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The Reactivity of Sulfur-Centred Radicals towards TMIO (1,1,3,3-Tetramethyl-2,3-dihydroisoindol-2-yloxyl). A New Type of Radical Fragmentation Reaction

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The thiyl radicals derived from 2-mercaptoethanol and thiophenol were found to undergo a complex series of reactions with 1,1,3,3-tetramethyl-2,3-dihydroisoindol-2-yloxyl (TMIO). Thus, treatment of 2-mercaptoethanol with di-t-butyl peroxyoxalate (DTBPO) in the presence of TMIO produced two N–S compounds—a sulfoxamide and a sufonamide—not the expected N–O–S adduct. The reaction between thiophenol and TMIO, which proceeded at a reasonable rate in the absence of DTBPO, produced 1,1,3,3-tetramethyl-2,3-dihydroisoindolin and its corresponding phenylsulfoxamide, diphenyl disulfide, phenylsulfinic acid, and 1,1,3,3-tetramethyl-2,3-dihydroisoindol-2-ylphenylsulfonate (the adduct of TMIO and the phenylsulfonyl radical). The mechanism of formation of these products, and the use of TMIO for trapping *S*-centred radicals, are discussed. A new radical fragmentation process, which appears to be general for aminoxyl adducts of electron-rich systems, is described.

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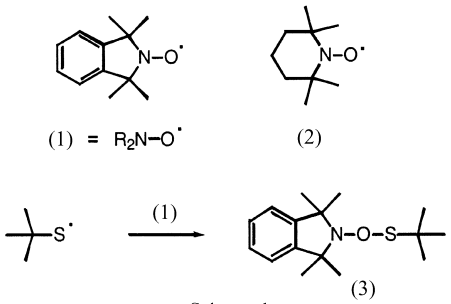
Introduction

TMIO [the aminoxyl or nitroxide 1,1,3,3-tetramethyl-2,3-dihydroisoindol-2-yloxyl (1)] has found extensive use as a free-radical trap for carbon-centred radicals, particularly in the study of the early stages of free-radical polymerizations.[1] The great advantage of TMIO over the commercially available aminoxyl TEMPO (2) (2,2,6,6-tetramethylpiperidin-1-yloxyl) is the presence of a UV chromophore, which allows for easy UV-detection and quantification of reaction products using high-performance liquid chromatography (HPLC).

Recently, we have employed TMIO to investigate the addition of phosphorus- and sulfur-centred radicals to alkenes.[2–4] In particular, we reported[3] that the t-butylthiyl radical reacts competitively with (1) to give an adduct, which was assigned the structure (3) (Scheme 1).



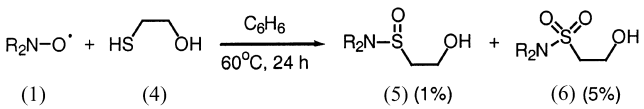
Scheme 1

However, more recent work by Greci et al.[5–9] has shown that aminoxyls such as TEMPO react with arylsulfinyl radicals to give a number of products including *N*-arylsulfinyl- and *N*-arylsufonyl-2,2,6,6-tetramethylpiperidines rather than the expected $R_2N–O–S–R$ adducts. These reports have prompted us to reexamine the reactions of sulfur-centred radicals with TMIO. The sulfur-centred radicals investigated were formed from 2-mercaptoethanol or from thiophenol by H-abstraction with t-butoxyl radicals or the aminoxyl itself.

Results and Discussion

Reaction Between TMIO (1) and 2-Mercaptoethanol (4)

A solution of (1) (0.42 mmol) and 2-mercaptoethanol (4) (0.21 mmol) in anhydrous benzene (10 mL) was heated at 60°C for 24 h (Scheme 2). The solution was evaporated to dryness (no salts precipitated on addition of pentane, 2 mL), and the crude mixture was analysed by HPLC–mass spectrometry (HPLC–MS). It was found that only 6% of (1) had been consumed. Two products were observed, the sulfoxamide (5) (1%) and the sulfonamide (6) (5%).



Scheme 2

The reaction was repeated but in the presence of di-t-butyl peroxyoxalate (DTBPO). Thermolysis of DTBPO produces t-butoxyl radicals, which abstract hydrogen from (4) at a more rapid rate than does (1). DTBPO (1.43 mmol) was mixed with (1) (1.80 mmol) and (4) (4.29 mmol) in benzene (5 mL). All of the TMIO (1) was consumed after 75 minutes and sulfoxamide (5) (59%) and sulfonamide (6) (14%) were isolated by preparative HPLC. Also present by HPLC but not isolated was a minor product (5%) assigned the structure (9) on the basis of MS data (MNa^+, 322).

