Nucleophilic Attack on 4,7-Disubstituted Benzofurazans and Their *N*-Oxides: Synthesis of Tetrazolo[1,5-*a*]azepines

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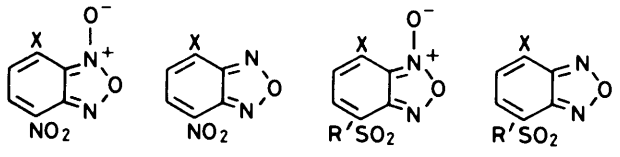
The reaction of various nucleophiles with benzofurazans and their *N*-oxides carrying electron-attracting substituents in the 4 and 7 positions has been reviewed and the study extended to include sulphonyl groups. As well as the simple replacement of leaving groups typical in chloronitrobenzofurazans, some unusual reactions were observed. Secondary amines attacked the heterocyclic N of benzofurazan *N*-oxide bis(methylsulphones) to give arylhydrazines, and this pathway was also followed to some extent in the reaction of the weaker base morpholine with bis(arylsulphones). Sodium azide reacted with benzofurazan *N*-oxide bis-sulphones to yield tetrazolo[1,5-*a*]azepines, possibly by a mechanism involving attack at the bridgehead carbon. Syntheses of tetrazoles are briefly reviewed with regard to mode of ring closure. Nitrobenzofurazan *N*-oxide sulphones yielded both azidosulphones and tetrazolo[1,5-*a*]azepines. The N→S migration of oxygen noted for nitrobenzofurazan *N*-oxide sulphoxides was also observed for sulphone sulphoxides.

Anticancer activity against lymphatic leukaemia P.388 in mice was demonstrated by 7-nitrobenzofurazan *N*-oxides (**1a**) carrying a substituted amino group (especially piperazinyl) in the 4-position.[1,2] These were prepared by reaction of the chloride (**1b**) with amines.[1] Thiolates and sulphinates also displace chlorine from the benzofurazan *N*-oxide (**1b**) and the benzofurazan (**2b**) to give the sulphides (**1c**) and (**2c**) and the sulphones (**2e**); the benzofurazan *N*-oxide sulphoxides (**1d**) undergo an intramolecular rearrangement, with N→S migration of oxygen, to the benzofurazan sulphones (**2e**).[3] We have now made a more systematic study of nucleophilic attack on 4,7-disubstituted benzofurazan *N*-oxides (**1**) and (**3**) and benzofurazans (**2**) and (**4**), and from this has emerged a new synthesis of the tetrazolo[1,5-*a*]azepine ring system.



(**1**) (**2**) (**3**) (**4**)

a; X = R_2N
b; X = Cl
c; X = RS
d; X = RSO
e; X = RSO_2
f; X = $R'SO_2$
g; X = RO
h; X = N_3

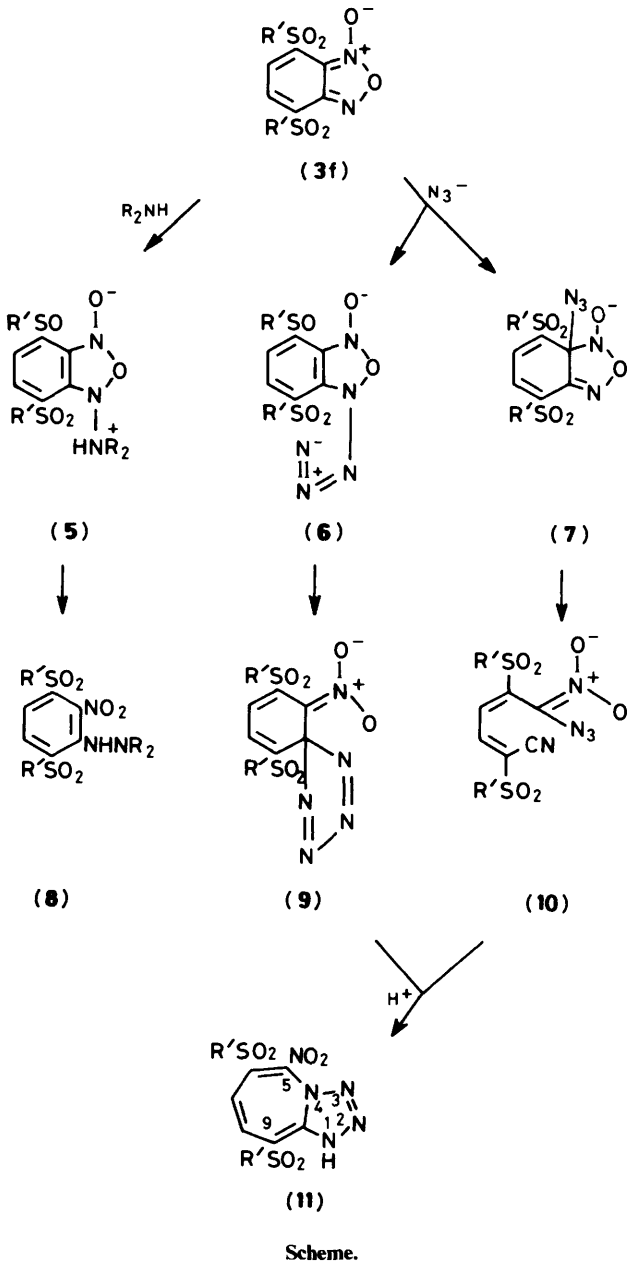
Investigation into the mode of reaction of nucleophiles with aromatic compounds bearing multiple electron-attracting substituents capable of acting as leaving or activating groups, has been in progress for many years.[4] Nitro, sulphonyl, and chloro are typical of such groups, and Loudon and Shulman[5] made a comprehensive study of the reactivity of chloronitrodiphenylsulphones towards amines, alkoxides, and thiolates. In the present paper we consider the behaviour of the nitrochlorides (**1b**) and (**2b**), the nitrosulphones (**1f**) and (**2f**), and the bis-sulphones (**3f**) and (**4f**), with a variety of nucleophiles including RO^-, RS^-, RSO_2^-, R_2NH, and N_3^-.

