Cycloadditions of Nitrile Oxides with Benzofurazan *N*-Oxides

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The reaction of benzofurazan *N*-oxides with nitrile oxides in refluxing dichloromethane affords the mono- and bis-adducts to the benzene ring, as well as benzo-*as*-triazine tri-*N*-oxides. The site-, regio-, and stereo-selectivity of the cycloadditions, the influence of substituents, and the isomeric composition of the isolated mono- and bis-adducts are discussed, and compared with the results of the cycloadditions to the corresponding benzofurazans.

Despite intensive work on benzofurazan *N*-oxides,[1] their reactivity towards 1,3-dipoles has been inadequately studied. Benzofurazan *N*-oxide reacts with diazodiphenylmethane[2] to give a variety of benzimidazole derivatives, depending upon the reaction conditions, while 5-nitrobenzofurazan 1-oxide undergoes cycloaddition[3] to the benzene ring with alkyl diazoacetates. *p*-Methoxyphenyl azide[2] reacts with benzofurazan *N*-oxide to open the furoxan ring, yielding bis-azo and bis-azoxy compounds. Nitrones[4] also react with benzofurazan *N*-oxide to afford high yields of 1-hydroxybenzimidazole 3-oxide derivatives.

In a preliminary communication[5] we reported that benzofurazan *N*-oxides react with nitrile oxides in refluxing dichloromethane to give mono- or bis-adducts to the benzene ring, as well as benzotriazine tri-*N*-oxides as by-products. The structure of the tri-*N*-oxides has been unequivocally assigned by X-ray analysis performed on one of them. We now report the results of our investigation of these reactions, including their site-, regio-, and stereo-selectivity, the influence of substitution of benzofurazan *N*-oxide on the reaction course, the isomeric composition of the cycloadducts, and we compare these results with those of cycloaddition to benzofurazans.

Results and Discussion

Cycloaddition Products of Nitrile Oxides **5** *and* **6** *to Benzofurazan* N-*Oxides* **1–4**.—Benzofurazan *N*-oxides **1–4** react with the stable nitrile oxides **5** and **6** in refluxing dichloromethane in a 1:1 to 1:2 molar ratio, to give the cycloadducts **8–12**, while the benzo-*as*-triazine tri-*N*-oxides **7a–l** are also formed in all cases as by-products (Scheme 1). The bis-adducts **8** and the mono-adducts **9** are the major products of the reactions of unsubstituted compound **1** and substituted benzofuroxans **2–4**, respectively. The cycloadducts **10–12** are also generated in certain reactions.

The reactions of unsubstituted benzofurazan *N*-oxide **1** with nitrile oxides **5** and **6** afforded, besides the tri-*N*-oxides **7a** and **7b**, the bis-adducts **8a** and **8b** as the major products, respectively. The regioisomers **11a** and **12b** were also formed, but in lower yields. 5,6-Dimethylbenzofurazan 1-oxide **2**, however, underwent, in analogous reactions, the formation of mono-adducts **9c** and **9d**, respectively, and also the tri-*N*-oxides **7c** and **7d** in low yields.

5(6)-Methylbenzofurazan 1-oxide **3** with nitrile oxides **5** and **6** afforded the mono-adducts **9e** and **9g** and, moreover, the bis-adducts **11e** and **11g**. The tri-*N*-oxides mixtures **7e**/**7f** and **7g**/**7h** were also formed in low yields. 5(6)-Methoxybenzofurazan 1-oxide **4** yielded the regioisomeric mono-adducts **9i** and **9k** and **10i** and **10k** in reactions with nitrile oxides **5** and **6**, besides the tri-*N*-oxide mixtures **7i**/**7j** and **7k**/**7l**, which were formed in low yields.

The yields in all reactions were based on the starting quantity of furoxan **1–4**,† whose unchanged excess was recovered in the separation of the reaction mixture by column chromatography.

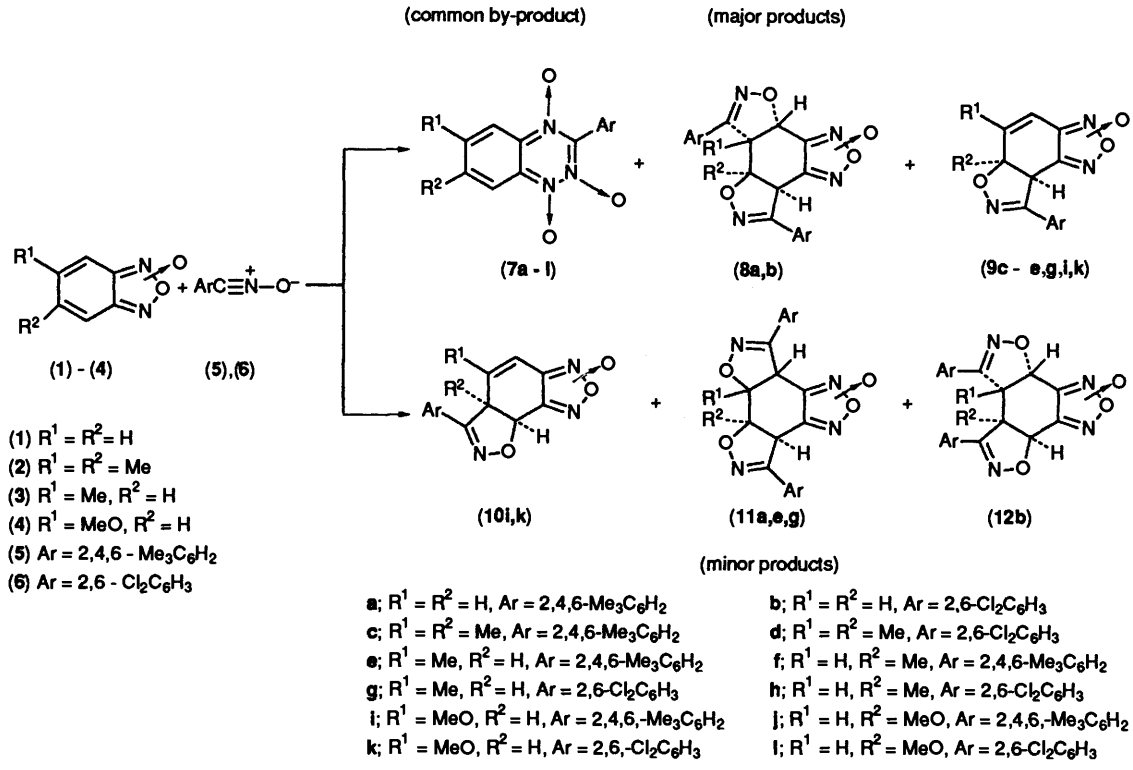
Cycloadditions of Nitrile Oxides **5** *and* **6** *to Benzofurazans* **13** *and* **14**.—In order to investigate the influence of the N→O group on the regioselectivity of cycloadditions to the benzofurazan ring, the reactions of benzofurazans **13** and **14** with nitrile oxides **5** and **6** were attempted, in refluxing dichloromethane, in a 1:2 molar ratio (Scheme 2).

Thus, benzofurazan **13** afforded, with mesitonitrile oxide **5**, exclusively the bis-adduct **15a** in 48% yield, while 5,6-dimethylbenzofurazan **14** underwent with the same nitrile oxide the formation of both the mono- **16c** and bis-adduct **15c** in yields 25 and 45%, respectively. The mono-adduct **16d** was the sole product in the addition of nitrile oxide **6** to 5,6-dimethylbenzofurazan **14**. However, no regioselectivity was observed in the reaction of benzofurazan **13** with the 2,6-dichlorobenzonitrile oxide **6**, where a mixture of all possible regioisomeric bis-adducts **15b**, **17b** and **18b** was isolated. The components of this mixture were not separated, and each compound was characterized from the ^{1}H NMR spectrum of the mixture.

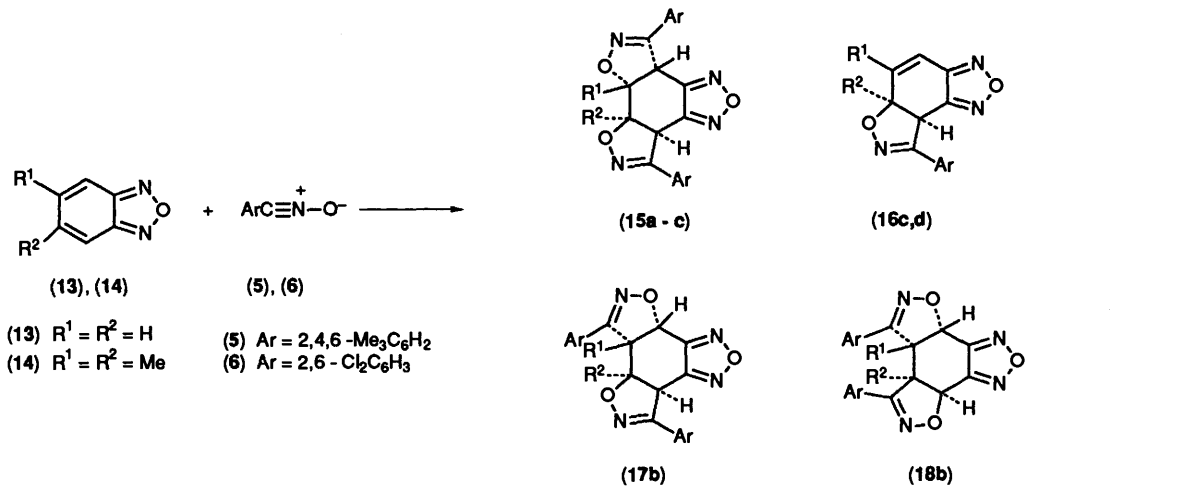
The structure of monoadducts **16c** and **16d** and of bis-adduct **15c** has been unequivocally assigned from their ^{13}C NMR spectra, where the chemical shifts of the quaternary aliphatic isoxazoline carbons at δ_C 86–89 indicate that these carbons are attached to O-atoms. The structure of bis-adduct **15a** is deduced by comparison of its ^{1}H NMR spectrum with the ^{1}H NMR spectra of compound **15c** and **16c** and **16d**. The 4-H protons close to the furazan ring have similar chemical shifts (δ *ca.* 5). Also, in a reverse regioisomeric structure for compound **15a**, its proton chemical shifts should have a larger dispersion, as happens in the case of **18b** or in the case of analogous cycloadducts to benzofurazan *N*-oxides (see next section).

