

mer,²² proton-transfer tautomers,²³ ring-chain tautomers,²⁴ and diastereoisomeric hemiacetals,²⁵ as well as the isomers related by 1,3-acyl migration discussed above. In many of the cases cited it is not clear whether the selectivity observed is due to preferential nucleation of one isomer or to a thermodynamic preference for one isomer in the crystalline state.

(22) I. R. Gault, W. D. Ollis, and I. O. Sutherland, *Chem. Commun.*, 269 (1970); N. A. Bailey and S. E. Hull, *ibid.*, 960 (1971); D. Y. Curtin and J. W. Hausser, *J. Amer. Chem. Soc.*, **83**, 3474 (1961); E. F. Schoenwaldt, R. B. Kinnel, and P. Davis, *J. Org. Chem.*, **33**, 4270 (1968); M. Raban and E. Carlson, *J. Amer. Chem. Soc.*, **93**, 685 (1971); A. G. Sanchez, A. M. Valle, and J. Bellanato, *J. Chem. Soc. B*, 2330 (1971); F. Sondheimer, *Accounts Chem. Res.*, **3**, 81 (1972); A. Rieker and H. Kessler, *Chem. Ber.*, **102**, 2147 (1969); A. J. Bellamy and R. D. Guthrie, *J. Chem. Soc. C*, 2090 (1968).

(23) B. H. Chase and J. Walker, *J. Chem. Soc.*, 3518 (1953); J. W. Schulerberg, *J. Amer. Chem. Soc.*, **90**, 1367 (1968); E. M. Peresleni, M. Y. Uritskaya, V. A. Loginova, Y. N. Sheinker, and L. I. Yakontov, *Dokl. Akad. Nauk SSSR*, **183**, 1102 (1968); G. A. Newman and P. J. S. Pauwels, *Tetrahedron*, **25**, 4605 (1969); E. Spinner and G. B. Yeh, *J. Chem. Soc. B*, 279 (1971); T. Shono, Y. Hayashi, and K. Shima, *Bull. Chem. Soc. Jap.*, **44**, 3179 (1971); D. Hadzi, *J. Chem. Soc.*, 2143 (1956); G. T'oth, I. T'oth, and L. Toldy, *Tetrahedron Lett.*, 5299 (1969); W. Walter and K. J. Reubke, *Chem. Ber.*, **102**, 2117 (1969).

(24) P. R. Jones and P. J. Desio, *J. Org. Chem.*, **30**, 4203 (1965); W. Flitsch, *Chem. Ber.*, **103**, 3205 (1970); A. F. McDonagh and H. E. Smith, *J. Org. Chem.*, **33**, 1 (1968); W. Schaefer and H. Schlude, *Tetrahedron Lett.*, 2161 (1968); H. Alper, E. C. Keung, and R. A. Partis, *J. Org. Chem.*, **36**, 1352 (1971), and earlier papers.

(25) M. C. Tanret, *Bull. Soc. Chim. Fr.*, **33**, 337 (1905); C. S. Hudson and E. Yanovsky, *J. Amer. Chem. Soc.*, **39**, 1013 (1917); R. W. King, C. F. Murphey, and W. C. Wildman, *ibid.*, **87**, 4912 (1965); J. Karle, J. A. Estlin, and I. L. Karle, *ibid.*, **89**, 6510 (1967).

Differential thermal analysis in which **2a** was heated at a rate of 10°/min showed an endotherm (partial melting) interrupted by an exotherm (heat of reaction and recrystallization of the **3a** which had been formed) and then a melting endotherm corresponding to the melting of the product **3a**.²⁶ From the areas of these peaks the thermal changes were estimated to be 4.7 kcal/mol for the first endotherm and -6.9 kcal/mol for the exotherm. At the end of those changes, if melting, reaction, and recrystallization had taken place, the net change for the process **2a** (solid) → **3a** (solid) was 4.7 + (-) 6.9 = 2.2 kcal/mol. These data are not of high accuracy but the result is reasonable. The final melting endotherm had an area which gave a value for the heat of fusion of 12 kcal/mol for the **3a** which had been formed. The value of the heat of fusion obtained with recrystallized **3a** was 9.3 kcal/mol. The reason for the greater stabilization of **3a** by crystal packing forces must await information about the crystal structures of these compounds.

Registry No.—1, 20178-62-5; **2a**, 20178-63-6; **2b**, 35454-86-5; **2c**, 35356-68-4; **3a**, 20178-64-7; **3b**, 35427-28-2; **3c**, 35356-69-5.

(26) We are indebted to Dr. S. R. Byrn for these results. The method employed has been described: D. Y. Curtin, S. R. Byrn, and D. B. Pendergrass, Jr., *J. Org. Chem.*, **34**, 3345 (1969).

Carbon-13 Nuclear Magnetic Resonance Spectroscopy. Conformational Analysis of Methyl-Substituted Cycloheptanes, Cycloheptanols, and Cycloheptanones¹

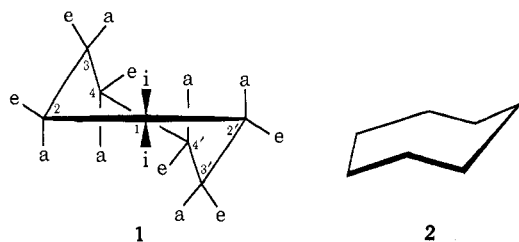
MANFRED CHRISTL² AND JOHN D. ROBERTS*

Contribution No. 4417 from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109

Received February 8, 1972

The ¹³C chemical shifts were determined of the carbons in 12 cycloheptanes, 21 cycloheptanols, and 8 cycloheptanones. In some cycloheptanols and cycloheptanones, the assignments have been obtained unambiguously by the synthesis of deuterated derivatives and the use of paramagnetic-shift reagents. Substituent effects for the different types of groups have been calculated. The most informative data about the cycloheptane conformations were provided by the relatively well understood γ effects. The results are generally in good agreement with predictions based on the twist-chair form, which has been predicted by Hendrickson to be the most stable conformation. Pairs of cis-trans isomers are found to have rather characteristic differences in their ¹³C spectra. This fact was used to assign the resonances found for cis-trans mixtures of methyl-substituted cycloheptanols to specific isomers.

In contrast to the many published studies of cyclohexane conformations, the results of relatively few experimental investigations of the cycloheptane conformations have been reported.³ One reason is complexity. The twist-chair conformation (1) of cyclo-



heptane is predicted to be most stable,⁴ and this form has three different equatorial (e) and axial (a) positions besides two identical isoclinal (i) or axis positions. Substituents at the i and the various e positions are calculated to have pretty much the same conformational energy.^{4d} To add to the complexities, and, in contrast to the rather rigid cyclohexane chair form, the cycloheptane twist form is quite flexible and an unsubstituted twist form can transform to another one by "pseudorotation" in which the axis of symmetry has moved by one carbon. The barrier to pseudorotation is estimated to be 1.4 kcal/mol^{4e} and the highest point of energy along the interconversion pathway is the chair form 2, which has a plane of symmetry.^{4e} The twist-boat (3) and the boat (4) are other cycloheptane con-

(1) Supported by the National Science Foundation.

(2) Max Kade Foundation, Inc., Fellow, 1970-1971.

(3) For a review see W. Tochtermann, *Fortschr. Chem. Forsch.*, **15**, 378 (1970).

(4) (a) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **83**, 4537 (1961); (b) *ibid.*, **84**, 3355 (1962); (c) *ibid.*, **89**, 7036 (1967); (d) *ibid.*, **89**, 7043 (1967); (e) *ibid.*, **89**, 7047 (1967).



formations which are also relatively stable. They can also be interconverted by pseudorotation, as for the chair forms. However, the calculated energies of **3** and **4** are higher by 2.4 and 2.7 kcal/mol than the twist-chair form.^{4c} It is expected, therefore, for simple substituted cycloheptanes that the boat family of forms should not be populated to more than 1% at room temperature. The results of calculations by Bixon and Lifson⁵ are similar to those of Hendrickson,⁴ except that they obtained an energy difference between twist-chair and chair conformations of only 0.7 kcal/mol. The substantial flexibility of the cycloheptane ring has been demonstrated by the fluorine-labeling technique.⁶ The low-temperature ¹⁹F spectra were found to be different from spectra taken at room temperature only if substituents like *gem*-methyl groups^{6a} or vicinal bromine atoms^{6b} were present. Pseudorotation is clearly very rapid unless relatively large substituents are present. No evidence was found which was not in agreement with the twist-chair conformation being favored at equilibrium. Heteroatoms, such as sulfur, in a saturated seven-membered ring also seem to increase the barrier to pseudorotation.⁷ X-Ray studies of 4-bromo-6,10-dimethylbicyclo[5.3.0]decan-3-one⁸ and the "dimeric cycloheptanone peroxide"⁹ show that the carbocyclic seven-membered rings in these compounds prefer the chair conformation in the solid state.

