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Atisine. The Synthesis of 1-Methyl-6-ethyl-3-azaphenanthrene[1a]

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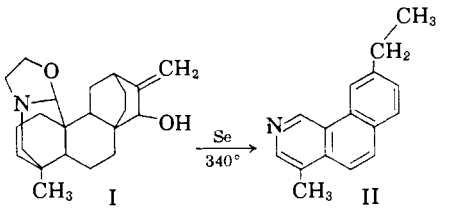
RECEIVED OCTOBER 10, 1958

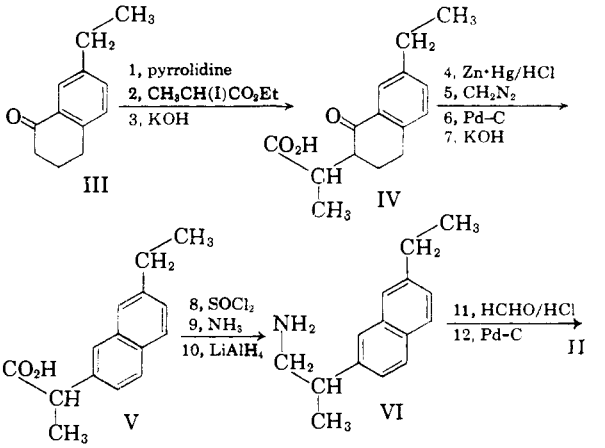
A key degradation product obtained from atisine by selenium dehydrogenation is the $C_{16}H_{15}N$ base of Jacobs and Craig. This compound has now been identified as 1-methyl-6-ethyl-3-azaphenanthrene by an unambiguous synthesis. Alkylation of the pyrrolidine enamine of 7-ethyltetralone-1 (III) with ethyl α-iodopropionate gave a crystalline mixture of diastereoisomers (IV). Reduction of IV by the Clemmensen method gave a resinous product which was dehydrogenated to α-methyl-7-ethyl-2-naphthaleneacetic acid (V). The acid was converted to the amine VI. Pictet–Spengler cyclization of this amine with formalin and hydrochloric acid followed by dehydrogenation over palladium furnished II, identical with an authentic sample from atisine. The identification of this base provides the first evidence establishing the position of the nitrogen atom in the atisine skeleton.

Recent work on the structure of atisine (I),[2] from *Aconitum heterophyllum*, and several closely related alkaloids[3,4] from various *Aconitum* and *Delphinium* spp., has emphasized the importance of the $C_{16}H_{15}N$ base[5] obtained on selenium dehydrogenation of atisine. This base contains all but six of the carbon atoms of atisine and relates the heterocyclic ring to the rest of the molecule. This paper reports the identification of the $C_{16}H_{15}N$ base as 1-methyl-6-ethyl-3-azaphenanthrene (9-ethyl-4-methylbenz[h]-isoquinoline)(II) by comparison with material prepared by an unambiguous synthesis.



The structure for the $C_{16}H_{15}N$ base was indicated by several considerations. The original data[5] showed that it was a tertiary base since it furnished a picrate and methiodide and contained no active hydrogen. It was found by us to contain no N-alkyl groups and to have a *pKa'* of 4.43 (66% methyl Cellosolve), both properties consistent with an aromatic base. A similar $C_{16}H_{15}N$ base subsequently was obtained by Wiesner, *et al.*, from veatchine, an alkaloid whose chemistry closely parallels that of atisine. This base was shown to be 1-methyl-7-ethyl-3-azaphenanthrene.[5a] Its ultraviolet absorption spectrum was very similar to, though not identical with, that of the base from atisine. The infrared spectra were clearly different. Since dehydrogenation of atisine furnished, in addition to the $C_{16}H_{15}N$ base, the hydrocarbon 1-methyl-6-ethylphenanthrene, while veatchine gave 1-methyl-7-ethylphenanthrene, it appeared likely that the atisine base was 1-methyl-6-ethyl-3-azaphenanthrene.

In projecting the synthesis of 1-methyl-6-ethyl-3-azaphenanthrene (II), it was decided to proceed from the known 7-ethyltetralone-1 (7-ethyl-3,4-dihydro-1-(2H)-naphthalenone) (III) which could be obtained by a direct reaction sequence from ethylbenzene.[6] It was anticipated that alkylation of the starting tetralone with an appropriate α-halopropionic ester would lead to a key intermediate, 7-ethyl-1-oxo-1,2,3,4-tetrahydro-α-methyl-2-naphthaleneacetic acid (IV). Reduction of the keto-function and dehydrogenation should then give 7-ethyl-α-methyl-2-naphthaleneacetic acid (V).



