SYNTHETIC ANALOGUES OF ADRENAL CORTICAL HORMONES: SOME 6:7:8:9-TETRAHYDRO-4:5-BENZINDANES

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6:7:8:9-Tetrahydro-1-oxo-4:5-benzindane and its 3′-methoxy analogue have been synthesised from 1-oxotetralin and 1-oxo-6-methoxytetralin. Side chains typical of cortical hormones have been built up by known methods via the intermediate ethynyl alcohols: 1-acetoxy-1-glycollyl-6:7:8:9-tetrahydro-4:5-benzindane has thus been produced. In the case of the corresponding methoxy analogue, ring expansion probably occurs to furnish the corresponding "homo" compound—a substituted hydrophenanthrene.

The action of basic reagents on 2-cyano-6-methoxy-2-methyl-1-oxotetralin leads to ring fission and the formation of γ(2-carboxy-5-methoxyphenyl) α-methylbutyronitrile.

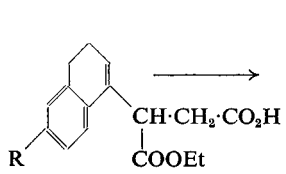
For the purpose of biological evaluation as adrenal cortical analogues, the attempted synthesis of two 4:5-benzindan derivatives I, (R = H, OMe) is described. This may be regarded as an extension of published work[1] on bicyclic steroid analogues.

Synthesis of the tricyclic ketones

Construction of the carbon skeleton of such compounds started most conveniently by attaching a five membered ring on to the readily available 1-oxo tetralin and 1-oxo-6-methoxytetralin, the method used being that described by Johnson[2] and outlined overleaf (formulae II → IV). Thus, starting from 1-oxo-tetralin, condensation with diethylsuccinate in presence of potassium *tert.*-butoxide gave the intermediate half ester II (R = H) which was smoothly cyclised with zinc chloride:acetic anhydride to yield 6:7-dihydro-1-oxo-4:5-benzindane (III, R = H)[2]. With 6-methoxy-1-oxo-tetralin, slight modification of the published details[3] led to considerable improvement in yield. Thus as a first step the half ester II (R = OMe) was obtained in 75 per cent yield from the corresponding tetralone. Ring closure of such half esters may conceivably take two courses, either on to the benzene ring to form a perinaphthane derivative or on to the double bond, forming the required benzindan structure. Thus Johnson and colleagues[2] found with II (R = H), that with zinc chloride, III (R = H) was obtained, whilst with anhydrous hydrogen fluoride, V resulted, accompanied by disproportionation products. Consideration, however, of the structure of II (R = OMe) led to the conclusion that position 8 would be deactivated towards attack by an electrophilic reagent and that during ring closure (attack by an acyl carbonium ion) only one product would obtain viz. III (R = OMe). This proved to be so and III (R = OMe) resulted with either anhydrous hydrogen fluoride or zinc chloride:acetic anhydride. The structure of the

product was confirmed by dehydrogenation to 1-oxo-4:5-(3′-methoxy) benzindane identical with a specimen previously described by Billeter and Miescher[4].

Hydrogenation of the unsaturated ketones III (R = H, OMe) was easily accomplished[5] to give the requisite saturated compounds IV (R = H, OMe). Although concomitant reduction of the ketone group to secondary alcohol took place to some extent, reoxidation with chromic anhydride was readily effected.



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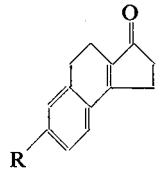

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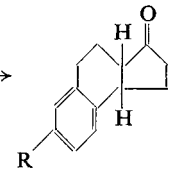

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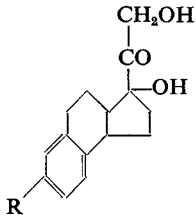

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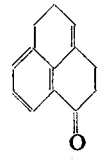

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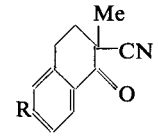

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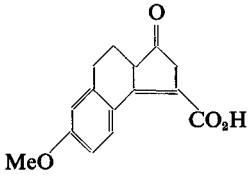

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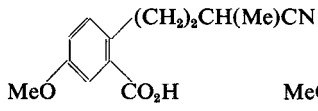

