(8) J. A. Franz and J. C. Martin, *J. Am. Chem. Soc.*, **97**, 583 (1975).
(9) N. Kunieda and S. Oae, *Bull. Chem. Soc. Jpn.*, **46**, 1745 (1973).
(10) H. R. Bentley, and J. K. Whitehead, *J. Chem. Soc.*, 2081 (1950).
(11) N. Furukawa, T. Omata, and S. Oae, *Chem. Commun.*, 590 (1973).
(12) (a) A. Fava, P. B. Sogs, and M. Calvin, *J. Am. Chem. Soc.*, **79**, 1078 (1957); (b) H. J. Shine and L. Piette, *ibid.*, **84**, 4798 (1962); (c) S. Oae and N. Kunieda, *Bull. Chem. Soc. Jpn.*, **41**, 696 (1968).
(13) N. Furukawa, T. Yoshimura, T. Omata, and S. Oae, *Chem. Ind.* (*London*), 702 (1974).
(14) (a) A. Kucsman, I. Kapovits, and F. Ruff, *Acta Chim. Acad. Sci. Hung.*, **40**, 75 (1964); (b) *Tetrahedron*, **22**, 1575, 1843 (1966); (c) S. Kucsman, F. Ruff, and I. Kapovits, *Acta Chim. Acad. Sci. Hung.*, **50**, 325 (1966); (d) A. Kalman, *Acta Crystallogr.*, **22**, 501 (1967); (e) K. Tsujihara, N. Furukawa, and S. Oae, *Bull. Chem. Soc. Jpn.*, **43**, 2153 (1970).
(15) Appel et al. claimed the formation of free nitrene which disproportionates to ammonia and nitrogen gas.
(16) W. Lwowski, Ed., "Nitrenes", Wiley, New York, N.Y., 1970.
(17) (a) L. Reiner and F. Flodalisi, U.S. Patent 2 648 705 (1953); (b) J. S. Berry, French Patent 1 377 794 (1964); U.S. Patent 3 255 116 (1966); (c) F. Misani, T. W. Fair, and L. Reiner, *J. Am. Chem. Soc.*, **73**, 459 (1951); (d) H. R. Bentley, E. E. McDermott, and J. K. Whitehead, *Proc. R. Soc. London, Ser. B*, **138**, 262 (1951); (e) J. K. Whitehead and H. R. Bentley, *J. Chem. Soc.*, 1572 (1952); (f) D. Jerchel, L. Dippelhofer, and D. Renner, *Chem. Ber.*, **87**, 947 (1954); (g) K. Hayashi, *Chem. Pharm. Bull.*, **8**, 177 (1960).
(18) (a) L. Horner and A. Christman, *Chem. Ber.*, **96**, 388 (1963); (b) L. Horner, G. Bauer, and J. Doerges, *ibid.*, **98**, 2631 (1965); (c) H. Kwart and A. A. Kahn, *J. Am. Chem. Soc.*, **89**, 1950 (1967).
(19) (a) D. Carr, T. P. Sesen, and R. Q. Turner, *Tetrahedron Lett.*, 477 (1969); (b) C. R. Johnson, R. A. Kirchhoff, R. J. Reisher, and G. F. Katekar, *J. Am. Chem. Soc.*, **95**, 4287 (1973); (c) M. Moriyama, T. Numata, and S. Oae, *Org. Prep. Proced. Int.*, **6**, 207 (1974).
(20) S. Oae, K. Harada, K. Tsujihara, and N. Furukawa, *Int. J. Sulfur Chem., Part A*, **2**, 49 (1972).
(21) H. J. Shine and J. J. Silber, *J. Am. Chem. Soc.*, **94**, 1026 (1972).
(22) Y. Tamura, K. Sumoto, H. Matushima, H. Taniguchi, and M. Ikeda, *J. Org. Chem.*, **38**, 4324 (1973).
(23) S. Oae, T. Masuda, K. Tsujihara, and N. Furukawa, *Bull. Chem. Soc. Jpn.*, **45**, 3586 (1972).
(24) Ordinarily esters such as ethyl acetate or ethyl benzoate did not react with free sulfilimine under the present reaction condition.
(25) K. Tsujihara, N. Furukawa, K. Oae, and S. Oae, *Bull. Chem. Soc. Jpn.*, **42**, 2631 (1969).
(26) N. Furukawa, T. Yoshimura, and S. Oae, unpublished result.
(27) All sulfilimines thus obtained have crystalline water but the content of it is not so clear so that some slightly erroneous elemental analyses data were obtained.

