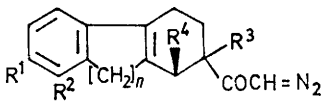
Intramolecular Keto-carbenoid Addition to Double Bonds: Stereochemistry of the Catalytic Reduction of $\Delta^{9(11)}$-Gibbenes and Related Compounds

By USHA R. GHATAK,* PRABIR C. CHAKRABORTI, BRINDABAN C. RANU, and BAIJAYANTI SANYAL (*née* Moitra)
(*Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta-32, India*)

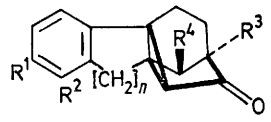
Summary Decomposition of some γδ-unsaturated α-diazomethyl ketones using an 'activated CuO catalyst' under irradiation with a tungsten lamp results in a significant increase in the yields of the corresponding intramolecular keto-carbenoid addition products; the substituents effect in controlling the stereoselectivity in the catalytic hydrogenation of a few pentacyclic ketones and $\Delta^{9(11)}$-gibbene derivatives have been evaluated, leading to stereocontrolled syntheses of some C-9 epimeric gibbane synthons and a degradation product of gibberellin A_{13}.

RECENTLY we reported[1] a route *via* intramolecular carbenoid addition, to tetracyclic bridged bicyclo[3,2,1]octanones, intermediates in diterpenoid synthesis. We also showed that the cyclopropyl ketone (**3a**) is hydrogenolysed regio- and stereo-specifically in the presence of Pd–C (10%) in EtOH, giving the 9α-gibbane (**6a**) as sole product. In contrast, reduction of the 9,11-styrenoid bond in the gibbene (**5a**) produces a mixture (69 : 31) of the C-9 epimeric ketones (**6a**) and (**7a**). We report here an efficient procedure for intramolecular keto-carbenoid addition to double bonds and our preliminary studies on stereospecificity in the catalytic reduction of other related cyclopropyl ketones and $\Delta^{9(11)}$-gibbene derivatives, leading to stereocontrolled routes to some C-9 epimeric gibbane synthons, including a degradation product of gibberellin A_{13}. Our studies demonstrate that although in the reductive cleavage of cyclopropyl ketones a high degree of stereospecificity is generally maintained, a small change in substitution pattern in the $\Delta^{9(11)}$-gibbenes can cause drastic change in the stereochemistry of the hydrogenation products.

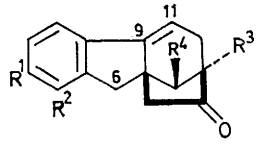
In our improved procedure,[2] solutions of the diazoketones (2 mmol) in 150—200 ml of anhydrous cyclohexane–tetrahydrofuran (7 : 3) or cyclohexane (if the diazoketone is soluble), in the presence of 'activated CuO catalyst†,' were heated under reflux and irradiated with two 250 W tungsten lamps until the diazoketone band at *ca.* 2110 cm^{-1} had disappeared (3—6 h). Thus the diazoketones (**1a**), (**2a**), and (**2c**) produced the known[1] pentacyclic ketones (**3a**), (**4a**), and (**4c**) in very good yields (50, 72, and 87%, respectively) after chromatography on basic or neutral alumina. Similarly, cyclisation of the diazoketones (**1b**—**d**), (**8a**), and (**8b**), prepared[1] from the carboxylic acids‡ afforded the corresponding pure cyclopropyl ketones (**3b**)§ m.p. 122°, (59%), (**3c**), m.p. 126—128° (76%), (**3d**), m.p. 134—135° (63%), (**9a**), b.p. 135° (0·4 mm Hg), (80%), and (**9b**), m.p. 61° (88%). The 'activated CuO catalyst' was the most satisfactory catalyst for intramolecular carbenoid additions of the γδ-unsaturated diazoketones that we have encountered. Decomposition of the diazoketones without irradiation required considerably longer reaction times and the yields of the cyclopropyl ketones were reduced by 15—25%.



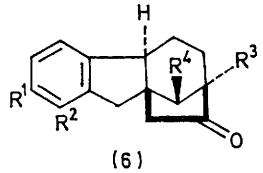
(1) $n = 1$
(2) $n = 2$



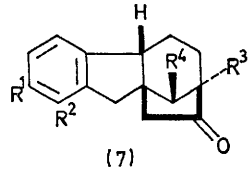
(3) $n = 1$
(4) $n = 2$



(5)



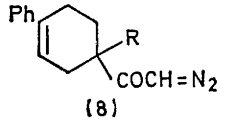
(6)



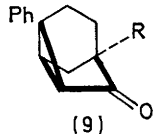
(7)

a; R^1 = OMe; R^2 = R^3 = R^4 = H
b; R^1 = R^3 = R^4 = H; R^2 = Me
c; R^1 = OMe; R^2 = R^4 = H; R^3 = Me
d; R^1 = R^4 = H; R^2 = R^3 = Me
e; R^1 = OMe; R^2 = R^3 = H; R^4 = Me

Acid-catalysed fragmentations[1] of the cyclopropyl ketones (**3b**), (**3c**), and (**3d**) produced the $\Delta^{9(11)}$-gibbene derivatives (**5b**)[4], m.p. 112°, (**5c**), m.p. 126°, and (**5d**),[5] m.p. 118° in 90—92% yields, which were also obtained in 60, 48, and 80% yield respectively by direct BF_3–Et_2O-catalysed cyclisations[1] of the corresponding diazoketones in CH_2Cl_2 or 1,2-dichloroethane solution.



