it is clear that $J_{5-8} \approx 1$ Hz, while $J_{6-8} \approx 0$. This fact apparently eluded Paudler and co-workers,[1b] who reversed H_5, H_6 chemical shift assignments even though their own data on 3,5-dideuterioimidazo[1,2-*a*]pyrazine (**3b**) showed no 6–8 coupling constant. The imidazo[1,2-*a*]pyridine analogue of **7** was previously synthesized in low yield from 2-bromoacetoacetaldehyde.[5]

To our knowledge the structure solution of **7** represents the first crystal structure of an imidazo[1,2-*a*]pyrazine.[6] Bond distances and angles are given in Figure 1 and Figure 2 is a two-dimensional representation of **7**. The nine atoms of the fused-ring system form a least-squares plane with a maximum deviation of 0.01 Å, while the maximum deviation from a plane for the four atoms of the keto group is also 0.01 Å. The angle between the two planes in the solid state is 6.7°.

Experimental Section

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were recorded on Varian T-60 or EM-390 spectrometers in $CDCl_3$ (unless otherwise specified) relative to Me_4Si internal standard. Infrared spectra were recorded on a Perkin-Elmer 621 grating spectrophotometer. Microanalyses were within ±0.4% of calculated values. The X-ray structure was determined on a Syntex Model P-2_1 four-circle automatic diffractometer.

X-ray Structure of 3-(1-Oxoethyl)imidazo[1,2-*a*]pyrazine (7). Crystallization of **7** from dilute solution in toluene gave suitable crystals having symmetry *Pbca* with $a = 6.686$ (1) Å, $b = 9.37$ (2), and $c = 23.906$ (7). The structure was solved by using standard direct methods and refined by using the full-matrix least-squares method. The final *R* factor calculated from the 730 observed reflections measured with Cu Kα radiation was 0.048. Table I contains the final fractional coordinates and temperature parameters (see supplementary material available paragraph).

The following library of crystallographic programs was used: MULTAN 78, University of York, York, England (1978); X-RAY 72, University of Maryland, College Park, MD (1972); ORTEP-II, Oak Ridge National Laboratory, Oak Ridge, TN (1970).

3-(1-Hydroxyethyl)imidazo[1,2-*a*]pyrazine (4b). A solution of 2.85 g (30.0 mmol) of aminopyrazine in 100 mL of CH_2Cl_2 was added to 28.5 g alumina (E. Merck, Darmstadt; activity I). The resulting stirred suspension was treated with a solution of 2,3-epoxypropanal (cis and trans; 2.58 g, 30.0 mmol) in 10 mL of CH_2Cl_2 and the suspension was stirred overnight at room temperature under N_2. The mixture was vacuum filtered, and the cake was washed with 100 mL of CH_2Cl_2 and two, 100-mL portions of 2% MeOH–CH_2Cl_2. The combined filtrate was concentrated under vacuum at 25 °C to give 3.6 g of orange solid, which was chromatographed on activity III alumina. Elution with CH_2Cl_2 gave fractions containing 1.25 g of pure 3-(1-hydroxyethyl)imidazo[1,2-*a*]pyrazine (26%): mp 152–153 °C; ^{1}H NMR (Me_2SO-d_6) δ 9.00 (1 H, d, $J = 1$ Hz), 8.50 (1 H, dd, $J = 1, 4$ Hz), 7.93 (1 H, d, $J = 4$ Hz), 7.75 (1 H, br s), 5.55 (1 H, d, $J = 6$ Hz), 5.27 (1 H, m), 1.62 (3 H, d, $J = 6$ Hz).

Anal. Calcd for $C_8H_9N_3O$: C, 58.88; H, 5.56; N, 25.75. Found: C, 58.63; H, 5.80; N, 26.03.

Extraction of the alumina in a Soxhlet thimble with boiling methanol caused partial decomposition of **4b** to imidazo[1,2-*a*]pyrazine, mp 83–85 °C (mixture melting point with authentic sample[1b] undepressed; isolated from the column chromatography).

