Synthesis and Reactions of C-Sulphenylketenimines

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The Horner–Wittig reaction of (1a,b) with phenyl isocyanate or dehydration of amides (4c—g) gave the C-sulphenylketenimines (3a—g) in moderate yields. Thermolysis of (3b) gave 2-ethoxy-3-phenylthioquinolin-4-ol (7) *via* intramolecular cyclization, and the reactions of (3e) and (3f) with CN-diphenylnitrone gave 3-methylthioindolones (10a) and (10b), respectively.

RECENTLY, some synthetic applications of ketenimines have been shown in the field of heterocyclic chemistry.[1] Our interest in heterocumulenes as the precursors of heterocycles has prompted us to synthesize heteroatom-substituted ketenimines,[2] since the reactions of such ketenimines are expected to give compounds bearing heteroatom-substituents. From this point of view, introduction of a sulphur substituent was of interest because of the possibility of replacing the sulphur substituent by other functional groups. Although a few examples of sulphur-substituted ketenimines have been described,[3] their chemistry is not well known. For the purpose of further investigation of their physical and chemical properties, the general synthesis and some reactions of C-sulphenylketenimines have been examined.

RESULTS AND DISCUSSION

Synthesis and ^{13}C *N.M.R. Spectra.*—The Horner–Wittig reaction of phenyl isocyanate and the carbanion of phosphonates (1a) and (1b), generated by sodium hydride in tetrahydrofuran, proceeded smoothly to give the ketenimines (3a) and (3b), which display characteristically the strong absorption bands at 2 000 and 2 040 cm^{-1}, respectively (Scheme 1). However, we were un-
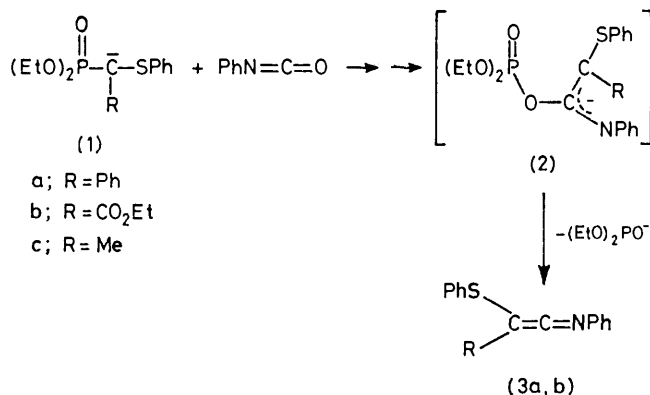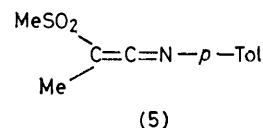

SCHEME 1

successful in our attempts to prepare N-phenylmethyl-(phenylthio)ketenimine (3c) by this method. In this case, the addition of phenyl isocyanate to the carbanion occurred, but subsequent elimination of the phosphoryl group could not proceed because of lack of stabilization of the carbanion adjacent to the sulphur atom in the intermediate (2). On the other hand, the dehydration[4]

of the α-alkylthioamide (4c—g) with triphenylphosphine, bromine, and triethylamine successfully gave the ketenimines (3c—g) in moderate yield (Scheme 2). The results
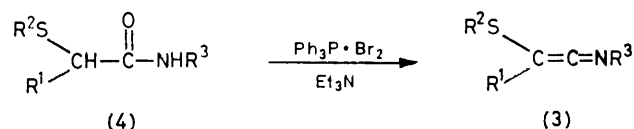
c; R^1=Me, R^2=R^3=Ph
d; R^1=Me, R^2=Ph, R^3=Et
e; R^1=Me, R^2=Me, R^3=Ph
f; R^1=Et, R^2=Me, R^3=Ph
g; R^1=Pr^i, R^2=Me R^3=Ph

SCHEME 2

are summarized in Table 1. Our attempts to isolate the sulphonylketenimine (5) was unsuccessful in spite of the observation of the absorption band at 2 000 cm^{-1} in the spectrum of the reaction mixture.

In Table 2 the ^{13}C n.m.r. chemical shifts of the unsaturated carbon atoms are listed. The resonances of the downfield imino-carbons (δ 183.99—189.13) are reasonable compared to those of other ketenimines, *e.g.* a triphenyl derivative (δ 190.16).[5] In comparison with alkyl- or aryl-substituted ketenimines, the tendency for both terminal and centre carbons to appear slightly to high field indicates the shielding effect of sulphur atoms as electron-donating groups.

