Autoassembly of cage structures
7.* Lactonization of methylene-bis-tartronates and methylene-bis-hydroxymethylmalonates

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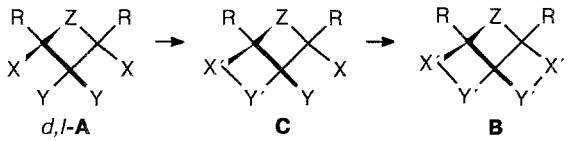
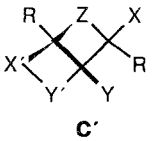
Methylene-bis-tartronates and methylene-bis-hydroxymethylmalonates form monolactones where the CO_2R and OH (or CH_2OH) groups are known to be *cis*-oriented. However, attempts to prepare the corresponding dilactones failed due to the unsufficient proximity of these functional groups. The results have been confirmed by NMR spectra.

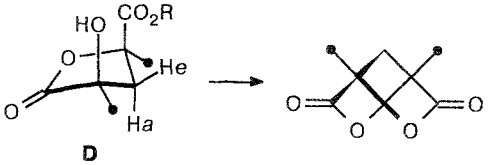
Key words: methylene-bis-tartronates, monolactones of methylene-bis-tartronic and methylene-bis-hydroxymethylmalonic acids, conformation, ^1H and ^{13}C NMR spectra.

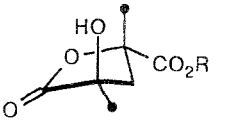
It was found previously that bicyclic systems **B** are formed only from *d,l*-forms of systems of type **A**, since the *meso*-form of **A** yields monocyclic structure C, which is incapable of repeated cyclization due to the *trans* mutual arrangement of the X and Y groups.[2–5]

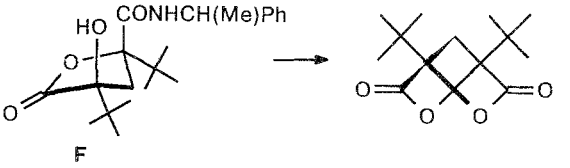


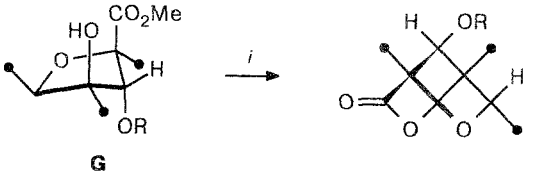


A necessary condition for preparing bicyclic systems **B** is either separation of the *d,l*- and *meso*-forms of the starting compound or stereospecific synthesis of the *d,l*-**A** or **C**. The latter has been carried out by us using monocyclic structures **C** with X = CN, Y = OH, Z = CH_2, R = Bu^t as examples.[4] The present work deals with directed synthesis of monolactones of type **C** with R = X = CO_2H or CO_2R, Y = OH or CH_2OH. In fact, there is no difference between forms **C** and **C'**, and the X and Y substituents are known to have *cis*-orientation. However, in this case, it is difficult to predict the possibility of repeated cyclization of monolactone to dilactone of type **B**. On the one hand, it is known that in monolactones **D** and **E** the conformations with pseudo-*a*-orientation of the OH group are populated preferentially, in conformity with the lower conformational energy of this group compared to the Me and CO_2R groups,[6] and therefore, monolactone **D** is readily con-









i. 1,8-Diazabicyclo[5.4.0]undec-7-ene, R = $MeOCH_2$

* For the previous paper in the series see Ref. 1.

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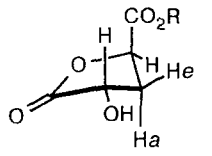
verted into dilactone.[2] Repeated lactonization of lactone amide **F** occurs even more easily,[7] since in this compound the bulkier *tert*-butyl groups "force out" the functional groups to axial positions (according to X-ray diffraction analysis, the O atom of the OH group and the carbonyl C atom of the CON group are brought together to a distance of ~3.2 Å).[8]

Lactonization of the key intermediate of the stereoselective synthesis of mycotoxins **G**, whose conformation at R = H has been determined by X-ray diffraction analysis (the O atom of the OH group and the carbonyl C atom of the CO_2Me group are brought together to a distance of ~2.7 Å), also occurs with quantitative yield.[9] On the other hand, in the case of monolactone H, the conformation with the pseudo-*e*-orientation of the OH group is unexpectedly realized.[3]



