

TERPENOIDS AND RELATED COMPOUNDS—XX¹

MOLECULAR REARRANGEMENTS INVOLVING 7-KETOFRIEDELENE SYSTEM

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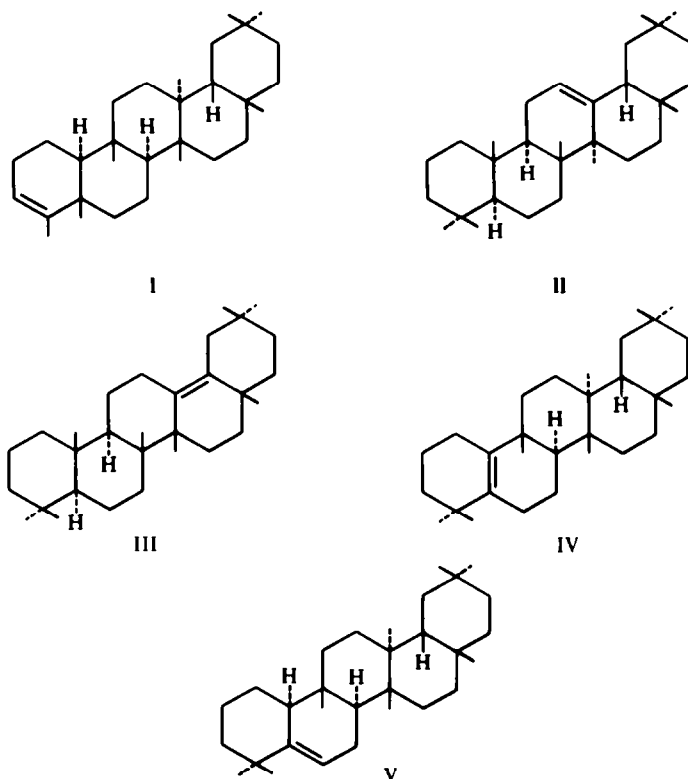
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(Received in the UK 5 November 1970; Accepted for publication 3 December 1970)

Abstract—Acid catalysed molecular rearrangement of friedel-3-en-7-one under mild conditions yielded an inseparable mixture of the starting material and friedel-5-en-7-one. Under more drastic conditions, friedel-5-en-7-one was obtained as the major product. 4- α -Bromofriedelan-3,7-dione on treatment with silver acetate furnished friedel-5-en-3,7-dione, which on Huang–Minlon reduction yielded friedel-5(10)-en-7-one.

SIMPLE friedel-3-ene (I) has been induced to undergo acid catalysed molecular rearrangement² to yield an equilibrium mixture of olean-12-ene (II) and olean-13(18)-ene (III). Under somewhat milder conditions I is rearranged³ to glut-5(10)-ene (IV),

CHART I

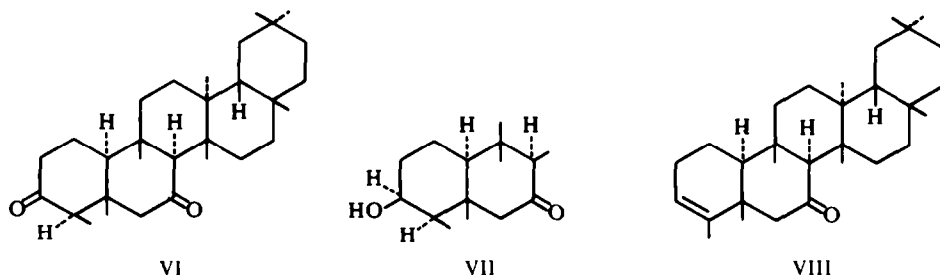


which on more vigorous treatment undergoes further methyl and hydride shifts to yield an olefinic mixture containing II and III.

It may be mentioned that glut-5-ene (V) on drastic treatment with acids⁴ gave the same mixture of olefins (II and III). But the olefin V or its derivatives furnished the derivatives of IV under milder conditions.^{4,5} Since the acid catalysed rearrangement is a thermodynamically controlled process, it is evident that olefins with higher energy content due to nonbonded steric interactions (e.g. I or V) tend to undergo methyl and hydride shifts, commonly known as "backbone rearrangement", to yield the thermodynamically more stable products II and III. But this transformation is not entirely a single step concerted process, but a two stage process,^{3d} each stage being an irreversible concerted process. The first stage represents the conversion I (or V) \rightarrow IV and the second stage consists of the conversion IV \rightarrow II and III.

