The Synthesis and Stereochemistry of 5-Substituted 2-Methylcycloheptanones

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The *cis* and *trans* isomers of 5-methyl- (**2b**), 5-isopropyl- (**2c**), 5-*t*-butyl- (**2d**), 5-isopropylol- (**2e**), and 5-carbethoxy-2-methylcycloheptanone (**2f**) were prepared in 80–90% yield *via* treatment of the appropriate 4-substituted cyclohexanone with diazoethane in 20% ethanol–ether. The initial (kinetic) distribution of the isomeric pairs was approximately 1:1. Equilibration of **2b–e** in methanolic sodium carbonate afforded isomer distributions of 2.5:1 (**2b**), 2:1 (**2c**), 3:1 (**2d**), and 3:1 (**2e**), respectively, favoring the *trans* isomer in each case. Stereorational syntheses of *trans*-2,5-dimethylcycloheptanone and *trans*-2-methyl-5-isopropylolcycloheptanone were carried out to determine the stereochemistry of the products derived from the ring-expansion reactions.

In connection with synthetic work on the guaiazulene sesquiterpenes[2] we required a number of 5-substituted 2-methylcycloheptanones. Of the potential routes to such compounds, the direct ring expansion of 4-substituted cyclohexanones with diazoethane[3] appeared most promising because of its directness and the ready availability of suitable starting materials. After some initial difficulties we discovered exceedingly efficient conditions for effecting the ring-expansion reaction. This discovery prompted us to examine the stereochemistry of the resulting disubstituted cycloheptanones with a view to obtaining the first concrete data on conformational–configurational relationships in such compounds.[4]

Previous workers[5] have noted that the conversion of cyclohexanone into 2-methylcycloheptanone *via* ring expansion with ethereal diazoethane proceeds very slowly and in poor yield. Our best efforts along this line resulted in a 38% yield of fairly pure 2-methylcycloheptanone after a reaction time of 4 days. Even then, over 30% of the unchanged cyclohexanone remained. Moreover, this material could be effectively removed from the product only through its bisulfite adduct, thereby rendering the over-all procedure not only time consuming, but laborious as well. We therefore decided to study the ring-expansion reaction further in the hope of improving its efficiency.

Some years ago, Mosettig[5a] found that methanol accelerated the reaction of cyclohexanone with diazomethane. Later work, which showed that this catalytic effect involves the addition step of the reaction,[6] suggested that this phenomenon might be general for a variety of ketones, diazoalkanes, and alcohols. Accordingly, we examined the effect of ethanol on the reaction of cyclohexanone with diazoethane.

The addition of ethanol to an ether solution of diazoethane and cyclohexanone caused the brisk evolution of nitrogen which subsided markedly and nearly ceased after several hours at room temperature. We made no attempt to determine the optimum solvent composition since our first choice of 20% ethanol in diethyl ether gave excellent results. The reaction was complete within 2 hr and afforded a 9:1 mixture of 2-methylcycloheptanone (**2a**) and the oxide **3a** in over 90% yield. Table I summarizes these findings and shows

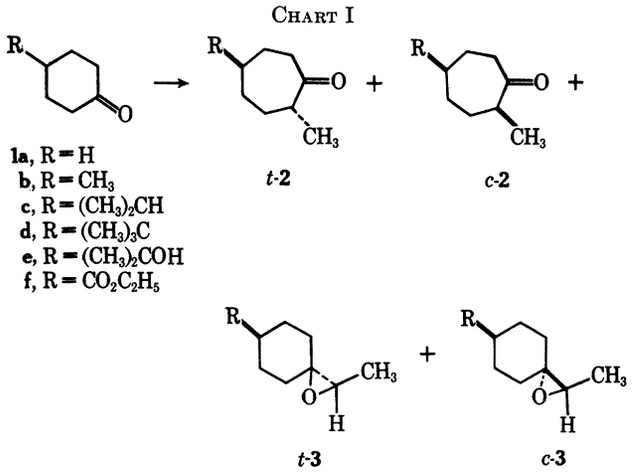
TABLE I
PRODUCT COMPOSITION OF DIAZOETHANE RING-EXPANSION REACTIONS

Cyclohexanone	2-Methylcycloheptanone (2), %	Oxide 3, %	Yield, %
1a	95	Trace	38[a]
1a	91	9	92[b]
1b	88	12	92[b]
1c	82	18	91[b]
1d	86	14	91[b]
1e	100	...	81[b]
1f	98	2	91[b]

[a] Diethyl ether was employed as the solvent. [b] A solution of 20% ethanol in diethyl ether was employed as the solvent.

the results of our studies on a number of 4-substituted cyclohexanones (**1b–f**) of interest in our projected synthetic work. In all cases, nitrogen evolution essentially ceased within 2–5 hr at room temperature signaling completion of the reaction. The 4-alkylcyclohexanones **1b–d**, as well as cyclohexanone itself, gave varying amounts (10–20%) of the related oxides **3a–d** in addition to the desired 2-methylcycloheptanones **2a–d** (Chart I). Surprisingly, those cyclohexanones (**1e**

CHART I



1a, R = H
b, R = CH_3
c, R = $(CH_3)_2CH$
d, R = $(CH_3)_3C$
e, R = $(CH_3)_2COH$
f, R = $CO_2C_2H_5$

and **1f**) with polar C-4 substituents gave high proportions of the cycloheptanone products **2e** and **2f**, and little or no oxides. Nmr analysis suggested that oxide **3b** derived from 4-methylcyclohexanone (**1b**) consisted

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(2) *Cf.* J. A. Marshall and J. J. Partridge, *J. Amer. Chem. Soc.*, **90**, 1090 (1968), and references therein.

(3) For a review, see C. D. Gutsche, *Org. Reactions*, **8**, 364 (1964).

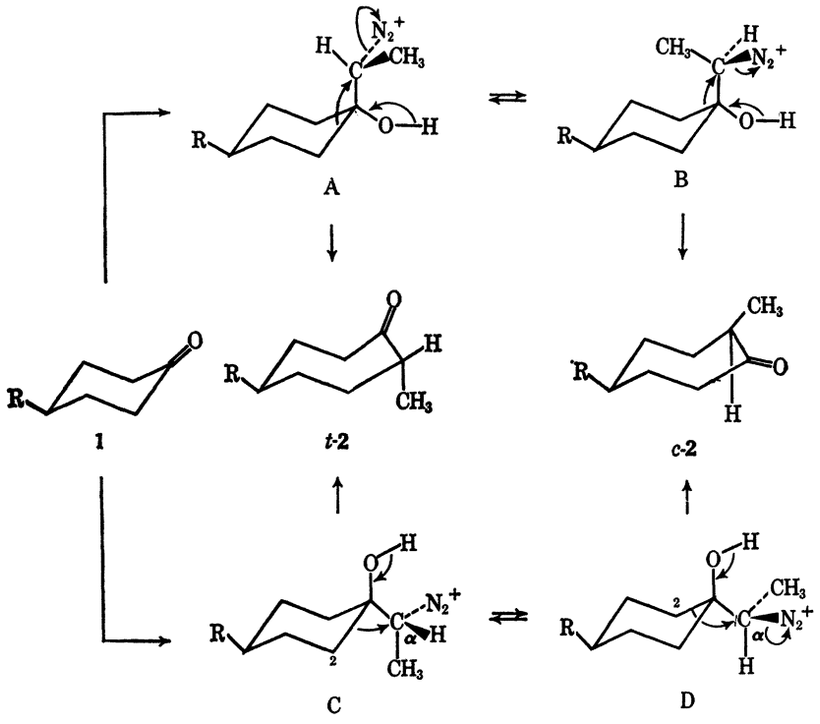
(4) *Cf.* J. B. Hendrickson, *J. Amer. Chem. Soc.*, **89**, 7043 (1967); **84**, 3355 (1962). J. B. Jones, J. M. Zander, and P. Price, *ibid*,. **89**, 94 (1967).

