HETEROCYCLIC STEROIDS-PART-V: STUDIES ON THE TOTAL SYNTHESIS OF RACEMIC 3-METHOXY-7-OXAESTRA-1,3,5(10),8-TETRAEN-17(e)-OL

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ABSTRACT

7-Methoxyisochroman-4-one(III), synthesised from m-methoxybenzyl alcohol, is converted into racemic 3-methoxy-7-oxaestra-1,3,5(10), 8-tetraen-17(e)-ol(IX).

Recent reviews on oxa-steroids(1) and on total syntheses of heterocyclic steroidal systems(2) mentioned that there has been no report on the total synthesis of 7-oxaestrone. This prompted us to report here the details of the total synthesis of the title compound (IX) (3).

The synthesis of the hitherto unknown 7-methoxy-isochroman-4-one(III) was achieved starting with m-methoxybenzyl alcohol(4). The sodio-derivative of the m-methoxybenzyl alcohol on treatment with ethyl bromo-acetate in refluxing benzene furnished ethyl m-methoxy-benzyloxyacetate(I) in 40% yield. Alkaline hydrolysis of the acetate(I) afforded the desired hitherto unknown m-methoxybenzyloxyacetic acid(II) in 68% yield. All attempts to cyclise this acid(II) using conventional Lewis acid catalysts such as $ZnCl_2$-Ac_2O/AcOH, PCl_5-$AlCl_3$, PPA

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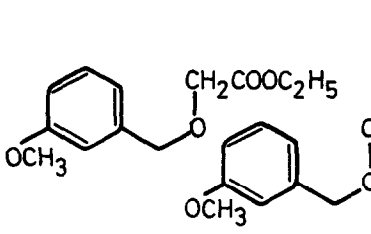

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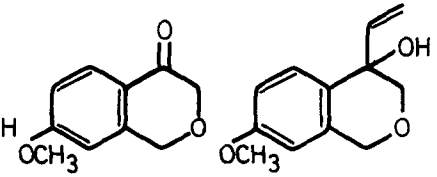

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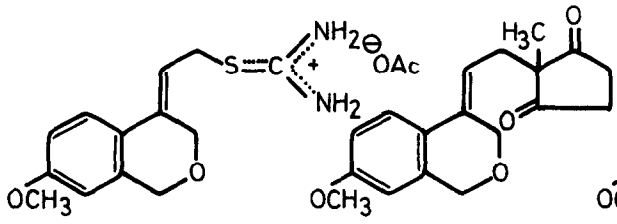

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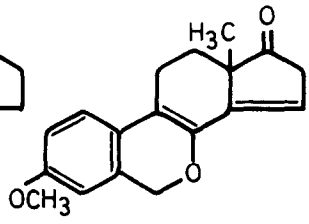

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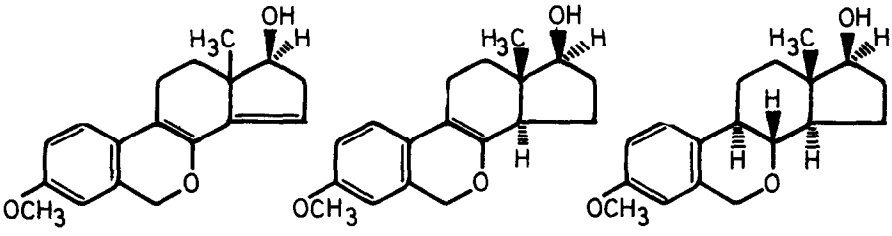

(VIII) (IX) (X)

(polyphosphoric acid) and also DCC (dicyclohexylcarbodiimide) (5) failed to furnish the desired Ketone(III). However, the acid chloride of the acid(II) on treatment with anhydrous $SnCl_4$ in benzene at 8-10°, gave the anticipated 7-methoxy-isochroman-4-one(III) as pale yellow needles, m.p. 78-80°, in 30% yield.