Reactions of C-Sulphenylketenimines.—Only one example of addition of water to a C-sulphenylketenimine has been reported previously,[3] where n-butyl(pentyl-amino)thioacetate was formed unexpectedly from N-pentyl-(n-butylthio)ketenimine (6). However, the addition of water to (3a) and (3c) seems to be very slow under neutral conditions because there is no change in the i.r. spectra after standing overnight; the acidic hydrolysis of (3a) and (3c) readily gave the corresponding anilides (4a) and (4c) in high yield. These differences between compounds (3) and (6) are due to the differences in the

TABLE 1

Spectral data of C-sulphenylketenimines (3a—g)

	Yield (%)	I.r. ν(C=C=N)/cm⁻¹	¹H N.m.r. (δ)[a]	M⁺
(3a)	43	2 000	7.04—7.60 (15 H, m, Ar-H)[b]	301.0900[d]
(3b)	83	2 040 [1 720 (C=O)]	1.24 (3 H, t, MeCH₂, J 7 Hz),[b] 4.57 (2 H, q, MeCH_2, J 7 Hz), 7.13—7.63 (10 H, m, Ar-H)	e
(3c)	60	2 000	2.0 (3 H, s, Me),[c] 7.40—7.50 (10 H, m, Ar-H)	239.0746[f]
(3d)	53	2 010	1.30 (3 H, t, MeCH₂, J 7.5 Hz),[c] 1.80 (3 H, s, MeC=), 3.51 (2 H, q, MeCH_2, J 7.5 Hz), 7.10—7.53 (5 H, m, Ar-H)	191.0776[g]
(3e)	61	1 995	2.00 (3 H, s, MeC=),[c] 2.29 (3 H, s, MeS), 7.1—7.36 (5 H, m, Ar-H)	177.0599[h]
(3f)	63	1 995	1.06 (3 H, t, MeCH₂, J 7.5 Hz),[b] 2.20 (3 H, s, MeS), 2.21 (2 H, q, MeCH_2, J 7.5 Hz), 7.16—7.52 (5 H, m, Ar-H)	191.0771
(3g)	57	1 990	1.25 (6 H, d, MeCH, J 6.75 Hz),[b] 2.18—2.92 (1 H, m, MeCH, J 6.75 Hz). 2.34 (3 H, s, MeS), 7.22—7.62 (5 H, m, Ar-H)	205.0904[j]

[a] Internal reference SiMe₄. [b] In CDCl₃. [c] In CCl₄. [d] C₂₀H₁₅NS requires M, 301.0928. [e] Not isolated. [f] C₁₅H₁₃NS requires M, 239.0767. [g] C₁₁H₁₃NS requires M, 191.0769. [h] C₁₀H₁₁NS requires M, 177.0609. [i] C₁₁H₁₃NS requires M, 191.0769. [j] C₁₂H₁₅NS requires M, 205.0924.
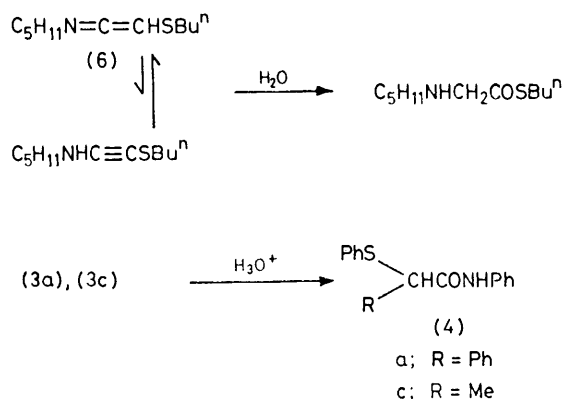
substituents. As pointed out previously, the ketenimine (6) exhibits reactivity characteristic of a triple bond by virtue of the tautomerism shown, but compounds (3) behave like alkyl- or aryl-substituted ketenimines and not like alkynyl sulphides.

TABLE 2

Selected ¹³C n.m.r. chemical shifts of (3a), (3d), and (3e) (δ in CDCl₃ from SiMe₄)

$$\text{R}^1\text{S} \diagdown \diagup \text{C}^1=\text{C}^2=\text{NR}^2$$
$$\text{R} \diagup$$

|	C¹	C²
(3a)	65.34	183.99
(3d)	54.02	184.42
(3e)	60.74	189.13

The thermolysis of (3b) in refluxing o-dichlorobenzene gave the quinolinol (7) (equilibrium with quinolone) in 54% yield, whose structure was established by the spectral data, elemental analysis, and the conversion to 2-ethoxyquinolin-4-ol (8) with Raney nickel. In aqueous

$$C_5H_{11}N=C=CHSBu^n$$
(6)
$$\xrightarrow{\text{H}_2\text{O}} C_5H_{11}NHCH_2COSBu^n$$
$$C_5H_{11}NHC{\equiv}CSBu^n$$

$$(3a), (3c) \xrightarrow{\text{H}_3\text{O}^+} \begin{matrix} \text{PhS} \diagdown \\ \diagup \\ \text{R} \end{matrix} \text{CHCONHPh}$$
(4)

a; R = Ph

c; R = Me

SCHEME 3

iron(III) chloride the latter compound showed the characteristic red colouration. The formation of (7) was considered to result via the intramolecular cyclization of

the imino-keten (9), generated by thermal migration of the ethoxy-group [6] (Scheme 4).

