Preparation, characterisation and slow quantitative dissociation of a novel asymmetric *N*-unsubstituted dialkylsulfimide

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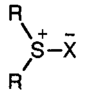
(±)-*S*-Imino-4,5-dihydro-3*H*-dinaphtho[2,1-*c*:1′,2′-*e*]thiepine, a novel asymmetric *N*-unsubstituted sulfimide, undergoes slow, quantitative N–S bond cleavage in $CDCl_3$ solution at 20 °C with a half-life of 20 h.

Sulfimides, sulfoxides and sulfur ylides **1** (X = NR, O or CR_2) belong to a general family of 'non-classical' molecules that are associated with three-centre, four-electron [3*c*-4*e*] bonds.[1]† This large family includes 1,3-dipoles, *e.g.* **2**,[2] and hypervalent compounds, *e.g.* **3**.[3,4] Whether represented by 1,3-dipolar, hypervalent or hetero-ylide structures, the fundamentally similar bonding in these non-classical molecules leads to common modes of reaction.[1] These include '*syn*-addition' and 'ligand coupling': in the latter mode of reaction the [3*c*-4*e*] bond is transformed into a lone pair and either a σ-bond between ligands X and Y (*e.g.* 1,3-dipoles **2** and hypervalent molecules **3**) or a second lone pair on a single ligand X (*e.g.* ylides and hetero-ylides **1**).[1] Transfer of nitrene or an alkylnitrene from a chiral sulfimide **1** (X = NH or N–alkyl) to prochiral substrates is a potentially useful application of ligand coupling and this has prompted us to seek a suitably reactive chiral *N*-unsubstituted sulfimide for evaluation.



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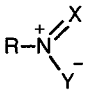

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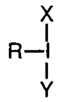

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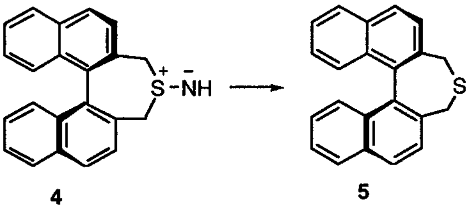
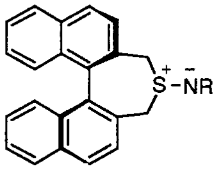
N-Unsubstituted diarylsulfimides **1** (R = Ar, X = NH) are stable compounds and relatively unreactive, decomposing to the diarylsulfide only at 100 °C or above.[5–7] In contrast, the dialkyl derivatives **1** (R = alkyl, X = NH) are reported to be very unstable with respect to decomposition to the dialkylsulfide.[7–9] To be synthetically useful a suitable sulfimide should be sufficiently stable for convenient preparation but ideally should be reactive at ambient temperature. The sulfide precursor must also be accessible and robust enough to facilitate recovery and regeneration of the sulfimide. We have now identified a novel chiral *N*-unsubstituted sulfimide that fulfils these requirements. In particular, we report the preparation of the asymmetric (C_1) unsubstituted sulfimide **4** from the dissymmetric (C_2) sulfide **5** and its slow and quantitative first-order thermal dissociation back to the sulfide precursor **5** (Scheme 1). The process **4** → **5** can be formally classified as a ligand coupling in which the ligand is nitrene (:NH), and in principle this reaction provides a source of singlet nitrene in a chiral environment. This behaviour is consistent with the general classification described above but the ease of dissociation is surprising since thioethers are not particularly good leaving groups in related reactions.[10] Since the enantiomers of sulfide **5** can be separated using column chromatography (triacetylcellulose),[11] sulfimide enantiomers **4** can be separately prepared by amination of homochiral sulfide **5** and, furthermore, homochiral sulfide regenerated during reactions of sulfimide enantiomers **4** can be recycled without the need for resolution.

