SYNTHESIS OF THE LACTONE OF 2-CARBOXY-4-HYDROXY-7-METHOXY-1, 2, 3, 4-TETRAHYDROPHENANTHRONE

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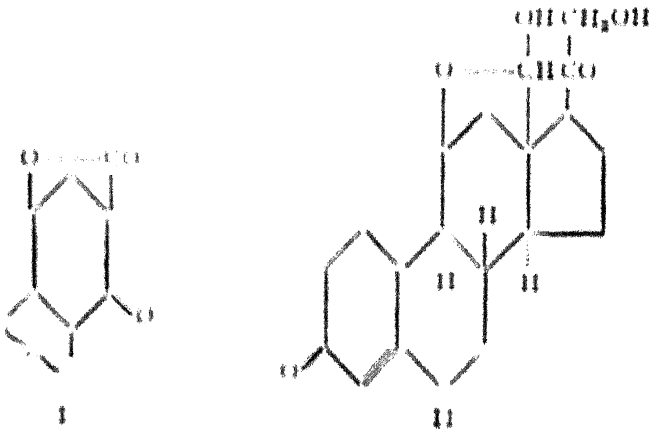
The high physiological activity of aldosterone prompted us to undertake the investigation on the synthesis of its analogues where the hydrindane system was fused with aromatic nuclei. These might be expected to have interesting physiological properties in view of Simpson and Tait's[1] observation that in its high biological potency and low concentration in biological fluids aldosterone resembles the oestrogens rather than the adrenal hormones.

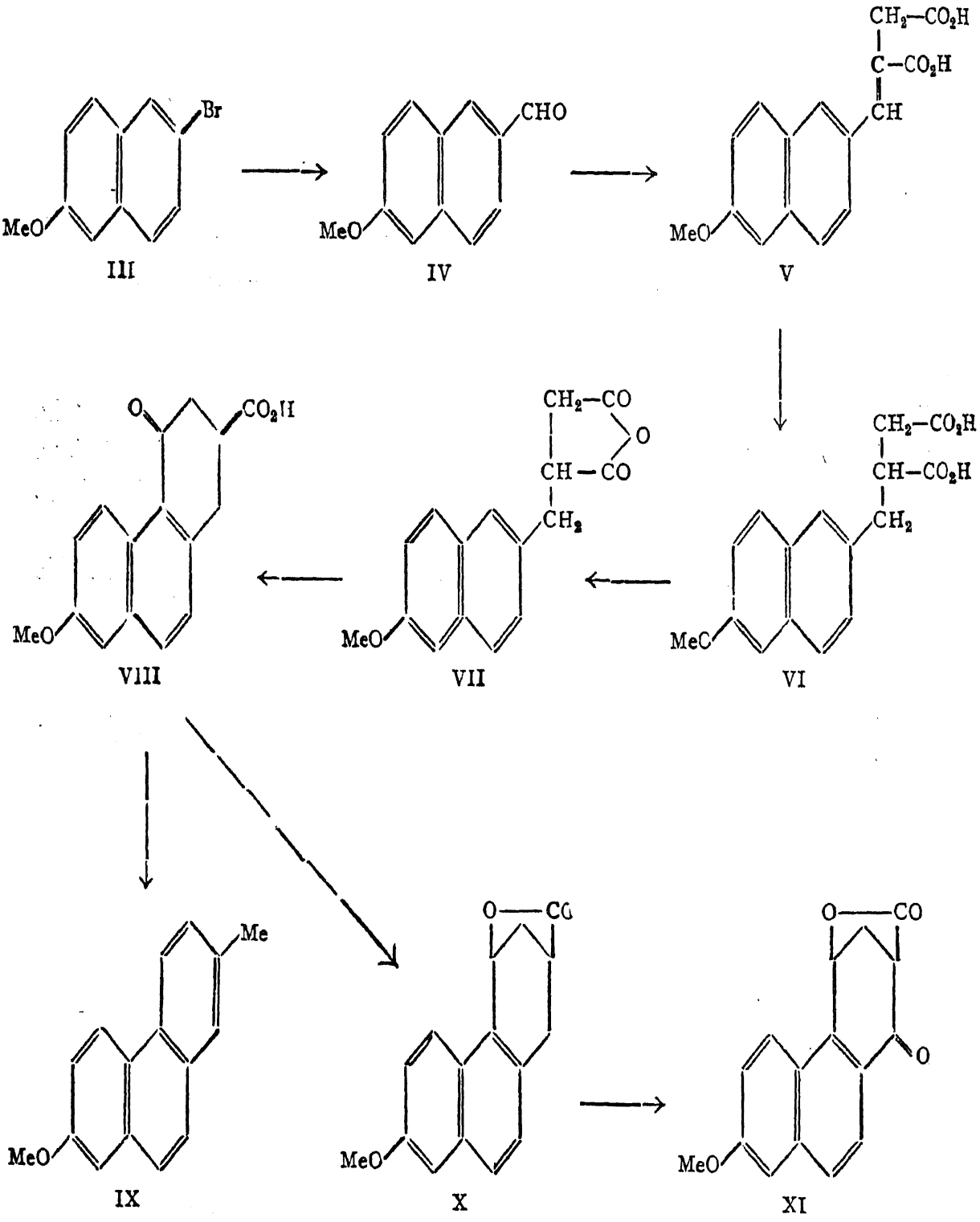
For these analogues it was considered desirable to build the five-membered ring on compounds with the partial structure (I) possessing a β-keto-