7-Methoxyisochroman-4-one(III), on treatment with vinylmagnesium bromide under Normant's reaction conditions (6) afforded the expected 4-hydroxy-4-vinyl-7-methoxy-isochroman(IV) as a colourless thick gum in 90% yield. The NMR spectrum of(IV)(CCl_4) indicated signals at δ3.25(s, 1H, OH, disappeared on D_2O exchange), 3.67(s, 3H, OCH_3), 4.45(s, 2H, benzylic CH_2) and 6.38 - 7.3(m, 3H, aromatic). The complex multiplet observed at δ 5.18 - 5.85, the intensity of which corresponded to three protons, and which represents the olefinic (- $C\underline{H}$ = $C\underline{H_2}$) protons, was in accordance with an ABC pattern expected for systems such as styrene and vinyl chloride(8). The methylene group at C_3(isochroman numbering) being adjacent to an asymmetric centre is expected to appear as an AB-quartet. In fact the NMR spectrum, as expected, indicated an AB-quartet centered at δ 3.62. The values for δ_{AB} and J_{AB} as calculated for the spectrum were found to be 7 and 11 Hz respectively. The ratio of δ_{AB}/J_{AB} was found to be 0.64. The intensities of the four lines of the AB-spectrum noticed

for the methylene group at C_3 in the NMR spectrum were found to correspond well to that calculated for an AB-system in which the ratio δ/J is less than unity(9). The mass spectrum indicated the most prominent peaks at m/e 206 (M^+ ion, 27%.), m/e 188(8%.), m/e 176(100%.), m/e 175(67%.), m/e 161(68%.), m/e 149(30%.) and m/e 121(16%.). The peaks at m/e 188(8%.) and m/e 175(67%.) seem best to support the structure (IV). The peaks at m/e 176(100%.) and m/e 149(30%.) not only supported the structure (IV) but also clearly ruled out the cleavage of the C-O bond in the heterocyclic ring during the Grignard reaction, incontradistinction to what was noticed earlier by Colonge and coworkers(7) in the case of the parent isochromanone and its 7-methyl derivative.

The allyl alcohol (IV) reacted smoothly with thiourea and glacial acetic acid (10) at room temperature, affording the expected 7-methoxyisochromanylideneethylisothiuronium acetate (V) as a white amorphous solid, m.p.137-8°, in 60% yield. Condensation of the isothiuronium acetate (V) with 2-methylcyclopentane-1,3-dione in a mixture of ether and water (1:1) furnished the expected 3-methoxy-8,14-seco-7-oxaestra-1,3,5(10),9(11)-tetraen-14,17-dione (VI) as a white crystalline solid, m.p. 86-7°, in 73% yield. Cyclodehydration of the secosteroid (VI) with methanolic hydrochloric acid gave 3-methoxy-7-

oxaestra-1,3,5(10),8,14-pentaen-17-one (VII) as a pale yellow crystalline solid, m.p. 142-4°, in 70% yield. The pentaene steroid (VII) appeared to be very unstable in solution but stable in the solid phase. The tetracyclic pentaene steroid (VII), on reduction with sodium borohydride in methanol, afforded an almost pure sample of racemic 3-methoxy-7-oxaestra-1,3,5(10),8,14-pentaen-17(e)-ol(VIII) as a pale yellow solid, m.p. 82-92°, in 90% yield. The triplet of 1 H intensity at δ 4.03(J = 8.5 Hz) was quite characteristic of an axial 17-hydrogen(11) and thus provided conclusive evidence in favour of an equatorial conformation of the 17-hydroxyl group. The mass spectrum of (VIII) indicated among other peaks a mass line at m/e 256, corresponding to a loss of 28 mass units. This has been rationalized by the elimination of 'CO' from the D-ring with the concomitant saturation of the 14, 15-olefinic bond (12).

The catalytic reduction of the 14, 15-double bond in the 17-hydroxy derivative (VIII) employing 10% palladium-on-carbon catalyst in dry benzene afforded the expected 3-methoxy-7-oxaestra-1,3,5(10), 8-tetraen-17(e)-ol(IX)(13) as a white crystalline solid, m.p. 123-7°, in 73% yield. The assignment of the equatorial configuration for the 17-hydroxyl and trans-stereochemistry for the C/D-ring junction was based on the findings of Banerjee

and his associates (14). Attempted reduction of the 8,9-olefinic bond in (IX) with lithium in liquid ammonia or by its saturation over 10% palladium-on-carbon catalyst failed to furnish the anticipated 3-methoxy-7-oxaestra-1,3,5(10)-trien-17(e)-ol(X).

