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Conformational Analysis of Seven-Membered Heterocycles. The 1,3-Dioxacycloheptanes—Proton and Carbon-13 Magnetic Resonance

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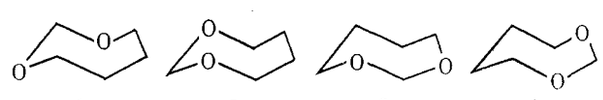
Configurational assignments are made for *cis*- and *trans*-4,7-dimethyl-1,3-dioxacycloheptane with the aid of proton and carbon-13 nmr spectroscopy. Five sets of steric interactions are defined which, when found in combinations of two, present effective pseudorotational and/or rotational barriers. Equilibrium studies for *cis*- and *trans*-2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane and *cis*- and *trans*-2-*tert*-butyl-5-methyl-1,3-dioxacycloheptane give $-\Delta G°$ of 0.45 ± 0.05 and 0.0 ± 0.05 kcal/mol, respectively. These values are in good agreement with values for 1,3-dimethylcycloheptane and 1,4-dimethylcycloheptane and reflect the availability of numerous low-energy conformations for each of the isomers.

Conformational analysis of seven-membered carbocyclics has received considerable recent attention.[1-7] Computer calculations by Hendrickson[1] have provided a detailed account of the symmetry and energetics of cycloheptane conformations. A study of coupling constants for cis and trans 2-substituted cycloheptanols[8] indicated that there were no conformational preferences for substituents and that the differences in coupling constants were due only to differences in configuration of the isomers. Thermochemical data[9] for *cis*- and *trans*-1,3-dimethylcycloheptane and *cis*- and *trans*-1,4-dimethylcycloheptane indicated enthalpy differences close to zero.

The initial results from our conformational studies of substituted 1,3-dioxacycloheptanes[10] are reported here. These compounds were selected for their ease of preparation and their amenability to equilibration studies.[11] They also provided an opportunity to study conformational preferences for alkyl substituents in a pseudorotating, heterocyclic system.

Conformational analysis of cyclohexane and 1,3-dioxacyclohexane is reasonably facilitated by the absence of a low-energy pseudorotational barrier and by the existence of only one chair conformation. A study of Dreiding models reveals that 1,3-dioxacycloheptane has four distinct chair conformations (**1**–**4**) in addition



1 2 3 4

to their respective twist–chair conformations. There are two conformations in which the syn-4,7-diaxial proton–proton interactions are absent plus two conformations in which the two-proton eclipsing interactions at C(5,6) are absent. On the basis of steric interactions alone, it would appear that chair conformation **4** is preferred over any of the twist–chair conformations. This is in contrast to the finding that the twist–chair conformation of cycloheptane is more stable than the chair conformation.[3] A comparison of Dreiding models reveals that the distance between the 1,3-diaxial positions for 1,3-dioxacyclohexane and 1,3-dioxacycloheptane are comparable. The distance between the 4,7-diaxial positions for 1,3-dioxacycloheptane is smaller than for 1,3-dioxacyclohexane. This suggests that 1,3-diaxial and 4,7-diaxial Me–H steric interactions should be more severe for both these heterocyclic compounds than for the corresponding carbocyclic compounds.[3,11,12]

Configurational and Conformational Assignments. *cis*- and *trans*-4,7-Dimethyl-1,3-dioxacycloheptanes.—The isomers of 4,7-dimethyl-1,3-dioxacycloheptane were separated by gas chromatography. Configurational assignments were made on the basis of proton and carbon-13 magnetic resonance spectra. A study of models indicated that there were seven possible chair conformations for the trans isomer and eight possible

(1) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **89**, 7036 (1967).
(2) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **89**, 7043 (1967).
(3) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **89**, 7047 (1967).
(4) J. D. Roberts, R. Knorr, and C. Ganter, *Angew. Chem., Int. Ed. Engl.* **6**, 556 (1967).
(5) M. Cristl and J. D. Roberts, *J. Org. Chem.*, **37**, 3443 (1972).
(6) E. S. Glazer, R. Knorr, C. Ganter, and J. D. Roberts, *J. Amer. Chem. Soc.*, **94**, 6026 (1972).
(7) H. Friebolin, R. Meck, S. Kabuss, and A. Luttringhaus, *Tetrahedron Lett.*, 1929 (1964).
(8) A. Bauman and H. Mohrle, *Tetrahedron*, **25**, 135 (1969).
(9) G. Mann, M. Muhlstadt, R. Muller, E. Kern, and W. Hadeball, *Tetrahedron*, **24**, 6941 (1968).
(10) H. Friebolin and S. Kabuss, "Nuclear Magnetic Resonance in Chemistry," B. Pesce, Ed., Academic Press, New York, N. Y., 1965, reports nmr studies for 2,2-dimethyl-1,3-dioxacyclohept-5-ene.
(11) E. L. Eliel and M. C. Knoeber, *J. Amer. Chem. Soc.*, **88**, 5347 (1966).
(12) W. Nader and E. L. Eliel, *J. Amer. Chem. Soc.*, **92**, 3050 (1970).

