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SELECTIVITY IN CYCLOADDITIONS—VII[1]

CYCLOADDITIONS OF NITRILE OXIDES TO THIOPHENE AND BENZO[b]THIOPHENE. REGIOCHEMISTRY

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Abstract—Thiophene adds benzo- and mesitonitrile oxide yielding mainly cycloadducts **1** or products derived from them. With benzothiophene the regioselectivity of the cycloadditions of the two nitrile oxides is lower and both the cycloadducts **10** and **11** could be isolated in a 78:22 and 26:74 ratio, respectively.

Frontier orbital considerations, using EH and MINDO/3 calculations, and a comparison with the regioselectivities of related systems allowed elucidation of the observed regiochemistry. Some differences in orientation between cycloadditions and electrophilic substitution reactions of benzothiophene are pointed out and discussed.

Although detailed investigations are available concerning the reactivity of heteroaromatics in electrophilic substitution reactions[2] or in cycloadditions where the heteroaromatics enter as $\pi 4$ components,[3] their dipolarophilic reactivity with 1,3-dipoles has been only briefly studied. The penta-atomic heteroaromatics such as furan, thiophene and pyrrole have frontier orbital energies and shapes similar to those of cyclopentadiene,[4,5] whose reactivity toward nitrile oxides[6] was carefully studied,[7] and have a well known propensity toward substitution rather than addition reactions. Therefore the study of their dipolarophilic activity appeared promising in order to gain insight in the mechanism[8] of the 1,3-dipolar cycloadditions. Because of the resistance of aromatics toward addition, diradical and zwitterionic pathways, which are normally of no importance in 1,3-dipolar cycloadditions,[8] may compete with the concerted reaction. The desire to restore the aromaticity should then provide a very convenient way for the diradical or zwitterionic intermediates to form substitution products rather than cycloaddition products.

Previous papers of this series dealt with the cycloadditions of nitrile oxides to furan[4] and benzofuran.[1] A competition between the concerted and a minor two-step pathway was ascertained in the case of furan. Interestingly enough, whereas the 1,3-dipolar cycloaddition to furan is highly regioselective, in the case of benzofuran the regioselectivity of the reaction is low and is reversed going from benzonitrile oxide to mesitonitrile oxide. The following is a study of the cycloadditions of benzo- and mesitonitrile oxide to thiophene and benzo[b]thiophene. The dipolarophilic reactivity of these heteroaromatics in Diels–Alder reactions with tetrazines[9] and in 1,3-dipolar cycloadditions with ozone,[10] carbonyl ylides[11] and 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide[12] has recently been reported.

RESULTS

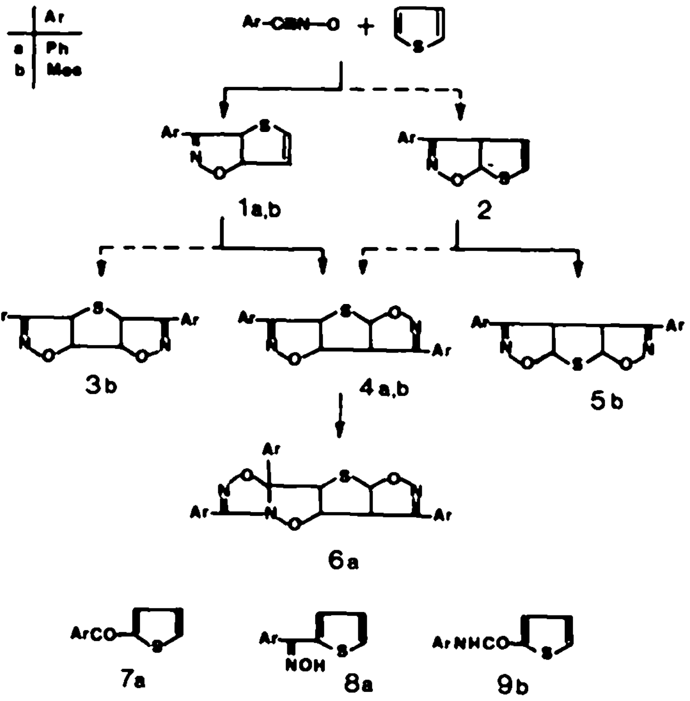
Thiophene is very slightly reactive with nitrile oxides and less reactive than furan. Only the slow generation *in situ* of benzonitrile oxide (BNO) in thiophene as solvent yielded, besides the dimerization products of BNO, a complex mixture of products, from which the monoadduct **1a** (1.9%) and the 2:1 and 3:1 adducts **4a** (2.5%) and **6a** (0.5%) could be isolated (Scheme 1). The formation of adducts **4a** and **6a** is easily understandable, since both the thioether double bond of **1a** and the strained isoxazoline C=N double bond are more reactive than the heteroaromatic system of thiophene. Under comparable conditions, up to a 30% yield of adducts was obtained with furan.[4]

