, wherein the solvent comprises water (e.g., H_2O or D_2O), methanol and/or ethanol.

23. The process of any one of the preceding claims, wherein step a) is conducted at a temperature of 20 °C to 90 °C.

24. The process of any one of the preceding claims, wherein the ratio of equivalents of inorganic fluoride source : activator : fluoride acceptor is from 1 : 1 : 4 to 4 : 4 : 1.

25. A fluorochemical obtained, directly obtained or obtainable by the process of any one of the preceding claims.

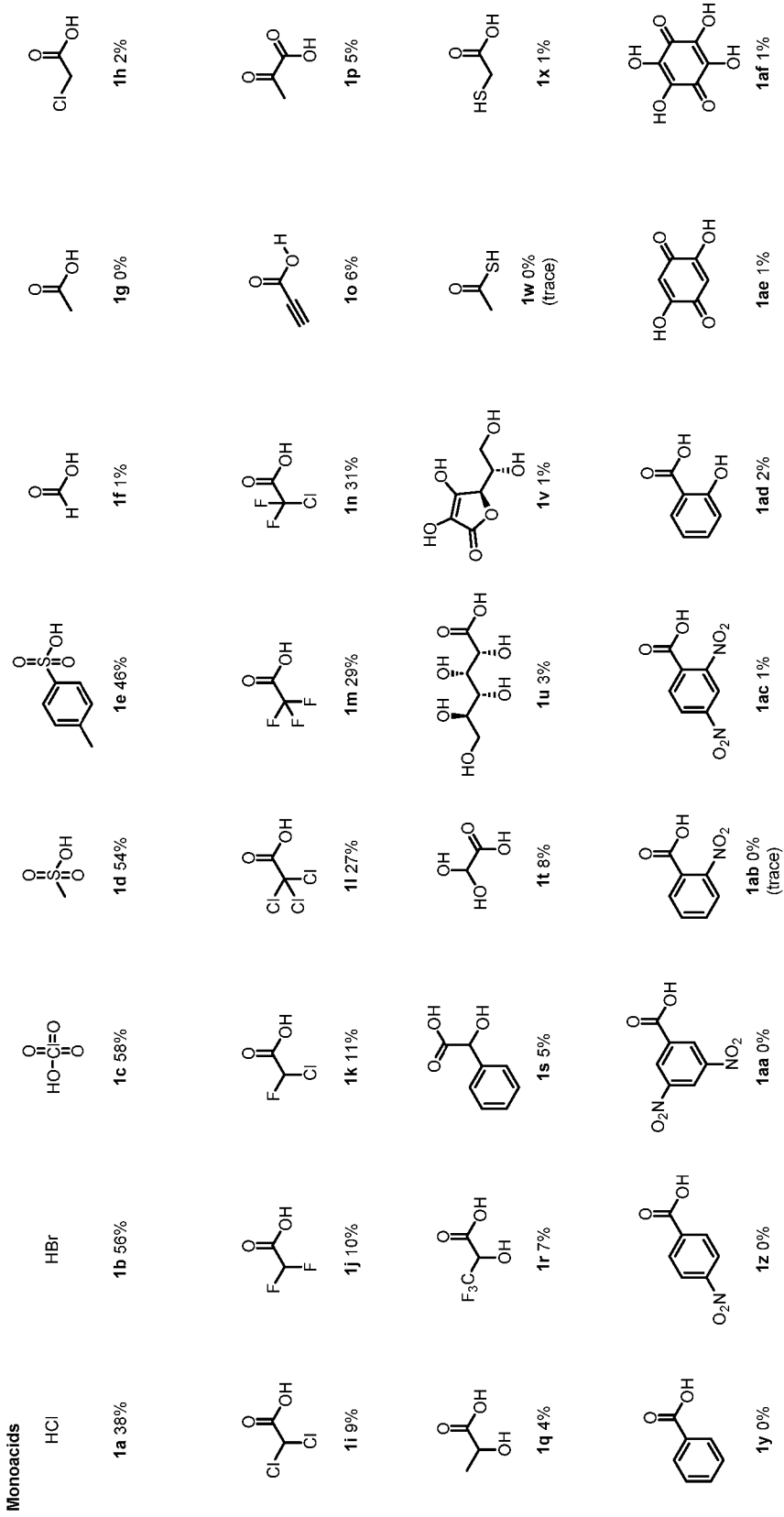


FIGURE 1

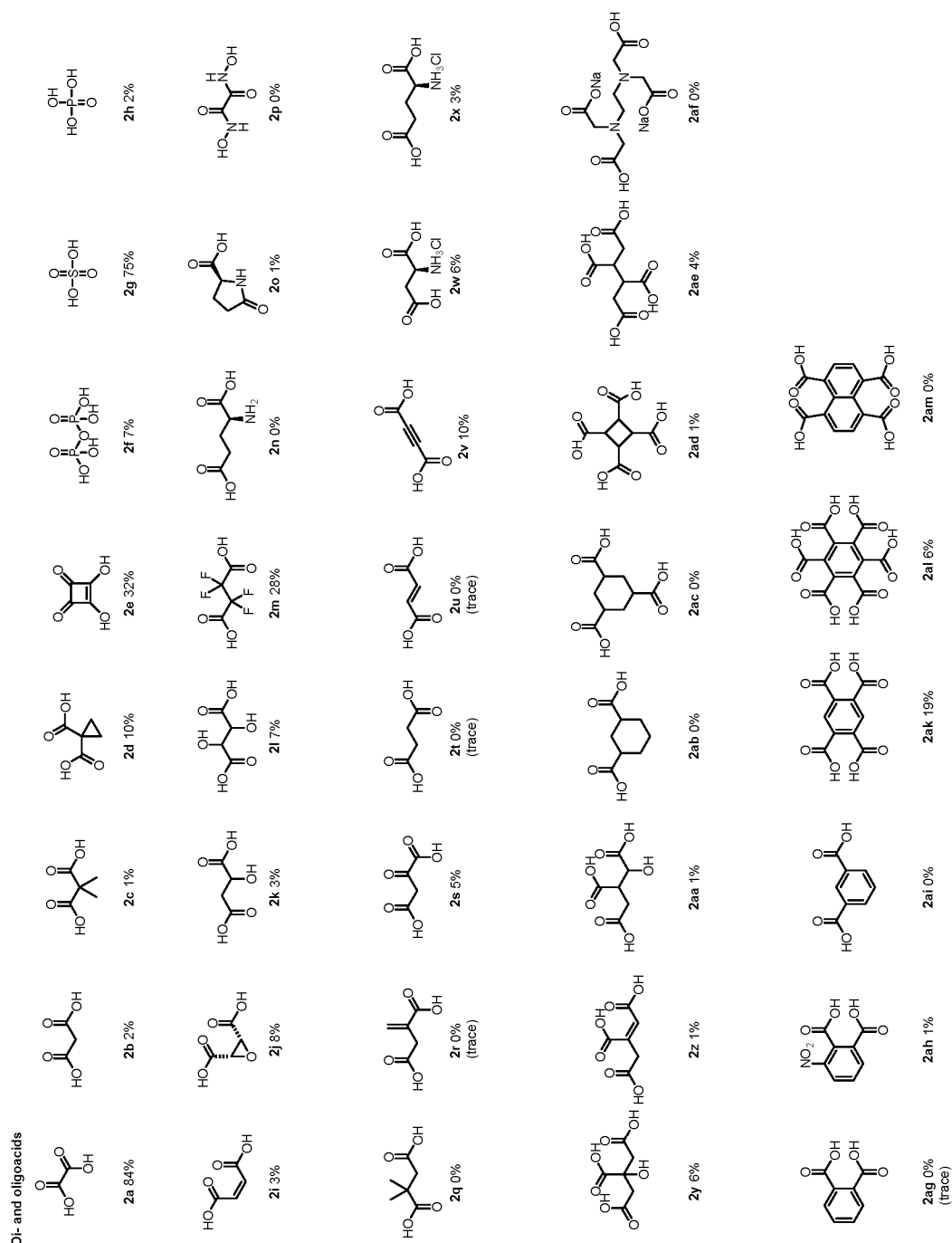
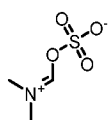
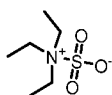
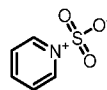


