Reactions of 3-iodolevoglucosenone with sodium derivatives of some CH acids. Chiral cyclopropanes and stable oxetenes

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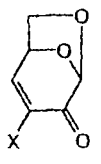
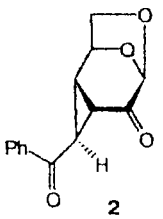
3-Iodolevoglucosenone reacts with the sodium derivative of ethyl cyanoacetate at −60 °C to give a tetrasubstituted cyclopropane derivative; similar reactions of the sodium derivatives of ethyl acetoacetate and acetylacetone at −60 °C afford the expected transformed Michael adducts, while at 20 °C, *O,C*-dialkylated products of the oxetene series are formed.

Key words: 3-iodolevoglucosenone, CH acids, Michael reaction, cyclopropanes, oxetenes.

Previously, trisubstituted cyclopropane **2** was prepared by the reaction of dimethylsulfonium phenacylide with levoglucosenone (**1**).[1] Recently we have shown[2] that 3-iodolevoglucosenone (**3**), readily accessible from compound **1**, reacts with the Na derivative of diethyl malonate in THF to give tetrasubstituted cyclopropane **4** in a high yield. In view of the increasing use of chiral functionalized cyclopropanes in syntheses[3–5] and in order to elucidate the synthetic potential of the reaction of halolevoglucosenones with anions of CH acids, in this work we studied the reactions of 3-iodo- (**3**) and 3-bromolevoglucosenone (**5**)[6] with the anions derived from ethyl malonate, ethyl cyanoacetate, and ethyl acetoacetate and from acetylacetone.



1, 3, 5



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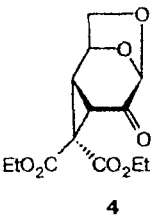

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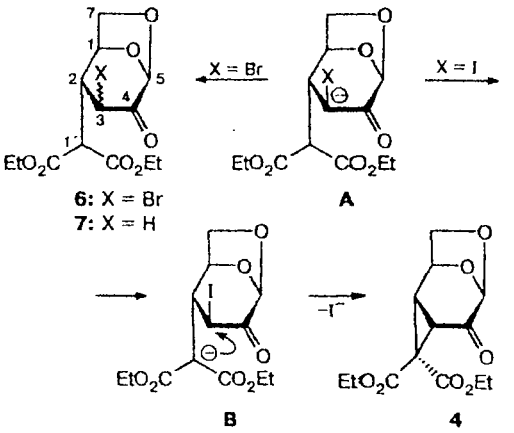
X = H (**1**), I (**3**), Br (**5**)

It was found that the nature of the halogen at the C(3) atom of levoglucosenone substantially influences the reaction pathway. Thus the reaction of compound **5** with the Na derivative of diethyl malonate in THF gave only Michael adduct **6**, which readily lost the halogen atom on treatment with an aqueous solution of Na_2SO_3 to give individual compound **7** in 48% yield (Scheme 1). In our opinion, the formation of different products in the reaction of compounds **3** and **5** with Na diethyl malonate is due to the specific features of charge delocalization in the intermediate Michael carbanion **A**. The electronegativity of the Br atom is known to be greater than that of I; therefore, when X = Br, anion **A** is fairly stable, whereas when X = I, the negative charge undergoes a 1,3-shift, resulting in the generation of more stable carbanion **B**, which leads to cyclopropane derivative **4**.

Scheme 1



6: X = Br
7: X = H

A

B

4

Thus, the study of the reactions of compounds **3** and **5** with the Na derivative of ethyl malonate demonstrated good prospects for using 3-iodolevoglucosenone in the construction of polycyclic structures. Therefore, subsequently we used only 3-iodolevoglucosenone (**3**) and involved it into reactions with the above-listed CH acids (Scheme 2).

The Na derivative of ethyl cyanoacetate in THF reacts with compound **3** at −60 °C to give tetrasubstituted cyclopropane **8** in 80% yield. The product is formed as a single diastereomer (it is shown in Scheme 2). Apparently, cyclization of carbanion **C** giving cyclopropane **8** is kinetically controlled; hence, the complete

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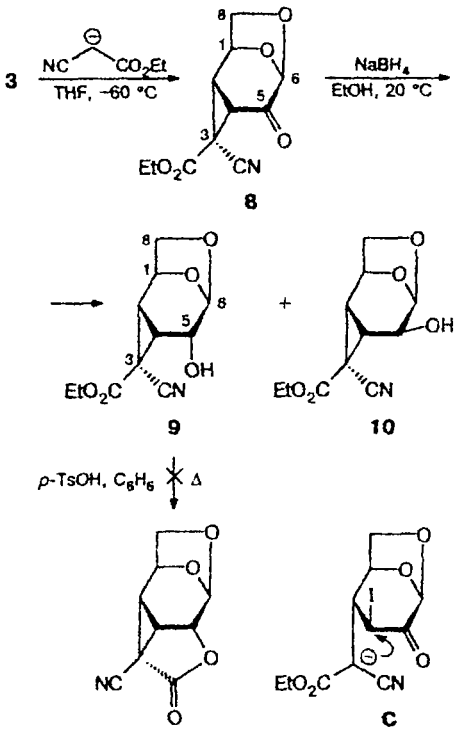
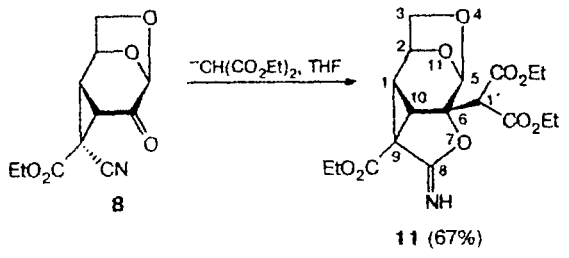
Scheme 2