TABLE I

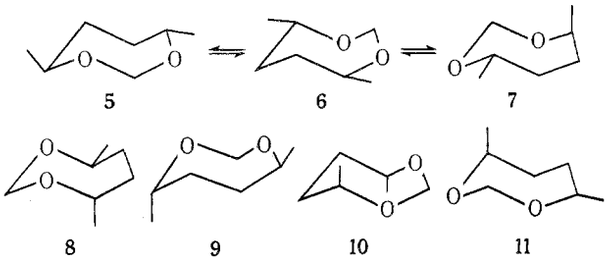
PROTON CHEMICAL SHIFTS FOR SOME 1,3-DIOXACYCLOHEPTANES

Registry no.	1,3-Dioxacycloheptanes	H-C(2)	H-C(4,7)	CH_3
41887-61-0	*cis*-4,7-Dimethyl	5.16, 5.47	6.17	8.84
41887-62-1	*trans*-4,7-Dimethyl	5.30	6.19	8.82
41887-63-2	*cis*-2-*tert*-Butyl-4-methyl	5.89	6.23	8.82
41887-64-3	*trans*-2-*tert*-Butyl-4-methyl	5.83	6.01	8.87
41887-65-4 (cis)	*cis*/*trans*-2-*tert*-Butyl-5-methyl	5.58		8.81, 9.01
41887-66-5 (trans)				
505-65-7	1,3-Dioxacycloheptane	5.49	6.46	
41887-67-6	2-*tert*-Butyl	5.96	6.31	

chair conformations for the cis isomer. The conformations for the trans isomer are shown in Chart I.

CHART I

CONFORMERS OF *trans*-4,7-DIMETHYL-1,3-DIOXACYCLOHEPTANE



5 6 7 8 9 10 11

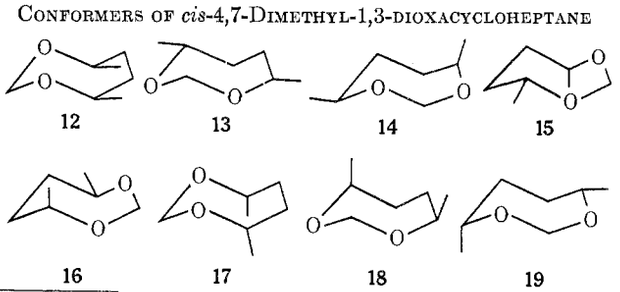
Using Hendrickson's values[3,13] for the steric interaction energies of a single methyl group with the other atoms of cycloheptane as a guide and recalling that 1,3-diaxial Me–H interactions are more severe in this heterocyclic system than in cycloheptane, it was estimated that conformers **8**, **9**, **10**, and **11** did not contribute more than 1% to the conformational array. Therefore they were excluded from further consideration.

Structures **5**, **6**, and **7** represent conformations of *trans*-4,7-dimethyl-1,3-dioxacycloheptane which differ by one pseudorotation. The twist–chair conformation which is obtained in the pseudorotation of **5** to **6** contains a C_2 axis which makes the C(2) protons equivalent. This pseudorotation inverts the C(2) protons but the methyl groups remain equatorial. The trans configuration was assigned to the isomer whose C(2) protons gave an A_2 nmr spectrum at τ 5.30. The proton nmr chemical shifts (τ) are listed in Table I.

Chart II shows the conformers of *cis*-4,7-dimethyl-1,3-dioxacycloheptane. Estimation of the steric interaction energies for all conformers indicates that **16**, **17**, **18**, and **19** contribute less than 1% to the conformational array and they were excluded from further consideration. The pseudorotational sequence **12**, **13**, **14**, and **15** is such that the C(2) protons retain their conformational integrity. In each of these conformations the C(2) protons are diastereotopic and should yield an AB nmr spectrum. Therefore, the compound which gave the AB nmr spectrum at τ 5.16 and 5.47 was assigned the cis configuration.