If a somewhat unreactive electron withdrawing group, like a CO group, is placed at C₇, it may be presumed that the second stage (IV \rightarrow II and III) will be completely prohibited. That this is indeed the case is demonstrated in the present communication. The starting material friedel-3-en-7-one (VIII) was prepared from putranjibadione (VI), whose structure and stereochemistry was settled by us.⁶ The latter on preferential reduction of the 3-keto group with sodium borohydride furnished 7-ketofriedelan-3 β -ol (VII)^{6,7} in which the C₃-OH group and C₄-H atom were in anti-periplanar orientation to undergo smooth elimination of a molecule of water on treatment with phosphorus oxychloride and furnish mainly friedel-3-en-7-one (VIII).

CHART II



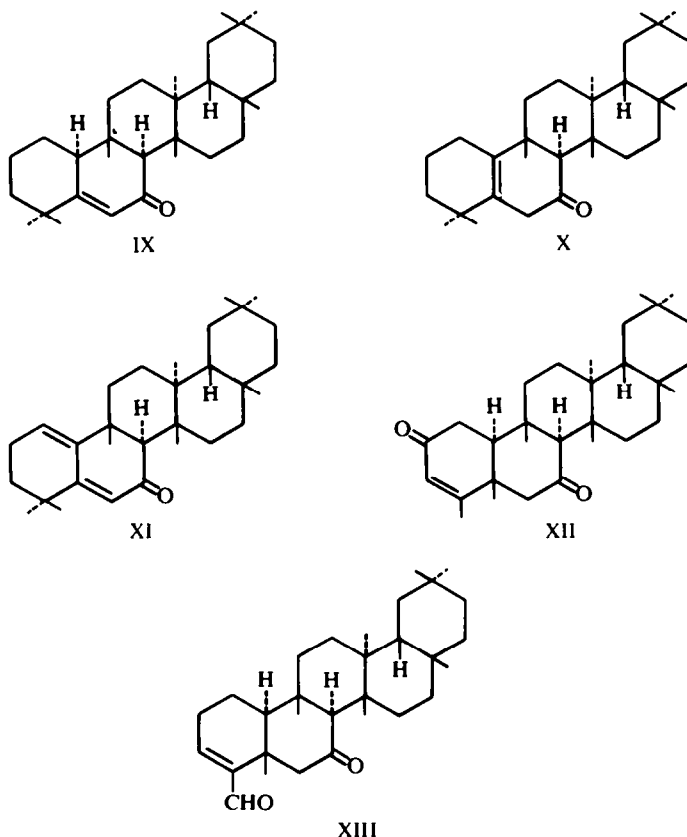
When anhydrous hydrogen chloride was bubbled through a refluxing solution of this enone (VIII) in glacial acetic acid for 3 to 6 hr a mixture of isomeric compounds having the molecular formula C₃₀H₄₈O was obtained. The mixture could not be resolved to give pure rearranged products, but its UV absorption spectra (λ_{\max} 243 m μ , E 4600) demonstrated that it contained *ca* 40% of glut-5-en-7-one (IX), which fact was supported by the IR spectra which showed peaks at 1700 cm⁻¹ (saturated 6-membered ring ketone) due to the presence of either the starting enone (VIII) or glut-5(10)-en-7-one (X) or both and at 1670 cm⁻¹ (conjugated 6-membered ring ketone) due to the presence of glut-5-en-7-one (IX).

The mixture on selenium dioxide oxidation⁸ furnished two compounds which could be separated by chromatography. The less polar compound, C₃₀H₄₆O, m.p. 235–238°, [α]_D 205° showed UV absorption maxima at 287 m μ (E 15,800). Its IR spectra showed a band at 1665 cm⁻¹ (conjugated 6-membered ring ketone). Hence this compound was glut-1(10),5-diene-7-one (XI) derived by selenium dioxide

oxidation of glut-5-en-7-one (IX) and glut-5(10)-en-7-one (X) present in the rearranged mixture.