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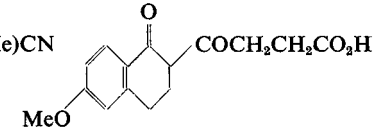


(VIII)

Several alternative routes to these and similar tricyclic ketones were explored and one unsuccessful attempt has already been described elsewhere[6]. Analogously with that report it has now been found that treatment of VI (R = OMe) with potassium *tert.*-butoxide (and other basic reagents) leads to ring fission and the production of the acid VII. For this reason we were unable to effect a Stobbe condensation between VI (R = OMe) and diethylsuccinate.

In place of potassium *tert.*-butoxide, the use of sodium hydride as a condensing agent[7,8] has been explored. With 1-oxo-tetralin, the dicarboxylic acid corresponding to II (R = H) resulted, that is the normal "Stobbe" type of condensation. With 6-methoxy-1-oxo-tetralin, however, nearly half of the product consisted of a monocarboxylic acid which displayed anomalous properties. It was assigned the structure VIII on the following evidence and would arise by the alternative "Claisen" type of condensation: (cf. Daub and Johnson[8]). (i) It gave a green colour

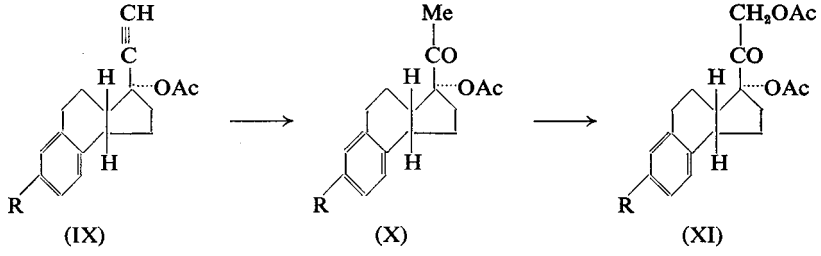
with ferric chloride, (ii) it proved stable to acid and was degraded by alkali to 6-methoxy-1-oxotetralin (iii), its spectroscopic properties are λmax 350 mμ ε 16,980 (ethanol): λmax 360 mμ ε 21,300 (0·1N NaOH). These spectral characteristics are in accord with the analogous case of benzoyl acetone, the bathochromic shift in 0·1N alkali being attributed by Morton, Hassan and Calloway[9] to the enolate ion.

Whilst 6:7:8:9:-tetrahydro-1-oxo benzindane IV (R = H) was a colourless oil and therefore difficult to assess from a stereochemical viewpoint, the methoxy analogue IV (R = OMe) proved to be a crystalline substance of sharp melting point and was deemed stereochemically homogenous. Comparison with other hexahydroindanes suggests that the more stable form of this substance would be *cis* about the C(8)–C(9) bond (cf. the classical work of Hückel and also references cited by Dreiding[10]).

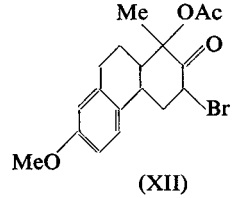
In addition, and more directly analogous, there remains the change from equilin to 14-*epi*-$\Delta^{8:9}$ equilin[11] and of 3-desoxyequilenin to 3-desoxy-14-*epi*-equilenin[12]: both isomerisations represent a change from a *trans* fusion of rings C and D to a *cis*. For these reasons the tentative assignment of the 6–5 membered ring junction in IV (R = OMe) is *cis*. Such is probably the case where R = H likewise.

Attachment of the Side Chain

By reacting the saturated ketones IV (R = H, OMe) with potassium acetylide in ether the corresponding ethynyl alcohols were obtained and these were converted to their acetates, IX (R = H, OMe).



