then steam-distilled. The organic phase was separated and then fractionated. Two well defined fractions were obtained. The first fraction (46 g., 27%), b.p. 137–138°, n_D^{20} 1.4029, was 2-ethoxy-3-methylbutyraldehyde.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.6; H, 10.8. Found: C, 64.8; H, 10.9.

The 2,4-dinitrophenylhydrazone melted at 125–126°.

Anal. Calcd. for $C_{13}H_{18}N_4O_5$: C, 50.3; H, 5.8. Found: C, 50.1; H, 5.8.

The second fraction (21 g., 12%), b.p. 160–162°, n_D^{20} 1.4132, was 4-ethoxy-3-methylbutyraldehyde.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.6; H, 10.8. Found: C, 64.9; H, 10.9.

The 2,4-dinitrophenylhydrazone, m.p. 48–50°, was very soluble and therefore difficult to purify.

Anal. Calcd. for $C_{13}H_{18}N_4O_5$: C, 50.3; H, 5.8. Found: C, 49.7; H, 6.1.

The structures of the two aldehydes were assigned on the basis of their nuclear magnetic resonance spectra. These spectra were in full agreement with the assigned structures and preclude the other possible isomer, ethoxypivalaldehyde.

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Studies of Configuration. VI. *cis-* and *trans-*4-Methoxycyclohexanol[1,2]

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The isomeric mixture of the 4-methoxycyclohexanols is well known, having been prepared frequently by hydrogenation of hydroquinone monomethyl ether.[3] However, there are only three reports concerning individual isomers. In 1941, Ruggli, Leupin, and Businger[4] reported that 4-methoxycyclohexyl tosylate could be separated into a solid, m.p. 87°, and a liquid. They suggested the *trans*-configuration for the solid 4-methoxycyclohexaneacetic acid prepared by treatment of the tosylate with sodio diethylmalonate, but made no assignment to the 4-methoxycyclohexyl tosylate.

Almost simultaneously with our preliminary report on the solvolysis of the *cis-* and *trans*-4-methoxycyclohexyl tosylates, Henbest and Nichols[5] reported the 3,5-dinitrobenzoate of the *trans*-isomer.

We have reported the separation of the isomers through the acid phthalates and a preliminary correlation of the configuration with the known 1,4-dihydroxycyclohexane by partial methylation. In view of the very interesting behavior of the two isomers, it seemed essential to present a definitive proof of configuration. Such is the purpose of the present report.

The known *cis*-4-hydroxycyclohexanecarboxylic acid[6] (I) was converted by methylation with methyl iodide and silver oxide following the procedure used by Noyce and Denney[7] to methyl *cis*-4-methoxycyclohexanecarboxylate (II). Ample evidence is available to show that this reaction proceeds without jeopardizing the stereochemical integrity of the system. The ester II was hydrolyzed to *cis*-4-methoxycyclohexanecarboxylic acid (III), m.p. 54.5–55.7°. This material was shown to be identical, by mixed melting point and comparison of infrared spectra, with the isomer of 4-methoxycyclohexanecarboxylic acid assigned the *cis*-configuration by Noyce and Weingarten.[8] Thus, confirmation of the previous assignment on the basis of rearrangement behavior is obtained.

Treatment of *cis*-4-methoxycyclohexanecarboxylic acid with methyllithium afforded the ketone *cis*-4-methoxy-1-acetylcyclohexane (IV). This reaction has been shown by Dauben and Hoerger[9] to proceed without any inversion or epimerization adjacent to the carbonyl group. Treatment of the ketone with perbenzoic acid afforded *cis*-4-methoxycyclohexylacetate (V), a reaction shown to proceed with retention of configuration by Turner.[10] Hydrolysis of the acetate afforded *cis*-4-methoxycyclohexanol (VI), which was characterized by infrared spectra and preparation of derivatives. Each of the steps proceeded in satisfactory yield.

The second method which was used was the partial methylation of the known *trans*-1,4-dihydroxycyclohexane.[11] Unfortunately, the yield of the monomethyl ether was low (10%) and the more definitive sequence above was carried through.

The chemical transformations are summarized in Chart I, and the properties of derivatives of *cis*- and *trans*-4-methoxycyclohexanol are given in Table I.

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(1) A portion of this work has been published in preliminary form [D. S. Noyce and B. R. Thomas, *J. Am. Chem. Soc.*, **79**, 755 (1957)].

(2) Supported in part by the National Science Foundation (G-2387).

(3) For recent examples, see F. Hunziker, F. X. Mullner, and H. Schaltegger, *Helv. Chim. Acta,* **38**, 1943 (1955); D. Papa, F. J. Villani, and H. F. Ginsberg, *J. Am. Chem. Soc.*, **76**, 4446 (1954).