predominance of steric factors in the transition state (the CO_2Et group is more bulky than the CN group) ensures the 100% optical induction in relation to the newly formed quaternary carbon center. The stereochemistry of compound **8** is confirmed experimentally by the fact that alcohol **9**, in which the hydroxy group occupies the *endo*-position with respect to the [4.1.0]bicyclic cage, does not undergo intramolecular lactonization upon prolonged refluxing in benzene in the presence of *p*-TsOH. The transformation of cyclopropane **8** into cyclic imine **11** on treatment with the diethyl malonate anion is more convincing chemical evidence for its structure (Scheme 3).

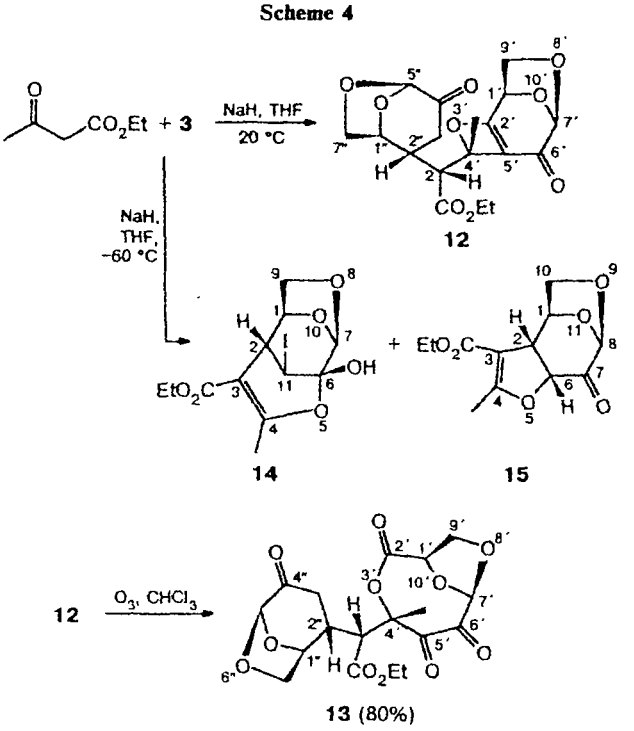
Scheme 3



Alcohols **9** and **10** in 4 : 1 ratio (^{1}H NMR spectroscopy data) were synthesized in 90% yield by the reduction of compound **8** ($NaBH_4$) under standard conditions. The most characteristic feature enabling the assignment of diastereomers **9** and **10** in the ^{1}H NMR spectra is the $J_{H(5),H(6)}$ = 3.0 Hz value found for the *exo*-isomer **10** and $J_{H(5),H(6)}$ = 0 for the *endo*-isomer **9**, which is consistent with the data reported for related structures.[7]

The reaction of the Na derivative of ethyl acetoacetate with 3-iodolevoglucosenone (**3**) follows a somewhat different pathway than that with ethyl cyanoacetate. When an excess of compound **3** (2 equiv.) is used and the reaction is carried out at room temperature, oxetene derivative **12** is formed in 73% yield (data on unstable oxetene and some its derivatives have been reported[8–11]). The reaction between equimolar amounts of the reactants at −60 °C affords cyclic enol ketol **14** and enol ether **15** in 42 and 40% yields, respectively (Scheme 4). The structure of the oxetene **12** was determined by converting it into lactone **13** by ozonolytic cleavage of the double bond and also relying on spectroscopic data, and the configurations of the C(2) atom and the quaternary chiral center were postulated based on the proposed stepwise pathway to this product.

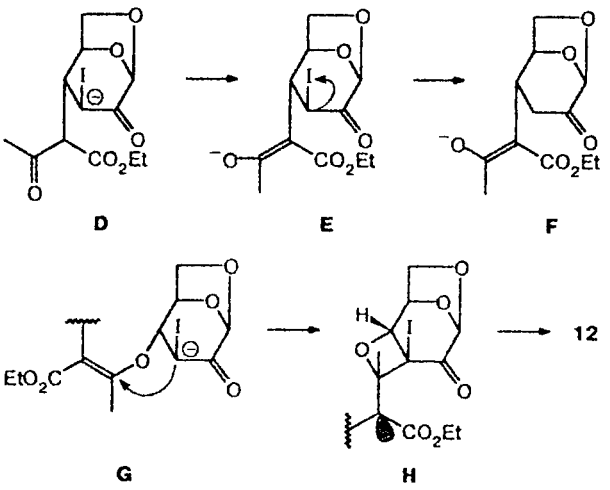
Scheme 4



It is known that in 1,4-conjugated addition reactions, nucleophilic reagents attack the activated double bond in levoglucosenone[12–15] and 3-iodolevoglucosenone[2] from the side opposite to the 1,6-anhydro bridge. Evidently, in this reaction, too, Michael carbanion **D** is generated in the initial step; this is followed by 1,5-shift of the carbanion to give *trans*-enolate **E**, which eliminates the mobile iodine atom on treatment with a base; apparently, this is accompanied by synchronous enolization of the oxo group in **E**, which also facilitates the elimination of the nucleofuge. As a whole, the formal outcome of these transformations is reductive elimination of the I atom from **E**. Subsequently *trans*-enolate **F** attacks one

