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Synthesis of Perhydrofluorenone Derivatives

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SEVERAL attempted total syntheses of gibberellins and related compounds have been reported. Matsui and his co-workers¹ synthesised the natural gibberellins A₂, A₄, A₆, and A₁₀ by using intermediates derived from natural gibberellins.

We have studied the conversion² of (I) into the γ -lactone derivatives, (II) and (III), which demonstrated the possibility of the application of Diels-Alder reaction of furan derivatives in the synthesis of the oxygenated A-ring of polycyclic terpenoids such as the gibberellins.

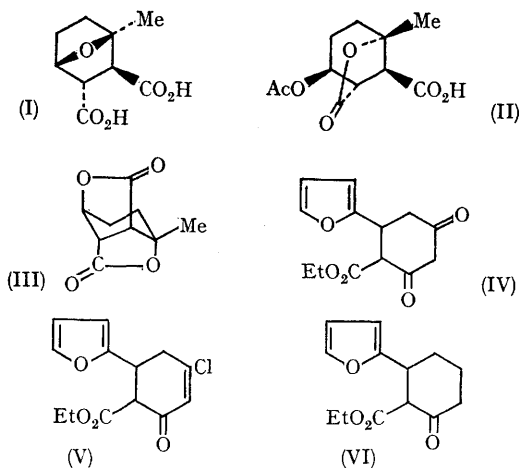
The furan derivative (VI), easily obtainable from (IV)³ by chlorination with phosphorous trichloride and subsequent hydrogenation of (V),

was used in an attempt at the total synthesis⁴ of gibberellins.

Addition of maleic anhydride to (VI) resulted in the predominant formation[†] of (VIIa) (75%, m.p. 113—114°). Although the formation of the stereoisomer (VIIb) was expected to be equally probable, only (VIIa) was isolated.

Catalytic hydrogenations of (VIIa) with palladium-charcoal and subsequent methanolysis of (VIII) afforded the half-ester (IXa) exclusively. Esterification of the remaining carboxyl-group of (IXa) failed under the usual conditions (diazomethane or dimethyl sulphate) and was only achieved by treatment with methyl iodide in the presence of dry potassium *t*-pentoxide in dimethyl sulphoxide, to give (IXb), {73%, from (VIIa), m.p. 153—154°; i.r. (KBr), 1740 and 1705 cm.⁻¹; n.m.r. (CDCl₃), 2.96 and 3.30 [H(1) and H(10a), AB-type quartet, *J* 10 c./sec.] and 4.98 p.p.m. [H(2), br s, half-band width 6 c./sec.]. The proton coupling between C(10a), C(1), and C(2) in the n.m.r. spectrum of (IXb) indicated retention of the *exo-cis* configuration of the two carbomethoxy-groups on conversion of (VIIa) into (IXb).

When (IXb) was treated with one equivalent of sodium hydride in absolute benzene, formation of the B ring with de-ethoxycarbonylation of (IXb) occurred unexpectedly, to afford the perhydrofluorenone derivatives, (Xa) {75%; m.p. 161—162°; i.r. (KBr), 1738, 1671, and 1605 cm.⁻¹; n.m.r. (CDCl₃), 8.63 [H(9a), s], 4.72 [H(2)] and 2.98 p.p.m. [H(1) and H(10a)]} and (Xb) {ca. 10%; m.p. 171—172°; n.m.r. (CDCl₃), 8.79 [H(9a)], 4.71



[†] Satisfactory elemental analyses were obtained for all new compounds.

[H(2)], 3.23 [H(1), t, J 4.7 c./sec.] and 3.03 [H(10a), d, J 4.7 c./sec.] p.p.m.}. The n.m.r. and i.r. spectra and the positive ferric chloride test demonstrate that H(9a) of (Xa) and (Xb) are in the enol form.

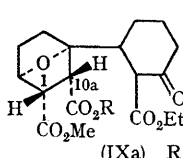
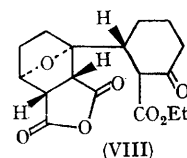
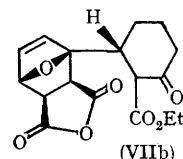
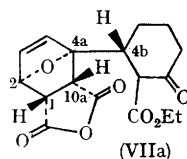
Alkylation of (Xa) with prop-2-ynyl bromide gave (XIa), {55%; m.p. 168—169°; i.r. (KBr), 3280, 1755, 1735, and 1697 cm^{-1} ; n.m.r.(CDCl_3), 4.72 [H(2)], 3.02, and 2.70 [H(1) and H(10a), AB-type quartet, J 9.7 c./sec.], ca. 2.7 [H(9)], 3.13 [H(4b)], and 2.08 ($\text{C}\equiv\text{CH}$, t, J 2.9 c./sec.) p.p.m.}. The *cis* B-c ring-junction was established as follows. In the n.m.r. spectrum of the tetrahydro-derivative (XIb), up-field shifts of H(4b) [Δ (XIb)–(XIa) 23.4 c./sec.] and H(10a) [Δ (XIb)–(XIa) 5.4 c./sec.] were observed, which were explained by the removal of an anisotropy effect of acetylenic bond.

Basic reagents react with (XIa) at H(10a) to give the ether-cleaved product (XII) {70%; m.p. 141°; i.r.(KBr), 3450, 3250, 1732, 1710, 1682, and 1642 cm^{-1} ; n.m.r.(CDCl_3), 4.27 [H(2)] and 3.55 [H(1)] p.p.m.}, which when treated with acetic anhydride and dimethyl sulphoxide, was oxidized to the phenolic compound (XIII) {m.p. 139°; i.r.(KBr), 3400 br, 3250, 1732, 1670, and 1601 cm^{-1} ; n.m.r.(CDCl_3), 10.45 (OH), 7.33 and 7.63 (aromatic protons, AB-type quartet, J 8.5 c./sec.), 3.77 [H(4b)], 2.57, and 3.00 [C(9)-protons, J 17.0 and 3.0 c./sec.] and 1.92 p.p.m. ($\text{C}\equiv\text{CH}$, t, J 3.0 c./sec.) }.

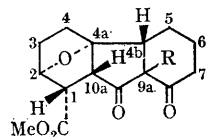
¹ K. Mori, M. Shiozaki, N. Itaya, T. Ogawa, M. Matsui, and Y. Sumiki, *Tetrahedron Letters*, 1968, 2183, and references therein.

² Y. Kitahara, T. Kato, N. Ototani, A. Inoue, and H. Izumi, *J. Chem. Soc. (C)*, in the press.

³ O. Neilands and J. Polis, *Latvijas P.S.R. Zinatnu Akad. Vestis, Khim. Ser.*, 1963, 192 (*Chem. Abs.*, 1964, 60, 5427).

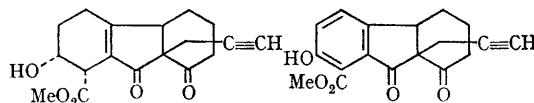
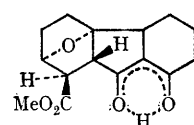


(IXb) R=Me



(XIa) R=CH₂C≡CH

(XIb) R=Prⁿ



(XIII)

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