BASE CATALYSED REACTION OF 2-CYANOMETHYL-1,3-BENZOTHIAZOLE WITH BENZOFUROXANES

Harsha Narayan Borah and Jagir Singh Sandhu*
Division of Drugs and Pharmaceuticals
Regional Research Laboratory, Jorhat 785006, India

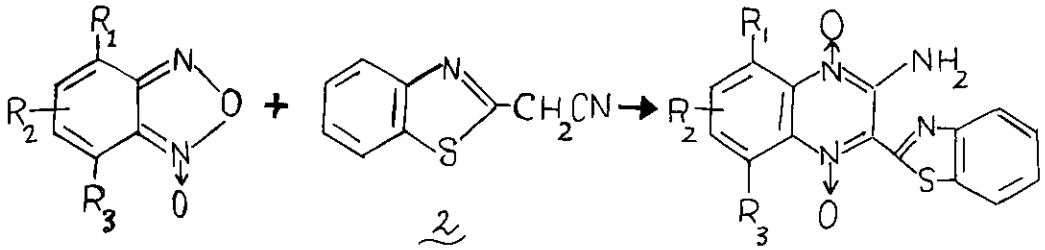
Abstract - 2-Cyanomethyl-1,3-benzothiazole (2) reacts with benzofuroxanes (1) to give quinoxaline N,N'-dioxides (3) in good yields.

Organic N-oxides are an attractive class of compounds and in particular quinoxaline-N,N'-dioxides are of significant biological importance. The versatile and fairly general procedure for the production of large number of N-oxides is reaction of benzofuroxanes with enamines which is quite often refered as Beirut reaction[1-3]. Dienamines have also been reported to react with benzofuroxanes, yielding quinoxaline N,N'-dioxides[4,5]. From this class of compounds Carbadox and Mecadox[6] are in clinical practice. In continuation of our studies on benzofuroxanes[7,8], herein we report the formation of quinoxaline N,N'-dioxide by the reaction of 2-cyanomethyl-1,3-benzothiazole with benzofuroxanes.

When reacted benzofuroxane (1a) and 2-cyanomethyl-1,3-benzothiazole (2) in equimolar quantities in ethanol at room temperature in presence of potassium carbonate gave bright red crystalline compound (3a) crystalisable from methanol, mp 240°C (dec.), in 80% yield. The structure of (3a) is fully corroborated by its spectral and elemental analysis, ν_{max} (KBr) 1348, 1355 (N→O), 3290, 3345, (NH_2) cm^{-1}, ^1H NMR (DMSO-d_6) δ : 7.44-8.56 (m, 10H), and m/z 310 (M^+). Anal. Calcd. for $C_{15}H_{10}N_4SO_2$: C, 58.06 ; H, 3.23 ; N, 18.06. Found : C, 58.55 ; H, 3.36 ; N, 18.05.

Similarly the reaction of (1b) and (1c) with (2) provided (3b) and (3c) in 72% and 82% yields respectively. (3b) ν_{max} (KBr) 1345, 1355 (N→O) 3290, 3330 (NH_2) cm^{-1}, m/z 324 (M^+) and ^1H NMR (DMSO-d_6) δ : 2.55 (s, 3H),