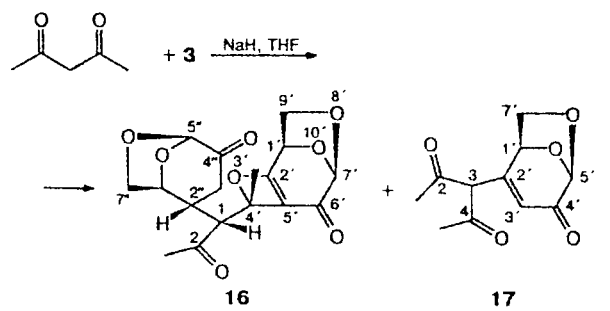
more molecule **3** to give carbanion **G**, which undergoes smooth stereospecific intramolecular 4-*exo*-trig-cyclization, being thus converted into carbanion **H**. In the latter species, the charge is localized in the *anti*-position in relation to the electronegative O atom of the oxetane ring; therefore, protonaton of this enolate occurs stereoselectively and, after *syn*-elimination of HI, oxetene **12** is produced (Scheme 5).

Scheme 5



Yet another CH acid, acetylacetone, reacts with 3-iodolevoglucosenone similarly to ethyl acetoacetate. In fact, the reaction of equimolar amounts of sodium acetylacetonate and compound **3** in THF at 20 °C gave oxetene **16** and the monoalkylation—dehydrohalogenation product, compound **17** (Scheme 6) in 40 and 20% yields, respectively.

Scheme 6



Thus, our studies resulted in the development of a new method for the synthesis of chiral cyclopropanes functionalized in different ways from 3-iodolevoglucosenone **3** and the Na derivative of ethyl cyanoacetate: realization of an original route for construction of substituted oxetene structures from compound **3** involving ambident nucleophiles, *viz.*, ethyl cyanoacetate and acetylacetone.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 and 75.47 MHz, respectively) using Me_4Si as the internal standard and $CDCl_3$ as the solvent. TLC analysis was carried out on Silufol chromatographic plates. The optical rotation was measured on a Perkin—Elmer-141 instrument. Mass spectra were recorded on an MX-1306 instrument (ionizing voltage 70 eV, temperature of the ionization chamber 30—50 °C).

(1*S*,2*R*,3*RS*,5*R*)-2-[Bis(ethoxycarbonyl)methyl]-3-bromo-6,8-dioxabicyclo[3.2.1]octan-4-one (6) and (1*S*,2*R*,5*R*)-2-[bis(ethoxycarbonyl)methyl]-6,8-dioxabicyclo[3.2.1]octan-4-one (7). Diethyl malonate (0.39 g, 2.4 mmol) was added dropwise to a suspension of NaH (0.12 g, 4.8 mmol) in 3 mL of THF, and the mixture was stirred for 30 min. A solution of 3-bromolevoglucosenone (**5**) (0.5 g, 2.4 mmol) in 2 mL of THF was added. After stirring for 5 min, the reaction mixture was acidified to pH 5 by adding 10% aqueous HCl, and the product was extracted with AcOEt (3×5 mL). The extracts were combined and separated into two portions. One portion was washed with water, dried with Na_2SO_4, and concentrated. Chromatography (using a 1 : 1 AcOEt—heptane mixture as the eluent) gave 0.21 g (24%) of a difficultly separable mixture of diastereomeric bromides **6** in the ratio (3*S*) : (3*R*) = 2 : 1 (^1H NMR data), R_f 0.36 (AcOEt—heptane, 1 : 1). **3*S*-Diastereomer 6.** ^1H NMR, δ: 1.20, 1.21 (both t, each 3 H, CH_3, J = 6.1 Hz); 2.96 (dd, 1 H, H(2), J = 5.0, 4.1 Hz); 3.70 (d, 1 H, H(1'), J = 5.0 Hz); 3.85 (dd, 1 H, $H(7)_{exo}$, J = 4.6, 7.7 Hz); 4.15 (m, 4 H, 2 OCH_2); 4.30 (d, 1 H, $H(7)_{endo}$); 4.50 (d, 1 H, H(3), J = 4.1 Hz); 4.78 (d, 1 H, H(1), J = 4.6 Hz); 5.20 (s, 1 H, H(5)). ^{13}C NMR, δ: 13.9 (2 CH_3); 42.8 (C(3)); 47.9 (C(2)); 53.7 (C(1')); 62.4, 62.2 (2 OCH_2); 68.6 (C(7)); 74.4 (C(1)); 99.8 (C(5)); 167.2, 167.7 (2 CO_2); 193.8 (C(4)). **2*R*-Diastereomer 6.** ^{13}C NMR, δ: 13.9 (2 CH_3); 48.8 (C(3)); 49.5 (C(2)); 50.0 (C(1')); 62.06, 62.98 (2 OCH_2); 67.8 (C(7)); 74.8 (C(1)); 100.9 (C(5)); 168.0, 168.6 (2 CO_2); 190.4 (C(4)).

