derived from the isoprene adduct was identical with that of an authentic sample.

Preparation of Methyl Vinyl Sulfone.—The method of Buckley, Charlish and Rose[13] was used to prepare methyl vinyl sulfone from β-chloroethyl methyl sulfide.[14] The sulfone was distilled; b.p. 115–120° (19 mm.).

1,2,5,6-Tetrahydrophenyl Methyl Sulfone.—A solution of 3.5 g. (0.033 mole) of methyl vinyl sulfone and 3.7 g. (0.074 mole) of 1,3-butadiene in 5 ml. of benzene was placed in a pressure bottle and kept in a 50°-bath for 11 days. After the solvent had been removed, the reaction mixture was distilled under diminished pressure to give 1.5 g. of methyl vinyl sulfone. The residue was dissolved in benzene–petroleum ether (89–92°) from which it crystallized upon cooling. After three recrystallizations from this solvent, 1,2,5,6-tetrahydrophenyl methyl sulfone was obtained; m.p. 43–44°.

Anal. Calcd. for $C_7H_{12}O_2S$: C, 52.47; H, 7.55. Found: C, 52.57; H, 7.57.

3,4-Dimethyl-1,2,5,6-tetrahydrophenyl Methyl Sulfone.—A solution of 5 g. (0.047 mole) of methyl vinyl sulfone and 3.87 g. (0.047 mole) of 2,3-dimethyl-1,3-butadiene in 4 ml. of benzene was left at room temperature for 12 hours and on the steam-cone for four days. The solvent was removed under reduced pressure, and the residue was distilled. There was obtained 7.2 g. (81%) of 3,4-dimethyl-1,2,5,6-tetrahydrophenyl methyl sulfone; b.p. 129° (0.6 mm.). Cubic crystals formed slowly in the distillate until it had completely solidified. It was recrystallized from benzene–petroleum ether (89–92°); m.p. 73–73.5°.

Anal. Calcd. for $C_9H_{16}O_2S$: C, 57.41; H, 8.57. Found: C, 57.41; H, 8.63.

2,5-Methylene-1,2,5,6-tetrahydrophenyl Methyl Sulfone.—A mixture of 7.4 g. (0.07 mole) of methyl vinyl sulfone and 5.0 g. (0.075 mole) of cyclopentadiene began to reflux slowly after a brief induction period. The mixture was left at room temperature for four days and then heated on a steam-cone for 15 minutes. Distillation of the reaction mixture gave 10 g. (83%) of a pale yellow viscous liquid; b.p. 132–134° (1.3 mm.). This liquid crystallized in an ice-bath. The 2,5-methylene-1,2,5,6-tetrahydrophenyl methyl sulfone was recrystallized from benzene–petroleum ether (89–92°); m.p. 55–56°.

Anal. Calcd. for $C_8H_{12}O_2S$: C, 55.78; H, 7.02. Found: C, 55.96; H, 7.26.

Isoprene–Methyl Vinyl Sulfone Adduct.—A solution of 10 g. (0.094 mole) of methyl vinyl sulfone, 6.8 g. (0.1 mole) of isoprene, and a few milligrams of hydroquinone in 5 ml. of benzene was heated under reflux for ten days. The benzene was removed under reduced pressure, and the residue was distilled. There was recovered 5.5 g. of methyl vinyl sulfone. The adduct (5.9 g., 80.5% based on unrecovered methyl vinyl sulfone) was a colorless liquid; b.p. 125–126° (1.2 mm.), $n^{20}D$ 1.5066. Crystals formed in this liquid on cooling. They were separated from an oil and recrystallized from ether–petroleum ether (40–42°); m.p. 55–56°.

Anal. Calcd. for $C_8H_{14}O_2S$: C, 55.14; H, 8.10. Found: C, 54.97; H, 8.10. The oil was distilled to give a colorless liquid; $n^{20}D$ 1.5070. This material could not be induced to crystallize and is probably a mixture of isomers. It represented *ca.* 25% of the product.

Anal. Calcd. for $C_8H_{14}O_2S$: C, 55.14; H, 8.10. Found: C, 55.33; H, 8.39.

URBANA, ILL. RECEIVED JANUARY 22, 1951

(13) G. D. Buckley, J. L. Charlish and J. D. Rose, *J. Chem. Soc.*, 1514 (1947).