(IX) (X) (XI)



(XII)

Addition of aniline to the triple bond by the method of Stavely[13] gave an anil which was readily hydrolysed to the ketone X. With X (R = H) the resulting ketone was brominated then treated with potassium acetate in acetone[14]: 1-glycollyl-1-hydroxy-6:7:8:9-tetrahydro-4:5-benzindan diacetate XI (R = H) thus resulted. With the ethynyl acetate IX (R = OMe), on the other hand, addition of aniline

undoubtedly gave a ketone and this in turn furnished a bromo ketone. Using a large variety of conditions, however, we were unable to effect replacement of this bromine atom either by the acetoxy or hydroxyl grouping. Under many conditions of hydroxylation of the triple bond ethynyl alcohols of the steroid series undergo at the same time a rearrangement similar to the pinacol rearrangement thus causing ring expansion to the so-called D-homo steroids[15]. With IX (R = OMe) the corresponding homo compound would probably have the structure shown in XII without the bromine atom. Although the conditions of Stavely[13] used here were specifically designed to avoid this rearrangement, such may in fact have occurred. Bromination of the "homo compound" would then furnish a substituted bromo*cyclo*hexanone XII where the bromine atom would be most likely to occupy an axial position[16] and thus be relatively inert to the action of alkali.

The ethynyl acetates IX (R = H, OMe) isolated in crystalline form would appear to be stereochemically homogenous and a tentative assignment of configuration is shown in IX (cf. reference 1). The same configuration applies to X and XI (R = H).

EXPERIMENTAL

β-Carbethoxy-β [1-(3:4-*dihydro*-6-*methoxy*) *naphthyl*] *propionic acid* (II, R = OMe). (i) *Stobbe condensation with potassium* tert.-*butoxide.* 6-Methoxy-1-oxotetralin (50 g.) and diethyl succinate (75 g.) were refluxed for 7 hours under nitrogen with potassium *tert.*-butoxide (from potassium (15 g.) and *tert.*-butanol (600 ml.)). After cooling, the *tert.*-butanol was removed *in vacuo*, water was added to the residue and this was extracted with ether. The acidic fraction was then removed therefrom with 10 per cent sodium carbonate solution, reprecipitated with hydrochloric acid and extracted again with ether. Evaporation gave a yellow gum, 66 g. (75 per cent) b.p. 190° at 0·5 mm.[3] Found: C, 66·9; H, 6·4; titration equivalent 300. Calc. for $C_{17}H_{20}O_5$, C, 67·1; H, 6·6 per cent. Titration equivalent 304. Light absorption in ethanol λmax 273 mμ (ε 10,000).

(ii) *With sodium hydride.* 6-Methoxy-1-oxotetralin (17·6 g.) and diethyl succinate (52 g.) were dissolved in benzene (300 ml.) and the solution dried azeotropically by distilling a 50 ml. portion of solvent. To the residual solution at 20° under nitrogen and with stirring, sodium hydride (4·8 g.) was quickly added followed by ethanol (1 drop). Evolution of hydrogen, negligible at first, markedly increased after 2 hours and ceased after 4–5 hours when the mixture was gelatinous and deep red. After pouring the mixture into water, the required compound was extracted therefrom with dilute sodium hydroxide. Acidification yielded a reddish-brown oil from which a crystalline material separated. On dissolving the oil in ether remained behind and was filtered off (2 g.). The ether layer was then re-extracted with 10 per cent sodium carbonate solution and this was reacidified. Ether extraction gave a solution of the required compound which was boiled with charcoal and on evaporation gave 22 g. (72·5 per cent) of a light brown oil from which crystals separated after a few days. This crystalline substance was separated with ether as described

above (3 g. thus resulted and the oily portion (II, R = OMe) distilled (b.p. 190° at 0·5 mm.) as a yellow gum. Found: C, 66·2; H, 6·35; titration equivalent, 300. Calculated for $C_{17}H_{20}O_5$; C, 67·1; H, 6·6 per cent. Titration equivalent 304.

The bulked crystalline material (5 g.) crystallised from ethanol in pale yellow prisms m.p. 166–167°. Found: C, 65·4; H, 5·6; OCH_3, 11·4. Molecular weight (ebullioscopic in acetone), 250; titration equivalent 280; $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8; OCH_3, 11·2 per cent; titration equivalent 276. Light absorption in ethanol λmax 241 mμ (ε 4,900); 272 mμ (ε 5,300); 350 mμ (ε 16,900). By adding sodium hydride to the reactants at 60° the induction period was reduced from 2 hours to several minutes and the yield of crystalline VIII (R = OMe) was increased to about 45 per cent of the total yield.