(8)



(9)

a; R = H
b; R = Me

High stereoselectivity was observed in the catalytic hydrogenolysis of the cyclopropyl ketones (**3c**), (**3d**), and (**3b**) in the presence of Pd–C (10%) in ethanol, affording the 9α-gibbanes (**6c**),[6] m.p. 131—132°, (**6d**), m.p. 100°, and (**6b**), m.p. 109°, in 94, 88, and 80% yield respectively. The

† CuO–Cu (*ca.* 95 : 5), prepared by heating freshly prepared Cu powder[3] for 16—20 h at 500—600 °C. We thank Dr. N. R. Sengupta for analyses of the catalyst.
‡ These acids were prepared by Diels–Alder reaction (ref. 1) and will be described elsewhere.
§ Compounds described here are all racemates; satisfactory analytical and spectral data were obtained for new compounds.

9β-ketone (**7b**), m.p. 110—111°, was also isolated from the hydrogenolysis of the ketone (**3b**) (*ca.* 2%). The stereochemistry of the epimeric ketones (**6b**) and (**7b**) were assigned from n.m.r. studies. In conformity with our previous finding[7] the C(6)-methylene protons in the 9α-gibbane (**6b**) [ABq; 100 MHz; $CDCl_3$; δ_A 2·82, δ_B 2·70, J_{AB} 16 Hz] resonate at a higher field than in the 9β-epimer (**7b**) [δ_A 3·01, δ_B 2·79, J_{AB} 16 Hz]. The i.r. spectrum of the 9β-ketone (**7b**) is identical with that of the optically active ketone, obtained[8] by degradation of gibberellin A_{13}, thereby establishing the stereochemistry at C-9 which was previously undefined.

In parallel to our previous finding[1] with (**5a**), catalytic hydrogenation of the 9,11-double bond [Pd–C (10%) in EtOH] in the $\Delta^{9(11)}$-gibbenes (**5c—e**)[9] produced the corresponding 9α and 9β-gibbanes (**6c**) and (**7c**); (**6d**) and (**7d**); and (**6e**) and (**7e**) [*ca.* 75:25; 62·5:37·5; and 74·6:25·4, respectively (n.m.r.)] with the 9α-epimer predominating in each case. In contrast, reduction of the double bond in the gibbene (**5b**), under similar conditions, afforded a mixture of (**6b**) and (**7b**) [*ca.* 20:80 (n.m.r.)]. The complete reversal of stereoselectivity[10] in this reduction¶ leading mainly to the 9β-epimer (**7b**), is interesting, from both synthetic and stereochemical viewpoints. The effects of the C-6 substituents in the gibbenes in the stereospecificity of the hydrogenation of the 9,11-double bond have been recorded in other cases.[11]

We thank Dr. A. J. Baker for the n.m.r. spectra and interpretations; thanks are due to C.S.I.R., New Delhi, for a Junior Fellowship to P.C.C.

(*Received, 19th April* 1973; *Com.* 563.)

¶ Mori *et al.* (ref. 4) observed the formation of mostly the 9α-epimer (**6b**) in the hydrogenation of (**5b**) in presence of Raney Ni, the stereochemistry of which has now been confirmed by direct comparison with our sample.

[1] P. N. Chakrabortty, R. Dasgupta, S. K. Dasgupta, S. R. Ghosh, and U. R. Ghatak, *Tetrahedron*, 1972, **28**, 4653.
[2] For the normal conditions see: W. Kirmse, 'Carbene Chemistry,' Academic Press, London, 1971, p. 338.
[3] R. Q. Brewster and T. Groening, *Org. Synth.*, 1959 Coll. Vol. II, 445.
[4] K. Mori, M. Matsui, and Y. Sumiki, *Agric. and Biol. Chem.* (*Japan*), 1961, **25**, 907.
[5] Y. Kos and H. J. E. Loewenthal, *J. Chem. Soc.*, 1963, 605.
[6] G. Stork, S. Malhotra, H. Thompson, and M. Uchibayashi, *J. Amer. Chem. Soc.*, 1965, **87**, 1148; we thank Professor Stork for comparison of our sample with that prepared by them through a stereospecific route.
[7] A. J. Baker, A. C. Goudie, U. R. Ghatak, and R. Dasgupta, *Tetrahedron Letters*, 1972, 1103.
[8] R. H. B. Galt, *J. Chem. Soc.*, 1965, 3143; we thank Professor Mori for these and comparisons.
[9] S. Chakrabarty and K. Rudra (*née* Dasgupta), unpublished results.
[10] *Cf.* B. E. Cross and R. E. Markwell, *J. Chem. Soc.* (*C*), 1971, 2980.
[11] J. F. Grove, J. MacMillan, T. P. C. Mulholland, and W. B. Turner, *J. Chem. Soc.*, 1960, 3049; H. J. E. Loewenthal and S. K. Malhotra, *ibid.*, 1965, 990; K. Mori, M. Shiozaki, N. Itaya, M. Matsui, and Y. Sumiki, *Tetrahedron*, 1969, **25**, 1293; A. J. Baker, J. Brown, and R. A. Raphael, *J.C.S. Perkin I*, 1972, 1256.