Carbon-13 nuclear magnetic resonance (¹³C nmr) has been used quite successfully in conformational studies with cyclohexane,^{10-12,13a} cyclopentane,¹⁴ and cyclononane^{13b} derivatives. Encouraged by these results, we have undertaken a ¹³C nmr investigation of cycloheptane derivatives, the results of which we report here.

Results and Discussion

The ¹³C chemical shifts were measured at about 40° and, of course, the rates of interconversion of the conformations are all exceedingly fast at this temperature. The shifts are therefore average values to which several conformations will contribute according to their popu-

lations as determined by the Boltzmann distribution. To assign the resonance lines to specific carbons, we used off-resonance proton decoupling and, whenever possible, specific proton decoupling.

A. Methylcycloheptanes.—The chemical shifts of methylcycloheptanes, kindly supplied by Professor James B. Hendrickson,¹⁵ have been determined in carbon disulfide as solvent, with tetramethylsilane as internal reference. Some representative cycloheptanes were also run in dioxane as solvent, which also served as internal reference. In dioxane, the shifts were uniformly upfield by about 1 ppm, compared to carbon disulfide. The results are summarized in Table I, while Table II gives the substituent effects of the methyl groups which result by comparison of the chemical shifts of a particular methyl-substituted cycloheptane with a corresponding cycloheptane having one less methyl group. The substituent effects are classified as α , β , γ , δ , and ϵ effects^{11a} and listed along with the previously determined methyl substituent effects for cyclohexanes.^{10a} The α effect is that produced by a methyl on a carbon to which it is directly attached, the β effect is on the carbon next removed, and so on.^{11a} Considerable difficulties will be encountered later in discussion of the shift changes by a need to distinguish between the numbering of positions for nomenclature purposes and the numbering of carbons in the twist-chair conformation where the isoclinal carbon will be taken as C-1. In order to clarify this, we will use C-1i, C-2e,a, etc., when we refer to the carbons of conformations, and omit the lower case letters otherwise.

In methylcycloheptane, the resonances of three methylene carbons can be readily distinguished. Compared to the unsubstituted cycloheptane, the resonance of C-2 at 155.0 ppm is shifted downfield by 9.3 ppm by the β effect of the methyl group. The position corresponding to C-3 is the result of a 1.3-ppm upfield γ effect, while the line for C-4 is 0.7 ppm downfield. The α and β effects have about the same magnitude as for methylcyclohexane.^{10a} The γ effect, however, is increased by 0.8 ppm. Because the γ effect appears to arise from direct steric interactions between the groups under consideration, it is believed to be relatively well understood.¹⁴ We assume here that the larger γ effect arises from a stronger average interaction between the methyl group and C-3 in methylcycloheptane than in methylcyclohexane. In this connection and in others to be discussed later, it is helpful to have Hendrickson's values for the steric interaction energies of a single methyl group with the other atoms of cycloheptane.^{4d}

Position	Calcd energy, kcal/mol
1i	0.5
2e,2e'	0.4
2a,2a'	3.0
3e,3e'	0.3
3a,3a'	3.3
4e,4e'	0.4
4a,4a'	1.8

The most stable conformation of 1,1-dimethylcycloheptane should be **5**, which is a twist-chair form with both methyl groups in the favorable isoclinal positions.

- (5) M. Bixon and S. Lifson, *Tetrahedron*, **23**, 769 (1967).
 (6) (a) J. D. Roberts, *Chem. Brit.*, 529 (1966); (b) R. Knorr, C. Ganter, and J. D. Roberts, *Angew. Chem.*, **79**, 577 (1967); *Angew. Chem., Int. Ed. Engl.*, **6**, 556 (1967); (c) E. S. Glazer, R. Knorr, C. Ganter, and J. D. Roberts, *J. Amer. Chem. Soc.*, **94**, 6026 (1972).
 (7) K. v. Bredow, H. Friebohn, and S. Kabuss, "Organic Chemistry, A Series of Monographs," Vol. 21, A. T. Blomquist, Ed., Academic Press, New York, N. Y., 1971, p 51.
 (8) T. Sato, H. Minato, M. Shiro, and H. Koyama, *Chem. Commun.*, 363 (1966).
 (9) P. Groth, *Acta Chem. Scand.*, **21**, 2631 (1967).
 (10) (a) D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.*, **89**, 6612 (1967); (b) D. K. Dalling, D. M. Grant, and L. F. Johnson, *ibid.*, **93**, 3678 (1971); (c) H. J. Schneider, R. Price, and T. Keller, *Angew. Chem.*, **83**, 759 (1971); *Angew. Chem., Int. Ed. Engl.*, **10**, 730 (1971).
 (11) (a) J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, and H. J. Reich, *J. Amer. Chem. Soc.*, **92**, 1338 (1970); (b) H. J. Reich, M. Jautelat, M. T. Messe, F. J. Weigert, and J. D. Roberts, *ibid.*, **91**, 7445 (1969).
 (12) G. W. Buchanan and J. B. Stothers, *Can. J. Chem.*, **47**, 3605 (1969).
 (13) (a) F. A. L. Anet, C. H. Bradley, and G. W. Buchanan, *J. Amer. Chem. Soc.*, **93**, 258 (1971); (b) F. A. L. Anet and J. J. Wagner, *ibid.*, **93**, 5266 (1971).
 (14) M. Christl, H. J. Reich, and J. D. Roberts, *ibid.*, **93**, 3463 (1971).

¹⁵ (15) J. B. Hendrickson and R. K. Boeckman, Jr., *J. Org. Chem.*, **36**, 2315 (1971).

TABLE I

¹³C CHEMICAL SHIFTS (IN PPM) OF METHYLCYCLOHEPTANES RELATIVE TO CARBON DISULFIDE

Registry no.	Cycloheptane	C-1	C-2	C-3	C-4	C-5	C-6	C-7	CH ₃
291-64-5	Cycloheptane ^a	164.3							
4126-78-7	Methyl	157.6	155.0	165.6	163.6				168.1
13151-49-0	1,1-Methyl	159.2	149.9	168.7	161.7				161.7
13151-50-3	<i>trans</i> -1,2-Dimethyl	151.2		156.7	165.8	162.8			169.9
13151-51-4	<i>cis</i> -1,2-Dimethyl	155.0		158.5	165.9	163.3			174.6
13151-52-5	<i>trans</i> -1,3-Dimethyl	161.4	147.8		155.0	163.4			168.2
13151-53-6	<i>cis</i> -1,3-Dimethyl	158.3	145.6		155.1	166.0			167.6
13151-54-7	<i>trans</i> -1,4-Dimethyl	157.3	155.9 ^b			155.7 ^b	168.4		168.2
14190-15-9	<i>cis</i> -1,4-Dimethyl	158.3	159.0			154.1	165.5		168.2
35099-89-9	1,1,2-Trimethyl	156.9	149.3	160.1	162.8 ^b	162.1 ^b	169.7	148.6	<i>trans</i> -1-CH ₃ 162.8 <i>cis</i> -1-CH ₃ 168.8 2-CH ₃ 173.7
24162-71-3	1,1,3-Trimethyl	160.1	141.1	163.0	153.1	162.4	169.0	150.0	<i>trans</i> -1-CH ₃ 163.0 <i>cis</i> -1-CH ₃ 160.1 3-CH ₃ 166.8
2158-55-6	1,1,4-Trimethyl	159.2	151.9 ^b	160.5	155.6	152.5 ^b	170.0	149.9	<i>trans</i> -1-CH ₃ 161.3 <i>cis</i> -1-CH ₃ 161.9 4-CH ₃ 168.4

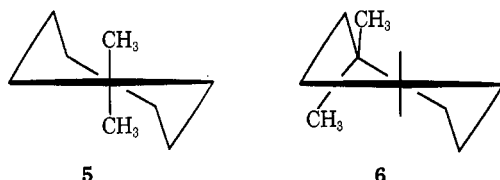
^a J. J. Burke and P. C. Lauterbur, *J. Amer. Chem. Soc.*, **86**, 1870 (1964). ^b Tentative assignments.