3-(1-Oxoethyl)imidazo[1,2-*a*]pyrazine (7). 3-(1-Hydroxyethyl)imidazo[1,2-*a*]pyrazine (1.47 g, 900 mmol) and manganese dioxide (7.2 g) were stirred in 50 mL of acetone for 1 week at room temperature. The mixture was filtered through Celite and the filtrate was concentrated to give 1.5 g of crude product. Chromatography on silica gel (MeOH–CH_2Cl_2) gave fractions containing 1.3 g (81%) of pure ketone **7**: mp 160–161.5 °C; ^{1}H NMR δ 9.40 (1 H, dd, $J = 1, 4.5$ Hz), 9.23 (1 H, d, $J = 1$ Hz), 8.42 (1 H, s), 8.18 (1 H, d, $J = 4.5$ Hz), 2.68 (3 H, s); IR (KBr) 1650, 1190 cm^{-1}.

Anal. Calcd for $C_8H_7N_3O$: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.21; H, 4.33; N, 26.20.

3-(1-Hydroxyethyl)imidazo[1,2-*a*]pyridine (4a). By a procedure similar to that for synthesis of **4b**, reaction of 2-aminopyridine (2.82 g, 30.0 mM) and 2,3-epoxypropanal (2.58 g, 30.0 mM) in CH_2Cl_2 on alumina gave, after chromatography on alumina, 2.6 g (53%) of 3-(1-hydroxyethyl)imidazo[1,2-*a*]pyridine: mp 141–142.5 °C (CH_3CN) [lit.[5] mp 148–150 °C ($PhCH_3$; corr.)]; ^{1}H NMR δ 8.43 (1 H, d, $J = 6.5$ Hz), 7.47 (1 H, d, $J = 9$ Hz), 7.17 (1 H, s), 7.17 (1 H, t), 6.77 (1 H, t), 5.14 (1 H, q, $J = 6$ Hz) 1.7 (3 H, d, $J = 6$ Hz).

Attempted sublimation of the product at 140 °C (0.2 torr) gave a mixture of **4a** and imidazo[1,2-*a*]pyridine identical by mixture TLC (R_f 0.57 on silica gel; 5% 2-propanol in $CHCl_3$ saturated with aqueous NH_3) and ^{1}H NMR.[7]

Registry No. 4a, 30489-50-0; **4b**, 78109-24-7; **5a**, 504-29-0; **5b**, 5049-61-6; *cis*-**6**, 78109-25-8; *trans*-**6**, 71403-93-5; **7**, 78109-26-9; imidazo[1,2-*a*]pyrazine, 274-79-3; imidazo[1,2-*a*]pyridine, 274-76-0.

Supplementary Material Available: The positional and thermal parameters from the X-ray structure of **7** (1 page). Ordering information is given on any current masthead page.

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Spin Trapping of Radicals Generated in the UV Photolysis of Alkyl Disulfides

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Disulfide (S–S) linkages, their formation as well as bond scission, play a vital role in the areas of biochemistry[1] and food science.[2] It has been frequently observed that photolysis of disulfides yielded thiyl radicals.[3,4] Callear and Dickson[5] concluded that both S–S and C–S bond scission occurred during the flash photolysis of dimethyl disulfide. Byers et al.[6] showed by product analysis that C–S bond cleavage is predominant in the photodecomposition of *tert*-butyl disulfide and benzyl disulfide. Shortly thereafter, Rosenfeld et al.[7] presented photo-CIDNP evidence for C–S bond rupture in the photolysis of *tert*-butyl disulfide in benzene solution. Recently Ito et al.[4] reported that flash photolysis of di-*tert*-butyl disulfide resulted in a transient absorption band at 370 nm and they attributed this absorption to the thiyl radicals generated by S–S bond cleavage. The S–S bond cleavage has also been achieved by vapor pyrolysis,[8] enzymatic,[9] and other chemical means. Rosenthal and Oster[10] observed that successive alkylation causes shift in the UV absorption maximum and they proposed that the acidity of the C–H bond situated α to the S–S linkage plays a vital role in the alkali cleavage.