CHART II

CONFORMERS OF *cis*-4,7-DIMETHYL-1,3-DIOXACYCLOHEPTANE



12 13 14 15 16 17 18 19

The unfavorable Me–H steric interactions found in conformers **8**, **9**, **10**, **11**, **16**, **17**, **18**, and **19** are as follows: A,[14] syn_0-diaxial 1,3-Me–H (1.16 Å); B, syn-diaxial 4,7-Me–H (1.88 Å); C, syn-diaxial 4,7-Me–Me (contact); D, syn-diaxial Me–H (contact); E, syn-diaxial 2,5-Me–Me (1.2 Å). Each of these conformers has a minimum of two unfavorable interactions, including at least one of type A. For this system of compounds, it appeared reasonable to exclude those conformations which contain at least two of these interactions from consideration when they appear in a pseudorotational or rotational sequence.[15]

Table II lists the carbon-13 chemical shifts for a series of 1,3-dioxacycloheptanes. Assignments were made by comparison with data for the 1,3-dioxacyclohexanes[16] and 1,3-dioxacyclohept-5-ene. The assignment for C(5,6) was made at 30.05 ppm, as this absorption did not occur in 1,3-dioxacyclohept-5-ene. The methyl assignments were made as indicated, since their absorptions did not occur in the spectrum of the unsubstituted compounds.

The carbon-13 chemical shifts for *trans*-4,7-dimethyl-1,3-dioxacycloheptane are, C(2), 91.95; C(4,7), 72.39;

(13) The Hendrickson values are reprinted here to aid in the estimation of steric interaction energies: 1i (0.5); 2e,2e′ (0.4); 2a,2a′ (3.0); 3e,3e′ (0.3); 3a,3a′ (3.3); 4e,4e′ (0.4); and 4a,4a′ (1.8). These values are not strictly applicable to this system owing to the replacement of two methylene groups by two oxygen atoms.

(14) The symbol syn_0 represents a 1,3-diaxial interaction which crosses an oxygen atom (CHOCH).

(15) It is interesting to note that conformer **12** is the rotamer (inversion) of conformer **17**, **13** is the mirror image of the rotamer of **18**, **14** is the mirror image of the rotamer of **19**, and **15** is the mirror image of the rotamer of **16**. If conformers **12–15** were inverting, the nmr spectrum for the C(2) protons would show the effects of averaging. The new spectrum could be A_2 due to accidental isochronicity or A′B′. The spectrum is not A_2. The question remains as to whether the observed spectrum is due to averaging of conformers **12–15**, as indicated by the steric interaction energies, or whether it is due to the averaging of conformers **12–19**. The chemical shift difference between the AB protons at C(2) for this compound is 17.9 Hz. This value is in good agreement with a value of 18.4 Hz for the chemical shift difference between the C(2) protons of *cis*-4,7-dimethyl-1,3-cyclohept-5-ene, which is conformationally locked so that no inversion is occurring (unpublished data of M. Adams). If in fact the conformers of *cis*-4,7-dimethyl-1,3-dioxacycloheptane were inverting, a difference in the chemical shifts between the C(2) protons would be expected to be small; for example, the nmr spectrum for the C(2) protons of 4-methyl-1,3-dioxacycloheptane gives an A_2 pattern. Therefore the assumption that conformers **16–19** do not contribute to the conformational array is consistent with the steric interaction energy estimates and the proton nmr spectrum.

(16) A. J. Jones, E. L. Eliel, D. M. Grant, M. C. Knoeber, and W. F. Baily, *J. Amer. Chem. Soc.*, **93**, 4772 (1971).