Reaction of the nitrochlorides (**1b**) and (**2b**) is uncomplicated and almost invariably only chlorine is substituted[6] by RO, RS,[3] R_2N,[1,7] or N_3.[7,8] Sulphinates are exceptional, displacing both groups and providing access to the bis-sulphones (**3f**) and (**4f**); however even sulphinates readily yield the nitrofurazans (**2f**) from (**2b**) under anhydrous conditions.[3] Sodium methanesulphinate affords compound (**3f**; R′ = Me) in considerably lower yield than that obtained for (**3f**; R′ = Ar). Attempts to prepare the benzofurazan (**4f**; R′ = Me) gave only dark-coloured mixtures.

In the nitrosulphone (**1f**), (**2f**) series, few reactions were carried out, since from a preparative point of view one can obtain the products of nucleophilic displacement of either group more conveniently starting with the chlorides (**1b**) and (**2b**). The transformation by sulphinates of compound (**2b**) into either the nitrosulphone (**2f**) or the bis-sulphone (**4f**), depending on the reaction conditions implies that these nucleophiles can displace the nitro group from (**2f**). We also found that sodium methoxide preferentially displaces the nitro group in compound (**2f**) to give an alkoxysulphone (**4g**; R = Me). The benzofurazan *N*-oxides (**1f**), however, are converted by thiolates into mixtures of the sulphonylsulphides (**3c**) and the nitrosulphides (**1c**), indicating displacement of either leaving group in these reactions. From the reaction between sodium azide and compound (**1f**; R′ = Ph) only the azidosulphone (**3h**; R′ = Ph), was isolated (36%); we shall refer to this reaction later

Greatest variety was observed in the reactions of the bis-sulphones (**3f**) and (**4f**). Alkoxides and thiolates smoothly yielded ethers (**3g**) and (**4g**) and sulphides (**3c**) and (**4c**) respectively. Similar reactions of piperidine were described earlier,[3] giving the amines (**3a**) and (**4a**), and pyrrolidine is also known to give the simple monosubstitution products. However the weaker base morpholine on reaction with compound (**3f**; R′ = Ph) yielded both the aminosulphone (**3a**), by displacement of a phenylsulphonyl group, and the arylhydrazine [**8**; R′ = Ph, $R_2 = (CH_2)_2O(CH_2)_2$], by attack at the heterocyclic N (Scheme). Such a reaction, with a variety of amines, was described previously[9] for monosubstituted benzofurazan *N*-oxides although it tended not to occur when the substituent was electron-attracting. We found that the alkylsulphone (**3f**; R′ = Me) afforded only the arylhydrazines (**8**; R′ = Me) on reaction with either morpholine or piperidine.

Sodium azide reacted with the benzofurazans (**4f**) to yield the azidosulphones (**4h**). However when a similar reaction mixture from the benzofurazan *N*-oxide (**3f**; R′ = Ph) was diluted with water, a yellow solution resulted which yielded a solid product only on acidification. Analysis indicated the addition of HN_3 to the starting-material $C_{18}H_{12}N_2O_6S_2$ without displacement of any leaving group whilst the i.r. spectrum showed the absence of an azide group but the presence of NH ($\nu_{max.}$ 3 200 cm^{-1}). An *N*-



Scheme.

acetyl derivative was readily obtained in good yield. These observations can be accommodated in the tetrazolo[1,5-*a*]azepine structure (**11**; R′ = Ph). The *p*-tolyl and methyl sulphones (**3f**; R′ = *p*-MeC_6H_4 or Me) gave, in good yield, products analogous to compound (**11**; R′ = Ph). The u.v. spectra ($\lambda_{max.}$ 302 and 344 nm) were characteristically different from those of the benzofurazan *N*-oxides (**3f**) ($\lambda_{max.}$ 269 and 394 nm).

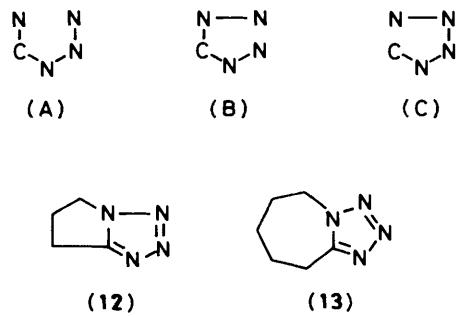
The n.m.r. spectra of the tetrazolo-azepines (**11**) were consistent with the assigned structure. The ^1H n.m.r. spectrum showed doublets at δ 8.28 and 8.09 for the two azepine protons and a broad singlet at δ 9.15 (NH). The ^{13}C n.m.r. spectrum showed eight doublets and six singlets, all in the aromatic-olefinic region. The C-7 and C-8 signals (interchangeable) were assigned to peaks at δ 122.5 and 125.3.

