Aliphatic Semidiones. XVI. Semidiones Derived from the Bicyclo[*n*.1.1]alkanes[1]

Glen A. Russell,* Philip R. Whittle,[2] and Robert G. Keske[3]

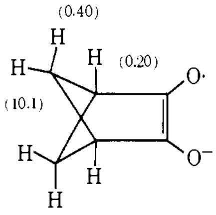
Contribution from the Department of Chemistry,
Iowa State University, Ames, Iowa 50010. Received May 29, 1970

Abstract: Bicyclo[2.1.1]hexane- and bicyclo[3.1.1]heptane-2,3-semidiones have been examined by electron spin resonance spectroscopy in dimethyl sulfoxide solution. The long-range hyperfine splitting by the anti hydrogen atoms of the methano bridges decreases from 10 G in the hexane to 3.5 G in the heptane. Bicyclo[4.1.1]octane-3,4-semidione was prepared and studied between −80 and +60°. Ring inversion was fast at all temperatures. A ring-expansion reaction of bicyclo[2.1.1]hexane-2,3-diones to bicyclo[3.1.1]heptane-2,3-diones by reaction with the methylsulfinylcarbanion has been detected.

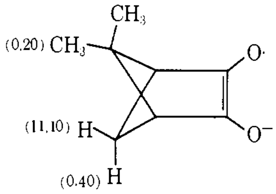
In a continuing study of long-range interactions,[4–11] and conformational effects in aliphatic semidiones,[12–19] we have synthesized the semidiones **1–3** in dimethyl sulfoxide solution. The semidiones have been detected by esr spectroscopy and the observed hyperfine splitting constants at ~25° are given with each structure.

Attempts to oxidize bicyclo[2.1.1]hexan-2-one or tricyclo[3.3.0.0^{2,6}]octan-3-one in DMSO solutions containing potassium *tert*-butoxide failed to produce a semidione. We thus turned to the acyloin condensation of *cis*-1,3-cyclobutanedicarboxylic esters (Scheme I).

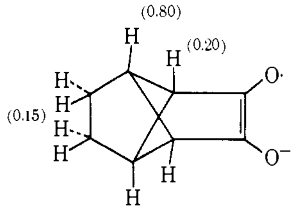
Reaction of the ester with sodium–potassium alloy in dimethoxyethane gave a poorly resolved esr spectrum. When this solution was diluted with a solution of potassium *tert*-butoxide in DMSO, the esr spectrum of Figure 1 was obtained. The same spectrum was obtained if the acyloin condensation was performed in the presence of trimethylchlorosilane and the unisolated bis(trimethylsiloxy)alkene treated with DMSO and base. Semidiones **1b** and **1c** were prepared from the appropriate esters by the acyloin condensation in the absence of trimethylchlorosilane.



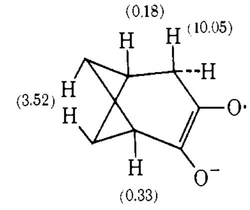
1a



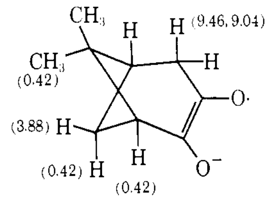
1b



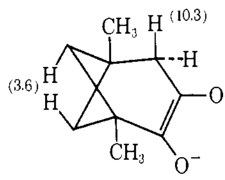
1c



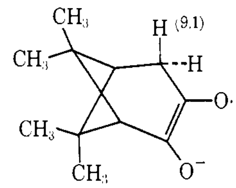
2a



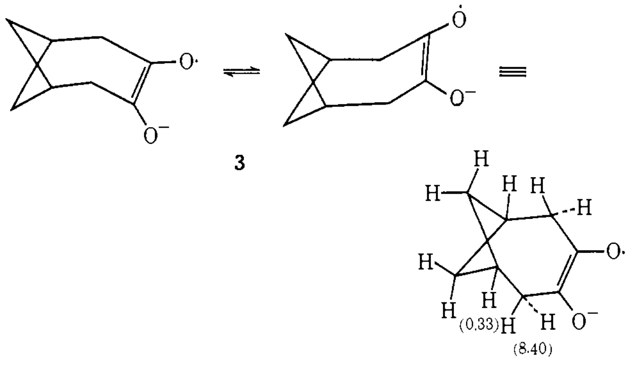
2b



2c



2d



3

---

(1) Application of Electron Spin Resonance Spectroscopy to Problems of Structure and Conformation. XXI. Supported by a grant from the National Science Foundation.