(4) P. Ruggli, O. Leupin, and A. Businger, *Helv. Chim. Acta*, **24**, 339 (1941).

(5) H. B. Henbest and B. Nichols, *Proc. Chem. Soc.*, 61 (1957); *J. Chem. Soc.*, 227 (1959).

(6) N. R. Campbell and J. H. Hunt, *J. Chem. Soc.*, 1379 (1950).

(7) D. S. Noyce and D. B. Denney, *J. Am. Chem. Soc.*, **76**, 768 (1954).

(8) D. S. Noyce and H. I. Weingarten, *J. Am. Chem. Soc.*, **79**, 3093 (1957).

(9) W. G. Dauben and E. Hoerger, *J. Am. Chem. Soc.*, **73**, 1504 (1951).

(10) R. B. Turner, *J. Am. Chem. Soc.*, **72**, 878 (1950).

(11) W. Nudenberg and L. W. Butz, *J. Am. Chem. Soc.*, **66**, 307 (1944).

Chart I

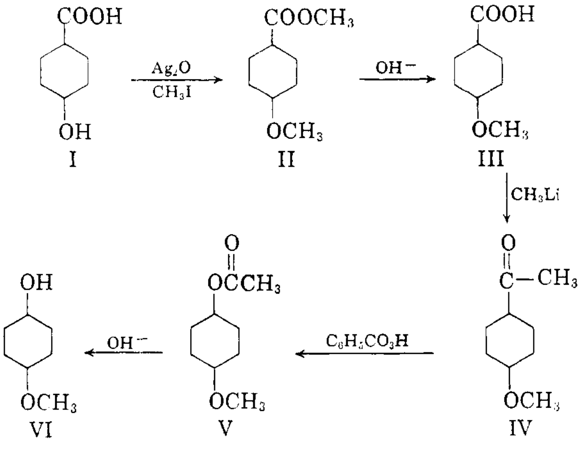

TABLE I

MELTING POINTS OF 4-METHOXYCYCLOHEXANOL DERIVATIVES

	M.P., °C.	
	cis-	*trans*-
3,5-Dinitrobenzoate	116.2–116.5	125.5–126.5
p-Toluene sulfonate	87.8–88.2	66.4–67.2
Acid phthalate	61–65	148.6–149.0

It is to be noted that the tosylate of the *cis*-isomer is the higher melting of the pair.

Another very interesting observation made during the course of this work is that the lithium aluminum hydroxide reduction of 4-methoxycyclohexanone affords 70% of the *cis*-isomer. Further study is in progress in this area.

EXPERIMENTAL[12]

cis-4-Hydroxycyclohexanecarboxylic acid (I). *p*-Hydroxybenzoic acid in acetic acid was hydrogenated over 5% rhodium-on-alumina at an initial hydrogen pressure of 45 p.s.i. After removal of the catalyst by filtration, the remaining solution was distilled at atmospheric pressure to afford a main fraction b.p. 235–245°. This fraction was redistilled to afford the lactone of *cis*-4-hydroxycyclohexanecarboxylic acid, b.p. 120–123° (11 mm.). Crystallization from benzene-pentane afforded the pure lactone, m.p. 127.2–128.0° (lit.[6] 126–128°).

The lactone was dissolved in a minimum amount of water and heated on a steam bath. The *cis*-4-hydroxycyclohexanecarboxylic acid (I) obtained by continuous ether extraction was crystallized from acetonitrile, m.p. 150.1–151.2° (lit.[6] 152°).

Methyl cis-4-methoxycyclohexanecarboxylate (II) was prepared by the procedure of Noyce and Fessenden[13] from 4.0 g. of *cis*-4-hydroxycyclohexanecarboxylic acid, 50 g. of freshly prepared silver oxide (anhydrous), and 150 ml. of methyl iodide. The crude ester was fractionally distilled at reduced pressure to afford 2.8 g. (58%) of methyl *cis*-4-methoxycyclohexanecarboxylate, II, b.p. 99–99.5° (10.5 mm.), n_D^{22} 1.4503.

cis-4-Methoxycyclohexanecarboxylic acid (III). The ester (2.35 g.) was heated under reflux with 15 ml. of water and 50 ml. of aqueous 1*N* sodium hydroxide for 3 hr. The acidified solution was continuously extracted with ether. The dried ether extracts were concentrated, and the residue crystallized from pentane (charcoal). The *cis*-4-methoxycyclohexanecarboxylic acid obtained had a m.p. 54.5–55.7° and weighed 1.33 g. (62%). When mixed with a sample of *cis*-4-methoxycyclohexanecarboxylic acid, m.p. 54.8–55.8°, prepared by Noyce and Weingarten,[8] the m.p. was 54.5–55.7°.

