Pergamon

Tetrahedron Letters, Vol. 35, No. 29, pp. 5275-5278, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00979-1

Alkylthionitroso and Arylthionitroso Compounds Generated from *N*-Trimethylsilyl-*N*-chlorothioalkylamine Precursors

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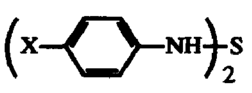
A range of alkylthionitroso and arylthionitroso compounds have been generated by thermal fragmentation of *N*-trimethylsilyl-*N*-chlorothioalkyl(aryl)amine precursors, and intercepted by reaction with dimethylbutadiene to afford Diels-Alder and ene adducts.

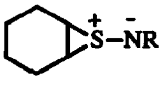
Organic thionitroso species, of general formula R-N=S, have been generated from a variety of precursors and intercepted *in situ* by reactions with conjugated dienes and alkenes, to form Diels-Alder and ene adducts, respectively.[1] Additional evidence for their intermediacy has been provided by matrix isolation experiments at low temperatures.[2] The instability of thionitroso species, and their high reactivity as heterodienophiles, is, in many ways, analogous to that of thioaldehydes. However, while the chemistry of thioaldehydes has developed rapidly over the last decade,[1,3,4] thionitroso compounds have remained in relative obscurity.

The principal precursors to thionitroso species are compounds **1**,[5] **2**,[6] **3**,[2,7,8] **4**[9] and **5**.[10] In view of our continuing interest in this area,[8,10] we were attracted by a recent brief report from Markovskii *et. al.* that thermal decomposition (toluene, 100°C) of two *N*-trimethylsilyl-*N*-chlorothioalkylamine derivatives **6a**, in the presence of dimethylbutadiene, afforded 2-alkyl-4,5-dimethyl-3,6-dihydro-1,2-thiazine Diels-Alder adducts presumably *via* intermediate alkylthionitroso species.[11] These workers claimed that analogous *N*-trimethylsilyl-*N*-chlorothioarylamines **6b** (which should be precursors to arylthionitroso compounds) could not be obtained. Hitherto, alkylthionitroso compounds had been reported only once; they had been generated from precursors **2**, and trapped with butadiene.[6]

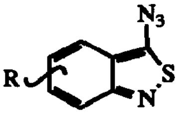
We now report our studies on the generation and trapping of new thionitroso compounds, using precursors **6**. The key features of this work are: (i) we have observed, for the first time, the formation of ene adducts of alkylthionitroso compounds; (ii) by judicious choice of substituents attached to nitrogen, the stability of the *N*-alkyl-1,2-thiazine Diels-Alder adducts **10** can be dramatically increased, and (iii) contrary to the claim of Markovskii *et. al.*[11] *N*-trimethylsilyl-*N*-chlorothioarylamines **6b** can be prepared, and, moreover, they serve as very convenient precursors to arylthionitroso compounds. Indeed, in this respect compounds **6b** offer advantages over compounds **5**,[10] which until now have been the precursors of choice for ArN=S systems.