(2) National Aeronautics and Space Agency Predoctoral Fellow, 1965–1968; Petroleum Research Fund Fellow, 1968–1969.

(3) National Science Foundation Predoctoral Fellow, 1967–1970.

(4) G. A. Russell and K.-Y. Chang, *J. Amer. Chem. Soc.*, **87**, 4381 (1965).

(5) G. A. Russell, K.-Y. Chang, and C. W. Jefford, *ibid.*, **87**, 4383 (1965).

(6) G. A. Russell, G. Holland, K.-Y. Chang, and L. H. Zalkow, *Tetrahedron Lett.*, 1955 (1967).

(7) G. A. Russell, P. R. Whittle, and J. McDonnell, *J. Amer. Chem. Soc.*, **89**, 5515 (1967).

(8) G. A. Russell, G. W. Holland, and K.-Y. Chang, *ibid.*, **89**, 6629 (1967).

(9) G. A. Russell and P. R. Whittle, *ibid.*, **89**, 6781 (1967).

(10) G. A. Russell and G. W. Holland, *ibid.*, **91**, 3968 (1969).

(11) G. A. Russell, P. R. Whittle, J. J. McDonnell, R. S. Givens, and R. G. Keske, *ibid.*, **93**, 1452 (1971).

(12) G. A. Russell and E. T. Strom, *ibid.*, **86**, 744 (1964).

(13) G. A. Russell and E. R. Talaty, *ibid.*, **86**, 5345 (1964); *Science*, **148**, 1217 (1965).

(14) E. T. Strom, G. A. Russell, and R. D. Stephens, *J. Phys. Chem.*, **69**, 2131 (1965).

(15) E. R. Talaty and G. A. Russell, *J. Amer. Chem. Soc.*, **87**, 4867 (1965).

(16) G. A. Russell, E. T. Strom, E. R. Talaty, and S. A. Weiner, *ibid.*, **88**, 1998 (1966).

(17) E. R. Talaty and G. A. Russell, *J. Org. Chem.*, **31**, 3455 (1966).

(18) G. A. Russell, E. R. Talaty, and R. H. Horrocks, *ibid.*, **32**, 353 (1967).

(19) G. A. Russell, G. R. Underwood, and D. C. Lini, *J. Amer. Chem. Soc.*, **89**, 6636 (1967).

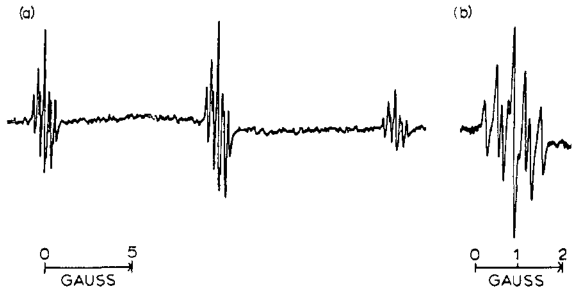


Figure 1. (a) First-derivative esr spectrum of bicyclo[2.1.1]hexanesemidione in DMSO solution; (b) central multiplet expanded.

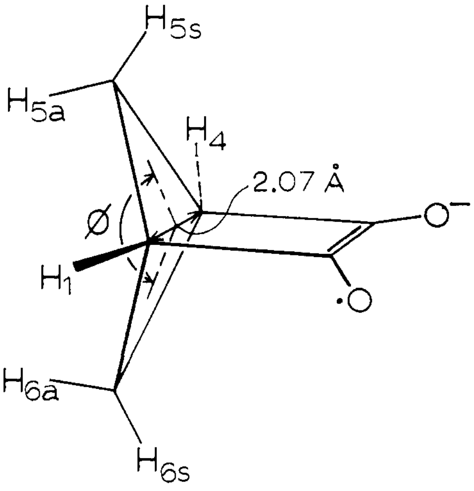
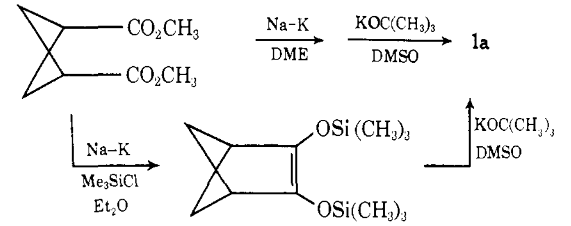


