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BENZOFUROXANS IN HETEROCYCLIC SYNTHESIS

REACTION OF BENZOFUROXANS WITH DIENAMINES; SYNTHESIS OF A NOVEL CLASS OF QUINOXALINE NN'-DIOXIDE ENAMINES

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Abstract—Benzofuroxanes react with dienamines to give a novel class of quinoxaline NN'-dioxide enamines in good yields.

Reaction of benzofuroxans (BFO) with a variety of nucleophiles has provided a facile entry to the synthesis of several either inaccessible N-oxides or which involved difficult or longer routes if prepared through conventional methods. A BFO also reacts with enamines and enolates providing an interesting range of N-oxides. The reaction of enamines with BFO has been extensively investigated in terms of the mechanism as well as the scope of the reaction. In all these reactions the furoxan ring transformation occurs providing novel heterocycles and these aspects has been reviewed recently.[1]

Nitro substituted BFO's place with butadienes through addition to the benzene ring.[2] Dienamines behave as typical dienes in Diels–Alder reaction and this behaviour has been exemplified by several workers.[3] We have investigated[4] the reaction of dienamines with benzofuroxans and have obtained quinoxaline NN'-dioxides in good yields.

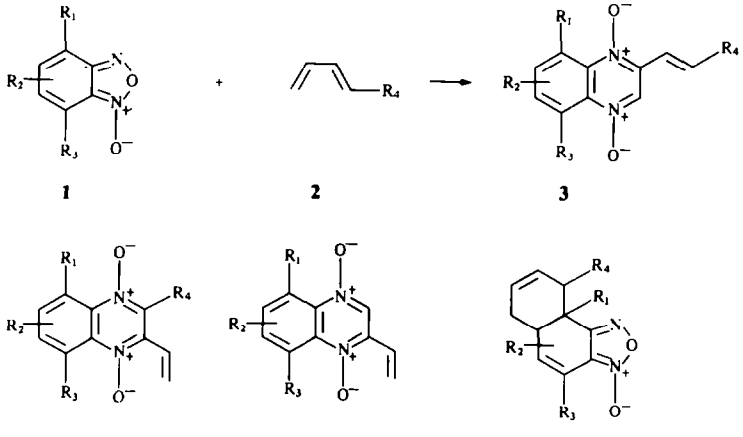
RESULTS AND DISCUSSION

Reaction of BFO (**1a**) and dienamine (**2a**) in equimolar quantities gave bright red crystals (**3a**); other possible structures (**4–6**) are easily excluded by spectroscopic data. The two spin-system at 8.46 and 5.37 with 13.5 Hz coupling constant proves beyond any doubt the presence of the trans CH=CH enamine side chain, further confirmed by spin–spin decoupling experiments. The isolated singlet at 8.25 arises from –CH=N(O)– unit, ruling out the structures (**4–6**) and in particular structure (**5**) which could have been the result of normal Beirut reaction. This is further confirmed by the mass spectrum showing two consecutive losses of 16 units typical and highly diagnostic for aromatic N-oxides from *m/e* 255 (at 243 and 227) as well as from *m/e* 260 (244 and 228). Two consecutive losses of 30 units (–NO) from *m/e* 259 (229, 199) are also typical of di N-oxides. Other quinoxaline NN' di-oxides (**3b–1**) were prepared similarly. When 5(6)-methyl substituted BFO or 5(6)-chloro substituted BFO were used the quinoxaline NN'-di-oxides were obtained in good yields. Also these products **3a–1** could be obtained in similar yields even if the reactions were carried out producing dienamines *in situ*. When 5(6)-nitro substituted BFOS were used the reaction was so fast and exothermic no characterisable product could be obtained even when the reaction was conducted at $-5°$.

EXPERIMENTAL

M.ps were taken in open capillary tubes on a Büchi apparatus and were uncorrected. NMR spectra were recorded on Varian 220 MHz or Bruker 270 MHz spectrometers at the Bangalore NMR facility, Indian Institute of Science, Bangalore, India and chemical shift values were recorded in δ units (parts per million), relative to TMS as the internal standard. The IR spectra were determined as potassium bromide discs recorded with a Perkin–Elmer 237B IR spectrometer. Mass spectra were determined on a AEI MS 30 instrument.

