

Photochemical Desulphurization of Indoline-2-thiones

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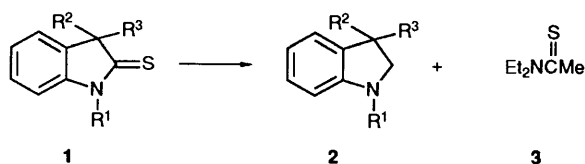
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The photochemical reactions of indoline-2-thiones in the presence of amines have been examined. Irradiation of indoline-2-thiones **1** in the presence of triethylamine yielded the desulphurization products, indolines **2**, along with *N,N*-diethylthioacetamide **3**. The photodesulphurization reactions of indoline-2-thiones **1** can be explained by a sequential electron/proton-transfer mechanism from the amine to the excited indoline-2-thione.

The photochemistry of thiocarbonyl compounds has been extensively studied over the past two decades. As a result of differences in chemical reactivity and thermodynamic properties, the observed photoreactions of thiocarbonyl compounds often follow a different course from those of analogous carbonyl compounds. The majority of those reported involving thioketones undergo [2 + 2]cycloaddition to alkenes, allenes, imines and alkynes, intramolecular or intermolecular hydrogen abstraction, and photooxidation.¹⁻⁸ However, relatively few reports have dealt with the photochemical properties involving the C=S group of thioamides. The observed reactions of thioamides are [2 + 2]photocycloadditions of alkenes at the C=S double bond to form aminothietanes, which are usually unstable and have not been isolated, and are transformed into fragmentation products. We recently reported photodesulphurization reactions⁹ of indoline-2-thiones, which have at least one hydrogen at the 3-position, as well as intramolecular¹⁰ and intermolecular¹¹ [2 + 2]photocycloaddition reactions to afford alkenes. We report here the photoreactions of indoline-2-thiones in the presence of an amine, which produced indolines by photodesulphurization.¹²

Results and Discussion

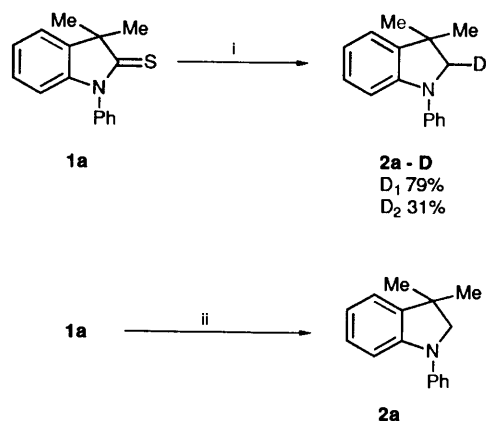
Although indoline-2-thiones which have at least one hydrogen at the 3-position gave indoles on irradiation,⁹ 3,3-disubstituted indoline-2-thiones **1** were inert to photolysis. However, irradiation of 3,3-dimethyl-1-phenylindoline-2-thione **1a** in benzene in the presence of triethylamine in a Pyrex vessel with a high-pressure mercury lamp under argon for 5 h at room temperature gave the desulphurization product, 3,3-dimethyl-1-phenylindoline **2a**, and *N,N*-diethylthioacetamide **3** in 45



Scheme 1 Reagent and conditions: *hν*, amine

and 43% isolated yields, respectively. The structure of these photoproducts (**2a** and **3**) was confirmed by direct comparison of their IR and NMR spectra with those of authentic materials, which were independently prepared by the reduction of 3,3-dimethyl-1-phenylindolin-2-one with lithium aluminium hydride¹³ and by the thionation of *N,N*-diethylacetamide with Lawesson's reagent [2,4-bis-(*p*-methoxyphenyl)-1,3-dithiaphosphetane 2,4-disulphide], respectively. Irradiation of indoline-2-thiones **1b-1j** and **1l** in the presence of triethylamine under the same conditions as described above similarly gave the

