Communications

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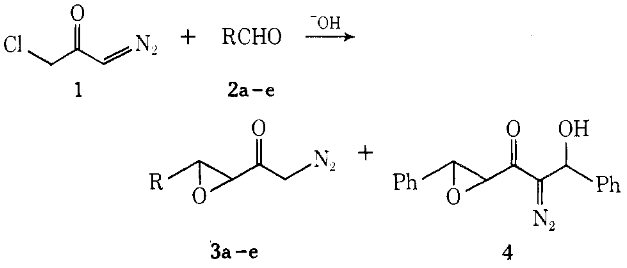
Darzens Condensation of 1-Chloro-3-diazopropanone

Summary: 1-Chloro-3-diazopropanone underwent Darzens condensation with various aldehydes leading to the synthesis of epoxy diazo ketones.

Sir: The ability of diazomethyl ketones to undergo various base-catalyzed condensation reactions similar to ordinary ketones is now well established. These include intramolecular aldol and Dieckman-type condensation[1] and intermolecular aldol condensation,[2,3] as well as an intramolecular alkylation reaction.[4] We now report the first example of Darzens condensation of a diazo ketone.

Treatment, in stoichiometric amounts, of a cold methanolic solution (20 ml) of 1-chloro-3-diazopropanone (**1**, 0.2 *M*) and benzaldehyde (0.2 *M*) with aqueous sodium hydroxide solution (4 ml, 1 *M*), followed by addition of water (30 ml) to the reaction mixture after 30 min, precipitated 1-diazo-3,4-epoxy-4-phenyl-2-butanone (**3a**) in 69% yield as a yellow solid (recrystallized from methanol–water): mp 95–96°; *m/e* 188 (M^+); nmr ($CDCl_3$) δ 7.33 (s, 5 H, Ph), 5.58 (s, 1 H, CHN_2), 3.91 (d, 1 H, J = 1.5 Hz, epoxymethine), 3.48 ppm (d, 1 H, J = 1.5 Hz, epoxymethine); ir ($CHCl_3$) 4.76 (s, CHN_2), 6.13 μ (s, CO). *Anal.* Calcd for $C_{10}H_8O_2N_2$: C, 63.83; H, 4.25; N, 14.87. Found: C, 63.77; H, 4.52; N, 14.85. The diazomethyl ketone nature of the product was further verified by treating a deuteriochloroform solution of **3a** with 1 drop of deuterium oxide containing a catalytic amount of sodium carbonate upon which the azomethine peak at δ 5.58 was completely removed from the nmr spectrum.[2] The formation of a single isomer and the magnitude of the coupling constant of the epoxymethine protons of **3a** implies stereoselective control of the reaction leading to the formation of the epoxide ring with trans stereochemistry. Darzens condensation of chloroacetone with benzaldehyde is known to proceed in a similar stereoselective manner.[5]

Treatment of a cold methanolic solution (20 ml) of diazo ketone **1** (0.2 *M*) containing an excess of benzaldehyde (2 ml) with an excess of aqueous sodium hydroxide (8 ml, 1 *M*) solution for 30 min, addition of water (30 ml), extraction with methylene chloride, and chromatography of the concentrate on Florisil (60 g, activity II) afforded 44% epoxy diazo ketone **3a** (eluted with CCl_4) and 41% a diastereomeric mixture of 2-diazo-1,5-diphenyl-4,5-epoxy-1-hydroxy-3-pentanone (**4**) (eluted with 9:1 benzene–ether). These products form as a result of Darzens and aldol condensations at the methylene and diazo carbons, respectively. The diastereomeric mixture had mp 77–106°;[6] *m/e* 266 ($M^+ - 28$); nmr ($CDCl_3$) δ 7.35 (d, 10 H, 2 Ph), 6.12 (d, 1 H, CHOH), 4.25 (d, 1 H), CHO**H**), 4.10 (d, J = 1.5 Hz, epoxymethine, isomer A), 4.02 (d, sum of A + B = 1 H, J = 1.5 Hz, epoxymethine, isomer B), 3.70 ppm (d, 1 H, J = 1.5 Hz, epoxymethine); nmr ($CDCl_3$–D_2O) same as above except for δ 6.12 (s, 1 H, **CH**OD), and lacking the 4.25-ppm peak; ir ($CHCl_3$) 2.95 (w, OH), 4.77 (s, CHN_2), 6.19 μ (s, CO). *Anal.* Calcd for $C_{17}H_{14}O_3N_2$: C, 69.41; H, 4.76; N, 9.52. Found: C, 69.17; H, 4.78; N, 9.40. The diastereomeric mixture of Darzens aldol product **4** dissolved in methanol was cleaved cleanly into epoxy diazo ketone **3a** and benzaldehyde by aqueous sodium hydroxide solution confirming the structure assigned to it.[3]



a, R = Ph
b, R = p-$NO_2C_6H_4$
c, R = p-$CH_3OC_6H_4$
d, R = *t*-PhCH=CH
e, R = 2-thienyl

Reaction of chloro diazo ketone **1** to give an epoxy diazomethyl ketone was found to be of general applicability as exemplified by reaction with representative aldehydes **2a–e** to give epoxy diazomethyl ketones **3a–e** in 46–88% yields.[7] The chemistry of epoxy diazomethyl ketones is currently under investigation.

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[6] From this diastereomeric mixture, isomer A, mp 110.5–111.5°, and isomer B, mp 78.5–80°, have been isolated. Isomer A and the diastereomeric mixture both are cleaved by base to **3a** in high yield.

[7] No attempt was made to prepare and isolate the diadducts similar to **4** from aldehydes **2b–e**.