Benzofuroxans were prepared by the oxidation of o-nitro-



1 **2** **3**

4 **5** **6**

Table 1. Quinoxaline NN′-dioxide enamines (3a–l)

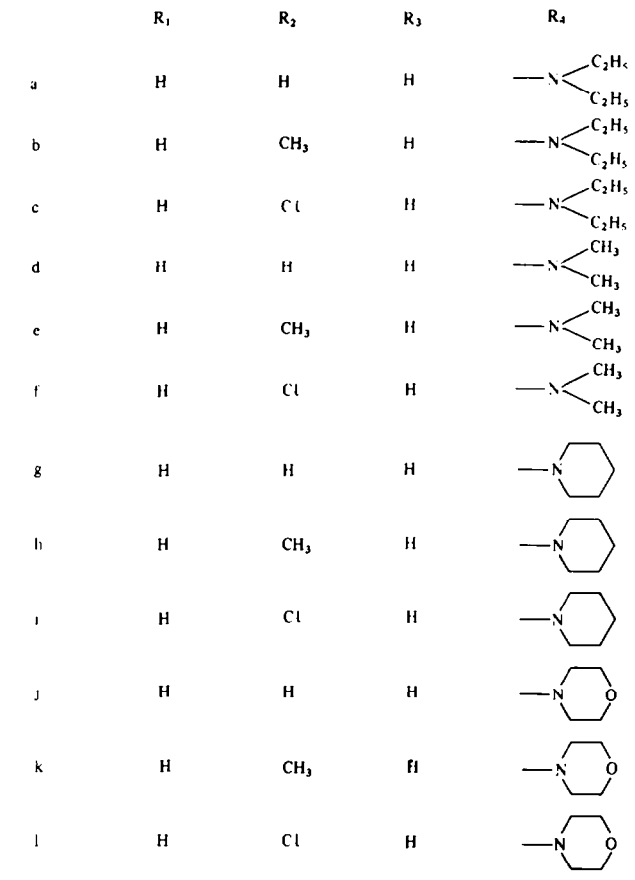
Product	Yield (%)	mp (°C)	Solvent for recrystallisation	Formula	Analyses					
					Percentage found			Percentage calculated		
					C	H	N	C	H	N
3a	80	173-75	Carbon Tetrachloride-pet ether(40-60) 1:1 mixture	$C_{14}H_{17}N_3O_2$	64.78	6.68	16.19	64.86	6.56	16.23
3b	75	174-78	Pet ether(40-60)-Dichloro-methane 4:1 mixture	$C_{15}H_{19}N_3O_2$	65.83	6.90	15.35	65.93	6.96	15.38
3c	85	159-61	Carbon Tetrachloride-pet ether(40-60) 2:1 mixture	$C_{14}H_{16}N_3O_2Cl$	57.24	5.40	14.28	57.24	5.45	14.31
3d	65	255-57	Carbon Tetrachloride-pet ether(40-60) 2:1 mixture	$C_{12}H_{13}N_3O_2$	62.24	7.70	18.09	62.34	5.63	18.18
3e	70	178-80	Carbon Tetrachloride-pet ether(40-60) 2:1 mixture	$C_{13}H_{15}N_3O_2$	67.10	6.12	17.20	63.67	6.12	17.14
3f	75	160-62	Benzene-pet ether (40-60) 1:1 mixture	$C_{12}H_{12}N_3O_2Cl$	54.00	4.38	15.34	54.24	4.52	15.82
3g	80	183-85	Benzene-pet ether (40-60) 1:1 mixture	$C_{15}H_{17}N_3O_2$	66.34	6.51	15.32	66.42	6.27	15.50
3h	75	198	Carbon Tetrachloride-pet ether(40-60) 2:1 mixture	$C_{16}H_{19}N_3O_2$	66.35	6.50	14.70	67.37	6.67	14.74
3i	85	189	Benzene-pet ether (40-60) 2:1 mixture	$C_{15}H_{16}N_3O_2Cl$	58.90	5.70	13.30	58.92	5.24	13.75
3j	75	255-56	Benzene-pet ether (40-60) 1:1 mixture	$C_{14}H_{15}N_3O_3$	61.45	5.66	15.29	61.54	5.49	15.38
3k	70	198	Benzene-pet ether (40-60) 1:1 mixture	$C_{15}H_{17}N_3O_3$	67.50	5.80	14.50	62.72	5.92	14.63
3l	80	Decom-posed at 200	Benzene-pet ether (40-60) 1:1 mixture	$C_{14}H_{14}N_3O_3Cl$	54.45	4.50	13.50	54.63	4.55	13.66