desulphurization products, **2b-2j** and **2l** in 11–70% isolated yield (Scheme 1). When indoline-2-thiones **1b-1g**, which have hydrogens intramolecularly abstractable in the side chain at C-3 by the thiocarbonyl group,¹⁴ were irradiated in the presence of amine no other photoproducts except the indolines **2b-2g** were detected. The photodesulphurization was not observed for the case of 1-methyl-3,3-diphenylindoline-2-thione **1k**. Photodesulphurization reactions of compound **1a** was examined under various conditions. The results are summarized in Table 1. Excitation of compound **1a** in the presence of tertiary amines such as tributylamine, tribenzylamine, dimethylaniline and diethylaniline resulted in the formation of desulphurization product, indoline **2a**, in moderate yields. Photodesulphurization of compound **1a** also took place in the presence of secondary amines, but in low yield. On the other hand, primary amines and triphenylamine, which does not have easily abstractable hydrogens, were not effective toward photodesulphurization of compound **1a**. Generally, amines with lower ionization potentials and aliphatic tertiary amines seem to be more favourable for the formation of desulphurization product, indoline **2a**. The photodesulphurization of compound **1a** was not observed when the indoline-2-thione **1a** was irradiated in ethanol, or in hydrogen-donating solvents such as diethyl ether and tetrahydrofuran (THF), or in the presence of hydrogen donors such as 9,10-dihydroanthracene and xanthene in benzene. Propan-2-ol was also unsuitable for the photodesulphurization, since the yield of indoline **2a** was low (8%). On the basis of relative reactivities of amines and hydrogen donors, the photodesulphurization is suggested to occur through an initial electron transfer from the amine to the electron-deficient sulphur atom of the excited thioamide thiocarbonyl group, followed by proton transfer and electron redistribution (Scheme 3). The photodesulphurization proceeds smoothly in benzene and acetonitrile, but does not proceed in



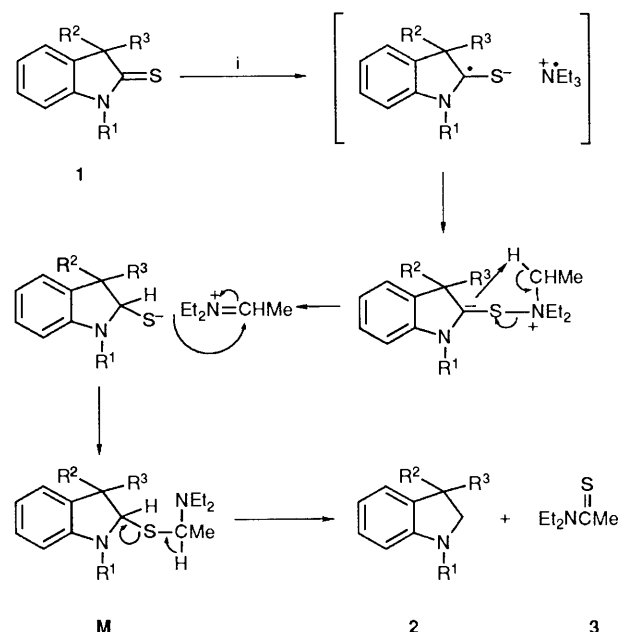
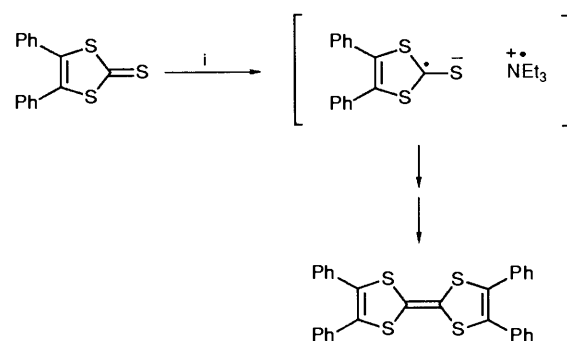
Scheme 2 Reagents and conditions: i, *hν*, PhN(CD₂Me)₂; ii, *hν*, Et₃N-C₆H₆