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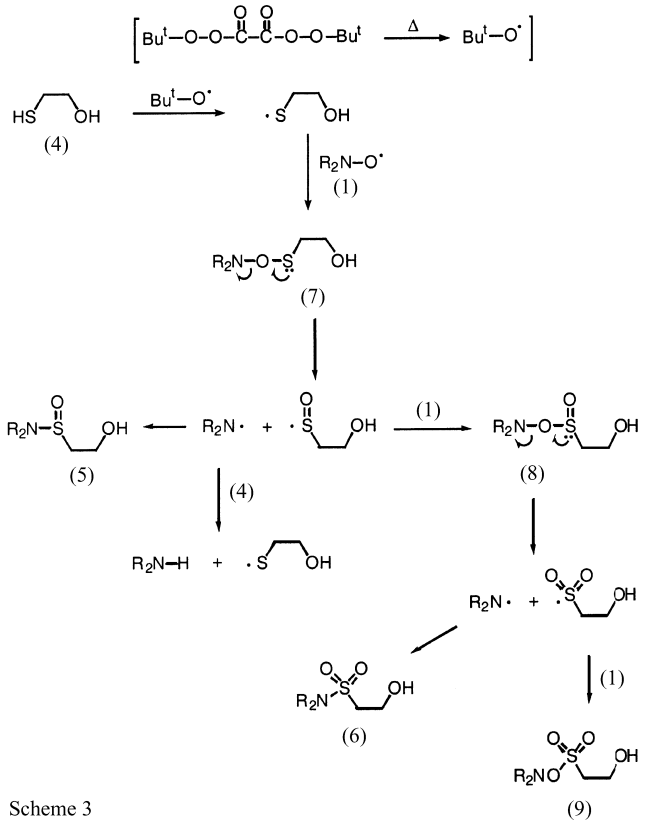
Sulfoxamide (5) and sulfonamide (6) were readily distinguished by ^{1}H nuclear magnetic resonance (NMR) spectroscopy, as the methylene hydrogens in (5) are diastereotopic and occur as complex multiplets, whereas the methylene hydrogens in (6) occur as clean triplets. Similarly, the isoindoline geminal methyl groups in (5) are magnetically non-equivalent, whereas in (6) they are equivalent. The presence of a characteristic S=O stretching frequency at 1060 cm^{-1} in the infrared (IR) spectrum constituted further evidence for the structure of (5). Compound (5) also underwent facile oxidation to (6) in high yield (96%) under mild conditions ($NaIO_4$ at 0–5°C). Products (5) and (6) were also characterized as their *O*-acetate (10) and *O*-benzoate (11) derivatives, respectively.

A mechanism for the formation of (5), (6) and (9) via homolytic fragmentation of the (presumed) intermediate (7) is suggested in Scheme 3. It is assumed that the driving force for this fragmentation is the formation of the strong S=O double bond (ΔH_{F298} ca. 520 kJ/mole,[10] cf. N–O, ca. 200 kJ/mole,[11] S–O, ca. 250 kJ/mole[12]). The ratio of products [(5) : (6) = 4.2 : 1] suggests that after fragmentation of intermediate (7), radical recombination to give the geminate product (5) is competitive with diffusion of the radicals from the solvent cage followed by trapping of the sulfinyl radical with the aminoxyl (1) to give a second intermediate (8). Similar fragmentation of (8) followed by radical recombination or trapping gives (6) and (9), respectively. It is clear that when the aminoxyl (1) is present in excess (as in the first experiment where only 6% of the aminoxyl was consumed), trapping of the sulfinyl radical by the aminoxyl is favoured (ratio of (5) to (6) 1 : 5).

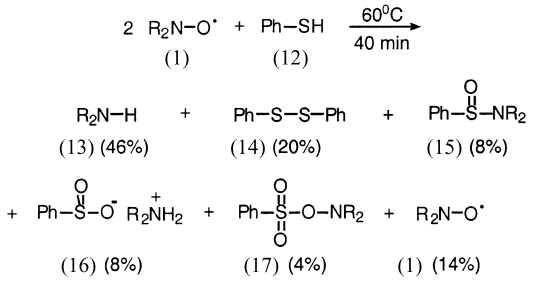


Scheme 3

Reaction Between TMIO (1) and Thiophenol (12)

When thiophenol (12) (1.4 mmol) and TMIO (1) (2.8 mmol) were mixed in anhydrous benzene (15 mL) at 60°C, an exothermic reaction occurred (Scheme 4). The reaction was stirred for a further 40 minutes, and the solution evaporated to dryness. On addition of pentane (5 mL), the benzenesulfinate salt (16) precipitated. The salt was collected by vacuum filtration, the filtrate was evaporated, and the pentane-soluble products were examined by HPLC–MS. The major products formed were the amine (13) (46%), the disulfide (14) (20%), the sulfoxamide (15) (8%), and the sulfonate (17) (4%). Some TMIO (14%) was also recovered.

