# Reactions of alkylenebisbromomalonates with nucleophiles

*R. G. Kostyanovsky,* O. N. Krutius, and Yu. I. El'natanov*

*N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, 4 ul. Kosygina, 117977 Moscow, Russian Federation. Fax: +7 (095) 938 2156*

Treatment of alkylenebisbromomalonates with nucleophiles (AcOK, AgOH, $KHCO_3$, 1,8-diazabicyclo[5.4.0]undec-7-ene, or $Ph_3P$) results mainly in their debromination to give cycloalkane-1,1,2,2-tetracarboxylates. When $H_2O$ and acids are present, the reaction gives products of the substitution of one or two bromine atoms by hydrogen. Alkaline hydrolysis results in oxacycloalkane-α,α,α′,α′-tetracarboxylic acids. The reaction mechanism is discussed.

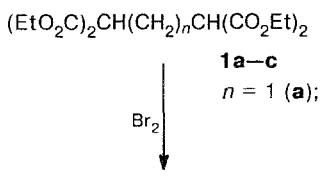
**Key words:** alkylenebisbromomalonates; nucleophilic and homolytic substitution; cycloalkane-1,1,2,2-tetracarboxylates; oxacycloalkane-α,α,α′,α′-tetracarboxylic acids.

We attempted to obtain alkylenebistartronates, the starting compounds for synthesizing bicyclic dilactones,[1] by treating readily accessible alkylenebisbromomalonates with O-nucleophiles.

Certain instances of the nucleophilic substitution of the Br atom in bromomalonates are known, *e.g.*, by treatment with AcOK [2] or with PhONa.[3] The transformation of ethylenebisbromomalonate into the monolactone of ethylenebistartronic acid by treatment with $Ba(OH)_2$ has also been reported.[4]

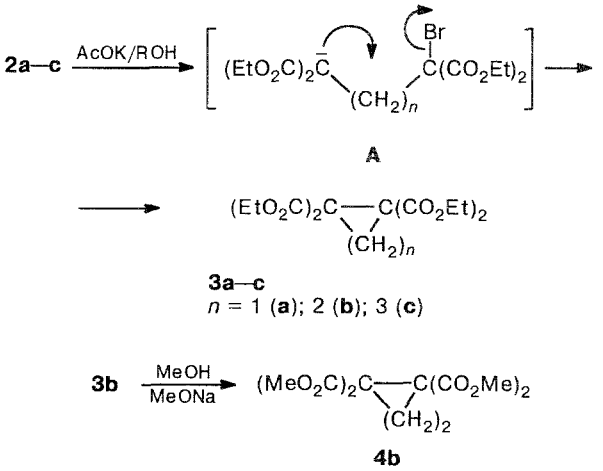
The bromination of alkylenebismalonates (**1a—c**)[5–8] according to the known procedure[5] resulted in tetraethyl alkylenebisbromomalonates (**2a—c**) (Scheme 1).

**Scheme 1**




When dibromides **2** are boiled with excess AcOK in dry EtOH or ethylcellosolve, the reaction gives, instead of the expected products of nucleophilic substitution, high yields (78—95 %) of the corresponding ethyl cycloalkane-1,1,2,2-tetracarboxylates (**3a—c**) (Scheme 2). These compounds were characterized by $^1H$ and $^{13}C$ NMR spectroscopy. They were found to be identical with those reported previously.[6,9–15] Compound **3b** was transformed by transesterification to tetramethyl ester **4b**.

**Scheme 2**




When dibromide **2b** was boiled with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dry ethanol, a mixture of compounds **3b** and **4b** in the ratio of 3 : 1 was obtained. Compound **2c** was transformed into tetraester **3c** by treatment with $KHCO_3$ under conditions of phase transfer catalysis.

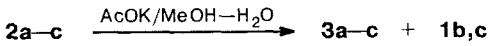
In essence, the above transformations of dibromides **2** closely represent the behavior of alkylenebismalonates during electrolysis in the presence of mediators, MHal;[12–15] in these reactions, an **A**-type anion is also believed to be the key intermediate of electrochemical cyclization. However, Scheme 2 is doubtful due to the absence of products of the nucleophilic substitution of the Br atoms by external nucleophiles. Therefore, it is not clear whether the reaction starts with electron transfer and whether homolytic substitution of a Br atom following the oxidation of an **A** anion to the correspond-

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2185—2189, December, 1994.

1066-5285/94/4312-2065 $12.50 

ing radical, is responsible for cyclization. However, the following facts support the formation of intermediate **A**.

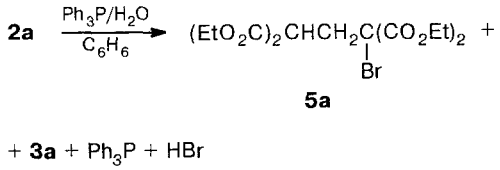
During the process given by Scheme 2, cyclization is inhibited when $H_2O$ is added to the system. This is due to the formation of products of the substitution of the Br atoms by H (tetraesters **1**).