TABLE II

¹³C CHEMICAL-SHIFT SUBSTITUENT EFFECTS (IN PPM) PRODUCED BY SUBSTITUTION OF A METHYL GROUP ON CYCLOHEPTANE (CYCLOHEXANE), METHYLCYCLOHEPTANE (METHYLCYCLOHEXANE), AND 1,1-DIMETHYLCYCLOHEPTANE (1,1-DIMETHYLCYCLOHEXANE)^a

Cycloheptane (cyclohexane)	α Effect	β Effect	γ Effect	δ Effect	ϵ Effect
Methyl	-6.7 (-6.0)	-9.3 (-8.7)	1.3 (0.5)	-0.7 (0.7)	
1,1-Dimethyl	1.6 (3.1)	-5.1, -6.4 ^b (-4.1, -6.1 ^b)	3.1 (4.0)	-1.9 (-0.1)	
<i>trans</i> -1,2-Dimethyl	-3.8 (-3.8)	-6.4, -8.9 (-6.5, -9.6)	2.2, 1.7, 1.8 ^b (-0.3, -0.5, 2.5 ^b)	-0.8, 0.2 (-0.3)	
<i>cis</i> -1,2-Dimethyl	0.0 (1.3)	-2.6, -7.1 (-1.4, -5.0)	2.3, 3.5, 6.5 ^b (2.7, 4.3, 7.0 ^b)	-0.3, 0.3 (2.9)	
<i>trans</i> -1,3-Dimethyl	-4.2 (-0.5)	-7.2, -8.6 (-5.7, -7.5)	3.8, -0.2 (5.8, 6.0)	-2.2, 0.0, 0.1 ^b (1.9, 2.2 ^b)	
<i>cis</i> -1,3-Dimethyl	-7.3 (-6.3)	-9.4, -8.5 (-8.9, -9.0)	0.7, 2.4 (-0.1, 0.2)	0.4, 0.1, -0.5 ^b (0.4, -0.1 ^b)	
<i>trans</i> -1,4-Dimethyl	-6.3 (-6.2)	-9.7, or -9.9 -7.9 or -7.7 (-9.1)	0.9 or 0.7 2.8 (0.2)	-0.3 0.7 or 0.9 (0.5)	0.1 (0.0)
<i>cis</i> -1,4-Dimethyl	-5.3 (-3.7)	-6.6, -9.5 (-4.4)	4.0, -0.1 (4.9)	0.7, -0.9 (3.0)	0.1 (2.6)
1,1,2-Trimethyl ^c	-0.6 (-2.0)	-2.3, -8.6 (-2.9, -8.7)	1.1, -1.3, 1.1, ^b 7.1 ^b (-0.1, -1.4, -1.7 ^b , 9.7 ^b)	0.4, 1.0 (-0.2)	
1,1,3-Trimethyl ^c	-5.7 (-5.7)	-8.8, -8.6 (-9.5, -9.0)	0.9, 0.7 (0.0, -0.8)	0.3, 0.1, 1.3, ^b -1.6 ^b (0.3, -4.9, ^b 3.9 ^b)	
1,1,4-Trimethyl ^c	-6.1	-8.2, -9.2 or -9.8	2.0 or 2.6, 1.3	0.0, 0.0	-0.4, 0.2

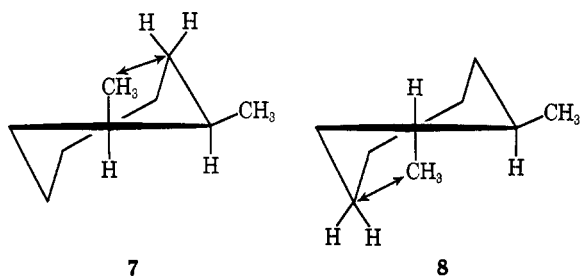
^a Parenthetical values are for cyclohexane derivatives. ^b Effect on the ¹³C nmr shift of a methyl already present. ^c Substituent effects relative to 1,1-dimethylcycloheptane.



The γ effect of the second methyl group is 3.1 ppm, which is 0.9 ppm less than in 1,1-dimethylcyclohexane, which indicates less axial character. The same trend is found in the α and β effects, which are less positive and more negative, respectively, than for 1,1-dimethylcyclohexane. However, 3.1 ppm for the γ effect is more than twice as much as in methylcycloheptane. Conformation 6, with the methyl groups in the 4e

and 4a positions, should be only about 1.2 kcal/mol less stable than 5, and may well be sufficiently populated to impose some average axial character to the methyl groups. The substituent effects seem to provide unambiguous assignments of the ¹³C nmr resonances of the *cis*- and *trans*-1,2-dimethylcycloheptanes. The serious steric interaction between the methyl groups in the *cis* isomer produces a large upfield shift of the methyl carbons, as has been observed in other similar compounds.^{10a, 11a, 14} The substituent effects in these isomers show the same regularities as in the 1,2-dimethylcyclohexanes. The α and β effects are more negative in the *trans* isomer, while the γ effects are larger in the *cis* isomer. In the most stable conformation of the latter, the methyl groups should occupy the

i and 2e or 2e' positions of the twist-chair (7). All the other conformations should be more than 1 kcal/mol

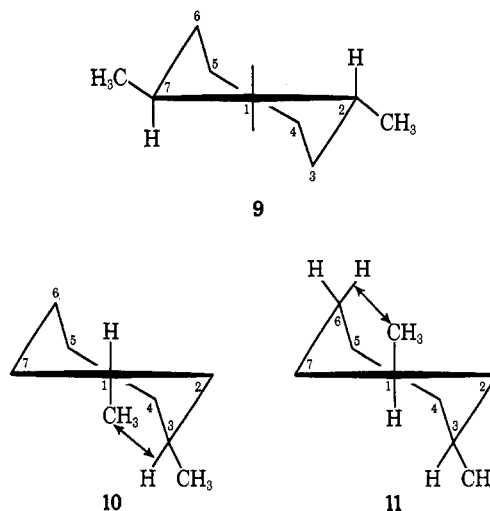


less stable but, because of their large number, they could well be considerably populated and, on the basis of Hendrickson's calculations,^{4d} the axial character of the methyl groups can be estimated to be 10%. For the trans isomer **8**, a much larger number of favorable conformations is possible and the axial character of the methyl groups should be below 1%. As a consequence of the relatively small difference in the conformational character of the methyl groups, their substituent effects do not differ so much between the cis and trans cycloheptane isomer as for the corresponding cyclohexanes, where the difference in the axial character is 50%. The two γ -methyl effects on the ring carbons in the cis isomer are different, being 2.3 and 3.5 ppm. This can be explained by an important contribution of **7**, in which introduction of an isoclinal methyl group will give a greater interference with the ring carbon adjacent to the methyl already present, rather than the one on the unsubstituted side. With the trans isomer, the situation is just reversed for the analogous conformation, as can be seen from **8**. However, both the size of the effects and their difference is smaller for the trans isomer because **8** is not the most favorable form. Other favorable conformations with the methyl groups in the 2e,3e, 3e,4e, 4e,4e', 4e',3e', and 3e',2e' positions should have smaller γ interactions, about the same magnitude as for methylcycloheptane itself. This is borne out by thermochemical data which show the enthalpy difference between the *cis*- and *trans*-1,2-dimethylcycloheptanes to be 0.7 kcal/mol¹⁶ compared to 1.87 kcal/mol¹⁷ between the corresponding cyclohexanes. The enthalpy differences between the *cis*- and *trans*-1,3- and -1,4-dimethylcycloheptanes are close to zero,¹⁶ while 1.96 and 1.90 kcal/mol have been determined for the corresponding cyclohexanes.¹⁷ These results follow from the average degree of axial character of the methyl groups which, from Hendrickson's^{4d} conformational energies of methyl groups, are indicated to be only about 6% for the 1,3-dimethylcycloheptanes and 2% for the 1,4-dimethylcycloheptanes. Nonetheless, the ¹³C nmr spectra seem sensitive to even the small differences for the 1,3 and 1,4 isomers. For the 1,2-dimethylcycloheptanes, the substituent effects resulting from introduction of the second methyl group are substantially different for the *cis* and *trans* isomers. With the 1,3-dimethylcycloheptanes, these differences decrease and become still smaller for the 1,4-dimethyl compounds.

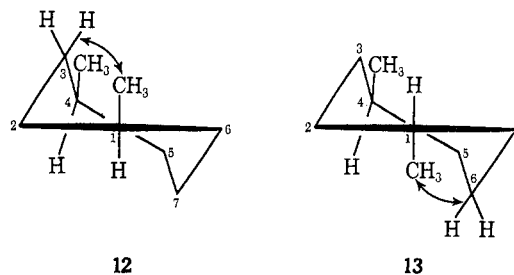
(16) G. Mann, M. Mülhstädt, R. Müller, E. Kern, and W. Hadeball, *Tetrahedron*, **24**, 6941 (1968).

(17) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, p 53.