FIGURE 1 (continued)

Proacids

**3a** 75%**3b** 26%**3c** 43%**FIGURE 1 (continued)**

potential Fluoride acceptor	Activator	yield (¹⁹ F NMR)
ZnCl ₂	(NH ₄) ₂ Ox	n.d.
InCl ₃	(NH ₄) ₂ Ox	n.d.
La(Oi-Pr) ₃	H ₂ Ox	n.d.
PbO ₂	H ₂ Ox	n.d.
ZrO ₂	H ₂ Ox	n.d.
CeO ₂	H ₂ Ox	n.d.
CoCl ₂	(NH ₄) ₂ Ox	n.d.
Fe(acac) ₂	H ₂ Ox	n.d.
NbO ₂	H ₂ Ox	9%
SeO ₂	H ₂ Ox	10%
SnO ₂	H ₂ Ox	10%
MoO ₂	H ₂ Ox	13%
Sb ₂ O ₃	H ₂ Ox	9%
SbCl ₃	(NH ₄) ₂ Ox	10%
VO ₂	H ₂ Ox	8%
WO ₂	H ₂ Ox	12%
As ₂ O ₃	H ₂ Ox	8%
P ₂ O ₅	H ₂ Ox	9%
Sb ₂ O ₃	H ₂ Ox	19%
SbCl ₅	(NH ₄) ₂ Ox	18%
TiO ₂	H ₂ Ox	11%
Ti ₂ O ₃	H ₂ Ox	3%
TiO	H ₂ Ox	3%
Nb(OEt) ₅	H ₂ Ox	10%
SiCl ₄	(NH ₄) ₂ Ox	59%
GeO ₂	H ₂ Ox	39%
Al ₂ O ₃	H ₂ Ox	27%
pTsCl	H ₂ Ox	92%
B(OH) ₃	H ₂ Ox	87%
B ₂ O ₃	H ₂ Ox	46%
SiO ₂	H ₂ Ox	97%
Ph ₃ SiCl	H ₂ Ox	48%