β-Carboxy-β [1-(3:4-*dihydro*)*naphthyl*] *propionic acid.* 1-Oxotetralin (14·6 g.) and diethylsuccinate (26 g.) in dry benzene (100 ml.) were treated as described above with sodium hydride (3·6 g.). There resulted a brown oil (14 g.) which partially solidified and on crystallisation from aqueous ethanol gave m.p. 184–186° (lit.[2] value m.p. 182–182·7°) (decomp.). Found: C, 68·1; H, 5·5; titration equivalent 123. Calculated for $C_{14}H_{14}O_4$, C, 68·3; H, 5·7 per cent, titration equivalent 123. Light absorption in ethanol, λmax 261 mμ (ε 8,900).

1-*Oxo*-6:7-*dihydro*-4:5-(3′-*methoxy*)*benzindane* (III, R = OMe). To redistilled half ester II, (R = OMe) (30 g.) in a polythene bottle, anhydrous hydrogen fluoride (250 ml.) was added and allowed to stand for two days. Evaporation of the reagent left a dark brown residue which was dissolved in a mixture of glacial acetic acid and concentrated hydrochloric acid (1:1) (200 ml.) and refluxed. When evolution of carbon dioxide had ceased (1 hour), acetic acid was removed under reduced pressure and the residual acid liquors neutralised and then extracted with ether. After washing with 10 per cent sodium hydroxide, then water, the solution was treated with charcoal, dried over sodium sulphate and evaporated. A mass of yellow crystals resulted whence crystallisation from ether gave the required ketone in colourless needles m.p. 96° in agreement with the literature value.[3]

The 2:4 *dinitrophenylhydrazone* crystallised from dioxan-ethanol in dark red needles charring at 255° (Birch, Quartey and Smith[3] cite m.p. 275°). Found: C, 61·3; H, 4·8; N, 14·6. $C_{20}H_{18}O_5N_4$ requires C, 60·9; H, 4·6; N, 14·2 per cent. Light absorption, (main bands in chloroform) λmax 423 mμ (ε 37,460) 326 mμ (ε 15,580).

The *semicarbazone* crystallised from glacial acetic acid in yellow micro needles m.p. 252° (decomp.). Found: C, 66·0; H, 6·0; N, 15·9; OCH_3, 11·31. $C_{15}H_{17}O_2N_3$ requires C, 66·4; H, 6·3; N, 15·5; OCH_3, 11·4 per cent.

From the residue left on evaporation of hydrogen floride, trituration with ether gave some crystalline material m.p. 141° (with gas evolution). The crystals were soluble in sodium carbonate and on attempted crystallisation from ethanol gave only the tricyclic ketone III (R = OMe). This was probably the intermediate keto acid IIIA.

1-*Oxo*-4:5-(3'-*methoxy*) *benzindane*. The above dihydro ketone (500 mg.) was heated with sublimed sulphur (100 mg.) at 220° (1½ hr.) when hydrogen sulphide evolution had almost ceased. The tarry residue was then extracted with boiling ether, the extract decolourised with charcoal and evaporated to yield a residue 211 mg. (42 per cent). Crystallisation from ether gave the required ketone in yellow needles m.p. 135°. The semicarbazone had m.p. 284° (decomp.) (lit. values[4] are m.p. 133° and 280–284° respectively).

1-*Oxo*-6:7:8:9-*tetrahydro*-4:5-(3'-*methoxy*) *benzindane*. The dihydro ketone (22·5 g.) in *iso*propanol (700 ml.) was hydrogenated (2 hr.) at a 5 per cent palladium:barium sulphate catalyst at 80 ats. and 80°. The filtered solution yielded a light yellow oil (23 g.) which contained 56 per cent ketone on assay with 2:4-dinitrophenylhydrazine. It was therefore dissolved in glacial acetic acid (25 ml.) and to it was slowly added with stirring a mixture of sodium dichromate (15 g.), conc. sulphuric acid (10 ml.) and water (50 ml.). The temperature was kept below 60°. After addition, the whole was kept at 55° for 1 hour, then sufficient ethanol added to destroy excess dichromate. Acetic acid was then removed and the whole extracted with ether. Evaporation gave an oil 18·3 g. (80 per cent) which had b.p. 145–150° at 0·4 mm. (16 g.). The distillate partly crystallised yielding thus the required *ketone* (8 g.) m.p. 63–64° on recrystallisation from ether. A further quantity of crystalline *ketone* (4 g.) was obtained from the oily residue by formation and hydrolysis of the semicarbazone. Found: C, 78·3; H, 7·0; OCH_3, 14·2. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4; CH_3O, 14·35 per cent.

