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UNUSUAL RING OPENING OF CONJUGATED PHENYLCYCLOPROPYL KETONE; A NEW ROUTE TO BICYCLO[3:3:1]NONANE INTERMEDIATE

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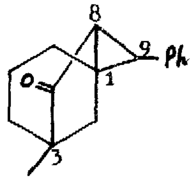
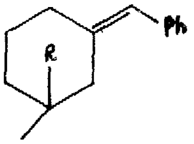
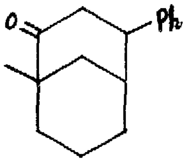
In connection with studies related to the syntheses of bridged ring systems present in diterpene group of alkaloids, the reductive fission of the conjugated phenylcyclopropyl ketone (I) with lithium in liquid ammonia has been investigated and a new route to bicyclo[3:3:1]nonane intermediate is described. In view of the analogies[1] relating to the conjugative properties of a cyclopropane ring having one or two adjacent unsaturated centres, the steric course of the C-C bond fission in (I) follows an unusual pathway, governed synergistically by the unique geometry of the ketone (I) and the conjugative effect of the keto group only (loc. cit). Usually, ring opening in systems analogous to that of (I) proclaims[1b,2] a high degree of regiospecificity involving cleavage of the benzylic C_8-C_9 bond enjoying maximum overlap with the aromatic ring. In our case, C_1-C_8 bond has undergone reductive fission.



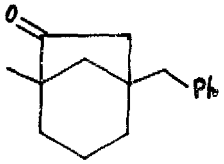
(I)



(II), R = $-CO_2Me$
(III), R = $-$ CO·CHN$_2$



(IV)



(V)

Wittig reaction on 3-carboxy-3-methylcyclohexanone with benzyltriphenylphosphonium chloride in presence of sodium hydride in DMSO followed by esterification of the resulting acid with ethereal diazomethane furnished in an excellent yield the ester (II)[3]; b.p. 120°/0.2 mm; ν_{max}(CHCl$_3$) 1725, 1600 cm^{-1}; λ_{max} (EtOH) 250 nm (ϵ =20,040); δ(CCl$_4$) 7.13 (5H, s), 6.2 (1H, s), 3.62 & 3.42 (3H, two singlets from $-CO_2Me$ protons), 1.2 & 1.1 (3H, two singlets from C-3 methyl protons). Conversion of the corresponding acid of (II) into the acid chloride and treatment of the latter with ethereal diazomethane resulted in the formation of the diazoketone (III); $\nu_{max}(CHCl_3)$ 2110, 1600 cm^{-1}. This crude diazoketone after purification (short-packed alumina column) was heated to reflux for 16 hr in tetrahydrofuran/cyclohexane (3:7) in the presence of 'activated copper oxide catalyst' under illumination leading to the formation of the ketone (I); b.p. 135-37°/0.05 mm; $\nu_{max}(CHCl_3)$ 1705, 1600 cm^{-1}; $\delta(CCl_4)$ 7.16 (5H, s), 3.33 (1H, m, C-9 proton), 0.93 (3H, s), 0.78 (1H, s, C-8 proton); m/e 226. The C-8 proton signal of (I) in the NMR reveals that the benzene ring is spatially prevented from exerting any conjugative effect on this proton as a result of the high degree of flexibility of the aromatic ring around the cyclopropane ring. In the alternative case[4], this particular proton appears in the range δ1.5-2.5 . The ketone (I) in ethanol did not take up hydrogen over Pd/C (10%) under atmospheric pressure. The ketone was next allowed to react with lithium in liquid ammonia for a short period leading to the formation of (IV); b.p. 95-100°/0.01 mm; $\nu_{max}(CHCl_3)$ 1715, 1600 cm^{-1}; $\delta(CCl_4)$ 7.19 (5H, s), 2.9-2.4 (3H, m), 0.95 (3H, s); m/e 228. The isomeric bicyclo [3:2:1] octane derivative (V), which might have been formed from alternative fission, has been synthesised[5] in an unambiguous method in our laboratory and the nonidentity between (IV) and (V) has been established from comparative spectral and chromatographic studies, particularly the complex NMR patterns of (IV) in the range δ2.9-2.4 for 3H as contrasted to two sharp 2H singlets at δ2.66 and δ2.00 in (V). In the absence of any interaction with the phenyl group, the sterically governed σ-π overlap between the C_1-C_8 bond in (I) and the carbonyl π-orbitals facilitates singularly this bond to open up leading to a new synthetic route for bicyclo [3:3:1] nonane intermediate (IV), an important skeletal feature of many natural products.

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3. Satisfactory analytical data were obtained for all new compounds. NMR spectra were recorded on 60 MHz T-60A spectrometer. Mass spectral fragmentation patterns were in full agreement with the structures shown.

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