(14) "Organic Syntheses," Col. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 136.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Conversion of Cholestanone to Cholesterol[1,2]

BY WILLIAM G. DAUBEN AND JEROME F. EASTHAM

When the enol acetate of cholestenone was reduced with excess lithium aluminum hydride, four stenols were formed in the following yields: cholesterol (32%), epicholesterol (16%), Δ^4-cholestene-3β-ol (4%) and Δ^4-cholestene-3α-ol (4%). In addition to these cholestenols, cholestenone was obtained in 34% yield. Inverse addition, temperature variation (−15 to 100°) and quantity of hydride had little effect on the course of this reaction. The stereochemical results exhibited no similarity to those reported for the reduction of either Δ^4- or Δ^5-cholestenone.

Cholesterol specifically labeled with isotopic carbon could serve as a useful tool for the study of the metabolic fate of this sterol in the animal body. Recently, methods for the preparation of cholesterol labeled at carbon atom twenty-six[3] and for the preparation of cholestenone labeled at carbon atom three[4] were described. The desirability of employing a ring-labeled sterol in other studies has led to a search for a convenient method for the transformation of cholestenone (I) to cholesterol (II). A procedure for such a conversion has been reported by Reich and Lardon[5] but the method is rather long and the over-all yield quite low.

The conversion of (I) to (II) posed two distinct problems, namely, effecting the migration of the carbon–carbon double bond and the reduction of the carbonyl group. McKennis and Gaffney[6] demonstrated that lithium aluminum hydride reduces this carbonyl group to an approximately equimolar mixture of the α(IV) and β(V) isomers of Δ^4-cholestenol. Furthermore, Shoppee[7] recently showed that a similar reduction of the isomeric Δ^5-cholestenone proceeds in high yield but, in contra-distinction to the foregoing, mainly the β-isomer (cholesterol) is formed. With respect to the migration of the double bond (Δ^4 to Δ^5), it has been found that such a rearrangement does occur in the preparation of the enol acetate (VI) of cholestenone.[8] These considerations made reduction of (VI) appear as an interesting possible approach to the preparation of cholesterol from cholestenone.

Catalytic hydrogenation of enol esters is known to lead to hydrogenolysis of the acyloxy group[9] and, indeed, Inhoffen[10] has reported that catalytic hydrogenation of (VI) itself yielded only cholestane. Since the conclusion of the present investigation,

(1) This work was supported by a grant from the University of California Cancer Fund.

(2) A preliminary announcement of this work was reported in a Communication to the Editor, THIS JOURNAL, **72**, 2305 (1950).

(3) A. I. Ryer, W. H. Gebert and N. M. Murrill, *ibid.*, **72**, 4247 (1950); W. G. Dauben and H. L. Bradlow, *ibid.*, **72**, 4248 (1950).

(4) R. B. Turner, *ibid.*, **72**, 579 (1950).

(5) H. Reich and A. Lardon, *Helv. Chim. Acta*, **29**, 671 (1946).

(6) H. McKennis and G. W. Gaffney, *J. Biol. Chem.*, **175**, 217 (1948).

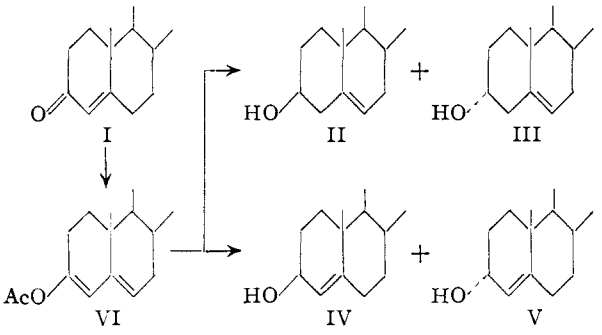
(7) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 687 (1950).

(8) V. Westphal, *Ber.*, **70**, 2128 (1937).

(9) E. J. Roll and R. Adams, THIS JOURNAL, **53**, 3469 (1931).

