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SYNTHESIS OF 4-METHYL-5-METHOXYINDAN-1-ONE

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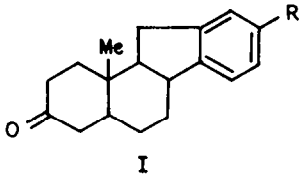
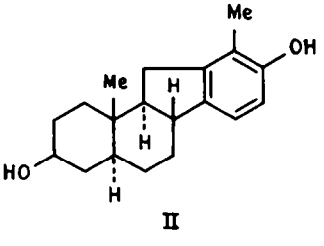
Abstract—PPA and Friedel-Crafts cyclizations of the bromo-acid (mixture) obtained by nuclear bromination of VII furnished three isomeric bromoketones characterised as XII, XI and XVI. The ketones XII and XI on catalytic debromination afforded 6-methoxy-7-methylindan-1-one (III) which on catalytic hydrogenolysis and subsequent oxidation furnished 4-methyl-5-methoxyindan-1-one (V). An unambiguous synthesis of this title compound (V) was also achieved using 2-methyl-3-methoxybenzyl chloride (XXIII) as the starting material. The change in the intensities of the K-bands of some indanone derivatives have been discussed in the light of buttressing effect.

THE steroidal alkaloids of the jerveratrum and ceveratrum type[1] possess C-nor-D-homo system. The growing interest in the biological properties of steroid hormones, in which the basic ring skeleton has been altered, has prompted the synthesis of hormone analogs possessing the C-nor-D-homo system from natural precursors.[2–5] Several methods have also been developed for the synthesis of C-nor-D-homosteroid ring system with the ultimate object of achieving the total synthesis of the parent alkaloids. These synthetic studies can broadly be classified into two subgroups, dealing with (a) the tricyclic system[6–9] comprising B, C and D rings and (b) the tetracyclic system[10–11] incorporating A, B, C and D rings. Very recently Bhattacharyya and his associates disclosed a different approach[12] for the total synthesis of C-nor-D-homosteroidal compounds such as I and 1-indanone derivatives have been utilised for this purpose. Extension of this procedure for the synthesis of the phenol (II),[3] a degradation product from hecogenin, appeared quite attractive and 4-methyl-5-methoxyindan-1-one (V) is expected to be a potential intermediate for this purpose. This paper describes two independent syntheses of V.



I

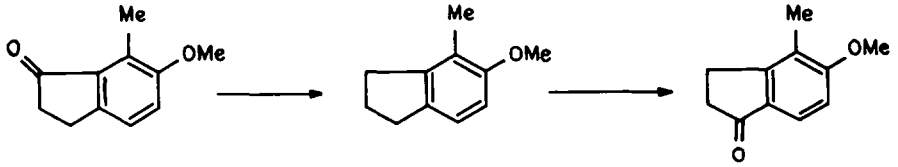
R = H and OMe



II

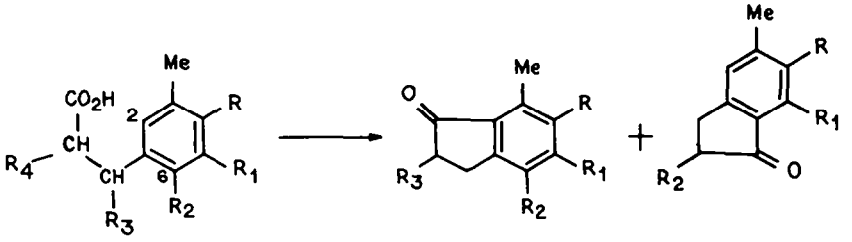
It was planned to prepare the desired indanone (V) from the isomeric ketone (III) according to the scheme depicted below.

It was reported by House *et al.*[13] that PPA cyclization of β-(*m*-tolyl)propionic acid (VI) furnishes a mixture of X and XIV in 96% yield and the two isomeric ketones present in approximately equal amounts, were separated by careful chromatography.



III IV V

Encouraged by this observation, the preparation of the indanone (III) through cyclization of β-(3-methyl-4-methoxyphenyl)propionic acid (VII) was attempted. Cyclization of this propionic acid by the above procedure furnished the ketone (XV), m.p. 108° in 67% yield and the desired ketone (III), m.p. 96° in only 11% yield. Evidence in favour of these structural assignments will be subsequently dealt with.



