[CONTRIBUTION FROM THE ROLLIN H. STEVENS MEMORIAL LABORATORY OF THE DETROIT INSTITUTE OF CANCER RESEARCH AND FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

The Dehydrogenation and Structure Proof of 1-Methylestrone[1]

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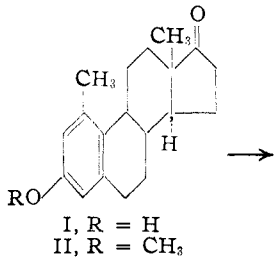
The palladium dehydrogenation of the methyl ether of 1-methylestrone (II) yielded the methyl ether of 1-methylisoequilenin (III) and 1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV). The latter substance was identical with a synthetic sample prepared *via* the key intermediates, 6-methoxy-8-methyl-1-tetralone (VIII) and 1-keto-2,5-dimethyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene (XIII).

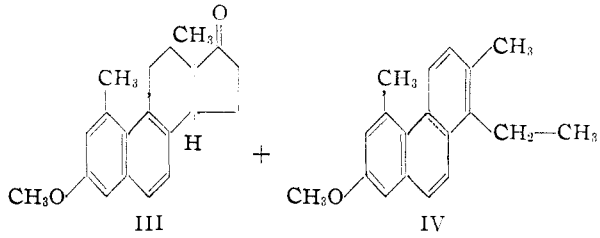
It has recently been shown[2] that the rearrangement of 1,4-androstadiene-3,17-dione with aqueous mineral acids yields largely a phenolic steroid identical with the substance which Djerassi and coworkers[3] had obtained from the rearrangement of 1,4,6-androstatriene-3,17-dione with acetic anhydride and *p*-toluenesulfonic acid, followed by hydrogenation. These authors assigned the 1-methylestrone structure I to this new estrogen on the basis of considerations of the reaction mechanism and from the evidence obtained in the study of a model dienone in the naphthalene series.[4]

To provide degradational evidence that this phenolic steroid actually has the 1-methylestrone structure I it was subjected to a dehydrogenation similar to the one which had proved successful in the elucidation of the structure of the "x-methylheterophenol."[5] When its methyl ether was treated with 5% palladium on charcoal at 350° for five minutes two products were obtained by fractional crystallization: compound A (70% yield), m.p. 140–142°, and compound B (7% yield), m.p. 115–117°. When the duration of this treatment was extended to 30 minutes only compound B was isolated in a 33% yield.

It has previously been shown that estrone methyl ether suffered a cleavage of ring D under a drastic palladium on charcoal treatment and was dehydrogenated to 1-ethyl-2-methyl-7-methoxyphenanthrene,[6] while a milder treatment afforded isoequilenin methyl ether. As expected, compound B, which was formed under the more drastic conditions, analyzed correctly (alone and in form of two derivatives) for an ethyldimethylmethoxyphenanthrene and showed an ultraviolet absorption spectrum similar to that of other methoxyphenanthrenes. Evidence will be presented below that compound B is identical with a synthetic sample



I, R = H
II, R = CH_3



III IV

of 1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV). Since it is considered unlikely that either the methyl group or the methoxyl group attached to the A-ring have migrated during the dehydrogenation, this result is evidence that these groups were attached at the 1- and 3-positions, respectively, in the original partially aromatic steroid and that the latter is indeed 1-methylestrone (I).

From the above-mentioned considerations it was expected that compound A was 1-methylisoequilenin methyl ether (III). This was confirmed by analysis, by the ultraviolet absorption spectrum which was almost identical with that of 1-methylequilenin,[3] by a peak at 5.77 μ in the infrared absorption spectrum (nujol) which suggested a C-17-carbonyl group, and by the analysis of its *sym*-trinitrobenzene complex. In confirmation of the conclusion that compound A, III, belonged to the iso-series (C/D *cis*) and that the catalyst had brought about an epimerization at carbon-14, it was compared with the methyl ether of 1-methylequilenin[3] (C/D *trans*), m.p. 205–207°, and found not to be identical with it. (That the described 1-methylequilenin[3] indeed belongs to the *normal* (C/D *trans*) series can be inferred from the fact that it was made by a reaction which was also used to convert 6,7-dehydroestrone into equilenin). The methyl ether of 1-methylequilenin was also dehydrogenated to compound B.

