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Graphical Abstract

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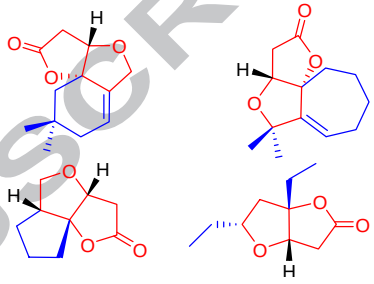

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A general, flexible, ring closing metathesis (RCM) based strategy for accessing the fused furo[3,2-b]furanone moiety present in diverse bioactive natural products

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ABSTRACT

A simple and straightforward methodology of general utility to construct sterically encumbered furo[3,2-*b*]furanone scaffolds present in a diverse range of bioactive natural products is delineated. The methodology emanates from readily available Morita-Baylis-Hillman adducts and employs sequential ring closing metathesis and oxy-Michael addition cascade as the key steps.

Functionally embellished furo[3,2-*b*]furanone moiety has been widely encountered as a distinctive sub-structure among a diverse range of natural products of mixed biosynthetic origin. Representative examples of natural products incorporating the furo[3,2-*b*]furanone segment (in red)) as part of their complex architecture are neovibsanin A & B (**1**, **2**),[1] lactonamycin (**3**),[2] schisandra nortriterpenoids (e,g micrandilactone A **4**),[3] plumericin (**5**),[4] pallavicinin (**6**) & neopallavicinin (**7**) [5] and plakortones (e,g plakortone E **8**).[6] All the natural products **1-8** displayed in Figure 1, exhibit wide ranging biological activities and even **8**, based exclusively on the furo[3,2-*b*]furanone platform, displays an impressive bioactivity profile.[6] For example, vibsane-type[7] natural products **1** & **2** bearing a fused furo[3,2-*b*]furanone core along with many of their recently reported structural siblings[7h,k] have been found to be potent promoters of neurite growth with implications in neurodegenerative disorders.[7] By contrast, **3** exhibits significant levels of antimicrobial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) strains apart from being cytotoxic against various tumoral cell lines.[2a] Similarly, other natural products **4-8** exhibit a range of biological activities ranging from cytotoxic, anti-HIV to cardiac SR-Ca^{2+} ATPase activators *etc.*[3-5,8] Thus, the furo[3,2-*b*]furanone core appears to be a promising and potent pharmacophoric group that imparts considerable therapeutic value to the natural products that embody it. This attribute along with the complex, challenging & diverse natural product

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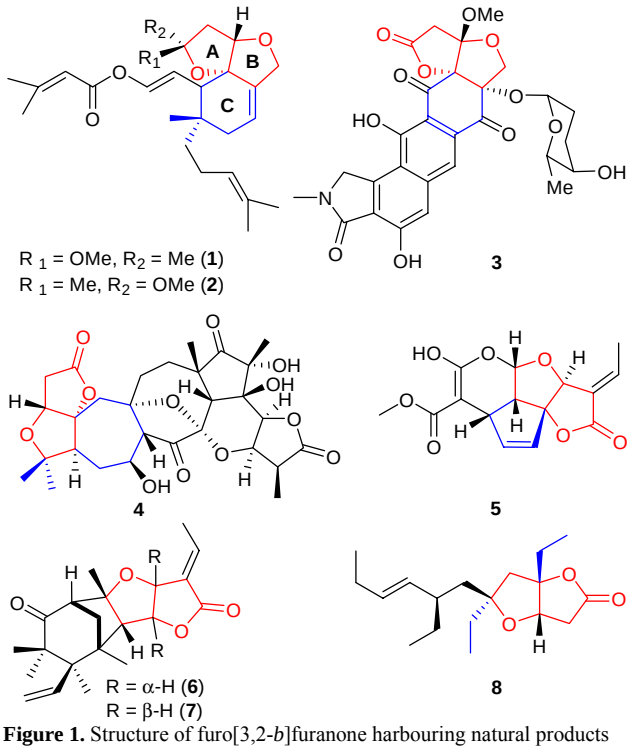
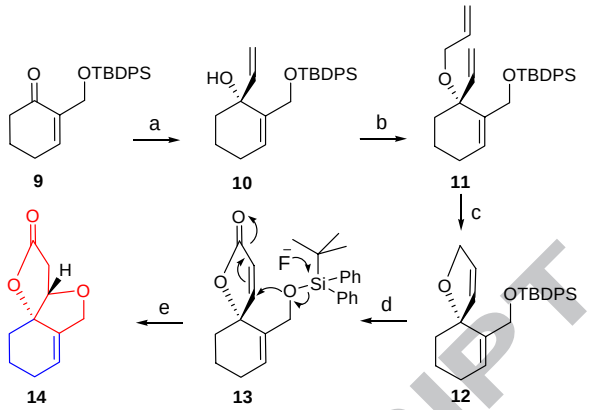