Figure 2. Geometry employed in extended Hückel calculations. All carbon–hydrogen bonds were 1.09 Å; all carbon–carbon single bonds were 1.54 Å; the H–C–H angles were 111°; the three H_1–C–C angles were set equal; the semidione carbon–carbon bond was 1.40 Å; the carbonyl carbon–oxygen distance was 1.22 Å; and a potassium gegenion located 2.4 Å from each oxygen atom was included in the calculation.

Scheme I



Extended Hückel MO calculations were performed for bicyclo[2.1.1]hexane-2,3-semidione using the technique described previously[11] and the geometry of Figure 2.[20] Calculations of the angle ϕ have predicted values of 139° (from angle strain) and 137° (from nonbonded repulsions).[20] We used values of 136 and 140° for ϕ and 2.07 Å for the C_1–C_4 distance in the calculations listed in Table I.

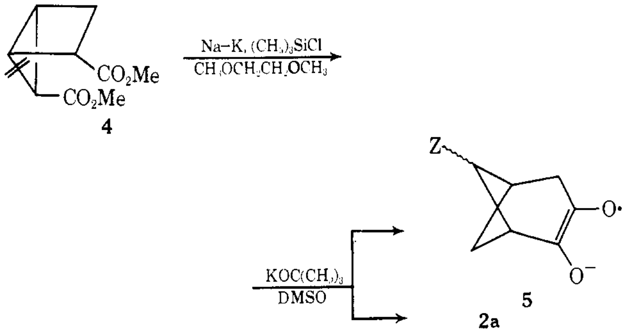
Table I. Calculated Hyperfine Splitting Constants for Bicyclo[2.1.1]hexane-2,3-semidione (Gauss)

Position	1 (4)	5 (6) syn	5 (6) anti
Obsd	0.20	0.40	10.10
Calcd ϕ = 140°	0	1.54	12.70
Calcd ϕ = 136°	0	0.79	10.89

Figure 3. Partial first-derivative esr spectrum of bicyclo[3.1.1]heptane-2,3-semidione in DMSO solution. The low-field triplet of a triplet of triplets is reproduced.

The bicyclo[3.1.1]heptane-2,3-semidione derivative **2b** was reported previously[4] as an oxidation product of nopinone.[21] Semidione **2a** (Figure 3) was prepared from the crude 2,3-bis(trimethylsiloxy)bicyclo[3.1.1]hept-2-ene by treatment with potassium *tert*-butoxide (0.2 *M*) in DMSO in the absence of oxygen. Semidione **2a** was also formed as a product in the acyloin condensation of the bicyclo[2.1.0]pentanedicarboxylic ester in the presence of trimethylchlorosilane. Semidiones **2a** and **5** were formed when the crude bis(trimethylsiloxy)alkene(s) were treated with excess potassium *tert*-butoxide in DMSO (Scheme II).[11] Hydrogenation of the cyclopropane (Scheme II) in **4** would lead to the formation of **2a**. Semidione **2a** is more stable than **5** and after a few hours in basic DMSO solution, only **2a** could be detected as a reaction product. Ring opening probably occurs prior to semidione formation because when the crude bistrimethylsiloxy derivative of **4** was treated in base and DMSO-d_6 the **2a** formed contained deuterium only at C-4, a^H = 3.50, 3.50, 0.35, 0.20; a^D = 1.55, 1.55. The hydrogen atom at C-4 in **2b** was previously observed to exchange readily in DMSO-d_6 containing potassium *tert*-butoxide.[11]