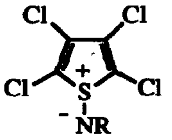
1 X = H, Cl, Br



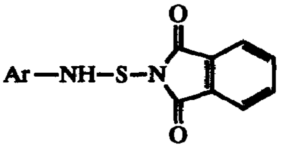
2 R = Me, Et, Pr



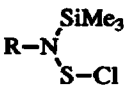
3 R = Cl, Br, NO_2



4 R = CO_2Et, CO_2Ph, tosyl



5 Ar = Ph, substituted phenyl, heteroaryl

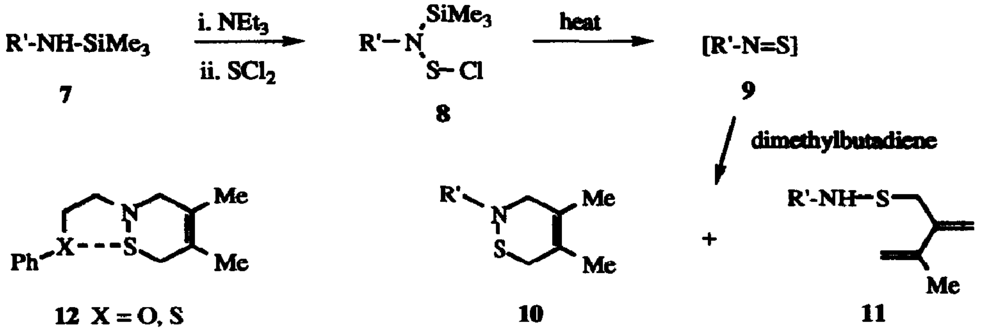


6 a R = *i*-Pr, *t*-Bu
b R = aryl

Silylated amines **7a-g** reacted with a mixture of triethylamine and sulfur dichloride at between -10°C and 20°C in ether to yield the corresponding sulfenyl chlorides **8a-g**, as unstable oils, which, without purification, were used in the next step within one hour of their preparation.[12] A mixture of compounds **8a-g** and dimethylbutadiene (10 molar equivalents) dissolved in toluene was heated (16h, 70°C) and after removal of volatile materials *in vacuo* at <70°C, the crude product mixture was analysed by ^1H NMR spectroscopy, which showed the presence of Diels-Alder adducts **10a-g**, accompanied in some cases by the corresponding ene adduct **11** (Scheme 1) in the ratios given in the Table.[13] The yield for the trapping reactions was *ca.* 20%, after purification. It is noteworthy that Markovskii *et. al.*[11] do not report the observation of any ene adducts in their reactions of thionitrosoalkanes **6a** with dimethylbutadiene (toluene, 100°C).[14]

Previous work on the trapping of thionitrosoarenes with dimethylbutadiene has established that the ratios of Diels Alder : ene adducts obtained are very sensitive to the electronic properties of substituents on the aryl group, with electron donating substituents favouring Diels-Alder reaction, while electron-withdrawing substituents result in a high proportion of the ene adduct.[8,10] The data in the Table show that benzylthionitroso compounds **9a**, **c** and **d**, afford the Diels-Alder and ene adducts, **10** and **11** in a 1:1 ratio, while α–methylbenzyl derivative **9b** gives a higher proportion of Diels-Alder adduct **10b**, *i.e.* the isomer distribution is not affected by substituents on the benzene ring, although it is affected by substitution at the methylene carbon. Both series of adducts **10a-d** and **11a-d** decompose upon storage under nitrogen for a few days at room temperature, with the ene adducts decomposing more rapidly (NMR evidence). In contrast to this, thionitroso compounds **9e-g**, which contain a phenoxyethyl- or phenylthioethyl-substituent attached to nitrogen, yield a product mixture containing the Diels-Alder adducts **10e-g**, exclusively, with no evidence for the presence of ene isomers **11e-g**, and the purified adducts **10e-g** are stable to storage at room temperature for at least six months! The absence of the ene adducts **11e-g** may be due to their rapid decomposition under the reaction conditions.

We suggest that the remarkable stability of **10e-g** arises from a non-bonded interaction between the oxygen or sulfur atom in the sidechain and the heterocyclic sulfur atom (general structure **12**). Close contacts of this type, involving five-membered ring interactions in solution and in the solid state, are well-documented in a variety of saturated and unsaturated sulfur heterocycles.[15] We have the following experimental evidence to support structure **12**. Compounds **10e-g** were recovered unchanged under conditions which readily converted compound **10j**[10c] into the corresponding sulfonamide (*meta*-chloroperbenzoic acid, 2h, 20°C, dichloromethane, 70% yield). Furthermore, in the ^1H NMR spectra of compound **10g** the CH_2S protons appear as an AB system, whereas the CH_2N protons are a broad singlet, typical of compounds **10a-d**. This clearly implies a rigidified ring system in the vicinity of sulfur in compound **10g**, which would be consistent with an intramolecular O---S interaction.



Scheme 1

Table. Product isomer ratios from dimethylbutadiene trapping of R'N=S species **9**, generated from precursors **8**.