(10) V. H. Inhoffen, G. Stoeck, G. Kolling and U. Stoeck, *Ann.*, **568**, 52 (1950).

a chemical reduction of the enol acetate has been achieved.[11] Birch, employing sodium and liquid ammonia, was able to isolate Δ^5-cholestenone which in turn could be reduced to cholesterol in the manner described by Shoppee and Summers.[7] The yield from (VI) to (II) apparently was about 40% of crude material (m.p. 135–140°); no yield of pure cholesterol (m.p. 148°) was indicated.



The enol acetate of cholestenone has now been found to be reduced by lithium aluminum hydride in still another characteristic fashion. When the reduction was carried out in the manner normally prescribed,[12] the product was a complex mixture, consisting of cholestenone (I), cholesterol (II), epicholesterol (III) and probably Δ^4-cholestene-3α-ol (IV) and Δ^4-cholestene-3β-ol (V). This rather imposing mixture was separated by the following scheme. The crude product was divided into "α" and "β" fractions by the use of digitonin. Each fraction was refluxed with dilute alcoholic hydrochloric acid solution to convert the Δ^4-isomers into cholestadiene and the resulting mixture was chromatographed on alumina to effect further separation.

The fact that the Δ^4-stenols could be formed does not seem illogical, but these two compounds, (IV) and (V), were never isolated directly. Evidence for their presence, however, was the isolation of cholestadiene from the mild acid treatment. Such conditions are known[6,13] to dehydrate the allylic Δ^4-sterols but to have no effect on cholesterol and practically none on epicholesterol.[14] If the dehydration step was not incorporated into the procedure after a "normal" reduction (ester solution added slowly to hydride solution) both cholesterol and epicholesterol were isolated in pure form only with difficulty. Direct chromatography of the reaction mixture from a normal reduction yielded a mixed stenol fraction which showed a positive Rosenheim test,[13,15] further evidence of Δ^4-isomers. When the reduction was conducted "inversely" (hydride added to ester), however, the formation of the Δ^4-isomers was prevented and the three products, (I), (II) and (III), could be isolated directly by chromatography. In this case none of the fractions obtained gave a positive Rosenheim test.

The effects of mode of addition of reactants and of reaction time are shown in Table I. Although slightly better yields of cholesterol were obtained when normal addition was used, the extra manipulations required for the isolation of cholesterol in this case offset the small additional yield. Little or no effect was found from the use of very large excesses of hydride (5–30-fold excess) or from variation in concentration of the reactants (0.02–0.10 mmole/ml.). The effect of temperature is summarized in Table II. It is seen that all manner of variation of reaction conditions (time, temperature, concentration, mode of addition) had no practical effect on the yield of cholestenone, cholesterol and epicholesterol. Normal addition and higher temperature seemed to allow formation of small quantities of the Δ^4-cholestenols.

TABLE I

EFFECT OF MODE OF ADDITION AND REACTION TIME ON YIELD OF CHOLESTEROL AND CHOLESTENONE[a]

Mode of addition	Time of addition, hours	Total time of reaction, hours	Yield, %[b] -ol	-one
Simultaneous	0	6.0	29	35
Normal	1.5	7.5	34	27
Normal	1.5	25.5	35	28
Inverse	5.0	25.0	31	36
Inverse	10.0	20.0	32	34

[a] Reaction conducted at 25° in ether. [b] Based upon starting ester.

TABLE II

EFFECT OF MODE OF ADDITION AND TEMPERATURE UPON YIELD OF REACTION

Temp., °C.	Solvent	Mode of addition	Yield, cholestane derivative, % 3β-ol	3α-ol	Δ^4-3-one	"β"-$\Delta^{3,5}$	"α"-$\Delta^{3,5\alpha}$
−10	Ether	Normal	34	15	32	4	4
25	Ether	Inverse	34	16	34	0	0
65	THF[b]	Normal	32	17	29	7	6
90	Bu ether[c]	Inverse	33	6	28	(9)[d]	

[a] "β" and "α" signify the diene from those fractions after digitonin precipitation. [b] Tetrahydrofuran. [c] *n*-Butyl ether. [d] Reaction mixture not separated by digitonin before acidic treatment.

Using cholestenone-4-C^{14} obtained by a modification[16] of the method of Turner,[4] cholesterol-4-C^{14} was prepared in 50% yield (based upon recovered cholestenone[17]).