Structure Assignment of Cycloadducts **8–12**.—The structure elucidation of the cycloadducts **8–12**, namely the determination of site-, regio-, and stereo-selectivity of the addition of the nitrile oxides, was based on their ^{1}H and ^{13}C NMR spectra, recorded in Tables 1 and 2. (The numbering used for compounds **8–12** and **15–18** is not the systematic one. However, it has the

† The yields in ref. 5 have been based on the *consumed* furoxan. The m.p. of compound **7a**, although adequately characterized, has been reported incorrectly as 210–212 °C instead of the correct value 195–196 °C.



Scheme 1.



Scheme 2.

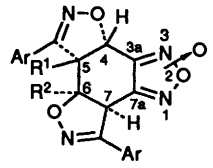
advantage of being common to all the compounds studied, and shows up more clearly their differences).

Two factors make the spectra complicated:

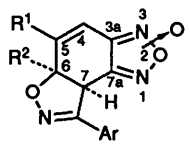
(*a*) The 1-oxide/3-oxide isomeric composition of most of the cycloadducts produces two isomers for every cycloadduct. This isomeric mixture exists in almost all cases, and the two isomers have their own individual peaks. Owing to the bulky substitution, the equilibrium rate is low, and the coalescence point is expected to be much higher than 20 °C. No attempt was made to undertake variable-temperature measurements in order to calculate the thermodynamic and kinetic parameters of these equilibria.

(*b*) The often appearing hindered rotation around the aryl–isoxazoline C–C bond yields additional peaks for the aromatic ring in both the ^1H and ^{13}C NMR spectra.

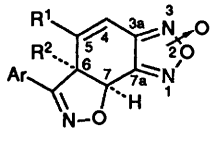
On the other hand, the existence of the two *N*-oxide isomeric forms, which makes the spectra complex, helped us in assigning the structure of the cycloadducts, allowing us to discern between the two *N*-oxide isomeric forms since the protons and carbons close to the *N*-oxide group are all (more or less strongly)



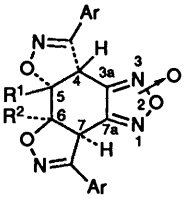
(8) [(17)= deoxide]



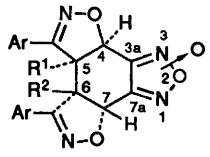
(9) [(16) = deoxide]



(10)



(11) [(15) = deoxide]



(12) [(18) = deoxide]

Table 1. ^{1}H NMR spectra (δ)[a] of cycloadducts **8**–**12** and **15**–**18**.

Compd.	Yield (%)[b]	Isomer	1-/3-Oxide proportions (%)	4-H	5-H	6-H	7-H	R^1	R^2	Aromatic ring ArH	2′-Me	4′-Me
8a[c]	25 (1:2)	3-oxide	100	5.99d	4.80dd	4.87dd	4.03d			6.91s,	2.07s,	2.29s,
	22 (1:1)			(9.8)	(9.8, 2.8)	(8.3, 2.8)	(8.3)			6.96s	2.20s	2.32s
8b	46 (1:2)	1-oxide	15	6.10d	4.92dd	5.14dd	4.88d			7.45m		
	22 (1:1.25)			(10)	(10, 2.6)	(9.5, 2.6)	(9.5)					
		3-oxide	85	6.07d	4.90dd	5.13dd	5.03d			7.45m		
				(10.1)	(10.1, 3)	(9.9, 3)	(9.9)					
9c	20 (1:1.1)	1-oxide	10	6.52q			4.73s	2.20d	1.78s	6.80s,	1.90s,	2.28s
				(1.3)				(1.3)		6.90s	2.38s	
		3-oxide	90	6.28q			4.80s	2.18d	1.80s	6.84s,	1.90s,	2.28s
				(1.4)				(1.4)		6.92s	2.38s	
9d	9 (1:1.1)	1-oxide	40	6.47q			4.84s	2.19d	1.79s	7.33m		
				(1.4)				(1.4)				
		3-oxide	60	6.24q			4.93s	2.16d	1.81s	7.33m		
				(1.3)				(1.3)				
9e	18 (1:1)	1-oxide	25	6.54s		5.51d	5.01d	2.19s		6.80s	1.87s,	2.27s
						(11.4)	(11.4)			6.90s	2.34s	
		3-oxide	75	6.30s		5.53d	5.06d	2.19s		6.89s	2.11s (br)	2.28s
						(11.7)	(11.7)					
9g	11(1:1.25)	1-oxide	5	6.57s		5.63d	5.20d	2.21s		7.36m		
						(11.5)	(11.5)					
		3-oxide	95	6.33s		5.65d	5.28d	2.20s		7.36m		
						(12)	(12)					
9i	7 (1:1.25)	1-oxide	20	5.86s		5.59d	5.09d	3.89s		6.82s,	1.91s,	2.28s
						(11.6)	(11.6)			6.90s	2.34s	
		3-oxide	80	5.60s		5.59d	5.13d	3.88s		6.90s	2.12s	2.29s
						(11.6)	(11.6)					
9k	*d*	1-oxide	10	5.87s		5.66d	5.27d	3.90s		7.39m		
						(12.1)	(12.1)					
		3-oxide	90	5.61s		5.70d	5.36d	3.89s		7.39s		
						(12.1)	(12.1)					
10i	33 (1:1.25)	1-oxide	100	5.69s		4.67d	6.00d	3.43s		6.86s,	2.04s,	2.29s
						(11.4)	(11.4)			6.87s	2.26s	
10k	*d*	1-oxide	100	5.77s		4.85d	6.05d	3.54s		7.38m		
						(11.7)	(11.7)					
11a[c]	15 (1:2)	1-oxide	100	4.84d	5.44dd	5.33dd	4.82d			6.87s,	1.94s,	2.29s,
	13 (1:1)			(9.3)	(9.3, 3.3)	(8.3, 3.3)	(8.3)			6.94s	2.20s,	2.30s
											2.36s	
11e	5 (1:1)	1-oxide	12	4.57s		5.18d	4.68d	*e*		*e*	*e*	*e*
	21 (1:1.25)					(7.5)	(7.5)					
		3-oxide	88	4.48s		5.17d	4.75d	1.87s		6.87s,	1.90s,	2.29s,
						(7.5)	(7.5)			6.92s,	2.25s (2	2.31s
										6.96s (2 H)	Me), 2.40s	
11g	14 (1:1.25)	1-oxide	10	4.82s,		5.33d (8)	5.02d (8)	1.82s		7.4m		
		3-oxide	90	4.67s		5.32d (8)	5.09d (8)	1.80s		7.4m		
12b	5 (1:1.25)	1-oxide	100	5.98d (10)	4.40m	4.40m	5.89d (9.7)			7.4m		
15a	48 (1:2)			4.96dd	5.50dd (10.3, 2.5)		4.96dd			6.93s	2.09s	2.31s
				(10.3, 2.5)			(10.3, 2.5)					
15b	*f*			5.30dd	5.60dd (10, 2.5)		5.30dd			7.4m		
				(10, 2.5)			(10, 2.5)					
15c	45 (1:2)			4.70s			4.70s	1.93s	1.93s	6.93s	2.07s(br)	2.31s
16c	26 (1:2)			6.66q (1.5)			4.90s	2.20d	1.77s	6.77s(br),	1.71s(br),	2.24s
								(1.5)		6.85s(br)	2.37s(br)	
16d	32 (1:2)			6.68q (1.4)			5.09s	2.22d (1.4)	1.82s	7.3m		
17b	*f*			6.26d	4.97dd	5.19m	5.19m			7.4m		
				(10.2)	(10.2, 2.1)							

Table 1. (*continued*)

Compd.	Yield (%)[b]	Isomer	1-/3-Oxide proportions (%)	4-H	5-H	6-H	7-H	R^1	R^2	Aromatic ring ArH	2'-Me	4'-Me
18b	*f*			6.12dd (11.7, 2.7)	4.41dd (11.7, 2.7)		6.12dd (11.7, 2.7)			7.4m		

[a] Obtained in $CDCl_3$ at 300 MHz. The coupling constants (Hz) are given in parentheses. [b] Based on starting benzofurazan at the molar ratio benzofurazan: nitrile oxide given in parentheses. [c] Compounds **8a**/**11a** were obtained as a mixture. [d] The isomers **9k**/**10k** did not separate; total yield 48%. [e] Overlapping with the peaks of the major 3-oxide isomer. [f] Not separated.

shielded compared with those further from the *N*-oxide group.[1a] This phenomenon is stronger in the ^{13}C NMR spectra, where the C-3 of the furoxan ring (close to N→O) is strongly shielded (δ_C 100–110) in comparison with C-4 (δ *ca.* 150).[1] By determination of the 1- and 3-oxide isomeric forms of the cycloadducts and their own peaks in the spectrum of the mixture (using the relative intensities and coupling constants), the differences in chemical shifts (in both the ^1H and ^{13}C NMR spectra) for the same proton or carbon in the two isomers allowed us to determine the regioaddition of the nitrile oxides.