FIGURE 2

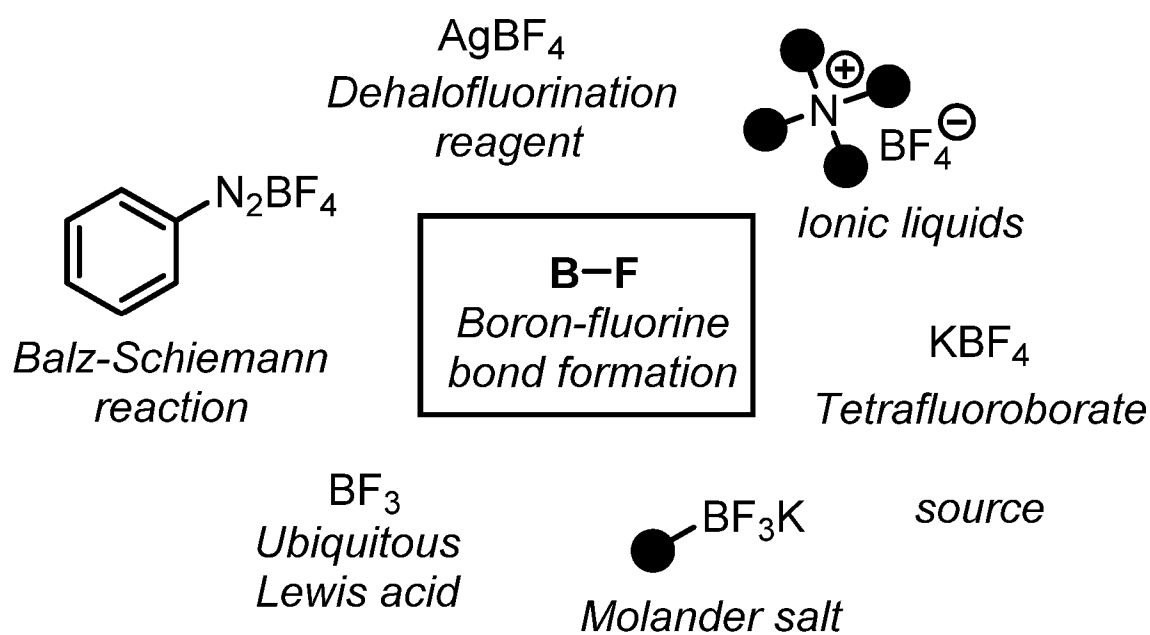


FIGURE 3

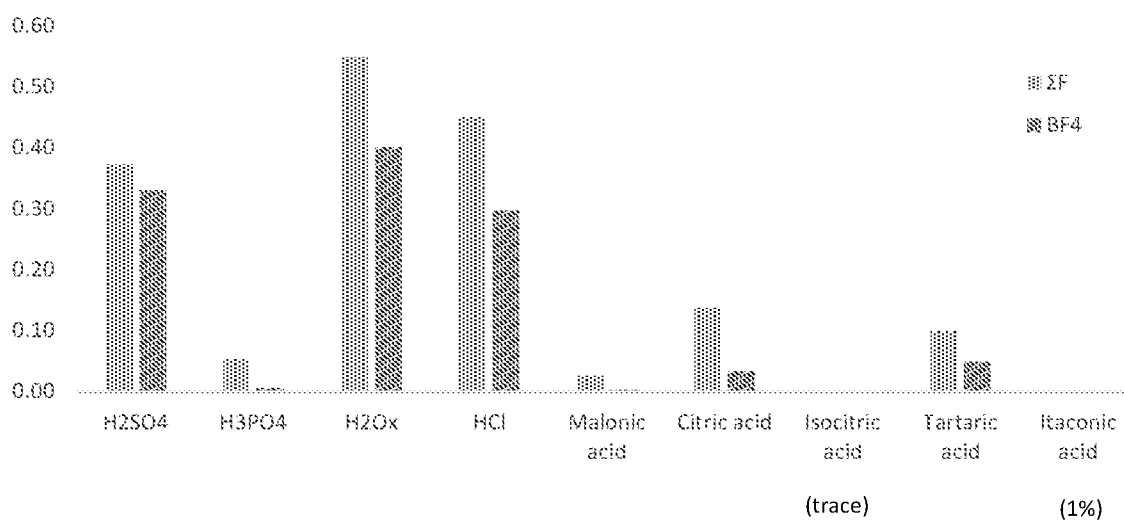


FIGURE 4

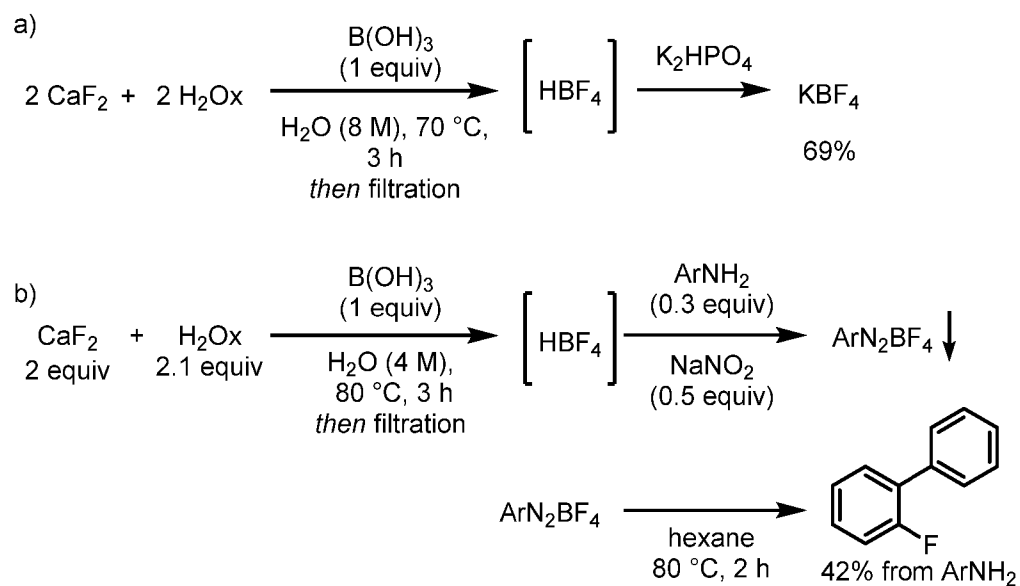


FIGURE 5

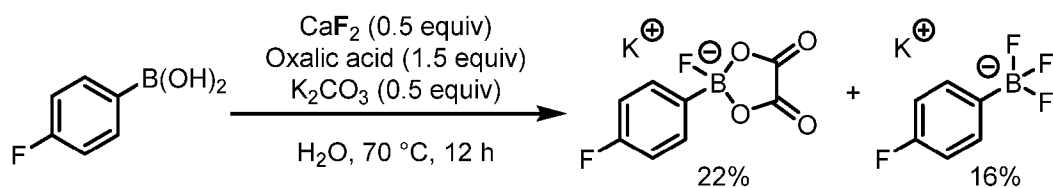