Table 1 Yields of the indolines 2

	R ¹	R ²	R ³	Amine	Solvent	Yield (%) ^a	
1a	Ph	Me	Me	Et ₃ N	Benzene	45 (78) ^b	
				(7.50) ^c	Et ₃ N	MeCN	(65)
				Et ₃ N	MeOH	(0)	
				Et ₂ NH	Benzene	(17)	
				(8.01)	Bu ₃ N	Benzene	(62)
				Bu ₂ NH	Benzene	(9)	
				(7.69)	BuNH ₂	Benzene	(0)
				(8.71)	PhNMe ₂	Benzene	(44)
				(7.10)	PhNEt ₂	Benzene	(22)
				(PhCH ₂) ₃ N	Benzene	(45)	
				Ph ₃ N	Benzene	(0)	
				(6.86)	Ph ₂ NEt	Benzene	(trace)
				PhNHEt	Benzene	(22)	
				PhNH ₂	Benzene	(0)	
				(7.71)		EtOH	(0)
						(10.50) ^c	
						Et ₂ O	(0)
		(9.53)					
		THF	(0)				
		Pr ⁱ OH	(8)				
		Benzene	(trace)				
		Benzene	(trace)				
		DHA ^d					
		Xanthene					
1b	Ph	-[CH ₂] ₄ -		Et ₃ N	Benzene	48	
1c	Ph	-[CH ₂] ₅ -		Et ₃ N	Benzene	48	
1d	Ph	-[CH ₂] ₂ O[CH ₂] ₂ -		Et ₃ N	Benzene	70	
1e	Ph	Me	Ph[CH ₂] ₃	Et ₃ N	Benzene	48	
1f	Ph	Me	Isopentyl	Et ₃ N	Benzene	44	
1g	Ph	Me	EtO[CH ₂] ₂	Et ₃ N	Benzene	50	
1h	PhCH ₂	Me	Me	Et ₃ N	Benzene	11	
1i	Bu	Me	Me	Et ₃ N	MeCN	32	
1j	Me	Me	Me	Et ₃ N	Benzene	33	
1k	Me	Ph	Ph	Et ₃ N	MeCN	0 ^e	
1l	H	Ph	Ph	Et ₃ N	MeCN	33	

^a Isolated yield. ^b Yields in parentheses determined by GLC. ^c Ionization potential (eV).¹⁵ ^d 9,10-Dihydroanthracene. ^e **1k** in benzene gave an intractable mixture on irradiation.

methanol. These results can be explained in terms of hydrogen-bonding interaction between the amine and the alcohol, which suppress the electron-transfer process.¹⁶ In this photo-desulphurization, hydrogen transfer from the amine to the indoline-2-thione **1** must be involved. In order to examine the mechanism for the formation of indolines **2** in detail, α -tetradeuteriated *N,N*-diethylamine (DEA-*d*) was prepared and photochemical reaction of the indoline-2-thione **1a** in the presence of DEA-*d* was carried out. When a solution of the indoline-2-thione **1a** in benzene was irradiated in the presence of DEA-*d* under the same conditions as described above, the indoline **2a-D**, which was deuteriated at C-2 position (D content: D₁ 79%, D₂ 31%, calculated from mass spectrum). Meanwhile, no deuteriated indoline **2a-D** was obtained when the indoline-2-thione **1a** was irradiated in hexadeuteriated benzene in the presence of triethylamine (Scheme 2). From these results, we postulate a plausible mechanism for the formation of desulphurization products, indolines **2**, as shown in Scheme 3, which involves the zwitterionic intermediates resulting from electron transfer from the amine to the excited indoline-2-thione **1** followed by proton transfer and electron redistribution, although we could not detect any evidence for the intermediacy of species **M**. An analogous intermediate has been proposed in the photochemical amine- or phosphite-promoted coupling of 2-

Scheme 3 Reagent and conditions: i, hv, Et₃NScheme 4 Reagent and conditions: i, hv, Et₃N

thioxo-1,3-dithioles¹⁷ as shown in Scheme 4. The photo-reactions described above could provide a convenient preparative route to indoline derivatives.