Scheme II



Semidiones **2c** and **2d** were also the products of an unexpected reaction. They were observed as the reaction products resulting when the crude acyloins from *cis*-1,3-dimethylcyclobutane-1,3-dicarboxylic and 2,2,4,4-tetramethyl-*cis*-1,3-cyclobutanedicarboxylic esters were treated with DMSO and potassium *tert*-butoxide. With DMSO-d_6 2,2,4,4-tetramethyl-*cis*-1,3-cyclobutanedicarboxylic ester yields a semidione with a^D = 1.40

---

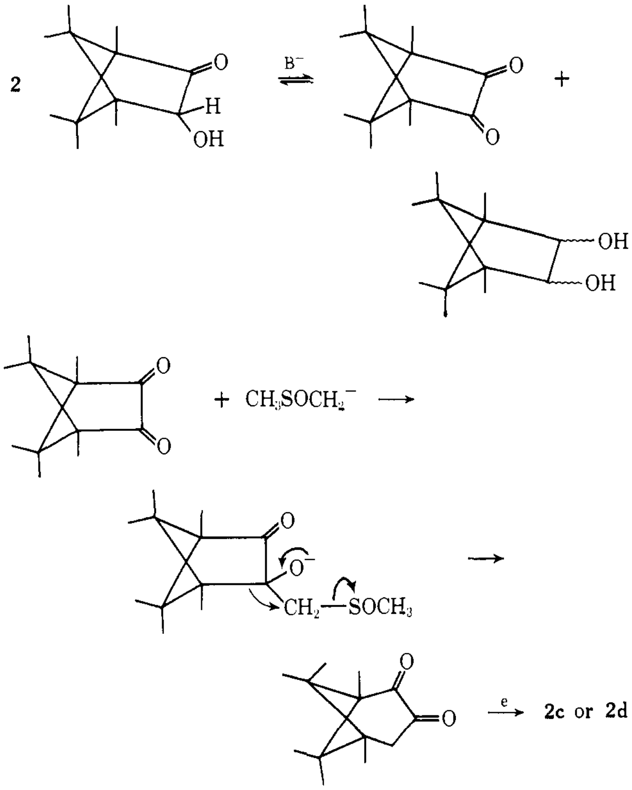
(20) C. F. Wilcox, *J. Amer. Chem. Soc.*, **82**, 414 (1960).

(21) V. B. Ipatieff, G. J. Czajkowski, and H. Pines, *ibid.*, **73**, 4098 (1951).

and 1.40 G, apparently the 4,4-dideuterio derivative of **2d**. The dideuterio semidione appeared to be the initial paramagnetic product of the treatment of the crude acyloin with DMSO-d_6 and no evidence for the intermediacy of undeuterated **2d** was found.

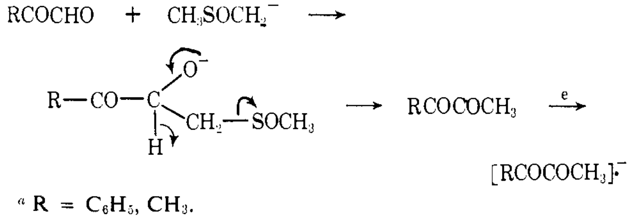
Scheme III lists a possible mechanism for the mysterious gain of a carbon atom for the products derived from the 1,3-dimethyl- and 2,2,4,4-tetramethyl-*cis*-cyclobutane-1,3-dicarboxylic esters.

Scheme III



A previous example of the addition of a methylene group from the methylsulfinylcarbanion to an α-dicarbonyl compound has been reported.[22] Monosubstituted glyoxals when treated with DMSO and base yield the corresponding propane-1,2-semidiones (Scheme IV).[22] Possible synthetic utilization of this chain-extension or ring-expansion reaction is being investigated.

Scheme IV



[a] R = C_6H_5, CH_3.

