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Synthesis of a pentacyclic lactone related to quinovaic acid and emmolactone using an anionic polycyclization strategy

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This article is dedicated to Professor Yoshito Kishi, the 2001 Recipient of the Tetrahedron Prize

Abstract—In an effort to discover a versatile and convergent synthesis of pentacylic triterpenes, we have synthesized a tetracyclic enone via a highly stereocontrolled cycloaddition between a Nazarov precursor and a cyclohexenone followed by an aldol condensation. Introduction of a C14 nitrile was made by hydrocyanation on a protected derivative of this tetracyclic enone. Reduction and subsequent hydrolysis of the latter intermediate concluded this expedient synthesis of a pentacyclic lactone.

1. Introduction

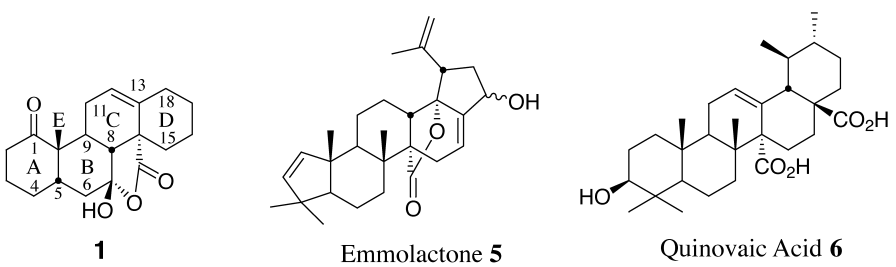
Pentacyclic triterpenes are abundant in nature and are usually bioactive compounds.[1] There is a need to conceive versatile and convergent new approaches to generate highly functionalized polycyclic analogues, or to simply accomplish the total synthesis of the large class of higher terpenoids. Herein we report the synthesis of pentacyclic lactone **1**, which bears resemblance to emmolactone **5**[2] and quinovaic acid **6**[3] (Fig. 1), using an anionic polycyclization mode of construction. In this strategy, a ring A is first coupled to a ring D to yield an ABD tricycle, which is then further transformed into an ABCD tetracycle in a stereocontrolled and concise manner.[4]

2. Results and discussion

The Nazarov intermediate **3b**, which will serve as a D ring, was made from commercially available 1,3-cyclohexadione. Monoalkylation using Hamanaka method[5] gave ester **7** (Scheme 1). Ketal protection was carried out under the usual acidic conditions using ethylene glycol. Since the ethyl ester had been partly transesterified, it was found necessary to treat the crude product with sodium methoxide to obtain methyl ester **8** in a good yield.

Reduction of ester **8** with Dibal-H in toluene at −78°C yielded aldehyde **9**. Homologation using a Wittig reaction between phosphorane **10**[6] and aldehyde **9** afforded the protected ethoxy enol ester **3a**. Deprotection of this enol ether to furnish the desired Nazarov reagent **3b** was achieved by stirring an acidic two phase solution (HCl 1 M, CH_2Cl_2).

Cycloaddition between Nazarov substrate **3b** and cyclohexenone **4**[7] gave the di-β-ketoester **11a** which exists as a mixture with its enol form. Selective palladium mediated decarboxylation[8] of **11a** yielded the *cis*-decalin **11b** as a single diastereomer.[4] Importantly, the stereochemistries at C10 and C9 (steroid numbering) correspond to the configuration found in most pentacyclic triterpenes. Even



1 Emmolactone **5** Quinovaic Acid **6**

Figure 1. Pentacyclic triterpenes.

Keywords: terpenoids; cycloadditions; aldol reactions.