TABLE II

CARBON-13 CHEMICAL SHIFTS FOR SOME 1,3-DIOXACYCLOHEPTANES

Registry no.	1,3-Dioxacycloheptanes	C(2)	C(4)	C(7)	C(5)	C(6)	CH_3
	1,3-Dioxacycloheptane	94.67	67.24		30.05		
	cis-4,7-Dimethyl	94.07	75.89		33.76		22.36
	trans-4,7-Dimethyl	91.95	72.39		36.51		22.58
	cis-2-*tert*-Butyl-4-methyl	108.70	76.98	70.68	28.31		22.32
	trans-2-*tert*-Butyl-4-methyl	106.39	71.23	66.87	29.29		22.51
2463-48-1	4-Methyl	93.50	75.32	66.80	36.95	29.29	22.51
	cis/*trans*-2-*tert*-Butyl-5-methyl	109.71	76.45	68.23	34.80	37.90	18.22
		110.19	72.45	64.59			17.09
41887-69-8	5-Methyl	94.65	72.40	64.84	34.95	38.44	17.27

C(5,6), 36.51 ppm. C(4,7) and C(5,6) each gave a single value, which indicated that these chemical shifts were averaged owing to a pseudorotation which was rapid compared with the carbon-13 nmr time scale. The same observation was evident from the cis isomer data. Carbon-13 studies by Eliel[16] and Grant[17] showed a substantial chemical shift difference between axial and equatorial methyl groups, 4.3 ppm for cyclohexane and 3.5 ppm for 1,3-dioxacyclohexane. Therefore the 0.2-ppm difference in chemical shift for the methyl groups of the cis and trans dimethyl isomers could not be considered the difference between axial and equatorial positions. It is clear that the methyl groups experience some averaged conformational atmosphere and that the axial contribution to the carbon-13 chemical shifts is important.

The chemical shift parameters of Eliel,[16] Grant,[17] and Roberts[5] provided a check for the configurational assignments. The trans-4,7-dimethyl isomer had chemical shifts which differed from 1,3-dioxacycloheptane as follows: C(2), +2.81; C(4,5), −5.15; C(5,6), −6.46. Calculated values (obtained by giving equal weight to conformers **5**, **6** and **7**, but excluding **8**–**11**) gave, C(2), +3; C(4,7), −5.2; C(5,6), −8.9.

The chemical shift values for the cis isomer differed from the chemical shift values of the parent as follows: C(2), +0.69; C(4,7), −8.65; C(5,6), −3.71. Calculated values obtained by giving equal weight to conformers **12**–**15**, but excluding **16**–**19**, were, C(2), +1.2; C(4,7), −4.9; C(5,6), −5.6. The parameter[5,17,18] which appeared to be most sensitive to conformation was a paramagnetic shift due to a 1,3-diaxial Me–H interaction. Therefore the calculations for the chemical shifts at C(2) were most sensitive to that interaction. Conformer **7** made the total paramagnetic contribution to the conformational array for the trans isomer. Conformers **14** and **15** made no paramagnetic contribution at C(2) for the cis isomer. The calculated values for C(2) were consistent with the configurational assignments made on the basis of proton nmr. When all conformers were weighted equally for each of the isomers, the cis C(2) value was greater than +7 and the trans value was greater than +6. The calculated chemical shift values also supported the conclusion that the methyl group experienced some averaged (axial–equatorial) conformational atmosphere.

2-*tert*-Butyl-4-methyl-1,3-dioxacycloheptane.—Configurational assignments for *cis*- and *trans*-2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane were made on the basis of proton and carbon-13 nmr spectra. Charts III and IV depict the chair conformers of *trans*-2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane and *cis*-2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane, respectively. Conformers with an axial *tert*-butyl group were excluded on the basis of severe steric interactions. Twist–boat and boat conformations were considered to be of sufficiently high energy so as to provide only a minor contribution to the conformational array. Only one twist–boat conformation could have been considered for the cis isomer but it required a paramagnetic carbon-13 chemical shift at C(7), which was not consistent with the spectrum. For the trans isomer the most reasonable twist–boat required a paramagnetic carbon-13 chemical shift at C(4), which was also not consistent with its spectrum.

CHART III

CONFORMERS OF

trans-2-*tert*-BUTYL-4-METHYL-1,3-DIOXACYCLOHEPTANE

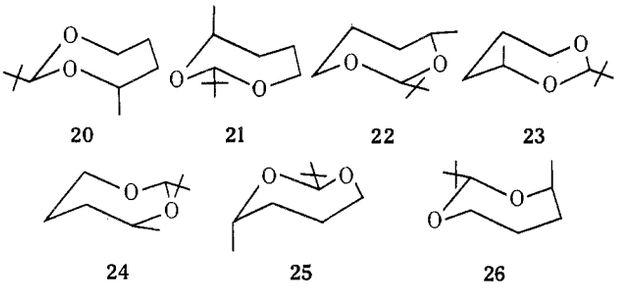
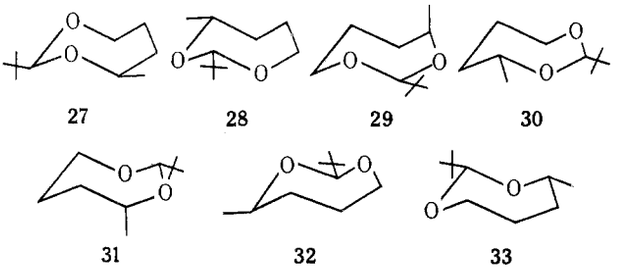