The reaction was also carried out with a higher ratio of TMIO to thiophenol (when the ratio of TMIO to thiophenol was 5 : 1, a precipitate was not observed) and at room temperature. The results are summarized in Table 1.



Scheme 4

Table 1. Relative percentage yields of products

Ratio of TMIO to PhSH (temperature)	Products (%)[A] (1)	(13)	(14)	(15)	(16)	(17)
2 (25°C)	30.5	27.5	28.0	5.3	8.5	0.3
2 (60°C)	14.4	45.8	20.1	7.4	8.4	4.2
5 (25°C)	72.1	17.4	7.2	2.5	0.0	0.7
5 (60°C)	72.3	17.8	7.4	1.2	0.0	1.5

[A] Yields are relative percentage yields based on HPLC responses, taking into account differences in extinction coefficients at 270 nm. (except for the salt (16) where the yield was determined by weighing).

The products 1,1,3,3-tetramethyl-2,3-dihydroisoindole (13) and diphenyl disulfide (14) were identified by comparison with authentic samples.

The structure of the sulfoxamide (15) followed from its MS, NMR and IR spectra. The electron ionization (EI) MS showed a parent ion at 299 corresponding to M^+, and a base peak at 125 corresponding to $PhSO^+$ (had the structure been Ph–S–O–NR_2 (19) a base peak at 190, corresponding to $[R_2N{=}O]^+$, would have been expected). The NMR spectrum showed magnetically non-equivalent methyl groups which is consistent with structure (15) rather than structure (19), while the IR spectrum showed strong absorption in the S=O region (1089 cm^{-1}).

Similarly, the IR spectrum of the sulfonate (17) showed strong absorption in the S=O region at 1189 cm^{-1}, while the mass spectrum showed a parent ion at 322, corresponding to MH^+, and a base peak at 190 corresponding to $[R_2N{=}O]^+$. There was also a strong peak at 174 (R_2N^+), which is

consistent with structure (17). As expected, and in contrast to (15), the NMR spectrum of (17) showed magnetically equivalent methyl groups.

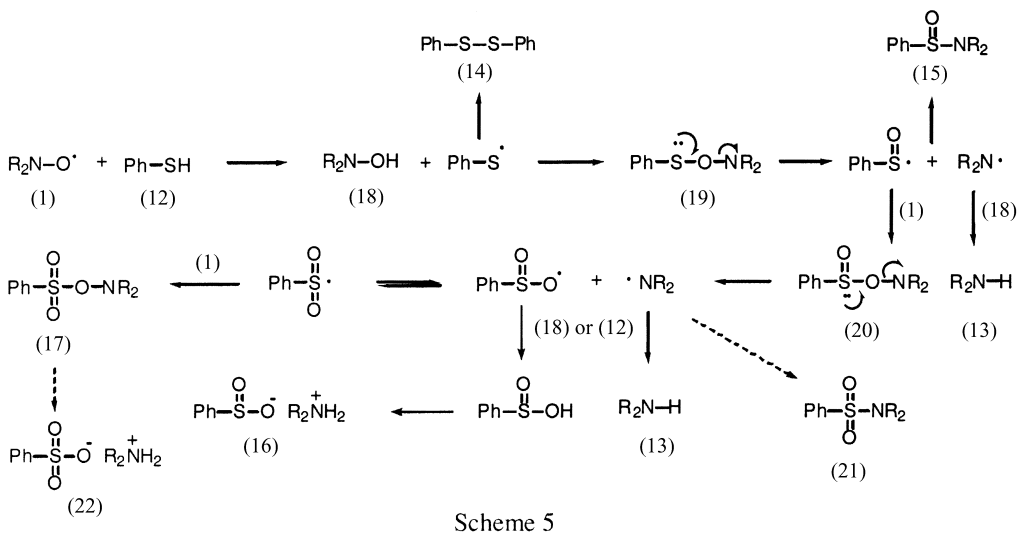
The structure of the 1,1,3,3-tetramethyl-2,3-dihydroisoindolinium benzenesulfinate salt (16) was deduced by comparison with the analogous 2,2,6,6-tetramethylpiperidinium benzenesulfinate salt prepared by Greci et al.[5] We repeated the Greci experiment and treated TEMPO with thiophenol (2:1) to give a mixture of tetramethylpiperidinium benzenesulfinate and benzenesulfonate salts. [We also carried out the reaction using a higher ratio (5:1) of TEMPO to thiophenol. Under these conditions, only the tetramethylpiperidinium benzenesulfonate salt was precipitated]. The benzenesulfinate and benzenesulfonate anions are readily distinguished by ^{1}H NMR spectroscopy. In $CDCl_3$, the H 2 and H 6 protons in the benzenesulfinate anion absorb at 7.73 ppm, whereas in the benzenesulfonate anion they occur further downfield at 7.89 ppm (these chemical shifts are well downfield of the isoindolinium signals at 7.1–7.4 ppm).