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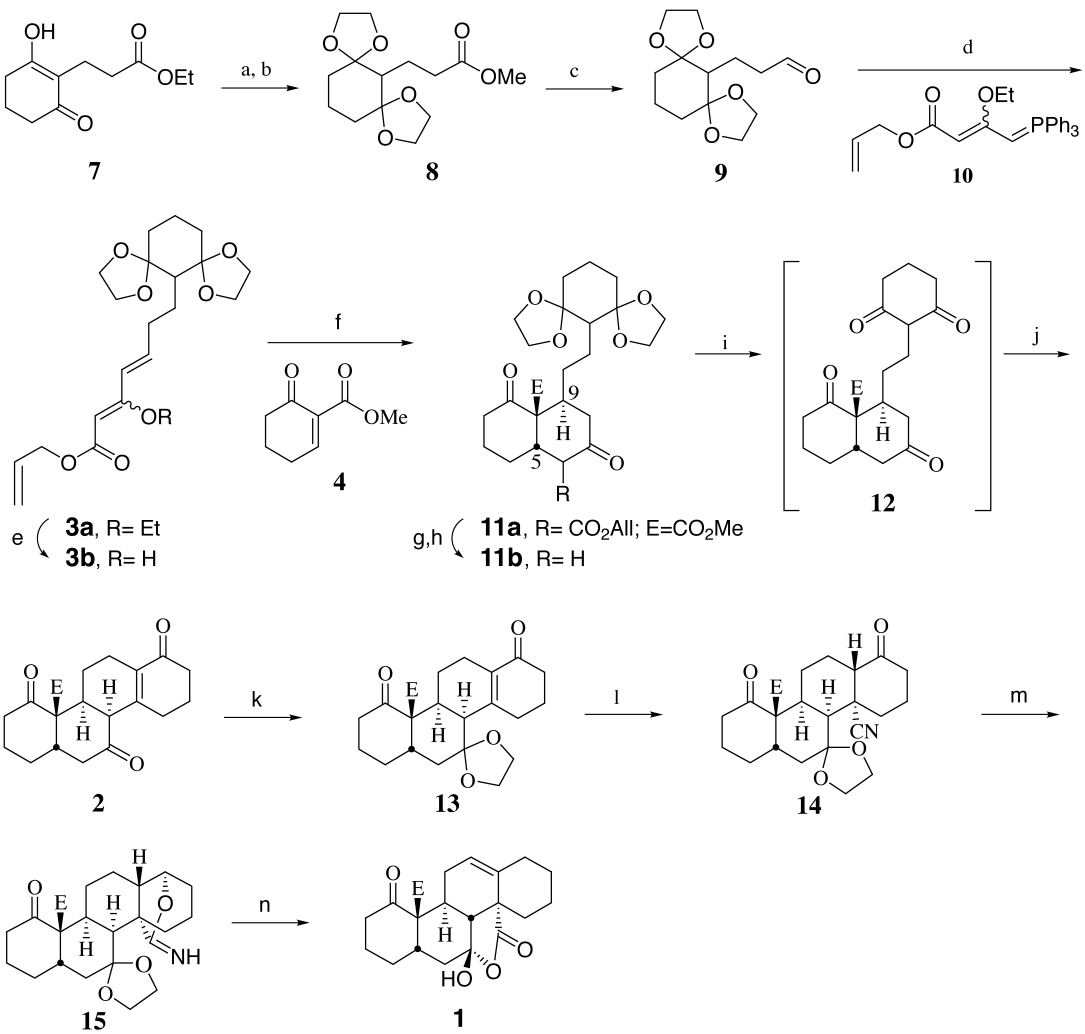

Scheme 1. (a) $HOCH_2CH_2OH$, PTSA, benzene, Dean–Stark 16 h; (b) MeONa (25% in MeOH), rt 16 h (81%); (c) Dibal-H (1.5 M in toluene), toluene, −78°C (50%); (d) **10**, $CHCl_3$, reflux 8 h (88%); (e) HCl (1 M), CH_2Cl_2 (99%); (f) **4**, Cs_2CO_3, CH_2Cl_2 (76%); (g) $Pd(PPh_3)_4$, morpholine, THF; (h) toluene, reflux (100%); (i) CHl (1 M), acetone, reflux; (j) PTSA, toluene, Dean–Stark (80%); (k) $HOCH_2CH_2OH$, PTSA, benzene, Dean–Stark (95%); (l) Et_2AlCN (1 M in toluene), isopropanol, CH_2Cl_2, rt, (60% (85% corrected)); (m) L-selectride (1 M in CH_2Cl_2), CH_2Cl_2, 78°C to rt (86%) (n) HCl (6 M), reflux 3 h (50%).

