SYNTHESIS OF 5-KETOTETRAZOLES UNDER HIGH PRESSURE

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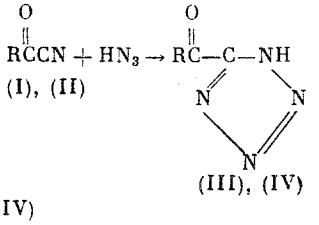
The reaction of nitriles with hydrazoic acid or its salts is a general method for the synthesis of 5-substituted tetrazoles [1]. However, attempts to extend this method to alkyl- and arylketonitriles in order to obtain 5-ketotetrazoles proved unsuccessful. In this case, the replacement of the nitrile group by an azide group predominates over ring formation to give acyl azides, which undergo subsequent transformations [2].

$$\underset{R=\text{Alk, Ph}}{RCOCN} \xrightarrow{N_3^{\ominus}} KCON_3 \rightarrow RNCO \xrightarrow{N_3^{\ominus}} RNHCON_3$$

Shifting the reaction toward tetrazole formation should be possible at high pressure, which is known to facilitate 1,3-dipolar cycloaddition [3].

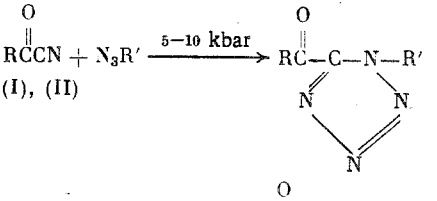
Indeed, in previous work [4], we have shown that 5-ketotetrazoles are formed in good yield upon the reaction of ketonitriles with hydrazoic acid at 5-10 kbar.



(I), (II) (III), (IV)

R = CH_3(I), (III), Ph(II), (IV)

The use of organic azides in this reaction permits the preparation of acyl- and benzoyl-1-N-tetrazoles.



(I), (II)

R = Ph, R′ = $CH_2COC_2H_5$(V); R = CH_3, R′ = $CH_2COC_2H_5$(VI); R = Ph, R′ = CH_2Ph(VII);

R = CH_3, R′ = CH_2Ph(VIII); R = CH_3, R′ = CH_2COCH_3(IX); R = CH_3, R′ = cyclohexyl (X)

Tetrazoles (III) and 1-benzyl-5-ethoxycarbonyltetrazole have been obtained by the reaction of ketonitriles with organic azides at atmospheric pressure. However, the tetrazole yields were low and the reaction required prolonged heating at high temperature [5].

Carrying out the reaction at high pressure provided for a sharp decrease in the reaction time and temperature, increase in the product yield, and the use of thermally unstble ketonitriles and azides in this reaction.

The product yields depend significantly on the presence employed. Thus, 35% (V) was obtained after 12 h at 5 kbar and 80°C, while this yield was raised to 90% at 10 kbar.

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No reaction was noted for (I) and (II) with phenyl azide, p-nitrophenyl azide, and o-nitrophenyl azide, apparently due to steric factors [3].

EXPERIMENTAL

The high pressure syntheses were carried out in units described in our previous work [6].

The IR spectra of the liquid were taken neat, while the IR spectra of solids were taken in KBr pellets on a UR-20 spectrophotometer. The PMR spectra were taken on a Perkin–Elmer R-12 spectrometer at 60 MHz in acetone-d_6 relative to HMDS. The mass spectra were taken on a Varian CH-6 mass spectrometer with direct sample inlet into the probe at 70 eV. The emission current was 100 μA and the control voltage was 1.75 kV.

5-Acetyltetrazole (III). A solution of 0.4 g CH_3COCN (I) in 2 ml 10.5% HN_3 in ether was maintained for 6 h at 40°C and 10 kbar. The solvent was removed to give 0.46 g (70%) (III), mp 89°C [7]. IR spectrum (ν, cm^{-1}): 1725 (C=O). Mass spectrum (m/z): 112 $(M)^+$.

5-Benzoyltetrazole (IV). A solution of 0.5 g PhCOCN (II) in 2 ml 10% HN_3 in benzene was maintained for 6 h at 70°C and 5 kbar. The solvent was removed to give 0.54 g (81%) (IV), mp 139°C [8]. IR spectrum (ν, cm^{-1}): 1670 (C=O). Mass spectrum (m/z): 174 $(M)^+$.

Ethyl Ester of 5-Benzyltetrazole-1-acetic Acid (V). a) A solution of 0.5 g (II) and 0.6 g ethyl azidoacetate in 1.5 ml acetonitrile was maintained in a Teflon ampul for 12 h at 80°C and 5 kbar. The solvent was removed to give 0.37 g (35%) (V), mp 65-67°C [5].

b) A solution of 0.5 g (II) and 0.6 g ethyl azidoacetate in 1.5 ml acetonitrile was maintained in a Teflon ampule for 12 h at 80°C and 10 kbar. The solvent was removed to give 0.94 g (90%) (V), mp 65-67°C.

Ethyl Ester of 5-Acetyltetrazole-1-acetic Acid (VI). A solution of 1 g (I) and 0.5 g ethyl azidoacetate was maintained for 12 h at 80°C and 10 kbar. The solvent was removed by distillation at 160-180°C (2 mm) to give 0.74 g (98%) (VI) as a viscous oil. Found, %: C 42.41; H 5.3; N 28.46. $C_7H_{10}N_4O_3$. Calculated, %: C 42.43; H 5.05; N 28.28. IR spectrum (ν, cm^{-1}): 1720 (C=O), 1765 (OC=O). PMR spectrum (δ, ppm): 1.2 t (3H), 2.7 s (3H); 4.2 q (2H), 5.5 s (2H).

