Reactions of levoglucosenone and its derivatives with diazo compounds*

R. A. Novikov, R. R. Rafikov, E. V. Shulishov, L. D. Konyushkin, V. V. Semenov, and Yu. V. Tomilov

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 6390. E-mail: tom@ioc.ac.ru

The reaction of levoglucosenone with methyl diazoacetate gives first 1-pyrazoline, which then, depending on the reaction conditions, either undergoes denitrogenation to form a mixture of cyclopropane and unsaturated compounds, or isomerizes into 2-pyrazoline capable of easy cyclodimerizing in the presence of pyridine through the addition of the N—H fragments to the carbonyl groups. The product of levoglucosenone reduction, 6,8-dioxabicyclo[3.2.1]oct-2-en-4-ol, affords the corresponding cyclopropane upon the action of diazomethane in the presence of a Pd catalyst, whereas its reaction with methyl diazoacetate in the presence of $Rh_2(OAc)_4$ leads to the insertion of methoxycarbonyl carbene into the OH bond. From the ester obtained, 1-diazo-3-{6,8-dioxabicyclo[3.2.1]oct-2-en-4-yloxy}propan-2-one was synthesized in several steps, its denitrogenation under the action of copper compounds is accompanied by the intramolecular insertion of the carbene into the C(4)—H bond of the levoglucosenone fragment to yield the corresponding spirane.

Key words: levoglucosenone, pyrazolines, diazomethane, methyl diazoacetate, cyclopropanation, insertion, NMR spectra.

6,8-Dioxabicyclo[3.2.1]octane derivatives possess a wide range of biological activity,[1,2] while optically active compounds of this series can be used as substrates in various enantioselective reactions.

In continuation of our studies in the field of chemistry of diazo compounds and in order to synthesize new optically active derivatives of 6,8-dioxabicyclo[3.2.1]octane including those with cyclopropane fragments, we synthesized derivatives of easily available carbohydrate enone, *viz.*, levoglucosenone (**1**), which can be obtained from cellulose of any origin by acid hydrolysis at 250—300 °C (see Refs 3 and 4).

Such chemical transformations of levoglucosenone and its derivatives as reactions with diazo compounds and synthesis of cyclopropane compounds based on them are virtually not investigated. In the literature, there are few works devoted to the study of reactions of diazo compounds with levoglucosenone or its derivatives, which can to a certain extent result from specific properties of this unsaturated ketone. Thus direct cyclopropanation of levoglucosenone by decomposition of diazomethane or methyl diazoacetate (MDA) in the presence of catalysts gives no cyclopropanation products because of lowered electron density on the double bond.[5] Though, 1,3-dipolar cycloaddition of diazomethane to the levoglucosenone C=C bond leads to the formation of 1-pyrazoline,[5] however, there are no data on possibility of its denitrogenation into the corresponding cyclopropane. The reaction of levoglucosenone with MDA in refluxing benzene (48 h) afforded two stereoisomeric hexacyclic adducts containing two levoglucosenone molecules per molecule of MDA as the isolated reaction products.[5] Presumably, after mixing of the reactants, 1-pyrazoline **2** is formed first followed by its easy isomerization to 2-pyrazoline **3**. Its Michael addition to the second molecule of levoglucosenone is followed by the intramolecular cyclization through the reaction of the active methylene fragment with the carbonyl group. It is of note that the reaction of sulfur ylides with the enone fragment of levoglucosenone proceeds also in different ways. Thus the reaction with $Me_2S{=}CH_2$ involves the carbonyl group and is accompanied by the formation of an unsaturated oxirane,[6] whereas acyl ylides add to the C=C bond and give cyclopropanated ketones.[7,8]

Cyclopropane derivatives were also obtained by the reaction of 3-iodo-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one[9] with ethyl cyanoacetate or diethyl malonate in the presence of a strong base; the yields of cyclopropane derivatives of levoglucosenone were 70—80% (see Refs 10 and 11).

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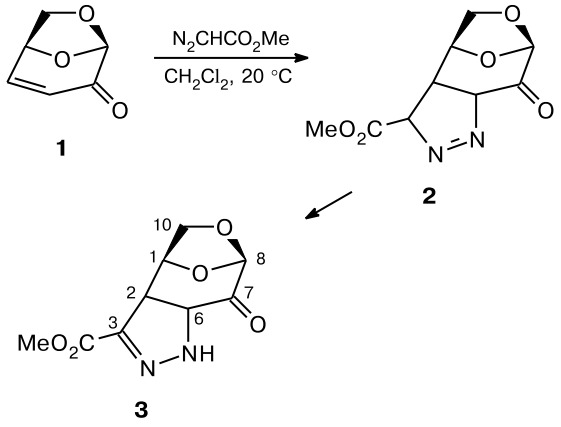
Results and Discussion

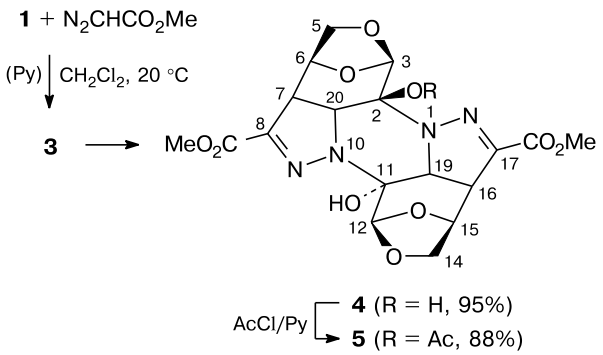
As was mentioned above, pyrazoline **3** formed in the reaction of levoglucosenone (**1**) with MDA cannot be isolated because of its reaction with the second molecule of **1**. To avoid (or, at least, considerably reduce) the aldol condensation of **3** with the starting levoglucosenone,[5] we studied the reaction of levoglucosenone with a 1.5—2-fold molar excess of MDA, the reaction being monitored by ^{1}H NMR spectroscopy. In a mixture of **1** and MDA kept in CH_2Cl_2 at ~20 °C for 1 h, two new sets of signals in the spectrum appear that belong to pyrazolines **2** and **3** in the ratio ~2 : 1. The conversion of levoglucosenone at this moment is ~30%. After 3.5 h, the conversion of **1** rises to 50—55% and the ratio of pyrazolines **2** and **3** changes to ~1 : 1 (Scheme 1). After 1 day, pyrazoline **3** is formed predominantly, however, this is accompanied by the appearance of "extra" signals in the spectrum. Pyrazoline **3** was isolated in ~58% yield using preparative TLC on SiO_2. The C(2)H and C(6)H methine protons are found at δ 3.71 and 4.50 in the ^{1}H NMR spectrum with vicinal spin-spin coupling constant $J_{2,6}$ equal to 11.2 Hz. It should be noted that the signal for the proton at the angular C(1) atom is shifted downfield as compared to the signal for the H(8) atom, which is apparently due to its deshielding by the ester substituent located in close proximity. In the ^{1}H NMR spectrum of pyrazoline **2**, the H(3) and H(6) atoms resonate at δ 5.35 and 5.86 and the vicinal spin-spin coupling constants $J_{2,3}$ and $J_{2,6}$ with the proton H(2) at δ 2.73 are equal to 9.0 and 9.8 Hz, respectively.

