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A NOVEL CYCLIZATION REACTION OF OXIDODIAZOALKANES: FORMATION OF PYRAZOLES AND PYRIDAZINES

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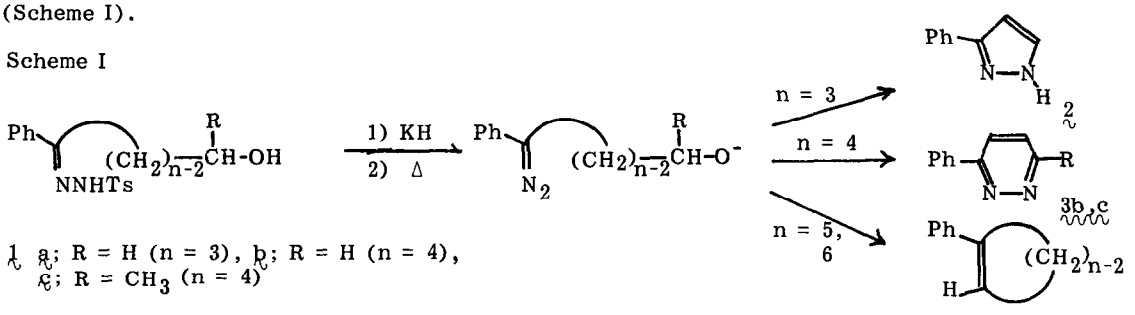
Abstract: The thermal decomposition of dialkali metal salts of β- and γ-hydroxyketone tosylhydrazones in refluxing DME produced pyrazoles and pyridazines, respectively.

In the preceding paper,[1] we have reported a novel cyclization reaction of δ- and ε-oxidodiazoalkanes in the thermal decomposition of dialkali metal salts of ω-hydroxyketone tosylhydrazones 1 (n = 5,6). When we examined the thermolysis of analogous substrates with a shorter alkanol skeleton, i.e., 1 (n = 3,4), we found that the cyclization takes place not between two carbon atoms but between carbon and nitrogen atom to give pyrazole or pyridazine derivatives (Scheme I).

Scheme I

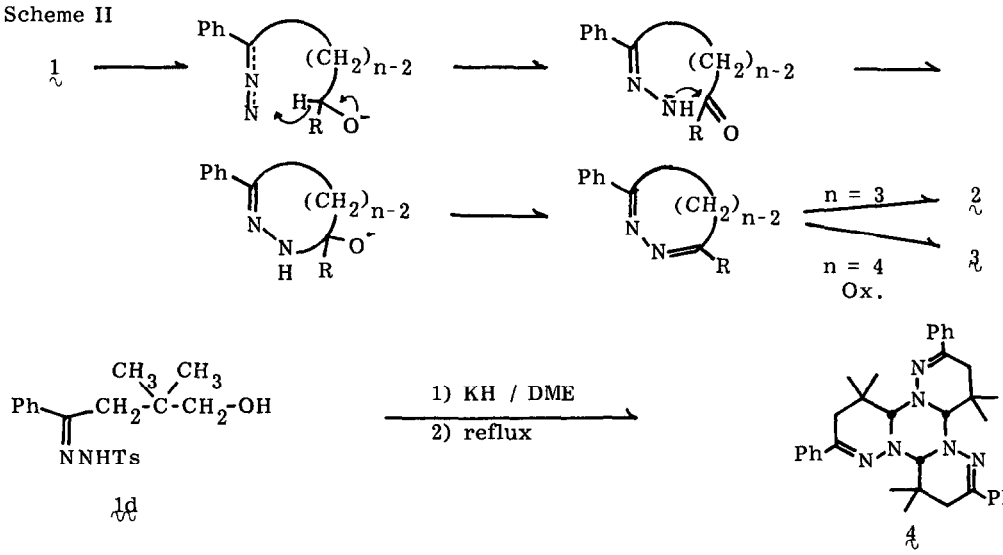


1 a; R = H (n = 3), b; R = H (n = 4), c; R = CH_3 (n = 4)

