## Generation and Trapping of Ortho-Substituted Thionitrosobenzenes: Competitive Diels-Alder and Ene Reactions with Dimethylbutadiene

Martin R. Bryce\* and Julie N. Heaton, Department of Chemistry, University of Durham, Durham, DH1 3LE, UK

Abstract: Transient thionitrosoarenes, ArN=S, (2) that bear a substituent (CN, Br or Me) *ortho* to the reactive N=S group have been generated by two entirely different routes and intercepted with dimethylbutadiene to afford mixtures of Diels-Alder and ene adducts, (3) and (4), respectively; the ene adduct predominates for each system.

We have recently developed an expedient route to transient thionitrosoarenes (ArN=S), e.g. (2a)-(2d), from N-(arylaminothio)phthalimides (1) and explored their trapping reactions with conjugated dienes.<sup>1</sup> With 2,3-dimethylbutadiene, Diels-Alder reaction of species (2a)-(2d) competes with ene reaction to yield isomeric products (3) and (4), respectively. Studies on a range of *para*-substituted derivatives (2a)-(2d) clearly established that electron-donating substituents on the benzene ring favour Diels-Alder reaction, while electronwithdrawing substitutents favour ene reaction<sup>1a,1c</sup> (Table 1). This was in accord with the previous observation by Meth-Cohn and van Vuuren that PhCO<sub>2</sub>N=S generated by an entirely different route, undergoes both Dicls-Alder and ene reactions.<sup>2</sup>

We now report the trapping of *ortho*-substituted thionitrosoarenes (2), generated analogously from precursors (1). A new feature of these reactions is that the distribution of products is now significantly influenced by both a steric effect from the o-substituent as well as an electronic effect. The steric contribution is clearly seen in the three systems for which we have studied both the o- and p-isomers, viz methyl-, bromoand cyano-thionitrosobenzene. In each case, when the substituent is *ortho* to the reactive N=S bond, there is a dramatic increase in the ratio of ene:Diels-Alder product, compared with the *para*-substituted isomer (Table 1). Indeed, comparison of the methyl-substituted derivatives (2b) and (2f) shows that while the Diels-Alder adduct (3b) predominates from the *para*-isomer (2b), an *ortho*-methyl substituent reverses the situation with the cne adduct (4f) emerging as the major product. Electron-withdrawing bromo- and cyano-substituents follow the same trend to the extent that for the *ortho*-substituted isomers the ene adducts (4g) and (4h) comprise *ca*. 90% of the adduct mixtures. (Table 1).





Reagents and Conditions : (i) triethylamine, acetone, dimethylbutadiene, 20°C. (ii) dimethylbutadiene, 20°C or 69°C.

<u>Table 1</u>. Product isomer ratios from dimethylbutadiene trapping of ArN=S species (2a)-(2h) generated from precursors (1a)-(1h). aCombined yield of adducts (3) + (4) was 55-65%; isomer ratios were based on proton NMR analysis of the crude reaction mixture (CDCl<sub>3</sub> at 250 MHz) as described previously (ref. 1c). <sup>b</sup>Reported previously in ref. 1c. <sup>c</sup>This work.

Precursor	Product	isomer ratio <sup>a</sup>	
	(3)	: (4)	
(1a)	85	15 <sup>b</sup>	
(1b)	60	40 <sup>b</sup>	
(lc)	20	80p	
(1d)	25	75b	
(1e)	20	80c	
(1 <b>f</b> )	35	65°	
(1g)	12	88c	
(1 <b>h</b> )	10	90¢	

Table 2.Product isomer ratios fordimethylbutadienetrapping of ArN=Sspecies (2h)-(2k) generated from precursors(5h) - (5k)."Same as Table 1. bThis work."

Precursor	Reaction	Product isomer ratio <sup>a</sup>	
	Temp/ºC	(3)	: (4)
(5h)	69	22	78b
(5h)	20	10	90ь
(5i)	69	22	78 <sup>b</sup>
(5j)	69	22	78 <sup>b</sup>
(5j)	20	10	90b
(5k)	69	20	80b

The foregoing results are entirely consistent with the accepted transition state geometries for Diels-Alder and ene reactions<sup>3,4</sup>: the presence of an *ortho* substituent on intermediate (2) should hinder the former reaction more than the latter. As pointed out recently by other workers,<sup>2b</sup> remarkably few dienophiles undergo both Diels-Alder and ene reactions with the same diene [the other systems are benzyne<sup>5</sup>, PhS- $O^{+6}$  EtO<sub>2</sub>CN $\approx$ NCO<sub>2</sub>Et <sup>7</sup> and R<sub>2</sub>NC(O)NO<sup>8</sup> and certain aldehydes<sup>9</sup>]. Our studies with substituted ArN=S derivatives (Table 1) provide the clearest results to date on how this competitive process is influenced by steric factors in the dienophile.