**2a–c** $\xrightarrow{AcOK/MeOH-H_2O}$ **3a–c** + **1b,c**

The transformation of compound **2a** to **3a** does not depend on the amount of $H_2O$ added; however, the reaction of compound **2b** in undried ethylcellosolve afforded a mixture of compounds **3b** and **1b** (3 : 1). When $H_2O$ was added in an equimolar or greater amount (with respect to AcOK), compound **2b** was transformed exclusively to **1b**. When dibromide **2a** was boiled with AgOH in aqueous ethanol, a mixture of compounds **1a** and **3a** (1.2 : 1) was obtained, while **2b** or **2c** gave esters **1b** or **1c** in virtually quantitative yields.

This is explained by the fact that $H_2O$ protonates anions **A** and the anions formed in the elimination of the second Br atom. The stronger acid, HBr, which is evolved in the reaction of $Ph_3P$ with dibromide **2a**, considerably inhibits cyclization. In this case, monobromide **5a** and cyclopropane **3a** are formed in the ratio of 4 : 1.



**2a** $\xrightarrow[C_6H_6]{Ph_3P/H_2O}$ $(EtO_2C)_2CHCH_2C(CO_2Et)_2$ + (Br)

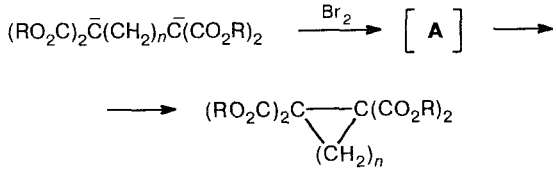
**5a**

+ **3a** + $Ph_3P$ + HBr

According to its $^1H$ NMR spectrum, monobromide **5a** is identical to an authentic sample obtained, along with **2a**, upon bromination of **1a**. When dibromide **2b** is boiled with monoethanolamine (1 equiv.) in dry EtOH, no cyclization occurs at all due to the evolution of HBr during *N*-bromination of the amine (the $^1H$ NMR spectrum showed only the formation of **1b**).

Dibromide **2a** does not react with an excess of the weaker C-nucleophile, $CH_2N_2$, in $Et_2O$.

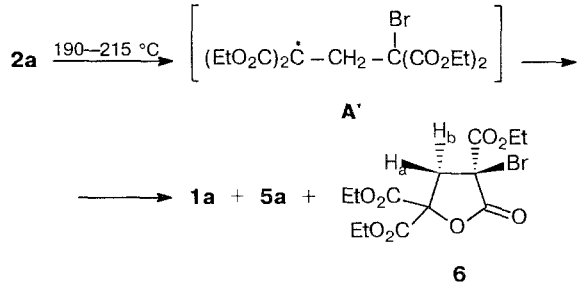
The intermediate formation of an **A**-type anion is strongly supported by the fact that it is also generated in an "independent synthesis" from disodium alkylenebismalonic esters treated with 1 equiv. $Br_2$ (*cf.* Refs. 14, 16) to give tetraalkyl cycloalkane-1,1,2,2-tetracarboxylates in high yields.



$(RO_2C)_2\bar{C}(CH_2)_n\bar{C}(CO_2R)_2$ $\xrightarrow{Br_2}$ [ **A** ] $\longrightarrow$ $(RO_2C)_2C(CH_2)_nC(CO_2R)_2$

The radical process could not be initiated by boiling compound **2a** with azoisobutyronitrile in $C_6H_6$ (18 h); the thermolysis of **2a** gave only compounds **1a**, **5a**, and α-bromo-α,γ,γ-tris(ethoxycarbonyl)-γ-butyrolactone (**6**) (in the ratio 1 : 4 : 2), which were identified by their $^1H$ NMR spectra (Scheme 3).

**Scheme 3**



**2a** $\xrightarrow{190–215\ °C}$ [ $(EtO_2C)_2\dot{C}-CH_2-C(Br)(CO_2Et)_2$ ] $\longrightarrow$

**A'**

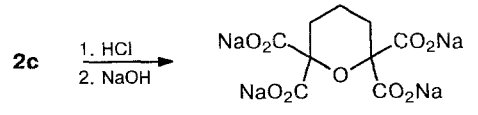
$\longrightarrow$ **1a** + **5a** + **6**

Similar radical lactonization has been reported previously.[17] The formation of cyclopropane **3a** was not detected in the reaction according to Scheme 3, hence **A'**-type radicals cannot be regarded as intermediates in the syntheses of tetraalkyl cycloalkanetetracarboxylates.

Thus, we did not succeed in performing the nucleophilic substitution of a Br atom in dibromides **2a–c**. This is due to polarization of the C←Br bond by the two electron-acceptor ethoxycarbonyl groups, as well as by steric factors facilitating the attack of a nucleophile on a Br atom. It is reasonable to assume that the situation could change if we transformed esters **2** into compounds containing the much less electron-accepting carboxylate groups. Therefore, we studied the alkaline hydrolysis of dibromides **2a,b** (Schemes 4 and 5).

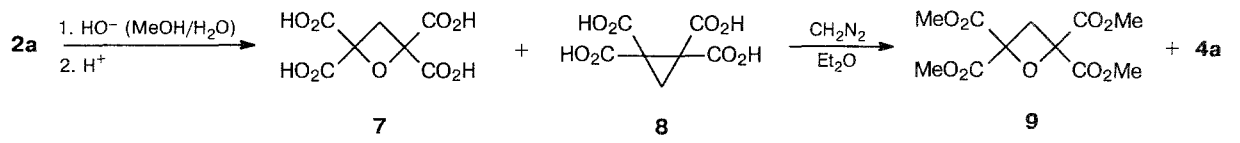
Ester **2a** was transformed into tetraacids **7** and **8** in the ratio of (3–4) : 1, which implies that saponification occurs more quickly than debromination. Treatment of the mixture of acids **7** and **8** with diazomethane gave cyclopropane **4a** and oxetane **9**, which was characterized by NMR and mass spectroscopy.