The process utilized to make these complex assignments can be exemplified by referring to the products **9e** and **11e**, mono- and bis-adducts, respectively, of mesitonitrile oxide **5** to 5(6)-methylbenzofurazan 1-oxide **3**. In this particular case, the two isomeric forms of compound **9e**, the 1- and 3-oxide, were separated chromatographically. They show relatively small differences in both the ^1H and ^{13}C NMR spectra, and then undergo a mutual change when refluxed in benzene solution, thus implying that they are the two N→O isomeric forms of the same cycloadduct.

That the nitrile oxide has added to the unsubstituted double bond of the benzene ring in substrate in **3** (6,7-positions) can easily be concluded from the presence of two tertiary aliphatic carbons for every isomer in the ^{13}C NMR spectrum of the product (in addition to methyl carbons). If the addition had been made to the 4,5-positions, one new aliphatic carbon in the cycloadduct should have been quaternary.

The 4-H proton chemical shift is δ 6.54 for the first isomer and δ 6.30 for the second one (Table 1). The two aliphatic isoxazoline protons have chemical shifts δ 5.51 and 5.01 for the first isomer and δ 5.53 and 5.06 for the second isomer. The shielding effect on the 4-H proton of the second isomer is evidently produced by the close N→O group, thus confirming that the second isomer is the 3-oxide isomer.

From the two isoxazoline proton pairs, the first one (δ 5.51 and 5.53), is practically unaffected by the N→O isomerization, and the second is affected by a factor of 0.05 ppm (δ 5.01 and 5.06). Thus, the peaks at 5.51 and 5.53 are assigned to the 6-H proton of the two N→O isomers and the peaks at δ 5.01 and 5.06 to the 7-H proton, which is shielded in the first isomer (1-oxide) by the neighbouring N→O group.

The aliphatic isoxazoline carbon chemical shifts of the two N→O isomers in the ^{13}C NMR spectra (Table 2) are δ_C 44.4 and 80.1 for the 1-oxide isomer and δ_C 47.0 and 80.4 for the 3-oxide isomer. The peaks at δ_C 80.1 and 80.4 ($\Delta\delta$ 0.3 ppm) are assigned to the isoxazoline aliphatic carbons attached to the O-atom, and the peaks at δ_C 44.4 and 47.0 ($\Delta\delta$ 2.6 ppm) to the other aliphatic isoxazoline carbons. The larger difference for the carbons at δ_C 44.4 and 47.0, indicates that these carbons of the isoxazoline ring are close to the furoxan ring, thus determining the regioselectivity of the addition and completing the structure assignment of product **9e**.

One more finding confirms the above assignment: the rotation around the mesityl–isoxazoline C–C bond is much more hindered in the first isomer, producing double signals for the 2'-Me/6'-Me and 3'-H/5'-H pairs in the ^1H NMR spectrum, as well as double peaks for the 2'-Me/6'-Me, C-2'/C-6' and C-3'/C-5' pairs in the ^{13}C NMR spectrum (Tables 1 and 2), at 20 °C, in accord with the suggested 1-oxide structure for this isomer of compound **9e**, where the N→O group is closer to the mesityl group than in the case of the 3-oxide isomer, and substantially restricts the free rotation around the mesityl–isoxazoline C–C bond. These signals coalesce at 20 °C in the isomeric **9e** 3-oxide.

The bis-adduct, isolated in the same reaction and assigned as having structure **11e**, consists of two isomers in an 88:12 ratio (^1H NMR), with small differences in their spectra, which evidently are the two isomeric N→O forms of the same cycloadduct. The major isomer has chemical shifts for the isoxazoline protons δ 4.48 (s), 4.75 (d) and 5.17 (d), and chemical shifts δ_C 45.7, 48.4, 81.8 and (quaternary) 84.3 for the aliphatic isoxazoline carbons. The minor isomer has for the isoxazoline protons δ 4.57 (s), 4.68 (d) and 5.18 (d), and δ_C 43.1, 50.6, 81.0 and (quaternary) 84.4 for the aliphatic isoxazoline carbons. The quaternary carbon signals at δ_C 84.3 and 84.4 determine the regioselectivity of the addition to the 4,5-positions: if the regioselectivity had been reversed, the quaternary carbons appear at δ_C *ca.* 50. This was verified by the singlet proton peaks at δ 4.48 and 4.57 assigned to the 4-H proton of the two isomers; in the reverse regioadduct the 4-H proton, attached to an O-atom, should have a chemical shift of δ *ca.* 5.5–6.

The shielded 4-H chemical shift of the major component compared with the respective chemical shift of the minor component of this mixture shows that the 3-oxide is the major product and the 1-oxide the minor product of the double addition. The regioselective addition of the adduct to the 6,7-positions is determined by the differences in the chemical shifts of the isoxazoline aliphatic carbons in the two isomers. The carbon attached to the O-atom of this isoxazoline ring is shielded in the minor product by a factor of 0.8 ppm (δ_C 81.0 and 81.8) and the other carbon is shielded by a factor of 2.6 ppm (δ_C 43.1 and 45.7), indicating that the carbon attached to the O-atom of the isoxazoline ring is far from the furoxan ring, thus showing that the bis-adduct of this reaction has the structure **11e** with the 3-oxide isomer as the major component of the product.

The structure of compound **11e** was also confirmed by chemical evidence. Both products **9e** and **11e** are formed in this reaction in an furoxan: nitrile oxide 1:1 molar ratio. No mono-adduct **9e**, however, was isolated when the reaction was repeated with a 25% excess of nitrile oxide: the mono-adduct **9e** intermediately formed is further converted into the bis-adduct in the presence of a certain excess of nitrile oxide. This finding reinforces our findings that the regioselectivity in the addition occurred at the 6,7-positions.

From the reaction of benzofurazan *N*-oxide **1** with mesitonitrile oxide **5**, there was isolated in 40% yield a solid (m.p. 210–220 °C) which was originally assigned as a mixture of the 1- and 3-oxide of the bis-adduct **8a**.[5] However, high-field ^1H NMR spectroscopy (300 MHz) indicated this solid to be a mixture of the isomers **8a**, which consists exclusively of one of the two possible isomeric *N*-oxide forms (most probably the 3-oxide) and the symmetric bis-adduct **11a**, in the ratio 62:38,

Table 2. ^{13}C NMR assignments (δ)[a] of cycloadducts **8–12** and **15–18**.[b]

