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(54) Title: PYRIDINE- OR PYRAZINE-CONTAINING COMPOUNDS

(57) Abstract: Described herein are selective bis-alkynyl pyrazines, bis-alkynyl pyridines, bispyridine substituted ellagic acid derivatives, and pyridine-substituted coumarin derivatives and methods of making thereof.

PYRIDINE- OR PYRAZINE-CONTAINING COMPOUNDS

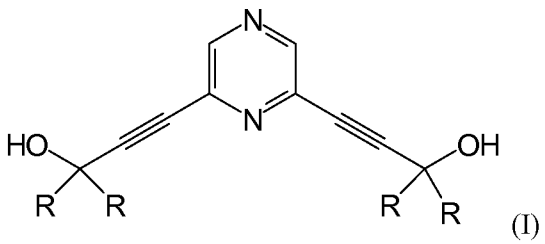
TECHNICAL FIELD

[0001] Pyridine- or pyrazine-containing compounds are described along with their methods of making.

SUMMARY

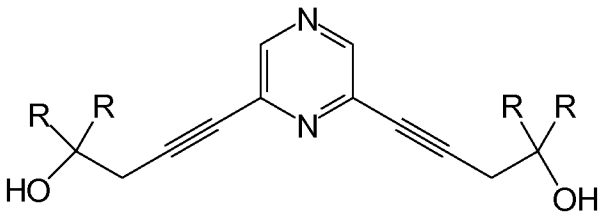
[0002] Pyridine- and pyrazine-containing compounds are valued materials in the fields of organic synthesis, supramolecular chemistry, and materials science. The presence of the nitrogen atoms, with their accompanying lone pair of electrons, renders pyridines and pyrazines both basic and nucleophilic, and thus can be used as highly soluble bases or catalysts in a variety of organic transformations. Pyridines and pyrazines are also valuable as synthons in organic synthesis, and are particularly useful in the preparation of pharmaceuticals and agrochemicals due to their propensity towards high biological activity. Pyridines and pyrazines also serve as ligands in the chelation of a variety of metals and metal ions, and the resultant organometallic complexes of pyridines and pyrazines are utilized, for example, as catalysts in asymmetric organic transformations, as dye sensitizers in solar cells, in organic light emitting diodes, and in the fields of artificial photosynthesis and related photogenerated energy transfer processes. Pyridines and pyrazines are also utilized industrially as components of adhesives, films, or other polymeric materials in which their properties, either alone or as metal complexes, impart valuable characteristics to the bulk material. Due to this widespread utility, there is a continuous desire to identify novel pyridine- and/or pyrazine-containing compounds.

[0003] In one aspect, pyridine- and pyrazine-containing compounds and their method of making are described, such compounds include those selected from the group consisting essentially of:
(a) bis-alkynyl pyrazine and bis-alkynyl pyridines of the formulas:



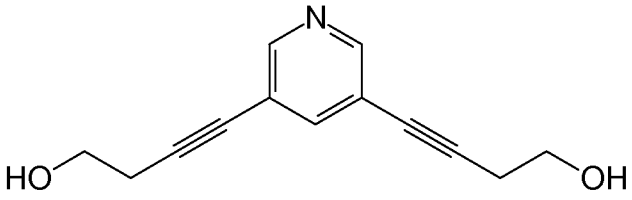
(I)

wherein R is selected from H, CH_3, or the two adjacent R groups join to form a cyclohexane ring;

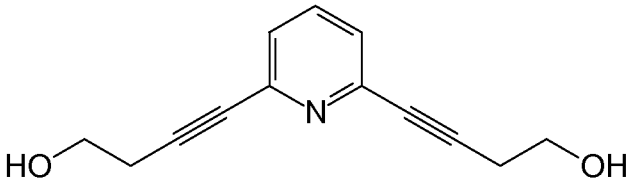


(II)

wherein R is selected from H, CH_3, or the two adjacent R groups join to form a cyclohexane ring;

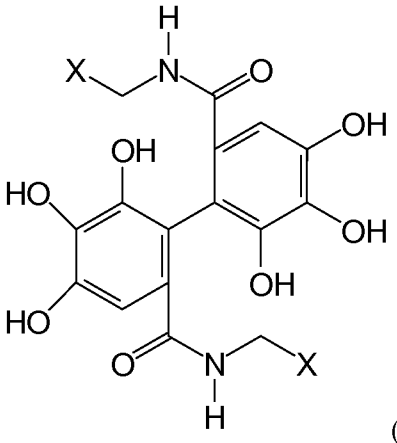


(III); and



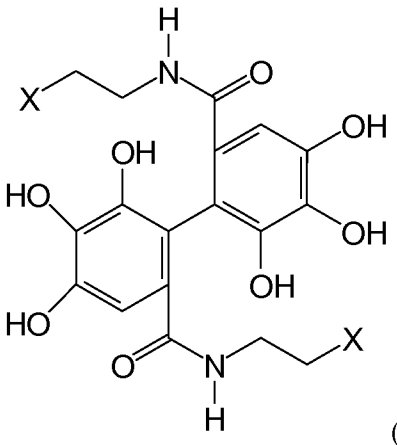
(IV);

(b) bispyridine substituted ellagic acid derivatives of the formulas:



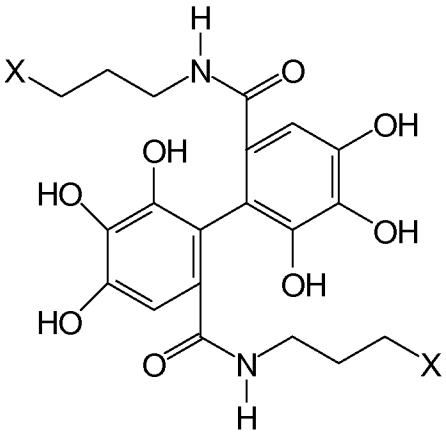
(V)

wherein X is a pyridyl group;