It was expected that this could be converted to the corresponding amine VI by a straightforward series of reactions and that the amine could be cyclized by the Pictet–Spengler reaction[7] to a tetrahydrobenzisoquinoline. A final dehydrogenation should then give the desired azaphenanthrene II.

After several unsuccessful attempts to alkylate the starting tetralone III with ethyl α-bromo- and α-iodopropionate using potassium *t*-butoxide as catalyst, it was suspected that the strong base and vigorous reaction conditions were causing dehydrohalogenation of the haloesters, followed by polymerization of the resulting acrylic ester. Accordingly recourse was had to the method of alkylation developed by Stork[8] which proceeds *via* the ena-

(1) (a) A preliminary report of this synthesis appeared as a Communication to the Editor, D. M. Locke and S. W. Pelletier, THIS JOURNAL, **80**, 2588 (1958). (b) To whom inquiries regarding this paper should be addressed.

(2) S. W. Pelletier and W. A. Jacobs, *ibid.*, **76**, 4496 (1954); K. Wiesner, *et al.*, *Chemistry & Industry*, 132 (1954); K. Wiesner and J. A. Edwards, *Experientia*, **11**, 255 (1955); D. Dvornik and O. E. Edwards, *Can. J. Chem.*, **35**, 860 (1957); *Chemistry & Industry*, 622 (1958); S. W. Pelletier, *ibid.*, 1116 (1958).

(3) S. W. Pelletier, *Science*, **126**, 1234 (1957); *Chemistry & Industry*, 1670 (1957).

(4) D. Dvornik and O. E. Edwards, *ibid.*, 952 (1957).

(5) W. A. Jacobs and L. C. Craig, *J. Biol. Chem.*, **143**, 589 (1942).

(5a) M. F. Bartlett and K. Wiesner, *Chemistry and Industry*, 542 (1954).

(6) W. E. Bachmann and R. O. Edgerton, THIS JOURNAL, **62**, 2219 (1940).

(7) W. M. Whaley and T. R. Govindachari, *Org. Reactions*, **6**, 151 (1951).

(8) G. Stork, R. Terrell and S. Szmuszkovicz, THIS JOURNAL, **76**, 2029 (1954). We wish to thank Prof. Stork for providing additional

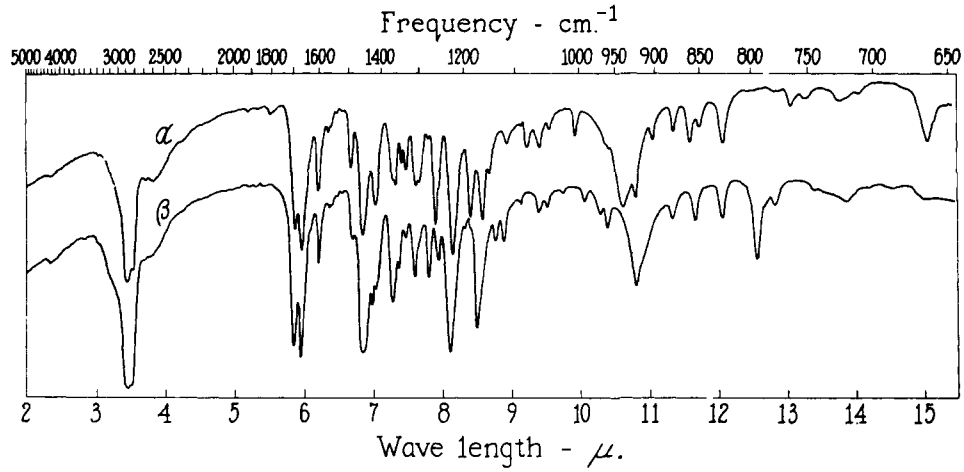
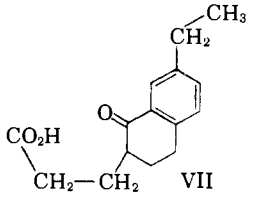


