ice-water, and the resulting oil solidified on standing. The crystals were collected, and washed with water; 0.86 g., m.p. 190–197.5°. Recrystallization from acetone afforded pure II; 0.6 g., m.p. 199–201°; infrared spectrum: λ_{max} 3540 and 3440 cm.$^{-1}$ (hydroxyl), 1730 cm.$^{-1}$ (acetate carbonyl), 1695 cm.$^{-1}$ (weak,?), 1260 and/or 1230 cm.$^{-1}$ (C–O stretch acetate), 1102 cm.$^{-1}$ (C–O stretch, ketal[5] and hydroxyl); $[\alpha]^{27}D$ −26° (16.05 mg., chloroform, α_D −0.21°), $[M]_D$ −128.

Anal. Calcd. for $C_{27}H_{40}O_8$ (492.58): C, 65.83; H, 8.19. Found: C, 65.83; H, 8.28.

$\Delta^{5,9(11)}$-Pregnadiene-17α,21-diol-3,20-dione-21-acetate-3,-20-bis-ethylene Ketal (III).—A solution of the bis-ethylene ketal (II) of hydrocortisone acetate (0.1 g.) in pyridine (1 ml.) was treated in the cold with phosphorus oxychloride (0.082 ml.). The mixture was allowed to stand at room temperature for 64 hours[6] when water was added (ice-cooling). The resulting crystals were collected; 84 mg., m.p. 195–197°. One recrystallization from acetone–petroleum ether gave 67 mg., m.p. 197–199° (70% yield). Two further recrystallizations did not alter the m.p. appreciably; 49 mg., m.p. 198–199°; λ_{max} none; infrared spectrum: λ_{max} 3560 cm.$^{-1}$ (hydroxyl), 1740 cm.$^{-1}$ (acetate carbonyl), 1259 and 1245 cm.$^{-1}$ (C–O stretch, acetate), 1096 cm.$^{-1}$ (C–O stretch, ketal and hydroxyl); negative Beilstein test for chlorine; $[\alpha]^{22}D$ −14° (14.8 mg., chloroform, α_D −0.10°), $[M]_D$ −66.

Anal. Calcd. for $C_{27}H_{38}O_7$ (474.57): C, 68.33; H, 8.07. Found: C, 68.22; H, 8.34.

$\Delta^{5,9(11)}$-Pregnadiene-17α,21-diol-3,20-dione-3,20-bis-ethylene Ketal (IV).—A solution of the bis-ketal acetate (III, 0.56 g.) in 2.5% alcoholic potassium hydroxide (15 ml.) was refluxed for one-half hour, treated with water, and cooled. The crystals were collected, m.p. 199–200°, cloudy melt. Recrystallization from acetone–petroleum ether gave 425 mg. (83% yield) of IV, m.p. 198–200°. Admixture m.p. determination with starting material (III) showed non-identity, m.p. 190–192°; infrared spectrum: λ_{max} 3470 cm.$^{-1}$ (hydroxyl), no carbonyl, 1094 cm.$^{-1}$ (C–O stretch, ketal and hyroxyl); $[\alpha]^{23}D$ −10° (21.2 mg., chloroform, α_D −0.11°), $[M]_D$ −43.

Anal. Calcd. for $C_{25}H_{36}O_6$ (432.54): C, 69.42; H, 8.39. Found: C, 69.62; H, 8.23.

$\Delta^{4,9(11)}$-Pregnadiene-17α,21-diol-3,20-dione (V). A.—A solution of III (250 mg.) in alcohol (20 ml.) was refluxed for 1 hour with 8.5 % (v./v.) sulfuric acid (2.5 ml.). Methanol was added; the solution was neutralized with sodium bicarbonate, and filtered. The filtrate was concentrated *in vacuo* until crystals separated. Water was added, and the crude product was collected; 147 mg., m.p. 239–241° dec., with previous softening. Five recrystallizations from acetone–petroleum ether afforded pure V; 21 mg., m.p. 259–260° dec. with previous softening; λ_{max} 237.5–239 mμ (ϵ 16000); infrared spectrum: λ_{max} 3530 and 3480 cm.$^{-1}$ (hydroxyl), 1715 cm.$^{-1}$ (C^{20}-carbonyl), 1665 cm.$^{-1}$ (C^3-carbonyl), 1620 cm.$^{-1}$ (double bond), 1102 cm.$^{-1}$ (C–O stretch, hydroxyl).