(1*S*,2*R*,5*R*)-2-[Bis(ethoxycarbonyl)methyl]-6,8-dioxabicyclo[3.2.1]octan-4-one (7). The remaining portion of the extract was washed with a saturated solution of Na_2SO_3, dried with Na_2SO_4, concentrated, and subjected to chromatography (using a 1 : 1 AcOEt—heptane mixture as the eluent) to give 0.17 g (24%) of compound **7** as an oil, R_f 0.30 (AcOEt—heptane, 1 : 1), $[\alpha]_D^{16}$ −138.1° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 930, 1060, 1140, 1200, 1260, 1320, 1390, 1465, 1485, 1730, 1750, 2930, 3000. ^1H NMR, δ: 1.25 (t, 6 H, 2 CH_3, J = 7.1 Hz); 2.25 (d, 1 H, H(3), J = 16.8 Hz); 2.76 (dd, 1 H, H(3), J = 16.8, 8.3 Hz); 2.87 (dd, 1 H, H(2), J = 8.4, 8.3 Hz); 3.62 (d, 1 H, H(1'), J = 8.4 Hz); 3.99 (dd, 1 H, $H(7)_{exo}$, J = 8.0, 5.1 Hz); 4.05 (dd, 1 H, $H(7)_{endo}$, J = 8.0, 1.1 Hz); 4.20 (q, 4 H, 2 CH_2O, J = 7.1 Hz); 4.69 (d, 1 H, H(1), J = 5.1 Hz); 5.03 (s, 1 H, H(5)). ^{13}C NMR, δ: 13.9 (2 CH_3); 34.6 (C(3)); 40.1 (C(2)); 53.6 (C(1')); 61.9, 62.0 (2 CH_2O); 67.9 (C(7)); 74.6 (C(1)); 101.3 (C(5)); 167.9, 168.0 (2 CO_2); 198.4 (C(4)). MS (EI), m/z (I_{rel} (%)): 286 $[M]^+$ (1), 285 $[M - H]^+$ (2), 258 $[M - CO]^+$ (20), 241 $[M - OEt]^+$ (12), 213 $[M - CO_2Et]^+$ (20), 185 $[M - CO_2Et - CO]^+$ (100), 139 (68), 111 (44), 99 (92), 85 (48), 81 (72), 67 (60), 53 (52), 43 (68), 29 (25).

Ethyl (1*S*,2*R*,3*S*,4*S*,6*R*)-3-cyano-5-oxo-7,9-dioxatricyclo[4.2.1.0^{2,4}]nonane-3-carboxylate (8). Ethyl cyanoacetate (0.24 mL, 2 mmol) was added dropwise to a suspension of NaH (0.08 g, 3.4 mmol) in 3 mL of THF, and the mixture was stirred for 30 min and cooled to −60 °C. A solution of 3-iodolevoglucosenone (0.5 g, 2 mmol) in 2 mL of THF was added. After stirring for 15 min, the temperature of the reaction mixture was

brought to 0 °C, the mixture was acidified to pH 5 by adding 10% HCl, and the product was extracted with AcOEt (3×5 mL). The combined extracts were washed with a saturated solution of Na_2SO_3, dried with Na_2SO_4, concentrated, and chromatographed (using a 9 : 1 AcOEt—heptane mixture as the eluent) to give 0.37 g (80%) of compound **8** as transparent crystals, R_f 0.43 (AcOEt—heptane, 9 : 1), m.p. 119.0—120.0 °C (AcOEt), $[\alpha]_D^{16}$ −121.9° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 760, 930, 1000, 1110, 1130, 1150, 1250, 1320, 1390, 1660, 1700, 1750, 2280, 2890, 2920, 2990. ^{1}H NMR, δ: 1.29 (t, 3 H, CH_3, J = 7.1 Hz); 2.38 (dd, 1 H, H(2), J = 8.4, 1.0 Hz); 2.63 (d, 1 H, H(4), J = 8.4 Hz); 3.90 (dd, 1 H, H(8)$_{exo}$, J = 7.5, 4.4 Hz); 4.11 (d, 1 H, H(8)$_{endo}$, J = 7.5 Hz); 4.22 (q, 2 H, OCH_2, J = 7.1 Hz); 4.98 (dd, 1 H, H(1), J = 4.4, 1.0 Hz); 5.00 (s, 1 H, H(6)). ^{13}C NMR, δ: 13.8 (CH_3); 28.3 (C(2)); 32.4 (C(4)); 64.0 (OCH_2); 68.6 (C(1)); 69.6 (C(8)); 99.0 (C(6)); 113.5 (CN); 164.9 (CO); 189.1 (C(5)). Found (%): C, 55.5; H, 4.6; N, 5.9. $C_{11}H_{11}NO_5$. Calculated (%): C, 55.7; H, 4.6; N, 5.9. MS (EI), m/z (I_{rel} (%)): 238 $[M + H]^+$ (1), 237 $[M]^+$ (3), 209 $[M - CO]^+$ (7), 192 (18), 191 (12), 181 (13), 178 (19), 163 (43), 149 (30), 134 (74), 123 (57), 121 (17), 106 (100).

