bath at the designated temperatures, and samples were periodically withdrawn for analysis. The product concentrations were determined by HPLC with a Waters Associates ALC 201 liquid chromatograph equipped with a Altex 4.6 mm × 250 mm Ultrasphere-ODS 5 μm column interface to a Hewlett-Packard 3380A integrator.

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation. A.P. wishes to thank the organic faculty at the University of Wurzburg for their gracious hospitality during his stay at the Institute as an Alexander von Humboldt Senior Awardee. Use of the high-field NMR spectrometer used in these studies was made possible through a NSF equipment grant.

Conformational Studies of Macrocyclic 1,2-Semidiones[1]

Glen A. Russell* and N. K. Suleman

Contribution from the Department of Chemistry, Iowa State University, Ames, Iowa 50011.

Received July 30, 1984

Abstract: The rate of internal rotation in *trans*-tetracosane-1,2-semidione (**3**) has been measured: $k(248\ \mathrm{K}) = 3.4 \times 10^7\ \mathrm{s}^{-1}$, $\Delta H^{\ddagger} = 5.7$ kcal/mol. Similar rates were observed for the *trans*-1,2-semidiones derived from *p*-cyclophanes **4** and **5**, while the *p*-cyclophane derivative **6** has $k(348\ \mathrm{K}) = 2.7 \times 10^7\ \mathrm{s}^{-1}$, $\Delta H^{\ddagger} = 10.8$ kcal/mol. For **7**, the *trans*-1,2-semidione is locked in an asymmetric conformation at 353 K. The *cis*-1,2-semidiones in macrocyclic rings also have appreciable barriers to conformational motion which time-averages pairs of α-hydrogen atoms. For *cis*-**7** this process has $\Delta H^{\ddagger} = 16$ kcal/mol while *cis*-**8** exists at 373 K in a locked conformation possessing two pairs of magnetically equivalent hydrogen atoms α to the dicarbonyl system.

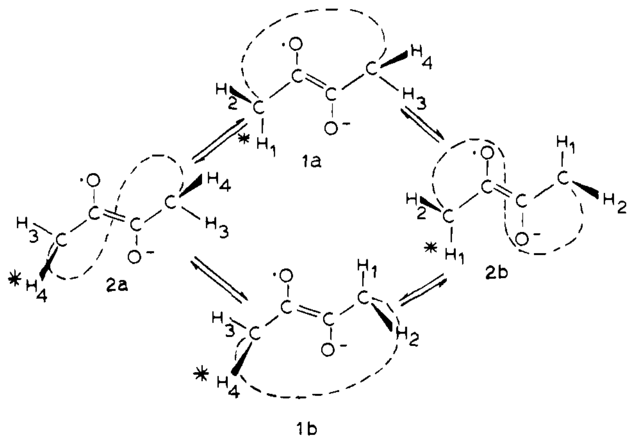
Cyclic 1,2-semidiones in rings of 11–15 atoms give complex ESR spectra in Me_2SO/K^+ because of the presence of trans and cis isomers both of which may display selective line broadening from conformational motion.[2] Ion pairing is more prominent for the cis isomer and leads to a lower *g* value.[3] In the presence of [2.2.2]-cryptand the trans isomer predominates for rings of more than 10 atoms.[2] Well-defined hyperfine splitting (hfs) by two pairs of α-hydrogen atoms has been observed in the trans isomers of cycloundecane-1,2-semidione at 170 °C,[2] 6,6-dimethyl-6-silacyclononane-1,2-semidione (25–110 °C),[4] 7,7-dimethyl-7-silacycloundecane-1,2-semidione (25–140 °C),[2] and cyclopentadecane-1,2-semidione (25–100 °C).[2] Heating the C_{15} semidione to 130 °C appeared to time average the pairs of α-hydrogen atoms, but the coalescence temperature was above the limit of thermal stability of the semidione.[2]

1,2-Semidiones give weak signals below 0 °C because of the disproportionation reaction 1 whose equilibrium is shifted to the right by complexing counterions, particularly in nonpolar solvents. However, in DMF at −20 °C a spectrum of *trans*-6,6-dimethyl-6-silacyclononane-1,2-semidione was obtained which was