(5) (a) E. Mosettig and A. Burger, *ibid.*, **52**, 3456 (1930); (b) E. P. Kohler, M. Tishler, H. Potter, and H. T. Thompson, *ibid.*, **61**, 1057 (1939); (c) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 181 (1939).

(6) J. N. Bradley, G. W. Cowell, and A. Ledwith, *ibid.*, 4334 (1964).

SCHEME I

PATHWAYS TO *cis*- AND *trans*-5-SUBSTITUTED 2-METHYLCYCLOHEPTANONES



of a nearly 1:1 mixture of the *trans* and *cis* isomers *t*-**3b** and *c*-**3b**, whereas the oxides **3c** and **3d** derived from 4-isopropyl- and 4-*t*-butylcyclohexanone appeared to be single stereoisomers.

As can be seen from Table II, the cycloheptanones **2b–f**, as obtained from the ring-expansion reaction, consist of nearly 1:1 mixtures of *cis* (*c*-**2**) and *trans* (*t*-**2**) isomers. Precise *cis*/*trans* ratios for the 5-alkylcycloheptanone mixtures **2b–d** could be obtained directly *via* gas chromatography, but the stereoisomers of the more polar compounds **2e** and **2f** failed to separate on a variety of columns. However, a fairly accurate estimate of isomer ratios could be secured from the integrated nmr spectra of these mixtures.

TABLE II

ISOMER COMPOSITION OF 5-SUBSTITUTED 2-METHYLCYCLOHEPTANONES

Cycloheptanone	Conditions	Composition, % *t*-2	*c*-2
2b	Kinetic	46	54[a]
	Equilibrium	71	29[a]
2c	Kinetic	46	54[a]
	Equilibrium	67	33[a]
2d	Kinetic	50	50[a]
	Equilibrium	75	25[a]
2e	Kinetic	~50	~50[b]
	Equilibrium	~75	~25[b]
2f	Kinetic	~50	~50[b]

[a] Gas chromatography was employed for the analysis. [b] The analysis is based on the integrated nmr spectrum.

Since the ring-expansion reactions were conducted under mild conditions in neutral solution, the observed 1:1 ratios of *cis* and *trans* isomers **2b–f** should represent the kinetic distribution and reflect the relative transition-state energies of the reactions leading to each. Scheme I outlines reasonable reaction pathways to each isomer.[7] From an inspection of molecular models, we estimate the energy of the transition state leading from conformer A to the *trans* product *t*-**2** to be lower than that of the transition state leading from conformer B to the *cis* product *c*-**2**. By the same token, the transition state leading from conformer D to *c*-**2** appears more favorable than that leading from conformer C to *t*-**2**. In the latter case the developing bond between C-2 and C-α restricts rotation of the ethyl diazonium grouping thereby forcing the methyl grouping to maintain an axial orientation. In the process leading from D to *c*-**2** this methyl grouping can remain equatorial.

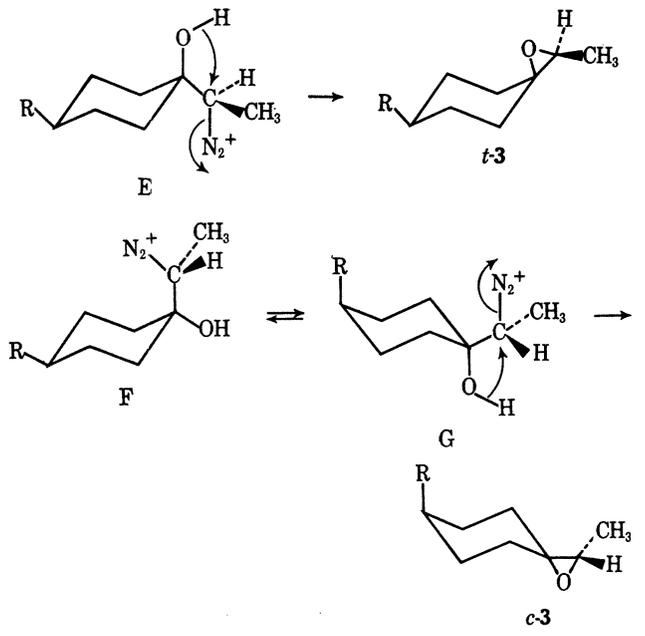
The adducts A and B, with axial ethyldiazonium groupings, should be somewhat higher in energy than their equatorially substituted counterparts C and D. However, this factor would influence the stereochemistry of the cycloheptanone products only if the additions leading to these intermediates were appreciably reversible. Such is probably not the case here, since protonation by ethanol should favor the addition reaction.[7] Thus, a reactantlike transition state for the addition process,[8] where topside and bottomside attack are about equally favored, followed by the rapid loss of nitrogen and synchronous bond migration preferentially *via* the lower energy transition states derived from adducts A and D, adequately accounts for the observed ratio of isomeric cycloheptanone products. We offer the foregoing explanation merely as one possible working hypothesis. Other possibilities exist, and we must await additional experimental evidence before a firm choice can be made.

(7) The assumption of protonated intermediates in this scheme seems justified in view of the high ethanol content of the reaction medium.

(8) See J. A. Marshall and R. D. Carroll, *J. Org. Chem.*, **30**, 2748 (1965), for comments bearing on this point.

As noted above, the oxide **3b** derived from 4-methylcyclohexanone (**1b**) consists of a 1:1 mixture of the stereoisomers *t*-**3b** and *c*-**3b**, whereas the oxides **3c** and **3d** appear stereochemically homogenous. This finding can be accommodated with the aid of Scheme II.[9]

SCHEME II
PATHWAYS TO *cis*- AND *trans*-4-SUBSTITUTED CYCLOHEXYLIDENE OXIDES



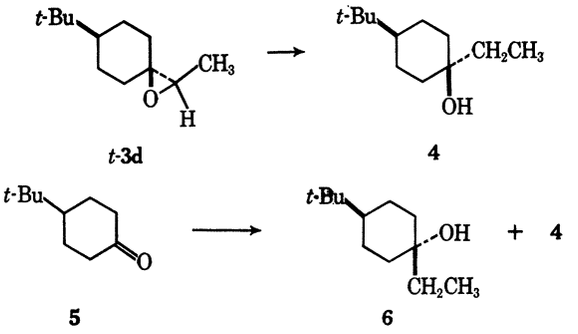
The transition states leading to the cyclohexylidene oxide products *t*-**3** and *c*-**3** require a *trans* relationship between the attacking hydroxyl oxygen and the departing diazonium grouping. Conformer E provides a low-energy pathway to the *trans* isomer *t*-**3**, but an analogous low-energy pathway to the *cis* isomer *c*-**3** must proceed mainly *via* conformer G as the transition state derived from F suffers from adverse steric crowding. The conversion of conformer F into conformer G requires reorientation of the R grouping from the equatorial to the axial position, a change which would be more favorable for a small group such as methyl than the larger isopropyl and *t*-butyl groupings present in cyclohexanones **1c** and **1d**. This analysis predicts the stereochemistry of the latter oxides to be *trans* (*t*-**3c** and *t*-**3d**).

The conversions outlined in Chart II confirmed this prediction for the *t*-butyl derivative **3d**. Reduction of this oxide with lithium aluminum hydride afforded the corresponding cyclohexanol **4**. This cyclohexanol was identical with the major alcohol, previously shown to be the *trans* isomer, obtained from the addition of ethylmagnesium bromide to 4-*t*-butylcyclohexanone.

