

A Novel Crystalline Tetrazolo-Azido Isomer Pair:
 Pyrido[2,3-*e*]tetrazolo[5,1-*c*]-*as*-triazine and 3-Azidopyrido[2,3-*e*]-*as*-triazine;
 The Synthesis of Tetrazolo[5,1-*c*]benzo-*as*-triazine and
 pyrido[2,3-*e*]triazolo[3,4-*c*]-*as*-triazine

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The deoxygenated derivative of 3-azidobenzo-*as*-triazine 1-oxide (II) exists in solution predominantly as 3-azidobenzo-*as*-triazine form (IVa) but in the crystalline state as tetrazolo[5,1-*c*]benzo-*as*-triazine (IVb), a new fused heteroaromatic ring system. With the pyrido[2,3-*e*]-*as*-triazine derivatives, however, both 3-azidopyrido[2,3-*e*]-*as*-triazine (X) and pyrido[2,3-*e*]tetrazolo[5,1-*c*]-*as*-triazine (XI) can be isolated in crystalline form, and these are interconvertible. Another new ring system, the pyrido[2,3-*e*]triazolo[3,4-*c*]-*as*-triazine (XVII) and its derivatives has also been synthesized.

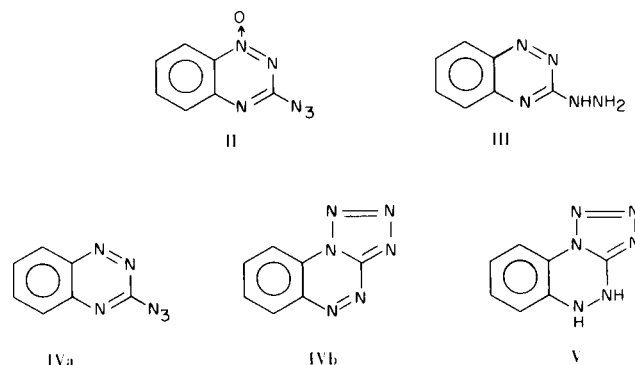
Earlier investigation (1) revealed that the presence of electron-withdrawing groups shifts the azidoazomethine (Ia)-tetrazole (Ib) equilibrium in solution towards the azido compound Ia. Generally, however, only one of



the two possible isomers has been isolated in crystalline form. It seemed reasonable that removal of the electron-withdrawing group from the molecule of the azido compound would be a suitable method to promote the formation of the tetrazole ring.

Interest in the synthesis of tetrazolo[5,1-*c*]benzo-*as*-triazine (IVb) led us to examine the deoxidation products of 3-azidobenzo-*as*-triazine 1-oxide (II) described by Sasaki *et al.* (2a). Removal of the electron-withdrawing *N*-oxide group should facilitate ring closure of the azide to give the tetrazole.

Indeed, it has been found that diazotization of 3-hydrazinobenzo-*as*-triazine (III) (2b) gives crystalline tetrazolo[5,1-*c*]benzo-*as*-triazine (IVb), the parent compound of a new heteroaromatic ring system, instead of the open-chain isomer. Sodium dithionite reduction of the product (IVb) yields 4,5-dihydrotetrazolo[5,1-*c*]benzo-*as*-triazine (V), similarly containing a tetrazole ring.