The hydrolysis of ester **2b** results in tetrahydrofuran-2,2,5,5-tetracarboxylic acid (**10**), whose structure was confirmed by NMR spectra and by comparing tetramethyl ester **11** with that obtained from the corresponding tetranitrile.[18] The formation of ethylenebistartronic acid monolactone in the saponification of ester **2b** has been reported previously.[4] However, our repeated attempts to reproduce these data resulted only in isomeric product **10**. It is also known that alkaline treatment of the dibromotetraacid obtained by acidic hydrolysis of tetraester **2c** results in a salt of tetrahydropyran-2,2,6,6-tetracarboxylic acid.[19]

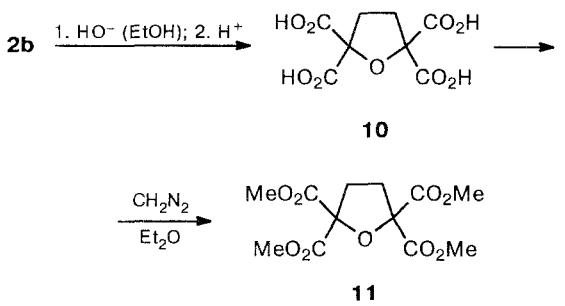


**2c** $\xrightarrow[2.\ NaOH]{1.\ HCl}$ $NaO_2C$, $CO_2Na$, O, $NaO_2C$, $CO_2Na$

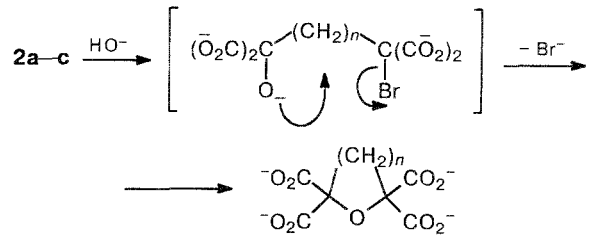
**Scheme 4**



**Scheme 5**



**Scheme 6**



Thus, dibromotetracarboxylates undergo nucleophilic substitution of a Br atom by OH. However, owing to the possibility of a suitable transition state, substitution of the second bromine atom by an internal nucleophile occurs to give oxacycloalkane-α,α,α',α'-tetracarboxylates (Scheme 6).

## Experimental

NMR spectra were recorded in $CDCl_3$ on a Bruker WM-400 spectrometer ($^1H$ 400.13; $^{13}C$ 100.62 MHz) relative to $Me_4Si$ as the internal standard. Mass spectra (EI) were obtained on Hitachi-M-80-A (ionizing voltages 12—20 and 70 eV) and URVG 7070E (70 eV) instruments with direct insertion of samples into the ion source. IR spectra were obtained for solutions in $CHCl_3$ and for KBr pellets on a UR-20 spectrophotometer. Melting points were measured on a Boetius PHMK-0.5 hot stage at a heating rate of 4—5 °C $min^{-1}$. Chromatography was performed on a 2×5 cm column packed with 40/100 μm silica gel.

**Alkylenebismalonates (1a—c)** were obtained by the known procedures.[5—8]

**Tetraethyl methylenebismalonate (1a).** B.p. 197—200 °C (10 Torr). $^1H$ NMR, δ: 1.28 (t, 12 H, 4 Me, $J$ = 7.0 Hz); 2.42 (t, 2 H, $CH_2$, $^3J$ = 7.6 Hz); 3.42 (t, 2 H, 2 CH, $J$ = 7.6 Hz); 4.2 (dq, 8 H, 4 $CH_2O$, $^3J$ = 2.2 Hz). $^{13}C$ NMR, δ: 13.16 (qt, Me, $^1J$ = 127.2 Hz, $^2J$ = 2.2 Hz); 26.82 (tt, $CH_2$, $^1J$ = 135.2 Hz, $^2J$ = 5.0 Hz); 48.8 (dd, CH, $^1J$ = 133.0 Hz, $^2J$ = 4.4 Hz, $^3J$ = 3.6 Hz); 61.22 (tq, $CH_2O$, $^1J$ = 4.4 Hz); 168.06 (dq, C=O, $^2J$ = 4.4 Hz, $^3J$ = 3.6 Hz). Based on the $^1H$ NMR spectrum, hexaethyl pentane-1,1,3,3,5,5-hexacarboxylate[20] was detected in the high-boiling fraction (δ): 1.27 (t, 6 H, 2 Me, $J$ = 7.0 Hz); 1.3 (t, 12 H, 4 Me, $J$ = 7.0 Hz); 2.5 (d, 4 H, 2 $CH_2$, $J$ = 7.0 Hz); 3.48 (t, 2 H, 2 CH); 4.16 (q, 4 H, 2 $CH_2O$); 4.24 (q, 8 H, 4 $CH_2O$). The spectrum agrees with that reported for the corresponding hexamethyl ester.[14]

