cal with previous crop (mixture melting point, ir, tlc): ir 1635, 1500, 860, 890 $cm^{-1}$; uv 275 nm ($\epsilon$ 2930), 238 (2300); nmr no signal above $\delta$ 2.4 ppm; mass spectrum *m/e* 460 ($M^+$), 445 ($M^+ - CH_3$), 432 ($M^+ - CO$), 400 ($M^+ - COS$), 316 ($M^+ - 144$).

*Anal.* Calcd for $C_{28}H_{44}OS_2$: C, 72.98; H, 9.63; S, 13.92. Found: C, 72.61; H, 9.48; S, 13.64.

**Lithium Aluminum Hydride Reduction of 3.**—A solution of **3** (0.5 g) in ether (50 ml) was added to a suspension of lithium aluminum hydride (2 g) in ether (100 ml); the mixture was refluxed for 32 hr, cooled, and decomposed with a saturated solution of $Na_2SO_4$ and then treated with dilute hydrochloric acid (10%) till acidic. The ether layer was separated and the aqueous portion was extracted with ether (140 ml). The combined ether solution was washed with water, dried ($Na_2SO_4$), and evaporated, when a colored oil (0.31 g) was obtained which was found to be a complex mixture of products by tlc. This was chromatographed on silica (25 g). Elution with benzene–petroleum ether (2:1) gave a highly colored oil (a complex mixture by tlc) (0.15 g) which could not be purified and identified. Elution of the column with benzene gave a solid (60 mg), which on several crystallizations from ether–methanol gave a colorless solid: mp 173–177° (sintering at 171°); ir 3400, 800 $cm^{-1}$; nmr $\delta$ 3.3–4.1 ppm (broad, 2 H); mass spectrum *m/e* 420 ($M^+$), 405 ($M^+ - CH_3$), 402 ($M^+ - H_2O$), 387 ($M^+ - SH$), 386 ($M^+ - H_2S$).

*Anal.* Calcd for $C_{27}H_{48}OS$: C, 77.06; H, 11.60. Found: C, 77.20; H, 11.48.

**Cholestan-3-one-2$\alpha$-thiol.**—A solution of cholestan-3-one 2$\alpha$-ethyl xanthate (0.5 g) in dry ethanol (30 ml) containing morpholine (5 drops) was refluxed in a nitrogen atmosphere for 5 hr. The solvent was removed and the residue was chromatographed on silica (25 g) using benzene–petroleum ether (1:1) as eluent, when a solid (0.22 g) was obtained which upon crystallization from ether–methanol in a nitrogen atmosphere gave colorless needles (0.172 g), mp 154–158°. This was found to be the cholestan-3-one-2$\alpha$-thiol by comparison of ir, nmr, and uv spectra with those of an authentic sample prepared by the known[5] procedure. However, when the reaction was carried out in the presence of air, the only identifiable product was the bischolestan-3-one 2,2′-disulfide[5] (identity established by mixture melting point, ir, and tlc comparison with an authentic sample).

**Attempted Rearrangement of Cholestan-3-one 2$\alpha$-Ethyl Xanthate. A.**—The xanthate (50 mg) was heated at 150° for 0.5 hr The residue was found to be identical with starting material by tlc (single spot with $R_f$ identical with that of the starting material) and ir comparison.

**B.**—A solution of the xanthate (0.2 g) in dry ethanol (25 ml) was refluxed for 6 hr. The solution was filtered from a small amount of insoluble residue and then concentrated. The oily residue was chromatographed on silica. Elution of the column with benzene–petroleum ether (1:2) gave an oil which on crystallization from methanol gave a solid (115 mg), mp 115–116°, identical with the starting material by mixture melting point and ir comparison.

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**Registry No.**—**2**, 42086-95-3; **4**, 42086-96-4; cholestan-3-one, 15600-08-5; cholestan-3-one-2$\alpha$-thiol, 42086-97-5; cholestan-3-one 2$\alpha$-ethyl xanthate, 42086-98-6; malononitrile, 109-77-3.