Figure 1. Structure of furo[3,2-*b*]furanone harbouring natural products

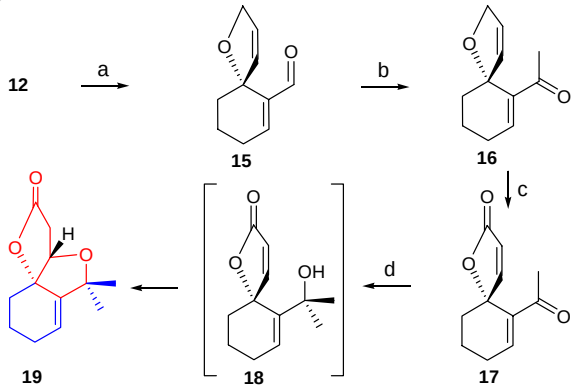
architecture into which furo[3,2-*b*]furanone core is embedded, has generated considerable interest in assembling this moiety.[9] However, synthetic efforts in this arena have largely focused on individual natural product targets[4,6,7f,7g] bearing the furo[3,2-*b*]furanone moiety and generally applicable solutions to construct this system, particularly in sterically constrained environment have been relatively few.[10] In an earlier report, we outlined the synthesis of a range of furo[3,2-*b*]furanone scaffolds from Morita-Baylis-Hillman (MBH) adducts of cyclic enones with alkyne addition/lactonization and intramolecular oxy-Michael addition constituting the key steps.[11] However, keeping in view the need for a simpler and versatile approach to furo[3,2-*b*]furanone scaffold to enable diversity creation and mapping of its therapeutic potential, an alternate approach of general utility was devised. Herein, we disclose this simple and straightforward methodology to construct a range of sterically constrained furo[3,2-*b*]furanones wherein ring closing metathesis (RCM) constitutes a key step.

To test the viability of our methodology, the readily available TBDPS-protected[12] MBH-adduct of cyclohexenone and formaldehyde **9** was subjected to vinylation with vinylmagnesium bromide to furnish a tertiary alcohol **10**, Scheme 1. Allylation of the hydroxyl group in **10** in the presence of potassium hydride furnished the desired precursor **11**[13] and setup the stage for the spiro-annulation of the carbonyl group of **9** through ring closing metathesis. Exposure of **11** to Grubbs-I catalyst smoothly delivered the spiro-annulated compound **12** in excellent yield. The spiro-fused dihydrofuran moiety in **12** now required activation to act as a Michael acceptor. After considerable trials employing various oxidizing agents[14] towards allylic oxidation in **12**, it was found that the classical Jones reagent,[15] readily delivered the required butenolide **13**[13] with TBDPS protection remaining intact. TBAF-mediated desilylation in **13** led to concomitant oxy-Michael addition to afford the tricyclic furo[3,2-*b*]furanone **14** whose stereochemistry, as well as of other oxy-Michael products to follow in the sequel, is based on earlier precedence[7l, 11b,c] and propensity towards preferred formation of *cis*- ring junction involving a spiro carbon centre. Thus, **14** is accessible in a short sequence bearing a segment ubiquitous among many natural products (see, **1-3**), particularly constituting the ABC core of neovibsanins **1** and **2**.