I II

lactone group which might be easily convertible to the hemi-acetal group of aldosterone (II) at a later stage, after formation of the D-ring. With this end in view the lactone of 2-carboxy-4-hydroxy-6-methoxytetralone (XII) was prepared and reported in an earlier paper.[2] The present paper deals with the synthesis of the lactone of 2-carboxy-4-hydroxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone (XI) starting from 6-methoxynaphthaldehyde-2 (IV).

6-Methoxynaphthaldehyde-2 (IV) was prepared by the method of Tard,



Lapin and Horeau,[3] which consisted of the condensation of the Grignard reagent prepared from 2-bromo-6-methoxynaphthalene (III) in tetrahydrofuran[4,5] with dimethyl formamide. Another method employed by us was to condense 2-lithium-6-methoxynaphthalene[3] with dimethyl formamide in ether without impairing the yield.

The Stobbe condensation of the aldehyde (IV) with dimethyl succinate in refluxing methanolic sodium methoxide followed by *in situ* hydrolysis of

the half-ester furnished γ-(6-methoxy-2-naphthyl)-itaconic acid (V). Reduction of an alkaline solution of the unsaturated diacid (V) with nickel aluminium alloy[7] at 90° yielded γ-(6-methoxy-2-naphthyl)-β-carboxybutyric acid (VI), the equivalent weight and analytical data indicated that the methoxyl group was not eliminated, as was observed in a few instances of similar reductions.[8] Treatment of the diacid (VI) with acetyl chloride yielded the anhydride (VII).