(VI)

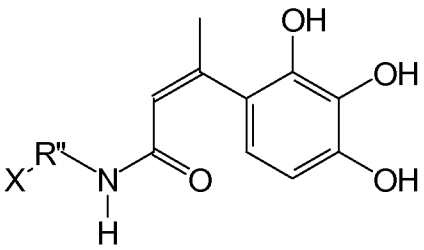
wherein X is a pyridyl group; and



(VII)

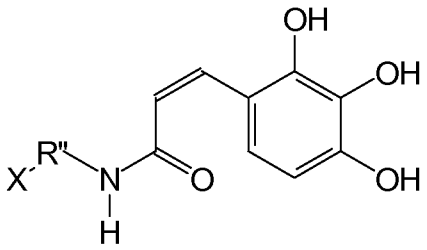
wherein X is selected from a pyridyl group; and

(c) pyridine-substituted coumarin derivatives of the formulas:



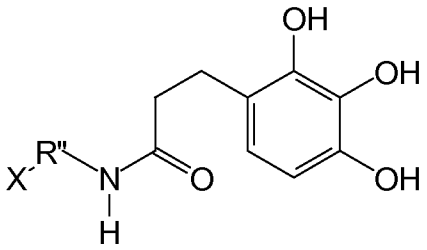
(VIII)

wherein (i) X is a 4-pyridyl group and R" is methylene, ethylene, or a propylene, or (ii)X is a 3-pyridyl group and R" is a methylene;



(IX)

wherein X is a 4-pyridyl group and R" is ethylene; and



(X)

wherein X is a 4-pyridyl group and R" is ethylene.

[0004] The above summary is not intended to describe each embodiment. The details of one or more embodiments of the invention are also set forth in the description below. Other features, objects, and advantages will be apparent from the description and from the claims.

DETAILED DESCRIPTION

[0005] As used herein, the term

"a", "an", and "the" are used interchangeably and mean one or more; and

"and/or" is used to indicate one or both stated cases may occur, for example A and/or B includes, (A and B) and (A or B).

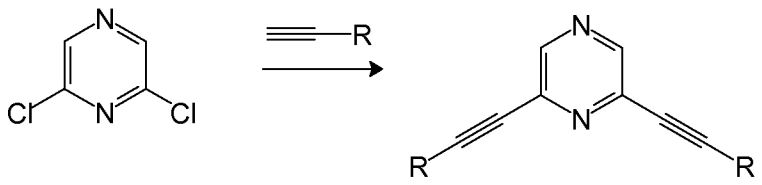
[0006] Also herein, recitation of ranges by endpoints includes all numbers subsumed within that range (e.g., 1 to 10 includes 1.4, 1.9, 2.33, 5.75, 9.98, etc.).

[0007] Also herein, recitation of "at least one" includes all numbers of one and greater (e.g., at least 2, at least 4, at least 6, at least 8, at least 10, at least 25, at least 50, at least 100, etc.).

[0008] In the present disclosure three groups of compounds comprising either a pyridine- or pyrazine ring are disclosed based on their method of making. These groups are divided into (a) bis-alkynyl pyrazine and bis-alkynyl pyridines; (b) bispyridine substituted ellagic acid derivatives; and (c) pyridine-substituted coumarin derivatives.

[0009] Bis-alkynyl Pyrazine and Bis-alkynyl Pyridines

[0010] In the present disclosure, compounds comprising two alkynyl groups (i.e., a triple bond between two carbon atoms) as well as a pyridine or pyrazine group may be prepared from a bis-chloro precursor as shown in the reaction below:



In the above reaction, the bis-chloro precursor is reacted with an alkynyl-terminated compound in the presence of a catalyst under basic conditions in a reaction known as the Sonogashira reaction.

[0011] In the present disclosure the bis-chloro precursor may be selected from 2,6-dichloropyrazine, 2,6-dichloropyridine, or 3,5-dichloropyridine.

[0012] In the present disclosure, the alkynyl-terminated compound may be selected from: alkynyl-terminated alcohols, comprising 2-10 carbon atoms, including for example, propargyl alcohol; 2-methyl-3-buyn-2-ol, 1-ethynyl-1-cyclohexanol, 3-butyn-1-ol.

[0013] The ratio of the alkynyl-terminated compound to the bis-chloro precursor to produce the bis-alkynyl pyrazine or bis-alkynyl pyridine should be at least 2:1 or even 3:1. Preferably there is an excess of alkynyl-terminated compound in the Sonogashira coupling reaction.

[0014] The reaction described above is run under basic pH conditions by adding an excess of a base. Exemplary bases include triethylamine, diisopropylamine, N,N-diisopropylethylamine, and cesium carbonate.

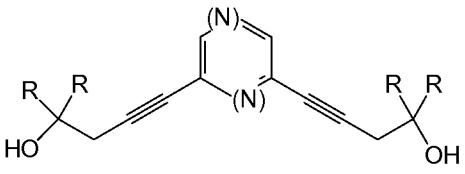
[0015] The reaction is also run in the presence of one or more catalysts. Such catalysts include palladium and copper. Exemplary palladium catalysts include: bis(triphenylphosphine)palladium (II) dichloride, 1,1'-bis(diphenylphosphino)ferrocene palladium (II) dichloride, and tetrakis(triphenylphosphine) palladium (0). Exemplary copper catalysts include copper (I) iodide. In one embodiment, one catalyst is used; in another embodiment, more than one catalyst is used. Typically the catalysts are added in small quantities such as no more than 5 mol%, 2.5 mol%, 1 mol%, or even 0.5 mol%.