Fig. 1.—The infrared spectra (Nujol) of the α- and β-isomers of 7-ethyl-α-methyl-1-oxo-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (IV).

mine[9] of the ketone in question. Alkylation of the pyrrolidine enamine of 7-ethyltetralone-1 with ethyl α-bromopropionate was found to proceed in small yield, and with ethyl α-iodopropionate in somewhat better yield. Since it was found difficult to purify the viscous, high-boiling product by distillation, the ester was saponified and the crude acid purified by crystallization and chromatography. The main crystalline product (22% of theoretical) had a wide melting-range, *ca.* 107–129°, but its analysis and infrared spectrum, 1707 (carboxylic acid) and 1680 cm.$^{-1}$ (conjugated ketone) (Nujol), were consistent with the structure IV. This material was followed on the chromatogram by an unidentified second substance whose analysis and infrared spectrum suggest that it contains a hydroxyl group in addition to the functions present in the main product.

The main fraction itself was considered to be a mixture consisting of the two *dl*-pairs corresponding to the desired ketoacid IV. The possibility was also considered that the reaction might have proceeded in part by an alternative path with some of the haloester undergoing dehydrohalogenation, followed by addition of the enamine in the Michael fashion to give the straight chain isomer VII.[10] Unlike the



VII

desired product, this material should consist of only one *dl*-pair, and it was thought that this substance might constitute part of the mixture. A C-methyl determination showed *ca.* 1.3 C-methyls as compared to *ca.* 0.5 for the starting tetralone. This was considered good evidence that the mixture consisted largely of the desired material. Nonetheless it was further investigated. Rechromatography of the crude product over silicic acid gave one pure isomer, m.p. 131–133°, in the earlier fractions, but all the subsequent fractions consisted of mixtures. A triangular fractional crystallization gave quite readily the same, apparently more abundant, isomer; but mixed crystal formation made it extremely difficult to obtain a pure sample of the other isomer. A pure sample, m.p. 125–128°, was finally obtained by a laborious fractional crystallization. The infrared spectra of the two isomers (Fig. 1) were quite similar, but definite differences were observed. For example, the α-isomer exhibits a doublet at 1188 and 1166 cm.$^{-1}$ and no maximum near 800 cm.$^{-1}$, while the β-isomer shows a single peak at 1179 cm.$^{-1}$ and a peak at 804 cm.$^{-1}$. These differences were sufficiently marked to demonstrate the presence of both isomers in the various mixtures (Fig. 2). Only these two substances could be detected in the material which comprised the main reaction product.

Treatment of each isomer with aqueous alcoholic base for short periods led to mixtures similar in melting point to the original mixture. The infrared spectra of these mixtures clearly indicated the presence of both isomers in each mixture (Fig. 2). This equilibration by base demonstrates that the two compounds do indeed represent the stereoisomers of the ketoacid IV and precludes the possibility that one of them is the Michael addition product VII. It is still possible that traces of the latter remained undetected in the crude reaction product.

Clemmensen reduction of the mixture of isomers of the ketoacid IV furnished a resinous product contaminated by a high-melting, highly crystalline bimolecular material, m.p. 195–199°, ν_{max} 1769 cm.$^{-1}$ (γ-lactone) (Nujol), mol. wt. 457, which might be considered to be VIII[11] by analogy with the formation of a similar bimolecular material from the Clemmensen reduction of β-benzoylpropionic acid which has been assigned the pinacol dilactone structure IX.[12] The purified resin from which the

experimental details and Prof. Carl Djerassi for making available to us reaction conditions for a closely related alkylation.

(9) M. E. Herr and F. W. Heyl, THIS JOURNAL, **75**, 5927 (1953).

(10) G. Stork and H. K. Landesman, *ibid.*, **78**, 5128 (1956).

(11) It is noted, however, that basic hydrolysis of the bimolecular material furnished on acidification a good yield of the mixture of isomers of the starting ketoacid, 7-ethyl-1-oxo-1,2,3,4-tetrahydro-α-methyl-2-naphthaleneacetic acid (II) (Fig. 2).

(12) S. C. Overbaugh, C. F. H. Allen, E. L. Martin and L. F Fieser, *Org. Syntheses*, **15**, 64 (1935).