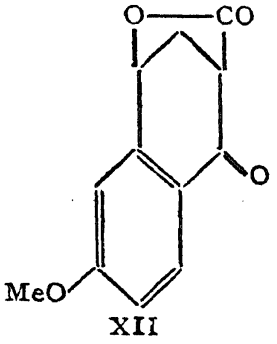
Friedel-Crafts cyclisation of the anhydride (VII) could theoretically yield the following four compounds: (i) 2-carboxy-7-methoxy-4-oxo-1, 2, 3, 4-tetrahydrophenanthrene (VIII); (ii) 3-carboxy-6-methoxy-1-oxo-1, 2, 3, 4-tetrahydroanthracene; (iii) 6, 7-(5′-methoxybenzo)-indanone-2-acetic acid; (iv) 5, 6-(5′-methoxybenzo)-indanone-2-acetic acid. It is known that the angularly-fused ring-formation is preferred to the linear one and that Friedel-Crafts cyclisation yields six-membered rings in preference to five-membered ones,[9] therefore, it was hoped that the phenanthroic acid (VIII) would be the major product. The reaction yielded a solid which after a single crystallisation melted at 217°. The ultra-violet absorption maxima at 245·5 mμ log ε 4·59, 310·5 mμ log ε 3·88 and 350 mμ log ε 3·57 have close resemblance to those reported for 3-methoxy-11-oxoequilenane by Newman *et al.*[6] The carbonyl region of the infra-red spectrum (in Nujol) showed two peaks at 1665 cm.$^{-1}$ (conjugated cyclohexane carbonyl) and 1705 cm.$^{-1}$ (acid dimer); a conjugated cyclopentane carbonyl and the acid dimer peaks might be expected to overlap.

Chemical proof in favour of the phenanthrene structure for the compound obtained by cyclisation of the anhydride (VII) was provided as follows. The keto-acid was treated with lithium aluminium hydride, and the crude diol on dehydration with potassium hydrogen sulphate followed by dehydrogenation with 30% palladium on charcoal yielded 7-methoxy-2-methylphenanthrene (IX).[10]

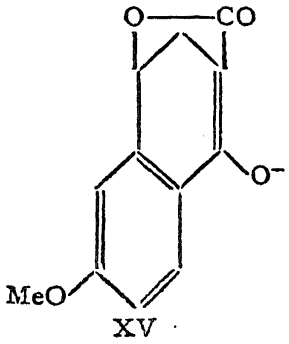
Reduction of a neutral aqueous solution of the sodium salt of 2-carboxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone-4 (VIII) with sodium borohydride afforded the lactone (X). Oxidation of the lactone (X) with chromium trioxide in acetic acid yielded the lactone of 2-carboxy-4-hydroxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone (XI).

We next investigated the alkylation of the β-keto-lactone system (I) in order to form the D-ring. Condensations of the keto-lactone (XII)[2] with diethylaminobutan-2-one methoiodide in the presence of sodium hydride

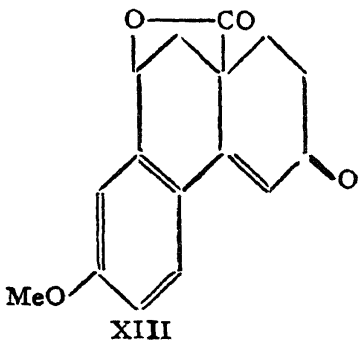
or potassium in benzene and with methallyl chloride in the presence of potassium carbonate and potassium iodide[11] resulted in the recovery of the keto-lactone (XII). Condensation with methyl vinyl ketone in the presence of



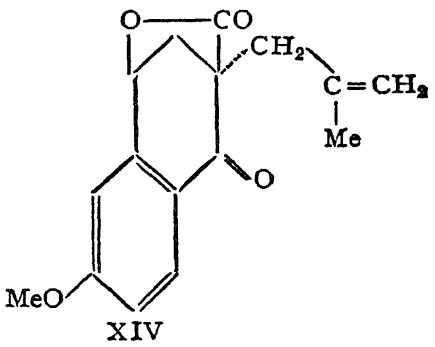
XII



XV



XIII



XIV

"Triton B"[12] or with diethylamino-butan-2-one methoiodide with sodium hydride in pyridine did yield a small quantity of a chromatographed fraction having the anticipated ultra-violet peak at 323 mμ (for the structure XIII), but the materials were extremely impure (ϵ *ca.* 500). When the potassio-derivative of the keto-lactone (XII), prepared by treating the keto-lactone (XII) with potassium *t*-butoxide and then completely removing the *t*-butanol under anhydrous conditions,[13] was treated with methallyl chloride in acetone, a small quantity of a material with ultra-violet peaks at 224·5 mμ log ϵ 4·01 and 277 mμ log ϵ 3·94, presumably (XIV), was obtained on repeated chromatography of the reaction product.

