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(54) **Title:** METHODS OF SYNTHESIZING HIGH-PURITY CANNABICYCLOL AND ARTIFICIAL RESINS COMPRISING CANNABICYCLOL

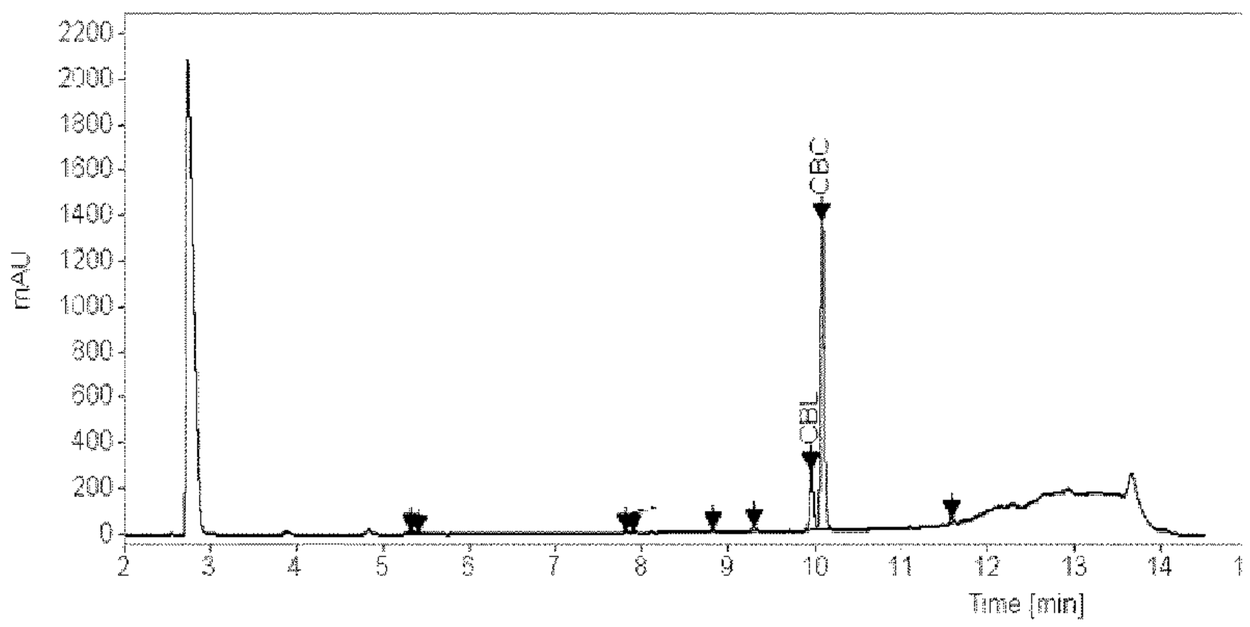

FIG.1

(57) **Abstract:** Compositions having enhanced cannabicyclol (CBL) or CBL derivative concentrations are disclosed herein as are methods of synthesizing CBL and CBL derivative in high-purity form. Relative to conventional methods, the methods of the present disclosure may: (i) be better suited to large-scale conditions in that they do not require dangerous and/or toxic solvents and/or reagents; (ii) be more tolerant of complex starting compositions, such as cannabinoid extracts, isolates and/or distillates; (iii) provide CBL and/or CBL derivative at higher yield; (iv) provide easier methods to purify product mixtures comprising CBL and/or CBL derivative; (v) provide product mixtures that comprise unique ratios of CBL or CBL derivative relative to other cannabinoids; (vi) provide product mixtures with reduced THC concentrations and/or (vii) provide artificial resins having of a mixture cannabinoids that cannot be produced by extracting cannabis plant material.

[Continued on next page]

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METHODS OF SYNTHESIZING HIGH-PURITY CANNABICYCLOL AND ARTIFICIAL RESINS COMPRISING CANNABICYCLOL

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to and benefit of United States Provisional Patent Application Serial Number 62/953,370 filed on December 24, 2019 and United States Provisional Patent Application Serial Number 62/987,179 filed on March 9, 2020, each of which is hereby incorporated by reference in its entirety.

TECHNICAL FIELD

[0002] The present disclosure generally relates to methods of synthesizing cannabinoids in high-purity forms and to methods for synthesizing cannabinoid compositions having unique ratios of cannabinoids. In particular, the present disclosure relates to methods for synthesizing high-purity cannabicyclol (CBL) and CBL derivatives and to cannabinoid compositions having enhanced CBL and/or CBL derivative concentrations.

BACKGROUND

[0003] Cannabicyclol (CBL) is a cannabinoid found in the *cannabis sativa* plant, and it is quickly gaining consumer and scientific interest. For example, scientific studies indicate that CBL has the potential for anti-inflammatory and anti-tumour activity. CBL is also known to provide a variety of benefits in association with other cannabinoids via the entourage effect. CBL also has utility as a synthon for chemical applications. In spite of this wide-ranging potential, CBL is not currently utilized at scale. CBL is typically found in low concentrations in cannabis plant material, extracts, distillates and/or the like. At the same time, separating CBL from such compositions can pose significant challenges as CBL has similar physical characteristics (*e.g.* solubility and/or affinity profile) to a number of other cannabinoids. Furthermore, mixtures of cannabinoids having CBL at a concentration (absolute or relative to other cannabinoids) not found in cannabis plant material, extracts, distillates, and/or the like may be desirable.

[0004] For similar reasons, CBL can be difficult to separate from reaction mixtures. Conventional synthetic methods for producing CBL typically lack selectivity and lead to significant quantities of other products, such as tetrahydrocannabinol (THC). Isolating CBL from reaction mixtures can pose significant challenges, as CBL is difficult to separate from other products by

typical purification methods (*e.g.* chromatography). This can make CBL difficult to obtain in pure form. THC is psychoactive, and compositions containing THC may be subject to regulatory restrictions or prohibitions on transportation or sale. This has the potential to limit the utility of the CBL compositions, because of the difficult associated with separating the two cannabinoids. This limitation is often compounded by the lack of scalability of conventional methods for synthesizing CBL.

[0005] For at least the foregoing reasons, methods for producing CBL and CBL derivatives in high-purity forms are desirable as are cannabinoid compositions with enhanced CBL and/or CBL derivative concentrations.

SUMMARY

[0006] The present disclosure is based on extensive research and development directed at overcoming at least some of the current impediments to advancing the start of the art in CBL-related applications. As exemplified by the examples set out herein, the present disclosure advances this field with the provision of methods of synthesizing CBL and derivatives thereof in high-purity form. The present disclosure also provides cannabinoid compositions having unique ratios of CBL or CBL derivative to other cannabinoids. The methods of the present disclosure may be better suited to industrial scale in that they do not require dangerous and/or toxic solvents and/or reagents. The methods of the present disclosure may provide for more efficient purification of CBL and CBL derivatives. The methods of the present disclosure may provide access to: (i) CBL and CBL derivatives in high purity; (ii) mixtures of cannabinoids, including mixtures of CBL and cannabichromene (CBC), and derivatives thereof, that have unique cannabinoid ratios; (iii) mixtures of cannabinoids with reduced THC concentrations and/or (iii) artificial resins comprising mixtures of cannabinoids in proportions that cannot be produced by extracting cannabis plant material. Importantly, the present disclosure also provides synthetic methods that may be tolerant to a variety of complex starting compositions, such as cannabis extracts, isolates, and/or distillates.

[0007] Select methods of the present disclosure allow for conversion of CBC to CBL, or CBC derivatives to CBL derivatives. Without being bound to any particular theory, the present disclosure asserts that the ability to convert CBC into CBL as demonstrated herein is associated with intramolecular cyclization. In particular, the examples of the present disclosure indicate that the intramolecular cyclization can be induced by contacting the CBC with an acidic heterogeneous

catalyst, contacting the CBC with a radical initiator, and/or by irradiating the CBC with UV light. The methods of the present disclosure may provide access cannabinoid compositions with unique ratios of CBL to CBC (or derivatives thereof). Select methods of the present disclosure allow for synthesizing CBL or a CBL derivative from citral and a modified resorcinol.

[0008] Select methods of the present disclosure allow for producing artificial resins from a starting material having a known composition. The starting material may include, for example, synthetic CBC and/or CBC isolate. Without being bound to any particular theory, the present disclosure asserts that conversion of at least a portion of the starting material to CBL provides access to the artificial resin that includes a mixture of cannabinoids with concentrations (relative or absolute) that cannot be produced by the extraction of cannabis plant material.

[0009] In select embodiments, the present disclosure relates to a method for converting CBC or a CBC derivative to CBL or a CBL derivative, the method comprising contacting the CBC or CBC derivative with an acidic heterogeneous material to form a product mixture comprising the CBL or CBL derivative.

[0010] In select embodiments, the present disclosure relates to a method for converting CBC or a CBC derivative to CBL or a CBL derivative, the method comprising contacting the CBC or CBC derivative with a radical initiator to form a product mixture comprising the CBL or CBL derivative.

[0011] In select embodiments, the present disclosure relates to a method for converting CBC or a CBC derivative to CBL or a CBL derivative, the method comprising irradiating the CBC or CBC derivative with UV light to form a product mixture comprising CBL or CBL derivative.

[0012] In select embodiments, the present disclosure relates to a method of preparing CBL or a CBL derivative, the method comprising: heating a reaction mixture comprising citral, a modified resorcinol, and an amine to form a first product mixture; and converting the first product mixture into a second product mixture by: (i) contacting the first product mixture with an acidic heterogeneous material to form the CBL or CBL derivative; (ii) contacting the first product mixture with a radical initiator to form the CBL or CBL derivative; or (iii) irradiating the first product mixture with UV light to form the CBL or CBL derivative.

[0013] In select embodiments, the present disclosure relates to a cannabinoid composition comprising (i) at least about 4% w/w CBL or a CBL derivative and (ii) at least about 4% w/w CBC or a CBC derivative.

[0014] In select embodiments, the present disclosure relates to a method of producing an artificial resin, the method comprising: contacting a starting material comprising CBC or a CBC derivative with an acidic heterogeneous material to form an artificial resin comprising at least about 4% w/w CBL or CBL derivative, a first cannabinoid, and a second cannabinoid.

[0015] In select embodiments, the present disclosure relates to a method of producing an artificial resin, the method comprising: contacting a starting material comprising CBC or a CBC derivative with a radical initiator to form an artificial resin comprising at least about 4% w/w CBL or CBL derivative, a first cannabinoid, and a second cannabinoid.

[0016] In select embodiments, the present disclosure relates to a method of producing an artificial resin comprising CBL or a CBL derivative, the method comprising: heating a reaction mixture comprising citral, a modified resorcinol, and an amine to form a product mixture; and converting the product mixture into the artificial resin by: (i) contacting the product mixture with an acidic heterogeneous material to form the CBL or CBL derivative; (ii) contacting the product mixture with a radical initiator to form the CBL or CBL derivatice; or (iii) irradiating the product mixture with UV light to form the CBL or CBL derivative.

[0017] In select embodiments, the present disclosure relates to an artificial resin comprising at least about 4% CBL or a CBL derivative, a first cannabinoid, and a second cannabinoid

[0018] Other aspects and features of the present disclosure will become apparent to those ordinarily skilled in the art upon review of the following description of specific embodiments.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] **FIG. 1** shows a high-performance liquid chromatogram for **EXAMPLE 1**;

[0020] **FIG. 2** shows a high-performance liquid chromatogram for **EXAMPLE 3**;

[0021] **FIG. 3** shows a high-performance liquid chromatogram for **EXAMPLE 4**;

[0022] **FIG. 4** shows a high-performance liquid chromatogram for **EXAMPLE 6**;

[0023] **FIG. 5** shows a high-performance liquid chromatogram for **EXAMPLE 7**;

[0024] **FIG. 6A** shows a perspective view of a crystal structure for CBL;

[0025] **FIG. 6B** shows a perspective view ORTEP drawing of a crystal structure for CBL;

[0026] **FIG. 6C** shows a stereoscopic view ORTEP drawing of a crystal structure for CBL;

[0027] **FIG. 7** shows high-performance liquid chromatograms for **EXAMPLE 9**.

DETAILED DESCRIPTION

[0028] As noted above, the present disclosure provides methods of synthesizing cannabicyclol (CBL) and derivatives thereof in high-purity forms. Relative to conventional methods, the methods of the present disclosure may: (i) be better suited to large-scale conditions in that they do not require dangerous and/or toxic solvents and/or reagents; (ii) be more tolerant of complex starting compositions, such as cannabinoid isolates and/or distillates; (iii) provide CBL and CBL derivative at higher yield; (iv) provide easier methods to purify product mixtures comprising CBL or CBL derivatives; (v) provide product mixtures that comprise unique ratios of CBL or CBL derivatives relative to other cannabinoids; (vi) provide product mixtures with reduced THC concentrations and/or; (vii) provide artificial resins having of a mixture cannabinoids that cannot be produced by extracting cannabis plant material. The present disclosure asserts that access to CBL and derivatives thereof via methods disclosed herein may be desirable in both medicinal and recreational contexts. Moreover, the present disclosure asserts that access to CBL and derivatives thereof via the methods disclosure herein is desirable to synthetic chemists.

[0029] The present disclosure provides cannabinoid compositions having unique ratios of cannabinoids, including unique ratios of cannabichromene (CBC) to CBL. Mixtures of cannabinoids may provide enhanced medicinal and/or recreational effects, for example via the entourage effect. The present disclosure provides cannabinoid compositions having reduced THC concentrations which may thereby avoid being subject to regulatory restrictions or prohibitions on transportation or sale. In some embodiments, the methods of the present disclosure provide access to high purity CBL and derivatives thereof, for example by converting CBC or a CBC derivative to CBL or a CBL derivative. High purity CBL or CBL derivative may be employed as an active pharmaceutical ingredient (API) for recreational and/or medicinal formulations, or as a synthon for chemical applications. High purity CBL or CBL derivative may be essentially free of THC, and thereby avoid being subject to regulatory restrictions or prohibitions on transportation

or sale. In some embodiments, the methods of the present disclosure may employ a cannabis extract or a synthesis reaction mixture as a starting material, as the methods of the present disclosure may be compatible with impure starting materials.

[0030] Without being bound to any particular theory, the present disclosure asserts that converting CBC into CBL as demonstrated herein results from an intramolecular cyclization reaction. The intramolecular cyclization of CBC may be performed with the addition of a catalyst, reagent, UV light, or a combination thereof. In particular, the examples of the present disclosure indicate that the intramolecular cyclization can be induced by contacting the CBC with an acidic heterogeneous catalyst, a radical initiator, and/or by irradiating the CBC with UV light.

[0031] In the context of the present disclosure, the term “artificial resin” refers to a mixture of cannabinoids with a defined composition produced from starting materials comprising one or more of the same or different cannabinoids. In an embodiment, the starting material has a known composition (e.g. known cannabinoid content). Artificial resins may include 2, 3, 4, or more cannabinoids. Without being bound to any particular theory, the present disclosure asserts that using starting materials with known composition provides increases the reproducibility of the artificial resins produced. In contrast, producing a mixture of cannabinoids from cannabis plant extracts may reduce the reproducibility of the resulting mixture of cannabinoids due to the batch-to-batch variation of cannabis plant extracts. Non-exclusive examples of starting materials with a known composition include synthetic CBC or CBC derivative, CBC isolate, CBC derivative isolate, and mixtures of citral and a modified resorcinol (e.g. olivetol). The CBC isolate may be derived from cannabis plant material so long as the CBC isolate is sufficiently pure to ensure batch-to-batch consistency.

[0032] Without being bound to any particular theory, the present disclosure asserts that conversion of at least a portion of the starting material to CBL or CBL derivative provides access to artificial resins that include a mixture of cannabinoids with concentrations (relative or absolute) that cannot be produced by the extraction of cannabis plant material. For example, an artificial resin including CBL at concentrations (relative to other cannabinoids) higher than the concentrations of CBL found in cannabis plant material.

[0033] As used herein, the term “cannabinoid” refers to: (i) a chemical compound belonging to a class of secondary compounds commonly found in plants of genus cannabis, (ii)

synthetic cannabinoids and any enantiomers thereof; and/or (iii) one of a class of diverse chemical compounds that may act on cannabinoid receptors such as CB1 and CB2..

[0034] In select embodiments of the present disclosure, the cannabinoid is a compound found in a plant, e.g., a plant of genus cannabis, and is sometimes referred to as a phytocannabinoid. One of the most notable cannabinoids of the phytocannabinoids is tetrahydrocannabinol (THC), the primary psychoactive compound in cannabis. Cannabidiol (CBD) is another cannabinoid that is a major constituent of the phytocannabinoids. There are at least 113 different cannabinoids isolated from cannabis, exhibiting varied effects.

[0035] In select embodiments of the present disclosure, the cannabinoid is a compound found in a mammal, sometimes called an endocannabinoid.

[0036] In select embodiments of the present disclosure, the cannabinoid is made in a laboratory setting, sometimes called a synthetic cannabinoid. In one embodiment, the cannabinoid is derived or obtained from a natural source (e.g. plant) but is subsequently modified or derivatized in one or more different ways in a laboratory setting, sometimes called a semi-synthetic cannabinoid.

[0037] Synthetic cannabinoids and semi-synthetic cannabinoids encompass a variety of distinct chemical classes, for example and without limitation: the classical cannabinoids structurally related to THC, the non-classical cannabinoids (cannabimimetics) including the aminoalkylindoles, 1,5 diarylpyrazoles, quinolines, and arylsulfonamides as well as eicosanoids related to endocannabinoids.

[0038] In many cases, a cannabinoid can be identified because its chemical name will include the text string “*cannabi*”. However, there are a number of cannabinoids that do not use this nomenclature, such as for example those described herein.

[0039] In the context of this disclosure, where reference is made to a particular cannabinoid, each of the acid and/or decarboxylated forms are contemplated as both single molecules and mixtures. In addition, salts of cannabinoids are also encompassed, such as salts of cannabinoid carboxylic acids.

[0040] As well, any and all isomeric, enantiomeric, or optically active derivatives are also encompassed. In particular, where appropriate, reference to a particular cannabinoid incudes both the “A Form” and the “B Form”. For example, it is known that THCA has two isomers, THCA-A

in which the carboxylic acid group is in the 1 position between the hydroxyl group and the carbon chain (A Form) and THCA-B in which the carboxylic acid group is in the 3 position following the carbon chain (B Form).

[0041] Examples of cannabinoids include, but are not limited to: cannabigerolic acid (CBGA), cannabigerolic acid monomethylether (CBGAM), cannabigerol (CBG), cannabigerol monomethylether (CBGM), cannabigerovarinic acid (CBGVA), cannabigerovarin (CBGV), cannabichromenic acid (CBCA), cannabichromene (CBC), cannabichromevarinic Acid (CBCVA), cannabichromevarin (CBCV), cannabidiolic acid (CBDA), cannabidiol (CBD), Δ6-cannabidiol (Δ6-CBD), cannabidiol monomethylether (CBDM), cannabidiol-C4 (CBD-C4), cannabidivarinic Acid (CBDVA), cannabidivarin (CBDV), cannabidiorcol (CBD-C1), tetrahydrocannabinolic acid A (THCA-A), tetrahydrocannabinolic acid B (THCA-B), tetrahydrocannabinol (THC or Δ9-THC), Δ8-tetrahydrocannabinol (Δ8-THC), *trans*-Δ10-tetrahydrocannabinol (*trans*-Δ10-THC), *cis*-Δ10-tetrahydrocannabinol (*cis*-Δ10-THC), tetrahydrocannabinolic acid C4 (THCA-C4), tetrahydrocannbinol C4 (THC-C4), tetrahydrocannabivarinic acid (THCVA), tetrahydrocannabivarin (THCV), Δ8-tetrahydrocannabivarin (Δ8-THCV), Δ9-tetrahydrocannabivarin (Δ9-THCV), tetrahydrocannabiorcolic acid (THCA-C1), tetrahydrocannabiorcol (THC-C1), Δ7-cis-iso- tetrahydrocannabivarin, Δ8-tetrahydrocannabinolic acid (Δ8-THCA), Δ9-tetrahydrocannabinolic acid (Δ9-THCA), cannabicyclolic acid (CBLA), cannabicyclol (CBL), cannabicyclovarin (CBLV), cannabielsoic acid A (CBEA-A), cannabielsoic acid B (CBEA-B), cnnabielsoin (CBE), cannabinolic acid (CBNA), cannabinol (CBN), cannabinol methylether (CBNM), cannabinol-C4 (CBN-C4), cannabivarin (CBV), cannabino-C2 (CBN-C2), cannabiorcol (CBN-C1), cannabinodiol (CBND), cannabinodivarin (CBDV), cannabitriol (CBT), 11-hydroxy-Δ9-tetrahydrocannabinol (11-OH-THC), 11-nor-9-carboxy- Δ9-tetrahydrocannabinol, ethoxy-cannabitriolvarin (CBTVE), 10 ethoxy-9-hydroxy- Δ6a-tetrahydrocannabinol, cannabitriolvarin (CBTV), 8,9 dihydroxy-Δ6a(10a)-tetrahydrocannabinol (8,9-Di-OH-CBT-C5), dehydrocannabifuran (DCBF), cannbifuran (CBF), cannabichromanon (CBCN), cannabicitran, 10-oxo-Δ6a(10a)-tetrahydrocannabinol (OTHC), Δ9-cis-tetrahydrocannabinol (cis-THC), cannabiripsol (CBR), 3,4,5,6-tetrahydro-7-hydroxy-alpha-alpha-2-trimethyl-9-n-propyl-2,6-methano-2h-1-benzoxocin-5-methanol (OH-iso-HHCV), trihydroxy-delta-9-tetrahydrocannabinol (triOH-THC), yangonin, epigallocatechin gallate, dodeca-2e, 4e, 8z, 10z-tetraenoic acid isobutylamide, hexahydrocannibinol, and dodeca-2e,4e-dienoic acid isobutylamide.

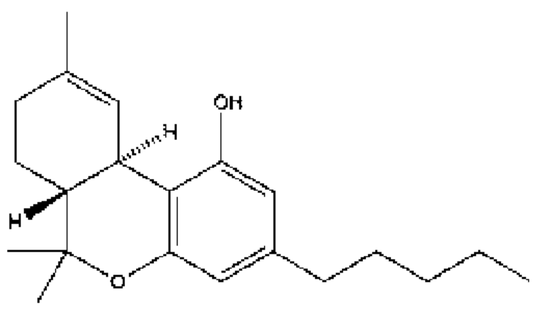
[0042] In some embodiments of the present disclosure, the cannabinoid is a cannabinoid dimer. The cannabinoid may be a dimer of the same cannabinoid (e.g. THC—THC) or different

cannabinoids. In an embodiment of the present disclosure, the cannabinoid may be a dimer of THC, including for example cannabisol.

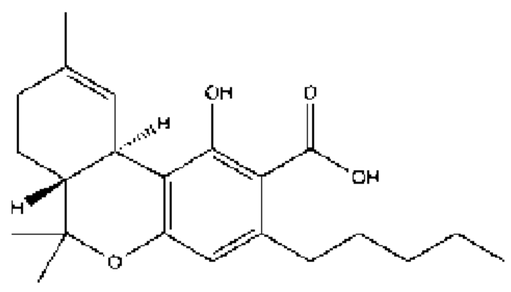
[0043] As used herein, the term "THC" refers to tetrahydrocannabinol. "THC" is used interchangeably herein with "Δ9-THC".