Scheme 1



When the reaction mixture was kept for longer time (for example, for 4 days), a decrease in intensity of the signals for pyrazoline **3** in the ^{1}H NMR spectrum and appearance of a double set of new signals of equal intensities was observed. It turned out that the compound with this set of signals is formed selectively and in high yield if 15—20 mol.% of pyridine is initially added to a mixture of levoglucosenone and MDA in CH_2Cl_2 and the mixture is kept for 2 days at ~20 °C. After the solvent and excess MDA were evaporated, a crystalline product was obtained, in which the ratio of the MDA and levoglucosenone fragments is 1 : 1. The ^{1}H and ^{13}C NMR spectra of this compound exhibit a double set of signals for these fragments (see Experimental); in the ^{13}C NMR spectrum, there are no low-field signals in the region of carbonyl group, while two signals of C atoms bearing no hydrogen atoms appear instead at δ ~100. All the spectral data indicate that the compound obtained has the heptacyclic structure **4** (Scheme 2) resulting from the dimerization of pyrazoline **3** through the double nucleophilic attack by the nitrogen atoms on two keto groups. These transformations result in a new six-membered heterocycle with conversion of the carbonyl groups to hydroxy groups. Different stereoisomers can be formed, however, compound **4** was obtained as a single isomer, which follows from the chromatographic homogeneity and the fact that the ^{1}H and ^{13}C NMR spectra of the products obtained after several crystallizations were identical. It thus follows that the addition of MDA to the double bond of **1** is highly selective and, as in the case of diazomethane,[5] the adduct with *exo*-orientation of the pyrazoline fragment is formed. This is inferred from the low spin-spin coupling constant ($J \leq 1$ Hz) of the vicinal bridgehead protons H(6), H(7) and H(15), H(16). The dimerization of pyrazoline **3** occurs also with high selectivity so that one of the arising OH groups is directed toward the anhydro bridge C(3)—O—C(5) and the other is directed toward the oxygen bridge C(12)—O—C(15) of the six-membered ring. This is the reason for the double set of signals in the ^{1}H and ^{13}C NMR spectra; the signals for the protons of the hydroxy groups in $CDCl_3$ resonate at δ 5.10 and 7.65.

Scheme 2



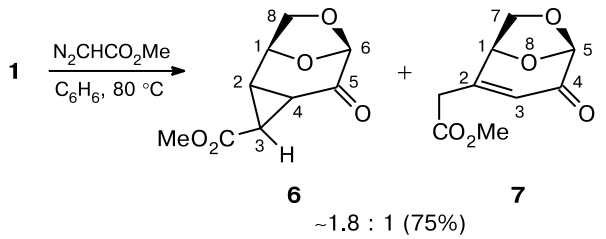
The nonequivalent spatial surroundings of the hydroxy groups is also confirmed by the results of acylation of compound **4**. Thus its treatment with a threefold molar excess of acetyl chloride in the presence of pyridine leads to the acetylation of only one hydroxy group to yield acetate **5**, in which it is the sterically hindered OH group

oriented toward the oxygen bridge that apparently remains unaffected. This is confirmed by a downfield shift of the proton at the C(20) atom in the ^{1}H NMR spectrum of acetate **5** by ~1 ppm as compared to the starting diol **4**, which results from its deshielding by the acetoxy substituent in the cisoid position to this proton. The EI mass spectrum of acetate **5** exhibits two fragments with *m/z* 226 and 268 resulting from the cleavage of the N(1)—C(2) and N(10)—C(11) bonds and differing only in the presence of OH and OCOMe substituents, respectively.

The reflux of a benzene solution of dimer **4** in the presence of acetic acid as a catalyst leads to its monomerization: after 1 h, the ^{1}H NMR spectrum of the reaction mixture indicates that it contains dimer **4** and pyrazoline **3** in the ratio ~1 : 1.5.

The character of chemical transformations is considerably different if levoglucosenone is added to a boiling benzene solution of MDA. In this case, neither pyrazoline **3** or its dimer **4**, nor a 2 : 1 adduct of levoglucosenone to MDA described earlier,[5] are virtually formed. Rather a ~1.8 : 1 mixture of methyl 5-oxo-7,9-dioxatricyclo-[4.2.1.0^{2,4}]nonane-3-carboxylate (**6**) and 2-(methoxycarbonylmethyl)-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (**7**), which is difficult to separate, was obtained in overall 75% yield (Scheme 3). Samples containing up to ~90% of each isomer were obtained using preparative TLC on SiO_2. It should be noted that the formation of cyclopropanes and substituted olefins is quite typical of thermal decomposition of 1-pyrazolines[12] and the presence of electron-withdrawing substituents in pyrazolines, as a rule, facilitates the process of denitrogenation. Apparently, in the thermal version of the reaction of levoglucosenone with MDA the initially forming 1-pyrazoline **2** much faster loses the nitrogen molecule giving compounds **6** and **7** than isomerizes to 2-pyrazoline **3**.

Scheme 3

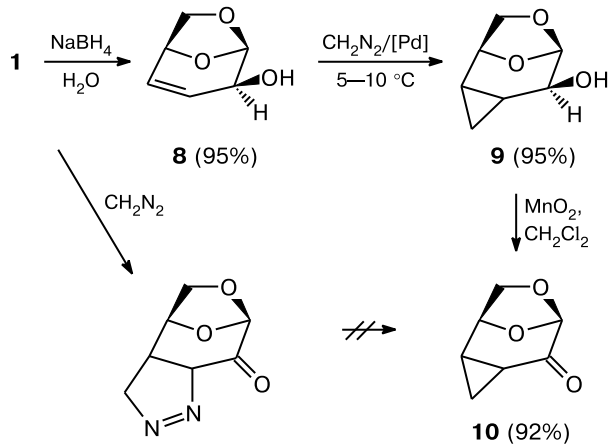


In the ^{1}H NMR spectrum of compound **6**, the signals for the protons of the cyclopropane ring are found at δ 2.04—2.54 and the spin-spin coupling constant $^3J_{3,2}$ = $^3J_{3,4}$ = 4.1 Hz corresponds to the *trans*-protons, which indicates the *anti*-orientation of the methoxycarbonyl substituent; the spin-spin coupling constant $^3J_{1,2}$, being near zero, indicates that the cyclopropane fragment is directed toward the oxygen atom of the six-membered ring. The ^{1}H and ^{13}C NMR spectra of compound **7**, instead of signals for the cyclopropane ring, exhibit signals characteristic of the CH_2—C=CH fragment, in which the protons of the methylene fragment are nonequivalent and resonate as two signals with the geminal spin-spin coupling constant of 16.3 Hz.

Since direct cyclopropanation of levoglucosenone by the catalytic decomposition of diazo compounds cannot be accomplished, we have reduced enone **1** to 6,8-dioxabicyclo[3.2.1]oct-2-en-4-ol (**8**) following a known scheme[13,14] and studied its reactions with diazomethane and methyl diazoacetate.

The addition of an ethereal solution of diazomethane (or passing of CH_2N_2 in a flow of nitrogen) to a solution of unsaturated alcohol **8** in CH_2Cl_2 containing a $Pd(OAc)_2$ or $Pd(acac)_2$ catalyst (0.5 mol.%) leads to 7,9-dioxatricyclo[3.2.1.0^{2,4}]nonan-5-ol (**9**) in high yield, in which the cyclopropane fragment is exclusively oriented toward the oxygen bridge.[8] The oxidation of this product with manganese dioxide affords the levoglucosenone cyclopropane derivative **10** in >90% yield (Scheme 4), which cannot be obtained by direct cyclopropanation of enone **1** or thermal denitrogenation of its adduct with diazomethane.