Experimental

M.p.s and b.p.s are uncorrected. IR spectra were recorded on a Hitachi 260-30 spectrophotometer. ¹H and ¹³C NMR spectra were run on a JEOL FX-100 (100 MHz) spectrometer, with CDCl₃ as solvent and tetramethylsilane as internal standard. Silica gel (Merck Kieselgel 60 or Wakogel C-300 for flash chromatography) was used for column chromatography.

Starting Materials.—Indoline-2-thiones **1a–1d**, **1f–1k** were prepared according to methods previously described in the literature,^{9–11} and indoline-2-thiones **1e** and **1l** were prepared by a modification of these methods.

3-Methyl-1-phenyl-3-(3-phenylpropyl)indoline-2-thione 1e, m.p. 99.5–91.5 °C (Found: C, 80.55; H, 6.5; N, 3.9. C₂₄H₂₃NS requires C, 80.65; H, 6.5; N, 3.9%); ν_{\max} (KBr)/cm⁻¹ 1595, 1495, 1365, 755, 725 and 695; δ_{H} 0.87–1.65 (2 H, m), 1.52 (3 H, s), 1.83–2.60 (4 H, m), 6.59–6.69 (1 H, m) and 6.98–7.63 (13 H, m); δ_{C} 26.0 (t), 28.3 (q), 35.8 (t), 41.9 (t), 59.2 (s), 110.4 (d), 123.0 (d), 124.2 (d), 125.6 (d), 127.6 (d), 128.2 (d), 128.3 (d), 129.0 (d), 129.8 (d), 137.0 (s), 138.1 (s), 141.8 (s), 145.7 (s) and 212.2 (s).

3,3-Diphenylindoline-2-thione 1l, m.p. 222–223 °C (Found: C, 79.95; H, 5.0; N, 4.5. C₂₀H₁₅NS requires C, 79.7; H, 5.0; N, 4.65%); ν_{\max} (KBr)/cm⁻¹ 1610, 1590, 1500, 1365, 765, 745 and

695; δ_{H} 6.97–7.36 (14 H, m) and 11.18 (1 H, br s); δ_{C} 72.81 (s), 110.4 (d), 124.3 (d), 136.3 (d), 127.3 (d), 128.2 (d), 128.9 (d), 139.0 (s), 141.5 (s), 142.7 (s) and 209.4 (s).

Preparation of N,N-Diethyl[$^2\text{H}_4$]aniline (DEA-d).—To a solution of acetanilide (1.35 g, 10 mmol) in THF (25 cm³) was added lithium aluminium deuteride (LAD) (420 mg, 10 mmol) and then the mixture was stirred for 15 h at room temperature, poured into dil. HCl, and extracted with diethyl ether. The extract was washed successively with dil. aq. NaOH and water, and then dried over anhydrous magnesium sulphate. After removal of the solvent under reduced pressure, the residual oil was chromatographed on a silica gel column with benzene to give *N*-ethyl[$^2\text{H}_2$]aniline (1.2 g, 98%).

To a solution of *N*-ethyl[$^2\text{H}_2$]aniline (1.2 g) and triethylamine (1 g) in benzene (30 cm³) was added dropwise a solution of acetyl chloride (0.8 g) in benzene (10 cm³). The mixture was stirred for 2 h at room temperature. Usual work-up gave *N*-ethyl[$^2\text{H}_2$]acetanilide (650 mg, 40%).

N-Ethyl[$^2\text{H}_2$]acetanilide (500 mg) was treated with LAD (180 mg) in diethyl ether under similar conditions as described above and the mixture was stirred for 1 h. Usual work-up gave *N,N*-diethyl[$^2\text{H}_4$]aniline (250 mg, 55%); δ_{H} 1.12 (6 H, s), 6.53–6.73 (3 H, m) and 7.09–7.34 (2 H, m); δ_{C} 12.4 (q), 43.6 (pent.), 111.9 (d), 115.4 (d), 129.3 (d) and 147.8 (s); m/z 153 (M^+). The peak corresponding to the methylene protons was not observed in the ^1H NMR spectrum, and the mass spectrum showed the parent peak at m/z 153. Therefore, the content of deuterium in DEA-*d* was estimated to be >95%.