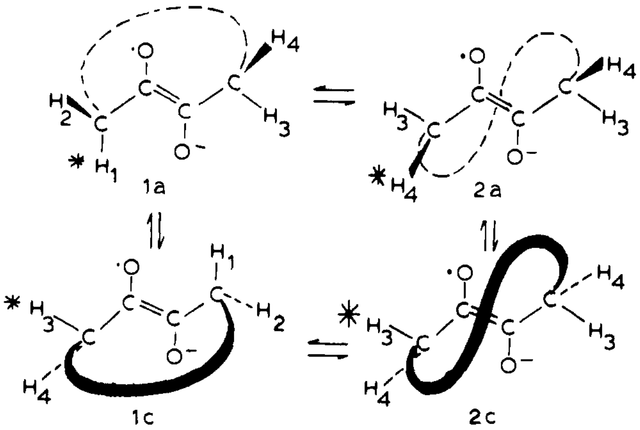
$$2\mathrm{RC(O\cdot){=}C(O^-)R} \rightleftharpoons \mathrm{RCOCOR} + \mathrm{RC(O^-){=}C(O^-)R} \qquad (1)$$

consistent with a selectively line broadened spectrum from a time-averaging process in which four magnetically different α-hydrogen atoms were being averaged to give two pairs of α-hydrogen atoms.[4] This observation led to the conclusion that in this case the preferred conformation of the *trans*-cyclic-1,2-semidione is asymmetric (**1a**,**b**) with different quasiaxial and quasiequatorial α-hydrogen atoms and with an appreciable energy barrier to the time-averaging process of Scheme I which produces pairs of hydrogen atoms ($H_1 \rightleftharpoons H_4$, $H_2 \rightleftharpoons H_3$). In conformation **1a** hydrogen atoms H(1) and H(3) are in the plane of the π-system (quasiequatorial) and their hyperconjugative interaction with the semidione spin should be much smaller than the interaction of the quasiaxial hydrogen atoms H(2) and H(4). The result of time averaging between **1a** and **1b** leads to two pairs of magnetically equivalent hydrogen atoms α to the dicarbonyl system (H(1)–H(4) and H(2)–H(3)) with nearly equivalent hfs. In the case of *trans*-6,6-dimethyl-6-silacyclononane-1,2-semidione, these hydrogens have $a^H = 3.5$ (2 H) and 2.5 (2 H) G at 25 °C.[4] *trans*-Cycloundecane-1,2-semidione at 170 °C also gave a time-averaged spectrum with $a^H = 4.7$ (2 H) and 3.1 (2 H) G.[2] On the other hand, the *trans*-1,2-semidiones of larger cycles, such as

Scheme I



Scheme II



---

[1] Aliphatic semidiones. Part 43. This work was supported by a grant from the National Science Foundation, CHE-8119343.

[2] Russell, G. A.; Osuch, C. E. *J. Am. Chem. Soc.* **1982**, *104*, 3353.

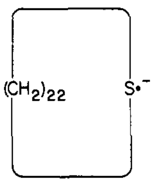
[3] Russell, G. A.; Osuch, C. E. *J. Am. Chem. Soc.* **1978**, *100*, 5979.

[4] Russell, G. A.; Osuch, C. E.; Senatore, G.; Morita, T.; Yamashita, M. *J. Org. Chem.* **1979**, *44*, 2780.

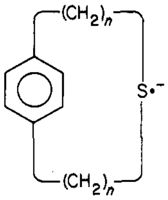
the 12- to 15-membered carbocyclics, the 7-sila- or 7-germacycloundecanes, or 8-silatridecane have an ESR spectrum at the highest observable temperature (~130 °C) which is a triplet of triplets with hfsc of 6–8 (2 H) and 1.7–2.0 (6 H) G. These observations seem more consistent with a preferred conformation such as **2a** or **2b** which possess a pair of quasiequatorial and a pair of quasiaxial hydrogen atoms α to the dicarbonyl system. Equal populations of **2a** and **2b** with rapid time averaging between them would lead to four nearly equivalent hydrogen atoms since again each hydrogen would spend equal time in the quasiequatorial and quasiaxial positions. However, again only the pairs H(1)–H(4) and H(2)–H(3) would be averaged. Equal population of all four conformations (**1a,b**; **2a,b**) would produce a similar result. However, since H(1) and H(3) or H(2) and H(4) are not exactly magnetically equivalent, four exactly magnetically equivalent hydrogen atoms can be achieved only if the internal rotations of Scheme II, which time averages H_1 with H_3 and H_2 with H_4, are combined with the conformational equilibria of Scheme I.