Compound	C-3a	C-4	C-5	C-6	C-7	C-7a	Isoxazoline C=N	R^1	R^2	Aryl groups C-1′	C-2′	C-3′	C-4′	2′-Me	4′-Me
8a 3 oxide	107.7	68.9	50.4	77.2	45.5	148.0	156.3, 157.6			122.5, 123.0	136.6, 136.8	129.0, 129.5	140.2, 140.3	19.9, 20.2	21.15, 21.2
9c 1-oxide	×	112.0	×	87.7	50.9	×	156.2	24.2	19.3	×	136.66, 136.74	128.6	139.8	19.3, 19.9	21.1
9c 3-oxide	109.4	107.5	147.4	87.8	53.6	148.6	156.4	24.3	18.5	123.0	136.3(br), 137.2(br)	128.8	139.7	19.8(br), 20.2(br)	21.1
9d 1-oxide	151.2	112.0	148.2	88.4	49.5	104.4	150.7	25.1	18.7	126.3	134.9(br), 135.7(br)	128.1, 128.2	132.0		
9d 3-oxide	109.5	107.6	145.9	88.7	52.2	148.8	152.2	24.8	18.5	125.8	135.0, 135.2	128.0, 128.1	131.9		
9e 1-oxide	150.9	112.8	146.1	80.1	44.4	104.0	154.6	20.5		122.7	136.7, 136.9	128.60, 128.62	139.9	19.3, 19.9	21.2
9e 3-oxide	109.6	108.5	142.4	80.4	47.0	148.2	154.8	20.7		122.5	136.9	128.8	139.8	19.8	21.1
9g 1-oxide	×	113.1	×	81.0	43.2	×	×	20.9		×	×	128.1, 128.6	132.13		
9g3-oxide	109.8	108.8	141.5	81.3	45.8	148.0	151.4	20.8		125.5	135.9	128.3	132.07		
9i 1-oxide	×	87.8	161.7	77.3	45.0	×	×	56.7		×	×	128.7	×	19.3	×
9i 3-oxide	111.0	83.9	159.1	77.8	47.9	146.8	154.7	56.8		122.3	137.0	128.9	140.0	19.9	21.2
9k 1-oxide	×	88.0	161.2	78.2	43.8	×	×	56.7		×	×	128.0	×		
9k 3-oxide	111.0	84.1	158.6	78.6	46.6	146.6	151.2	56.8		125.2	135.9	128.3	132.2		
10i 1-oxide	106.0	87.1	160.5	54.9	70.3	152.3	155.9	56.2		123.7	136.3, 137.1	128.4	139.2	19.7, 19.9	21.1
11a 1-oxide	148.5	78.4	45.4	43.4	77.1	105.7	156.0 157.8			123.04, 123.7	136.36, 136.4, 136.9	128.82, 128.95, 129.03	140.00, 140.17	19.5, 20.0, 20.1	21.1
11e 1-oxide	×	50.6	84.4	81.0	43.1	×	×	23.7		×	×	128.8	×	×	×
11e 3-oxide	106.6	48.4	84.3	81.8	45.7	148.8	155.2 159.0	24.2		123.5, 124.1	136.5, 136.6, 137.1	128.9, 129.1, 129.2	139.9, 140.2	19.1, 20.2, 20.3	21.2
15a	145.1	44.3	77.3	77.3	44.3	145.1	157.7			122.9	137.0	129.0	140.1	19.8	21.2
15c	145.5	50.3	86.9	86.9	50.3	145.5	157.8	20.2	20.2	123.1	137.6	129.2	140.0	21.0	21.2
16c	147.7	110.7	149.7	87.8	52.0	145.3	156.7	24.6	18.6	123.1	136.4(br), 137.2(br)	128.7	139.5	19.5(br), 19.9(br)	21.1
16d	147.8	110.9	148.3	88.8	50.7	145.0	152.7	25.1	18.7	125.9	135.2	128.1	131.8		

[a] Obtained at 75 MHz in $CDCl_3$. [b] Peaks indicated by a × did not appear.

respectively. That the product is not a mixture of 1-/3-oxide isomers of the same cycloadduct was concluded from the large differences in the chemical shifts of the analogous protons (Table 1) and carbons (Table 2), taking into account that the *N*-oxide group usually produces a shielding effect on the neighbouring protons of the magnitude of 0.2 ppm.[1] The large dispersion of the chemical shifts of the 4-H, 5-H, 6-H, 7-H protons of the major component corroborates our contention that this compound is the unsymmetric adduct **8a**. An alternative structure, like **12a** (analogous to **12b**, where Ar = mesityl, Scheme 1), for the minor component can be excluded by comparison of its spectral shifts with those of the cycloaddition products to benzofurazan, which are similar, while the proton chemical shifts of the hypothetical structure **12a** should be different (4-H and 7-H downfield, 5-H and 6-H upfield), as happens in the case of compound **12b**, which was isolated from reaction of substrate **1** with nitrile oxide **6**. Attempted deoxygenation of the mixture **8a**/**11a** with Ph_3P or $P(OEt)_3$ failed, probably due to the bulky substitution of the adducts.

Using the process outlined above for compounds **9e** and **11e**, the structures of cycloadducts **8**–**12** have been elucidated, and their 1-/3-oxide isomeric forms assigned. Compounds **8a** and **10i** and **10k** were, however, isolated in only one of the two possible isomeric *N*-oxide forms, and it was not possible to determine which isomer this was by simply following the above process.

However, the 3-oxide isomer is a reasonable suggestion for product **8a**, from the lack of hindered rotation in both the ^1H and ^{13}C NMR spectra at 20 °C, which shows that the mesityl group is far from the N→O group. The 1-oxide isomer is expected to show such a restricted rotation around the isoxazoline–mesityl C–C bond, similar to that observed in the case of one mesityl group of compound **11a**. For compounds **10i** and **10k** the 1-oxide was formed, as found by refluxing of cycloadduct **10i** in benzene solution for 10 h. The formation of the 3-oxide isomer was detected in the mixture by ^1H NMR spectroscopy.

For cycloadducts **8b**, **10k**, **11g** and **12b**, ^{13}C NMR spectra have not been obtained, either because they were isolated in trace amounts (**10k**) or because they are not very soluble in $CDCl_3$ (**8b**, **11g** and **12b**), and were dehydrogenated when $(CD_3)_2SO$ was utilized as NMR solvent. However, their ^1H NMR spectra leave no doubt as to their structures.

Table 3. FMO energies and coefficients of mesitonitrile oxide **5** and 2,6-dichlorobenzonitrile oxide **6**.

Compd.	FMO	*E* (eV)	C_a[a]	C	N	O
5[b]	LUMO	0.03	0.44	0.24	−0.40	0.25
	HOMO	−9.42	−0.37	0.44	0.28	−0.52
5[c]	LUMO	5.58	0.50	0.27	−0.42	0.28
	HOMO	−6.12	−0.32	0.41	0.21	−0.69
6[c]	LUMO	4.43	0.55	0.22	−0.40	0.29
	HOMO	−6.89	−0.24	0.46	0.18	−0.73

[a] Carbon attached to the dipole moiety. [b] Ref. 7. [c] Ref. 8.

Regarding the stereochemistry of the bis-adducts formed in the reactions discussed here, it would not be surprising to expect a *trans* arrangement for the two isoxazoline rings. Indeed, this was confirmed by the ^3J coupling constant between the 5-H and 6-H protons (*ca.* 3 Hz), which according to the simplified Karplus equations[6] corresponds to dihedral angles θ of *ca.* 120° or 50°. Stereochemical models show that for the more stable *cis* and *trans* arrangements of the isoxazoline rings in these compounds, θ has values of *ca.* 5° and 115°, respectively.

Regularities in the Cycloadditions to Benzofurazans and Benzofurazan N-*Oxides*.—The regio- and site-selectivity of these reactions can be approximated by using Frontier Molecular Orbital (FMO) terms of the reacting species. Geneste and co-workers[7] have reported FMOs of mesitonitrile oxide by the CNDO/S method, and Shiraishi and co-workers[8] reported calculations on both mesitonitrile and 2,6-dichlorobenzonitrile oxides by an *ab initio* SCF method with STO-3G basis set (Table 3).

An inspection of the reported data shows that the relative magnitudes of the AO coefficients are essentially the same, although there are different values for the frontier orbitals, caused presumably by the different level of approximations. Another noteworthy point is that in the case of 2,6-dichlorobenzonitrile oxide the LUMO orbital energy is more stabilized than the HOMO orbital is destabilized, in respect to the mesitonitrile oxide.

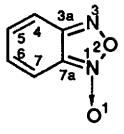
Analogous data for benzofurazan *N*-oxide have been taken by a CNDO/CI calculation on the unsubstituted benzofurazan *N*-oxide; these data are recorded in Table 4. The computations were run at the CNDO level of approximation using the semiempirical integral values proposed by Jaffé.[9] The input geometry was the one obtained by full optimization at the MNDO level.[10] During this optimization no symmetry conditions were imposed except for the planarity of the system.

From the FMOs of benzofurazan *N*-oxide we concluded that the HOMO dipole-controlled first addition might occur at the C(4)–C(5) double bond, with the LUMO dipole-controlled first addition at the C(6)–C(7) double bond, assuming that the energy change associated with those two different modes of FMO approaches is roughly proportional to the sum of the squares of the coefficients on the sites of attachment. On the other hand, FMOs of nitrile oxides **5** and **6** showed that a HOMO dipole-controlled interaction is more probable for mesitonitrile oxide than for 2,6-dichlorobenzonitrile oxide, and that a LUMO dipole-controlled addition is more probable for the 2,6-dichlorobenzonitrile oxide.