[0044] In an embodiment of the present disclosure, the cannabinoid is THC (Δ9-THC), Δ8-THC, *trans*-Δ10-THC, *cis*-Δ10-THC, THCA, THCV, Δ8-THCA, Δ9-THCA, Δ8-THCV, Δ9-THCV, THCVA, CBD, CBDA, CBDV, CBDVA, CBC, CBCA, CBCV, CBCVA, CBG, CBGA, CBGV, CBGVA, CBN, CBNA, CBNV, CBNVA, CBND, CBNDA, CBNDV, CBNDVA, CBE, CBEA, CBEV, CBEVA, CBL, CBLA, CBLV, CBLVA, CBT, cannabicitran, or any combination thereof.

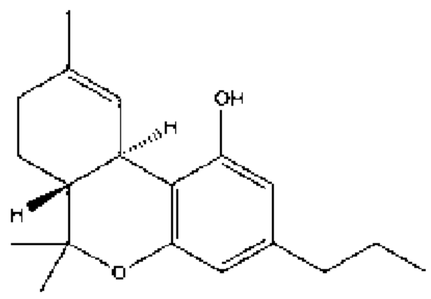
[0045] Structural formulae of cannabinoids of the present disclosure may include the following:



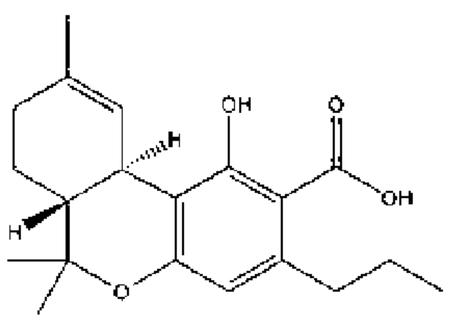
THC



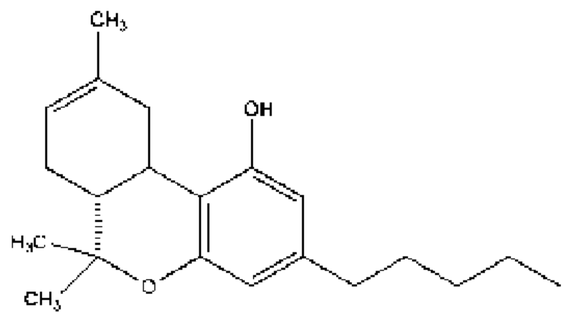
THCA



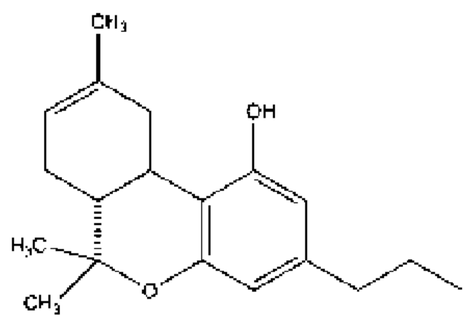
THCV



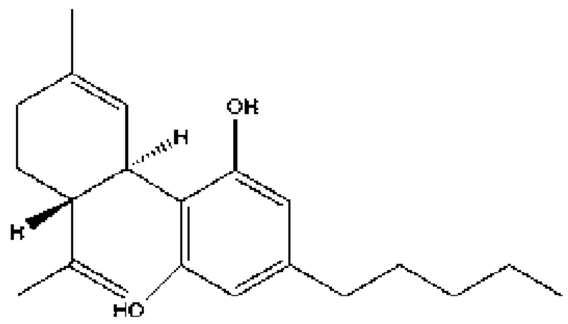
THCVA



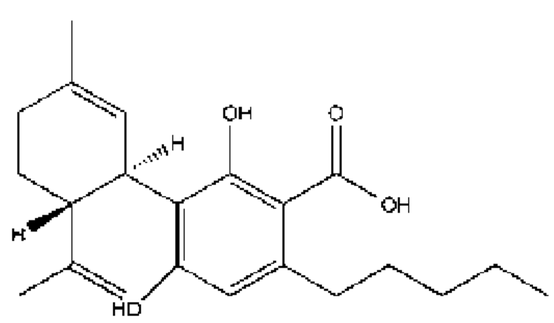
Δ8-THC



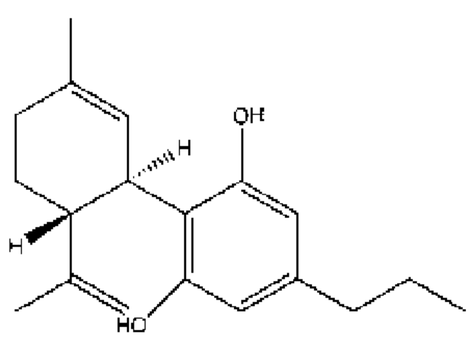
Δ8-THCV



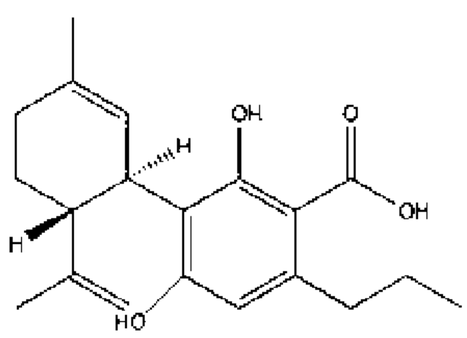
CBD



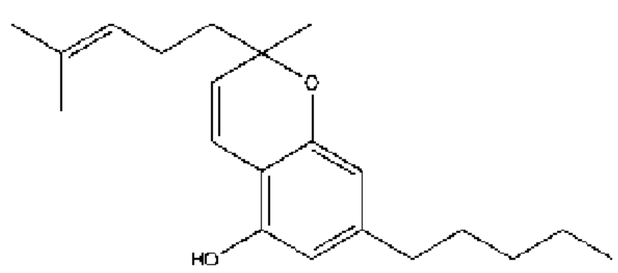
CBDA



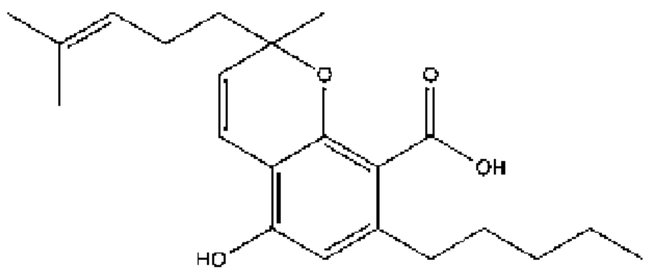
CBDV



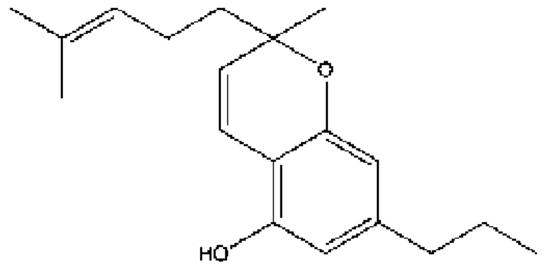
CBDVA



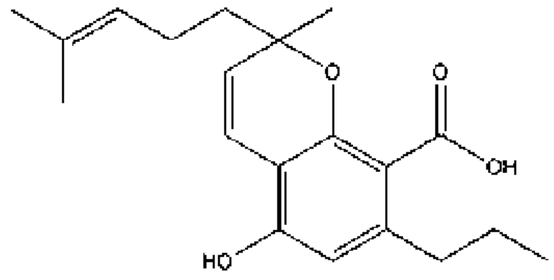
CBC



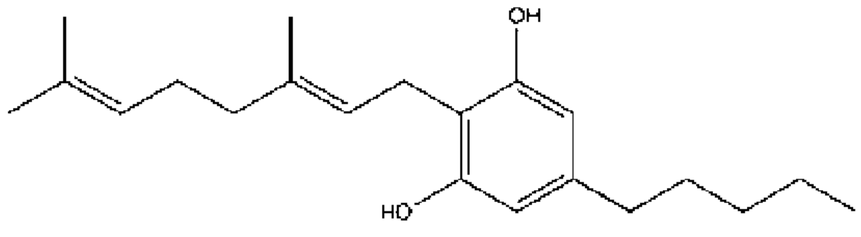
CBCA



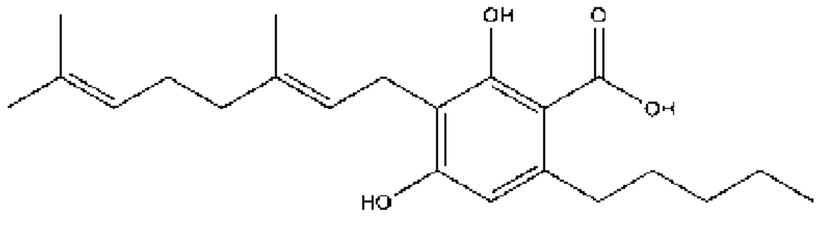
CBCV



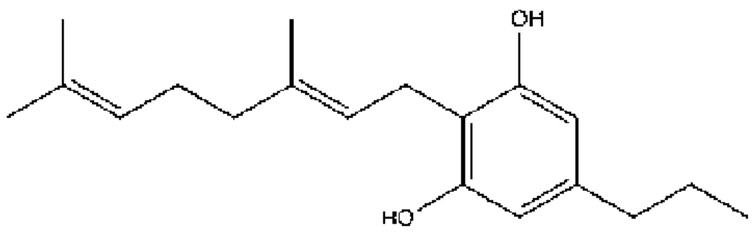
CBCVA



CBG



CBGA



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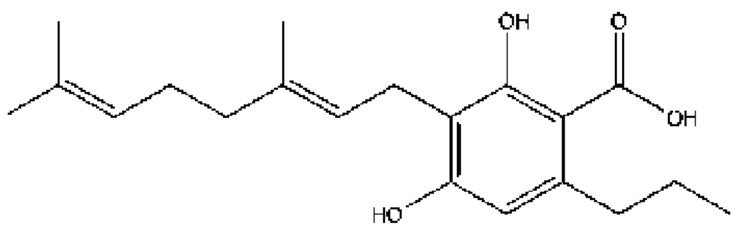
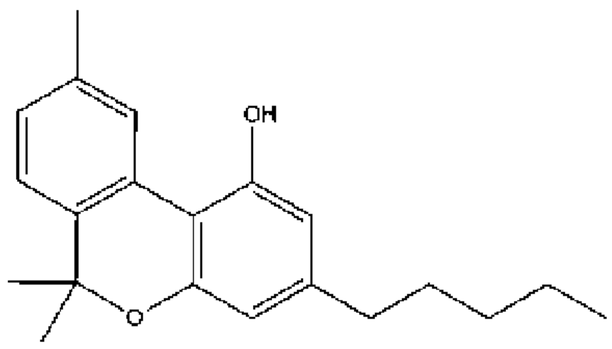
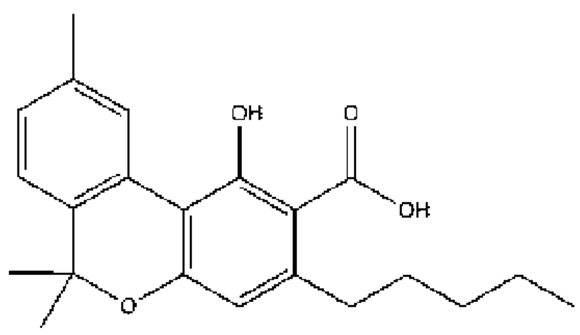


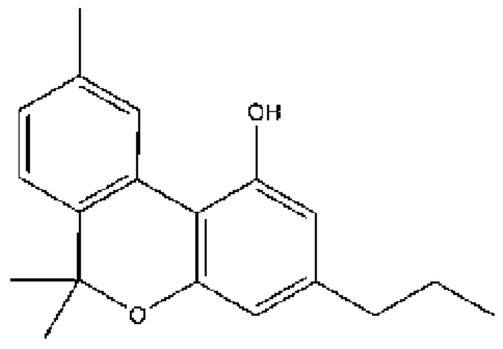
CBGVA



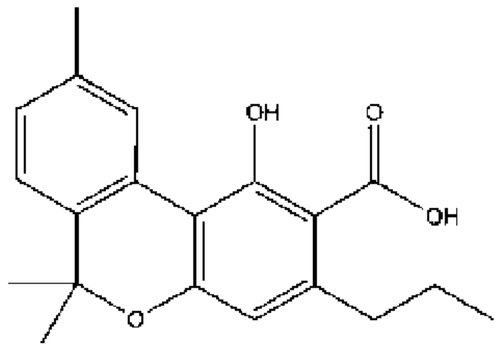
CBN



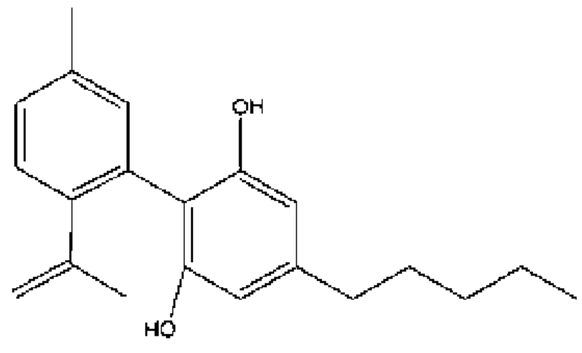
CBNA



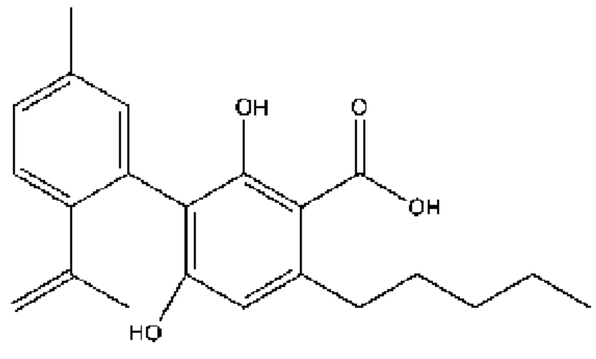
CBNV (or CBV)



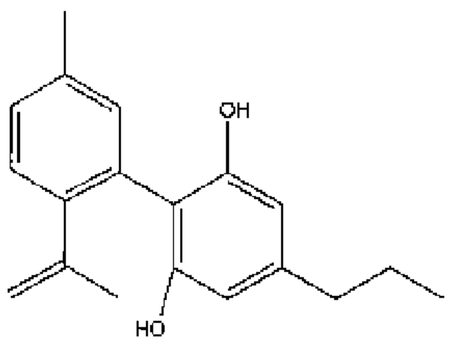
CBNVA



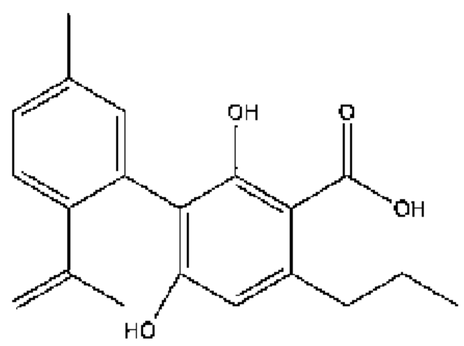
CBND



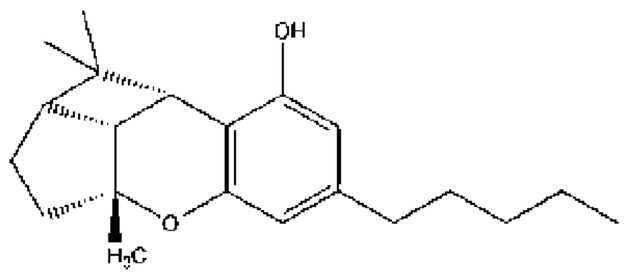
CBNDA



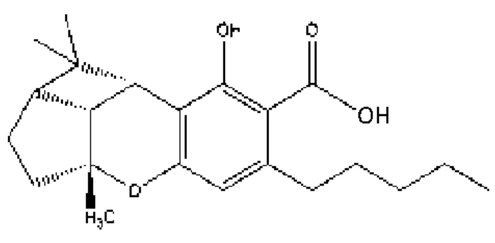
CBNDV



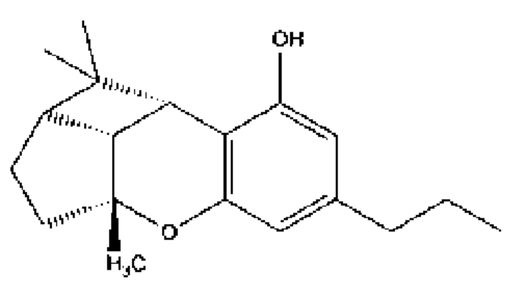
CBNDVA



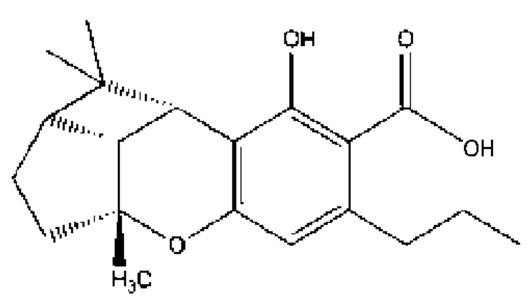
CBL



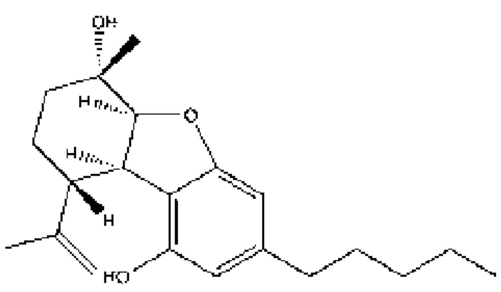
CBLA



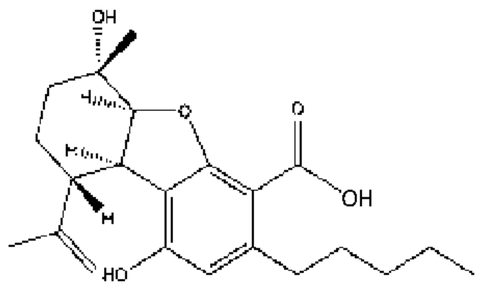
CBLV



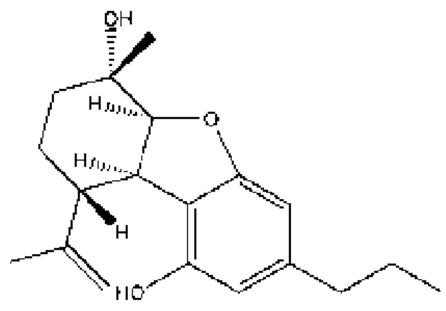
CBLVA



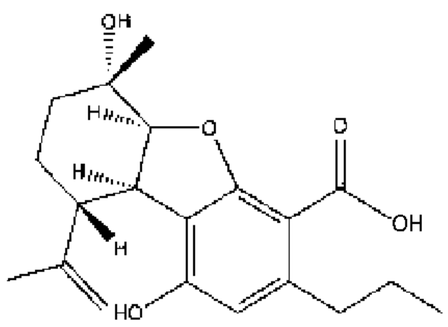
CBE



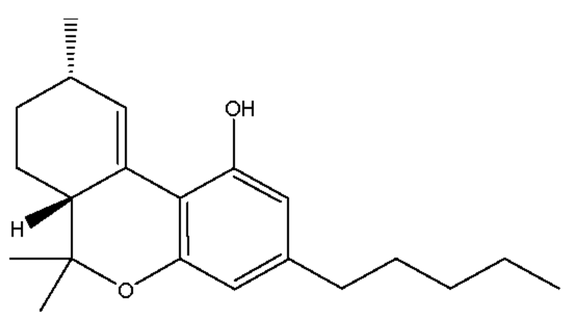
CBEA



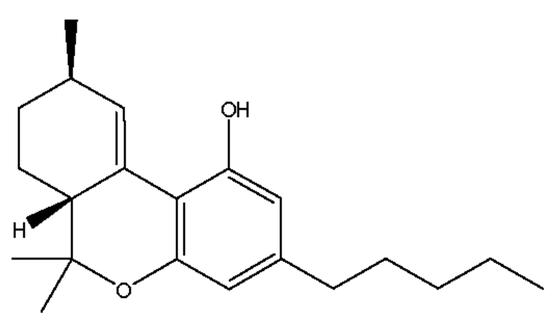
CBEV



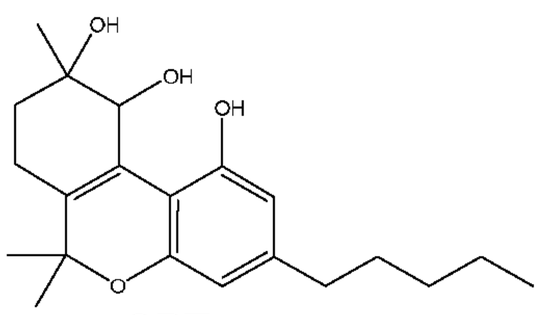
CBEVA



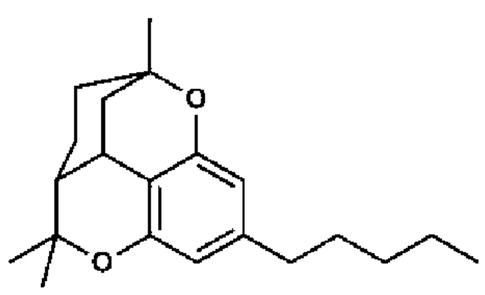
trans-Δ10-THC



cis-Δ10-THC



CBT
(cannabitriol)



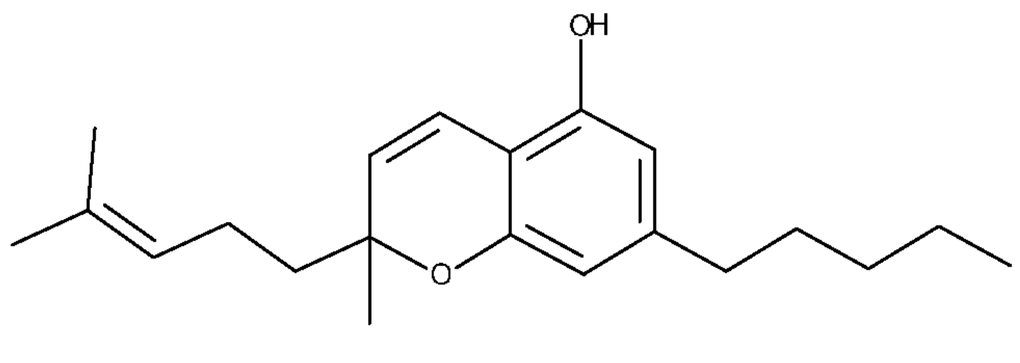
cannabicitran

[0046] In select embodiments, the present disclosure relates to a method for converting cannabichromene (CBC) or a CBC derivative to cannabicyclol (CBL) or a CBL derivative, the method comprising contacting the CBC or CBC derivative with an acidic heterogeneous material to form a product mixture comprising the CBL or CBL derivative.

[0047] In the context of the present disclosure, the term "contacting" and its derivatives is intended to refer to bringing the CBC or CBC derivative and the acidic heterogeneous material into proximity such that a chemical reaction can occur. In some embodiments of the present disclosure, the contacting may be by adding the acidic heterogeneous material to the CBC or CBC derivative. In some embodiments, the contacting may be by combining, mixing, or both.