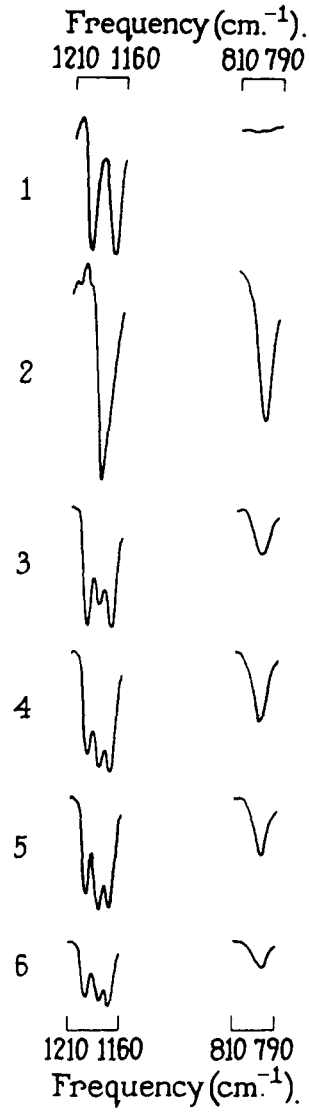
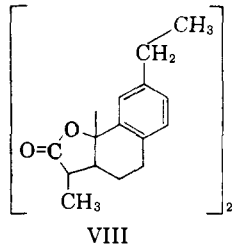
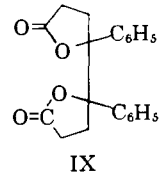


Fig. 2.—Infrared spectra (Nujol): 1, α-isomer of 7-ethyl-α-methyl-1-oxo-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (IV); 2, β-isomer of IV; 3, reaction mixture of α- and β-isomers of IV (partially purified by chromatography); 4, reaction mixture from epimerization of α-isomer of IV; 5, reaction mixture from epimerization of β-isomer of IV; 6, reaction mixture from hydrolysis of bimolecular by-product (VIII).

above by-product was removed exhibited carbonyl absorption in the infrared corresponding only to a carboxylic acid (1712 cm.$^{-1}$) (film). This informa-



VIII



IX

tion, together with an elementary analysis, indicated that the main resinous product was the desired acid, 7-ethyl-α-methyl-1,2,3,4-tetrahydro-2-naphthaleneacetic acid. Repetition of this experiment with the more abundant of the two pure isomers of the ketoacid IV, m.p. 131–133°, gave results identical with the above.

A preliminary dehydrogenation of the pure resinous acid led to a good yield of the desired α-methyl-7-ethyl-2-naphthaleneacetic acid (V), but attempts to repeat this experiment gave a decarboxylated product, apparently 2,7-diethylnaphthalene (identified as the picrate, m.p. 79–81°). This inconsistent decarboxylation of the acid was later avoided by preliminary esterification with diazomethane, dehydrogenation and finally saponification to the desired acid V. A dehydrogenation of the crude Clemmensen reduction product from which the bimolecular by-product had not been renoved, gave in addition to the decarboxylated material a small amount of a high-melting mixture which on separation by a triangular fractional crystallization proved to be the bimolecular material previously isolated (VIII) and a new material, m.p. 182–184°. This is believed to have arisen from VIII during the dehydrogenation, and its analysis, molecular weight (464) and infrared spectrum, ν_{max} 1772 (Nujol), suggest that it is an isomer of VIII.

Treatment of α-methyl-7-naphthaleneacetic acid (V) with thionyl chloride led to the corresponding acid chloride. Without isolation this substance was taken up in benzene, and the resulting solution was saturated with ammonia. The crystalline amide, m.p. 105–107°, ν_{max} 1651 (Nujol), obtained in this way was reduced by lithium aluminum hydride to the amine VI which was isolated as the hydrochloride, m.p. 208–209°, picrate, m.p. 215–218°. Treatment of this hydrochloride with formalin in 20% aqueous ethanolic hydrochloric acid gave the Pictet–Spengler cyclization product,[7] the tetrahydroisoquinoline (tetrahydro II), which was also isolated as the hydrochloride. Dehydrogenation of the free base was accomplished with 10% palladium-on-carbon at 225–235° to give 1-methyl-6-ethyl-3-azaphenanthrene (II). The melting points of this base and its picrate and trinitrobenzene adduct were identical with those of the corresponding materials from the dehydrogenation of atisine.[5,13] In each case mixture melting points showed no depression. Infrared (Fig. 3) and ultraviolet absorption spectra of the two bases were also identical.