Presumably, the reason for the failure of alkylation of the keto-lactone (XII) is that the formation of the enolate ion (XV) constitutes the violation of Bredt's rule.[14, 15, 16]

EXPERIMENTAL

6-Methoxynaphthaldehyde-2 (IV).—To a vigorously stirred and cooled (ice and salt) solution of dry 2-bromo-6-methoxynaphthalene (III) (12·0 g.) in anhydrous benzene (75 ml.) under a stream of nitrogen was added an ethereal solution of *n*-butyllithium[17] (from 1·08 g. of lithium and 8·56 g. of *n*-butyl

bromide and 100 ml. of ether) over a period of 5 min. After stirring the reaction mixture for a further 20 min. at — 5°, a solution of dimethyl formamide (4·4 g.) in dry benzene (5 ml.) was added slowly within 5 min. The pale green reaction mixture was left under the nitrogen atmosphere for 2 hours at 0° and then slowly raised to room temperature overnight. The reaction mixture was decomposed (0°) with aqueous ammonium chloride. The organic phase was separated and the aqueous phase extracted with ether. The combined organic phase was washed with water and dried, and the solvent was removed. The crude residue was crystallised from ether-light petroleum (40-60°) to yield 6-methoxy-naphthaldehyde-2 (IV) (5·9 g.) m.p. 74-79°. It was recrystallised from benzene-hexane, m.p. 81° (reported[3] 79°); U.V.: $\lambda_{max.}^{rlc.}$ 243 mμ log ε 4·56, 248 mμ log ε 4·56, 261 mμ log ε 4·44 and 310-12 mμ log ε 4·20 (Found: C, 77·2; H, 5·5. Calc. for $C_{12}H_{10}O_2$. C, 77·4; H, 5·4%).

γ-(6-Methoxy-2-naphthyl)-itaconic Acid (*V*).—To a vigorously stirred refluxing solution of methanolic sodium methoxide, prepared from sodium (1·92 g.) and methanol (20 ml.), was cautiously added a solution of the naphthaldehyde (IV) (6·2 g.) and freshly distilled dimethyl succinate (5·35 g.) in methanol (50 ml.) and benzene (10 ml.). The stirring and refluxing were continued for 2·5 hours, then water (100 ml.) was added cautiously (considerable bumping occurs due to the separation of solid) with simultaneous distillation of the methanol. When the methanol had ceased to distil, the contents were cooled and added to water (100 ml.). The aqueous solution of the sodium salt was washed with ether and then run into an excess of cold 6N-hydrochloric acid. The pale yellow precipitate (5·43 g.), m.p. 175–185° d., was crystallised from aqueous alcohol (norit). The *itaconic acid* (V) melted at 196–197° d.; U.V.: $\lambda_{max.}^{alc.}$ 220 mμ log ε 4·50, 263 mμ log ε 4·52 and 301 mμ log ε 4·26 (Found: C, 66·8; H, 5·1%; eq. wt. 146·3. $C_{16}H_{14}O_5$ requires C, 67·2; H, 4·9%; eq. wt. 143·1).

γ-(6-Methoxy-2-naphthyl)-β-carboxybutyric Acid (*VI*).—To a well-stirred solution of the unsaturated diacid (V) (3·6 g.) in 10% aqueous sodium hydroxide (100 ml.), kept at 92–93°, was added a few drops of octyl alcohol and then, in small portions, 1 : 1-nickel-aluminium alloy (10 g.) over a period of 25 min. The stirring was continued for 1 hour at 95°, and then the hot material was filtered carefully under suction, the catalyst being washed well with hot water. The warm filtrate was slowly run into concentrated hydrochloric acid (300 ml.) with efficient stirring. The milky solution deposited a white precipitate (2·35 g.), m.p. 168–170°. *γ-(6-methoxy-2-naphthyl)-β-carboxybutyric acid* (*VI*) was crystallised from aqueous alcohol, m.p. 170–71°;

U.V.: $\lambda_{max.}^{alc.}$ 227 mμ log ε 4·79, 262 mμ log ε 3·75, 272 mμ log ε 3·75, 318 mμ log ε 3·27 and 332 mμ log ε 3·35 (Found: C, 66·7; H, 5 4%; eq. wt. 145·3. $C_{13}H_{16}O_3$ requires C, 66·7; H, 5·6%; eq. wt. 144·1).