Experimental[18]

Cholestenone Enol Acetate.—A solution of cholestenone (5.0 g., 13 mmoles) in 5 ml. of isopropenyl acetate[19] and 0.02 ml. of concentrated sulfuric acid was refluxed for two hours. At the end of the first hour the pressure was re-

(11) A. J. Birch, *J. Chem. Soc.*, 2325 (1950).

(12) R. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 1197 (1947).

(13) R. Schoenheimer and E. A. Evans, *J. Biol. Chem.*, **114**, 567 (1936).

(14) This is somewhat in contrast to the report of Marker and coworkers (THIS JOURNAL, **58**, 1948 (1936)) who "found that epicholesterol behaves very similarly in instability to" Δ^4-cholestenols. We have found that upon employing the milder conditions of Schoenheimer and Evans[13] epicholesterol can be recovered in better than 90% yield.

(15) O. Rosenheim, *Biochem. J.*, **23**, 47 (1929).

(16) Dr. George Fujimoto, private communication.

(17) In addition to the cholestenone obtained directly from the reaction mixture, this also allows for ketone prepared by oxidation of all other sterol fractions and by hydrolysis of the residual products from the preparation of the enol acetate.

(18) All analyses are by the Microanalytical Laboratory of the Department of Chemistry, University of California, Berkeley; analytical samples were sublimed at 10^{-5} mm. All melting points are corrected.

(19) H. J. Hagemeyer and D. C. Hull, *Ind. Eng. Chem.*, **41**, 2920 (1949).

duced for a short period and 1 ml. of liquid distilled from the solution. At the end of the second hour, 0.1 g. of anhydrous sodium acetate was added and the mixture concentrated at reduced pressure. The residual blue-green fluorescent oil was diluted with a few ml. of chloroform and decanted from the sodium acetate into 65 ml. of methanol. Additional chloroform was added to bring the oil into solution in the refluxing methanol. Seeding and slow cooling of this solution yielded 4.8 g. (87%) of the cholestenone enol acetate, m.p. 76–78° (lit.[8] 81°).

Stability of Stenols to Dehydration.—A solution of 200 mg. of epicholesterol (m.p. 139.5–140.5°) in 10 ml. of ethanol and 0.2 ml. of concentrated hydrochloric acid was refluxed for five hours. While still refluxing, this solution was brought to turbidity by addition of water. Slow cooling of the solution to ice temperature yielded 180 mg. (90%) of unchanged epicholesterol, m.p. 139–140°. Under similar conditions, a mixture of the Δ^4-stenols was completely dehydrated to $\Delta^{3,5}$-cholestadiene. Cholesterol was recovered virtually unaffected from such treatment.

Reduction of Enol Acetate (A) Normal Reduction.—Lithium aluminum hydride (2.0 g., 53 mmoles) was refluxed for about 30 minutes with 50 ml. of anhydrous tetrahydrofuran. To this refluxing mixture there was added slowly (requiring about one hour) a solution of 1.969 g. (4.6 mmoles) of the enol acetate in tetrahydrofuran. The mixture then was refluxed for an additional three hours. The entire reaction was conducted in a nitrogen atmosphere under rigorously dry conditions.

The reduction complex and the excess hydride remaining were decomposed with 70 ml. of 20% sulfuric acid. The aqueous phase was extracted once with 60 ml. of ether and this extract was added to the furan phase.

The ethereal solution was washed with a saturated sodium potassium tartrate solution and dried over magnesium sulfate. Distillation of the solvent left an amorphous residue (1.780 g.).

Precipitation of "β" Fraction.—The above residue was dissolved in 50 ml. of hot 90% ethanol and to it there was added a solution of 2.5 g. of digitonin in 100 ml. of hot 90% ethanol. After cooling the mixture at ice-bath temperature for 12 hours, the digitonide was filtered (3.03 g.).

The digitonide was dissolved in 35 ml. of dry pyridine and then 200 ml. of ether was added. The suspension was centrifuged and decanted, the residue diluted with another 100 ml. of ether, stirred, centrifuged, decanted and the process repeated once more. The combined supernatant liquids were filtered, washed with 20% sulfuric acid, saturated sodium chloride solution, dried and evaporated. The residue (0.73 g.) was then dissolved in a mixture of 50 ml. of ethanol and 1.5 ml. of concentrated hydrochloric acid and refluxed for six hours. After cooling, the alcoholic solution was diluted with 150 ml. of ether. Water was added, the ether phase separated and washed with aqueous sodium bicarbonate and saturated sodium chloride solutions. The ethereal solution was dried over anhydrous potassium carbonate, evaporated and the residue dissolved in hexane for chromatography on 25 g. of Merck and Co., Inc., Reagent Aluminum Oxide. The solvent sequence employed was hexane, 15% ether (by volume) in hexane, and 25% ether in hexane. Table III summarizes the results.