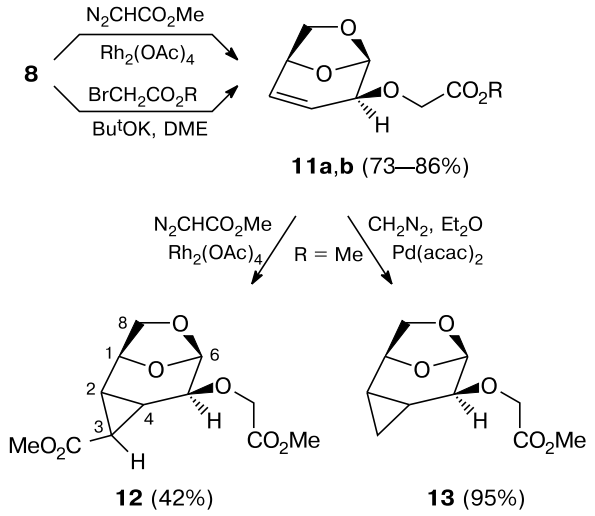
Scheme 4



In contrast to diazomethane, the decomposition of MDA in the presence of $Pd(OAc)_2$ at 25 °C gives no reaction products with unsaturated alcohol **8**, only the starting alcohol, dimethyl fumarate, and dimethyl maleate were found in the reaction mixture. When $Rh_2(OAc)_4$ is used instead of the palladium catalyst, MDA readily reacts with compound **8**, however, the denitrogenation of MDA is accompanied not by cyclopropanation of the double bond, but by insertion of methoxycarbonylcarbene[15,16a] into the O—H bond to form unsaturated ester **11a**, the yield of which reaches 86% (Scheme 5).

We also obtained esters **11** alternatively, *i.e.*, by the reaction of alcohol **8** with methyl (or ethyl) bromoacetate

Scheme 5



R = Me (**a**), Et (**b**)

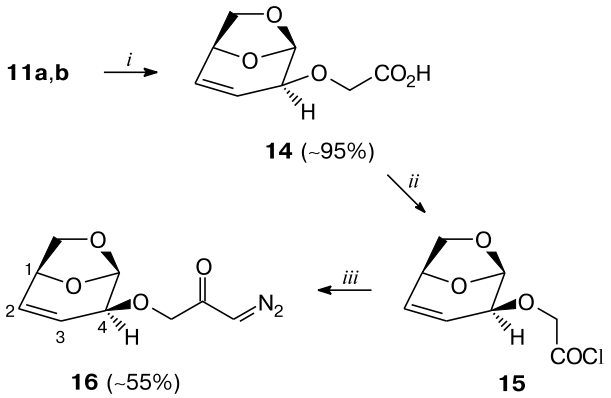
in the presence of a strong nonnucleophilic base, in particular, potassium *tert*-butoxide in dimethoxyethane. However, in this case the reaction is less efficient and esters **11a**,**b** are obtained in lower yields and purities, than in the generation of methoxycarbonylcarbene.

The ^{1}H and ^{13}C NMR spectra of compounds **11a**,**b** clearly trace the structure of unsaturated alcohol **8** with additional signals characteristic of the CH_2CO_2R fragment. And the protons of the methylene group due to their magnetic nonequivalence are found at δ_H 4.0—4.3 as two doublets with the spin-spin coupling constant of 16.4 Hz.

With compound **11a** as an example, we showed that using a fivefold excess of MDA in the presence of $Rh_2(OAc)_4$, cyclopropanation of the double bond can also be accomplished to afford diester **12** in ~42% yield (see Scheme 5). In this case, despite the large excess of MDA, the conversion of the starting compound **11a** is only ~50%. Dimethyl fumarate and dimethyl maleate are formed in the reaction, which makes the isolation of the target product difficult. In contrast to MDA, diazomethane easily cyclopropanates the double bond of **11a** in the presence of a palladium catalyst, for example $Pd(acac)_2$. The yield of 7,9-dioxatricyclo[4.2.1.0^{2,4}]nonane derivative **13** is no less than 95% (see Scheme 5) and the compound obtained can virtually be distilled *in vacuo* entirely. Both cyclopropanation reactions proceed stereospecifically and produce only one isomer. As in the preceding cases, the attack at the double bond occurs from the sterically less hindered side, *i.e.*, from the side of the oxygen atom of the six-membered ring ($^3J_{2,4}$ = 9.1 Hz; $^3J_{1,2}$ and $^3J_{4,5}$ are near zero) and in the case of compound **12**, the methoxycarbonyl group in the tricyclic fragment is in the *anti*-position, which is testified by the spin-spin coupling constant values for the protons of the cyclopropane ring $^3J_{trans} \approx {}^3J_{2,3} \approx {}^3J_{3,4} \approx 4.4$ Hz.

On heating in aqueous ethanolic solution of KOH and subsequent acidification to pH 2.5—3, esters **11a**,**b** are converted to 2-{6,8-dioxabicyclo[3.2.1]oct-2-en-4-yloxy}-acetic acid (**14**) in up to 95% yield. Acid **14** is not very stable in air and changes with time from a light orange oil to a dark viscous mass. Despite the fact that the majority of levoglucosenone derivatives are sensitive to HCl, which opens the dioxolane ring,[14,17] we succeeded in the transformation of acid **14** to acyl chloride **15** on treatment with oxalyl chloride in the presence of a catalytic amount of pyridine; one-pot reaction with excess of an ethereal solution of diazomethane and chromatography on silica gel afforded diazoketone **16** in moderate yield with the dioxabicyclo[3.2.1]octene fragment remaining intact (Scheme 6).

Scheme 6



Reagents and conditions: *i.* 1) KOH, EtOH/H_2O, 2) HCl, H_2O; *ii.* $(COCl)_2$, Et_3N, C_6H_6/DME; *iii.* CH_2N_2, Et_2O.

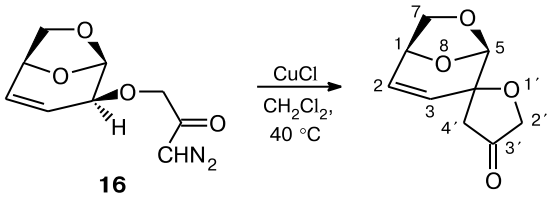
The ^{1}H and ^{13}C NMR spectra of compounds **14** and **16** with allowance for the change in the nature of the functional groups very much resemble the corresponding spectra of ester **11a**. In diazoketone **16**, the signals for the CHN_2 fragment are observed at δ_H 5.88 and δ_C 53.4, whereas in the ^{14}N NMR spectrum, two signals for the nitrogen atoms of the diazo group are at δ_N −119 and −10.

Further, we have studied decomposition of diazoketone **16** in CH_2Cl_2 in the presence of various catalysts. Dilute solutions were used to make intramolecular transformations predominant over intermolecular processes. It turned out that $Rh_2(OAc)_4$ in catalytic amounts does not virtually decompose diazoketone **16** even in boiling CH_2Cl_2. Dirhodium tetrakis(trifluoroacetate) proved to be a more active catalyst, however, it brings about nonselective decomposition of the diazoketone and a mixture of nonidentified compounds was obtained.

For the directed decomposition of diazoketone **16**, copper compounds proved to be the most suitable catalysts.

For instance, the reflux of diazoketone **16** in CH_2Cl_2 in the presence of a freshly prepared cuprous chloride leads to its denitrogenation and intramolecular insertion[16b,18] of a transient carbene into the C(4)—H bond to furnish 1′,6,8-trioxaspiro[bicyclo[3.2.1]oct-2-en-4,5′-cyclopentan-3′-one] (**17**) in up to 55% yield (Scheme 7). A similar reaction takes place also in the presence of cupric acetylacetonate, however, the process is less efficient, and spirane **17** is obtained in ≤40% yield.