Anhydride of γ-(6-Methoxy-2-naphthyl)-β-carboxybutyric Acid (VII).—To the diacid (VI) (2·20 g.) was added an excess of acetyl chloride (50 ml.); the flask became cold during the dissolution of the acid and a clear pale yellow solution was obtained. After 6 hours at room temperature, the acetyl chloride was completely removed, and the residue (2·00 g.), m.p. 139–40°, was crystallised from dry benzene-light petroleum (40–60°) to yield the *anhydride of γ-(6-methoxy-2-naphthyl)-β-carboxybutyric acid (VII)*, m.p. 140° (Found: C, 70·8; H, 5·1% $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%).

2-Carboxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone-4 (VIII).—A solution of the anhydride (VII) (1·87 g.) in nitrobenzene (50 ml.) was run into a well-stirred solution of aluminium chloride (2·7 g.) in nitrobenzene (20 ml.) at room temperature (23°). After stirring overnight the product was decomposed with ice and hydrochloric acid. After removal of the nitrobenzene by steam-distillation, a solid (1·84 g.), m.p. 200–10°, was isolated by filtration of the cooled mixture. *2-Carboxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone-4 (VIII)* was crystallised from aqueous alcohol (norit), m p. 217°; U.V.: $\lambda_{max.}^{alc.}$ 245·5 mμ log ε 4·59, 310·5 mμ log ε 3·88 and 350 mμ log ε 3·57; I.R. (Nujol): 3·39 μ (hydroxyl), 5·87 μ (acid dimer), 6·01 μ (conjugated cyclohexane carbonyl) (Found: C, 70·8; H, 5·1%; eq. wt. 269·7. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%; eq. wt. 270·3).

Conversion of 2-Carboxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone-4 (VIII) into 7-Methoxy-2-methylphenanthrene (IX).—A solution of the keto-acid (VIII) (0·5 g.) in tetrahydrofuran (75 ml.) was added slowly with swirling to lithium aluminium hydride (0·15 g.) in tetrahydrofuran (100 ml.). After standing the mixture for 1 hour at room temperature, it was refluxed for 2 hours. It was then decomposed at 0° by cautious addition of a little water followed by cold 10% sulphuric acid (20 ml.). The mixture was poured into water and repeatedly extracted with ether. The ethereal extract was washed successively with cold potassium carbonate solution and brine, and then dried. After removal of the solvent, the neutral viscous residue (0·18 g.) was heated with freshly fused potassium bisulphate (2 g.) at 170–175° in an atmosphere of nitrogen. The dehydrated product (0·094 g.), isolated by short-path distillation at 150–60° (bath)/1 mm., was dehydrogenated in a Heymann's apparatus with 30% palladium on carbon (100 mg.) under a stream of carbon dioxide at 310–30° for 2·5 hours. The sublimate (0·04 g.), m.p. 130–40°,

was crystallised as described by Bachmann and Chemerda,[10] when 7-methoxy-2-methylphenanthrene (8 mg.), m.p. 142–43° (reported[10] 144·5–45·5°), was obtained (Found: C, 86·2; H, 6·2%. $C_{16}H_{14}O$ requires C, 86·5; H, 6·4%).