From the previous results, it appears that the internal rotation of Scheme II is a higher energy process than the ring flip of Scheme I, and for *trans*-cyclopentadecane-1,2-semidione, the internal rotation has a rate constant $<2 \times 10^7$ s^{-1} at 130 °C since the coalescence temperature has not been reached.[2]

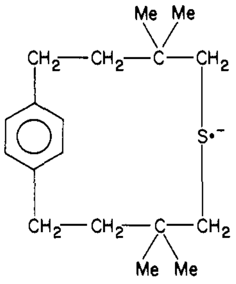
In hope of clarifying the conformational preferences and interconversions of macrocyclic *trans*-1,2-semidiones, we have examined a series of macrocyclic semidiones **3–8** ($S\cdot^- = -C(O\cdot)=C(O^-)-$) prepared by treatment of the corresponding acyloins with Me_3COK in Me_2SO or Me_2SO/DMF mixtures in the presence of either [2.2.2]-cryptand or excess KI.



3



4, n = 11
5, n = 9
6, n = 7
7, n = 4



8

Results and Discussion

Treatment of the acyloin of cyclotetracosane with Me_3COK in Me_2SO gives a mixture of *cis*- and *trans*-semidiones **3**. Addition of KI increases the cis/trans ratio which is ~1:1 at 25 °C in the presence of 0.4 M K^+ or at 65 °C in the presence of 0.8 M K^+. The *cis*-semidione ion pair has $g = 2.00485$, $a^H = 5.2$ (4 H), 0.08 (4 H) G at 65 °C. The 2nd and 4th peaks of the major pentet show selective line broadening at 35 °C which disappears to give a binomial pentet at 95 °C. Unfortunately, cooling solutions of *cis*-**3** below 25 °C in the presence of K^+ results in a reversible loss of the ESR signal from reaction 1.

In the presence of an excess of [2.2.2]-cryptand, *trans*-**3** is observed from −65 to 85 °C (Figure 1) with a cis/trans ratio of ~1/100 at 25 °C. The *trans*-semidione (free ion) at 25 °C has $g = 2.005046$, $a^H = 4.2$ (4 H) and 0.1 (4 H) G. The 2nd and 4th peaks of the major pentet show selective line broadening up to 85 °C. Upon cooling to −25 °C (Me_2SO/DMF, 1:1), the 2nd and 4th peaks are extensively broadened (Figure 1c) to yield a 1:4:1 triplet which evolves to a crudely resolved triplet of triplets at −65 °C (Figure 1d). We interpret the −65 °C spectrum as hfs from two pairs of hydrogen atoms in a slow exchange limit with $a^H = 7.6$ (2 H) and 1.9 (2 H) G.[5] At the coalescence temperature (−25 °C), the rate constant for the internal rotation which time averages the pairs of α-hydrogen atoms is 3.4×10^7 s^{-1}. Line broadening of the coalesced spectrum from −15 to 85 °C yields $\Delta H^\ddagger = 5.7 \pm 0.2$ kcal/mol and $\Delta S^\ddagger = 1$ eu for the internal rotation.

Semidiones **4** and **5** gave results essentially the same as **3**. *cis*-**4** can be observed in the presence of K^+, $g = 2.00485$, $a^H = 5.2$ (4 H), 0.08 (4 H) G at 25 °C. The spectrum shows broadening of the 2nd and 4th peaks of the main pentet at 25 but not at 85 °C. *trans*-**4** in the presence of cryptand has $g = 2.005045$, $a^H = 4.25$ (4 H), 0.12 (4 H) G at 25 °C with selective broadening of the 2nd and 4th peaks which disappears upon warming above 75 °C. Cooling to −25 °C gives the 1:4:1 triplet while at −65 °C the spectrum is consistent with pairs of hydrogen atoms in a slow exchange limit with $a^H = 6.9$ (2 H) and 1.9 (2 H) G.