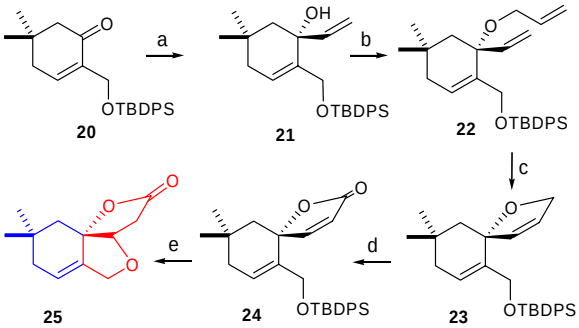
Scheme 1. Reagents and conditions: (a) vinylmagnesium bromide, THF, 0 °C, 1h, 92%; (b) Allyl bromide, KH, THF, 0 °C, 1h, 83%; (c) Grubbs-Ist, CH_2Cl_2, rt, 2h, 93%; (d) Jones reagent, acetone, 0 °C -rt, 1h, 80%; (e) TBAF, THF, rt, 30 minutes, 95%

Bearing in mind the promise and relevance of neovibsanin based scaffold **14** and desirability of creating diversity around it, the generality of the protocol depicted in Scheme 1 had to be further demonstrated. Towards this objective, bicyclic intermediate **12** was subjected to OTBDPS deprotection and the resulting allylic alcohol on PDC oxidation furnished the aldehyde **15**[13] (Scheme 2). MeLi addition to aldehyde **15** led to a diastereomeric mixture of secondary alcohols which upon PDC-oxidation directly furnished the methylketone **16** (Scheme 2). Jones oxidation in **16** afforded the spiro-fused -butenolide **17**. [13] Chemoselective MeLi addition of **17** furnished an intermediate carbinol **18** which underwent concomitant oxa-Michael addition to afford ring-B modified neovibsanin core **19** [13] (Scheme 2).



Scheme 2. Reagents and conditions: (a) (i) TBAF, THF, rt, 30 minutes; (ii) PDC, CH_2Cl_2, rt, 2h, 88% (over two steps); (b) (i) MeLi, THF, 0 °C, 30 min.; (ii) PDC, CH_2Cl_2, rt, 2h, 90% (over two steps); (c) Jones reagent, acetone, 0 °C-rt, 2h, 82%; (d) MeLi, THF, 0 °C, 30 minutes, 92%.

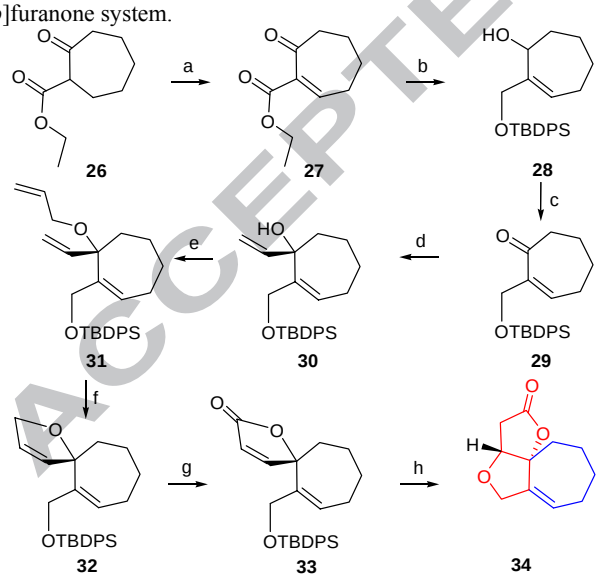
Furthermore, commercially available dimedone was smoothly converted to the TBDPS-protected MBH-adduct **20** through a known procedure[11b, 16] and further elaborated to a ring-A substituted neovibsanin scaffold. Thus, **20** was subjected to vinylation to **21**, allylation of the tertiary hydroxyl group in it yielded **22**[13] (Scheme 3). RCM in **22** to **23**, Jones oxidation to butenolide **24** and fluoride-mediated desilylation resulted in concomitant oxa-Michael addition to furnish ring A modified tricyclic furo[3,2-*b*]furanone derivative **25**.[13]



