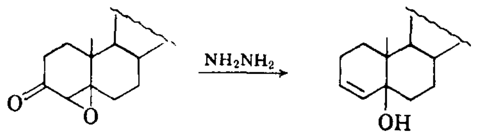

I II

90° for 10 min. followed by refluxing (118°) for a further 15 min. A single crystallization of the crude product from methylbutane at −15° yielded needles of the desired 3-coprosten-5-ol (II) in 68% yield, m.p. 89–91°: analytical sample, m.p. 93.5–94.5°, $[\alpha]_D^{23}$ + 98° (chloroform) (*c* 2.9), $\lambda_{max}^{CS_2}$ 2.75 μ (found: C, 83.58; H, 11.93). The tertiary allylic alcohol II was characterized by its facile dehydration which was readily demonstrated in acidic 95% ethanol (*ca.* 0.05*N* in hydrochloric acid): the characteristic maxima of 3,5-cholestadiene (228, 235, and 242 mμ)[11] appeared in the ultraviolet spectrum and increased in intensity over a period of several hours. Hydrogenation of II with platinum oxide in ethanol proceeded rapidly at room temperature with the uptake of one equivalent of hydrogen and yielded coprostan-5-ol,[12] (99%), m.p. 79–81°, $[\alpha]_D^{23}$ +35° (chloroform) (*c* 3.2), $\lambda_{max}^{CS_2}$ 2.75 μ.

The mild conditions necessary for the rapid succession of steps which presumably involve hydrazone formation, opening of the epoxide and *elimination of nitrogen*[13] were even more strikingly demonstrated when it was found that the reaction of hydrazine with other α,β-epoxy ketones proceeded at room temperature in alcohol solutions in the presence of acetic acid. Preparatively, using these conditions, 1,5,5-trimethyl-2-cyclohexen-1-ol, b.p. 59.0–60.5° (6 mm.), was readily isolated in 66% yield from the reduction of isophorone oxide (10 g.): analytical sample, b.p. 60.5–61.0° (7 mm.), n_D^{27} 1.4653, $\lambda_{max}^{CCl_4}$ 2.8 and 2.9 μ (found: C, 76.87; H, 11.28). Hydrogenation with platinum oxide in ethanol resulted in the uptake of one equivalent of hydrogen and yielded 1,3,3-trimethylcyclohexan-1-ol[14] (78%), m.p. 71.5–72.5°, $\lambda_{max}^{CCl_4}$ 2.8 and 2.9 μ.

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DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
MADISON, WIS.

P. S. WHARTON
D. H. BOHLEN

Received May 5, 1961

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[11] H. E. Stavely and W. Bergmann, *J. Org. Chem.*, **1**, 567 (1937).

[12] A. S. Hallsworth and H. B. Henbest, *J. Chem. Soc.*, 4604 (1957).

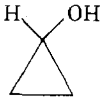
[13] The closely related (but nonreductive) reaction of α-halo ketones with substituted hydrazines also occurs under very mild conditions: V. R. Mattox and E. C. Kendall, *J. Am. Chem. Soc.*, **72**, 2290 (1950).

[14] A. W. Crossley and C. Gilling, *J. Chem. Soc.*, 2218 (1910); K. v. Auwers and E. Lange, *Ann.*, **401**, 303 (1913).

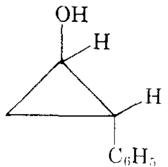
The Synthesis of Cyclopropanols

Sir:

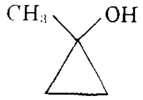
Although cyclopropanol and simply substituted cyclopropanols would be of interest for numerous synthetic and mechanistic studies, no general methods for their preparation are available. Cyclopropanol itself, in very impure form, was prepared by Cottle and co-workers,[1,2] and again in low yield and also impure by Roberts and Chambers,[3] but neither method appeared applicable for the synthesis of substituted cyclopropanols of known structure.[4] We wish to report the synthesis of cyclopropanol (I), *trans*-2-phenylcyclopropanol (II), and 1-methylcyclopropanol (III) by methods which are general enough to be extended to the synthesis of other cyclopropanols.