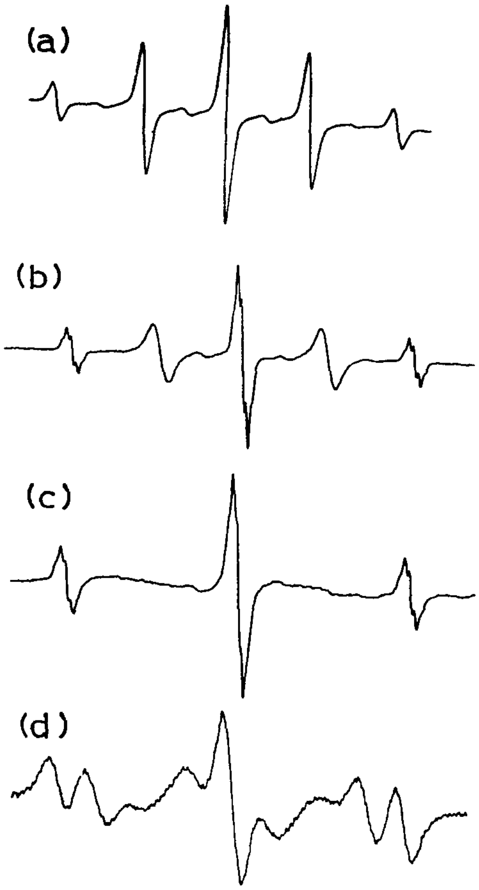


Figure 1. ESR spectrum of *trans*-**3** in Me_2SO/DMF in the presence of K^+[2.2.2]-cryptand: (a) 85 °C, (b) 15 °C, (c) −25 °C, (d) −65 °C.

Semidiones **5** in the presence of 0.4 M K^+ at 25 °C exist as a ~1:1 ratio of cis and trans isomers. *cis*-**5** has $g = 2.00485$, $a^H = 5.1$ (4 H), 0.1 (4 H) at 25 °C. Again the 2nd and 4th peaks of the main pentet show selective line broadening which is lost upon warming to 85 °C. In the presence of [2.2.2]-cryptand, *trans*-**5** can be observed free of the cis isomer, $g = 2.005061$, $a^H = 4.2$ (4 H), 0.2 (4 H) G. Warming to 105 °C gives a binomial pentet while cooling to −40 °C gives the 1:4:1 triplet. At −100 °C the spectrum consists of triplets of triplets in the slow exchange limit with $a^H = 6.8$ (2 H), 1.8 (2 H) G.

In semidione **6** the conformational equilibria are clearly slower. In the presence of K^+ a mixture of *cis*-**6** (ion pair, low g value) and *trans*-**6** (free ion) is observed. At 120 °C the cis isomer has four equivalent α-hydrogen atoms, $a^H = 5.0$ G. The *trans*-semidione approaches a binomial pentet at 120 °C with $a^H = 3.9$ G. Below this temperature the 2nd and 4th peaks of the pentet are broadened, and at the coalescence temperature of 75 °C a spectrum similar to that in Figure 1c is observed. At −10 °C the spectrum (Figure 2) is a triplet of triplets ($a^H = 6.1$ (2 H), 1.7 (2 H) G). The rate constant for the internal rotation is calculated to be 2.7×10^7 s^{-1} at the coalescence temperature, and from line broadening between 82 and 102 °C values of $\Delta H^\ddagger = 10.8$ kcal/mol and $\Delta S^\ddagger = 6$ eu are estimated.