Treatment of the 1:1 mixtures of epimeric 2-methylcycloheptanones **2b–e** with refluxing methanolic sodium carbonate led to new mixtures ranging in composition from 3:1 (**2d** and **2e**) to 2:1 (**2c**) as shown in Table II. The major epimers of the alkyl-substituted cycloheptanones **2b–d** exhibited the shorter gas chromato-

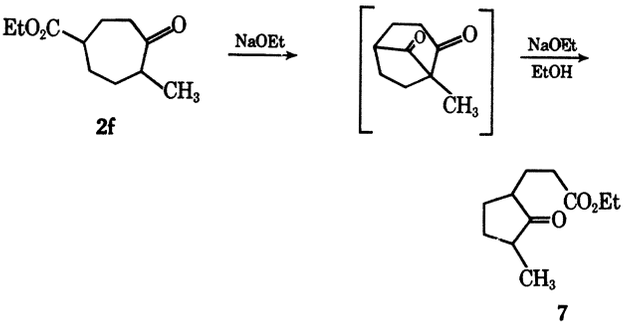
(9) Essentially the same analysis has been used by R. G. Carlson and N. S. Behn [*J. Org. Chem.*, **33**, 2069 (1968)] in their studies on the Tiffeneau–Demjanov rearrangement. Their findings also lend support to Scheme I. For an alternative mechanism of oxirane formation, see C. D. Gutsche and J. E. Bowers, *ibid.*, **32**, 1203 (1967).

CHART II



graphic retention times. As noted above, the epimers derived from the isopropylol derivative **2e** failed to separate on a variety of columns. Interestingly, the predominant component of this mixture, and the mixtures related to **2b–d** as well, gave rise to higher field methyl doublets in the nmr spectrum. These observations suggest that the major epimer of each pair belongs to the same stereochemical series.

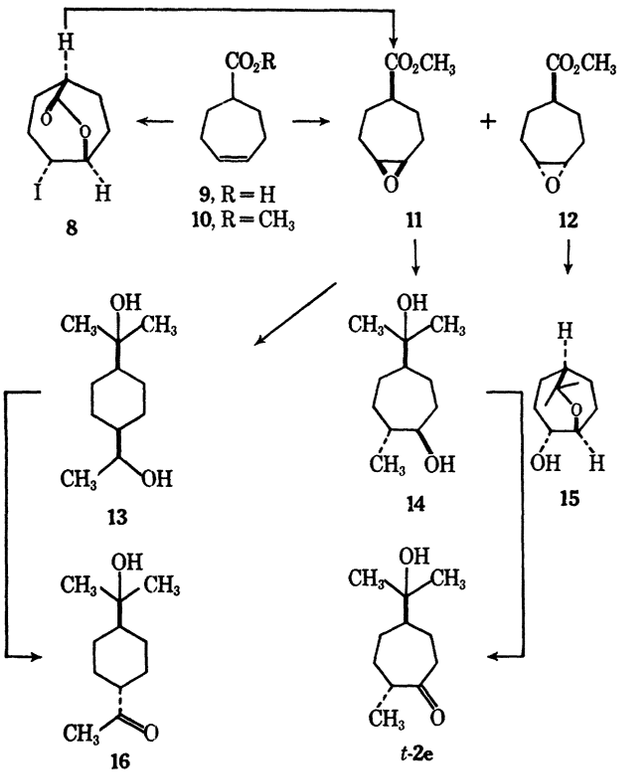
Our efforts to equilibrate the carbethoxy-substituted cycloheptanone **2f** were foiled by a combination of circumstances. Fearing saponification of this keto ester under the equilibrating conditions (Na_2CO_3–H_2O–CH_3OH) employed for the other cycloheptanones **2b–e**, we attempted to carry out this reaction with ethanolic sodium ethoxide. Unfortunately, this reagent effected skeletal isomerization of the cycloheptanone **2f** leading, as shown below, to the cyclopentanone derivative **7**.



The conformational analysis of cycloheptane and its derivatives has been considered in great detail by Hendrickson.[4] We applied his concepts to the calculation of conformational energies of the *cis*- and *trans*-2,5-disubstituted cycloheptanones (**2**) in an attempt to deduce the correct stereochemistry of these compounds. Each of these cycloheptane derivatives can adopt 14 different pseudorotomeric forms. For each of these forms there exists an energetically distinct chair–twist, chair–boat, and twist–boat conformation. To simplify our calculations we rejected those conformers which appeared from an inspection of models to possess serious nonbonded eclipsing interactions. Considering the remaining conformers in the light of Hendrickson's ring-substituent energy values,[4] we computed an energy difference of 0.1 kcal/mol favoring the *trans*-dimethylcycloheptanone *t*-**2b** over the *cis* isomer *c*-**2b**.

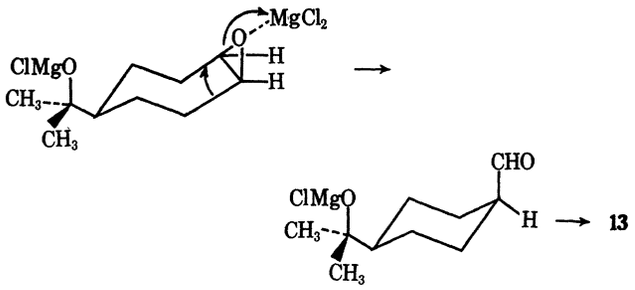
Since conformational analysis failed to provide a clear-cut assignment of stereochemistry to the 2,5-disubstituted cycloheptanones **2b–f**, we decided to seek this information through the stereoselective synthesis

CHART III



of selected members of this group. Our first efforts, outlined in Chart III, were directed toward the isopropylolcycloheptanones *t*-**2e** and *c*-**2e**. The methyl ester **10** of 4-cycloheptenecarboxylic acid (**9**) afforded a nearly 1:1 mixture of the *cis* and *trans* oxides **11** and **12** upon treatment with *m*-chloroperoxybenzoic acid in benzene. A pure sample of each isomer was secured *via* preparative gas chromatography. The iodo lactone **8**, derived from the unsaturated acid **9**, yielded an authentic sample of the *cis*-oxido ester **11** when treated with slightly less than 1 mol equiv of sodium methoxide in 1,2-dimethoxyethane at room temperature. Equilibration in refluxing methanolic sodium methoxide afforded a 62:38 mixture of the *cis* (**11**) and *trans* (**12**) isomers.