Acknowledgment.—We wish to express our appreciation to The Lilly Research Laboratories, Eli Lilly and Co., for a grant which partially supported this work. Analyses are by Mr. D. Rigakos of this Laboratory. The technical assistance of Mrs. Vera Barna is gratefully acknowledged.

Experimental[14]

7-Ethyl-1-oxo-1,2,3,4-tetrahydro-α-methyl-2-naphthaleneacetic Acid (IV).[8,9]—A solution of 33.4 ml. (0.40 mole) of pyrrolidine in 400 ml. of toluene was refluxed for 2 hours in a three-necked flask equipped with stirrer, condenser, dropping funnel and a Bidwell-Sterling moisture collector previously filled with toluene. At the end of this time no

(13) We wish to thank Dr. W. A. Jacobs and Dr. L. C. Craig for kindly furnishing a sample of the dehydrogenation base from atisine.

(14) For general experimental procedures, see S. W. Pelletier and D. M. Locke, THIS JOURNAL, **79**, 4531 (1957).

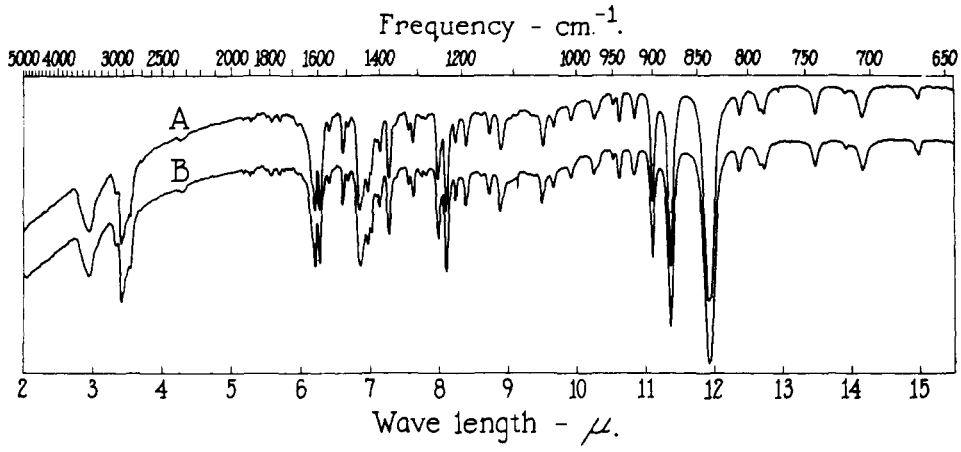


Fig. 3.—The infrared spectra (0.6% in KBr) of 1-methyl-6-ethyl-3-azaphenanthrene: A, synthetic; B, from dehydrogenation of atisine.

more water collected in the trap, and 34.8 g. (0.20 mole) of 7-ethyltetralone-1 (III)[6,15] was added with 100 mg. of *p*-toluenesulfonic acid. After refluxing for 48 hours no more water collected in the trap, the reflux condenser was replaced with a downward condenser, and toluene was removed until no more came over readily. Refractive index measurements indicated that the last portion of the distillate consisted of pure toluene.

A sample of ethyl α-iodopropionate was prepared from 39.8 g. (0.22 mole) of ethyl α-bromopropionate and 33 g. (0.22 mole) of sodium iodide in 300 ml. of dry acetone. After removal of the precipitated inorganic salts and distillation of the acetone, the residue was subjected to azeotropic distillation with 250 ml. of benzene to remove any traces of moisture. This material was added to the dark red enamine, followed by 300 ml. of dioxane and, after refluxing for 8.5 hours, the solution was concentrated *in vacuo*, diluted with water, and warmed on the steam-bath for 1 hour. The aqueous layer was separated and extracted several times with benzene. The combined organic layers were concentrated *in vacuo* and saponified on the steam-bath with 250 ml. of 2 *N* aqueous methanolic KOH for 1 hour. The solution was then concentrated *in vacuo*, diluted with water, and extracted exhaustively with benzene. The aqueous layer was then acidified with hydrochloric acid and extracted with benzene. The benzene layer was extracted several times with sodium carbonate solution. The aqueous solution then was exhaustively extracted with benzene to remove further neutral material, and finally reacidified and extracted with benzene. The benzene extract on concentration *in vacuo* gave 18.4 g. of a dark brown viscous oil which was taken up in a large volume of cold ether and filtered. The ethereal solution was concentrated somewhat and refrigerated to give 5.95 g. of nearly colorless crystals, m.p. 103–129°, with a second crop of brownish crystals, 2.68 g., m.p. 107–129°. These fractions were combined and recrystallized from ether to give 3.11 g. of nearly colorless crystals, and a second crop of 4.41 g.