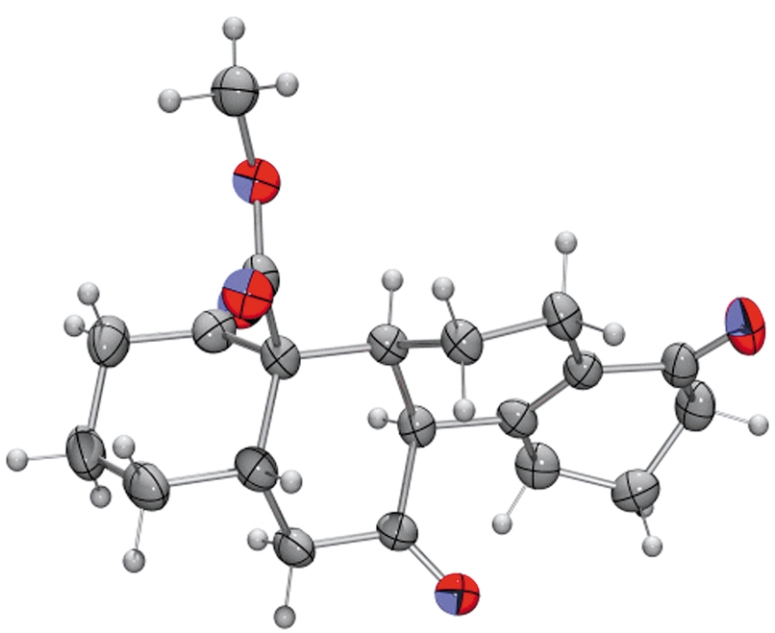

Figure 2. Single crystal X-ray structure of tetracyclic enone **2**.

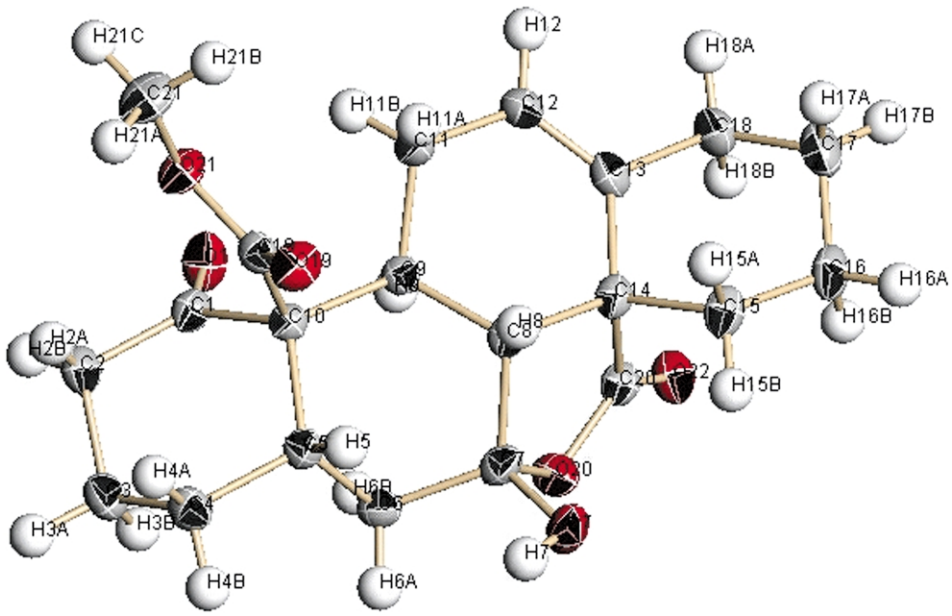

Figure 3. Single crystal X-ray structure of pentacyclic lactone **1**.

though epimerization at C5, which would complete the AB ring stereochemistry, can in theory be realized using the C7 ketone functionality, this step was postponed to a later stage.