Ethyl (1*S*,2*R*,3*S*,4*S*,5*RS*,6*S*)-3-cyano-5-hydroxy-7,9-dioxatricyclo[4.2.1.0^{2,4}]nonane-3-carboxylate (diastereomers 9 and 10). $NaBH_4$ (0.11 g, 2.8 mmol) was added to a solution of compound **8** (0.27 g, 1.1 mmol) in 6 mL of EtOH and 4 mL of THF cooled to 0 °C. After stirring for 1 h, the reaction mixture was neutralized by the addition of concentrated AcOH, the resulting mixture was concentrated on a rotary evaporator, the residue was diluted with 2 mL of water, and the products were extracted with AcOEt (3×5 mL). The combined organic extracts were dried with $MgSO_4$, concentrated, and chromatographed (using a 7 : 3 AcOEt—heptane mixture as the eluent) to give 0.2 g (90%) of a mixture of compounds **9** and **10** as an oil, R_f 0.20 (AcOEt—heptane, 7 : 3). Crystallization from an AcOEt—Et_2O mixture gave the *endo*-isomer of **9**. **5*R*-Diastereomer 9.** M.p. 124—125 °C (AcOEt—heptane), $[\alpha]_D^{16}$ −120.7° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 760, 840, 870, 900, 970, 1020, 1100, 1180, 1280, 1330, 1400, 1750, 2270, 2930, 3000, 3540. ^{1}H NMR, δ: 1.35 (t, 3 H, CH_3, J = 7.1 Hz); 2.09 (dd, 1 H, H(2), J = 8.5, 1.0 Hz); 2.45 (dd, 1 H, H(4), J = 8.7, 8.5 Hz); 2.90 (br.s, 1 H, OH); 3.80 (dd, 1 H, H(8)$_{exo}$, J = 7.3, 4.0 Hz); 3.98 (d, 1 H, H(8)$_{endo}$, J = 7.3 Hz); 4.07 (d, 1 H, H(5), J = 8.7 Hz); 4.27 (q, 2 H, OCH_2, J = 7.1 Hz); 4.90 (d, 1 H, J = 4.0 Hz); 5.36 (s, 1 H, H(6)). ^{13}C NMR, δ: 14.05 (CH_3); 19.8 (C(3)); 29.1 (C(4)); 30.5 (C(2)); 63.6 (OCH_2); 65.8 (C(5)); 68.3 (C(2), C(8)); 102.2 (C(6)); 116.2 (CN); 167.2 (CO_2). **5*S*-Diastereomer 10.** The spectra were recorded for the **9** + **10** mixture. ^{1}H NMR, δ: 1.25 (t, 3 H, CH_3, J = 7.1 Hz); 1.96 (d, 1 H, H(2), J = 9.4 Hz); 2.10 (d, 1 H, H(4), J = 9.4 Hz); 3.80 (dd, 1 H, H(8)$_{exo}$, J = 4.1, 7.5 Hz); 3.88 (d, 1 H, H(5), J = 3.0 Hz); 4.08 (d, 1 H, H(8)$_{endo}$, J = 7.5 Hz); 4.18 (q, 2 H, OCH_2, J = 7.1 Hz); 4.80 (d, 1 H, H(1), J = 4.1 Hz); 5.25 (d, 1 H, H(6), J = 3.0 Hz). ^{13}C NMR, δ: 13.7 (CH_3); 22.1 (C(3)); 29.9 (C(4)); 30.6 (C(2)); 64.6 (OCH_2); 68.5 (C(1)); 70.3 (C(8)); 98.7 (C(6)); 114.5 (CN); 166.5 (CO_2).

Ethyl (1*R*,2*S*,5*R*,6*S*,9*S*,10*S*)-6-[bis(ethoxycarbonyl)-methyl]-8-imino-4,7,11-trioxatetracyclo[4.3.1.1^{2,5}.0^{9,10}]-undecane-9-carboxylate (11). Diethyl malonate (0.27 g, 1.7 mmol) was added dropwise to a suspension of NaH (0.06 g, 2.5 mmol) in 2 mL of THF, the mixture was stirred for 30 min, and a solution of cyclopropane **8** (0.4 g) in 2 mL of THF was added. The reaction mixture was stirred for 20 min and quenched by adding a 3% aqueous solution of HCl to pH 7, and the product was extracted with CH_2Cl_2 (3×5 mL). The combined extracts were washed with brine, dried with $MgSO_4$, concentrated, and chromatographed (AcOEt—heptane, 7 : 3) to give 0.45 g (67%) of imine **11** as an oil and 0.08 g of the initial cyclopropane **8**, R_f 0.19 (AcOEt—heptane, 7 : 3), $[\alpha]_D^{25}$ +112.4° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 760, 880, 980, 1030, 1130, 1270, 1390, 1730, 2900, 2980. ^{1}H NMR, δ: 1.25 (m, 9 H, 3 CH_3); 2.20 (d, 1 H, H(10), J = 8.7 Hz); 2.93 (d, 1 H, H(1), J = 8.7 Hz); 3.72 (s, 1 H, H(1)); 3.95 (dd, 1 H, H(3)$_{exo}$, J = 7.0, 3.8 Hz); 4.07 (d, 1 H, H(3)$_{endo}$, J = 7.0 Hz); 4.22 (m, 6 H, 3 OCH_2); 4.88 (br.s, 1 H, H(2)); 5.38 (s, 1 H, H(5)); 5.84 (s, 1 H, NH). ^{13}C NMR, δ: 13.89, 13.95, 14.04 (3 CH_3); 30.7 (C(10)); 31.8 (C(1)); 37.0 (C(9)); 54.3 (C(1′)); 58.1 (C(3)); 62.0, 62.2, 62.3 (3 OCH_2); 70.7 (C(2)); 73.7 (C(6)); 100.9 (C(5)); 166.2, 166.4 167.7 (CO_2); 171.6 (C=NH). MS (EI), m/z (I_{rel} (%)): 397 $[M]^+$ (1.5), 396 $[M - H]^+$ (3), 369 $[M - C_2H_4]^+$ (1), 352 $[M - OEt]^+$ (24), 351 $[M - EtOH]^+$ (43), 324 $[M - CO_2Et]^+$ (52), 309 (19), 305 (10), 234 (14), 232 (10), 279 (38), 206 (100), 178 (14), 160 (81), 134 (19), 132 (12), 106 (6), 104 (8).