Scheme 7



16 **17** (55%)

Compound **17** was isolated by preparative TLC on SiO_2, its structure was confirmed by the ^1H and ^{13}C NMR and mass spectral data. Thus in the ^1H NMR spectrum the signal at δ 4.32 related to the proton at C(4) in the starting diazoketone **16** disappears with simultaneous simplification of the signals for the H(3) and H(5) protons. In the five-membered ring of spirane **17** formed, the signals for the protons of the methylene fragments are found in different regions of the spectrum and have different multiplicity: the low-field signal for the OCH_2 fragment resonates as a singlet, whereas the signal for the protons at C(4′), appears as two doublets with the spin-spin coupling constant ^2J of 18.7 Hz.

In conclusion, we synthesized and described a number of levoglucosenone derivatives including those with a fused cyclopropane fragment in the molecule and developed procedures for their synthesis. A possibility of intramolecular carbene-type transformations of levoglucosenone diazocarbonyl derivative with the formation of new spirane structure has been demonstrated. In all the cases, an efficient face discrimination due to the presence of the anhydro bridge and influence of the acetal oxygen atoms provides high regio- and stereoselectivity of the reactions described, which in most cases give rise to only one isomer.

Experimental

^1H, ^{13}C, and ^{14}N NMR spectra were recorded on a Bruker AVANCE II 300 spectrometer (300, 75.5 and 21.7 MHz, respectively) for solutions in $CDCl_3$ or DMSO-d_6 containing 0.05% Me_4Si as the internal standard. Mass spectra were recorded on a Finnigan MAT INCOS-50 (EI, 70 eV, direct inlet) and Finnigan LCQ (ESI) instruments. Optical rotation was measured on a Perkin-Elmer 341 polarimeter at 20 °C (λ 589 nm, a 2.5-cm cuvette). Thin-layer chromatography was performed on Silicagel 60 plates (Merck), visualization of compounds was made by the iodine vapor. For preparative separations, column or plate chromatography was used (silica gel 60, 0.040—0.063 mm, Merck) with the ratio of compound : sorbent being equal to ~1 : 100. Levoglucosenone[3,4] (96% purity) and 6,8-dioxabicyclo[3.2.1]oct-2-en-4-ol (**8**)[12,13] were synthesized according to the described procedures. Solvents of chemically pure grade (>99.5%) were used in the work without additional purification. Copper(I) chloride was precipitated from its hydrochloric acid solution by dilution with distilled water, filtered off under argon, sequentially washed with acetone and CH_2Cl_2, and dried in a vacuum desiccator.

3-Methoxycarbonyl-4,5-diaza-9,11-dioxatricyclo-[6.2.1.0^{2,6}]undec-3-en-7-one (3). Methyl diazoacetate (0.24 g, 2.4 mmol) was added to a solution of levoglucosenone (**1**) (0.19 g, 1.5 mmol) in CH_2Cl_2 (4 mL) and this was left for 4 days at room temperature, monitoring the reaction course by ^1H NMR spectroscopy. After evaporation of the solvent *in vacuo*, pyrazoline **3** (0.20 g, 58%) was isolated by preparative TLC on SiO_2 (benzene—AcOEt, 1 : 3, R_f 0.6) with 95% purity as a colorless oily liquid. MS *m/z* (I_{rel} (%)): 226 (8) $[M]^+$, 195 (6) $[M - OMe]^+$, 152 (76), 139 (33), 95 (100), 59 (32). ^1H NMR ($CDCl_3$), δ: 3.71 (dd, 1 H, H(2), $J_{2,6}$ = 11.2 Hz, $J_{1,2}$ = 1.0 Hz); 3.88 (s, 3 H, OMe); 4.02 (dd, 1 H, *exo*-H(10), ^2J = 7.7 Hz, ^3J = 4.7 Hz); 4.11 (dd, 1 H, *endo*-H(10), ^2J = 7.7 Hz, ^3J = 1.0 Hz); 4.50 (dd, 1 H, H(6), $J_{2,6}$ = 11.2 Hz, $J_{6,8}$ 1.0 Hz); 5.16 (br.s, 1 H, H(8)); 5.60 (br.d, 1 H, H(1), $J_{1,10}$ = 4.7 Hz); 6.96 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 49.7 (C(2)); 52.6 (OMe); 62.6 (C(6)); 68.8 (C(10)); 71.7 (C(1)); 99.4 (C(8)); 141.3 (C(3)); 162.9 (COO); 198.4 (C=O). When aliquots were taken after 1 and 3.5 h, the ^1H NMR spectra showed the presence (along with signals for 2-pyrazoline **3**) of the signals related to 1-pyrazoline **2** ($CDCl_3$), δ: 2.73 (br.dd, 1 H, H(2), $J_{2,3}$ = 9.0 Hz and $J_{2,6}$ = 9.8 Hz); 3.93 (s, 3 H, OMe); 3.90 (2 H(10), overlapped with the same-type signals for levoglucosenone); 4.84 (br.d, 1 H, H(1), $J_{1,10}$ = 4.4 Hz); 5.18 (d, 1 H, H(8), $J_{6,8}$ ≈ 2.0 Hz); 5.35 (H(3), partially overlapped with the signal for levoglucosenone); 5.86 (dd, 1 H, H(6), $J_{2,6}$ = 9.8 Hz, $J_{6,8}$ = 2.0 Hz).

Dimethyl 2,11-dihydroxy-1,9,10,18-tetraaza-4,13,21,22-tetraoxaheptacyclo[9.7.1.1^{2,7}.1^{3,6}.1^{12,15}.0^{10,20}.0^{16,19}]docosa-8,17-diene-8,17-dicarboxylate (4). Methyl diazoacetate (320 mg, 3.2 mmol) and pyridine (25 mg, 0.3 mmol) were added to a solution of levoglucosenone (203 mg, 1.6 mmol) in anhydrous benzene (5 mL) and this was left for 2 days at room temperature. Then, the solvent was evaporated *in vacuo* and the residue was recrystallized from CCl_4 to yield colorless fine crystalline powder (343 mg, 95%) of compound **4** with admixture of 2-pyrazoline **3** (~4%), m.p. 127—129 °C. Found (%): C, 47.42; H, 4.56; N, 12.06. $C_{18}H_{20}N_4O_{10}$. Calculated (%): C, 47.79; H 4.46; N, 12.39. MS (ESI, $CHCl_3$/MeOH), *m/z* (I_{rel} (%)): 453 (5) $[M + H]^+$, 227 (100) $[M/2 + H]^+$. ^1H NMR ($CDCl_3$), δ: 3.32 (ddd, 1 H, H(7), $J_{7,20}$ = 10.8 Hz, J ≈ 1.2 Hz); 3.48 (ddd, 1 H, H(16), $J_{16,19}$ = 12.0 Hz, J ≈ 0.9 Hz); 3.83 and 3.87 (both s, 3 H each, 2 OMe); 3.85 (dd, 1 H, *endo*-H(14), ^2J = 7.9 Hz, ^3J = 1.6 Hz); 3.90 (dd, 1 H, *exo*-H(5), ^2J = 7.6 Hz, ^3J = 4.8 Hz); 3.93 (dd, 1 H, *exo*-H(14), ^2J = 7.9 Hz, ^3J = 6.1 Hz); 4.01 (br.d, 1 H, *endo*-H(5), ^2J = 7.6 Hz); 4.32 (d, 1 H, H(19), ^3J = 12.0 Hz); 4.61 (d, 1 H, H(20), $J_{7,20}$ = 10.8 Hz); 4.99 (br.dd, 1 H, H(15), ^3J = 6.1 Hz, ^3J = 1.6 Hz); 5.24 (br.s, 1 H, H(12)); 5.26 (d, 1 H, H(3), $J_{3,6}$ = 1.2 Hz); 5.56 (br.d, 1 H, H(6),

^3J = 4.8 Hz); 5.10 and 7.65 (both br.s, 1 H each, 2 OH). ^{13}C NMR ($CDCl_3$), δ: 47.8 and 49.6 (C(7) and C(16)); 52.2 and 52.7 (2 OMe); 65.1 and 67.8 (C(19) and C(20)); 68.6 and 69.3 (C(5) and C(14)); 70.3 and 70.6 (C(6) and C(15)); 97.6 and 99.7 (C(2) and C(11)); 99.5 and 100.2 (C(3) and C(12)); 140.3 and 145.9 (C(8) and C(17)); 161.7 and 162.7 (2 COO).