VI , R=R1=R2=R3=R4=H
VII , R=OMe; R1=R2=R3=R4=H
VIII , R=OMe; R1=Br; R2=R3=R4=H
IX , R=OMe; R1=R3=R4=H; R2=Br
XVII , R=OMe; R1=R2=R4=H; R3=Br
XVIII , R=OMe; R1=R2=R3=H; R4=Br

X , R=R1=R2=R3=H
XI , R=OMe; R1=Br; R2=R3=H
XII , R=OMe; R1=R3=H; R2=Br
XIII , R=OH; R1=Br; R2=R3=H
XIX , R=OMe; R1=R2=H; R3=Br

XIV , R=R1=R2=H
XV , R=OMe; R1=R2=H
XVI , R=OMe; R1=Br; R2=H
XX , R=OMe; R1=H; R2=Br

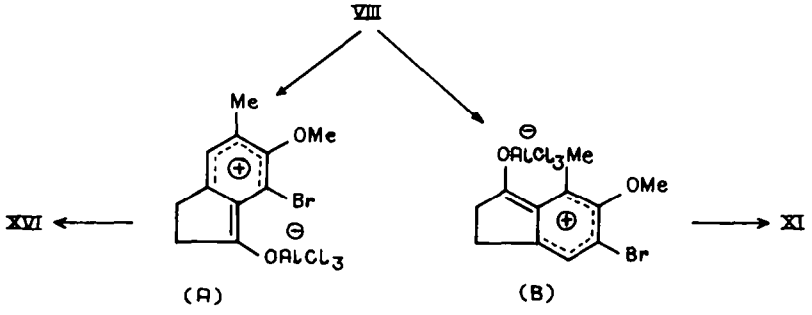
The OMe group in VII is situated *meta* to the two possible cyclization centres i.e., C_2 and C_6. The intramolecular acylation *meta* to the methoxy group is difficult and there are ample precedents[14] known. The predominant formation of XV in PPA cyclization of VII may be explained by the fact that the rate of cyclization becomes much slower compared to that of the acid (VI) studied by House *et al.*[13] In a slow reaction of this type, cyclization takes place selectively at C_6 in VII which is sterically and probably electronically more favourable. It may be mentioned here that γ-(3-methyl-4-methoxyphenyl)butyric acid cyclizes exclusively at the position *para* to the Me group under all possible cyclization conditions.[15]

In view of the above findings, synthesis of the indanone (III) through cyclization of the bromo acid (VIII) appeared a better possible method.[16] Bromination of the acid (VII) in glacial acetic acid afforded an oily material and consisted of a mixture of isomeric bromo acids, which provided expected elemental analyses. On careful chromatography over silica gel, it furnished two crystalline bromo acids: A is present to the extent of 6% in the mixture and melts at 131–132° and B, m.p. 73–74° constitutes 70% of the mixture. It may be mentioned that the procedure followed for the bromination of the acid (VII) always resulted in nuclear bromination in other similar

system[6, 17] The acid A, on PPA cyclization, furnished a single indanone derivative (XII) in excellent yield. The acid B, on similar cyclization, afforded after chromatography two crystalline bromo indanones (XVI and XI), and these were present in the ratio 1:1·7. The Friedel-Crafts cyclization of the acid B through its acid chloride yielded the same two indanones (XVI and XI) in the ratio 1:2. The two bromo acids A and B can now therefore be represented respectively by the expressions IX and VIII. The structures XI, XII and XVI for the bromo indanones mentioned above have been unambiguously established from their NMR spectra (Experimental). The alternative structures* XVII and XVIII for the bromo acids (IX and VIII) respectively can therefore be altogether ruled out. Incidentally two α-bromo indanones (XIX and XX), which are the expected cyclization products of the bromo acid (XVIII), were prepared from the indanones (III and XV) respectively by well established procedure.[18] These α-bromo indanones having characteristic NMR spectra (Experimental), were found to be completely different from XI and XVI in all respects.

The separation of the bromo acids was tedious and time consuming. Therefore the cyclization of the bromo acid mixture was attempted under different cyclization conditions (Experimental). Cyclization with polyphosphoric acid gave a much better yield of the ketonic material as compared to that of Friedel-Crafts procedure. This is not surprising due to the fact that during cyclization with PPA, more reactive acylium ion is involved.[19] During Friedel-Crafts cyclization, a crystalline phenolic ketone was isolated as the alkali soluble product. This phenol was characterised to be XIII as it has been found to be identical with the demethylated product of XI. The phenol (XIII) on methylation also furnished the indanone (XI).

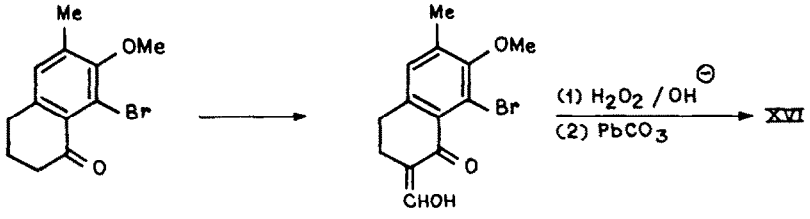
The two types of mechanism, namely ionic and substitution mechanisms, are generally accepted for Friedel-Crafts acylation.[20] In the present case we are tempted to propose that the substitution mechanism as shown below is more significant for explaining the experimental findings. The intermediate (A) leading to the product (XVI) is destabilized due to both steric and electronic considerations than (B) leading to the indanone (XI). This explains the low yield of the cyclized products and also the formation of the indanone (XI) in greater proportions when $AlCl_3$ is used as the cyclizing agent.