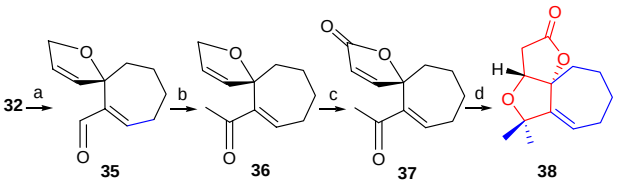
Scheme 3. Reagents and conditions: (a) vinylmagnesium bromide, THF, 0 °C, 30 min., 92%; (b) Allyl bromide, KH, THF, 0 °C-rt, 1h, 82%; (c) Grubbs-Ist, CH_2Cl_2, rt, 2h, 92%; (d) Jones reagent, acetone, 0 °C -rt, 2h, 82%; (e) TBAF, THF, rt, 30 minutes, 93%

With some degree of confidence in our simple strategy, we decided to apply it for the construction of the ABC core of schisandra nortriterpenoids (e,g micrandilactone A, **4** etc.). Readily available compound **26**[17] was subjected to phenylselenylation-H_2O_2 oxidative elimination to furnish cycloheptenone **27**. DIBAL-H reduction of **27** yielded a diol, in which the primary hydroxyl group was chemoselectively protected as TBDPS-derivative **28**[13] and further oxidation led to **29,** formally a protected MBH adduct of cycloheptenone and formaldehyde (Scheme 4). Compound **29** was smoothly elaborated to **34** via **30**-**33**[13] following the vinylation, tertiary-alcohol allylation, ring closing metathesis, Jones oxidation and fluoride mediated deprotection protocol (Scheme 4) outlined above.

In order to gain access to the ABC core of natural product **4**, installation of a *gem*-dimethyl substitution in ring-B was mandated. This was achieved through a diversion, akin to that described in Scheme 2, from the spiro-fused dihydrofuran derivative **32**. Elaboration of **32** to tricyclic **38**, [13] representing ABC core of micrandilactone-A **4** through the intermediacy of **35**-**37**[13] is displayed in Schme 5 and reaffirms the efficacy of our short sequence for the construction of the fused furo[3,2-*b*]furanone system.



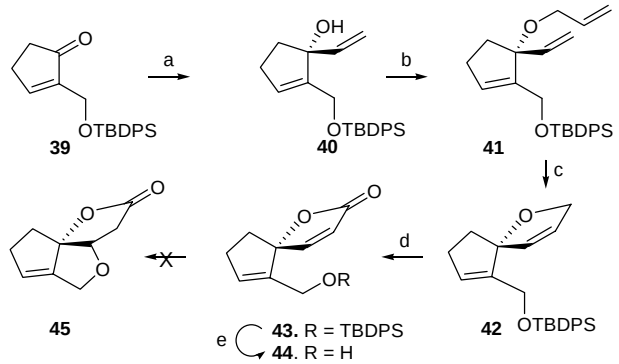
Scheme 4. Reagents and conditions: (a) (i) PhSeBr, LDA, THF, -78 °C; 2h; (ii) H_2O_2, CH_2Cl_2, °C , 30 minutes, 85% (over two steps); (b) (i) DIBAL-H, THF, rt, 2h; (ii) TBDPSCl, DMAP, imidazole, DMF, 6h, 70% (over two steps); (c) PCC, CH_2Cl_2, rt, 2h, 91%; (d) vinylmagnesium bromide, THF, 0 °C, 30 minutes, 90%; (e) Allyl bromide, KH, THF, 0 °C-rt, 1h, 80%; (f) Grubbs-Ist, CH_2Cl_2, rt, 3h, 89%; (g) Jones reagent, acetone, 0 °C -rt, 5h, 80%; (h) TBAF, THF, rt, 30 minutes, 92%.



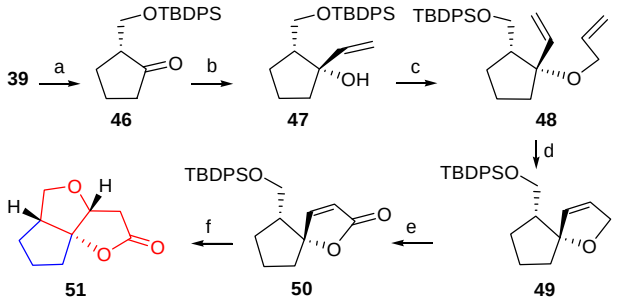
Scheme 5. Reagents and conditions: (a) (i) TBAF, THF, rt, 30 minutes; (ii) PDC, CH_2Cl_2, rt, 2h, 85% (over two steps); (b) (i) MeLi, THF, 0 °C, 30 min.; (ii) PDC, CH_2Cl_2, rt, 2h, 80% (over two steps); (c) Jones reagent, acetone, 0 °C-rt, 5h, 87%; (d) MeLi, THF, 0 °C, 30 minutes, 93%.