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In our present work, a spin-trapping technique is used to detect the photodecomposition of disulfides in organic solvents. This technique involves the use of nitroso[11] or nitrone[12] compounds as spin traps which react with short-lived radicals to produce more stable spin adducts. The spectral information contained in the adduct is often less than that of the parent radical. However, on the basis of the previously known spin adducts of similar compounds, many conclusions can be drawn by comparing their spectral characteristics. With the prolonged lifetime, both the alkyl and thiyl radicals may be simultaneously trapped and detected in a single experiment.

Materials and Methods

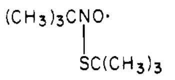
The spin trap, 2-methyl-2-nitrosopropane (tNB), and alkyl disulfides were purchased from Aldrich Chemical Co., Milwaukee, WI. Nitrosamines were obtained from Eastman Organic Chemicals, Eastman Kodak Co., Rochester, NY. In spin-trapping experiments, the concentration of disulfides in benzene ranges between 0.5 and 4 M and tNB between 0.01 and 0.05 M, while *N*-nitrosamine is approximately 1 M.

Samples were irradiated in an ESR quartz flat cell by using a high-pressure Schoffel mercury lamp. ESR spectra were obtained with a Varian E9 ESR spectrometer. The *g* values were calculated, using DPPH as a standard. The magnetic fields were calibrated with Mn^{2+}, an impurity in strontium oxide powder.

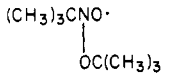
Di-*tert*-butyl nitroxide radical was separated by using a Perkin-Elmer 601 HPLC with a Perkin-Elmer LC55 spectrophotometer as detector.

Results

Photolysis of a benzene solution containing 0.01 M tNB and 1–4 M *tert*-butyl disulfide yielded the ESR spectrum shown in Figure 1a. Lines labeled A, a triplet with a_N = 1.50 + 0.02 mT, are probably due to a spin adduct of thiyl radical with tNB (I). Other similar spin adducts were observed by Wargon and Williams[13] and Leaver and Ramsay.[14] In our experiment, the trapping of the thiyl radical resulting from S–S bond cleavage of *tert*-butyl disulfide will yield radical I. Lines marked B are a larger triplet with a_N = 2.71 ± 0.02 mT, which closely resemble the previously published spin-adduct spectrum of *tert*-butoxy radical (II) observed by Sargent and Gardy[15] in the γ irradiation of *tert*-butyl alcohol in the presence of tNB. Formation of peroxy radicals is also possible in the photolysis of the disulfide. Trapping of the peroxy radical by tNB, however, has not been observed previously. The peroxy radical could very easily combine with a *tert*-butyl radical to yield di-*tert*-butyl peroxide. Homolytic cleavage of this followed by spin trapping could lead to II.

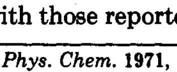

$(CH_3)_3CN(O\cdot)SC(CH_3)_3$

I


$(CH_3)_3CN(O\cdot)OC(CH_3)_3$

II

In N_2-bubbled solution, lines marked B in Figure 1a were considerably suppressed, while extended photolysis yielded the well-known ESR spectrum of the di-*tert*-butyl nitroxide radical (III),[17-20] shown in Figure 1b, with A_N = 1.54 ± 0.02 mT and $A(^{13}C)$ = 0.4 ± 0.02 mT and g = 2.0063, which agree closely with those reported earlier in benzene solutions (A_N = 1.543 mT, A_{13C} = 0.426 mT).[20] Lemaire et al.[19] by comparing di-*tert*-butyl nitroxide and hexamethylacetone attributed the ^{13}C satellite lines to the coupling of the unpaired electron with the naturally abundant ^{13}C ($I = 1/2$) of the methyl groups through hyperconjugation.


$(CH_3)_3CN(O)C(CH_3)_3$

III

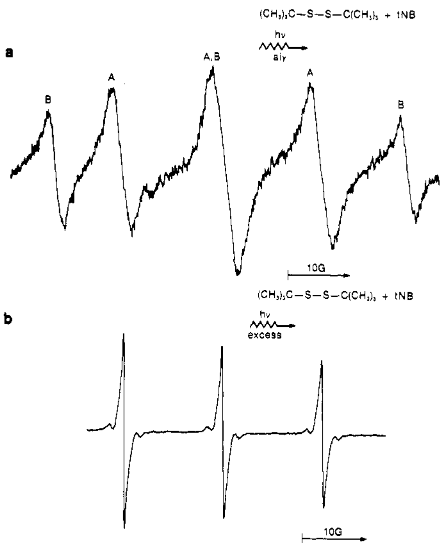


Figure 1.