The assignment is made easier by examination of the tetrazolo-azepine (**11**; R′ = Me). For this, the ^1H n.m.r. spectrum indicated the presence of two methyl groups (singlets at δ 3.48 and 3.57), two neighbouring olefinic hydrogens [doublets (*J* 9.1 Hz) at δ 8.15 and 8.60 p.p.m.], and an NH group (δ 11.88). The corresponding doublets for the neighbouring hydrogens in the benzene ring of the bis(methylsulphone) (**3f**; R′ = Me) have δ 8.07 and 8.17 (*J* 7.2 Hz). The ^{13}C n.m.r. spectrum of compound (**11**; R′ = Me) showed the two methyl carbon signals at δ 40.4 and 44.8, two doublets at δ 123.1 and 125.7, and four singlets at 130.4, 134.7, 137.6, and 145.7. The $^1J_{CH}$ couplings for the olefinic doublets, as determined by a gated decoupling experiment, were 174.6 and 172.7 Hz. The singlets showed long-range coupling constants of 9.8, 6.1, 9.1, and 11.0 Hz respectively. With the possible exception of that of the signal at δ 134.7, these coupling constants are characteristic $^3J_{CH}$ values, indicating that the quaternary carbons are all β to C–H groups. Taking into consideration the evidence adduced earlier, the n.m.r. spectra of compound (**11**; R′ = Me) cannot be reconciled with any other plausible structure.

Two possible mechanisms for the transformations (**3f**)→(**11**) were considered (Scheme). Attack by azide at the heterocyclic N would give an intermediate (**6**) corresponding to the type (**5**) postulated for secondary amines.[9] The terminal N of the tetrazene fragment in (**6**) could interact with the benzene ring attached to the other terminus to form the spiro-tetrazole (**9**). A 1,2-shift would stabilise the system by ring enlargement, protonation giving the tetrazolo-azepine (**11**).

More likely, however, is attack by azide at the bridgehead C giving adduct (**7**).* Cycloreversion of the type observed in 3,4-disubstituted furoxans[10] would then yield the conjugated azidonitrile (**10**). The rigid, planar nature of this anion and its strongly electron-attracting substituents would facilitate cycloaddition to the bicyclic system, protonation yielding compound (**11**).

These mechanisms led us to survey the various modes of tetrazole ring closure reported in the literature. The most usual would seem to be N–N bond formation (1—2 ring closure) (**A**),



and existing syntheses[11] from inorganic azides are of this type. The intermediate imidoyl azides $RC(N_3)=NR'$ are usually generated from nitriles or isonitriles, or in the von Braun-Rudolph[12] or Schmidt[13] reactions; they also arise from thermal or photolytic decomposition of *gem*-diazides *via* 1,2-shifts in azido-nitrenes.[14] Diazotisation of amidrazones[15] often proceeds in this way, although when it leads to 2- or 3-substituted tetrazoles, azide intermediates cannot be involved and indeed ring closure may sometimes be of the 2—3 type (**B**). Other 2—3 ring closures[16] have been described.

1—5 Ring closure (**C**) is represented by C–N bond formation in tetrazenes arising either from hydrazides and diazonium salts,[12] or by oxidation of carbazates.[17] A mechanism leading to tetrazolo[1,5-*a*]azepines (**11**) *via* intermediate (**6**) would also be of type (**C**). However, that involving intermediate (**10**) is a concerted cycloaddition, of which some earlier reactions[18] have

* We thank a referee for this suggestion.

Table 1. Benzofurazan (*N*-oxide) ethers (**3g**) and (**4g**) and sulphides (**3c**) and (**4c**)

Compound[b]	R	M.p. (°C)	Formula	Analysis (%)[a] C	H	N	S
(**3g**)	Me	196—198	$C_{13}H_{10}N_2O_5S$	50.9 (51.0)	3.4 (3.3)	8.9 (9.2)	10.5 (10.5)
(**3g**)	Et	164—165	$C_{14}H_{12}N_2O_5S$	52.3 (52.5)	3.9 (3.8)	8.5 (8.8)	10.1 (10.0)
(**3g**)[c]	Et	179—180	$C_{15}H_{14}N_2O_5S$	53.9 (53.9)	4.3 (4.2)	8.3 (8.4)	9.6 (9.6)
(**4g**)	Me	159—160	$C_{13}H_{10}N_2O_4S$	54.0 (53.8)	3.5 (3.4)	9.6 (9.7)	11.0 (11.0)
(**3c**)	*p*-ClC_6H_4	195—196	$C_{18}H_{11}ClN_2O_4S_2$[d]	51.5 (51.6)	2.5 (2.6)	6.7 (6.7)	15.4 (15.3)
(**3c**)	Ph	190	$C_{18}H_{12}N_2O_4S_2$	56.3 (56.3)	3.2 (3.1)	7.3 (7.3)	16.8 (16.7)
(**3c**)	*p*-MeC_6H_4	194	$C_{19}H_{14}N_2O_4S_2$	57.3 (57.3)	3.5 (3.5)	7.0 (7.0)	16.0 (16.1)
(**3c**)[c]	*p*-ClC_6H_4	186—187	$C_{19}H_{13}ClN_2O_4S_2$[e]	53.0 (52.7)	3.0 (3.0)	6.5 (6.5)	14.8 (14.8)
(**3c**)	$PhCH_2$	185—187	$C_{19}H_{14}N_2O_4S_2$	57.6 (57.3)	3.5 (3.5)	6.8 (7.0)	15.9 (16.1)
(**4c**)	*p*-ClC_6H_4	167—168	$C_{18}H_{11}ClN_2O_3S_2$[f]	53.4 (53.7)	2.7 (2.7)	6.7 (7.0)	15.9 (15.9)
(**4c**)[c]	*p*-ClC_6H_4	162—163	$C_{19}H_{13}ClN_2O_3S_2$[g]	55.0 (54.7)	3.1 (3.1)	6.4 (6.7)	15.3 (15.4)

[a] Required values in parentheses. [b] R′ = Ph except where stated. [c] R′ = *p*-MeC_6H_4. [d] Found: Cl, 8.6. Required: Cl, 8.5%. [e] Found: Cl, 8.1. Required: Cl, 8.2%. [f] Found: Cl, 8.8. Required: Cl, 8.8%. [g] Found: Cl, 8.2. Required: Cl, 8.5%.