[0048] In the context of the present disclosure, the term "convert" includes a reaction involving a reagent initially present as an isolate, a component of a mixture (including a cannabis extract or distillate), and/or a reagent formed *in situ*.

[0049] In the context of the present disclosure, the term "CBC" refers to cannabichromene or, more generally, to cannabichromene-type cannabinoids. Accordingly the term "CBC" includes: (i) acid forms, such as "A-type", "B-type", or "AB-type" acid forms; (ii) salts of such acid forms, such as Na^+ and/or Ca^{2+} salts of such acid forms; (iii) ester forms, such as those formed by hydroxyl-group esterification to form traditional esters, sulphonate esters, and/or phosphate esters; and/or (iv) various stereoisomers. In select embodiments of the present disclosure, CBC may have the following structural formula:



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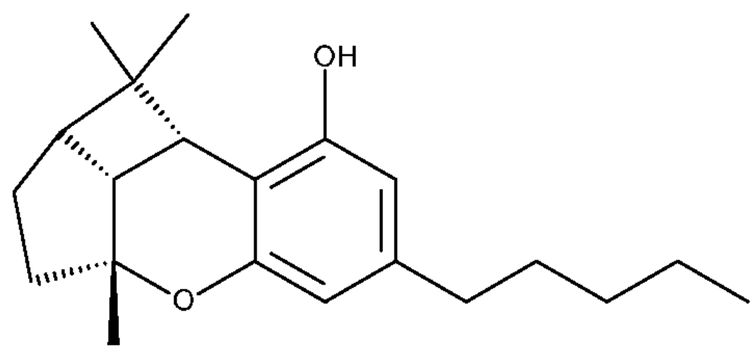
[0050] In the context of the present disclosure, the term “CBL” refers to cannabicyclol or, more generally, to cannabicyclol-type cannabinoids. Accordingly the term “CBL” includes: (i) acid forms, such as “A-type”, “B-type”, or “AB-type” acid forms; (ii) salts of such acid forms, such as Na^+ and/or Ca^{2+} salts of such acid forms; (iii) ester forms, such as those formed by hydroxyl-group esterification to form traditional esters, sulphonate esters, and/or phosphate esters; and/or (iv) various stereoisomers. In select embodiments of the present disclosure, CBL may have the following structural formula:



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[0051] In the context of the present disclosure, an acid heterogeneous reagent is one which: (i) comprises one or more sites that are capable of accepting an electron pair from an electron pair donor or donating a proton to a proton-acceptor. A person of skill in the art will appreciate that acidic heterogeneous catalysts may thereby be Lewis-acidic or Bronsted/Lowry acidic, where Bronsted-Lowry acids are also Lewis acids. Importantly, the term “reagent” is used in the present disclosure to encompass both reactant-type reactivity (*i.e.* wherein the reagent is at least partly consumed as reactant is converted to product) and catalyst-type reactivity (*i.e.* wherein the reagent is not substantially consumed as reactant is converted to product). The acidity of the acidic heterogeneous reagent may be determined using Hammet indicators or temperature-programmed desorption (TPD). Acidity determined by TPD may more accurately reflect the number of acid sites able to react with reagents that are not small molecules.

[0052] Non-exclusive examples of acidic heterogeneous material include: montmorillonite, activated montmorillonite, amberlyst resins, and ZSM-5. In select embodiments of the present disclosure, the acidic heterogeneous material is activated montmorillonite.

[0053] In select embodiments of the present disclosure, the contacting is performed in the presence of a solvent (e.g. the reaction conditions comprise the components in a solvent). The solvent may dissolve at least a portion of the CBC or CBC derivative and/or a portion of the CBL or CBL derivative. Dissolving the CBC and/or the CBL (or derivatives thereof) may increase the rate of reaction. Without being bound to any particular theory, the present disclosure asserts that

the properties of the solvent, including the polarity of the solvent, may affect the rate of reaction, the yield of the reaction, and/or the amount of side products formed. In select embodiments of the present disclosure, the solvent is chloroform. In select embodiments of the present disclosure, the solvent is a class 3 solvent. Any suitable class 3 solvent may be used. In select embodiments of the present disclosure, the class 3 solvent is heptane, acetic acid, or a combination thereof.

[0054] In select embodiments of the present disclosure, the contacting is at a reaction temperature of less than about 100°C. In select embodiments of the present disclosure, the reaction temperature is between about -40°C and about 100°C, more particularly between about -25°C and about 75°C, between about -20°C and about 60°C, or between about -10°C and about 10°C. In an embodiment, the reaction temperature is at about room temperature. In an embodiment, the reaction temperature is about -25°C, about -20°C, about -15°C, about -10°C, about -5°C, about 0°C, about 5°C, about 10°C, about 15°C, about 20°C, about 25°C, about 30°C, about 35°C, about 40°C, about 45°C, about 50°C, about 55°C, or about 60°C. A higher temperature may increase the rate of reaction, where a higher rate of reaction increases throughput and is thereby more compatible with large scale reactions. A lower temperature may increase the yield of the reaction or reduce the amount of side products formed.

[0055] In select embodiments of the present disclosure, the contacting is for a reaction time of at least about 30 minutes, more particularly at least about 60 minutes. In an embodiment, the reaction time is between about 30 minutes and about 72 hours, more particularly between about 2 hours and about 48 hours, between about 4 hours and about 36 hours, between about 6 hours and about 24 hours, or between about 12 hours and about 24 hours. In an embodiment, the reaction time is between about 2 hours and 24 hours. In an embodiment, the reaction time is between about 18 hours and about 24 hours. In an embodiment, the reaction time is about 30 minutes, about 60 minutes, about 90 minutes, about 2 hours, about 4 hours, about 6 hours, about 8 hours, about 10 hours, about 12 hours, about 18 hours, about 24 hours, about 30 hours, about 36 hours, about 42 hours, about 48 hours, or longer. A shorter reaction time may increase the throughput of the reaction, which increases the rate at which CBL or CBL derivative is produced. A longer reaction time may increase the yield of the reaction.

[0056] In select embodiments of the present disclosure, the contacting is under a reaction pressure below about 1 bar (below about 100 kPa). In an embodiment, the reaction pressure is between about 0.1 mbar and 1000 mbar, more particularly between about 0.1 mbar and 100 mbar, or between about 0.5 mbar and 10 mbar. Executing the reaction under conditions of reduced

pressure may reduce the amount of side products present in a product of the reaction. Non-exclusive examples of side products include CBC, tetrahydrocannabinol (THC), cannabacitran, cannabigerol (CBG), cannabidiol (CBD), and cannabinol (CBN).

[0057] In select embodiments of the present disclosure, the product mixture comprises at least about 1% w/w CBL and at least about 1% w/w CBC (or derivatives thereof).

[0058] In select embodiments of the present disclosure, the product mixture comprises between about 1% w/w CBC and about 95% w/w CBC, or more particularly between about 1% w/w CBC and about 75% w/w CBC, between about 1% w/w CBC and about 50% w/w CBC, or between about 1% w/w CBC and about 25% w/w CBC. In an embodiment, the product mixture comprises between about 1% w/w CBC and about 25% w/w CBC, more particularly between about 1% w/w CBC and about 25% w/w CBC, or between about 1% w/w CBC and about 5% w/w CBC. In an embodiment, the product mixture comprises between about 5% w/w CBC and about 25% w/w CBC. In an embodiment, the product mixture comprises about 1.0%, about 2.5%, about 5.0%, about 7.5%, about 10.0%, about 12.5%, about 15.0%, about 17.5%, about 20.0%, about 22.5%, about 25%, about 27.5%, about 30%, or greater w/w CBC. As will be appreciated from the disclosure herein, reference to CBC in this paragraph equally applies to CBC derivatives and the amounts thereof.

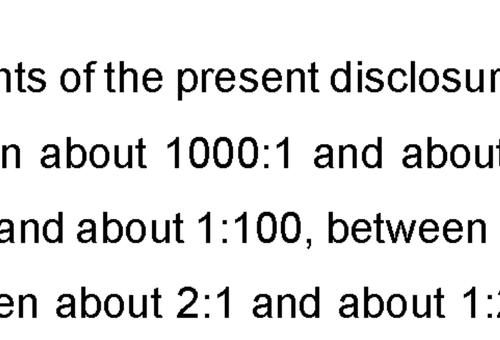
[0059] In select embodiments of the present disclosure, the product mixture comprises between about 1% w/w CBL and about 99% w/w CBL, more particularly between about 10% w/w CBL and about 90% w/w CBL, between about 25% w/w CBL and about 75% w/w CBL or between about 40% w/w CBL and about 50% CBL. In an embodiment, the product mixture comprises about 1.0%, about 2.5%, about 5.0%, about 7.5%, about 10.0%, about 12.5%, about 15.0%, about 17.5%, about 20.0%, about 22.5%, about 25%, about 27.5%, about 30%, about 32.5%, about 35%, about 37.5%, about 40%, about 42.5%, about 45%, about 47.5%, about 50%, or greater w/w CBL. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives and the amounts thereof.

[0060] In the context of the present disclosure, the relative quantities of CBL and CBC in a particular composition may be expressed as a ratio – CBL:CBC. Those skilled in the art will recognize that a variety of analytical methods may be used to determine such ratios, and the protocols required to implement any such method are within the purview of those skilled in the art. By way of non-limiting example, CBL:CBC ratios may be determined by diode-array-detector

high pressure liquid chromatography, UV-detector high pressure liquid chromatography, nuclear magnetic resonance spectroscopy, mass spectroscopy, flame-ionization gas chromatography, gas chromatograph-mass spectroscopy, or combinations thereof. As will be appreciated from the disclosure herein, reference to CBL:CBC ratios may be equally applicable to ratios of derivatives of these compounds.

[0061] In select embodiments of the present disclosure, the CBL and the CBC are present in a CBL:CBC ratio that is between about 1000:1 and about 1:1000, between about 500:1 and about 1:500, between about 100:1 and about 1:100, between about 10:1 and about 1:10, between about 5:1 and about 1:5, or between about 2:1 and about 1:2. In an embodiment, the CBL:CBC ratio of the product mixture is between about 100:1 and about 1:20, between about 95:1 and about 1:10, or between about 20:1 and about 1:1. In an embodiment, the CBL:CBC ratio of the product mixture is about 20:1, about 15:1, about 10:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 1:2, about 1:3, about 1:4, about 1:5, about 1:10, about 1:15, or about 1:20.

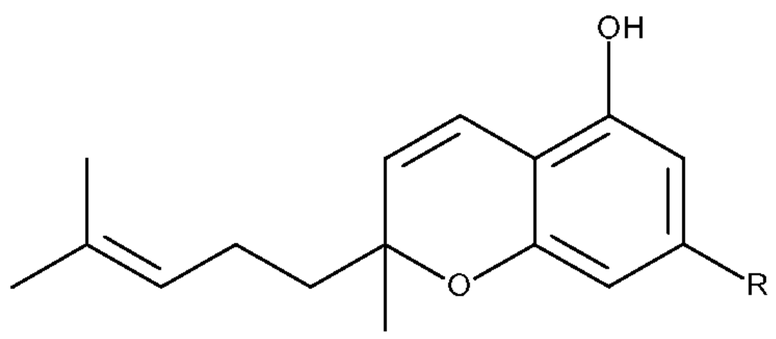
[0062] In select embodiments of the present disclosure, the CBL derivative of the form:



,

wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. A CBL derivative may possess enhanced or modified medicinal and/or recreational effect, and may provide additional functionality for synthetic chemists.

[0063] In select embodiments of the present disclosure, the CBC derivative of the form:



,

wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. As will be appreciated by those skilled in the art who have benefitted from the teachings of the present disclosure, a derivative of CBL converted from a CBC derivative will typically share the same R group.

[0064] In select embodiments of the present disclosure, the method further comprises purifying the product mixture to provide CBL or CBL derivative that is at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% pure. In an embodiment, the CBL or CBL derivative is at least 95% pure. CBL or CBL derivative with such purity may be more readily used as an API. Non-exclusive examples of purification methods include chromatography, flash chromatography, reversed phase C18 flash chromatography, simulated moving bed chromatography, liquid-liquid extraction, distillation, short-path distillation, and crystallization. Chromatography methods may be surprisingly effective for the isolation of CBL or CBL derivative from CBC or CBC derivative. In select embodiments of the present disclosure, purifying the product mixture comprises flash chromatography. In select embodiments of the present disclosure, the flash chromatography is reversed phase C18 flash chromatography. Flash chromatography and/or reversed phase C18 flash chromatography may be particularly effective for purifying CBL or CBL derivative. In select embodiments, purifying the product mixture includes crystallizing the product mixture to produce CBL or CBL derivative that has a purity of at least 95%, at least 99%, or greater than 99%. Crystalline CBL or CBL derivative that has a purity of at least 95% may be a CBL isolate or CBL derivative isolate.

[0065] In select embodiments of the present disclosure, the CBC or CBC derivative is a component of a cannabis extract, a cannabis distillate, a cannabis isolate, or a cannabis synthesis reaction mixture. As the CBC derivative may not be a naturally occurring substance, in particular embodiments the CBC derivative is a component of a cannabis synthesis reaction mixture. In the context of the present disclosure, a cannabis synthesis reaction mixture comprises a reaction mixture comprising the products of a reaction between citral and a modified resorcinol. In select embodiments of the present disclosure, the cannabis extract, the cannabis distillate, the cannabis isolate, or the cannabis synthesis reaction mixture comprises at least 40% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the cannabis extract, the cannabis distillate, the cannabis isolate, or the cannabis synthesis reaction mixture comprises between about 40% w/w and about 95% w/w, between about 50% w/w and about 95% w/w, or between about 85% w/w and about 90% w/w CBC or CBC derivative. The methods of the present disclosure allow conversion of CBC to CBL (or derivatives thereof) where the CBC or CBC

derivative is a component of a mixture (e.g. a cannabis extract, a cannabis distillate, a cannabis isolate, or a cannabis synthesis reaction mixture), which allows the use of reagents with reduced CBC or CBC derivative purity that may be more readily available or less expensive than reagents of higher purity.

[0066] In select embodiments of the present disclosure, the CBL or CBL derivative has a yield of at least 10%. In some embodiments, the yield of CBL or CBL derivative may be at least 25%, at least 50%, or more. A higher yield increases the amount of CBL or CBL derivatives obtained via the methods of the present disclosure.

[0067] In select embodiments of the present disclosure, the product mixture comprises less than about 30% w/w tetrahydrocannabinol (THC). In an embodiment, the product mixture comprises less than 30% w/w THC, less than 25% w/w THC, less than 20% w/w THC, less than 15% w/w THC, less than 10% w/w THC, less than 5% w/w THC, less than 2.5% w/w THC, less than 1% w/w THC, less than 0.5% w/w THC, less than 0.3% w/w THC, less than 0.1% w/w THC, or even less. In an embodiment, the product mixture comprises only trace amounts of THC (e.g. less than 0.01% w/w THC). In an embodiment, the product mixture comprises no THC or at least no detectable THC. In the context of the present disclosure, the phrase “less than” includes amounts below the detection limit of appropriate analytical methods.

[0068] A lower amount of THC may allow a product mixture to avoid regulatory restrictions. In select embodiments of the present disclosure, a CBL:THC ratio of the product mixture is between about 10,000:1 and about 1:1, between about 1000:1 and about 1:1, between about 500:1 and about 1:1, between about 100:1 and about 1:1, or between about 10:1 and about 1:1. In an embodiment, the CBL:THC ratio is between about 100:1 and about 10:1, between about 100:1 and about 25:1, between about 100:1 and about 50:1, or between about 100:1 and about 75:1. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[0069] In select embodiments of the present disclosure, the product mixture comprises less than about 50% w/w cannabidiol (CBD), less than about 25% w/w CBD, less than about 20% w/w CBD, less than about 15% w/w CBD, less than about 10% w/w CBD, less than about 5% w/w CBD, less than about 1% w/w CBD, less than about 0.3% w/w CBD, less than about 0.2% w/w CBD, or less than about 0.1% w/w CBD.

[0070] In select embodiments of the present disclosure, a CBL:CBD ratio of the product mixture may be between about 100:1 and about 1:100, more particularly between about 100:1 and about 1:10. In select embodiments of the present disclosure, the CBL:CBD ratio of the product mixture may be between about 1000:1 and about 900:1, about 900:1 and about 700:1, about 700:1 and about 500:1, about 500:1 and about 300:1, about 100:1 and about 50:1, about 50:1 and about 25:1, about 25:1 and about 10:1, about 10:1 and about 1:1, or about 1:1 and about 1:10. In an embodiment, the CBL:CBD ratio of the product mixture may be about 10:1, about 5:1, about 2:1, about 1:1, about 1:2, about 1:5 or about 1:10. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[0071] In select embodiments, the present disclosure relates to a method for converting cannabichromene (CBC) or a CBC derivative to cannabicyclol (CBL) or a CBL derivative, the method comprising contacting the CBC or CBC derivative with a radical initiator to form a product mixture comprising the CBL or CBL derivative.

[0072] In the context of the present disclosure, the term “contacting” and its derivatives is intended to refer to bringing the CBC or CBC derivative and the radical initiator into proximity such that a chemical reaction can occur. In some embodiments of the present disclosure, the contacting may be by adding the radical initiator to the CBC or CBC derivative. In some embodiments, the contacting may be by combining, mixing, or both.

[0073] In the context of the present disclosure, a radical initiator is a source of free radicals. The radical initiator may generate free radicals under the conditions disclosed herein at a higher rate than under ambient conditions. Non-exclusive examples of free radical initiators include metal ions and organic compounds. Non-exclusive examples of metal ion free radical initiators include transition metal ions (e.g. Cu^{2+}, Fe^{3+}), their corresponding complexes, and their corresponding salts. Non-exclusive examples of organic free radical initiators include organic peroxides. In select embodiments of the present disclosure, the radical initiator is $Fe(ClO_4)_3$.

[0074] In select embodiments of the present disclosure, the contacting of the CBC or CBC derivative with the radical initiator is performed in the presence of a solvent. The solvent may dissolve at least a portion of the CBC or CBC derivative and/or a portion of the formed CBL or CBL derivative. Dissolving the CBC and/or the CBL (or derivatives thereof) may increase the rate of reaction. Without being bound to any particular theory, the present disclosure asserts that the properties of the solvent, including the polarity of the solvent, may affect the rate of reaction, the

yield of the reaction, and/or the amount of side products formed. In select embodiments of the present disclosure, the solvent is a class 3 solvent. Any suitable class 3 solvent may be used. In select embodiments of the present disclosure, the solvent is ethyl acetate.

[0075] In select embodiments of the present disclosure, the contacting with the radical initiator is at a reaction temperature of less than about 77°C, more particularly between about 0°C and about 77°C, between about 10°C and about 50°C, or between about 15°C and about 25°C. In an embodiment, the reaction temperature is about 0°C, about 5°C, about 15°C, about 20°C, about 25°C, about 30°C, about 35°C, about 40°C, about 45°C, or about 50°C.

[0076] In select embodiments of the present disclosure, the contacting with the radical initiator is for a reaction time of at least about 1 minute, more particularly between about 1 minute and about 60 minutes, between about 5 minutes and about 60 minutes, between about 10 minutes and about 30 minutes, or between about 10 minutes and about 20 minutes. In an embodiment, the reaction time is about 1 minute, about 5 minutes, about 10 minutes, about 15 minutes, about 20 minutes, about 25 minutes, about 30 minutes, about 35 minutes, about 40 minutes, about 45 minutes, about 50 minutes, about 55 minutes, about 60 minutes, or longer.

[0077] In select embodiments of the present disclosure, the contacting with the radical initiator is under a reaction pressure below about 1 bar (below about 100 kPa). In an embodiment, the reaction pressure is between about 0.1 mbar and 1000 mbar, more particularly between about 0.1 mbar and 100 mbar, or between about 0.5 mbar and 10 mbar.

[0078] In select embodiments of the present disclosure, the product mixture comprises at least about 1% w/w CBL and at least about 1% w/w CBC (or derivatives thereof).

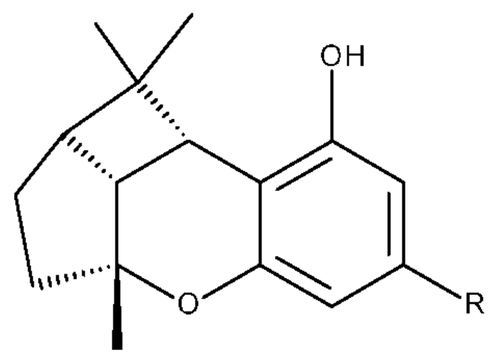
[0079] In select embodiments of the present disclosure, the product mixture comprises between about 1% w/w CBC and about 95% w/w CBC, or more particularly between about 1% w/w CBC and about 75% w/w CBC, between about 1% w/w CBC and about 50% w/w CBC, or between about 1% w/w CBC and about 25% w/w CBC. In an embodiment, the product mixture comprises between about 1% w/w CBC and about 25% w/w CBC, more particularly between about 1% w/w CBC and about 25% w/w CBC, or between about 1% w/w CBC and about 5% w/w CBC. In an embodiment, the product mixture comprises between about 5% w/w CBC and about 25% w/w CBC. In an embodiment, the product mixture comprises about 1.0%, about 2.5%, about 5.0%, about 7.5%, about 10.0%, about 12.5%, about 15.0%, about 17.5%, about 20.0%, about 22.5%, about 25%, about 27.5%, about 30%, or greater w/w CBC. As will be appreciated from

the disclosure herein, reference to CBC in this paragraph equally applies to CBC derivatives and the amounts thereof.

[0080] In select embodiments of the present disclosure, the product mixture comprises between about 1% w/w CBL and about 99% w/w CBL, more particularly between about 10% w/w CBL and about 90% w/w CBL, between about 25% w/w CBL and about 75% w/w CBL or between about 40% w/w CBL and about 50% CBL. In an embodiment, the product mixture comprises about 1.0%, about 2.5%, about 5.0%, about 7.5%, about 10.0%, about 12.5%, about 15.0%, about 17.5%, about 20.0%, about 22.5%, about 25%, about 27.5%, about 30%, about 32.5%, about 35%, about 37.5%, about 40%, about 42.5%, about 45%, about 47.5%, about 50%, or greater w/w CBL. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives and the amounts thereof.

[0081] In select embodiments of the present disclosure, the CBL and the CBC are present in a CBL:CBC ratio that is between about 1000:1 and about 1:1000, between about 500:1 and about 1:500, between about 100:1 and about 1:100, between about 10:1 and about 1:10, between about 5:1 and about 1:5, or between about 2:1 and about 1:2. In an embodiment, the CBL:CBC ratio of the product mixture is between about 100:1 and about 1:20, between about 95:1 and about 1:10, or between about 20:1 and about 1:1. In an embodiment, the CBL:CBC ratio of the product mixture is about 20:1, about 15:1, about 10:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 1:2, about 1:3, about 1:4, about 1:5, about 1:10, about 1:15, or about 1:20. As will be appreciated from the disclosure herein, reference to CBL:CBC ratios may be equally applicable to ratios of derivatives of these compounds.

