1,3-Dipolar Additions of Glycosyl Azides to Substituted Acetylenes

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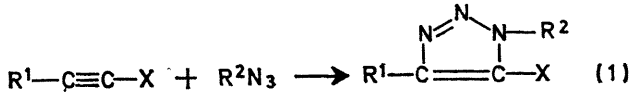
Summary The 1,3-dipolar additions of fully acetylated β-D-glycosyl azides to ynamines, ethoxyacetylene, and 1-ethylthio-2-phenylacetylene led to the formation of the corresponding *N*-glycosyl-2,3,4-triazoles.

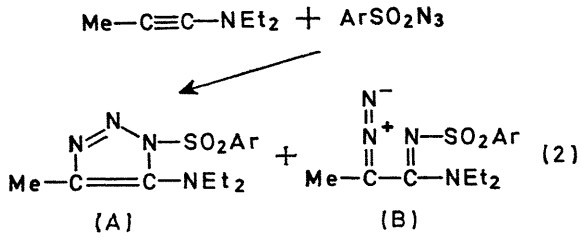
IT has been known for some time that the 1,3-dipolar additions of simple alkyl and aryl azides to various substituted acetylenes afford the corresponding triazoles (equation 1).[1]



(1)

X = OEt, NMe_2, NEt_2, *etc.*
and R^1 and R^2 = alkyl or aryl

According to Huisgen,[2] the 1,3-dipolar cycloadditions take place *via* a concerted mechanism as opposed to that involving a spin-paired diradical intermediate, as suggested by Firestone.[3] Recently, we reported[4] that the addition of a number of substituted benzenesulphonyl azides to ynamines gave equilibrium mixtures of *NN*-dialkylamino-1,2,3-triazole (A) and α-diazoamidine (B) tautomers (equation 2).



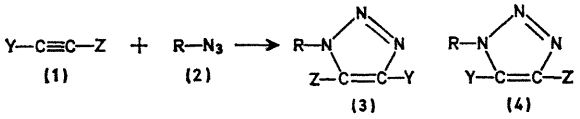
(2)

(A) (B)

We now report the first example of the 1,3-dipolar addition of several fully acetylated-β-D-glycosyl azides to acetylenes substituted by *NN*-dialkylamino-, ethoxy- and ethylthio-groups. Our results indicate marked differences in the relative reactivities of these acetylenes substituted by different electron-donating groups. The addition of hepta-*O*-acetyl-β-D-maltosyl and of hepta-*O*-acetyl-β-D-cellobiosyl azide to ethoxyacetylene was significant because each of them yielded both the possible isomeric triazoles. Previously reported additions of azides to ethoxyacetylene afforded only one of the two triazoles.[1]

The per-*O*-acetyl-β-D-glycosyl azides (**2**a—d) were prepared by heating (90°) the corresponding per-*O*-acetyl-α-D-glycosyl halides with sodium azide in dimethylformamide. This procedure is similar to that used in the preparation of 2-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-glucosyl azide[5] and 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl azide.[6] This method was preferred over the well-known literature procedures involving the hazardous use of silver azide.[7]

The addition of glycosyl azides, (**2**a—d), to *NN*-diethylaminoprop-1-yne (**1**a) and *NN*-dimethylaminophenylacetylene (**1**b) (equation 3) was accomplished by heating solutions of the azide and the ynamine in tetrahydrofuran under reflux for 2—8 h. In each case t.l.c. of the reaction mixture showed only one new spot. The adducts, which were identified as 1,2,3-triazoles, (**3**a—g)† were isolated either by crystallization or column chromatography over silica gel. In each case, only one of the two possible triazoles was isolated. These results are in general agreement with the known additions of azides[1] and sulphonyl azides[4] to ynamines but contrast with the addition of glycosyl azides to phenylacetylene,[1] where both the isomeric triazoles were isolated. The structures assigned to the



(1) (2) (3) (4)

a; Y = Me, Z = NEt_2 a; R = Gluco
b; Y = Ph, Z = NMe_2 b; R = Galacto
c; Y = OEt, Z = H c; R = Malto
d; Y = SEt, Z = Ph d; R = Cellobio

a; Y = Me, Z = NEt_2, R = Gluco
b; Y = Me, Z = NEt_2, R = Galacto
c; Y = Me, Z = NEt_2, R = Malto
d; Y = Me, Z = NEt_2, R = Cellobio
e; Y = Ph, Z = NMe_2, R = Gluco
f; Y = Ph, Z = NMe_2, R = Galacto
g; Y = Ph, Z = NMe_2, R = Malto
h; Y = H, Z = OEt, R = Gluco
i; Y = H, Z = OEt, R = Galacto
j; Y = H, Z = OEt, R = Cellobio
k; Y = H, Z = OEt, R = Malto

a; Y = H, Z = OEt, R = Cellobio
b; Y = H, Z = OEt, R = Malto
c; Y = Ph, Z = SEt, R = Cellobio