I



II



III

Our initial interest in the isolation and investigation of cyclopropanols was aroused by the observation that cyclopropanol accumulates during the basic hydrolysis of cyclopropyl acetate,[5] despite its known sensitivity to alkali.[1] Lithium aluminum hydride reduction of the acetate in ether, followed by careful work-up and purification by isolative gas chromatography gave cyclopropanol as a colorless, stable, water-soluble liquid. Its derivatives agreed in melting point with those reported by Cottle.

This method of synthesis was extended to the preparation of II and III. *trans*-2-Phenylcyclopropanecarboxylic acid[6] was converted in good yield to the methyl ketone by reaction with methyllithium[7] and thence to *trans*-2-phenylcyclopropyl acetate with peroxytrifluoroacetic acid.[8] Reaction with lithium aluminum hydride, or better still, with methyllithium, gave II, b.p. 75°/0.2 mm., m.p. 41.5–42.0°. Although II decomposes slowly, its structure was supported by its infrared and NMR spectrum. It readily formed a 1-naphthyl

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[1] J. K. Magrane and D. L. Cottle, *J. Am. Chem. Soc.*, **64**, 484 (1942).

[2] C. W. Stahl and D. L. Cottle, *J. Am. Chem. Soc.*, **65**, 1782 (1943).

[3] J. D. Roberts and V. C. Chambers, *J. Am. Chem. Soc.*, **73**, 3176 (1951).

[4] At least one natural product contains a cyclopropanol ring. P. Lipp and C. Padberg., *Ber.*, **54**, 1316 (1921).

[5] L. R. Mahoney, Ph.D. Thesis, Iowa State University, 1960.

[6] M. Julia, S. Julia and B. Bémont, Compt. Rend., **245**, 2304 (1957).

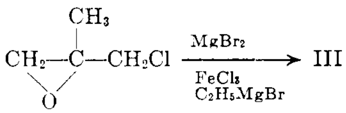
[7] C. Tegner, Acta Chem. Scand., **6**, 782 (1952).

[8] W. D. Emmons and G. B. Lucas, *J. Am. Chem. Soc.*, **77**, 2287 (1955).

urethane, m.p. 130.0–130.5°, *anal.* C, 78.75; H, 5.55; N, 4.41 and a *p*-nitrobenzoate, m.p. 102.0–102.5°, *Anal.* C, 67.38; H, 4.59; N, 4.84.

Cyclopropyl acetates may also be prepared by the addition of iodomethylzinc iodide to enol esters.[9] In this way 1-methylcyclopropyl acetate was formed in low yield from isopropenyl acetate. Hydride reduction and gas chromatographic purification gave a colorless liquid, b.p. 103°, which was assigned the structure III on the basis of infrared and NMR spectrum and its ready conversion by alkali to methyl ethyl ketone.

Cottle[1,2] prepared cyclopropanol from epichlorohydrin, magnesium bromide, ferric chloride, and ethylmagnesium bromide. The mechanism of this conversion is obscure and its applicability to the preparation of other cyclopropanols has never been tested. We have found that III can conveniently be prepared in 35% yield by this method from 2-methylepichlorohydrin.



$$\underset{\diagdown\,O\,\diagup}{CH_2\text{—}\overset{CH_3}{C}}\text{—}CH_2Cl \xrightarrow[\substack{FeCl_3\\ C_2H_5MgBr}]{MgBr_2} \text{III}$$

These results make it clear that cyclopropanols are stable molecules, readily prepared and purified. Extension of these methods to the preparation of other cyclopropanols of interest is being investigated.

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DEPARTMENT OF CHEMISTRY
IOWA STATE UNIVERSITY
AMES, IOWA

C. H. DEPUY
L. R. MAHONEY[10]
K. L. EILERS

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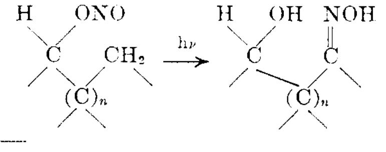
[9] H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959).

[10] National Science Foundation Cooperative Fellow, 1959–60.