The synthesis of the previously unknown 1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV), required for the comparison with compound B, was accomplished in the following manner: γ-(2-Methyl-4-methoxyphenyl)-butyric acid (V) was cyclized in 80% yield by a modification of the Gil-

(1) (a) Based on a thesis submitted by Walter Pummer in partial fulfillment of the requirements for the degree of Master of Science at Wayne University, August, 1952. (b) The work reported in this paper was supported in part by grants from the Atomic Energy Commission, the American Cancer Society, Inc., the Michigan Cancer Foundation and The Kresge Foundation.

(2) A. S. Dreiding, W. J. Pummer and A. J. Tomasewski, THIS JOURNAL, **75**, 3159 (1953).

(3) C. Djerassi, G. Rosenkranz, J. Romo, J. Pataki and St. Kaufmann, *ibid.*, **72**, 4540 (1950).

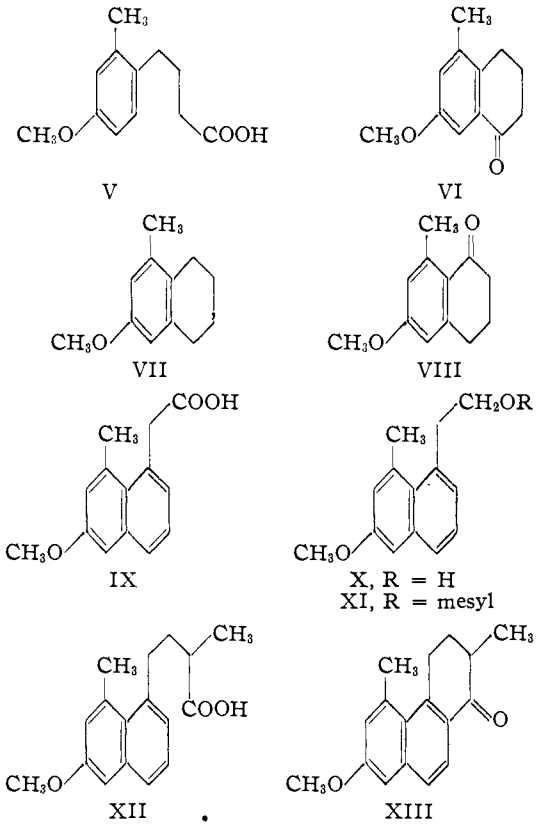
(4) A. Sandoval, L. Miramontes, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 990 (1951).

(5) A. S. Dreiding and A. Voltman, abstract of paper presented before the Division of Organic Chemistry, Boston, April 3, 1951, p. 21 M.; A. S. Dreiding and A. J. Tomasewski, abstract of paper presented before the Division of Organic Chemistry, Milwaukee, April 5, 1952, p. 82 K; J. Herran, O. Mancera, G. Rosenkranz and C. Djerassi, *J. Org. Chem.*, **16**, 899 (1951).

(6) W. E. Bachmann and A. S. Dreiding, THIS JOURNAL, **72**, 1324 (1950).

more and Horton[7] method with a 1:1 mixture of phosphoric acid and phosphorus pentoxide to 5-methyl-7-methoxy-1-tetralone (VI). This method is more convenient and gives better yields than the two methods[8,9] which have been previously reported.

A Wolff–Kishner reduction of VI at atmospheric pressure[10] afforded 6-methoxy-8-methyltetralin (VII) which was readily purified by codistilling it with ethylene glycol directly from the reaction mixture. Of the three benzyl-type positions in VII only the 1-position is activated by a *p*-methoxyl group and, as expected, the chromic anhydride[11] oxidation took place at that center to give 6-methoxy-8-methyl-1-tetralone (VIII). Comparison of the ultraviolet absorption spectra of the two ketones, VI and VIII (see experimental part), clearly showed the two isomers to be different. The difference in the spectra is the same as observed with 7-methoxy-1-tetralone and 6-methoxy-1-tetralone.[12]



A Reformatsky condensation of the ketone VIII and ethyl bromoacetate followed by dehydration, dehydrogenation and saponification yielded 6-methoxy-8-methyl-1-naphthylacetic acid (IX) which was reduced with lithium aluminum hydride in the form of the methyl ester to the crystalline alcohol X. The conversion of the latter to α-methyl-γ-(6-methoxy-8-methyl-1-naphthyl)-butyric acid (XII) was fashioned after a synthesis described by Wilds, Beck and Close,[13] with the exception that the mesylate XI was used in a condensation with the potassium salt of diethyl malonate. The substituted naphthylbutyric acid XII was also prepared in a very low yield by a Reformatsky reaction with methyl γ-bromotiglate[14] and 6-methoxy-8-methyl-1-tetralone (VIII), followed by dehydration, disproportionation and saponification.