Table 2. Spectral data of compounds (3a–l)

Product	I.R. (KBr) [cm^{-1}]	^{1}H NMR ($CDCl_3$) δ [ppm]	Mass m/e [M$^+$]
1	2	3	4
3a	975, 1348, 1355, 1625, 1592	1.271(t,6H); 3.382(q,4H); 5.36(d,1H, J=13.5Hz); 7.56(m,1H); 7.74(m,1H); 8.25(s,1H); 8.47(m,2H); 8.62(d,1H, J=13.5Hz)	260(7.5%), 259(37.5%), 243(75%), 242(78%), 229(30.2%), 227(37.5%), 226(100%), 214(25%), 199(37.7%), 185(85%), 129(30%), 102(42.5%), 84(37.5%), 77(37.2%)
3b	979, 1353, 1403, 1596, 1600	1.289(t,6H); 2.561(s,3H); 3.374(q,4H); 5.408(d,1H,J=13.5Hz); 7.595(m,1H); 8.085(s,1H); 8.102(s,1H); 8.391(d,1H); 8.544(d,1H,J=13.5Hz)	273(8%), 272(36.5%), 256(73%), 255(77.5%), 242(29.8%), 240(38%), 239(100%), 227(26%), 211(37.8%), 198(88%), 142(34%), 115(43%), 97(38%), 90(39.5%)
3c	976, 1347, 1400, 1596, 1625	1.260(t,6H); 3.374(q,4H); 5.37(d,1H, J=13.5Hz); 7.86(d,1H); 8.238(s,1H); 8.39(s,1H); 8.469(d,1H); 8.63(d,1H, J=13.5Hz)	295(7.7%), 293(36.3%), 292(73.5%), 276(77%), 275(29.5%), 262(37.7%), 260(100%), 259(27%), 247(36,9%), 232(87.7%), 218(35%), 162(42.9%), 135(38.3%), 117(37.9%), 110(36.5%)
3d	974, 1352, 1626, 1600	3.02(s,6H); 5.25(d,1H,J=13.5Hz); 7.51(m,1H); 7.66(m,1H); 8.18(s,1H); 8.41(m,1H); 8.54(d,1H,J=13.5Hz)	231(21.5%), 215(43%), 214(78.9%), 201(30%), 199(96.5%), 198(100%), 183(85%), 168(42.5%), 158(70.5%), 143(56%), 129(37.5%), 130(25%), 115(14.5%), 102(47.5%), 77(22.5%)
3e	975, 1353, 1600 1627	2.561(s,3H); 3.051(s,6H); 5.306(d,1H, J=13.5Hz); 7.595(m,1H); 8.238(s,1H); 8.272(m,1H); 8.391(m,1H); 8.544(d,1H, J=13.5Hz)	245(20%), 229(45%), 228(78.7%), 215(29.9%), 212(100%), 196(85.5%), 182(42%), 172(70.4%), 157(56.3%), 143(38%), 134(24.9%), 129(14.8%), 116(48%), 91(22%)
3f	972, 1355, 1590, 1625	3.102(s,6H); 5.306(d,1H,J=13.5Hz); 7.714(m,1H); 8.255(s,1H); 8.442(m,1H); 8.476(m,1H); 8.663(d,1H,J=13.5Hz)	267(15.8%), 265(21.2%), 249(45%), 248(77.9%), 235(29%), 233(96.2%), 232(100%), 217(82%), 202(39%), 192(68%), 177(55%), 163(38%), 154(24.9%), 149(14%), 136(48.3%), 111(21%)
3g	990, 1355, 1625, 1600	1.70(s,6H); 3.36(s,4H); 5.47(d,1H, J=13.5Hz); 7.56(m,1H); 7.70(m,1H); 8.20(s,1H); 8.5(m,3H)	271(6.26%), 255(25%), 254(18.6%), 241(17.5%), 239(83.5%), 238(100%), 219(4.5%), 211(4.5%), 183(25%), 170(6.79%), 160(15%), 143(27.5%), 129(36.5%), 102(38.9%), 77(10%)
3h	987, 1354, 1590, 1626	1.714(s,6H); 2.578(s,3H); 3.374(s,4H); 5.527(d,1H,J=13.5Hz); 7.595(m,1H);	285(4%), 269(7%), 268(24%), 255(17.9%), 254(16.5%), 253(85%), 234(100%), 225(4%),