The γ effects are especially interesting. The *trans*-1,3-dimethylcycloheptane should only be favorably disposed as **9** and **10**, because in these conformations

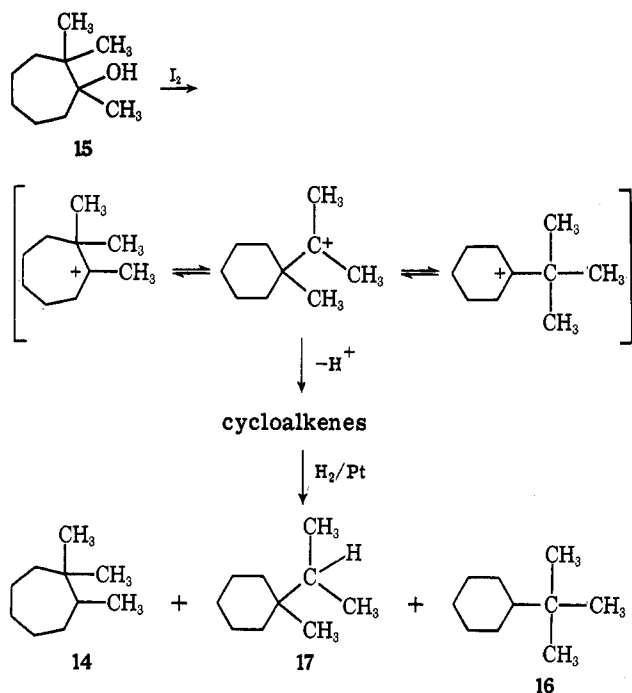


both methyl groups are placed in positions of minimum strain. The other trans conformations have at least one axial-type interaction. It is evident from **10** that an isoclinal methyl group should interact more strongly with C-3 than with C-6, which is reflected in the corresponding 3.8- and -0.5-ppm γ effects. The interaction with C-6 is the stronger one (2.4 ppm) in *cis*-1,3-dimethylcycloheptane, while the C-3 resonance is shifted upfield only by 0.7 ppm, both of which can be accounted for by **11**. The effects are smaller than in the trans compound, because for the cis compound there are two other conformations, 2e,4e and 3e,5e, which are quite favorable. This analysis is borne out by the shifts of the methyl carbons of the trans isomer, which appear at 0.6 ppm higher field than those of the cis isomer, in accord with greater average steric interactions of trans methyl groups. The methyl carbons of the *cis*- and *trans*-1,4-dimethylcycloheptanes have the same chemical shift. This is not surprising on the basis of the predicted difference in the interactions of the methyl groups in both the isomers. Again, the γ effects show a remarkable asymmetry. The C-3 interaction expected for conformation **12** of the cis isomer amounts to 4.0 ppm, which is close to the 4.9 ppm found for *cis*-1,4-dimethylcyclohexane. Practically no effect is found on the shift of C-7. Conformation **12**, one of



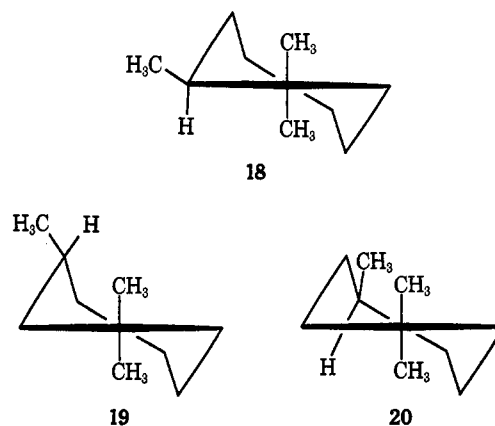
the favorable forms of the cis isomer, explains this well, while the interactions expected for **13** account for the reverse situation with the trans compound.

1,1,2-Trimethylcycloheptane (**14**) was not obtained pure. Dehydration of 1,2,2-trimethylcycloheptanol (**15**) yielded a mixture of cycloalkanes which, on hydrogenation, give a mixture of cycloalkanes. Gas chro-



matography of this mixture with two different columns showed it to be composed largely (88%) of two substances in equal amounts, one of which, from the ¹³C nmr spectrum, was clearly *tert*-butylcyclohexane (16).^{11a} Twelve other ¹³C nmr resonances remained to be identified. Taking into account only tertiary carbonium ions in the dehydration of 15, the reasonable other products appear to be 1-methyl-1-isopropylcyclohexane (17) or the desired 1,1,2-dimethylcycloheptane (14). One would expect 17 to exhibit seven ¹³C nmr resonance lines, while 14 should have ten. Prediction of the line positions of 17 from related compounds^{10a,18} gives a poor fit to the observed shifts, and the intensity ratios of the peaks are also incorrect. The most appropriate fit to the ten resonances expected for 14 are shown in Table I. Each of these assignments agrees with the off-resonance proton decoupled spectra. Two further resonances at 156.1 and 170.5 ppm were not assigned and were believed to arise from the 12% of remaining impurities. The substituent effects of the 2-methyl group (Table II) relative to 1,1-dimethylcycloheptane fit well in the general pattern of the substituent effects in methylcycloheptanes. 1,1,4-Trimethylcycloheptane was obtained by dehydration of 1,4,4-trimethylcycloheptanol and hydrogenation of the cycloalkene product. No rearrangement was detected.

It is evident from Table II that the γ effects of the 2-, 3-, and 4-methyl groups in 1,1,2-, 1,1,3-, and 1,1,4-trimethylcycloheptanes, respectively, are relatively small. If an additional methyl group is substituted on 1,1-dimethylcycloheptane, it can go to an equatorial position (18, 19, and 20) in which, at most, only a small γ interaction would be expected. In 1,1,2-dimethylcycloheptane, the assignment of the 1-methyl group, which is *cis* to the 2-methyl group, is facilitated by the direct steric interaction of these two groups, which produces a considerable differential between the shifts of the *gem*-methyl carbons (168.8 and 162.8 ppm). These γ effects of the 2-methyl are 1.1 and 7.1 ppm, slightly smaller than for *trans*-1,2-dimethyl- (1.8 ppm) and



slightly larger than for *cis*-1,2-dimethylcycloheptane (6.5 ppm).

B. Methylcycloheptanols.—There have been several studies in recent years dealing with the conformations of substituted cycloheptanols.^{19–22} In general, the results show the same kinds of regularities in spectra which are characteristic of the corresponding cyclohexanols, *i.e.*, that, in the *trans*-2-, *cis*-3-, and *trans*-4-methyl cycloheptanols, the hydroxyl group has more equatorial character than in the corresponding *cis*, *trans*, and *cis* isomers. However, the differences between *cis*–*trans* isomeric pairs are not usually so large as between the cyclohexanols. In the monomethylcycloheptanols, differences are greatest for the 2-methyl isomers. Borsdorf and coworkers²¹ have used Hendrickson's conformational energies^{4d} to calculate the differences in the axial character of the hydroxyl groups between *cis*–*trans* isomers for the 2-, 3-, and 4-methylcycloheptanols to be 23, 16, and 7%, respectively. With the corresponding methylcyclohexanols, the difference is expected to be about 70% for all three isomer pairs, if the conformational energy of a hydroxyl group is taken to be about one-half of that of a methyl group. For this kind of analysis, the proton spectra of dimethyl sulfoxide solutions are especially informative,²¹ because they give the chemical shift of the hydroxyl proton, and with secondary alcohols, the coupling constant with the carbinyl proton. These parameters have been shown to depend systematically on the axial character of the hydroxyl group.^{23,24} We have used this approach to characterize the secondary cycloheptanols used in this study, especially for mixtures, to determine which of the two isomers is the more abundant. It has also turned out that, for pairs of tertiary cycloheptanol isomers, the one with the more axial hydroxyl group has the more upfield hydroxyl proton chemical shift. The hydroxyl proton chemical shifts and coupling constants are collected in Table III.

All the cycloheptanols reported here were prepared by reduction of the corresponding ketones, which, in turn, were obtained by published procedures. Lithium aluminum hydride reduction of 3- and 4-methyl- and *cis*-3,5-dimethylcycloheptanone produced *cis*–*trans* mixtures of alcohols in ratios too close to 1:1 to permit

(18) D. M. Grant and E. G. Paul, *J. Amer. Chem. Soc.*, **86**, 2984 (1964).

(19) W. Hüchel and J. Wächter, *Justus Liebig's Ann. Chem.*, **672**, 64 (1964).
 (20) W. Hüchel and O. Honecker, *ibid.*, **678**, 10 (1964).
 (21) A. Zschunke, F.-J. Strüber, and R. Borsdorf, *Tetrahedron*, **24**, 4403 (1968).
 (22) H. Baumann, H. Moehrl, and A. Dieffenbacher, *ibid.*, **25**, 135 (1969).
 (23) O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **86**, 1256 (1964).
 (24) C. P. Rader, *ibid.*, **91**, 3248 (1969).

TABLE III
HYDROXYL PROTON CHEMICAL SHIFTS (IN PPM DOWNFIELD FROM EXTERNAL TETRAMETHYLSILANE^a) AND H-C-OH COUPLING CONSTANTS (IN HZ) OF CYCLOHEPTANOLS IN DIMETHYL SULFOXIDE SOLUTION

Registry no.	Substituent	δ	J
502-41-0	None ^b	4.26	4.0
19790-05-7	<i>trans</i> -2-Methyl ^c	4.23	5.0
19790-04-6	<i>cis</i> -2-Methyl ^c	4.05	4.4
933-16-4	<i>trans</i> -3-Methyl ^c	4.13	3.8
933-15-3	<i>cis</i> -3-Methyl ^c	4.17	4.2
10126-52-0	<i>trans</i> -4-Methyl ^c	4.23	4.0
19790-06-8	<i>cis</i> -4-Methyl ^c	4.20	4.0
1194-32-7	2,2-Dimethyl	4.11	4.6
35099-83-3	3,3-Dimethyl	4.12	4.1
35099-84-4	4,4-Dimethyl	4.27	4.3
35099-37-7	<i>trans,trans</i> -3,5-Dimethyl	4.17	4.0
35099-38-8	<i>cis,cis</i> -3,5-Dimethyl	4.17	4.0
3761-94-2	1-Methyl	3.96	
35099-39-9	<i>trans</i> -1,2-Dimethyl	3.67	
35099-40-2	<i>cis</i> -1,3-Dimethyl	3.91	
35099-41-3	<i>trans</i> -1,3-Dimethyl	3.94	
35099-42-4	<i>trans</i> -1,4-Dimethyl	3.91	
35099-43-5	<i>cis</i> -1,4-Dimethyl	3.95	
35099-86-6	1,2,2-Trimethyl	3.63	
35099-87-7	1,3,3-Trimethyl	3.79	
35099-88-8	1,4,4-Trimethyl	3.93	

^a The low-field ¹³C satellite of the dimethyl sulfoxide protons at δ 3.68²³ was used as internal reference. ^b From ref 21. ^c Slightly different values are reported in ref 21.

assignment of the resonances to specific isomers on the basis of resonance intensities. In these cases, one of the two isomers was concentrated by chromatography on neutral alumina, or else a different ratio from 1:1 of alcohols was obtained by catalytic hydrogenation. The tertiary cycloheptanols were synthesized from the ketones and methylolithium. In these reactions, the isomers were not formed in the same amount.