Precursor	R'	Product isomer ratio	
		10 :	**11**
8a	$PhCH_2$-	50	50
8b	PhCH(Me)-	92	8
8c	4-MeO-C_6H_4-CH_2-	50	50
8d	4-Cl-C_6H_4-CH_2-	50	50
8e	Ph-O-CH_2-CH_2-	100	0
8f	Ph-S-CH_2-CH_2-	100	0
8g	Ph-O-CH_2-CH(Me)-	100	0
8h	4-Br-C_6H_4-	25	75
8i	2-Br-C_6H_4-	15	85
8j	4-Me-C_6H_4-	60	40
8k	2-*n*-Pr-C_6H_4-	50	50

We have extended the methodology in Scheme 1 to the generation and trapping of thionitrosoarenes **9h-k** (acetonitrile, 20°C, 16h). The combined yields of adducts **10h-k** and **11h-k** are 60-80% after purification. The ratios of adducts **10h-j** : **11h-j** (Table) are, within experimental error, the same as those obtained using the same solvent, temperature and reaction time, from the corresponding precursors in the phthalimide series **5**.[8,10c,d] This provides compelling evidence that the same transient thionitroso intermediate **9** is produced from both series of precursors **8** and **5**. It is noteworthy that 1-propyl-2-thionitrosobenzene **9k** is obtained from precursor **8k** and trapped efficiently; the analogous precursor **5** (Ar = 2-propyl-C_6H_4-) could not be prepared, presumably for steric reasons.

We have demonstrated, therefore, that compounds **8** are straightforward to prepare from a wide variety of silylated alkylamines and arylamines; they fragment under mild conditions to yield thionitrosoalkanes and thionitrosoarenes, respectively, making them the most versatile family of thionitroso precursors reported to date. There would now appear to be unprecedented scope for attaching functionalised and branched substituents to the nitrogen atom of thionitroso groups (*cf.* **9b** and **9g**) thereby paving the way for new developments in the chemistry of this neglected functional group.

Acknowledgments. We thank SERC for funding this work, and Shell Research Ltd. (Sittingbourne) for CASE awards (to J.N.H. and G.N.M.).

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12. Compounds **8**, **10** and **11**: General procedure. To a solution of silylated amine **7** dissolved in ether under nitrogen at -10°C was added sequentially triethylamine (1 equivalent) and sulfur dichloride (1 equivalent). The mixture was stirred for 0.5h at -10°C, then allowed to warm to 20°C over 1h. The precipitate of triethylammonium hydrochloride was separated by filtration and the filtrate was evaporated *in vacuo* to yield compound **8** as a red oil. Without purification, compound **8** was dissolved in toluene (for derivatives **8a-g**) or acetonitrile (for derivatives **8h-k**) and dimethylbutadiene (10 equivalents) was added. The mixture was stirred for 16h at 70°C (for **8a-g**) or 20°C (for **8h-k**). Volatile materials were then removed *in vacuo* to yield the crude product mixture. Integration of the ^{1}H NMR spectra of this mixture, obtained immediately after removal of solvent, gave the isomer ratios in Scheme 1. Purification of the adducts was then achieved by colum chromatography on neutral alumina (eluant hexane). For systems where the adducts **10** and **11** are both formed, it was generally not possible to separate them cleanly.
13. All new compounds gave satisfactory high resolution mass spectra and ^{1}H NMR spectra (250 or 400 MHz, in $CDCl_3$). By analogy with our previous work on arylthionitroso compounds,[10] generated from precursors **5**, the Diels-Alder adducts **10** were identified by characteristic peaks due to the dihydrothiazine ring protons at δ *ca.* 3.3 ppm (CH_2N) and *ca.* 3.05 ppm (CH_2S), while the signature of the ene adducts **11** is a peak at δ *ca.* 3.2 ppm (CH_2 adjacent to the sulfenamide sulfur) together with the NH and two vinylic CH_2 peaks in the region δ 4.8-5.3 ppm.
14. The trapping of R-N=S [R = Me, Et, *n*-Pr and benzyl (**9a**) generated from the corresponding ylids **2**, chloroform, reflux, 16h, following the procedure of Hata and Watanabe[6]] with dimethylbutadiene, also led to mixtures of Diels-Alder and ene adducts: J.N.Heaton, Ph.D. Thesis, University of Durham, **1992**.
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(*Received in UK* 11 *April* 1994; *accepted* 20 *May* 1994)