Ketal hydrolysis of **11b** was realized under mild acidic conditions and the crude product was treated with *p*-toluenesulfonic acid in refluxing toluene. Aldol condensation and dehydration occurred to produce the tetracyclic enone **2** as a single racemic diastereoisomer in 80% yield. The structure of compound **2** was determined by single crystal X-ray crystallography (Fig. 2).[†]

Interestingly, compound **2** underwent a selective monoketalization at C7 to yield enone **13** in high yield (95%).[9] Hydrocyanation of **13** yielded the nitrile addition product **14** along with some starting material which could be separated by chromatography. Examination of a molecular model of enone **13** clearly suggested that the nitrile addition should take place on the α-face. The *J*-resolved experiment of compound **14** confirmed the CD *trans* ring junction (C13-H: J=1.5, 8.0 Hz). Compound **14** has thus the terpenoid configuration at C9, C10, C13 and C14. Potential epimerization at C5 and β-alkylation at C8 would lead to an ABCD *trans-anti-trans-anti-trans* configuration identical to that in most pentacyclic triterpenes.

β-face reduction of compound **14** with L-selectride led to the iminolactone **15**. The latter was then converted to lactone **1** in refluxing HCl (6 M) aqueous solution for 3 h. Lactone **1** was obtained from ketal and iminolactone hydrolysis, epimerization at C8, elimination at C18, lactonization on C7 ketone and double bound migration of iminolactone **15**. Basic hydrolysis was not successful probably due to a retro-Claisen of the β-keto ester in the A ring. The structure of compound **1** was also determined by single crystal X-ray diffraction crystallography (Fig. 3). The overall yield of **1** is 7.4% starting from **7**.

[†] Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 181212 and CCDC 180106. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

3. Conclusion

We have elaborated in this model study, a very short and efficient stereocontrolled route for the synthesis of tetracycles related to terpenoids. Current efforts in our laboratories are now directed at the synthesis of chiral A ring intermediates[10] which contain the *gem*-dimethyl group at C4 in order to effect the cycloaddition step with complete stereocontrol. This would lead to the construction of far more advanced chiral tetracyclic intermediates in a very efficient convergent manner, in order to subsequently achieve the total synthesis of complex terpenoids such as emmolactone **5** or quinovaic acid **6**.

4. Experimental

4.1. General

All reactions were performed under N_2 atmosphere with oven or flame dried glassware. Solvents were distilled and dried according to standard procedures. Analytical TLC were performed on precoated glass plates (0.25 mm) with silica gel 60F-250 (Merck). Flash chromatography was performed with 230–400 mesh gel 60 (Merck). ^{1}H and ^{13}C NMR spectra were recorded on a Brüker AC-300 and are referenced with respect to the residual signals of the solvent; they are described using standard abbreviations. IR spectra were recorded on a Perkin–Elmer 1600 FT-IR. Mass spectra were recorded on a ZAB-1F micromass spectrometer.

4.1.1. 1,3-Ethyldioxolane-2-(propionic acid methyl ester)-cyclohexane (8). Ethylene glycol (1.05 mL, 18.90

mmol) and PTSA (9.00 mg, 47.00 μmol) were added to a solution of methyl ester **7** (1.00 g, 4.70 mmol) in benzene (10 mL). The mixture was refluxed on a Dean–Stark apparatus. After 16 h, the mixture was cooled at room temperature, neutralized with a saturated aqueous solution of $NaHCO_3$, extracted with dichloromethane, dried over Na_2SO_4, decanted and concentrated. The crude product was solubilized with methanol (10 mL), sodium methoxide 25% in methanol (2 mL) was added and the mixture was stirred over 16 h. Acetic acid (5 mL, 4.70 mmol) was added and methanol was evaporated. The residue was extracted with dichloromethane, dried over Na_2SO_4, decanted and concentrated. The crude product was purified by flash chromatography (hexanes–ethyl acetate 5:5, R_f 0.35) to give the methyl ester **8** (1.091 g, 81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20–3.89 (8H, m, CH_2CH_2O); 3.65 (3H, s, CH_3); 2.49 (2H, dd, J=8.5, 10.0 Hz, $CH_2CH_2CO_2CH_3$); 1.99 (1H, t, J=5.0 Hz, $CHCH_2$); 1.85–1.76 (4H, m); 1.62–1.54 (2H, m); 1.40–1.28 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6, 111.2, 65.3, 64.0, 51.4, 50.7, 34.9, 33.8, 19.2, 18.5. IR (film) ν 2950, 2884, 1732, 1621, 1440, 1346, 1263, 1176, 1132, 1060, 1029, 950, 932, 908, 853. MS (EI): 286 $(M)^+$. HRMS $(M)^+$ calcd for $C_{14}H_{22}O_6$: 286.1416; found: 286.1410.