It appears from the values of α^H that *trans*-**6** at −10 °C is mainly in conformation **2**. However, further cooling to −50 °C gives the spectrum of Figure 2b in a reversible manner. Figure 2b is consistent with hfs by four magnetically nonequivalent hydrogens, $\alpha^H = 7.6, 6.3, 1.3, <0.05$ G. However, there is no possible

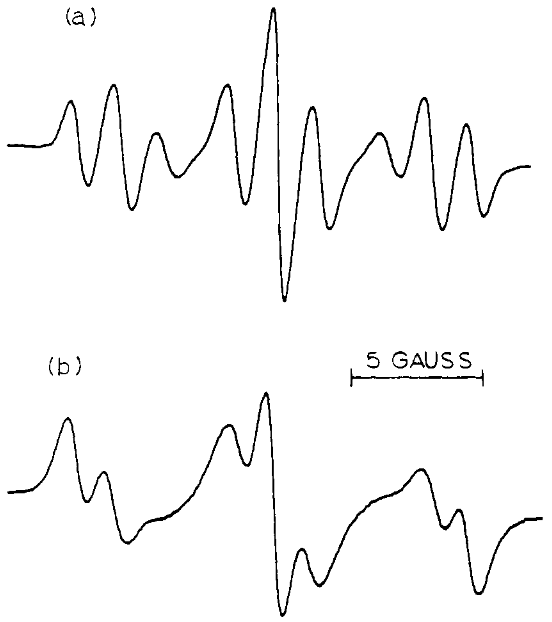


Figure 2. ESR spectrum of *trans*-**6** in Me_2SO/DMF (1:1) in the presence of K^+[2.2.2]-cryptand at (a) −10 °C and (b) −50 °C.

time-averaging process for this asymmetric conformation which could yield the spectrum observed at −10 °C (α^H = 6.1 (2 H), 1.7 (2 H) G).[6] Time averaging of the asymmetric conformation (**1a** ⇌ **1b**) would be expected to average large and small hfsc and yield a spectrum with either $\alpha^H \cong 3.8$ (4 H) G or α^H = 4.5 (2 H), 3.2 (2 H) G, a prediction inconsistent with the observed effect of temperature upon *trans*-**6** but consistent with observations made for 9- and 11-membered-ring semidiones.[2] For the 9- and 11-membered rings, the symmetric conformations **2** are not accessible and the **1a** ⇌ **1c** interconversion is observed at elevated temperatures without the occurrence of an internal ring rotation up to temperatures of 170 °C.[2] For larger rings such as **3–6**, as well as the 12- to 15-membered rings previously investigated,[2] one of the symmetric conformations **2** (or an unequal mixture of **2a** and **2b**) is preferred. With **3–6** the internal rotation can be readily observed, but whether this is a direct **2a** ⇌ **2c** process or involves **2a** ⇌ **1a** ⇌ **1c** ⇌ **2c** cannot be specified.

Semidione **7** was investigated in hopes of isolating the **1a** ⇌ **1b** process without complication from internal rotation. Indeed, no evidence for the internal rotation was observed for *trans*-**7** up to 80 °C, the highest temperature at which this semidione could be studied. However, the **1a** ⇌ **1b** process is also not observed and *trans*-**7** exists in a frozen asymmetric conformation showing no effect of temperature on hfs from −20 to 80 °C. The spectrum (Figure 3) requires a^H = 6.5 (1 H), 4.8 (2 H), and 1.7 (1 H) G.

In the presence of K^+, *cis*-**7** predominantes, and at K^+ = 0.8 M a cis/trans ratio of >10 is observed at 25 °C. *cis*-**7** at −10 °C gives a sharp triplet of triplets: a^H = 5.5 (2 H), 1.5 (2 H) G with a coalescence temperature of 25 °C where a 1:4:1 triplet is observed. At 90 °C a binomial pentet is observed with a^H = 3.5 (4 H) G ($\Delta H^\ddagger$ = 16 kcal/mol; $\Delta S^\ddagger$ = 29 eu). The hfs observed for *cis*-**7** is in sharp contrast to the observed spectrum for the tetra-β-methyl derivative, **8**. Reaction of the acyloin precursor to **8** with Me_3COK gives a triplet of triplets (Figure 4) with hfsc which do not change between −20 and 100 °C. The same spectrum is observed in the presence of excess K^+ or excess