Synthesis of [1]Benzothieno[3,2-*d*]-*v*-triazine Derivatives. A Unique Diazonium Ion Cyclization

James R. Beck* and Joseph A. Yahner

Lilly Research Laboratories, Division of Eli Lilly and Company, Greenfield, Indiana 46140

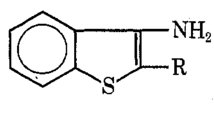
Received December 9, 1975

Diazotization of 3-aminobenzo[*b*]thiophene-2-carbonitrile in hydrochloric acid yielded 4-chloro[1]benzothieno[3,2-*d*]-*v*-triazine. Various derivatives were prepared by nucleophilic displacement using methoxide, methylamine, dimethylamine, hydrazine, and hydroxide ion. The parent heterocycle, [1]benzothieno[3,2-*d*]-*v*-triazine, was obtained by oxidation of the hydrazine derivative.

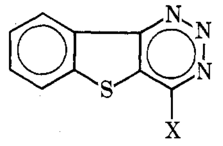
Diazonium ion condensation with an adjacent nucleophilic function to form a five- or six-membered ring has proved valuable for synthesizing various nitrogen heterocycles. Among these are numerous 1,2,3-benzotriazines, including 4-ones from carboxamides,[1] 4-imines from amidines,[2] 3-amino-4-ones from carboxhydrazides,[3] 3-oxides from oximes,[4] and 4-amino-3-oxides from amidoximes.[5] Other examples involving cyclization with nitrogen nucleophiles include the preparation of benzothiatriazine *S*,*S*-dioxides from sulfonamides[6] and benzotriazoles from amines.[7] Examples of cyclization with carbon nucleophiles are the synthesis of 4-cinnolones from ketones[8] and nitroindazoles from activated methyl functions.[9] Indazole itself has been prepared in high yield from diazotized *o*-toluidine.[10]

We were unable to find any examples in the literature that involved condensation of a diazonium ion with an adjacent cyano function. Therefore, we were surprised when the product obtained by diazotization of 3-aminobenzo[*b*]thiophene-2-carbonitrile (**1a**)[11] in hydrochloric acid was 4-chloro[1]benzothieno[3,2-*d*]-*v*-triazine (**2a**, 77% yield). The product underwent normal halide displacement with a variety of nucleophiles, including methoxide ion, methylamine, dimethylamine, and hydrazine, to yield the derivatives **2b** (87%), **2c** (70%), **2d** (63%), and **2e** (55%), respectively. Complex mixtures were obtained with ammonia, azide, and excess methyl mercaptan anion, indicating possible triazine ring fission with these nucleophiles. Oxidation of the hydrazine derivative **2e** with mercuric oxide[12] yielded the parent heterocycle **2f** (54%). The ultraviolet spectrum of **2f** was similar to that of **2a** (see Experimental Section).

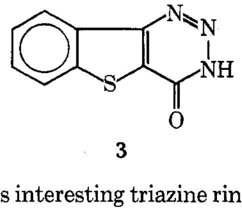
An unequivocal synthesis of **2a** was attempted by, first of all, hydrolyzing **1a** in alcoholic potassium hydroxide to form the carboxamide **1b** (82%). Diazotization of **1b** in sulfuric acid yielded the triazinone **3** (88%).[13] Attempts to prepare **2a** from **3** utilizing standard reagents (phosphorus oxychloride, phosphorus trichloride, and thionyl chloride–DMF) were unsuccessful, apparently owing to the instability of the triazine ring. Nevertheless, a proof of structure was accomplished by treating **2a** with aqueous potassium hydroxide and obtaining a triazinone (79%) identical in all respects with **3**. When **3** was subjected to the same reaction conditions utilized in the formation of **2a** from **1a**, it was recovered unchanged, indicating that it is not an intermediate in that transformation.



1a, R = CN
b, R = CONH$_2$



2a, X = Cl
b, X = OCH$_3$
c, X = NHCH$_3$
d, X = N(CH$_3$)$_2$
e, X = NHNH$_2$
f, X = H



3

The scope of this interesting triazine ring closure will receive our further attention. No evidence for the presence of 4-chloro-1,2,3-benzotriazine was found when anthranilonitrile was diazotized under identical reaction conditions. The only product isolated after chromatography was the corresponding linear triazine (9%) formed by condensation of the diazonium ion with unreacted anthranilonitrile. Similarly, diazotization of 3-amino-4-chloro-2-benzofurancarbonitrile[14] under the same conditions led to a complex mixture.