The ¹³C chemical shifts of 21 cycloheptanols and the substituent effects of the hydroxyl groups are shown in Table IV. Based on these parameters, the assignment of most of the resonance lines to specific carbons seems to be rather unambiguous. A few critical choices have been examined in detail, as by introduction of deuterium instead of hydrogen in specific locations, which causes almost complete loss of the signal of the directly attached carbon in the noise-decoupled spectra.^{11b} Thus, investigation of *cis*- and *trans*-2-methylcycloheptanol-2,7,7-*d*₃ led to the unambiguous assignment of C-7 in these compounds. The ¹³C nmr spectra of *cis*- and *trans*-3-methylcycloheptanol-2,2,7,7-*d*₄ and -2,2,6,6-*d*₄, as well as *cis*- and *trans*-4-methylcycloheptanol-2,2,7,7-*d*₄ and -3,3,7,7-*d*₄, permitted conclusive assignment of all of the carbons of the 3- and 4-methylcycloheptanols. Lanthanide shifts induced by europium tris(dipivaloylmethane), Eu(DPM)₃, and europium tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione), Eu(fod)₃, have been useful with our cycloheptanols. Downfield shifts of the resonances in the proton^{25,26} and carbon-13 spectra^{14,27} were observed and, because the effects normally (but by no means invariably) decrease with increasing distance of the nu-

cleus under consideration from the europium atom, assignments can be made on the basis of the relative size of the pseudocontact shifts within a molecule. The measured shifts for benzene solutions of the alcohols are shown in Table V. In the absence of the lanthanide complexes, the ¹³C nmr shifts differ only a few tenths of a part per million from those in Table IV, all of which were obtained for dioxane solutions. In contrast, the shifts of the methylcycloheptanes (Table I) are for carbon disulfide solutions, in which all resonances are shifted downfield by about 1 ppm, compared to dioxane. This should be kept in mind in discussion of the hydroxyl group substituent effects, which are calculated by subtraction of the chemical shifts of the corresponding cycloheptane from those of the cycloheptanol. Thus, the solvent influence makes all hydroxyl group substituent effects more positive by about 1 ppm.

The magnitudes of the hydroxyl group γ effects are sufficiently large for the monomethylcycloheptanols to make the uncertainties in them due to solvent effects unimportant. This should be no surprise after the discussion of the substituent effects in the dimethylcycloheptanes, where the axial character, if any, is divided between the two methyl groups. In the methylcycloheptanols, the methyl group, being the larger group, tends to occupy the equatorial positions, thus imposing axial character on the hydroxyl group which results in substantial γ interactions. For *trans*-2-, *cis*-3-, and *trans*-4-methylcycloheptanol, the sum of both the γ effects is smaller than in the corresponding *cis*, *trans*, and *cis* isomers, in accordance with expectations of the axial character of the hydroxyl groups in these compounds.²¹ However, the γ effects in the former isomers are relatively large compared to those for corresponding cyclohexanols^{11a} or for cycloheptanol itself. This may indicate some degree of population of conformations with axial hydroxyl groups or an increased γ effect of hydroxyl groups when forced into the isoclinal positions of the twist-chair (1) by having the methyl groups go equatorial.

The general pattern of the substituent effects in the cycloheptanols is very similar to that for the methylcycloheptanes. *Cis*-*trans* isomeric pairs display the same systematic differences in the α , β , and γ effects which decrease in going from the 2-methyl- to the 3-methyl- and finally to the 4-methylcycloheptanols. The asymmetry of the γ interactions discussed earlier is also observed. For *cis*-2-methylcycloheptanol, a large chemical-shift effect on the methyl carbon results from the direct steric interaction of the substituents, as has been observed also for *cis*-2-methylcyclohexanol^{11a} and cyclopentanol.¹⁴

The γ effects of the hydroxyl groups in the geminal dimethylcycloheptanols are larger than expected because of the tendency of the hydroxyl group to be forced into axial positions. The difference between the chemical shifts of the two methyl carbons in 2,2-dimethylcycloheptanol is larger than between those of the methyl carbons in the two 2-methylcycloheptanols and, because of the direct steric interaction with the hydroxyl group, the resonance of the *cis* methyl group should be the one at the higher field.

In 4,4-dimethylcycloheptanol, the asymmetry introduced by the hydroxyl group is not sufficient to make

(25) J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, **93**, 641 (1971), and references cited therein.

(26) R. E. Rondeau and R. E. Sievers, *ibid.*, **93**, 1524 (1971).

(27) J. Briggs, F. A. Hart, G. P. Moss, and E. W. Randall, *Chem. Commun.*, 364 (1971).

TABLE IV
¹³C CHEMICAL SHIFTS OF CYCLOHEPTANOLS^a

Substituents	C-1	C-2	C-3	C-4	C-5	C-6	C-7	1-CH ₃	2-, 3-, 4-, 5-CH ₃
None ^b	120.1	154.8	169.2	163.9					
	-44.2	-9.5	4.9	-0.4					
<i>trans</i> -2-Methyl	115.2	150.8	160.8	166.8	164.7	170.7	156.5	<i>trans</i> -2-CH ₃	172.3
	-39.8	-6.8	5.8	1.2	1.1	7.1	-9.1		4.2
<i>cis</i> -2-Methyl	119.3	154.1	163.1	167.0	164.8	170.6	158.2	<i>cis</i> -2-CH ₃	175.2
	-35.7	-3.5	8.1	1.4	1.2	7.0	-7.4		7.1
<i>trans</i> -3-Methyl	124.3	147.6	165.1	155.7	165.1	169.1	155.7	<i>trans</i> -3-CH ₃	169.1
	-41.3	-7.4	7.5	0.7	-0.5	5.5	-7.9		1.0
<i>cis</i> -3-Methyl	121.9	146.0	162.9	156.3	166.9	170.4	155.3	<i>cis</i> -3-CH ₃	168.9
	-43.7	-9.0	5.3	1.3	1.3	6.8	-8.3		0.8
<i>trans</i> -4-Methyl	121.0	157.1	161.1	158.6	156.4	172.3	155.7	<i>trans</i> -4-CH ₂	169.3
	-42.6	-8.5	6.1	1.0	1.4	6.7	-7.9		1.2
<i>cis</i> -4-Methyl	121.9	158.7	163.1	159.0	155.4	170.4	155.1	<i>cis</i> -4-CH ₄	169.3
	-41.7	-6.9	8.1	1.4	0.4	4.8	-8.5		1.2
2,2-Dimethyl	113.8	155.6	153.6	171.0	164.6	168.6	159.9	<i>trans</i> -2-CH ₃	164.6, <i>cis</i> -2-CH ₃
	-36.1	-3.6	3.7	1.3	2.9	6.9	-8.8		2.9, 8.8
3,3-Dimethyl	124.9	141.2	162.0	150.7	170.1	166.8	153.5	<i>trans</i> -3-CH ₃	163.7, <i>cis</i> -3-CH ₃
	-43.8	-8.7	2.8	0.8	1.4	5.1	-8.2		2.0, -0.7
4,4-Dimethyl	120.6	161.2	153.4	160.3	150.8	174.0	157.6	<i>trans</i> -4-CH ₃	162.4, <i>cis</i> -4-CH ₃
	-41.1	-7.5	3.5	1.1	0.9	5.3	-4.1		0.7, 0.7
<i>trans,trans</i> -3,5-Dimethyl	123.7	147.2	165.5	145.7	157.6	160.1	157.6	<i>trans</i> -3-CH ₃	169.1, ^c <i>trans</i> -5-CH ₃
	-42.3	-7.9	7.2	0.1	-0.7	5.0	-8.4		<i>d</i> , <i>d</i>
<i>cis,cis</i> -3,5-Dimethyl	122.6	145.7	162.6	145.7	159.8	162.6	158.5	<i>cis</i> -3-CH ₃	168.5, ^c <i>cis</i> -5-CH ₃
	-43.4	-9.4	4.3	0.1	1.5	7.5	-7.5		<i>d</i> , <i>d</i>
1-Methyl	120.3	150.1	170.5	163.3				162.0	
	-37.3	-4.9	4.9	-0.3				-6.1	
<i>trans</i> -1,2-Dimethyl ^e	120.1	149.3	162.0	165.0 ^e	164.2 ^e	171.1	149.9	163.8	<i>trans</i> ^e -2-CH ₃
	-31.1	-1.9	5.3	<i>f</i>	<i>g</i>	5.3	-6.8	-6.1	175.9, 6.0
<i>cis</i> -1,3-Dimethyl ^e	121.1	141.1	163.0	154.6	164.3	170.5	150.2	160.7	<i>cis</i> ^e -3-CH ₃
	-37.2	-4.2	4.7	-0.5	-1.7	4.5	-4.9	-6.9	168.1, 0.5
<i>trans</i> -1,3-Dimethyl ^e	120.7	141.1	165.4	154.0	163.6	170.5	149.8	163.0	<i>trans</i> ^e -3-CH ₃
	-40.7	-6.7	4.0	-1.0	0.2	7.1	-5.2	-5.2	168.0, -0.2
<i>trans</i> -1,4-Dimethyl ^e	120.6	152.0	162.7	157.4	154.4	171.4	150.1	161.6	<i>trans</i> ^e -4-CH ₃
	-36.7	<i>h</i>	<i>i</i>	0.1	<i>j</i>	3.0	<i>k</i>	-6.6	169.3, 1.1
<i>cis</i> -1,4-Dimethyl ^e	120.4	152.7	161.8	157.2	154.0	171.6	149.7	162.2	<i>cis</i> ^e -4-CH ₃
	-37.9	-6.3	2.8	-1.1	-0.1	6.1	-4.4	-6.0	169.5, 1.3
1,2,2-Trimethyl	117.9	152.8	155.5	171.2	166.6	172.0	153.6	167.3	<i>trans</i> ^e -2-CH ₃
	-31.4	-4.1	6.9	1.5	<i>l</i>	<i>m</i>	-6.5	-6.4	168.0, ^c <i>cis</i> ^e -2-CH ₃
1,3,3-Trimethyl	120.4	138.6	159.9	150.2	167.9	168.3	149.6	160.1	<i>trans</i> ^e -3-CH ₃
	-42.6	-2.5	-0.2	0.2	-1.1	5.9	-3.5	-6.7	162.3, <i>cis</i> ^e -3-CH ₃
1,4,4-Trimethyl	121.5	156.6	158.4	160.2	149.7	173.9	148.0	161.4	<i>trans</i> ^e -4-CH ₃
	-34.1	-3.9	<i>p</i>	1.0	-0.2	3.9	<i>q</i>	-7.0	162.6, <i>cis</i> ^e -4-CH ₃