EXPERIMENTAL (15)

Ethyl m-methoxybenzyloxyacetate(I).- To a suspension of finely divided sodium (4.6g) in 250 ml of dry thiophene-free benzene was added dropwise m-methoxybenzyl alcohol (27.6g) in 30 ml of dry thiophene-free benzene with stirring under anhydrous conditions at room temperature. The entire mixture was left overnight under stirring followed by a gentle reflux for one hour the following day. The sodio-derivative was precipitated as a pale yellow solid.

To the well-stirred suspension of the above obtained sodio-derivative of the m-methoxybenzyl alcohol, ethyl bromoacetate(22.2 ml, 33.4 g) in 30 ml of dry thiophene-free benzene was added dropwise. During the addition, the colour of the precipitate changed from pale yellow to reddish yellow. After the addition was over, the resulting solution was refluxed for 15 hours under anhydrous conditions. The unreacted sodium, if any, was destroyed by adding cautiously methanol and later the reaction mixture was treated with water. The yellow gelatinous product in the aqueous layer was extracted with ether (2 x 200 ml). The organic layer, dried over anhydrous sodium sulphate, was evaporated. The residual liquid on vacuum distillation at 140°/12 mm furnished a colourless liquid with a fruity odour (17.9g) in an overall 40% yield which showed a single spot in TLC [benzene:ethyl acetate (20:1)] ; UV λ max 274(ε 1,721) and 280 nm (ε 1,549); IR(smear) ν max 1740, 1595, 1585, 1485 and 1265 cm^{-1}; NMR (CCl_4) δ 1.17 (t, 3H,$-CH_2-CH_3$), 3.65(s, 3H, OCH_3), 3.85 (s, 2H,$-O-CH_2-CO-$), 4.07(q, 2H,$-CH_2-CH_3$), 4.45(s,2H,benzylic CH_2) and 6.62-7.1(m,4H,aromatic).

m-Methoxybenzyloxyacetic acid(II).- Ethyl m-methoxybenzyloxyacetate(1) (15.4g) was refluxed with 60 ml of a 10% methanolic KOH solution for 18 hours. After this period, the reaction mixture was extracted with

ether (2 x 50 ml). The resulting aqueous alkaline solution was acidified and then extracted with ether. The ethereal layer was washed several times with water and finally extracted with a saturated sodium bicarbonate solution. The bicarbonate layer was acidified carefully with ice-cold concentrated hydrochloric acid. The liberated free acid (II) was extracted with ether (2 x 100 ml). The ethereal layer, dried over anhydrous sodium sulphate, was evaporated. The resulting crude acid on vacuum distillation at 125°/0.18 mm furnished an analytically pure sample of m-methoxybenzyloxyacetic acid (II) (9.2g) in 68% yield. UV λ max 222 (ϵ 4,937) and 274 nm (ϵ 1,721); IR ($CHCl_3$) ν max 3000, 1720, 1590, 1480 and 1260 cm^{-1}; NMR (CCl_4) δ 3.72 (s, 3H, OCH_3), 4.05 (s, 2H, -O-CH_2-COO-), 4.52(s,2H,benzylic CH_2) and 6.62-7.3 (m, 4H, aromatic).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.65; H, 6.33%.

7-Methoxyisochroman-4-one (III).- A mixture of 1.98g of m-methoxybenzyloxyacetic acid (II) and a large excess of freshly distilled thionyl chloride (5 ml) was stirred at room temperature till the evolution of HCl gas ceased. Later, the solution was refluxed with stirring for 15 minutes under anhydrous conditions. After this period, the excess of thionyl chloride was removed under reduced pressure. The acid chloride thus obtained as a brown liquid (2g) was characterised by its IR spectrum; IR(smear) ν max 1790, 1590, 1500, 1420 and 1260 cm^{-1}.