Anal. Calcd. for $C_{21}H_{28}O_4$ (344.44): C, 73.22; H, 8.19. Found: C, 73.07; H, 8.12.

B.—A solution of IV (375 mg.) in methanol (25 ml.) was refluxed for 1 hour with 8.5% (v./v.) sulfuric acid (3 ml.). Addition of water followed by cooling gave 265 mg., m.p. 245–246°. Pure V was obtained by recrystallization from acetone–petroleum ether; 0.22 g. (73% yield), m.p. 259–261° dec., with previous softening, positive Blue Tetrazolium test for α-ketol moiety; $[\alpha]^{23}D$ +88° (12.3 mg., pyridine, α_D +0.54°), $[M]_D$ +302.

$\Delta^{4,9(11)}$-Pregnadiene-17α,21-diol-3,20-dione 21-Acetate (VI).—The free steroid (V, 38 mg.) in pyridine (2 ml. was acetylated with acetic anhydride (1 ml.) (15 hr., room temperature). Ether was added; the mixture was cooled, and the crystals were collected; 41 mg., m.p. 235–236° with previous softening. Two recrystallizations from acetone–ether gave pure VI; 20 mg., m.p. 239.5–241°, with previous softening; λ_{max} 238.5–240 mμ (ϵ 16600); infrared spectrum: λ_{max} 3450 cm.$^{-1}$ (hydroxyl), 1755 cm.$^{-1}$ (acetate carbonyl), 1730 cm.$^{-1}$ (C^{20}-carbonyl), 1660 cm.$^{-1}$ (C^3-carbonyl), 1620 cm.$^{-1}$ (double bond), 1238 cm.$^{-1}$ (C–O stretch, acetate), 1100 cm.$^{-1}$ (weak C–O stretch, hydroxyl); $[\alpha]^{23}D$ +120° (9.2 mg., chloroform, α_D +0.55°), $[M]_D$ +463.

Anal. Calcd. for $C_{23}H_{30}O_5$ (386.47): C, 71.48; H, 7.82. Found: C, 71.64; H, 8.00.

$\Delta^{4,9(11)}$-Androstadiene-3,17-dione (VII).—The free steroid (V, 125 mg.) in glacial acetic acid (10 ml.) was oxidized with a solution of chromic anhydride (160 mg.) in water (4 drops) and glacial acetic acid (10 ml.) (18 hours, room temperature). The mixture was evaporated *in vacuo* at below 30°. The product was extracted with ether, and the residue obtained on evaporation was submitted to chromatographic analysis (10 g. of aluminum oxide, Merck). The product was eluted from the column with 100% ether; 28 mg. Recrystallization from acetone–petroleum ether (Norit treatment) gave 10 mg. of the dione (VII), m.p. 203–205.5° with previous softening and darkening. Admixture m.p. determination with authentic sample (m.p. 204–206°) gave no depression, m.p. 203–206.5°, λ_{max} 238–239 mμ (ϵ 14800); infrared spectrum: λ_{max} no hydroxyl, 1745 cm.$^{-1}$ (C^{17}-carbonyl), 1670 cm.$^{-1}$ (C^3-carbonyl), 1620 cm.$^{-1}$ (double bond). The infrared spectrum was identical with that of an authentic sample.

Bis-dinitrophenylhydrazone.—M.p. 290° dec., literature[1] m.p. 292.5–293.5° dec.

Acknowledgment.—We are indebted to Messrs. Louis M. Brancone and Samuel S. Modes for the microanalytical data, and to Mr. William Fulmor for the infrared spectra.

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(5) *One* of the principal C–O stretch bands of an ethylene ketal.

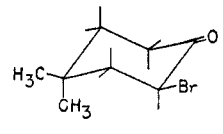
(6) The minimal time required for this dehydration was not investigated.