The methylene hydrogen atoms of **2a** showed no magnetic nonequivalence at 25° and we presume that the energy barrier to conformation interconversion is very low. The corresponding bicyclo[3.2.2]nonan-2,3-semidione also gave no evidence of conformational stability at 25° although molecular models predict that a ring flip should be occurring.[5]

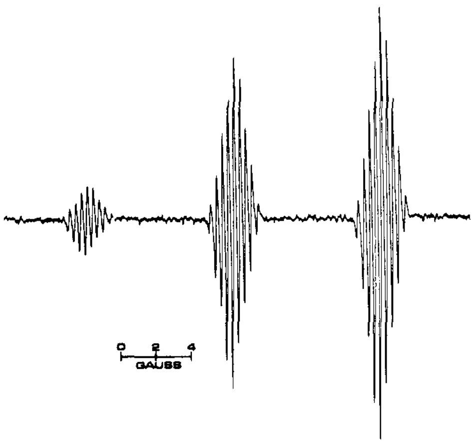
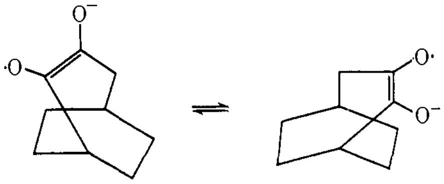
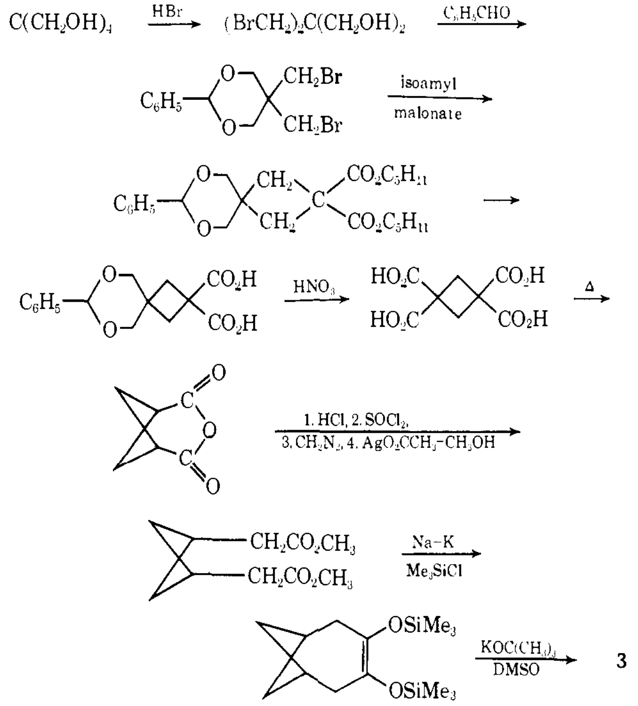


Figure 4. Partial first-derivative esr spectrum of bicyclo[4.1.1]-octane-3,4-semidione in DMSO solution. The first (low-field) three lines of the 1:4:6:4:1 quintet are reproduced.



Semidione **3** was prepared from the crude bis(trimethylsiloxy)alkene according to the syntheses of Scheme V following the procedures of Allinger and Tushaus for the preparation of 1,3-cyclobutanedicarboxylic anhydride.[23]

Scheme V



Semidione **3** was examined between +60 and −80°. Below 0° a mixture of 80% DMF and 20% DMSO was employed as the solvent. The spectrum observed for **3** is given in Figure 4. We conclude that this spectrum is the result of a very rapid ring inversion process with E_a less than 2.5 kcal/mol and probably less than 2 kcal/

---

[22] G. A. Russell, R. D. Stephens, and E. R. Talaty, *Tetrahedron Lett.*, 1139 (1965).

[23] N. L. Allinger and L. A. Tushaus, *J. Org. Chem.*, **30**, 1945 (1965).

mol. The ease of ring inversion in the bicyclo[*n*.*x*.*x*]2-alkenes with $n = 3$ or 4, $x = 1$ or 2, is noteworthy.