[0082] In select embodiments of the present disclosure, the CBL derivative is of the form:



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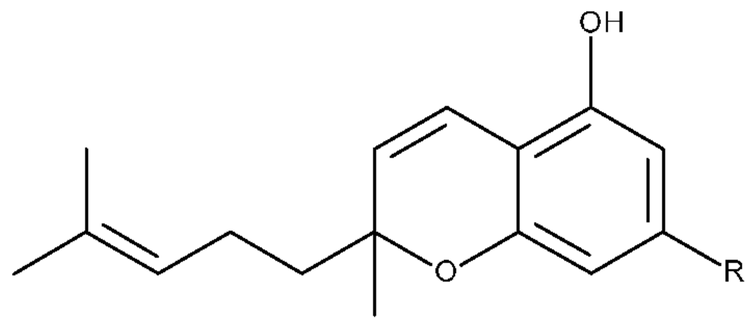
wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

[0083] In select embodiments of the present disclosure, the CBC derivative is of the form:



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wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. As will be appreciated by those skilled in the art who have benefitted from the teachings of the present disclosure, a derivative of CBL converted from a CBC derivative will typically share the same R group.

[0084] In select embodiments of the present disclosure, the method further comprises purifying the product mixture to provide CBL or CBL derivative that is at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% pure. In an embodiment, the CBL or CBL derivative is at least 95% pure. In select embodiments of the present disclosure, purifying the product mixture comprises flash chromatography. In select embodiments of the present disclosure, the flash chromatography is reversed phase C18 flash chromatography. In select embodiments, purifying the product mixture includes crystallizing the product mixture to produce CBL or CBL derivative that has a purity of at least 95%, at least 99%, or greater than 99%. Crystalline CBL or CBL derivative that has a purity of at least 95% may be a CBL isolate or CBL derivative isolate.

[0085] In select embodiments of the present disclosure, the CBC or CBC derivative is a component of a cannabis extract, a cannabis distillate, a cannabis isolate, or a cannabis synthesis reaction mixture. As the CBC derivative may not be a naturally occurring substance, in particular embodiments the CBC derivative is a component of a cannabis synthesis reaction mixture. In select embodiments of the present disclosure, the cannabis extract, distillate, or isolate comprises at least 40% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the cannabis extract, the cannabis distillate, the cannabis isolate, or the cannabis synthesis reaction mixture comprises between about 40% w/w and about 95% w/w, between about 50% w/w and about 95% w/w, or between about 85% w/w and about 90% w/w CBC or CBC derivative.

[0086] In select embodiments of the present disclosure, the CBL or CBL derivative has a yield of at least 10%. In some embodiments, the yield of CBL or CBL derivative may be at least 25%, at least 50%, or more. In select embodiments of the methods of the present disclosure involving contacting with a radical initiator, the concentration of CBC or CBC derivative prior to

contacting the CBC or CBC derivative with the radical initiator is between 0.1 mM and 10 mM, and the concentration of the radical initiator prior to contacting the CBC or CBC derivative is between 0.01 mM and 1 mM.

[0087] In select embodiments of the present disclosure, the product mixture comprises less than about 30% w/w tetrahydrocannabinol (THC). In an embodiment, the product mixture comprises less than 30% w/w THC, less than 25% w/w THC, less than 20% w/w THC, less than 15% w/w THC, less than 10% w/w THC, less than 5% w/w THC, less than 2.5% w/w THC, less than 1% w/w THC, less than 0.5% w/w THC, less than 0.3% w/w THC, less than 0.1% w/w THC, or even less. In an embodiment, the product mixture comprises only trace amounts of THC (e.g. less than 0.01% w/w THC). In an embodiment, the product mixture comprises no THC or at least no detectable THC.

[0088] In select embodiments of the present disclosure, a CBL:THC ratio of the product mixture is between about 10,000:1 and about 1:1, between about 1000:1 and about 1:1, between about 500:1 and about 1:1, between about 100:1 and about 1:1, or between about 10:1 and about 1:1. In an embodiment, the CBL:THC ratio is between about 100:1 and about 10:1, between about 100:1 and about 25:1, between about 100:1 and about 50:1, or between about 100:1 and about 75:1. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[0089] In select embodiments of the present disclosure, the product mixture comprises less than about 50% w/w cannabidiol (CBD), less than about 25% w/w CBD, less than about 20% w/w CBD, less than about 15% w/w CBD, less than about 10% w/w CBD, less than about 5% w/w CBD, less than about 1% w/w CBD, less than about 0.3% w/w CBD, less than about 0.2% w/w CBD, or less than about 0.1% w/w CBD.

[0090] In select embodiments of the present disclosure, a CBL:CBD ratio of the product mixture may be between about 100:1 and about 1:100, more particularly between about 100:1 and about 1:10. In select embodiments of the present disclosure, the CBL:CBD ratio of the product mixture may be between about 1000:1 and about 900:1, about 900:1 and about 700:1, about 700:1 and about 500:1, about 500:1 and about 300:1, about 100:1 and about 50:1, about 50:1 and about 25:1, about 25:1 and about 10:1, about 10:1 and about 1:1, or about 1:1 and about 1:10. In an embodiment, the CBL:CBD ratio of the product mixture may be about 10:1, about 5:1,

about 2:1, about 1:1, about 1:2, about 1:5 or about 1:10. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[0091] In select embodiments, the present disclosure relates to a method for converting CBC or a CBC derivative to CBL or a CBL derivative, the method comprising irradiating the CBC or CBC derivative with UV light to form a product mixture comprising CBL or CBL derivative.

[0092] In the context of the present disclosure, irradiating comprises contacting with UV light. The UV light may be of a single wavelength, multiple wavelengths, or a spectrum of wavelengths. The UV light may be a portion of an irradiating light. In an embodiment, the UV light is of a wavelength between 100 nm and 400 nm. In an embodiment, the UV light is of a wavelength between 300 nm and 350 nm.

[0093] In select embodiments of the present disclosure, the irradiating the CBC or CBC derivative is performed under inert atmosphere. Irradiating under an inert atmosphere may reduce the formation of side products.

[0094] In select embodiments of the present disclosure, the irradiating is performed in the presence of a solvent. The solvent may dissolve at least a portion of the CBC or CBC derivative and/or a portion of the CBL or CBL derivative. In select embodiments of the present disclosure, the solvent is a class 3 solvent. Any suitable class 3 solvent may be used. In select embodiments of the present disclosure, the solvent is a 1:1 v/v mixture of isopropyl alcohol and acetone. In select embodiments of the present disclosure, the solvent is acetone.

[0095] In select embodiments of the present disclosure, the irradiating is at a reaction temperature of less than about 60°C. In select embodiments of the present disclosure, the reaction temperature is between about 10°C and about 60°C, more particularly between about 10°C and about 50°C, between about 15°C and about 35°C, or between about 15°C and about 25°C. In an embodiment, the reaction temperature is at about room temperature. In an embodiment, the reaction temperature is about 10°C, about 15°C, about 20°C, about 25°C, about 30°C, about 35°C, about 40°C, about 45°C, about 50°C, about 55°C, or about 60°C. A higher temperature may increase the rate of reaction, where a higher rate of reaction increases throughput and is thereby more compatible with large scale reactions. A lower temperature may increase the yield of the reaction or reduce the amount of side products formed.

[0096] In select embodiments of the present disclosure, the irradiating is for a reaction time of at least about 30 minutes, more particularly at least about 60 minutes. In an embodiment, the reaction time is between about 30 minutes and about 7 days, more particularly between about 2 hours and about 7 days, between about 2 hours and about 48 hours, between about 2 hours and about 12 hours, or between about 2 hours and about 6 hours. In an embodiment, the reaction time is about 30 minutes, about 60 minutes, about 90 minutes, about 2 hours, about 4 hours, about 6 hours, about 8 hours, about 10 hours, about 12 hours, about 18 hours, about 24 hours, about 30 hours, about 36 hours, about 42 hours, about 48 hours, or longer. A shorter reaction time may increase the throughput of the reaction, which increases the rate at which CBL is produced. A longer reaction time may increase the yield of the reaction.

[0097] In select embodiments of the present disclosure, the irradiating is under a reaction pressure below about 1 bar (below about 100 kPa). In an embodiment, the reaction pressure is between about 0.1 mbar and 1000 mbar, more particularly between about 0.1 mbar and 100 mbar, or between about 0.5 mbar and 10 mbar.

[0098] In select embodiments of the present disclosure, the product mixture comprises at least about 1% w/w CBL and at least about 1% w/w CBC (or derivatives thereof).

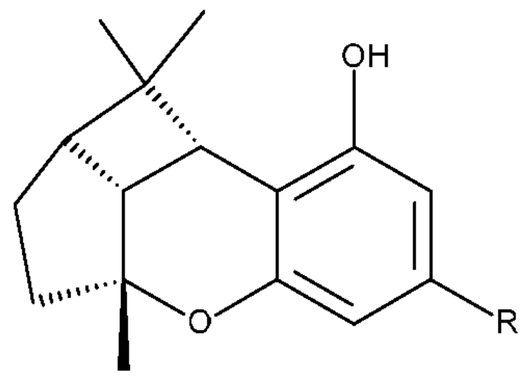
[0099] In select embodiments of the present disclosure, the product mixture comprises between about 1% w/w CBC and about 95% w/w CBC, or more particularly between about 1% w/w CBC and about 75% w/w CBC, between about 1% w/w CBC and about 50% w/w CBC, or between about 1% w/w CBC and about 25% w/w CBC. In an embodiment, the product mixture comprises between about 1% w/w CBC and about 25% w/w CBC, more particularly between about 1% w/w CBC and about 25% w/w CBC, or between about 1% w/w CBC and about 5% w/w CBC. In an embodiment, the product mixture comprises between about 5% w/w CBC and about 25% w/w CBC. In an embodiment, the product mixture comprises about 1.0%, about 2.5%, about 5.0%, about 7.5%, about 10.0%, about 12.5%, about 15.0%, about 17.5%, about 20.0%, about 22.5%, about 25%, about 27.5%, about 30%, or greater w/w CBC. As will be appreciated from the disclosure herein, reference to CBC in this paragraph equally applies to CBC derivatives and the amounts thereof.

[00100] In select embodiments of the present disclosure, the product mixture comprises between about 1% w/w CBL and about 99% w/w CBL, more particularly between about 10% w/w CBL and about 90% w/w CBL, between about 25% w/w CBL and about 75% w/w CBL or between

about 40% w/w CBL and about 50% CBL. In an embodiment, the product mixture comprises about 1.0%, about 2.5%, about 5.0%, about 7.5%, about 10.0%, about 12.5%, about 15.0%, about 17.5%, about 20.0%, about 22.5%, about 25%, about 27.5%, about 30%, about 32.5%, about 35%, about 37.5%, about 40%, about 42.5%, about 45%, about 47.5%, about 50%, or greater w/w CBL. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives and the amounts thereof.

[00101] In select embodiments of the present disclosure, the CBL and the CBC are present in a CBL:CBC ratio that is between about 1000:1 and about 1:1000, between about 500:1 and about 1:500, between about 100:1 and about 1:100, between about 10:1 and about 1:10, between about 5:1 and about 1:5, or between about 2:1 and about 1:2. In an embodiment, the CBL:CBC ratio of the product mixture is between about 100:1 and about 1:20, between about 95:1 and about 1:10, or between about 20:1 and about 1:1. In an embodiment, the CBL:CBC ratio of the product mixture is about 20:1, about 15:1, about 10:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 1:2, about 1:3, about 1:4, about 1:5, about 1:10, about 1:15, or about 1:20. As will be appreciated from the disclosure herein, reference to CBL:CBC ratios may be equally applicable to ratios of derivatives of these compounds.

[00102] In select embodiments of the present disclosure, the CBL derivative of the form:



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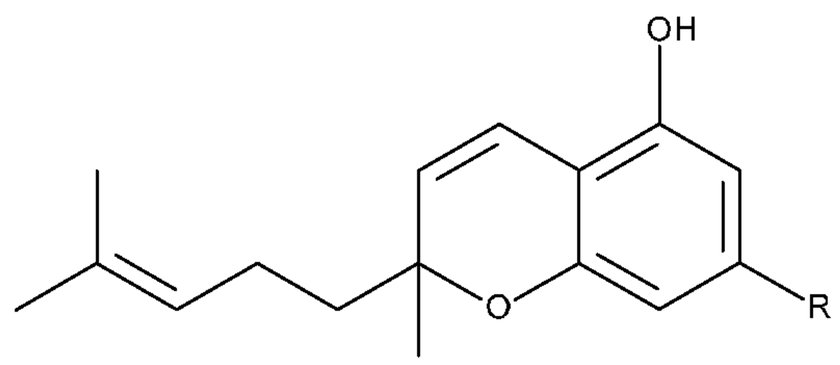
wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

[00103] In select embodiments of the present disclosure, the CBC derivative of the form:



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wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. As will be appreciated by those skilled in the art who have benefitted from the teachings of the present disclosure, a derivative of CBL converted from a CBC derivative will typically share the same R group.

[00104] In select embodiments of the present disclosure, the method further comprises purifying the product mixture to provide CBL or CBL derivative that is at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% pure. In an embodiment, the CBL or CBL derivative is at least 95% pure. In select embodiments of the present disclosure, purifying the product mixture comprises flash chromatography. In select embodiments of the present disclosure, the flash chromatography is reversed phase C18 flash chromatography. In select embodiments, purifying the product mixture includes crystallizing the product mixture to produce CBL or CBL derivative that has a purity of at least 95%, at least 99%, or greater than 99%. Crystalline CBL or CBL derivative that has a purity of at least 95% may be a CBL isolate or CBL derivative isolate.

[00105] In select embodiments of the present disclosure, the CBC or CBC derivative is a component of a cannabis extract, a cannabis distillate, a cannabis isolate, or a cannabis synthesis reaction mixture. As the CBC derivative may not be a naturally occurring substance, in particular embodiments the CBC derivative is a component of a cannabis synthesis reaction mixture. In select embodiments of the present disclosure, the cannabis extract, the cannabis distillate, the cannabis isolate, or the cannabis synthesis reaction mixture comprises at least 40% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the cannabis extract, the cannabis distillate, the cannabis isolate, or the cannabis synthesis reaction mixture comprises between about 40% w/w and about 95% w/w, between about 50% w/w and about 95% w/w, or between about 85% w/w and about 90% w/w CBC or CBC derivative.

[00106] In select embodiments of the present disclosure, the CBL or CBL derivative has a yield of at least 10%. In some embodiments, the yield of CBL or CBL derivative may be at least 25%, at least 50%, or more. A higher yield increases the amount of CBL or CBL derivatives obtained via the methods of the present disclosure.

[00107] In select embodiments of the present disclosure, a wavelength of the UV light is between 300 nm and 350 nm. In select embodiments of the present disclosure, the UV light has

a power between 30 W and 500 W. In the context of the present disclosure, the power of the UV light is defined as the electrical power consumed by the light source in W.

[00108] In select embodiments of the present disclosure, the product mixture comprises less than about 30% w/w tetrahydrocannabinol (THC). In an embodiment, the product mixture comprises less than 30% w/w THC, less than 25% w/w THC, less than 20% w/w THC, less than 15% w/w THC, less than 10% w/w THC, less than 5% w/w THC, less than 2.5% w/w THC, less than 1% w/w THC, less than 0.5% w/w THC, less than 0.3% w/w THC, less than 0.1% w/w THC, or even less. In an embodiment, the product mixture comprises only trace amounts of THC (e.g. less than 0.01% w/w THC). In an embodiment, the product mixture comprises no THC or at least no detectable THC.

[00109] In select embodiments of the present disclosure, a CBL:THC ratio of the product mixture is between about 10,000:1 and about 1:1, between about 1000:1 and about 1:1, between about 500:1 and about 1:1, between about 100:1 and about 1:1, or between about 10:1 and about 1:1. In an embodiment, the CBL:THC ratio is between about 100:1 and about 10:1, between about 100:1 and about 25:1, between about 100:1 and about 50:1, or between about 100:1 and about 75:1. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[00110] In select embodiments of the present disclosure, the product mixture comprises less than about 50% w/w cannabidiol (CBD), less than about 25% w/w CBD, less than about 20% w/w CBD, less than about 15% w/w CBD, less than about 10% w/w CBD, less than about 5% w/w CBD, less than about 1% w/w CBD, less than about 0.3% w/w CBD, less than about 0.2% w/w CBD, or less than about 0.1% w/w CBD.

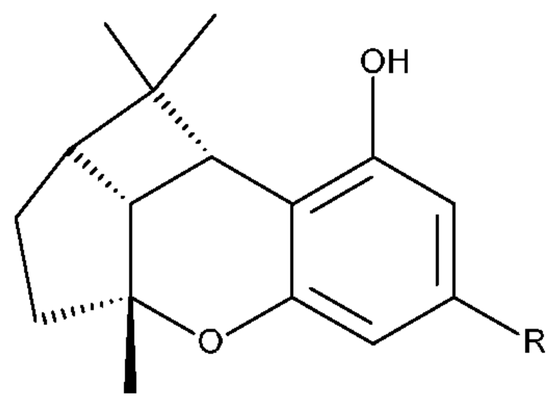
[00111] In select embodiments of the present disclosure, a CBL:CBD ratio of the product mixture may be between about 100:1 and about 1:100, more particularly between about 100:1 and about 1:10. In select embodiments of the present disclosure, the CBL:CBD ratio of the product mixture may be between about 1000:1 and about 900:1, about 900:1 and about 700:1, about 700:1 and about 500:1, about 500:1 and about 300:1, about 100:1 and about 50:1, about 50:1 and about 25:1, about 25:1 and about 10:1, about 10:1 and about 1:1, or about 1:1 and about 1:10. In an embodiment, the CBL:CBD ratio of the product mixture may be about 10:1, about 5:1, about 2:1, about 1:1, about 1:2, about 1:5 or about 1:10. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[00112] In select embodiments, the present disclosure relates to a cannabinoid composition comprising (i) at least about 4% w/w CBL or a CBL derivative and (ii) at least about 4% w/w CBC or a CBC derivative. The cannabinoid composition may, for example, be prepared by any of the methods disclosed herein.

[00113] In select embodiments of the present disclosure, the cannabinoid composition comprises between about 4% w/w CBL and about 99% w/w CBL, between about 10% w/w CBL and about 90% w/w CBL, between about 25% w/w CBL and about 75% w/w CBL or between about 40% w/w CBL and about 50% CBL. In select embodiments of the present disclosure, the cannabinoid composition comprises about 5%, about 15%, about 25%, about 35%, about 50%, about 60%, about 75%, about 85%, about 90%, or about 95% w/w CBL. In select embodiments of the present disclosure, the cannabinoid composition comprises between 4% w/w CBC and about 10% w/w CBC, between about 10% w/w CBC and about 25% w/w CBC, or greater than about 25% w/w CBC. In select embodiments of the present disclosure, the cannabinoid composition comprises between 40% w/w CBC and about 50% w/w CBC, between about 50% w/w CBC and about 70% w/w CBC, or greater than about 70% w/w CBC. In select embodiments of the present disclosure, the cannabinoid composition comprises about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, or about 95% w/w CBC. As will be appreciated from the disclosure herein, reference to CBL and CBC in this paragraph equally applies to CBL derivatives and CBC derivatives, respectively, and the amounts thereof.

[00114] In select embodiments of the present disclosure, the CBL and the CBC are present in a CBL:CBC ratio that is between about 1000:1 and about 1:1000, between about 500:1 and about 1:500, between about 100:1 and about 1:100, between about 10:1 and about 1:10, between about 5:1 and about 1:5, or between about 2:1 and about 1:2. In an embodiment, the CBL:CBC ratio of the cannabinoid composition is between about 100:1 and about 1:20, between about 95:1 and about 1:10, or between about 20:1 and about 1:1. In an embodiment, the CBL:CBC ratio of the cannabinoid composition is about 20:1, about 15:1, about 10:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 1:2, about 1:3, about 1:4, about 1:5, about 1:10, about 1:15, or about 1:20. As will be appreciated from the disclosure herein, reference to CBL:CBC ratios may be equally applicable to ratios of derivatives of these compounds.

[00115] In select embodiments of the present disclosure, the cannabinoid composition comprises a CBL derivative of the form:



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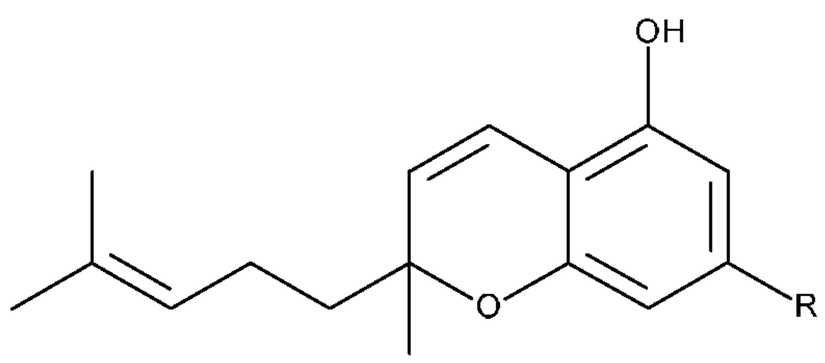
and comprises a CBC derivative of the form:



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wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. As will be appreciated by those skilled in the art who have benefitted from the teachings of the present disclosure, the CBL derivative and CBC derivative in the cannabinoid composition will typically share the same R group.

[00116] In select embodiments of the present disclosure, the cannabinoid composition comprises less than about 30% w/w tetrahydrocannabinol (THC). In an embodiment, the cannabinoid composition comprises less than 30% w/w THC, less than 25% w/w THC, less than 20% w/w THC, less than 15% w/w THC, less than 10% w/w THC, less than 5% w/w THC, less than 2.5% w/w THC, less than 1% w/w THC, less than 0.5% w/w THC, less than 0.3% w/w THC, less than 0.1% w/w THC, or even less. In an embodiment, the cannabinoid composition comprises only trace amounts of THC (e.g. less than 0.01% w/w THC). In an embodiment, the cannabinoid composition comprises no THC or at least no detectable THC.

[00117] In select embodiments of the present disclosure, a CBL:THC ratio of the cannabinoid composition is between about 1000:1 and about 1:1 or between about 100:1 and about 10:1. In select embodiments of the present disclosure, the CBL:THC ratio of the cannabinoid composition is between about 10,000:1 and about 1:1, between about 1000:1 and about 1:1, between about 500:1 and about 1:1, between about 100:1 and about 1:1, or between about 10:1 and about 1:1. In an embodiment, the CBL:THC ratio is between about 100:1 and

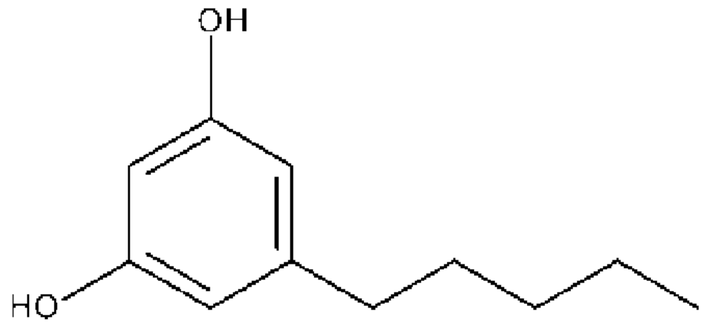
about 10:1, between about 100:1 and about 25:1, between about 100:1 and about 50:1, or between about 100:1 and about 75:1. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[00118] In select embodiments of the present disclosure, the cannabinoid composition comprises less than about 50% w/w cannabidiol (CBD), less than about 25% w/w CBD, less than about 20% w/w CBD, less than about 15% w/w CBD, less than about 10% w/w CBD, less than about 5% w/w CBD, less than about 1% w/w CBD, less than about 0.3% w/w CBD, less than about 0.2% w/w CBD, or less than about 0.1% w/w CBD.