The Stereochemistry of α-Haloketones. IV. The Stable Orientation of Bromine in 2-Bromocholestane-3-one

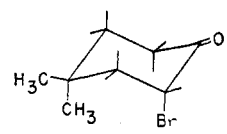
BY ELIAS J. COREY

RECEIVED APRIL 30, 1953

Recently[1] we have described a method for predicting the stable orientation of bromine in α-bromoketosteroids of both the normal and allo series. Application of this method to 2-bromo-3-ketoallosteroids leads to the expectation that the stable epimer should be that in which bromine is α-oriented. This conclusion follows from the fact that the stable molecular configuration of 2-bromo-4,4-dimethylcyclohexanone is IA and not IB.[2]



IA



IB

We have found that 2-bromocholestane-3-one, m.p. 170–170.5°,[3] is not subject to epimerization under the influence of hydrogen bromide in acetic acid, and hence should be formulated as the 2α-bromo epimer. This assignment, which is also indicated by the infrared spectrum of the substance,[4] has now been proved by a chemical method.

After the completion of this work a paper appeared in which the very same reaction sequence that we used was reported to afford results entirely

(1) E. J. Corey, Part III, *Experientia*, in press.

(2) E. J. Corey, THIS JOURNAL, **75**, 2301 (1953).

(3) A. Butenandt and A. Wolff, *Ber.*, **68**, 2091 (1935); J. von Euw and T. Reichstein, *Helv. Chim. Acta*, **29**, 654 (1935).

(4) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

different from ours.[5] The conclusion was reached that the bromine substituent in 2-bromocholestane-3-one is β-oriented. Furthermore, it was felt that the infrared data could be explained by postulating that ring A adopts a boat conformation.[6] Since these results are in sharp disagreement with ours we wish to report here our findings on 2-bromocholestane-3-one (II).[6a]

Reduction of II with sodium borohydride in methanol–ether or ethanol–ether at 25° affords a mixture of products which, in our hands, could not be completely resolved by recrystallization, but which could be separated by chromatography on acid-washed alumina. The main reduction product is a bromohydrin, $C_{27}H_{47}OBr$, m.p. 111.5–112.5°, $[\alpha]^{25}D$ +14.0 ± 1.5°, which is not changed by further chromatography or partial precipitation with digitonin. The infrared spectrum of the product exhibits bands at 2.79 μ (3590 cm.$^{-1}$) (OH stretching), 4.62 μ (2165 cm.$^{-1}$) (overtone of C–O stretching), 9.45 μ (1060 cm.$^{-1}$) (C–O stretching)[7] and no carbonyl absorption.

The bromohydrin reacts smoothly with isopropanolic potassium hydroxide at 55° to give pure 2β,3β-oxidocholestane[8] in 75–77% yield. The β-oxide was identified by m.p., rotation, elemental analysis, infrared spectrum (no carbonyl or hydroxyl absorption) and by reduction with lithium aluminum hydride to cholestane-2β-ol.[8] The β-oxide also can be obtained in good yield from the bromohydrin using ether–methanol as solvent. The bromohydrin is reduced with palladium-on-Darco catalyst to cholestane-3β-ol, identified by m.p. and mixture m.p.

Thus, *the bromohydrin, m.p. 111.5–112.5°, must be 2α-bromocholestane-3β-ol and the original bromoketone 2α-bromocholestane-3-one.* It is exceedingly unlikely that the orientation of the bromine in the bromoketone and in the bromohydrin are different, since this would require that the reduction of the 2β-bromoketone be tremendously slower than that of the 2α-bromoketone which might be in equilibrium with it.

In addition to the above-mentioned bromohydrin we have isolated in several instances from the reduction of II appreciable quantities of cholestane-3-one, identified by m.p., mixture m.p. and infrared spectrum. Since this substance is readily reduced by sodium borohydride[9] and since an excess of sodium borohydride was invariably used, cholestane-3-one could hardly have been present as a primary reaction product. The ketone may have been formed from 2β-bromocholestane-3α-ol which is probably present in the crude reaction product (*vide infra*) by acid-catalyzed rearrangement on the acid-washed alumina used for chromatography. This point is now under further investigation.

It seems likely from our work that, in contrast to the results reported previously,[5] some 2β-bromocholestane-3α-ol is produced by the sodium borohydride reduction of II. Purification of the crude reduction product by recrystallization afforded, in our hands, mixtures of m.p. anywhere from 95–97° to 103–106° which yield a correct analysis for the bromohydrin, show no carbonyl absorption in the infrared and, therefore, seem best regarded as mixtures of isomeric bromohydrins (probably epimeric at C_3).