The combined mother liquors were chromatographed over 250 g. of silicic acid to give 3.12 g. of crystalline fractions, with melting points in the range 103–133°, for a total of 10.64 g. or 22% of theoretical. An analytical sample prepared by several recrystallizations from ether had m.p. 112–120°, ν_{max} 1707, 1680 cm.$^{-1}$ (Nujol).

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37; two C–CH_3, 12.21. Found: C, 73.38; H, 7.44; C–CH_3, 8.27.[16]

Rechromatography of the combined fractions over 250 g. of silicic acid gave a first fraction of 1.10 g. of colorless crystals, m.p. 130–135°. The remaining fractions consisted of mixed crystals, m.p. 106–130°. Recrystallization of the first fraction from ethyl acetate gave a fraction α of m.p. 131–133°, ν_{max} 1706, 1677 cm.$^{-1}$ (Nujol) (Fig. 1).

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.20; H, 7.43.

The use of ether, benzene–light petroleum ether and ethyl acetate, in turn, as solvents for a lengthy fractional crystallization of the material from a similar run gave 2.72 g. of the α-isomer together with mixed crystals and 293 mg. of a β-isomer, 125–128°, ν_{max} 1710, 1681 cm.$^{-1}$ (Nujol) (Fig. 1).

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.27; H, 7.38.

Chromatography of the mother liquors from a run in which the heating of the enamine with the iodoester in dioxane had been extended to 22 hours (and in which the yield of main product had fallen to 17%) gave a fraction following the main fraction amounting to 200 mg., m.p. 155–156°, ν_{max} 3401–3077, 1728, 1690 cm.$^{-1}$ (Nujol).

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.39; H, 6.92.

Traces of this material in other runs may have remained undetected. It was not investigated further.

Basic Equilibration of Both Isomers of 7-Ethyl-α-methyl-1-oxo-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid.—A 60-mg. sample of the α-isomer, m.p. 131–133°, of the above ketoacid was heated at reflux for 30 minutes in 10 ml. of 1% aqueous methanolic potassium hydroxide and then allowed to stand overnight at room temperature. The solution was concentrated *in vacuo*, diluted with water, acidified with hydrochloric acid and extracted with chloroform. The chloroform extracts were evaporated to dryness *in vacuo* and the residue was recrystallized from ethyl acetate giving 30 mg., m.p. 109–129°.

A 60-mg. sample of the β-isomer was treated in the same manner with aqueous ethanolic potassium hydroxide and furnished on crystallization from benzene–petroleum ether 43 mg., m.p. 103–124°.

The infrared spectra of these products showed them both to be mixtures of the α- and β-isomers of IV (Fig. 2).

7-Ethyl-α-methyl-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid.—A 7.31-g. sample of ketoacid IV (m.p. 107–129°) was reduced by the procedure of Martin[17] to give a crude oily product which on standing deposited a small amount of a crystalline by-product. This was removed by filtration, washed with ligroin, and recrystallized from ligroin to give 308 mg. of VIII, m.p. 195–199°, ν_{max} 1769 cm.$^{-1}$ (Nujol).

Anal. Calcd. for $C_{30}H_{34}O_4$: C, 78.57; H, 7.47; mol. wt., 459. Found: C, 78.71; H, 7.63; mol. wt., 457 (Rast in camphor).

A 50-mg. sample of this crystalline by-product VIII was heated in 10 ml. of 1% aqueous ethanolic potassium hydroxide for 2 hr. on the steam-bath. The reaction mixture was concentrated *in vacuo*, acidified, diluted with water and extracted with chloroform. The chloroform extracts were evaporated to dryness and the crude product recrystallized, m.p. 119–170°. An infrared spectrum indicated some of the 1769 cm.$^{-1}$ peak still present so the above treatment was repeated. The crude product then was chromatographed

(15) Purchased from Distillation Products Industries, Eastman Kodak Co.