**Tetraethyl ethylenebismalonate (1b).** B.p. 192—195 °C (3 Torr), $n_D^{18}$ 1.4426. $^1H$ NMR, δ: 1.26 (t, 12 H, 4 Me, $^3J$ = 7.0 Hz); 1.88 (m, 4 H, 2 $CH_2$); 3.28 (m, 2 H, 2 CH); 4.17 (m, 8 H, 4 $CH_2O$, Δν = 2.5 Hz). $^{13}C$ NMR, δ: 13.39 (q, Me, $^1J$ = 126.4 Hz); 25.8 (t, $CH_2$, $^1J$ = 130.7 Hz); 51.01 (d, CH, $^1J$ = 130.8 Hz); 60.58 (t, $CH_2O$, $^1J$ = 148.23 Hz); 168.14 (s, C=O). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 346 $[M]^+$ (1.1), 302 (1.6), 301 (14.5), 255 (27.7), 227 (25.6), 201 (12.1), 187 (66.5), 186 (16.3), 183 (32.3), 181 (31.9), 173 (43.0), 160 (100), 141 (45.3), 109 (25.3), 101 (28.4), 85 (71.4), 83 (64.8).

**Tetraethyl propylenebismalonate (1c).** B.p. 210 °C (5 Torr). $^1H$ NMR, δ: 1.25 (t, 12 H, 4 Me, $^3J$ = 7.0 Hz); 1.33 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 1.88 (dt, 4 H, $C\underline{H}_2CH_2C\underline{H}_2$, $^3J$ = 7.2 Hz); 3.24 (t, 2 H, 2 CH, $^3J$ = 7.2 Hz); 4.15 (dq, 8 H, 4 $CH_2O$, Δν = 2.2 Hz). $^{13}C$ NMR, δ: 13.57 (qt, Me, $^1J$ = 126.4 Hz, $^2J$ = 2.9 Hz); 24.53 (tt, $CH_2\underline{C}H_2CH_2$, $^1J$ = 126.5 Hz, $^2J$ = 4.4 Hz); 27.8 (tt, $\underline{C}H_2CH$, $^1J$ = 129.3 Hz, $^2J$ = 4.4 Hz); 51.00 (dt, CH, $^1J$ = 132.2 Hz, $^2J$ = 2.9 Hz); 60.81 (tq, $CH_2O$, $^1J$ = 148.2 Hz, $^2J$ = 4.4 Hz); 168.64 (dq, C=O, $^3J$ = 3.6 Hz, $^2J$ = 4.4 Hz).

**Synthesis of alkylenebisbromomalonates (2a—c) (general procedure).** Bromine (0.1 mol) was added dropwise to a solution of an alkylenebismalonate (0.05 mol) in $CHCl_3$ (40—50 mL). When the reaction started (sometimes, during the addition of $Br_2$, or after a short period of heating to 50 °C), self-heating of the mixture and intense evolution of HBr occurred. Then the mixture was refluxed for 8 h and cooled; $CHCl_3$ (50—70 mL) and sodium hydrosulfite (0.5 g) were added. The mixture was washed with $H_2O$ (3×100 mL), dried with $CaCl_2$, and concentrated. The residue was recrystallized from EtOH. The yield of compounds **2a—c** was 80—90 %.

**Tetraethyl methylenebisbromomalonate (2a).** M.p. 53—55 °C. $^1H$ NMR ($CD_3OD$), δ: 1.28 (t, 12 H, 4 Me, $J$ = 7.0 Hz); 3.62 (s, 2 H, $CH_2$); 4.26 (q, 8 H, 4 $CH_2O$). $^{13}C$ NMR, δ: 13.08 (qt, Me, $^1J$ = 127.2 Hz, $^2J$ = 2.2 Hz); 41.92 (t, $CH_2$, $^1J$ = 136.6 Hz); 58.79 (t, $\underline{C}Br$, $^2J$ = 3.6 Hz); 62.97 (tq, $CH_2O$, $^1J$ = 149.7 Hz, $^2J$ = 4.4 Hz); 165.1 (dq, C=O, $^3J$ = 2.9 Hz).

**Tetraethyl ethylenebisbromomalonate (2b).** M.p. 78—80 °C. $^1H$ NMR, δ: 1.29 (t, 12 H, 4 Me, $J$ = 7.0 Hz); 2.40 (s, 4 H, 2 $CH_2$); 4.27 (q, 8 H, 4 $CH_2O$). $^{13}C$ NMR, δ: 13.57 (qt, Me, $^1J$ = 127.9 Hz, $^2J$ = 2.9 Hz); 27.06 (tt, $CH_2$, $^1J$ = 132.2 Hz, $^2J$ = 3.5 Hz); 53.15 (t, $\underline{C}Br$, $^2J$ = 3.6 Hz); 60.91 (tq, $CH_2O$, $^1J$ = 148.2 Hz, $^2J$ = 4.4 Hz); 170.53 (br.s, C=O).