Catalytic debromination of the indanones (XI and XII) in presence of triethylamine provided the desired indanone (III) in good yield. Similar reductive removal of bromine from the bromo ketone (XVI) afforded the ketone XV. This procedure for

* These possibilities were pointed out by a learned referee

the removal of nuclear bromine without affecting the carbonyl group is well known[21] in the literature. An authentic sample of the bromo ketone (XVI) was prepared from the tetralone derivative (XXI) of established[22] structure. The formyl compound (XXII), prepared in excellent yield, on oxidation with alkaline hydrogen peroxide furnished an acidic material which failed to crystallize even after chromatography on silica gel. The crude acid on pyrolysis with lead carbonate afforded the desired bromo indanone (XVI) in low yield.



XXI XXII

The UV absorption characteristics of the isomeric bromo indanones (XI, XVI and XII) are quite informative. It has been shown by Braude *et al.*[23] that the intensity of the K-bands of the UV spectra of this class of compounds provides a good measure of coplanarity of the CO group. The change in the intensities of the K-bands of the ketones tabulated in Table 1, may be rationalized by considering the "buttressing effect"[24] due to a *meta* substituent in the benzene ring. Convincing evidence for the operation of this effect has been provided through studies in the rates of racemization of certain optically active biphenyls.[25] Further examples showing possible buttressing interaction are available in other benzene,[24] biphenyl[26] and α-tetralone[27] derivatives.

TABLE 1

Bromo ketone	K-band (λ_{max}^{EtOH} in mμ)	ε
XI	260	15,490
XVI	259	10,960
XII	256	7,586

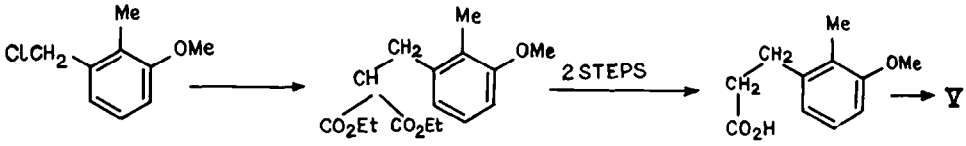
The OMe group buttresses on the Me group and on the Br atom in XI and XVI respectively. The effective interference value of bromine[24] (2·0 ± 0·4 Å) being greater than that of Me[28] (1·7 Å), the ketone (XVI) is expected to show decreased absorption intensity. The dipole-dipole interaction between the Br atom and the CO group in XVI may also result in a slight out of plane twisting of the CO group. The very low absorption intensity of XII is probably due to the combined buttressing effects of the OMe group and the Br atom both being situated *meta* to the CO group. The intensities of the K-bands of the indanones (X, III, XIV and XV) are summarized in Table 2 and can be accounted for by the reasons discussed above. Although the quantitative aspects of the buttressing effects are difficult to evaluate, the general trend of the experimental data is quite convincing and is suggestive of the presence of this effect in these molecules.

TABLE 2

Indanones	K-band (λ_{max}^{EtOH} in mμ)	ε
X[13]	248	13,600
III	251	10,230
XIV[13]	253	15,500
XV	256	11,670

The indanone (III) on catalytic reduction in presence of a trace of perchloric acid afforded the crystalline indane (IV) in excellent yield. The synthesis of 4-methyl-5-methoxyindan-1-one (V) was then completed through chromic acid oxidation of IV.

An unambiguous synthesis of V was achieved by the following sequence of reactions.



XXIII XXIV XXV

2-Methyl-3-methoxybenzyl chloride (XXIII), prepared from 2-chloro-6-nitrotoluene, was condensed with ethyl malonate to furnish XXIV in excellent yield. This malonic ester derivative on alkaline hydrolysis followed by decarboxylation provided the propionic acid (XXV) in high yield. PPA cyclization of this acid afforded the desired indanone (V) in nearly quantitative yield and was found to be identical in all respects with the indanone (V) prepared by the route described earlier.

EXPERIMENTAL

All the m.p.s are uncorrected. Neutral Brockman alumina (Merck & Co.) and silica gel for chromatography (BDH) were used for column chromatographic experiments. IR spectra were measured on Perkin-Elmer Infra cord Model 137 in $CHCl_3$ as solvent and UV spectra on a Unicam S.P. 500 spectrophotometer. NMR spectra were recorded on Varian associates, Model A-60-D instrument, using $CDCl_3$ as solvent and TMS as internal standard. The form of signals is expressed as s = singlet, d = doublet and qu = quartet.

β-(3-Methyl-4-methoxyphenyl)propionic acid (VII). This compound was prepared from 3-methyl-4-methoxybenzyl chloride[29] by malonic ester synthesis according to the known procedure,[30] m.p. 98–99° (lit.[30] m.p. 100°).