Epimerization in a Nitrite Ester Photolysis

Sir:

An elegant method for functionalizing an "unactivated" aliphatic site was recently reported by Barton, Beaton, Geller, and Pechet.[1] The method involves photochemical rearrangement of a nitrite ester to an oximino alcohol, and its power as a synthetic tool has been convincingly demonstrated.[2,3]



In connection with research in the caryophyllene-humulene field we have been investigating the constitution of "α"-caryophyllene alcohol[4] and have used the nitrite reaction as a degradative step. We have encountered in our work a case in which the *C—O bond undergoes a change of configuration* in the course of the nitrite→oximino alcohol transformation. Because of the significance of this finding to those who may use the nitrite reaction in synthesis or in structural studies we wish to report relevant experiments that establish this configurational change, even though we are not ready to propose complete structures for our compounds.

"α"-Caryophyllene alcohol (henceforth abbreviated "α"-alcohol; $C_{15}H_{26}O$, m.p. 118.5–119.5°[5]; 3,5-dinitrobenzoate, m.p. 176.5–177°) was prepared as reported[4a] and was oxidized (97%) to a ketone $C_{15}H_{24}O$ (m.p. 40.5–41.5°; 2,4-dinitrophenylhydrazone m.p. 158.5–159°). This ketone responded negatively to several tests for enolizable hydrogens, and its infrared band at 1742 cm.$^{-1}$ (carbon tetrachloride) indicates a strained carbonyl comparable to that in a five-membered ring. Reduction of the ketone with sodium in 2-propanol regenerated "α"-alcohol (87%), whereas hydrogenation (platinum/ethyl acetate/perchloric acid) gave in about equal amounts "α"-alcohol and a liquid, isomeric alcohol (designated *epi*-"α"-alcohol) whose 3,5-dinitrobenzoate has a m.p. of 129.5–130.5°. The epimeric alcohols are readily separated by chromatography and can be differentiated by infrared spectroscopy. Oxidation of *epi*-"α"-alcohol with chromium trioxide reformed the original ketone (80%). These experiments show that "α"-alcohol and *epi*-"α"-alcohol are epimeric secondary alcohols.

Nitrosation of *epi*-"α"-alcohol (sodium nitrite in acetic acid) gave the crdue *epi*-nitrite as a liquid [ν (carbon tetrachloride) 1642, 1621, 915 cm.$^{-1}$] from which *epi*-"α"-alcohol could be regenerated by saponification. Irradiation of this *epi*-nitrite in benzene with a mercury lamp gave an oximino alcohol $C_{15}H_{25}O_2N$ (m.p. 226.5–227° dec., ν (potassium bromide) 3500, 1632 cm.$^{-1}$; yields, 50–60%). Acid hydrolysis of the oxime provided the corresponding keto alcohol $C_{15}H_{24}O_2$ [m.p. 98.5–

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[1] D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Am. Chem. Soc.*, **82**, 2640 (1960).

[2] D. H. R. Barton and J. M. Beaton, *J. Am. Chem. Soc.*, **82**, 2641 (1960); D. H. R. Barton and J. M. Beaton, *J. Am. Chem. Soc.*, **83**, 750 (1961).

[3] An alternate photolytic pathway has been discovered for the case of steroid C-17β nitrites (C. H. Robinson, O. Gnoj, A. Mitchell, R. Wayne, E. Townley, P. Kabasakalian, E. P. Oliveto, and D. H. R. Barton, *J. Am. Chem. Soc.*, **83**, 1771 (1961)).

[4] Y. Asahina and T. Tsukamoto, *J. Pharm. Soc. (Japan)*, **484**, 463 (1922); (b) J. Bell and G. G. Henderson, *J. Chem. Soc.*, 1971 (1930); (c) D. H. R. Barton, T. Brunn, and A. S. Lindsey, *J. Chem. Soc.*, 2210 (1952); (d) D. H. R. Barton and A. Nickon, *J. Chem. Soc.*, 4665 (1954); (e) S. Dev, *Current Sci. (India)*, **20**, 296 (1951).

[5] Satisfactory analyses were obtained for all compounds whose melting points are reported here.