There is a significant difference between the results reported here for TMIO and those reported by Greci et al.[5] for TEMPO. When thiophenol is treated with TEMPO, the major product formed (49%) is the 2,2,6,6-tetramethylpiperidinium salt of benzenesulfonic acid. With TMIO under similar reaction conditions, the major products formed (28% each) were the free amine [1,1,3,3-tetramethyl-2,3-dihydroisoindole (13)] and diphenyl disulfide (14). No benzenesulfonic salt was formed. Conversely, the unusual hydroxylamine sulfonate ester (17) was formed with TMIO but the analogous TEMPO product was not observed. Indeed, Greci et al. [5] proposed that the TEMPO analogue of (17) is the precursor of their major product, the 2,2,6,6-tetramethylpiperidinium salt of benzenesulfonic acid.

These results, and the intriguing differences with the results of Greci et al. are best discussed with reference to a mechanistic scheme (Scheme 5).

In Scheme 5, the relative yield of disulfide (14) was much higher with TMIO than with TEMPO (28 versus 8%, respectively, for reactions performed at room temperature). At first inspection this seems to be contrary to expectation, as TMIO is a somewhat more reactive trap than TEMPO (at least towards carbon-centred radicals, though the difference in reactivity is not large).[13] However, if TMIO is more reactive than TEMPO towards H-abstraction from thiophenol, then as the reaction proceeds the concentration of TMIOH (18) will increase, with a consequent decrease in TMIO concentration (relative to TEMPO). If it is further assumed that trapping of the phenylthiyl radical by the aminoxyl [to give (19)] is reversible, then the relative yield of disulfide (14) could well be higher in the case of the TMIO reaction. Another factor that would influence the yield of the disulfide is the rate of N–O fragmentation of (19) (reversible formation of (19), combined with a more rapid fragmentation in the case of the TEMPO analogue would result in a relatively higher yield of disulfide in the TMIO reaction).

Following fragmentation of the intermediate (19), there is significant geminate coupling of the aminyl and sulfoxyl radicals to give the sulfoxamide (15). This result is consistent with that reported by Greci[5] using TEMPO, where a comparable yield of the TEMPO analogue of (15) was obtained. In competition with geminate coupling, the phenylsulfoxyl radical can undergo trapping by the aminoxyl (1) to give the intermediate (20). Fragmentation of (20), as shown in Scheme 5, would give the aminyl and phenylsulfonyl radicals, which would also be expected to undergo geminate coupling. Strangely, the sulfonamide (21) was not observed. However, Greci[5] reported that the TEMPO analogue of (21) was a significant product (7%). A possible explanation for this difference is that the concentration of hydroxylamine (18) is higher than that of TEMPOH in the analogous TEMPO reaction (as suggested earlier). Competitive H-abstraction from (18), to give phenylsulfinic acid and the amine (13), or aminoxyl trapping, to give the sulfonate (17), must be favoured over geminate radical coupling, which would give (21). Evidence in support of this is that when the TMIO concentration was increased (to 5 : 1 TMIO/PhSH), no phenylsulfinic acid salt (16) was formed and the relative yield of sulfonate (17) also increased [relative to sulfoxamide (15)]. As expected, increasing the TMIO concentration also resulted in a reduction in the relative yield of disulfide (14).