Our initial plans called for the conversion of the isomeric oxido esters **11** and **12**, respectively into the corresponding 2-methyl-5-isopropylolcycloheptanols (*e.g.*, **11** → **14**) with the methyl Grignard reagent. Subsequent oxidation of these alcohols would then complete the stereochemically rational synthesis of *c*-**2e** and *t*-**2e**. However, ensuing developments forced a slight tactical modification of both methodology and objectives. The *cis*-oxido ester **11**, upon treatment with either methylmagnesium chloride or bromide in refluxing tetrahydrofuran, yielded a crystalline diol in high yield. Although the spectral properties of this substance seemed in accord with those expected for the desired diol **14**, its subsequent oxidation to the methyl ketone **16** betrayed its true identity as the rearranged cyclohexane derivative **13**. Related rearrangements of oxiranes are well documented.[10] In the present case the pinacolic-type rearrangement of the oxido ester **11** or, more likely, its isopropylol derivative can be viewed as shown below. The methyl ketone **16**

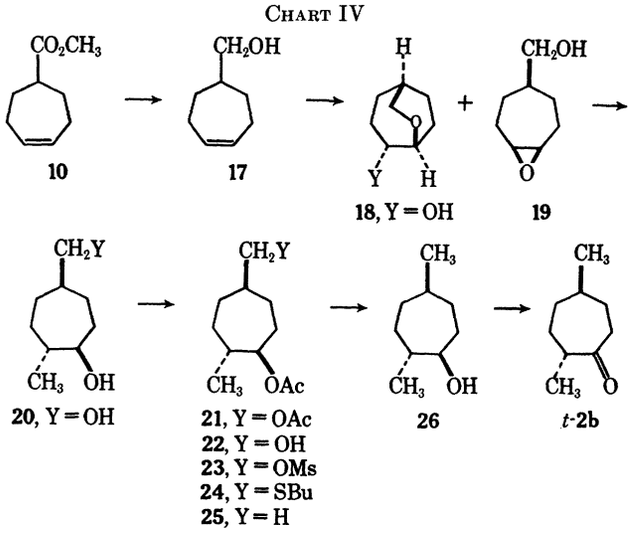


failed to epimerize in refluxing methanolic sodium carbonate and can therefore be regarded as the more stable *trans* isomer. Since concerted rearrangement of the above *cis* oxide would afford the *cis*-diol **13**, isomerization of the initially formed labile[11] axial acetyl grouping of the *cis* product must occur under the acidic conditions of the oxidation step.

Dimethylmagnesium smoothly added to the oxido ester **11** in refluxing dioxane to give the desired cycloheptanol **14** in high yield.[10] Upon oxidation with chromic acid, this material afforded *trans*-2-methyl-5-isopropylolcycloheptanone (*t*-**2e**). The nmr spectrum of this substance corresponded to that of the major component in the equilibrium mixture. Unfortunately, the above sequence could not be employed to synthesize the minor component of this mixture. The addition of dimethylmagnesium to the *trans*-oxido ester **12** afforded the bicyclic hydroxy ether **15** as the only isoluble product.

We next set out to synthesize stereorationally the 2,5-dimethylcycloheptanones *t*-**2b** and *c*-**2b** using an approach which parallels that described above for the isopropylol analog *t*-**2e**. Once again, a transannular reaction prevented us from fully realizing complete success. Nonetheless, a satisfactory synthesis of the *trans* isomer *t*-**2b** could be effected as shown in Chart IV. The alcohol **17**, obtained *via* reduction of the

CHART IV



unsaturated ester **10** with lithium aluminum hydride, afforded a 35:65 mixture of hydroxy ethers **18** and **19** upon treatment with *m*-chloroperoxybenzoic acid in

(10) *Cf.* B. G. Christensen, R. G. Strachan, N. R. Trenner, B. H. Arison, R. Hirschmann, and J. M. Chemerda, *J. Amer. Chem. Soc.*, **82**, 3995 (1960).

(11) *Cf.* H. E. Zimmerman, *ibid.*, **79**, 6554 (1957).

benzene. The major hydroxy ether **19** decomposed during attempts at column or preparative gas chromatography, but these techniques could be used to purify the minor isomer **18** Since this substance was unaffected by dimethylmagnesium in refluxing dioxane, the 35:65 mixture of hydroxy ethers **18** and **19** could be subjected to this reagent whereupon the unreacted isomer **18** and the desired diol **20** could be easily separated by column chromatography.

In view of the *cis* relationship between the alcohol functions of diol **20** and the marked propensity of such compounds for transannular reactions, we rejected some of the usual sequences for converting methylol into methyl groupings. Thus, no attempts were made at hydrogenolysis of the methylol tosylate or mesylate derivatives (*e.g.*, **20**, Y = OTs or OMs). Instead a more circuitous but less hazardous route was chosen which began with the conversion of diol **20** into diacetate **21** with acetic anhydride in pyridine. Selective saponification afforded the hydroxy acetate **22**, which was subsequently converted into the mesylate derivative **23**. Displacement of the mesylate grouping without cleavage of the acetate could be readily effected with a combination of butanethiol and sodium hydride in tetrahydrofuran. The resulting thio ether **24** underwent reductive desulfurization upon treatment with Raney nickel in ethanol giving the dimethylcycloheptyl acetate **25**. Cleavage of the acetate with lithium aluminum hydride followed by oxidation of the resulting alcohol **26** yielded *trans*-2,5-dimethylcycloheptanone (*t*-**2b**) identical with the thermodynamically favored isomer of the mixture **2b**. In view of the similar physical properties found for the mixtures of 5-substituted 2-methylcycloheptanones **2b–e**, we feel justified in assigning the *trans* stereochemistry to the thermodynamically favored isomer of the isopropyl (**2c**) and *t*-butyl (**2d**) ketones, as well.

Experimental Section[12]

Ring Expansion of Cyclohexanones with Diazoethane in 20% Ethanol–Diethyl Ether.—Ethereal diazoethane was prepared by a modification of the procedure of Arndt[13] and Werner.[14] In a typical preparation, a mixture of 100 ml of 50% aqueous potassium hydroxide and 500 ml of ether in a 1-l. erlenmeyer flask was cooled to −10°, and 62.0 g of solid N-ethyl-N-nitrosourea[15] was added in small portions over a 1.5-hr period. The mixture was stirred magnetically with cooling for 0.5 hr, and 400 ml of the solution was decanted into a second 1-l. erlenmeyer flask containing 25 g of potassium hydroxide pellets. An additional 100 ml of ether was added to the initial erlenmeyer flask, and, after 15 min of continued stirring, 160 ml of the ethereal solution was decanted into the second flask bringing the total volume to about 560 ml. Titration with ethereal benzoic acid and back titration with standard aqueous sodium hydroxide to the phenolphthalein end point indicated that the solution was 0.64 *M* in diazoethane.

The ring-expansion reactions were carried out by adding dropwise a solution of the cyclohexanone in ethanol to 1.25 mol equiv of 0.4–0.5 *M* ethereal diazoethane maintained at −10° and stirred magnetically. Sufficient ethanol was used to bring the final solvent composition to 20% ethanol in ether. After the addition was complete, the cooling bath was removed, a mercury bubbler was attached, and the mixture was stirred until nitrogen evolution ceased (2–5 hr). The excess diazoethane was destroyed by the dropwise addition of acetic acid, and the mixture was washed with saturated aqueous sodium bicarbonate and dried over anhydrous magnesium sulfate.

2-Methylcycloheptanone (**2a**).—According to procedure described above, 8.4 g of cyclohexanone was converted into 9.8 g (91%) of a 91:9 mixture of 2-methylcycloheptanone (**2a**) and the oxide **3a**, bp 66–71° (15 mm). The pure ketone, obtained *via* preparative gas chromatography,[16] had the following properties: $n^{25}D$ 1.4576; λ_{max}^{film} 5.87 (CO), 7.27 8.51, 8.60, and 10.65 μ; $\delta_{TMS}^{CCl_4}$ 1.02 ppm (CH_3, doublet, J = 7 Hz); semicarbazone derivative mp 129–130° (lit.[17] mp 129–131°).

2-Methyl-1-oxaspiro[2.5]octane (**3a**).—The sample secured from the above mixture *via* preparative gas chromatography[16] had the following properties: λ_{max}^{film} 7.23, 9.68, 9.84, 10.08, 11.13, and 11.77 μ; $\delta_{TMS}^{CCl_4}$ 2.70 (H-2, quartet, J = 5.5 Hz), 1.55 (ring envelope), and 1.23 ppm (CH_3, doublet, J = 5.5 Hz). The analytical sample, bp 55° (bath temperature) at 24 mm, was secured by distillation.