## Cyclopropylamine Rearrangement[1]

H. M. WALBORSKY* AND P. E. RONMAN

*Department of Chemistry, Florida State University, Tallahassee, Florida 32306*

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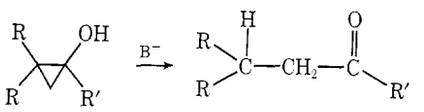
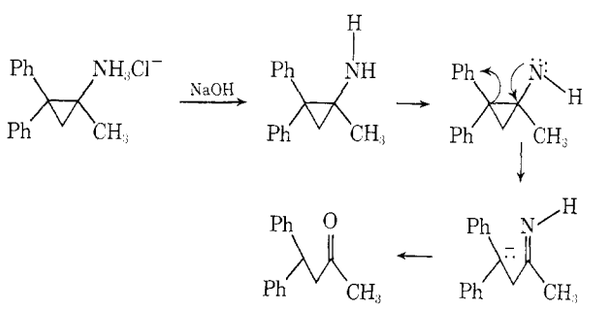
The cyclopropanol rearrangement was originally observed by Magrane and Cottle[2] and extensively explored by DePuy and coworkers.[3] The rearrangement involves the reaction of cyclopropanols with base to yield the corresponding aldehydes or ketones.



In a recent paper Kuehne and King[4] noted that cyclopropylamines were remarkably stable toward both acidic and basic conditions. The amines studied were all tertiary amines and therefore lacking amino hydrogens. We wish to report an example in which a facile rearrangement, comparable with the cyclopropanol rearrangement, occurs when a primary cyclopropylamine reacts with base. A similar rearrangement has been postulated for the hydride reduction of *N*-cyclopropylimines[5] and *N*-cyclopropylformamide[6] derivatives. However, it is not clear from these latter experiments whether the rearrangement occurs during hydride reduction as postulated by these workers or during the subsequent base work-up of the reduction product.

1-Methyl-2,2-diphenylcyclopropylamine was prepared by refluxing 1-methyl-2,2-diphenylcyclopropyl isocyanate[7] with hydrochloric acid. The amine is isolated as its stable hydrochloride salt. Treatment of the amine salt with aqueous or methanolic sodium hydroxide results not in the formation of the free cyclopropylamine but rather one obtains 4,4-diphenyl-2-butanone as the sole product. The propensity for this rearrangement is remarkable since one can achieve this reaction by treatment of the amine salt with aqueous sodium bicarbonate.



The scope, limitations, and stereochemistry of the cyclopropylamine rearrangement are currently under investigation.

### Experimental Section

**1-Methyl-2,2-diphenylcyclopropylamine Hydrochloride.**—A solution of 7.2 g (0.29 mol) of 1-methyl-2,2-diphenylcyclopropyl isocyanate,[7] 45 ml of concentrated hydrochloric acid, and 90 ml of water was refluxed overnight. On cooling the amine hydrochloride precipitated out of solution and was removed by filtration,

(1) The support of this work by a Public Health Service Grant No. 04065 from the National Cancer Institute is gratefully acknowledged.

(2) J. K. Magrane and D. L. Cottle, *J. Amer. Chem. Soc.*, **64**, 484 (1942).

(3) C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *J. Amer. Chem. Soc.*, **88**, 3347 (1966), and earlier references cited therein. See also A. Nickon, J. L. Lambert, S. J., R. O. Williams, and N. H. Werstuik, *ibid.*, **88**, 3354 (1966).

(4) M. E. Kuehne and J. C. King, *J. Org. Chem.*, **38**, 304 (1973).

(5) C. L. Bumgardner, E. L. Lawton, and J. G. Carver, *J. Org. Chem.*, **37**, 407 (1972).

(6) C. Kaiser, A. Berger, L. Zirngibl, C. S. Davis, and C. L. Zirkle, *J. Org. Chem.*, **27**, 768 (1962).