The cyclization of the acid chloride of XII to 1-keto-2,5-dimethyl-7-methoxyphenanthrene (XIII) was carried out with stannic chloride, and treatment of XIII with ethylmagnesium iodide, followed by dehydrogenation led to the desired 1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV). The evidence for the identity of this sample with the dehydrogenation product (compound B) from 1-methylestrone (I) consisted of undepressed mixture melting points of the free phenanthrenes and two derivatives, as well as superimposable infrared absorption spectra of the phenanthrenes.

Acknowledgments.—We wish to express our thanks to Dr. J. M. Vandenbelt and Mr. Bruce Scott of Parke, Davis and Co., Detroit, Michigan, for the infrared and some of the ultraviolet absorption spectra. We are grateful to Dr. Carl Djerassi, and Syntex, S.A., Mexico City, Mexico, for a sample of 1,4,6-androstatriene-3,17-dione, which was used for the preparation of 1-methylequilenin.

Experimental[15]

Dehydrogenation of the Methyl Ether of 1-Methylestrone (II). (a) For Five Minutes.—A mixture of 238 mg. of II and 220 mg. of 5% palladium-on-charcoal was heated at 350° for five minutes under a nitrogen atmosphere. The contents were allowed to cool and extracted with boiling benzene, the solution was filtered and the solvent removed. The residue was recrystallized from methanol to give 164 mg. (70%) of the **methyl ether of 1-methylisoequilenin (III**, compound A), m.p. 140.5–142°.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.17; H, 7.85.

The ultraviolet absorption spectrum was taken in 95% ethanol, λ_{max}^{alc} 236, 268, 278, 323 and 337 mμ (ε 75,660, 6,360, 6,570, 1,720, 2,250), and was similar to that of 1-methylequilenin.[3] The infrared spectrum showed $\lambda_{max}^{mineral\ oil}$ 5.77 μ (isoequilenin methyl ether, 5.75 μ).

The ***sym*-trinitrobenzene complex** crystallized from methanol as orange needles, m.p. 129–130°.

Anal. Calcd. for $C_{26}H_{25}N_3O_8$: C, 61.53; H, 4.97; N, 8.28. Found: C, 61.84; H, 4.85; N, 8.20.

By concentrating the mother liquors of the crystallization of III, 15 mg. (7%) of **1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV**, compound B) was obtained, m.p. 115–116.7°. The ultraviolet absorption spectrum in 95% ethanol exhibited the following maxima: λ_{max}^{alc} 228, 262, 305, 328, 343 and 360 mμ (ε, 12,900, 69,690, 9,610, 600, 890, 890). The infrared spectrum showed $\lambda_{max}^{mineral\ oil}$ 6.11(s), 6.34(w), 7.10(w), 7.42(m), 7.72(w), 7.86(s), 8.17(m), 8.30(m), 8.56(s), 9.10(m-s), 9.37(m-s), 9.42(m-s), 9.71(m), 10.10(m), 11.28(m-s), 11.65(s), 11.85(w), 12.13(m), 12.79(m), 13.73 (m-s) μ.

Anal. Calcd. for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.52; H, 8.16.

The ***sym*-trinitrobenzene** complex crystallized from methanol in yellow needles, m.p. 133–135°, while the picrate

(7) R. C. Gilmore, Jr., and W. J. Horton, *ibid.*, **73**, 1413 (1951).
(8) L. Ruzicka and L. Sternbach, *Helv. Chim. Acta*, **23**, 360 (1940).
(9) R. B. Woodward and T. Singh, THIS JOURNAL, **72**, 494 (1950).
(10) Huang-Minlon, *ibid.*, **68**, 2487 (1946).
(11) V. C. E. Burnop, G. H. Elliot and R. P. Linstead, *J. Chem. Soc.*, 727 (1940).
(12) W. E. Bachmann and J. Controulis, private communication.
(13) A. L. Wilds and L. W. Beck, THIS JOURNAL, **66**, 1688 (1944); A. L. Wilds and W. J. Close, *ibid.*, **69**, 3079 (1947).
(14) A. S. Dreiding and R. J. Pratt, unpublished results from this Laboratory.
(15) The analyses were performed by the Micro-Tech Laboratories, Skokie, Illinois. The melting points are not corrected.

crystallized from the same solvent as orange needles, m.p. 118–119°.