The *semicarbazone* crystallised from glacial acetic acid in small yellow needles m.p. 245°. Found: C, 66·2; H, 7·1; N, 15·5. $C_{15}H_{19}O_2N_3$ requires C, 66·0; H, 7·0; N, 15·4 per cent.

The 2:4-*dinitrophenylhydrazone* crystallised from ethanol-dioxan in red needles m.p. 220°. Found: C, 60·7; H, 4·8; N, 14·4. $C_{20}H_{20}O_5N_4$ requires C, 60·7; H, 5·1; N, 14·14 per cent. Light absorption (main band in chloroform) λmax 367·5 mμ (ϵ 24,000).

2-*Hydroxymethylene*-6-*methoxy*-1-*oxo tetralin*. Ethyl formate (5 g.) in dry benzene (40 ml.) was added at 0° over 30 minutes to sodium methoxide (from sodium 1·6 g.) under nitrogen. 6-methoxy-1-oxotetralin (5 g.) in dry benzene (40 ml.) was then added under the same conditions. After stirring (1 hr.) the mixture was allowed to stand at room temperature overnight. Water was added and the benzene layer extracted with 5 per cent sodium hydroxide. Acidification and ether extraction yielded a brown oil on evaporation of solvent. This crystallised on standing and was carried forward thus to the next stage. A sample distilled (b.p. 140–142° at 0·5 mm.) and crystallised from ether in pale greenish-yellow plates m.p. 67–68°, had the following analysis: found: C, 70·6; H, 5·5. $C_{12}H_{12}O_3$ requires C, 70·5; H, 5·9 per cent.

2-*Cyano*-6-*methoxy*-1-*oxo tetralin*. The above substance (25 g.) and hydroxylamine hydrochloride (17·5 g.) in glacial acetic acid (200 ml.) were stirred at 75° for 8 hours. Most of the acetic acid was removed, water added and the whole extracted with ether. After washing this with

sodium bicarbonate, evaporation gave the crude isoxazole (25 g.). To this was slowly added a 10 per cent solution of sodium methoxide in methanol and after standing 2 hours, the whole was diluted with water and impurities extracted with ether. Acidifying the aqueous phase followed by ether extraction, furnished 22·8 g. (90 per cent) of the required *cyano ketone* which crystallised from ether in colourless needles m.p. 98–99°. Found: C, 71·9; H, 5·7; N, 7·3. $C_{12}H_{11}O_2N$ requires C, 71·6; H, 5·5; N, 7·0 per cent.

2-*Cyano*-6-*methoxy*-2-*methyl*-1-*oxotetralin*. The above ketone (14 g.) with sodium ethoxide (from sodium 2·3 g.) in ethanol (120 ml.) was refluxed for 8 hours with methyl iodide (14 g.). There resulted 12 g. (80 per cent) crude product which crystallised from ether in colourless plates m.p. 70–70·5°. Found: C, 73·05; H, 6·0; N, 6·7. $C_{13}H_{13}O_2N$ requires C, 72·5; H, 6·1; N, 6·5 per cent.

γ-(2-*Carboxy*-5-*methoxy phenyl*) α-*methylbutyronitrile* (VII, R = OMe). The above ketone (1·05 g.) was stirred (5 hr. at 55°) with potassium *tert.*-butoxide (from potassium 1 g. in *tert.*-butanol 30 ml.). The acidic fraction of the resulting mixture weighed 1·21 g. and crystallised from ether in colourless prisms m.p. 108–110°. Found: C, 66·5; H, 6·4; N, 6·1; Titration equivalent, 228. $C_{13}H_{15}O_3N$ requires C, 66·9; H, 6·5; N, 6·0; titration equivalent 233.