Dimethyl 2-acetoxy-11-hydroxy-1,9,10,18-tetraaza-4,13,21,22-tetraoxaheptacyclo[9.7.1.1^{2,7}.1^{3,6}.1^{12,15}.0^{10,20}.0^{16,19}]-docosa-8,17-diene-8,17-dicarboxylate (5). Acetyl chloride (47 mg, 0.6 mmol) and pyridine (47 mg, 0.6 mmol) were added to a solution of dimer **4** (91 mg, 0.2 mmol) in CH_2Cl_2 (5 mL) and this was stirred for 6 h at 20 °C. The reaction mixture was quenched with water, extracted twice with CH_2Cl_2, dried with anhydrous $MgSO_4$, and concentrated *in vacuo*. After recrystallization from diethyl ether, acetate **5** was obtained (87 mg, 88%) as colorless crystals, m.p. 93—94 °C. Found (%): C, 48.21; H, 4.26. $C_{20}H_{22}N_4O_{11}$. Calculated (%): C, 48.59; H 4.49. MS, *m/z* (I_{rel} (%)): 326 (2), 283 (6), 268 (11), 226 (20), 194 (75), 152 (100). ^{1}H NMR ($CDCl_3$), δ: 2.35 (s, 3 H, Me); 3.37 (d, 1 H, H(16), ^3J = 12.3 Hz); 3.46 (dt, 1 H, H(7), ^3J = 10.4 Hz, J = 1.2 Hz); 3.78 (dd, 1 H, *exo*-H(5) or *exo*-H(14), ^2J = 8.0 Hz, ^3J = 1.8 Hz); 3.86 and 3.92 (both s, 3 H each, 2 OMe); 3.91 (m, 2 H, *exo*-H(5) or *exo*-H(14) and *endo*-H(5) or *endo*-H(14)); 4.02 (d, 1 H, *endo*-H(5) or *endo*-H(14), ^2J = 8.0 Hz); 4.45 (d, 1 H, H(19), ^3J = 12.3 Hz); 4.93 (br.d, 1 H, H(15), ^3J = 6.0 Hz); 5.11 (br.s, 1 H, OH); 5.27 and 5.31 (both s, 1 H each, H(3) and H(12)); 5.43 (d, 1 H, H(20), ^3J = 10.4 Hz); 5.52 (br.d, 1 H, H(6), ^3J = 4.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 22.3 (Me); 48.9 and 49.6 (C(7) and C(16)); 52.6 and 53.0 (2 OMe); 61.1 and 66.8 (C(19) and C(20)); 68.3 and 69.0 (C(5) and C(14)); 70.0 and 70.5 (C(6) and C(15)); 96.2 (C(11)); 99.9 (C(2)); 100.0 and 101.0 (C(3) and C(12)); 145.1 and 145.9 (C(8) and C(17)); 162.0 and 162.1 (2 COO).

3-Methoxycarbonyl-7,9-dioxatricyclo[4.2.1.0^{2,4}]nonan-5-one (6) and 2-(2-methoxy-2-oxoethyl)-6,8-dioxabicyclo-[3.2.1]oct-2-en-4-one (7). A solution of levoglucosenone (**1**) (101 mg, 0.8 mmol) and methyl diazoacetate (480 mg, 4.8 mmol) in benzene (8 mL) was refluxed for 20 h under argon. Then, the reaction mixture was concentrated *in vacuo* and the residue was passed through a column with SiO_2 eluting with diethyl ether to obtain a colorless oily liquid (119 mg, 75%), which was a 1.8 : 1 mixture of compounds **6** and **7** (^{1}H NMR data). The mixture obtained was separated by preparative TLC on SiO_2 with three-fold development (benzene—AcOEt, 4 : 1) to yield compound **7** (24 mg) with R_f = 0.27 and compound **6** (45 mg) with R_f = 0.32 (the content of the major isomer in each of them was ~90%), as well as a fraction with approximately the same ratio of compounds **6** and **7** as in the starting mixture.

Compound **6**. MS, *m/z* (I_{rel} (%)): 198 (3) $[M]^+$, 170 (9), 155 (19), 124 (17), 111 (31), 95 (29), 83 (73), 59 (58), 39 (100). ^{1}H NMR ($CDCl_3$), δ: 2.04 (ddd, 1 H, H(2), $J_{2,4}$ = 7.9 Hz, $J_{2,3}$ = 4.1 Hz, $J_{1,2}$ = 1.4 Hz); 2.30 (br.dd, 1 H, H(4), $J_{2,4}$ = 7.9 Hz, $J_{3,4}$ = 4.1 Hz); 2.54 (t, 1 H, H(3), J_{trans} = 4.1 Hz); 3.74 (s, 3 H, OMe); 3.92 (dd, 1 H, *exo*-H(8), ^2J = 7.1 Hz, ^3J = 4.7 Hz); 4.08 (d, 1 H, *endo*-H(8), ^2J = 7.1 Hz); 4.90 (br.d, 1 H, H(1), $J_{1,8a}$ = 4.7 Hz); 5.01 (br.s, 1 H, H(6)). ^{13}C NMR ($CDCl_3$), δ: 22.1, 22.5 and 22.6 (C(2), (C(3) and C(4)); 52.5 (OMe); 68.4 (C(8)); 70.7 (C(1)); 99.7 (C(6)); 170.8 (COO); 193.6 (C(5)).

Compound **7**. MS, *m/z* (I_{rel} (%)): 198 (8) $[M]^+$, 170 (67), 153 (28), 138 (22), 124 (59), 110 (80), 81 (83), 59 (100), 39 (100). ^{1}H NMR ($CDCl_3$), δ: 3.40 and 3.48 (both dd, 1 H each, CH_2, ^2J = 16.4 Hz, ^4J = 1.2 Hz); 3.76 (s, 3 H, OMe); 3.90 (dd, 1 H, *endo*-H(7), ^2J = 7.1 Hz, J = 1.0 Hz); 3.96 (dd, 1 H, *exo*-H(7), ^2J = 7.1 Hz, ^3J = 4.7 Hz); 5.04 (br.d, 1 H, H(1), J = 4.7 Hz); 5.36 (d, 1 H, H(5), J = 1.5 Hz); 5.97 (m, 1 H, H(3)). ^{13}C NMR ($CDCl_3$), δ: 37.4 (CH_2); 52.7 (OMe); 67.3 (C(7)); 75.0 (C(1)); 100.1 (C(5)); 125.3 (C(3)); 156.0 (C(2)); 169.0 (COO); 188.8 (C(4)).