From the physical properties reported for the bromohydrin by previous workers,[5] m.p. 104–105°, $[\alpha]D$ +25°, it seems probable that they were dealing with a mixture of C_3-epimers. In order to explain the results which they obtained we have studied the reaction of impure samples of bromohydrin with base. When bromohydrin of m.p. 107–108° is treated with potassium hydroxide in methanol–ether at room temperature for 48 hours the β-oxide which is obtained is impure and gives a positive Beilstein test. We have been unable to remove the impurity (presumably 2α-bromocholestane-3α-ol) by repeated recrystallization, although pure oxide is obtained easily by chromatography. When still less pure bromohydrin is used the β-oxide formed does not crystallize and, hence, is easily overlooked. It can, however, be isolated by chromatography. Thus, it seems not unreasonable that the previous workers failed to isolate the oxide because of the impurity of their starting material and probably also because of the fact that they added hydrochloric acid, which rapidly destroys the oxide, to the reaction mixture before attempted isolation. Their isolation of cholestane-3-one (in *ca.* 6.5% yield) might be explained in a number of ways.

Experimental[10]

2α-Bromocholestane-3β-ol.—A solution of 1.90 g. of 2α-bromocholestane-3-one,[3] m.p. 170–170.5°, in 90 ml. of ether was added to 0.80 g. of sodium borohydride in 70 ml. of methanol and the solution was allowed to stand at 25° for 30 minutes. Pentane (100 ml.) was added and the solution was extracted with three 150-ml. portions of water, dried over calcium chloride and evaporated under reduced pressure to a colorless oil (1.88 g.). The residue was taken up in 10 ml. of cyclohexane and adsorbed on a 19 × 1.8 cm. column of acid-washed alumina. The following fractions (40 ml. each) were collected using the solvent specified.

Fraction	Solvent	Eluted material Mg.	Form
1–5	Pure cyclohexane to pure benzene	45	Oil
6–10	Benzene–ether (6:1) to benzene–ether (1:4)	215	Solid
11–18	Ether	93	Oil
19–23	Acetone–ether (1:10)	995	Solid
24–29	Acetone–ether (1:5)	258	Solid
30–35	Acetone–ether (1:3) to acetone	82	Oily solid

(5) L. F. Fieser and X. A. Dominguez, THIS JOURNAL, **75**, 1704 (1953).

(6) According to rough calculations of the type made previously [C. W. Beckett, K. S. Pitzer and R. Spitzer, *ibid.*, **69**, 2488 (1947); R. B. Turner, *ibid.*, **74**, 2118 (1952); ref. 2] either of the two possible boat forms of ring A should be much less stable than the chair conformation with bromine α-oriented.

(6a) *Note added May 22:* Our results were communicated to Dr. Fieser immediately after the article of Fieser and Dominguez appeared. We have since been informed (private communication, May 5, 1953) that the work described herein has been repeated in the Harvard Laboratory and that our conclusion regarding the stereochemistry of 2-bromocholestane-3-one has been confirmed.

(7) The position of this band is in better agreement with a β- than an α-oriented hydroxyl function (a) A. R. H. Cole, R. N. Jones and K. Dobriner, THIS JOURNAL, **74**, 5571 (1952); (b) H. Rosenkrantz and L. Zablow, *ibid.*, **75**, 903 (1953); (c) A. Fürst, H. H. Kuhn, R. Scotoni, Jr., and Hs. H. Günthard, *Helv. Chim. Acta*, **35**, 951 (1952).

(8) A. Fürst and Pl. A. Plattner, *ibid.*, **32**, 275 (1949).

(9) W. G. Dauben, R. A. Micheli and J. F. Eastham, *ibid.*, **74**, 3852 (1952).

(10) We are indebted to Mr. Joseph Nemeth, Mrs. Esther Fett and Mrs. Lucy Chang for the microanalyses and to Miss Helen Miklas and Mrs. Rosemary Hill for the infrared determinations.