TABLE III

Compound eluted	Wt. in mg.	M.p., °C. crude	M.p., °C. recrystd.
Diene	97	65–70	78–79
I[a]	36	86–87[b]	81.0–81.5
II	577	145–147	146–148

[a] Hazelwood (*Biochem. J.*, 41, 639 (1947)) has reported that cholestenone is precipitated by digitonin. [b] Barton and Cook (*J. Chem. Soc.*, 602 (1943)) have found that cholestenone is dimorphic and exhibits melting points of 82° and 88°.

Analysis of "α" Fraction.—The filtrate from the preparation of the digitonide was acidified with 5 ml. of concentrated hydrochloric acid and the solution refluxed for six hours. After cooling, 500 ml. of ether was added and then processed as above, crude yield 1.01 g. Table IV summarizes the chromatographic results.

(B) **Inverse Reduction.**—To a solution of 0.83 g. of enol acetate in 25 ml. of ether, there was added very slowly a clear solution of 0.60 g. of lithium aluminum hydride in 25 ml. of ether. The reaction mixture became quite turbid initially, then cleared when about one-fifth of the hydride solution had been added. The complete addition required approximately ten hours and the solution was stirred for an additional ten hours. At the end of this time the crude product was isolated and chromatographed directly without acid or digitonin treatment. The results are summarized in Table V.

TABLE IV

Compound eluted	Wt. in mg.	M.p., °C. crude	M.p., °C. recrystd.
Diene	129	.....	76–78
I	478	87.0–87.5	80.0–80.5
III	298	132–137	139.5–140.5

TABLE V

Compound eluted	Wt. in mg.	M.p., °C. crude	M.p., °C. recrystd.
I	254	84–87	80.0–80.5
III	105	136–139	138–140
II, III	10	120–130	131–132[20]
II	245	144–146	146–148

The cholesterol, epicholesterol and cholestenone obtained have been characterized by mixed melting points, optical activity, infrared spectra, ultraviolet spectra and carbon and hydrogen analyses. The values obtained were those expected with the exception of the rotation of epicholesterol. A value $[\alpha]^{25}D$ −47.5° (*c* 1.500, $CHCl_3$) was consistently obtained for the epicholesterol isolated from various runs of the reduction. This value is significantly higher than previously reported values of −44.5°,[21a] −41.4°[21b] and −37.5°.[22] Other workers have reported[23] even lower values. Since this value is important in structural deductions,[24] our epicholesterol was carefully characterized.

This epicholesterol does not give a coloration with trichloroacetic acid and is not precipitated by digitonin. Its melting point after two recrystallizations from methanol is 140.2–140.6°; when admixed with cholesterol it melts 129–132°.[20] *Anal.* of a sublimed sample: Calcd.: C, 83.89; H, 11.97. Found: C, 83.80; H, 12.09. The acetate, prepared in pyridine with acetic anhydride in the usual manner, melts 83–84° (lit.[22,23] 84–85°). The ultraviolet spectrum of the epicholesterol indicates that even if all the absorption at 235 mμ (λ_{max}, $\Delta^{3,5}$-cholestadiene) was due to diene (this being the only logical contaminant that would increase levorotation), there would still be less than 1% of the diene present.[25] For comparison purposes, epicholesterol was prepared by the method of Plattner.[21] By this process, epicholesterol, m.p. 139.5–140.5° and $[\alpha]^{25}D$ −47.8°, was obtained. This epicholesterol showed no depression of melting point on admixture with the material obtained by reduction of the enol acetate. The two samples have identical infrared spectra.