[00119] In select embodiments of the present disclosure, a CBL:CBD ratio of the cannabinoid composition may be between about 100:1 and about 1:100, more particularly between about 100:1 and about 1:10. In select embodiments of the present disclosure, the CBL:CBD ratio of the cannabinoid composition may be between about 1000:1 and about 900:1, about 900:1 and about 700:1, about 700:1 and about 500:1, about 500:1 and about 300:1, about 100:1 and about 50:1, about 50:1 and about 25:1, about 25:1 and about 10:1, about 10:1 and about 1:1, or about 1:1 and about 1:10. In an embodiment, the CBL:CBD ratio of the cannabinoid composition may be about 10:1, about 5:1, about 2:1, about 1:1, about 1:2, about 1:5 or about 1:10. As will be appreciated from the disclosure herein, reference to CBL in this paragraph equally applies to CBL derivatives.

[00120] In select embodiments, the present disclosure relates to a method of preparing CBL or a CBL derivative, the method comprising: heating a reaction mixture comprising citral, a modified resorcinol, and an amine to form a first product mixture; and converting the first product mixture into a second product mixture by: (i) contacting the first product mixture with an acidic heterogeneous material to form the CBL or the CBL derivative; (ii) contacting the first product mixture with a radical initiator to form the CBL or the CBL derivative; or (iii) irradiating the first product mixture with UV light to form the CBL or the CBL derivative. In select embodiments of the present disclosure, the first reaction mixture is a cannabis synthesis reaction mixture.

[00121] In select embodiments of the present disclosure, and in relation to methods for preparing CBL, the modified resorcinol may be of the form:



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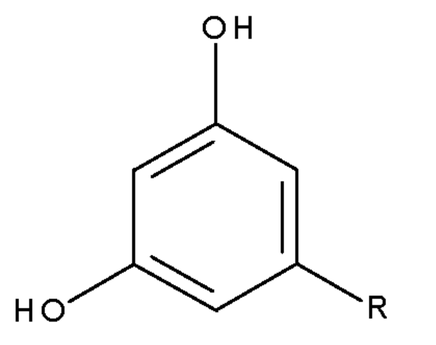
[00122] In select embodiments of the present disclosure, and in relation to methods for preparing CBL derivatives, the modified resorcinol may be of the form:



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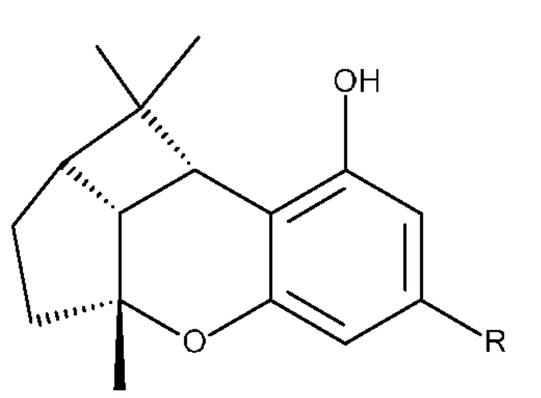
and the CBL derivative of the form:



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wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. As will be appreciated by those skilled in the art who have benefitted from the teachings of the present disclosure, a derivative of CBL prepared from a modified resorcinol will typically share the same R group.

[00123] In select embodiments, the present disclosure relates to a method of producing an artificial resin, the method comprising: contacting a starting material comprising CBC or a CBC derivative with an acidic heterogeneous material to form an artificial resin comprising at least about 4% w/w CBL or CBL derivative, a first cannabinoid, and a second cannabinoid.

[00124] In select embodiments of the present disclosure, the acidic heterogeneous material converts CBC to CBL or CBC derivative to CBL derivative in the presence of at least one

additional cannabinoid to produce the artificial resin. Unreacted CBC or CBC derivative may form a portion of the artificial resin.

[00125] Non-exclusive examples of acidic heterogeneous material include: montmorillonite, activated montmorillonite, amberlyst resins, and ZSM-5. In select embodiments of the present disclosure, the acidic heterogeneous material is activated montmorillonite.

[00126] In select embodiments of the present disclosure, the contacting is performed in the presence of a solvent. In select embodiments of the present disclosure, the solvent is chloroform. In select embodiments of the present disclosure, the solvent is a class 3 solvent. Any suitable class 3 solvent may be used. In select embodiments of the present disclosure, the class 3 solvent is heptane, acetic acid, or a combination thereof.

[00127] In select embodiments of the present disclosure, the contacting is at a reaction temperature of less than about 100°C. In select embodiments of the present disclosure, the reaction temperature is between about -40°C and about 100°C, more particularly between about -25°C and about 75°C, between about -20°C and about 60°C, or between about -10°C and about 10°C. In an embodiment, the reaction temperature is at about room temperature. In an embodiment, the reaction temperature is about -25°C, about -20°C, about -15°C, about -10°C, about -5°C, about 0°C, about 5°C, about 10°C, about 15°C, about 20°C, about 25°C, about 30°C, about 35°C, about 40°C, about 45°C, about 50°C, about 55°C, or about 60°C.

[00128] In select embodiments of the present disclosure, the contacting is for a reaction time of at least about 30 minutes, more particularly at least about 60 minutes. In an embodiment, the reaction time is between about 30 minutes and about 72 hours, more particularly between about 2 hours and about 48 hours, between about 4 hours and about 36 hours, between about 6 hours and about 24 hours, or between about 12 hours and about 24 hours. In an embodiment, the reaction time is between about 2 hours and 24 hours. In an embodiment, the reaction time is between about 18 hours and about 24 hours. In an embodiment, the reaction time is about 30 minutes, about 60 minutes, about 90 minutes, about 2 hours, about 4 hours, about 6 hours, about 8 hours, about 10 hours, about 12 hours, about 18 hours, about 24 hours, about 30 hours, about 36 hours, about 42 hours, about 48 hours, or longer.

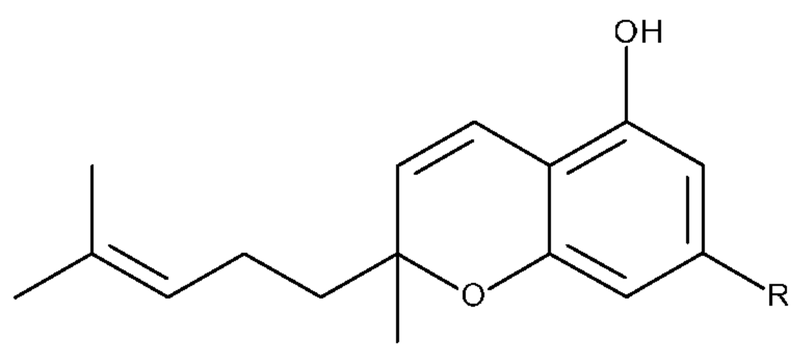
[00129] In select embodiments of the present disclosure, the contacting is under a reaction pressure below about 1 bar (below about 100 kPa). In an embodiment, the reaction pressure is

between about 0.1 mbar and 1000 mbar, more particularly between about 0.1 mbar and 100 mbar, or between about 0.5 mbar and 10 mbar.

[00130] In select embodiments of the present disclosure, the artificial resin comprises between about 4% w/w and about 90% w/w CBL or CBL derivative, more particularly between about 10% and about 90%, between about 25% and about 75%, or between about 40% and about 50% w/w CBL or CBL derivative. In select embodiments of the present disclosure, the artificial resin comprises about 5%, about 15%, about 25%, about 35%, about 50%, about 60%, about 75%, about 85%, about 90%, or about 95% w/w CBL or CBL derivative.

[00131] In select embodiments of the present disclosure, the first cannabinoid in the artificial resin is CBC or CBC derivative. In an embodiment, the artificial resin comprises at least about 4% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises between about 4% and about 10% w/w CBC or CBC derivative, more particularly between about 10% and about 25% w/w CBC or CBC derivative, or greater than about 25% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises between about 40% and about 50%, between about 50% and about 70%, or greater than about 70% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, or more w/w CBC or CBC derivative.

[00132] In select embodiments of the present disclosure, the CBC derivative of the artificial resin is of the form:



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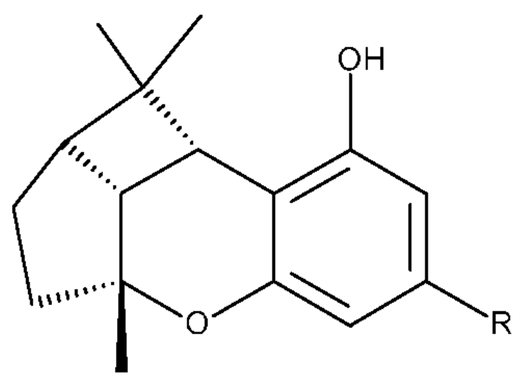
wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

[00133] In select embodiments of the present disclosure, the CBL derivative of the artificial resin is of the form:



wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. In an embodiment, the CBC derivative and CBL derivative have the same R group.

[00134] In select embodiments of the present disclosure, the second cannabinoid is a modified cannabinoid comprising the same R group as the CBC derivative and/or the CBL derivative. As used herein, the term “modified cannabinoid” refers to a natural or synthetic cannabinoid (e.g. THC, CBD, CBG, CBN, etc) having a modified substituent in place of the common pentyl chain in the position of the R group, above. A person of ordinary skill in the art, with the benefit of the present disclosure, will appreciate that CBC derivative converted to cannabinoids other than CBL derivative will also typically have the same R group as CBC derivative.

[00135] In select embodiments of the present disclosure, the second cannabinoid is any one of the cannabinoids described herein. In an embodiment, the second cannabinoid is THC (Δ9-THC), Δ8-THC, CBD, CBT, CBN, CBG, CBDV, THCA, or cannabicitran. Conversion of CBC may produce various cannabinoids. In select embodiments of the present disclosure, the second cannabinoid is cannabicitran or a cannabicitran derivative. In select embodiments of the present disclosure, the artificial resin comprises at least about 1% w/w of the second cannabinoid. In an embodiment, the artificial resin comprises between about 1% and about 25% w/w of the second cannabinoid, more particularly between about 2% and about 10% w/w of the second cannabinoid. In an embodiment, the artificial resin comprises about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, or more w/w of the second cannabinoid.

[00136] In select embodiments of the present disclosure, the CBC of the starting material and/or artificial resin comprises synthetic CBC or synthetic CBC derivative. In select embodiments of the present disclosure, the starting material comprises at least 40% w/w synthetic CBC or synthetic CBC derivative, more particularly between about 40% and about 95%, between about 50% and about 95%, or between about 50% and about 75% w/w synthetic CBC or synthetic CBC

derivative. In an embodiment, the starting material comprises between about 85% w/w and about 90% w/w synthetic CBC or synthetic CBC derivative. In select embodiments of the present disclosure, the CBC of the starting material comprises a CBC isolate or CBC derivative isolate.

[00137] In select embodiments of the present disclosure, the artificial resin further comprises a third cannabinoid. In select embodiments of the present disclosure, the third cannabinoid is THC or CBD. In select embodiments of the present disclosure, the artificial resin comprises at least about 1% w/w of the third cannabinoid. In an embodiment, the artificial resin comprises between about 1% and about 25% w/w of the third cannabinoid, more particularly between about 2% and about 10% w/w of the third cannabinoid. In an embodiment, the artificial resin comprises about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, or more w/w of the third cannabinoid. In some embodiments, the amount of the third cannabinoid in the artificial resin is less than the amount of the second cannabinoid.

[00138] In select embodiments, the present disclosure relates to a method of producing an artificial resin, the method comprising: contacting a starting material comprising CBC or a CBC derivative with a radical initiator to form an artificial resin comprising at least about 4% w/w cannabicyclol (CBL) or CBL derivative, a first cannabinoid, and a second cannabinoid.

[00139] Non-exclusive examples of free radical initiators are described elsewhere herein. In select embodiments of the present disclosure, the radical initiator is $Fe(ClO_4)_3$.

[00140] In select embodiments of the present disclosure, the contacting is in the presence of a solvent. In select embodiments of the present disclosure, the solvent is a class 3 solvent. Exemplary class 3 solvents are described elsewhere herein. In select embodiments of the present disclosure, the solvent is ethyl acetate.

[00141] In select embodiments of the present disclosure, the contacting with the radical initiator is at a reaction temperature of less than about 77°C, more particularly between about 0°C and about 77°C, between about 10°C and about 50°C, or between about 15°C and about 25°C. In an embodiment, the reaction temperature is about 0°C, about 5°C, about 15°C, about 20°C, about 25°C, about 30°C, about 35°C, about 40°C, about 45°C, or about 50°C.

[00142] In select embodiments of the present disclosure, the contacting with the radical initiator is for a reaction time of at least about 1 minute, more particularly between about 1 minute

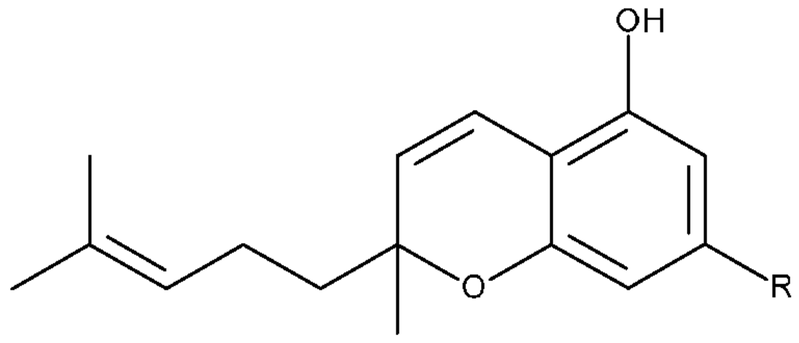
and about 60 minutes, between about 5 minutes and about 60 minutes, between about 10 minutes and about 30 minutes, or between about 10 minutes and about 20 minutes. In an embodiment, the reaction time is about 1 minute, about 5 minutes, about 10 minutes, about 15 minutes, about 20 minutes, about 25 minutes, about 30 minutes, about 35 minutes, about 40 minutes, about 45 minutes, about 50 minutes, about 55 minutes, about 60 minutes, or longer.

[00143] In select embodiments of the present disclosure, the contacting with the radical initiator is under a reaction pressure below about 1 bar (below about 100 kPa). In an embodiment, the reaction pressure is between about 0.1 mbar and 1000 mbar, more particularly between about 0.1 mbar and 100 mbar, or between about 0.5 mbar and 10 mbar.

[00144] In select embodiments of the present disclosure, the artificial resin comprises between about 4% w/w and about 90% w/w CBL or CBL derivative, more particularly between about 10% and about 90%, between about 25% and about 75%, or between about 40% and about 50% w/w CBL or CBL derivative. In select embodiments of the present disclosure, the artificial resin comprises about 5%, about 15%, about 25%, about 35%, about 50%, about 60%, about 75%, about 85%, about 90%, or about 95% w/w CBL or CBL derivative.

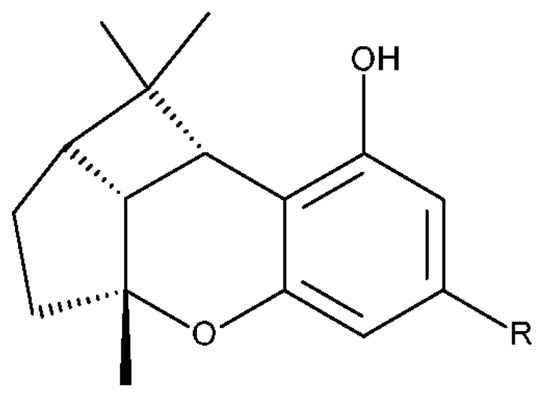
[00145] In select embodiments of the present disclosure, the first cannabinoid in the artificial resin is CBC or CBC derivative. In an embodiment, the artificial resin comprises at least about 4% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises between about 4% and about 10% w/w CBC or CBC derivative, more particularly between about 10% and about 25% w/w CBC or CBC derivative, or greater than about 25% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises between about 40% and about 50%, between about 50% and about 70%, or greater than about 70% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, or more w/w CBC or CBC derivative.

[00146] In select embodiments of the present disclosure, the CBC derivative of the artificial resin is of the form:



wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

[00147] In select embodiments of the present disclosure, the CBL derivative of the artificial resin is of the form:



[00148] wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. In an embodiment, the CBC derivative and CBL derivative have the same R group.

[00149] In select embodiments of the present disclosure, the second cannabinoid is a modified cannabinoid comprising the same R group as the CBC derivative and/or CBL derivative.

[00150] In select embodiments of the present disclosure, the second cannabinoid is any one of the cannabinoids described herein. In an embodiment, the second cannabinoid is THC (Δ9-THC), Δ8-THC, CBD, CBT, CBN, CBG, CBDV, THCA, or cannabicitran. In select embodiments of the present disclosure, the second cannabinoid is cannabicitran. In select embodiments of the present disclosure, the artificial resin comprises at least about 1% w/w the second cannabinoid. In an embodiment, the artificial resin comprises between about 1% and about 25% w/w of the second cannabinoid, more particularly between about 2% and about 10% w/w of the second cannabinoid. In an embodiment, the artificial resin comprises about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, or more w/w of the second cannabinoid.

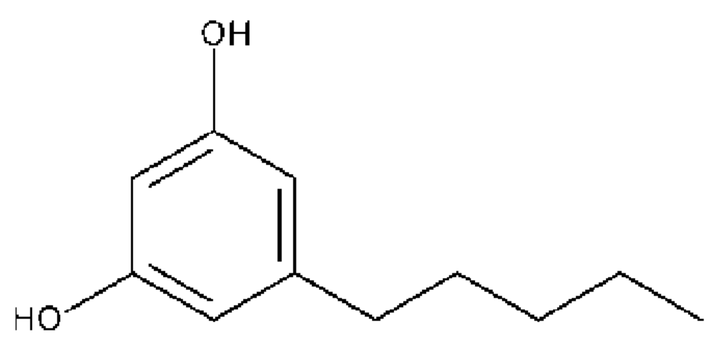
[00151] In select embodiments of the present disclosure, the CBC of the starting material and/or artificial resin comprises synthetic CBC or synthetic CBC derivative. In select embodiments

of the present disclosure, the starting material comprises at least 40% w/w synthetic CBC or synthetic CBC derivative, more particularly between about 40% and about 95%, between about 50% and about 95%, or between about 50% and about 75% w/w synthetic CBC or synthetic CBC derivative. In an embodiment, the starting material comprises between about 85% w/w and about 90% w/w synthetic CBC or synthetic CBC derivative. In select embodiments of the present disclosure, the CBC of the starting material comprises a CBC isolate or CBC derivative isolate.

[00152] In select embodiments of the present disclosure, the artificial resin further comprises a third cannabinoid. In select embodiments of the present disclosure, the third cannabinoid is THC or CBD. In select embodiments of the present disclosure, the artificial resin comprises at least about 1% w/w of the third cannabinoid. In an embodiment, the artificial resin comprises between about 1% and about 25% w/w of the third cannabinoid, more particularly between about 2% and about 10% w/w of the third cannabinoid. In an embodiment, the artificial resin comprises about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, or more w/w of the third cannabinoid. In some embodiments, the amount of the third cannabinoid in the artificial resin is less than the amount of the second cannabinoid.

[00153] In select embodiments, the present disclosure relates to a method of producing an artificial resin, the method comprising: heating a reaction mixture comprising citral, a modified resorcinol, and an amine to form a product mixture; and converting the product mixture into the artificial resin by: (i) contacting the product mixture with an acidic heterogeneous material to form CBL or CBL derivative; (ii) contacting the product mixture with a radical initiator to form CBL or CBL derivative; or (iii) irradiating the product mixture with UV light to form CBL or CBL derivative.

[00154] In select embodiments of the present disclosure, and in relation to methods for preparing an artificial resin comprising CBL, the modified resorcinol may be of the form:



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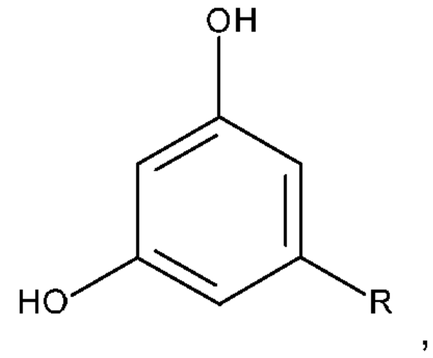
[00155] In select embodiments of the present disclosure, and in relation to methods for preparing an artificial resin comprising a CBL derivative, the modified resorcinol may be of the form:



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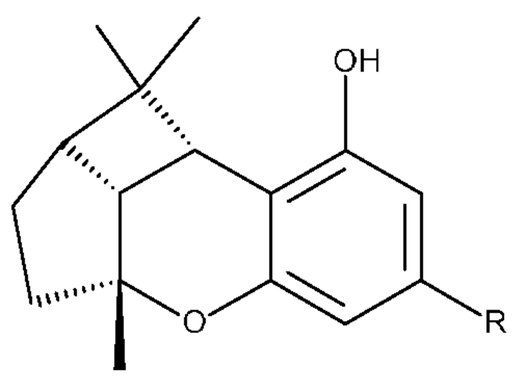
and the CBL derivative of the form:



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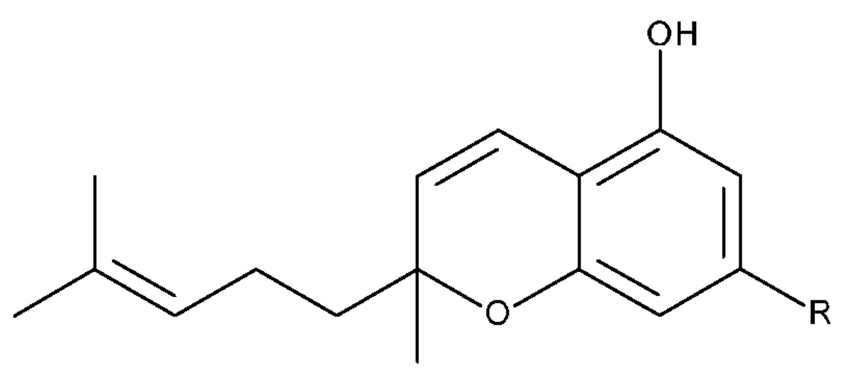
wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. As will be appreciated by those skilled in the art who have benefitted from the teachings of the present disclosure, a derivative of CBL prepared from a modified resorcinol will typically share the same R group.

[00156] In select embodiments, the present disclosure relates to an artificial resin comprising at least about 4% CBL or CBL derivative, a first cannabinoid, and a second cannabinoid.

[00157] In select embodiments of the present disclosure, the artificial resin comprises between about 4% w/w and about 90% w/w CBL or CBL derivative, more particularly between about 10% and about 90%, between about 25% and about 75%, or between about 40% and about 50% w/w CBL or CBL derivative. In select embodiments of the present disclosure, the artificial resin comprises about 5%, about 15%, about 25%, about 35%, about 50%, about 60%, about 75%, about 85%, about 90%, or about 95% w/w CBL or CBL derivative.