cis-4-Methoxy-1-acetylcyclohexane (IV). To a solution of 9.5 g. of *cis*-4-methoxycyclohexanecarboxylic acid in anhydrous ether was added dropwise 300 ml. of a freshly prepared 0.52 molar methyllithium solution in anhydrous ether.[14] After addition was complete, the cloudy solution was stirred for an additional 20 min., and then poured onto 100 g. of ice. The crude ketone was distilled to afford 6.4 g. (69%) of *cis*-4-methoxy-1-acetylcyclohexane, b.p. 99–102° (12 mm.), n_D^{27} 1.4576.

The dinitrophenylhydrazone was prepared in aqueous ethanol and crystallized from 50% ethanol, m.p. 104.2–105.4°.

Anal. Calcd. for $C_{15}H_{20}O_5N_4$: C, 53.56; H, 5.98; N, 16.73. Found: C, 53.7; H, 5.95; N, 16.70.

Conversion of cis-4-methoxy-1-acetylcyclohexane to cis-4-methoxycyclohexyl acetate (V). *cis*-4-Methoxy-1-acetylcyclohexane, 5.3 g., was treated with a 50% excess of freshly prepared perbenzoic acid in chloroform,[15] and allowed to stand at room temperature for 14 days. The solution was diluted with ether, washed with dilute sodium hydroxide and water, and dried over magnesium sulfate. Fractionation afforded *cis*-4-methoxycyclohexyl acetate (V), b.p. 98–100° (12.5 mm.) n_D^{28} 1.4438. The yield was 3.0 g. (52%).

cis-4-Methoxycyclohexanol (VI). Hydrolysis of V, 3.0 g., with 1*N* sodium hydroxide was followed by continuous extraction with ether. Fractionation of the dried ether extract afforded 1.3 g. (57%) of *cis*-4-methoxycyclohexanol, b.p. 98–99° (11 mm.) n_D^{27} 1.4641.

cis-4-Methoxycyclohexyl 3,5-dinitrobenzoate was prepared in the usual manner and crystallized from hexane, m.p. 115.6–116.2°.

Separation of isomers of 4-methoxycyclohexanol. 4-Methoxycyclohexyl hydrogen phthalate was fractionally crystallized from benzene. Three crystallizations afforded the *trans*-4-methoxycyclohexyl hydrogen phthalate, m.p. 148.6–149.0°.

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.71; H, 6.49.

From the mother liquors a low melting form, m.p. 61–65°, was obtained, which subsequent investigation showed to be primarily *cis*-4-methoxycyclohexyl hydrogen phthalate.

Anal. Found: C, 64.66; H, 6.45.

The *p-toluenesulfonates* were prepared in the usual manner, m.p. *cis*-, 87.8–88.2°; *trans*-, 66.4–67.2°. The *p*-toluenesulfonates may also be separated by fractional crystallization of the mixed isomers from petroleum ether.

Anal. Calcd. for $C_{14}H_{20}O_4S$: C, 59.13; H, 7.09; S, 11.27. Found (*cis*-): C, 59.25; H, 7.18; S, 11.16. Found (*trans*-): C, 59.03; H, 7.13; S, 11.18.

The 3,5-dinitrobenzoates were prepared in the usual manner from the regenerated alcohol. *cis-4-Methoxycyclohexyl 3,5-dinitrobenzoate* was crystallized from hexane, m.p. 116.2–116.5°. *trans-4-Methoxycyclohexol 3,5-dinitrobenzoate* was crystallized from methanol, m.p. 125.5–126.5°.

Anal. Calcd. for $C_{14}H_{16}O_7N_2$: C, 51.85; H, 4.95; N, 8.64. Found (*cis*-): C, 52.03; H, 4.73; N, 8.65. Found (*trans*-): C, 51.61; H, 4.93; N, 8.79.

trans-4-Methoxycyclohexanol from trans-1,4-cyclohexanediol. Treatment of 5 g. of *trans*-1,4-cyclohexanediol with an eightfold excess of methyl iodide and silver oxide using methanol as a solvent afforded 0.6 g. (10%) of *trans*-4-

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(12) Melting points are corrected; boiling points are uncorrected. Analyses are by the Microanalytical Laboratory of the University of California.

(13) D. S. Noyce and J. S. Fessenden, *J. Org. Chem.*, **24**, 715 (1959).

(14) D. A. Van Dorp and J. A. Arens, *Rec. trav. chim.*, **65**, 338 (1946).