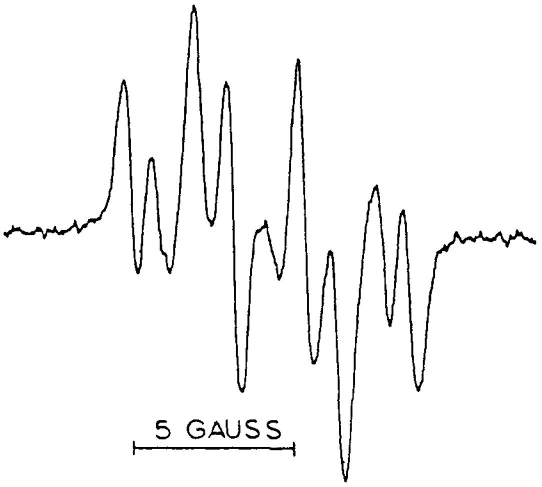


Figure 3. ESR spectrum assigned to *trans*-**7** in Me_2SO in the presence of K^+[2.2.2]-cryptand at 25 °C.

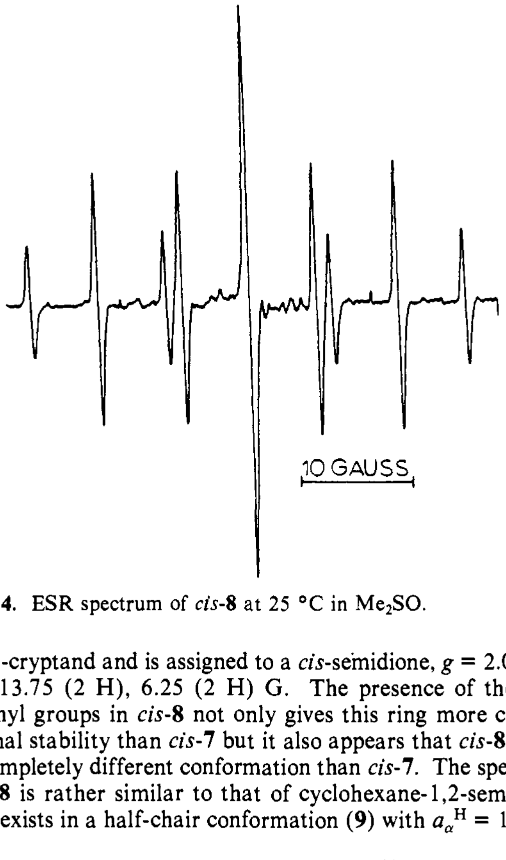
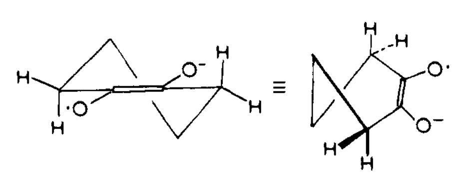
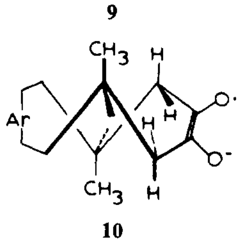


Figure 4. ESR spectrum of *cis*-**8** at 25 °C in Me_2SO.

[2.2.2]-cryptand and is assigned to a *cis*-semidione, g = 2.00488, a^H = 13.75 (2 H), 6.25 (2 H) G. The presence of the four β-methyl groups in *cis*-**8** not only gives this ring more conformational stability than *cis*-**7** but it also appears that *cis*-**8** exists in a completely different conformation than *cis*-**7**. The spectrum of *cis*-**8** is rather similar to that of cyclohexane-1,2-semidione which exists in a half-chair conformation (**9**) with a_α^H = 13.0 (2



9



10

---

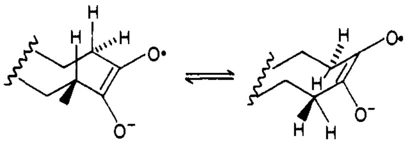
(5) A small temperature effect on Σa^H is observed. Although Figure 1d appears to be a triplet of triplets in the slow exchange limit, the possibility exists that at low temperatures a different conformation is populated. In fact, Figure 1d can also be rationalized with an asymmetric conformation (**1**) with a^H = 8.5, 6.6, 1.9, <0.05 G.