**Tetraethyl propylenebisbromomalonate (2c).** M.p. 38—40 °C. $^1$H NMR ($CD_3OD$), δ: 1.27 (t, 12 H, 4 Me, $J$ = 7.1 Hz); 1.5 (m, 2 H, $CH_2\underline{CH_2}CH_2$); 2.28 (m, 4 H, $CH_2CBr$); 4.25 (q, 8 H, 4 $CH_2O$, $J$ = 7.1 Hz). $^{13}$C NMR, δ: 13.34 (qt, Me, $^1J$ = 127.9 Hz, $^2J$ = 2.9 Hz); 20.95 (tt, $CH_2\underline{C}H_2CH_2$, $^1J$ = 129.3 Hz, $^2J$ = 3.6 Hz); 37.02 (tt, $\underline{C}H_2CBr$, $^1J$ = 132.2 Hz, $^2J$ = 3.5 Hz); 62.25 (t, CBr, $^2J$ = 3.6 Hz); 62.5 (tq, $CH_2O$, $^1J$ = 149, $^2J$ = 4.4 Hz); 165.78 (tt, C=O, $^3J$ = 2.9 Hz, $^3J$ = 3.6 Hz).

**Reactions of alkylenebisbromomalonates 2a—c with AcOK (general procedure).** A mixture of compounds **2a—c** (2 mmol) and AcOK (8.15 mmol) in a dry solvent (6 mL) was refluxed (for 30 h in EtOH; for 14 h in ethylcellosolve) and concentrated. The brown residue was washed with saturated aqueous $NaHCO_3$, extracted with ether (3×100 mL), dried with $MgSO_4$, and concentrated. The residue was passed through silica gel using ether as the eluent. The ether was distilled off from the eluate to give almost pure compound **3a** (yield 78—80 %). Distillation *in vacuo* gave compounds **3b** and **3c** (85—95 %) and **1b** and **1c** (5—7 %). When unpurified commercial-grade solvents were used, the fraction of compounds **1b** and **1c** increased to 25 %; when water (12—16 mmol) was added to the reaction mixture, only **1b** and **1c** were obtained.

**Tetraethyl cyclopropane-1,1,2,2-tetracarboxylate (3a).** M.p. 44—46 °C. $^1$H NMR, δ: 1.29 (t, 12 H, 4 Me, $J$ = 7.0 Hz); 2.12 (s, 2 H, $CH_2$); 4.20 (q, 8 H, 4 $CH_2O$). $^{13}$C NMR, δ: 12.98 (qt, Me, $^1J$ = 127.2 Hz, $^2J$ = 2.2 Hz); 22.62 (t, $CH_2$, $^1J$ = 170 Hz); 40.47 (t, $\underline{C}(COOEt)_2$, $^2J$ = 2.9 Hz); 61.29 (tq, $CH_2O$, $^1J$ = 148.2 Hz, $^2J$ = 4.4 Hz); 164.84 (m, COO, $^3J$ = 3.6 Hz).

**Tetraethyl cyclobutane-1,1,2,2-tetracarboxylate (3b).** B.p. 162—167 °C (3 Torr). $^1$H NMR, δ: 1.26 (t, 12 H, 4 Me, $J$ = 7.0 Hz); 2.54 (s, 4 H, 2 $CH_2$); 4.19 (q, 8 H, 4 $CH_2O$, $J$ = 7.0 Hz). $^{13}$C NMR, δ: 13.07 (t, Me, $^1J$ = 126.4 Hz); 24.87 (t, $CH_2$, $^1J$ = 143.87 Hz); 59.02 (s, $\underline{C}(COOEt)_2$); 60.48 (tq, $CH_2O$, $^1J$ = 148.2 Hz, $^2J$ = 4.4 Hz); 168.46 (s, C=O). MS (EI, 12 eV), $m/z$ ($I_{rel}$ (%)): 344 $[M]^+$ (13.3), 299 (100), 298 (50), 271 (21), 270 (20), 252 (24.1), 226 (49.5), 199 (71), 180 (12.5), 153 (10.5), 72 (29), 59 (8.0). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 344 $[M]^+$ (8.0), 299 (38.1), 298 (9), 271 (10), 252 (9), 227 (16), 225 (19), 199 (28.1), 153 (35.2), 29 (100).

**Tetraethyl cyclopentane-1,1,2,2-tetracarboxylate (3c).** B.p. 172—173 °C (2 Torr). $^1$H NMR, δ: 1.26 (t, 12 H, 4 Me, $J$ = 7.0 Hz); 1.91 (m, 2 H, $CH_2\underline{CH_2}CH_2$); 2.51 (t, 4 H, $\underline{CH_2}CH_2\underline{CH_2}$, $J$ = 7.2 Hz); 4.15 (q, 8 H, 4 $CH_2O$). $^{13}$C NMR, δ: 12.98 (qt, Me, $^1J$ = 127.2 Hz, $^2J$ = 2.2 Hz); 21.26 (t.quint, $CH_2\underline{C}H_2CH_2$, $^1J$ = 133.0 Hz, $^2J$ = 3.6 Hz); 35.14 (ttt, $\underline{C}H_2CH_2\underline{C}H_2$, $^1J$ = 135.2 Hz, $^2J$ = 4.4 Hz, $^3J$ = 2.9 Hz); 60.54 (tq, $CH_2O$, $^1J$ = 148.2 Hz, $^2J$ = 4.4 Hz); 65.68 (s, $\underline{C}(COOEt)_2$); 169.36 (tt, C=O, $^3J$ = 3.6 Hz, $^3J$ = 2.9 Hz). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 358 $[M]^+$ (2.2), 314 (8.0), 313 (40.4), 285 (43.7), 241 (11.9), 239 (41.5), 211 (77.1), 167 (100), 139 (94.4), 93 (14.9).