(3b)   (9)

(7)   Raney nickel   (8)
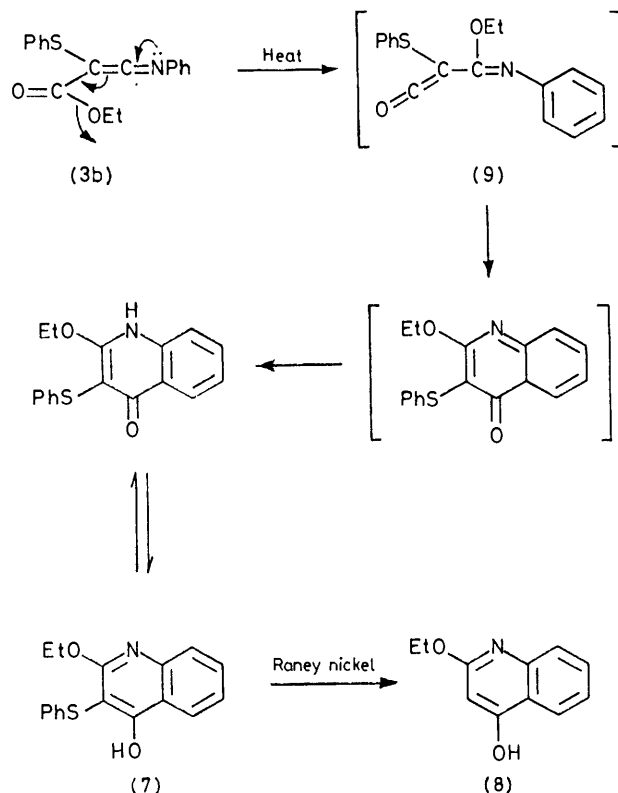
SCHEME 4

It is known that the reactions of N-phenyldialkylketen-imines and nitrone give indolones.[1a,b] We also obtained 3-methylthioindolones (10a) and (10b) from (3e) and (3f) with CN-diphenylnitrone in 40 and 22% yields, respectively, but the 1 : 1 adducts (11)[1b] could not be isolated (Scheme 5). This reaction depended upon the substituents at the terminal carbons of the ketenimine, since indolones could not be obtained when (3a) and (3g) were

used. Probably steric as well as electronic effects influence the formation of indolones.

Thus the properties of C-sulphenylketenimines (3) are very similar to other ketenimines, and they have some use as precursors to heterocycles with sulphur substituents.
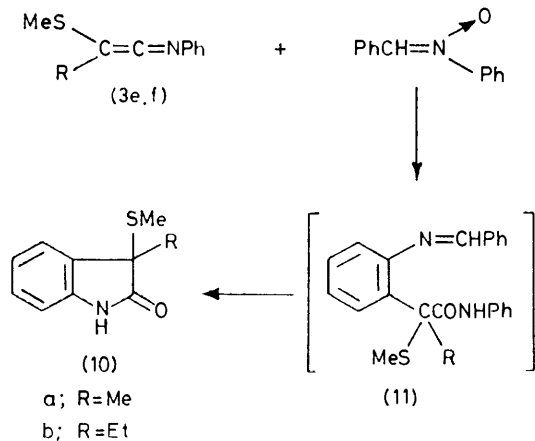
SCHEME 5

EXPERIMENTAL

B.p.s and m.p.s are uncorrected. I.r. spectra were obtained using JASCO IR-E and JASCO IRA-1 spectrometers. ^{1}H N.m.r. spectra were recorded with JEOL JNM-C-60HL and JNM-PMX-60 spectrometers, and ^{13}C n.m.r. spectra were taken with a JNM-FX 90 Q spectrometer using tetramethylsilane as internal reference. Mass spectra were obtained from JEOL JMS-01SH-2 spectrometer on-line to a JEOL JEC-6 spectrum computer and Hitachi RMU-6E spectrometer. Gas chromatographic–mass spectral data were obtained from a JMS-D300 mass spectrometer attached to a JGC-20KD gas chromatograph.