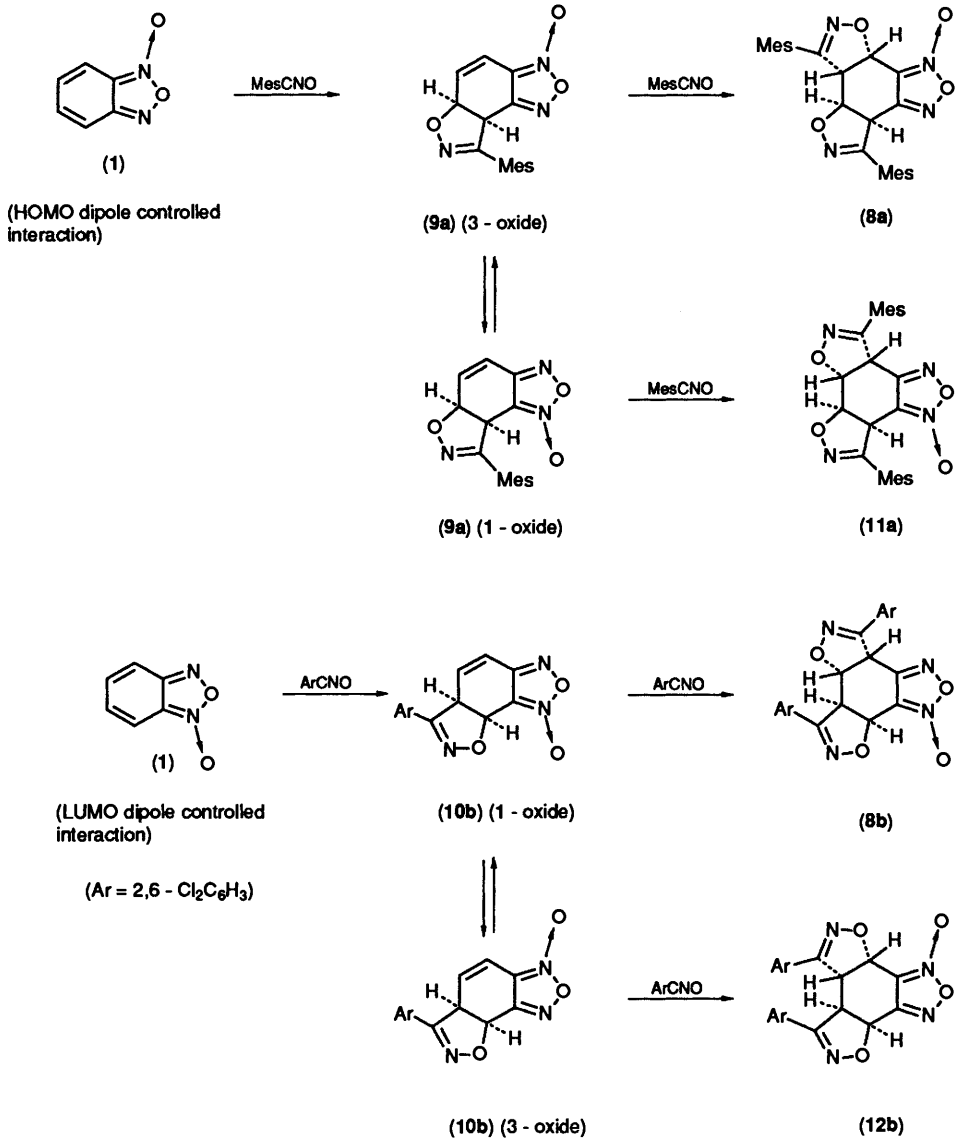
A HOMO dipole-controlled interaction should lead to the formation of the 3-oxide monoadduct of type (**9**). Although the magnitudes of coefficients on both C-4 and C-5 of benzofurazan *N*-oxide (Table 4) are almost equal (0.29 and 0.31, respectively), secondary orbital bonding interactions between the aromatic *ipso*-C of nitrile oxide HOMO and the N-3 furoxan LUMO stabilize this transition state.

A LUMO dipole-controlled interaction should also give rise to the mono-adduct **10** (1-oxide), whose transition state is better

Table 4. FMO energies and coefficients of benzofurazan *N*-oxide **1**.



FMO	*E* (eV)	O-1	N-1	O-2	N-3	C-3a	C-4	C-5	C-6	C-7	C-7a
LUMO	−1.835	0.42	−0.50	0.21	−0.36	0.22	0.29	−0.31	−0.23	0.32	0.11
HOMO	−9.87	0.43	−0.27	−0.10	0.58	−0.05	−0.34	−0.11	0.37	0.28	−0.33



Scheme 3.

stabilized because of the maximum overlapping as well as the secondary bonding orbital interactions between anionic termini of both nitrile oxide and furoxan.

The second addition to intermediate products **9** (3-oxide) and **10** (1-oxide) is expected to be governed by the same rules. However, this addition could occur before or after their isomerization to **9** (1-oxide) and **10** (3-oxide), respectively, as the isomerization reverses the orientation of the new adduct.

The following conclusions could be made by considering the structures of cycloadducts **8–12** and **15–18**:

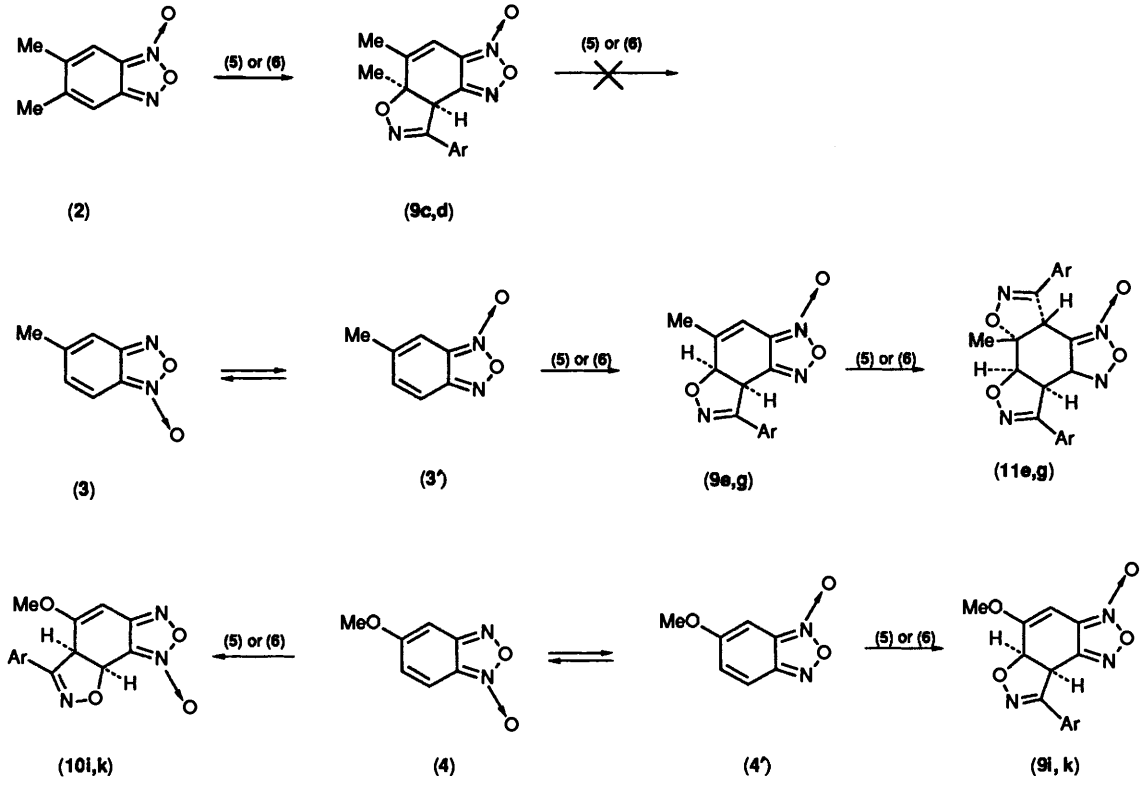
(*a*) Isolated cycloadducts **8–12** consist, mainly, of a pair of the two N→O isomers in an average ratio 90:10. This ratio reflects, predominantly, their formation pathway, and is partially a result of the equilibrium between the two isomers. Indeed, while compound **11e** was isolated in a 88:12 ratio of the two N→O isomers, the equilibrium restoration by refluxing of compound **11e** in benzene solution for 48 h yielded a *ca.* 1:1 ratio of the two N→O isomers.

(*b*) According to the previous discussion the first addition of mesitonitrile oxide (**5**) to benzofurazan *N*-oxide **1** could be regarded as a HOMO dipole-controlled interaction, while the first addition of 2,6-dichlorobenzonitrile oxide **6** to substrate **1** is a LUMO dipole-controlled one. Thus, mesitonitrile oxide **5**, when added to compound **1**, forms the intermediate **9a** (3-oxide), which can be isomerized to **9a** (1-oxide) (Scheme 3). A second addition to **9a** (3-oxide) affords the bis-adduct **8a** (3-oxide) as a LUMO dipole-controlled interaction, while the second addition to **9a** (1-oxide) is a HOMO dipole-controlled interaction and forms the bis-adduct isomer **11a**.

A LUMO dipole-controlled addition of nitrile oxide **6** to substrate **1** (Scheme 3) gives the intermediate **10b** (1-oxide), which reacts further, before and after its isomerization to **10b** (3 oxide). The second additions to **10b** (1 oxide) and **10b** (3-oxide) are HOMO and LUMO dipole-controlled interactions, respectively, and give the bis-adducts **8b** (3-oxide) and **12b** (Scheme 3).

(*c*) While the addition of mesitonitrile oxide **5** to benzofurazan **13** is highly regioselective, 2,6-dichlorobenzonitrile oxide **6** does not regioselectively add to benzofurazan **13**, and all possible isomeric bis-adducts are formed (Scheme 2). This might be attributed to the less nucleophilic character of compound **6** compared with **5**, which allows both HOMO- and LUMO-controlled interactions in the addition to benzofurazan **13**.

(*d*) Substitution at the benzene ring with electron-releasing



Scheme 4.