(b) **For Thirty Minutes.**—When the dehydrogenation of 345 mg. of II, m.p. 125–127°, was carried out as described in the previous experiment, except that the duration of the heating at 350° was extended to 30 minutes, 165 mg. of a crude yellow solid was obtained. On recrystallization from methanol, this yielded 103 mg. (33%) of 1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV, compound B) as colorless crystals, m.p. 110–112°. A sublimation at 130° and 0.08 mm. raised the melting point to 114–116°, undepressed on admixture with the sample obtained in the previous experiment.

The *sym*-**trinitrobenzene complex** crystallized from methanol as yellow needles, m.p. 133–135° alone and when mixed with this derivative from the previous experiment.

Anal. Calcd. for $C_{25}H_{23}N_3O_7$: N, 8.80. Found: N, 8.73.

The **picrate** was recrystallized from methanol as orange needles, m.p. 118–119°, which was not depressed on admixture with the sample described above.

Anal. Calcd. for $C_{25}H_{23}N_3O_8$: N, 8.52. Found: N, 8.75.

1-Methylequilenin Methyl Ether.—1-Methylequilenin was prepared as described by Djerassi and co-workers.[3] It was converted to the methyl ether by dissolving 50 mg. in 10 ml. of 95% ethanol and adding alternately 1 ml. of 10% sodium hydroxide and 1 ml. of dimethyl sulfate four times. After allowing the solution to stand at room temperature for one-half hour, the pink precipitate was filtered and recrystallized from methanol as short pink needles, m.p. 205–207°.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.24; H, 7.74.

Dehydrogenation of 1-Methylequilenin Methyl Ether.—The dehydrogenation of 7 mg. of the methyl ether of 1-methylequilenin, m.p. 203–205°, was carried out as described above, but for 15 minutes. The crude residue was converted to the *sym*-trinitrobenzene derivative of 1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV), m.p. 132–134°, yield 4 mg. (35%). On admixture with this derivative of IV as described above (m.p. 133–135°) the melting point was 132–135°. When mixed with this derivative of III (m.p. 129–130°) the melting point was depressed to 115–130°.

5-Methyl-7-methoxy-1-tetralone (VI).—γ-(2-Methyl-4-methoxyphenyl)-butyric acid (V) was cyclized by essentially the procedure developed by Gilmore and Horton[7] for δ-phenylvaleric acid. Instead of an almost 3:2 ratio of phosphorus pentoxide to phosphoric acid, a 1:1 ratio was used. By heating 30 g. of the acid (V) in 200 g. of phosphorus pentoxide and 200 ml. of 85% phosphoric acid for 1.5 hours in a water-bath, pouring on ice and recrystallizing the residue from an ether–petroleum ether mixture was obtained 21.5 g. (78%) of 5-methyl-7-methoxy-1-tetralone (**VI**) as yellow needles, m.p. 55.5–57° (reported[8,9] m.p. 57–57.5° and 50% yield). The ultraviolet absorption spectrum had the following maxima: λ_{max}^{alc} 220.8, 258.5, 323 mμ (ε 20,120, 8,900 and 3,170). The infrared spectrum exhibited the intense carbonyl group absorption at 5.95 μ (mineral oil). The ketone VI formed a **2,4-dinitrophenylhydrazone** as orange needles after recrystallization from ethyl acetate, m.p. 243° dec.

Anal. Calcd. for $C_{18}H_{18}N_4O_5$: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.36; H, 5.21; N, 15.03.