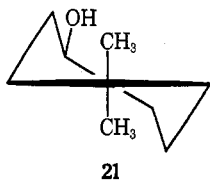
^a The upper numbers for each alcohol are the experimentally determined chemical shifts in parts per million upfield from carbon disulfide; the second values are substituent effects obtained by subtracting the chemical shifts in parts per million of cycloheptane or the corresponding methylcycloheptanes. ^b From ref 11a. ^c Tentative assignments. ^d 0.9 or 1.5 ppm. ^e Cis and trans refers to the 1-methyl group. ^f -0.8 or -1.6 ppm. ^g 1.4 or 2.2 ppm. ^h -3.9 or -3.7 ppm. ⁱ 6.8 or 7.0 ppm. ^j -1.3 or -1.5 ppm. ^k -5.6 or -5.8 ppm. ^l 4.5 or 3.8 ppm. ^m 9.2 or 9.9 ppm. ⁿ 5.2 or 5.4 ppm. ^o 0.6 or 0.8 ppm. ^p 6.5 or 5.9 ppm. ^q -4.5 or -3.9 ppm.

TABLE V
PSEUDOCONTACT SHIFTS OF ¹³C RESONANCES IN SOME CYCLOHEPTANOLS (IN PPM)

Substituents	Molar ratio complex/cycloheptanols	C-1	C-2	C-3	C-4	C-5	C-6	C-7	1-CH ₃	2-, 3-, 4-, 5-CH ₃
<i>trans,trans</i> -3,5-Dimethyl ^a	0.14	-6.9	-1.8	-1.0	-0.8	-0.8	-1.2	-2.2		3,5-CH ₃
	0.22	-10.2	-3.0	-1.7	-1.3	-1.4	-1.6	-3.5		-0.4, -0.2
<i>cis,cis</i> -3,5-Dimethyl ^a	0.14	-8.0	-2.6	-1.1	-0.8	-0.9	-1.1	-2.2		-0.6, -0.4
	0.22	-12.8	-4.1	-1.8	-1.3	-1.3	-1.8	-3.5		-0.4, -0.2
1,2,2-Trimethyl ^a	0.24	<i>b</i>	-3.5	-2.6	-1.8	<i>c</i>	-2.8	-5.4	-6.8	2-CH ₃ , <i>c</i>
1,3,3-Trimethyl ^d	0.15	-6.2	-1.6	-0.6	-0.6	-0.5	-0.8	-1.6	-2.1	<i>trans</i> ^e -3-CH ₃
										-0.5, -0.2
1,4,4-Trimethyl ^d	0.10	<i>b</i>	-1.2	-0.7	-0.5	-0.6	-0.8	-1.0	-1.6	<i>cis</i> ^e -3-CH ₃
										4-CH ₃ , -0.3

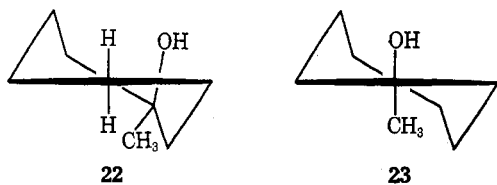
^a Shift reagent Eu(DPM)₃. ^b Not observed. ^c Obscured by the *tert*-butyl methyl carbon resonance of Eu(DPM)₃ at 164.5 ppm. ^d Shift reagent Eu(fod)₃. ^e Cis and trans refer to the 1-methyl group.

the methyl carbons nonequivalent. Presumably, there is a relatively small effect of the equatorial hydroxyl on the environment of the methyls in **21**, which is expected to be the most stable conformation for this substance.



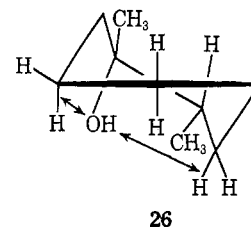
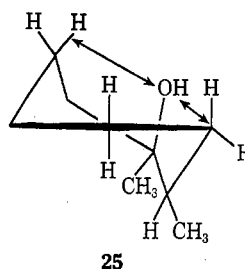
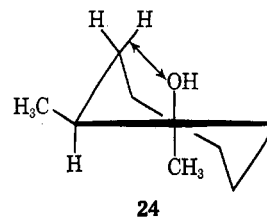
The two isomeric 3,5-dimethylcycloheptanols which have the methyl groups *cis* to each other show characteristic differences in the ^{13}C nmr spectrum. The hydroxyl protons, however, have the same chemical shift and the same coupling constant as the carbinyl proton (Table III), indicating similar conformational positions for the hydroxyl groups. The pseudorotation itinerary of the twist-chair model, which contains 14 conformations, predicts a more equatorial hydroxyl group for the *cis,cis* isomer than for the *trans,trans* isomer. The substituent effects of the hydroxyl groups on the ^{13}C resonances reflect this trend. In one isomer, the α effect and the sum of the β effects are more negative, while the sum of the γ effects is less positive than for the other isomer, as would be expected for a higher equatorial character for the hydroxyl group of the former isomer which, therefore, should be the *cis,cis* structure.

The γ interaction of the hydroxyl group in 1-methylcycloheptanol, as reflected by the chemical shifts, is somewhat larger than the γ effect of a methyl group in 1,1-dimethylcycloheptane. This may indicate that **22**



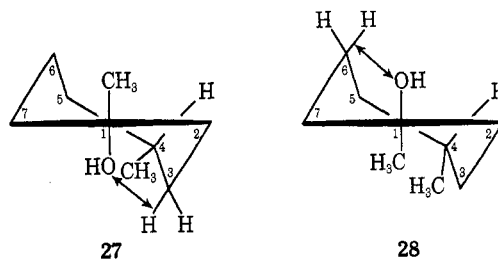
has some significant population relative to **23**. The principal product from 2-methylcycloheptanone and methyl lithium appears to be the one with *trans*-methyl groups, because the chemical shift of the 1-methyl carbon is only 1.8 ppm upfield from the corresponding peak in 1-methylcycloheptanol. If the addition were to give *cis*-methyls, about a 6.5-ppm upfield shift would be expected (compare *cis*- and *trans*-1,2-dimethylcycloheptane). The γ effects of the hydroxyl in this compound are both 5.3 ppm, which appears to rule out **24** from being the only important conformation because it has only one strong γ interaction. Significant population of **25** and **26** would balance the γ effects of the hydroxyl, and these conformations are expected to be substantially more important than the corresponding ones for 1,1,2-trimethylcycloheptane because the relatively small hydroxyl group should not be so unfavorably situated in a 4a or 4a' position of the twist-chair (1) as a methyl group.