Polyphosphoric acid cyclization of β-(3-methyl-4-methoxyphenyl)propionic acid (VII). To well stirred polyphosphoric acid[19] (58 g) heated in an oil bath (80°) was added VII (5 g) in four equal instalments during a period of 45 min. After complete addition the stirring was continued at that temp for 4 hr more. The reaction mixture was then cooled, poured into ice-water and extracted with ether to furnish 4·3 g (93%) of a yellow solid. This material was then chromatographed over alumina (240 g). Elution with 10% benzene-light petroleum furnished 450 mg (11% of the mixture) of III, m.p. 96° in the forefractions; UV(EtOH), 251 (ε 10,230) and 321 mμ (ε 3,202); IR 1698 cm^{-1} (cyclopentenone); NMR τ 7·46 (3H, s, CH_3), 7·24 (2H, s, CH_2), 7·07 (2H, s, CH_2), 6·11 (3H, s, OCH_3), 2·78 (2H, qu, J = 8 c/s, aromatic protons). [Found C, 74·96; H, 6·92. $C_{11}H_{12}O_2$ requires: C, 74·98; H, 6·86%]. The 2,4-dinitrophenylhydrazone separated from MeOH and was recrystallized from $CHCl_3$–EtOAc to furnish nice red crystals, m.p. 276° (dec); UV ($CHCl_3$), 387 mμ (ε 25,370). [Found: C, 57·42; H, 4·82; N, 15·78. $C_{17}H_{16}O_5N_4$ requires: C, 57·30; H, 4·53; N, 15·72%]. The

latter fractions of the above chromatography furnished 2·9 g (67% of the mixture) of XV, m.p. 108°; UV (EtOH), 256 (ε 11,670) and 316 mμ (ε 5,379); IR 1692 cm^{-1} (cyclopentenone). [Found C, 75·26; H, 7·12. $C_{11}H_{12}O_2$ requires: C, 74·98; H, 6·86%]. The 2,4-dinitrophenylhydrazone separated from MeOH and was recrystallized from $CHCl_3$, m.p. 281° (dec); UV($CHCl_3$), 395 mμ (ε 30,970). [Found C, 57·49; H, 4·67; N, 15·81. $C_{17}H_{16}O_5N_4$ requires: C, 57·30; H, 4·53; N, 15·72%].

Bromination of β-(3-methyl-4-methoxyphenyl)propionic acid (VII); *formation of β-(6-bromo-3-methyl-4-methoxyphenyl)propionic acid* (IX) *and β-(5-bromo-3-methyl-4-methoxyphenyl)propionic acid* (VIII).

To a soln of VII (4·8 g) in glacial AcOH (72 ml), a soln of Br_2(4·7 g) in glacial AgOH (30 ml) was added, kept at room temp for 1 hr and then at 50° for 30 hr. The reaction mixture was then diluted with water and extracted with ether. The organic layer was washed with water, dried (Na_2SO_4) and evaporated. The residue was distilled at 180–185°/0·4 mm to furnish 6 g (89%) of a highly viscous oil. A middle cut was analysed. [Found C, 48·26; H, 4·82. $C_{11}H_{13}O_3Br$ requires: C, 48·35; H, 4·76%]. This material solidified on standing, m.p. 55–60° which was chromatographed over silica gel (150 g). Elution with 5% ether-light petroleum furnished 300 mg (6%) of IX, in the forefractions which on two recrystallizations from light petroleum furnished the analytical material, m.p. 131–132°. [Found C, 48·11; H, 4·50. $C_{11}H_{13}O_3Br$ requires: C, 48·35; H, 4·76%]. The latter fractions of the above chromatography furnished 3·5 g (70%) of VIII which on two recrystallizations from light petroleum furnished the analytical material, m.p. 73–74°. [Found C, 48·53; H, 5·05. $C_{11}H_{13}O_3Br$ requires: C, 48·35; H, 4·76%]. Since the separation of the acids were difficult and time consuming, experiments were performed sometimes with the oily bromo acid mixture.

4-Bromo-6-methoxy-7-methylindan-1-one (XII). A mixture of IX (45 mg) and polyphosphoric acid[19] (10 g) was heated on a free flame till homogeneous reaction mixture was attained. This was heated on a steam bath for 30 min, then cooled, decomposed with ice-water and extracted with ether. The ethereal soln was washed with 2% KOH aq, dried (Na_2SO_4) and evaporated to furnish a yellow material which on one recrystallization from light petroleum furnished 30 mg (71%) of XII, m.p. 159–160°; UV(EtOH), 256 (ε 7,586) and 327 mμ (ε 4,074); IR 1713 cm^{-1} (cyclopentenone); NMR τ 7·52 (3H, s, CH_3), 7·22 (2H, s, CH_2), 7·14 (2H, s, CH_2), 6·11 (3H, s, OMe), 2·83 (1H, s, aromatic proton). [Found: C, 51·90; H, 4·44. $C_{11}H_{11}O_2Br$ requires: C, 51·76; H, 4·31%]. The 2,4-dinitrophenylhydrazone separated from MeOH and was recrystallized from $CHCl_3$, m.p. 297° (dec). UV($CHCl_3$), 388 mμ (ε 27,170). [Found C, 47·15; H, 3·61; N, 12·68. $C_{17}H_{15}N_4O_5Br$ requires: C, 46·89; H, 3·21; N, 12·87%].