The more polar component was a dicarbonyl compound, $C_{30}H_{46}O_2$, m.p. 306–310°, $[\alpha]_D^{25} 47^\circ$ which, we believed, could be either friedel-3-en-2,7-dione (XII) or 7-keto-friedel-3-en-23-al (XIII). That it was not the endione (XII) was shown by the preparation of the latter from the enone (VIII) by dichromate oxidation. The endione (XII), m.p. 284–286°, $[\alpha]_D^{25} 26.6^\circ$ showed UV absorption maxima at 235 $m\mu$ (E 13,700) and IR bands at 1720 cm^{-1} (saturated 6-membered ring ketone) and 1670 cm^{-1} ($\alpha\beta$ -unsaturated ketone). The NMR spectra showed singlets at 0.95 (3H), 1.00 (6H), 1.11 (3H), 1.17 (3H) and 1.4 (6H) ppm for the seven angular Me groups. The vinyl methyl at C_4 appeared as a doublet ($J = 2.5\text{ c/s}$) at $\delta 1.85$ ppm due to coupling with the vinyl proton at C_3 . The latter proton appeared as a broad signal (1H) at $\delta 5.73$ ppm due to long range coupling.

CHART III

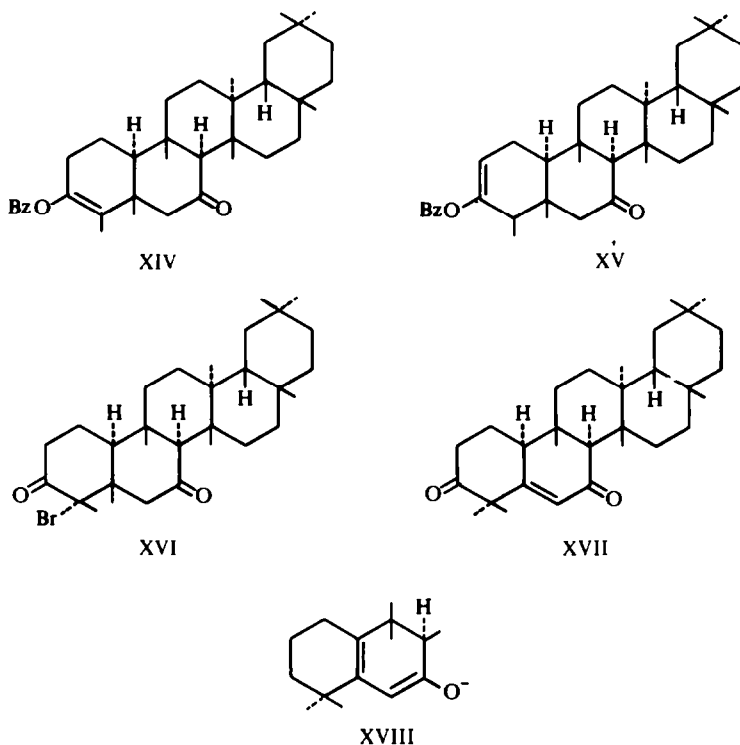


The dicarbonyl compound, m.p. 306–310° was therefore the ketoaldehyde (XIII), which structure was supported by its spectral data. It showed UV absorption maxima at 226 $m\mu$ (E 7200) and IR bands at 1715 cm^{-1} (saturated 6-membered ring ketone), 1680 and 2770 cm^{-1} ($\alpha\beta$ -unsaturated aldehyde) and 1640 cm^{-1} (conjugated $C=C$). The NMR spectra showed signals due to seven tertiary Me groups at $\delta 0.95$, 1.00,

1.18, 1.32, 1.36 and 1.40 ppm. The vinyl Me signal was absent, but instead an aldehyde proton signal (1H) appeared at δ 9.28 ppm. The signal for the olefinic proton at C₃ moved downfield and appeared as a broad multiplet at δ 6.6 ppm, since it was now on the β -carbon of an $\alpha\beta$ -unsaturated aldehyde system. Obviously the ketoaldehyde (XIII) was formed from the unchanged enone (VIII) present in the above mentioned rearranged mixture. This was substantiated by the conversion of the pure enone (VIII) to the same ketoaldehyde (XIII) by oxidation with selenium dioxide in the same manner.

Next we attempted to prepare pure friedel-5-en-7-one (IX) through a different route starting from putranjivadione (VI). The latter on heating^{2c} with benzoyl chloride furnished the Δ^3 -enolbenzoate (XIV), m.p. 292–294°, $[\alpha]_D$ 51.7°. That it was