Experimental Section

Dimethyl *cis*-1,3-cyclobutanedicarboxylate was prepared by the method of Allinger and Tushaus.[23] Pure material was isolated by glpc with a 20% SF-96 on Chromosorb W at 150°. **Dimethyl bicyclo[2.1.1]hexane-*exo*,*exo*-5,6-dicarboxylate** was prepared by oxonolysis of tricyclo[3.3.0.0^{2,6}]oct-3-ene[24] in methanol at −75°. Ozone was passed through a solution of 200 mg of the olefin in 25 ml of methanol until the solution retained a purple color. The methanol was removed under vacuum and the residue treated with 10 ml of formic acid and 5 ml of 30% hydrogen peroxide. The solution was stirred at 25° for 12 hr and refluxed 1 hr, and the solvent removed under vacuum to yield 250 mg of a crystalline residue. The crude diacid was dissolved in 30 ml of ether and treated with the diazomethane prepared from 4 g of Diazald in 50 ml of ether. After 16 hr at 25° the excess diazomethane was decomposed with acetic acid and the etheral solution worked with saturated sodium bicarbonate and sodium chloride solutions and dried over MgSO$_4$. The solution was concentrated to give a residue that could be crystallized from pentane. Preparative glpc (15% Carbowax 20M on Chromosorb W at 160°) gave 125 mg of the diester: mp 84–86; ir (CCl$_4$) 1735, 1340, 1200, 1162 cm^{-1}; pmr (CCl$_4$) δ 1.82 (s, 4), 2.24 (s, 2), 3.04 (s, 2), 3.60 (s, 6); mass spectrum (70 eV) 198, 167, 139.

Anal. Calcd for C$_{10}$H$_{14}$O$_4$ (198): C, 60.59; H, 7.11. Found: C, 60.51; H, 7.09.

Dimethyl 2,2-dimethyl-*cis*-1,3-cyclobutanedicarboxylate was prepared by esterification of *cis*-norpinic acid[25] with methanol and a trace of sulfuric acid. Pure material was isolated by glpc (15% Carbowax 20M on Chromosorb W at 160°): ir (CCl$_4$) 1740, 1385, 1370, 1335, 1190, 1165 cm^{-1}; pmr (CCl$_4$) δ 0.9 (s, 3), 1.30 (s, 3), 1.85–2.70 (m, 2), 2.64 (t, 2, J = 4 Hz), 3.61 (s, 6); mass spectrum (70 eV) 200, 169, 141, 140.

Dimethyl *cis*-1,3-dimethyl-1,3-cyclobutanedicarboxylate was prepared[26] and pure material isolated by glpc (15% Carbowax 20M at 160°). **Dimethyl 2,2,4,4-tetramethyl-*cis*-1,3-cyclobutanedicarboxylate** was prepared by esterification of the acid,[27] mp 230–232° (lit.[27] mp 235–236°), using diazomethane. The diester was isolated by glpc (15% Carbowax 20M at 155°): pmr (CCl$_4$) δ 1.27 (s, 12), 2.63 (s, 2), 3.60 (s, 6); mass spectrum (70 eV) 213, 197, 181. **Dimethyl bicyclo[2.1.0]pentane-*endo*,*endo*-2,5-dicarboxylate (4)** was described previously.[11]

Dimethyl *cis*-1,3-cyclobutane-1-acetate-3-carboxylate was prepared from *cis*-cyclobutane-1,3-dicarboxylic anhydride[23] *via* the monomethyl ester. Treatment of 6.4 g of the anhydride with 1.2 equiv of methanol at reflux for 1 hr gave the monoester: pmr (CH$_2$Cl$_2$) δ 2.15–2.65 (m, 4), 2.70–3.25 (m, 2), 3.61 (s, 3), 7.60 (s, 1). The ester was dissolved in 40 ml of benzene and 10 ml of thionyl chloride and a few drops of pyridine was added. The mixture was stirred for 3 hr at 25° and 1 hr at 50°. The solvent and excess thionyl chloride were removed under vacuum. An additional 50 ml of benzene was added to the crude acid chloride and the solvent again removed under vacuum. The crude acid chloride was dissolved in 100 ml of ether and the solution filtered through a glass wool plug into a solution of diazomethane prepared from 21.5 g of Diazald in ether at 0°. The mixture was allowed to warm slowly to room temperature and after 24 hr at 25°, the solvent was removed under reduced pressure. The diazo ketone was dissolved in 60 ml of methanol and a mixture of 0.5 g of silver acetate in 5 ml of triethylamine was added slowly. The resulting solution was heated to reflux, decolorized with charcoal, filtered, and cooled. After removal of the solvent under reduced pressure, the residue was dissolved in 150 ml of ether and the resulting solution was washed with dilute hydrochloric acid followed by 10% sodium bicarbonate. The solution was dried over MgSO$_4$ before removal of the solvent under reduced pressure to yield 5.9 g (58%) of the crude diester, >90% pure by glpc: ir (neat) 1730 cm^{-1}; pmr (CCl$_4$) 1.55–3.15 (m, 6), 3.61 (s, 6); mass spectrum (70 eV) *m/e* (rel intensity) 186 1), 155 (36), 154 (11), 127 (14), 126 (23).