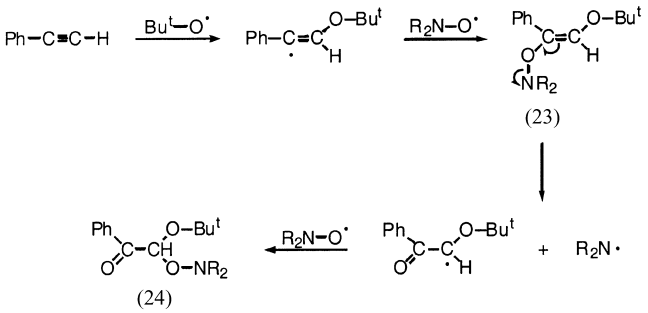
Scheme 5

The major difference between the results for TEMPO and TMIO, is that in our work, we did not observe any sulfonic acid salt (22), whereas in the Greci experiment, the sulfonic acid salt was the major (49%) product. Greci et al.[5] propose that the sulfonic acid salt [TEMPO analogue of (22)] is formed via reduction of the hydroxylamine sulfonate ester [TEMPO analogue of (17)] with either TEMPOH or the thiophenol (12). If the thiophenol is the reductant, it is not clear why the TEMPO analogue of (17) should be more easily reduced. However, it is possible that TEMPOH is a more powerful reductant than TMIOH (18). This would explain the difference between our results and those of Greci et al.,[5] and would be consistent with our earlier suggestion that TMIO is the more reactive aminoxyl towards H-abstraction.

One slightly puzzling feature of the Greci work is that although a 2 : 1 molar ratio of N : S compounds (aminoxyl/thiophenol) was employed, all of the products (with the exception of PhSSPh, 8% and R_2NH, 9%) contain N and S in equimolar amounts. This suggests that considerable aminoxyl (or R_2NOH) was present at the end of the reaction (as observed in our work with TMIO). This, however, was not reported.

Are Aminoxyl Adducts of Electron-Rich Systems Generally Susceptible to Homolytic Fragmentation?

It is interesting to compare the apparent instability of aminoxyl adducts of di- and tetra-valent sulfur [such as (7), (8), (19) and (20)] with that of the aminoxyl adduct of an electron-rich alkene. In earlier work,[14] we investigated the reaction of t-butoxyl radicals with phenylacetylene in the presence of TMIO. The expected product was (23), the adduct of TMIO and an electron-rich alkene. Instead of (23), the phenylglyoxal derivative (24) was obtained in high yield. A fragmentation mechanism analogous to that in Schemes 3 and 5 can be envisaged for this reaction (Scheme 6).

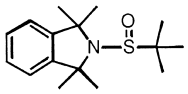


Scheme 6

We suggest that this type of radical fragmentation is probably a general phenomenon and would be expected to occur whenever an aminoxyl is attached to an electron-rich (or easily oxidized) centre.

In particular, it will be favoured when a strong X=O bond (such as S=O, C=O, P=O) and/or a resonance-stabilized radical is formed. Other examples of this type of radical fragmentation occur with aminoxyl adducts of trivalent phosphorus compounds,[9,15] while a case of intermediate stability is provided by the TMIO adduct of the phenyl radical (2-phenoxy-1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindole), which decomposes slowly upon storage.[16]

Finally, just as the aminoxyl radical trapping technique[1] provides useful information about reactions involving carbon-centred radicals, the same is clearly true for reactions involving sulfur-centred radicals. However, one has to be aware that aminoxyls react with thiols to form a range of different products rather than a single alkoxyamine as is usually the case with carbon-centred radicals. Moreover, it is clear from the results reported here and from the work of Greci et al. that the range of products depends on both the type of sulfur radical involved (i.e. alkylthiyl versus arylthiyl), and the structure of the aminoxyl employed (e.g. TMIO versus TEMPO). One common product that appears in all of the reactions reported here and in those reported by Greci et al. is the sulfoxamide [e.g. (5),(15)]. The sulfoxamide is simply the product of rearrangement of the (presumed) initially formed adduct (R_2N–O–S–R), and it is the instability of this adduct that gives rise to the range of different products observed. In light of this observation, and following a reexamination of the spectral data, we have reassigned the structure of adduct (3) to the corresponding sulfoxamide (25). The t-butyl group of the adduct exhibits a quaternary carbon chemical shift of 58.8 ppm,[17] which is consistent with the sulfoxamide (25).



(25)

The corresponding carbon in (3) would be expected to absorb some 10–15 ppm upfield of this (cf. di-t-butyl sulfide and disulfide, δ_{Cquat} 45.6 ppm[18]).

Conclusions and Significance

Whereas carbon-centred radicals generally react cleanly and efficiently with aminoxyls such as TMIO to produce stable alkoxyamine products, the quantity and structure of which reflect the quantity and structure of the precursor radicals (divalent), sulfur-centred radicals react with aminoxyls such as TMIO to produce a range of different products and do so in proportions that depend on the type of sulfur radical, and on the type and concentration of aminoxyl employed. The formation of the corresponding sulfoxamide provides good qualitative evidence for the presence of a particular sulfur-centred radical. However, because the aminoxyl-trapping technique results in the formation of varying amounts of different products, it would be difficult to use this technique for quantitative work with sulfur-centred radicals.

