the residue gave 1.4 g of ketone X, bp 92–102° (22 mm) and $[\alpha]^{25}_{D}$ +1.43° (neat, 1-dm tube).

The **semicarbazone**, mp 169–170° (lit.[9] mp 170–171°), had[15] $[\alpha]^{22}_{D}$ +1.11°, $[\alpha]^{27}_{450}$ +3.0°, $[\alpha]^{27}_{300}$ +13.2° (c 1.8, chloroform).

Anal. Calcd for $C_{10}H_{17}ON_3$: C, 61.51; H, 8.78; N, 21.52. Found: C, 61.00; H, 8.96; N, 21.31.

Registry No.—IX semicarbazone, 15643-73-9; X, 15562-33-1; X semicarbazone, 15562-34-2.

[15] We thank Dr. P. Laur for determining the rotations at 300 and 450 mμ on a Cary spectropolarimeter.

The Absolute Configuration of 2-Cyclohexen-1-ol[1]

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During the course of a study of asymmetric induction in thermal rearrangements of derivatives of cyclic allylic alcohols,[2] it became necessary to provide an unambiguous assignment of the absolute configuration of 2-cyclohexen-1-ol (I). Additional impetus for this investigation comes from the formation of optically active 2-cyclohexen-1-ol in several reactions involving optically active catalysts. Denney, *et al.*,[3] found recently that the use of copper salts of optically active carboxylic acids to catalyze the *t*-butyl hydroperoxide oxidation of cyclohexene affords optically active I. Elucidation of the role played by the metal salt in this striking example of asymmetric induction by an optically active catalyst will depend on a knowledge of the absolute configuration and optical purity of the product. Dextrorotatory I may also be obtained by enzymatic oxidation,[4] using liver alcohol dehydrogenase and NAD with acetaldehyde as the hydrogen acceptor to oxidize selectively the levorotatory enantiomer. Here again a knowledge of the absolute configuration is necessary to correlate this result with theories of stereospecificity in enzymatic oxidations and reductions.[5]

Though Denney's synthesis was the first report of optically active 2-cyclohexen-1-ol, the absolute configuration had already been predicted by Mills.[6] Mills formulated an empirical rule based on rotations of terpene alcohols which states that cyclohexenols containing the moiety II are more levorotatory than their epimers. The same conclusion is reached in the empirical rule of Bose and Chatterjee[7] correlating configuration with rotation of cyclic compounds and in Brewster's conformational asymmetry arguments for optical rotations of cyclic olefins.[8]

In order to provide an unambiguous chemical proof of configuration, we have correlated I with a standard of known configuration. The method chosen was to introduce a new asymmetric center in a stereospecific manner and then determine its configuration. A suitable reaction for this purpose is the Simmons–Smith reaction to form *cis*-bicyclo[4.1.0]heptan-2-ol (III). Dauben and Berezin[9] have shown that the directing influence of the hydroxyl group in the Simmons–Smith reaction results in addition exclusively *cis* to the hydroxyl in I. Consequently the determination of configuration at either of the two new asymmetric centers of III would permit an assignment of configuration to I.

Racemic I was converted into the acid phthalate and partially resolved with dehydroabietylamine. Alcohol resolved in this way had $[\alpha]_{D}$ −15°, a rotation comparable with that obtained by Denney's method. Reaction with methylene iodide and zinc–copper couple afforded optically active III, which was oxidized with chromic acid to optically active bicyclo-[4,1,0]-heptan-2-one (IV). Though IV was unaffected by zinc in refluxing acetic acid, it was readily reduced by lithium in liquid ammonia to optically active 3-methylcyclohexanone (V). The lithium–ammonia reduction of cyclopropyl ketones has been shown to be highly stereospecific;[10,11] the cyclopropane bond cleaved is that which possesses maximum overlap with the π orbital system of the carbonyl group.

Beginning with (+)-I, this sequence yielded (*S*)-(−)-3-methylcyclohexanone, whose absolute configuration has been firmly established.[12] Repetition of the sequence with (−)-I led to (*R*)-(+)-V. These correlations provide a conclusive assignment of configuration to (*R*)-(+)-I and confirm the validity of Mills' rule.

From the maximum rotation ($[\alpha]^{26}_{D}$ 12.01°, neat, 1 dm) reported[12] for 3-methylcyclohexanone and assuming that no racemization occurs during the sequence I → V, it is possible to calculate a minimum value of 152° for the rotation of optically pure I.[13] This value allows an estimate of the optical yield in Denney's synthesis as about 7%. Despite the low optical yield, the rotation of the pure alcohol is high enough that his convenient synthesis gives material with an optical rotation adequate for most purposes.