7,9-Dioxatricyclo[4.2.1.0^{2,4}]nonan-5-ol (9). An ethereal solution of diazomethane (0.56 *M*, 268 mL, 0.15 mol) was added dropwise to a solution of 6,8-dioxabicyclo[3.2.1]oct-2-en-4-ol (**8**) (10.2 g, 0.08 mol) and $Pd(acac)_2$ (49 mg, 0.16 mmol) in CH_2Cl_2 (50 mL) at 0—5 °C with gentle stirring over 30 min and stirring was continued for another 1 h. Then, the reaction mixture was filtered, the solvent was evaporated, and the residue distilled *in vacuo* to yield compound **9** (10.8 g, 95%) as colorless needle-like crystals hygroscopic in air, b.p. 41—42 °C (0.03 Torr), m.p. 48—49 °C, $[\alpha]_D^{20}$ −90.0° (*c* 0.54; $CHCl_3$). Found (%): C, 59.12; H, 7.22. $C_7H_{10}O_3$. Calculated (%): C, 59.14; H, 7.10. MS, *m/z* (I_{rel} (%)): 96 (51) $[M - H_2O - CO]^+$; 95 (52); 67 (100); 55 (51); 41 (85); 39 (89). ^{1}H NMR ($CDCl_3$), δ: 0.60 (m, 2 H, C(3)H_2); 0.83 and 1.02 (both m, 1 H each, H(2) and H(4)); 2.33 (d, OH, J = 11.6 Hz); 3.69 (dd, 1 H, H(5), $J_{5,6}$ = 3.5 Hz, J = 11.6 Hz); 3.82 (dd, 1 H, *exo*-H(8), $J_{1,8\text{-}exo}$ = 4.1 Hz, ^2J = 6.7 Hz); 4.01 (d, 1 H, *endo*-H(8), ^2J = 6.7 Hz); 4.62 (d, 1 H, H(1), $J_{1,8\text{-}exo}$ = 4.1 Hz); 5.16 (d, 1 H, H(6), $J_{5,6}$ = 3.5 Hz). ^{13}C NMR ($CDCl_3$), δ: 6.6 (C(3)); 13.4 and 14.8 (C(2) and C(4)); 67.1 (C(1)); 70.9 (C(8)); 71.3 (C(5)); 99.6 (C(6)).

7,9-Dioxatricyclo[4.2.1.0^{2,4}]nonan-5-one (10). Freshly prepared activated manganese dioxide was added in excess (10—11 g) to a solution of 7,9-dioxatricyclo[4.2.1.0^{2,4}]nonan-5-ol (**9**) (0.50 g, 3.5 mmol) in CH_2Cl_2 (50 mL) and this was stirred for 20 h at room temperature. Solids were filtered off, washed with ethyl acetate (30 mL) and the solvents were evaporated *in vacuo*. The product was purified by column chromatography on SiO_2 (eluent, benzene : AcOEt, 7 : 1) to yield ketone **10** (0.45 g, 92%) as a colorless oil. MS, *m/z* (I_{rel} (%)): 140 (12) $[M]^+$, 113 (18) $[M - C_2H_3]^+$, 94 (69), 83 (45), 66 (100), 55 (94), 39 (83). ^{1}H NMR ($CDCl_3$), δ: 1.16 (ddd, 1 H, *anti*-H(3), ^2J = 4.8 Hz, $^3J_{cis}$ = 7.6 Hz and 9.9 Hz); 1.43 (dt, 1 H, *syn*-H(3), ^2J = 4.8 Hz, $^3J_{trans}$ = 5.0 Hz); 1.58 and 1.71 (both m, 1 H each, H(2) and H(4)); 3.88 (dd, 1 H, *exo*-H(8), ^2J = 6.8 Hz, $J_{1,8\text{-}exo}$ = 4.7 Hz); 4.03 (d, 1 H, *endo*-H(8), ^2J = 6.8 Hz); 4.77 (d, 1 H, H(1), $J_{1,8\text{-}exo}$ = 4.7 Hz); 4.95 (s, 1 H, H(6)). ^{13}C NMR ($CDCl_3$), δ: 9.1 (C(3)); 14.8 and 20.0 (C(2) and C(4)); 68.5 (C(8)); 71.3 (C(1)); 99.9 (C(6)), 197.4 (C=O).

4-(Methoxycarbonylmethoxy)-6,8-dioxabicyclo[3.2.1]oct-2-ene (11a). ***Method A.*** A $Rh_2(OAc)_4$ catalyst (68 mg, 0.15 mmol) was added to a solution of 6,8-dioxabicyclo[3.2.1]oct-2-en-4-ol (**8**) (9.61 g, 0.075 mol) in CH_2Cl_2 (230 mL) followed by a dropwise addition of a solution of methyl diazoacetate (15.0 g, 0.15 mol) in CH_2Cl_2 (30 mL) with stirring at 20 °C over 3 h. The reaction mixture was stirred for another 1 h, concentrated *in vacuo* to 2/3 of the original volume, and passed through a short layer of silica gel. The solvent was evaporated and the residue was distilled *in vacuo* to yield ester **11a** (12.9 g, 86%) as a colorless oily liquid, b.p. 109—112 °C (0.03 Torr), $[\alpha]_D^{20}$ −23.5° (*c* 0.39; $CHCl_3$). Found (%): C, 53.70; H, 5.87. $C_9H_{12}O_5$. Calculated (%): C, 54.00; H, 6.04. MS, *m/z* (I_{rel} (%)): 200 (2) $[M]^+$, 155 (12), 127 (12), 97 (21), 81 (90), 39 (100). ^{1}H NMR ($CDCl_3$), δ: 3.76 (s, 3 H, OMe); 3.78 (br.dd, 1 H, *exo*-H(7),

^2J = 6.5 Hz, ^3J = 4.1 Hz); 3.94 (br.d, 1 H, *endo*-H(7), ^2J = 6.5 Hz); 4.28 and 4.30 (both d, 1 H each, OCH_2, ^2J = 16.5 Hz); 4.36 (m, 1 H, H(4)); 4.68 (dd, 1 H, H(1), $J_{1,2} \approx J_{1,7a}$ = 4.1 Hz); 5.65 (br.dd, 1 H, H(5), $J_{4,5} \approx J_{3,5}$ = 2.3 Hz); 5.78 (ddd, 1 H, H(3), $J_{2,3}$ = 9.8 Hz, $J_{3,4} \approx J_{3,5}$ = 2.3 Hz); 6.08 (ddd, 1 H, H(2), $J_{2,3}$ = 9.8 Hz, $J_{1,2}$ = 4.1 Hz, $J_{2,4}$ = 1.1 Hz). ^{13}C NMR ($CDCl_3$), δ: 51.3 (OMe); 65.5 (OCH_2); 70.8 (C(7)); 70.9 (C(1)); 76.6 (C(4)); 99.7 (C(5)); 125.2 (C(3)); 131.5 (C(2)); 170.3 (COO).

Method B. A solution of potassium *tert*-butoxide (0.30 g, 2.6 mmol) and unsaturated alcohol **8** (0.31 g, 2.4 mmol) in anhydrous dimethoxyethane (4 mL) was stirred under argon for 30 min, then a solution of methyl bromoacetate (0.38 g, 2.5 mmol) in dimethoxyethane (1 mL) was added and this was stirred for another 2 h. A precipitate formed was filtered off, washed with $CHCl_3$ (2×5 mL), the filtrate was concentrated *in vacuo*, and the residue was separated by column chromatography on SiO_2 (benzene—AcOEt, 1 : 1) to yield compound **11a** (0.36 g, 75%) as a colorless oil identical to the sample obtained by method ***A***.