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.4; H, 11.3.

trans-**2,5-Dimethylcycloheptanone** (*t*-**2b**). **A. From** *trans,cis*-**2,5-Dimethylcycloheptanol** (**26**).—To a solution of 48 mg of alcohol **26** in 5 ml of acetone at 0° was added 5 drops of standard chromic acid reagent.[18] After 5 min, isopropyl alcohol was added to destroy the excess oxidizing agent; the mixture was diluted with water; and the product was isolated with ether[12a] giving 42 mg (89%) of ketone *t*-**2b** which gave a single peak on gas chromatography.[19] The spectral and chromatographic properties of this substance exactly matched those of the thermodynamically favored dimethylcycloheptanone whose isolation is described below.

B. *Via* **Ring Expansion of 4-Methylcyclohexanone** (**1b**) **with Diazoethane.**—By the procedure described above, 10.0 g of 4-methylcyclohexanone (**1b**) was converted into 11.6 g (92%) of a 41:47:12 mixture of ketones *t*-**2b** and *c*-**2b** and oxide **3b**,[20] bp 77–83° (14 mm). The pure *trans* isomer *t*-**2b**, secured from the above mixture *via* preparative gas chromatography,[16] had the following properties: $n^{25}D$ 1.4534; λ_{max}^{film} 5.88 (CO), 7.48, 8.50, 9.53, 10.84, and 11.3 μ; $\delta_{TMS}^{CCl_4}$ 0.98 ppm (CH_3, doublet, J = 7 Hz).

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.1; H, 11.6.

cis-**2,5-Dimethylcycloheptanone** (*c*-**2b**).—The sample secured from the ring-expansion reaction mixture *via* preparative gas chromatography[16] had the following properties: $n^{25}D$ 1.4576; λ_{max}^{film} 5.88 (CO), 8.60, 8.82, 9.33, 9.53, 9.68, 9.89, and 11.1 μ; $\delta_{TMS}^{CCl_4}$ 1.00 (CH_3, doublet, J = 7 Hz) and 0.91 ppm (CH_3, doublet, J = 7 Hz).

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.0; H, 11.6.

2,6-Dimethyl-1-oxaspiro[2.5]octane (**3b**).—The sample secured from the ring-expansion reaction mixture *via* preparative gas chromatography[16] had the following properties: $n^{25}D$ 1.4464; λ_{max}^{film} 7.25, 9.65, 10.10, 10.25, 11.30, and 14.80 μ; $\delta_{TMS}^{CCl_4}$ 2.73 (H-2, quartet, J = 6 Hz), 1.22 (CH_3, doublet, J = 6 Hz), and 0.98 ppm (two pairs of unresolved CH_3 doublets). The relative intensities of the latter peaks indicated that this sample was approximately a 1:1 mixture of *t*-**3b** and *c*-**3b**.

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.9; H, 11.5.

Equilibration of *cis*- **and** *trans*-**2,5-Dimethylcycloheptanones** (*c*-**2b and** *t*-**2b**).—A 1.4-g sample of a 54:46 mixture of ketones *c*-**2b** and *t*-**2b** was heated at reflux for 18 hr in 10 ml of methanol containing 1 ml of *M* aqueous sodium carbonate. The product was isolated with hexane[12a] and distilled affording 1.3 g (92%)

(12) (a) The isolation procedure consisted of diluting the reaction mixture with water or saturated brine, thoroughly extracting the mixture with the specified solvent, washing the combined extracts with saturated brine, and drying the organic phase over anhydrous magnesium sulfate. The solvent was removed on a rotary evaporator. (b) Gas chromatography was performed on an F & M Model 700 or 720 instrument using helium as the carrier gas. (c) Microanalyses were performed by Micro-Tech Laboratories, Inc. Skokie, Ill.

(13) F. Arndt, "Organic Syntheses," Coll. Vol II, John Wiley & Sons, Inc., New York N. Y., 1943, p 165.

(14) J. Werner, *J. Chem. Soc.*, 1093 (1919).

(15) Reference 13, p 461.

(16) A 12 ft by 0.5 in. column packed with 16% Carbowax 20M on 60–80 mesh Diatoport S was used for this separation.

(17) O. Wallach, *Ann.*, **345**, 146 (1906).

(18) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

(19) A 17 ft by 1/4 in. column packed with 12% Carbowax 20M on 60–80 mesh Chromosorb W was used for this analysis.

(20) A 20 ft by 1/8 in. column packed with 20% Carbowax 20M on 60–80 mesh Chromosorb W was used for this analysis.

of a 29:71 mixture of *c*-**2b** and *t*-**2b**,[20] bp 75–85° (15 mm). The same mixture was obtained when each of the pure ketones was subjected to the equilibration conditions.

Ring Expansion of 4-Isopropylcyclohexanone (1c) with Diazoethane.—By the procedure described above, 9.6 g of 4-isopropylcyclohexanone (**1c**) was converted into 10.6 g (91%) of a 38:44:18 mixture of ketones *t*-**2c** and *c*-**2c** and oxide **3c**,[21] bp 101–110° (15 mm). The *cis* and *trans* ketones could be separated from the oxide, but not from each other, by preparative gas chromatography.

2-Methyl-6-isopropyl-1-oxaspiro[2.5]octane (*t*-3c).—The sample secured from the above ring-expansion reaction mixture *via* preparative gas chromatography[16] had the following properties: $n^{25}D$ 1.4605; λ_{max}^{film} 7.25, 9.65, 9.99, 10.78, 11.25, and 14.81 μ; $\delta_{TMS}^{CCl_4}$ 2.72 (H-2, quartet, J = 6 Hz), 1.21 (CH_3, doublet, J = 6 Hz), and 0.92 ppm [$(CH_3)_2C$, doublet, J = 6 Hz].

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, C, 78.3; H, 12.1.

Equilibration of *cis*- and *trans*-2-Methyl-5-isopropylcyclohexanones (*c*-2c and *t*-2c).—The previously described procedure was applied to 1.7 g of a 54:46 mixture of ketones *c*-**2c** and *t*-**2c**, affording 1.5 g (91%) of a 33:67 mixture[21] of the same ketones, bp 103–110° (15 mm). Those ketones could not be separated by preparative gas or column chromatography and were therefore characterized as the equilibrium mixture: λ_{max}^{film} 5.86 (CO), 7.20, 7.29, 7.48, 8.54, 10.80, and 11.10 μ; $\delta_{TMS}^{CCl_4}$ 1.02 (CH_3, doublet of *c*-**2c**, J = 7 Hz), 0.99 (CH_3, doublet of *t*-**2c**, J = 7 Hz), and 0.88 ppm [$(CH_3)_2C$ doublet, J = 7 Hz].

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.7; H, 12.0.

Ring Expansion of 4-*t*-Butylcyclohexanone (1d) with Diazoethane.—By the procedure described above, 12.0 g of 4-*t*-butylcyclohexanone (**1d**) was converted into 13.0 g (91%) of a 43:43:14 mixture of ketones *t*-**2d** and *c*-**2d** and oxide *t*-**3d**,[21] bp 118–123° (16 mm). The *cis* and *trans* ketones could be separated from the oxide, but not from each other by preparative gas chromatography.

2-Methyl-6-*t*-butyl-1-oxaspiro[2.5]octane (*t*-3d).—The sample secured from the above ring-expansion reaction mixture *via* preparative gas chromatography[16] had the following properties: $n^{25}D$ 1.4639; λ_{max}^{film} 7.30, 9.67, 10.00, 10.78, 11.26, and 14.70 μ; $\delta_{TMS}^{CCl_4}$ 2.73 (H-2, quartet, J = 6 Hz), 1.22 (CH_3, doublet, J = 6 Hz), and 0.89 ppm [$(CH_3)_3C$].