To an ice-cold stirred solution of the acid chloride (1.11g) in 50 ml of dry thiophene-free benzene was added under anhydrous conditions 0.61 ml of anhydrous stannic chloride in 10 ml of thiophene-free benzene dropwise for a period of 10-15 minutes. After the addition was over, the mixture was stirred for 30 minutes at 5-10°. The reaction mixture was then decomposed by the addition of 15 ml of ice-cold 2N HCl. The resulting product was extracted with ether (2 x 50 ml). The ethereal layer was washed thoroughly with a saturated solution of $NaHCO_3$ (3 x 25 ml). Evaporation of the dried ether layer gave a brown gummy solid (0.47 g) in 50% yield. This was chromatographed over Brockman neutral alumina (15g). The solid obtained from petroleum ether-benzene (1:1) eluates was further purified by repeated recrystallization from acetone-petroleum ether to furnish the analytical sample of the ketone (III) (0.28g) as pale yellow needles, m.p. 78-80°, in 30% yield; UV λ max 224 (ϵ 11,440) and 276 nm (ϵ 15,640); IR (CCl_4) ν max 1680, 1585, 1465, 1445 and 1265 cm^{-1}; NMR (CCl_4) δ 3.77 (s, 3H, OCH_3), 4.1(s, 2H, O-CH_2-CO-), 4.68 (s,2H,benzylic CH_2), 6.49-6.92 (m,2H,

aromatic protons at C_6 and C_8) and 7.86 (d,1H,J = 8.5 Hz, periproton at C_5); mass peaks at m/e 178 (M^+ ion, 48%.), m/e 148 (100%.), m/e 120 (49%.), m/e 105 (11%.), m/e 91(25%.), m/e 90 (11%.) and m/e 77 (27%.).

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.4; H, 5.66. Found: C, 67.7; H, 6.01%..

4-Hydroxy-4-vinyl-7-methoxyisochroman (IV).- To a stirred suspension of vinylmagnesium bromide (11g) (from 10 ml of vinyl bromide and 2g of magnesium turnings) cooled to -20° was added dropwise a solution of 7-methoxyisochroman-4-one (III) (2.5g) in dry tetrahydrofuran precooled to -20° in an atmosphere of dry nitrogen. The pale yellow reaction mixture was slowly brought to room temperature and then refluxed for 12 hours. The yellowish green product obtained on decomposition with ice cold NH_4Cl was extracted with ether to give rise to (IV). The crude product on vacuum distillation at 140°/0.00001 mm furnished the analytical sample of (IV) (2.34g) as a colourless thick gum in 90% yield; UV λmax 217 (ε 5,971), 227 (ε 6,812) and 278 nm (ε 4,473); IR (CCl_4) ν max 3420, 1595, 1565, 1285, 1255, 990 and 915 cm^{-1}.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.9%.; H, 6.79. Found: C, 70.02; H, 6.92%..

7-Methoxyisochromanylideneethylisothiuronium acetate (V).- A mixture of allyl alcohol (IV) (0.5g), thiourea (0.186g) and glacial acetic acid (1.4 ml) was stirred at room temperature for 16 hours. The precipitated solid obtained on addition of 20 ml of ether was filtered and washed repeatedly with dry acetone to furnish the isothiuronium acetate (V) (0.474g, 60%.), m.p.137-8°; UV λ max 221 (ε 12,380), 258 (sh) (ε 8,461), 273 (ε 15,460) and 298 nm (sh) (ε 4,704); IR (KBr) ν max 3170, 1590, 1550, 1485, 1230 and 840 cm^{-1}; NMR(DMSO-d_6) δ 1.74 (s,3H, -O-CO-CH_3), 3.77(s,3H,OCH_3), 3.83 (d, 2H, J = 8.5 Hz, -S-CH_2), 4.53 (s, 2H, OCH_2), 4.63 (s, 2H, benzylic CH_2), 6.04(t,1H,J=8 Hz, olefinic), 6.65-6.90(m,2H,aromatic), 7.2-7.53 (broad,4H,NH_2) and 7.64 (d, 1H, J=8.5 Hz, aromatic proton at C_5); mass peaks at m/e 222 (25%.),m/e 189 (100%.), m/e 188 (41%.), m/e 161 (58%.), m/e 159 (43%.), m/e 146 (17%.), m/e 144 (21%.), m/e 129 (15%.), m/e 116 (11%.) and m/e 115 (29%.).

Anal. Calcd. for $C_{15}H_{20}O_4N_2S$: C, 55.66; H,6.17; N, 8.64. Found: C, 55.54; H, 6.24; N, 8.33%.