6-Methoxy-8-methyltetralin (VII).—The ketone VI was reduced by the Huang-Minlon modification of the Wolff–Kishner method. Eighteen grams of the ketone VI, 14 g. of potassium hydroxide, 12 ml. of 85% hydrazine hydrate and 250 ml. of ethylene glycol were refluxed vigorously for one hour. The apparatus was arranged for distillation and the temperature gradually raised to the boiling point of the glycol (198–200°), when the tetralin derivative VII codistilled with the solvent. Distillation was continued until no cloudiness appeared on adding water to the distillate. The distillate was diluted with water and extracted with ether. The yellowish viscous product was purified by distillation to give 14 g. (85%) of 6-methoxy-8-methyltetralin (VII) as a colorless liquid, b.p. 86.5° (0.3 mm.), $n^{25}D$ 1.5474, m.p. 16–17° (determined in an equilibrium mixture of liquid and solid). Cleavage of the ether linkage in a small sample with hydriodic acid and red phosphorus yielded 4-methyl-2-ar-tetralol, m.p. 104–105° (reported[9] 104–105°).

6-Methoxy-8-methyl-1-tetralone (VIII).—To a stirred solution of 15 g. of 6-methoxy-8-methyltetralin (VII) in 106 ml. of glacial acetic acid and 21.2 ml. of propionic acid, cooled in an ice-bath, was added dropwise a solution of 22.5 g. of chromic anhydride in 7.5 ml. of water and 65 ml. of glacial acetic acid over a two-hour period. At the end of this time, the black reaction mixture was stored at 0° for three weeks, followed by dilution with an equal amount of water and extraction with ether. After the usual operations, a solution of the crude yellow solid product (9.89 g.) in benzene was filtered through a column of 40 g. of Fischer chromatographic alumina to yield 7.13 g. (44.5%) of **6-methoxy-8-methyl-1-tetralone (VIII)** as colorless plates, m.p. 67–69°. The analytical sample was recrystallized from methanol, m.p. 69.5–70.5°. The following maxima were observed in the ultraviolet absorption spectrum: λ_{max}^{alc} 225.8 and 275.5 mμ (ε 15,900, 17,000). The infrared spectrum showed a strong peak at 6.01 μ (mineral oil) which is probably due to the carbonyl group.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.62; H, 7.30.

The ketone VIII formed a red **2,4-dinitrophenylhydrazone** which crystallized from ethyl acetate, m.p. 236° dec.

Anal. Calcd. for $C_{18}H_{18}N_4O_5$: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.14; H, 4.95; N, 15.03.

6-Methoxy-8-methyl-1-naphthylacetic Acid (IX).—The Reformatsky reaction was carried out in the usual manner.[16] From 4 g. of the ketone VIII and 30 ml. of ethyl bromoacetate in an ether–benzene (4:1) mixture was obtained 7.2 g. of the crude Reformatsky ester. Dehydration with 6 g. of fused potassium acid sulfate at 160° and dehydrogenation with 1.5 g. of 5% palladium–charcoal at 250°, followed by saponification, afforded 2.64 g. (55% from the ketone, VIII) of the crude **6-methoxy-8-methyl-1-naphthylacetic acid (IX)** as a tan solid. The analytical sample was recrystallized from an ether–benzene mixture as long transparent needles, m.p. 197–198°.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.05; H, 6.13. Found: C, 73.37; H, 6.24.

β-(6-Methoxy-8-methyl-1-naphthyl)-ethanol (X).—A suspension of 2 g. of lithium aluminum hydride in 50 ml. of anhydrous ether was treated over a two-hour period with an ethereal solution of the methyl ester of IX (prepared from 780 mg. of IX with diazomethane) and refluxed for two hours more. After decomposition of the excess hydride with water, followed by addition of dilute acid, the ethereal layer was separated and washed well with acid and alkali. The addition of petroleum ether (b.p. 30–60°) to the dried ether concentrate led to 656 mg. (88%) of **β-(6-methoxy-8-methyl-1-naphthyl)-ethanol (X)**, m.p. 67–70°. Recrystallization from cyclohexane yielded the analytical sample as colorless needles, m.p. 70–71°.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.73; H, 7.43.

Mesylate of β-(6-Methoxy-8-methyl-1-naphthyl)-ethanol (XI).—To a solution of 654 mg. of the alcohol X in 15 ml. of pyridine was added 7 ml. of methanesulfonyl chloride while cooling the solution in an ice-bath. The mixture was allowed to stand at room temperature for 15 minutes with occasional shaking and decomposed with ice and saturated sodium bicarbonate solution. The white solid was filtered and recrystallized from diisopropyl ether to give 753 mg. (85%) of the **mesylate of β-(6-methoxy-8-methyl-1-naphthyl)-ethanol (XI)** as long colorless needles, m.p. 112.5–113.5°.