Table 2. Nitrotetrazolo[1,5-*a*]azepine sulphones [(**11**) and analogues]

R′	M.p. (°C)	Formula	Analysis (%)[a] C	H	N	S
Me	234—236	$C_8H_9N_5O_6S_2$[b]	28.6 (28.7)	2.7 (2.7)	21.0 (20.9)	19.3 (19.1)
Me[c]	184—185	$C_{10}H_{11}N_5O_7S_2$[d]	31.8 (31.8)	2.9 (2.9)	18.6 (18.6)	16.7 (17.0)
Ph	212—214	$C_{18}H_{13}N_5O_6S_2$	46.9 (47.1)	3.0 (2.8)	14.7 (15.3)	13.9 (13.9)
Ph[c]	184—186	$C_{20}H_{15}N_5O_7S_2$	48.2 (47.9)	3.3 (3.0)	13.2 (14.0)	12.6 (12.8)
p-MeC_6H_4	237—242	$C_{20}H_{17}N_5O_6S_2$[e]	49.4 (49.3)	3.5 (3.5)	14.3 (14.4)	12.8 (13.1)
p-MeC_6H_4[c]	228—230	$C_{22}H_{19}N_5O_7S_2$	49.9 (49.9)	3.7 (3.6)	12.8 (13.2)	12.1 (12.1)
Ph[f]	266—267	$C_{19}H_{15}N_5O_4S_2$	51.5 (51.7)	3.2 (3.4)	15.7 (15.9)	14.8 (14.5)
Ph[g]	267—268	$C_{18}H_{12}ClN_5O_4S_2$[h]	47.2 (46.8)	2.6 (2.6)	15.6 (15.2)	14.0 (13.9)

[a] Required values in parentheses. [b] $\nu_{max.}$ 3 235, 1 550, 1 355, 1 320, 1 155, and 1 140 cm^{-1}; δ_H 11.88 (br s, NH), 8.60 and 8.15 (both d, *J* 9.1 Hz, 7- and 8-H), 3.57 (s, Me), and 3.48 (s, Me); δ_C 40.4 (q, Me), 44.8 (q, Me); 123.1 (d, *J* 174.6 Hz), 125.7 (d, *J* 172.7 Hz) (C-7 and C-8); 130.4, 134.7, 137.6, and 145.7 (all s; C-5, C-6, C-9, C-9a). [c] NAc for NH. [d] $\nu_{max.}$ 1 735 cm^{-1}. [e] δ_H 8.31 and 8.08 (both d, *J* 9 Hz, 7- and 8-H), 8.0—7.4 (m, 2 × Ph), 6.59 (br s, NH), 2.49 (s, Me), 2.48 (s, Me); δ_C 20.76 (q, Me), 20.82 (q, Me); 121.1 (d), 124.2 (d) (C-7 and C-8); 127.5, 127.7, 129.0, and 130.1 (all d); 128.1, 136.8, 143.2, and 145.3 (all s). [f] *p*-MeC_6H_4S for one SO_2Ph. [g] *p*-ClC_6H_4S for one SO_2Ph. [h] Found: Cl, 7.7. Required: Cl, 7.7%'.

also been considered examples. Most relevant is the interaction of organic azides and nitriles.[19] Electronic or steric requirements in the latter are high: perfluoronitriles react intermolecularly with azides to give tetrazoles, and the saturated C_4-nitrile $N_3(CH_2)_3CN$ yields the pyrrolo-tetrazole (**12**), but compound (**13**) cannot be prepared from the corresponding C_6-nitrile.

The tetrazolo[1,5-*a*]azepine system has few representatives in the literature, and none with a conjugated azepine ring. Pentylenetetrazole (**13**), the best known, is widely used as a stimulant of the central nervous system. It is a classical example of type (**A**) tetrazole synthesis above, made from cyclohexanone[20] and hydrazoic acid or from caprolactam[21] by diazotisation of the derived amidrazone; the perhydroazepine ring is formed prior to fusion of the tetrazole in a sequence quite different from either of the mechanisms considered for formation of compound (**11**).