3-Methoxy-8,14-seco-7-oxaestra-1,3,5(10),9(11)-tetraen-14,17-dione(VI).- The isothiuronium acetate(V) (0.878g) and 2-methylcyclopentane-1,3-dione(0.3g) were

vigorously agitated in a mixture of water (10 ml) and ether (10 ml) for 6 hours. The aqueous layer was extracted with ether (2 x 20 ml) and then the combined ether extracts were washed successively with a 10% K_2CO_3 solution (3 x 10 ml) and water (2 x 15 ml). The dried ether layer on evaporation of the solvent afforded a pale yellow solid which on repeated recrystallization from methanol gave the seco steroid (VI) (0.59g) as a white crystalline solid, m.p. 86-7°, in 73% yield; UV λ max 221 (ε 17,370), 258 (sh) (ε 17,290), 268 (ε 21,750) and 297 nm (sh) (ε 6,874); IR ($CHCl_3$) ν max 1750, 1705, 1595, 1485, 1270, 1045, 1025 and 840 cm^{-1}; NMR (CCl_4) δ 1.07 (s,3H,methyl at C_{13}), 2.38 (d,2H,J=8 Hz, methylene at C_{12}), 2.58 (s,4H,-CO-CH_2-CH_2-CO-), 3.72 (s,3H,OCH_3), 4.33 (d,2H,J=1 Hz, allylic coupling -OCH_2), 4.56 (s,2H, benzylic CH_2), 5.68 (t, 1H, vinylic), 6.43-6.75(m,2H, aromatic) and 7.42 (d,1H,J=8.5 Hz, aromatic proton at C_1); mass peaks at m/e 300 (M^+ ion, 30%.), m/e 189 (100%.), m/e 188(25%.), m/e 161 (77%.), m/e 159 (37%.), m/e 146 (13%), m/e 144 (12%.), m/e 129 (11%.) and m/e 115(16%.).

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 72; H, 6.67. Found: C, 71.85; H, 6.89%..

3-Methoxy-7-oxaestra-1,3,5(10),8,14-pentaen-17-one (VII).- To a solution of the seco steroid(VI) (0.598 g) in a minimum quantity of methanol (8 ml) was added dropwise with stirring conc. HCl until the solution became turbid. After stirring the contents for 45 minutes, complete precipitation was observed. The precipitate was filtered and washed several times with a mixture of water and methanol (1:1) and finally dried. Preparative TLC [benzene:ethyl acetate (20:1)]of the solid followed by rapid recrystallization from acetone-petroleum ether furnished the analytical sample of the pentaene steroid (VII) (0.394g) as a pale yellow crystalline solid, m.p. 143-4°, in 70% yield; UV λmax 221 (ε 12,330), 297 (ε 9,204) and 320 nm (ε 13,170); IR($CHCl_3$) ν max 1730, 1595, 1585, 1555, 1245 and 1035 cm^{-1}; NMR ($CDCl_3$) δ 1.13 (s,3H,methyl at C_{13}), 1.49-1.96 (m,2H, methylene at C_{12}), 2.63 (m,2H,methylene at C_{11}), 3.08 (d,2H,J=8 Hz, methylene at C_{16}), 3.75 (s,3H,OCH_3), 5.0 (s,2H,benzylic CH_2), 6.07 (t, 1H, olefinic proton at C_{15}) and 6.55-7.3(m,3H,aromatic); mass peaks at m/e 282 (M^+ ion, 100%.), m/e 254 (74%.), m/e 253 (7%.), m/e 239(20%.) and m/e 211 (8%.).

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.61; H,6.38. Found: C, 76.18; H, 6.74%..

3-Methoxy-7-oxaestra-1,3,5(10),8,14-pentaen-17(e)-ol(VIII).- To a stirred ice-cold methanolic solution of the tetracyclic 17-ketone (VII) (0.207g) was added sodium borohydride (0.099g) in one lot. The reaction

mixture was stirred for 3 hours after bringing it slowly to room temperature. The yellow precipitate obtained on neutralization (pH7) with ice-cold 2N HCl was recrystallized from methanol to furnish the analytical sample of the 17-hydroxy derivative (VIII) (0.188g) as a pale yellow solid, m.p. 85-92°, in 90% yield; UV λ max 225 (ϵ 9,961), 282 (sh) (ϵ 4,842) and 321 nm (ϵ 17,660); IR ($CHCl_3$) ν max 3400, 1590, 1555, 1485, 1275, 1240 and 1035 cm^{-1}; NMR ($CDCl_3$) δ 0.97 (s,3H,CH_3 at C_{13}), 1.03-2.65 (m,7H, methylene protons at C_{11},C_{12} and C_{16} and the OH proton at C_{17}), 3.7 (s,3H,OCH_3), 4.9 (s,2H,benzylic CH_2), 5.62 (t,1H,olefinic proton at C_{15}) and 6.47-7.2 (m,3H,aromatic); mass peaks at m/e 284 (M^+ ion, 100%.), m/e 256 (14%.), m/e 255 (10%.), m/e 241 (8%.) and m/e 213 (7%.).