FIGURE 6

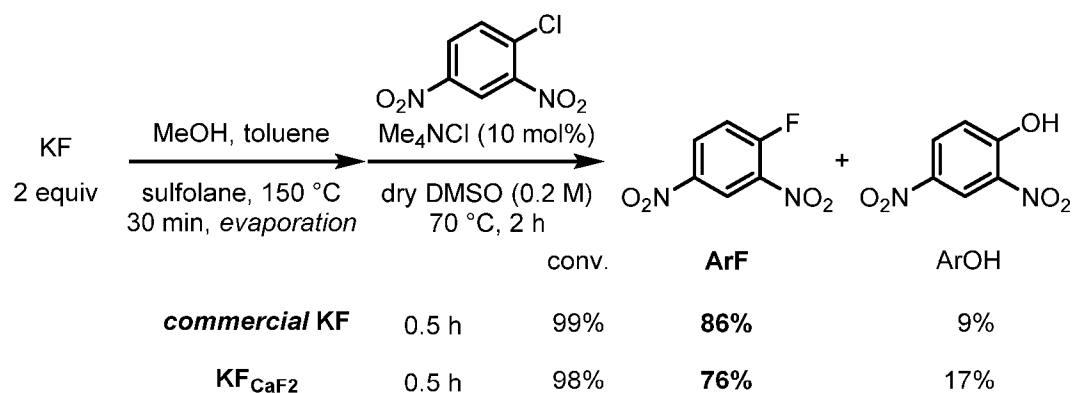


FIGURE 7

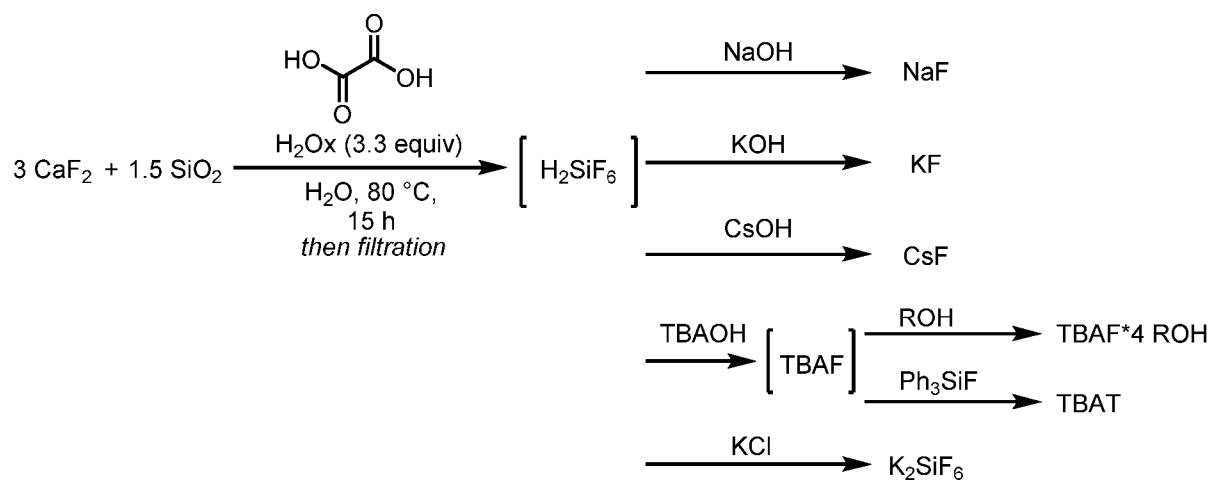


FIGURE 8

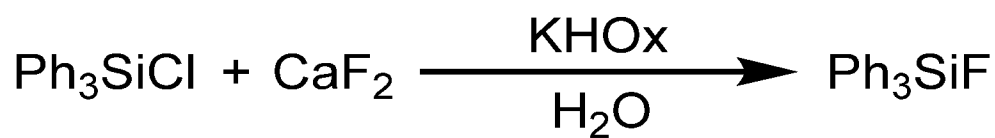


FIGURE 9

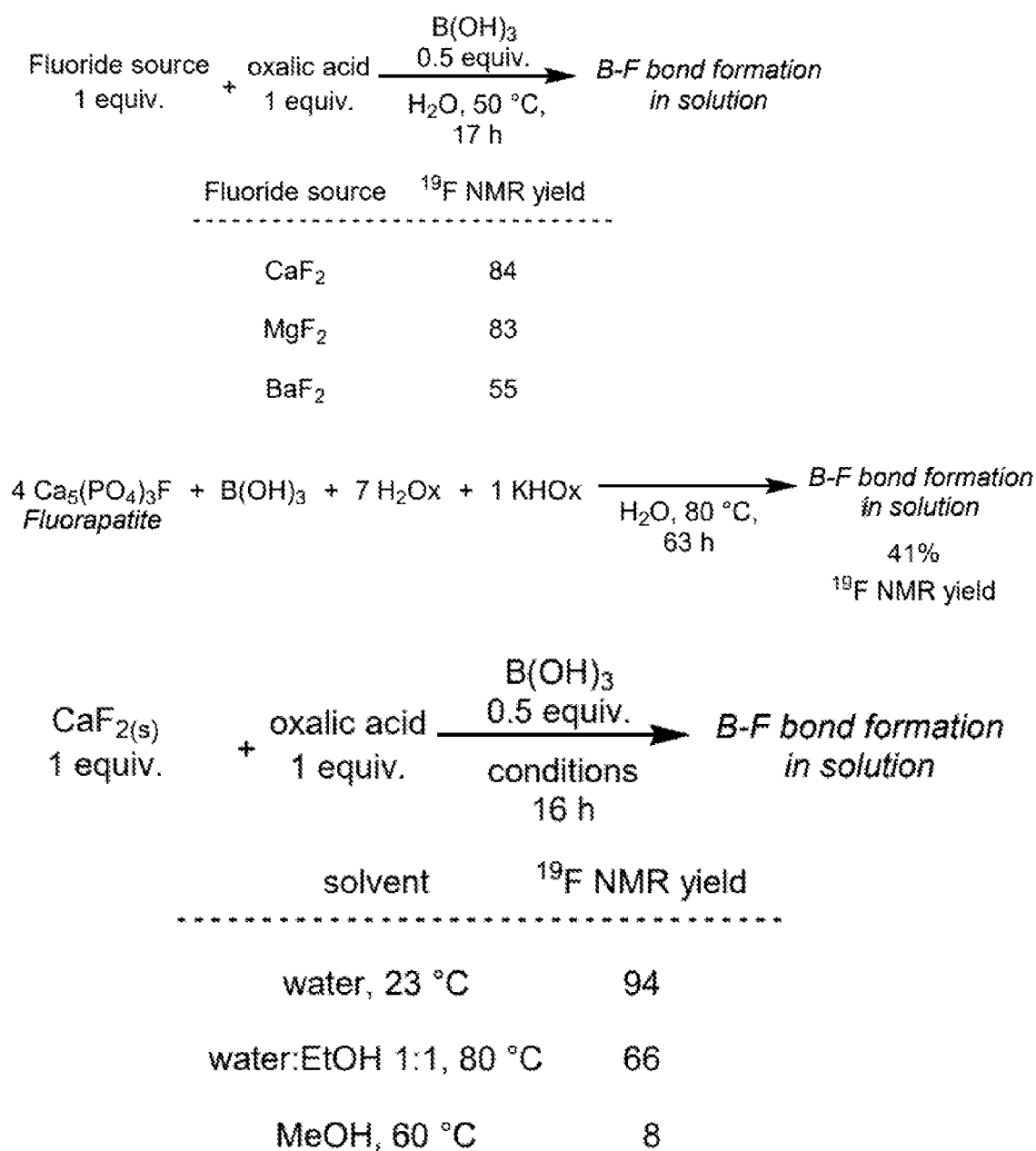