The structures of the adducts are based on chemical and NMR evidence (Table 1). Acidic hydrolysis of **1a** gave the isoxazoline ring cleavage product, 2-benzoylthiophene **7a**. Compound **1a** added BNO on the thioether double bond with the same regiospecificity observed with enol ethers[4,13] to yield **4a**. Compound **6a** was obtained from **4a** and excess BNO. The NMR spectra of the adducts closely correspond to similar adducts obtained with cyclopentadiene.[7]

Because of the effect of sulphur,[14] the hydrogens α to the sulphur are shifted downfield by 1.3–1.5 ppm, and the coupling constants of the isoxazolinic hydrogens are in the usual range reported for *cis*-4,5-disubstituted isoxazolines.[15] The bridgehead proton of **1a**, adjacent to the C=C bond, couples with the olefinic protons and the values of the coupling constants are almost identical to those reported for 2,3-dihydrothiophene itself.[16] The asymmetric structure of **4a** is supported by spectral patterns which show all the ring protons distinguishable. The *anti* stereochemistry could be safely deduced by the lack of appreciable coupling (<1 Hz) in **4a** (and in **6a**) between the adjacent protons on the side joining the two heterocyclic rings, as previous examples show.[4,7]

Regioisomer **2a** or products deriving from it could not be detected in the reaction mixture. Furthermore the presence of significant amounts of 2-benzoylthiophen oxime **8a**—which can arise from a competing 1,3-addition reaction analogous to that observed with furan[4]—could be safely ruled out by tlc comparison of the reaction mixture with authentic samples of *syn* and *anti* oximes.[17]

Similar mono and bis cycloadducts were obtained with mesitonitrile oxide. This stable nitrile oxide, kept in thiophene for 7 months at r.t., yielded cycloadducts **1b** and **4b** in fair yields (1.6% and 40% resp.) along with the symmetrical bisadducts **3b** (2%) and **5b** (3%). Acidic hydrolysis cleaved the isoxazolinic ring of **1b**, giving the 2,4,6-trimethyl anilide of thiophene-2-carboxylic acid, **9b**.



Scheme 1.

Table 1. Chemical shifts[a] and coupling constants[b] of cycloadducts[c]

Compd	4-H[d]	5-H[d]	$J_{4,5}$
1a[e]	5.56 d	6.18 o	10.6
1b[f]	5.42 d	6.18 o	10.6
3b	5.27 d	5.82 d	7.3
4a	5.13 d 5.13 d	5.65 d 6.73 d	8.0 8.0
4a[g]	5.37 d 5.30 d	5.62 d 6.80 d	7.3 8.0
4b	4.98 d 4.97 d	5.17 d 6.74 d	8.0 7.7
5b	4.22 d	6.54 d	7.4
6a	5.31 d[h] 5.03 d[h]	6.72 d[h] 5.40 d[h]	8.0[h] 3.3[h]
10a	5.62 d	6.39 d	9.6
10b	5.48 d	6.43 d	9.8
11a	5.52 d	6.68 d	9.2
11b	5.37 d	7.08 d	9.2

[a] Chemical shifts in parts per million (δ) from internal Me_4Si. Multiplicity: d, doublet; q, quartet; o, octet. Solvent: $CDCl_3$.

[b] In Hz.

[c] Satisfactory combustion analytical data C, H, N (±0.4%) have been obtained for these compounds. Ed.

[d] Numbering refers to the isoxazoline ring.

[e] Dihydrothiophene ring: 2-H 6.47 q; 3-H 5.84 q; $J_{2,3}$ 6.3; $J_{3,5}$ 2.5; $J_{2,5}$ 1.1

[f] Dihydrothiophene ring: 2-H 6.43 q; 3-H 5.81 q; $J_{2,3}$ 6.2; $J_{3,5}$ 2.6; $J_{2,5}$ 1.1.

[g] In acetone-D_6.