4.1.2. 1,3-Ethyldioxolane-2-(propionaldehyde)-cyclohexane (9). To a solution of methyl ester **8** (37.80 g, 132.00 mmol) in toluene (130 mL) at −78°C was added slowly a solution of Dibal-H 1.5 M in toluene (132 mL, 198.00 mmol). The solution was stirred for 1 h, neutralized with an aqueous solution of tartaric acid 0.5 M, warmed to rt, extracted with dichloromethane, dried over Na_2SO_4, decanted and concentrated. The crude product was purified by flash chromatography (hexanes–ethyl acetate 4:6, R_f 0.23) to give the aldehyde **9** (16.5 g, 50%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (1H, t, J=2.0 Hz, HC=O); 4.11–3.85 (8H, m, OCH_2CH_2O); 2.60 (2H, td, J=2.0, 8.0 Hz, CH_2CH_2HC=O); 1.99 (1H, t, J=5.0 Hz, $CHCH_2$); 1.86–1.77 (4H, m); 1.62–1.53 (2H, m); 1.40–1.30 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.5, 111.1, 65.2, 63.9, 50.7, 44.9, 33.7, 19.1, 15.6. IR (film) ν 2948, 2884, 2719, 1721, 1445, 1346, 1268, 1159, 1136, 1067, 1029, 950, 910, 858. MS (EI): 228 $(M)^+$. HRMS $(M)^+$ calcd for $C_{13}H_{20}O_5$: 228.1361; found: 228.1359.

4.1.3. 1,3-Ethyldioxolane-2-(3-ethoxy-hepta-2,4-dienoic acid allyl ester) cyclohexane (3a). To a solution of aldehyde **9** (2.00 g, 7.80 mmol) in chloroform (125 mL) was added the phosphorane **10** (3.69 g, 8.58 mmol). The mixture was refluxed over 8 h, concentrated and purified by flash chromatography (hexanes–ethyl acetate 4:6, R_f 0.33) to give the ester **3a** (2.73 g, 88%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (major isomer) 7.29 (1H, d, J=16.0 Hz, CH_2CHCHC); 6.52 (1H, td, J=16.0, 7.0 Hz, CH_2CHCHC); 5.90 (1H, tdd, J=11.0, 10.5, 6.0 Hz, CH_2CHCH_2); 5.29 (1H, d, J=16.0 Hz, CH_2CHCH_2); 5.19 (1H, d, J=10.5 Hz, CH_2CHCH_2); 4.98 (1H, s, $CCHC$); 4.56 (2H, d, J=5.5 Hz, OCH_2CH); 4.06–3.81 (10H, m, OCH_2CH_2O and CH_3CH_2O); 2.34 (2H, td, J=8.5, 7.0 Hz, CH_2CH_2CH); 1.93 (1H, t, J=5.0 Hz, C_2CHCH_2); 1.76 (2H, td, J=13.0, 4.0 Hz, $CHCH_2CH_2$); 1.59–1.52 (4H, m, $CCH_2CH_2CH_2C$); 1.49–1.30 (5H, m, CH_3CH_2 and $CCH_2CH_2CH_2C$). ^{13}C NMR (75 MHz, $CDCl_3$) δ (major isomer) 167.1, 166.8, 140.3, 132.9, 122.0, 117.7, 111.3, 90.4, 65.2, 64.2, 63.7, 51.0, 34.0, 33.7, 22.9, 19.2, 14.3. IR (film) ν 2943, 2881, 1705, 1648, 1580, 1443, 1385, 1265, 1140, 1067, 1036, 948, 810. MS (EI): 408 $(M)^+$. HRMS $(M)^+$ calcd for $C_{22}H_{32}O_7$: 408.2148; found: 408.2150.

