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PHOTOCHEMISTRY OF 2-AZIDOADENINE IN ALCOHOLS

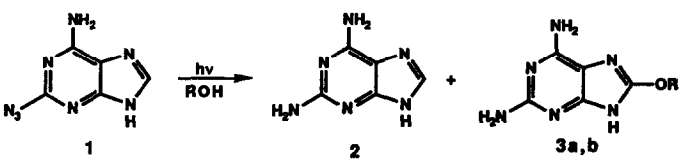
Yi-de Xing,† Stephen S. Hixson,†* and Robert A. Zimmermann‡
Departments of Chemistry† and Biochemistry,‡ University of Massachusetts, Amherst MA 01003

Summary: Photolysis of 2-azidoadenine in methanol (ethanol) gives 2,6-diaminopurine plus 8-methoxy(ethoxy)-2,6-diaminopurine.

2-Azidoadenosine is one of a group of azidopurine nucleoside analogs which have seen extensive use as photoaffinity probes of biological macromolecular systems.[1-6] We have recently used transfer RNAs (tRNAs) in which 2-azidoadenosine has been substituted, site-selectively, for the natural nucleoside adenosine as probes of the structure of the tRNA binding sites on the bacterial ribosome.[7,8] As an aid in carrying out and interpreting such photoaffinity labeling studies we have examined the photochemistry of the parent base, 2-azidoadenine (1), in alcohols. We find that 1 reacts in a manner significantly different from that commonly observed with other aryl azides.[9]

The irradiation of azide 1 (50 mg) in methanol (220 mL) under nitrogen was carried out at room temperature with Pyrex-filtered light from a Hanovia 450-watt medium pressure mercury arc. After 70 min, silica gel TLC indicated the virtual disappearance of 1 and the formation of two slower moving products, 2 and 3a. NMR analysis revealed the products were each formed in 37% yield. Preparative TLC afforded pure samples of 2 and 3a.

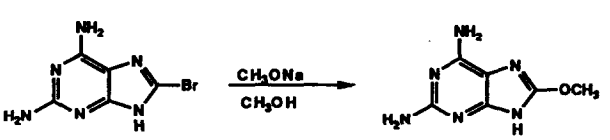
Product 2 was determined to be 2,6-diaminopurine by comparison of its NMR and UV spectra with those reported in the literature,[10-12] while 3a, mp 302°C (d), was tentatively identified as 8-methoxy-2,6-diaminopurine on the basis of its spectral data: ^{1}H-NMR (DMSO-d_6) δ 5.65 (s, 2H, exchangeable with D_2O), 6.63 (s, 2H, exchangeable with D_2O), and 7.67 (s, 1H); ^{13}C-NMR (DMSO-d_6) δ 112.40, 135.69, 152.82, 155.58, and 160.11 ppm; UV (CH_3OH) λ_{max} 286 nm (ε 8700); IR (KBr) 3355, 1618, 1407, 946, 790 and 636 cm^{-1}; MS 150 (M^+). Confirmation of the proposed structure of 3a was achieved by independent synthesis of 3a from 8-bromo-2,6-diaminopurine, 4[13,14] (equation 2).



1 2 3a,b (1)

Product Yields

R	2	3
CH_3	37%	37% (3a)
CH_3CH_2	75%	11% (3b)
$(CH_3)_2CH$	65%	---
$(CH_3)_2C$	59%	---



4 3a

Irradiation of azide **1** in ethanol followed a similar course, giving, however, a greater proportion of 2,6-diaminopurine (**2**) than the ethoxy-substituted product **3b** (^{1}H-NMR (DMSO-d_6) δ 1.34 (t, 3H, J = 6.8 Hz), 4.37 (q, 2H, J = 6.8 Hz), 5.43 (s, 2H) and 6.20 (s, 2H) ppm). Photolysis of **1** in either 2-propanol or tert-butyl alcohol gave **2** as the only isolable product (see equation 1).

We assume that products **2** and **3a,b** arise via a nitrene, and that the nitrene arises directly from azide **1** and not from the tetrazole tautomers with which **1** is in equilibrium.[3,15] The latter have been reported to be photochemically inert.[3]

The formation of reduction product **2**, presumably by nitrene hydrogen-atom abstraction, has ample analogy in aryl azide photochemistry.[9] On the other hand alkoxy derivatives **3a,b** are unusual azide photoproducts. Addition of nucleophilic solvents to photochemically-derived aryl nitrenes commonly proceeds via heterocumulene or azirine intermediates, generally providing ring-expanded azepine or ortho-substituted aromatic amine products.[9,16] Insertion of the nitrene into H-X bonds is another, but less often observed, reaction pathway.[9] In the present case we have net conjugate addition of ROH to the nitrene at a site (C-8) quite remote from the electron-deficient nitrogen. Formation of **3a,b** via direct reaction of the nitrene with methanol (ethanol) is the most straightforward of possible mechanisms. However, involvement of an unstable intermediate such as an azirine is also a possibility. In any case it is important to note that photoaffinity labeling of nucleophilic sites by azide **1** incorporated into tRNAs[7,8] and in other systems studied likely involves C-8. Further studies on this interesting reaction are underway.

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