Unknown Steroid Isolated.—In a few of the runs of the reduction there was isolated a compound coming off the alumina column after all of the previously discussed isomers had been eluted. The yield of this compound was never more than 2–3% except in the case of a reduction carried out at −70° when the yield amounted to approximately 10%. The compound melts 168–169°, is difficultly soluble in organic solvents, gives no color with either trichloroacetic

(20) An intimate mixture of 20% epicholesterol and 80% cholesterol melts sharply at 132°. However, if this mixture is recrystallized from ethanol–water, the material melts over a range below 130°.

(21) (a) Pl. A. Plattner and W. Long, *Helv. Chim. Acta*, **27**, 1872 (1944); (b) Pl. A. Plattner, A. Furst, F. Koller and W. Long, *ibid.*, **31**, 1455 (1948).

(22) L. Ruzicka and M. W. Goldberg, *ibid.*, **19**, 1407 (1936).

(23) R. DeFazzia and F. Pirrone, *Gazz. chim. ital.*, **70**, 18 (1940); see also reference in footnote 14.

(24) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, p. 216.

(25) H. E. Stavely and W. Bergmann (*J. Org. Chem.*, **1**, 567 (1936)) and Schoenheimer and Evans[13] report for the diene a molecular extinction coefficient of 22,000 at 235 mμ. Our epicholesterol showed only a value of 80 at this wave length.

acid or acetic anhydride and sulfuric acid, is not affected by refluxing with alcoholic hydrochloric acid, and has an analysis which best fits a dihydroxycholestene. This compound has not been further characterized.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.5; H, 11.5. Found: C, 80.0; H, 11.2.

BERKELEY, CALIF. RECEIVED DECEMBER 21, 1950

[JOINT CONTRIBUTION FROM THE INSTITUTO DE QUÍMICA DE LA UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO, THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY AND THE RESEARCH LABORATORIES OF SYNTEX, S. A.]

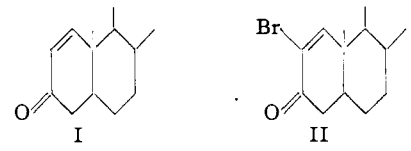
The Effect of Bromine Substitution upon the Ultraviolet Absorption Spectra of α,β-Unsaturated Ketones

BY A. L. NUSSBAUM,[1a] O. MANCERA,[1a] RALPH DANIELS,[1b] G. ROSENKRANZ[1c] AND CARL DJERASSI[1c]

A study of the ultraviolet absorption spectra of a series of aliphatic α-bromo-α,β-unsaturated ketones has demonstrated that α-bromine substitution results in a bathochromic shift of approximately 23 mμ, thus providing additional evidence for the structure of a number of brominated steroid ketones. The presence of a phenyl group in conjugation with either the carbonyl group or the double bond reduces the bathochromic shift due to a bromine atom to 8–14 mμ.

Notably through the work of Woodward[2] and of Gillam[3] it has been possible to correlate with a fair degree of accuracy, ultraviolet absorption spectra with the constitution of α,β-unsaturated ketones. Their measurements and literature analyses, indicating a bathochromic shift of *ca.* 10 mμ for each alkyl substituent and one of 5 mμ for an exocyclic double bond, have proved very valuable in structure assignments of natural products including those of the steroids.

At that time, the tentative suggestion was made[2] that a bromine substituent had almost the same effect as an alkyl group in shifting the maximum. Fieser and Fieser,[4] proceeding on this assumption in correlating ultraviolet absorption with structure in the field of α,β-unsaturated ketosteroids, have been led to question the correctness of structures assigned to the Δ[1]-2-bromo-3-ketosteroids (II),[5,6] since they exhibit maxima around 255 mμ as compared to 230 mμ for the unsubstituted Δ[1]-3-ketosteroid (I). In our opinion, the structure of the bromo ketones II appeared to be conclusively established by their mode of synthesis (dehydrobromination of a *gem*-2,2-dibromo-3-ketone or bromination of a Δ[1]-3-ketone[6c]) and by their reactions, notably the reduction (by zinc in ethanol) to the Δ[1]-3-ketone I. On the basis of these observations the bathochromic effect of a bromine substituent upon the spectrum should be close to 25 mμ[7] rather than 10 mμ as believed earlier.[4] This in turn has made untenable the structure assignments[8] of a series of bromination products of Δ[4]-3-ketosteroids and has subsequently led to a revision[9] of their constitution.