Lactone of 2-*Carboxy*-4-*hydroxy*-7-*methoxy*-1, 2, 3, 4-*tetrahydrophenanthrene* (*X*).—Sodium borohydride (0·50 g.) was added to a solution oft he keto-acid (VIII) (4·50 g.) in 1 N-sodium hydroxide (16·7 ml.), and the contents were allowed to stand overnight at room temperature (23°). Dilute suphuric acid (5·1 ml. of concentrated acid in 100 ml. of water) was added and the contents heated for 15 min. on a boiling water-bath. It was cooled and poured into a large quantity of ether (*ca.* 1 l.) and the aqueous phase separated. The ether solution was washed with cold sodium bicarbonate solution and brine, and then dried. After removal of the solvent, the white waxy material (0·38 g.) was repeatedly triturated with hexane containing a trace of benzene. After removal of the liquid portion, the *lactone of* 2-*carboxy*-4-*hydroxy*-7-*methoxy*-1, 2, 3, 4-*tetrahydrophenanthrene* (*X*) was left as a white waxy solid, m.p. 48–51°; U.V.: $\lambda_{max.}^{alc.}$ 234 mμ log ε 4·74, 263 mμ log ε 3·76, 319 mμ log ε 3·28 and 334 mμ log ε 3·32; I.R. ($CHCl_3$): 5·66 μ (γ-lactone) (Found: C, 75·5; H, 5·7%. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%).

Lactone of 2-*Carboxy*-4-*hydroxy*-7-*methoxy*-1, 2, 3, 4-*tetrahydrophenanthrone* (*XI*).—To a solution of the lactone (X) (0·24 g.) in glacial acetic acid (2·1 ml.) and propionic acid (0·4 ml.), kept at 0°, was added a solution of chromium trioxide (0·2 g.) in water (0·2 ml.) and acetic acid (1·1 ml.) over a period of 7 min. It was kept for 40 min. at 0° and overnight at room temperature. After destroying any excess oxidising mixture with a little methanol, the contents were poured into water (50 ml.) and extracted with ether. The ether extract was washed with cold potassium carbonate solution and brine, and then dried (Na_2SO_4). After removal of the solvent, the white waxy residue was triturated with light petroleum (40–60°), when an amorphous powder (0·08 g.), m.p. 62–67°, was obtained. Crystallisation from ether-light petroleum (40–60°) yielded the *lactone of* 2-*carboxy*-4-*hydroxy*-7-*methoxy*-1, 2, 3, 4-*tetrahydrophenanthrone* (*XI*), m.p. 66–69°; U.V.: $\lambda_{max.}^{alc.}$ 254 mμ log ε 4·56, 265·5 mμ log ε 4·56, 290 mμ log ε 3·99, 301 mμ log ε 4·06 and inflexions at 245 mμ log ε 4·48, 282 mμ log ε 4·40 and 312 mμ log ε 3·92; I.R. ($CHCl_3$): 5·62 μ (γ-lactone), 5·8 μ (conjugated cyclohexane carbonyl) (Found: C, 71·2; H, 4·7.% $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%).

Alkylation Experiments with the Keto-lactone (*XII*)

(*a*) *Using Methallyl Chloride in the presence of Potassium Carbonate and Potassium Iodide.*[11]—To a stirred mixture of the keto-lactone (XII) (1·09 g.)

dry potassium iodide (1·0 g.), freshly prepared potassium carbonate (1·36 g.) and anhydrous acetone (40 ml.) under a dry nitrogen atmosphere was added freshly distilled methallyl chl ride (10 ml.) in fi e lots over 72 hours at room temperature. The reaction product was cocentrated in vacuum, water (100 ml.) was added, and the product extracted with ether (3 × 100 ml.). The ether solution was washed with brine and dried (Na_2SO_4), and the solvent was removed. The solid residue (1·0 g.) melted at 134–36° and was identified as the starting keto-lactone (XII).