It is proposed that aminoxyl adducts of electron-rich or readily oxidized systems, such as divalent sulfur, trivalent phosphorus and electron-rich alkenes, undergo facile homolytic fragmentation with loss of the corresponding aminyl radical.

Experimental

General

IR spectra were recorded as thin films for liquids. NMR spectra were recorded in $CDCl_3$ on a Varian UNITY-400 or a Varian Gemini 200

spectrometer. Chemical shifts are referenced to TMS (^{1}H and ^{13}C) unless otherwise stated, and *J* values are given in Hz. LSIMS mass spectra were run by Dr Noel Davies at the University of Tasmania on a Kratos ISQ high-resolution magnetic sector mass spectrometer using *m*-nitrobenzoic acid as the liquid matrix. The ESI mass spectra were run on a VG Platform II mass spectrometer, coupled to a MassLynx data system. Di-t-butyl diperoxyoxalate (DTBPO),[19] and 1,1,3,3-tetramethyl-2,3-dihydroisoindol-2-yloxyl (TMIO, 1)[20] were prepared using literature procedures. Products were analysed using reverse-phase HPLC–MS (electrospray mass spectrometry, ES^+) using mixtures of methanol/water with 270 nm for detection. Peak areas from the HPLC chromatogram were converted directly into relative yields of products (taking into account differences in extinction coefficients, ε). The extinction coefficients (ε) were measured relative to TMIO (713 L mol^{-1} cm^{-1} at 270 nm).[21]

Reaction of DTBPO, 2-Mercaptoethanol (4) and (1)

A solution of DTBPO (0.335 g, 1.43 mmol) and (1) (0.342 g, 1.80 mmol) in benzene (5 mL) and a solution of (4) (0.335 g, 4.29 mmol) in benzene (5 mL) were prepared separately in the two legs of a Y-flask under argon. Slowly the two solutions were mixed and an immediate exothermic reaction was observed. The solution was heated at 60°C for 75 min. (approximately six half-lives for DTBPO), cooled and evaporated to dryness. The crude product was analysed by HPLC–MS and products (5) and (6) were isolated by preparative HPLC using 60–100% mixtures of methanol in water as eluent. The order of elution from the HPLC column was (5) (ε = 390 L mol^{-1} cm^{-1} at 270 nm), followed by (6) (ε = 418 L mol^{-1} cm^{-1} at 270 nm), followed by (9) [several unsuccessful attempts were made to isolate this minor product. It was tentatively identified as the hydroxylamine sulfonate ester (9) by HPLC–MS (MNa^+, 322)].

New Compounds

*2-(2′-Hydroxyethylsulfinyl)-1,1,3,3-tetramethyl-2,3-dihydro-1*H-*isoindole (5)* was isolated as white needles, m.p. 127–128°C (Found: M^+, 267.1295. $C_{14}H_{21}NO_2S$ requires M^+, 267.1293). ν_{max} (cm^{-1}) 2974, 2254, 1466, 1383, 1095, 1060 (S=O). ε = 390 L mol^{-1} cm^{-1} at 270 nm. ^{1}H NMR δ 1.72, s, 6H, CH_3; 1.80, s, 6H, CH_3; 2.97–3.07, m, 1H, SCH_2; 3.42–3.45, m, 1H, OH; 3.79–3.92, m, 1H, SCH_2; 4.07–4.18, m, 2H, C**H**$_2$OH; 7.10–7.14, m, 2H, Ar-4,7-CH; 7.27–7.32, m, 2H, Ar-5,6-CH. ^{13}C NMR δ 32.0 (CH_3); 32.8 (CH_3); 55.6 ($SOCH_2$); 58.8 (CH_2OH); 70.7 (1,3-C); 121.1 (Ar-4,7-CH); 127.7 (Ar-5,6-CH); 128.0 (Ar-5,6-CH); 145.3 (3a,7a-C). Mass spectrum (ES^+): *m/z* 557 (M_2Na^+, 20%); 290 (MNa^+, 23); 268 (MH^+, 5); 176 (100). (EI): *m/z* 267 (MH^+, 19%); 252 (78); 222 (100); 160 (59).