I II

From a consideration of the manner in which light in the near ultraviolet region is presumed to be absorbed by α,β-unsaturated ketones to produce activated forms such as $-\overset{|}{\overset{+}{C}}-C=C-O^-$ and a comparison of the electronic environment of a bromine atom *vs.* an alkyl group, it would not be expected *a priori* that they would have the same quantitative effect in shifting the maxima. Bromine might be expected to have an effect intermediate between an alkyl and an alkoxyl or hydroxyl group and in that connection it is pertinent to mention that recent work has indicated a bathochromic shift of 35 mμ for an α-hydroxyl group[10] and one of nearly 50 mμ for a β-hydroxyl substituent.[11] The primary evidence for the assumption by Fieser and Fieser[4] of an equal effect for alkyl and bromine rests on data for three compounds, the structures of which are almost certainly incorrect.[9,12] In or-

(1) Present locations: (a) Instituto de Química, Tacuba, D. F.; (b) Department of Chemistry, University of Wisconsin, Madison 6, Wisconsin; (c) Syntex, S. A., Laguna Mayrán 413, Mexico City, D. F.

(2) R. B. Woodward, THIS JOURNAL, **63**, 1123 (1941); **64**, 76 (1942).

(3) L. K. Evans and A. E. Gillam, *J. Chem. Soc.*, 815 (1941); A. E. Gillam and T. F. West, *ibid.*, 486 (1942).

(4) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., 1949, pp. 196–197.

(5) (a) H. H. Inhoffen and G. Zuehlsdorff, *Ber.*, **76**, 233 (1943); (b) B. Ellis and V. Petrow, *J. Chem. Soc.*, 2194 (1950).

(6) (a) A. L. Wilds and C. Djerassi, THIS JOURNAL, **68**, 2125 (1946); (b) C. Djerassi and C. R. Scholz, *ibid.*, **69**, 2404 (1947); (c) **70**, 1911 (1948); (d) *J. Org. Chem.*, **13**, 697 (1948); (e) C. Djerassi and G. Rosenkranz, *Experientia*, **7**, 93 (1951).

(7) R. Adams and W. Herz, THIS JOURNAL, **71**, 2546 (1949), recorded a shift of 25 mμ in the conversion of helenalin to bromohelenalin in excellent agreement with the values observed in the steroid series (refs. 5 and 6).

(8) A. Butenandt, G. Schramm and H. Kudszus, *Ann.*, **531**, 176 (1937); H. H. Inhoffen, *Angew. Chem.*, **53**, 473 (1940).

(9) C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann and J. Pataki, THIS JOURNAL, **72**, 4534 (1950). It was also pointed out in this paper that a bromine atom in the γ-position has a variable influence depending upon the configuration. In the steroid series, a 6α-substituent showed a very slight bathochromic shift, while the 6β-isomer exhibited a bathochromic shift of nearly 8 mμ. This has since been confirmed by D. H. R. Barton, University of London (private communication).

(10) L. F. Fieser, M. Fieser and S. Rajagopalan, *J. Org. Chem.*, **13**, 800 (1948).

(11) C. H. Shunk and A. L. Wilds, THIS JOURNAL, **71**, 3947 (1949). footnote 8.

(12) Of the three compounds (Nos. 43–45 in ref. 4), Δ[4]-4-bromocholesten-3-one (No. 43) is the most important one and the fallacy in its structure assignment is herewith illustrated. The Fiesers (ref. 4) obtained the spectrum from Dannenberg's monograph, who in turn quotes Barkow, Dissertation, Danzig, 1938 (publ. 1940). An inspection of this thesis (a copy was obtained from the Library of the University, Basle) yields the following information: Δ[4]-cholesten-3-one was tetra- or hexabrominated for 24 hours, the resulting solution was refluxed to complete spontaneous loss of hydrogen bromide and the polyunsaturated dibromo derivative refluxed in amyl alcohol in an atmosphere of hydrogen with palladium–barium sulfate catalyst for eight hours. The product, isolated in poor yield, was characterized by a bromine analysis (2.4% *too high*) and an ultraviolet maximum at 250 mμ, and on *the basis of the latter* was assigned the Δ[4]-4-bromocholesten-3-one structure. According to our present results (*cf.* ref. 9, footnote 16) such a substance should exhibit a maximum at *ca.* 265 mμ.