Two recrystallizations of fractions 19–23 from ether–ethanol–water afforded the bromohydrin (810 mg.) as colorless needles, m.p. 111–112°. This material (150 mg.) was subjected to chromatography and the heart fraction (88 mg.) recrystallized for analysis, m.p. 111.5–112.5°, $[\alpha]^{25}D$ 14.0 ± 1.5° (*c* 1.78, chf).

Anal. Calcd. for $C_{27}H_{47}OBr$: C, 69.35; H, 10.13; Br, 17.09. Found: C, 69.35; H, 10.11; Br, 17.17.

A sample of 200 mg. of bromohydrin, m.p. 111–112°, in 6 ml. of acetone was treated with a solution of 130 mg. of digitonin in 11 ml. of 95% ethanol, and the resulting mixture was filtered. The filtrate was evaporated under reduced pressure and the residual solid was extracted well with pentane. Removal of the pentane and recrystallization of the residue from ether–ethanol–water yielded 125 mg. of bromohydrin, m.p. and mixture m.p. with starting material 111–112°. The digitonide was dissolved in 3.5 ml. of dry pyridine and the solution was diluted with pentane (40 ml.). The mixture was filtered, the filtrate was washed with water, dilute hydrochloric acid and again with water and evaporated. Recrystallization of the residue gave 30 mg. of bromohydrin, m.p. and mixture m.p. 111–112°.

Two recrystallizations of fractions 24–29 yielded 160 mg. of a mixture of epimeric bromohydrins, m.p. 103–106° not changed appreciably by two further recrystallizations.

Anal. Found: C, 69.39; H, 10.16.

The same bromohydrin, m.p. and mixture m.p. 111–112°, could be obtained by chromatography when the sodium borohydride reduction is carried out in ether–ethanol or in absolute ethanol alone. When the reaction mixture was worked up by fractional crystallization, the various crops obtained showed melting points ranging from 95–97° to 103–106°. The infrared spectra of the mixtures were very much like that of the pure bromohydrin, m.p. 111–112° (see Discussion), the important difference being a small shoulder at 9.60 μ (1042 cm.$^{-1}$) in the spectra of the mixtures. Absorption at this position might be due to the C–O stretching vibrations of a 3α-hydroxyl group.

Recrystallization of fractions 6–10 from ether–methanol afforded 153 mg. of cholestane-3-one, m.p. 127–128.5°, undepressed upon admixture with a pure sample, m.p. 129.3–130.3°. In addition the infrared spectrum of this substance was identical with that of cholestane-3-one.

2β,3β-Oxidocholestane.—A solution of 370 mg. of the bromohydrin, m.p. 111–112°, and 3.0 g. of potassium hydroxide in 50 ml. of isopropyl alcohol was heated in an atmosphere of purified nitrogen at 55° for 1.5 hours. A precipitate of potassium bromide appeared after *ca.* 5 minutes of heating. The product crystallized from the reaction mixture after addition of water and cooling. Recrystallization from ether–ethanol–water yielded 232 mg. (75.5%) of the β-oxide, m.p. 89–90°. Two evaporative distillations (160° at 0.05 mm.) yielded pure β-oxide, m.p. 90.8–91.4°, $[\alpha]^{25}D$ +57.4 ± 1.0° (*c* 1.53, chf) (reported for 2β,3β-oxidocholestane,[8] m.p. 87.5–88.5, $[\alpha]D$ +50.5°; reported for 2α,3α-oxidocholestane[8], m.p. 105°, $[\alpha]D$ +36°).

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.60; H, 12.02.

The infrared spectrum of the oxide showed no hydroxyl or carbonyl absorption.

Reduction of the β-oxide (52 mg.) with lithium aluminum hydride (40 mg.) in ether (15 ml.) at room temperature yielded cholestane-2β-ol (31.5 mg.) as glistening plates, m.p. 153–154°, $[\alpha]^{25}D$ +35.6° (*c* 1.03, chf) (reported[9] m.p. 154°, $[\alpha]D$ +34.2°). The infrared spectrum of this material was identical with that published for cholestane-2β-ol.[7c]

Reaction of the pure bromohydrin with potassium hydroxide in methanol–ether at room temperature for 48 hours afforded after recrystallization a 66.5% yield of β-oxide, m.p. 89–90.5°.