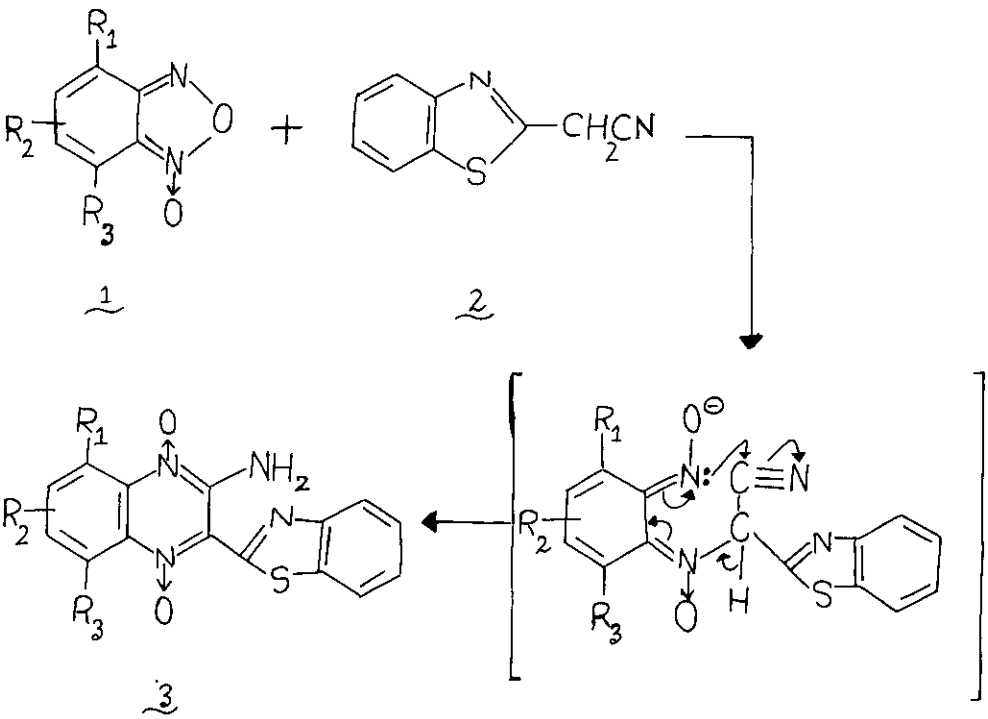
7.55-8.40 (m, 9H) ; (3c) ν_{max} (KBr) 1340, 1355 (N→O), 3290, 3340 (NH_2) cm^{-1}. m/z 345 (M^+) and ^1H NMR (DMSO-d_6) δ : 7.50-8.60 (m, 9H).



1 2 3

	R_1	R_2	R_3
a	H	H	H
b	H	CH_3	H
c	H	Cl	H

Concerning the mechanism of this reaction, a plausible reaction scheme is given below ;



Scheme - 1

EXPERIMENTAL

Melting points were obtained in open capillaries on a Büchi apparatus and are uncorrected. The ir spectra were measured on a Perkin-Elmer 237B spectrophotometer for potassium bromide discs. The mass spectra were determined on a AEIMS 30 instrument. The nmr spectra were recorded on Varian 220 MHz spectrometer.

Benzofuroxane was prepared by the oxidation of o-nitroaniline with sodium hypochlarite solution[9]. 5(6)-Methyl and 5(6)-chloro-substituted benzofuroxanes were prepared by pyrolysis of the corresponding nitrophenylazides[10]. 2-Cyanomethyl-1,3-benzothiazole was obtained by the reaction of 2-aminobenzenethiol with malononitrile as reported earlier[11].

Preparation of 3a

Equimolar quantities of benzofuroxane(1a) (1.36 g, 10 mmol) and 2-cyanomethyl-1,3-benzothiazole(2) (1.74 g, 10 mmol) were dissolved in ethanol in the presence of catalytic amount of K_2CO_3. This reaction mixture was stirred magnetically till the solution turned to red colour in about 30 min. The reaction was followed by tlc and completion of reaction was concluded from the disappearance of benzofuroxane spot. The red crystals precipitated were filtered and were recrystallised from methanol (2.5 g, 80%) ; mp 240°C (dec.) ms m/z : 310 (M^+) ; ir ν_{max} (KBr) cm^{-1}: 1348, 1355 (N→O), 3290, 3345 (NH_2); ^1H NMR (DMSO-d_6) δ: 7.44-8.56 (m, 10H) ; Anal. Calcd. for $C_{15}H_{10}N_4SO_2$: C, 58.06 ; H, 3.23 ; N, 18.06. Found : C, 58.55, H, 3.36 ; N, 18.05.