**Reaction of alkylenebisbromomalonates 2a—c with AgOH (general procedure).** A mixture of compound **2a—c** (3.06 mmol), $Ag_2O$ (obtained from 8.24 mmol of $AgNO_3$), $H_2O$ (4 mL), and EtOH (10 mL) was refluxed for 11—20 h. The precipitate was separated, the filtrate was evaporated, and the residue was dispersed in ether. The ethereal solution was passed through silica gel and concentrated. Compounds **2b** and **2c** gave **1b** and **1c**, respectively, in almost quantitative yields, while compound **2a** gave a mixture of compounds **1a** and **3a** in the ratio of 1.2 : 1.

**Reaction of dibromide 2b with DBU.** A mixture of ester **2b** (1.75 g, 3.47 mmol) and DBU (1.35 g, 8.86 mmol) in dry EtOH (13 mL) was refluxed for 10 h, the solvent was evaporated, and the residue was dispersed in ether. The ethereal extract was passed through silica gel (to remove the unchanged DBU) and concentrated to give 0.97 g of a mixture of compounds **1b** and **3b** in the ratio of 1 : 3.

**Reaction of dibromide 2c with $KHCO_3$.** A mixture of compound **2c** (1.2 g, 2.32 mmol), $KHCO_3$ (3 g, 29.9 mmol), and dicyclohexano-18-crown-6 (0.02 g, 0.054 mmol) in dry MeCN (30 mL) was refluxed for 35 h with vigorous stirring. The precipitate was separated, the filtrate was concentrated, the residue was dispersed in aqueous ether, and the ethereal solution was passed through silica gel to give 0.96 g of a mixture of compounds **2c** and **3c** (1 : 1).

**Tetramethyl cyclobutane-1,1,2,2-tetracarboxylate (4b).** A solution of compound **3b** (0.2 g, 0.58 mmol) and a catalytic amount of MeONa in MeOH (10 mL) was kept for 7 days at ~20 °C and evaporated to dryness. The residue was dissolved in $Et_2O$ and the solution was filtered and concentrated again. The residue was recrystallized from MeOH to give 0.09 g (54 %) of ester **4b**, m.p. 82 °C. $^1$H NMR, δ: 2.56 (s, 4 H, 2 $CH_2$); 3.74 (s, 12 H, 4 MeO). $^{13}$C NMR, δ: 25.76 (tt, $CH_2$, $^1J$ = 142.4 Hz, $^2J$ = 5.6 Hz); 52.68 (q, MeO, $^1J$ = 148.2 Hz); 58.51 (s, $\underline{C}(COOMe)_2$); 169.93 (s, C=O). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): $[M]^+$ not found, 257 (100), 256 (25.2), 229 (25.3), 199 (31.6), 185 (99.8), 171 (36.5), 169 (56.5), 138 (58.8), 136 (30.6), 127 (26.6), 112 (83.1), 110 (21.5), 83 (26.7), 81 (30.2).

**The reaction of dibromide 2a with $Ph_3P$.** A mixture of ester **2a** (0.36 g, 0.73 mmol) and aqueous $Ph_3P$ (0.19 g, 0.73 mmol) in $C_6H_6$ (4 mL) was kept for 20 h at ~20 °C (a white precipitate was formed, and the mixture turned orange). A portion (0.5 mL) of the mixture was concentrated to dryness. The $^1$H NMR spectrum indicated the formation of a mixture of compounds **3a** and **5a** (1 : 4).

**Tetraethyl 1-bromopropane-1,1,3,3-tetracarboxylate (5a).** $^1$H NMR, δ: 1.3 and 1.31 (both t, 6 H, 2 Me, $J$ = 7.0 Hz); 2.97 (d, 2 H, $CH_2$, $J$ = 6.1 Hz); 3.68 (t, 1 H, CH, $J$ = 6.1 Hz); 4.18 and 4.22 (both q, 4 H, 2 $CH_2O$).

**Thermolysis of dibromide 2a.** Dibromide **2a** (1.15 g, 2.34 mmol) was heated for 35 min on an oil bath (190—215 °C) with a reflux condenser. Evolution of gas bubbles was observed. After cooling, a portion of the reaction mixture (0.2 g, black resin) was extracted with light petroleum (40—70 °C, 2×20 mL) and the extract was concentrated to dryness. According to the $^1$H NMR spectrum, the residue contained a mixture of compounds **1a** and **5a** and lactone **6** in the ratio of 1 : 4 : 2. $^1$H NMR of lactone **6**, δ: 1.32, 1.34, and 1.35 (all t, 3 H, Me, $J$ = 7.0 Hz); 3.27 ($H_A$, 1 H, $CH_AH_B$, $^2J$ = 15.0 Hz); 3.75 ($H_B$, 1 H); 4.28 (q, 8 H, 4 $CH_2O$); 4.30 (q, 4 H, 2 $CH_2O$).