Polyphosphoric acid cyclization of β-(5-bromo-3-methyl-4-methoxyphenyl)propionic acid (VIII)

A mixture of VIII (500 mg) and polyphosphoric acid[19] (38 g) was heated on a steam bath for 1 hr. The reaction mixture was then cooled, decomposed with ice-water and extracted with ether. The organic layer was washed with 2% KOH aq, dried (Na_2SO_4) and evaporated. The residue was evaporatively distilled at 125°/0·4 mm to furnish an oil which soon solidified to furnish 370 mg (79%) of a pale yellow solid, m.p. 60–75°. This material was chromatographed over alumina (15 g). Elution with 10% benzene-light petroleum furnished 200 mg (59% of the mixture) of XI which on one recrystallization from light petroleum furnished the analytical material, m.p. 80–81°; UV(EtOH), 260 (ε 15,490) and 304 mμ (ε 3,715); IR 1710 cm^{-1} (cyclopentenone); NMR τ 7·44 (3H, s, CH_3), 7·22 (2H, s, CH_2), 7·04 (2H, s, CH_2), 6·15 (3H, s, OCH_3), 2·65 (1H, s, aromatic proton). [Found C, 51·35; H, 4·72. $C_{11}H_{11}O_2Br$ requires: C, 51·76; H, 4·31%]. The 2,4-dinitrophenylhydrazone separated from MeOH and was recrystallized from $CHCl_3$, m.p. 271° (dec), UV ($CHCl_3$), 338 mμ (ε 31,270). [Found C, 46·75; H, 3·33; N, 12·79. $C_{17}H_{15}N_4O_5Br$ requires: C, 46·89; H, 3·21; N, 12·87%]. Elution of the column with 50% benzene-light petroleum furnished 130 mg (35% of the mixture) of XVI which on one recrystallization from light petroleum furnished the analytical sample, m.p. 110–111°; UV(EtOH), 259 (ε 10,960) and 307 mμ (ε 3,467); IR 1711 cm^{-1} (cyclopentenone); NMR τ 7·57 (3H, s, CH_3), 7·19 (2H, s, CH_2), 7·07 (2H, s, CH_2), 6·13 (3H, s, OMe), 2·72 (1H, s, aromatic proton). [Found C, 51·73; H, 4·61. $C_{11}H_{11}O_2Br$ requires: C, 51·76; H, 4·31%]. The 2,4-dinitrophenylhydrazone separated from MeOH and was recrystallized from $CHCl_3$, m.p. 286 (dec); UV ($CHCl_3$), 388 mμ (ε 27,180). [Found C, 46·93; H, 3·62; N, 12·71. $C_{17}H_{15}N_4O_5Br$ requires: C, 46·89; H, 3·21; N, 12·87%].

Friedel-Crafts cyclization of β-(5-bromo-3-methyl-4-methoxyphenyl)propionic acid (VIII)

(A) *In tetrachloroethane solvent.* A mixture of VIII (3 g) and PCl_5 (3 g) was heated on a steam bath for 30 min, then diluted with dry benzene (20 ml) and the benzene was slowly distilled off to remove $POCl_3$. The crude acid chloride was dissolved in dry tetrachloroethane (5 ml) and was added to an ice cold stirred suspension of $AlCl_3$ (8 g) in dry tetrachloroethane (50 ml). The reaction mixture was allowed to stand at

room temp for 14 hr and then decomposed with ice-water (150 ml) and HCl (15 ml). This was then extracted with ether, the organic layer was washed with $NaHCO_3$, dried (Na_2SO_4) and evaporated. The residue was evaporatively distilled at 120°/0·4 mm to furnish a pale yellow oil which solidified to give 850 mg (30%) of a pale yellow solid, m.p. 60–78°. This material was chromatographed over alumina (51 g). Elution with 10% benzene-light petroleum furnished 450 mg (53% of the mixture) of XI, m.p. 80–81° and elution with 50% benzene–light petroleum furnished 125 mg (28% of the mixture of XVI, m.p. 110–111°. These two ketones were identical in all respects with the ketones previously prepared.