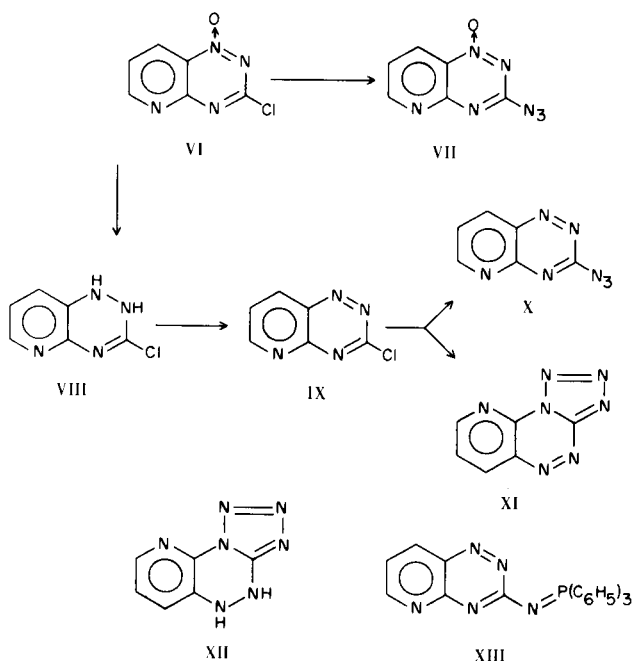
The open-chain or cyclic structure of the products can be readily decided from the presence or absence of the azide band in the infrared spectrum, taken both in the solid phase (potassium bromide) and in solution (chloroform).

While Sasaki's compound II has the azide structure both in the solid phase and in solution, dihydrotetrazolo[5,1-*c*]benzo-*as*-triazine (V) prepared by us exists as the tetrazole isomer in both phases, in accord with the presence of an electron-releasing amino group in place of the electron-withdrawing *N*-oxide group. Compound IV occupies an intermediate position between these two extremes (II and V); the absence of the *N*-oxide group gives rise to the tetrazole form IVb in the solid phase only, while in solution the open 3-azidobenzo-*as*-triazine

structure (IVa) remains predominant.

These observations prompted us to extend our examinations to the analogous case of azido derivatives with pyrido[2,3-*e*]-*as*-triazine ring system, containing one more nitrogen atom.

Treatment of 3-chloropyrido[2,3-*e*]-*as*-triazine 1-oxide (VI), described by Carbon and Tabata (3), with sodium azide gives 3-azidopyrido[2,3-*e*]-*as*-triazine 1-oxide (VII), which, like compound II, has the azide structure both in the solid phase and in solution. In order to prepare the deoxidized derivative of the azido *N*-oxide (VII), the chloro-*N*-oxide (VI) was reduced with sodium dithionite to 3-chloro-1,2-dihydropyrido[2,3-*e*]-*as*-triazine (VIII) and the latter oxidized with potassium ferricyanide to 3-chloropyrido[2,3-*e*]-*as*-triazine (IX). Interestingly, treatment of this latter (IX) with sodium azide gave rise to the formation of two crystalline products of identical composition. The aqueous acetone reaction medium deposited pale yellow crystals melting at 129° dec. in 47% yield, while extraction of the filtrate with dichloromethane and treatment of the partially concentrated extract with petroleum ether gave a bright yellow crystalline substance, of melting point 62°, in 26% yield. The infrared spectrum of the lower melting product had a strong azide band both in the solid phase and in solution,



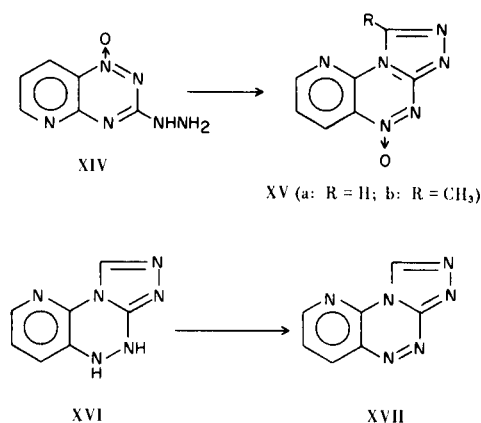
accordingly, the structure of 3-azidopyrido[2,3-*e*]-*as*-triazine (X) was assigned to it. The other product, which contains no azide band in the infrared, should thus be regarded as pyrido[2,3-*e*]-tetrazolo[5,1-*c*]-*as*-triazine (XI), the first representative of a new heteroaromatic ring system.