FIGURE 10

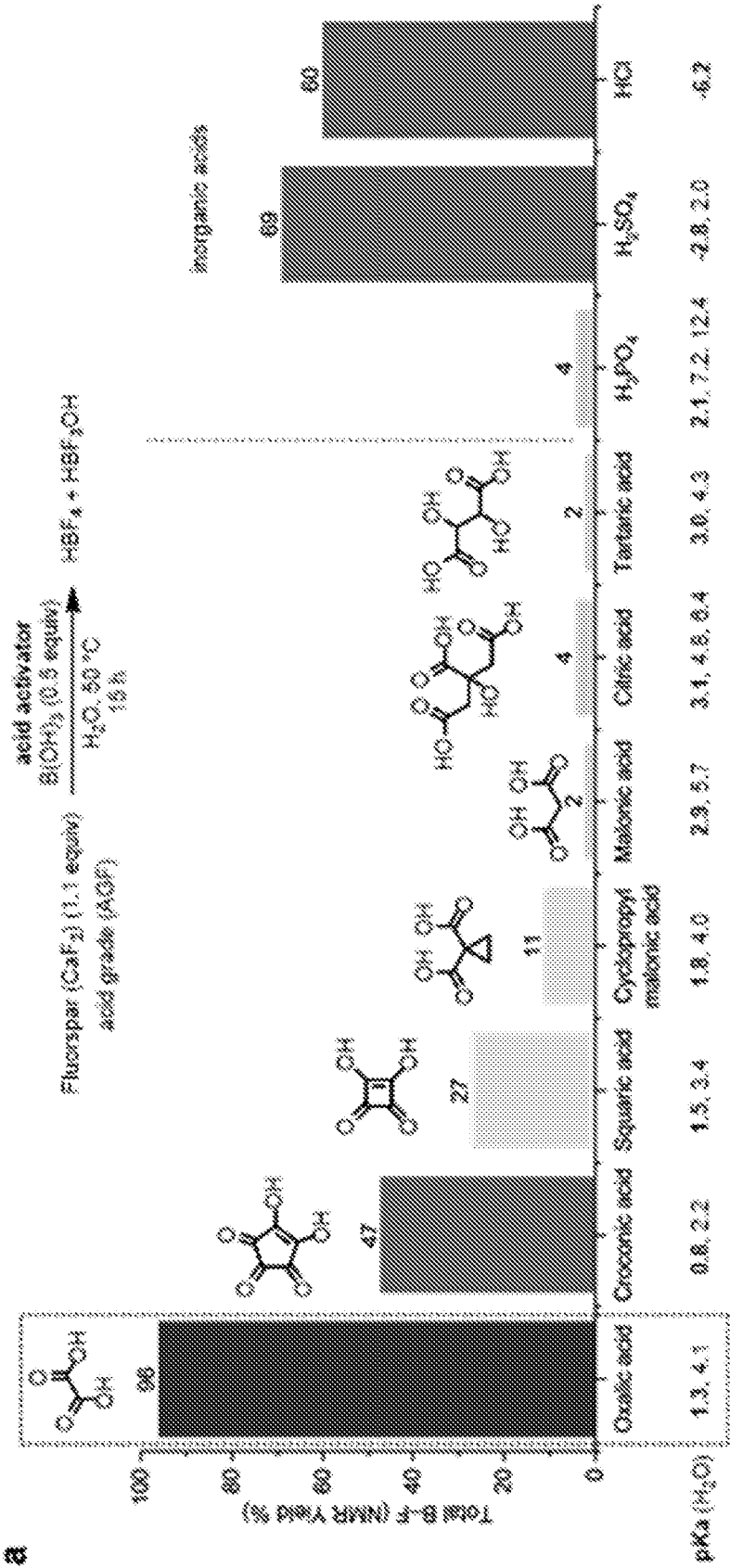


FIGURE 11

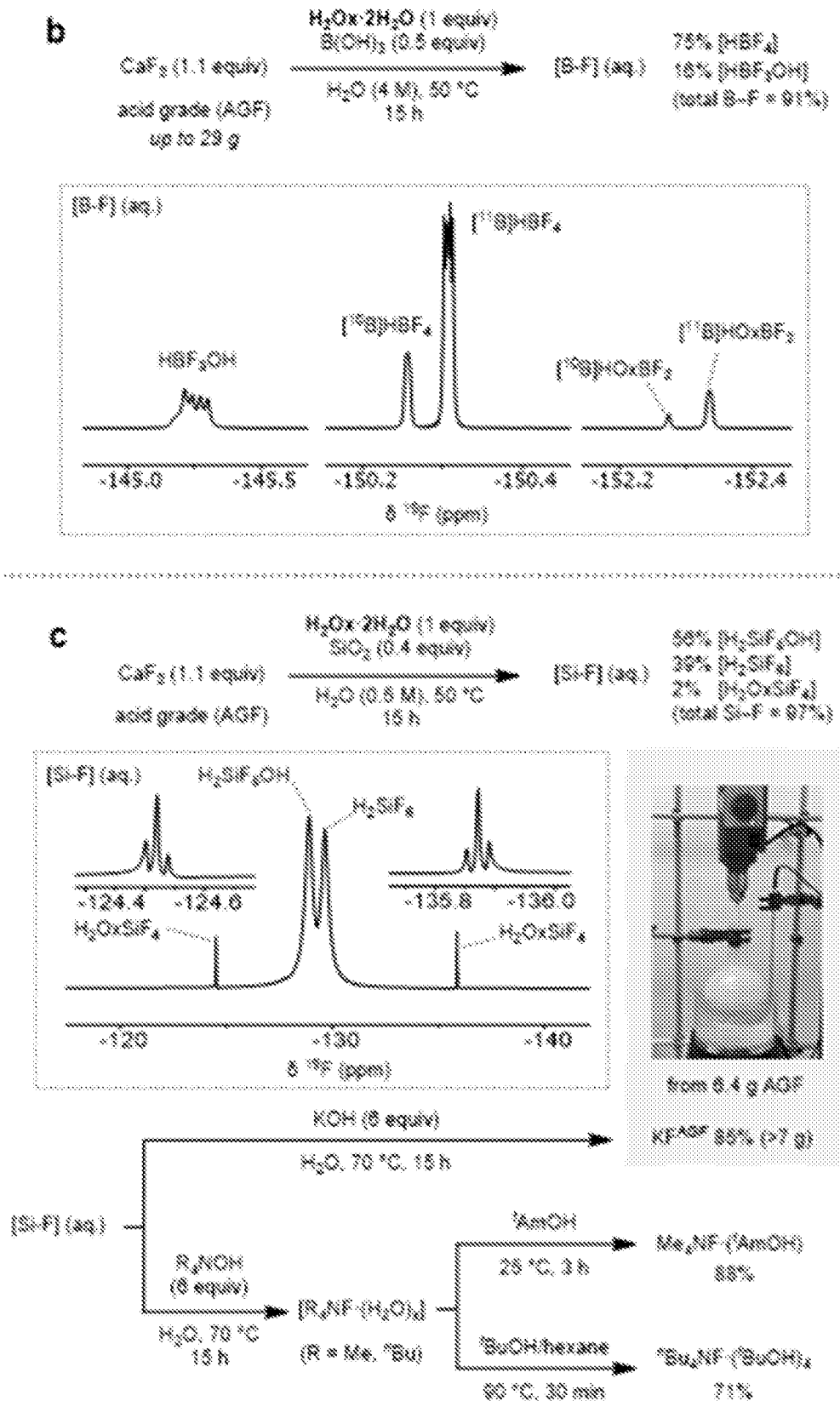


FIGURE 11 (continued)

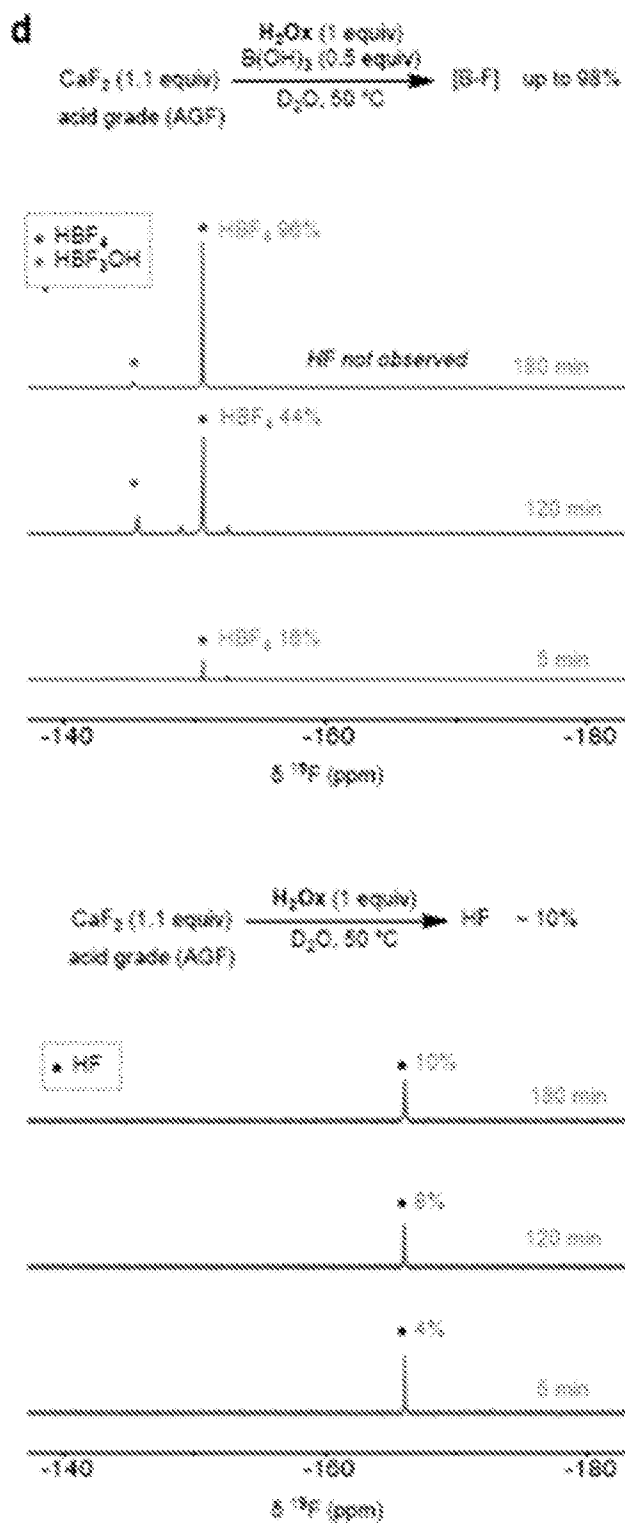


FIGURE 11 (CONTINUED)