4-Ethoxycarbonylmethoxy-6,8-dioxabicyclo[3.2.1]oct-2-ene (11b). This was prepared as a liquid similarly to the preceding experiment (*method **B***), from alcohol **8** (10.2 g, 0.08 mol), ethyl bromoacetate (15.0 g, 0.09 mol), and Bu^tOK (10.1 g, 0.09 mol). The residue was distilled *in vacuo* to yield compound **11b** (12.5 g, 73%) as a colorless oil, b.p. 118—121 °C (0.03 Torr), $[\alpha]_D^{20}$ −22.1° (*c* 0.39; $CHCl_3$). Found (%): C, 55.80; H, 6.79. $C_{10}H_{14}O_5$. Calculated (%): C, 56.07; H, 6.59. MS, *m/z* (I_{rel} (%)): 214 (58) $[M]^+$, 169 (12), 127 (22), 81 (100). ^{1}H NMR ($CDCl_3$), δ: 1.29 (t, 3 H, Me, J = 7.1 Hz); 3.79 (ddd, 1 H, *exo*-H(7), ^2J = 6.6 Hz, ^3J = 4.2 Hz, J = 1.3 Hz); 3.96 (br.d, 1 H, *endo*-H(7), ^2J = 6.6 Hz); 4.21 and 4.27 (both d, 1 H each, OCH_2, J = 16.5 Hz); 4.23 (q, 2 H, $COOCH_2$, J = 7.1 Hz); 4.38 (m, 1 H, H(4)); 4.67 (dd, 1 H, H(1), $J_{1,2} \approx J_{1,7\text{-}exo}$ = 4.2 Hz); 5.69 (dd, 1 H, H(5), $J_{4,5}$ = 2.4 Hz, $J_{3,5}$ = 2.2 Hz); 5.78 (ddd, 1 H, H(3), $J_{2,3}$ = 9.9 Hz, $J_{3,4} \approx J_{3,5}$ = 2.2 Hz); 6.17 (ddd, 1 H, H(2), $J_{2,3}$ = 9.9 Hz, $J_{1,2}$ = 4.2 Hz, $J_{2,4}$ = 1.4 Hz). ^{13}C NMR ($CDCl_3$), δ: 14.3 (Me); 61.1 ($COO\underline{C}H_2$); 66.4 (OCH_2); 71.5 (C(7)); 71.6 (C(1)); 77.3 (C(4)); 100.4 (C(5)); 126.0 (C(3)); 131.9 (C(2)); 170.6 (C=O).

3-Methoxycarbonyl-5-methoxycarbonylmethoxy-7,9-dioxatricyclo[4.2.1.0^{2,4}]nonane (12). A $Rh_2(OAc)_4$ catalyst (5.5 mg, 0.012 mmol) was added to a solution of compound **11a** (0.50 g, 2.5 mmol) in CH_2Cl_2 (10 mL), followed by a slow addition of methyl diazoacetate (1.20 g, 12 mmol) in CH_2Cl_2 (3 mL) over 3 h with stirring. The reaction mixture was stirred for another 2 h at 30 °C, then, passed through a short layer of silica gel, the sorbent was washed with CH_2Cl_2 (2 mL), and the eluate was concentrated *in vacuo*. The residue was separated by column chromatography on SiO_2 (eluent, benzene—AcOEt, 1 : 1). The starting **11a** (0.22 g, ~45%) and compound **12** (0.29 g, 42%) as a colorless oil were isolated. ^{1}H NMR ($CDCl_3$), δ: 1.63 (ddd, 1 H, H(4), $J_{2,4}$ = 9.1 Hz, $J_{3,4}$ = 4.4 Hz, $J_{4,6}$ = 1.5 Hz); 1.69 (br.dd, 1 H, H(2), $J_{2,4}$ = 9.1 Hz, $J_{2,3}$ 4.4 Hz); 1.80 (dd, 1 H, H(3), $J_{2,3} \approx J_{3,4}$ = 4.4 Hz); 3.63 (d, 1 H, H(5), $J_{5,6}$ = 3.1 Hz); 3.70 and 3.77 (both s, 3 H each, 2 OMe); 3.86 (dd, 1 H, *exo*-H(8), ^2J = 7.1 Hz, $J_{1,8\text{-}exo}$ = 4.1 Hz); 4.14 (d, 1 H, *endo*-H(8), ^2J = 7.1 Hz); 4.23 and 4.29 (both d, 1 H each, OCH_2, ^2J = 16.6 Hz); 4.65 (br.d, 1 H, H(1), $J_{1,8\text{-}exo}$ = 4.1 Hz); 5.40 (br.dd, 1 H, H(6), $J_{5,6}$ = 3.1 Hz, $J_{4,6}$ = 1.5 Hz). ^{13}C NMR ($CDCl_3$), δ: 20.3 (C(4)); 22.0 (C(3)); 24.3 (C(2)); 51.92 and 51.96 (2 OMe); 66.3 (OCH_2); 70.2 (C(1)); 70.6 (C(8)); 74.6 (C(5)); 98.1 (C(6)); 170.4 and 172.8 (2 COO).

5-Methoxycarbonylmethoxy-7,9-dioxatricyclo[4.2.1.0^{2,4}]nonane (13). An ethereal solution of diazomethane (0.57 *M*, 158 mL, 0.09 mol) was added to a stirred solution of compound **11a** (10.0 g, 0.05 mol) and $Pd(acac)_2$ (76 mg, 0.25 mmol) in dichloromethane (60 mL) at 0—5 °C over 2 h and this was stirred for another 1 h. The reaction mixture was filtered through a short layer of alumina, the solvents were evaporated, and the residue was distilled *in vacuo* of an oil pump to obtain compound **13** (10.1 g, 95%) as a colorless oily liquid, b.p. 121—125 °C (0.01 Torr), $[\alpha]_D^{20}$ −41.2° (*c* 0.39; $CHCl_3$). Found (%): C, 56.45; H, 6.85. $C_{10}H_{14}O_5$. Calculated (%): C, 56.07; H, 6.59. MS, *m/z* (I_{rel} (%)): 168 (5) $[M - H_2O - CO]^+$; 95 (40), 78 (100), 67 (40). ^{1}H NMR ($CDCl_3$), δ: 0.48 (dt, 1 H, *syn*-H(3), ^2J = 4.9 Hz, $J_{trans} \approx$ 5.0 Hz); 0.69 (dd, 1 H, *anti*-H(3), ^2J = 4.9 Hz, J_{cis} = 7.8 Hz and 9.4 Hz); 0.96 and 1.02 (both m, 1 H each, H(2) and H(4)); 3.55 (d, 1 H, H(5), $J_{5,6}$ = 3.1 Hz); 3.77 (s, 3 H, OMe); 3.85 (dd, 1 H, *exo*-H(8), $J_{1,8\text{-}exo}$ = 4.1 Hz, ^2J = 6.7 Hz); 4.11 (d, 1 H, *endo*-H(8), ^2J = 6.7 Hz); 4.25 and 4.27 (both d, 1 H each, OCH_2, ^2J = 16.6 Hz); 4.61 (br.d, 1 H, H(1), $J_{1,8\text{-}exo}$ = 4.1 Hz); 5.35 (dd, 1 H, H(6), $J_{5,6}$ = 3.1 Hz, $J_{4,6}$ = 1.3 Hz). ^{13}C NMR ($CDCl_3$), δ: 7.1 (C(3)); 10.2 and 14.7 (C(2) and C(4)); 51.9 (OMe); 66.4 (OCH_2); 71.1 (C(8)); 71.3 (C(1)); 76.1 (C(5)); 98.2 (C(6)); 170.8 (COO).