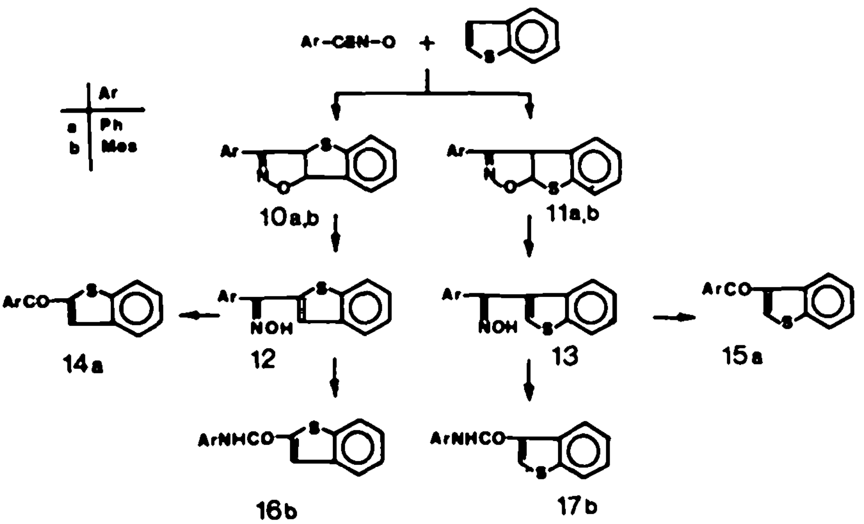
[h] Isoxazolidine ring protons.

The different behaviour of the mesityl derivative **1b**, with respect to **1a**, can be ascribed to the high migratory aptitude of the mesityl group, which causes a facile Beckmann rearrangement of the intermediate oxime. Compound **1b** added mesitonitrile oxide yielding bisadducts **4b** and **3b** in the same ratio (*ca.* 20:1) observed in the cycloaddition to thiophene. The NMR spectra support the assignments. The spectra of **1b** and **4b** closely correspond to those of the phenyl derivatives. In the symmetrical bisadduct **5b** the C-5 isoxazolinic protons appear at low field, 6.54 δ, because of the deshielding effect of oxygen and sulphur whereas the doublet of the other isoxazolinic protons is well separated at 4.22 δ, in the usual range reported for C-4 isoxazolinic protons. In adduct **3b** both the isoxazolinic protons experience the deshielding effect of oxygen and sulphur, resp., and have close chemical shifts. An *anti* stereochemistry is suggested for the symmetrical adducts **3b** and **5b**, by analogy to **4b** and to the predominant formation of the *anti* bisadducts on cyclopentadiene, where the stereochemistry could be safely deduced from the equivalence of the methylene protons.[7]

Benzo[b]thiophene is also slightly reactive toward nitrile oxides. By generating BNO in the presence of 10 equivs of benzothiophene in ether, we isolated a 2% yield of cycloadducts **10a** and **11a** in a 78:22 ratio in addition to the products of the heavily competing dimerization of BNO. With mesitonitrile oxide a mixture of adducts **10b** and **11b** in the ratio 26:74 was obtained with a total yield of 30% (Scheme 2).

A neat inversion of regiochemistry occurs here, analogous to that observed in the cycloaddition to benzofuran.[1]

The structures of the adducts rely upon chemical and NMR evidence. The protons α to sulphur are deshielded by 1.1 ppm with respect to the analogous indene adducts.[7] Acidic hydrolysis of the BNO adducts **10a** and **11a** yielded the known 2- and 3-benzoyl benzothiophene **14a** and **15a** resp., whereas the mesitonitrile oxide ad-



Scheme 2.

ducts **10b** and **11b** were cleaved to yield the 2,4,6-trimethylanilides of the benzo[b]thiophene-2- and 3-carboxylic acids, **16b** and **17b** resp.

This behaviour differs from the results obtained with the analogous adducts to benzofuran, where only the adducts corresponding to **11** are easily cleaved on the benzofuran ring, yielding isoxazole derivatives.[1]

The oximes **12a** and **13a** have been obtained by oximation of the ketones. They are stable under the cycloaddition conditions and could not be detected by tlc in the reaction mixtures.

