Synthesis of Perhydrofluorenone Derivatives

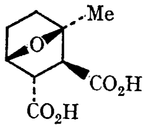
By YOSHIO KITAHARA,* TADAHIRO KATO, MAKOTO FUNAMIZU, NOBORU OTOTANI, AKIRA INOUE, and HIDEO IZUMI
(*Department of Chemistry, Faculty of Science, Tohoku University, Katahiracho No. 75, Sendai, Japan*)

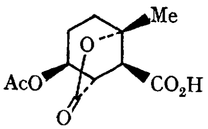
SEVERAL attempted total syntheses of gibberellins and related compounds have been reported. Matsui and his co-workers[1] synthesised the natural gibberellins A_2, A_4, A_9, and A_{10} by using intermediates derived from natural gibberellins.

We have studied the conversion[2] 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 synthesis of gibberellins.

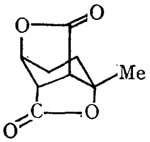
(I)

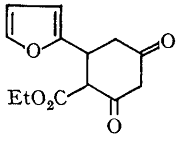




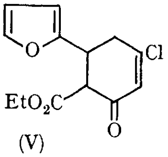
(II)

(III)

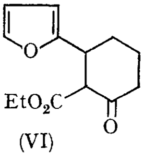




(IV)



(V)



(VI)

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-pentyloxide in dimethyl sulphoxide, to give (IXb), {73%, from (VIIa), m.p. 153—154°; i.r. (KBr), 1740 and 1705 cm.$^{-1}$; n.m.r. ($CDCl_3$), 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.($CDCl_3$), 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.($CDCl_3$), 8·79 [H(9a)], 4·71

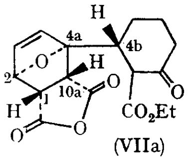
---

† Satisfactory elemental analyses were obtained for all new compounds.

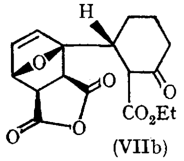
[H(2)], 3·23 [H(1), t, *J* 4·7 c./sec.] and 3·03 [H(10a), d, *J* 4·7 c./sec.] p.p.m.}. The n.m.r. and i.r. spectra and the positive ferric chloride test demonstrate that H(9a) of (Xa) and (Xb) are in the enol form.

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 (C≡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.

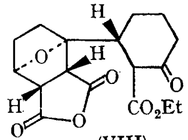
Basic reagents react with (XIa) at H(10a) to give the ether-cleaved product (XII) {70%; m.p. 141°; i.r.(KBr), 3450, 3250, 1732, 1710, 1682, and 1642 cm.$^{-1}$; n.m.r.($CDCl_3$), 4·27 [H(2)] and 3·55 [H(1)] p.p.m.}, which when treated with acetic anhydride and dimethyl sulphoxide, was oxidized to the 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. (C≡CH, t, *J* 3·0 c./sec.)}.



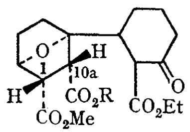
(VIIa)



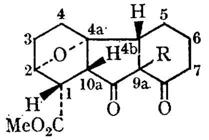
(VIIb)



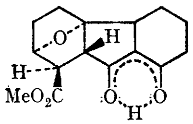
(VIII)



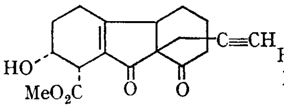
(IXa) R=H
(IXb) R=Me



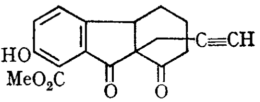
(Xa) R=H
(XIa) R=$\overset{9}{\mathrm{C}}\mathrm{H_2}\cdot\overset{8}{\mathrm{C}}$:CH
(XIb) R=Pr^n



(Xb)



(XII)



(XIII)

(*Received, October 3rd,* 1968; *Com.* 1356.)

---

[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).