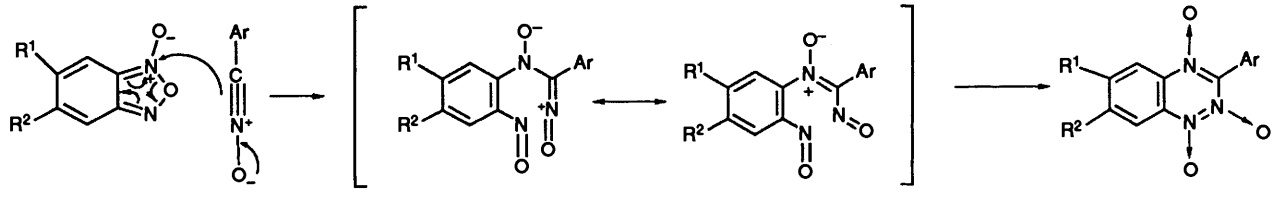
groups deactivates the attached double bond towards the cycloaddition in both benzofurazans and their *N*-oxides. On the other hand, it increases in some cases the regioselectivity, *e.g.* for reaction of compound **2** or compound **14** with nitrile oxide **6**. Indeed, while nitrile oxide **6** added to benzofurazan *N*-oxide **1** and benzofurazan **13**, affording bis-adducts with limited or no regioselectivity, its addition to the respective dimethyl derivatives **2** and **14** gave only one regioisomer mono-adduct. Steric factors may well be the reason for this non-generation of bis-adducts.

Furthermore, nitrile oxides **5** and **6** are added to the unsubstituted double bond of species **3'**, a form of 5(6)-methylbenzofurazan 1-oxide **3** that has the N→O group far from the unsubstituted double bond (Scheme 4), to afford regioselectively the mono-adducts **9e** and **9g**. No regioisomeric adduct from nitrile oxide **6** similar to species **10g** was isolated. Mono-adducts **9e** and **9g** react subsequently with an excess of nitrile oxide **5** and **6**, to give the bis-adducts **11e** and **11g**. The second addition is also regioselective and no product such as **8e** or **8g** was detected. The regioselectivity of this second addition is evidently dominated by the presence of the substituent (Me), which determines the orientation of the adduct, because of steric and electronic reasons.

The methoxy group in compound **4** strongly deactivates the attached double bond and furthermore favours[11] isomer **4** against isomer **4'** (Scheme 5), by a factor of 2:1. Thus, nitrile oxides **5** and **6**, when added to the unsubstituted double bond of isomer **4'**, give the mono-adducts **9i** and **9k**, whereas when added to the unsubstituted double bond of isomer **4** they undergo the reverse regioisomeric reaction to afford mono-adducts **10i** and **10k**. The presumption that compounds **10i** and **10k** are produced by addition to isomer **4** and not to **4'** is confirmed by the fact that products **10i** and **10k** (Scheme 4) consist exclusively of the 1-oxide isomeric form.

Benzo-as-*triazine Tri*-N-*oxides* **7**.—As already mentioned, these products are formed by a Beirut-type addition[1a] of the nitrile oxides to the furoxan ring of benzofurazan *N*-oxides, in yields up to 12%. The unsymmetrically substituted benzofurazan *N*-oxides **3** and **4** afforded pairs of isomeric 6- and 7-substituted benzo-*as*-triazine tri-*N*-oxides **7e/7f**, **7g/7h**, **7i/7j** and **7k/7l**, which were not separated, but characterized as mixtures.

The reaction affording the formation of these products seems to be a [4 + 2] cycloaddition, where the benzofurazan *N*-oxide and the nitrile oxide contribute four and two electrons, respectively. This reaction may involve an intermediate bis(nitroso)nitrone **20** (Scheme 5), possibly produced by a nucleophilic attack from the carbon of the nitrile oxide, which carries a considerable negative charge,[12] on the *N*-oxide nitrogen of the furoxan ring to afford the intermediate **19**. When



Scheme 5.

considering the '*o*-dinitroso equivalence' of benzofurazan *N*-oxides, this reaction is similar to that reported[13] between nitrile oxides and nitrosobenzene, where an analogous intermediate nitrosonitrone has been isolated. An intermediate similar to **20** has also been proposed in the reaction of benzofurazan *N*-oxides with nitrones.[4]

The suggested nucleophilic attack by the nitrile oxide at the furoxan ring might occur on the N-1 position (Scheme 5), which is a stronger electrophilic centre (Table 4) rather than on the N-3 position. The nucleophilic centre of the nitrile oxide is the carbon rather than the oxygen atom, because the C–N bond formed is stronger than the N–O bond.[14]

This proposed nucleophilic attack is in line with the results discussed here: the yields of tri-*N*-oxides decrease substantially when electron-releasing groups are added to the furoxan ring, as well as in the reactions of the less nucleophilic 2,6-dichlorobenzonitrile oxide **6** compared with those of mesitonitrile oxide **5**. When the electrophilic character of the furoxan ring was strengthened, as in the case of furoxano[3,4-*b*]quinoxalines,[15] the corresponding tri-*N*-oxides were formed in high yield as the only reaction products.

The structure assignment of tri-*N*-oxides **7a–1** was based on their ^{1}H and ^{13}C NMR data, as well as on an X-ray analysis performed on compound **7c**.[5] Owing to low yields, ^{13}C NMR spectra have not been obtained for all compounds.

Conclusion.—Two competitive reaction pathways occur when benzofurazan *N*-oxides react with nitrile oxides. The main reaction leads to a cycloaddition to the benzene ring, whose regioselectivity depends on the substituents on that ring. Electron-releasing substituents decrease the reactivity of the double bond, while the unsubstituted benzofurazan *N*-oxide affords exclusively the bis-adducts. The corresponding benzofurazans also react with nitrile oxides, and adducts with different orientations are formed.

A side reaction produced the novel triazine tri-*N*-oxides. We have shown and discussed elsewhere[15] the synthetic possibilities of this reaction, in which by entering a fused electron-withdrawing ring, such as quinoxaline, to the furazan *N*-oxide the tri-*N*-oxides were formed in high yield as the sole products.

Taking into account the high stereoselectivity of the bis-adducts, the controlled regioselectivity, depending on the substituents, the presence of the N→O group, and the nucleophilicity of the nitrile oxides, as well as the synthetic importance of the isoxazoline rings[12,16] which act as masked aldols and which can easily be opened[16] with retention of the construction of the rest of the molecule, it may be assumed that the reactions discussed here could become a powerful tool for the highly stereoselective synthesis of polysubstituted cyclohexane derivatives.

It should be emphatically noted that the real yields of the reaction products are much higher than the given ones, which have been calculated on the basis of the starting quantities of benzofurazan *N*-oxides. Use of a higher excess of nitrile oxides will significantly improve the yields of the products.

Experimental

M.p.s were determined on a Kofler hot-stage microscope and are uncorrected. IR spectra were recorded on a Perkin-Elmer 297 Infrared spectrophotometer for Nujol mulls, while mass spectra were obtained on a Hitachi–Perkin-Elmer MU-6L spectrometer at 70 eV. ^{1}H NMR spectra were recorded at 300 MHz on a Varian VXR-300 spectrometer and ^{13}C NMR spectra at 75 MHz on the same spectrometer and are quoted relative to tetramethylsilane as internal reference, in deuteriochloroform solutions. Microanalyses were performed on a Perkin-Elmer 240B element analyser. All reactions were monitored by TLC on precoated silica gel 60F-254 plates. All reaction solvents used were reagent grade and were distilled prior to use. Column chromatography was carried out on Kieselgel 60G (Merck) and solvents were distilled before use. Benzofurazan *N*-oxides **1–4**,[17] and nitrile oxides **5** and **6**,[18] were prepared according to the literature methods. Benzofurazans **13** and **14** were prepared by deoxygenation of the corresponding *N*-oxides **1** and **2** with Ph_3P. For compound **13**, m.p. 50–52 °C (lit.,[19] 51–53 °C). For compound **14**, m.p. 75–78 °C (lit.,[19] 81–82.5 °C).

Reaction of Benzofurazan N-*Oxide* **1** *with Mesitonitrile Oxide* **5**.—A solution of benzofurazan *N*-oxide (0.544 g, 4 mmol) and mesitonitrile oxide (1.23 g, 8 mmol) in dichloromethane (20 ml) was refluxed for 5 days. After evaporation of the solvent, the mixture was chromatographed on a column of silica gel with ethyl acetate–hexane (35:65) as eluant. Unchanged benzofurazan *N*-oxide and nitrile oxide were eluted first, followed by a mixture of the *isomers* **8a** and **11a** (0.733 g, 40%) in the ratio 62:38 (^{1}H NMR), m.p. 210–220 °C (Found: C, 68.2; H, 5.8; N, 12.0. $C_{26}H_{26}N_4O_4$ requires C, 68.10; H, 5.72; N, 12.22%); ν_{max} 1620 cm^{-1}; *m/z* 458 (M^+, 11%).

3-*Mesitylbenzo*-as-*triazine tri*-N-*oxide* **7a** (0.14 g, 12%) was then eluted (ethyl acetate eluant) as a yellow solid (Found: C, 64.5; H, 5.2; N, 14.2. $C_{16}H_{15}N_3O_3$ requires C, 64.63; H, 5.09; N, 14.14%), m.p. 195–196 °C; ν_{max} 1610 and 1595 cm^{-1}; δ_H 2.15 (6 H, s), 2.37 (3 H, s), 7.04 (2 H s), 7.90 (2 H, m), 8.40 (1 H, dd, *J* 8.3 and 1.5 Hz) and 8.57 (1 H, dd, *J* 2.0 and 8.2 Hz); δ_C 18.9, 21.3, 118.2, 120.7 (two peaks), 128.8, 130.9, 132.0, 133.6, 133.7, 137.7, 141.9 and 148.0; *m/z* 297 (M^+, 3%).