(*b*) *Using Methallyl Chloride in the presence of Potassium t-Butoxide.*[13]—A solution of the keto-lactone (XII) (1·09 g.) in *t*-butanol (10 ml.) was added to a stirred solution of potassium *t*-butoxide, from potassium (0·21 g.) and *t*-butanol (20 ml.), under an atmosphere of nitrogen. The suspension was stirred overnight at room temperature and then made completely free from solvent under suction. To the residue, kept under nitrogen, was added dry acetone (50 ml.), anhydrous potassium iodide (1 g.) and methallyl chloride (3·2 g.) in acetone (30 ml.). After 50 hours at room temperature, the acetone was removed under reduced pressure, water (50 ml.) was added and the material extracted with ether. The ether solution was washed with sodium thiosulphate solution and brine, and then dried (Na_2SO_4). After removal of the solvent, the crude material (1·1 g.) was chromatographed over acid-washed alumina (30 g.) when a fraction (0·17 g.) showing ultra-violet absorption maxima at 224 mμ and 277 mμ was obtained in the benzene eluates. Short-path distillation, 100° (bath)/0·005 mm., and rechromatography over acid-washed alumina yielded the *lactone of 2-carboxy-4-hydroxy-2-methallyl-6-methoxytetralone* (*XIV*); U.V.: $\lambda_{max.}^{alc.}$ 224·5 mμ log ε 4·01 and 277 mμ log ε 3·94 (Found: C, 70·8; H, 6·3. $C_{16}H_{18}O_4$ requires C, 70·6; H, 5·9%).

(*c*) *Using Diethylaminobutan-2-one Methoiodide in the presence of Potassium.*—A solution of the keto-lactone (XII) (1·1 g.) in benzene (30 ml.) was added in 5 min. to a suspension of potassium dust (0·20 g.) in benzene (10 ml.) in an atmosphere of nitrogen. The contents were refluxed for 8 hours and to the cooled (0°) material diethylaminobutan-2-one methoiodide[18] (1·70 g.) in pyridine (8 ml.) was added. After 3 hours at room temperature and 14 hours under reflux, the product was decomposed with 6 N-hydrochloric acid (50 ml.). The material was extracted with ether, and after washing the organic phase with sodium bicarbonate solution and brine, the solvent was removed. The gummy residue (0·85 g.) on crystallisation from benzene-light petroleum (40–60°) yielded the starting keto-lactone (XII), m.p. and mixed m.p. 136–37°.

(*d*) *Using Diethylaminobutan-2-one Methoiodide in the presence of Sodium Hydride in Benzene.*—A solution of the keto-lactone (XII) (0·55 g.) in benzene

(35 ml.) was added to a suspension of sodium hydride (0·12 g.) in benzene (30 ml.) under nitrogen. After refluxing for 4 hours, to the cooled contents was added diethylaminobutan-2-one methoiodide[18] (0·84 g.) in pyridine (8 ml.), and after stirring the mixture for 8 hours at room temperature, it was kept under reflux for 5 hours. The reaction product was decomposed and worked up as usual, when the starting keto-lactone (XII) (0·35 g.), m.p. 135–36°, was obtained.

(*e*) *Using Diethylaminobutan-2-one Methoiodide in the presence of Sodium Hydride in Pyridine.*—A solution of the keto-lactone (XII) (0·90 g.) in pyridine (35 ml.), and sodium hydride (0·12 g.) was stirred for 18 hours under nitrogen at room temperature (26–28°). The contents were cooled (0°) and diethylaminobutan-2-one methoiodide[18] (1·40 g.) in pyridine (10 ml.) was added. After leaving the mixture for 3 hours in an ice-bath and overnight at room temperature, dry ether (100 ml.) was added and the contents gently refluxed for 1 hour. It was cooled, dry ether (100 ml.) was added, and the contents were poured with stirring into crushed ice (500 g.) and hydrochloric acid (100 ml.). The ether layer was separated and the aqueous layer extracted with ether. The combined ether solution was washed successively with water-sodium bicarbonate solution and brine. After drying (Na_2SO_4), the solvent was removed and the residue (0·70 g.) on short-path distillation at 150–70° (bath)/0·005 mm. yielded a viscous material (0·50 g.). Chromatography of the distillate over acid-washed alumina (15 g.) yielded in the 1 : 1 benzene-light petroleum (40–60°) eluates a material having ultra-violet absorption maxima at 322 mμ log ε 2·81 and 336 mμ log ε 2·42 (log ε calc. for XIII).