R = H, Me

H

We showed that treatment of methylene-bis-*O*-benzoyltartronate (1)[10] with an alcoholic alkali followed by acidification yields a mixture of methylene-bis-tartronic acid (**2**) and monolactones (**3** and **4**) in a ratio of 2.5 : 5 : 1 (according to the ^{1}H NMR spectrum) (Scheme 1). The products were characterized by NMR spectra, and hydroxylactone **3** was isolated in the individual state. Treatment of a mixture of **2**, **3**, and **4** with diazomethane gave the corresponding methyl esters **2a**, **3a**, and **4a**, which were isolated and characterized (Scheme 1).

Monolactone **3a** was prepared from methylene-bis-tartronate **2a** in quantitative yield, by heating **2a** at ~250 °C (15 min) or by boiling it with TsOH in toluene (45 min). The reverse transformation occurs during acid-catalyzed methanolysis.

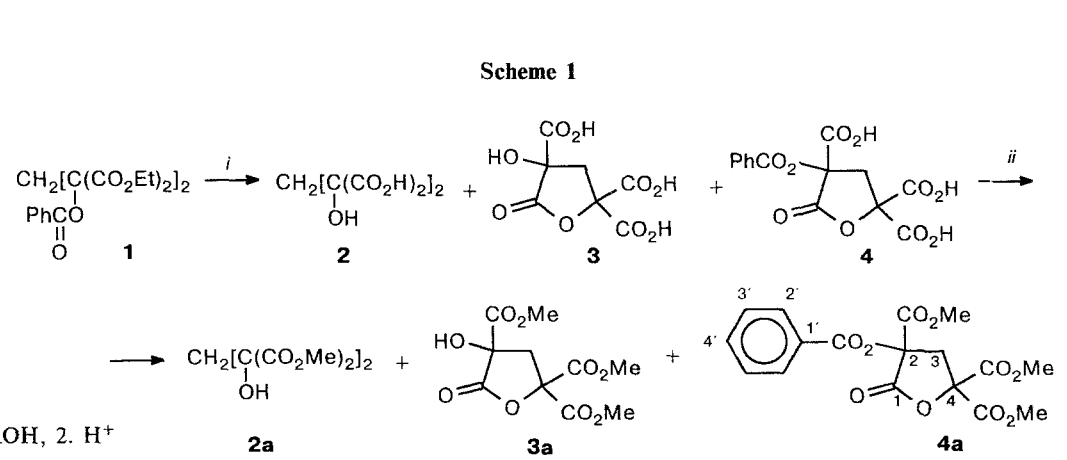
Monolactone **3a** is distilled *in vacuo* unchanged and does not undergo subsequent lactonization under the action of dry HCl in ether (3 days at 20 °C), when stored over Amberlyst-15 in benzene (30 days at 20 °C), when boiled with TsOH in toluene (20 h) or in *o*-xylene with a Dean—Stark distillation head (12 h), or upon heating. Dilactone also cannot be obtained from monolactone **3** under the action of dicyclohexylcarbodiimide in pyridine or under conditions of thermolysis (~250 °C; in this case, the reaction yields a mixture of unidentified products containing unsaturated compounds, probably products of dehydration and decarboxylation).

The fact that repeated lactonization of monolactones **3** and **3a** does not occur can be explained by the decrease in the nucleophilicity of the hydroxyl group owing to the two neighboring electron-withdrawing carbonyl groups and by the insufficient proximity of the reactive sites (OH and CO_2H or CO_2R). In fact, the ^{13}C NMR spectra of monolactones **3** and **3a** exhibit a triplet for the 3-CH_2 methylene carbon atom, whereas for similar monolactones with a fixed envelope conformation, where the protons at C-3 have pseudo-*a* and -*e* orientations, this signal is a doublet of doublets.[3,4] Thus, in the case of **3** and **3a**, due to the slight difference between the conformational energies of the substituents, rapid interconversion of the ring, rather than a fixed conformation, occurs. This is also confirmed by equalization of the spin-spin coupling constants $^3J_{CH}$ of the carbonyl C atoms of the CO_2H and CO_2Me groups with the 3-CH_2 group protons and by the fact that the spin-spin coupling constant $^4J_{HH}$ of the hydroxyl proton with pseudo-*a*-H at C(3), which is observed for lactones with a fixed conformation of type **D**,[4,8] is equal to zero.