[00158] In select embodiments of the present disclosure, the first cannabinoid is CBC or CBC derivative. In an embodiment, the artificial resin comprises at least about 4% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises between about 4% and about 10% w/w CBC or CBC derivative, more particularly between about 10% and about 25% w/w CBC or CBC derivative, or greater than about 25% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises between about 40% and about 50%, between about 50% and about 70%, or greater than about 70% w/w CBC or CBC derivative. In select embodiments of the present disclosure, the artificial resin comprises about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, or more w/w CBC or CBC derivative.

[00159] In select embodiments of the present disclosure, the CBC derivative of the artificial resin is of the form:



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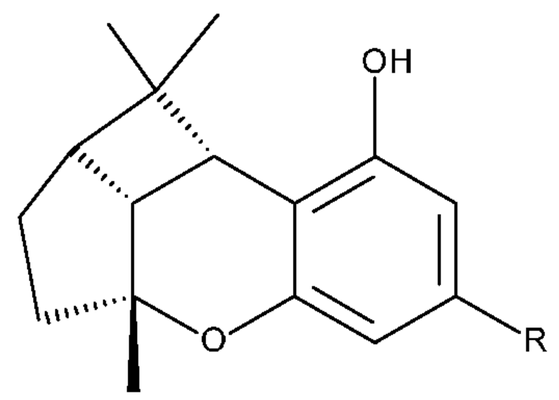
wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

[00160] In select embodiments of the present disclosure, the CBL derivative of the artificial resin is of the form:



wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl. In an embodiment, the CBC derivative and CBL derivative have the same R group.

[00161] In select embodiments of the present disclosure, the second cannabinoid of the artificial resin is a modified cannabinoid comprising the same R group as the CBC derivative and/or CBL derivative.

[00162] In select embodiments of the present disclosure, the second cannabinoid is any one of the cannabinoids described herein. In an embodiment, the second cannabinoid is THC (Δ9-THC), Δ8-THC, CBD, CBT, CBN, CBG, CBDV, THCA, or cannabicitran. In select embodiments of the present disclosure, the second cannabinoid is cannabicitran or a cannabicitran derivative. In select embodiments of the present disclosure, the artificial resin comprises at least about 1% w/w of the second cannabinoid. In an embodiment, the artificial resin comprises between about 1% and about 25% w/w of the second cannabinoid, more particularly between about 2% and about 10% w/w of the second cannabinoid. In an embodiment, the artificial resin comprises about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, or more w/w of the second cannabinoid.

[00163] In select embodiments of the present disclosure, the CBC of the artificial resin comprises synthetic CBC or synthetic CBC derivative. In select embodiments of the present disclosure, the CBC of the artificial resin is from a CBC isolate or CBC derivative isolate.

[00164] In select embodiments of the present disclosure, the artificial resin further comprises a third cannabinoid. In select embodiments of the present disclosure, the third cannabinoid is THC or CBD. In select embodiments of the present disclosure, the artificial resin comprises at least about 1% w/w of the third cannabinoid. In an embodiment, the artificial resin comprises between about 1% and about 25% w/w of the third cannabinoid, more particularly between about 2% and about 10% w/w of the third cannabinoid. In an embodiment, the artificial resin comprises about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, or more w/w of the third cannabinoid. In some embodiments, the amount of the third cannabinoid in the artificial resin is less than the amount of the second cannabinoid.

EXAMPLES

[00165] **EXAMPLE 1**: CBC (202 mg, produced synthetically from citral and olivetol) was dissolved in 48 mL 1:1 isopropyl alcohol:acetone and transferred to an 80 mL Quartz test tube. The reaction was left unstirred at room temperature for 96 hours under irradiation by a UV lamp.

The solvent was evaporated to give 0.196 g of crude reaction mixture. Analysis by HPLC (**FIG. 1**) showed CBL as a product with a yield in the crude reaction mixture of 5% w/w.

[00166] **EXAMPLE 2**: CBC (250 mg, produced synthetically from citral and olivetol) was dissolved in 5 mL pentane and transferred to an 80 mL Quartz test tube. The reaction was left unstirred at room temperature for 24 hours under irradiation by a UV lamp. The solvent was evaporated to give 0.200 g of crude reaction mixture. Analysis by HPLC (not shown) showed no observable CBL as a product.

[00167] **EXAMPLE 3**: CBC (272 mg, 1 mmol) was transferred to a beaker (1 L capacity) and dissolved in 432 mL ethyl acetate followed by $Fe(ClO_4)_3$ (30 mg, 0.1 mmol, Sigma-Aldrich). The reaction was stirred at room temperature for 15 minutes. The solvent was evaporated to give 0.066 g of crude reaction mixture. Analysis by HPLC (**FIG. 2**) showed CBL as a major product with a yield in the crude reaction mixture of 16% w/w with no CBC remaining. Additional reaction time did not increase the yield of CBL.

[00168] **EXAMPLE 4**: CBC (250 mg, 0.8 mmol) was transferred to a round-bottomed flask (100 mL capacity) and dissolved in 13 mL chloroform followed by activated montmorillonite (250 mg, k30, Sigma-Aldrich). The montmorillonite was activated by heating in a 200°C oven for 2 hours. The reaction was stirred for 2 hours at room temperature under nitrogen. The solvent was evaporated to give 0.196 g of crude reaction mixture. Analysis by HPLC (**FIG. 3**) showed CBL as a major product with a yield in the crude reaction mixture of 25% w/w with 75% w/w CBC remaining.

[00169] **EXAMPLE 5**: CBC (250 mg-500mg, 0.8-0.16 mmol) was transferred to a round-bottomed flask (100 mL capacity) and dissolved in 100 mL chloroform or dichloromethane followed by one of: 0.375g p-Tosyl (Sigma-Aldrich, 0.280g camphorsulfonic acid (Sigma-Aldrich), 0.256g Amberlyst-15 (Sigma-Aldrich), and 0.520g ZSM-5 (MR38, ACS). The reaction was stirred for 2 hours at 0°C under nitrogen. The solvent was evaporated to give a crude reaction mixture. Analysis by HPLC (not shown) showed no significant CBL as a product (maximum 1% CBL w/w in product mixture).

[00170] **EXAMPLE 6**: CBC (2.005 g, 6.4 mmol, 90% pure) was transferred to a round-bottomed flask (250 mL capacity) and dissolved in 100 mL chloroform followed by activated montmorillonite (2.022 g). The reaction was stirred for 48 hours at 0°C under nitrogen. The solvent was evaporated to give 0.713 g of crude reaction mixture. The crude reaction mixture was

recrystallized from heptane. Analysis by HPLC of the purified product (**FIG. 4**) showed CBL as a major product with a purity of 97% w/w with no CBC remaining. The yield of purified CBL was 35%.

[00171] **EXAMPLE 7**: To a round bottomed flask with a stopcocked side arm (100 ml capacity), was charged with 640 µL citral, 800 µL piperdine and 7.5 mL ethyl acetate. The resulting mixture was cooled to 0°C and 800 µL acetic anhydride was added dropwise. The resulting mixture was heated at 90°C for 1 hour, before adding a 15 mL solution toluene containing 1 g olivetol. The reaction mixture was stirred at 130°C for 65 hours under nitrogen, after which time it was cooled to room temperature. The solvent was removed by evaporation to yield 3.1 g of crude product. Analysis by HPLC (**FIG. 5**) showed CBC as the major product with a yield of 30% w/w, however no CBL was observed. Replacement of 7.5 mL ethyl acetate with 15 mL toluene and 0.8 mL acetic anhydride produced no significant CBC and no observable CBL. An alternative reaction mixture of: 0.30 mL citral, 300 mg olivetol, 0.25 mL acetic anhydride, 1.8 mL toluene, and a single drop of formic acid at room temp temperature under N2 gas for 24 hours produced no significant CBC and no observable CBL.

[00172] **EXAMPLE 8:** A single crystal of CBL was sample was mounted on a Mitegen polyimide micromount with a small amount of Paratone N oil. All X-ray measurements were made on a Bruker Kappa Axis Apex2 diffractometer at a temperature of 110 K. The unit cell dimensions were determined from a symmetry constrained fit of 9884 reflections with $6.0° < 2\theta < 71.12°$. The data collection strategy was a number of ω and φ scans which collected data up to 71.346° (2θ). The frame integration was performed using SAINT. The resulting raw data was scaled and absorption corrected using a multi-scan averaging of symmetry equivalent data using SADABS.

[00173] The structure was solved by using a dual space methodology using the SHELXT program. Most non-hydrogen atoms were obtained from the initial solution. The remaining atomic positions were obtained from subsequent difference Fourier maps. The hydrogen atoms were introduced at idealized positions and were allowed to ride on the parent atom. The n-pentyl group exhibited a disorder where the chain adopted three different conformations. The normalized occupancies refined to values 0.488(2), 0.345(2), and 0.167(2). The structural model was fit to the data using full matrix least-squares based on F2. The calculated structure factors included corrections for anomalous dispersion from the usual tabulation. The structure was refined using the SHELXL program from the SHELX suite of crystallographic software. A graphic plot of the structure of CBL was produced using the NRCVAX program suite and is shown in **FIG. 6A**.

Drawings of the structure elucidated for CBL were also produced using the Oak Ridge Thermal Ellipsoid Plot (ORTEP) program. **FIG. 6B** shows a perspective view ORTEP drawing of a crystal structure for CBL. **FIG. 6C** shows a stereoscopic view ORTEP drawing of a crystal structure for CBL.

[00174] **EXAMPLE 9:** A series of reactions between CBC and Montmorillonite (K30) were performed. Unless noted otherwise below, 50 mg CBC was transferred to a round-bottomed flask (100 mL capacity) and dissolved in 2.5 mL solvent followed by activated montmorillonite (100% mass equivalent, k30, Sigma-Aldrich). The montmorillonite was activated by heating in a 200°C oven for 2 hours. The reaction was stirred under nitrogen at a temperature and time listed in Table 1. The solvent was evaporated to give a crude reaction mixture that was analyzed by HPLC to determine the CBC, CBL, and cannabicitran content (**FIG. 7** shows HPLC results for experiments 12, 15, and 16 having solvents of heptane, tert-butyl methyl ether, and acetic acid, respectively) The product compositions are shown in Table 1. Cannabicitran contents marked with "*" indicate a reaction where the CBC included 14% w/w cannabicitran. cannabicitran contents marked with a "?" contained cannabicitran at a concentration below the detection limit of the HPLC system.

TABLE 1: Reaction conditions and crude yield for Example 9.

#	Time (h)	Temperature	Solvent	variant	Product % w/w (CBC/CBL/cannabicitran)
1	2	R.T.	chloroform	300 mg CBC, 13 mL solvent	73 / 25 / 2
2	24	R.T.	chloroform	product separation via cooling to form precipitate and mother liquor	4 / 95 / trace
3		0°C	chloroform		35 / 25 / 5
4	24	0°C	chloroform	none	71 / 10 / ND
5	24	0°C	chloroform	catalyst over-activated	69 / 9.5 / ND
6	24	0°C	chloroform	catalyst un-activated	82 / 5 / ND
7	18	R.T.	heptane	200% Mass Eq. catalyst	1 / 22 / 28
8	18	R.T.	heptane	50% Mass Eq. catalyst	1 / 22 / 28
9	18	R.T.	heptane	none	67 / 14 / 4
10	48	R.T.	heptane	none	59 / 9 / 4
11	18	0°C	heptane	50% Mass Eq. catalyst	65 / 2.5 / 14
12	18	0°C	heptane	none	46 / 8 / 15
13	18	0°C	heptane	200% Mass Eq. catalyst	62 / 5 / 13
14	18	40°C	heptane	none	48 / 12 / 10

15	18	0°C	tBME	none	64 / 0.3 / 13
16	18	R.T.	acetic acid	none	40 / 4 / 7

[00175] In the present disclosure, all terms referred to in singular form are meant to encompass plural forms of the same. Likewise, all terms referred to in plural form are meant to encompass singular forms of the same. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure pertains.

[00176] As used herein, the term “about” refers to an approximately +/-10 % variation from a given value. It is to be understood that such a variation is always included in any given value provided herein, whether or not it is specifically referred to.

[00177] It should be understood that the compositions and methods are described in terms of "comprising," "containing," or "including" various components or steps, the compositions and methods can also "consist essentially of or "consist of” the various components and steps. Moreover, the indefinite articles "a" or "an," as used in the claims, are defined herein to mean one or more than one of the element that it introduces.

[00178] For the sake of brevity, only certain ranges are explicitly disclosed herein. However, ranges from any lower limit may be combined with any upper limit to recite a range not explicitly recited, as well as, ranges from any lower limit may be combined with any other lower limit to recite a range not explicitly recited, in the same way, ranges from any upper limit may be combined with any other upper limit to recite a range not explicitly recited. Additionally, whenever a numerical range with a lower limit and an upper limit is disclosed, any number and any included range falling within the range are specifically disclosed. In particular, every range of values (of the form, "from about a to about b," or, equivalently, "from approximately a to b," or, equivalently, "from approximately a-b") disclosed herein is to be understood to set forth every number and range encompassed within the broader range of values even if not explicitly recited. Thus, every point or individual value may serve as its own lower or upper limit combined with any other point or individual value or any other lower or upper limit, to recite a range not explicitly recited.

[00179] Therefore, the present disclosure is well adapted to attain the ends and advantages mentioned as well as those that are inherent therein. The particular embodiments disclosed above are illustrative only, as the present disclosure may be modified and practiced in

different but equivalent manners apparent to those skilled in the art having the benefit of the teachings herein. Although individual embodiments are discussed, the disclosure covers all combinations of all those embodiments. Furthermore, no limitations are intended to the details of construction or design herein shown, other than as described in the claims below. Also, the terms in the claims have their plain, ordinary meaning unless otherwise explicitly and clearly defined by the patentee. It is therefore evident that the particular illustrative embodiments disclosed above may be altered or modified and all such variations are considered within the scope and spirit of the present disclosure. If there is any conflict in the usages of a word or term in this specification and one or more patent(s) or other documents that may be incorporated herein by reference, the definitions that are consistent with this specification should be adopted.

[00180] Many obvious variations of the embodiments set out herein will suggest themselves to those skilled in the art in light of the present disclosure. Such obvious variations are within the full intended scope of the appended claims.

Claims:

1. A method for converting cannabichromene (CBC) or a CBC derivative to cannabicyclol (CBL) or a CBL derivative, the method comprising contacting the CBC or CBC derivative with an acidic heterogeneous material to form a product mixture comprising the CBL or CBL derivative.

2. The method of claim 1, wherein the acidic heterogeneous material is activated montmorillonite.

3. The method of claim 1 or 2, wherein the contacting is in the presence of a solvent chosen from chloroform or a class 3 solvent.

4. The method of any one of claims 1 to 3, wherein the contacting is at a reaction temperature of less than about 100°C.

5. The method of claim 4, wherein the reaction temperature is between about -10°C and about 10°C.

6. The method of any one of claims 1 to 5, wherein the contacting is at a reaction pressure below about 1 bar.

7. A method for converting cannabichromene (CBC) or a CBC derivative to cannabicyclol (CBL) or a CBL derivative, the method comprising contacting the CBC or CBC derivative with a radical initiator to form a product mixture comprising the CBL or CBL derivative.

8. The method of claim 7, wherein the radical initiator is $Fe(ClO_4)_3$.

9. The method of claim 7 or 8, wherein the contacting is in the presence of a class 3 solvent.

10. The method of claim 9, wherein the class 3 solvent is ethyl acetate.

11. The method of any one of claims 7 to 10, wherein the contacting is at a reaction temperature of less than about 77°C.

12. The method of claim 11, wherein the reaction temperature is between about 15°C and about 25°C.

13. The method of any one of claims 7 to 12, wherein the contacting is at a reaction pressure below about 1 bar.

14. The method of any one of claims 7 to 13, wherein the concentration of CBC or CBC derivative prior to contacting the CBC or CBC derivative with the radical initiator is between 0.1 mM and 10 mM, and wherein the concentration of the radical initiator prior to contacting the CBC or CBC derivative with the radical initiator is between 0.01 mM and 1 mM.

15. A method for converting cannabichromene (CBC) or a CBC derivative to cannabicyclol (CBL) or a CBL derivative, the method comprising irradiating the CBC or CBC derivative with UV light to form a product mixture comprising CBL or CBL derivative.

16. The method of claim 15, wherein the UV light is of a wavelength between 300 nm and 350 nm.

17. The method of claim 15 or 16, wherein the UV light has a power between 30 W and 500 W.

18. The method of any one of claims 15 to 17, wherein the irradiating is performed under inert atmosphere.

19. The method of any one of claims 15 to 18, wherein the irradiating is performed in the presence of a class 3 solvent.

20. The method of claim 19, wherein the class 3 solvent is a 1:1 v/v mixture of isopropyl alcohol and acetone.

21. The method of any one of claims 15 to 20, wherein the irradiating is at a reaction temperature of less than about 70°C.

22. The method of claim 21, wherein the reaction temperature is between about 15°C and about 25°C.

23. The method of any one of claims 15 to 22, wherein the irradiating is under a reaction pressure below about 1 bar.

24. The method of any one of claims 1 to 23, wherein the product mixture comprises at least about 1% w/w CBL or CBL derivative and at least about 1% w/w CBC or CBC derivative.

25. The method of claim 24, wherein the CBL or CBL derivative and the CBC or CBC derivative are present in a CBL:CBC ratio or a CBL derivative:CBC derivative ratio that is between about 100:1 and about 1:20.

26. The method of claim 25, wherein the CBL:CBC ratio or CBL derivative:CBC derivative ratio is between about 95:1 and about 1:10.

27. The method of claim 25 or 26, wherein the CBL:CBC ratio or CBL derivative:CBC derivative ratio is between about 20:1 and about 1:1.

28. The method of any one of claims 1 to 27, further comprising purifying the product mixture to provide CBL or CBL derivative that is at least 95% pure.

29. The method of claim 28, wherein the purifying of the product mixture comprises flash chromatography.

30. The method of claim 29, wherein the flash chromatography is reversed phase C18 flash chromatography.

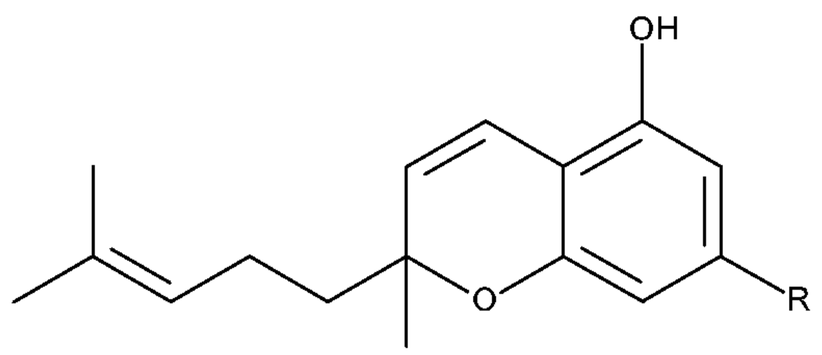
31. The method of claim 28, wherein the purifying of the product mixture comprises crystallizing the product mixture to produce crystalline CBL or CBL derivative that has a purity of at least 99%.

32. The method of any one of claims 1 to 31, wherein the CBL or CBL derivative has a yield of at least 10%.

33. The method of any one of claims 1 to 32, wherein the CBL or CBL derivative comprises a crystalline polymorph.

34. The method of any one of claims 1 to 33, wherein the CBC or CBC derivative is a component of a cannabis extract, a cannabis distillate, a cannabis isolate, or a cannabis synthesis reaction mixture.

35. The method of claim 34, wherein the cannabis synthesis reaction mixture comprises a CBC derivative of the form:



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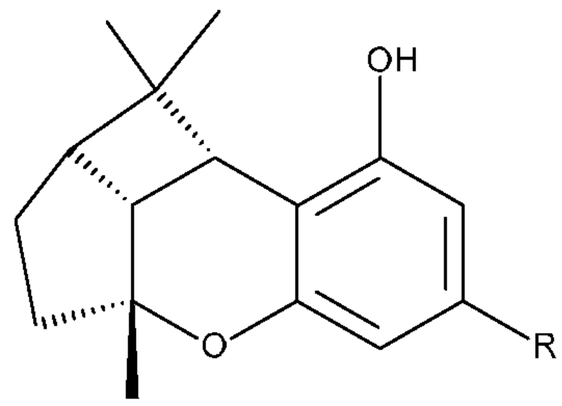
wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

36. The method of claim 35, wherein the product mixture comprises a CBL derivative of the form:



,

wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

37. The method of any one of claims 1 to 36, wherein the product mixture comprises less than about 1% w/w tetrahydrocannabinol (THC).

38. The method of claim 37, wherein the product mixture comprises less than about 0.3% w/w THC.

39. The method of claim 37, wherein the product mixture comprises less than about 0.1% w/w THC.

40. The method of any one of claims 1 to 39, wherein a CBL:THC ratio or CBL derivative:THC ratio of the product mixture is between about 1000:1 and about 1:1.

41. The method of any one of claims 1 to 40, wherein a CBL:CBD ratio or CBL derivative:CBD ratio of the product mixture is between about 100:1 and about 1:10.

42. A cannabinoid composition comprising (i) at least about 4% w/w cannabicyclol (CBL) or a CBL derivative and (ii) at least about 4% w/w cannabichromene (CBC) or a CBC derivative.

43. The cannabinoid composition of claim 42, wherein the cannabinoid composition comprises between about 4% w/w and about 99% CBL or CBL derivative.

44. The cannabinoid composition of claim 42 or 43, wherein the cannabinoid composition comprises between about 10% w/w and about 90% w/w CBL or CBL derivative.

45. The cannabinoid composition of any one of claims 42 to 44, wherein the cannabinoid composition comprises between about 4% w/w and about 10% w/w CBC or CBC derivative.

46. The cannabinoid composition of any one of claims 42 to 44, wherein the cannabinoid composition comprises between about 10% w/w and about 25% w/w CBC or CBC derivative.

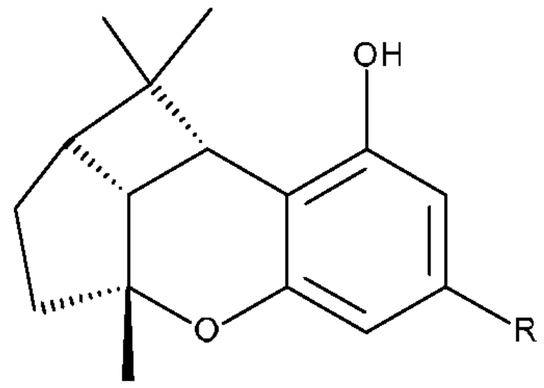
47. The cannabinoid composition of any one of claims 42 to 46, which comprises the CBL and CBC.

48. The cannabinoid composition claim 47, wherein the CBL and the CBC are present in a CBL:CBC ratio that is between about 100:1 and about 1:20.