Ethyl 2(*R*)-{(1*S*,2*R*,5*R*)-4-oxo-6,8-dioxabicyclo[3.2.1]-octan-2-yl}-2-{(1*S*,4*S*,7*R*)-4-methyl-6-oxo-3,8,10-trioxa-tricyclo[5.2.1.0^{2,5}]dec-2(5)-en-4-yl}acetate (12) was obtained in 73% yield by the reaction of iodolevoglucosenone with the Na derivative of ethyl acetoacetate (ratio 2 : 1) at 20 °C by the procedure described above for cyclopropane **8**; R_f 0.50 (AcOEt—heptane, 7 : 3), m.p. 132—133 °C (Et_2O), $[\alpha]_D^{16}$ −321.3° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 1000, 1120, 1260, 1330, 1400, 1480, 1680, 1700, 1760, 2880, 2950. ^{1}H NMR, δ: 1.28 (t, 3 H, CH_3, J = 7.1 Hz); 2.12 (d, 1 H, H(3″), J = 17.5 Hz); 2.22 (s, 3 H, CH_3); 2.70 (dd, 1 H, H(3″), J = 17.5, 9.6 Hz); 2.88 (d, 1 H, H(2″), J = 9.6 Hz); 3.58 (br.s, 1 H, C(2)HCO_2); 3.78 (dd, 1 H, H(9′)$_{exo}$, J = 7.8, 4.8 Hz); 3.88 (d, 1 H, H(9′)$_{endo}$, J = 7.8 Hz); 4.0 (m, 2 H, 2 H(7″)); 4.20 (q, CH_2, J = 7.1 Hz); 4.60 (d, 1 H, H(1″), J = 4.6 Hz); 4.92 (d, 1 H, H(1′), J = 4.8 Hz); 5.08 (s, 1 H, H(5″)); 5.20 (s, 1 H, H(7′)). ^{13}C NMR, δ: 13.9, 14.3 (2 CH_3); 31.0 (C(3″)); 43.5 (C(2″)); 48.3 (C(2)); 60.2 (OCH_2); 68.1 (C(7″)); 69.0 (C(9′)); 72.3 (C(1″)); 74.8 (C(1′)); 88.0 (C(4′)); 98.5 (C(5″)); 101.1 (C(7′)); 104.9 (C(5′)); 164.4 (C(2′)); 166.9 (CO_2); 192.3 (C(6′)); 199.1 (C(4″)). Found (%): C, 57.4; H, 5.4. $C_{18}H_{20}O_9$. Calculated (%): C, 56.8; H, 5.3. MS (EI), m/z (I_{rel} (%)): 380 $[M]^+$, 352 $[M - C_2H_4]^+$ or $[M - CO]^+$ (6), 335 $[M - OEt]^+$ (12), 306 (38), 293 (100), 279 (6), 265 (46), 219 (15), 206 (15), 193 (23), 180 (10), 99 (28), 71 (21), 57 (18).

Ethyl 2(*R*)-{(1*S*,2*R*,5*R*)-4-oxo-6,8-dioxabicyclo[3.2.1]-octan-2-yl}-2-{(1*S*,4*S*,7*R*)-4-methyl-2,5,6-trioxo-3,8,10-trioxabicyclo[5.2.1]dec-4-yl}acetate (13). An ozone—oxygen mixture was passed for 5 min at 0 °C through a solution of oxetene **12** (0.25 g) in 10 mL of $CHCl_3$ (TLC monitoring). The reaction mixture was purged with argon, Me_2S (0.2 mL) was added, and the mixture was stirred for 1 h (test for peroxides!). The solvent was evaporated at a reduced pressure, and the residue was crystallized from a 1 : 1 AcOEt—Et_2O mixture to give 0.21 g (80%) of the crystalline lactone **13**, m.p. 175—176 °C (AcOEt—Et_2O, decomp.), R_f 0.50 (AcOEt—heptane, 9 : 1), $[\alpha]_D^{26}$ −123.6° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 920, 1145, 1250, 1400, 1485, 1770, 2860—3000. ^{1}H NMR, δ: 1.35 (t, 3 H, CH_3, J = 7.0 Hz); 2.05 (s, 3 H, CH_3); 2.48 (d, 1 H, H(3″), J = 16.4 Hz); 2.63 (s, 1 H, H(2)); 2.78 (dd, 1 H, H(3″), J = 16.4, 9.2 Hz); 2.80 (d, 1 H, H(2″), J = 9.2 Hz); 3.83 (dd, 1 H, H(7″)$_{exo}$, J = 9.3, 4.3 Hz); 3.88 (d, 1 H, H(7″)$_{endo}$, J = 9.3 Hz); 3.95 (d, 1 H, H(9′), J = 21.5 Hz); 4.02 (d, 1 H, H(9′), J = 21.5 Hz); 4.80 (d, 1 H, H(1″), J = 4.3 Hz); 4.89 (br.s, 1 H, H(1′)); 5.05 (s, 1 H, H(5″)); 5.44 (s, 1 H, H(7′)). ^{13}C NMR, δ: 13.8 (CH_3); 20.0 (CH_3); 32.1 (C(3″)); 46.3 (C(2″)); 50.8 (C(2)); 63.3 (OCH_2); 69.0 (C(7″)); 69.1 (C(9′)); 72.6 (C(1″)); 72.7 (C(1′)); 78.7 (C(4′)); 100.1 (C(7′)); 100.8 (C(5″)); 161.6 (C(2′)); 168.7 (CO_2Et); 189.1