A final point concerns the sign of the Cotton effect of the bicyclic ketone IV. It has been shown recently that the Cotton effects of most optically active cyclopropyl ketones can be correlated with absolute configuration using a reversed cyclohexanone octant rule.[14] Unfortunately, the simplest bicyclo[4.1.0]heptanone studied to date, (+)-carone (VI), does not fit this generalization. Djerassi, *et al.*,[14] have suggested that the geminal dimethyl group makes a strong contribution to the positive Cotton effect of VI and accounts for its failure to follow a reversed octant rule. The ORD

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[1] This investigation was supported by a research grant, GP-3811, from the National Science Foundation, and by a predoctoral fellowship to J. W. Morgan from the Public Health Service, to whom we express our appreciation.

[2] R. K. Hill and M. E. Synerholm, in press.

[3] D. B. Denney, R. Napier, and A. Cammarata, *J. Org. Chem.*, **30**, 3151 (1965).

[4] J. Rétey, private communication, 1966.

[5] See, *e.g.*, V. Prelog, *Pure Appl. Chem.*, **9**, 119 (1964).

[6] J. A. Mills, *J. Chem. Soc.*, 4976 (1952).

[7] A. K. Bose and B. G. Chatterjee, *J. Org. Chem.*, **23**, 1425 (1958).

[8] J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5493 (1959).

[9] W. G. Dauben and G. H. Berezin, *ibid.*, **85**, 468 (1963).

[10] T. Norin, *Acta Chem. Scand.*, **19**, 1289 (1965).

[11] W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, **31**, 3794 (1966).

[12] E. J. Eisenbraun and S. M. McElvain, *J. Am. Chem. Soc.*, **77**, 3383 (1955).

[13] An attempt was made to determine the optical purity of partially resolved I by the nmr method of M. Raban and K. Mislow, *Tetrahedron Letters*, 4249 (1965), but the nmr spectrum of the O-methylmandelate ester of I showed no splitting of the benzylic hydrogens.

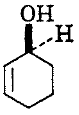
[14] C. Djerassi, W. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, **21**, 163 (1965).

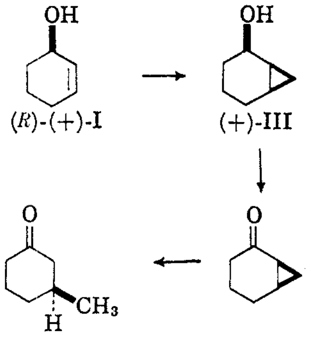
spectrum of bicyclo[4,1,0]heptan-2-one (IV) strongly supports this argument; (−)-IV shows, as predicted by the reversed octant rule, a negative Cotton effect, with a trough at 311 mμ.

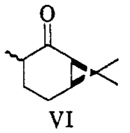
Experimental Section[15]

Partial Resolution of 2-Cyclohexen-1-ol (I).—A mixture of racemic 2-cyclohexen-1-ol (110.3 g), phthalic anhydride (169 g), and dry pyridine (100 ml) was heated on the steam bath for 3 hr, then cooled, poured into a mixture of ice water (1500 ml) and concentrated hydrochloric acid (115 ml), and extracted with chloroform. The extracts were dried and concentrated to leave an oil which solidified after several days. After washing the solid with petroleum ether (bp 60–70°), the acid phthalate[16] (233 g, 83%) was sufficiently pure for resolution.

A solution of the phthalate (300 g) in 900 ml of acetone was mixed with a solution of dehydroabietylamine (346 g) in 3 l. of acetone. The solid (322 g, mp 153–156°) which precipitated after one day was recrystallized twice from acetone to yield 94 g of salt, mp 158–161°. This salt was decomposed with 1 l. of saturated sodium carbonate solution, washed with several portions of ether, then acidified with 6 *N* hydrochloric acid and extracted thoroughly with ether. The ethereal extracts were dried over magnesium sulfate and concentrated to leave 40.8 g of optically active phthalate.