CHART IV

CONFORMERS OF

cis-2-*tert*-BUTYL-4-METHYL-1,3-DIOXACYCLOHEPTANE



A study of models for the conformers of the trans isomer indicated that conformations **20**, **21**, **23**, and **25** would make little contribution to the conformational array by virtue of the severe steric interactions. For example, conformer **20** showed one syn-diaxial 1,3-Me–H interaction and one syn-diaxial 4,7-Me–H interaction. Accordingly, only conformers **22**, **24**, and **26** were left to account for the proton and carbon-13 nmr spectra.

(17) D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.*, **94**, 5318 (1972).
(18) J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, and H. J. Reid, *J. Amer. Chem. Soc.*, **92**, 1388 (1970).

Conformers **22** and **24** were expected to give low-field chemical shifts for the axial methine C(4) protons because they were directly opposed to an oxygen atom across the ring and conformer **26** had an equatorial proton, which normally absorbs at lower field than an axial proton. The high-field C(4) proton absorption for the cis isomer was consistent with that conformational array, since the proton was axial for five of the conformations and was not found in a position opposed to oxygen.

The carbon-13 data were consistent with this interpretation, since the C(2) absorption for the trans isomer indicated a paramagnetic shift from conformer **26**. Examination of models for the conformers of the cis isomer dictated that none of the conformers could be discarded due to severe steric interactions and none of the conformers would give a paramagnetic shift at C(2). Accordingly, the assignments were made as indicated in the tables with the C(2) chemical shift for the trans isomer at 106.39 ppm. The remaining chemical shifts were found to be consistent with parameters from Eliel, Grant, and Roberts.

Equilibrium Studies. *cis*- and *trans*-2-*tert*-Butyl-5-methyl-1,3-dioxacycloheptane.—All attempts to separate the isomers of 2-*tert*-butyl-5-methyl-1,3-dioxacycloheptane were unsuccessful. The carbon-13 nmr indicated that both isomers were present in equal concentration. This isomer mixture was equilibrated (see Experimental Section) until the carbon-13 nmr spectra gave consistent areas[19] for the methyl, C(4), and C(7) peaks. Fortunately, the peaks were of equal area, so that it was not necessary to make unequivocal assignments for each of the absorptions. A $-\Delta G°_{82°}$ of 0.0 ± 0.5 kcal/mol was calculated for the 1:1 mixture.[20]

***cis*- and *trans*-2-*tert*-Butyl-4-methyl-1,3-dioxacycloheptane.**—Equilibrium for the *cis*- and *trans*-2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane was approached from both directions using samples of 95% purity. Relative concentrations of isomers were determined by integration of each of the nmr peaks for the C(2) axial proton and by integration of the appropriate peaks of the gas chromatograms. The cis:trans equilibrium ratio was found to be 1.9:1 and the $-\Delta G°_{355°}$ value was calculated to be 0.45 ± 0.05 kcal/mol.

Discussion

The low $-\Delta G°$ values for the 2-*tert*-butyl-4-methyl- and 2-*tert*-butyl-5-methyl-1,3-dioxacycloheptane isomerizations indicate that there are numerous low-energy conformations available for each of the systems. The $-\Delta G°$ of 0.45 kcal/mol for 2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane isomerization compares favorably with Eliel's $-\Delta G°$ value of 0.27 kcal/mol for the isomerization of 2-*tert*-butyl-4-methyl-1,3-dioxolane,[21] for which he suggested the availability of numerous low-energy conformations. The $-\Delta G°$ values of 2.9 kcal/mol for 2-*tert*-butyl-4-methyl-1,3-dioxacyclohexane[11] and 1.96 kcal/mol for 1,4-dimethylcyclohexane[22] are high in contrast to those mentioned above, since they are restricted to chair conformations in which the substituent must assume either axial or equatorial positions.