[0016] To facilitate the reaction, a solvent is used, typically a polar aprotic solvent system, however polar protics solvents have also been used. Exemplary solvents include: tetrahydrofuran, diethyl ether, methyl tert-butyl ether, dimethylformamide, and acetonitrile.

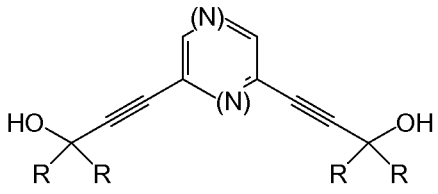
[0017] In one embodiment, the reaction between the bis-chloro precursor and the alkynyl-terminated compound may be conducted at a temperature of between at least room temperature, 25, 30, or even 35°C; at most 90, 100, or even 150°C.

[0018] Final reaction products must be separated from remaining catalysts, catalyst by-products, bases, and other salts present. Such techniques are known in the art. Typically this accomplished by filtration of the reaction mixture through a stationary phase such as diatomaceous earth (Celite) and/or washing the reaction mixture with an aqueous phase. Upon removal of the solvent and/or other volatile components under reduced pressure, the reaction product can optionally be purified by silica gel chromatography and/or crystallization from an appropriate solvent.

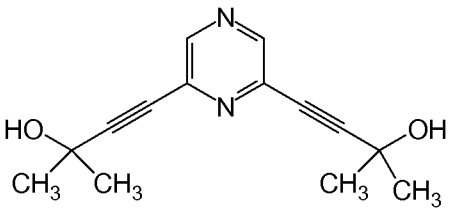
[0019] Exemplary compounds made according to the above reaction include:

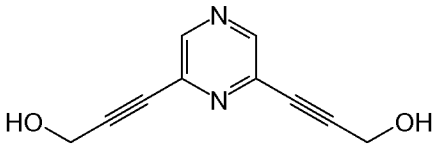


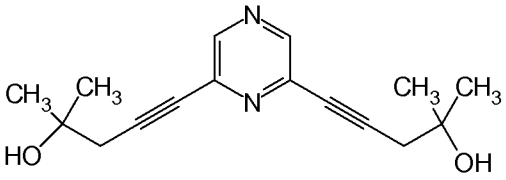
and



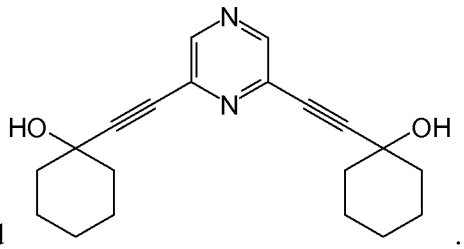
wherein R is selected from H or a C1-C4 alkyl group or the two adjacent R groups join to form a cyclohexane ring and the aromatic ring comprises 1 or 2 nitrogen atoms. Specific pyrazine-containing compounds include for example:







and



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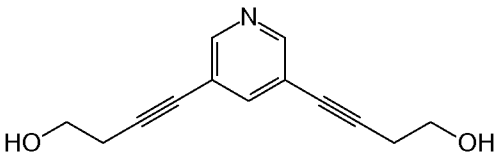
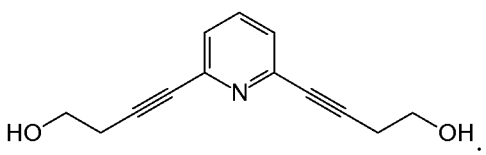
Specific pyridine-containing compounds include:



and



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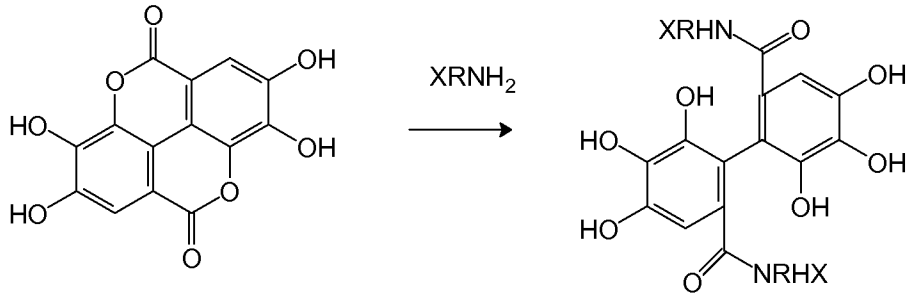
[0020] Bispyridine Substituted Ellagic Acid Derivatives

[0021] In the present disclosure, compounds comprising two pyridine groups (i.e., C5H5N) are prepared from Ellagic acid as shown in the reaction below:



In the above reaction, Ellagic acid is reacted with a primary amine-substituted pyridine compound ($XRNH_2$) to form bis-pyridine derivatives.

[0022] In the present disclosure, Ellagic acid may be used and/or alternatively a salt or hydrate form of Ellagic acid.

[0023] As used herein, $XRNH_2$ represents a primary amine-substituted pyridine compound, wherein R is a bond, or a C1-C4 alkylene group. The pyridine may be a 2-, 3-, or 4-pyridyl group. Exemplary primary amine-substituted pyridine compounds include: 2-(aminomethyl)pyridine, 3-(aminomethyl)pyridine,4-(aminomethyl)pyridine, 2-(2-aminoethyl)pyridine, 3-(2-aminoethyl)pyridine, 4-(2-aminoethyl)pyridine, 3-(2-pyridyl)-1-propanamine, 3-(3-pyridyl)-1-propanamine, and 3-(4-pyridyl)-1-propanamine.