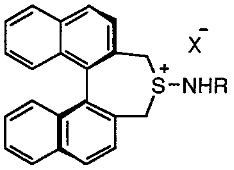


Scheme 1

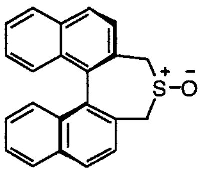
Initially we attempted to prepare the novel sulfimide **4** *via* the *N*-tosyl derivative **6**. Treatment of the racemic sulfide **5**[11] in CH_2Cl_2 with chloramine-T (1.12 equiv.) and hexadecyltributylphosphonium bromide (0.06 equiv.) gave the (±)-*N*-tosylsulfimide **6**, mp 225 °C (decomp.) (86%).‡ All attempts to obtain the free sulfimide **4** by acid catalysed removal of the tosyl group[5,6] were unsuccessful. In an alternative approach, reaction of the sulfide **5** with *O*-mesitylenesulfonylhydroxylamine[12] (1.5 equiv.) gave the (±)-*S*-aminosulfonium salt **8**, mp 199 °C (decomp.) (87%). All spectroscopic properties of compounds **6** and **8** supported the assigned structures. In particular, the ^1H NMR spectrum ($CDCl_3$) of the salt **8** showed two pairs of doublets (*J* 12 and 14.5 Hz) at δ 3.71, 3.94, 4.42 and 4.78 due to the four non-equivalent methylene protons.



6 R = Ts
7 R = CONHPh



8 R = H, X = OMes
9 R = Ts, X = Cl



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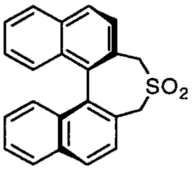

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For direct comparison of spectroscopic properties we have also made the asymmetric (C_1) sulfoxide **10** and the dissymmetric (C_2) sulfone **11**. Oxidation of the sulfide **5** with sodium perborate tetrahydrate (1.0 equiv.) in glacial AcOH gave the novel sulfoxide **10**, mp 239–241 °C (92%) and use of 2 equiv. gave the novel sulfone **11**, mp > 260 °C (75%). As expected the ^1H NMR spectrum ($CDCl_3$) of the sulfoxide showed four discrete doublets (δ 3.26, 3.51, 3.92 and 4.36), (*J* 12 or 14 Hz) for the non-equivalent methylene protons. In $CDCl_3$ the spectrum of the sulfone showed only a singlet (δ 4.11) for the four methylene protons but in C_6D_6 solution two doublets (δ 3.49, *J* 14 Hz and δ 3.62, *J* 14 Hz) consistent with the dissymmetric structure **11** were observed.

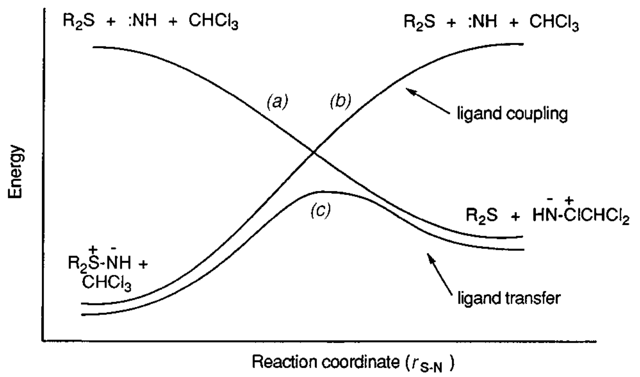

Fig. 1 A bond forming–bond breaking analysis and the possible role of solvent in the S–N bond dissociation of *N*-unsubstituted sulfimides.

The salt **8** can be converted into the free sulfimide **4** in solution by treatment with a number of bases including LDA, DBU and DABCO. The *N*-unsubstituted sulfimide **4** is too unstable to be isolated but is sufficiently stable in solution at room temperature to allow investigation of its properties, and it appears to be indefinitely stable in solution at 0 °C and below. Treatment of a toluene solution of compound **8** at −80 °C with LDA (1.0 equiv.) followed by addition of phenyl isocyanate (3.0 equiv.) gave the adduct **7**, mp 142 °C (decomp.) (67%). In a similar manner the *N*-tosylsulfimide **6** (88%), identical to an authentic sample, was obtained *via* the salt **9** by *in situ* treatment of the sulfimine **4** with TsCl. The ^1H NMR spectrum of the free sulfimide **4** in $CDCl_3$ solution was obtained by treatment of the salt **8** with 1 equiv. of base. Using DBU, a spectrum with two pairs of doublets (δ 3.03, 3.56, 3.72 and 4.16), (J 12 or 14 Hz) assignable to the four non-equivalent methylene protons was obtained. As expected, this spectrum closely resembles that of the stable and closely related sulfoxide **10** and the signals are up-field relative to those for the corresponding protons in the cation **8**. In agreement with their C_1 symmetry, non-equivalence of the CH_2 groups was also observed in the ^{13}C NMR spectra of sulfimide **4** (δ 54.25 and 56.59) and sulfoxide **10** (δ 54.62 and 57.08). In contrast, the C_2 symmetric sulfide **5** and sulfone **11** each show a single CH_2 signal, which appear at δ 32.35 and δ 58.24, respectively.