The enthalpy difference between *cis*- and *trans*-1,3-dimethylcycloheptane is approximately zero.[9] Calculation of the enthalpy difference between *cis*- and *trans*-2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane gives a value of 0.14 kcal/mol, assuming that the entropy contribution is due entirely to entropy of mixing ($R \ln {}^7/_3$). All allowable conformers in Charts I and II were given equal weight for this calculation.[23,24]

The $\Delta G°$ value of 0.0 kcal/mol for 2-*tert*-butyl-5-methyl-1,3-dioxacycloheptanes contrasts with a $\Delta G°$ value of −0.84 kcal/mol for 2-*tert*-butyl-5-methyl-1,3-dioxacyclohexanes and a $\Delta G°$ of −1.9 kcal/mol for 1,4-dimethylcyclohexanes. The enthalpy difference for the 1,4-dimethylcyclohexanes is also close to zero. Calculation of the enthalpy difference for the 2-*tert*-butyl-5-methyl-1,3-dioxacycloheptanes, assuming that the entropy contribution is due to mixing ($R \ln {}^7/_5$), gives a value of 0.24 kcal/mol, in good agreement with the value for 1,4-dimethylcyclohexanes.

The data support the concept of numerous low-energy conformations as an explanation for the low $\Delta G°$ values in pseudorotating systems. The suggestion that a combination of any two of the steric interactions is sufficiently severe to prohibit a pseudorotational sequence or severely limit the conformational array is strengthened by the enthalpy calculations.

Experimental Section

Proton nmr spectra were recorded on a Varian A-60A instrument. Samples were run as 10% solutions in carbon tetrachloride. All chemical shifts are reported in τ units. The carbon-13 nmr spectra were recorded at 25.15 MHz on a HA-100D nmr spectrometer interfaced to a Digilab NMR-FTS-3 pulse and data system. The samples were neat liquids. The number of data points was 8K or 16K as required to obtain satisfactory resolution. Spectra were recorded with broad band decoupling. All chemical shifts were referenced to internal TMS and reported in parts per million. All *m/e* values were determined on a AEI MS-9 high-resolution mass spectrometer. Separations were

(19) To reduce the probability that areas for the C(2), C(7), and methyl sets of absorptions were not the results of different relaxation rates, the spectra were run at three different pulse rates. The ratios of the areas remained constant.

(20) These equilibrations were run for 8, 24, and 148 hr in order to give reasonable assurance that equilibrium had been reached. These times exceed those required for the equilibration of 2-*tert*-butyl-4-methyl-1,3-dioxacycloheptanes and the 1,3-dioxolanes.

(21) W. E. Willy, G. Bensch, and E. L. Eliel, *J. Amer. Chem. Soc.*, **92**, 5394 (1970).

(22) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965.

(23) The steric interaction energies required to estimate the percentages of each of the conformers are not available. The best (or worst) that can be done is to assume equal concentrations. This assumption is consistent with the values calculated for the C(2) carbon-13 chemical shifts.

(24) A reviewer has expressed concern that the anomeric effect may have a major role in the determination of conformer concentrations [G. Baddely, *Tetrahedron Lett.*, 1645 (1973), and references cited therein]. A study of models indicates that the anomeric effect will disfavor **5** and **7** (Table I). Conformer **5** is probably best represented as a twist-chair, as indicated earlier, but a twist-chair for **7** will severely diminish the required paramagnetic shift at C(2). A twist-boat for **5** makes the anomeric effect less significant while a twist-boat for **7** reduces the anomeric effect but creates new steric interactions at C(4) and C(7). Anomeric effects for **8**, **9**, **10**, and **11** (Table I) are probably small compared with the highly unfavorable steric interactions for both the chair and twist-chair conformations. Conformations **16**, **17**, **18**, and **19** (Table II) have been rejected on the basis of steric effects and the nmr spectra. The twist-chair conformations must be rejected on the same basis, ref 15. The anomeric effect will disfavor **12**, **13**, and **14**. Twist-chair conformations for **12** and **14** relieve the 4,7-diaxial interactions and the anomeric effects would be less significant. However, conformer **14** accounts very well for the paramagnetic shift at C(5). There is no evidence that only one conformer in any of these compounds predominates. It is not clear how important energetically the anomeric effect is in these compounds. The chemical shift parameters would indicate that the anomeric effect is not strong enough to completely disfavor conformations such as **7** and **14**.

carried out on a Hewlett-Packard F & M 5752 gas chromatograph. The infrared spectra were recorded on a Beckman IR-8 instrument and the absorpton values are reported in microns.