Anal. Calcd. for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.17; S, 10.89. Found: C, 61.52; H, 6.53; S, 11.19.

α-Methyl-γ-(6-methoxy-8-methyl-1-naphthyl)-butyric Acid (XII). (a) By a Malonic Ester Synthesis with the Mesylate (XI).—The synthesis of the butyric acid XII from the mesylate XI was carried out by the method of Wilds, Beck and Close[13] without purifying the intermediates. The addition of 693 mg. of the mesylate XI to a suspension of the salt prepared from 0.5 g. of potassium metal and 3 g. of diethyl malonate in benzene afforded 605 mg. of the crude malonic acid after saponification, apparent m.p. 212–220° dec. Esterification (diazomethane), conversion to the po-

(16) R. L. Shriner, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 18.

tassio-salt, and treatment with methyl iodide in portions until the mixture was neutral to phenolphthalein, yielded, after saponification and decarboxylation at 160°, 115 mg. (18% from the mesylate, XI) of α-methyl-γ-(6-methoxy-8-methyl-1-naphthyl)-butyric acid (XII) as a yellow solid. The analytical sample was recrystallized from an ether–petroleum ether mixture as slightly yellow microcrystals, m.p. 116–118°.

Anal. Calcd. for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.03; H, 7.86.

(b) **By a Methyl γ-Bromotiglate Reformatsky Reaction with the Ketone (VIII).**—The crude Reformatsky ester, obtained from 2 g. of the ketone VIII and 4 g. of methyl γ-bromotiglate[14] in a 3:1 ether–benzene mixture, was dehydrated with 1.5 g. of potassium acid sulfate, isomerized with 0.5 g. of 5% palladized charcoal by the method of Stork[17] and saponified to yield 50 mg. (1.8%; based on unrecovered ketone, 5%) of α-methyl-γ-(6-methoxy-8-methyl-1-naphthyl)-butyric acid (XII), m.p. 115–117°, undepressed on admixture with the substance obtained from method (a). The amount of starting ketone recovered was 1.31 g. (65%).

1-Keto-2,5-dimethyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene (XIII).—The butyric acid (XII, 66 mg.) was converted to the acid chloride with 1 ml. of oxalyl chloride in benzene solution and then cyclized with stannic chloride exactly as described by Bachmann, Cole and Wilds[18] for the corresponding intermediate in their equilenin synthesis; yield of **1-keto-2,5-dimethyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene (XIII)** was 36 mg. (59%), m.p. 175–176.5°, after recrystallization from an ether–petroleum ether mixture.

(17) G. Stork, THIS JOURNAL, **69**, 2937 (1947).

(18) W. E. Bachmann, W. Cole and A. L. Wilds, *ibid.*, **62**, 824 (1940).

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.14. Found: C, 80.52; H, 7.51.

1-Ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV).—A solution of a Grignard reagent, prepared from 1 g. of magnesium turnings and 5 g. of ethyl iodide in 20 ml. of anhydrous ether under an atmosphere of nitrogen was added to 36 mg. of the ketone XIII in 10 ml. of dry ether and refluxed for one hour. After decomposition of the excess reagent with water and addition of dilute acid, the organic layer was separated and washed well with dilute acid, dried and evaporated. The oily residue was covered with methanol when the oil solidified, weight 33 mg. (87%), m.p. 104–114°. Recrystallization from methanol gave the **1-ethyl-2,5-dimethyl-7-methoxy-3,4-dihydrophenanthrene** as colorless microcrystals, m.p. 114.5–116°.

Dehydrogenation of 23 mg. of the dihydro derivative with 23 mg. of palladized charcoal at 250–260° for seven minutes gave 14 mg. (61%) of **1-ethyl-2,5-dimethyl-7-methoxyphenanthrene (IV)**, which melted at 115–116.5° after recrystallization from methanol as colorless plates. When this sample was mixed with compound B (m.p. 115–116.7°) the melting point was 115–116.5°. The infrared absorption spectrum exhibited the following peaks: $\lambda_{max}^{mineral\ oil}$ 6.12(s), 6.35(w), 7.11(w), 7.43(m), 7.73(w), 7.86(s), 8.18(m), 8.31(m), 8.57(s), 9.12(m-s), 9.38(m-s), 9.43(m-s), 9.72(m), 10.50(m), 11.28(m-s), 11.66(s), 11.86(w), 12.14(m), 12.80(m), 13.75 (m-s) μ.