(B) *In nitrobenzene solvent.* The crude acid chloride prepared from VIII (1·3 g) and PCl_5 (1 g) was dissolved in dry nitrobenzene (10 ml) and added slowly to an ice cold soln of anhyd $AlCl_3$ (2 g) in dry nitrobenzene (20 ml). The reaction mixture was allowed to stand at the room temp for 20 hr, then decomposed and steam distilled. The solid residue was dissolved in ether, washed with $NaHCO_3$ soln and then extracted repeatedly with 4% KOH aq. The neutral soln on evaporation furnished 380 mg of a pale yellow oil. The 4% KOH extract on acidification followed by ether extraction furnished a grey coloured solid material which on sublimation at 130°/0·4 mm furnished 300 mg of a colourless compound. This material on repeated recrystallizations from MeOH furnished a pure sample of XIII, m.p. 188–189°. [Found C, 50·00; H, 4·02. $C_{10}H_9O_2Br$ requires: C, 49·81; H, 3·76%]. This phenolic material (300 mg) was dissolved in a soln of NaOH (150 mg) in water (5 ml) and was methylated with Me_2SO_4 (0·4 ml) by stirring at room temp for 2 hr. The reaction mixture was then extracted with ether to furnish a neutral oil (110 mg). The alkaline soln on acidification furnished 170 mg of unreacted phenolic material. This material was again methylated by refluxing in acetone (10 ml) for 6 hr with anhyd K_2CO_3 (500 mg) and MeI (1 ml). The reaction mixture was diluted with water, extracted with ether and the ethereal soln was washed with 4% KOH aq. The neutral ethereal soln on evaporation furnished 170 mg of a pale yellow oil. The total neutral materials were mixed up and evaporatively distilled at 120°/0·4 mm to furnish 560 mg (46%) of the cyclized product.

Cyclization of the bromo acid mixture (VIII and IX)

(A) *By polyphosphoric acid method.* To polyphosphoric acid[19] (65 g) the oily bromo acid mixture (VIII and IX) (4·6 g) was added and the mixture was warmed on a steam bath for 1·5 hr. The brown reaction mixture was cooled, decomposed with ice-water and the brown oil that separated was extracted with ether. The ethereal soln on evaporation and the residue on evaporation distillation at 110°/0·4 mm furnished 2·25 g (52%) of a pale yellow oil which readily solidified. This material (1·5 g) was chromatographed over alumina (60 g). Elution with 10% benzene-light petroleum furnished 30 mg (1·7% of the mixture) of XII, m.p. 159–160° in the forefractions. The latter fractions from the above chromatography furnished 760 mg (51% of the mixture) of XI, m.p. 80–81°. Elution with 50% benzene-light petroleum furnished 370 mg (25% of the mixture) of XVI, m.p. 110–111°. These three ketones were identical in all respects with the ketones previously prepared.

(B) *By Friedel-Crafts method.* The crude acid chloride prepared from the oily bromo acid mixture (VIII and IX; 5 g) and PCl_5 (4·2 g) was dissolved in dry nitrobenzene (20 ml) and added slowly to an ice cold soln of anhyd $AlCl_3$ (8·2 g) in dry nitrobenzene (100 ml). The reaction mixture was allowed to stand at room temp for 60 hr, then decomposed and steam distilled. The solid residue was dissolved in ether, washed with $NaHCO_3$aq and then extracted repeatedly with 2% KOHaq. The neutral ethereal soln on evaporation furnished 500 mg of a pale yellow oil. The 2% KOH extract on acidification followed by ether extraction furnished 3 g of XIII (impure), m.p. 140–165°. The crude phenolic material (2·5 g) was dissolved in a soln of NaOH (1 g) in water (10 ml) and was methylated with Me_2SO_4 (2 ml). Further quantity of NaOH (1 g) and Me_2SO_4 (2 ml) was added and the mixture was heated at the steam bath for 45 min. cooled and extracted with ether. Large amounts of tarry material separated and the ethereal soln was evaporated to furnish 1 g of pale yellow oil which was mixed up with neutral material produced directly in Friedel-Crafts cyclization. The total material (1·5 g, 33%) was chromatographed over alumina (45 g). Elution with 10% benzene-light petroleum furnished 50 mg (3·3% of the mixture) of XII, m.p. 159–160° in the forefractions. The latter fractions of the above chromatography furnished 820 mg (55% of the mixture) of XI, m.p. 80–81°. Elution with 50% benzene-light petroleum furnished 230 mg (17% of the mixture) of XVI, m.p.110–111°. These three ketones were identical in all respects with ketones previously prepared.

Preparation of an authentic sample of 5-bromo-6-hydroxy-7-methylindan-1-one (XIII). A mixture of XI (200 mg) and 48% HBr (5 ml) was refluxed for 35 min. The solid material thus obtained was filtered, dried and sublimed at 125°/0·3 mm. This material on two recrystallizations from MeOH furnished 150 mg (80%) of the pure material XIII, m.p. 188–189°, identical in all respects with the ketone previously prepared.