Reaction of the impure bromohydrin, m.p. 97–100°, with isopropanolic potassium hydroxide under the conditions described above gave a brown mixture which upon dilution deposits only a rather small amount of oily solid. The pure β-oxide was obtained by evaporation of alcohol under reduced pressure, addition of water, extraction with pentane, evaporation of the pentane under reduced pressure and chromatography of the residue on basic alumina. The oxide was eluted with 1:1 benzene–cyclohexane and had m.p. 90.5–91.0°.

Hydrogenolysis of 2α-Bromocholestane-3β-ol.—A solution of 50.6 mg. of the pure bromohydrin and 50 mg. of potassium hydroxide in 7 ml. of absolute ethanol was stirred with 15 mg. of 11% palladium-on-Darco catalyst for two hours. The catalyst was removed by filtration and water was added to the filtrate to precipitate the sterol. Recrystallization from ethanol–water gave 33 mg. of cholestane-3β-ol as glistening plates, m.p. 140.6–141.5°, undepressed upon admixture with an authentic sample, m.p. 141.8–142.0°.

NOYES CHEMICAL LABORATORY
DIVISION OF ORGANIC CHEMISTRY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

2-Fluoropropene

BY PAUL R. AUSTIN, DONALD D. COFFMAN, HARVEY H. HOEHN AND MAYNARD S. RAASCH

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The synthesis of 2-fluoropropene was undertaken in order to investigate the polymerizability of this new fluoroölefin. Although its isomer, 3-fluoropropene, had been known for many years,[1] 2-fluoropropene had been unreported. Two procedures for preparing the olefin are described here. The compound has been synthesized[2] (1) by the thermal dehydrofluorination of 2,2-difluoropropane at 731°, which is comparable to the conversion of 1,1-difluoroethane to vinyl fluoride under similar conditions,[3] and (2) by the dechlorination of 1,2-dichloro-2-fluoropropane (a commercial research chemical) with magnesium, a reagent that has also been used to obtain vinyl fluoride from 1,1-difluoro-2-iodoethane[4] and vinylidene fluoride from 1,1,1-trifluoro-2-iodoethane.[5] The intermediate 2,2-difluoropropane was prepared by the addition of hydrogen fluoride to propyne[6] or to allene.

A comparison of the boiling point of 2-fluoropropene with those of related compounds shows it to fall in the expected position:

	B.p., °C.		"I.C.T." b.p., °C.
2-Fluoropropene	−24.0	2-Chloropropene	22.7
3-Fluoropropene	−3[1]	3-Chloropropene	44.6
2-Fluoropropane	−9.5[7]	2-Chloropropane	36.5

The infrared spectrum of 2-fluoropropene exhibits the absorption bands of the carbon–fluorine bond and the double bond at 7.9 and 5.8 μ, respectively. The compound forms copolymers and low molecular weight homopolymers.[2]

Acknowledgment.—The authors are indebted to Miss Doris Huck for determination of the infrared spectra.

Experimental

Hydrofluorination of Allene.—Anhydrous hydrogen fluoride (100 g., 5 moles) was charged into a silver reactor cooled in Dry Ice–acetone and fitted with oil-sealed nickel stirrer, thermocouple, inlet line and off-gas line protected with a calcium chloride tube. Ten grams (0.25 mole) of allene

(1) M. Meslans, *Ann. chim. phys.*, [7] **1**, 374 (1894).

(2) P. R. Austin, U. S. Patent 2,585,529 (Feb. 12, 1952).

(3) F. B. Downing, A. F. Benning and R. C. McHarness, U. S. Patent 2,480,560 (Aug. 30, 1949); D. D. Coffman and R. D. Cramer, U. S. Patent 2,461,523 (Feb. 15, 1949); O. W. Cass, U. S. Patent 2,442,993 (June 8, 1948).

(4) A. L. Henne, THIS JOURNAL, **60**, 2275 (1938).

(5) H. Gilman and R. G. Jones, *ibid.*, **65**, 2037 (1943).

(6) A. V. Grosse and C. B. Linn, *ibid.*, **64**, 2289 (1942).

(7) A. V. Grosse, R. C. Wackher and C. B. Linn, *J. Phys. Chem.*, **44**, 275 (1940).