When the same reaction was repeated in a 1:1 molar ratio, the bis-adduct mixture **8a**/**11a**, and tri-*N*-oxide **7a** were again isolated in 35 and 9% yield respectively.

Reaction of Benzofurazan N-*Oxide* **1** *with* 2,6-*Dichlorobenzonitrile Oxide* **6**.—A solution of benzofurazan *N*-oxide (0.544 g, 4 mmol) and 2,6-dichlorobenzonitrile oxide (0.935 g, 5 mmol), in dichloromethane (20 ml), was refluxed for 5 days. The solvent was then partly evaporated off and crystals of the *bis-adduct* **8b** separated out (0.45 g, 22%), m.p. 235 °C (decomp.) (Found: C, 46.7; H, 1.95; N, 11.1. $C_{20}H_{10}Cl_4N_4O_4$ requires C, 46.90; H, 1.97; N, 10.94%); ν_{max} 1625, 1610 and 1605 cm^{-1}; *m/z* 510 (M^+, 1%).

The residue was chromatographed on silica gel with ethyl acetate–hexane (35:65). Unchanged benzofurazan *N*-oxide and nitrile oxide dimer were eluted at first, followed by the *bis-adduct isomer* **12b** (0.1 g, 5%), m.p. 234–235 °C (Found: C, 46.7; H, 2.1; N, 10.9%); ν_{max} 1620 and 1590 cm^{-1}; *m/z* 510 (M^+, 2%).

Tri-N-*oxide* **7b** (0.040 g, 2%) was eluted with ethyl acetate, m.p. 205–207 °C (decomp.) (from Et_2O) (Found: C, 47.9; H, 2.0; N, 12.8. $C_{13}H_7Cl_2N_3O_3$ requires C, 48.17; H, 2.18; N, 12.97%); ν_{max} 1600 cm^{-1}; δ_H 7.54 (3 H, s), 7.95 (2 H, m), 8.44 (1 H, dd, *J* 8.5 and 1.2 Hz) and 8.65 (1 H, dd, *J* 8.5 and 1.2 Hz); *m/z* 323 (M^+, 3%).

The bis-adduct **8b** and tri-*N*-oxide **7b** were formed in 46 and 3% yield, respectively, when the reaction was repeated in a 1:2 molar ratio, under the same conditions.[5]

Reaction of 5,6-*Dimethylbenzofurazan* N-*Oxide* **2** *with Mesitonitrile Oxide* **5**.—A solution of compound **2** (1.148 g, 7 mmol) and nitrile oxide **5** (1.207 g, 7.5 mmol) in dichloromethane (20 ml) was refluxed for 10 days. The reaction mixture was chromatographed on silica gel with ethyl acetate–hexane (35:65) as eluant. Unchanged nitrile oxide **5** was eluted first, followed by a mixture of starting *N*-oxide **2** and adduct **9c**, which were separated by a second column chromatography, with ethyl acetate–hexane (10:90) to give unchanged **2** (0.63 g recovery) and

adduct **9c** (0.45 g, 20%), m.p. 140–145 °C (from EtOH) (Found: C, 66.5; H, 6.0; N, 13.1. $C_{18}H_{19}N_3O_3$ requires C, 66.44; H, 5.89; N, 12.92%); ν_{max} 1630 and 1610 cm^{-1}; *m/z* 325 (M^+, 40%).

The yellow *3-mesityl-6,7-dimethylbenzo-as-triazine tri-N-oxide isomer* **7c** (0.16 g, 7%) was eluted with ethyl acetate, m.p. 195–197 °C (decomp.) (Found: C, 66.3; H, 6.0; N, 12.7%); ν_{max} 1 600 cm^{-1}; δ_H 2.13 (6 H, s,), 2.36 (3 H, s), 2.52 (3 H, s), 2.55 (3 H, s), 7.03 (2 H, s), 8.15 (1 H, s) and 8.31 (1 H, s); δ_C 18.8, 20.3, 20.4, 21.3, 117.4, 119.8, 120.9, 128.7, 129.1, 131.6, 137.7, 141.7, 143.6, 145.3 and 147.1; *m/z* 325 (M^+, 5%).

Reaction of 5,6-*Dimethylbenzofurazan* N-*Oxide* **2** *with* 2,6-*Dichlorobenzonitrile Oxide* **6**.—A solution of compound **2** (1.148 g, 7 mmol) and nitrile oxide **6** (1.41 g, 7.5 mmol) in dichloromethane (20 ml) was refluxed for 10 days, and the resulting mixture was chromatographed on silica gel with ethyl acetate–hexane (10:90) as eluant. A mixture of the excess of substrate **2** and nitrile oxide dimer were eluted at first, followed by the *adduct* **9d** (0.23 g, 9%), which was separated as crystals, m.p. 167–170 °C (from EtOH) (Found: C, 51.25; H, 3.15; N, 11.85. $C_{15}H_{11}Cl_2N_3O_3$ requires C, 51.15; H, 3.15; N, 11.93%); ν_{max} 1635, 1610 and 1580 cm^{-1}; *m/z* 351 (M^+, 100%).

Yellow *tri-N-oxide isomer* **7d** (0.025 g, 1%) was eluted with ethyl acetate, m.p. 194–195 °C (Found: C, 51.1; H, 3.2; N, 11.75%); ν_{max} 1600w and 1570 cm^{-1}; δ_H 2.54 (3 H, s), 2.57 (3 H, s), 7.52 (3 H, s), 8.18 (1 H, s) and 8.32 (1 H, s); *m/z* 351 (M^+, 2%).

Reaction of 5(6)-*Methylbenzofurazan* N-*Oxide* **3** *with Mesitonitrile Oxide* **5**.—A solution of 5(6)-methylbenzofurazan *N*-oxide **3** (0.6 g, 4 mmol) and mesitonitrile oxide **5** (0.644 g, 4 mmol) in dichloromethane (20 ml) was refluxed for 6 days. After evaporation of the solvent, the mixture was chromatographed on silica gel with ethyl acetate–hexane (20:80) as eluant. Unchanged *N*-oxide **3** was eluted first, followed by the *bis-adduct* **11e** (0.1 g, 5%), m.p. 285–295 °C (Found: C, 68.7; H, 6.0; N, 11.8. $C_{27}H_{28}N_4O_4$ requires C, 68.62; H, 5.97; N, 11.86%); ν_{max} 1610 cm^{-1}; *m/z* 472 M^+, 25%).

Mono-adduct **9e** (0.22 g, 18%) was then eluted, of which the two isomeric *N*-oxide forms (1- and 3-oxide) were separated chromatographically under the same conditions, to give **9e** 1-*oxide* and **9e** 3-*oxide* in pure form. For **9e** 3-oxide: m.p. 124–126 °C (Found: C, 65.7; H, 5.6; N, 13.7. $C_{17}H_{17}N_3O_3$ requires C, 65.58; H, 5.50; N, 13.50%); ν_{max} 1650 and 1600 cm^{-1}; *m/z* 311 (M^+, 50%). For **9e** 1-oxide: m.p. 155–157 °C (Found: C, 65.7; H, 5.6; N, 13.7%); ν_{max} 1640 and 1620 cm^{-1}; *m/z* 311 (M^+, 30%).

The mixture of *isomeric tri-N-oxides* **7e**/**7f** (0.148 g, 12%) was eluted with ethyl acetate, m.p. 220–222 °C (decomp.) (Found: C, 65.8; H, 5.5; N, 13.7%); ν_{max} 1600 cm^{-1}; δ_H 2.14 (6 H, s), 2.37 (3 H, s), 2.64 (3 H, s), 7.04 (2 H, s), 7.76 (1 H, d, *J* 8.6 Hz), 8.27 (1 H, d, *J* 8.6 Hz) and 8.37 (1 H, s), for the one isomer, and 2.14 (6 H, s), 2.37 (3 H, s), 2.66 (3 H, s), 7.04 (2 H, s), 7.69 (1 H, d, *J* 8.9 Hz), 8.20 (1 H, s) and 8.46 (1 H, d, *J* 8.9 Hz) for the other isomer, in the ratio 4:3; *m/z* 311 (M^+, 2%).

When the reaction was repeated under the same conditions with a 1:1.25 molar ratio only the bis-adduct **11e** (21%) and tri-*N*-oxides **7e**/**7f** (9%) were isolated.

Reaction of 5(6)-*Methylbenzofurazan* N-*Oxide* **3** *with* 2,6-*Dichlorobenzonitrile Oxide* **6**.—A solution of compound **3** (0.6 g, 4 mmol) and nitrile oxide **6** (0.935 g, 5 mmol) in dichloromethane (20 ml) was refluxed for 5 days. The solvent was evaporated off, and the resulting mixture was treated with diethyl ether to give microcrystals of *bis-adduct* **11g** (0.29 g, 14%), m.p. 230 °C (decomp.) (from $CHCl_3$) (Found: C, 47.7; H, 2.2; N, 10.9. $C_{21}H_{12}Cl_4N_4O_4$ requires C, 47.93; H, 2.30; N, 10.65%); ν_{max} 1610 cm^{-1}; *m/z* 524 (M^+, 5%).