Hydrolysis with ethanolic potassium hydroxide gave γ(2-*carboxy*-5-*methoxy phenyl*)α-*methylbutyramide* m.p. 181–183° from ethanol. Found: C, 61·9; H, 6·5; N, 5·5; titration equivalent 246. $C_{13}H_{17}O_4N$ requires C, 62·2; H, 6·7; N, 5·6 per cent. Titration equivalent 252.

1-*Ethynyl*-6:7:8:9-*tetrahydro*-1-*hydroxy*-4:5-*benzindane*. Dry ether (1000 ml.) was saturated with acetylene at 20° by bubbling the gas through for 1 hour. To this was then added over 30 minutes with stirring a mixture of 6:7:8:9-tetrahydro-1-oxo-4:5-benzidane (9·3 g.) in dry ether (100 ml.) and potassium *tert.*-amylate (from potassium 13 g. and dry *tert.*-amyl alcohol 300 ml.). After 8 hours stirring and passage of acetylene, water was added, the aqeous layer made faintly acid to litmus and saturated with sodium chloride. The organic layer was removed, the aqueous portion extracted with ether and the combined extracts evaporated to give the *acetylenic alcohol* (7·25 g.) b.p. 112–114° at 0·1 mm. Found: C, 84·7; H, 7·6. $C_{15}H_{16}O$ requires C, 84·9; H, 7·6 per cent.

1-*Acetoxy*-1-*ethynyl*-6:7:8:9-*tetrahydro*-4:5-*benzindane* (IX, R = H). The above ethynyl carbinol (7 g.) was refluxed under nitrogen for 20 hours with freshly distilled pyridine (40 ml.) and acetic anhydride (40 ml.). After pouring into water and extracting with ether, there resulted a mass of yellow crystals 7 g. (84 per cent). Crystallisation from light petroleum (b.p. 40–60°) gave colourless prisms m.p. 92–93°. Found: C, 79·9; H, 7·3; $COCH_3$ 16·7; absorbed 2·07 H_2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·14; $COCH_3$, 16·9 per cent.

1-*Acetoxy*-1-*acetyl*-6:7:8:9-*tetrahydro*-4:5-*benzindane* (X). The above ethynyl acetate (3 g.) and redistilled aniline (1·4 g.) were dissolved in benzene (160 ml.) at 60°. To this was added mercuric chloride (8 g.) in boiling distilled water (40 ml.) and the two-phase system

vigorously stirred for 8 hours at 60°. After standing a further 16 hours at 25°, benzene was removed by steam distillation and in the aqueous residue there remained an insoluble brown gum. Water was decanted and the gum dissolved in acetone. Hydrogen sulphide was bubbled through until precipitation of mercury was complete. The filtered solution was then evaporated to give a brown oil, and treated with charcoal in ether to leave on evaporation, a crystalline mass 2·3 g. (70 per cent). Crystallisation from ether:light petroleum (b.p. 40–60°) (1:1) gave colourless needles m.p. 74°. Found: C, 74·7; H, 7·4. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·4 per cent. Infra-red absorption in carbon tetrachloride (NaCl prism) 1743 cm.$^{-1}$ (carbonyl) 1370 cm.$^{-1}$ (acetate methyl) 1419 cm.$^{-1}$ (active methylene).

This substance failed to form a semicarbazone and on prolonged boiling with 2:4-*dinitrophenylhydrazine* in 10 per cent ethanol:sulphuric acid gave the 2:4-dinitrophenylhydrazone of an $\alpha\beta$ unsaturated ketone—probably formed by elimination of acetic acid and consequent formation of a double bond in the 1:8 position (cf. ref. 1). It crystallised from ethanol-dioxan in dark red needles m.p. 187–188°. Found: C, 64·7; H, 5·6; N, 14·3. $C_{21}H_{20}O_4N_4$ requires C, 64·3; H, 5·1; N, 14·3 per cent. Light absorption (main band in chloroform) λmax 386 mμ (ϵ 27,300).