*2-(2′-Hydroxyethylsulfonyl)-1,1,3,3-tetramethyl-2,3-dihydro-1*H-*isoindole (6)* was isolated as cream-coloured needles, m.p. 153–154°C (Found: MH^+, 284.1329. $C_{14}H_{22}NO_3S$ requires MH^+, 284.1320). ν_{max} (cm^{-1}) 1646, 1465, 1384, 1322, 1147. ε = 1154 l mol^{-1} cm^{-1} at 270 nm. ^{1}H NMR δ 1.79, s, 12H, CH_3; 3.31–3.37, t, *J* 5.5 Hz, 2H, $SO_2CH_2CH_2$; 4.11–4.16, t, *J* 5.5 Hz, 2H, C**H**$_2$OH; 7.10–7.15, m, 2H, Ar-4,7-CH; 7.30–7.35, m, 2H, Ar-5,6-CH. ^{13}C NMR δ 30.9 (CH_3); 57.7 (SO_2**C**H_2CH_2); 60.6 (CH_2OH); 70.1 (1,3-C); 121.2 (Ar-4,7-CH); 126.1 (Ar-5,6-CH); 144.3 (3a,7a-C). Mass spectrum (EI): *m/z* 284 (MH^+, 100%); 268 (65); 159 (52).

General Procedure for Acetylation of (5) and Benzoylation of (6)

Acetic anhyride (1 drop) was added to a stirred solution of (5) (10 mg, 0.04 mmol) in pyridine (0.5 mL) at 5°C. The reaction was left overnight at 0–5°C, water (2 mL) was added and the solution was left to stand at room temperature for a further 15 min. The aqueous mixture was extracted with dichloromethane (5 × 5 mL). The organic extracts were washed with hydrochloric acid solution (2 × 5 mL, 2 M), saturated sodium hydrogen carbonate solution (5 mL), water (5 mL), dried ($MgSO_4$) and the solvent was evaporated to dryness to yield white crystals of *2-(2′-Acetoxyethylsulfinyl)-1,1,3,3-tetramethyl-2,3-dihydro-1*H-*isoindole (10)* (12 mg, 97%), m.p. 63–64°C (Found: MH^+, 310.1477. $C_{16}H_{23}O_3S$ requires MH^+, 310.1477). ν_{max} (cm^{-1}) 1741 (C=O), 1653, 1458, 1383, 1245, 1061 (S=O). ^{1}H NMR δ 1.71, s, 6H, CH_3; 1.79, s, 6H, CH_3; 2.11, s, 3H, $OCCH_3$, 3.48–3.56, m, 2H, $SOCH_2CH_2$; 4.42–4.49, m, 2H, CH_2OCO; 7.10–7.14, m, 2H, Ar-4,7-CH; 7.29–7.33, m, 2H, Ar-5,6-CH. ^{13}C NMR δ 20.8 (OC**C**H_3); 32.0 (CH_3); 32.5 (CH_3); 53.9 (S**C**H_2CH_2); 59.7 (**C**H_2OCO); 70.5 (1,3-C); 121.1 (Ar-4,7-CH); 127.7 (Ar-5,6-CH); 127.9 (Ar-5,6-CH); 145.3 (3a,7a-C). Mass spectrum (EI): *m/z* 310 (MH^+, 25%); 293 (26); 222 (100); 159 (67).

Similarly, *2-(2′-Benzoyloxyethylsulfonyl)-1,1,3,3-tetramethyl-2,3-dihydro-1*H-*isoindole (11)* was isolated as white needles, m.p. 125–126°C (Found: MH^+, 388.1572. $C_{21}H_{26}NO_4S$ requires MH^+, 388.1572). ν_{max} (cm^{-1}) 1723 (C=O), 1452, 1422, 1335, 1266, 1149. ^{1}H NMR δ 1.80, s, 12H, CH_3; 3.53–3.59, t, *J* 6.6 Hz, 2H, SO_2C**H**$_2CH_2$; 4.78–4.84, t, *J* 6.6 Hz, 2H, CH_2OCO; 7.10–7.56, m, 8H, Ar-H; 8.04–8.08, m, 1H, Ar-H. ^{13}C NMR δ 30.8 (CH_3); 57.0 (SO_2C**H**$_2CH_2$); 59.1 (C**H**$_2$OCO); 69.9 (1,3-C); 121.2 (Ar-4,7-CH); 128.1 (Ar-CH); 128.5 (Ar-CH); 129.6 (Ar-CH); 133.2 (Ar-CH); 144.4 (3a,7a-C). Mass spectrum (ES^+): *m/z* 797 (M_2Na^+, 20%); 410 (MNa^+, 100). (EI): *m/z* 388 (MH^+, 100%); 213 (61); 149 (66).