4.1.4. 1,3-Ethyldioxolane-2-(3-hydroxy-hepta-2,4-dienoic acid allyl ester) cyclohexane (3b). A solution of HCl 1 M (8.57 mL) was added to a solution of ester **3a** (500 mg, 1.22 mmol) in dichloromethane (25 mL). The mixture was stirred at rt until completion (followed by ^{1}H NMR), decanted, extracted with dichloromethane, dried over Na_2SO_4, decanted and concentrated to give the ester **3b** (476 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (β-keto ester form) 6.88 (td, 1H, J=6.7, 15.9 Hz, H_2C-HC=CH); 6.15 (d, 1H, J=15.9 Hz, O=C–HC=CH); 5.75–6.00 (m, 1H, H_2C-HC=CH_2); 5.26 (dd, 2H, J=1.0, 12.8 Hz, H_2C=CH); 4.61 (d, 2H, O=C–H_2C–HC=CH_2); 4.11–3.82 (m, 8H, $(OCH_2)_2$); 3.60 (s, 2H, O=C–CH_2–C=O); 2.30–2.45 (m, 2H, CH_2CH_2CH=); 1.94 (t, 1H, J=4.7 Hz, C–CH–CH_2); 1.19–1.83 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (β-keto ester form) 192.5, 167.2, 151.1, 142.0, 129.4, 118.5, 111.2, 65.9, 65.3, 64.0, 50.6, 46.5, 33.7, 33.4, 21.3, 19.2. IR (film) ν 2947, 2882, 1742, 1668, 1629, 1597, 1444, 1413, 1345, 1269, 1230, 1152, 1069, 1031, 949, 851, 795, 720. MS (EI): 380 $(M)^+$. HRMS $(M)^+$ calcd for $C_{20}H_{28}O_7$: 380.1835; found: 380.1826.

4.1.5. 1,7-Dioxo-5β-hydrido-9β-(2-(2,6-ethyldioxolane cyclohexane)ethyl)-10β-methyl ester decaline (11b). A solution of enone **4** (1.36 g, 8.85 mmol) in dichloromethane (160 mL) freshly prepared was added to a solution of Nazarov **3b** (2.34 g, 5.90 mmol) and cesium carbonate (2.89 g, 8.85 mmol) in dichloromethane (320 mL). The mixture was stirred over 16 h, filtered on silica and concentrated. The crude product was purified by flash chromatography (hexanes–ether 1:3, R_f 0.28) to give the decalin **11a** (2.36 g, 76%). Morpholine (9.44 mL, 89.68 mmol) and tetrakis(triphenylphosphine)palladium (52 mg, 44.84 μmol) were added to a solution of allyl ester **11a** (2.36 g, 4.46 mmol) in THF (262 mL). The mixture was stirred over 3 h, concentrated, dissolved in toluene (157 mL), refluxed 1 h and concentrated. The crude product was purified by flash chromatography (hexanes–ethyl acetate 2:8, R_f 0.26) to give the decalin **11b** (2.00 g, 100%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.04–3.76 (8H, m, OCH_2CH_2O); 3.68 (3H, s, CH_3); 3.03 (1H, m, CH_2CH_2-$CHCH_2$); 2.64–2.60 (2H, m); 2.42–2.05 (6H, m); 1.96–1.75 (3H, m); 1.70 (2H, m); 1.50–1.15 (9H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 206.6, 170.5, 111.1, 65.4, 65.2, 64.5, 64.0, 63.8, 52.5, 50.6, 42.9, 41.3, 40.2, 39.7, 38.7, 33.9, 33.7, 30.1, 27.0, 22.7, 20.6, 19.1. IR (film) ν 3020, 2954, 2886, 1713, 1453, 1435, 1374, 1347, 1269, 1236, 1130, 1072, 1025, 950, 908, 861. MS (EI): 450 $(M)^+$. HRMS $(M)^+$ calcd for $C_{24}H_{34}O_8$: 450.2253; found: 450.2257.