To our knowledge, 3-azidopyrido[2,3-*e*]-*as*-triazine (X) and pyrido[2,3-*e*]-tetrazolo[5,1-*c*]-*as*-triazine (XI) constitute the third type of simple azide-tetrazole isomer pair (4,5) isolated in crystalline form. The two isomers are interconvertible. In the solid phase, the tetrazole, and in solution, the azide isomer is the more stable, but the latter is stable enough to exist for a few days in the crystalline form. After standing for a week, the solid azide has undergone spontaneous transformation to the tetrazole. Both X and XI have ABX nmr spectra. Isomerization can be followed by the signal of the proton 7: freshly prepared solutions of tetrazole XI and azide X in dimethylsulphoxide gave two different quartets. Some minutes later the quartet of the other isomer slowly appeared and in an hour the same pattern could be observed in both cases, indicating that equilibrium has been established.

The solubility features of the two isomers differ considerably. The azide X is readily soluble in chloroform and benzene; on heating with triphenylphosphine in benzene solution it gave the greenish-yellow triphenylphosphine imine XIII in 71% yield. In contrast, the tetrazole XI is insoluble in chloroform and benzene at room temperature. On heating, dissolution takes place slowly, the process being accompanied by conversion into the azide X, which is easily isolated on evaporation of the solvent. The tetrazole XI, dissolved carefully in cold dimethylformamide and treated with aqueous sodium dithionite solution is converted to 4,5-dihydropyrido[2,3-*e*]-tetrazolo[5,1-*c*]-*as*-triazine (XII).

Comparison of the infrared spectra reveals that the electron-withdrawing effect exerted upon the azide group in pyrido[2,3-*e*]-*as*-triazine derivatives changes more gradually than in benzo-*as*-triazines. In consequence, while compound IV exists merely as the tetrazole isomer in solid phase, the azide isomer X of the tetrazole compound XI can also be isolated as a crystalline solid.

3-Hydrazinopyrido[2,3-*e*]-*as*-triazine 1-oxide (XIV), easily available from 3-chloropyrido[2,3-*e*]-*as*-triazine 1-



oxide (VI) by the procedure of Carbon and Tabata (3), reacts with orthoesters to give 1-substituted pyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine 5-oxide (XV). Sodium dithionite reduction of compound XVa yields 4,5-dihydropyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine (XVI), which on oxidation with ferric chloride gives the heteroaromatic pyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine (XVII). An unambiguous proof for the structure of the new ring system XVII is provided by the nmr spectrum recorded in DMSO and its comparison with that of *s*-triazolo[3,4-*c*]benzo-*as*-triazine, described by Sasaki and Murata (2a), of related structure but containing one nitrogen atom less. The signals of the protons in position 1 of the two compounds are identical, while those of the remaining three protons are shifted towards higher δ values in the new ring system, in agreement with the structural feature that the latter compound contains also a nitrogen atom in the ring bearing these protons.

EXPERIMENTAL

Tetrazolo[5,1-*c*]benzo-*as*-triazine (IV).

A suspension of 1.0 g. (6.2 mmoles) of 3-hydrazinobenzo-*as*-triazine (III) in 8 ml. of glacial acetic acid was treated dropwise with a solution of 0.45 g. (7.2 mmoles) of sodium nitrite in 5 ml. of water over a period of 10 minutes, when a homogeneous solution resulted which was stirred for a further 5 minutes to deposit a greenish-yellow solid substance. It was isolated by filtration, dried and purified by precipitation with petroleum ether from a chloroform solution to give 0.60 g. (58%) of pale yellow crystals, m.p. 115-117°; ν max cm^{-1} (chloroform): 2150 (azide); (potassium bromide): no azide band.

Anal. Calcd. for $\text{C}_7\text{H}_4\text{N}_6$: C, 48.9; H, 2.3; N, 48.9. Found: C, 49.2; H, 2.4; N, 49.2.

4,5-Dihydropyrido[2,3-*e*]benzo-*as*-triazine (V).