Gluco = 2,3,4,6-tetra-O-acetyl-β-D-glucosyl

Galacto = 2,3,4,6-tetra-O-acetyl-β-D-galactosyl

Malto = 2,3,4,6,2',3',6'-hepta-O-acetyl-β-D-maltosyl

Cellobio = 2,3,4,6,2',3',6'-hepta-O-acetyl-β-D-cellobiosyl

triazoles are based on literature analogies.[1,4] They were also supported by elemental analyses and n.m.r. data. The addition of glycosyl azides, (**2**a—d), to ethoxyacetylene (**1**c) required much more severe conditions than the corresponding additions to ynamines. The reactions were conducted by heating a tetrahydrofuran solution of an azide and (**1**c) in a sealed tube at 60—70° for 12 d. Higher temperatures were avoided to prevent excessive decomposition of (**1**c). The reactions yielded complex mixtures and isolation of the products required extensive column chromatography over silica gel. The resulting triazoles, (**3**h—k) and (**4**a—b), could only be isolated in low yields (<35%). As before, they were characterized by elemental analyses

† Analytically pure samples of (**3**a), (**3**c), (**3**d—e), (**3**h—k), and (**4**a—c) were obtained as colourless crystals whereas those of (**4**b) (**3**f), and (**3**g) were colourless gums.

and n.m.r. data. The addition of (2a) and (2b) led to the isolation of only one of the two possible isomeric triazoles in each case, (3h) and (3i), respectively. On the other hand, all the possible triazoles, (3j), (4a), (3k), were isolated from the addition of hepta-*O*-acetyl-β-D-cellobiosyl azide (2c) and hepta-*O*-acetyl-β-D-maltosyl azide (2d). The n.m.r. spectra of each set of these isomeric triazoles were similar and consistent with the structures. This is the first time that both the possible isomeric triazoles have been isolated from the addition of azides to ethoxyacetylene.

The reaction of (2a—d) with 1-ethylthio-2-phenylacetylene (1d) under the usual conditions was slow and led to extensive decomposition when more severe conditions [heating the tetrahydrofuran solution containing an azide and (1d) in a sealed tube at 130—140° for 5 d] were used. Only the addition of hepta-*O*-acetyl-β-D-cellobiosyl azide (2d) gave a low yield (18%) of a crystalline triazole, (4c). Of particular interest was the appearance of the phenyl hydrogens as a singlet at τ 2·52. In accordance with the earlier observations of Garcia-Lopez *et al.*,[1] the structure (4c) was preferred over the other possible isomeric structure, in which case the phenyl hydrogens would have appeared as a complex multiplet. This is also consistent with the observations of Groen and Arens,[8] who demonstrated that the 1,3-dipolar addition of diazomethane to (1d) takes place in a manner opposite to the 1,3-dipolar additions to ynamines or acetylenic ethers.

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[1] R. Fuks, R. Buijle, and H. G. Viehe, *Angew. Chem.*, 1966, **78**, 594; R. Huisgen, R. Knorr, L. Mobius, and G. Szeimies, *Chem. Ber.*, 1965, **98**, 623; M. T. Garcia-Lopez, G. Garcia-Monoz, J. Iglesias, and R. Madronero, *J. Heterocyclic Chem.*, 1969, **6**, 639; P. Grunanger, P. Finzi, and E. Fabbri, *Gazzetta*, 1967, **55**, 11397.
[2] R. Huisgen, *J. Org. Chem.*, 1968, **33**, 2291.
[3] R. A. Firestone, *J. Org. Chem.*, 1968, **33**, 2285.
[4] R. E. Harmon, F. Stanley, jun., S. K. Gupta, and J. Johnson, *J. Org. Chem.*, 1970, **35**, 3444.
[5] A. Yamamoto, C. Miyashita, and H. Tsukamoto, *Chem. and Pharm. Bull.* (*Japan*), 1965, **13**, 1036.
[6] R. Carrington, G. Shaw, and D. V. Wilson, *J. Chem. Soc.*, 1965, 6864.
[7] F. Mitchell and A. Klemer, *Adv. Carbohydrate Chem.*, 1961, **16**, 85.
[8] S. H. Goren and J. F. Arens, *Rec. Trav. chim.*, 1961, **80**, 879.