6-Methoxy-7-methylindan-1-one (III)

(A) *By catalytic debromination of* XI. A soln of XI (3·5 g) in 95% EtOH (70 ml) was hydrogenated over 10% Pd-C (250 mg) in presence of Et_3N (2 ml) at room temp and atmo press. After the absorption of the theoretical quantity of H_2 (314 ml), the catalyst was filtered off, solvent evaporated, the residue was taken up in ether and washed with 5% HCl. The solvent was evaporated to furnish 2·4 g (100%) of solid material which was recrystallized from light petroleum to furnish the pure material, m.p. 96°, identical in all respects with III, obtained before by the polyphosphoric acid cyclization of VII.

(B) *By catalytic debromination of* XII. A soln of XII (100 mg) in 95% EtOH (10 ml) was hydrogenated over 10% Pd-C (10 mg) at room temp and atmo press in presence of Et_3N (1 drop). The theoretical amount of H_2 (9 ml) was absorbed in 2 min. The reaction mixture was then worked up as before to furnish 65 mg (100%) of the pure material, m.p. 96°, identical in all respects with III described before.

2-Bromo-6-methoxy-7-methylindan-1-one (XIX)

To a soln of III (0·5 g) in dry ether (50 ml) was added a soln of Br_2 (0·55 g) in ether (30 ml) at 10° with stirring, each drop being added after the decolourization of the previous drop. After complete addition the ethereal soln was washed with $NaHCO_3$ aq, dried (Na_2SO_4) and evaporated. The residue on 3 recrystallizations from light petroleum furnished the pure material (0·5 g, 68%), m.p. 107°; UV(EtOH), 221 (ε 17,380), 260 (ε 9,550) and 335 mμ (ε 2,884); IR 1710 cm^{-1} (cyclopentenone); NMR τ 7·44 (3H, s, Me), 6·45 (2H, qu, J = 7·2 and 4·0 c/s, CH_2), 6·10 (3H, s, OMe), 5·32 (1H, qu, J = 7·2 c/s, CHBr), 2·75 (2H, s, ring protons). [Found C, 51·52; H, 4·56. $C_{11}H_{11}O_2Br$ requires: C, 51·76; H, 4·31%].

6-Methoxy-5-methylindan-1-one (XV)

By catalytic debromination of XVI. A soln of XVI (3·2 g) in 95% EtOH (70 ml) was hydrogenated over 10% Pd-C (250 mg) at room temp and atmo press in presence of Et_3N (1·7 ml). The theoretical amount of H_2 (310 ml) was absorbed in 40 min. The reaction mixture was then worked up as before to furnish 2·2 g (100%) of the debrominated compound, m.p. 108°, identical in all respects with XV obtained before by the polyphosphoric acid cyclization of VII.

2-Bromo-6-methoxy-5-methylindan-1-one (XX)

A soln of XV (1 g) in dry ether (80 ml) was brominated by using a soln of Br_2 (0·95 g) in dry ether (30 ml) following the same experimental procedure as in the preparation of XIX. The crude material on three recrystallizations from light petroleum furnished the pure material (0·8 g, 54%), m.p. 83°; UV(EtOH), 219 (ε 19,050), 266 (ε 12,300) and 325 mμ (ε 5,623); IR 1705 cm^{-1} (cyclopentenone); NMR τ 7·68 (3H, s, Me), 6·44 (2H, qu, J = 7·2 and 4·0 c/s, CH_2), 6·10 (3H, s, OMe), 5·32 (1H, qu, J = 7·2 c/s, CHBr), 2·75 (2H, s, ring protons). [Found C, 51·29; H, 4·31. $C_{11}H_{11}O_2Br$ requires: C, 51·76; H, 4·31%].

Preparation of an authentic sample of 7-bromo-6-methoxy-5-methylindan-1-one (XVI)

2-Formyl-8-bromo-7-methoxy-6-methyl-1-tetralone (XXII). To dry NaOMe prepared from Na (170 mg) and MeOH (10 ml) suspended in dry benzene was added ethyl formate (550 mg) followed by the addition of authentic sample of XXI[22] (1 g) with stirring under N_2. The stirring was continued for 4 hr more and then left overnight. The reaction mixture was then decomposed with ice-water, the aqueous layer separated and the organic layer was extracted with 5% NaOH aq. The combined alkaline soln was acidified and extracted with ether to furnish the solid derivative which on one recrystallization from light petroleum furnished 800 mg (72%), of XXII m.p. 116–117°. [Found C, 52·68; H, 4·42. $C_{13}H_{13}O_3Br$ requires: C, 52·52; H, 4·31%].