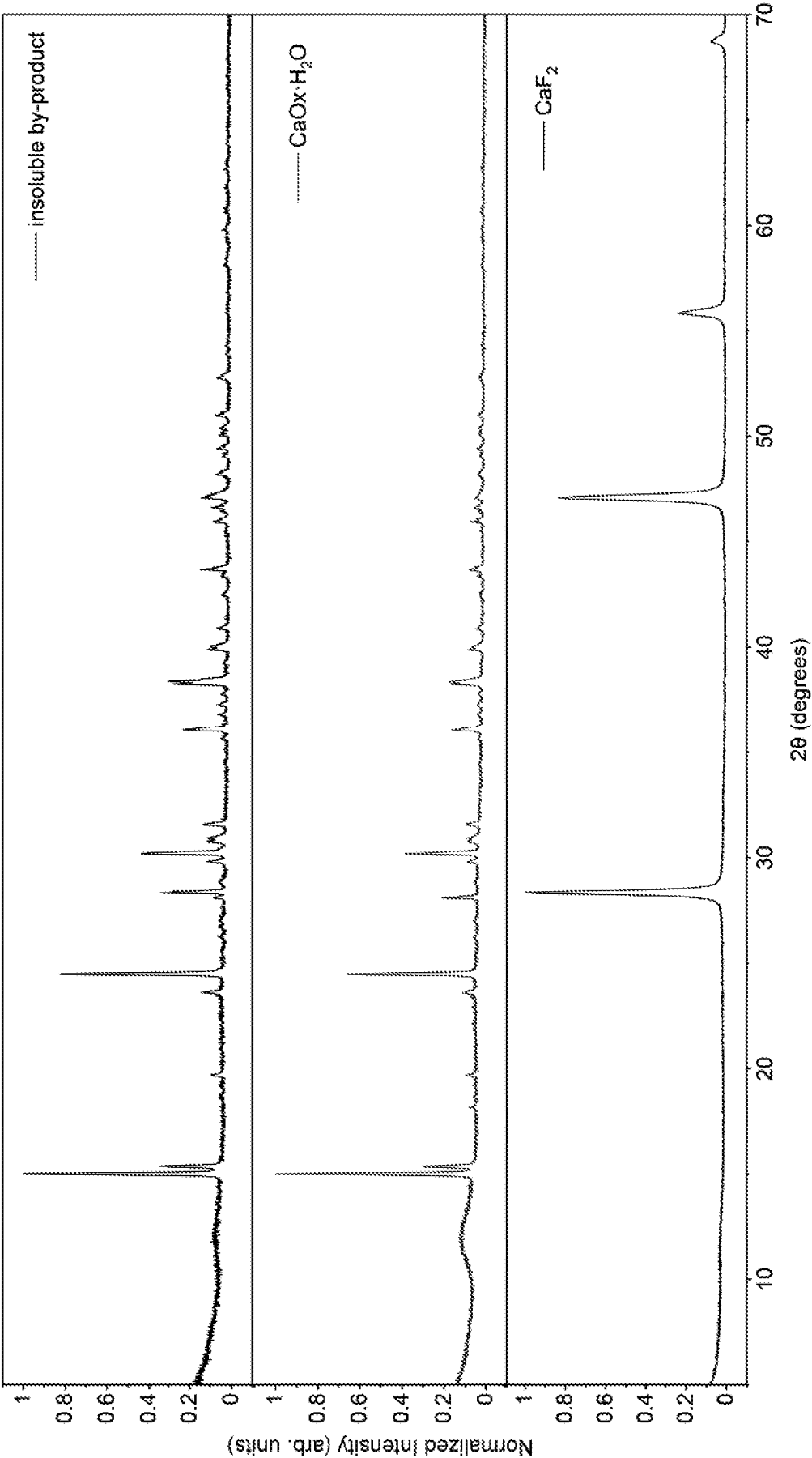


FIGURE 12

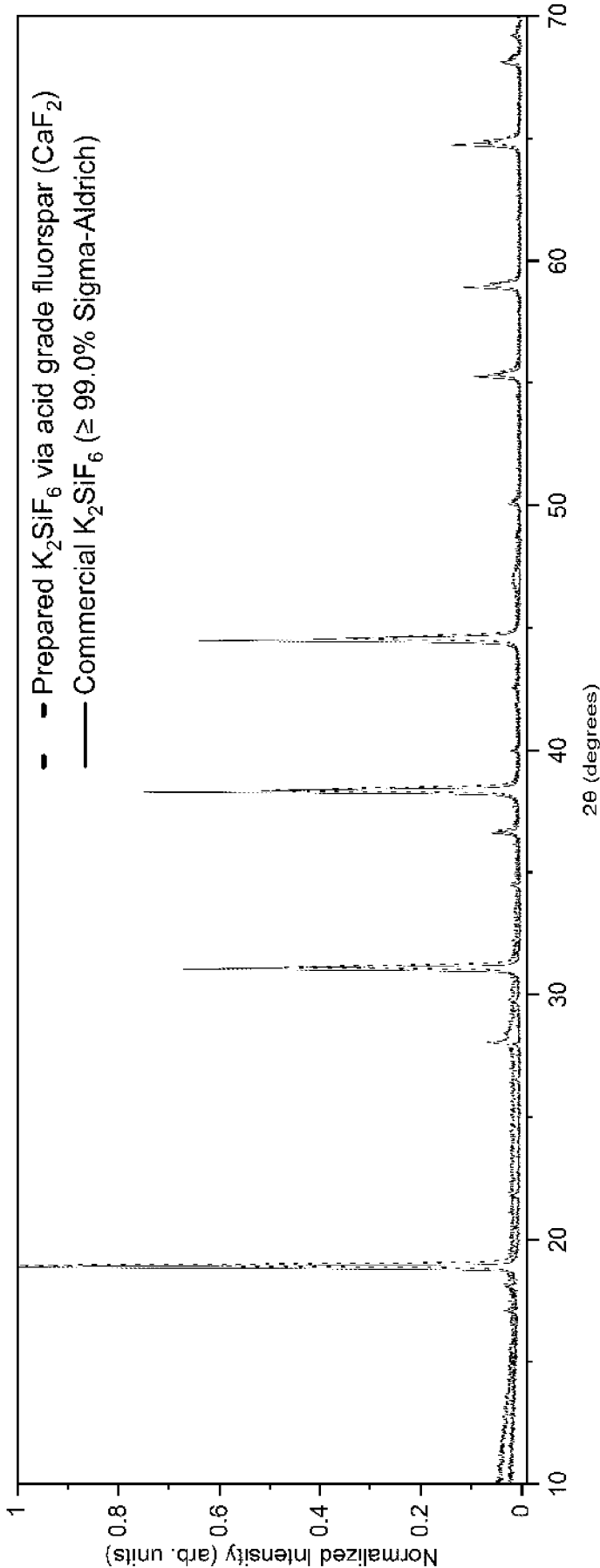


FIGURE 13