(16) For purposes of comparison the results of a similar determination on 7-ethyltetralone are included: *Anal.* Calcd. for $C_{12}H_{14}O$: 1 C–CH_3, 8.63. Found: C–CH_3, 4.09.

(17) E. L. Martin, THIS JOURNAL, **58**, 1438 (1936).

over 2 g. of silicic acid. The crystalline fractions were combined and recrystallized from benzene–petroleum ether to give 27 mg., m.p. 114–129°. The infrared spectrum of this sample was identical with that of the mixture obtained by basic equilibration of the α-isomer of the keto acid IV (Fig. 2).

A portion of the non-crystalline residues (after separation of VIII) was purified by chromatography over silicic acid and sublimation to give an analytical sample of 7-ethyl-α-methyl-1,2,3,4-tetrahydro-2-naphthaleneacetic acid, ν_{max} 1712 cm.$^{-1}$ (film).

Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.57; H, 8.60.

7-Ethyl-α-methyl-2-naphthaleneacetic Acid (V). A.—The non-crystalline portion of the above reaction (*ca.* 7 g.) was treated with diazomethane in acetone and evaporated to dryness several times with benzene. The residue, mixed with 700 mg. of 10% palladium-on-carbon, was heated for 5 hr. at 265–270°. After cooling, the reaction mixture was taken up in benzene, filtered, and evaporated to dryness *in vacuo*. The residue was saponified with 100 ml. of 5 *N* aqueous methanolic potassium hydroxide for 4 hours on the steam-bath, concentrated *in vacuo*, diluted with water and extracted with benzene several times. The aqueous layer was acidified and extracted with benzene to give 3.1 g. of crude product, which after repeated crystallization from ligroin gave 867 mg., m.p., 105–109°. Chromatography of the mother liquors over silicic acid and recrystallization of the product from ligroin gave an additional 477 mg., for a total yield of 1.34 g. (21% in two steps from the keto-acid IV. An analytical sample crystallized from ligroin had m.p. 109–110°.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.08; H, 7.05.

B.—A 10-g. sample of ketoacid IV was reduced by the Martin procedure,[17] and the total crude product was treated directly with 1 g. of palladium-on-carbon catalyst with nitrogen bubbled through the reaction mixture and the temperature maintained at 225 ± 5° for 4 hours. The crude product was taken up in hot ligroin and filtered to remove the catalyst. Concentration of the resulting solution and chromatography over 200 g. of silicic acid gave a 4.7-g. fraction consisting of a colorless liquid with a faint violet fluorescence. From this material was prepared a picrate which was recrystallized from ethanol, m.p. 79–81° (reported[18] for picrate of 2,7-diethylnaphthalene, m.p. 77–78°).

Anal. Calcd. for $C_{14}H_{16}\cdot C_6H_3N_3O_7$: C, 58.11; H, 4.63. Found: C, 58.21; H, 4.50.

Further elution of the column furnished 1.75 g. of crystalline material, m.p. 155–182°. A triangular fractional crystallization from benzene–ligroin furnished a sample of m.p. 203–205°, infrared spectrum identical with that of the bimolecular by-product from the Clemmensen reduction (VIII). A second material was obtained, m.p. 182–184°, $\nu_{max.}$ 1772 (Nujol).

Anal. Calcd. for $C_{30}H_{34}O_4$: C, 78.57; H, 7.47; mol. wt., 459. Found: C, 78.44; H, 7.37; mol. wt., 464 (Rast in camphor).

7-Ethyl-α-methyl-2-naphthaleneacetamide.—A 1.42-g. sample of 7-ethyl-α-methyl-2-naphthaleneacetic acid was heated with 1 ml. of thionyl chloride on the steam-bath for 1 hour. The excess thionyl chloride was removed by evaporation *in vacuo* on the steam-bath. The residue was taken up in *ca.* 15 ml. of benzene, and anhydrous ammonia was bubbled through the solution for 1 hour. The solution was treated with chloroform–water. The aqueous layer was separated and extracted several times with chloroform. The combined chloroform layers were evaporated to dryness *in vacuo*, and the residue was chromatographed over alumina. Recrystallization of the crystalline fraction from ethyl acetate gave a total of 1.10 g. (78% of theoretical). An analytical sample crystallized from benzene–ligroin as long fine needles, m.p. 105–107°, ν_{max} 1651 (Nujol).