(6) The spectra of Figure 2b and possibly Figure 1d could also be explained as a selectively line broadened spectrum from the exchange between two different species. Exchange between unequal populations of **2a** and **2b** or exchange between **1a,b** and **2** is possible. Upon further cooling of the semidione solutions, the quality of the spectra rapidly diminished.

(7) Russell, G. A.; Underwood, G. R.; Lini, D. C. *J. Am. Chem. Soc.* **1967**, *89*, 6636.

H), 6.5 (2 H) G ($\Delta H^{\ddagger}$ for ring-flip = 4 kcal/mol).[7] *cis*-**8** apparently exists in a similar but frozen conformation (**10**).

In the absence of the nonbonded interactions of the β-methyl groups, *cis*-**7** appears to prefer the more boat-like conformation **11** which undergoes a ring-flip which time averages the α-hydrogen atoms. Such a conformation has been assigned to the cyclic C_7 and C_9 *cis*-1,2-semidiones[4,8] and is apparently the preferred conformation for the *cis*-1,2-semidiones in the larger rings including **3**–**7**.



11

7a, a_α^H = 5.5 (2 H), 1.5 (2 H) G
C_9, a_α^H = 5.28 (2 H), 2.18 (2 H) G
6-Me_2Si-9, a_α^H = 7.35 (2 H), 1.40 (2 H) G

Although rate data could not be obtained for conformational motion in *cis*-**3**–**6**, the line broadening observed at 25 °C or above indicates that the ring-flip of conformation **11** has an appreciable activation energy even in these macrocyclic semidiones. The value of $\Delta H^{\ddagger}$ for ring-slip of *cis*-**7** of 16 kcal/mol is remarkably high but is, of course, required by the strong temperature dependence observed in which a fully resolved triplet of triplets at −10 °C coalesces at 25 °C with time averaging being complete at 90 °C.[9]

Experimental Section

General Procedures. Acyloins were prepared from the appropriate dimethyl esters by the procedure of Allinger.[10] Semidiones were prepared by mixing deoxygenated solutions of the acyloins with Me_3COK in an H-cell mixing chamber[11] in the presence of [2.2.2]-cryptand or KI. Spectra were recorded in flat, fused silica aqueous sample cells with a Bruker ER-200D spectrometer at 100 kHz field modulation. For *g*-value measurements, a dual cavity with perylene radical cation in H_2SO_4 (g = 2.002569) was employed. Field differences were measured to 1 mG with a Bruker ER-035 NMR gaussmeter and the spectrometer frequency measured to 100 Hz with a Systron Donner frequency counter Model 4254A calibrated to 1 part in 10^6.

1-Hydroxy-2-ketocyclotetracosane (Precursor to 3). Dimethyl tetracosanedioate was prepared,[12] mp 73,5–74.5 °C (lit.[12] mp 74.5–74.8 °C). The ester (1 g, 2.5 mmol) in 100 mL of xylene was added dropwise over a 24-h period to 1 g (0.034 mmol) of sodium dispersion in 150 mL of xylene. The product was acidified at 0 °C with 10 mL of CH_3CO_2H and washed with water and the xylene was distilled under reduced pressure to leave a yellow oil in 60% yield: IR (neat) 1710, 3450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3; HRMS calcd for $C_{24}H_{46}O_2$ 366.34979, found 366.35051. The starting ester, δ 3.5 (s, 3), 1.0–2.3 (m, 22), could not be detected in the reaction product by ^1H NMR.

1,4-(5-Hydroxy-6-ketodecamethylene)benzene (Precursor to 7). This compound was prepared according to the literature procedure in 50% yield as a waxy solid: bp 130–133 °C (0.06 torr) (lit.[13] bp 158–161 °C (0.4 torr)); IR (neat) 1720, 3400–3500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.0 (s, 4), 0.8–3.0 (m, 18).