CHART IV



not the isomeric Δ^2 -enolbenzoate (XV) was demonstrated by the absence of any olefinic proton signal in the NMR spectra. The seven tertiary Me signals appeared at δ 0.84, 0.90, 1.00, 1.10, 1.20 and 1.40 ppm. The vinyl Me at C₄ appeared upfield as a singlet (3H) at δ 1.50 ppm due to shielding by the benzoate group at C₃. The five aromatic protons gave signals in the region δ 7.40 to 8.2 ppm. It showed UV absorption maxima at 231 m μ (E 14,600) and IR bands at 1730 cm⁻¹ (saturated 6-membered ring ketone) and 1700 and 1275 cm⁻¹ (benzoate). The enolbenzoate (XIV) on bromination^{2c} furnished the bromoketone (XVI), m.p. 172–174°, $[\alpha]_D$ 62.5° which did not exhibit any UV maxima in the region 220–250 m μ . In the IR spectra the two saturated CO groups showed a broad band at 1715 cm⁻¹. This bromoketone (XVI) on refluxing

with silver acetate in glacial acetic acid solution gave glut-5-en-3,7-dione (XVII), m.p. 305–307°, $[\alpha]_D -91.7^\circ$ which showed an UV absorption maxima at 243 m μ and IR bands at 1710 cm $^{-1}$ (saturated 6-membered ring ketone) and 1665 cm $^{-1}$ ($\alpha\beta$ -unsaturated ketone). The NMR spectra showed singlets at δ 1.02, 1.08, 1.14, 1.20, 1.25, 1.34, 1.36 and 1.42 ppm for the eight tertiary Me groups. The olefinic proton at C₆ appeared as a doublet (1H, $J = 2$ c/s) at 5.95 ppm split by the α -hydrogen at C₁₀. We expected that this endione (XVII) on Huang–Minlon reduction would preferentially reduce the keto group at C₃ to yield the enone (IX). But instead the reduction gave a mixture which on purification provided only the unconjugated enone (X) as the major component. The enone (X), m.p. 258–260° did not exhibit any maxima in the UV absorption spectra in the region 210–250 m μ but showed an IR band at 1709 cm $^{-1}$ due to the $\beta\gamma$ -unsaturated CO system. The NMR spectra revealed the absence of any olefinic proton. On treatment with selenium dioxide this enone (X) provided the same conjugated dienone (XI) described earlier.

We next carried out the acid treatment on friedel-3-en-7-one (VIII) under more drastic conditions i.e. (i) refluxing with aqueous hydrochloric acid in glacial acetic acid for 24 hr and (ii) refluxing with anhydrous hydrogen chloride in glacial acetic acid for 12 hr. Under these conditions simple friedel-3-ene (I) furnished a mixture of II and III as stated before. In either case we isolated the conjugated enone (IX), m.p. 279–280°, $[\alpha]_D 54.5^\circ$ as the major product. It showed a band at 1660 cm $^{-1}$ in the IR spectra and a maxima at 243 m μ (E 10,700) in the UV spectra. The NMR spectra showed singlets (3H each) at δ 0.90, 0.98, 1.02, 1.06, 1.10, 1.12, 1.20 and 1.35 ppm for the eight tertiary Me groups. The vinyl proton at C₆ appeared as a doublet (1H, $J = 2$ c/s) at δ 5.84 ppm split by the α -hydrogen at C₁₀.

As pointed out earlier in this communication simple glut-5(10)-ene (IV) is thermodynamically more stable than glut-5-ene (V). This difference in energy should be attributed to the more intense nonbonded interaction between the olefinic proton at C₆ in V and the equatorial Me group at C₄, since the shorter olefinic linkage between C₅ and C₆ has brought these two interacting centres closer than in IV. But the situation is quite different with the corresponding 7-keto derivatives. Since the conjugated enone (IX) is formed as the major product in the drastic proton catalysed rearrangement which is a thermodynamically controlled process, this enone (IX) must be of lower energy than the nonconjugated enone (X) and the backbone rearrangement does not proceed any further. Obviously the enone (IX) has greater stability due to resonance of the $\alpha\beta$ -unsaturated CO system.

The formation of the nonconjugated enone (X) by the Huang–Minlon reduction of the endione (XVII) is not unexpected. It has obviously been formed by a kinetically controlled⁹ protonation of the enolate anion (XVIII) formed in the alkaline medium used. In order to test this conclusion the enone (IX) was treated with base. It remained unchanged with methanolic alkali, but on vigorous refluxing (Huang–Minlon condition) with potassium hydroxide in diethylene glycol, it furnished a mixture from which the nonconjugated enone (X) was obtained as the major product.

EXPERIMENTAL

M.p.s are not corrected. UV absorption spectra were taken in 95% EtOH. Rotations were measured in CHCl₃. NMR spectra were taken in 60 Mc instruments in CDCl₃ using TMS as reference standard.