A solution of 1.0 g. (5.7 mmoles) of sodium dithionite in 10 ml. of water was added to a solution of 0.5 g. (2.91 mmoles) of tetrazolo[5,1-*c*]benzo-*as*-triazine (IV) in 4 ml. of dimethylformamide, when colorless needles separated from the reaction mixture. The product was filtered off, dried, dissolved in acetone and the solution treated with petroleum ether to deposit 0.28 g. (61%) of a colorless substance, m.p. 194° dec.; ν max cm^{-1} either in chloroform solution or in potassium bromide; ν max cm^{-1} 3150 and 3210 (NH); ν max (ethanol) 309 nm (ϵ , 6,360) and 390 nm (ϵ , 1,855).

Anal. Calcd. for $\text{C}_7\text{H}_6\text{N}_6$: N, 48.2. Found: N, 47.5.

3-Azidopyrido[2,3-*e*]-*as*-triazine 1-Oxide (VII).

A solution of 0.4 g. (2.2 mmoles) of 3-chloropyrido[2,3-*e*]-*as*-triazine 1-oxide (VI) in 4 ml. of acetone was treated with 0.2 g. (3.2 mmoles) of sodium azide in 2 ml. of water, when the solution (remaining deep yellow) slightly warmed up. After standing 0.5 hour, the mixture was diluted with 10 ml. of water and extracted with 20 ml. of chloroform three times. The combined extracts were dried, concentrated to about 5 ml. and diluted with petroleum ether to precipitate 0.30 g. (73%) of yellow crystals. Purification was achieved by precipitation with petroleum ether from benzene, m.p. 114-115°; ν max cm^{-1} 2150 (azide); (both in potassium bromide and chloroform); ν max (ethanol)

265 nm (ϵ , 19,500) and 370 nm (ϵ , 5,560).

Anal. Calcd. for $\text{C}_6\text{H}_3\text{N}_7\text{O}$: N, 51.9. Found: N, 52.1.

3-Chloropyrido[2,3-*e*]-*as*-triazine (IX).

Sodium dithionite (3.4 g.) in 17 ml. of water was added to 1.7 g. (9.4 mmoles) of 3-chloropyrido[2,3-*e*]-*as*-triazine 1-oxide (VI) in 8 ml. of acetonitrile, when the mixture slightly warmed up and copious precipitation commenced. The mixture was diluted with 15 ml. of water and the voluminous crystalline product filtered off to obtain 0.9 g. (57%) of crude 3-chloro-1,2-dihydropyrido[2,3-*e*]-*as*-triazine (VIII), m.p. 151-153° dec.

This 0.9 g. of VIII was added to a mixture of 17 ml. of 20% aqueous potassium ferricyanide and 10 ml. of 10% sodium bicarbonate solutions. The resulting suspension was stirred for 0.5 hour and extracted with chloroform. The combined extracts were dried, and evaporated to dryness to give 0.55 g. (63%) of a bright yellow crystalline residue, which was purified by crystallization from chloroform-petroleum ether. Pure 3-chloropyrido[2,3-*e*]-*as*-triazine (IX) melted at 124-126°; ν max (ethanol) 273 nm (ϵ , 4,520); 327 nm (ϵ , 9,990) and 336 nm (ϵ , 9,320).

Anal. Calcd. for $\text{C}_6\text{H}_3\text{N}_4\text{Cl}$: N, 33.7; Cl, 21.2. Found: N, 33.7; Cl, 20.9.

3-Azidopyrido[2,3-*e*]-*as*-triazine (X) and Pyrido[2,3-*e*]tetrazolo[5,1-*c*]-*as*-triazine (XI).

3-Chloropyrido[2,3-*e*]-*as*-triazine (IX) (0.4 g., 2.4 mmoles) in 4 ml. of acetone was treated with 0.2 g. of sodium azide in 2 ml. of water to give a homogeneous solution which slightly warmed up. After standing 20 minutes, bright crystals commenced to separate. The mixture was concentrated to about half of its volume, the crystals were filtered off, washed with water and acetone and dried to obtain 0.20 g. (47.8%) of pyrido[2,3-*e*]tetrazolo[5,1-*c*]-*as*-triazine (XI), m.p. 129° dec.; ν max (potassium bromide): no azide band; nmr (dimethylsulphoxide) 6, 7 and 8 hydrogens: 9.61; 8.40, and 9.48 ppm (ABX spectrum); coupling constants: J_{6-7} 8.2 Hz; J_{7-8} 4.9 Hz; J_{6-8} 1.8 Hz.