Dipotassium salt of 3-hydroxypropiophenone tosylhydrazone (1a) (mp 96-98 °C)[2] in DME was heated at 85 °C for 24 h. After aqueous workup followed by column chromatography, 3-phenylpyrazole (2) was isolated in 76% yield. Under similar reaction conditions, the decomposition of dipotassium salts of 4-hydroxybutyrophenone tosylhydrazone (1b) (mp 111-112 °C) and 4-hydroxyvalerophenone tosylhydrazone (1c) (mp 131-134 °C) provided 3-phenylpyridazine (3b) in 41% yield and 5-methyl-3-phenylpyridazine (3c) in 39% yield, respectively.

It was ascertained from the following observation that the present reaction proceeds not directly from dipotassium salts of hydroxytosylhydrazones but through an intermediate formation of oxidodiazoalkanes: When (3-hydroxypropyl)(phenyl)diazomethane in benzene-THF, prepared from the corresponding hydrazone by the oxidation with Ag_2O, was heated in the presence of KH at 65 °C for 5 h, pyridazine 3b was obtained in 9 % yield. In the preceding paper for the mechanism of cyclization reaction of δ- and ε-oxidodiazoalkanes, we have proposed an intramolecular

Scheme II



hydride transfer from α position of alkoxides to the nitrogen terminus of a diazo group. The present reaction of β- and γ-oxidodiazoalkanes can also be rationalized by the same intramolecular hydride transfer. In these cases, however, the hydride transfer was followed by the attack of the terminal nitrogen on the carbonyl group and then by the subsequent elimination of KOH (Scheme II). If we can isolate dihydropyridazine intermediates in the reaction of 1 (n = 4), it will be a strong evidence supporting the mechanism proposed above. Therefore, we carried out the decomposition of the dipotassium salt derived from 3,3-dimethyl-4-hydroxybutyrophenone tosylhydrazone (1d) (mp 139-141 °C)(eq 1). Although the reaction was not clean, tetracyclic trimer (4, 10% yield)[3] was formed besides several uncharacterized products, and this clearly demonstrates the intermediate formation of 5,5-dimethyl-3-phenyl-4,5-dihydropyridazine in the present reaction.

In connection with recent reports on a novel nitrene-type intramolecular 1,1-cycloaddition of allyldiazomethanes,[4] it should be emphasized here that the mechanism proposed in Scheme II involves a formal nitrene-type insertion reaction by the terminal nitrogen atom of a diazo group into α C-H bond of alkoxide.

References and Notes

(1) Harada, T.; Akiba, E.; Oku, A. preceding paper of this issue.

(2) Tosylhydrazones (1a-d) showed satisfactory spectral (^{1}HNMR, IR) and analytical data.

(3) 4: mp 224-226 °C; IR (KBr disk) 2980 (s), 2920 (s), 1595 (s), 1115 (s), 760 (s), 720 (s), and 690 cm^{-1} (s); ^{1}HNMR (200 MHz, $CDCl_3$) 1.12 (9H, s), 1.25 (9H, s), 2.25 (3H, d, J = 16.8 Hz), 3.12 (3H, d, J = 16.8 Hz), 4.10 (3H, s), 6.80-7.16 (9H, m), and 7.16-7.30 (6H, m); mass spectrum, m/e (relative intensity) 559 (M, 3%), 372 (5), 186 (26), and 171 (100); high resolution mass spectrum, m/e 558.3470 (calcd for $C_{36}H_{42}N_6$, 558.3475).

(4) (a) Padwa, A.; Rodriguez, A.; Tohidi, M.; Fukunaga, T. J. Am. Chem. Soc. 1983, 105 933. (b) Miyashi, T.; Yamakawa, K.; Komata, M.; Mukai, T. Ibid., 1983, 105, 6342.

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