Friedel-3-en-7-one (VIII)

Phosphorus oxychloride (4 ml) was slowly added to a soln of VII^{6,7} (0.5 g) in pyridine (40 ml) and the mixture was allowed to stand overnight. It was finally refluxed for 5 min, cooled and poured into crushed ice. The ppt was extracted with ether and the ether soln was washed with 2% HCl aq, then water, dried (Na₂SO₄) and evaporated to yield a residue (0.35 g), which was chromatographed over activated alumina (30 g). Elution with a mixture of light petroleum and benzene (4:1) furnished a solid (0.29 g), which on crystallisation from CHCl₃-acetone furnished VIII, m.p. 280–283°, [α]_D 72.1°. (Found: C, 84.96; H, 11.13. C₃₀H₄₈O requires: C, 84.84; H, 11.39%); IR spectra showed peaks at 1710 cm⁻¹ (saturated 6-membered ring ketone) and 796 cm⁻¹ (trisubstituted double bond).

Proton catalysed rearrangement of Friedel-3-en-7-one (VIII)

A stream of dry HCl was bubbled through a suspension of VIII (0.1 g) in boiling glacial AcOH (100 ml). The solid material soon dissolved and the soln was refluxed for 3 to 6 hr, then poured into ice and the ppt was filtered off and chromatographed over activated alumina (10 g). Elution with light petroleum gave a solid which on crystallisation from CHCl₃-acetone furnished the isomeric mixture (see Introduction), m.p. 253–258°, [α]_D 2.8°. (Found: C, 84.78; H, 11.43. C₃₀H₄₈O requires: C, 84.84; H, 11.39%); IR and UV: See Introduction.

Selenium dioxide oxidation of the isomerised mixture

Gluta-1(10),5-dien-7-one (IX) and *7-ketofriedel-3-en-23-al* (XIII). A soln of SeO₂ (0.25 g) in water (0.6 ml) was added to a suspension of the above isomerised mixture (0.2 g) in glacial AcOH (140 ml) and the mixture was refluxed for 4 hr. The hot soln was filtered and diluted with cold water. The ppt was filtered off and chromatographed over a column of activated alumina (30 g). Elution with light petroleum and benzene (7:3) yielded a solid (0.05 g), which on crystallisation from CHCl₃-acetone furnished XI, m.p. 235–238°, [α]_D 205°. (Found: C, 85.47; H, 11.09. C₃₀H₄₆O requires: C, 85.24; H, 10.97%); IR and UV: See Introduction.

Further elution of the above column with benzene gave a solid (0.06 g), which on crystallisation from CHCl₃-acetone furnished XIII, m.p. 306–310°, [α]_D 47°. (Found: C, 82.17; H, 10.71. C₃₀H₄₆O₂ requires: C, 82.13; H, 10.57%); IR, UV and NMR: See Introduction.

Selenium dioxide oxidation of friedel-3-en-7-one (VIII)

7-Ketofriedel-3-en-23-al (XIII). The enone VIII (0.17 g) in glacial AcOH (120 ml) was treated as above with a soln of SeO₂ (0.2 g) in water (0.5 ml). After usual working up the same XIII (0.1 g), m.p. 305–309° was obtained.

Sodium dichromate oxidation of friedel-3-en-7-one (VIII)

Friedel-3-en-2,7-dione (XII). A mixture of VIII (0.34 g), sodium dichromate (0.34 g), benzene (27 ml) and glacial AcOH (27 ml) was refluxed for 4 hr. Water was added and the organic materials were taken up in ether. The solid residue (0.36 g) obtained after the evaporation of ether was chromatographed over a column of activated alumina (20 g). After a forerun of 0.17 g of unchanged VIII, elution with light petroleum and benzene (3:2) furnished a solid (0.12 g), which on crystallisation from CHCl₃-MeOH gave XII, m.p. 284–286°, [α]_D 26.6°. (Found: C, 82.27; H, 10.33. C₃₀H₄₆O₂ requires: C, 82.13; H, 10.57%); IR, UV and NMR: See Introduction.

 Δ^3 -Enolbenzoate of purranjivadione (XIV)

A mixture of VI, 1.1 g and benzoyl chloride (15 ml) was heated at 180° for 3 hr, cooled and treated slowly with EtOH (200 ml). The ppt was filtered off and crystallised from CHCl₃-acetone to furnish XIV, m.p. 292–294°, [α]_D 51.7°. (Found: C, 81.51; H, 9.42. C₃₇H₅₂O₂ requires: C, 81.57; H, 9.62%); IR, UV and NMR: See Introduction.