Ring enlargement of benzene to azepine is well known, but it usually involves nitrene insertion. These intermediates are generated by thermal or photolytic decomposition of azides, of both inter- or intra-molecular types.[22] Various fused ring systems can be formed,[23] sometimes when the reacting azide group is in a more remote position.[24]

The reactions of sodium azide with the benzofurazan *N*-

Table 3. Benzofurazan (*N*-oxide) sulphoxides (**3d**) and (**4d**) and sulphones (**3e**) and (**4e**)

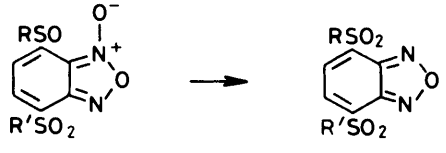
R[b]	M.p. (°C)	Formula	Analysis (%)[a] C	H	N	S	Cl
(**3d**) Ph	200[c]	$C_{18}H_{12}N_2O_5S_2$	54.0 (54.0)	3.0 (3.0)	6.6 (7.0)		
(**3d**) *p*-MeC_6H_4	212[c]	$C_{19}H_{14}N_2O_5S_2$	54.7 (55.1)	3.3 (3.4)	6.7 (6.7)	15.5 (15.5)	
(**3d**) *p*-ClC_6H_4	230[c]	$C_{18}H_{11}ClN_2O_5S_2$	49.9 (49.7)	2.3 (2.5)	6.4 (6.4)	14.7 (14.7)	8.2 (8.2)
(**3d**)[d] *p*-ClC_6H_4	210[c]	$C_{19}H_{13}ClN_2O_5S_2$	50.2 (50.8)	2.6 (2.9)	6.1 (6.2)	13.9 (14.3)	8.3 (7.9)
(**3d**) $PhCH_2$	207[c]	$C_{19}H_{14}N_2O_5S_2$	54.9 (55.1)	3.3 (3.4)	6.6 (6.7)	15.4 (15.5)	
(**3e**) *p*-MeC_6H_4	257—259	$C_{19}H_{14}N_2O_6S_2$	53.4 (53.0)	3.3 (3.3)	6.5 (6.5)	14.8 (14.9)	
(**3e**) *p*-ClC_6H_4	270—271	$C_{18}H_{11}ClN_2O_6S_2$	48.1 (47.9)	2.4 (2.4)	6.2 (6.2)	14.2 (14.2)	7.9 (7.9)
(**4d**) *p*-ClC_6H_4	247—249	$C_{18}H_{11}ClN_2O_4S_2$	51.5 (51.6)	2.7 (2.6)	6.6 (6.7)	15.3 (15.3)	7.9 (8.5)
(**4d**)[d] *p*-ClC_6H_4	216—218	$C_{19}H_{13}ClN_2O_4S_2$	52.4 (52.7)	3.0 (3.0)	6.2 (6.5)	14.9 (14.8)	7.9 (8.2)
(**4e**) *p*-MeC_6H_4	265	$C_{19}H_{14}N_2O_5S_2$	55.6 (55.1)	3.5 (3.4)	6.7 (6.7)	15.2 (15.5)	
(**4e**) *p*-ClC_6H_4	271—272	$C_{18}H_{11}ClN_2O_5S_2$	49.8 (49.7)	2.5 (2.5)	6.4 (6.4)	14.7 (14.7)	8.2 (8.2)
(**4e**)[d] *p*-ClC_6H_4	268—270	$C_{19}H_{13}ClN_2O_5S_2$	50.5 (50.8)	2.8 (2.9)	6.1 (6.2)	14.3 (14.3)	7.8 (7.9)
(**4e**) $PhCH_2$	245—247	$C_{19}H_{14}N_2O_5S_2$	55.2 (55.1)	3.4 (3.4)	6.6 (6.7)	15.5 (15.5)	

[a] Required values in parentheses. [b] R′ = Ph except where stated. [c] Benzofurazan *N*-oxide sulphoxides (**3d**) melt with decomposition. [d] R′ = *p*-MeC_6H_4.

oxides (**1b**) and (**3f**) are thus radically different. As might perhaps have been expected, the nitrosulphones (**1f**) represent intermediate cases. The mediocre yield of azidosulphone (**3h**; R′ = Ph) referred to above was due to partial attack on the nitrosulphone in the manner undergone by the bis-sulphones. Acidification of the mother liquor after filtration of the azidosulphone led to a fraction which could not be recrystallised but which had a u.v. spectrum indicative of tetrazolo[1,5-*a*]-azepine. From the *p*-tolylsulphone (**1f**; R′ = *p*-MeC_6H_4) could be isolated in approximately equal yields (25—30% of each) the azidosulphone (**3h**; R′ = *p*-MeC_6H_4) and a tetrazolo[1,5-*a*]azepine which proved to be (**11**; R′ = *p*-MeC_6H_4). The starting nitrosulphone (**1f**; R′ = *p*-MeC_6H_4) can be recovered (90%) from aqueous dimethylformamide, with no evidence of disproportionation. The probable course of reaction of the nitrosulphone with azide ion involves attack at both the nitro group (giving the azidosulphone and nitrite) and the sulphone group (giving nitroazide and sulphinate), in the manner demonstrated above for thiolate ion. Since sulphinate converts the nitrosulphone very readily into bis-sulphone [only bis-sulphones can be isolated from the nitrochloride (**1b**)], some bis-sulphone (**3f**; R′ = *p*-MeC_6H_4) is formed which then reacts with azide to yield the tetrazolo[1,5-*a*]azepine (**11**; R′ = *p*-MeC_6H_4).

Reaction of the tetrazolo[1,5-*a*]azepine (**11**; R′ = Ph) with toluene-*p*-thiol caused displacement of one sulphonyl group, presumably that next to the nitro. One of the doublets in the ^1H n.m.r. spectrum of this compound due to the azepine protons (δ 8.03, 6.90; *J* 9 Hz) is shifted upfield relative to the corresponding signal in the starting bis-sulphone (azepine proton doublets at δ 8.28 and 8.09), and the u.v. spectrum ($\lambda_{max.}$ 386 nm) also showed an appropriate shift (from $\lambda_{max.}$ 344 nm). The doublets for the neighbouring protons in the central benzene ring of the benzofurazan *N*-oxide (**3c**; R = *p*-MeC_6H_4, R′ = Ph) are at δ 7.99 and 6.39 (*J* 7.6 Hz). Treatment of the bis-sulphone (**11**; R′ = Ph) with piperidine caused extensive decomposition, and attempts to reduce the nitro group were also unsuccessful.