Reaction of Thiophenol (12) and (1)

Solutions of (1) (0.532 g, 2.8 mmol) in benzene (10 mL) and (12) (0.154 g, 1.4 mmol) in benzene (5 mL) were prepared separately in the two legs of a Y-flask under argon. The two solutions were mixed and allowed to stir for 40 min. at room temperature or at 60°C. The solution was evaporated to dryness, and pentane (10 mL) was added. A thick white precipitate formed, which was collected by vacuum filtration. By comparison with the ^{1}H NMR spectra of 2,2,6,6-tetramethylpiperidinium benzenesulfonate and the corresponding sulfinate prepared by the procedure of Greci et al.,[5] the precipitate was found to consist only of 1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindolinium benzenesulfinate (16). The filtrate was evaporated to dryness and the products quantified by HPLC–MS [taking into account the yield of compound (16)]. The same reaction conditions were employed for the 5 : 1 TMIO : thiophenol experiments, using thiophenol (62 mg, 0.56 mmol) and TMIO (0.532 g, 2.8 mmol). Phenyl disulfide (14) (ε = 1154 L mol^{-1} cm^{-1}) was identified by comparison with an authentic sample. Products (13) (ε = 179 L mol^{-1} cm^{-1} at 270 nm), (15) (ε = 906 L mol^{-1} cm^{-1} at 270 nm), (17) (ε = 793 L mol^{-1} cm^{-1} at 270 nm) and (14) were isolated in sequential order of elution by preparative HPLC using 70–100% mixtures of methanol in water as eluent.

New Compounds

*2-(Benzenelsulfinyl)-1,1,3,3-tetramethyl-2,3-dihydro-1*H-*isoindole (15)* was isolated as white crystals, m.p. 86–87°C (Found: M^+, 299.1344. $C_{18}H_{21}NOS$ requires M^+, 299.1344). ν_{max} (cm^{-1}) 2306, 1422, 1266, 1089 (S=O). ε = 906 L mol^{-1} cm^{-1} at 270 nm. ^{1}H NMR δ 1.57, s, 6H, CH_3; 1.77, s, 6H, CH_3; 7.06–7.11, m, 2H, Ar-H; 7.25–7.30, m, 2H, Ar-H; 7.46–7.60, m, 3H, Ar-H; 7.79–7.84, m, 2H, Ar-H. ^{13}C NMR δ 32.1 (CH_3); 32.8 (CH_3); 70.8 (C); 121.4 (Ar-CH); 126.9 (Ar-CH); 127.8 (Ar-CH); 128.7 (Ar-CH); 130.6 (ArCH); 146.0 (3a,7a-C). Mass spectrum (ES^+): *m/z* 621 (M_2Na^+, 100%); 322 (MNa^+); 300 (MH^+), 176. (EI): *m/z* 299 (M^+, 23%); 284 (62); 125 (100).

*1,1,3,3-Tetramethyl-2,3-dihydro-1*H-*isoindolinium benzenesulfinate (16)* was isolated as white crystals, m.p. 223–224°C (Found: C, 67.8; H, 7.2; N, 4.2%. $C_{18}H_{23}NO_2S$ requires C, 68.1; H, 7.3; N, 4.4%). ^{1}H NMR δ 1.73, s, 12H, CH_3; 7.10–7.15, m, 2H, Ar-H; 7.33–7.42, m, 5H, Ar-H; 7.71–7.75, m, 2H, Ar-H. ^{13}C NMR δ 29.6 (CH_3); 67.3 (C); 121.6 (Ar-CH); 124.9 (Ar-CH); 128.5 (Ar-CH); 129.1 (Ar-CH); 129.4 (Ar-CH); 143.6 (C); 155.8 (C).

*1,1,3,3-Tetramethyl-2,3-dihydro-1*H-*isoindolinium benzenesulfonate (17)* was isolated as a gum (Found: MH^+, 332.1316. $C_{18}H_{22}NO_3S$ requires MH^+, 332.1320). ν_{max} (cm^{-1}) 2252, 1640, 1467, 1380, 1189. ^{1}H NMR δ 1.51, s, 12H, CH_3; 6.94–6.99, m, 2H, Ar-H; 7.15–7.20, m, 2H, Ar-H; 7.49–7.53 m, 3H, Ar-H; 7.97–8.01, m, 2H, Ar-H. ^{13}C NMR δ 30.0 (CH_3); 70.8 (1,3-C); 97.2 (C), 121.8 (Ar-CH); 128.0 (Ar-CH); 129.1 (Ar-CH), 129.9 (Ar-CH), 134.3 (Ar-CH); 146.7 (3a,7a-C). Mass spectrum (ES^+): *m/z* 685 (M_2Na^+, 100%); 354 (MNa^+, 40); 332 (MH^+, 10). (LSIMS): *m/z* 332 (MH^+, 73%); 190 (100); 174 (50); 154 (80); 136 (52).

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