In view of the limitations on repeated lactonization of monolactones **3** and **3a** considered above, we studied bis-homologs of dihydroxy tetraesters **2a**, *viz.*, methylene-bis-hydroxymethylmalonates, the hydroxyl groups of which should possess increased nucleophilicity. In addition, it is known that bis-aza analogs of these compounds readily form bicycles: aminomethylation of methylene-bis-malonates gives the corresponding dilactams in high yields.[11]

Hydroxymethylation of malonic systems, specifically, ethylene-bis-malonate, followed by mono- and dilac-

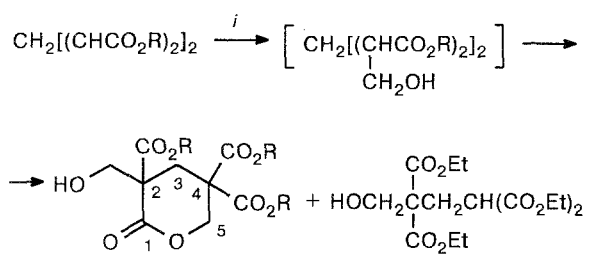
Scheme 1



i. 1. KOH/ROH, 2. H^+
ii. CH_2N_2

tonization has been studied by Piskov.[12] However, the author used a strong base, EtONa, as the catalyst, under the action of which methylene-bis-malonate decomposes. Therefore, we carried out purely chemical reproduction of the known electrochemical synthesis of monolactones of methylene-bis-hydroxymethylmalonates.[13] We prepared methyl and ethyl esters **5a,b** by hydroxymethylation of methylene-bis-malonates[14] with formaldehyde in alcohols in the presence of AcOK (Scheme 2).

Scheme 2



5a: R = Me
5b: R = Et

6

i. CH_2O/ROH/AcOK

The structure of monolactones **5a,b** was confirmed by IR and NMR spectra. Compound **5a** was identified by comparing with the specimen prepared as described in Ref. 12.

The expected increase in the nucleophilicity of the OH group in methylene-bis-hydroxymethylmalonates compared to that in tartronates **2**, **2a** is manifested in their spontaneous monolactonization. However, compounds **5a,b** did not undergo repeated lactonization under the action of dry HCl in ether (7 days at ~20 °C) or of Amberlyst-15 in benzene (30 days at 20 °C), on prolonged boiling with TsOH in toluene, or during vacuum distillation. In the latter case, lactone **5b** affords a mixture of malonic and methylenemalonic esters (which were identified by the ^1H NMR spectrum).

In order to elucidate the reasons why monolactones **5a,d** do not undergo lactonization, we studied their conformation by NMR spectroscopy. The signals for methylene protons in the ^1H NMR spectra of lactones **5a,b** were assigned by comparison with lactone **5a** and model compounds described previously.[13] A typical feature of these spectra (Fig. 1) is that the long-range spin-spin coupling constant $^4J_{HH}$ (which was not observed by Elinson *et al*[13]) is present for just one proton of each of the methylene groups at C(3) and C(5). Moreover, the spectrum does not change when a solution of **5a** in toluene-d_8 is heated to 100 °C. This indicates that the six-membered ring in this compound exists in a fixed conformation with an orientation of these protons close to *W*.

The signals in the ^{13}C NMR spectrum of compounds **5a,b** were assigned using selective heteronuclear double resonance. The following feature of these spectra, which is significant for conformational analysis, has been identified. The signal for the 2′ carbon atom of the CH_2OH group is a triplet of doublets ($^1J_{CH}$ = 149.0; $^3J_{CH_a}$ = 5.1 Hz); the small spin-spin coupling constant $^3J_{CH_a}$ disappears in the case of selective proton decoupling from H_a, which has the long-range constant $^4J_{HH}$, but is retained under conditions of proton decoupling from H_b. This implies that the dihedral angle C(2′)—C(2)—C(3)—H_b should be close to 90°. The two conditions, *viz.* the presence of the spin-spin interaction ^4J of the H_a proton with H_f and with the C(2′) carbon atom and the absence of the spin-spin interaction between C(2′) and H_b, are satisfied only in the case of the