Anal. Calcd. for $C_{15}H_{17}ON$: C, 79.26; H, 7.54; two C–CH_3, 13.22. Found: C, 79.25; H, 7.41; C–CH_3, 9.83.[18]

7-Ethyl-β-methyl-2-naphthaleneëthylamine (VI).—A 1.1-g. sample of the above amide in 100 ml. of anhydrous ether was added slowly to a stirred suspension of 1.8 g. of lithium aluminum hydride in ether. After the solution had refluxed for 4 hours it was allowed to cool, and ethyl acetate was added dropwise until reflux ceased. Moist ether was then added in small portions until no vigorous evolution occurred and finally several milliliters of water were added with stirring until the precipitated salts became white and coagulated. The inorganic material was collected and washed repeatedly with ether to give 825 mg. of crude resinous product. This material then was taken up in benzene and extracted with dilute hydrochloric acid. The acid layer was basified and extracted with benzene. Saturation of the benzene solution with anhydrous hydrogen chloride, with subsequent evaporation to dryness *in vacuo* several times gave, after repeated crystallization from benzene, 780 mg. of hydrochloride (65% of theoretical), m.p. 209–211°. An analytical sample prepared by recrystallization from ethanol–ether had m.p. 208–209°.

Anal. Calcd. for $C_{15}H_{19}N\cdot HCl$: C, 72.12; H, 8.07. Found: C, 72.03; H, 8.00.

Picrate, from acetone–ether, m.p. 215–218°.

Anal. Calcd. for $C_{15}H_{19}N\cdot C_6H_3N_3O_7$: C, 57.01; H, 5.01. Found: C, 57.09; H, 4.93.

1-Methyl-6-ethyl-1,2,3,4-tetrahydro-3-azaphenanthrene (9-Ethyl-4-methyl-1,2,3,4-tetrahydrobenz[h]isoquinoline).—To a solution of 445 mg. of the above amine hydrochloride in 10 ml. of 2 *N* hydrochloric acid containing a minimum of ethanol, was added 2 ml. of a 40% formalin solution. The reaction mixture was heated on the steam-bath for 2.5 hours, and allowed to stand at room temperature overnight. It then was evaporated to dryness *in vacuo* several times with benzene. The residue was taken up in ethanol and diluted with ether. A crop of yellow crystals was obtained, 367 mg. (78% of theoretical), m.p. 217–220°. Several recrystallizations from ethanol–ether gave an analytical sample, m.p. 217–221°.

Anal. Calcd. for $C_{16}H_{19}N\cdot HCl$: C, 73.40; H, 7.70. Found: C, 73.70; H, 7.66.

A 350-mg. sample of hydrochloride was hydrolyzed with dilute sodium hydroxide, taken up in benzene and evaporated to dryness *in vacuo* to give 276 mg. of nearly colorless oil.

1-Methyl-6-ethyl-3-azaphenanthrene (9-Ethyl-4-methylbenz[h]isoquinoline) (II).—A sample of the above material (262 mg.) was treated with 100 mg. of 10% palladium-on-carbon at 225–235° for 45 minutes. After cooling, the material was taken up in hot ligroin, filtered to remove catalyst, and concentrated. On standing there was obtained 121 mg. (55% of theoretical) of crystals, m.p. 74.5–82.5°. Recrystallization from ligroin gave an analytical sample, m.p. 83.5–85°. A mixture with an authentic sample from the dehydrogenation of atisine[5,13] showed m.p. 83.5–85°. The infrared (Fig. 3) and ultraviolet absorption spectra were identical with those of the material from atisine.

Anal. Calcd. for $C_{16}H_{15}N$: C, 86.84; H, 6.83. Found: C, 86.71; H, 6.67.

Picrate, m.p. 220–221° (undepressed on admixture with the picrate of material from atisine).

Anal. Calcd. for $C_{16}H_{15}N\cdot C_6H_3N_3O_7$: C, 58.66; H, 4.03. Found: C, 58.75; H, 3.98.

Trinitrobenzene adduct, m.p. 122.5–123.5° (undepressed on admixture with TNB of material from atisine).

Anal. Calcd. for $C_{16}H_{15}N\cdot C_6H_3N_3O_6$: C, 60.82; H, 4.18. Found: C, 60.94; H, 4.09.

NEW YORK, N. Y.

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