II


(*R*)-(+)-I (+)-III (*S*)-(−)-V (−)-IV


VI

The phthalate (35 g) in 150 ml of ether was reduced with lithium aluminum hydride (38 g) in 450 ml of ether, refluxing the mixture for 3 hr and destroying excess hydride with 2 *N* sodium hydroxide solution. After filtering from precipitated solids, distillation of the filtrate afforded 9.15 g of 2-cyclohexen-1-ol, bp 75–76° (23 mm), $[\alpha]^{25}\mathrm{D}$ −15.2° (*c* 5.32, chloroform). The mother liquors from the recrystallization of the salt were concentrated to a thick residue which was steam-distilled from aqueous sodium hydroxide. The distillate was saturated with potassium carbonate and extracted with ether; distillation of the extracts gave the enantiomer, 10.24 g, bp 73° (22 mm), and $[\alpha]^{25}\mathrm{D}$ +7.3° (*c* 4.68, chloroform).

(+)-*cis*-Bicyclo[4.1.0]heptan-2-ol (III).—2-Cyclohexen-1-ol (10.0 g, $[\alpha]^{25}\mathrm{D}$ +7.3°) was treated with the Simmons–Smith reagent exactly as described by Dauben and Berezin,[9] yielding 6.6 g (58%) of III, bp 89–90° (23 mm) (lit.[9] bp 76–77° (10 mm)) and $[\alpha]^{23}\mathrm{D}$ +4.2° (*c* 8.65, chloroform). The product was shown to be free of starting material by the absence of olefinic protons in the nmr spectrum and by the presence of a single peak on vpc analysis.[17]

The **phenylurethan**, after recrystallization from petroleum ether (bp 60–70°), melted at 111.5–112.5°, $[\alpha]^{25}\mathrm{D}$ +4.9° (*c* 0.92, chloroform); Dauben and Berezin[9] report mp 109–110.5° for the racemic phenylurethan.

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.53; H, 7.43; N, 5.70.

(−)-Bicyclo[4.1.0]heptan-2-one (IV).—Following the procedure of Dauben and Berezin,[9] 2.0 g of bicycloheptanol (III), $[\alpha]^{23}\mathrm{D}$ +4.2°, was oxidized with chromic acid in an acetone–aqueous sulfuric acid solution. The distilled ketone, bp 94–95° (22 mm) (lit.[9] bp 85.0–85.5° (10 mm)), weighed 1.26 g (64%) and had $[\alpha]^{23}\mathrm{D}$ −0.61° (*c* 13.1, chloroform). The nmr spectrum showed the absence of starting alcohol and the vpc[17] showed a single peak.

The **2,4-dinitrophenylhydrazone**, after recrystallization from ethanol, melted at 161–163° (lit. mp 159.5–161.5°[9] and 162–163°[18]).

Anal. Calcd for $C_{13}H_{14}N_4O_4$: C, 53.79; H, 4.87; N, 19.30. Found: C, 53.59; H, 5.08; N, 19.28.

(−)-3-Methylcyclohexanone (V).—To a solution of 1.0 g of IV, $[\alpha]^{23}\mathrm{D}$ −0.61°, in 50 ml of liquid ammonia was added 0.25 g of lithium. The solution was stirred for 2 hr after the blue color developed. Ammonium chloride was added, followed by ether; after the ammonia had evaporated, the ethereal solution was decanted and the precipitated salts washed well with ether. The combined ether solutions were dried and concentrated, and the residue purified by preparative vpc,[19] yielding 0.30 g of 3-methylcyclohexanone, $[\alpha]^{23}\mathrm{D}$ −0.58° (neat, 1 dm). In an identical run the product was purified by preparative vpc followed by distillation and had $[\alpha]^{26}\mathrm{D}$ −0.65° (*c* 16.9, methanol). The infrared spectrum and vpc retention time were identical with those of an authentic racemic sample.

Registry No.—(*R*)-(+)-I, 3413-44-3; III, phenylurethan, 15562-36-4; IV 2,4-dinitrophenylhydrazone, 15562-37-5.

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[15] Melting points were taken in open capillaries and are uncorrected. Optical rotations were measured on a Rudolph spectropolarimeter. We thank Mr. Grant Krow for obtaining the ORD spectrum on a Cary recording spectropolarimeter.

[16] F. D. Greene and W. W. Rees, *J. Am. Chem. Soc.*, **80**, 3432 (1958).

[17] Using a 10-ft column of 15% Carbowax 20M at 180°, III had a retention time of 5 min and IV a retention time of 7 min.

[18] G. Stork and J. Ficini, *ibid.*, **83**, 4678 (1961).

[19] Using a 20-ft column of DC 710 at 225°.