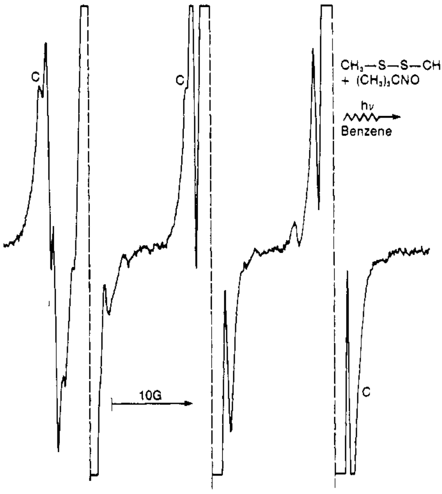


Figure 2.

In order to demonstrate that *tert*-butyl radicals, which by addition to tNB give radical III, were also generated by the photolytic cleavage of the C–S bond in di-*tert*-butyl disulfides with photodecomposition of tNB,[17] nitrosamines (diethylnitrosamine, nitrosopiperidine, dibutylnitrosamine) in benzene solution or $NaNO_2$ in methanol solution, both of which do not contain a *tert*-butyl functional group, were used in place of tNB spin trap. An ESR spectrum identical with that attributed to III (Figure 1b) was observed for nitrosamines, while identical hyperfine value with that of the di-*tert*-butyl nitroxide in methanol[18] was observed for the case of $NaNO_2$. In addition, HPLC fractions (reverse phase; methanol–water, 1:1) which contain the respective

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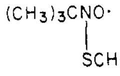
3738 J. Org. Chem. 1981, 46, 3738–3741

paramagnetic species of both experiments, tNB or nitrosamine as spin traps, occurred at the identical retention times and presented identical ESR spectra. Consequently, it is concluded that *tert*-butyl radicals were also generated by the photolytic cleavage of the C–S bond.

Photolysis of dimethyl disulfide in the presence of tNB in benzene solution gave the ESR spectrum shown in Figure 2. The intense triplet was attributed to radical III. A weaker set of lines was also observed (labeled C in Figure 2) with $A_N = 1.88 \pm 0.02$ mT and $A_{CH_3} = 0.08 \pm 0.02$ mT, which was attributed to radical IV, resulting from S–S bond cleavage in the photolysis of dimethyl disulfide.

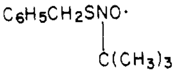


$(CH_3)_3CN(O\cdot)SCH_3$

IV

The spectral intensity increases at higher field due to continuous illumination and growth of radical III during the scan. In addition $M_I = 0$ and -1 peaks of both radicals overlap. Consequently, ^{13}C lines of radical III severely interfere with radical IV. The ESR spectral parameters of radical IV were reported by Wargon and Williams[13] as $A_N = 1.89$ mT and $A_{CH_3} = 0.12$ mT in their low-temperature (−103 °C) radiolysis of alkanethiol, using tNB as the spin trap.

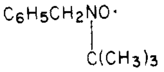
For dibenzyl disulfide, a triplet spectrum with $A_N = 1.72$ mT and $g = 2.0068$ was observed, due presumably to radical V, arising from S–S bond cleavage. Since this radical has not been reported in the literature thus far, it was compared with the ESR parameters for $(CH_3)_3CN(O\cdot)SCH(CH_3)_2$ reported by Wargon and Williams[13] ($A_N = 1.699$ mT, $g = 2.0068$) and by Leaver and Ramsay[14] ($A_N = 1.67$ mT and $g = 2.0062$).



$C_6H_5CH_2SN(O\cdot)C(CH_3)_3$

V

Another set of lines with $A_N = 1.50 \pm 0.02$ mT and $A_{CH_2} = 0.75 \pm 0.02$ mT and $g = 2.0062$ was also observed, which was assigned to radical VI, arising from C–S bond cleavage.

