Intramolecular C-Alkylation in βγ-Unsaturated Diazo Ketones : A New Synthetic Route to Angularly fused Cyclobutanones and γ-Lactones

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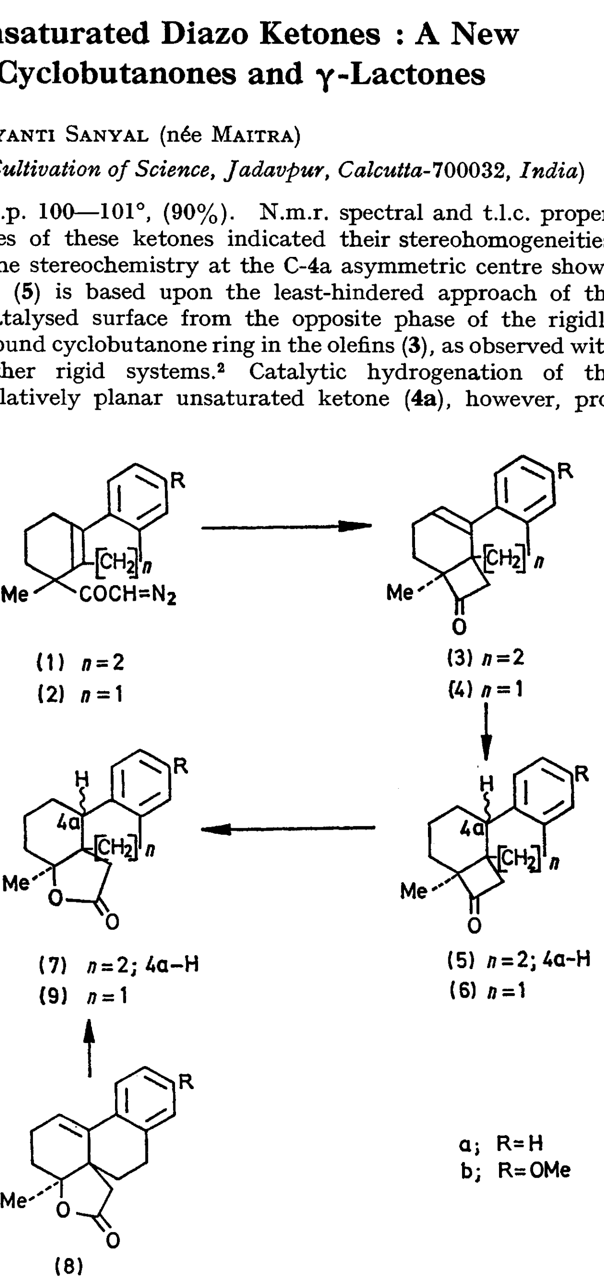
Summary A new synthesis of angularly fused cyclobutanones by the acid-catalysed intramolecular *C*-alkylation of *βγ*-unsaturated α-diazomethyl ketones is described along with their transformation into γ-lactones.

RECENTLY a new annelation reaction of synthetic potentiality has been developed[1,2] for the introduction of a bicyclo[3,2,1]octanone group into a number of monocyclic and polycyclic systems by intramolecular acid-catalysed cyclisation of the corresponding γδ-unsaturated α-diazomethyl ketones. We now present some novel examples in which an angularly fused four-membered ring ketone is formed in high yields by π-bond participation in the displacement of nitrogen from the protonated diazomethyl carbonyl function in a few *βγ*-unsaturated α-diazomethyl ketones. To our knowledge, these represent the first reported intramolecular electrophilic addition reaction of diazo-ketones leading to four-membered ring ketones.[3,4]