(7) H. M. Walborsky and G. E. Niznik, *J. Org. Chem.*, **37**, 187 (1972).

washed with acetone, and recrystallized from ethanol to yield 7.5 g (0.29 mol): mp 112–120° dec after drying under vacuum at 80°; nmr (TFA) δ 1.64 (s, 3), 2.12 (d, 2, $J$ = 3.5 Hz), 6.96 (s, br, 3), 7.27 (m, 10).

*Anal.* Calcd for $C_{16}H_{18}NCl$: C, 73.82; H, 6.93; N, 5.41. Found: C, 73.62; H, 6.98; N, 5.26.

**4,4-Diphenyl-2-butanone.**—To a solution of 231 mg (0.84 mmol) of 1-methyl-2,2-diphenylcyclopropyl amine hydrochloride dissolved in 150 ml of water was added 100 ml of saturated sodium bicarbonate and the reaction mixture was allowed to stir for 24 hr at ambient temperatures. The mixture was extracted with ether and the ether extracted was washed with 5% hydrochloric acid [36 mg (0.13 mmol, 16%) of starting material was recovered]. The residue from the ether extract gave ir ($CHCl_3$) 1715 $cm^{-1}$; nmr ($CDCl_3$) δ 2.02 (s, 3, $CH_3$), 3.15 (d, 2, $J$ = 7.5 Hz), 4.60 (t, 1, $J$ = 7.0 Hz), 7.23 (s, 10). The residue was treated with 2,4-dinitrophenylhydrazine and 256 mg (0.64 mmol, 76%) of the hydrazone was isolated, mp 172–175° (lit.[8] mp 173–175°).

Using aqueous sodium hydroxide as the base instead of sodium bicarbonate yielded 63% of ketone and alcoholic sodium hydroxide gave a 69% yield.

**Registry No.**—1-Methyl-2,2-diphenylcyclopropylamine hydrochloride, 42253-75-8; 1-methyl-2,2-diphenylcyclopropyl isocyanate, 42253-76-9; 4,4-diphenyl-2-butanone, 5409-60-9.

(8) H. O. House, D. D. Traficanti, and R. A. Evans, *J. Org. Chem.*, **28**, 348 (1963).

## Conformational Analysis of Hydroxyl by the Nuclear Magnetic Resonance Chemical Shift Method. Equivalence of Cyclohexanol and 4,4-Dimethylcyclohexanol as Mobile Systems

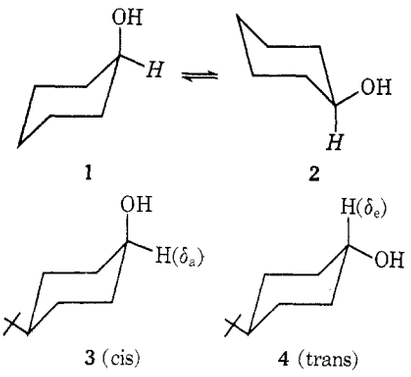
EUGENE C. GILBERT*[1] AND JORMA KOSKIMIES

*John Stuart Research Laboratories, The Quaker Oats Company, Barrington, Illinois 60010, and Department of Chemistry, University of Notre Dame, South Bend, Indiana 46556*

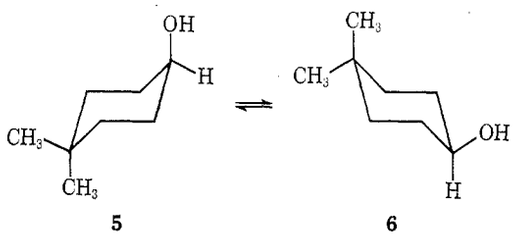
*Received April 11, 1973*

With a view to determining the change of conformational energy with solvent, we had in an earlier study[2] subjected the hydroxyl group to nmr chemical shift analysis[3,4] in a variety of solvents using 2,2,6,6-tetradeuterated cyclohexanol (**1** ⇌ **2**) as substrate and similarly deuterated *cis*- (**3**) and *trans*-4-*tert*-butylcyclohexanol (**4**) as conformationally rigid models.

