[13] *J. S. Fruton,* 'The Proteins', Vol. I, p. 208 (1963).
[14] *A. M. Dannenberg & E. L. Smith,* J. biol. Chemistry *215,* 55 (1955).
[15] *L. A. Sluyterman & J. Wijdenes,* Biochim. biophys. Acta *289,* 194 (1972).
[16] *C. Toniolo & G. M. Bonora,* Makromol. Chem. *175,* 1665 (1974).
[17] *J. M. Becker & F. Naider,* Biopolymers *13,* 1747 (1974).
[18] *E. Peggion, M. Palumbo, G. M. Bonora & C. Toniolo,* Biorg. Chemistry *3,* 125 (1974).
[19] *J. R. Kimmel & E. L. Smith,* Adv. Enzymol. *19,* 305 (1957).
[20] *S. Fox & C. Pettinga,* Arch. Biochemistry Biophysics *25,* 13 (1950).
[21] *E. Bennett & C. Niemann,* J. Amer. chem. Soc. *72,* 1798 (1950).
[22] *W. Schulter & C. Niemann,* J. Amer. chem. Soc. *73,* 1644 (1951).
[23] *J. S. Fruton, R. Johnston & M. Fried,* J. biol. Chemistry *190,* 39 (1951).
[24] *E. Bayer & M. Mutter,* Chem. Ber. *107,* 1344 (1974).
[25] *M. Mutter, R. Uhmann & E. Bayer,* Liebigs Ann. Chem. 901 (1975).
[26] *J. Engel, E. Liehl & S. Clemens,* European J. Biochemistry *21,* 22 (1971).

50. *ipso*-Substitution with Sodium-*N*-alkyl-(*p*-nitrobenzene)sulfonamide. A Novel Anionic Rearrangement

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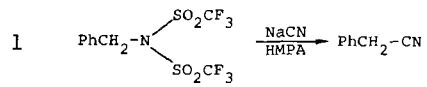
(26.I.79)

Summary

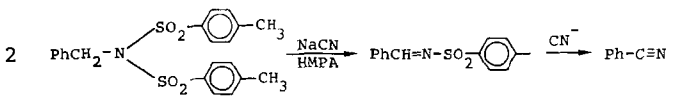
Reaction of *N*-benzyl-*N*,*N*-di-(*p*-nitrobenzene)sulfonamide (**3**) with NaCN/HMPA at 140° affords *N*-benzyl-*p*-nitroaniline (**4**). The same product is obtained upon heating of the sodium salt of *N*-benzyl-(*p*-nitrobenzene)sulfonamide (**5**). The transformation **5**→**4** is believed to proceed *via* an anionic episulfonyl compound **6**.

N-Benzyl-*N*,*N*-ditrifluoromethanesulfonamide (**1**) reacts with sodium cyanide in HMPA *via* nucleophilic displacement to give benzyl cyanide [1] *(Scheme 1).* The corresponding tosylamide **2** however, under the same conditions is converted to benzonitrile by formal two-fold elimination of *p*-toluene sulfinic acid [2] *(Scheme 2).*

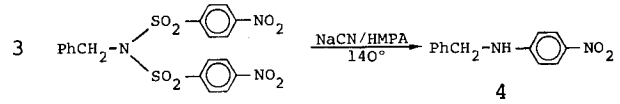
Scheme 1



Scheme 2



Scheme 3

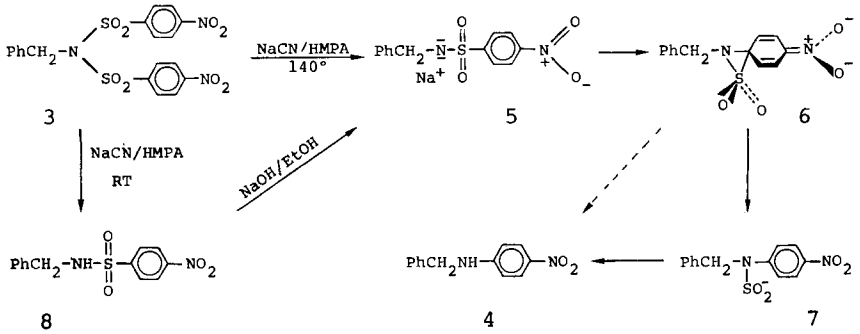


In connection with our interest in nucleophilic displacement of sulfone-activated amino groups [3], we have investigated the reaction of *N*-benzyl-*N*,*N*-di-(*p*-nitrobenzene)sulfonamide (**3**) [4] with NaCN/HMPA. To our surprise this compound reacts by yet another pathway: One of the sulfonyl groups is lost, while the other undergoes substitution at the *ipso* position accompanied by extrusion of sulfur dioxide to give *N*-benzyl-*p*-nitroaniline (**4**, *Scheme 3*). The reaction consisted in heating **3** with 2 equiv. of NaCN in HMPA at 140° for 1 h. After removal of the solvent by distillation, the dark residue was dissolved in dichloromethane and purified by column chromatography with silica gel. *N*-Benzyl-*p*-nitroaniline, isolated in 70% yield, was identified by its m.p. (142°) [5] and by comparison of its spectral data with the reported values [6].