**Oxetane-2,2,4,4-tetracarboxylic acid (7), cyclopropane-1,1,2,2-tetracarboxylic acid (8), tetramethyl cyclopropane-1,1,2,2-tetracarboxylate (4a), and tetramethyl oxetane-2,2,4,4-tetracarboxylate (9).** *A.* Water (29 mL) was added to a solution of ester **2a** (4.13 g, 8.19 mmol) in MeOH (115 mL), then a solution of KOH (3.34 g, 50.6 mmol; 85 %) in a mixture of MeOH (17 mL) and $H_2O$ (8 mL) was added dropwise. The reaction mixture was kept for 18 h and concentrated, then $Et_2O$ (20 mL) and concentrated HCl (15 mL) were added to the residue. The mixture was extracted with ether (3×100 mL). The extract was dried with $MgSO_4$ and concentrated to dryness to give 1.9 g of a yellowish viscous liquid, which consisted of a mixture of acids **7** and **8** (4 : 1 according to the $^1$H NMR spectrum ($CD_3OD$), δ: 3.38 (s, 2 H, $CH_2$) (**7**) and 2.04 (s, 2 H, $CH_2$) (**8**)). The mixture was dissolved in MeOH (15 mL), the solution was filtered and treated with a solution of $CH_2N_2$ in $Et_2O$ until the yellow coloring no longer disappeared. The reaction mixture was concentrated to give 1.1 g of a mixture of esters **4a** and **9** (1 : 4). Distillation gave 0.6 g of a viscous fluid,

b.p. 187—188 °C (6 Torr), a mixture of compounds **4a** and **9** (1 : 8). $^1$H NMR of ester **4a** ($CD_3OD$), δ: 2.12 (s, 2 H, $CH_2$); 3.72 (s, 12 H, 4 MeO). $^1$H NMR of ester **9** ($CD_3OD$), δ: 3.47 (s, 2 H, $CH_2$); 3.82 (s, 12 H, 4 MeO). $^{13}$C NMR of ester **9**, δ: 34.96 (t, $CH_2$, $^1J$ = 147.5 Hz); 53.44 (q, MeO, $^1J$ = 149.0 Hz); 80.11 (m, $C(COOMe)_2$); 167.36 (dq, C=O, $^3J$ = 4.4 Hz, $^3J$ = 3.6 Hz). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 290 $[M]^+$ (1.8), 231 (8.1), 214 (6.2), 201 (2.4), 200 (4.0), 173 (4.4), 171 (12.2), 159 (82.3), 113 (60.7), 105 (40.1), 87 (16.2), 59 (100).

***B.*** A mixture of ester **2a** (1.9 g, 3.77 mmol) and $Ba(OH)_2 \cdot 8H_2O$ (3.67 g, 11.64 mmol) in $H_2O$ (10 mL) was refluxed for 8 h, then the same amount of $Ba(OH)_2 \cdot 8H_2O$ was added. The reaction mixture was refluxed for an additional 8 h and cooled, then conc. HCl (7 mL) was added, and the mixture was extracted with ether (4×70 mL). The extract was dried with $MgSO_4$, filtered, concentrated, and the residue was dried *in vacuo* for 2 h to give 1.08 g of a mixture of acids **7** and **8** (3 : 1). A portion (0.3 g) of this mixture was treated with $CH_2N_2$ as described above to give a mixture of esters **4a** and **9** (3 : 1), which was purified by gradient chromatography on a column with silica gel. The mixture was eluted with ether and hexane in 20 mL portions, starting from 100 % *n*-hexane and gradually increasing the fraction of ether by 2—3 % to 40 %. The initial and middle fractions contained compounds **4a** and **9**. The final fractions, which contained almost pure ester **9**, were combined and concentrated. The residue was dried *in vacuo* to give 0.05 g of ester **9** as a colorless transparent liquid.

**Tetrahydrofuran-2,2,5,5-tetracarboxylic acid (10).** The reaction was carried out in a silver-plated vessel (*cf.* Ref. 4). A mixture of compound **2b** (9 g, 18 mmol) and $Ba(OH)_2 \cdot 8H_2O$ (recrystallized from water; 11.29 g, 35.8 mmol) in $H_2O$ (35 mL) was refluxed for 6 h, the same amount of $Ba(OH)_2 \cdot 8H_2O$ was added, and the mixture was refluxed for an additional 6 h. The resulting solid was ground, placed on a Schott filter, washed with water (500 mL; 60—70 °C) and dry dioxane (70 mL), and dried in air. The residue was treated with a solution of conc. $H_2SO_4$ (3.7 g) in $H_2O$ (10 mL). The mixture was triturated for 0.5 h and kept for 12 h. The precipitate was filtered off and the filtrate was concentrated *in vacuo*. The residue was extracted with MeCN (20 mL), and the extract was passed through a column with silica gel and concentrated. The residue was recrystallized from ether to give 1.93 g (43 %) of acid **10**, m.p. 105 °C. $^1$H NMR ($CD_3OD$), δ: 2.53 (s, $CH_2$). Found (%): C, 38.51; H, 3.71. $C_8H_8O_9$. Calculated (%): C, 38.71; H, 3.23.