The diazo ketone (**1a**),† m.p. 104—106°, prepared quantitatively from the corresponding acid,[5] in $CHCl_3$ (0·1—0·05 M) rapidly loses nitrogen when treated with 2 to 4 equivalents of 70% aqueous $HClO_4$ or 48% aqueous HBF_4 or conc. H_2SO_4 at 5—10° to give the unsaturated cyclobutanone (**3a**), m.p. 91—92° [ν_{max} ($CHCl_3$) 1765 cm^{-1}; λ_{max} (EtOH) 255 nm (log ϵ 4·07); δ ($CDCl_3$) 1·20 (3H, s) and 6·37 (1H, br t, *J* 4Hz)] (80—99%). Reaction of the diazoketone (**1a**) in $CHCl_3$ with 57% HI, under Wolfrom reduction conditions[6] again gave the cyclobutanone (**3a**) (60%), as the only isolable product after chromatography. The methoxy-analogue (**1b**),[7] likewise with $HClO_4$ or HI, produced the cyclobutanone (**3b**), m.p. 102—103° (50—70%) The hydrofluorene derivative (**2a**),[8] m.p. 102—103° with $HClO_4$ or HI afforded the strained cyclobutanone (**4a**), m.p. 77—78° [ν_{max} ($CHCl_3$) 1768 cm^{-1}; λ_{max} (EtOH) 255 (log ϵ 4·12) and 290 nm (log ϵ 3·68); δ ($CDCl_3$) 1·30 (3H, s), 6·26 (1H, br t, *J* 5 Hz)] (50—55%). Compared to (**3**) this cyclobutanone is relatively unstable at room temperature.

Catalytic hydrogenation of the styrenoid bond in the ketones (**3a**) and (**3b**) [Pd–C (10%) in EtOH] gave the corresponding saturated ketones (**5a**), m.p. 102° and (**5b**), m.p. 100—101°, (90%). N.m.r. spectral and t.l.c. properties of these ketones indicated their stereohomogeneities. The stereochemistry at the C-4a asymmetric centre shown in (**5**) is based upon the least-hindered approach of the catalysed surface from the opposite phase of the rigidly bound cyclobutanone ring in the olefins (**3**), as observed with other rigid systems.[2] Catalytic hydrogenation of the relatively planar unsaturated ketone (**4a**), however, pro-



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

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

(5) $n=2$; 4a-H
(6) $n=1$

(7) $n=2$; 4a-H
(9) $n=1$

(8)

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† Compounds described here are all racemates; satisfactory analytical and spectral data were obtained for new compounds.

duced a mixture of the diastereoisomers (**6a**) in ratio of *ca.* 80:20 (n.m.r.). The stereochemistry of the main stereoisomer of (**6a**), m.p. 79—80°, separated from the mixture (*ca.* 60%) could not be assigned at this stage.[9]

Baeyer-Villiger oxidation of the saturated ketone (**5a**) with *m*-chloroperbenzoic acid in CH_2Cl_2 produced the γ-lactone (**7a**), m.p. 173—174° [ν_{max} ($CHCl_3$) 1750 cm^{-1}; δ ($CDCl_3$) 1·42 (3H, s)] (68—72%). The same lactone was also obtained as the sole product through hydrogenation [Pd–C (10%) in EtOH] of the corresponding unsaturated lactone (**8a**), m.p. 149° [ν_{max} ($CHCl_3$ 1755 cm^{-1}; λ_{max} (EtOH) 250 nm (log ϵ 4·18); δ ($CDCl_3$) 1·42 (3H, s) and 6·20 (1H, br t, *J* 5 Hz)], which was prepared (90%) by alkaline hydrogen peroxide oxidation of the unsaturated ketone (**3a**). Similarly the methoxy analogues (**5b**) and (**3b**) were converted into the corresponding γ-lactones (**7b**), m.p. 177—178° and (**8b**) m.p. 166–167 °. The stereochemical results in the hydrogenation of rigid unsaturated lactones (**8a**) and (**8b**) to the corresponding saturated lactones support the stereostructures assigned to (**5a**) and (**5b**). The saturated ketone (**6a**), m.p. 79—80° also gave the corresponding γ-lactone (**9a**) m.p. 122° [ν_{max} ($CHCl_3$) 1755 cm^{-1}, δ ($CDCl_3$) 1·42 (3H, s)] (80%) through oxidation with *m*-chloroperbenzoic acid in CH_2Cl_2.

The present investigations thus provide a simple synthetic route to angularly fused polycyclic cyclobutanones[10] which have potentialities, particularly for stereospecific introduction of angular substituents[11] in polycyclic systems.

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