The assignment of the two sets of lines of different intensities in the mixture of the 1,3-dimethylcycloheptanols to specific isomers has been made on the basis of the chemical shifts of the methyl carbons, the isomer with the low field 1-methyl being taken to have the methyl groups *cis*. With the exception of these and

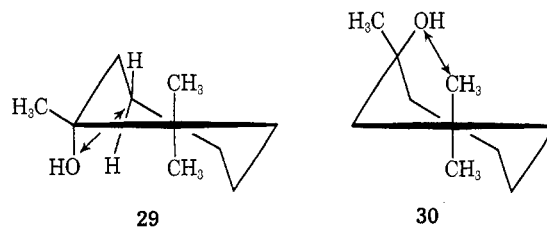


the resonances of C-3, all the chemical shifts are rather similar.

Still more similar in their ^{13}C nmr spectra are the two 1,4-dimethylcycloheptanols. The assignments followed those for the 1,3-dimethyl compounds except that now *cis* and *trans* were exchanged. The number of favorable conformers with both the methyl groups in equatorial or isoclinal positions are five for the *trans* and four for the *cis*. The similarity in the chemical shifts of the two isomers is therefore not surprising. The asymmetry of the γ interactions in these isomers can be explained by conformations **27** and **28**. The



1,2,2-, 1,3,3-, and 1,4,4-trimethylcycloheptanols are rather highly substituted. Based on Hendrickson's conformational energies of the methyl group, and assuming half of these values for a hydroxyl group, one can calculate the energies of the possible conformations. The results suggest that, for all three cases, twist-chair forms should be more stable than other conformations by about 1 kcal/mol. The most favorable conformer of 1,2,2-trimethylcycloheptanol should be **29**, which



reflects the asymmetry of the γ effect of the hydroxyl group on the resonances of C-6 and C-3. The small chemical-shift difference between the two 2-methyl carbons allows only an arbitrary assignment, while the peak for the 1-methyl carbon was positively identified by specific proton decoupling.

TABLE VI

¹³C CHEMICAL SHIFTS OF CYCLOHEPTANONES RELATIVE TO CARBON DISULFIDE (IN PPM)

Registry no.	Cycloheptanane	C-1	C-2	C-3	C-4	C-5	C-6	C-7	2-CH ₃	3-CH ₃	4-CH ₃
502-42-1	Cycloheptanone ^a	-18.9	150.1	169.3	163.1						
932-56-9	2-Methyl	-19.9	147.2	159.9	164.5	163.3	168.8	150.9	176.1		
933-17-5	3-Methyl	-17.7	141.7	162.0	153.9	164.5	168.9	149.4		169.9	
5452-36-8	4-Methyl	-18.9	151.1	160.8	156.5	154.3	170.0	149.6			170.0
7228-52-6	2,2-Dimethyl	-21.7	146.1	154.0	168.2	162.5	166.7	153.5	167.6		
23438-70-2	3,3-Dimethyl	-16.9	137.5	160.8	148.4	168.9 ^b	168.1 ^b	149.5		163.9	
35099-49-1	4,4-Dimethyl	-18.6	154.1	156.9	159.9	149.8	173.3	149.8			164.6
24291-91-6	<i>cis</i> -3,5-Dimethyl	-18.0	141.2	162.2	144.6	157.0	160.4	150.4		168.9	168.9

^a From ref 31. ^b Uncertain assignments.

TABLE VII

¹³C CHEMICAL SHIFT SUBSTITUENT EFFECTS (IN PPM) ON CYCLOHEPTANE, METHYLCYCLOHEPTANE, AND 1,1-DIMETHYLCYCLOHEPTANE PRODUCED BY A KETONE GROUP

Cycloheptanone	α Effect	β Effect	γ Effect	δ Effect	Effect on the Methyl C ^a
Cycloheptanone	-183.2	-14.3	5.0	-1.2	
2-Methyl	-174.9	-10.4, -14.7	4.9, 5.2	-1.1, -0.3	8.0 (γ)
3-Methyl	-183.3	-13.3, -14.2	4.4, 5.3	-1.1, -1.1	1.8 (δ)
4-Methyl	-182.5	-14.5, -14.0	5.8, 4.4	-1.1, -0.7	1.9 (ε)
2,2-Dimethyl	-171.6	-13.1, -15.2	4.1, 5.0	-0.5, 0.8	5.9 (γ)
3,3-Dimethyl	-185.6	-12.4, -12.2	1.6, 6.4, or 5.7	-1.5, 0.2, or -0.5	2.2 (δ)
4,4-Dimethyl	-180.3	-14.6, -11.9	7.0, 4.6	0.7, -0.1	2.9 (ε)
<i>cis</i> -3,5-Dimethyl	-184.0	-13.9, -15.6	3.9, 5.3	-1.0, -1.3	1.3 (δ), 1.3 (ε)

^a Type of interaction in parentheses.

The most stable conformation of 1,3,3-trimethylcycloheptanol should be 30. The data in Table IV show that the C-3 shift is not influenced by the hydroxyl group. However, C-3 has no attached hydrogens and is likely to be less susceptible to a γ effect, as judged from other examples.¹⁴ The hydroxyl group does interact with the 1-methyl group which is on the same side of the ring, and this one is therefore assigned the upfield resonance. Compared to other 1-methylcycloheptanols, the α-substituent effect of the hydroxyl group is quite high (-42.6 ppm). Apparently, as C-1 loses its directly attached hydrogen on introduction of the hydroxyl group, there is at least partial loss of the positive γ shift exerted by the 3-methyl groups. The result is a 8.5-ppm more negative shift than is found for the corresponding carbon of 1,4,4-trimethylcycloheptanol.

C. Methylcycloheptanones.—Studies of the conformational problems of cycloheptanones have been carried out with halogen²⁸ and alkyl derivatives.^{29,30} It has been concluded from ir spectra that for *cis*-2,7-dichlorocycloheptanone the conformer with two equatorial chlorines is more stable by 1.1 kcal/mol than the diaxial one.²⁸ Allinger has reported the enthalpy difference between *cis*- and *trans*-3,5-dimethylcycloheptanone to be 0.8 kcal/mol, the *cis* isomer being the more stable.²⁹ Evidence for the twist-chair conformation of alkylcycloheptanones has been derived from benzene-induced shifts on the proton spectra.³⁰

The chemical shifts obtained from the ¹³C nmr spectra of some methylcycloheptanones in dioxane are given in Table VI. (See also Table VII.) The resonances of C-2 and C-7 have been identified by selective decoupling of the attached protons. Further assignments have been obtained unambiguously by compari-

son of the spectra of 3-methylcycloheptanone-2,2,6,6-*d*₄ and 4-methylcycloheptanone-3,3,7,7-*d*₄ with those of the corresponding nondeuterated ketones. Earlier³¹ we did not properly characterize the resonances of C-3 and C-4 of the unsubstituted cycloheptanones. This has now been achieved with Eu(DPM)₃ in benzene solutions (in which the chemical shifts differ from those in dioxane by less than 1 ppm, in the absence of the paramagnetic chelate). At a molar ratio of ketone/complex of 3.0, the four different carbons moved downfield by 10.8, 3.4, 2.4, and 1.2 ppm, and we have assumed that the 1.2-ppm shift is that of C-4. For the 2-, 3-, and 4-methylcycloheptanones, the methine carbon resonances are easy to identify, and we have used these as references for the carbonyl substituent effects.³¹ It is evident that the γ-shift effect of a carbonyl group in a cycloheptanone is much more positive than for cyclohexanones.³¹ The small γ effects of carbonyl groups on cyclohexane resonances has been interpreted as evidence for flattening of the six-membered ring by the sp² hybridized carbonyl carbon.³¹ The large γ carbonyl effects in cycloheptanones suggest that a sp² center does not critically affect the geometry of the cycloheptane ring. This could be a consequence of the relatively large bond angles in cycloheptane, which are, on the average, about 3° larger than in cyclohexane, according to the predictions of Hendrickson⁴⁶ and the experiments of Groth.⁹ It is noteworthy that the carbonyl carbon resonances are relatively invariant as respects methyl substitution on the ring. This was also observed for alkylcyclohexanones.³¹

Experimental Section

2-Methyl-,³² 3-methyl-,^{20,33} 4-methyl-,³³ 2,2-dimethyl-,³² 3,3-dimethyl-,³⁴ 4,4-dimethyl-,⁶⁰ and *cis*-3,5-dimethylcyclohepta-

(28) R. Borsdorf, W. Flamme, H. Kumpfert, and M. Mühlstädt, *Tetrahedron*, **24**, 65 (1968), and references cited therein.

(29) N. L. Allinger, *J. Amer. Chem. Soc.*, **81**, 232 (1959).