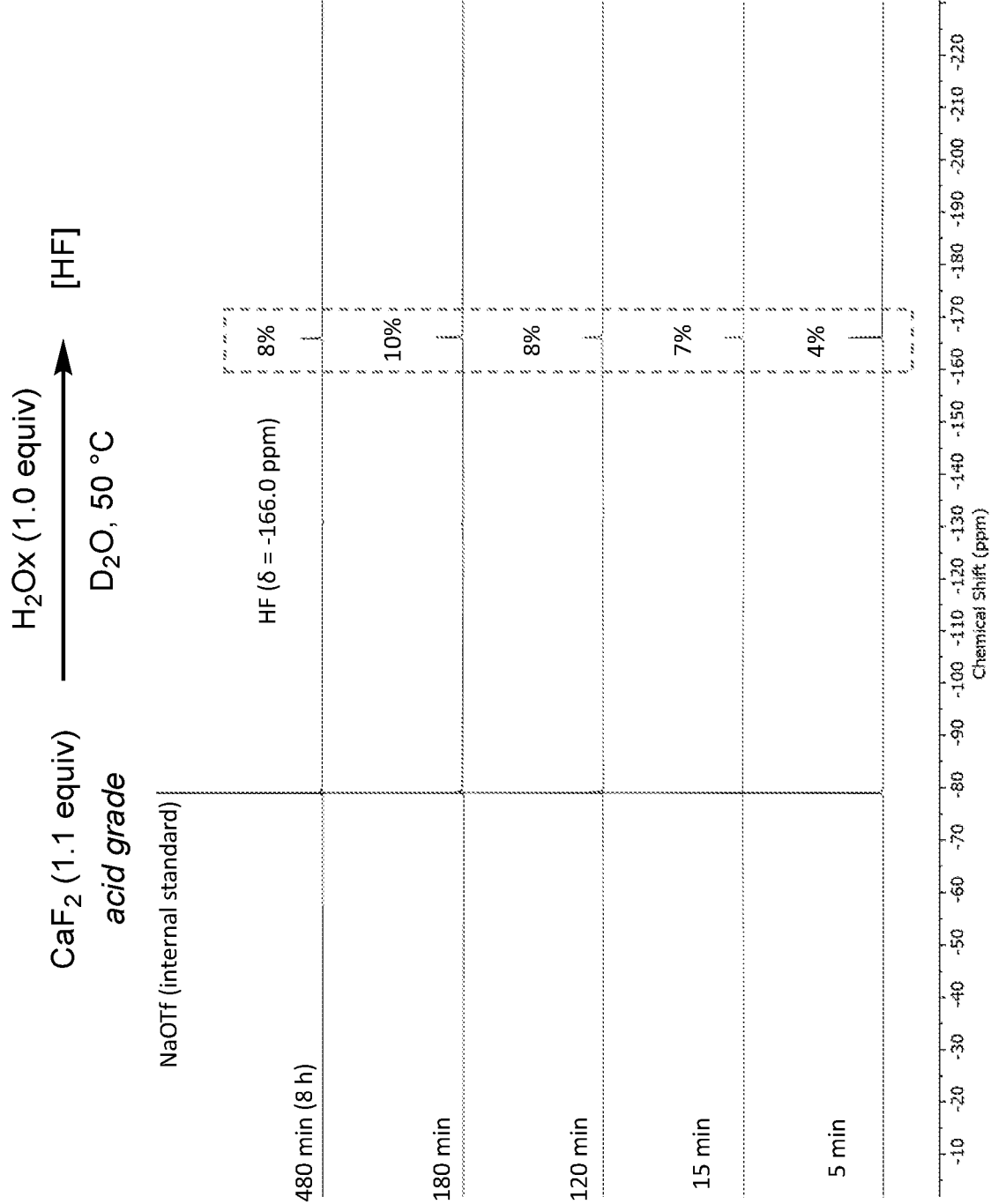


FIGURE 14

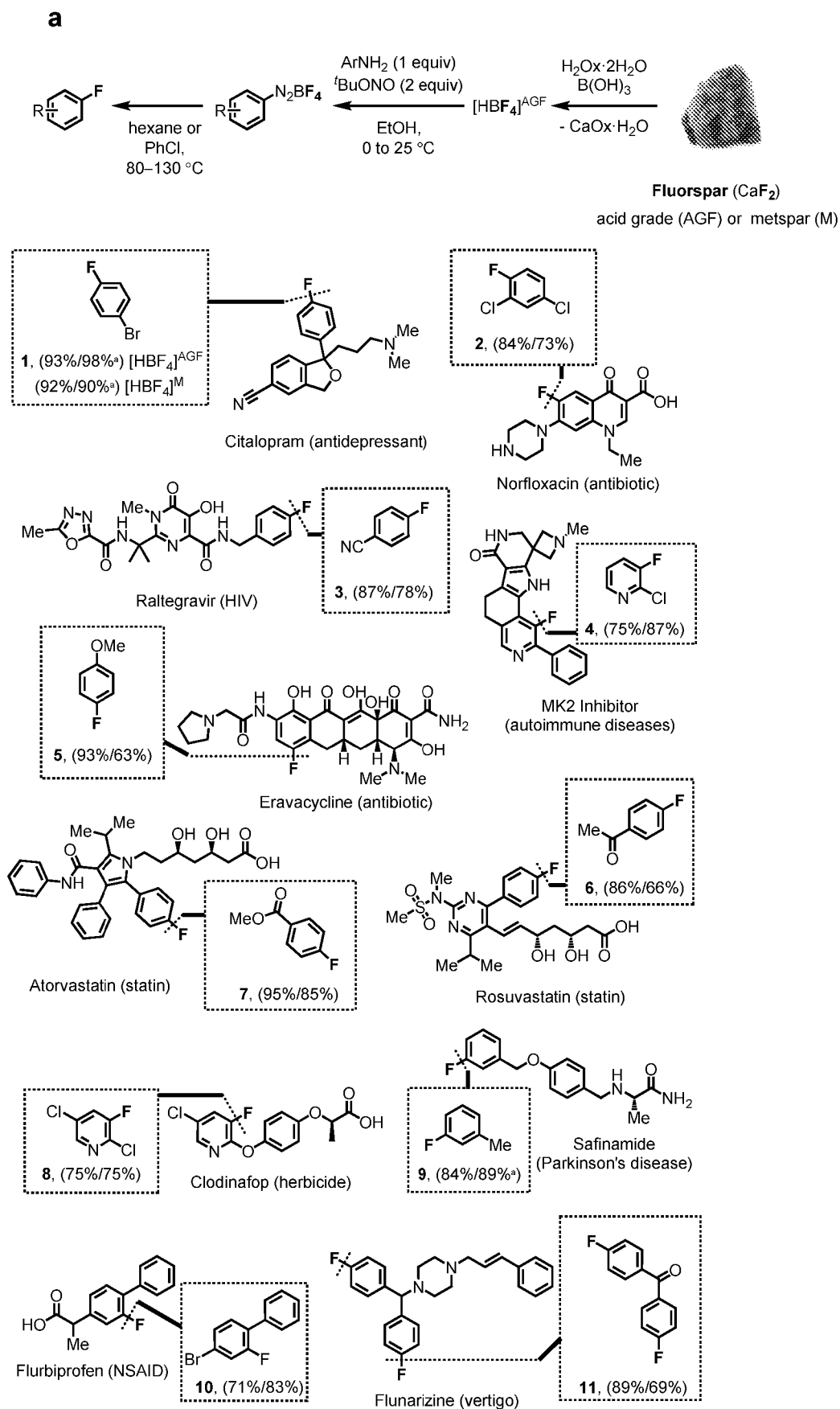
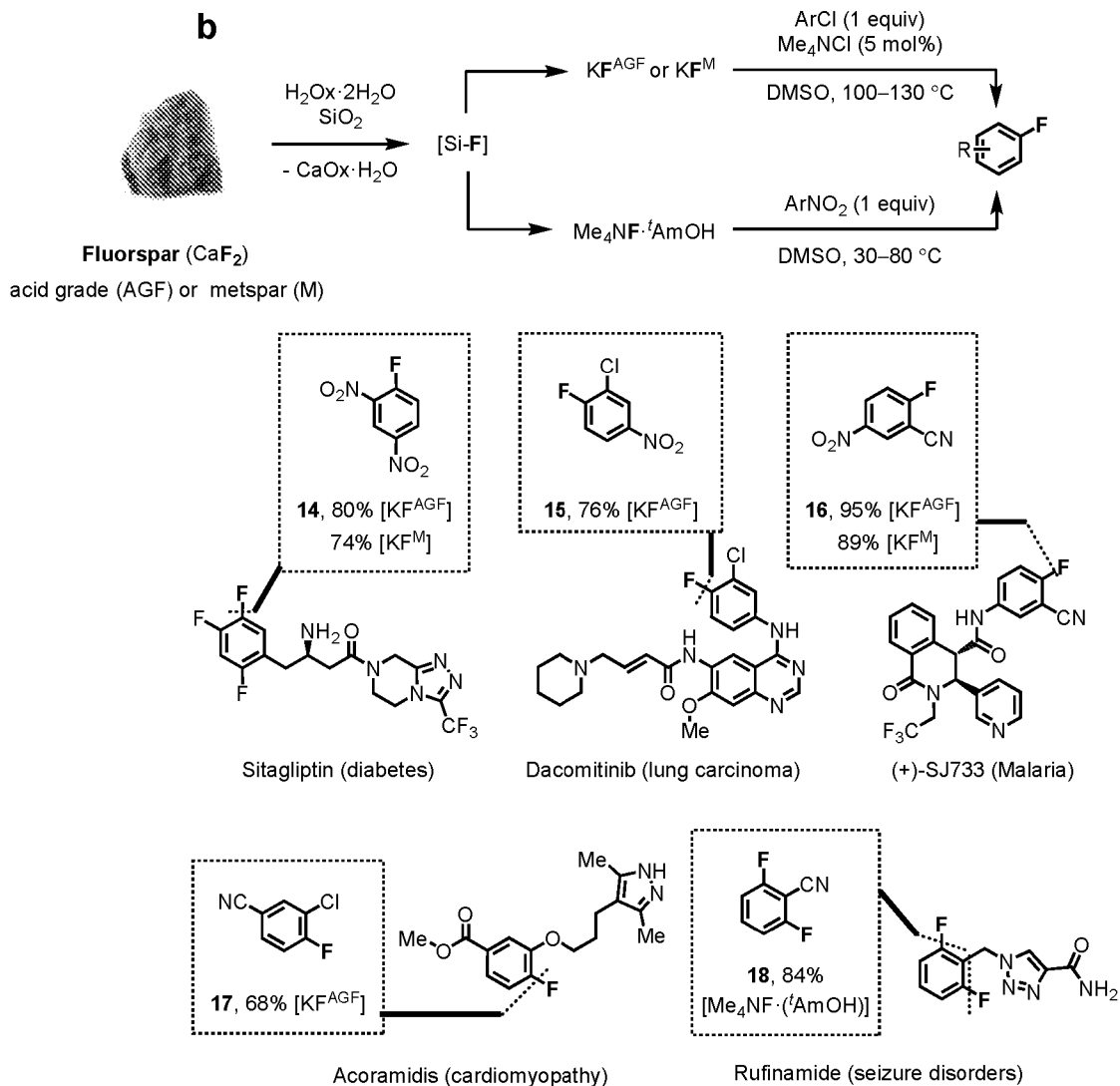