To further probe the generality of our strategy, it was of interest to apply it for the construction of the tricyclic furo[3,2-*b*]furanone core present in the natural product plumericin **5**. This endeavour emanated from the -OTBDPS protected MBH-adduct of cyclopentenone and formaldehyde **39**.[11a] Vinylation, O-allylation, ring closing metathesis and Jones oxidation afforded compound **43** smoothly via **40**-**42**, Scheme 6. However, when **43** was subjected to TBAF-mediated desilylation, it only led to the deprotected **44**.[13] The hydroxymethyl arm of **44** could not be coaxed into oxa-Michael reaction to deliver **45** even when hydroxyl activation was provided by exposure to bases like DBU, KO^{t}Bu etc. It appeared that the hydroxylmethyl arm on the planar, inflexible cyclopentene double bond of **43** could not manoeuvre the requisite geometry for the intramolecular oxa-Michael addition to eventuate in a highly strained tricyclic furo[3,2-*b*]furanone **45**. To substantiate this surmise, it was decided to execute our strategy on the reduced derivative **46**, obtained by the hydrogenation of **39** (Scheme 7). Vinylation of the carbonyl group in **46** was stereoselective and furnished **47**. O-allylation to **48** and RCM with Grubbs I catalyst led to **49** in excellent yield. Jones oxidation on **49** resulted in the -butenolide **50** which on desilylation and subsequent treatment with DBU underwent oxa-Michael addition to deliver **51**,[13] a structural segment present in natural product **5** (Scheme 7).

Finally, the methodology was tested to target the furo[3,2-*b*]furanone scaffold present in plakortones represented by natural product **8**. In this endeavor, commercially available 3,5-heptandione **52** was subjected to selective vinyl addition to afford **53.** The tertiary hydroxyl group in **53** could be esterified with acrolylchloride to **54**[13] and further ring closing metathesis using Gubbs-II catalyst furnished the -butenolide **55**. Chemoselective

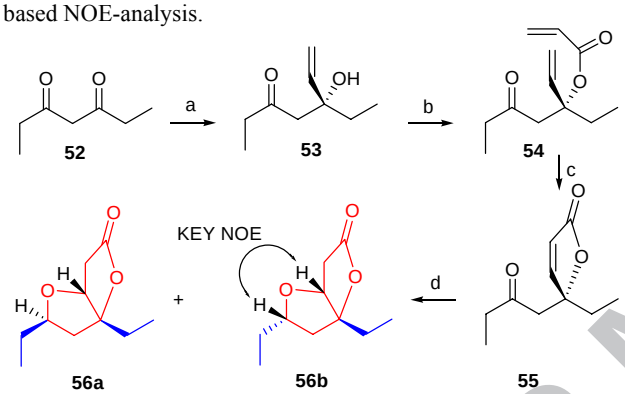


Scheme 6. Reagents and conditions: (a) vinylmagnesium bromide, THF, 0 °C, 30 min., 88%; (b) Allyl bromide, KH, THF, 0 °C, 1h, 89%; (c) Grubbs-Ist, CH_2Cl_2, rt, 3h, 93%; (d) Jones reagent, acetone, 0 °C -rt, 2h, 83%; (e) TBAF, THF, rt, 1h, 92% .



Scheme 7. Reagents and conditions: (a) H_2, Pd/C, Hexane, rt, 2h, 92%; (b) vinylmagnesium bromide, THF, 0 °C, 1h, 90%; (c) Allyl bromide, KH, THF, 0 °C, 1h, 89%; (d) Grubbs-Ist, CH_2Cl_2, rt, 3h, 93%; (e) Jones reagent, acetone, 0 °C -rt, 5h, 90%; (f) (i) TBAF, THF, rt, 30 minutes; (ii) DBU, THF, reflux; 6h, 70% (over two steps).

reduction of the carbonyl group in **55**[13] with $NaBH_4$ was only moderately stereoselective and through concomitant oxa-Michael addition delivered plakortone-type frameworks **56a** and **56b**[13] as a diastereomeric mixture (3:7 respectively), Scheme 8. Stereostructures of **56a** and **56b** were deduced from the 2D-NMR based NOE-analysis.