The *sym*-trinitrobenzene complex melted at 134–135°. When it was mixed with this derivative of compound B (m.p. 133–135°) the melting point was 133–135°. The picrate melted at 116–118° alone and when mixed with this derivative of compound **B** (m.p. 118–119°).

DETROIT, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND LABORATORY FOR NUCLEAR SCIENCE AND ENGINEERING, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Mechanisms of Racemization of Camphene-8-C^{14} [1]

BY JOHN D. ROBERTS* AND JOEL A. YANCEY

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It has been shown by C^{14}-tracer studies that optically-active camphene racemizes by at least two different mechanisms in the presence of hydrated titanium dioxide, pyruvic acid or aniline hydrochloride. One of these mechanisms does not cause isotope-position rearrangement of camphene-8-C^{14} and probably involves successive hydride and Wagner rearrangements. This mechanism predominates with hydrated titanium dioxide and aniline hydrochloride. Racemization of camphene-8-C^{14} with pyruvic acid is accompanied by extensive isotope-position rearrangement and is well formulated by assuming interconversion of enantiomorphic "camphenonium" (camphene-hydro) cations through methyl group shifts (Nametkin rearrangements).

Camphene (I) is racemized more or less readily by a variety of acidic reagents.[2–4] Two types of mechanisms have been suggested for these processes which may be illustrated (and experimentally distinguished) with optically active camphene-8-C^{14} (Ia).

Both mechanisms involve formation of the "camphenonium" (camphene-hydro) cation (IIa) by addition of a proton to Ia. Mechanism A then proceeds by 2,6-hydride migration to yield the isomeric non-classical cation III,[5] or possibly the symmetrical tricyclonium ion IV,[5b] either of which would yield Ia and Ib thus giving racemic camphene. Mechanism A stems from an early suggestion of Meerwein[6] regarding the mode of racemization of isobornyl chloride and is given substantial support by the findings that: (1) 2,6-hydrogen migrations occur readily in cationic reactions of norbornyl[5b,7] and fenchyl[8] derivatives and (2) 8-substituted camphenes appear to racemize without substantial rearrangement.[3,9]

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(1) Supported in part by the program of research of the U. S. Atomic Energy Commission.

(2) (a) P. Lipp and G. Stutzinger, *Ber.*, **65**, 241 (1932); (b) S. Yamada, *Bull. Chem. Soc. Japan*, **16**, 336 (1941).

(3) J. J. Ritter and G. Vlases, Jr., THIS JOURNAL, **64**, 583 (1942).

(4) For refs. to related reactions and discussion see J. L. Simonsen and L. N. Owen, "The Terpenes," Vol. II, 2nd Ed., University Press, Cambridge (1949), Chap. V, particularly pp. 290–293.

(5) For extensive studies of intermediates of this type in other reactions see (a) S. Winstein and D. S. Trifan, THIS JOURNAL, **71**, 2953 (1949); **74**, 1147, 1154 (1952); (b) J. D. Roberts and C. C. Lee, *ibid.*, **73**, 5009 (1951); (c) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan and H. Marshall, *ibid.*, **74**, 1127 (1952.)

(6) H. Meerwein and F. Montfort, *Ann.*, **435**, 207 (1924).

(7) J. D. Roberts, paper presented at the 75th Anniversary Meeting of the American Chemical Society, Sept. 7, 1951.

(8) W. v. E. Doering and A. P. Wolf, Abstracts of the XIIth International Congress of Pure and Applied Chemistry, New York, N. Y., Sept. 11, 1951, p. 437.

(9) The argument here is not rigorous since as Ritter and Vlases[3] point out the structures of the racemization products were not confirmed by chemical means. Furthermore, even if racemization occurred by mechanism B (above), the 8-substituted camphenes may be more thermodynamically stable than their 9- or 10-substituted isomers and hence no apparent rearrangement need accompany racemization.