Preparation of 3b

In a similar experiment as above and workup(3b) was obtained in (2.3 g, 72%) ; mp 220°C (dec.) ; ms m/z : 324 (M^+) ; ir ν_{max} (KBr) cm^{-1} : 1345, 1355 (N→O), 3290, 3330 (NH_2) : ^1H NMR (DMSO-d_6) δ : 2.55 (s, 3H), 7.55-8.40 (m, 9H). Anal. Calcd. for $C_{16}H_{12}N_4SO_2$: C, 59.26 ; H, 3.70 ; N, 17.28. Found : C, 59.30 ; H, 3.76 ; N, 17.30.

Preparation of 3c

The N-oxide(3c) was obtained following the procedure as in given for(3a) in (2.8 g, 82%) ; mp 254°C (dec.) ; ms m/z : 345 (M^+) ; ir ν_{max} (KBr) cm^{-1} : 1340, 1355 (N→O), 3290, 3340 (NH_2) : ^1H NMR (DMSO-d_6) δ : 7.50-8.60 (m, 9H). Anal. Calcd. for $C_{15}H_9N_4SO_2Cl$: C, 52.25 ; H, 2.61 ; N, 16.26 Found : C, 52.31 ; H, 2.65 ; N, 16.51.

ACKNOWLEDGEMENTS

The authors wish to express their thanks to Prof. W. Pfleiderer, Universität Konstanz, West Germany for spectral and elemental analysis of one of the compounds and analytical division of Central Drug Research Institute, Lucknow and this Laboratory for the rest of the compounds.

REFERENCES

1. M.J. Haddadine and C.H. Issidorides, Heterocycles, 1976, 4, 767.
2. K. Ley and F. Sung, Synthesis, 1975, 415.
3. A. Gasco and A.J. Boulton, Advances in Heterocyclic Chemistry, Edited by A.R. Katritzkey and A.J. Boulton, Academic Press, 1981, 29, 251.
4. P. Devi, J.S. Sandhu and G. Thyagarajan, J. Chem. Soc., Chem. Commun., 1979, 710.
5. H.N. Borah, P. Devi, J.S. Sandhu and J.N. Baruah, Tetrahedron, 1984, 40, 1617.
6. See, e.g. V. Russo, A. Catelano and S. Vitali, Atti. Soc. Ital. Sci. Vet., 1968, 22, 354 (Chem. Abstr., 1969, 71, 47137) : G.W. Thrasher, J.E. Shively, C.E. Askelson, W.E. Babcock and R.R. Chalquest, J. Anim. Sci., 1969, 28, 208 (Chem. Abstr., 1969, 70, 75593) ; 1970, 31, 333 (Chem. Abstr.,1970, 73, 74402) ; V. Dzapo and H. Reuter, Arch. Tierernaehr., 1972, 22, 615 (Chem. Abstr., 1973, 78, 70577) ; J.P. Raynaud and H. Bretheau, Rev. Med. Vet., 1973, 124, 375. (Chem. Abstr., 1973, 79, 13629).
7. H.N. Borah, R.C. Boruah and J.S. Sandhu, Heterocycles, 1984, 22, 2323.
8. H.N. Borah, R.C. Boruah and J.S. Sandhu, Heterocycles, 1985, 23, 1625.
9. a) A. Smith and A. Boyer, Organic Synthesis, 1951, 31, 14.
   b) A. Gaughran, A. Picard and A. Kaufman, J. Am. Chem. Soc., 1954, 76, 2233.
10. a) M.O. Farster and M.F. Basker, J. Chem. Soc., 1913, 103, 1918.
    b) A.J. Boulton, A.C. Gripper Gray and A.R. Katritzky, J. Chem. Soc., (B) 1967, 910.
11. K. Saito, S. Kambe and Y. Nakano, Synthesis, 1983, 210.

Received, 22nd October, 1985