Oxidation of the sulphonylsulphides (**3c**) and (**4c**) with *m*-chloroperbenzoic acid yielded the corresponding sulphoxides (**3d**) and (**4d**) or sulphones (**3e**) and (**4e**). The N→S migration of oxygen noted[3] in the nitrobenzofurazan *N*-oxide sulphoxides (**1d**) was also observed when the sulphoxides (**3d**) were heated in toluene, resulting in formation of the benzofurazans (**4e**) in good yield. As before, the rearrangement was considerably slower for R = *p*-chlorophenyl than for R = *p*-tolyl, the compound with R = benzyl requiring an intermediate time.



(**3d**) (**4e**)

Experimental

I.r. spectra were run in Nujol on a Unicam SP1000 spectrophotometer, u.v. spectra in methanol on a Unicam SP-800 instrument, and n.m.r. spectra in $(CD_3)_2SO$ (^1H n.m.r. on a Varian XL-200 instrument, ^{13}C n.m.r. on a Bruker WP-80). M.p.s. were determined in capillaries and are uncorrected. Light petroleum had b.p. 40—60 °C except where stated otherwise.

4,7-*Bis*(*methylsulphonyl*)*benzofurazan* N-*Oxide* (**3f**; R′ = Me).—A solution of 4-chloro-7-nitrobenzofurazan *N*-oxide

(2.15 g, 10 mmol) in acetone (50 ml) was added portionwise to sodium methanesulphinate (2.24 g, 22 mmol) in water (20 ml) and acetone (20 ml). After 30 min the mixture was diluted with water and the *bis-sulphone* (1.1 g, 38%) filtered off, m.p. 243—245 °C (from acetone) (Found: C, 32.9; H, 2.9; N, 9.7; S, 21.9. $C_8H_8N_2O_6S_2$ requires C, 32.9; H, 2.7; N, 9.6; S, 21.9%); $\lambda_{max.}$ 268 sh and 384 nm; $\nu_{max.}$ 1 612, 1 325, 1 195, 1 140, and 964 cm^{-1}; δ_H 8.17, 8.07 (both d, *J* 7.2 Hz, 5- and 6-H), 3.48 (s, Me), and 3.44 (s, Me).

4-*Methoxy*-7-*phenylsulphonylbenzofurazan* N-*Oxide* (**3g**; R = Me, R′ = Ph).—4,7-Bis(phenylsulphonyl)benzofurazan *N*-oxide[3] (2.08 g, 5 mmol) ($\lambda_{max.}$ 269 and 394 nm) was heated in refluxing 0.05M NaOMe (100 ml) for 1 h until a solution was obtained. Concentration gave the *ether* (1.3 g, 85%) which was recrystallised from ethanol as long yellow needles. Other ethers (**3g**) and (**4g**) were prepared similarly in good yield (Table 1).

4-*Methoxy*-7-*phenylsulphonylbenzofurazan* (**4g**; R = Me, R′ = Ph).—4-Nitro-7-phenylsulphonylbenzofurazan[3] (0.5 g) was added to sodium (40 mg) in methanol (100 ml) and the solution heated to reflux, upon which the initial green colour darkened. After 20 min, the methanol was evaporated, water was added, and the product was filtered off, m.p. 160—161 °C (from ethanol); $\lambda_{max.}$ 350 nm; i.r. spectrum identical with that of the ether obtained (Table 1) from the bis-sulphone (**4f**; R′ = Ph).

Reaction of 4-*Nitro*-7-(p-*tolylsulphonyl*)*benzofurazan* N-*Oxide* (**1f**; R′ = *p*-MeC_6H_4) *with* p-*Chlorobenzenethiol*.—The nitrosulphone (168 mg, 0.5 mmol) [$\lambda_{max.}$ 275sh and 411 nm] was added to a solution of the thiol (79 mg, 0.55 mmol) in methanol (20 ml) containing a few drops of 2M NaOH. Refluxing for 30 min, concentration, and filtration yielded a solid (131 mg), m.p. 172—182 °C. Recrystallisation from benzene–light petroleum (b.p. 60—80 °C) gave red and yellow crystals, m.p. 180—184 °C; t.l.c. (4:1 light petroleum–ethyl acetate) and the u.v. spectrum [$\lambda_{max.}$ 422 and 440sh nm] indicated a mixture of the sulphonylsulphide (**3c**; R′ = *p*-MeC_6H_4) [m.p. 186—188 °C (golden yellow needles from MeOH); $\lambda_{max.}$ 276 and 419 nm] and the slightly faster-running nitrosulphide (**1c**), [m.p. 203—205 °C (orange–red needles from EtOAc); $\lambda_{max.}$ 322 and 451 nm], with R = *p*-ClC_6H_4 in each case.

4-(p-*Chlorophenylthio*)-7-*phenylsulphonylbenzofurazan* N-*Oxide* (**3c**; R = *p*-ClC_6H_4, R′ = Ph).—4,7-Bis(phenylsulphonyl)benzofurazan *N*-oxide (832 mg, 2 mmol) and *p*-chlorobenzenethiol (289 mg, 2 mmol) in ethanol (100 ml) containing a few drops of 2M NaOH were refluxed for 30 min. Dilution of the deep yellow solution with water, followed by cooling and filtration yielded the *sulphide* (650 mg, 78%), recrystallised from benzene–light petroleum (Table 1).