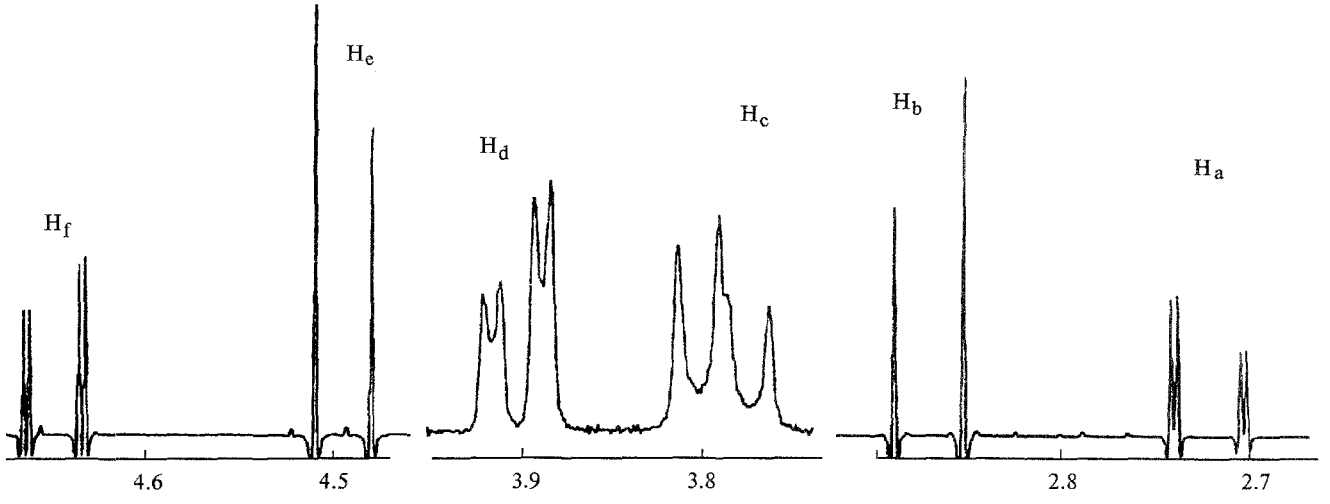
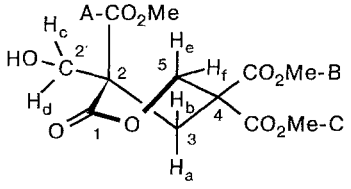
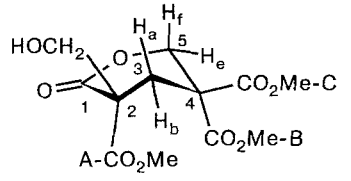


Fig. 1. ^1H NMR spectrum of the ring protons of monolactone **5a** in C_6D_6 recorded under the conditions of narrowing of lines at various amplifications.

conformation of a somewhat distorted boat (**I**). The arrangement of H_a and H_f protons in this conformation is close to a planar *W* orientation and the dihedral angle C(2′)—C(2)—C(3)—H_b is close to 90°. At first glance it would seem that the half-boat conformation **J** fits these requirements. However, in this conformation, the C(2′) atom is orthogonal to the proton at C(3) that has a perfect *W* arrangement with the proton at C(5).



I



J

It is easy to see that the CO_2Me-C and $HOCH_2$ functional groups in conformation **I** are widely separated, which accounts for the fact that these compounds do not undergo repeated lactonization.

Experimental

The NMR spectra were recorded on a Bruker WM-400 spectrometer (400.13 MHz for ^1H and 100.62 MHz for ^{13}C) in $CDCl_3$ using TMS as the internal standard. Electron impact (EI) mass spectra were obtained on a VG 7070E instrument at an ionizing potential of 70 eV with direct injection of the sample into the ion source; IR spectra were measured on a UR-20 spectrophotometer in $CHCl_3$. Melting points were determined on a Boetius PHMK-0.5 hot-stage apparatus at a heating rate of 4—5 °C min^{-1}.