(15) G. Braun, *Org. Syntheses*, **Coll. Vol. I,** 431 (1941).

methoxycyclohexanol (VII), b.p. 90–95° (10 mm.) n_D^{25} 1.4650.

The distillation residue afforded 2 g. of recovered *trans*-1,4-cyclohexanediol on crystallization from acetone, m.p. 141–142°.

The *p*-toluene sulfonate and 3,5-dinitrobenzoate of VII were prepared, m.p. 65–66° and 126–127°, respectively.

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Conformational Analysis. VII. The Dipole Moment of 2-Bromocyclooctanone[1,2]

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Recently a conformational analysis of the 2-bromocyclooctanone molecule (I) was reported.[3] This molecule was predicted to exist as a mixture of the five conformational species III–VI[4] depicted in Fig. 1. (There are two species having the gross geometry of III which differ in dihedral angle.) The percentage compositions of the equilibrium mixtures of III–VI (see Table I) in the solvents *n*-heptane benzene, and dioxane were calculated from theoretical considerations and these values predicted rather small changes in the position of the conformational equilibrium with respect to the effective dielectric constant of the medium. A small influence of solvent upon the equilibrium composition was detected by experimental measurements of the absorption intensities of the infrared and ultraviolet carbonyl absorption maxima of I in various media and these spectral data were qualitatively consistent with the theoretical predictions. The exact extent of the agreement between theory and experiment was somewhat obscured, however, by the fact that at present there is no theory available which could be used to quantitatively predict the results of the spectral measurements. On the other hand, the determination of the dipole moment of I in benzene solution did provide an accurate physical measurement which could be directly compared to a calculated value. The experimental value of 3.36 D was in excellent agreement with the predicted dipole moment of 3.28 D for the compound in this solvent.

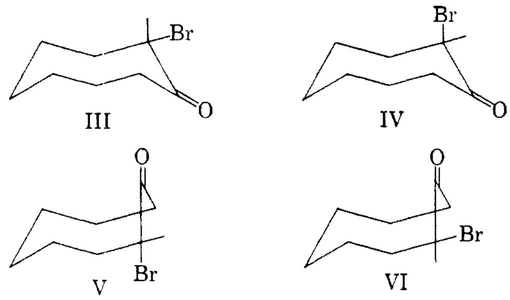

Figure 1

TABLE I

CALCULATED PERCENTAGE CONFORMATIONAL ISOMER COMPOSITION OF 2-BROMOCYCLOOCTANONE

Conformational Isomer	Dihedral Angle	Solvent (D_{effec}) *n*-Heptane (4.83)	Benzene (6.44)	Dioxane (10.3)
IIIa	40°	16	19	22
IIIb	63°	26	27	28
IV	166°	2	1	1
V	132°	47	41	34
VI	12°	9	12	15

The present study was undertaken to extend the dipole moment data for 2-bromocyclooctanone to the solvents *n*-heptane and dioxane and thus to provide a more extensive experimental test of the theoretical analysis. The dipole moments of I were obtained from dielectric constant measurements and had the values 3.29 D and 3.42 D in the solvents *n*-heptane and dioxane, respectively. These values, along with the experimental dipole moment of I in benzene solution and the dipole moments calculated from the estimated compositions for each solvent of Table I, are listed in Table II.

TABLE II

DIPOLE MOMENT OF 2-BROMOCYCLOOCTANONE AT 25°

Solvent	μ Calcd.	μ Observed
n-Heptane	3.13	3.29
Benzene	3.28	3.36
Dioxane	3.41	3.42

The qualitative prediction that only small changes in the conformational composition of the equilibrium mixture of IIIa–VI would result from the changing effective dielectric constant is substantiated by the small differences observed between the magnitudes of the dipole moment in each solvent. The deviations between the calculated and observed moments as the solvent is varied appear to be systematic, but are certainly as small as could be hoped for. The variation of the dipole moment of 2-bromocyclooctanone with solvent is to be compared with the similar corresponding changes in the moment of 2-bromocyclohexanone.[5]

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(1) Sponsored by the Office of Ordnance Research, U. S. Army.

(2) Paper VI, *J. Org. Chem.*, **25**, in press (1959).

(3) J. Allinger and N. L. Allinger, *J. Am. Chem. Soc.*, **81**, 5736 (1959).

(4) For reference, the numbers assigned to these isomers in Paper V (ref. 3) have been retained herein.

(5) The dipole moments of 2-bromocyclohexanone in *n*-heptane, benzene, and dioxane, respectively, are 3.37, 3.50, and 3.64 D. [W. D. Kumler and A. C. Huitric, *J. Am. Chem. Soc.*, **78**, 3369 (1956)].