3-Methoxy-7-oxaestra-1,3,5(10),8-tetraen-17(e)-ol(IX).- A solution of the pentaene steroid (VIII) (0.29g) in 10 ml of thiophene-free dry benzene was stirred with 10% palladium-on-carbon catalyst (0.29g) in an atmosphere of hydrogen until 1 mole of hydrogen was absorbed. The catalyst was filtered and the white solid obtained on removal of the solvent, was chromatographed over Brockman neutral alumina (20g). The benzene-chloroform (1:1) eluates on evaporation gave a solid which on repeated recrystallization afforded the tetracyclic tetraene steroid (IX) (0.22g) as a white crystalline solid, m.p. 123-7°, in 73% yield; UV λ max 221 (ϵ 9,770) and 286 nm (ϵ 10,006); mass peaks at m/e 286 (M^+ ion, 100%.), m/e 228 (9%.), m/e 227 (20%.), m/e 226 (3%.), m/e 225 (9%.), m/e 213 (13%.), m/e 199 (23%.), m/e 148 (25%.) and m/e 147 (18%.).

Anal. Calcd. for $C_{18}H_{22}O_3$: C, 75.53; H, 7.69. Found: C, 75.1; H, 8.01%.

N.B. Prolonged hydrogenation of (IX) over the same catalyst, however. failed to saturate the 8,9-olefinic bond.

Attempted saturation of the 8,9-olefinic bond in 3-methoxy-7-oxaestra-1,3,5(10),8-tetraen-17(e)-ol (IX) with lithium in liquid ammonia:- To a stirred solution of 100 ml of liquid ammonia and the tetraene steroid (0.09g) in 50 ml of dry ether were added small bits of lithium (7 mg) in one lot. Stirring was continued until the reaction was complete as indicated by the disappearance of the blue colour. After the evaporation of liquid ammonia, the ethereal layer was washed with water (3 x 10 ml). The dried ether layer on evaporation of the solvent afforded an almost pure resinous solid (0.075g) which on evaporative distillation at 180°/0.0005 mm gave a pure sample. Examination of its NMR spectrum revealed that the compound had suffered a cleavage (16,17) of the

heterocyclic ring resulting in the formation of a polymeric material.

ACKNOWLEDGEMENTS

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REFERENCES

1. Ramadas, S.R. and Radhakrishnan, J., J.SCI.IND.RES., INDIA, 31, 145-60 (1972).
2. Huisman, H.O., 'TOTAL SYNTHESIS OF HETEROCYCLIC STEROIDAL SYSTEMS' in MTP INTERNATIONAL REVIEW OF SCIENCE, 'STEROIDS', VOL.8, Ed. by Johns, W.F., BUTTERWORTHS, LONDON, (1973).
3. Ramadas, S.R. and Chaudhuri, A.P., J.CHEM.SOC.CHEM. COMMUN., 521 (1974).
4. Davidson, D. and Begert, M.T., J.AMER.CHEM. SOC., 57, 905 (1935).
5. Ramadas, S.R., Ramana, D.V. and Chaudhuri, A.P., INDIAN J.CHEM., 11, 400 (1973).
6. Normant, H., ADV. ORG. CHEM., 2, 1(1960).
7. Colonge, J., Descotes, G. and Fournier, M., COMPT. REND., 258, 4083 (1964).
8. NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY, Ed. by Bovey, F.A., 2ND EDITION, ACAD. PRESS, NEW YORK AND LONDON, 114-6 (1969).
9. APPLICATION OF NMR SPECTROSCOPY IN ORGANIC CHEMISTRY, Ed. by Jackman, L.M. and Sternhell, S., 2ND EDITION, PERGAMON PRESS, LONDON, 129 (1969).
10. Kuo, C.H., Taub, D. and Wendler, N.L., J.ORG.CHEM., 33, 3126 (1968).
11. APPLICATION OF NMR SPECTROSCOPY IN ORGANIC CHEMISTRY, Ed. by Bhacca, N.S. and Williams, D.H., HOLDEN-DAY, INC. SAN FRANCISCO, LONDON, AMSTERDAM, 77-8 (1964).
12. The generality of the loss of 28 mass units as 'CO' from the D-ring is noticed in a series of heterocyclic and carbocyclic 17β-hydroxy steroids possessing a 14, 15-olefinic bond. The exact mechanism and its confirmation by high resolution mass spectral data will form part of our future communication.
13. The tetracyclic compounds (VIII, IX and X) are racemates and the full and dotted lines do not represent absolute configurations.
14. Banerjee, D.K., Chatterjee, S., Pillai, C.N. and Bhatt, M.V., J.AMER.CHEM.SOC., 78, 3769 (1956).

