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NORMAL BASE CATALYZED INTRAMOLECULAR ALKYLATION OF A DIAZO KETONE

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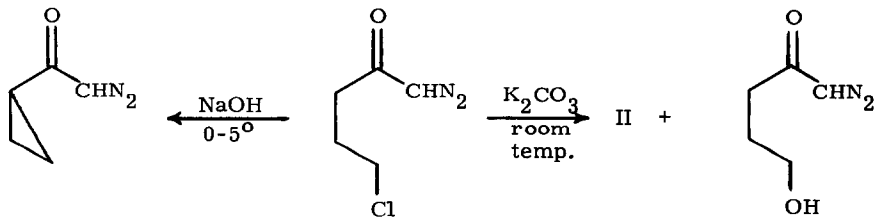
A number of new nondestructive reactions of diazo ketones at the α-diazocarbon have been reported (1) including normal base catalyzed aldol condensations (2). We report here the first example of a normal base catalyzed intramolecular alkylation of an aliphatic diazomethyl ketone at the α-methylene carbon.

As part of a mechanistic study, we sought to prepare 1-diazo-5-hydroxy-2-pentanone (III). Diazoketones are known to be relatively stable to dilute aqueous base at room temperature but in warm basic solution a variety of reactions ensue (3). More concentrated aqueous or anhydrous base also cause facile reaction at room temperature (4). In an attempt to utilize the low temperature base stability of the diazo ketone group to prepare III, the readily available 5-chloro-1-diazo-2-pentanone (I) (5) [ir (neat) 4.73 (CHN_2), 6.09 μ ($\underline{C}OCHN_2$); nmr (CCl_4) δ 5.43 (s, 1H, $C\underline{H}N_2$), 3.58 (t, 2H, J = 6 Hz, $ClC\underline{H}_2$); 2.50 (br t, 2H, $COC\underline{H}_2$), ca. 2.07 ppm (m, 2H, $COCH_2C\underline{H}_2$)] was dissolved in 1 N sodium hydroxide solution and allowed to stand at 0-5° for 22 hr. Extraction with methylene chloride, evaporation and evaporative distillation at 32-36° (1mm) gave what proved to be cyclopropyl diazomethyl ketone (II) in 67% yield. The infrared bands at 4.74 μ and 6.11 clearly established the presence of the diazo ketone moiety. The nmr spectrum of II, nmr ($CDCl_3$) δ 5.92 (s, 1H, $C\underline{H}N_2$), ca. 1.8 (m, 1H, cyclopropyl $C\underline{H}CO$), ca. 1.0 ppm (m, 4H, cyclopropyl $C\underline{H}_2$), closely resembled that of methyl cyclopropyl-



II I III

carboxylate in the δ 2.3-1.6 ppm region (6). The structure II was further verified by reaction with hydrogen chloride to form chloromethyl cyclopropyl ketone, nmr (CCl_4) δ 4.22 (s, 2H, $COCH_2Cl$), ca. 2.20 (m, 1H, cyclopropyl CHCO), ca. 0.97 ppm (m, 4H, cyclopropyl CH_2), which was identified by conversion to a 2,4-DNP derivative, mp 125-126° (lit. (7) mp 126-127°).

Treatment of the chloro diazo ketone I with sodium carbonate solution (2.8%) for nine days at room temperature gave in addition to the cyclopropyl diazo ketone II (removed by extraction with methylene chloride), the desired hydroxy diazo ketone III which was separated from the aqueous solution by continuous extraction with ether, then chromatographed on basic alumina and evaporatively distilled at 50-53° (1 mm) to give 24% of the hydroxy diazo ketone III; ir (neat) 2.86 μ (OH), 4.72 (CHN_2), 6.13 ($COCHN_2$); nmr ($CDCl_3$) δ 5.40 (s, 1H, CHN_2), 3.64 (t, 2H, J = 6 Hz, OCH_2), 3.33 (s, 1H, OH), 2.48 (br t, 2H, $COCH_2$), ca. 1.9 ppm (m, 2H, $COCH_2CH_2$). The spectral data for III and its thermal Wolff rearrangement (in refluxing o-xylene) to o-valerolactone (identical by ir with an authentic sample) conclusively established the structure of the hydroxy diazo ketone as III.

The ability of diazo ketones to undergo normal base catalyzed reactions at the α-carbon opposite the diazocarbon has not been previously recognized nor exploited. We are currently investigating the scope of this type of condensation as well as the reactions of the hydroxy diazo ketone III.

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