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HETEROCYCLE FORMATION IN THE REACTION OF α-DIAZOACETOPHENONE WITH BASES

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A RECENT report from this Laboratory[1] has described an investigation of the reaction of α-diazoacetophenone with sodium methoxide in dilute solution. We now report on the reactions of α-diazoacetophenone with sodium methoxide in concentrated solution and with potassium t-butoxide, which have additional features of interest.

Addition of an equimolar amount of 7 M methanolic sodium methoxide to 5 M methanolic α-diazoacetophenone led to a violent exothermic reaction which was moderated by external cooling; after three hours the mixture was poured into aqueous sodium bicarbonate. The following products were isolated:[2] methyl benzoate, benzoic acid, (hydrogen cyanide), acetophenone, 3-benzoyl-4-phenylpyrazole (I), 3-benzoyl-4-hydroxy-5-phenylpyrazole (II), 3-benzoyl-5-hydroxy-4-phenylpyrazole (III), 5-benzoyltetrazole (IV), and a compound $C_{17}H_{11}N_5O$. Compounds I - IV were identified by direct comparison with authentic samples: the preparation of I[1,3] has been described elsewhere;

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[1] P. Yates and B. L. Shapiro, J. Amer. Chem. Soc. 81, 212 (1959).

[2] Satisfactory elementary analyses have been obtained for all new compounds.

[3] L. I. Smith and W. B. Pings, J. Org. Chem. 2, 23 (1937).

II - IV were synthesized in the following manner. Photolysis of 3-benzoyl-4-diazo-5-phenylpyrazole[4] in aqueous acetone gave II, pale yellow needles, m.p. 209-210°, λ_{max}^{Nujol} 2.97, 3.07, 6.16, 8.60, 10.28 11.05 μ. Treatment of the higher melting epimer of methyl dl-α-phenyl-β-bromo-β-benzoylpropionate[5] in boiling ethanol with hydrazine and sodium carbonate while air passed through the solution gave III, pale yellow needles, m.p. 252-254°, λ_{max}^{Nujol} 3.03, 3.18, 6.13, 6.50, 11.02 μ; two other products were obtained from this reaction: 3,5-dephenylpyrazoline-5-carboxylic acid (as its CH_2Cl_2 complex), colorless square plates, m.p. 152-155° dec., λ_{max}^{Nujol} 3.00, 4.0, 5.30, 5.90, 6.30, 6.42 μ, and 3,5-diphenyl-6-pyridazinone.[6] Oxidation of 5-benzyltetrazole[7] with chromic acid gave IV, colorless leaflets, m.p. 139-140°, $\lambda_{max}^{CH_2Cl_2}$ 2.95, 6.00, 10.85 μ.[8] The product $C_{17}H_{11}N_5O$, yellow needles with blue-green fluorescence under ultraviolet illumination, m.p. 203-204° dec., λ_{max}^{Nujol} 6.07, 6.50, 11.00 μ, is provisionally formulated as V since it is hydrolyzed in basic medium to 5-benzamido-4-benzoyl-1,2,3-triazole (VI), m.p. 266-268° dec., λ_{max}^{Nujol} 3.12, 5.97, 6.11, 6.30, 10.70 μ, identified by independent synthesis.

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[4] P. Yates and D. G. Farnum, Chem. & Ind. 659 (1960).

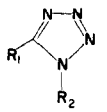
[5] E. P. Kohler and R. C. Goodwin, J. Amer. Chem. Soc. 49, 219 (1927).

[6] G. K. Almström, Ann. 400, 131 (1913).

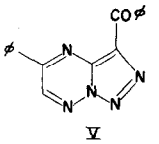
[7] W. G. Finnegan, R. A. Henry and R. Lofquist, J. Amer. Chem. Soc. 80, 3908 (1958).

[8] Since the completion of this work, an alternative synthesis of 5-benzoyltetrazole (m.p. 140-141°) has been reported: B. E. Fisher, A. J. Tomson and J. P. Horwitz, J. Org. Chem. 24, 1650 (1959).