[0024] The ratio of the primary amine-substituted pyridine compound to the Ellagic acid to produce the bispyridine substituted ellagic acid derivative is at least 2:1 or even 3:1. Preferably there is an excess of the primary amine-substituted pyridine compound in the addition reaction.

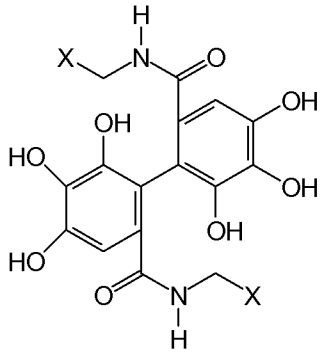
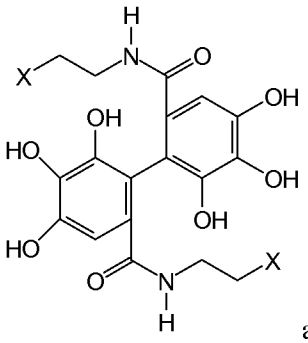
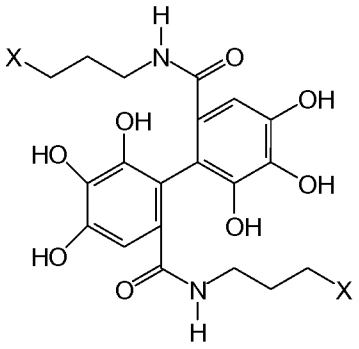
[0025] To facilitate the reaction, a solvent is used, specifically a polar aprotic solvent system. Exemplary solvents include: tetrahydrofuran, methyl tert-butyl ether, dimethylformamide, and acetonitrile.

[0026] In one embodiment, the reaction between the primary amine-substituted pyridine compound and the Ellagic acid is conducted at temperatures higher than room temperature. Typically at the reflux temperature of the solvent is used, for example, temperatures between at least room temperature, 25, 30, or even 35°C; at most 90, 100, or 150°C.

[0027] To facilitate the reaction, in one embodiment, a catalyst may be added. The catalyst may increase the rate of reaction at any given temperature, or allow the reaction to be performed at a lower temperature. Exemplary catalysts include 4-dimethylaminopyridine and 1,4-diazabicyclo[2.2.2]octane. Amounts of catalysts added may be no more than 10 mol%, 5 mol%, or even 2 mol%.

[0028] In one embodiment, the resulting product may be collected via filtration and washed with solvent.

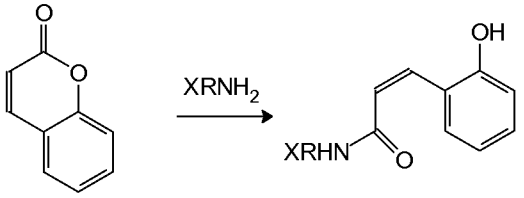
[0029] Exemplary compounds made according to the above reaction include:



and


wherein X is selected from a pyridyl group (2-, 3-, or 4-pyridyl group).

[0030] Pyridine-substituted Coumarin Derivatives

[0031] In the present disclosure, compounds comprising a pyridine group (i.e., C5H5N) are prepared from a coumarin ring opening reaction as shown in the reaction below:



In the above reaction, a coumarin is reacted with a primary amine-substituted pyridine compounds to form a pyridine-substituted coumarin derivative.

[0032] Coumarin starting materials include: 4-methylesculetin, coumarin, dihydrocoumarin, and 7, 8-dihydroxy-4-methylcoumarin.

[0033] As used herein, $XRNH_2$ represents a primary amine-substituted pyridine compound, wherein R is a bond, or a C1-C4 alkylene group. In the present disclosure, the primary amine-substituted pyridine compounds may be selected from: 2-(aminomethyl)pyridine, 3-(aminomethyl)pyridine,4-(aminomethyl)pyridine, 2-(2-aminoethyl)pyridine, 3-(2-aminoethyl)pyridine, 4-(2-aminoethyl)pyridine, 3-(2-pyridyl)-1-propanamine, 3-(3-pyridyl)-1-propanamine, and 3-(4-pyridyl)-1-propanamine.

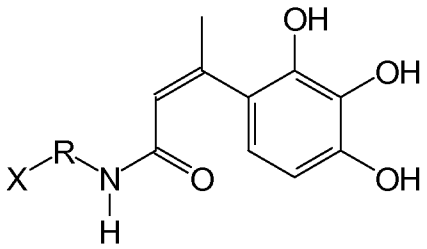
[0034] The ratio of the primary amine-substituted pyridine compound to the coumarin to produce the pyridine substituted coumarin derivative should be at least 1:1 or even 1.5:1. Preferably there is an excess of the primary amine-substituted pyridine compound in the addition reaction.

[0035] To facilitate the reaction, a solvent is used, specifically a polar aprotic solvent system. Exemplary solvents include: tetrahydrofuran, methyl tert-butyl ether, dimethylformamide, and acetonitrile.

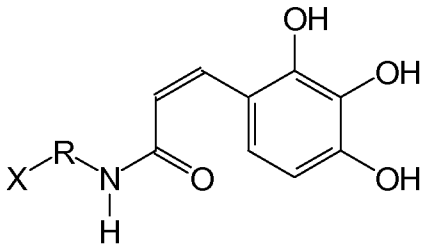
[0036] In one embodiment, the reaction between the primary amine-substituted pyridine compound and the coumarin is conducted at temperatures higher than room temperature. Typically at the reflux temperature of the solvent used, for example, temperatures between at least room temperature, 25, 30, or even 35°C; at most 90, 100, or even 150°C.