1,3-Dioxacycloheptane, 1,3-dioxacyclohept-4-ene,[25] 2-methyl-1,4-butanediol,[26] and 1,4-pentanediol[27] were prepared as described in the literature.

1,3-Dioxacycloheptanes. General Procedure.—The preparation of 4-methyl-1,3-dioxacycloheptane is described as a representative example. A mixture of 10.4 g (0.1 mol) of 1,4-pentanediol, 3.0 g (0.1 mol) of paraformaldehyde, 100 ml of benzene, and 50 mg of *p*-toluenesulfonic acid was refluxed using a Dean–Stark distillation trap. The reaction was terminated when 1.8 ml of water was evolved. The mixture was fractionally distilled at atmospheric pressure to give 10.8 g (89%) of the desired product: bp 105–107° (760 Torr); n^{25}D 1.4226; ir (neat) 3.41, 8.46, 8.71, 8.90 μ; *m/e* 116 (parent peak).

4,7-Dimethyl-1,3-dioxacycloheptane.—The mixture of isomers had bp 65° (760 Torr) and the yield was 37%. The relative concentrations of the isomers were 78% cis and 22% trans. The diastereoisomers were separated by glpc (8 ft 10% Apiezon–Chromosorb column). The trans isomer was the first peak: n^{25}D 1.4269; ir 3.43, 3.49, 7.32, 8.68, 8.87, 9.09, and 9.26 μ; ^{1}H nmr CH_2(5,6) 8.27 ppm; *m/e* 130 (parent peak).

The cis isomer was the second peak: n^{25}D 1.4214; ir (neat) 3.38, 3.44, 7.35, 8.68, 8.87, and 9.06 μ; *m/e* 130 (parent peak).

2-*tert*-Butyl-4-methyl-1,3-dioxacycloheptane.—The mixture of isomers was distilled at 35° (1 Torr) and the yield was 72%. The isomers were separated by glpc (8 ft 10% Apiezon–Chromosorb column) and the cis isomer was the first peak: n^{25}D 1.4291; ir 3.43, 3.49, 6.74, 8.77, 9.15, and 9.52 μ; ^{1}H nmr *tert*-butyl 9.15, CH_2 (5,6) multiplet 8.30 ppm; ^{13}C nmr *tert*-butyl (C) 36.64, *tert*-butyl (CH_3) 25.10 ppm; *m/e* 116 (P − *tert*-butyl).

The trans isomer was the second peak: n^{25}D 1.4304; ir (neat) 3.41, 3.49, 6.73, 8.82, 9.03, 9.21, and 9.47 μ; ^{1}H nmr (CCl_4) *tert*-butyl 9.15, CH_2(5,6) multiplet 8.33 ppm; ^{13}C nmr *tert*-butyl (C) 36.21, *tert*-butyl (CH_3) 25.36 ppm.

2-*tert*-Butyl-5-methyl-1,3-dioxacycloheptane.—The mixture of isomers was isolated in 45% yield: bp 44° (1 Torr); n^{25}D 1.4323; ir (neat) 3.38, 3.48, 6.79, 6.90, 7.38, 8.33, and 8.93 μ; ^{1}H nmr (CCl_4) *tert*-butyl 8.92; ^{13}C nmr *tert*-butyl (C) 36.57, *tert*-butyl (CH_3) 25.17; *m/e* 116 (P − *tert*-butyl).

4-Methyl-1,3-dioxacycloheptane.—The product was isolated in 89% yield: bp 105° (760 Torr); n^{25}D 1.4226; ir (neat) 3.41, 8.46, 8.71, and 8.90 μ; ^{1}H nmr (CCl_4) Me 8.83, OCH_2O 5.32, CH 6.15, OCH_2C multiplet at 6.26 ppm; *m/e* 116 (parent peak).

5-Methyl-1,3-dioxacycloheptane.—The product was isolated in 44% yield: bp 48° (0.3 Torr); n^{25}D 1.4266; ir (neat) 3.41, 8.71, 8.90, and 9.43 μ; ^{1}H nmr (CCl_4) Me 9.33, OCH_2O 5.37, CH_2-OCH_2O multiplet 6.49, CH 8.41, CH_2 multiplet 8.35 ppm; *m/e* 116 (parent peak).