49. The cannabinoid composition of claim 48, wherein the CBL:CBC ratio is between about 95:1 and about 1:10.

50. The cannabinoid composition of claim 48 or 49, wherein the CBL:CBC ratio is between about 20:1 and about 1:1.

51. The cannabinoid composition of any one of claims 42 to 46, which comprises a CBL derivative of the form:



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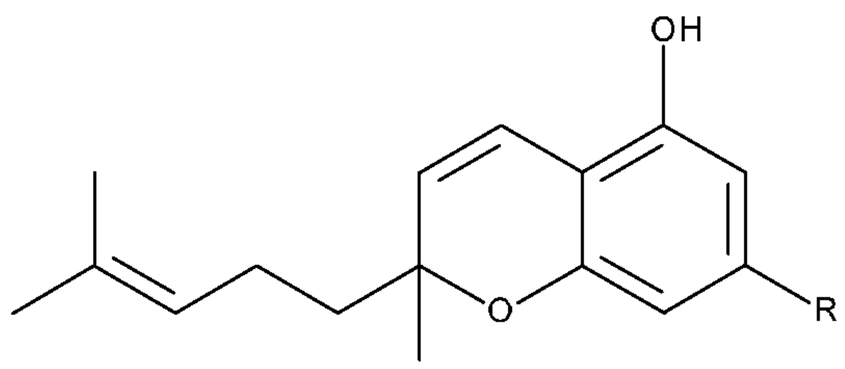
and a CBC derivative of the form:



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wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

52. The cannabinoid composition of any one of claims 42 to 51, wherein the CBL or CBL derivative comprises a crystalline polymorph.

53. The cannabinoid composition of any one of claims 42 to 52, which comprises less than about 1% w/w tetrahydrocannabinol (THC).

54. The cannabinoid composition of claim 53, which comprises less than about 0.3% w/w THC.

55. The cannabinoid composition of claim 53, which comprises less than about 0.1% w/w THC.

56. The cannabinoid composition of any one of claims 42 to 56, wherein a CBL:THC ratio or CBL derivative:THC ratio of the cannabinoid composition is between about 1000:1 and about 1:1.

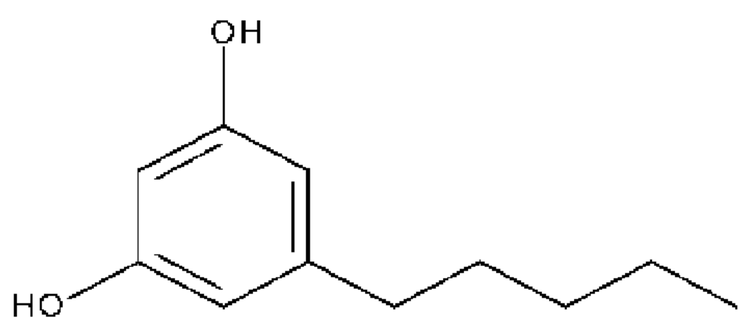
57. The cannabinoid composition of any one of claims 42 to 57, wherein a CBL:CBD ratio or CBL derivative:CBD ratio of the cannabinoid composition is between about 100:1 and about 1:10.

58. A method of preparing cannabicyclol (CBL) or a CBL derivative, the method comprising:

heating a reaction mixture comprising citral, a modified resorcinol, and an amine to form a first product mixture; and

converting the first product mixture into a second product mixture by: (i) contacting the first product mixture with an acidic heterogeneous material to form the CBL or CBL derivative; (ii) contacting the first product mixture with a radical initiator to form the CBL or CBL derivative; or (iii) irradiating the first product mixture with UV light to form the CBL or CBL derivative.

59. The method of claim 58, which is for preparing CBL, and the modified resorcinol is of the form:



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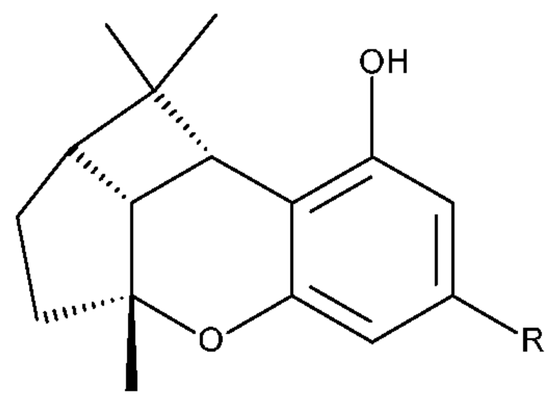
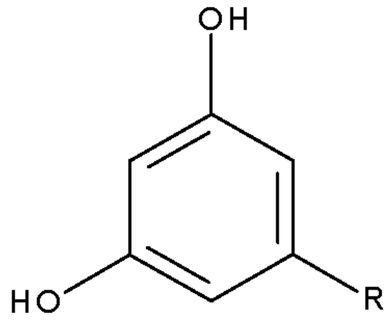
60. The method of claim 59, which is for preparing a CBL derivative of the form:



,

and the modified resorcinol is of the form:



wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

61. A method of producing an artificial resin, the method comprising: contacting a starting material comprising cannabichromene (CBC) or a CBC derivative with an acidic heterogeneous material to form an artificial resin comprising at least about 4% w/w cannabicyclol (CBL) or CBL derivative, a first cannabinoid, and a second cannabinoid.

62. The method of claim 61, wherein the acidic heterogeneous material is activated montmorillonite.

63. The method of claim 61 or 62, wherein the contacting is performed in the presence of a solvent chosen from chloroform or a class 3 solvent.

64. The method of any one of claims 61 to 63, wherein the contacting is performed at a reaction temperature of less than about 100°C.

65. The method of claim 64, wherein the reaction temperature is between about -10°C and about 10°C.

66. The method of any one of claims 61 to 65, wherein the contacting is under a reaction pressure below about 1 bar.

67. A method of producing an artificial resin, the method comprising: contacting a starting material comprising cannabichromene (CBC) or a CBC derivative with a radical initiator to form an artificial resin comprising at least about 4% w/w cannabicyclol (CBL) or CBL derivative, a first cannabinoid, and a second cannabinoid.

68. The method of claim 67, wherein the radical initiator is $Fe(ClO_4)_3$.

69. The method of claim 67 or 68, wherein the contacting is performed in the presence of a class 3 solvent.

70. The method of claim 69, wherein the solvent is ethyl acetate.

71. The method of any one of claims 67 to 70, wherein the contacting is at a reaction temperature of less than about 77°C.

72. The method of claim 71, wherein the reaction temperature is between about 15°C and about 25°C.

73. The method of any one of claims 67 to 72, wherein the contacting is under a reaction pressure below about 1 bar.

74. The method of any one of claims 61 to 73, wherein the artificial resin comprises between about 4% w/w and about 90% w/w CBL or CBL derivative.

75. The method of any one of claims 61 to 74, wherein the CBC or CBC derivative is a synthetic CBC or synthetic CBC derivative.

76. The method of claim 75, wherein the starting material comprises at least 40% w/w synthetic CBC or synthetic CBC derivative.

77. The method of claim 75 or 76, wherein the starting material comprises between about 40% w/w and about 95% w/w synthetic CBC or synthetic CBC derivative.

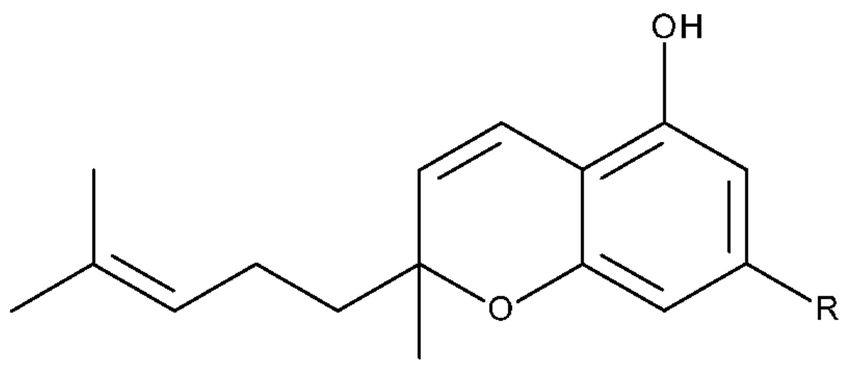
78. The method of any one of claims 75 to 77, wherein the starting material comprises between about 85% w/w and about 90% w/w synthetic CBC or synthetic CBC derivative.

79. The method of any one of claims 61 to 74, wherein the CBC or CBC derivative is an isolate.

80. The method of any one of claims 61 to 79, wherein the first cannabinoid is the CBC or CBC derivative and the artificial resin comprises at least about 4% w/w CBC or CBC derivative.

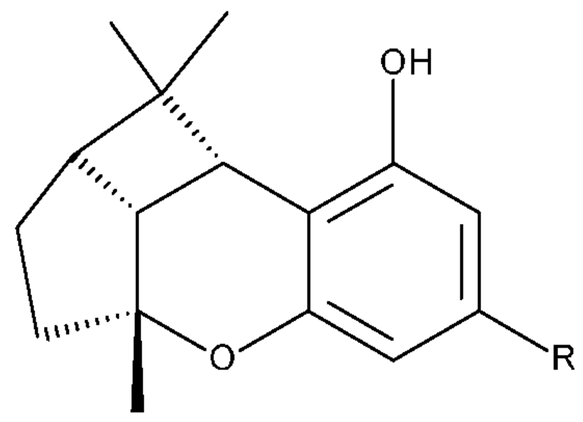
81. The method of claim 80, wherein the artificial resin comprises between about 4% w/w and about 50% w/w CBC or CBC derivative.

82. The method of any one of claims 61 or 81, wherein the CBC derivative is of the form:



,

and the artificial resin comprises a CBL derivative of the form:



wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl, and the CBC derivative and CBL derivative have the same R group.

83. The method of claim 82, wherein the second cannabinoid is a modified cannabinoid comprising the same R group as the CBC derivative and CBL derivative.

84. The method of any one of claims 61 to 83, wherein the second cannabinoid is tetrahydrocannabinol (THC or Δ9-THC), Δ8-tetrahydrocannabinol (Δ8-THC), cannabidiol (CBD), cannabinol (CBN), cannabitriol (CBT), cannabigerol (CBG), cannabidivarin (CBDV), tetrahydrocannabinolic acid (THCA), or cannabicitran.

85. The method of claim 84, wherein the second cannabinoid is cannabicitran.

86. The method of any one of claims 61 to 85, wherein the artificial resin comprises at least about 1% w/w the second cannabinoid.

87. The method of any one of claims 61 to 86, wherein the artificial resin further comprises a third cannabinoid.

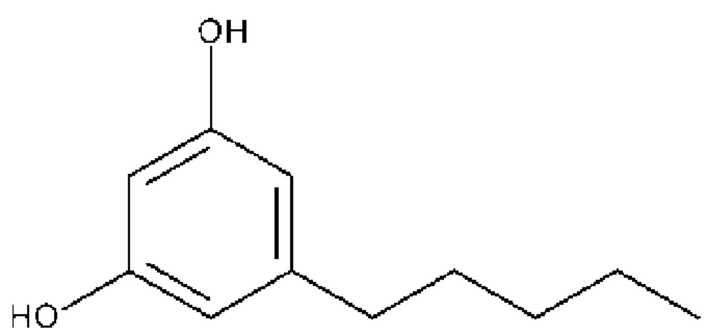
88. The method of claim 87, wherein the third cannabinoid is THC or CBD.

89. A method of producing an artificial resin comprising CBL or a CBL derivative, the method comprising:

heating a reaction mixture comprising citral, a modified resorcinol, and an amine to form a product mixture; and

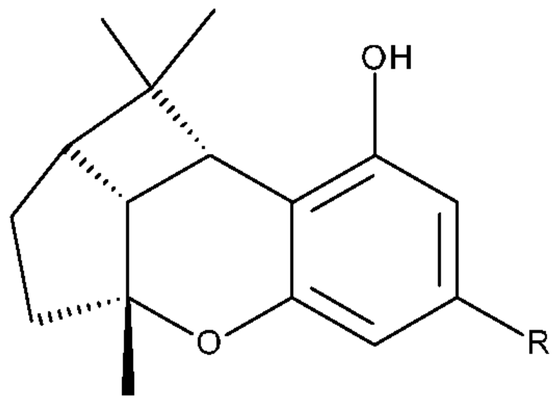
converting the product mixture into the artificial resin by: (i) contacting the product mixture with an acidic heterogeneous material to form the CBL or CBL derivative; (ii) contacting the product mixture with a radical initiator to form the CBL or CBL derivatice; or (iii) irradiating the product mixture with UV light to form the CBL or CBL derivative.

90. The method of claim 89, which is for producing the artificial resin comprising CBL, and the modified resorcinol is of the form:



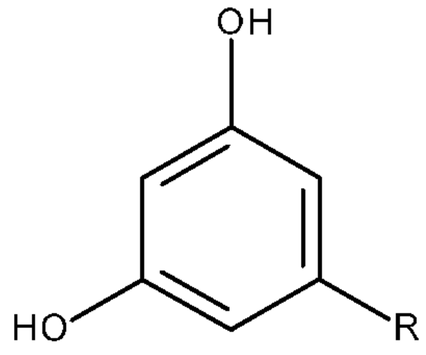
.

91. The method of claim 89, which is for producing the artificial resin comprising a CBL derivative of the form:



,

and the modified resorcinol is of the form:



wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

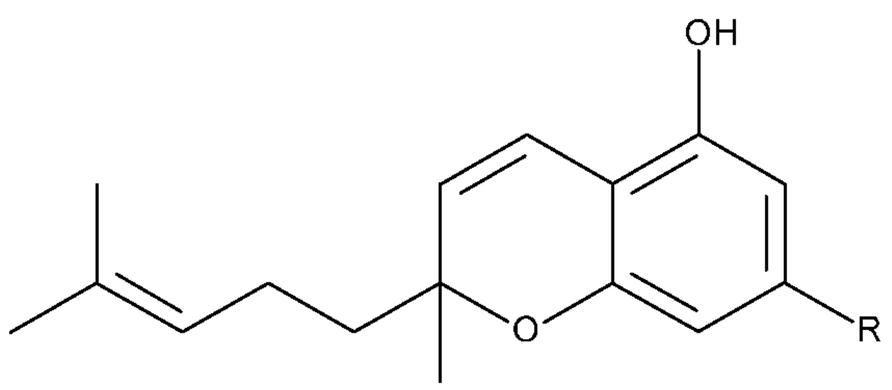
92. An artificial resin comprising at least about 4% cannabicyclol (CBL) or a CBL derivative, a first cannabinoid, and a second cannabinoid.

93. The artificial resin of claim 92, which comprises between about 4% w/w and about 90% w/w CBL or CBL derivative.

94. The artificial resin of claim 92 or 93, wherein the first cannabinoid is CBC or a CBC derivative and the artificial resin comprises at least about 4% w/w CBC or CBC derivative.

95. The artificial resin of claim 94, wherein the artificial resin comprises between about 4% w/w and about 50% w/w CBC or CBC derivative.

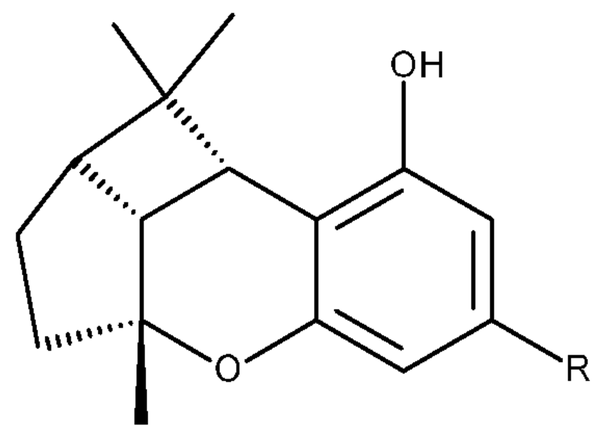
96. The artificial resin of claim 94 or 95, which comprises the CBC derivative and the CBC derivative is of the form:



,

wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl.

97. The artificial resin of claim 96, which comprises the CBL derivative and the CBL derivative is of the form:



,

wherein R is methyl, propyl, heptyl, 1,1-dimethylheptyl, phenylethyl, or phenylvinyl, and the CBC derivative and CBL derivative have the same R group.

98. The artificial resin of claim 97, wherein the second cannabinoid is a modified cannabinoid comprising the same R group as the CBC derivative and CBL derivative.

99. The artificial resin of any one of claims 92 to 98, wherein the second cannabinoid is tetrahydrocannabinol (THC or Δ9-THC), Δ8-tetrahydrocannabinol (Δ8-THC), cannabidiol (CBD), cannabitriol (CBT), cannabinol (CBN), cannabigerol (CBG), cannabidivarin (CBDV), tetrahydrocannabinolic acid (THCA), or cannabicitran.

100. The artificial resin of claim 99, wherein the second cannabinoid is cannabicitran.

101. The artificial resin of any one of claims 92 to 100, wherein the artificial resin comprises at least about 1% w/w of the second cannabinoid.

102. The artificial resin of any one of claims 92 to 101, wherein the artificial resin further comprises a third cannabinoid.

103. The artificial resin of claim 102, wherein the third cannabinoid is THC or CBD.

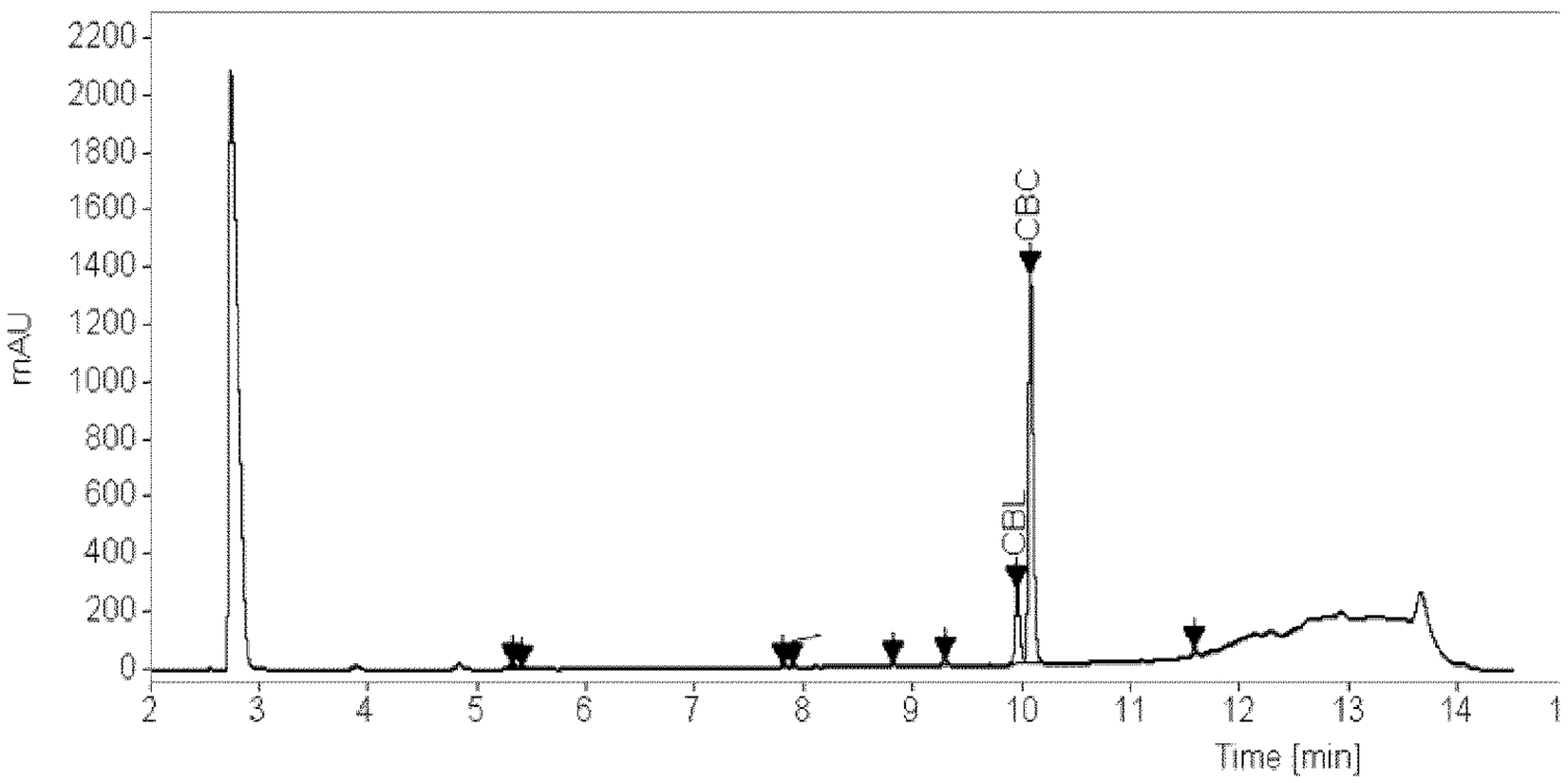

2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
mAU
CBC
CBL
2
3
4
5
6
7
8
9
10
11
12
13
14
1
Time [min]

FIG.1

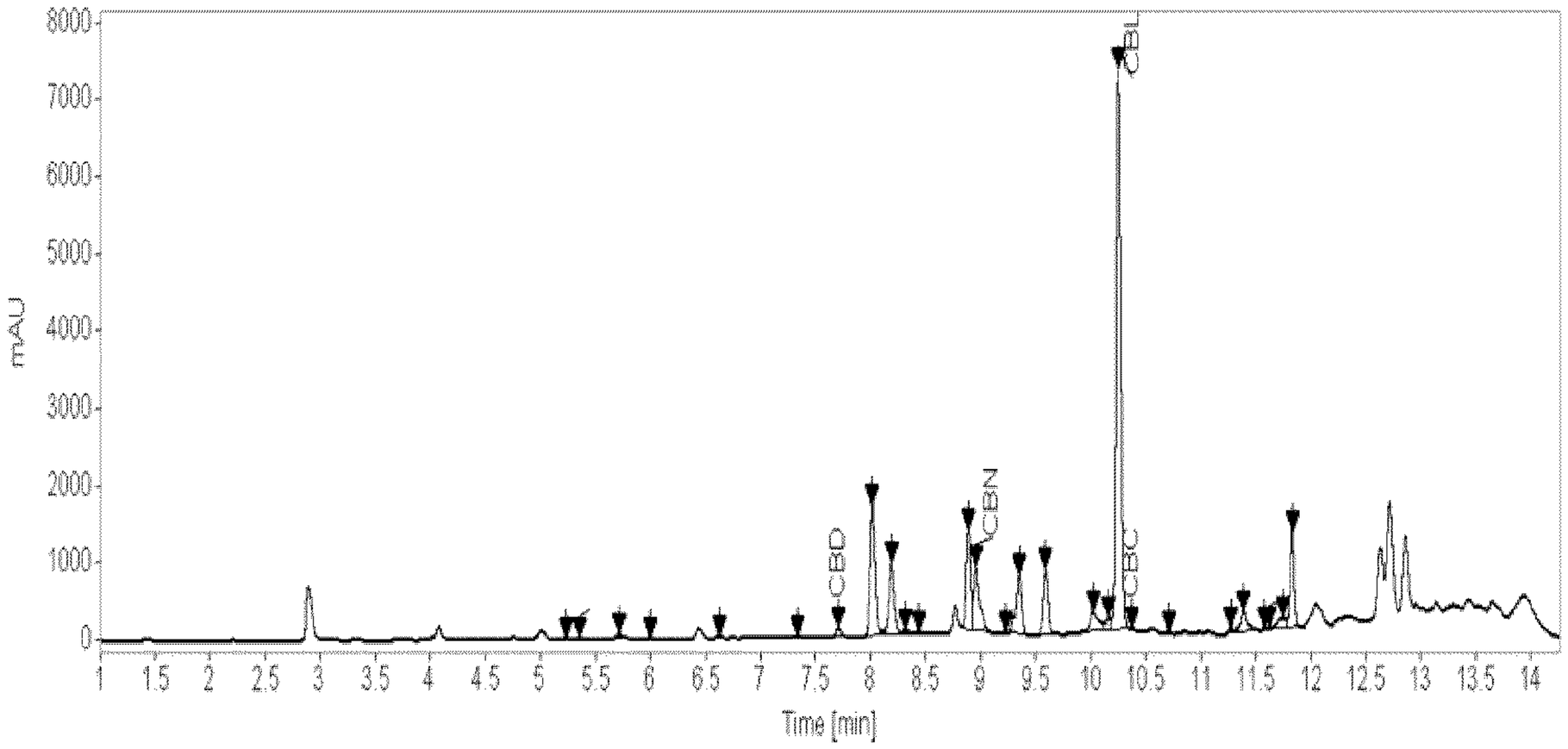

mAU
8000
7000
6000
5000
4000
3000
2000
1000
0
CBD
CBN
CBC
1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8 8.5 9 9.5 10 10.5 11 11.5 12 12.5 13 13.5 14
Time [min]