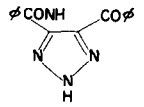
I, $R_1=\phi, R_2=H$
III, $R_1=OH, R_2=\phi$
III, $R_1=\phi, R_2=OH$



IV, $R_1=CO\phi, R_2=H$
VII, $R_1=CO\phi, R_2=CH_2CO\phi$
VIII, $R_1=H, R_2=CH_2CO\phi$



V



VI

Treatment of α-diazoacetophenone woth potassium t-butoxide in t-butyl alcohol gives a dimeric product.[9] This product, colorless needles, m.p. 114-114.5°, $\lambda_{max}^{CH_2Cl_2}$ 5.85, 5.95, 10.82 μ, λ_{max}^{EtOH} 250 mμ (log ε 4.39), has now been shown to be 5-benzoyl-1-phenacylpyrazole (VII) by its independent synthesis from IV by phenacylation; the isomeric 5-benzoyl-2-phenacyltetrazole m.p. 126-126.5°, $\lambda_{max}^{CH_2Cl_2}$ 5.85, 5.97, 10.80 μ, λ_{max}^{EtOH} 252 mμ (log ε 4.29), 272 mμ (shoulder, log ε 4.19) was also formed in this reaction. When the reaction of α-diazoacetophenone and potassium t-butoxide was carried out under heterogeneous conditions with ether as diluent, sodium benzoate precipitated; treatment of the ethereal solution with aqueous ammonium chloride gave 1-phenacyltetrazole (VIII), colorless needles, m.p. 104-104.5°, $\lambda_{max}^{CH_2Cl_2}$ 5.85, 8.15 μ. This was identified by its independent synthesis from tetrazole[10] by phenacylation; the isomeric 2-phenacyltetrazole, colorless needles, m.p. 110.5-111.5°, $\lambda_{max}^{CH_2Cl_2}$ 5.86, 8.51, 9.09 μ, was obtained as the major product from this reaction.

The following reaction scheme accomodates the formation of the several

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[9] C.H. DePuy, unpublished results; we are greatly indebted to Professor DePuy, Iowa State University, for communicating to us the directions for this preparation and suggesting that we pursue the investigation of this reaction.

[10] R. Stollé, Ber. 62, 1118 (1929).

tetrazoles and V in the reaction of α-diazoacetophenone with bases ($B^{\ominus}$):

$$\phi COCHN_2 + B^{\ominus} \rightleftharpoons [O{=}C(\phi){-}CH{=}N{=}N{-}B]^{\ominus}$$

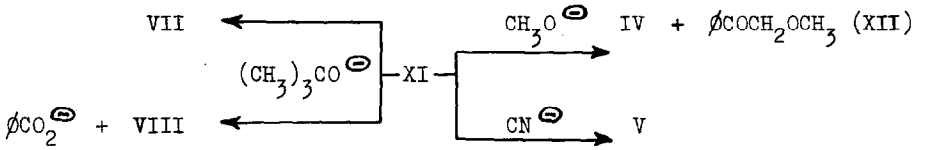
IX

$$IX + \phi COCHN_2 \rightleftharpoons [\phi COCH{=}N{-}N(B){-}N{=}N{=}CH{-}C(\phi){=}O]^{\ominus}$$

X

$$X \rightleftharpoons \phi COCH{=}N{-}N{=}N{-}N{=}CHCO\phi + B^{\ominus}$$

XI



The postulated intermediate XI may be compared with that involved in the reaction of diazonium salts with azide ion.[11] The path proposed for the formation of the chain of four nitrogen atoms is preferred to one involving removal of a proton from α-diazoacetophenone followed by attack of the anion on a second molecule of the diazoketone since it provides a rationalization for the divergence of path in the homogeneous and heterogeneous reactions with potassium t-butoxide.[12,13] Reasonable routes are available from XI and

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[11] K. Clusius and M. Vecchi, Ann. 607, 16 (1957).

[12] It is planned to discuss this in detail in a later publication. It may be noted that VII is not converted to VIII under the conditions of the heterogeneous t-butoxide reaction, nor is it converted to IV under the conditions of the methoxide reaction.

[13] An alternative pathway for the formation of IV could involve the reduction of diazoacetophenone with sodium methoxide followed by attack of the anion of the resulting hydrazone[14] on the diazoketone. Such a route is not available, however, in the reactions with potassium t-butoxide.

[14] Cf. L. Wolff, Ann. 394, 23 (1912).

from the reaction products of XII with diazoketone to all of the other products obtained from the reaction with sodium methoxide in concentrated solution.[15]

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[15] In dilute solution, no evidence was obtained for the formation of IV or V, and the reaction may well follow a different route after the initial terminal addition step.[1]