The oily residue was chromatographed on silica gel with ethyl acetate–hexane (35:65) as eluant, to give, first, unchanged substrate **3** and nitrile oxide and then the *mono-adduct* **9g** (0.15 g, 11%), m.p. 142–144 °C (from CH_2Cl_2–hexane) (Found: C, 49.6; H, 2.5; N, 12.5. $C_{14}H_9Cl_2N_3O_3$ requires C, 49.72; H, 2.68; N, 12.43%); ν_{max} 1640 and 1620 cm^{-1}; *m/z* 337 (M^+, 4%).

A mixture of *tri-N-oxides* **7g**/**7h** 0.014 g, 1%) was eluted with ethyl acetate, m.p. 207–213 °C (Found: C, 50.1; H, 2.5; N, 12.35%); ν_{max} 1610, 1585 and 1560 cm^{-1}; δ_H 2.66 (3 H, s), 7.53 (3 H, s), 7.81 (1 H, d, *J* 8.6 Hz), 8.32 (1 H, d, *J* 8.6 Hz) and 8.37 (1 H, s) for the one isomer, and 2.69 (3 H, s), 7.53 (3 H, s), 7.71 (1 H, d, *J* 8.8 Hz), 8.22 (1 H, s) and 8.46 (1 H, d, *J* 8.8 Hz) for the other isomer, in the ratio 4:3; *m/z* 337 (M^+, 2%).

Reaction of 5(6)-*Methoxybenzofurazan* N-*Oxide* **4** *with Mesitonitrile Oxide* **5**.—A solution of compound **4** (0.664 g, 4 mmol) and nitrile oxide **5** (0.805 g, 5 mmol) in dichloromethane (20 ml) was refluxed for 6 days. The reaction mixture was then chromatographed on silica gel with ethyl acetate–hexane (35:65) as eluant. Unchanged substrate **4** and nitrile oxide were eluted first, followed by the *mono-adduct* **10i** (0.43 g, 33%), m.p. 182–184 °C (Found: C, 62.35; H, 5.3; N, 12.8. $C_{17}H_{17}N_3O_4$ requires C, 62.37; H, 5.24; N, 12.84%); ν_{max} 1640 cm^{-1}; *m/z* 327 (M^+, 24%), followed by the isomeric mono-adduct **9i** (0.09 g, 7%), m.p. 157–158 °C (Found: C, 62.5; H, 5.2; N, 13.0%); ν_{max} 1650, 1640 and 1610 cm^{-1}; *m/z* 327 (M^+, 14%).

A mixture of *tri-N-oxides* **7i**/**7j** (0.08 g, 6%) was eluted with ethyl acetate, m.p. 217–220 °C (Found: C, 62.0; H, 5.2; N, 12.7%); ν_{max} 1600 cm^{-1}; δ_H 2.15 (6 H, s), 2.37 (3 H, s), 4.04 (3 H, s), 7.04 (2 H, s), 7.52 (1 H, dd, *J* 9.5 and 2.7 Hz), 7.88 (1 H, d, *J* 2.7 Hz) and 8.30 (1 H, d, *J* 9.5 Hz) for the one isomer, and 2.14 (6 H, s), 2.37 (3 H, s), 4.05 (3 H, s), 7.04 (2 H, s), 7.44 (1 H, dd, *J* 9.5 and 2.6 Hz), 7.65 (1 H, d, *J* 2.6 Hz) and 8.46 (1 H, d, *J* 9.5 Hz) for the other isomer, in the ratio 5:1; *m/z* 327 (M^+, 5%).

Reaction of 5(6)-*Methoxybenzofurazan* N-*Oxide* **4** *with* 2,6-*Dichlorobenzonitrile Oxide* **6**.— A solution of compound **4** (0.664 g, 4 mmol) and nitrile oxide **6** (0.94 g, 5 mmol) in dichloromethane (20 ml) was refluxed for 6 days. The mixture was then chromatographed on silica gel with dichloromethane as eluant to give, first, unchanged *N*-oxide **4** and nitrile oxide dimer, followed by the regioisomers **10k** and **9k** as a mixture (0.68 g, total yield 48%). Analytical samples of both regioisomers **10k** and **9k** were obtained by chromatography of their mixture on silica gel with hexane–ethyl acetate (3:1) as eluant, where isomer **10k** was eluted first, followed by isomer **9k**. For compound **10k**: m.p. 142–148 °C (from CH_2Cl_2–hexane) (Found: C, 47.6; H, 2.5; N, 12.1. $C_{14}H_9Cl_2N_3O_4$ requires C, 47.48; H, 2.56; N, 11.87%); ν_{max} 1650 and 1610 cm^{-1}; *m/z* 353 (M^+, 12%).

For *compound* **9k**: m.p. 195–196 °C (from CH_2Cl_2–hexane) (Found: C, 47.6; H, 2.6; N, 11.9%); ν_{max} 1645 and 1630 cm^{-1}; *m/z* 353 (M^+, 10%).

A mixture of *tri-N-oxides* **7k**/**7l** (0.02 g, 1%) was eluted with ethyl acetate, m.p. 185–188 °C (Found: C, 47.6; H, 2.6; N, 11.7%); ν_{max} 1600 cm^{-1}; *m/z* 353 (M^+, 1%).

Reaction of Benzofurazan **13** *with Mesitonitrile Oxide* **5**.—A solution of benzofurazan **13** (0.24 g, 2 mmol) and mesitonitrile oxide (0.644 g, 4 mmol) in dichloromethane (10 ml) was refluxed for 3 days. *Bis-adduct* **15a** (0.29 g) crystallized out on cooling, while a second crop (0.13 g) of the same product was isolated after partial evaporation of the solvent, and addition of hexane (5 ml). Total yield 48%; m.p. 262–263 °C (decomp.) (from CH_2Cl_2–hexane) (Found: C, 70.6; H, 6.0; N, 12.8. $C_{26}H_{26}N_4O_3$ requires C, 70.57; H, 5.92; N, 12.66%); ν_{max} 1610 and 1600 cm^{-1}; *m/z* 442 (M^+, 5%).

Reaction of Benzofurazan **13** *with* 2,6-*Dichlorobenzonitrile*

Oxide **6**.—A solution of benzofurazan **13** (0.18 g, 1.5 mmol) and nitrile oxide **6** (0.55 g, 3 mmol) in dichloromethane (10 ml) was refluxed for 3 days. The solvent was then partly removed and hexane (5 ml) was added to give crystals (0.2 g) of a mixture of compounds **15b**, **17b** and **18b** in the proportions 1:1:2 (^{1}H NMR).

Reaction of 5,6-*Dimethylbenzofurazan* **14** *with Mesitonitrile Oxide* **5**.—A solution of compound **14** (0.222 g, 1.5 mmol) and nitrile oxide **5** (0.483 g, 3 mmol) in dichloromethane (10 ml) was refluxed for 6 days. After evaporation of the solvent, the reaction mixture was chromatographed on silica gel with ethyl acetate–hexane (1:3) as eluant to give, first, a mixture of starting benzofurazan **14** and nitrile oxide **5**, followed by a mixture of mono- and bis-adducts **15c** and **16c**. This mixture was fractionally crystallized from dichloromethane–hexane to give crystals of the *bis-adduct* **15c** (0.32 g, 45%), m.p. 286–288 °C (decomp.) (Found: C, 71.5; H, 6.7; N, 12.1. $C_{28}H_{30}N_4O_3$ requires C, 71.47; H, 6.43; N, 11.91%); ν_{max} 1610 and 1595 cm^{-1}; *m*/*z* 470 (M^+, 24%).

Mono-adduct **16c** was isolated chromatographically from the filtrate with diethyl ether–hexane as eluant (0.12 g, 26%), m.p. 88–89 °C (Found: C, 69.95; H, 6.2; N, 13.7. $C_{18}H_{19}N_3O_2$ requires C, 69.88; H, 6.19; N, 13.58%); ν_{max} 1635 and 1610 cm^{-1}; *m*/*z* 309 (M^+, 18%).

Reaction of 5,6-*Dimethylbenzofurazan* **14** *with* 2,6-*Dichlorobenzonitrile Oxide* **6**.—A solution of compound **14** (0.222 g, 1.5 mmol) and nitrile oxide **6** (0.56 g, 3 mmol) in dichloromethane (10 ml) was refluxed for 6 days. The mixture was then chromatographed on silica gel with ethyl acetate–hexane (35:65) as eluant to give starting material **14** and nitrile oxide dimer, followed by the *adduct* **16d** (0.16 g, 32%), m.p. 110–113 °C (Found: C, 53.7; H, 3.2; N, 12.3. $C_{15}H_{11}Cl_2N_3O_2$ requires C, 53.59; H, 3.29; N, 12.50%); ν_{max} 1635 and 1600 cm^{-1}; *m*/*z* 335 (M^+, 17%).

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