Bridged Bicyclo[3,2,1]octane Ring System by Intramolecular Carbene Insertion Reaction: a New Synthetic Approach to Tetracyclic Diterpenoids

By S. K. DASGUPTA, R. DASGUPTA, S. R. GHOSH, and U. R. GHATAK*

(*Department of Organic Chemistry, Indian Association for the Cultivation of Science, Calcutta-32, India*)

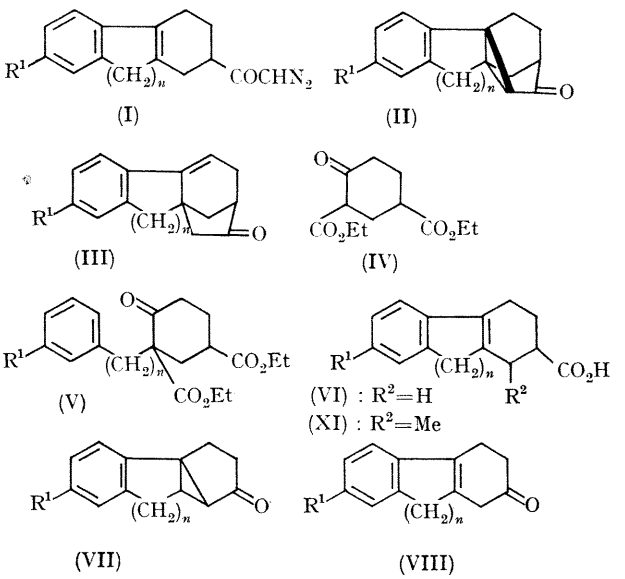
Summary Syntheses of the basic skeletal structures of gibberelins and some tetracyclic diterpenoids have been achieved by intramolecular carbene insertion reaction and subsequent cleavage of the cyclopropane ring.

THE recent disclosure[1] of the preparation of a bicyclo[3,2,1]-octane derivative by intramolecular alkylation *via* a carbenoid intermediate prompts us to report a few of the related results of our investigations. The intramolecular cyclisation of the diazo-ketones (I) to the cyclopropane derivatives (II) and subsequent acid-catalysed cleavage to the bridged-ring compounds (III), having the basic skeletal structures of gibberellins and phyllocladene are now reported.

Alkylation of the keto-diester (IV) with *m*-methoxybenzyl chloride and *β*-phenethyl bromide led to the products (Va) [b.p. 190—195°/0·2 mm., λ_{max} (EtOH) 275 nm. (log ϵ 3·41)] and (Vb) [b.p. 135—136°/0·15 mm., λ_{max} 255 nm. (log ϵ 3·27)] in 61% and 38% yields, respectively. These underwent simultaneous hydrolysis, decarboxylation, and dehydration on being refluxed with HCl–AcOH to afford the tricyclic *βγ*-unsaturated acids (VIa) [m.p. 213°, λ_{max} 266 nm. (log ϵ 4·31)] and (VIb) [m.p. 203—204°, λ_{max} 267 nm. (log ϵ 4·01)]. These two acids were converted into the corresponding unsaturated diazo-ketones (Ia) (m.p. 103°, ν_{max} 2112, 1630 cm.$^{-1}$) and (Ib) [ν_{max} ($CHCl_3$) 2115, 1630 cm.$^{-1}$] in excellent yields by treatment of the corresponding acid chlorides with diazomethane. The crude diazo-ketones were subjected to cyclisation[3] leading to the formation of the cyclopropane derivatives (IIa) [m.p. 121°, λ_{max} 248 nm. (log ϵ 4·01). ν_{max} 1710 cm.$^{-1}$] and (IIb) [m.p. 99–100°, λ_{max} 238 nm. (log ϵ 4·1), ν_{max} 1715 cm.$^{-1}$].

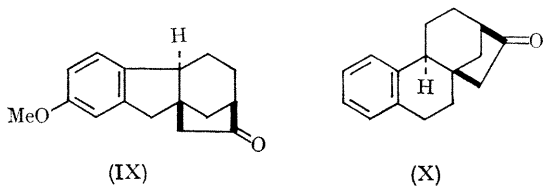
Cleavage of the cyclopropane derivatives (IIa) and (IIb) with dry HCl in $CHCl_3$ produced the bridged-ring compounds (IIIa) [m.p. 128°, λ_{max} 266 nm. (log ϵ 4·30), ν_{max} 1735 cm.$^{-1}$] and (IIIb) [b.p. 135°/0·1 mm., λ_{max} 265 nm. (log ϵ 4·17), ν_{max} 1730 cm.$^{-1}$; 2,4-dinitrophenylhydrazone, m.p. 190—192°] in over 90% yield. The spectral data of these two compounds indicated[4] the preferential cleavage of the cyclopropane bond which is in conjunction with both the aromatic ring and the carbonyl function. These observations are in accord with those for similar cleavages of compounds (VIIa) and (VIIb) in which the preferential fission of the benzylic bonds led to the formation of compounds (VIIIa) and (VIIIb), respectively.[5]

Catalytic hydrogenation of (IIIa) and (IIIb) in the presence of 10% palladium–charcoal afforded the tetracyclic saturated ketones (IX) [m.p. 115°, λ_{max} 230 nm. (log ϵ 3·75), 280 nm. (log ϵ 3·45), ν_{max} 1730 cm.$^{-1}$] and (X) [b.p. 140°/0·2 mm., λ_{max} 266 nm. (log ϵ 2·74), 274 nm. (log ϵ 2·73), ν_{max} 1735 cm.$^{-1}$; 2,4-dinitrophenylhydrazone, m.p. 164—166°] in quantitative yields. *trans*-Fused stereochemistry



(I)—(VIII): a; R^1=OMe,n=1
b; R^1=H,n=2

has been tentatively assigned to these products by analogy with similar reported[6] hydrogenation results.



Experiments are also under way with (XI) to study the formation of the cyclopropane ring and its fission, in order to evaluate the effect of a substituent on the course of these reactions.

(*Received, September 8th,* 1969; *Com.* 1351.)

[1] D. J. Beames and L. N. Mander, *Chem. Comm.*, 1969, 498.
[2] A. Chatterjee and D. Banerjee, *J. Indian Chem. Soc.*, 1968, **45**, 78.
[3] S. K. Dasgupta and A. S. Sarma, *Tetrahedron Letters*, 1968, 2983 and references cited therein.
[4] *Cf.* R. McCrindle, A. Martin, and R. D. H. Murray, *J. Chem. Soc.*, 1968, 2353.
[5] S. K. Dasgupta and S. R. Ghosh, unpublished results.
[6] J. F. Grove, J. McMillan, T. P. C. Mulholland, and W. B. Turner, *J. Chem. Soc.*, 1960, 3049; Y. Kos and H. J. E. Loewenthal, *ibid.*, 1963, 605; H. J. E. Loewenthal and Z. Neuwirth, *J. Org. Chem.*, 1967, **32**, 517.