Scheme 8. Reagents and conditions: (a) vinylmagnesium bromide, THF, 0 °C, 1h, 87%; (b) acrolylchloride, pyridine, THF, 0 °C, 1h, 84%; (c) Grubbs-II, Toluene, 80 °C, 6h, 92%; (d) $NaBH_4$, $CeCl_3.7H_2O$, MeOH, 1h, 80.

In summary, a short, simple and flexible methodology, based on readily available building blocks has been developed to target substituted and sterically congested furo[3,2-*b*]furanone scaffolds present in a diverse range of bioactive natural products.

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13. All compounds reported here are racemic and were fully characterized on the basis of IR, ^{1}H NMR, ^{13}C-NMR and HRMS spectral data. Spectral data of selected compounds: *compound* **11** IR (neat) 3063, 3013, 2931, 2860, 1462, 1419, 1112, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (4H, m), 7.44-7.35 (6H, m), 6.34 (1H, bs), 5.76 (2H, m), 5.13-4.97 (4H, m), 4.16 (2H, m), 3.85 (1H, dd, *J* = 10.0 & 5.0 Hz), 3.63 (1H, dd, *J* = 10 & 5.0 Hz), 2.12 (2H, m), 1.92 (1H, m), 1.73-1.59 (3H, m), 1.08 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 136.9, 135.5 (4C), 133.8, 133.7, 129.5 (2C), 127.6 (4C), 127.5, 126.1, 115.3, 114.2, 79.0, 63.2, 62.2, 31.5, 27.4 (3C), 25.0, 19.5, 19.3; HRMS (ES): 455.2381 [M+Na]$^+$; *compound* **13** IR (neat) 2931, 2860, 1758, 1101, 695 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (1H, d, *J* = 7.0 Hz), 7.61 (4H, m), 7.43-7.35 (6H, m), 6.12 (1H, m), 5.97 (1H, d, *J* = 7.0 Hz), 3.92 (2H, m), 2.18 (2H, m), 1.84 (4H, m), 1.03 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 160.4, 135.5 (4C), 134.8, 133.4, 132.5, 131.5, 129.7 (2C), 127.7 (4C), 120.0, 86.7, 62.8, 34.2, 26.7 (3C), 26.6, 24.9, 19.1; HRMS: 441.1862 [M+Na]$^+$; *compound* **15** IR (neat) 2922, 2853, 1738, 1643, 1444, 1949 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.44, (1H, s), 6.93 (1H, m), 6.02 (m, 1H), 5.71 (m, 1H), 7.87-4.70 (m, 2H), 2.50-2.20 (m, 2H), 1.87-170 (m, 4), ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.2, 151.3, 141.3, 130.4, 127.0, 86.2, 75.4, 36.3, 26.5, 19.2; HRMS: 197.0721 [M+Na]$^+$; *compound* **17** IR (neat) 3439, 3088, 2926, 2854, 1761, 1745, 1674, 1631, 1439 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (1H, d, *J* = 8.0 Hz), 7.19 (1H, m), 6.08 (1H, d, *J* = 8.0 Hz), 2.61-2.33 (2H, m), 2.25 (3H, s), 1.91-1.81 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 173.0, 160.1, 147.2, 136.1, 119.6, 84.0, 35.4, 26.8, 26.2, 18.2; HRMS: 215.0684 [M+Na]$^+$; *compound* **19** IR (neat) 2974, 2932, 1774, 1687, 1439, 1406, 1379 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (1H, m), 4.25 (1H, m), 2.75 (2H, bs), 1.87-1.79 (4H, m), 1.62-1.29 (2H, m), 1.33 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 143.1, 124.8, 89.9, 83.2, 80.0, 37.5, 29.9, 29.8, 28.5, 24.3, 17.0; HRMS: 231.0997 [M+Na]$^+$; *compound* **22** IR (neat) 3072, 3050, 2957, 2932, 2895, 2859, 1962, 1892, 1726, 1678 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (4H, m), 7.44 (6H, m), 6.23 (1H, bs), 5.78 (2H, m), 5.20-4.98 (4H, m), 4.28 (2H, m), 3.81-3.62 (2H, m), 1.97 (2H, bs), 1.85 (1H, d, *J* = 14.0 Hz), 1.55 1H, d, *J* = 14.0 Hz), 1.10 (9H, s), 1.05 (3H, s), 0.95 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 137.0, 135.7 (2C), 135.5, 133.9, 129.5 (2C), 127.6 (6C), 121.9, 114.9, 113.9, 113.8, 77.8, 62.7, 62.3, 43.8, 39.3, 30.5, 30.4, 26.9 (3C), 26.8, 19.3; HRMS: 483.2696 [M+Na]$^+$; *compound* **25** IR (neat) 2953, 2870, 1778, 1137, 914 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (1H, m), 4.56-4.51 (1H, m), 4.35 (1H, d, *J* = 11.3 Hz), 4.23 (1H, m), 2.74 (2H, bs), 2.04 (2H, m), 1.79 (1H, d, *J* = 14.1 Hz), 1.58 (1H, d, *J* = 14.1 Hz), 1.12 (3H, s), 1.06 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 133.5, 125.5, 88.7, 83.2, 70.1, 42.1, 39.2, 36.9, 31.8, 29.3, 27.1; HRMS: 231.0997 [M+Na]$^+$; *compound* **28** IR (neat) 3320, 3034,1624 1613 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (4H, m), 7.44 (6H, m), 5.61 (1H, m), 4.58 (1H, m), 4.29 (2H, bs), 3.55 (1H, s), 2.19-1.66 (8H, m), 1.09 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 135.7, 135.6 (2C), 134.8, 133.1, 133.0, 129.8, 129.5, 128.4, 127.8, 127.7 (3C), 73.1, 69.1, 35.4, 27.2, 26.8 (3C), 26.4, 25.3,