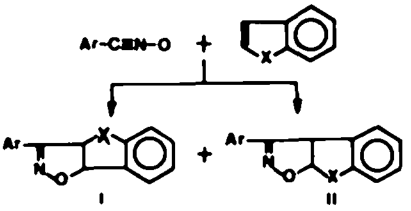
DISCUSSION

Thiophene and benzo[b]thiophene are slightly reactive toward nitrile oxides. The competing dimerization complicates isolation and detection procedures. However the results are in accord with a predominant concerted cycloaddition of nitrile oxides to thiophene and benzothiophene. The 1,3-addition products —the 2-benzoylthiophen oxime and the oximes **12a** and **13a** or products derived from them— were not detected in the reaction mixtures to any significant extent. As in the case of furan,[4] they are probably in the order of a few % of the total yield of the cycloadducts and easily escape isolation and detection.

Oximes were isolated in the cycloaddition of nitrile oxides to 3-pyrrolidinothiophene and their formation was attributed to the easy ring-chain tautomerism of the [not detected] cycloadduct.[18]

The regioselectivity of the cycloadditions of the two nitrile oxides is high with thiophene and is analogous to those reported for furan,[4] cyclopentadiene[7] and butadiene.[6] On the contrary a wide variation occurs in the series of the benzoderivatives (Table 2). In the cycloadditions of BNO to styrene[6] and indene[7] the ratio I/II is still high and lowers with benzofuran and benzothiophene. On going from BNO to mesitonitrile oxide, the regiochemical effect is noteworthy, affecting the $\Delta\Delta G^{\neq}$ by similar values, 1–1.3 kcal/mole. In the case of indene, the regiochemistry is reduced, and in the case of

Table 2. Regioisomer distribution in the cycloaddition of nitrile oxides with styrene, indene, benzofuran and benzothiophene



X	I/II Ph[c]	I/II Mes[d]	$\Delta\Delta G^{\neq}_{I/II}$[a] Ph	$\Delta\Delta G^{\neq}_{I/II}$[a] Mes	Change[a,b]
H,H	100: 0	100: 0			
CH_2	96: 4	76:24	1.72	0.68	1.04
O	70:30	26:74	0.46	−0.62	1.08
S	78:22	26:74	0.68	−0.62	1.30

[a] kcal/mole, ±0.1 kcal/mole.

[b] $\Delta\Delta G^{\neq}_{I/II}(Ph) - \Delta\Delta G^{\neq}_{I/II}(Mes)$.

[c] 0°, ether.

[d] 25°, benzene.

benzofuran and benzothiophene a change in the preferred regioisomer occurs. The simple frontier molecular orbital (FMO) treatment[19] satisfactorily accounts for the observed trends.

The HOMOs of thiophene and benzothiophene are high lying. The lowest vertical ionization potentials are 8.9 eV[20,21] and 8.2 eV[21] respectively and were assigned to ionization from π orbitals. Ionizations from orbitals mainly localized on the sulphur lone pair occur at 9.5 and 8.76 eV respectively. The lowest IP's are comparable to those reported for furan (8.88 eV),[22] cyclopentadiene (8.57 eV)[3c] and butadiene (9.03 eV)[22] and to those of benzofuran (8.66 eV),[21b] indene (8.20 eV)[21b] and styrene (8.55 eV).[21b] Moreover the similarity of the values of the singlet $\pi \rightarrow \pi^*$ UV transitions for cyclopentadiene and the penta-atomic heteroaromatics[23] as well as for their benzoderivatives[24] suggests[25] that the LUMO energies are also comparable. Therefore —as previously discussed for cyclopentadiene and indene,[7] furan[4] and benzofuran[1]— the HOMO(dipolarophile)-LUMO(nitrile oxide) interaction is expected to govern the cycloaddition with benzonitrile oxide. A similar HOMO-dipolarophile control is expected for the cycloaddition to the 2,3-dihydrothiophene system of 1, whose regioselectivity is formally reversed with respect to thiophene. The IP of 2,3-dihydrothiophene can be estimated at 8.1 eV from model compounds.[26]

The shapes of the π-orbitals are shown in Fig. 1, as obtained from Extended Hückel (EH)[27] calculations. The EH and MINDO/3[28] eigenvalues and eigenvectors are given in Table 3.[29] Also in the table is the polarization of the FMOs, defined as the difference between the squares of the coefficients on the C=C double bond of the heterocyclic ring. Both methods of calculations show a fair agreement upon the values of the HOMO polarizations, and upon the trend of the LUMO polarizations. The FMOs correspond essentially to the familiar FMOs of butadiene, styrene and enol ethers, whose double bonds are highly polarized. In benzothiophene, however, quantitative changes occur in the HOMO. The polarization of the double bond is remarkably reduced with respect to styrene and indene, similar to what found for benzofuran.[1] This can be attributed to the second order mixing of the styrene FMOs induced by interaction with the sulphur and oxygen lone pairs.[1,30]