4-Methoxycarbonyl-6,8-dioxabicyclo[3.2.1]oct-2-ene (14). Ester **11b** (10.1 g, 47 mmol) was added to an aqueous ethanolic (1 : 1) solution of KOH (0.8 *M*, 200 mL) and this was refluxed for 3 h. Ethanol was evaporated on a rotary evaporator, the residue was washed with CH_2Cl_2 (3×50 mL), the aqueous layer was acidified with 10% aq. hydrochloric acid to pH 2.5—3, the solution was half-concentrated *in vacuo*, and repeatedly extracted with ethyl acetate (8×80 mL). The combined organic extracts were dried no less than for 3 h with anhydrous $MgSO_4$, then the solvent was evaporated on a rotary evaporator, and the residue was dried *in vacuo* of 0.01 Torr to obtain acid **14** (8.39 g, 96%) with ~95% purity as a light orange oil, which darkens in air. MS, *m/z* (I_{rel} (%)): 141 (6) $[M - COOH]^+$, 127 (3) $[M - CH_2COOH]^+$, 111 (4) $[M - OCH_2COOH]^+$, 102 (9), 81 (100), 53 (46). ^{1}H NMR ($CDCl_3$), δ: 3.80 (ddd, 1 H, *exo*-H(7), ^2J = 6.6 Hz, $J_{1,7\text{-}exo}$ = 4.2 Hz, J = 1.1 Hz); 3.97 (d, 1 H, *endo*-H(7), ^2J = 6.6 Hz); 4.26 and 4.34 (both d, 1 H each, OCH_2, ^2J = 16.8 Hz); 4.42 (m, 1 H, H(4)); 4.69 (dd, 1 H, H(1), $J_{1,2} \approx J_{1,7\text{-}exo}$ = 4.2 Hz); 5.68 (br.dd, 1 H, H(5), $J_{4,5}$ = 2.4 Hz, $J_{3,5}$ = 2.2 Hz); 5.75 (ddd, 1 H, H(3), $J_{2,3}$ = 9.9 Hz, $J_{3,4} \approx J_{3,5}$ = 2.2 Hz); 6.21 (ddd, 1 H, H(2), $J_{2,3}$ = 9.9 Hz, $J_{1,2}$ = 4.2 Hz, J = 1.4 Hz); 8.70 (br.s, 1 H, COOH). ^{13}C NMR ($CDCl_3$), δ: 64.6 (OCH_2); 70.9 (C(7)); 71.1 (C(1)); 76.5 (C(4)); 99.8 (C(5)); 125.1 (C(3)); 131.6 (C(2)); 174.3 (COO).

4-(3-Diazo-2-oxopropoxy)-6,8-dioxabicyclo[3.2.1]oct-2-ene (16). A solution of acid **14** (0.97 g, 5.2 mmol) in a mixture of anhydrous benzene and dimethoxyethane (3 : 1, 30 mL) was added dropwise to a solution of distilled oxalyl chloride (0.66 g, 5.2 mmol) in anhydrous benzene (15 mL) containing pyridine (1 drop) with stirring under dry nitrogen at 18 °C over 30 min and this was stirred for 2.5 h. Then a solution of triethylamine (0.51 g, 5 mmol) in anhydrous benzene (3 mL) was added to the reaction mixture at 0 °C over 10 min and the mixture obtained was added dropwise without filtration to a stirred ethereal solution of diazomethane (25 mL, ~15 mmol) at 0 °C over 30 min. The mixture was stirred for an additional 1 h at 20 °C,

a precipitate formed was filtered off and the solvents were evaporated *in vacuo*. The oily red residue was extracted with Et_2O (3×20 mL), the combined extracts were concentrated *in vacuo*, and the residue was purified by column chromatography on SiO_2 (eluent, Et_2O) to yield diazo ketone **16** (0.61 g, ~55%) with ~95% purity as a yellow oil. MS, *m/z* (I_{rel} (%)): 182 (1.5) $[M - N_2]^+$, 137 (14), 108 (26), 95 (43), 81 (100), 78 (79), 55 (98). ^{1}H NMR ($CDCl_3$), δ: 3.80 (ddd, 1 H, *exo*-H(7), ^2J = 6.6 Hz, $J_{1,7\text{-}exo}$ = 4.2 Hz, J = 1.1 Hz); 3.96 (d, 1 H, *endo*-H(7), ^2J = 6.6 Hz); 4.14 and 4.21 (both d, 1 H each, OCH_2, ^2J = 15.9 Hz); 4.32 (m, 1 H, H(4)); 4.68 (dd, 1 H, H(1), $J_{1,2} \approx J_{1,7\text{-}exo}$ = 4.2 Hz); 5.61 (dd, 1 H, H(5), $J_{4,5}$ = 2.4 Hz, $J_{3,5}$ = 2.2 Hz); 5.71 (ddd, 1 H, H(3), $J_{2,3}$ = 9.8 Hz, $J_{3,4} \approx J_{3,5}$ = 2.2 Hz); 5.88 (br.s, 1 H, HCN_2); 6.19 (ddd, 1 H, H(2), $J_{2,3}$ = 9.8 Hz, $J_{1,2}$ = 4.2 Hz, J = 1.5 Hz). ^{13}C NMR ($CDCl_3$), δ: 53.4 (CN_2); 71.4 (C(1)); 71.5 (C(7)); 72.5 (OCH_2); 77.6 (C(4)); 99.9 (C(5)); 125.3 (C(3)); 131.1 (C(2)); 193.4 (C=O). ^{14}N NMR ($CDCl_3$), δ: –119.0 (=N); –9.7 (HC=N).

1′,6,8-Trioxaspiro[bicyclo[3.2.1]oct-2-ene-4,4′-cyclopentan-3′-one] (17). Freshly prepared CuCl (5 mg) was added to a solution of diazo ketone **16** (21 mg, 0.1 mmol) in CH_2Cl_2 (10 mL) and this was refluxed for 1 h. Then, the reaction mixture was filtered, the solvent was evaporated *in vacuo*, and the oily residue obtained was separated by preparative TLC on SiO_2 (eluent, AcOEt) to yield compound **17** (10 mg, 55%) as a colorless oil, R_f = 0.79. MS, *m/z* (I_{rel} (%)): 181 (2) $[M - H]^+$, 153 (2), 137 (27), 86 (60), 84 (100), 79 (44). ^{1}H NMR ($CDCl_3$), δ: 2.48 and 2.70 (both d, 1 H each, H(4′), ^2J = 18.7 Hz); 3.82 (dd, 1 H, *exo*-H(7), ^2J = 6.6 Hz, $J_{1,7\text{-}exo}$ = 4.1 Hz); 3.96 (d, 1 H, *endo*-H(7), ^2J = 6.6 Hz); 4.14 (br.s, 2 H, H(2′)); 4.71 (dd, 1 H, H(1), $J_{1,7\text{-}exo}$ = 4.1 Hz, $J_{1,2}$ = 4.3 Hz); 5.39 (d, 1 H, H(5), $J_{3,5}$ = 2.3 Hz); 5.74 (dd, 1 H, H(3), $J_{2,3}$ = 10.0 Hz, $J_{3,5}$ = 2.3 Hz); 6.17 (dd, 1 H, H(2), $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.3 Hz). ^{13}C NMR ($CDCl_3$), δ: 45.4 (C(4′)), 70.4 and 70.6 (C(7) and C(2′)), 71.6 (C(1)), 76.2 (C(4)), 102.5 (C(5)), 128.2 (C(2)); 130.6 (C(3)); 212.9 (C=O).

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