Hydrolysis of methylene-bis-benzoyloxymalonate. a. A solution of KOH (3.96 g, 60 mmol) in 30 mL of 95 % EtOH was added to a solution of methylene-bis-benzoyloxymalonate[10] (5.72 g, 10 mmol) in 420 mL of the same solvent, and the mixture was held at 20 °C for 3 days. The mixture, which turned yellow, was evaporated, ethyl benzoate was extracted with Et_2O (200 mL), and the residue was diluted with ether, and then 20 mL of conc. HCl was carefully added to it. The mixture was extracted with ether (8×150 mL), the extract was concentrated to half its volume, the precipitated $PhCO_2H$ was filtered off, and the mother liquor was dried with $MgSO_4$ and evaporated to dryness to give 2.53 g of a mixture of methylene-bis-tartronic (**2**), 2-hydroxy-γ-butyrolactone-2,4,4-tricarboxylic (**3**), and 2-benzoyloxy-γ-butyrolactone-2,4,4-tricarboxylic (**4**) acids in a ratio of 2.5 : 5 : 1 (according to ^1H NMR). ^1H NMR (CD_3OD), δ, **2**: 2.97 (s, CH_2); **3**: 3.08 (dd, AB, 2 H, CH_2, Δν = 212, $^2J_{AB}$ = −14.3 Hz); **4**: 3.53 (dd, AB, 2 H, CH_2, Δν = 228, $^2J_{AB}$ = −15 Hz), 7.45 (t, 2 H, H-3, ^3J = 8.2 Hz), 7.61 (t, 1 H, H-4, ^3J = 8.2 Hz), 8.06 (d, 2 H, H-2, ^3J = 8.2 Hz). The mixture of acids (2.45 g) was dissolved in 30 mL of MeOH, and 50 mL of ether was added. The mixture was filtered, treated with an ethereal solution of CH_2N_2 until the yellow color no longer vanished, and evaporated, and the residue was dried *in vacuo* to give 2.15 g of a mixture comprised of **2a**, **3a**, and **4a** in a ratio of 2.5 : 5 : 1. The mixture was dissolved in 50 mL of anhydrous benzene with heating and allowed to stand for 1 h, and the precipitated crystals were isolated by filtration to give 0.68 g (22 %) of tetramethyl methylene-bis-tartronate (**2a**), identical to that described previously.[10]

The mother liquor was evaporated to dryness, and the residue was extracted with hot ether (3×50 mL). Concentration of the extract followed by vacuum distillation gave 2-hydroxy-2,4,4-tris-methoxycarbonyl-γ-butyrolactone (**3a**) as a colorless viscous liquid, yield 0.85 g (30.8 %), b.p. 205—210 °C (3 Torr), IR ($CHCl_3$), ν/cm^{-1}: 1445, 1760 vs (C=O); 1810 (ring C=O); 2945—3025 (CH); 3500 (OH). ^1H NMR, δ: 3.16 (dd, AB, 2 H, CH_2, Δν = 180, $^2J_{AB}$ = −14.3 Hz); 3.87 (s, 3 H, MeO^1); 3.89 (s, 3 H, MeO^2); 3.9 (s, 3 H, MeO^3); 4.0 (s, 1 H, HO). ^{13}C NMR, δ: 40.03 (t, 3-CH_2, ^1J = 140.6 Hz); 53.66 (q, MeO, ^1J = 149 Hz), 53.69 (q, MeO, ^1J = 149 Hz), 53.79 (q, MeO, ^1J = 149 Hz), 75.5 (dd, C-2, ^2J = 2.2 and 6.2 Hz), 82.03 (t, C-4, ^2J = 3.3 Hz), 165.7 (m, 2-CO_2, $^3J_{Me}$ = 3.7 Hz), 166 (m, 4-CO_2, $^3J_{Me}$ = 3.7 Hz), 168.63 (m, 4-CO_2, $^3J_{Me}$ = 3.7 Hz), 170.3 (dd, 1-CO, ^3J = 3.3 and 4.7 Hz). MS, *m/z* (I_{rel} (%), EI, 70 eV at 20 °C): $[M]^+$ is absent; 233 (12.9), 214 (10.3), 201 (10.2), 189 (11.3), 174 (12.4), 173 (12), 172 (19.1), 171 (19.7), 162 (12.8), 161 (13.3), 160 (11.1), 159 (15.9), 155 (16.2), 149 (17.4), 148 (25.1), 147 (27.4), 146 (51.9), 145 (57), 144 (14.4), 143 (23.1), 141 (10.2), 134 (10.6), 133 (12.3), 132 (11.1), 131 (10.7), 130 (14.6), 129 (25.1), 127 (11.9), 118 (12.6), 117 (15.3), 116 (32.3), 115 (32.4), 114 (53.1), 113 (100), 105 (21), 104 (15), 103 (17), 102 (31.6), 101 (38.4), 91 (18.2), 89 (11), 88 (17.2), 87 (28.3), 85 (12), 77 (15.4), 71 (13.9), 69 (21.7), 62 (11.5), 61 (11), 60 (30), 59 (89.5), 57 (13.9), 55 (41), 45 (20.2), 44 (35.6), 43 (48.7), 42 (28.7).