Dimethyl *cis*-1,3-cyclobutanediacetate was prepared from 1,3-cyclobutanedicarboxylic anhydride.[23] A mixture of 3.2 g of the anhydride and 3.2 g of 6 *N* hydrochloric acid was refluxed for 10 min. The mixture was extracted twice with 50 ml of ether and the ethereal extracts were dried (MgSO$_4$). Removal of the ether under vacuum left the solid diacid which was treated in the same manner as described for chain extension of the monomethyl ester of cyclobutane-1,3,-cyclobutane-1-acetate-3-carboxylate. The crude diester (3.1 g, 61%) was purified by glpc on a 5-ft 10% QF-1 column at 160°: ir (neat) 1730; pmr (CCl$_4$) δ 1.1–1.7 (m, 2), 2.10–2.60 (m, 8), 3.60 (s, 6); mass spectrum (70 eV) *m/e* (rel intensity) 169 (12), 168 (2), 141 (5), 140 (4).

Preparation of Crude Samples of 3,4-Bis(trimethylsiloxy)bicyclo[4.1.1]oct-3-ene and 2,3-Bis(trimethylsiloxy)bicyclo[3.1.1]hept-2-ene. The diester (0.3 g) was added to a mixture of 20 ml of ether and 1 ml of trimethylsilyl chloride. The solution was kept under nitrogen while 0.5 g of sodium–potassium alloy was added. The mixture was stirred vigorously for 3 hr and then filtered. Removal of the volatile components under vacuum left the crude product. This product gave the same esr signal before or after glpc purification on a 15% Carbowax 20M on Chromosorb W column at 160°.

Semidiones were prepared from 3 to 5 drops of the crude bissiloxyalkene dissolved in 0.5 ml of DMSO and placed in one side of an inverted U cell.[28] In the other side of the cell 20 mg of potassium *tert*-butoxide was dissolved in 0.5 ml of DMSO. Both solutions were thoroughly deoxygenated by a stream of prepurified nitrogen before being mixed. The final solutions were examined at 25° with a Varian E-3 spectrometer using a V-4548 aqueous solution cell or at variable temperatures in a Varian V-4500 spectrometer with V-4540 variable temperature controller and V-4548-1 cell.

Acknowledgment. Bicyclo[2.1.1]hexan-2-one and tricyclo[3.3.0.0^{2,6}]octan-3-one were generously supplied by Professors F. T. Bond and J. Meinwald,[24] respectively. 1-Methylbicyclo[4.4.0.0^{2,7}]decan-8-one obtained from Dr. C. H. Heathcock failed to produce a semidione upon oxidation in basic DMSO solution.

---

[24] J. Meinwald and B. E. Kaplan, *J. Amer. Chem. Soc.*, **89**, 2611 (1967); F. T. Bond and L. Scerbo, *Tetrahedron Lett.*, 2789 (1968).

[25] W. H. Perkin, Jr., and J. L. Simonsen, *J. Chem. Soc.*, **95**, 1166 (1909).

[26] R. T. LaLonde and R. I. Aksentijevich, *Tetrahedron Lett.*, 23 (1965).

[27] F. Lautenschlaeger and C. F. Wright, *Can. J. Chem.*, **41**, 863 (1963).

[28] G. A. Russell, E. G. Janzen, and E. T. Strom, *J. Amer. Chem. Soc.*, **86**, 1807 (1964).