[0037] To facilitate the reaction, a catalyst may be added. The catalyst may increase the rate of reaction at any given temperature, or allow the reaction to be performed at a lower temperature. Exemplary catalysts include 4-dimethylaminopyridine and 1,4-diazabicyclo[2.2.2]octane. Amounts of catalysts added may be no more than 10 mol%, 5 mol%, or even 2 mol%.

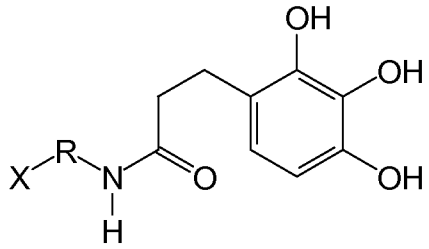
[0038] Exemplary compounds made according to the above reaction include:



wherein (i) X is a 4-pyridyl group and R is methylene, ethylene, or a propylene, or (ii)X is a 3-pyridyl group and R is a methylene;



wherein X is a 4-pyridyl group and R is ethylene; and



wherein X is a 4-pyridyl group and R is ethylene.

[0039] In one embodiment, the compounds as disclosed herein may be used as starting materials, or may be used in compositions such as epoxy adhesives and epoxy powder coatings as disclosed in U.S. Appl. No. 61/823111, filed May 14, 2013, the disclosure herein incorporated by reference in its entirety.

EXAMPLES

[0040] Advantages and embodiments of this disclosure are further illustrated by the following examples, but the particular materials and amounts thereof recited in these examples, as well as other conditions and details, should not be construed to unduly limit this invention. In these examples, all percentages, proportions and ratios are by weight unless otherwise indicated.

[0041] All materials are commercially available, for example from Sigma-Aldrich Chemical Company; Milwaukee, WI, or known to those skilled in the art unless otherwise stated or apparent.

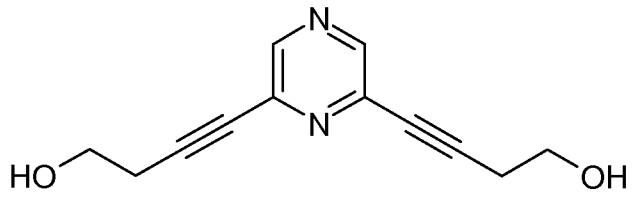
[0042] These abbreviations are used in the following examples: g = gram, kg = kilograms, min = minutes, mol = mole; cm= centimeter, mm = millimeter, ml = milliliter, L = liter, psi=pressure per square inch, MPa = megaPascals, and wt = weight.

Materials

Material	Source
Acetonitrile	EMD Chemicals, Inc.; Gibbstown, NJ
4-Acetylpyridine	Sigma Aldrich; St. Louis, MO
4-(2-Aminoethyl)pyridine	TCI America; Portland, OR
Aminoguanidine sulfate	Alfa Aesar; Ward Hil, MA
Bis(triphenylphosphine) palladium(II) dichloride	TCI America; Portland, OR
3-Butyn-1-ol	Sigma Aldrich; St. Louis, MO
Copper (I) iodide	Sigma Aldrich; St. Louis, MO
Dichloromethane	EMD Chemicals, Inc.; Gibbstown, NJ
2,6-Dichloropyrazine	Sigma Aldrich; St. Louis, MO
7,8-Dihydroxy-4-methylcoumarin	Sigma Aldrich; St. Louis, MO
Ellagic acid	AmplaChem, Inc.; Carmel, IN
Ethyl acetate	EMD Chemicals, Inc.; Gibbstown, NJ
Hexane	EMD Chemicals, Inc.; Gibbstown, NJ
Silica gel (230-400 Mesh)	Alfa Aesar; Ward Hil, MA
Tetrahydrofuran	EMD Chemicals, Inc.; Gibbstown, NJ
Triethylamine	EMD Chemicals, Inc.; Gibbstown, NJ

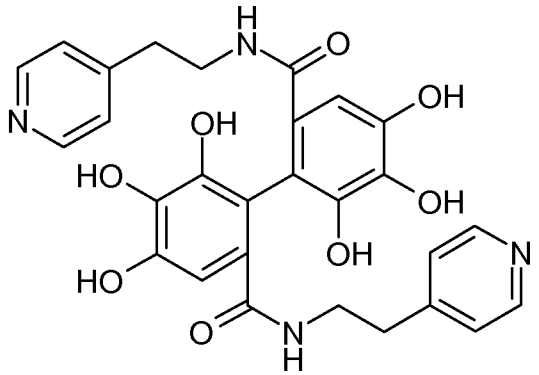
[0043] NMR: Nuclear magnetic resonance spectra (proton – 1H NMR) were analyzed and recorded using an NMR spectrometer (UltraShield™Plus 500 MHz NMR spectrometer; Bruker Corporation; Billerica, MA).

[0044] Preparation of Bis-alkynyl pyrazine



[0045] A 500 mL three neck round-bottomed flask was equipped with a reflux condenser, pressure-equalizing addition funnel, and magnetic stirbar. 2,6-dichloropyrazine (14.0 g, 94.0 mmol), 3-butyn-1-ol (16.5 g, 235 mmol), triethylamine (39.4 mL, 282 mmol), and 200 mL acetonitrile were added to the flask, and the resultant solution was degassed using several cycles of evacuation / nitrogen back flow. Copper iodide (1.80 g, 9.40 mmol) and bis(triphenylphosphine) palladium(II) dichloride (1.65 g, 2.35 mmol) were added to the solution, and the degassing procedure was repeated. The reaction mixture was heated at reflux overnight under nitrogen atmosphere with vigorous stirring. Silica gel was added to the reaction mixture, and the volatile components were evaporated under reduced pressure. The adsorbed material was loaded onto a silica gel filter column and eluted with ethyl acetate to afford the product (11.6 g, 57% of theoretical yield) as a yellow solid. 1H NMR (500 MHz, $CDCl_3$): δ 8.51 (s, 2H), 3.91 (q, J = 6.4 Hz, 4H), 3.56 (t, J = 6.4 Hz, 2H), 2.77 (t, J = 6.4 Hz, 2H).