The residue was extracted with ether, and 2-benzoyloxy-2,4,4-tris-methoxycarbonyl-γ-butyrolactone (**4a**) was isolated as white lustrous crystals, yield 0.34 g (9 %), m.p. 126—127 °C. IR ($CHCl_3$), ν/cm^{-1}: 1450, 1605 (Ph), 1760 vs (C=O), 1815 (ring C=O), 2950—3030 (CH). ^1H NMR, δ: 3.52 (dd, AB, 2 H, CH_2, Δν = 228, $^2J_{AB}$ = −15 Hz), 3.85, 3.87, and 3.93 (s, 3 H, MeO), 7.48 (t, 2 H, H-3, ^3J = 8.2 Hz), 7.63 (t, 1 H, H-4, ^3J = 8.2 Hz), 8.08 (d, 2 H, H-2, ^3J = 8.2 Hz). ^{13}C NMR, δ: 38.99 (dd, 3-CH_2, J = 140 and 143.9 Hz), 53.86 (q, MeO, ^1J = 148.2 Hz), 54.04 (q, MeO, ^1J = 148.2 Hz), 54.09 (q, MeO, ^1J = 148.2 Hz), 78.75 (dd, C-2, ^2J = 3 and 6.5 Hz), 82.39 (dd, C-4, ^2J = 1.4 and 4.3 Hz), 127.46 (t, C-1′, ^2J = 8 Hz), 128.52 (dd, C-2′,6′, ^1J = 160 and ^2J = 10 Hz), 130.06 (dt, C-3′,5′, ^1J = 162 and ^2J = 7 Hz), 134.24 (dt, C-4′, ^1J = 162.8 and ^2J = 8 Hz), 164.64 (t, Ph-C=O, ^3J = 4.3 Hz), 164.93 (qt, *e*-2-CO, ^3J = 4.3 and 4.3 Hz), 165.65 (qdd, *a*-4-CO, ^3J = 4.3, 2.9, and 6.2 Hz), 166 (q.t, *e*-4-CO, ^3J = 4.3 and 4.3 Hz), 166.35 (dd, 1-CO, ^3J = 1.4 and 5.1 Hz).

b. A solution of KOH (3.12 g, 47.2 mmol) in a mixture of MeOH (18 mL) and H_2O (4 mL) was added to a solution of methylene-bis-benzoyloxymalonate[10] (3 g, 5.24 mmol) in 70 mL of MeOH and 10 mL of H_2O, and the mixture was held at 20 °C for 2 days and concentrated. 30 mL of Et_2O and 13 mL of conc. HCl were added. The mixture was extracted

with ether (2×30 mL), and the extract was concentrated to give 1.22 g of $PhCO_2H$ (95.3 %). To the aqueous solution, 200 mL of CH_3CN was added, the precipitated KCl was separated by filtration, the mother liquor was evaporated to dryness, 50 mL of dry CH_3CN was once again added, and the mixture was once again evaporated. The residue (0.94 g) was a viscous liquid, which partially crystallized when it was stored at 20 °C for 3 weeks. The product was washed with dry CH_3CN (2×30 mL) and dried *in vacuo* to give 0.3 g of crystals of 2-hydroxy-γ-butyrolactone-2,4,4-tricarboxylic acid **3** as colorless needles, m.p. 97—99 °C. Evaporation of CH_3CN from the mother liquor yielded an additional 0.6 g of product **3** as a viscous liquid. ^{13}C NMR (CD_3OD), δ: 41.88 (t, 3-CH_2, ^1J = 140.2 Hz), 77.05 (dd, C-2, ^2J = 1.8 and 4.7 Hz), 83.76 (br.s, C-4), 168.88 (t, 2-CO_2, ^3J = 4 Hz), 169.33 (t, 4-CO_2, ^3J = 4 Hz), 171.56 (t, 4-CO_2, ^3J = 3.3 Hz), 173.3 (dt, 1-CO, ^3J = 3.3 and 4.3 Hz).

