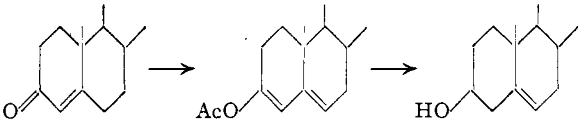
COMMUNICATIONS TO THE EDITOR

ON THE CONVERSION OF CHOLESTENONE TO CHOLESTEROL

Sir:

Turner[1] has recently reported the preparation of C^{14}-labeled cholestenone and discussed its possible use in the study of cancer. The desirability of a similarly labeled cholesterol for other biological studies has prompted us to investigate the transformation of cholestenone to cholesterol. Reich and Lardon[2] previously have devised a seven step process for such a conversion but the over-all yield was only 12%. It has now been found that cholesterol (III) can be obtained more directly and in better yield by the reduction of the enol acetate (II) of cholestenone with lithium aluminum hydride.



I II III

Cholestenone was converted to its enol acetate in 90% yield by the method of Westphal.[3] The product from the lithium aluminum hydride reduction of II at −15° was fractionated with digitonin. Each crude fraction was heated with dilute alcoholic hydrochloric acid in order to dehydrate the Δ^4-isomers present.[4] Marker and co-workers have reported[5] that *epi*-cholesterol also undergoes dehydration upon treatment with alcoholic hydrochloric acid. We found, however, that the mild conditions employed in this research did not affect *epi*-cholesterol to any appreciable extent (<5%).

The material obtained after dehydration of the reduction product was separated by chromatography using alumina. Cholesterol (m. p. 146–148°), M^{24}_{D} −154° ($\mathrm{CHCl_3}$), was isolated from the β-fraction and *epi*-cholesterol (m. p. 137–138°), M^{25}_{D} −149° ($\mathrm{CHCl_3}$), from the α-fraction. The yields based on the enol acetate of cholestenone were 34 and 15%, respectively. No depression of melting point upon admixture with authentic samples was noticed with either of the sterols. Further work is in progress with regard to other aspects of this transformation.

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(1) Turner, This Journal, **72**, 579 (1950).

(2) Reich and Lardon, *Helv. Chim. Acta*, **29**, 671 (1946).

(3) Westphal, *Ber.*, **70**, 2128 (1937).

(4) Schoenheimer and Evans, *J. Biol. Chem.*, **114**, 567 (1936); McKennis and Gaffney, *ibid.*, **175**, 217 (1948).

(5) Marker, Kamm, Oakwood and Laucius, This Journal, **58**, 1948 (1936).

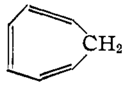
SYNTHESIS OF TROPOLONE

Sir:

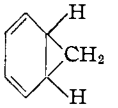
Following Dewar's original and stimulating conception of tropolone (cycloheptatriene-2,4,6-ol-2-one-1) as a unit possessing resonance stabilization and unique chemical characteristics and constituting a part of colchicine and stipitatic acid,[1] much evidence of a degradative nature has been accumulated supporting the presence of a tropolone system in these molecules, in purpurogallin and the thujaplicins as well,[2] while syntheses have been limited to 3,4-benztropolone[3] and 4,5-benztropolone.[4] We wish to report the synthesis in two steps of tropolone itself.

A benzene solution of diazomethane is irradiated[5] to give nitrogen and I, $\mathrm{C_7H_8}$, b. p. 114.5° after fractionation in an 80-plate column. While I has the same infrared spectrum as Kohler's "cycloheptatriene,"[6] its chemistry which we are presently investigating is formulated equally well as cycloheptatriene (Ia) or norcaradiene (Ib).

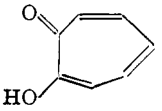
$$\mathrm{C_6H_6 + CH_2N_2 \xrightarrow[365\ \mu]{h\nu} C_7H_8\ (I) \xrightarrow{KMnO_4} C_7H_6O_2\ \ (II)}$$



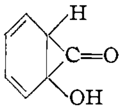
Ia



Ib



IIa



IIb

The oxidation of I with 4% aqueous potassium permanganate produces a small amount of material extractable at *p*H 4 with chloroform. Shaking the concentrated extract with aqueous cupric acetate and evaporating to dryness affords a green, crystalline, chloroform-soluble copper complex (1% yield), m. p. 320° with dec., from which hydrogen sulfide liberates II. II is recrystallized from hexane as colorless needles, m. p. 48°. (*Anal.* Calcd. for $\mathrm{C_7H_6O_2}$: C, 68.85; H, 4.95; neut. equiv., 122.1. Found: C, 68.86; H, 4.96; neut. equiv., 122.8). II sublimes easily, is soluble in water and most organic solvents, is colored deep green by ferric chloride, and is an acid of *pK* 6.7 forming a yellow anion. The ultraviolet absorption spectrum has maxima in

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(1) Dewar, *Nature*, **155**, 50, 141, 479 (1945).

(2) Reviewed by Loudon, *Ann. Rep. on Progress Chem.* (*Chem. Soc. London*), **45**, 187 (1948).

(3) Cook and Somerville, *Nature*, **163**, 410 (1949).

(4) Tarbell, Scott and Kemp, This Journal, **72**, 379 (1950).

(5) Meerwein, Rathjen and Werner, *Ber.*, **75**, 1610 (1942), who discovered the photochemical reaction of diazomethane with ether and isopropyl alcohol, imply that benzene gives toluene.

(6) Kohler, Tishler, Potter and Thompson, This Journal, **61**, 1057 (1939).