Therefore in the cycloadditions of BNO —whose dipole carbon is the electrophilic site[31] and bonds to the HOMO position of the dipolarophile with the largest HOMO coefficient— the regioselectivity nicely reflects the change of the HOMO polarization. The effect of the stronger LUMO(dipole)-HOMO(dipolarophile) interaction is moderated somewhat in the case of these diene- and styrene-like dipolarophiles by the weaker HOMO(dipole)-LUMO(dipolarophile) interaction, which has opposite regioselectivity consequences because of the higher nucleophilicity of the oxygen of the dipole.[31] Since the regioselectivity effects are proportional to the alkene polarizations,[19c] the strong increase of the LUMO polarization observed in the case of benzofuran also concurs sizably in determining the lowering of regioselectivity with this dipolarophile.[1]

In the cycloadditions with the more nucleophilic mesitonitrile oxide the weaker HOMO(dipole)-LUMO(dipolarophile) interaction gains importance because of the raising of the orbitals of the dipole. The IPs of mesitonitrile oxide and BNO are 8.35 and 8.98 eV, resp.[32] and the EAs have been estimated at −0.11 and 0.50 eV, resp.[1] The balance between regioisomers is then shifted toward the minor isomers. This causes a decrease of regioselectivity with thiophene, as inferred by the isolation of bisadduct 5b, and a change of the preferred regioisomer with benzothiophene. A similar situation should hold for 2,4,6-trimethyl-3,5-dichloro benzonitrile oxide, which gives with benzothiophene a ratio of regioisomers I/II of 3:7,[12] close to that observed with mesitonitrile oxide.

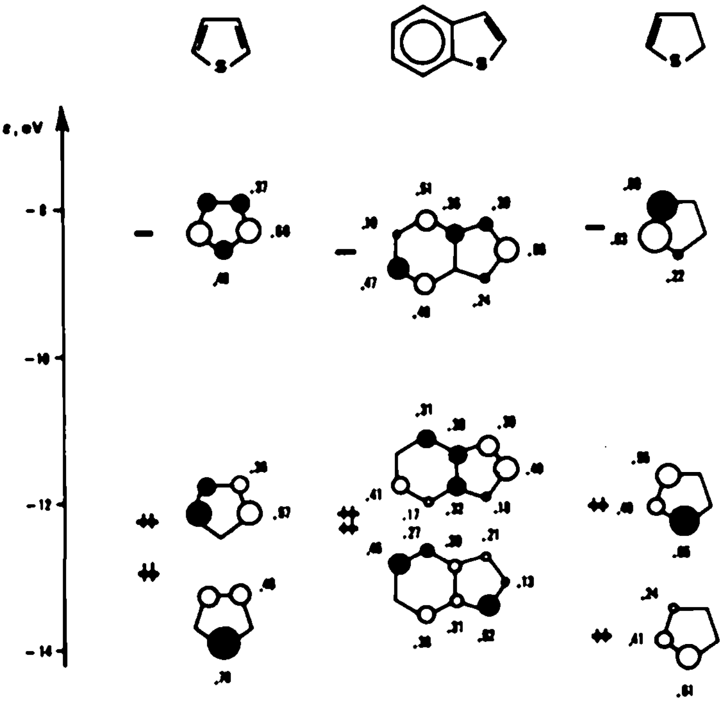
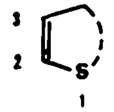


Fig. 1. Frontier molecular orbitals of thiophene, benzo[b]thiophene and 2,3-dihydro thiophene (EH).