Anal. Calcd. for $\text{C}_6\text{H}_3\text{N}_7$: C, 41.6; H, 1.7; N, 56.6. Found: C, 41.0; H, 2.0; N, 56.4.

Extraction of the aqueous acetone filtrate with dichloromethane and treatment of the dried and concentrated (to about ¼ volume), extract with petroleum ether gave 0.11 g. (26.2%) of 3-azidopyrido[2,3-*e*]-*as*-triazine (X), a bright yellow crystalline product, m.p. 61-62°; ν max cm^{-1} (potassium bromide): 2150 (azide); (chloroform): 2150 (azide); nmr (dimethylsulphoxide) 6, 7, and 9 hydrogens: 9.60, 8.04, and 9.11 ppm (ABX spectrum); coupling constants: J_{6-7} 8.3 Hz; J_{7-8} 4.0 Hz; J_{6-8} 2.0 Hz.

Anal. Calcd. for $\text{C}_6\text{H}_3\text{N}_7$: C, 41.6; H, 1.7; N, 56.6. Found: C, 41.6; H, 2.1; N, 56.7.

Interconversion of the Azido (X) and Tetrazole (XI) Isomers.

3-Azidopyrido[2,3-*e*]-*as*-triazine (0.10 g.) was kept in a sealed container for a week at room temperature, when it completely lost its yellow color and a pale blue tint appeared on the surface. The product was triturated with acetone and the insoluble material was isolated by filtration to obtain 0.08 g. of a yellowish-green solid, m.p. 126-128° dec. No mixed melting point depression was observed with the above tetrazole derivative.

This latter tetrazole derivative slowly dissolved when warmed in chloroform or benzene and on evaporation of the solvent the azide modification of m.p. 62° was recovered.

4,5-Dihydropyrido[2,3-*e*]tetrazolo[5,1-*c*]-*as*-triazine (XII).

Sodium dithionite (0.5 g., 2.9 mmoles) in 5 ml. of water was added in one portion to a solution of 0.2 g. (1.6 mmoles) of pyrido[2,3-*e*]tetrazolo[5,1-*c*]-*as*-triazine (XI) in 3 ml. of dimethylformamide. The resulting cloudy, pale yellow solution slowly deposited needles. The mixture was kept for 1 hour in a refrigerator and the pale yellow crystals were filtered off, washed with water and cold methanol and dried to obtain 0.12 g. (60%) of a product which did not melt up to 300°. On standing in air the crystals turned to bluish-green; the material can be stored for longer periods in closed containers only; ν max cm^{-1} (potassium bromide): 3150 (NH), no azide band; $\text{uv } \lambda$ max (dimethylsulphoxide) 326 nm (ϵ , 5,530).

Anal. Calcd. for $\text{C}_6\text{H}_5\text{N}_7$: N, 56.0. Found: N, 56.2.

3-Triphenylphosphiniminopyrido[2,3-*e*]-*as*-triazine (XIII).

3-Azidopyrido[2,3-*e*]-*as*-triazine (X) (0.2 g., 1.15 mmoles) and 0.35 g. (1.33 mmoles) of triphenylphosphine were refluxed 5 minutes in 5 ml. of benzene. On cooling, the solution deposited greenish-yellow crystals, which were filtered off and recrystallized from toluene to give 0.33 g. (71%) of a dark greenish-yellow crystalline product, m.p. 180-182°; $\text{uv } \nu$ max (ethanol) 351 nm (ϵ , 19,500) and 408 nm (ϵ , 4,070).

Anal. Calcd. for $\text{C}_{24}\text{H}_{18}\text{N}_5\text{P}$: C, 71.1; H, 4.4; P, 7.6. Found: C, 71.4; H, 4.4; P, 7.2.