Equilibration of *cis*-2-*tert*-Butyl-4-methyl-1,3-dioxacycloheptane.—A 50-ml three-neck flask equipped with a condenser, thermometer, and drying tube was charged with 0.54 g of *cis*-2-*tert*-butyl-4-methyl-1,3-dioxacycloheptane, 5 mg of *p*-toluenesulfonic acid, and 10 ml of dry benzene. The mixture was heated to reflux for periods of 8, 24, and 148 hr and analyzed by glpc. The response ratio for the glpc was found to be 1.0. The equilibrium ratios were identical with those found by integrating the C(2) proton areas of the nmr spectra. The cis:trans equilibrium ratio was found to be 1.91:1.

Equilibration of *trans*-2-*tert*-Butyl-4-methyl-1,3-dioxacycloheptane.—The procedure for this equilibration was the same as described for the cis isomer. The cis:trans equilibrium ratio was 1.9:1.

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(25) K. C. Brannock and G. Lappin, *J. Org. Chem.*, **21**, 1366 (1956).
(26) R. Rossi, P. Diversi, and G. Ingrosso, *Gazz. Chim. Ital.*, **98**, 391 1968).
(27) C. Fuganti and D. Ghiringhelli, *Gazz. Chim. Ital.*, **99**, 316 (1969).

Nonclassical Condensed Thiophenes. III. Studies in the Benzo[1,2-*c*:4,5-*c'*]dithiophene System

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The reaction of phosphorus pentasulfide and xylene with 1,2,4,5-tetrabenzoylbenzene (**13**) and with 1,3,6,7-tetraphenyl-4,5-dibenzoylisothianaphthene (**19**) affords 4,8-dihydro-1,3,5,7-tetraphenylbenzo[1,2-*c*:4,5-*c'*]dithiophene (**14**) and 4,8-dihydrohexaphenylbenzo[1,2-*c*:4,5-*c'*]dithiophene (**20**), respectively. Dehydrogenation of **14** and **20** affords diketones **18** and **19**. The intermediacy of **9** and **10** in these transformations is consistent with similar reactions carried out on the recently synthesized compound **10**.

We have reported the synthesis of a number of nonclassical isocondensed thiophenes for which the only uncharged resonance contributors are those structures containing tetracovalent sulfur (**1–3**).[1] Other five-membered heterocycles containing tetracovalent sulfur have been reported. In these compounds, at least one sulfur is directly bonded to a heteroatom (**4–6**)[2,3] or is in conjugation with a heteroatom whose lone electron pair is not used in π bonding (**7** and **8**).[4] We have now examined an approach to the synthesis of several derivatives (**9** and **10**) of the benzo[1,2-*c*:4,5-*c'*]dithiophene system which, although unsuccessful, involves the generation of compounds **9** and **10** as reaction intermediates.[5]

Tetrakisbromodurene (**11**)[6] was converted to 1,2,4,5-tetrabenzylbenzene (**12**) by reaction with benzene in the presence of anhydrous ferric chloride.[7] Chromic acid oxidation of **12** afforded the corresponding tetraketone **13** in 70% yield.[8] Treatment of **13** with phosphorus pentasulfide in boiling xylene yielded, as the

(1) (a) M. P. Cava and G. E. M. Husbands, *J. Amer. Chem. Soc.*, **91**, 3952 (1969), and references cited therein; (b) M. P. Cava and M. A. Sprecker, *ibid.*, **94**, 6214 (1972); (c) for a general review of this work see M. P. Cava, *Int. J. Sulfur Chem.*, in press.
(2) M. Carmack, R. W. Street, and R. Y. Wen, 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, Abstract ORGN-54.
(3) J. D. Bower and R. H. Schlessinger, *J. Amer. Chem. Soc.*, **91**, 6891 (1969).
(4) K. T. Potts and D. McKeough, *J. Amer. Chem. Soc.*, **94**, 6215 (1972).
(5) The isolation of crystalline compound **10** was reported after the writing of the first draft of this paper: K. T. Potts and D. McKeough, *J. Amer. Chem. Soc.*, **95**, 2750 (1973).
(6) W. Reid and H. Boden, *Ber.*, **89**, 2328 (1956).
(7) The preparation of **12** from the less readily available tetrakischlorodurene has been reported: V. G. Dreschler and W. Genill, *J. Prakt. Chem.*, **26**, 24 (1964).
(8) E. Profft, V. G. Dreschler, and H. Oberender, *Chem. Abstr.*, **55**, 2564 (1961).