Table 2 (*Contd*)

Product	I.R. (KBr) [cm^{-1}]	^{1}H NMR ($CDCl_3$) δ [ppm]	Mass m/e [M^+]
1	2	3	4
		8.238(s,1H); 8.272(m,1H); 8.374(d,1H); 8.408(d,1H,J=13.5Hz)	197(4.5%), 184(24%), 174(7.2%), 158(14%), 145(28.2%), 133(36%), 129(37.5%), 116(20%), 90(10%)
3i	985, 1353, 1595, 1623	1.731(s,6H); 3.408(s,4H); 5.493(d,1H, J=13.5Hz); 7.680(m,1H); 8.289(s,1H); 8.408(m,1H); 8.442(m,1H); 8.510(d,1H, J=13.5Hz)	307(3.9%), 305(7.5%), 289(25.5%), 288(18%), 275(17.2%), 273(85.3%), 272(100%), 254(4.3%), 245(4.8%), 217(24%), 204(7.5%), 194(14.5%), 177(28%), 163(35.9%), 136(30.3%), 111(20.5%)
3j	975, 1350, 1625, 1600	3.53(m,4H); 3.86(m,4H); 5.44(d,1H); 7.54(m,1H); 7.68(m,1H); 8.16(s,1H); 8.55(m,3H)	273(9.9%), 274(2.2%), 257(29.7%), 256(39.6%), 241(59.4%), 240(100%), 228(5%), 222(3.9%), 210(35.65%), 196(9.9%), 181(49.5%), 169(33.65%), 158(29.7%), 143(29.7%), 129(24.75%), 100(29.7%), 86(2.5%), 77(10%)
3k	950, 1355, 1600, 1625	2.578(s,3H); 3.391(m,4H), 3.816(m,4H); 5.527(d,1H,J=13.5Hz); 7.612(m,1H); 8.238(s,1H); 8.289(m,1H); 8.392(d,1H); 8.425(d,1H,J=13.5Hz)	287(2.5%), 286(9%), 270(28%), 269(38.9%), 254(58%), 253(100%), 241(6%), 235(5.5%), 223(35.5%), 209(10.2%), 194(49.5%), 182(33.6%), 171(30.3%), 165(29.1%), 142(25.1%), 113(31%), 99(3%), 89(12%)
3l	922, 1350, 1595, 1624	3.425(m,4H); 3.816(m,4H); 5.476(d,1H); (J=13.5Hz); 7.714(m,1H); 8.510(s,1H); 8.442(m,1H); 8.476(m,1H); 8.578(d,1H, J=13.5Hz)	309(1.2%), 307(2.8%), 306(9.3%), 290(27%), 289(34.5%), 274(59.2%), 273(100%), 261 (6.9%), 255(6.2%), 243(36.2%), 229(11.2%), 214(47.2%), 202(33.6%), 291(31%), 276(31%), 262(25.3%), 234(32%), 119(4.5%), 109(9.2%)



aniline with sodium hypochlorite solution.[5] 5(6)-Methyl and 5(6)-chloro-substituted benzofuroxan were prepared by pyrolysis of the corresponding nitrophenylazides.[6]

Dienamines were prepared by condensing freshly distilled crotonaldehyde with freshly distilled corresponding secondary amines.

General procedure

Freshly prepared dienamines (0.01 mole) were added to an etheral solution of BFO or (Cl/Me-substituted BFO) (0.01 mole) at room temperature. The colour of the solution slowly turned red and after some time red crystalline solids began to separate. The reaction was followed by TLC and worked up after the BFO was consumed. The solvent was removed under vacuum and the residue crystallised from an appropriate solvent, giving a red crystalline solid (see Tables 1, 2).

In situ *generation*

Freshly distilled crotonaldehyde (4.8 ml) was added slowly to a solution of corresponding secondary amines (12.4 ml) dissolved in dry ether over anhydrous potassium carbonate, keeping the temp. at -5 to $-10°$. The reaction mixture was left at 0° for 1 h and at 20° for 4 h until the crotonaldehyde was consumed (followed by TLC).

The mixture was filtered off and then 0.01 mole of BFO or (Cl/Me-substituted BFO) dissolved in dry ether was added. The reaction mixture was kept at room temp. for some time. Red crystalline product separated out.

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