2-Hydroxy-2,4,4-tris-methoxycarbonyl-γ-butyrolactone (3a). a. Tetramethyl methylene-bis-tartronate **2a** (0.15 g, 0.49 mmol) was heated in the open flame of a burner for 15 min. The residue was extracted with 20 mL of ether, and Et_2O was evaporated to give 0.12 g (89 %) of **3a** as a colorless viscous liquid.

b. A mixture of tetramethyl methylene-bis-tartronate **2a** (0.07 g, 0.23 mmol) and $TsOH \cdot H_2O$ (0.08 g, 42 mmol) in 20 mL of toluene was boiled for 45 min. After filtration and concentration of the mixture, compound **3a** was detected in the residue by ^1H NMR spectroscopy.

Tetramethyl methylene-bis-tartronate (2a). A mixture of 2-hydroxy-2,4,4-tris-methoxycarbonyl-γ-butyrolactone **3a** (0.21 g, 0.76 mmol) and TsOH (0.14 g, 0.74 mmol) in 10 mL of MeOH was kept at 20 °C for 3 days. Then the mixture was evaporated to dryness, and the residue was recrystallized from benzene to give 0.21 g (90 %) of **2a** as white lamellar crystals, m.p. 141 °C. (*cf.* Ref. 10).

2-Hydroxymethyl-2,4,4-tris-methoxycarbonyl-δ-valerolactone (5a). Paraform (0.5 g, 16.67 mmol) and AcOK (0.77 g, 7.85 mmol) were added to a solution of tetramethyl methylene-bis-malonate (2.17 g, 7.86 mmol) in 30 mL of anhydrous MeOH. The mixture was heated until the reactants completely dissolved (3 min) and allowed to stand at 20 °C for 4 days. The solvent was evaporated, and the residue was extracted with ether (2×100 mL). The extract was concentrated *in vacuo* to give 2.2 g of an oily residue. Gradient chromatography of the residue (0.8 g) on a column (2×6.5 cm) with silica gel (40—100 μm, using *n*-hexane—AcOEt mixtures (0—25% AcOEt) as eluents) yielded 0.25 g of the product as an oil, which crystallized from a solution in 3 mL of Et_2O after storing in a refrigerator. 0.2 g of lactone **5a** as colorless needle crystals was isolated, m.p. 91 °C (*cf.* Ref. 13). IR (CCl_4), ν/cm^{-1}: 1750 and 1766 (sh) (vs, C=O), 2960 (CH), 3560 (br, w, HO). ^1H NMR (C_6H_6), δ: 2.8 (m, 2 H, 3-CH_2, Δν = 60, $^2J_{ab}$ = −15.0, $^4J_{af}$ = 1.2 Hz), 3.15 (s, 3 H, MeO), 3.16 (s, 3 H, MeO), 3.21 (s, 3 H, MeO), 3.5 (m, 1 H, *e*-HO), 3.84 (m, 2 H, CH_2OH, Δν = 44, $^2J_{cd}$ = −11.3, $^3J_{ce}$ = 9, $^3J_{de}$ = 3.8 Hz), 4.57 (m, 2 H, 5-CH_2, Δν = 64, $^2J_{ef}$ = −12.2, $^4J_{fa}$ = 1.2 Hz). ^{13}C NMR (C_6D_6), δ: 31.54 (ddt, 3-CH_2, ^1J = 136.6 and 138.8, $^3J_{CH_f}$ = 5.8, $^3J_{CH_e}$ = 2.9, $^3J_{CH_{c,d}}$ = 2.7 Hz), 52.68 (m, C-4, $^2J_{CH}$ = 4.4 Hz), 53.04 q, 53.31 q, 53.47 q (MeO, ^1J = 148.2 Hz), 54.73 (m, C-2, $^2J_{CH}$ = 4.4 Hz), 66.71 (td, CH_2OH, ^1J = 149.0, $^3J_{CH_a}$ = 5.1 Hz), 68.5 (ddd, 5-CH_2, $^1J_{CH}$ = 155.5 and 158.4, $^3J_{CH_a}$ = 2.9, $^3J_{CH_b}$ = 1.5 Hz), 168.66 (m, A-CO, $^3J_{COCH}$ = 3.6, $^3J_{CH_a}$ = 5.1, $^3J_{CH_b}$ = 3.6 Hz), 169.4 (m, C-CO, $^3J_{COCH}$ = 3.6, $^3J_{CH}$ = 5.1 and 2.9 Hz), 169.85 (m, 3 1-CO, $^3J_{CH_f}$ = 5.8, $^3J_{CH_b}$ = 5.1, $^3J_{CH_e}$ = 4.4 Hz), 170.25 (m, B-CO, $^3J_{COCH}$ = 3.6, $^3J_{CH}$ = 5.1, 4.4, and 2.9 Hz). ^{13}C NMR spectrum of **5a** in $CDCl_3$ refined by Elinson *et al*[13]: 31.2 (t, CH_2), 52.36 (s, C), 53.4 (q), 53.7 (q), 53.9 (q, MeO), 54.19 (s, C), 66.6 (t, CH_2OH), 68.3 (t, CH_2O), 168.3 (s), 170 (s), 170.1 (s), 170.3 (s, C=O).