19.1; HRMS: 381.2172 $[M+H]^+$; c*ompound* **31** IR (neat) 3072, 1892, 1678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (4H, m), 7.41 (6H, m), 6.42 (1H, m), 5.79 (2H, m), 5.14-4.97 (4H, m), 4.15 (2H, m), 3.87-3.65 (2H, m), 2.34-2.19 (2H, m), 1.70-1.56 (6H, m), 1.09 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 140.1, 135.5 (4C), 135.4, 134.3, 133.9, 133.8, 129.4, 128.9, 127.5 (4C), 115.3, 114.2, 82.9, 64.3, 63.4, 35.3, 26.9 (3C), 26.0, 25.8, 22.8, 19.3; HRMS: 447.2641$[M+H]^+$; c*ompound* **33** IR (neat) 3483, 3072, 2932, 2857, 1767, 1461, 1427, 1391, 1261 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (4H, m), 7.60 (1H, d, *J* = 7.0 Hz), 7.45-7.36 (6H, m), 6.11 (1H, m), 5.94 (1H, d, *J* = 7.0 Hz), 4.01 (2H, m), 2.43-1.90 (4H, m), 1.81-1.56 (4H, m), 1.04 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 158.1, 137.7, 135.5 (3C), 133.3, 131.1, 129.7, 129.7, 127.6 (6C), 119.5, 92.3, 64.5, 37.9, 26.8 (3C), 26.8, 26.1, 25.5, 19.2; HRMS: 455.2019$[M+Na]^+$; c*ompound* **34** IR (neat) 2924, 1773, 1177, 1053 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.93, (1H, m), 4.55 (1H, d, *J* = 12.0 Hz), 4.34(1H, d, *J* = 12.0 Hz), 4.29 (1H, bs), 2.70 (2H, m), 2.44-2.20 (2H, m), 2.05-1.82 (4H, m), 1.80-1.42 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 139.8, 128.0, 93.2, 84.1, 72.1, 35.8, 33.7, 27.6, 27.0, 24.6; HRMS: 217.0841 $[M+Na]^+$; c*ompound* **37** IR (neat) 1739, 1715, 1540, 1345 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (1H, d, *J* = 7 Hz), 7.18 (1H, m), 6.07 (1H, d, *J* = 7 Hz), 2.54-2.30 (2H, m), 2.25 (3H, s), 1.96-1.76 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 173.0, 160.1, 147.1, 136.0, 119.6, 83.9, 35.4, 29.3, 26.8, 26.2, 18.2; HRMS: 206.0913 $[M]^+$; c*ompound* **38** IR (neat) 2927, 1774, 1540, 1178 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (1H, m), 4.28 (1H, d, *J* = 4.0 Hz), 2.75 (1H, dd, *J* = 18.0 Hz, 5.0 Hz), 2.65 (1H, d, *J* = 18.0 Hz), 2.44-2,33 (1H, m), 2.25-2.16 (1H, m), 2.00-182 (4H, m), 1.73-1.66 (1H, m), 1.57 (3H, s), 1.47-1.42 (1H, m), 1.36 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 