FIGURE 15



C Compounds featuring multiple fluoroarenes

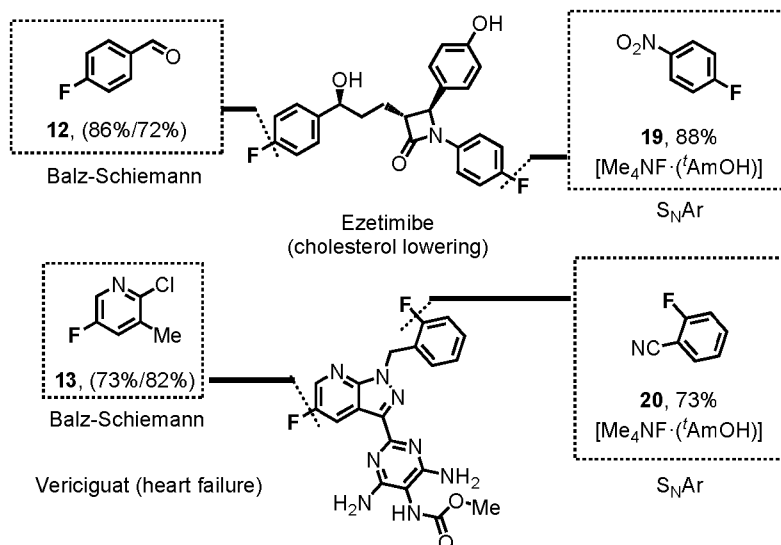


FIGURE 15 (continued)

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2024/051525

A. CLASSIFICATION OF SUBJECT MATTER					
INV.	C07B39/00	C07C25/13	C07C247/16	C07F5/02	C07F7/12
	C07C201/12	C07C253/30			
ADD.					
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)					
C07B C07C C07F					
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					
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category*	Citation of document, with indication, where appropriate, of the relevant passages				Relevant to claim No.
X	WO 2011/155666 A1 (KCC CORP [KR]; KANG KYUNG HOON [KR] ET AL.)				25
	15 December 2011 (2011-12-15)				
Y	A method of producing a fluorochemical (SiF ₄) comprising the steps of mixing in a single reactor an inorganic fluoride source (CaF ₂ or NaAlF ₄ , see examples 1-2) a fluoride acceptor (amorphous silica) and an activator (sulfuric acid), whereby a gaseous product of SiF ₄ is formed: see claim 1 and paragraph [56]				2-6, 14, 15, 19, 20

	- / - -				
☒ 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			"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		
"E" earlier application or patent but published on or after the international filing date			"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		
"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)			"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		
"O" document referring to an oral disclosure, use, exhibition or other means			"&" document member of the same patent family		
"P" document published prior to the international filing date but later than the priority date claimed					
Date of the actual completion of the international search			Date of mailing of the international search report		
23 August 2024			13/09/2024		
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 Lange, Tim		

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2024/051525

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HE JINGUI ET AL: "Study on the coordination properties of [CeFx] ₄ -x and [BFy] ₃ -y in sulfuric acid medium by complexometric potentiometric titration", JOURNAL OF FLUORINE CHEMISTRY, ELSEVIER, NL, vol. 156, 20 September 2013 (2013-09-20), pages 106-111, XP028786017, ISSN: 0022-1139, DOI: 10.1016/J.JFLUCHEM.2013.09.007	25
Y	A process for the preparation of a fluorochemical (KBF ₄), the process comprising reacting an inorganic fluoride source (CeF ₂), an activator (acid at a concentration of 1 mol/L) and a fluoride acceptor (H ₃ BO ₃): see paragraph 4.3.3 on page 110	2-6,14, 15,19,20
X	----- SPRENGER JAN A P ET AL: "Convenient synthesis of perfluoroalkyltrifluoroborates", JOURNAL OF FLUORINE CHEMISTRY, ELSEVIER, NL, vol. 206, 7 December 2017 (2017-12-07), pages 54-60, XP085337468, ISSN: 0022-1139, DOI: 10.1016/J.JFLUCHEM.2017.12.004	1,7-12, 16-18, 21-25
Y	Process for preparation of a fluorochemical (K[C ₂ F ₅ -BF ₃]) by mixing together in a one-pot reaction an inorganic fluoride source (KHF ₂), an activator (trifluoroacetic acid, with pK _a of 0,52) and a boron-based fluoride acceptor (pentafluoroethyltrimethoxyborate K[C ₂ F ₅ -B(OMe) ₃]): see scheme 5	2-6,14, 15,19,20
A	other activators used: MeCO ₂ H (see 3.2.1) and H ₂ SO ₄ (see 3.2.5) -----	13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2024/051525

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011155666 A1	15-12-2011	CN 102275934 A	14-12-2011
		EP 2473442 A1	11-07-2012
		JP 2012519651 A	30-08-2012
		KR 20110135785 A	19-12-2011
		TW 201144225 A	16-12-2011
		WO 2011155666 A1	15-12-2011