1-Benzyl-5-benzoyltetrazole (VII). A solution of 0.5 g (II) and 0.51 g benzoyl azide in 1 ml acetonitrile was maintained in a Teflon ampul for 25 h at 100°C and 10 kbar. The solvent was removed and the residue was subjected to thin-layer chromatography on silica gel with ether as the eluent to give 0.9 g (90%) (VII) as a viscous oil. Found, %: C 67.92; H 4.55; N 21.19. $C_{15}H_{12}N_4O$. Calculated, %: C 68.18; H 4.55; N 21.21. IR spectrum (ν, cm^{-1}): 1680 (C=O). PMR spectrum (δ, ppm): 5.8 s (2H), 7.1-8.3 m (10H).

1-Benzyl-5-acetyltetrazole (VIII). A solution of 0.6 g (I) and 0.4 g benzyl azide in 1 ml acetonitrile was maintained in a Teflon ampul for 10 h at 80°C and 10 kbar. The solvent was distilled off at 180-200°C (2 mm) to give 0.56 g (92%) (VIII) as a viscous oil. Found, %: C 59.17; H 5.00; N 27.98. $C_{10}H_{10}N_4O$. Calculated, %: C 59.41; H 4.95; N 27.72. IR spectrum (ν, cm^{-1}): 1725 (C=O). PMR spectrum (δ, ppm): 2.7 s (3H), 5.75 s (2H), 7.25 m (5H).

1-(2'-Oxopropyl)-5-acetyltetrazole (IX). A solution of 1 g (I) and 0.4 g azidoacetone in 1 ml acetonitrile was maintained for 10 h at 80°C and 10 kbar. The solvent was removed and the residue was subjected to thin-layer chromatography on silica gel with ether as the eluent to give 0.24 g (35%) (IX) as a viscous oil. Found, %: C 43.62; H 4.85; N 32.97. $C_6H_8N_4O_2$. Calculated, %: C 42.85; H 4.76; N 33.33. IR spectrum (ν, cm^{-1}): 1725 (C=O), 1755 (OC=O). PMR spectrum (δ, ppm): 2.3 s (3H), 2.6 s (3H), 5.6 s (2H).

1-Cyclohexyl-5-acetyltetrazole (X). A solution of 0.6 g (I) and 0.4 g cyclohexyl azide was maintained for 8 h at 80°C and 10 kbar. The solvent was removed to give 1.54 g (92%) (X), mp 74°C (from hexane). IR spectrum (ν, cm^{-1}): 1723 (C=O). Found, %: C 55.07; H 6.54; N 28.02. $C_9H_{14}ON_4$. Calculated, %: C 55.67; H 7.21; N 28.86.

CONCLUSIONS

The reaction of α-ketonitriles with hydrazoic acid and organic azides at high pressure is an effective method for the synthesis of 5-acyltetrazoles.

LITERATURE CITED

1. R. M. Elderfield, Heterocyclic Compounds, Vol. 8, Wiley New York (1961).
2. O. Gryszkiewicz-Trochimowoki, Comptes Rendus Acad. Sci., 246, 2627 (1958).
3. M. M. Krayushkin, A. M. Beskopyl'nyi, S. G. Zlotin, et al., Dokl. Akad. Nauk SSSR, 259, 370 (1981).
4. USSR Inventor's Certificate No. 1,018,942; Byull. Izobret., No. 19 (1983).
5. USSR Patent No. 576,935; Byull. Izobret., No. 11 (1977).
6. V. M. Zhulin, M. T. Gonikberg, and V. N. Zagrobin, Izv. Akad. Nauk SSSR, Ser. Khim., 716 (1962); V. M. Zhulin and A. S. Suprun, Vysokomol. Soedin., A13, 2518 (1971); G. I. Nikishin, S. S. Spektor, and G. P. Shakhovskoi, Izv. Akad. Nauk SSSR, Ser. Khim., 1664 (1976).
7. B. E. Fisher, A. J. Tomson, and J. P. Horwitz, J. Org. Chem., 24, 1650 (1959).
8. P. Yates and D. G. Farmum, J. Am. Chem. Soc., 86, 2967 (1963).

HYDROGENATION OF DEHYDROAMINO ACIDS IN THE PRESENCE OF PALLADIUM(II) COMPLEXES WITH METHIONINE

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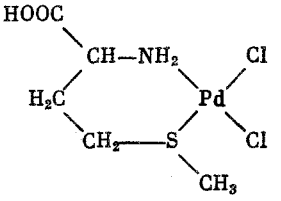
There have been recent attempts to find asymmetric hydrogenation catalysts derived from metal complexes with various chiral nonphosphine ligands, including complexes with natural amino acids [1, 2].

In the present work, we studied the catalytic activity of Pd(II) complexes with R- and S-methionine reduced by H_2 or $NaBH_4$. The $Pd(MetH)Cl_2$ complexes are



stable chelates and their structure has been readily established [3-6]. However, the catalytic properties of systems containing these complexes have not yet been studied.

We have shown that these systems at 20°C with 0.1 MPa H_2, 10:1 substrate/catalyst ratio, and 1:2 catalyst/$NaBH_4$ ratio have high catalytic activity in the hydrogenation of cinnamic acid derivatives (see Table 1).

$$PhCH = C(NHCOR^1)COOR + H_2 \rightarrow PhCH_2CH(NHCOR^1)COOR$$

A quantitative yield of the hydrogenation product at atmospheric pressure may be achieved after 5-8 h but the enantioselectivity is virtually zero. This is probably related to the formation of a metallic Pd phase such that the hydrogenation of most of the substrate proceeds on palladium. Indeed, the precipitate of the black collected after the reaction contains only traces of carbon and hydrogen (as indicated by elemental analysis). If, on the other hand, an excess of free methionine is introduced into the reaction mixture, the hydrogenation does not proceed.

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