1,4-(3,3,8,8-Tetramethyl-5-hydroxy-6-ketodecamethylene)benzene (Precursor to 8). This compound was prepared according to a literature procedure[14] in 20% yield as a yellow oil, bp 130–133 °C (0.05 torr) (lit.[12] bp 144 °C (2 torr)). The acyloin was purified by column chromatography on alumina with ethyl acetate–hexane (1:1) eluate: ^1H NMR ($CDCl_3$) δ 7.1 (s), 2.6–2.8 (m), 1.0–1.7 (m); HRMS calcd for $C_{22}H_{34}O_4$ 302.22459, found 302.22398.

1,4-(12-Hydroxy-13-ketotetracosanomethylene)benzene (Precursor to 4). The diester and acyloin were prepared in a manner similar to the acyloin precursor to **7**. The diester was recrystallized from CH_3OH: mp 65–67 °C; IR ($CDCl_3$) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7 (s, 4), 3.5 (s, 6), 1–2.8 (m, 44). The acyloin was obtained in 30% yield as a yellow gum: IR (neat) 3500, 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1 (m), 1.0–2.5 (m); HRMS calcd for $C_{30}H_{50}O_2$ 442.38109, found 442.38218.

1,4-(8-Hydroxy-9-ketohexadecamethylene)benzene (Precursor to 6). The diester had mp 30–31 °C: IR 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.0 (s, 4), 3.6 (s, 6), 1.0–2.8 (m, 28); ^{13}C NMR ($CDCl_3$) δ 25.58, 29.38 (3 C), 31.85, 34.56, 36.03, 51.66, 128.68, 140.38, 174.36. The acyloin was obtained in 10% yield as a yellow oil: IR (neat) 3000, 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.9 (s, 4), 1.0–3.0 (m, 30); HRMS calcd for $C_{22}H_{34}O_2$ 330.25589, found 330.25676.

1,4-(10-Hydroxy-11-ketoeicosamethylene)benzene (Precursor to 5). A sample of this acyloin was kindly provided by Professor Y. Murakami.[15]

Registry No. 3, 94929-90-5; **4**, 94929-91-6; **5**, 94929-92-7; **6**, 94929-93-8; **7**, 94929-94-9; **8**, 94929-95-0; 1-hydroxy-2-ketocyclotetracosane, 94929-96-1; 1,4-(5-hydroxy-6-ketodecamethylene)benzene, 94929-97-2; 1,4-(3,3,8,8-tetramethyl-5-hydroxy-6-ketodecamethylene)benzene, 94929-98-3; 1,4-(12-hydroxy-13-ketotetracosanomethylene)benzene, 94929-99-4; 1,4-(8-hydroxy-9-ketohexadecamethylene)benzene, 94930-00-4; 1,4-(10-hydroxy-11-ketoeicosamethylene)benzene, 58380-71-5.

---

(8) Russell, G. A.; Keske, R. G.; Holland, G.; Mattox, J.; Givens, R. S.; Stanly, K. *J. Am. Chem. Soc.* **1975**, *97*, 1892.

(9) Estimates of $\Delta H^{\ddagger}$ for the ring flip of *cis*-cyclononane-1,2-semidione and *cis*-6,6-dimethyl-6-silacyclononane-1,2-semidione are 5.0 and 2.3 kcal/mol, respectively.[4] Unfortunately, it was not possible to study these semidiones above the coalescence temperature which was observed to be 120 °C for C_9 and >130 °C for the 6-sila analogue.

(10) Allinger, N. L. *Org. Synth.* **1956**, *36*, 79.

(11) Russell, G. A.; Janzen, E. G.; Strom, E. T. *J. Am. Chem. Soc.* **1964**, *86*, 1807.

(12) Marosi, L.; Schlenk, W. *Justus Liebigs Ann. Chem.* **1973**, 584.

(13) Cram, D. J.; Daeniker, H. V. *J. Am. Chem. Soc.* **1954**, *76*, 2743.

(14) Blomquist, A. T.; Jaffe, F. *J. Am. Chem. Soc.* **1958**, *80*, 3405.

(15) Murakami, Y.; Sunamoto, J.; Kano, K. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1238.