Table 3. Eigenvectors and eigenvalues for the frontier orbitals[a]



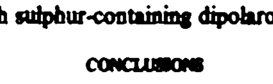
	C_1	C_2	C_3	p^b	E(eV)	C_1	C_2	C_3	p^b	E(eV)
EH										
2,3-Dihydrothiophene	-.65	.40	.55	-.13	-12.06	.22	-.83	.80	.05	-7.79
Thiophene	.00	.57	.36	.19	-12.21	.48	-.66	.37	.29	-8.35
Benzo[b]thiophene	-.16	.49	.39	.09	-12.16	.24	-.56	.30	.22	-8.64
MINDO/3										
2,3-Dihydrothiophene	-.70	.36	.50	-.11	- 8.58	.13	-.70	.62	.10	1.77
Thiophene	.00	.58	.40	.18	- 8.64	.26	.57	.36	.20	1.19
Benzo[b]thiophene	-.20	.48	.39	.08	- 8.38	.19	-.47	.26	.15	0.82

[a] Experimental geometries of 2,3-dihydrothiophene and thiophene were used for the calculations. 2,3-Dihydrothiophene: T. Ueda and T. Shimanouchi, *J. Chem. Phys.* 47, 5018 (1967). Thiophene: B. Bak, D. Christensen, L. Hansen-Nygaard and J. Rastrup-Andersen, *J. Mol. Spectrosc.* 7, 58 (1961). For the geometry of benzo[b]thiophene see Ref. 21b.

[b] Polarization defined as $C_2^2 - C_3^2$.

No significant wide change in regioselectivity is expected for dihydrothiophene, where the two interactions favor the same regioisomer. The minor regioisomer 3 could, however, be isolated with mesitonitrile oxide.

Finally it should be noted that also the second HOMO of thiophene and benzothiophene are high lying and show definite lone pair character. They will cause the facile formation of internal salts such as 18.[33]



18

Although never isolated, they could explain the formation of diphenyl- or dimesitylureas, always present in varying amounts in the reaction mixtures from cycloadditions with sulphur-containing dipolarophiles.[34]

CONCLUSIONS

BNO adds to furan, benzofuran and thiophene respecting the rules of orientation of electrophilic substitution reactions. However with benzothiophene the major isomer results from attack of the nitrile oxide carbon on the α-position, whereas the classical site of the attack of electrophiles is the β-position.[2,35] Since the frontier orbital treatment consistently accounts for the regioselectivity of the concerted cycloadditions of BNO with the heteroaromatics so far investigated, explanations for this apparent anomaly have to be offered.

In electrophilic substitutions the stability of the Wheland intermediates are believed to be mainly responsible for orientation.[2,36] The recently demonstrated[37] large effect of sulphur and second-row elements in stabilizing adjacent cationic sites then provides the rationale for the predominant β orientation of electrophiles.

Although the reactivity of heteroaromatics toward nitrile oxides is low because of the loss of aromaticity, the transition state of these concerted cycloadditions occurs early,[38] so that frontier orbital interactions still control the regiochemistry.

EXPERIMENTAL

All m.ps are uncorrected. IR spectra: "Perkin-Elmer" model 257 spectrophotometer, Nujol mulls. NMR spectra: "Perkin-Elmer" R12 spectrometer, 60 MHz. Gaschromatographic analyses were carried out on a glass column, 1% Carbowax 20 M and 1% Apiezon L on Gaschrom P, with a column temp. of 175° on a "Carlo Erba" Fractovap instrument. Microanalyses were performed by Dr. L. Maggi Dacrema. Satisfactory analytical data (±0.4% for C,H,N) were obtained for all the compounds listed in Table 1. Column chromatography and tlc: silica gel H and GF_{254} (Merck), respectively, eluant cyclohexane: EtOAc 9:1 to 7:3 unless otherwise specified. The identification of samples from different experiments was secured by mixed m.ps and superimposable IR spectra.

Cycloadditions of benzonitrile oxide

(a) *Thiophene.* To a stirred ice-cooled soln of benzhydroximic acid chloride (10g, 64 mmoles) in thiophene (100 ml), a stoichiometric amount of Et_3N was added over a 2 hr period. After keeping overnight at 0° and 2 days at r.t., the mixture was diluted with anhyd benzene (200 ml), the Et_3NHCl was filtered off and the filtrate was evaporated under reduced pressure, leaving a residue. Column chromatography gave 4.1g of 3,4-diphenylfuroxan impure of 3,5-diphenyl-1,2,4-oxadiazole (53%) along with the following products: (i) monoadduct 1a, (250 mg, 1.9%), m.p. 104–105° from EtOH; (ii) trisadduct 6a (50 mg, 0.5%), m.p. 160–162° from EtOH; (iii) bisadduct 4a (260 mg, 2.5%), m.p. 195–196° from EtOH; (iv) 330 mg of diphenylurea.