15. The recorded temperatures are uncorrected. UV spectra were determined in 95 percent methanol using a Carl-Zeiss spectrophotometer DMR-21. IR spectra were taken using a Perkin-Elmer grating infrared spectrophotometer, model 257. NMR spectra were recorded on Varian A 60-D and 100 XL spectrometers using TMS as the internal standard, the chemical shifts are reported in 'δ' values. Mass spectra were taken using a MAT-CH7 Spectrometer. Microanalyses were carried out by Dr.S.Selvavinayakam and his associates, Microbiological Laboratory, CIBA Research Centre, Goregaon, Bombay-63, India and by Messrs. P.N. Khanna and J. Saran of the Department of Medicinal Chemistry, CDRI, Lucknow, U.P., India.
16. Birch, A.J., QUART. REV., 4, 69 (1950).
17. Birch, A.J., and Smith, H., QUART. REV., 12, 17 (1958).

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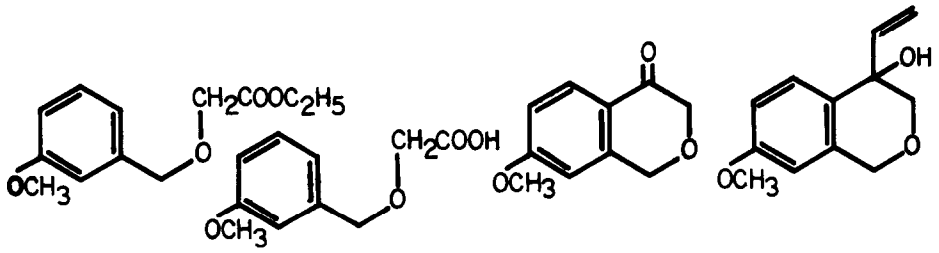
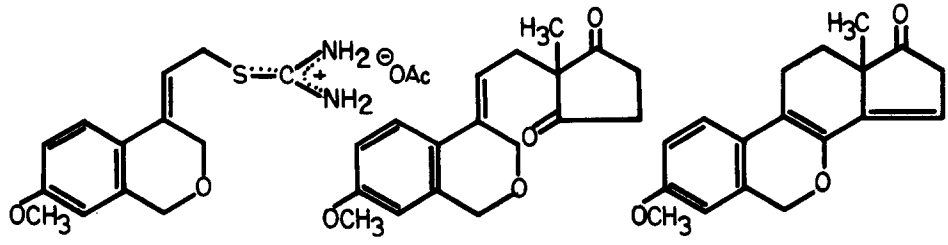
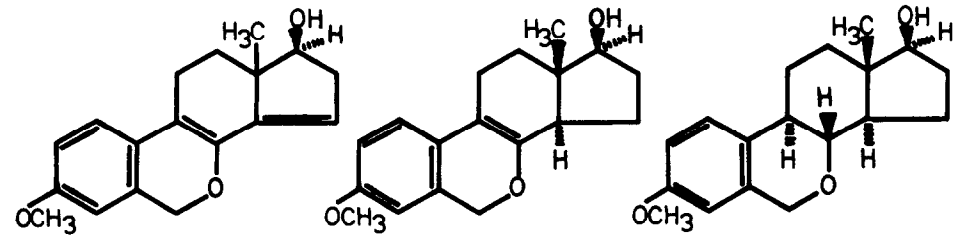


(I) (II) (III) (IV)



(V) (VI) (VII)



(VIII) (IX) (X)