2-Hydroxymethyl-2,4,4-tris-ethoxycarbonyl-δ-valerolactone (5b). A mixture of paraform (0.65 g, 21.67 mmol) and anhydrous AcOK (0.7 g, 7.13 mmol) in 50 mL of anhydrous EtOH was heated for 3 min until the reactants completely dissolved. Tetraethyl methylene-bis-malonate (3.32 g, 10 mmol) was added to the resulting solution, and the mixture was kept at 20 °C for 66 h. Then the mixture was concentrated, and the residue was extracted with ether (2×70 mL). Evaporation of the extract *in vacuo* gave 3.04 g (88 %) of light-yellow oil, which was a mixture (1 : 1) of **5b** and the product of monohydroxymethylation, *viz.* α-hydroxymethylmethylene-bis-malonate [^1H NMR (CD_3OD) δ: 1.25 (t, 12 H, Me_3, J = 7 Hz), 2.55 (d, 2 H, CH_2, ^3J = 6 Hz), 3.63 (t, H, CH), 4.14 (q, 8 H, CH_2O)]. Gradient chromatography as described in the previous procedure gave 1.2 g (34.7 %) of **5b** as a yellow oil. IR (CCl_4), ν/cm^{-1}: 1770 (vs, C=O), 2910—3050 (CH), 3550 (vw, OH). ^1H NMR, δ: 1.25, 1.26, and 1.27 (three t, 9 H, 3 Me, ^3J = 7.5 Hz), 2.68 (m, 2 H, 3-CH_2, ABX, Δν = 42, $^2J_{AB}$ = −15, $^4J_{af}$ = 1.4 Hz), 2.9 (br.s, 1 H, *e'*-*e*-OH), 3.88 (m, 2 H, CH_2OH, AB, Δν = 56, $^2J_{cd}$ = −11.3 Hz), 4.26—4.42 (m, 6 H, 3 CH_2O), 4.56 (m, 2 H, 5-CH_2, ABX, Δν = 130.7, $^2J_{ef}$ = −12.2, $^4J_{fa}$ = 1.4 Hz). ^{13}C NMR, δ: 13.12 (q, Me, ^1J = 126.4 Hz), 13.13 (q, 2 Me, ^1J = 126.4 Hz), 30.16 (ddm, 3-CH_2, ^1J = 137 and 138.1, ^2J = 2.2 Hz), 51.62 (s, C-4), 53.67 (s, C-2), 60.81; 61.58 (t, 2 CH_2O, ^1J = 149.0 Hz), 62.04 (t, CH_2O, ^1J = 149.7 Hz), 65.42 (td, CH_2OH, ^1J = 149, ^3J = 5.1 Hz), 67.4 (dd, C-5, ^1J = 155.5 and 157 Hz), 167.21; 167.55; 168.56 and 168.9 (m, 3 CO and C-1).

Attempt to prepare dilactone from 2-hydroxymethyl-2,4,4-tris-methoxycarbonyl-δ-valerolactone 5a. Monolactone **5b** was distilled *in vacuo* to give 0.15 g of a colorless liquid, b.p. 70—75 °C (6 Torr), which was a mixture of methylenemalonic (MME) and malonic (ME) esters. ^1H NMR (CD_3OD), δ MME: 1.26 (t, 6 H, CH_3, ^3J = 7 Hz), 4.17 (q, 4 H, CH_2O), 6.49 (s, 2 H, CH_2=); ME: 1.3 (t, 6 H, CH_3, ^3J = 7 Hz), 3.39 (s, 2 H, CH_2), 4.25 (q, 4 H, CH_2O).

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