The fact that both of these aminonitriles failed to undergo the cyclization probably indicates stabilization of the diazotized **1a** intermediate by the sulfur atom. A possible mechanism could involve the intermediacy of an imidoyl chloride,[15] whose geometry would be suitable for condensation with the adjacent diazonium ion.

Experimental Section[16]

3-Aminobenzo[*b*]thiophene-2-carboxamide (1b). A solution containing 4.4 g (25 mmol) of **1a**[11] and 2.2 g of potassium hydroxide in 100 ml of alcohol was refluxed for 4 h. The mixture was cooled and filtered to yield 3.9 g (82%) of product, mp 218–220 °C.

Anal. Calcd for $C_9H_8N_2OS$: C, 56.23; H, 4.19; N, 14.57. Found: C, 56.25; H, 4.30; N, 14.27.

4-Chloro[1]benzothieno[3,2-*d*]-*v*-triazine (2a). To a cold slurry (ice bath) containing 4.4 g (25 mmol) of **1a**,[11] 30 ml of concentrated hydrochloric acid, and 30 ml of acetic acid was added dropwise a solution containing 2.1 g (30 mmol) of sodium nitrite in 20 ml of water. The mixture was warmed to room temperature and stirred for 2 h and then poured into ice water. The solid was collected and crystallized from DMF–water to yield 4.2 g (77%) of product: mp 163–165 °C dec; uv λ_{max} (alcohol) 225 nm (ϵ 26 100), 267 (18 070), 315 (sh).

Anal. Calcd for $C_9H_4ClN_3S$: C, 48.77; H, 1.82; N, 18.96. Found: C, 48.55; H, 1.96; N, 19.08.

4-Methoxy[1]benzothieno[3,2-*d*]-*v*-triazine (2b). A solution containing 2.2 g (10 mmol) of **2a** and 0.7 g (12 mmol) of sodium methoxide in 100 ml of methanol was refluxed for 1 h. The mixture was cooled and filtered to yield 1.9 g (87%) of product, mp 165–167 °C dec.

Anal. Calcd for $C_{10}H_7N_3OS$: C, 55.29; H, 3.25; N, 19.34. Found: C, 55.05; H, 3.47; N, 19.25.

4-(Methylamino)[1]benzothieno[3,2-*d*]-*v*-triazine (2c). Methylamine was bubbled into a refluxing solution of 4.4 g (20 mmol) of **2a** in 100 ml of absolute alcohol for 1 h. The mixture was cooled and the solid was collected. Crystallization from alcohol–water yielded 3.1 g (70%) of product, mp 231–232 °C dec.

Anal. Calcd for $C_{10}H_8N_4S$: C 55.54; H, 3.73; N, 25.91. Found: C, 55.81; H, 4.02; N, 25.93.

4-(Dimethylamino)[1]benzothieno[3,2-*d*]-*v*-triazine (2d). Dimethylamine was bubbled slowly into a solution containing 2.0 g (9 mmol) of **2a** in 50 ml of DMF at 100 °C for 90 min. The mixture was cooled and filtered to yield 1.3 g (63%) of product, mp 207–209 °C dec.

Anal. Calcd for $C_{11}H_{10}N_4S$: C, 57.37; H, 4.38; N, 24.31. Found: C, 57.43; H, 4.61; N, 24.27.

4-Hydrazino[1]benzothieno[3,2-*d*]-*v*-triazine (2e). A solution of 2.5 g (12 mmol) of **2a** and 10 ml of hydrazine hydrate in 75 ml of alcohol was refluxed for 2 h. The mixture was cooled and the solid was collected. Crystallization from DMF–water yielded 1.3 g (55%) of product, mp 194–196 °C dec.

Anal. Calcd for $C_9H_7N_5S$: C, 49.76; H, 3.25; N, 32.24. Found: C, 49.99; H, 3.27; N, 32.43.

[1]Benzothieno[3,2-*d*]-*v*-triazine (2f). A mixture containing 2.1 g (10 mmol) of **2e** and 5.4 g (25 mmol) of mercuric oxide in 130 ml of water was refluxed for 4 h. The slurry was cooled and filtered. The crude solid was triturated with hot ethyl acetate. Filtration and removal of the solvent yielded a residue which was chromatographed on silica gel (Woelm, 250 g) using ethyl acetate–hexane (1:1) as the eluent. The solid obtained was crystallized from alcohol–water to yield 1.0 g (54%) of product: mp 190–191 °C dec; uv λ_{max} (alcohol) 225 nm (ϵ 25 770), 265 (14 810), 320 (sh).