148.4, 128.1, 84.3, 79.9, 77.1, 35.8, 34.6, 29.0, 28.4, 27.4, 27.1, 24.7; HRMS: 245.115 $[M+Na]^+$; c*ompound* **44** IR (neat) 3217, 3035, 1737, 1463, 1430 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (1H, d, *J* = 4.0 Hz), 6.19 (1H, s), 6.09 (1H, d, *J* = 4.0 Hz), 4.11 (1H, d, *J* = 16.0 Hz), 3.99 (1H, d, *J* =16.0 Hz), 2.65 (1H, m), 2.51 (1H, m), 2.33 (2H, m), 1.7 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 157.9, 140.4, 135.8, 120.5, 99.0, 57.9, 34.4, 30.0; HRMS: 166.1735 $[M]^+$; c*ompound* **51** IR (neat) 3856, 3752, 3397, 2927, 2855, 1785, 1598, 1458, 1261 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.80 (1H, m), 3.70 (1H, m), 3.58 (1H, m), 2.56 (1H, m), 2.33-2.21 (2H, m), 1.81 (1H, m), 1.56 (3H, m), 1.45-1.29 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 95.1, 91.6, 78.9, 53.2, 37.8, 36.1, 29.9, 25.4; HRMS: 191.0684 $[M+Na]^+$; c*ompound* **54** IR (neat) 3045, 1716, 1625, 1421 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.40 (1H, d, *J* = 17.2 Hz), 6.12 (1H, dd, *J* = 10.4, 17.6 Hz), 5.94 (1H, dd, J = 11.2, 17.6 Hz), 5.82 (1H, d, *J* = 16.4Hz), 5.22 (2H, m), 3.26 (1H, d, *J* = 15.2 Hz), 3.13 (1H, d, J =15.6Hz), 2.40 (2H, q, *J* = 7.2 Hz), 2.23 (1H, m), 1.90 (1H, m), 1.01 (3H, t, *J* = 7.6 Hz), 0.83 (1H, t, *J* = 7.6 Hz); HRMS: 233.1154 $[M+Na]^+$; c*ompound* **55** IR (neat) 3033, 1734, 1617, 1511 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (1H, d, *J* = 6.0 Hz), 6.05 (1H, d, *J* = 5.6 Hz), 3.10 (1H, d, *J* = 16.4 Hz), 2.73 (1H, d, *J* = 16.4 Hz), 2.45 (2H, q, *J* = 7.2 Hz), 1.89 (2H, m), 1.03 (3H, t, *J* =7.2Hz), 0.83 (3H, t, J = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.4, 172.1, 159.1, 121.0, 89.1, 49.1, 37.2, 29.2, 7.6, 7.4; HRMS: 205.0841 $[M+Na]^+$; c*ompound* **56b** IR (neat) 2927, 2855, 1785, 1598, 1458 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.22 (1H, m), 3.88 (1H, m), 2.73 (2H, m), 2.22 (2H, m), 1.5-1.1 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 96.7, 81.1, 80.9, 42.4, 36.7, 29.6, 28.1, 10.1, 8.3; HRMS: 185.1098$[M+H]^+$

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