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.2; H, 12.3.

Equilibration of *cis*- and *trans*-2-methyl-5-*t*-Butylcycloheptanones (*c*-2d and *t*-2d).—The previously described procedure was applied to 1.8 g of a 50:50 mixture of ketones *c*-**2d** and *t*-**2d** affording 1.6 g (92%) of a 25:75 mixture[21] of the same ketones, bp 120–124° (17 mm). These ketones could not be separated by preparative gas chromatography or column chromatography and were therefore characterized as the equilibrium mixture: λ_{max}^{film} 5.87 (CO), 7.31, 8.09, 8.53, 9.90, 10.78, and 11.23 μ; $\delta_{TMS}^{CCl_4}$ 1.01 (CH_3, doublet of *c*-**2d**, J = 7 Hz), 0.98 (CH_3, doublet of *t*-**2d**, J = 7 Hz), and 0.88 ppm [$(CH_3)_3C$].

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.2; H, 12.2.

4-(1-Hydroxy-1-methylethyl)cyclohexanone (1e).—A solution of 1.3 g of ethyl 4-hydroxycyclohexanecarboxylate[22] in 50 ml of ether was slowly added to a stirred solution of 50 ml of 1.8 *M* ethereal methyllithium at 0°. The mixture was allowed to reach room temperature, and after 24 hr aqueous ammonium chloride was added slowly. The product was isolated with ethyl acetate,[12a] affording 1.04 g (89%) of a sticky oil that crystallized on standing: λ_{max}^{film} 3.00 (OH), 7.28, 8.68, 9.32, 9.66, 10.33, 10.48, and 10.95 μ.

A 402-mg sample of the above diol in 25 ml of acetone was treated at 0° with 1.0 ml of standard chromic acid reagent.[18] Isopropyl alcohol was added after 5 min, and the product was isolated with ether[12a] and distilled affording 390 mg (84%) of an oil, bp 72° (bath temperature) at 0.2 mm, that crystallized on standing. The analytical sample, mp 37–38°, was obtained *via* recrystallization from ether–hexane: λ_{max}^{KBr} 2.88 (OH), 5.83 (CO), 8.40, 8.72, 10.56, 10.92, and 11.68 μ; $\delta_{TMS}^{CCl_4}$ 2.25 (OH), and 1.19 ppm [$(CH_3)_2C$–].

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.4; H, 10.2.

Ring Expansion of 4-(1-Hydroxy-1-methylethyl)cyclohexanone (1e) with Diazoethane.—By the procedure described above, 208 mg of hydroxy ketone **1e** was converted into 198 mg (81%) of a 50:50 mixture (nmr analysis—see below) of ketones *t*-**2e** and *c*-**2e**, bp 58° (bath temperature) at 0.05 mm. Only one component was detected by gas chromatography.[19]

Equilibration of *cis*- and *trans*-2-Methyl-5-(1-hydroxy-1-methylethyl)cycloheptanones (*c*-2e and *t*-2e).—The previously described procedure was applied to 88 mg of a 50:50 mixture of ketones *c*-**2e** and *t*-**2e** affording 79 mg (90%) of a 25:75 mixture (by nmr analysis) of the same ketones: bp 60° (bath temperature) at 0.05 mm; λ_{max}^{film} 2.90 (OH), 5.87 (CO), 7.27, 8.57, 8.82, 10.70, and 11.22 μ; $\delta_{TMS}^{CCl_4}$ 2.01 (OH), 1.12 [$(CH_3)_2C$], 1.04 (CH_3, doublet of *c*-**2e**, J = 7 Hz), and 1.01 ppm (CH_3, doublet of *t*-**2e**, J = 7 Hz).

***trans*-2-Methyl-5-(1-hydroxy-1-methylethyl)cycloheptanone (*t*-2e).**—To a stirred solution of 97 mg of diol **14** in 5 ml of acetone at 0° was added 0.2 ml of standard chromic acid reagent.[18] Isopropyl alcohol was added after 10 min, and the product was isolated with ether.[12a] Distillation afforded 82 mg (85%) of a colorless oil: bp 60° (bath temperature) at 0.05 mm; λ_{max}^{film} 2.90 (OH), 5.88 (CO), 7.27, 8.57, 8.82, 10.72, and 11.20 μ; $\delta_{TMS}^{CCl_4}$ 3.38 (OH), 1.12 [$(CH_3)_2C$–], and 1.01 ppm (CH_3, doublet, J = 7 Hz). The spectra indicated that this hydroxy ketone is identical with the major isomer of the above equilibration experiment. Satisfactory analytical values could not be obtained for this material.

Ethyl 5-Methyl-4-oxocycloheptanecarboxylate (2f).—By the ring-expansion procedure described above, 55.6 g of keto ester **1f** was converted into 58.8 g (91%) of a 1:1 mixture (nmr analysis) of ketones *t*-**2f** and *c*-**2f**, bp 69–72° (0.1 mm). The gas chromatogram indicated the presence of 2% shorter retention time component, conceivably the oxide **3e**. The analytical sample, bp 68–70° (0.05 mm), was secured after three distillations: λ_{max}^{film} 5.78 (ester CO), 5.87 (ketone CO), 7.25, 7.62, 8.01, 8.45, and 9.62 μ; $\delta_{TMS}^{CCl_4}$ 4.10 (OCH_2 quartet, J = 7 Hz), 1.23 (CH_3, triplet, J = 7 Hz), 1.02 (CH_3, doublet, J = 7 Hz, 1.5 H), and 1.00 ppm (CH_3, doublet, J = 7 Hz, 1.5 H). Only one component was detected in the gas chromatogram[23] of this sample.

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 67.0; H, 9.2.

***trans*-1-Ethyl-4-*t*-butylcyclohexanol (4). A. From Oxide *t*-3d.**—A solution of 108 mg of oxide *t*-**3d** in 1 ml of ether was added to a stirred suspension of 80 mg of lithium aluminum hydride in 5 ml of ether. After 14 hr, 0.16 ml of water and 0.12 ml of 10% aqueous sodium hydroxide were carefully added, and the mixture was stirred for 1 hr and filtered. Distillation of the filtrate gave 89 mg (82%) of an oil: bp 46° (bath temperature) at 0.1 mm; $n^{25}D$ 1.4675 (lit.[24] $n^{25}D$ 1.4638); λ_{max}^{film} 2.97 (OH), 7.30, 8.35, 9.92, 10.52, and 12.04 μ; $\delta_{TMS}^{CCl_4}$ 1.33 (OH), 0.98 (CH_3, triplet, J = 7 Hz), and 0.82 ppm [$(CH_3)_3C$–]. The gas chromatogram[23] showed a single peak.