4.1.6. Tetracyclic enone (2). A solution of HCl 1 M (7.77 mL) was added to a solution of diketal **11b** (500 mg, 1.11 mmol) in acetone (111 mL). The mixture was heated to reflux 1 h, cooled to rt, neutralized with pH 7 buffer (100 mL) and a solution of sodium hydroxide 1 M (7.77 mL), extracted with CH_2Cl_2, dried over Na_2SO_4,

decanted. Toluene (111 mL) was then added and dichloromethane was evaporated. PTSA (317 mg, 1.61 mmol) was added to this toluene solution and heated to reflux over a Dean–Stark apparatus over 16 h, cooled to rt, neutralized with solid $NaHCO_3$ (140 mg), filtered on silica, and concentrated. The crude product was purified by flash chromatography (hexanes–ethyl acetate 5:5, R_f 0.31) to give the tetracycle enone **2** (300 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (3H, s, CH_3); 3.57 (1H, d, J=5.0 Hz, $C_{(8)}$H); 3.21–3.17 (1H, m, $CH_2CH_2CHCH_2$); 2.92–2.85 (1H, m, CH_2CHCH); 2.58–1.89 (14H, m); 1.57–1.54 (2H, m); 1.30–1.14 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.2, 206.4, 199.1, 170.0, 152.7, 132.7, 64.6, 53.6, 53.2, 43.2, 41.4, 40.5, 40.0, 38.2, 31.2, 30.0, 27.3, 26.4, 22.4, 21.3. IR (film) ν 2928, 1714, 1664, 1456, 1431, 1385, 1240, 1211, 1152, 1086, 754. MS (EI): 344 $(M)^+$. HRMS $(M)^+$ calcd for $C_{20}H_{24}O_5$: 344.1624; found: 344.1632.

4.1.7. Ketal (13). Ethylene glycol (18 μL, 326 μmol) and PTSA (3 mg, 16 μmol) were added to a solution of enone **2** (56 mg, 163 μmol) in benzene (10 mL). The mixture was refluxed over a Dean–Stark apparatus over 2 h, cooled to rt, filtered on silica and concentrated. The crude product was purified by flash chromatography (hexanes–ethyl acetate 5:5, R_f 0.48) to give ketal **13** (60 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.89–3.72 (4H, m, OCH_2CH_2O); 3.71 (3H, s, CH_3); 2.98–2.92 (1H, m); 2.82 (1H, d, J=5.0 Hz, CC*H*CH); 2.73–2.55 (2H, m); 2.50–2.21 (7H, m); 2.15–1.81 (6H, m); 1.53–1.45 (3H, m); 1.04–0.99 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.4, 199.5, 170.6, 154.9, 134.0, 110.5, 65.6, 64.2, 63.3, 52.5, 45.4, 40.9, 38.4, 37.5, 36.3, 34.8, 33.3, 27.0, 23.5, 22.4, 22.1, 19.4. IR (film) ν 2948, 2882, 1714, 1662, 1454, 1434, 1385, 1347, 1240, 1216, 1142, 1085, 1033, 949, 912, 755. MS (EI): 388 $(M)^+$. HRMS $(M)^+$ calcd for $C_{22}H_{28}O_6$: 388.1886; found: 388.1891.