(C(5′)); 192.5 (C(6′)); 198.6 (C(4″)). Found (%): C, 51.8; H, 4.7. $C_{18}H_{20}O_{11}$. Calculated (%): C, 52.4; H, 4.8. MS (EI), *m/z* (I_{rel} (%)): 412 $[M]^+$ (0.2), 411 $[M - H]^+$ (0.6), 381 $[M - OCH_3]^+$ (14.6), 367 $[M - OEt]^+$ (0.2), 364 (0.6), 339 $[M - CO_2Et]^+$ (25.3), 295 (1.2), 267 (22), 248 (14.6), 229 (23.3), 221 (20), 195 (26), 177 (26), 149 (40.0), 121 (73.3), 43 (100.0), 29 (66.7).

Ethyl (1*S*,2*R*,6*S*,7*R*,11*S*)-6-hydroxy-11-iodo-4-methyl-5,8,10-trioxatricyclo[5.2.1.1^{2,6}]dec-3(*E*)-ene-3-carboxylate (14) and (1*S*,2*R*,6*R*,8*R*)-4-methyl-7-oxo-5,9,11-trioxatricyclo[6.2.1.0^{2,6}]undec-3(*E*)-ene-3-carboxylate (15) were prepared in 42 and 40% yields, respectively by the procedure described above at a 3 : ethyl acetoacetate ratio of 1 : 1 and a temperature of −60 °C. **Enol ketol 14.** R_f 0.50 (AcOEt—heptane, 7 : 3), m.p. 117—118 °C (AcOEt—heptane), $[\alpha]_D^{26}$ −120.4° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 780, 824, 876, 912, 960, 1000, 1112, 1200, 1240, 1276, 1280, 1300, 1384, 1476, 1640, 1688, 1704, 1724, 1736, 2912, 2976, 3304. ^{1}H NMR ($(CD_3)_2SO$), δ: 1.20 (t, 3 H, CH_3, *J* = 7.1 Hz); 2.22 (s, 3 H, CH_3); 3.20 (dd, 1 H, H(2), *J* = 3.1, 3.2 Hz); 3.68 (m, 1 H, C(11)HI, *J* = 3.1 Hz); 4.08 (q, 2 H, CH_2O, *J* = 7.0 Hz); 4.35 (m, 2 H, 2 H(9)); 4.82 (d, 1 H, H(1), *J* = 3.2 Hz); 5.21 (s, 1 H, H(7)). ^{13}C NMR ($(CD_3)_2SO$), δ: 14.5 (CH_3); 19.5 (CH_3); 25.3 (C(11)); 44.9 (C(2)); 59.8 (CH_2O); 68.3 (C(9)); 77.4 (C(1)); 98.0 (C(6)); 102.9 (C(4)); 103.0 (C(7)); 165.2 (C(3)); 166.9 (CO_2). Found (%): C, 38.1; H, 4.1. $C_{12}H_{15}IO_6$. Calculated (%): C, 37.7; H, 3.9; I, 33.2.

Enol ether 15. R_f 0.40 (AcOEt—heptane, 7 : 3), $[\alpha]_D^{18}$ −150.5° (*c* 1.0, $CHCl_3$). ^{1}H NMR, δ: 1.23 (t, 3 H, CH_3, *J* = 7.1 Hz); 2.18 (s, 3 H, CH_3); 3.72 (d, 1 H, H(2), *J* = 10.5 Hz); 3.84 (dd, 1 H, H(10)$_{exo}$, *J* = 7.5, 4.6 Hz); 3.92 (d, 1 H, H(10)$_{endo}$, *J* = 7.5 Hz); 4.15 (q, 2 H, CH_2O, *J* = 7.1 Hz); 5.00 (d, 1 H, H(6), *J* = 10.5 Hz); 5.11 (s, 1 H, H(8)); 5.25 (d, 1 H, H(1), *J* = 4.6 Hz). ^{13}C NMR, δ: 14.1 (CH_3); 14.3 (CH_3); 50.0 (C(2)); 60.1 (CH_2O); 68.5 (C(10)); 72.5 (C(1)); 78.7 (C(6)); 99.5 (C(8)); 102.3 (C(4)); 164.7 (C(3)); 169.8 (CO_2); 195.4 (C(7)O). MS (EI), *m/z* (I_{rel} (%)): 254 $[M]^+$ (1), 228 $[M - CO]^+$ (11), 226 $[M - OCH_2O]^+$ (8), 224 (3), 209 $[M - OEt]^+$ (13), 199 (2), 183 (5), 181 (5), 180 $[M - OEt - CHO]^+$ (30), 167 (100), 168 (7), 154 (10), 151 (11), 139 (22), 125 (13), 109 (17), 99 (17), 72 (12), 43 (67).