B. From 4-*t*-Butylcyclohexanone (5).—A 69:31 mixture of *trans*- and *cis*-1-ethyl-4-*t*-butylcyclohexanols (**4** and **6**) was prepared by the addition of ethylmagnesium bromide to 4-*t*-butylcyclohexanone (**5**) in diethyl ether according to the procedure of Hennion and O'Shea.[24] The major alcohol (**4**) was shown to be identical with the alcohol obtained *via* reduction of oxide *t*-**3d**, as outlined above, by comparison of the ir spectra and the gas chromatographic retention times (peak enhancement).[23]

Attempted Equilibration of Ethyl 5-Methyl-4-oxocycloheptanecarboxylate (2f). Ethyl 3-(3-Methyl-2-oxocyclopentyl)propanoate (7).—A solution of 15 mg of sodium ethoxide and 1.02 g of keto ester **2f** in 10 ml of ethanol was heated at reflux for 5 hr. The product was isolated with ether[12a] and distilled affording 0.80 g (79%) of an oil: bp 80° (bath temperature) at 0.1 mm; λ_{max}^{film} 5.77 (CO), 7.27, 7.58, 8.05, 8.46, and 9.62 μ; $\delta_{TMS}^{CCl_4}$ 4.08 (OCH_2, quartet, J = 7 Hz), 1.23 (CH_3, triplet, J = 7 Hz), and 1.06 ppm (CH_3 doublet, J = 6.5 Hz). The gas chromatogram[23] exhibited a single peak. The 2,4-dinitrophenylhydrazone derivative had mp 120–121° after three recrystallizations from ethanol.

(21) A 40 ft by 1/8 in. column packed with 8% Carbowax 20M on 60 mesh Chromosorb W was used for this analysis.

(22) R. A. Finnegan and P. L. Bachman, *J. Org. Chem.*, **30**, 4145 (1965).

(23) A 15 ft by 1/8 in. column packed with 10% DC-550 oil on 60–80 mesh Chromosorb W was used for this analysis.

(24) G. F. Hennion and F. X. O'Shea, *J. Amer. Chem. Soc.*, **80**, 614 (1958).

Anal. Calcd for $C_{17}H_{22}N_4O_6$: C, 53.96; H, 5.86; N, 14.81. Found: C, 54.1; H, 5.8; N, 14.9.

***trans,cis*-5-Iodo-4-hydroxycycloheptanecarboxylic Acid Lactone (8).**—The method of van Tamelen[25] was employed. A solution of 4.9 g of 4-cycloheptenecarboxylic acid[26] in 210 ml of 0.5 *M* sodium bicarbonate was added to a solution of 12.7 g of iodine and 24.9 g of potassium iodide in 75 ml of water. The mixture was allowed to stand in the dark for 12 hr at room temperature, and the product was isolated with ether[12a] affording 9.3 g of yellow solid. Recrystallization from ether–hexane gave 8.3 g (89%) of white elongated prisms: mp 77–78°; λ_{max}^{KBr} 5.73 (CO), 7.22, 7.92, 7.98, 9.42, 9.72, 10.44, 10.68, 13.18, and 14.38 μ; $\delta_{TMS}^{CCl_4}$ 4.91 (H-4, broad doublet, J = 4 Hz), 4.47 (H-5, triplet, J = 8.5 Hz); and 2.78 ppm (H-1, broad unresolved peak). An additional recrystallization afforded the analytical sample, mp 77–78°.

Anal. Calcd for $C_8H_{11}IO_2$: C, 36.11; H, 4.17; I, 47.69. Found: C, 36.1; H, 4.4; I, 47.9.

Methyl 4-Cycloheptenecarboxylate (10).—To 500 ml of 0.28 *M* ethereal diazomethane at −10° was added slowly a solution of 14.4 g of acid 9[26] in 100 ml of ether. The solution was magnetically stirred at 0° for 30 min, and acetic acid was added to destroy the excess diazomethane. Distillation afforded 14.5 g

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ml of tetrahydrofuran (THF) and 25 ml of 3 *M* methylmagnesium chloride in THF was heated at reflux for 48 hr. Aqueous ammonium chloride was added, and the product was isolated with ether[12a] affording 571 mg of solid material. Recrystallization from ethyl acetate–heptane yielded 478 mg (84%) of diol **13** as white platelets: mp 120–122°; λ_{max}^{KBr} 3.02 (OH), 7.22, 7.29 8.78, 8.98, 9.24, 9.36, 10.58, and 10.76 μ; $\delta_{TMS}^{CDCl_3}$ 3.54 [–CH(OH)–, broad peak], 1.38 (OH), 1.15 [$(CH_3)_2COH$], and 1.14 ppm (CH_3, doublet, J = 6.5 Hz). The analytical sample, mp 122–123°, was secured after two additional recrystallizations.

Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.8; H, 11.7.

The same product was obtained in high yield when the above procedure was repeated with methylmagnesium bromide.

***cis*-5-(1-Hydroxy-1-methylethyl)-*trans*-2-methylcycloheptanol (14).**—The method of Christensen, *et al.*,[10] was employed. A mixture of 75 ml of 0.5 *M* dimethylmagnesium in dioxane and 600 mg of *cis*-oxido ester **11** in 5 ml of dioxane was heated at reflux for 48 hr. Aqueous ammonium chloride was added, and the product was isolated with ether[12a] affording 520 mg (80%) of crystalline diol **14**: λ_{max}^{KBr} 2.98 (OH), 7.30, 8.81, 9.70, 9.80, 10.83, and 11.24 μ; $\delta_{TMS}^{CDCl_3}$ 3.37 [–CH(OH)–, broad peak], 1.72 (OH), 1.15 [$(CH_3)_2COH$], and 1.04 ppm (CH_3 doublet,

chloride in THF was heated at reflux for 48 hr. Aqueous ammonium chloride was added, and the product was isolated with ether[12a] affording 571 mg of solid material. Recrystallization from ethyl acetate–heptane yielded 478 mg (84%) of diol **13** as white platelets: mp 120–122°; λ_{max}^{KBr} 3.02 (OH), 7.22, 7.29 8.78, 8.98, 9.24, 9.36, 10.58, and 10.76 μ; $\delta_{TMS}^{CDCl_3}$ 3.54 [–CH(OH)–, broad peak], 1.38 (OH), 1.15 [$(CH_3)_2COH$], and 1.14 ppm (CH_3, doublet, J = 6.5 Hz). The analytical sample, mp 122–123°, was secured after two additional recrystallizations.

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with 10% aqueous sodium hydroxide, dried over anhydrous magnesium sulfate, and distilled affording 4.76 g (91%) of a 35:65 mixture[28] of alcohols **18** and **19**. The minor alcohol (**18**) was secured *via* preparative gas chromatography[28] or column elution chromatography on silica gel. A sample secured *via* gas chromatography exhibited the following properties: mp 132–138° from hexane; λ_{max}^{KBr} 2.94 (OH), 8.26, 8.82, 9.48, 9.67, 9.98, 11.35, and 11.67 μ. The acetate derivative, bp 94° (bath temperature) at 18 mm, was prepared for combustion analysis.

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.9; H, 8.6.

The major alcohol (**19**) of the above mixture decomposed during attempted chromatographic purifications.

***cis*-5-Hydroxymethyl-*trans*-2-methylcycloheptanol (20).**—A 4.03-g sample of the above 35:65 mixture of alcohols **18** and **19** in 5 ml of dioxane was refluxed with 250 ml of 0.5 *M* dimethylmagnesium[10] in dioxane for 36 hr. Aqueous ammonium chloride was added, and the product was isolated with ethyl acetate and distilled affording 3.25 g of an oil. A 440-mg sample was chromatographed on deactivated alumina.[31] The unchanged bicyclic alcohol **18** (126 mg) was eluted with 50% ether–benzene. Elution with ether afforded 250 mg of diol **20**: λ_{max}^{film} 3.00 (OH), 9.12, 9.47, and 11.30 μ; $\delta_{TMS}^{CDCl_3}$ 3.41 (CH_2OH, broad peak), 3.33 (H-1, broad peak), 2.51 (OH), and 1.04 ppm (CH_3, doublet, J = 6 Hz).

The diacetate derivative, bp 66° (bath temperature) at 0.1 mm, was prepared for analysis.

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.4; H, 9.2.