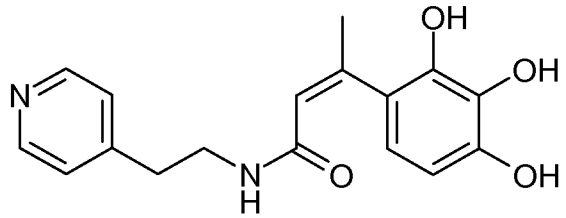
[0046] Preparation of Ellagic acid adduct:



[0047] To a 250 mL round-bottomed flask equipped with magnetic stirbar was added ellagic acid (9.07 g, 30.0 mmol) and tetrahydrofuran (40 mL). A solution of 4-(2-aminoethyl)pyridine (7.33 g, 60.0 mmol) in tetrahydrofuran (20 mL) was added via pipette, and the resultant mixture was heated at reflux overnight while stirring vigorously. After cooling to ambient temperature, the precipitated product was collected via filtration, washing with additional tetrahydrofuran. Drying

under vacuum provided the product (13.5 g, 83% of theoretical yield) as a tan solid. 1H NMR (500 MHz, d_6-DMSO): δ 8.50 (d, J = 5.8 Hz, 4H), 7.29 (d, J = 5.8 Hz, 4H), 7.20 (s, 2H), 3.07 (m, 4H), 2.84 (m, 4H).

[0048] Preparation of Coumarin derivative:



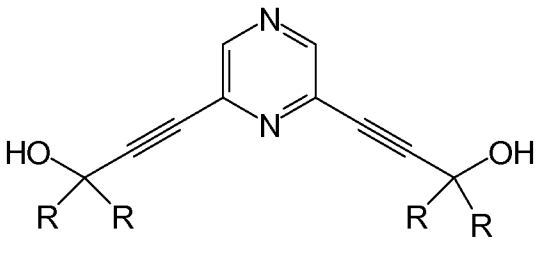
[0049] To a 250 mL round-bottomed flask equipped with magnetic stirbar was added 7,8-dihydroxy-4-methyl coumarin (3.64 g, 20.0 mmol) and tetrahydrofuran (30 mL). A solution of 4-(2-aminoethyl)pyridine (2.44 g, 20.0 mmol) in tetrahydrofuran (20 mL) was added via pipette, and the resultant mixture was heated at reflux overnight while stirring vigorously. The majority of the tetrahydrofuran was evaporated under reduced pressure to afford a thick orange oil. A 1:1 Ethyl acetate / dichloromethane solution (100 mL) was added, and the resultant mixture was heated at reflux while stirring vigorously. The yellow precipitate which formed was collected via filtration and dried under vacuum to afford the product (4.56 g, 75% of theoretical yield). 1H NMR (500 MHz, d_6-DMSO): δ 8.46 (dd, J1 = 1.6 Hz, J2 = 4.4 Hz, 2H), 7.25 (dd, J1 = 1.6 Hz, J2 = 4.4 Hz, 2H), 7.05 (d, J = 8.6 Hz, 1H), 6.77 (d, J = 8.6 Hz, 1H), 6.07 (d, J = 1.0 Hz, 1H), 2.87 (t, J = 7.4 Hz, 2H), 2.72 (t, J = 7.4 Hz, 2H), 2.35 (d, J = 1.0 Hz, 3H).

[0050] Foreseeable modifications and alterations of this invention will be apparent to those skilled in the art without departing from the scope and spirit of this invention. This invention should not be restricted to the embodiments that are set forth in this application for illustrative purposes.

What is claimed is:

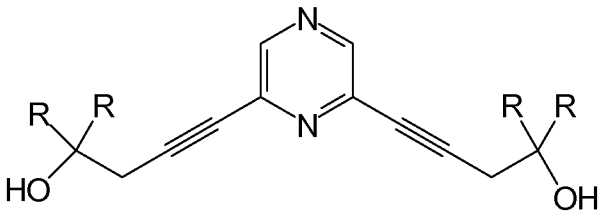
1. A composition comprising a compound selected from the group consisting essentially of:

(a) bis-alkynyl pyrazine and bis-alkynyl pyridines of the formulas:



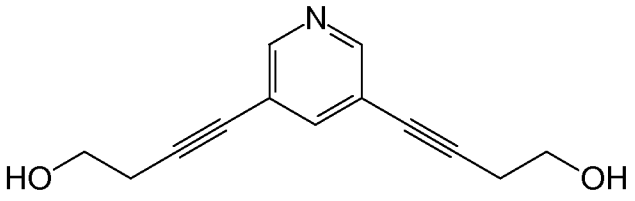
(I)

wherein R is selected from H, CH_3, or the two adjacent R groups join to form a cyclohexane ring;

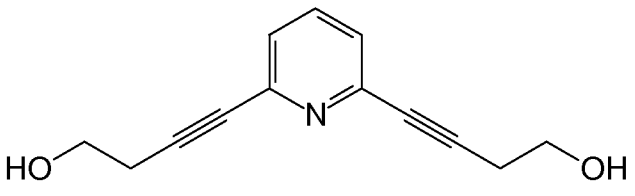


(II)

wherein R is selected from H, CH_3, or the two adjacent R groups join to form a cyclohexane ring;