1-*Acetoxy*-1-*bromoacetyl*-6:7:8:9-*tetrahydro*-4:5-*benzindane*. The above ketone (1·36 g.) in glacial acetic acid (10 ml.) was treated with bromine (0·8 g.) also in acetic acid; on warming to 50–60° the bromine colour was discharged. Acetic acid was then removed. The residue was treated with charcoal in either to yield the *bromoketone* (1·2 g.) which crystallised from light petroleum (b.p. 60–80°) in colourless prisms. m.p. 106–109° (softens at 100°). Found: C, 58·8; H, 5·3; Br, 20·9. $C_{17}H_{19}O_3Br$ requires C, 58·1; H, 5·5; Br, 22·7 per cent.

1-*Acetoxy*-1-*glycollyl*-6:7:8:9-*tetrahydro*-4:5-*benzindane* (XI, R = H). The bromoketone (2 g.) in acetone (100 ml.) was refluxed for 30 minutes with potassium iodide (2 g.). Potassium acetate (6 g.) was then added and the whole refluxed 15 hours. Working up in the usual way gave 1·77 g. (94 per cent) of crystalline material which crystallised from ether in colourless needles m.p. 135–137°. Found: C, 69·0; H, 6·9; CH_3CO, 26·5. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7; CH_3CO, 26·1 per cent.

Infra-red absorption in carbon tetrachloride (NaCl prism) 1743 cm.$^{-1}$, 1758 cm.$^{-1}$ (carbonyl), 1372 cm.$^{-1}$ (acetate methyl), 1418 cm.$^{-1}$ (methylene in $COCH_2OAc$).

Attempts to form the free glycollyl side chain either by direct replacement of Br by OH in the bromoketone, or by hydrolysis of the diacetate, gave oily mixtures which could not be evaluated.

1 - *Ethynyl* - 6:7:8:9 - *tetrahydro* - 1 - *hydroxy* - 4:5 - (3′ - *methoxy*) *benzindane*. Starting from 6:7:8:9-tetrahydro-1-oxo-4:5-(3′-methoxy) benzindane (5 g.) and proceeding in an identical manner to that described above for the desmethoxy compound, the required *acetylenic alcohol* was obtained as a yellow oil b.p. 150–152° at 0·4 mm. 3·4 g. (60 per cent). It was carried on thus to the next stage.

1 - *Acetoxy* - 1 - *ethynyl* - 6:7:8:9 - *tetrahydro* - 4:5 - (3′ - *methoxy*) *benzindane* (IX, R = OMe). The above ethynyl alcohol (2·1 g.) was acetylated as described for the desmethoxy compound to yield 2·36 g. (95 per cent) of the required *ethynyl carbinol acetate* which crystallised from light petroleum (b.p. 60–80°) in colourless prisms. m.p. 98–99°. Found: C, 76·7; H, 7·2; OCH_3, 10·4; absorbed 2·04 moles H_2. $C_{18}H_{20}O_3$ requires C, 76·0; H, 7·1; OCH_3, 10·5 per cent.

1-*Acetoxy*-1-*acetyl*-6:7:8:9-*tetrahydro*-4:5-(3′-*methoxy*) *benzindane?* Treatment of the above ethynyl acetate in the same manner as described above for the desmethoxy compound gave a *compound* crystallising in colourless plates m.p. 93–94° from ether-light petroleum (b.p. 40–60°). Found: C, 71·6; H, 7·4; OCH_3, 10·1. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3; OCH_3, 10·3 per cent. Infra-red absorption in carbon tetrachloride (NaCl prism) 1743 cm.$^{-1}$ (carbonyl), 1372 cm.$^{-1}$ (acetate methyl).

1 - *Acetoxy* - 1 - *bromoacetyl* - 6:7:8:9 - *tetrahydro* - 4:5 (3′ *methoxy*) *benzindane?* (XIII). Bromination of the above compound in the usual manner gave a *bromoketone* crystallising from ether in colourless prisms m.p. 189–190°. Found: C, 57·1; H, 5·6; Br, 20·8; CH_3CO, 11·4. $C_{18}H_{21}O_4Br$ requires C, 56·7; H, 5·6; Br, 20·9; CH_3CO, 11·3 per cent.

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