Compounds 16 and 17 were synthesized at 20 °C as crystalline materials in 21 and 43% yields, respectively by a procedure similar to that described for compound **12** at a 3 : acetylacetone ratio of 1 : 1.

1(*R*)-1-{(1*S*,2*R*,5*R*)-4-Oxo-6,8-dioxabicyclo[3.2.1]oct-2-yl}-1-{(1*S*,4*S*,7*R*)-4-methyl-6-oxo-3,8,10-trioxatricyclo[5.2.1.0^{2,5}]dec-2(5)-en-4-yl}propan-2-one (16). R_f 0.15 (AcOEt—heptane, 7 : 3), m.p. 240 °C (AcOEt—heptane, decomp.), $[\alpha]_D^{16}$ −295.5° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 970, 1010, 1130, 1260, 1325, 1400, 1480, 1650, 1755, 2880—3000. ^{1}H NMR, δ: 2.15 (d, 1 H, H(3″), *J* = 17.0 Hz); 2.33 (s, 3 H, CH_3); 2.38 (s, 3 H, CH_3); 2.75 (dd, 1 H, H(3″), *J* = 17.0, 7.5 Hz); 2.88 (d, 1 H, H(2″), *J* = 7.5 Hz); 3.68 (br.s, 1 H, H(1)); 3.82 (dd, 1 H, H(7″)$_{exo}$, *J* = 7.8, 4.6 Hz); 3.93 (d, 1 H, H(7″)$_{endo}$, *J* = 7.8 Hz); 4.00 (br.s, 2 H, 2 H(9′)); 4.62 (br.s, 1 H, H(1′)); 4.90 (d, 1 H, H(1″), *J* = 4.6 Hz); 5.01 (s, 1 H, H(5″)); 5.25 (s, 1 H, H(7′)). ^{13}C NMR, δ: 15.1 (CH_3); 29.5 (CH_3); 31.0 (C(3″)); 43.5 (C(2″)); 48.8 (C(1)); 68.4 (C(7″)); 68.8 (C(9′)); 72.3 (C(1″)); 74.5 (C(1′)); 87.6 (C(4′)); 98.3 (C(5″)); 101.0 (C(7′)); 116.3 (C(5′)); 165.8 (C(2′)); 192.3 (C(6′)); 192.9 (C(2)); 198.7 (C(4″)). Found (%): C, 57.5; H, 5.2. $C_{17}H_{18}O_8$. Calculated (%): C, 58.3; H, 5.2. MS (EI), *m/z* (I_{rel} (%)): 350 $[M]^+$ (1), 349 $[M - H]^+$ (1), 320 $[M - CH_2O]^+$, $[M - CH_2CO]^+$ (3), 276 $[M - CH_2OH]^+$, $[M - CH_3CO]^+$ (18), 263 (100), 249 (13), 239 (90), 221 (7), 203 (10), 202 (11), 189 (19), 176 (13), 163 (30), 150 (7), 137 (12), 71 (11), 43 $[COCH_3]^+$ (63).

3-{(1*S*,5*R*)-4-Oxo-6,8-dioxabicyclo[3.2.1]oct-2-en-2-yl}pentane-2,4-dione (17). R_f 0.45 (AcOEt—heptane, 7 : 3), m.p. 140—141 °C (AcOEt—heptane), $[\alpha]_D^{16}$ −457.3° (*c* 1.0, $CHCl_3$). IR, ν/cm^{-1}: 888, 976, 1024, 1104, 1280, 1298, 1320, 1376, 1464, 1612, 1636, 1676, 1688, 1844, 2856, 2880, 2920. ^{1}H NMR, δ: 2.00 (s, $CHAc_2$); 2.20 (s, 6 H, 2 CH_3); 3.75 (d, 1 H, H(7′)$_{endo}$, *J* = 7.2 Hz); 3.95 (dd, 1 H, H(7′)$_{exo}$, *J* = 7.2, 5.0 Hz); 4.90 (d, 1 H, H(1′), *J* = 5.0 Hz); 5.40 (s, 1 H, H(5′)); 6.00 (s, 1 H, H(3′)). ^{13}C NMR, δ: 23.5 (C(3)); 24.0 (2 C, 2 CH_3); 66.6 (C(7′)); 76.8 (C(1′)); 101.0 (C(5′)); 127.4 (C(3′)); 157.2 (C(2′)); 188.7 (2 CO); 192.7 (C(4′)). MS (EI), *m/z* (I_{rel} (%)): 224 $[M]^+$ (2), 223 $[M - H]^+$ (10), 196 $[M - CO]^+$ (4), 182 $[M - CH_2{=}C{=}O]^+$ (3), 178 $[M - CO - H_2O]^+$, $[M - C_2H_5OH]^+$ (28), 163 (5), 150 (100), 137 (30), 135 (65), 122 (13), 95 (9), 43 (46).

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