Although we have not rigorously established the reaction mechanism, a plausible scheme may be outlined *(Scheme 4)*. Cyanide attack on the sulfonamide **3** takes place *via* N,S-bond cleavage [7] and generates the anion **5**. The latter, in turn, undergoes intramolecular addition to the *p*-nitrobenzene ring to form the anionic episulfonyl compound **6**. Loss of SO_2 could occur either directly from **6** or, more likely, after rearrangement to the sulfinate **7** [8].

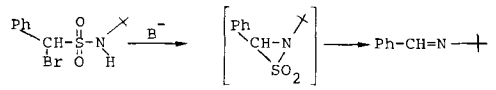
The following reactions were carried out in order to test this mechanism. Reaction of **3** with NaCN/DMF (140°, 1 h) afforded rearrangement product **4** and sulfonamide **8** each in 40% yield. This demonstrates that the solvent HMPA is not required for the rearrangement. When **3** was reacted with NaCN/HMPA at room temperature for 15 min the sulfonamide **8** was isolated in 51% yield. The sodium salt **5** was obtained by deprotonation of **8** with NaOH/EtOH. On heating to 140° in HMPA **5** rearranged to **4** (25% yield). The observations that cyanide attacks the nosylamide **3** at the sulfur atom and that the anion **5** rearranges to **4** are compatible with our mechanistic scheme. Nevertheless, other pathways involving intermolecular or radical reactions cannot be excluded. The same rearrangement was observed with *N*-hexyl-*N*,*N*-di-*p*-nitrobenzenesulfonamide, although for as yet unknown reasons, the yield with this compound was only 11%.

Scheme 4



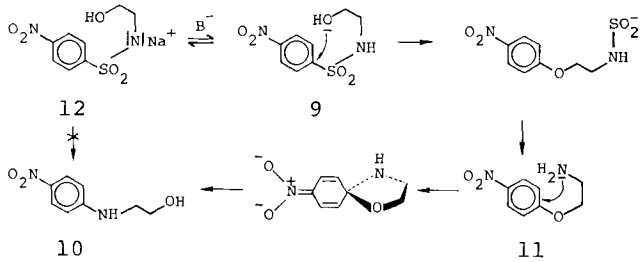
The mechanism proposed for the rearrangement of **5** to **4** is an aromatic variant of the well-known *Ramberg-Bäcklund* reaction of aliphatic α-halosulfones [9]. Moreover, this same transformation has also been reported for α-halosulfonamides [10] *(Scheme 5)*.

Scheme 5



In the aromatic series, the *Smiles* rearrangement [11] provides a mechanistic analogy, in that the reaction proceeds *via* five-membered transition states or intermediates rather than by 3-membered ones. For example, *N*-(2-hydroxyethyl)-*p*-nitrobenzenesulfonamide (**9**) rearranges in hot sodium hydroxide solution to 2-hydroxyethyl-*p*-nitroaniline (**10**) [12]. However, it has been shown [13] that this reaction involves a double *Smiles* rearrangement *via* 2-(*p*-nitrophenoxy)ethylamine (**11**) *(Scheme 6)*, and not an intramolecular attack of the sodium salt **12**. In our case, the double *Smiles* rearrangement is impossible, so that **5** is obliged to follow the less favorable pathway to the episulfonyl compound **6**.

Scheme 6



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REFERENCES

[1] *R.S. Glass*, Chem. Commun. *1971*, 1546.
[2] *R.S. Glass & R.C. Hoy*, Tetrahedron Letters *1976*, 1777.
[3] *P. Müller & M.P. Nguyen-Thi*, Tetrahedron Letters *1978*, 4727.
[4] *P.J. De Christopher, J.P. Adamek, G.D. Lyon, S.A. Klein & R.J. Baumgarten*, J. org. Chemistry *39*, 3525 (1974).
[5] *J.H. Billman & A.C. Diesing*, J. org. Chemistry *22*, 1068 (1957).
[6] *A.G. Moritz*, Spectrochim. Acta *16*, 1176 (1960).
[7] *P.J. De Christopher*, Ph. D. Thesis, University of Illinois, Chicago Circle, Chicago, Illinois 1971; Diss. Abstr. Int. B. 1972, 32 (10) 5687.
[8] *E. Bloch*, 'Reactions of Organosulfur Compounds', Academic Press, New York 1978, pp. 268–280.
[9] *F.G. Bordwell*, Accounts Chem. Res. *3*, 281 (1970); *L.A. Paquette*, ibid. *1*, 209 (1968).
[10] *J.C. Sheehan, U. Joller & D. Ben-Ishai*, J. org. Chemistry *39*, 1817 (1974).
[11] *W.E. Truce, E.M. Kreider & W.W. Brand*, Organic Reactions *18*, 99 (1970).
[12] *K.G. Kleb*, Angew. Chem. *80*, 284 (1968).
[13] *A.C. Knipe & J. Lound-Keast*, Tetrahedron Letters *1976*, 2289; J. chem. Soc., Perkin II, *1976*, 1741; *A.C. Knipe, J. Lound-Keast & N. Sridhar*, Chem. Commun. *1976*, 765.