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Note

Pyridazines. LXXI. Addition of Azidoazolopyridazines to Triple Bonds

B. Mihelčič, S. Simonič, B. Stanovnik, and M. Tišler

Department of Chemistry, University of Ljubljana, 61000 Ljubljana, Slovenia, Yugoslavia

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Cycloaddition reactions of azidoazolopyridazines to triple bonds are described. In the case of unsymmetrical acetylenes, for example phenylacetylene, the preference for the formation of substituted 4-phenyl 1,2,3-triazole has been established.

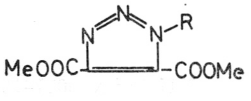
It is well known that azides, as reactive 1,3-dipoles, undergo cycloaddition reactions. The concept of 1,3-dipolar cycloadditions and its implications were elaborated in detail by Huisgen and his collaborators[1]. Cycloaddition reactions of azides to different polarophiles have been reviewed[1-4] and theoretical principles have been discussed[5].

In contrast to 1,3-dipolar cycloadditions of azides to olefins whereby in most cases thermally unstable Δ^2-1,2,3-triazolines are formed, addition of azides to triple bonds yields stable 1,2,3-triazoles. Kinetic results, although limited, present evidence that the reactivity of alkynes is comparable to that of alkenes[6].

In connection with our studies concerning the reactivity and azido-tetrazolo isomerizations of azidoazolopyridazines[7] it seemed of interest to investigate 1,3-dipolar cycloadditions of these compounds to multiple bonds. In this paper we wish to report some reactions with acetylenic compounds.

The addition of dimethyl acetylenedicarboxylate in ethanol or toluene proceeded as anticipated to give the 1 : 1 molar adduct and the corresponding triazoles (*1*) were obtained in moderate yield. In addition to the spectroscopic evidence for the triazole ring formation, chemical evidence was presented by formation of a triazolopyridazine ring (*2*, or tautomer) after treatment with hydrazine hydrate.

The addition of azides to unsymmetrical acetylenes is of particular interest since two products are conceivable. From previous studies it is known that the orientation is governed by electronic and steric effects[8,9]. When 6-azidotetrazolo(1,5-*b*)pyridazine reacted with phenylacetylene in boiling toluene a mixture of the 4- and 5-phenyl isomers (*3c* and *4c*) was obtained. From the n.m.r. spectrum of the mixture it was concluded that both compounds were present in a ratio of about 1 : 5. The structure of both compounds is supported by n.m.r. spectral evidence. The 4-phenyl group exhibits in the n.m.r. spectrum a multiplet, whereas the signal for the 5-phenyl group is a broadened singlet. This is in agreement with the observations on related products[10] as well as



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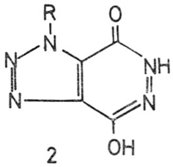

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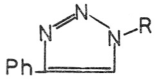

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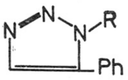

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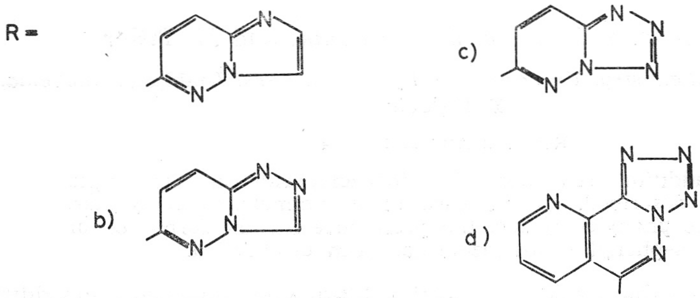

with our findings on addition products of azides and 1,3-dicarbonyl compounds[11]. As already mentioned, the 4-phenyl isomer is the major product and this contrasts the reaction between phenylacetylene and phenyl azide. Here, the 4-phenyl isomer was formed in 43% yield and the 5-phenyl isomer in 52% yield[8]. The preference for the formation of the 4-phenyl isomer from 6-azidoazolopyridazines is understandable if we take into consideration the electronic pathway of 1,3-dipolar cycloaddition[12] and the lesser steric hindrance exerted by the bulky azolopyridazine ring. This has also been confirmed in other cases. Phenylacetylene afforded with 6-azido-*s*-triazolo(4,3-*b*)pyridazine or with 6-azidoimidazo(1,2-*b*)pyridazine exclusively the 4-phenyl isomer (*3b* and *3a*).

EXPERIMENTAL

Melting points were determined on a Kofler micro hot stage. N.m.r. measurements were made on a JEOL JNM-C-60HL spectrometer (TMS as internal standard) and mass spectra were recorded on a Hitachi-Perkin-Elmer RMU—6L mass spectrometer.

1-[Tetrazolo(1,5-b)pyridazinyl-6′]-4,5-dicarbomethoxy-1,2,3-triazole (1c)

A mixture of 6-azidotetrazolo(1,5-*b*)pyridazine (1.62 g), dimethyl acetylenedicarboxylate (1.42 g) and toluene (30 ml) was heated under reflux for 10 h. The separated product was filtered off and crystallized from ethanol and *N,N*-dimethylformamide, 3 : 1. M. p. 205 °C (yield 0.5 g, 16%).