**Tetramethyl tetrahydrofuran-2,2,5,5-tetracarboxylate (11).** A solution of acid **10** (0.57 g, 2.3 mmol) in dry $Et_2O$ (35 mL) was treated with an ethereal solution of $CH_2N_2$ until the yellow coloring no longer disappeared. The ether was distilled off and the residue was recrystallized from an ether—light petroleum mixture to give 0.54 g (77 %) of ester **11** (white crystals), m.p. 100—101 °C. $^1$H NMR, δ: 2.58 (s, 4 H, 2 $CH_2$); 3.82 (s, 12 H, 4 MeO). $^{13}$C NMR, δ: 32.43 (tt, $CH_2$, $^1J$ = 138.7 Hz, $^2J$ = 4.2 Hz); 52.82 (q, MeO, $^1J$ = 148.4 Hz); 88.0 (s, $\underline{C}(COOMe)_2$); 167.94 (m, C=O, $^3J$ = 4.2 Hz). MS (EI, 12 eV), *m/z* ($I_{rel}$ (%)): $[M]^+$ not present, 246 (12.3), 245 (100), 229 (7.9), 217 (34.6), 214 (7.2), 185 (24.2), 159 (12.1), 145 (8.3), 141 (6.2), 85 (5.3). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): $[M]^+$ not present, 246 (12.9), 245 (100), 243 (6.5), 231 (6.6), 217 (43.7), 214 (9.0), 186 (10.8), 185 (60.3), 159 (12), 158 (5.9), 157 (11.6), 155 (11.9), 153 (29.0), 145 (12.6), 141 (34.7), 129 (18.0), 127 (12.9), 113 (25.3), 99 (10.4), 95 (14.3), 85 (13.5), 71 (16.3), 59 (58.8), 57 (19.2). IR ($CHCl_3$), ν/cm$^{-1}$: 2960 (CH), 1760 (C=O). Found (%): C, 47.07; H, 5.53. $C_{12}H_{16}O_9$. Calculated (%): C, 47.37; H, 5.30.

The authors are grateful to G. I. Nikishin, M. N. Elinson, and S. K. Fedukovich for their helpful discussion of the results obtained and for providing an authentic sample of compound **4b**. The study was financially supported by the Russian Foundation for Basic Research (Project No. 94-03-08730), NATO (Grant No. LG 921193), and the International Science Foundation (Grant No. MCO 000).

## References

1. R. G. Kostyanovsky and Yu. I. El'natanov, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 650 [*Russ. Chem. Bull.*, 1994, **43**, 599 (Engl. Transl.].
2. M. Conrad and C. Brückner, *Chem. Ber.*, 1891, **24**, 2993.
3. K. H. Takemura, M. Pulickal, and F. O. Hoff, *J. Org. Chem.*, 1971, **36**, 3646.
4. R. Lean, *J. Chem. Soc.*, 1900, **77**, 103.
5. J. J. Lennon and W. H. Perkin, *J. Chem. Soc.*, 1928, 1513.
6. *Sintezy organicheskikh preparatov* [*Syntheses of Organic Compounds*], sb. 1, Izd-vo inostr. lit., Moscow, 1949 (Russ. Transl.).
7. N. S. Zefirov, N. K. Sadovaya, and S. V. Kambarova, *Zh. Org. Khim.*, 1988, **24**, 116 [*J. Org. Chem. USSR*, 1988, **24** (Engl. Transl.)].
8. C. S. Marvel and R. D. Vest, *J. Am. Chem. Soc.*, 1959, **81**, 984.
9. F. Effenberger, W. Müller, and H. Isak, *Chem. Ber.*, 1987, **120**, 53.
10. F. Caudemar-Bartone and M. Caudemar, *Bull. Soc. Chim. Fr.*, 1973, 3467.
11. N. S. Zefirov, K. A. Lukin, S. I. Kozhushkov, T. S. Kuznetsova, A. M. Domarev, and I. M. Sosonkin, *Zh. Org. Khim.*, 1989, **25**, 312 [*J. Org. Chem. USSR*, 1989, **25** (Engl. Transl.)].
12. D. A. White, *J. Electrochem. Soc.*, 1977, **124**, 1177.
13. M. N. Elinson, S. K. Fedukovich, and G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1987, 228 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1987, **36**, 206 (Engl. Transl.)]; M. N. Elinson, S. K. Fedukovich, and G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 2783 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 2523 (Engl. Transl.)].
14. M. N. Elinson, S. K. Fedukovich, S. V. Lindeman, M. S. Aleksanyan, Yu. T. Struchkov, and G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 1603 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 1467 (Engl. Transl.)].
15. M. N. Elinson, S. K. Fedukovich, B. I. Ugrak, and G. I. Nikishin, *Izv. Akad. Nauk, Ser. Khim.*, 1992, 2332 [*Bull. Russ. Acad. Sci., Div. Chem. Sci.*, 1992, **41**, 1827 (Engl. Transl.)].
16. K. W. Kohlrausch and R. Sabathy, *Monatsh.*, 1939, 303; 309.
17. D. P. Curran, M.-H. Chen, E. Spletzer, C. M. Seong, and C.-T. Chang, *J. Am. Chem. Soc.*, 1989, **111**, 8872.
18. W. L. Linn and R. E. Benson, *J. Am. Chem. Soc.*, 1965, **87**, 3657.
19. H. J. Kraus and E. Schmadel, FRG Pat. 2714956, *Chem. Abstrs.*, 1979, **90**, P25154z.
20. J. F. Bottomley and W. H. Perkin, *J. Chem. Soc.*, 1900, **77**, 298.

*Received April 6, 1994;*
*in revised form July 5, 1994*