When an NMR sample of the sulfimide **4** was re-examined after 24 h the spectrum showed that a significant amount of the sulfide **5** was present. The rate of transformation of the sulfimide, generated in $CDCl_3$ solution using LDA (1.0 equiv.), was followed by monitoring the decay of the proton doublet at δ 4.16 using $CHCl_2CHCl_2$ in a sealed capillary (δ 5.96) as internal reference. Slow but quantitative transformation to the sulfide **5** took place over a period of 4 days, during which the sulfide proton signals appeared and simultaneously the sulfimide signals decayed. The dissociation **4** → **5** has a half-life (*ca.* 20 h) which is independent of concentration, suggesting reaction kinetics that are first-order or pseudo-first-order. We have not yet been able to determine the fate of the NH fragment, the products of which may include N_2 and NH_3.[5–9]

Thermal dissociation of a simple *N*-unsubstituted sulfimide to a sulfide and singlet nitrene at room temperature is an unexpected process in which an electron-rich nitrogen atom is transformed in one step into an electron-deficient nitrogen. In the gas phase this process is also extremely endothermic. Using the AM1 semi-empirical MO method,[13] we have calculated the energy of dissociation for the process $Me_2S^+\text{–}N^-\text{–}H \rightarrow Me_2S + NH$ to be 106.8 kcal mol^{-1} and to have an energy profile of the type described by the curve (*b*) in Fig. 1. Solvation of the sulfimide and sulfide are unlikely to change this profile but solvation of the nitrene may be significant. Singlet nitrene has a low energy, unoccupied p-orbital that can interact with a lone pair on solvent molecules such as $CHCl_3$ to form a hetero-ylide (*i.e.* $HN^-\text{–}Cl^+\text{–}R$). Participation of the solvent may therefore facilitate the reaction by providing an alternative mechanism ('ligand transfer') as shown by curve (*c*) in the Bell–Evans–Polanyi analysis[14] in Fig. 1. This mechanism is consistent with pseudo-first-order kinetics and the proposed iminochlorinane intermediate is analogous to the isolable iminoiodinanes, *e.g.* $TsN^-\text{-}I^+Ph$.[15] This mode of stabilisation of singlet nitrenes is consistent with experimental observations that CH_2Cl_2 stabilises the singlet-state character of nitrenes.[16] A similar model for lone pair stabilisation of nitrenes has been proposed by Gleiter and Hoffmann.[17] NMR studies in inert solvents to eliminate solvent participation, *e.g.* saturated hydrocarbons, were precluded by solubility and availability. When the sulfimide **4** was generated in C_6D_6 solution sulfide formation still occurred but the reaction was not as clean as in $CHCl_3$: a very complex mixture of additional products was observed and none were formed in any significant amount.

In conclusion, we have obtained a chiral *N*-unsubstituted sulfimide having sufficient levels of stability and reactivity to enable studies of its nitrene transfer onto prochiral substrates. Cleavage of the S–N bond probably occurs by interaction with solvent (ligand transfer) to give a reactive intermediate rather than by formation of the free nitrene (ligand coupling). These preliminary results may be relevant to the role of solvent in nitrene mediated reactions. We plan further investigations of the chemistry and modes of reaction of this interesting system and related species.

Notes and references

† These bonds are sometimes described as two-centre, four-electron [2*c*-4*e*] bonds but in this context 'centre' strictly refers to the centres of the three atomic orbitals that interact to form molecular orbitals. In these bonds two of the atomic orbitals happen to be on the same atom but it is important to retain the description [3*c*-4*e*] to emphasise the similarity of bonding and properties to closely related systems, *e.g.* **2** and **3**.

‡ All new compounds were characterised by spectroscopy and elemental analysis.

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