7-Bromo-6-methoxy-5-methylindan-1-one (XVI)

To an ice cold soln of XXII (800 mg) in 10% NaOH (94 ml) and MeOH (70 ml) was added 30% H_2O_2 (30 ml). After 20 min a fresh lot of 10% NaOH (94 ml) and 30% H_2O_2 (60 ml) was added and the mixture was allowed to stand overnight. Next day the reaction mixture was acidified and extracted with ether to furnish 500 mg of an oil which was chromatographed over silica gel (30 g). Elution with 10% ether-light petroleum furnished 300 mg of colourless viscous oil, IR 1712 cm^{-1} (saturated acid). This material could not be solidified by keeping in the freeze with solvents even after 8 months and was directly pyrolysed by heating with $PbCO_3$ (1 g) under nitrogen at 230–310°. The yellow oil that was obtained readily solidified which on one recrystallization from light petroleum furnished 35 mg (5%) of XVI, m.p. 110–111°. This ketone was identical in all respects with the ketone previously described.

5-Methoxy-4-methylindane (IV)

A soln of III (2·5 g) in AcOH (90 ml) was hydrogenated over 10% Pd-C (550 mg) at room temp and atmo press in presence of 70% $HClO_4$ (5 drops). The theoretical amount of H_2 (720 ml) was absorbed in 2 hr. The catalyst was filtered off, the filtrate was made alkaline with NaOH and was extracted with ether. The residue obtained after the evaporation of the solvent was distilled at 130–135°/15 mm to furnish 2 g (87%) of a colourless oil which soon solidified to a colourless solid, m.p. 39°; UV(EtOH) 276 (ε 1,950) and 280 mμ (ε 1,950). [Found C, 81·26; H, 8·58. $C_{11}H_{14}O$ requires: C, 81·44; H, 8·70%].

5-Methoxy-4-methylindan-1-one (V)

To a stirred ice cold soln of IV (2 g) in glacial AcOH (13 ml) was added dropwise a soln of CrO_3 (2·2 g) in water (1·2 ml) and AcOH (6·6 ml). The mixture was allowed to stand at room temp for 20 hr, then diluted with water and extracted with ether. Evaporation of the solvent furnished a yellow solid material which on sublimation at 80°/0·01 mm and then on recrystallization from light petroleum furnished 1·4 g (64%) of colourless solid, m.p. 90–91°; UV(EtOH), 226 (ε 19,410), 277 (ε 13,490) and 282 mμ (ε 13,490); IR 1691 cm^{-1} (cyclopentenone). [Found C, 74·99; H, 7·02. $C_{11}H_{12}O_2$ requires: C, 74·98; H, 6·86%]. The 2,4-dinitrophenylhydrazone separated from MeOH which on recrystallization from $CHCl_3$–EtOAc furnished red crystals, m.p. 254°(dec); UV($CHCl_3$), 406 mμ (ε 30,080). [Found C, 57·42; H, 4·62; N, 15·62. $C_{17}H_{16}O_5N_4$ requires: C, 57·30; H, 4·53; N, 15·72%].

Diethyl(2-methyl-3-methoxybenzyl)malonate (XXIV)

To an ice cold soln of NaOEt prepared from Na (450 mg) and dry EtOH (8 ml) was added diethyl malonate (6 g) and the pasty mass thus obtained was allowed to stand at room temp for 15 min. 2-Methyl-3-methoxybenzyl chloride* (XXIII, 3 g) was added dropwise with stirring, the mixture was allowed to stand at room temp for 14 hr and then refluxed for 6 hr. The reaction mixture was cooled, diluted with water and extracted with ether. The solvent was evaporated and the residue on distillation at 150°/0·2 mm furnished 4·4 g (85%) of XXIV as colourless oil. [Found C, 65·23; H, 7·67. $C_{16}H_{22}O_5$ requires: 65·29; H, 7·53%].

β-*(2-Methyl-3-methoxyphenyl)propionic acid* (XXV)

A soln of XXIV (1·2 g) in MeOH (12 ml) was hydrolysed with KOH (1·25 g) by heating under reflux for 3 hr. The reaction mixture was diluted with water and acidified. The liberated acid was extracted with ether, solvent evaporated and the residue was decarboxylated by heating at 180° for 3 hr. On cooling 800 mg (100%) of the solid acid was obtained which was recrystallized from benzene to furnish colourless crystals, m.p. 149–150°. [Found C, 67·72; H, 7·46. $C_{11}H_{14}O_3$ requires: C, 68·02; H, 7·27%].

5-Methoxy-4-methylindan-1-one (V)

To polyphosphoric acid[19] (43 g) was added XXV (1·96 g) and heated over a free flame to obtain a homogeneous mixture. This was then heated on a steam bath for 30 min, cooled, decomposed with ice-water and extracted with ether. The ethereal soln was washed with $NaHCO_3$aq dried (Na_2SO_4), evaporated, the residue was sublimed at 80°/0·01 mm and then recrystallized from light petroleum to furnish 1·6 g (91%) of the pure material, m.p. 90–91°. The ketone was identical in all respects with the ketone obtained by the chromic acid oxidation of IV.

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