4 α -Bromofriedelan-3,7-dione (XVI)

A soln of Br₂ (0.11 ml) in CHCl₃ (2 ml) was added dropwise with stirring to a soln of XIV, 1 g in CHCl₃ (10 ml). The soln was concentrated under reduced pressure and the residue was chromatographed over silica gel (25 g). Elution with light petroleum and benzene (3:2) furnished a solid (0.4 g), which on crystallisation from CHCl₃-MeOH gave XVI, m.p. 172–174°, [α]_D 62.5°. (Found: C, 69.29; H, 9.11; Br, 15.49. C₃₀H₄₇BrO₂ requires: C, 69.36; H, 9.05; Br, 15.4%); IR and UV: See Introduction.

Glut-5-en-3,7-dione (XVII)

The above XVI (0.5 g) was added to a hot soln of AgOAc (0.15 g) in glacial AcOH (84 ml) and the mixture was refluxed for 3 hr, cooled and poured into ice and HCl. The ppt was extracted with CHCl_3 , and the CHCl_3 extract was washed with water, dried (Na_2SO_4) and evaporated to yield a solid which was chromatographed over a column of silica gel (10 g). Elution with light petroleum and benzene (2:3) furnished a solid (0.28 g) which on crystallisation from CHCl_3 -acetone gave XVII, m.p. 305–307°, $[\alpha]_D -91.7^\circ$. (Found: C, 82.02; H, 10.30. $\text{C}_{30}\text{H}_{46}\text{O}_2$ requires: C, 82.13; H, 10.5%); IR, UV and NMR: See Introduction.

Huang-Minlon reduction of glut-5-en-3,7-dione (XVII)

Glut-5(10)-en-7-one (X). The endione XVII (0.12 g) in diethylene glycol (37 ml) was refluxed with 85% hydrazine hydrate (5 ml) for 12 hr. Then KOH (0.8 g) was added and the mixture was refluxed for 1 hr when the condenser was removed and the inner temp was raised to 190°. After refluxing for further 24 hr the mixture was worked up in the usual manner to furnish a solid (0.1 g), which was chromatographed over activated alumina (10 g). Elution with light petroleum yielded a solid, which on crystallisation from CHCl_3 -acetone yielded X, m.p. 258–260°. (Found: C, 84.74; H, 11.17. $\text{C}_{30}\text{H}_{48}\text{O}$ requires: C, 84.84; H, 11.39%); IR and UV: See Introduction.

Selenium dioxide oxidation of glut-5(10)-en-7-one (X)

Gluta-1(10),5-dien-7-one (XI). The enone X (40 mg) in glacial AcOH (34 ml) was oxidised in the usual manner with a soln of SeO_2 (50 mg) in water (0.1 ml) to yield XI, m.p. 235–238°, identical with XI described earlier.

Glut-5-en-7-one (IX)

Dry HCl was passed through a soln of VIII (0.25 g) in boiling glacial AcOH (200 ml) for 12 hr. The residue obtained after usual working up was chromatographed over activated alumina (20 g). Elution with light petroleum and benzene (9:1) gave a solid, which on crystallisation from CHCl_3 -acetone afforded IX, m.p. 279–280°, $[\alpha]_D 54.5^\circ$. (Found: C, 85.10; H, 11.21. $\text{C}_{30}\text{H}_{48}\text{O}$ requires: C, 84.84; H, 11.39%); IR, UV and NMR: See Introduction.

The same enone IX was obtained by refluxing VIII in AcOH with HCl aq for 24 hr.

Glut-5(10)-en-7-one (X) from glut-5-en-7-one (IX)

Glut-5-en-7-one (IX), 0.08 g was refluxed with a soln of KOH (1 g) in diethylene glycol (28 ml) for 12 hr. After usual work up, the solid obtained was chromatographed over alumina and crystallised from CHCl_3 -acetone to yield X, m.p. 258–260° identical with X mentioned earlier.

Acknowledgements—We are highly indebted to Prof. K. H. Overton of Glasgow University and to Prof. P. C. Mukherjee of Presidency College, Calcutta for the NMR spectra and to Prof. D. K. Banerjee of the Indian Institute of Science, Bangalore, to Prof. J. N. Chatterjee of Patna University and to Dr. S. C. Pakrashi of the Indian Institute of Experimental Medicine, Calcutta for the IR spectra. We are also indebted to the Council of Scientific and Industrial Research, India for the award of a Junior Research Fellowship to one of us (M.S.).

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