4.1.8. Nitrile (14). A solution of diethylaluminiumcyanide 1 M (2.58 mL, 2.58 mmol) in toluene was added to a solution of enone **13** (190 mg, 490 μmol) and isopropanol (40 μL, 516 μmol) in dichloromethane (5.16 mL). The mixture was stirred at rt over 16 h, poured into a mixture of ice and a solution of sodium hydroxide 1 M (6 mL), extracted with dichloromethane, dried over Na_2SO_4, decanted and concentrated. The crude product was purified by flash chromatography (hexanes–ethyl acetate 5:5, R_f 0.21) to give nitrile **14** (122 mg, 60%) and starting enone **13** (48 mg, 25%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.09–3.90 (4H, m, OCH_2CH_2O); 3.71 (3H, s, CH_3); 3.02–2.94 (2H, m); 2.82–2.77 (1H, m); 2.72 (1H, d, J=5.0 Hz, CC*H*CH); 2.50–1.99 (10H, m); 1.87–1.55 (5H, m); 1.45–1.22 (2H, m); 1.03–0.86 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.8, 205.0, 170.4, 120.4, 111.2, 64.6, 64.1, 61.3, 52.7, 50.1, 48.7, 42.8, 40.9, 40.7, 37.7, 36.4, 34.3, 34.2, 29.7, 26.7, 23.4, 22.7, 22.3. IR (film) ν 3020, 2953, 2232, 1715, 1454, 1436, 1348, 1300, 1240, 1145, 1107, 1087, 1046, 1029, 991, 947, 909, 738. MS (EI): 415 $(M)^+$. HRMS $(M)^+$ calcd for $C_{23}H_{29}O_6N$: 415.1995; found: 415.1984.

4.1.9. Iminolactone 15. A solution of L-selectride 1 M (251 μL, 251 μmol) in dichloromethane was added to a solution of diketone **14** (104 mg, 251 μmol) in dichloromethane (4 mL) at −78°C. The mixture was stirred over 1 h, warmed to rt, stirred 3 h, neutralized with a saturated solution of ammonium chloride, extracted with dichloromethane, dried over Na_2SO_4, decanted and concentrated. The crude product was purified by flash chromatography (ethyl acetate 100%, R_f 0.11) to give the iminolactone **15** (89 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20–3.67 (m, 5H); 3.65 (s, 3H, CH_3O_2C); 3.62 (s, 1H, =N*H*); 2.80–2.74 (m, 1H); 2.58–2.50 (m, 2H); 2.41–2.15 (m, 3H); 2.08–0.73 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 177.5, 170.7, 111.1, 81.6, 64.8, 64.3, 61.0, 52.5, 51.3, 46.2, 40.8, 40.0, 37.5, 36.3, 34.2, 34.2, 28.6, 27.2, 26.6, 22.2, 21.5, 19.4. IR (film) ν 3323, 2947, 2878, 2223, 1740, 1712, 1668, 1451, 1434, 1368, 1301, 1276, 1238, 1211, 1190, 1124, 1100, 1020, 981, 918, 818, 731, 695, 599, 570. MS (EI): 417 $(M)^+$. HRMS $(M)^+$ calcd for $C_{23}H_{31}O_6N$: 417.2151; found: 417.2145.

4.1.10. Pentacyclic lactone (1). Iminolactone **15** (89 mg, 213 μmol) was refluxed in a 6 M HCl aqueous solution (5 mL) over 3 h, extracted with dichloromethane, dried over Na_2SO_4, decanted and concentrated. The crude product was purified by flash chromatography (hexanes–ethyl acetate 5:5, R_f 0.43) to give the lactone **1** (40 mg, 50%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.56 (d, 1H, J=6.3 Hz, *H*C=C); 3.76 (s, 3H, CH_3O_2C); 3.07 (m, 1H, *H*$C_{(5)}$); 2.9030 (t, 1H, J=13.7 Hz, *H*$C_{(9)}$); 2.86 (s, 1H, *H*OC); 2.68 (d, 1H, J=13.7 Hz, *H*$C_{(8)}$); 2.60–2.50 (m, 1H); 2.46–2.38 (m, 1H); 2.29–2.01 (m, 4H); 1.97–1.19 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 176.5, 171.6, 135.9, 121.2, 104.7, 62.8, 52.4, 48.9, 48.6, 40.7, 39.7, 39.0, 37.5, 33.5, 32.1, 28.4, 27.6, 26.5, 22.9, 21.9. IR (film) ν 3359, 3017, 2930, 2857, 1766, 1743, 1708, 1419, 1435, 1310, 1221, 1146, 756. MS (EI): 374 $(M)^+$. HRMS $(M)^+$ calcd for $C_{21}H_{26}O_6$: 374.1729; found: 374.1719.

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