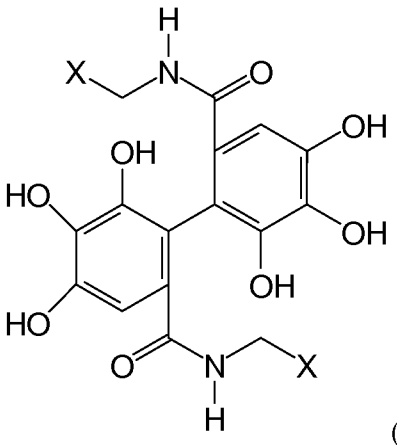


(III); and



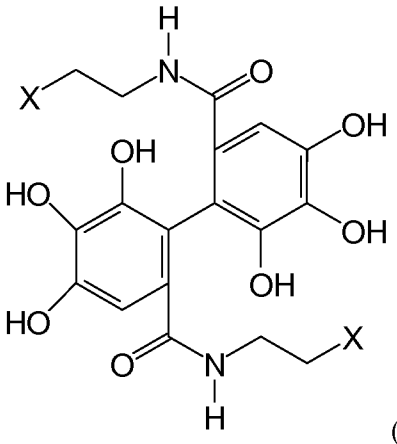
(IV);

(b) bispyridine substituted ellagic acid derivatives of the formulas:



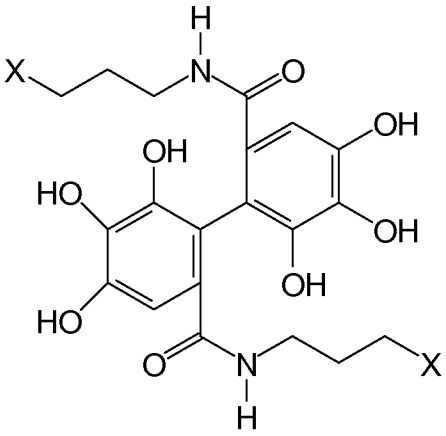
(V)

wherein X is a pyridyl group;



(VI)

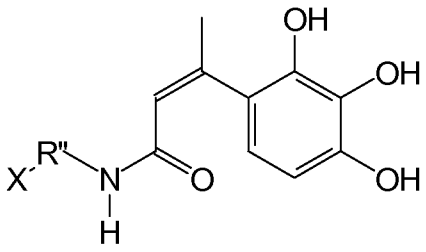
wherein X is a pyridyl group; and



(VII)

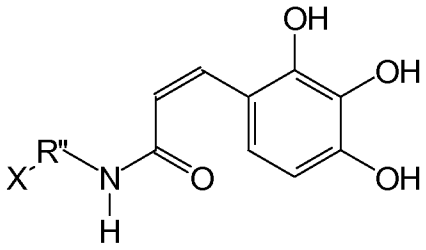
wherein X is selected from a pyridyl group; and

(c) pyridine-substituted coumarin derivatives of the formulas:



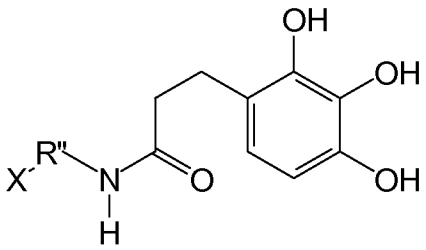
(VIII)

wherein (i) X is a 4-pyridyl group and R" is methylene, ethylene, or a propylene, or (ii)X is a 3-pyridyl group and R" is a methylene;



(IX)

wherein X is a 4-pyridyl group and R" is ethylene; and



(X)

wherein X is a 4-pyridyl group and R" is ethylene.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/035132

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Claim 1 (partly) is directed to a composition comprising a bis-alkynyl pyrazine or a bis-alkynyl pyridine derivative.

Claim 1 (partly) is directed to a composition comprising a bispyridine-substituted elagic acid derivative.

Claim 1 (partly) is directed to a composition comprising a pyridine-substituted coumarin derivative.

1. ☐ As all required addtional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1 (partly, regarding a composition comprising a bis-alkynyl prazine or a bis-alkynyl pyridine)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/035132

A. CLASSIFICATION OF SUBJECT MATTER

C07D 211/90(2006.01)i, C07D 241/10(2006.01)i, C07D 241/14(2006.01)i

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)
C07D 211/90; C07D 487/04; A61K 31/4985; C07D 403/04; C07D 241/10; C07D 241/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: bis-alkynyl pyrazine, bis-alkynyl pyridine

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JEAN, A. et al, `Stereoselective access to heteroarylmethylene-substituted pyrrolidines: fully organocatalytic Mannich-hydroamination reactions`, Chemical Communications, January 2013, Vol. 49, pp. 1651-1653 See page 1652; electronic supplementary material, S7, compound 8i.	1
A	US 2009-0215785 A1 (DUBOIS DAISY JOE et al.) 27 August 2009 See column 22, paragraphs [0260]-[0261], example 16.	1
A	KR 10-2010-0114094 A (F.HOFFMANN-LA ROCH AG) 22 October 2010 See page 72, paragraphs [0505]-[0508], example 5.	1
A	GOTO, H. et al., `Single-Site Modifications and Their Effect on the Folding Stability of m-Phenylene Ethynylene Oligomers, Organic Letters, February 2004, Vol. 6, No. 6, pp.889-892 See scheme 1; compounds 9, 10 and 12 in table 1.	1
A	NAKAMURA, H. et al., `Bimodal Chemiluminescence of 8-Chlorostyryl-6-phenylethynylimidazopyrazinone: Large Bathochromic Shift Caused by a Styryl Group at 8-Position, Tetrahedron Letters, 1998, Vol. 39, pp. 301-304 See compound 4 in scheme 1.	1