General Procedure for the Photochemical Reactions of the Indoline-2-thiones 1 in the Presence of Amine.—A solution of an indoline-2-thione **1** (200 mg) in dry solvent (70 cm³) in the presence of an excess of amine (10 equimolar) in a Pyrex vessel was irradiated with a high-pressure mercury lamp (300 W) under argon at room temperature for 5 h. After removal of the solvent, the residue was chromatographed on a silica gel column with benzene–hexane (1:1–1:10) as eluent to yield the corresponding indolines **2**. The photochemical reactions of compounds **1** in the absence of amine or in the presence of a hydrogen donor were carried out under similar conditions. The indolines **2a–2d**, **2g–2i**, **2l** thus obtained were determined by direct comparison of their spectral properties with those of authentic materials, which were independently prepared¹³ by reduction of the indolin-2-ones with lithium aluminium hydride or desulphurization of the indoline-2-thiones with Raney nickel.

3-Methyl-1-phenyl-3-(3-phenylpropyl)indoline 2e, b.p. 175 °C at 2 mmHg (Found: C, 87.85; H, 7.8; N, 4.2. $\text{C}_{24}\text{H}_{25}\text{N}$ requires C, 88.0; H, 7.7; N, 4.25%); ν_{max} (film)/cm⁻¹ 1585, 1495, 1380, 740 and 690; δ_{H} 1.30 (3 H, s), 1.52–1.74 (4 H, m), 2.46–2.65 (2 H, m), 3.64 (2 H, dd, J 9.3, 12.7 Hz) and 6.65–7.39 (14 H, m); δ_{C} 25.9 (q), 26.4 (t), 36.3 (t), 40.5 (t), 43.0 (s), 64.2 (t), 108.1 (d), 117.3 (d), 118.8 (d), 120.6 (d), 122.8 (d), 125.6 (d), 127.1 (d), 128.2 (d), 128.3 (d), 129.0 (d), 138.9 (s), 142.1 (s), 143.9 (s) and 145.8 (s).

3-Isopentyl-3-methyl-1-phenylindoline 2f, b.p. 160 °C at 2

mmHg (Found: C, 85.65; H, 9.15; N, 5.0. $\text{C}_{20}\text{H}_{25}\text{N}$ requires C, 85.95; H, 9.0; N, 5.0%); ν_{max} (film)/cm⁻¹ 1590, 1500, 1385, 745 and 695; δ_{H} 0.85 (6 H, d, J 5.9 Hz), 1.32 (3 H, s), 0.95–1.73 (2 H, m), 3.67 (2 H, dd, J 9.3, 14.7 Hz) and 6.67–7.48 (9 H, m); δ_{C} 22.6 (q), 26.1 (q), 28.5 (d), 33.6 (t), 38.6 (t), 43.0 (s), 64.1 (t), 108.1 (d), 117.4 (d), 118.8 (d), 120.6 (d), 122.8 (d), 127.0 (d), 129.0 (d), 139.3 (s), 114.0 (s) and 145.8 (s).

Preparation of N,N-Diethylthioacetamide 3.—A mixture of *N,N*-diethylacetamide (0.6 g) and Lawesson's reagent (1.25 g) in 1,2-dimethoxyethane (30 cm³) was stirred at room temperature for 40 min. The solvent was removed under reduced pressure and then the residue was chromatographed on a silica gel column with benzene–ethyl acetate (4:1) as eluent to yield *N,N*-diethylthioacetamide **3** (615 mg, 90%), b.p. 45 °C at 3 mmHg (Found: C, 54.65; H, 10.0; N, 10.65. $\text{C}_6\text{H}_{13}\text{NS}$ requires C, 54.9; H, 10.0; N, 10.65%); ν_{max} (CHCl_3)/cm⁻¹ 1590, 1500, 1480 and 1380; δ_{H} 1.27 (6 H, t, J 6.8 Hz), 2.65 (3 H, s), 3.59 (2 H, q, J 6.8 Hz) and 3.99 (2 H, q, J 6.8 Hz); δ_{C} 11.2 (q), 13.1 (q), 32.0 (q), 46.7 (t), 48.0 (t) and 198.0 (s).

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