FIG. 2

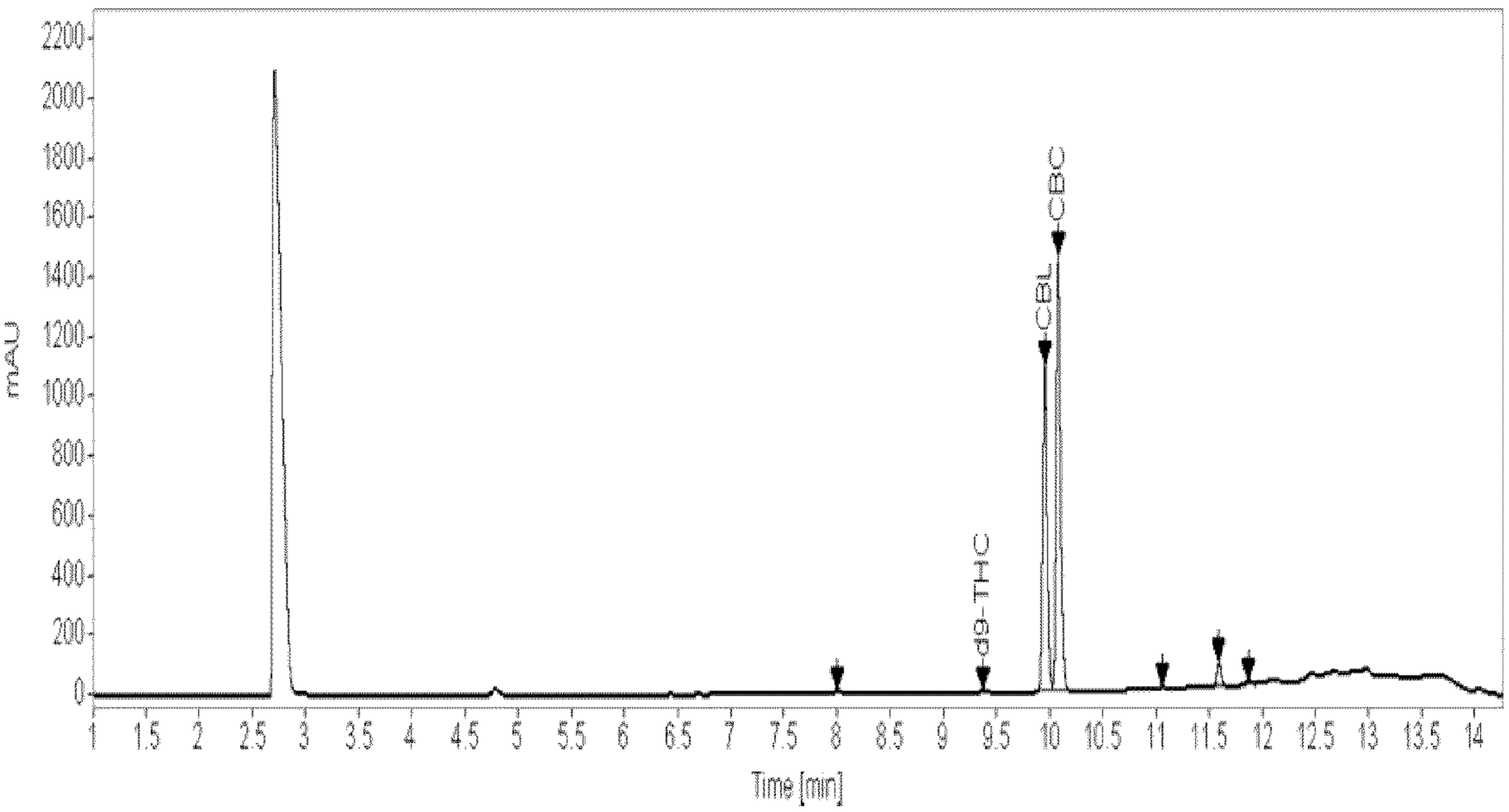

mAU
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
CBL
CBC
Δ9-THC
1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8 8.5 9 9.5 10 10.5 11 11.5 12 12.5 13 13.5 14
Time [min]

FIG.3

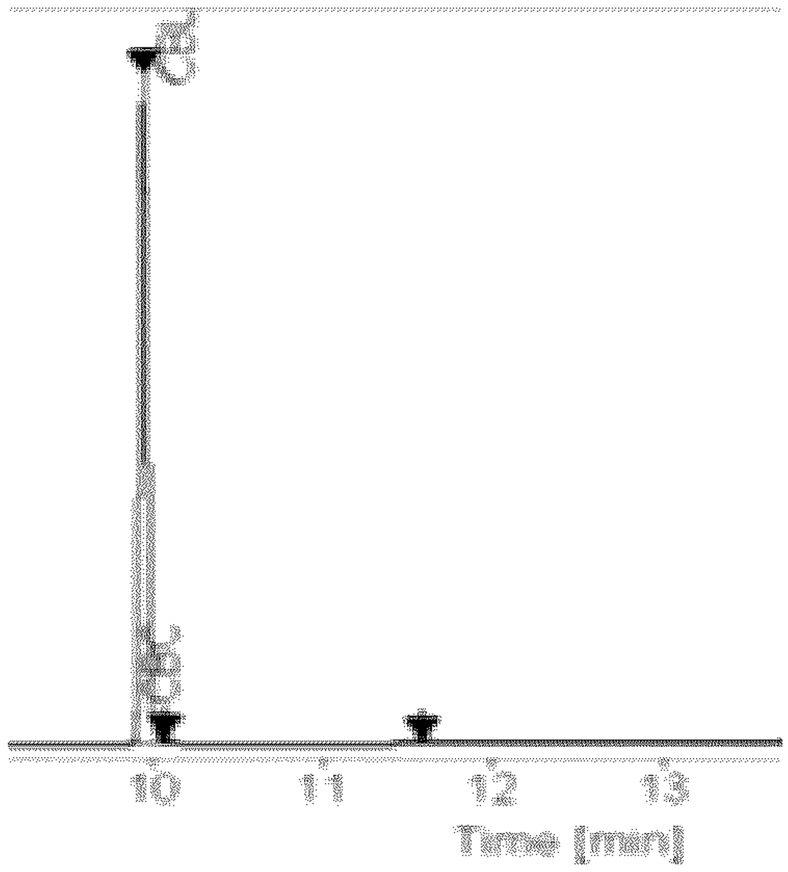


FIG. 4

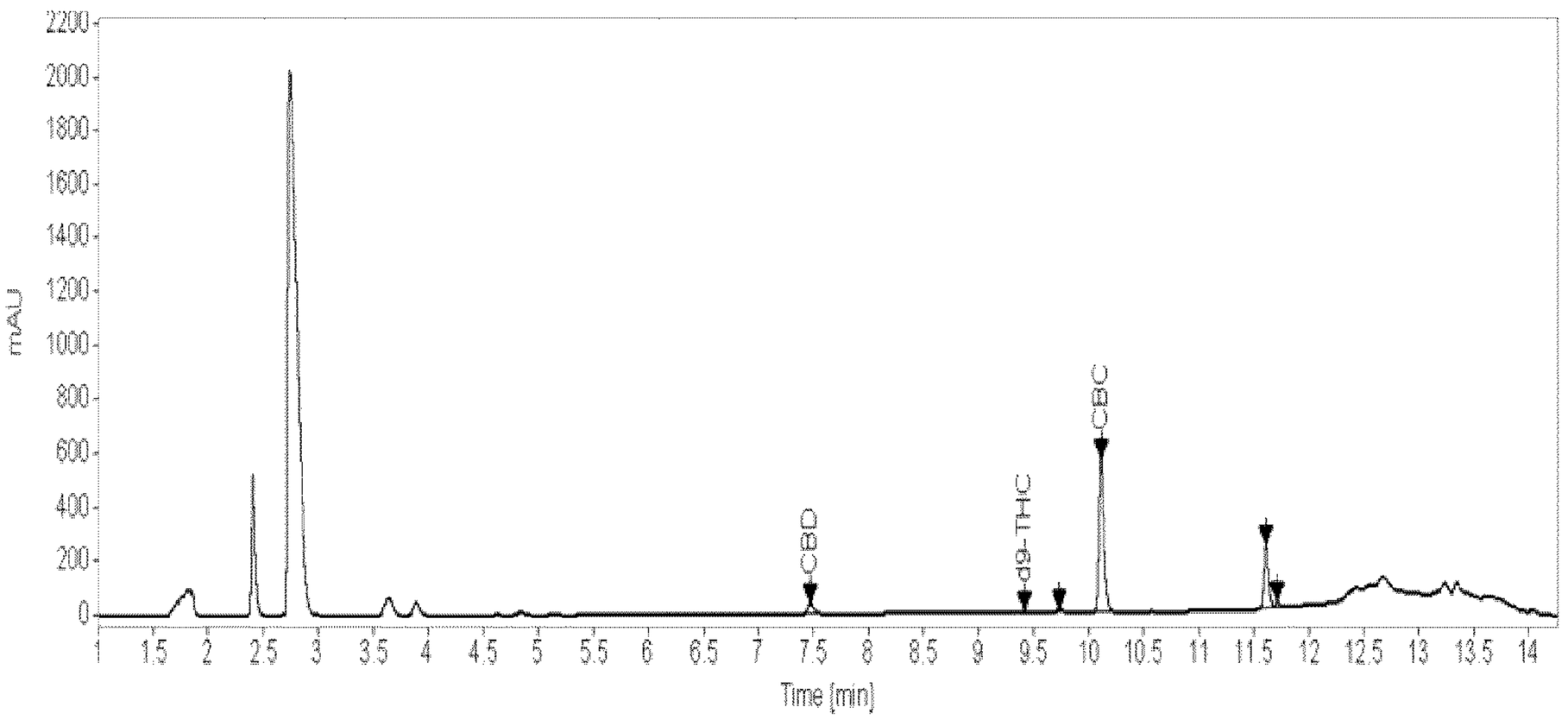


FIG. 5

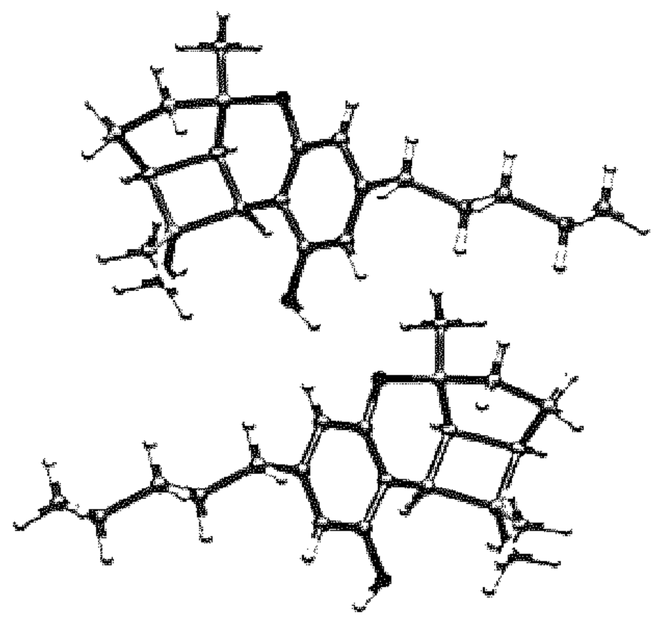


FIG. 6A

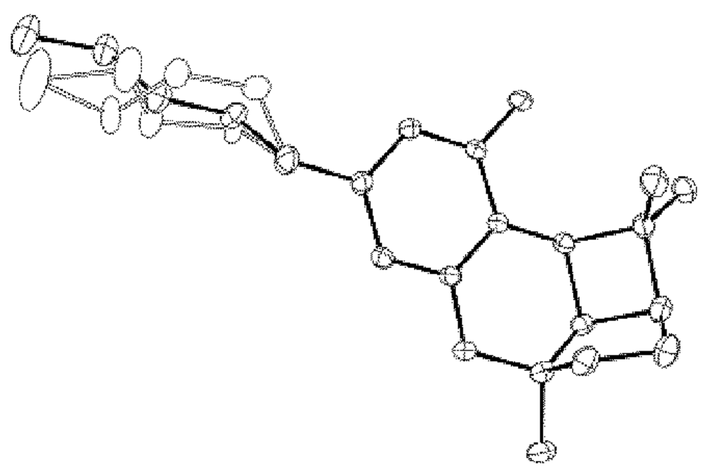


FIG. 6B

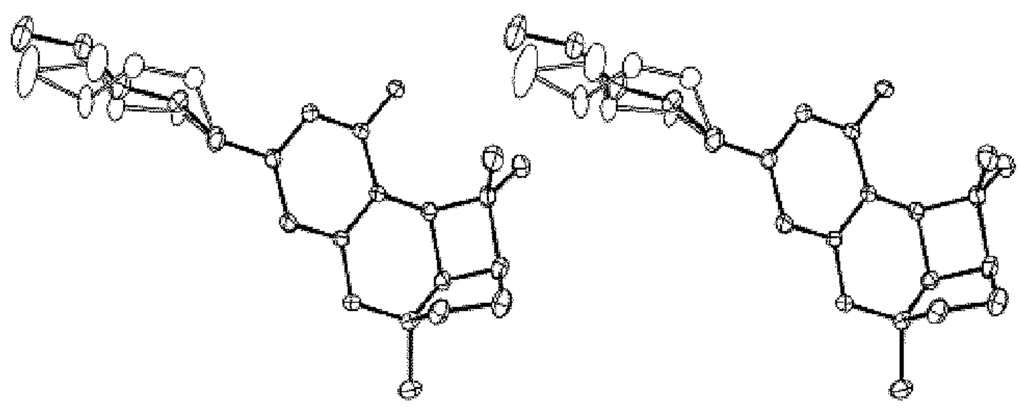


FIG. 6C

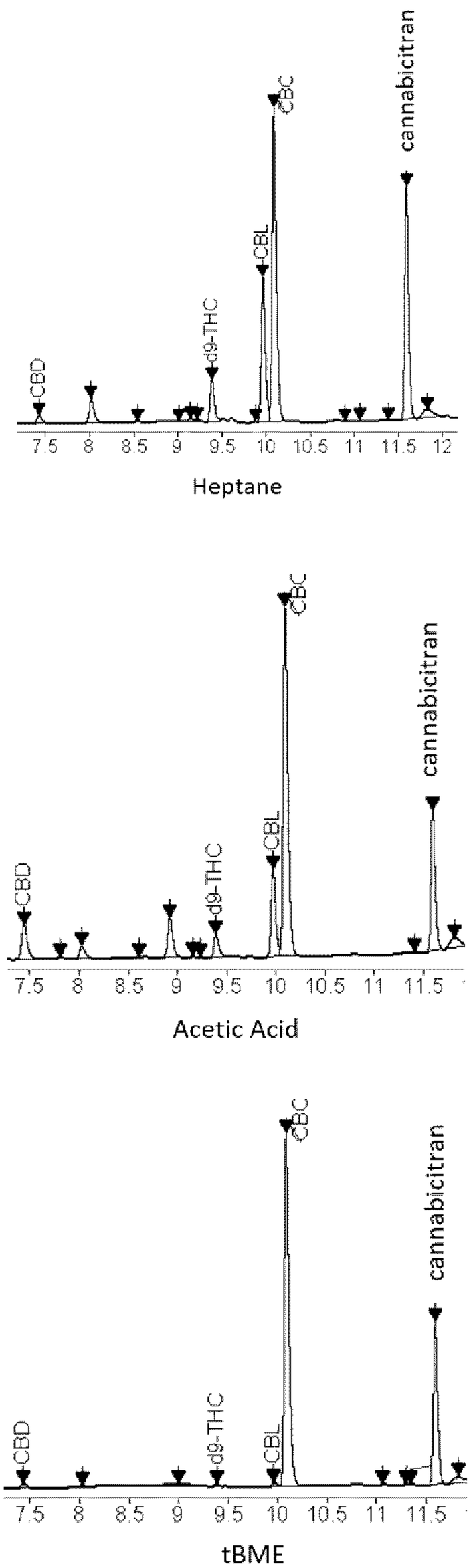

CBC
cannabicitran
CBL
d9-THC
CBD
7.5 8 8.5 9 9.5 10 10.5 11 11.5 12
Heptane
CBC
cannabicitran
CBL
d9-THC
CBD
7.5 8 8.5 9 9.5 10 10.5 11 11.5
Acetic Acid
CBC
cannabicitran
CBL
d9-THC
CBD
7.5 8 8.5 9 9.5 10 10.5 11 11.5
tBME

FIG. 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2020/051801

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **A61K 31/353** (2006.01) , ***A61P 25/00*** (2006.01) , ***C07D 493/18*** (2006.01)

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)
A61K 31/353, A61P 25/00, C07D 493/18

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
STN (CASREACT, Registry, CAPlus), Scopus, Questel-Orbit (FamPat)
Keywords : cannabichromene, cannabicyclol, citral, cannabinoid, cannabis, montmorillonite, iron(III) perchlorate, UV light, extract?, distil?, isolate?, radical initiator

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CROMBIE, L. et al.: "Synthesis of Cannabinoids by Pyridine-catalysed Citral-Olivetol Condensation: Synthesis and Structure of Cannabicyclol, Cannabichromen, (Hashish Extractives), Citrylidene-cannabis, and Related Compounds" *Journal of the Chemical Society C: Organic*, pages 796-804, 1971 *page 804, right-hand column, "Photolysis of cannabichromene"*	15-17, 19-27, 32, 33, 37-39, 42-55, 58-60, 89-91
Y		34-36, 40, 41, 56, 57, 102, 103
X	CROMBIE, L. W. et al.: "Synthesis of Bibenzyl Cannabinoids, Hybrids of Two Biogenetic Series Found in *Cannabis sativa*" *Journal of the Chemical Society, Perkin Transactions 1*, pages 1263-1270, 1978 *page 1270, left-hand column, reaction of bibenzyl 17 with citral and photolysis of chromene 24*	15-23, 29, 30, 32, 33, 37-39, 42-55, 58-60, 89-101
Y		34-36, 40, 41, 56, 57, 102, 103

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

*	Special categories of cited documents:	"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"D"	document cited by the applicant in the international application	"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
"E"	earlier application or patent but published on or after the international filing date	"&"	document member of the same patent family
"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		

Date of the actual completion of the international search 25 February 2021 (25-02-2021)	Date of mailing of the international search report 10 March 2021 (10-03-2021)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 819-953-2476	Authorized officer Geneviève Fortier, PhD (819) 639-8658

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CROMBIE, L. et al.: "Hashish Components. Photochemical Production of Cannabicyclol from Cannabichromeme" *Tetrahedron Letters*, (55), pages 5771-5772, 1968 *page 5771, second paragraph*	15-23, 28, 31-33, 37-39, 42-55
Y		34-36, 40, 41, 56, 57, 102, 103
X	WO2009/125198A2 (De MEIJER, E.) 15 October 2009 (15-10-2009) *Table 6*	42, 43, 47, 48, 51, 53-55
Y		34-36, 40, 41, 56, 57, 61-66, 74-88, 102, 103
X	CAPRIOGLIO, D. et al.: "One-Pot Total Synthesis of Cannabinol via Iodine-Mediated Deconstructive Annulation" *Organic Letters*, Vol. 21, pages 6122-6125, August 2019 *Figure 2*	92, 93, 99-101
X	YEOM, H.-S. et al.: "Total Syntheses of Cannabicyclol, Clusiacyclol A and B, Iso-Eriobrucinol A and B, and Eriobrucinol" *Organic Letters*, Vol. 15(12), pages 3130-3133, 2013 *Schemes 3 and 4*	1-6, 58-60, 89-91
Y		34-36, 40, 41, 56, 57, 61-66, 74-88, 102, 103

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2020/051801

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim 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. ☐ Claim 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:

Groups A-C
See explanation on page 6

1. ☐ As all required additional 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 additional fees, this Authority did not invite payment of 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 claim 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 claim Nos.:

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.

(Continuation from page 2)

Group A - Claims 1-6 (in full), 24-60 (in part), 61-66 (in full) and 74-103 (in part) are directed to a method for converting CBC or a CBC derivative into CBL or a CBL derivative using an acidic heterogeneous material and product mixture thereof; a two-step method to prepare CBL or a CBL derivative starting from citral and a modified resorcinol wherein the second step involves converting CBC or a CBC derivative using an acidic heterogeneous material; and artificial resin comprising at least CBL;

Group B – Claims 7-14 (in full), 24-60 (in part), 67-73 (in full) and 74-103 (in part) are directed to methods for converting CBC or a CBC derivative into CBL or a CBL derivative using a radical initiator and product mixture thereof; a two-step method to prepare CBL or a CBL derivative starting from citral and a modified resorcinol wherein the second step involves converting CBC or a CBC derivative using a radical initiator; and artificial resin comprising at least CBL; and

Group C – Claims 15-23 (in full), 24-60 (in part) and 89-103 (in part) are directed to methods for converting CBC or a CBC derivative into CBL or a CBL derivative by irradiating with UV light and product mixture thereof; a two-step method to prepare CBL or a CBL derivative starting from citral and a modified resorcinol wherein the second step involves converting CBC or a CBC derivative by irradiating with UV light; and artificial resin comprising at least CBL.

The common linking feature between the claims of Groups A, B and C is the conversion of CBC into CBL. This feature however is not novel or inventive and cannot serve as a single general inventive concept unifying the claims. The conversion of CBC to CBL is known at least from **D1**-**D3**, **D5** and **D6**. It therefore results that the claims of Groups A, B and C are not linked by any single general inventive concept. Further, it should be noted that the conversion of CBC to CBL by irradiating with UV light is known from **D1**-**D3**

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2020/051801

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO2009125198A2	15 October 2009 (15-10-2009)	WO2009125198A3	07 January 2010 (07-01-2010)
		EP2282630A2	16 February 2011 (16-02-2011)
		GB0806553D0	14 May 2008 (14-05-2008)
		GB2459125A	14 October 2009 (14-10-2009)
		GB2459125B	02 January 2013 (02-01-2013)
		US2011098348A1	28 April 2011 (28-04-2011)
		US2016360721A1	15 December 2016 (15-12-2016)