Pyrido[2,3-*e*]-*as*-triazolo[3,4-*c*]-*as*-triazine 5-Oxide (XVa).

A mixture of 0.5 g. (2.75 mmoles) of 3-hydrazinopyrido[2,3-*e*]-*as*-triazine 1-oxide (XIV) and 10 ml. of ethyl orthoformate was refluxed for 2 hours to deposit 0.48 g. (93%) of a reddish material, while the initial red color of the solution gradually turned to pale yellow. Recrystallization of the crude product from 50% aqueous ethanol afforded 0.36 g. (70%) of yellowish-green needles, m.p. 278°; $\text{uv } \lambda$ max (ethanol) 328 nm (ϵ , 9,780) and 336 nm (ϵ , 9,620).

Anal. Calcd. for $\text{C}_7\text{H}_4\text{N}_6\text{O}$: C, 44.7; H, 2.1. Found: C, 44.9; H, 2.5.

1-Methylpyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine 5-Oxide (XVb).

A mixture of 0.3 g. (1.66 mmoles) of 3-hydrazinopyrido[2,3-*e*]-*as*-triazine 1-oxide (XIV) and 6 ml. of ethyl orthoacetate was refluxed for 2 hours. The starting material gradually dissolved, while another solid product was deposited from the reaction mixture, the process being accompanied by a change in color of the mixture from red to pale yellow. Recrystallization of the deposited crude product (0.26 g., 80%) from pyridine afforded 0.15 g. (46%) of the pure product, m.p. 260-261°; $\text{uv } \lambda$ max (ethanol) 328 nm (ϵ , 9,020) and 338 nm (ϵ , 9,020).

Anal. Calcd. for $\text{C}_8\text{H}_6\text{N}_6\text{O}$: C, 47.5; H, 3.0. Found: C, 47.7; H, 3.0.

4,5-Dihydropyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine (XVI).

A solution of 2.0 g. (11.5 mmoles) of sodium dithionite in 15 ml. of water was added to 0.8 g. (4.3 mmoles) of pyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine 5-oxide (XVa) and the mixture was heated. After refluxing for about 2 minutes, the material dissolved and the brown color of the mixture gradually turned to reddish-yellow. The solution was filtered while hot and it deposited on cooling colorless needles, 0.5 g. (68%), m.p. 196-198°; ν max cm^{-1} (potassium bromide): 3120 and 3200 (NH); $\text{uv } \lambda$ max (ethanol) 315 nm (ϵ , 5,180) and 338 nm (ϵ , 6,090).

Anal. Calcd. for $\text{C}_7\text{H}_6\text{N}_6$: C, 48.2; H, 3.5. Found: C, 48.0; H, 3.9.

Pyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine (XVII).

To 0.5 g. (2.88 mmoles) of 4,5-dihydropyrido[2,3-*e*]-*s*-triazolo[3,4-*c*]-*as*-triazine (XVI) was added a solution of 2.0 g. (9.5 mmoles) of crystalline ferric chloride in 20 ml. of water. The starting material rapidly dissolved to give a dark brown solution, from which the deposition of crystals commenced within 2 minutes. The mixture was allowed to stand for 2 hours and filtered off to obtain 0.34 g. of product (70%), m.p. 226-228°; $\text{uv } \lambda$ max (ethanol) 323 nm (ϵ , 9,400); nmr (dimethylsulphoxide): 10.30 ppm (1-H); 9.17 ppm, 8.12 ppm, 9.31 ppm (6, 7, and 8 hydrogens giving an ABX spectrum); coupling constants: J_{6-7} 4.8 Hz; J_{7-8} 8.2 Hz; J_{6-8} 1.8 Hz.

Anal. Calcd. for $\text{C}_7\text{H}_4\text{N}_6$: C, 48.8; H, 2.3. Found: C, 49.3; H, 2.4.

Melting points were determined on a Büchi apparatus and are uncorrected. The infrared, ultraviolet, and nuclear magnetic resonance spectra were obtained with a Unicam SP 200, Unicam SP 800, and Varian A-60 instrument, respectively.

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