The lack of correlation of free energy with solvent that was found at the time was attributed to possible ring distortion and anisotropy effects introduced by the *tert*-butyl holding group in the model systems.[5] It has recently been suggested, however, that substitution of 4,4-dimethylcyclohexyl systems in place of cyclohexyl would largely compensate for any disturbing factors imposed by the *tert*-butyl holding group and thus allow




for accurate free-energy determinations by nmr.[6] From this viewpoint, it seemed worthwhile to repeat our earlier work using tetradeuterated 4,4-dimethylcyclohexanol (**5** ⇌ **6**) as a hopefully more appropriate mobile system.




Use of the low-temperature nmr method is not practical for a solvent study of this type owing to potential solubility problems, complications from solute–solute association through hydrogen bonding (which would be very serious under these conditions especially in nonpolar solvents), and a lack of choice of a suitable solvent series due to freezing point problems.[7]

The results obtained in the course of this work are presented in Table I along with those of earlier work

TABLE I

FREE ENERGY VALUES FOR THE HYDROXYL GROUP BY THE CHEMICAL SHIFT METHOD OF ELIEL

| Solvent | Free energy values at 30°[a] Cyclohexyl | 4,4-DMC[b] |
|---|---|---|
| Cyclohexane | 0.61 ± 0.03[c] | 0.60 ± 0.03 |
| Acetone-$d_6$ | 0.76 ± 0.06[d] | 0.72 ± 0.04 |
| Chloroform-*d* | 0.82 ± 0.05 | 0.88 ± 0.04 |
| Benzene | 0.89 ± 0.05[d] | 0.85 ± 0.06 |
| *tert*-Butyl alcohol | 0.91 ± 0.07[e] | 0.97 ± 0.06 |

[a] Total concentrations in all cases were 0.03 *M* or less in order to minimize complications from solute–solute hydrogen bonding. Error limits are standard deviations from the mean. [b] 4,4-Dimethylcyclohexyl. [c] Compared with value of 0.60 ± 0.02 obtained from Raney nickel equilibration of 4-*tert*-butyl cyclohexanones, ref 2b. [d] Revised value. [e] Compared with value of 0.95 ± 0.04 obtained from Raney nickel equilibration of 4-*tert*-butylcyclohexanones, ref 2b.

with deuterated cyclohexanols.[2] Some of the cyclohexanol data are revised values,[8] and, while the shifts in benzene, cyclohexane, and chloroform-*d* are in excellent

(1) Author to whom inquiries should be directed: John Stuart Research Laboratories, The Quaker Oats Company.

(2) (a) E. L. Eliel, D. C. Neilson, and E. C. Gilbert, *Chem. Commun.*, 360 (1968); (b) E. L. Eliel and E. C. Gilbert, *J. Amer. Chem. Soc.*, **91**, 5487 (1969).

(3) (a) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, pp 152–156; (b) E. L. Eliel, *Angew Chem.*, **77**, 784 (1965); *Angew. Chem., Int. Ed. Engl.*, **4**, 761 (1965).

(4) E. L. Eliel, *Chem. Ind. (London)*, 568 (1959).

(5) F. R. Jensen and B. H. Beck, *J. Amer. Chem. Soc.*, **90**, 3251 (1968); F. R. Jensen, C. H. Bushweller, and B. H. Beck, *ibid.*, **91**, 344 (1969); (b) F. R. Jensen and H. C. Bushweller, *Advan. Alicyclic Chem.*, **3**, 139 (1971).

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(7) C. H. Bushweller, J. A. Beach, J. W. O'Neil, and G. U. Rao, *J. Org. Chem.*, **35**, 2086 (1970).

(8) The present data were obtained by single scans on a Varian XL-100 instrument. The earlier results[2b] were derived from data obtained on a Varian A-60A instrument by repeated scanning and computer averaging with a CAT. Such scanning of dilute solutions may be affected by drift and by false triggering caused by impurity peaks.