***exo*-2-Oxabicyclo[3.2.2]nonan-7-yl Acetate (18, Y = OAc) and *cis*-5-Acetoxymethyl-*trans*-2-methylcycloheptyl Acetate (21).**—A 610-mg sample of the *ca.* 1:2 mixture of alcohols **18** and **20**, prepared in the experiment described above, was allowed to stand with 1.25 g of acetic anhydride in 10 ml of pyridine at room temperature for 24 hr. The product was isolated with ether[12a] affording 840 mg of an oil shown by gas chromatography to be a 30:70 mixture of acetates **18** (Y = OAc) and **21**. This mixture was chromatographed on silica gel. The diacetate **21** was eluted with 5% ether in benzene and distilled affording 450 mg of oil: bp 66° (bath temperature) at 0.1 mm; λ_{max}^{film} 5.74–5.76 (CO), 7.28, 8.02, 9.72, and 10.16 μ; $\delta_{TMS}^{CCl_4}$ 4.54 (H-1, broad peak), 3.81 (CH_2OAc, doublet, J = 5.5 Hz) 1.93 (CH_3CO), and 0.92 ppm (CH_3, doublet, J = 6.5 Hz). This material was identical with the acetate derivative prepared from a purified sample of diol **20**.

Acetate **18** (Y = OAc) was eluted from the aforementioned column with 10% ether in benzene and distilled giving 155 mg of an oil: bp 94° (bath temperature) at 18 mm; λ_{max}^{film} 5.74 (CO), 7.28, 8.03, 8.26, 8.78, 9.28, 9.58, 9.68, 10.17, and 11.46 μ; $\delta_{TMS}^{CCl_4}$ 4.80 (H-7, broad peak), 3.92, (H-1, broad peak), 3.70 (H-3, doublet, J = 5 Hz), and 1.93 ppm (CH_3CO). This material was identical with the acetate derivative prepared from a purified sample of alcohol **18**.

***cis*-5-Hydroxymethyl-*trans*-2-methylcycloheptyl Acetate (22).**—A solution containing 650 mg of diacetate **21** in 85 ml of ethanol and 27 ml of 0.1 *M* aqueous sodium hydroxide was stirred at room temperature for 14 hr. The product was isolated with ether and distilled affording 496 mg (93%) of hydroxy acetate **22**: bp 88° (bath temperature) at 0.1 mm; λ_{max}^{film} 2.92 (OH), 5.77, 5.81 (split CO), 7.26, 8.00, 9.74, and 10.12 μ; $\lambda_{max}^{CCl_4}$ 5.77 μ (CO); $\delta_{TMS}^{CCl_4}$ 4.50 (H-1, broad peak), 3.31 (CH_2OH, broad peak), 3.24 (OH), 1.97 (CH_3CO), and 0.93 ppm (CH_3, doublet, J = 6 Hz). The analytical sample was secured after two additional distillations.

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.9; H, 10.2.

(31) The deactivated alumina was prepared by stirring 1 kg of Fisher alumina with 1 l. of benzene 10 g of pyridine, and 20 g of water for 1 hr.

***cis*-5-(2-Thiahexyl)-*trans*-2-methylcycloheptyl Acetate (24).**—A stirred solution of 384 mg of hydroxy acetate **22** in 8 ml of pyridine was cooled to 0°, and 242 mg of methanesulfonyl chloride was carefully added. After 2 hr at 0°, the mixture was poured onto crushed ice, and the product was isolated with ether,[12a] after the pyridine had been removed *via* thorough washing with 2% aqueous sulfuric acid, affording 498 mg (93%) of oily mesylate **23**: λ_{max}^{film} 5.78 (CO), 7.38, 8.00, 8.49, 9.73, 10.2–10.8, and 11.8–12.2 μ.

To a mixture derived from 85 mg of sodium hydride and 324 mg of butanethiol in 20 ml of tetrahydrofuran (THF) was added 498 mg of mesylate **23** in 5 ml of THF. The resulting mixture was heated at reflux for 12 hr, and the product was isolated with ether[12a] affording 388 mg (80%) of oily sulfide **24**: bp 96° (bath temperature) at 0.1 mm; λ_{max}^{film} 5.76 (CO), 7.26, 8.00, 9.72, 10.16, and 10.30 μ; $\delta_{TMS}^{CCl_4}$ 4.53 (H-1, broad peak), 2.42 ($-SCH_2$, broad triplet), 2.35 ($-SCH_2$, doublet, J = 6.5 Hz), 1.94 (CH_3CO), 0.98 (CH_3, triplet, J = 4 Hz), and 0.90 ppm (CH_3, doublet, J = 5 Hz). The analytical sample was secured after an additional distillation.

Anal. Calcd for $C_{15}H_{28}O_2S$: C, 66.13; H, 10.36; S, 11.77. Found: C, 66.1; H, 10.5; S, 12.0.

***trans*, *cis*-2,5-Dimethylcycloheptyl Acetate (25).**—A mixture containing 258 mg of the sulfide **24** and 6 g of W-2 Raney nickel in 100 ml of ethanol was heated at reflux for 2 hr. The cooled mixture was filtered, and the product was isolated with ether[12a] and distilled affording 133 mg (76%) of acetate **25**: bp 82° (bath temperature) at 16 mm: λ_{max}^{film} 5.75 (CO), 7.26, 8.00, 9.77, 10.05, and 10.27 μ; $\delta_{TMS}^{CCl_4}$ 4.53 (H-1, broad peak), 1.94 (CH_3CO), and 0.92 ppm (CH_3, doublet, J = 6 Hz). The analytical sample was secured after an additional distillation.

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.6; H, 10.8.

***trans*,*cis*-2,5-Dimethylcycloheptanol (26).**—To a stirred suspension of 40 mg of lithium aluminum hydride in 3 ml of ether was added 97 mg of acetate **25** in 2 ml of ether. After 4 hr, 0.08 ml of water and 0.07 ml of 10% aqueous sodium hydroxide was added, and the mixture was stirred for several hours, filtered, and distilled, affording 62 mg (83%) of alcohol **26**: bp 65° (bath temperature) at 16 mm: λ_{max}^{film} 2.97 (OH), 7.23, 9.58, 9.70, and 9.90 μ; $\delta_{TMS}^{CCl_4}$ 3.29 (H-1, broad peak), 2.01 (OH), and 0.99 ppm (CH_3, doublet, J = 6 Hz).

Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.76. Found: C, 75.8; H, 12.6.

Registry No.—**1e**, 17328-67-5; **2a**, 932-56-9; ***t*-2b**, 17328-68-6; ***c*-2b**, 17328-69-7; **2c**, 17328-98-2; **2d**, 17328-70-0; ***c*-2e**, 17328-71-1; ***t*-2e**, 17477-88-2; **2f**, 17328-73-3; **3a**, 17328-74-4; **3b**, 17328-75-5; ***t*-3c**, 17328-76-6; ***t*-3d**, 17328-77-7; **4**, 17328-78-8; **7**, 17328-79-9; **7** 2,4-dinitrophenylhydrazene derivative, 17328-80-2; **8**, 17328-99-3; **10**, 17328-81-3; **11**, 17328-82-4; **12**, 17329-00-9; **13**, 17328-83-5; **14**, 17328-84-6; **15**, 17328-85-7; **16**, 17328-86-8; **17**, 17328-87-9; **18**, 17328-88-0; **18** (Y = OAc), 17328-89-1; **19**, 17328-90-4; **19** acetate, 17329-01-0; **20**, 17328-91-5; **21**, 17328-92-6; **22**, 17328-93-7; **23**, 17328-94-8; **24**, 17328-95-9; **25**, 17328-96-0; **26**, 17328-97-1.

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