The overwhelming predominance of ene adduct (4h) over Diels-Alder adduct (3h) from interception of o-cyanothionitrosobenzene (2h) was inconsistent with a previous report from other workers<sup>10</sup> who discovered that o-cyanothionitrosobenzenes, formed by mild thermolysis of 3-azido-2,1-benzisothiazoles (5)<sup>11</sup>, could be trapped with dienes: Diels-Alder adduct (3i) was identified, but, surprisingly, there was no mention of the corresponding ene adduct (4i).<sup>10</sup>

We have, therefore, reinvestigated the reaction of dimethylbutadiene with o-cyanothionitrosobenzene derivatives generated from 3-azido-2,1-benzisothiazole precursors. Dissolution of compounds (5h)-(5k) in neat dimethylbutadiene, followed by heating at reflux (69°C) for 16 h, as described previously,<sup>10</sup> yielded a mixture of products (3) and (4) in the ratios shown (Table 2). <sup>1</sup>H NMR spectroscopy of the crude reaction mixture shows, unambiguously, that the ene adduct (4) is the major product in each case. Indeed, when the same reaction with precursors (5h) and (5j) was carried out at lower temperature (20°C for 3-6 days) the percentage of ene adduct in the product mixture further increased to 90%, *i.e.* the ratio of products was the same as when thionitroso intermediate (2h) was generated from precursor (1h) at the same temperature. The ratio of products (3h) and (4h) obtained from reaction at 20°C was unchanged when the isolated adduct mixture was subsequently heated at 69°C for 16 h. This demonstrates that the significant effect of reaction temperature on product ratio is not due to interconversion of the Diels-Alder and ene isomers, or to thermal decomposition of the adducts. Product ratios from (5h) and (5j) were unchanged when the trapping reaction was performed at 20°C under photolytic conditions (1 kW high-pressure mercury lamp).

In conclusion, we have established that ene adducts (4) greatly predominate over the Diels-Alder isomers (3) when thionitrosobenzenes (2) bearing an *ortho*-CN,  $\cdot$ Br, or  $\cdot$ Me substituent react with dimethylbutadiene. That the same adduct ratios are found from the structurally very different precursors (1) and (5), provides compelling evidence that both pathways proceed *via* the same intermediates (2).

<u>Acknowledgements</u>. We thank SERC and Shell (Sittingbourne) for a CASE award (to J N H), Professor C.W. Rees and Dr. E. Haddock for many helpful discussions, and Dr. D. Waring, Kodak Ltd., for the gift of 3-amino-2,1-benzisothiazoles.

## References

- (a) Bryce, M.R.; Taylor, P.C. J. Chem. Soc. Chem. Commun. 1988, 950-951; (b) Bryce, M.R.;
  Taylor, P.C. Tetrahedron Lett. 1989, 30, 3835-3836; (c) Bryce, M.R; Taylor, P.C. J. Chem. Soc.
  Perkin Trans. 1 1990, 3225-3235.
- (a) Meth-Cohn, O.; van Vuuren, G. J. Chem. Soc. Chem. Commun. 1984, 1144-1146; (b) Meth-Cohn, O.; van Vuuren, G. J. Chem. Soc. Perkin Trans 1 1986, 245-250.
- 3 Hoffmann, H.M.R. Angew. Chem. Int. Edn. Engl. 1969, 8, 556-577
- 4 Carruthers, W. 'Cycloaddition Reactions in Organic Synthesis', Pergamon, Oxford, 1990.
- 5 Wittig, G.; Dürr, H. Justus Liebigs Ann. Chem. 1964, 672, 55-62.
- 6 Moiseenkov, A.M.; Veselovsky, V.V.; Makarova, Z.G.; Zholin, V.M.; Smit, W.A. Tetrahedron Lett. 1984, 25 5929-5932.
- Jacobson, B.M.; Arvanitis, G.M.; Eliasen, C.A.; Mitelman, R. J. Org. Chem. **1985**, 50, 194-201 and references therein.
- 8 Christie, C.C.; Kirby, G.W.; McGuigan, H.; Mackinnon, J.W.M. J. Chem. Soc. Perkin Trans 1 1985, 2469-2473.
- 9 Klimova, E.I.; Treshchova, E.G.; Arbuzov, Y.A. Dolk. Akad. Nauk SSSR, 1968, 180, 865-868 (Chem. Abs. 1968, 69, 67173b; formula II in the abstract is wrong).
- 10 Joucla, M.F.; Rees, C.W. J. Chem. Soc. Chem. Commun, 1984, 374-375.
- 11 Low temperature photolysis of 3-azido-2,1-benzisothiazoles has recently been used for spectroscopic detection of a sterically-crowded ArN=S intermediate: Okazaki, R.; Takahashi, M.; Inamoto, N.; Sugawara, T.; Iwamura, H. Chem. Lett, 1989, 2083-2086.

(Received in UK 30 September 1991)