(30) A. Zschunke, F.-J. Strüber, and R. Borsdorf, *J. Prakt. Chem.*, **311**, 296 (1969).

(31) F. J. Weigert and J. D. Roberts, *J. Amer. Chem. Soc.*, **92**, 1347 (1970).

(32) M. Godchot and G. Cauquil, *C. R. Acad. Sci.*, **188**, 795 (1929).

(33) C. Djerassi, B. F. Burrows, C. G. Overberger, T. Takekoshi, C. D. Dutsche, and C. T. Chang, *J. Amer. Chem. Soc.*, **85**, 949 (1963).

(34) M. Mousseron and G. Manon, *Bull. Soc. Chim. Fr.*, 392 (1949).

TABLE VIII
YIELDS, BOILING POINTS, AND ¹H CHEMICAL SHIFTS^a (IN PPM DOWNFIELD FROM TETRAMETHYLSILANE) OF
SOME CYCLOHEPTANOLS

Substituents	Yield, %	Bp, °C (Torr)	1-H	2 H-7 H	1-CH ₃	2-, 3-, 4-, 5-CH ₃
<i>cis-cis</i> -3,5-Dimethyl } <i>trans-trans</i> -3,5-Dimethyl }	80	84-86 (8)	3.88	1.1-2.0		~0.9
2,2-Dimethyl	80	92-94 (12)	3.41	1.0-2.1		0.89, 0.97
3,3-Dimethyl	75	92-94 (9)	3.75	1.2-1.9		0.91, 0.97
4,4-Dimethyl	79	97-99 (9)	3.76	1.1-2.1		0.88, 0.91
<i>trans</i> -1,2-Dimethyl	81	83-86 (8)		1.1-2.0		0.97
<i>cis</i> -1,3-Dimethyl ^b } <i>trans</i> -1,3-Dimethyl ^b }	80	70-74 (4)		1.1-2.0	{ 1.23 } { 1.26 }	0.95
<i>trans</i> -1,4-Dimethyl ^c } <i>cis</i> -1,4-Dimethyl ^c }	88	79-82 (6)		1.1-2.0	1.21	0.90
1,2,2-Trimethyl	93	86-90 (6)		1.1-2.1	1.15	0.90, 0.95
1,3,3-Trimethyl	86	83-87 (8)		1.3-1.9	1.22	0.92, 1.02
1,4,4-Trimethyl	85	89-91 (10)		1.0-1.9	1.22	0.89, 0.91

^a Taken in CDCl₃ as solvent. ^b *Cis*:*trans* ratio, 60:40. ^c *Trans*:*cis* ratio, 55:45.

none¹⁶ were prepared as described in the literature. 2-Methylcycloheptanone-2,7,7-*d*₃ and 3-methyl- and 4-methylcycloheptanone-2,2,7,7-*d*₄ were obtained from the nondeuterated ketones by means of sodium carbonate and deuterium oxide as described for other cyclic ketones.³⁵ 3-Methylcyclohexanone-2,2,6,6-*d*₄, obtained by exchange³⁵ with diazomethane,³³ gave a mixture of 3-methylcycloheptanone-2,2,6,6-*d*₄ and 4-methylcycloheptanone-3,3,7,7-*d*₄ which was separated on our efficient spinning-band column.

Reduction of 2-methylcycloheptanone with H₂/Pt or Na/C₂H₅OH resulted in mixtures of the 2-methylcycloheptanols in which one or the other of the two isomers was in excess.^{19,36} The 3-methylcycloheptanols were obtained as 1:1 mixture of *cis*-*trans* isomers by LiAlH₄ reduction of the corresponding ketone.¹⁹ Chromatography of 1 g of this mixture on 50 g of neutral Al₂O₃ (Woelm, activity III) was assayed with pentane and pentane-ether as solvents. The first eight 100-ml portions eluted with pentane contained no alcohol. With pentane-ether, the ninth fraction contained 130 mg of the practically pure *trans* isomer, while in fractions 12 and 13 (200 mg) the *cis*-*trans* ratio was 2:1. Reduction of 4-methylcycloheptanone with lithium aluminum hydride resulted in a 1:1 mixture of *cis*-*trans* isomers. However, hydrogenation, as described for 2-methylcycloheptanone,^{19,36} produced a mixture in which the *cis* compound was the more abundant component (about 60%). Reduction of *cis*-3,5-dimethylcycloheptanone with lithium aluminum hydride also gave a 1:1 mixture of two isomers which, by chromatography on neutral Al₂O₃ as above, led to enrichment of the *cis,cis* isomer to about 60% in the last fraction. A mixture of about the same ratio was obtained by reduction of the ketone with H₂/Pt. The deuterated cycloheptanones were all reduced by lithium aluminum hydride and the ¹³C nmr spectra were examined without further attempts at separation. The 2,2,3,3- and 4,4-dimethylcycloheptanols were obtained by lithium aluminum hydride reduction of the corresponding ketones. Table VIII summarizes the properties of some secondary and tertiary cycloheptanols prepared in this work. The latter alcohols were obtained in addition of 30 mmol of methylolithium (about 15 cc of a commercial 2.1 M solution in ether) to 15 mmol of the appropriate cycloheptanone, dissolved in 10 cc of anhydrous ether. The mixture was heated gently under reflux for 15 hr, then hydrolyzed by addition of water. The ether phase was separated, dried over anhydrous sodium sulfate, and distilled. The products were found to be free of major impurities from their proton and ¹³C nmr spectra. The isomer ratios of the cycloheptanol mixtures were estimated either from the hydroxyl proton intensities in the spectra in dimethyl sulfoxide or from the ¹³C nmr spectra.

1-Methylcycloheptanol, Eu(DPM)₃, Eu(fod)₃, and methylcycloheptane were commercial materials used without further

(35) E. Premuzic and L. W. Reeves, *Can. J. Chem.*, **40**, 1870 (1962).

(36) M. Godehot and G. Cauquil, *C. R. Acad. Sci.*, **190**, 642 (1930).

purification. The samples of the dimethyl- and 1,1,3-trimethylcycloheptanes were provided by Professor J. B. Hendrickson.

1,1,4-Trimethylcycloheptane.—1,4,4-Trimethylcycloheptanol (2.9 g) and 1 g of iodine were mixed and heated to 80-100° under a pressure of about 1 Torr. The volatile products were collected at -75°, taken up in ether, washed with aqueous sodium bisulfite solution to remove some iodine, dried over sodium sulfate, and distilled. After removal of the ether, a fraction of 900 mg was obtained, bp 71-75° (30 Torr). The vpc on Carbowax 20M showed two peaks of equal intensity. The distillate in 10 ml of acetic acid took up 275 ml of hydrogen in the presence of 150 mg of PtO₂ over 2 hr. The catalyst was removed by filtration, the filtrate was neutralized with potassium hydroxide solution and extracted with ether, and the extract was dried over sodium sulfate. Distillation gave a fraction of bp 72-75° (30 Torr), amounting to 700 mg (27%) which, in the vpc (Carbowax 20M), showed only one peak. The proton spectrum (neat + TMS) showed 2 H-7 H at δ 0.98-2.03 and CH₃ at δ 0.88. The same procedure, starting with 1,2,2-trimethylcycloheptanol, gave a 39% yield of a mixture of C₁₀H₂₀ hydrocarbons which, by vpc on two different columns (UCC/W98, silicon oil SE-30), showed two major products, each abundant to the extent of about 44%. The carbon-13 spectrum showed one of these substances to be *tert*-butylcyclohexane.^{11a} The other product was assumed to be 1,1,2-trimethylcycloheptane (see text).

Nmr Spectra.—The ¹³C spectra of the cycloheptanols and cycloheptanones were taken on dioxane solutions. The measurements of the pseudocontact shifts, however, were made on benzene solutions. The cycloheptanes were run in carbon disulfide with 20-30% (v/v) of tetramethylsilane, as required. The resonances of the carbons of the solvents were used as internal references. The chemical shifts reported here have all been corrected to carbon disulfide as external reference by the relationship δ_C = δ_C^{dioxane} + 126.2 ppm, δ_C = δ_C^{benzene} + 64.55 ppm, and δ_C = δ_C^{tetramethylsilane} + 192.5 ppm, and were reproducible to ±0.1 ppm. Most of the spectra were taken with a digital frequency sweep spectrometer, operating at 15.08 MHz, with its associated proton decoupler equipped with a narrow-band pseudorandom noise generator.^{11a} The proton signals of the solvents provided a proton-field frequency lock. Some of the spectra were obtained with a Varian HR-220 spectrometer, operating at 55.34 MHz, and equipped with a proton decoupler and a pseudorandom noise generator. This instrument was used in the continuous-wave or the Fourier-transform mode. For the latter purpose, a Varian 620i computer was interfaced with the spectrometer.

Acknowledgment.—We are deeply indebted to Professor James B. Hendrickson of Brandeis University for the loan of samples of the dimethyl- and 1,1,3-trimethylcycloheptanes studied in this research.