Other aryl sulphides (**3c**) and (**4c**) were prepared similarly (Table 1), but for the benzyl sulphide (**3c**; R = CH_2Ph, R′ = Ph), the bis-sulphone (8 mmol), toluene-ω-thiol (1 ml), 0.5M NaOMe (16 ml), and dry methanol (150 ml) were refluxed for 15 min to yield the product (2.6 g, 82%); $\lambda_{max.}$ 274 and 415 nm. The sulphide (**3c**; R = *p*-MeC_6H_4, R′ = Ph) has δ_H 7.99, 6.39 (2 H, both d, *J* 7.6 Hz, 5- and 6-H), 7.9—7.3 (9 H, m, C_6H_4 and Ph), and 2.41 and 2.09 (3 H, both s, Me).

Reaction of Bis-sulphones (**3f**) *with Secondary Amines*.—(*a*) *Piperidine*. The methyl sulphone (**3f**; R′ = Me) (0.2 g, 0.7 mmol) was dissolved in dimethylformamide (5 ml) and treated with piperidine (1 ml). After 3 h the solution was poured into ice–water. Addition of a few drops of 2M HCl precipitated the yellow *phenylhydrazine* [**8**; R′ = Me, R_2 = $(CH_2)_5$] (0.1 g, 38%), m.p. 201—203 °C (from benzene–light petroleum) (Found: C, 41.3; H, 5.1; N, 11.0; S, 16.6. $C_{13}H_{19}N_3O_6S_2$ requires C, 41.4; H, 5.0; N, 11.1; S, 16.9%); $\nu_{max.}$ 3 295 and 1 595 cm^{-1}.

(*b*) *Pyrrolidine*. The phenyl sulphone (**3f**; R′ = Ph) treated with pyrrolidine under the foregoing conditions gave the *benzofurazan* N-*oxide* [**3a**; R′ = Ph, R_2 = $(CH_2)_4$] as red needles, m.p. 202—204 °C (from ethanol) (Found: C, 55.5; H, 4.4; N, 12.1; S, 9.6. $C_{16}H_{15}N_3O_4S$ requires C, 55.7; H, 4.4; N, 12.2; S, 9.3%).

(*c*) *Morpholine*. The methyl sulphone (**3f**; R′ = Me) yielded only the *phenylhydrazine* [**8**; R′ = Me, R_2 = $(CH_2)_2O(CH_2)_2$], m.p. 210—211 °C (from ethyl acetate–light petroleum) (Found: C, 38.0; H, 4.4; N, 11.2; S, 16.9. $C_{12}H_{17}N_3O_7S_2$ requires C, 38.0; H, 4.5; N, 11.2; S, 16.9%); $\nu_{max.}$ 3 285 and 1 595 cm^{-1}. The phenyl sulphone (**3f**; R′ = Ph) gave the yellow *phenylhydrazine* [**8**; R′ = Ph, R_2 = $(CH_2)_2O(CH_2)_2$], m.p. 212—213 °C (from benzene–ethanol) (Found: C, 52.8; H, 4.3; N, 8.2; S, 12.3. $C_{22}H_{21}N_3O_7S_2$ requires C, 52.3; H, 4.2; N, 8.3; S, 12.7%); $\nu_{max.}$ 3 240, 1 575, and 1 555 cm^{-1}. Concentration of the aqueous mother liquor caused separation of the red *benzofurazan* N-*oxide* [**3a**; R′ = Ph, R_2 = $(CH_2)_2O(CH_2)_2$], m.p. 230 °C (from ethanol) (Found: C, 53.1; H, 4.3; N, 11.5; S, 8.9. $C_{16}H_{15}N_3O_5S$ requires C, 53.2; H, 4.2; N, 11.6; S, 8.7%).

4-*Azido*-7-(p-*tolylsulphonyl*)*benzofurazan* (**4h**; R′ = *p*-MeC_6H_4).—The bis-sulphone (**4f**; R′ = *p*-MeC_6H_4) (0.85 g, 2 mmol) and sodium azide (0.14 g, 2.15 mmol) were stirred in dimethylformamide (20 ml). The solution (clear after 20 min) was poured into ice–water after 1 h, and following refrigeration the golden yellow *azide* was filtered off in good yield, with m.p. 148—149 °C (from benzene–light petroleum) (Found: C, 50.0; H, 2.8; N, 21.7; S, 10.1. $C_{13}H_9N_5O_3S$ requires C, 49.5; H, 2.9; N, 22.2; S, 10.2%); $\lambda_{max.}$ 253 and 366 nm.