Cycloaddition of BNO (3 mmoles) to the monoadduct 1a (1 mmole) in anhyd benzene (20 ml) at r.t. led to the bisadduct 4a, which was isolated by column chromatography with a 34% yield, along with diphenylfuroxan and unchanged 1a (40%). Cycloaddition of excess BNO (10 equivs) to 4a gave similarly a low yield (10%) of trisadduct 6a. Unchanged 4a (30%) was recovered.

(b) *Benzo[b]thiophene.* To a stirred ice-cooled soln of benzhydroximic acid chloride (5g, 32 mmoles) and benzothiophene (43g, 320 mmoles) in anhyd ether (150 ml), a stoichiometric amount of Et_3N was added over a 2 hr period. After 2 days the mixture was diluted with anhyd benzene (150 ml), the Et_3NHCl was filtered off and the filtrate was evaporated under reduced pressure, leaving a residue. Column chromatography yielded unreacted benzothiophene, a mixture of 3,4-diphenylfuroxan and 3,5-diphenyl-1,2,4-oxadiazole (6.2g, about 54% yield), cycloadduct **10a** (115 mg, 1.4%), m.p. 147-8° from EtOH, and cycloadduct **11a** (30 mg, 0.4%), m.p. 132° from EtOH.

In a duplicate experiment the unreacted benzothiophene was distilled (bath up to 100° at 0.1 mm). The residue was chromatographed, yielding a mixture of **10a** and **11a** (150 mg, 1.9%) in a 78:22 ratio, as determined by NMR integration of the doublets of the isoxazolinic protons.

Cycloadditions with mesitonitrile oxide

(a) *Thiophene.* A soln of mesitonitrile oxide (3.22g, 20 mmoles) in thiophene (50 ml) was stored at r.t. for 7 months. Dimesitylurea (0.2g, 6%) was filtered off. After evaporation of the solvent the residue was crystallized from EtOH, affording 1.26g (31%) of bisadduct **4b**, m.p. 229–230°. The mother liquors were evaporated. Column chromatography gave, besides dimesitylfuroxan (5%), (i) monoadduct **1b**, (83 mg, 1.6%), m.p. 111–112° from EtOH, (ii) a mixture of bisadducts **4b** (0.36g, 9%) and **5b** (0.12g, 3%), m.p. 262–3° from EtOH, which was separated by column chromatography, $CHCl_3$ serving as eluant, (iii) bisadduct **3b** (80 mg, 2%), m.p. 257–8° from EtOH, (iv) 0.9g (21%) of N-mesityl ethyl carbamate.

(b) *Benzo[b]thiophene.* A soln of mesitonitrile oxide (3.22g, 20 mmoles) and benzo[b]thiophene (13.4g, 0.1 mole) in anhyd benzene (20 ml) was held at r.t. for 4 months, until the nitrile oxide was no longer detectable by tlc. Dimesitylurea (0.14g, 4%) was filtered off. Evaporation of the solvent left a thick oil from which unreacted benzothiophene was removed under vacuum (bath up to 100°, 0.1 mm). The residue was chromatographed giving **11b** (1.31 g, 22%), m.p. 150–151° from EtOH, and **10b** (0.52 g, 8%), m.p. 155–156° from EtOH.

In a duplicate experiment the ratio of cycloadducts **10b**/**11b** was determined by glc and was found to be 26:74 ± 2.

Oximes **8a**, **12a** *and* **13a**. The *syn* and *anti* oximes **8a** have been prepared by oximation of 2-benzoyl thiophene according to the literature.[17,39] Chromatographic separation, eluant benzene, of the mixture of the two oximes m.p. 91–2° yielded the E oxime, colorless crystals m.p. 113–4° from aqueous EtOH (20%) and the Z oxime, colorless crystals m.p. 114° from aqueous EtOH (40%). The phenyluretane of the Z oxime was crystallized from EtOH, m.p. 122–3°, ν_{CO} 1735 cm^{-1} and ν_{NH} 3270 cm^{-1}. Beckmann rearrangement [39a] of the major oxime afforded quantitatively the thiophene-2-carboxanilide **9a**, m.p. 144–5°, identical with an authentic specimen.[40]