Anal. $C_{10}H_8N_8O_4$ (304.24) calc'd.: C 39.48; H 2.65; N 36.83%
found: C 39.62; H 2.82; N 37.01%

The above compound, when heated with an ethanolic solution of hydrazine hydrate, formed the corresponding triazolo(4,5-*d*)pyridazine derivative (*2c*) in 85% yield, m. p. 188—190 °C (from *N,N*-dimethylformamide and ethanol, 1 : 2).

Anal. $C_8H_4N_{10}O_2$ (272.18) calc'd.: C 35.30; H 1,48; N 51.46%
found: C 35.48; H 1.70; N 51.24%

*4,5-Dicarbomethoxy-1[pyrido(2,3-d)tetrazolo(1,5-*b*)pyridazinyl-6')1,2,3--triazole (1d)*

6-Azidopyrido(2,3-*d*)tetrazolo(1,5-*b*)pyridazine (1.07 g), dimethyl acetylenedicarboxylate (0.85 g) and ethanol (10 ml) were heated under reflux for 6 h. The separated crystals were filtered off and crystallized from *N,N*-dimethylformamide and ethanol, m. p. 190 °C (yield 1,0 g, 52%). Mass spectrum: $M^+ = 355$. N.m.r. spectrum (DMSO-d_6): $\tau = 0.75$ (dd, $H_{9'}$), 1.75 (dd, $H_{8'}$), 0.80 (dd, $H_{7'}$), 6.03 and 6.45 (s, COOMe); $J_{8'9'} = 6.0$, $J_{7'9'} = 2.0$, $J_{7'8'} = 9.0$ Hz.

Anal. $C_{13}H_9N_9O_4$ (355.29) calc'd.: C 43.95; H 2.55; N 35.48%
found: C 44.12; H 2.68; N 35.88%

*4-Phenyl-1-[tetrazolo(1,5-*b*)pyridazinyl-6']-1,2,3-triazole (3c)*

6-Azidotetrazolo(1,5-*b*)pyridazine (0.8 g), toluene (10 ml) and phenylacetylene (0.55 g) were heated under reflux for 2 h. The reaction mixture was evaporated *in vacuo* to dryness and the residue was found by examining its n.m.r. spectrum to be a mixture of the 4-phenyl isomer (*3c*) and 5-phenyl isomer (*4c*) in ratio of about 1 : 5. Upon crystallization from *N,N*-dimethylformamide and ethanol, 1 : 2, the 5-phenyl isomer (0.7 g, 52%) was obtained pure, m. p. 165—166 °C. N.m.r. spectrum (DMSO-d_6): 4-phenyl isomer (*3c*): $\tau = 1.28$ (d, $H_{7'}$), 0.85 (d, $H_{8'}$), 0.10 (s, H_5), 2.40 and 1.90 (m, Ph), $J_{7'8'} = 9.5$ Hz. 5-Phenyl isomer: $\tau = 1.63$ (d, $H_{7'}$), 0.85 (d, $H_{8'}$), 1.65 (s, H_4), 2.45 (s, Ph), $J_{7'8'} = 9.5$ Hz.

Anal. $C_{12}H_8N_8$ (264.25) calc'd.: C 54.54; H 3.05; N 42.41%
found: C 54,27; H 3.48; N 42.40%

*4-Phenyl-1-[*s*-triazolo(4,3-*b*)pyridazinyl-6']-1,2,3-triazole (3b)*

The compound was obtained in the same way as described above in 60% yield, m. p. 231 °C (from ethanol and *N,N*-dimethylformamide, 4 : 1). N.m.r. spectrum (DMSO-d_6): $\tau = 0.40$ (s, $H_{3'}$), 2.02 (d, $H_{7'}$), 1.50 (d, $H_{8'}$), 0.70 (s, H_5), 2.70 and 2.10 (m, Ph), $J_{7'8'} = 9.5$ Hz.

Anal. $C_{13}H_9N_7$ (263.26) calc'd.: C 59.31; H 3.45; N 37.25%
found: C 59.60; H 3.81; N 37.50%

*4-Phenyl-1-[imidazo(1,2-*b*)pyridazinyl-6']-1,2,3-triazole (3a)*

was obtained in a similar way in 84% yield, m. p. 235 °C (from ethanol and *N,N*--dimethylformamide, 3 : 1). N.m.r. spectrum (DMSO-d_6): $\tau = 2.28$ (d, $H_{2'}$), 1.85 (d, $H_{3'}$), 2.15 (d, $H_{7'}$), 1.78 (d, $H_{8'}$), 0.92 (s, H_5), 2.70 and 2.10 (m, 4-Ph); $J_{2'3'} = 1.0$, $J_{7'8'} = 9.5$ Hz.

Anal. $C_{14}H_{10}N_6$ (262.27) calc'd.: C 64.11; H 3.84; N 32.05%
found: C 64.23; H 3.98; N 32.45%

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IZVLEČEK

Piridazini. LXXI. Adicije azidoazolopiridazinov na trojne vezi

B. Mihelčič, S. Simonič, B. Stanovnik in M. Tišler

Opisane so reakcije cikloadicije azidoazolopiridazinov na trojne vezi. V primeru nesimetričnih acetilenov, kot na primer fenilacetilena, je bilo mogoče ugotoviti da nastane prednostno substituiran 4-fenil 1,2,3-triazol.

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