(*f*) *Using Methyl Vinyl Ketone in the presence of "Triton B".*[12]—To a solution of the keto-lactone (XII) (0·55 g.) in absolute ethanol (5 ml.) was added 37% methanolic "Triton B" (1·3 ml.) and 85% methyl vinyl ketone (0·65 ml.), and the contents were refluxed for 2 hours on a steam-bath. It was cooled to 0°, 3 N-hydrochloric acid (2 ml.) was added and the mixture then heated for 30 min. on a steam-bath. The contents were concentrated under reduced pressure and then worked up as usual. Chromatography of the crude residue (0·42 g.), obtained after removal of the solvent, on acid-washed alumina (14 g.), yielded in the alcohol eluates a material (0·08 g.) having ultra-violet absorption maximum at 322–24 mμ log ε 3·1 (log ε calc. for XIII).

Summary

Starting from 6-methoxynaphthaldehyde-2, 2-carboxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone-4 was prepared. Sodium borohydride reduction of the keto-acid followed by chromic acid oxidation yielded the lactone of

2-carboxy-4-hydroxy-7-methoxy-1, 2, 3, 4-tetrahydrophenanthrone. Alkylation of the lactone of 2-carboxy-4-hydroxy-6-methoxytetralone was not promising.

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REFERENCES

1. Simpson, S. A. and Tait, J. F. — *Recent Progress in Hormone Research*, 1955, **11**, 208.
2. Banerjee, D. K. and Bagavant, G. — *Proc. Ind. Acad. Sci.*, 1959, **50 A**, 282.
3. Tard, C., Lapin, H. and Horeau, A. — *Compt. Rend.*, 1958, **246**, 3644.
4. Robinson, R. and Slater, S. N. — *J. Chem. Soc.*, 1941, 376.
5. Woodward, R. B. and Eastman, R. H. — *J. Amer. Chem. Soc.*, 1944, **66**, 674.
6. Eglinton, G., Nevenezel, J. C., Scott, A. I. and Newman, M. S. — *Ibid.*, 1956, **78**, 2331.
7. Papa, D., Schwenk, E. and Whitman, B. — *J. Org. Chem.*, 1942, **7**, 587.
8. —— and Ginsberg, H. F. — *Ibid.*, 1944, **9**, 1.
9. Johnson, W. S. .. — *Organic Reactions*, Vol. II, John Wiley and Sons, Inc., New York, 1944, p. 116.
10. Bachmann, W. E. and Chemerda, J. M. — *J. Amer. Chem. Soc.*, 1948, **70**, 1472.
11. Uehlinger, H. P., Ch. Tamm and Reichstein, T. — *Hel. Chim. Acta*, 1957, **40**, 2234.
12. Poos, G. I., Arth, G. E., Bayler, R. E. and Sarett, L. H. — *J. Amer. Chem. Soc.*, 1953, **75**, 425.
13. Stork, G., Loweenthal, H. J. E. and Mukharji, P. C. — *Ibid.*, 1956, **78**, 501.
14. Bredt, J., Thoubet, H. and Schmitz, H. — *Ann.*, 1924, **437**, 4.
15. Fawcett, F. S. .. — *Chem. Revs.*, 1950, **47**, 249.
16. Prelog, V. .. — *J. Chem. Soc.*, 1950, 425.
17. Gilman, H., Beel, J. A., Brannen, C. G., Bullock, M. W., Dunn, G. E. and Miller, L. S. — *J. Amer. Chem. Soc.*, 1949, **71**, 1499.
18. Wilds, A. L. and Shunk, C. H. — *Ibid.*, 1943, **65**, 471.

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