5-*Nitro*-6,9-*bis*(*phenylsulphonyl*)-1H-*tetrazolo*[1,5-a]*azepine* (**11**; R′ = Ph).—Sodium azide (1.1 g, 17 mmol) was added to 4,7-bis(phenylsulphonyl)benzofurazan *N*-oxide (6.24 g, 15 mmol) dissolved in dimethylformamide (60 ml) causing an immediate red colouration. The mixture was stirred (2 h) and poured into ice–water (300 ml) to give a yellow solution. On acidification with 2M HCl, the *product* (5.0 g, 73%) separated and was filtered off after a few hours in the refrigerator. It was recrystallised from ethyl acetate–light petroleum (details of analysis in Table 2) and had $\nu_{max.}$ 3 200, 1 542, 1 320, 1 180, and 1 155 cm^{-1}; $\lambda_{max.}$ 302 and 344 nm; δ_H 9.15 (s, NH, disappears on addition of D_2O), 8.28 and 8.09 (both d, *J* 9 Hz, 7- and 8-H), and 8.0—7.4 (m, 2 × Ph); δ_C 122.5 (d), 125.3 (d) (C-7 and C-8); 127.9, 128.1, 129.2, 130.0, 133.7, and 134.8 (all d); 130.0, 134.4, 136.7, 138.4, 139.7, and 145.5 (all s). After treatment with refluxing acetic anhydride (1 h) the solution was poured into ice–water to yield the 1-*acetyl derivative* ($\lambda_{max.}$ 295 and 345sh nm), which was also recrystallised from ethyl acetate–light petroleum. Other bis-sulphones (**11**) and their *N*-acetyl derivatives were prepared similarly (Table 2).

4-*Azido*-7-*phenylsulphonylbenzofurazan* N-*Oxide* (**3h**; R′ = Ph).—A solution of the nitrosulphone (**1f**; R′ = Ph) (674 mg, 2.1 mmol) in dimethylformamide (10 ml) was treated with sodium azide (150 mg, 2.3 mmol), stirred for 2 h, and poured into ice–water (50 ml). The following day the *azidosulphone* (239 mg, 36%) was filtered off and recrystallised from ethyl acetate, m.p. 145—146 °C (Found: C, 45.4; H, 2.15; N, 22.0; S, 10.1. $C_{12}H_7N_5O_4S$ requires C, 45.45; H, 2.2; N, 22.05; S, 10.1%); $\lambda_{max.}$ 272, 305sh and 408 nm; $\nu_{max.}$ 2 130 (N_3), 1 325, and 1 150 (SO_2) cm^{-1}.

Reaction of 4-*Nitro*-7-(p-*tolylsulphonyl*)*benzofurazan* N-*Oxide* (**1f**; R′ = *p*-MeC_6H_4) *with Sodium Azide*.—Treatment of the nitrosulphone (1.34 g, 4 mmol) with sodium azide as in the

foregoing example yielded the *azidosulphone* (**3h**; R′ = *p*-MeC_6H_4) (325 mg, 25%), m.p. 144—145 °C (from ethyl acetate) (Found: C, 47.5; H, 2.7; N, 21.5; S, 9.7. $C_{13}H_9N_5O_4S$ requires C, 47.15; H, 2.75; N, 21.15; S, 9.7%).

Acidification of the mother liquor caused turbidity. After being left overnight in the refrigerator, the product (358 mg) was filtered off, much time being required for this process. The product proved to be bis-sulphone (**11**; R′ = *p*-MeC_6H_4) (Found: C, 49.4; H, 3.5; N, 14.5%); m.p. 232—234 °C (from ethyl acetate), undepressed when mixed with sample prepared as above from the bis-sulphone (**3f**; R′ = *p*-MeC_6H_4). The yield was *ca.* 36%, based on formation of 0.5 mole per mole of nitrosulphone (**1f**).

5-Nitro-9-phenylsulphonyl-6-(p-*tolylthio*)-1H-*tetrazolo*-[1,5-a]-*azepine*.—A solution of the bis-sulphone (**11**; R′ = Ph) (0.92 g, 2 mmol) and toluene-*p*-thiol (0.25 g, 2 mmol) in ethanol (85 ml) containing aqueous 1M NaOH (2 ml) was refluxed for 45 min. Concentration and addition of water afforded the yellow p-*tolyl sulphide* (0.6 g, 68%), recrystallised from benzene–ethanol; $\lambda_{max.}$ 291 and 386 nm; δ_H 8.03 and 6.90 (both d, *J* 9 Hz, 7- and 8-H), 5.85 (br s, NH), and 2.40 (s, Me). The p-*chlorophenyl sulphide* was prepared similarly (Table 2).

Sulphoxides (**3d**) *and* (**4d**) *and Sulphones* (**3e**) *and* (**4e**).—A solution of the appropriate sulphide (**3c**) or (**4c**) in methylene dichloride was treated at 0 °C with *m*-chloroperbenzoic acid (85%; 1 or 2 equiv.) in the same solvent. After 1 h the solution was allowed to reach room temperature. The next day it was washed with saturated aqueous $NaHCO_3$ and evaporated, and the product, obtained in good yield, recrystallised from methylene dichloride or chloroform (Table 3). For compounds with two aryl substituents, the sulphoxides (**3d**) had $\lambda_{max.}$ 260sh, 292sh, and 387 nm, and the sulphones (**3e**) $\lambda_{max.}$ 269, 295sh, and 394 nm; the benzofurazan sulphones (**4e**) had $\lambda_{max.}$ 280, 318, and 331sh nm.

Thermal Rearrangement of 7-Phenylsulphonylbenzofurazan N-Oxide Sulphoxides (**3d**; R′ = Ph).—A solution of the sulphoxide (R = *p*-MeC_6H_4) (0.3 g) in toluene (50 ml) was refluxed and the reaction monitored by t.l.c. After 3 h the reaction was complete, and the benzofurazan bis-sulphone (**4e**; R = *p*-MeC_6H_4, R′ = Ph) (0.21 g) crystallised out on cooling the solution.

Similarly obtained in high yield were the sulphones (**4e**; R′ = Ph) after 8 h (for R = CH_2Ph) and 10 h (for R = *p*-ClC_6H_4).

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