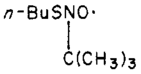


$C_6H_5CH_2N(O\cdot)C(CH_3)_3$

VI

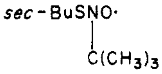
Radical VI is the H adduct of α-phenyl-*N*-*tert*-butylnitrone (PBN); the ESR parameters for VI have been reported by Leaver and Ramsay[14] ($A_N = 1.498$ mT, $A_{CH_2} = 0.727$ mT, $g = 2.0062$) and several others (Mao and Kevan,[21] Mao and Kevan,[22] and Janzen and Blackburn[23]). Hence there is less uncertainty about this structure assignment.

Lastly, di-*n*-butyl and di-*sec*-butyl disulfides yielded triplets ($A_N = 1.81 \pm 0.02$ mT and $A_N = 1.72 \pm 0.02$ mT, respectively), presumably due to radicals VII and VIII.



$n\text{-BuSN}(O\cdot)C(CH_3)_3$

VII

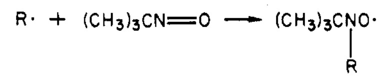


$sec\text{-BuSN}(O\cdot)C(CH_3)_3$

VIII

Discussion

We have utilized the spin-trapping technique to observe alkoxy, alkyl, and thiyl radicals simultaneously in the photodecomposition of various disulfides. In our present work, both S–S and C–S bond cleavage were observed by spin trapping the radicals generated in the photolysis of alkyl disulfides in the presence of tNB.



$$R\cdot + (CH_3)_3CN{=}O \longrightarrow (CH_3)_3CN(O\cdot)R$$

For di-*tert*-butyl disulfides, depending on the duration of UV irradiation, *tert*-butyl, alkoxy, and thiyl radicals were trapped. The hyperfine parameters of all four spin adducts (III, IV, V, and VI) agree well with the previously published results even though their methods of generation are quite different. We have also demonstrated that di-*tert*-butyl nitroxide radical (III) can be obtained simply by the recombination of phytolytic fragments of C–S bond cleavage from disulfides and N–N bond cleavage from nitrosamines. Unlike the tNB spin trap, nitrosamine does not contain *tert*-butyl functional group and thus di-*tert*-butyl nitroxide radical (III) must necessarily contain fragments of C–S bond breakage from disulfide molecule. The HPLC–ESR analysis further strengthened the identification of di-*tert*-butyl nitroxide radical. Di-*n*-butyl, di-*sec*-butyl, and dimethyl disulfides gave spin adducts consisting of only the S–S bond fragments, while di-*tert*-butyl and dibenzyl disulfide spin adducts indicated the trapping of both S–S and C–S bond scission products.

In summary, as most biological systems and food components contain disulfide linkages, spin-trapping techniques can be used to study their photodecomposition products since alkyl, alkoxy, and thiyl radical spin adducts give distinct ESR spectra and may be detected simultaneously.

Acknowledgment. Many helpful discussions with Dr. A. E. Pohland are deeply appreciated.

Registry No. I, 78109-57-6; II, 52323-95-2; III, 2406-25-9; IV, 58921-64-5; V, 74928-99-7; VI, 24293-08-1; VII, 58921-68-9; VIII, 78109-58-7.

Total Synthesis of the Alleged (±)-Chiloscyphone

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Chiloscyphone is a main component of the essential oil collected from the plant *Chiloscyphus polyanthus* (L) corda, hepaticae.[1] The structural assignment of chiloscyphone, based on its spectral properties and products derived from hydrogenation, led to the formulation 1. In this paper we describe a total synthesis of 1 by a stereospecific route, the key intermediates of which were derived by antithetic analysis (Scheme I).

Owing to the relative instability of α-methylene ketones, our initial focus was on the synthesis of octalone 2. It was envisioned that 2 could in turn be prepared via the intramolecular variant of the Diels–Alder reaction,[2] thereby forming the two six-membered rings with the simultaneous introduction of the three requisite chiral centers.[3] Accordingly, the stereospecific construction of the requisite

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