Anal. Calcd for $C_9H_5N_3S$: C, 57.74; H, 2.67; N, 22.44. Found: C, 57.82; H, 2.81; N, 22.41.

[1]Benzothieno[3,2-*d*]-*v*-triazin-4(3*H*)-one (3). Method A. A solution of 2.2 g (10 mmol) of **2a** and 1.0 g of potassium hydroxide in 75 ml of water was refluxed for 30 min. The mixture was cooled and acidified with concentrated hydrochloric acid. The solid was collected and crystallized from DMF–water to yield 1.6 g (79%) of product: mp 179–181 °C dec (lit.[13] mp 180–182 °C); uv λ_{max} (alcohol) 234 nm (ϵ 31 275), 253 (17 575), 320 (6375).

Anal. Calcd for $C_9H_5N_3OS$: C, 53.19; H, 2.48; N, 20.68. Found: C, 53.47; H, 2.62; N, 20.90.

Method B. To a cold mixture (ice bath) of 1.3 g (18 mmol) of sodium nitrite in 30 ml of concentrated sulfuric acid was added dropwise a solution containing 3.5 g (18 mmol) of **1b** in 35 ml of acetic acid. The mixture was stirred for 30 min and then poured into ice water. The crude solid was collected and crystallized from DMF–water to yield 2.3 g (63%) of product, mp 185 °C dec. Concentration of the mother liquors yielded an additional 0.9 g of product, mp 185 °C dec. The combined yield was 3.2 g (88%). This product was identical with that obtained by method A (NMR, ir, and uv spectra).

Acknowledgment. The authors thank Mr. Paul Unger and associates for spectral measurements and Mr. George Maciak and associates for microanalytical data.

Registry No.—**1a,** 34761-14-3; **1b,** 37839-59-1; **2a,** 58374-96-2; **2b,** 58374-97-3; **2c,** 58374-98-4; **2d,** 58374-99-5; **2e,** 58375-00-1; **2f,** 40826-40-2; **3,** 55557-47-6.

References and Notes

(1) A. König and A. Reissert, *Ber.*, **32,** 782 (1899).

(2) (a) M. W. Partridge and M. F. G. Stevens, *J. Chem. Soc.*, 3663 (1964); (b) K. F. Yip and K. C. Tsou, *Tetrahedron Lett.*, 3087 (1973).

(3) S. Petersen, H. Herlinger, E. Tietze, and W. Siefken, *Angew. Chem., Int. Ed. Engl.*, **2,** 24 (1963).

(4) J. Meisenheimer, O. Senn, and P. Zimmermann, *Ber.*, **60,** 1736 (1927).

(5) E. W. Parnell, *J. Chem. Soc.*, 4930 (1961).

(6) F. Ullmann and C. Gross, *Ber.*, **43,** 2694 (1910).

(7) C. Graebe and F. Ullmann, *Justus Liebigs Ann. Chem.*, **291,** 16 (1896).

(8) (a) W. Borsche and A. Herbert, *Justus Liebigs Ann. Chem.*, **546,** 293 (1941); (b) J. R. Keneford and J. C. E. Simpson, *J. Chem. Soc.*, 917 (1947).

(9) E. Noelting, *Ber.*, **37,** 2556 (1904).

(10) R. Huisgen and H. Nakaten, *Justus Liebigs Ann. Chem.*, **573,** 181 (1951).

(11) (a) J. R. Beck and J. A. Yahner, *J. Org. Chem.*, **39,** 3440 (1974); (b) D. E. L. Carrington, K. Clarke, and R. M. Scrowston, *J. Chem. Soc. C*, 3903 (1971).

(12) A. Albert and G. Catterall, *J. Chem. Soc. C*, 1533 (1967).

(13) During the writing of this manuscript, a similar synthesis of **3** was reported: S. W. Schneller and F. W. Clough, *Heterocycles*, **3,** 135 (1975).

(14) J. R. Beck and R. G. Suhr, *J. Heterocycl. Chem.*, **11,** 227 (1974).

(15) H. Ulrich, "The Chemistry of Imidoyl Halides", Plenum Press, New York, N.Y., 1968, p 66.

(16) Melting points were determined on a Mel-Temp apparatus and are uncorrected.