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
07 October 2014 (07.10.2014)	**07 October 2014 (07.10.2014)**

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2014/035132

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2009-0215785 A1	27/08/2009	AR 070467 A1	07/04/2010
		AT 519763 T	15/08/2011
		AU 2009-218607 A1	03/09/2009
		AU 2009-218609 A1	03/09/2009
		CA 2712507 A1	03/09/2009
		CA 2713324 A1	03/09/2009
		CA 2713710 A1	03/09/2009
		CA 2713718 A1	03/09/2009
		CA 2716223 A1	03/09/2009
		CN 101939324 A	05/01/2011
		CN 101945877 A	12/01/2011
		CN 101945877 B	03/07/2013
		CN 101952294 A	19/01/2011
		CN 101952295 A	19/01/2011
		CN 101952295 B	20/11/2013
		CN 101952296 A	19/01/2011
		CN 101952296 B	21/08/2013
		EP 2245033 A1	03/11/2010
		EP 2245033 B1	31/08/2011
		EP 2247592 A1	10/11/2010
		EP 2247592 B1	31/08/2011
		EP 2247593 A1	10/11/2010
		EP 2247593 B1	10/08/2011
		EP 2247595 A1	10/11/2010
		EP 2247595 B1	20/07/2011
		EP 2250172 A1	17/11/2010
		EP 2250172 B1	31/08/2011
		IL 206818 D0	30/12/2010
		JP 05-284377 B2	11/09/2013
		JP 05-368484 B2	18/12/2013
		JP 05-368485 B2	18/12/2013
		JP 05-485178 B2	07/05/2014
		JP 05-529049 B2	25/06/2014
		JP 2011-513210 A	28/04/2011
		JP 2011-513261 A	28/04/2011
		JP 2011-513262 A	28/04/2011
		JP 2011-513263 A	28/04/2011
		JP 2011-513263 T	28/04/2011
		JP 2011-513264 A	28/04/2011
		KR 10-1261514 B1	07/05/2013
		KR 10-2010-0114095 A	22/10/2010
		MX 2010009023 A	07/09/2010
		PE 17382009A1	13/11/2009
		RU 2010139284 A	10/04/2012
		TW 200942543 A	16/10/2009
		US 2009-0215724 A1	27/08/2009
		US 2009-0215750 A1	27/08/2009
		US 2009-0215788 A1	27/08/2009
		US 2010-0267666 A1	21/10/2010

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2014/035132

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 7902197 B2	08/03/2011
		US 7932254 B2	26/04/2011
		US 7939531 B2	10/05/2011
		US 8008298 B2	30/08/2011
		US 8119636 B2	21/02/2012
		WO 2009-106441 A1	03/09/2009
		WO 2009-106442 A1	03/09/2009
		WO 2009-106443 A1	03/09/2009
		WO 2009-106444 A1	03/09/2009
		WO 2009-106445 A1	03/09/2009
KR 10-2010-0114094 A	22/10/2010	AU 2009-218607 A1	03/09/2009
		AU 2009-218609 A1	03/09/2009
		CA 2712507 A1	03/09/2009
		CA 2713324 A1	03/09/2009
		CA 2713710 A1	03/09/2009
		CA 2713718 A1	03/09/2009
		CA 2716223 A1	03/09/2009
		CN 101939324 A	05/01/2011
		CN 101945877 A	12/01/2011
		CN 101945877 B	03/07/2013
		CN 101952294 A	19/01/2011
		CN 101952295 A	19/01/2011
		CN 101952295 B	20/11/2013
		CN 101952296 A	19/01/2011
		CN 101952296 B	21/08/2013
		EP 2245033 A1	03/11/2010
		EP 2245033 B1	31/08/2011
		EP 2247592 A1	10/11/2010
		EP 2247592 B1	31/08/2011
		EP 2247593 A1	10/11/2010
		EP 2247593 B1	10/08/2011
		EP 2247595 A1	10/11/2010
		EP 2247595 B1	20/07/2011
		EP 2250172 A1	17/11/2010
		EP 2250172 B1	31/08/2011
		JP 05-284377B2	11/09/2013
		JP 05-368484B2	18/12/2013
		JP 05-368485B2	18/12/2013
		JP 05-485178B2	07/05/2014
		JP 05-529049B2	25/06/2014
		JP 2011-513210 A	28/04/2011
		JP 2011-513261 A	28/04/2011
		JP 2011-513262 A	28/04/2011
		JP 2011-513263 A	28/04/2011
		JP 2011-513264 A	28/04/2011
		KR 10-2010-0114095 A	22/10/2010
		TW 200942543 A	16/10/2009
		TW 200942543 A	16/10/2009
		US 2009-0215724 A1	27/08/2009

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/US2014/035132

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 2009-0215750 A1	27/08/2009
		US 2009-0215785 A1	27/08/2009
		US 2009-0215788 A1	27/08/2009
		US 2010-0267666 A1	21/10/2010
		US 7902197 B2	08/03/2011
		US 7932254 B2	26/04/2011
		US 7939531 B2	10/05/2011
		US 8008298 B2	30/08/2011
		US 8119636 B2	21/02/2012
		WO 2009-106441 A1	03/09/2009
		WO 2009-106442 A1	03/09/2009
		WO 2009-106443 A1	03/09/2009
		WO 2009-106444 A1	03/09/2009
		WO 2009-106445 A1	03/09/2009