Compounds **14a** and **15a** have been synthetized from benzo[b]thiophene, benzoyl chloride and $SnCl_4$.[41] They have been separated by column chromatography, where **15a** is eluted first. The oximes **12a** and **13a** have been obtained with fair yields refluxing **14a** and **15a** with an excess of $NH_2OH \cdot HCl$ (5 equivs) in ethanol for 24 hr. The mixtures were concentrated, diluted with water and extracted with $CHCl_3$. The extracts were dried and the solvent evaporated, yielding mixtures of *syn* and *anti* oximes, which were separated by column chromatography, benzene serving as eluant. Oximes **12a**: E oxime, colorless crystals m.p. 170–1° from benzene (30%) and Z oxime, colorless crystals m.p. 165–6° from benzene (50%). (Found: C, 70.95; H, 4.41; N, 5.71. $C_{15}H_{11}NOS$ requires: C, 71.11; H, 4.37; N, 5.52%.) The phenyl uretane of the Z oxime was crystallized from EtOH, m.p. 193–5°, ν_{CO} 1731 cm^{-1} and ν_{NH} 3270 cm^{-1}. Oximes **13a**: E oxime, colorless crystals m.p. 120–1° from hexane (25%) and Z oxime, colorless crystals m.p. 161–2° from benzene (50%). (Found: C, 70.96; H, 4.42; N, 5.80. $C_{15}H_{11}NOS$ requires: C, 71.11; H, 4.37; N, 5.52%.) The phenyl uretane of the Z oxime was crystallized from EtOH, m.p. 197–8°, ν_{CO} 1730 cm^{-1} and ν_{NH} 3300 cm^{-1}. All the oximes were hydrolyzed to the starting benzoyl derivatives **14a** or **15a** on boiling for 1 hr with a 1:1 mixture of HOAc and 20% sulfuric acid. Beckmann rearrangement of the Z oximes **12a** and **13a** with PCl_5 in ether, 0°, 24h yielded quantitatively **16a**, m.p. 187.5–188.5°, and **17a**, m.p. 172–3°, resp., identical with samples prepared according to the literature.[42,43]

The oximes are stable under the conditions of the cycloaddition reactions, in ether in the presence of $NEt_3/NEt_3 \cdot HCl$. A comparison of the oximes with the cycloaddition mixtures by tlc allowed to exclude the presence of significant amounts of the oximes in the cycloaddition mixtures.

Cleavage of monoadducts **1**. A soln of **1a** (1 mmole) in HOAc (3 ml) and 20% H_2SO_4 (3 ml) was refluxed for 1 hr. After cooling, the mixture was poured on ice and extracted with $CHCl_3$. The extracts were washed with 10% NaOH and dried on Na_2SO_4. The solvent was evaporated giving a 64% yield of **7a**, b.p. 100–130° (bath) at 0.1 mm, m.p. 55–56° from petroleum ether, identical with an authentic sample.[39a]

Under similar conditions **1b** gave with a 70% yield **9b**, as colorless crystals m.p. 164–5° from EtOH, ν_{CO} 1630 cm^{-1} and ν_{NH} 3250 cm^{-1}. (Found: C, 68.28; H, 6.23; N, 5.56. $C_{14}H_{15}NOS$ requires: C, 68.53; H, 6.16; N, 5.70.) The carboxamide was independently obtained from thiophen-2-carbonyl chloride[40] and 2,4,6-trimethylaniline.

Cleavage of cycloadducts **10** *and* **11**. A soln of the cycloadducts (1 mmole) in HOAc (3 ml) and 20% H_2SO_4 (3ml) was refluxed until they were no longer detectable by tlc (5 hr). Operating as above cycloadducts **10a** and **11a** led with almost quantitative yield to **14a** and **15a** resp.

Similarly, **10b** and **11b** yielded **16b** and **17b**, resp. The carboxamide **16b** was crystallized from EtOH, colorless needles m.p. 210–11°, ν_{CO} 1630 cm^{-1} and ν_{NH} 3270 cm^{-1}. (Found: C, 72.90; H, 5.62; N, 4.69. $C_{18}H_{17}NOS$ requires: C, 73.18; H, 5.80; N, 4.74%.) The carboxamide **17b** was crystallized from EtOH, soft needles m.p. 182–3°, ν_{CO} 1640 cm^{-1} and ν_{NH} 3210 cm^{-1}. (Found: C, 72.87; H, 5.94; N, 4.82. $C_{18}H_{17}NOS$ requires: C, 73.18; H, 5.80; N, 4.74%.) The carboxamides were independently obtained from benzothiophene 2- and 3-carbonyl chloride[42,43] and 2,4,6-trimethylaniline.

Calculations. The computations were executed with the EH,[27] MINDO/3[28] and CNINDO[29a] programs on a Honeywell 6030 computer.

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