Phenyl- and Ethoxycarbonyl- N-phenyl(phenylthio)ketenimines (3a) *and* (3b).—To a suspension of sodium hydride (50% in oil, 2.95 g) in tetrahydrofuran (THF) (5 ml) was added dropwise diethyl[phenyl(phenylthio)methyl]phosphonate (1a) (20.62 g, 61.4 mmol) in THF (15 ml), and then heated at 40 °C for 5.5 h. After cooling to room temperature phenyl isocyanate (7.30 g, 61.3 mmol) in THF (20 ml) was added slowly and the mixture was stirred for 1 h at ambient temperature. The supernatant solution was concentrated and the residue was chromatographed on silica gel with benzene–hexane as eluant to give (3a) in 43% (7.85 g) yield as yellow crystals, m.p. 78—80 °C (benzene–hexane). The other spectral data are shown in Tables 1 and 2. In a similar manner, (3b) was obtained in 83% (9.65 g) yield as a viscous oil from (1b) (13 g, 39.2 mmol) and phenyl isocyanate (4.66 g, 39.2 mmol).

Dehydration of α-Sulphenylamides (4).—A mixture of triphenylphosphine (7.35 g, 28 mmol), bromine (1.44 ml, 28 mmol), triethylamine (10 ml), and α-phenylthiopropion-anilide (7.25 g, 28 mmol) in dichloromethane (70 ml) was stirred at room temperature for 3 h. After evaporation of the solvent the residue was treated with light petroleum and filtered. The filtrate was concentrated and distilled to give (N-*phenyl*)methyl(*phenylthio*)ketenimine (3c) in 60% (4.04 g) yield, b.p. 159 °C at 2 mmHg.

In a similar manner, the ketenimines (3d—g) were obtained as follows; (N-*ethyl*)methyl(*phenylthio*)ketenimine (3d), b.p. 94—95 °C at 1 mmHg; (N-*phenyl*)methyl(*methylthio*)keten-

imine (3e), b.p. 98—100 °C at 2 mmHg; (N-*phenyl*)ethyl(*methylthio*)ketenimine (3f), b.p. 103—104 °C at 2 mmHg; (N-*phenyl*)isopropyl(*methylthio*)ketenimine (3g), b.p. 113—114 °C at 2 mmHg.

Acidic Hydrolysis of (3a) *and* (3c).—A solution of (3a) (0.41 g, 1.36 mmol) in aqueous THF (5 ml) containing a catalytic amount of hydrochloric acid was stirred at room temperature for 3 h. After removal of the solvent the residue was extracted with chloroform and washed with brine. Drying (Na$_2$SO$_4$) and evaporation of the solvent gave α-*phenylthio(phenyl)acetanilide* (4a) (0.41 g, 95%), m.p. 148—150 °C (from ethanol) (Found: C, 74.85; H, 5.25; N, 4.2. C$_{20}$H$_{17}$NOS requires C, 75.22; H, 5.37; N, 4.39%); ν$_{max.}$ (Nujol) 3 300 (NH), 1 660 (CO) cm^{-1}; δ (CDCl$_3$) 5.05 (s, 1 H, CH), 7.04—7.30 (m, 15 H, Ar-H), and 8.01 (br, 1 H, NH); m/e 319 (M$^+$).

Similarly α-*phenylthiopropionanilide* (4c) (94%, 0.51 g) was obtained from (3c) (0.50 g, 2.1 mmol), m.p. 110—111 °C (from ethanol) (Found: C, 69.85; H, 5.9; N, 5.25. C$_{15}$H$_{15}$-NOS requires C, 70.02; H, 5.88; N, 5.44%); ν$_{max.}$ (Nujol) 3 200 (NH) and 1 650 (CO) cm^{-1}; δ (CDCl$_3$) 1.53 (d, 3 H, Me, *J* 6.75 Hz), 3.87 (q, 2 H, MeC*H*, *J* 6.75 Hz), 6.94—7.54 (m, 10 H, Ar-H), and 10.57 (br, 1 H, NH); m/e 257 (M$^+$).

Thermolysis of (3b).—A solution of (3b) (7.4 g, 25 mmol) in o-dichlorobenzene (50 ml) was refluxed for 1 h. The precipitate was collected by filtration and washed with ether to give 2-*ethoxy-3-phenylthioquinolin-4-ol* (7) in 54% (4.0 g) yield, m.p. 229—232 °C (Found: C, 68.65; H, 5.1; N, 4.7; S, 10.75. C$_{17}$H$_{15}$NO$_2$S requires C, 68.98; H, 5.09; N, 4.56; S, 10.65%); δ ([^{2}H$_6$]Me$_2$SO) 1.23 (t, 3 H, MeCH$_2$), 4.46 (q, 2 H, MeC*H$_2$*), 7.03—7.73 (m, 6 H, ArS and 6-H), 7.73—7.84 (m, 2 H, 5-H and 7-H), 8.32 (m, 1 H, 8-H), and 11.45 (br, 1 H, NH); m/e 297 (M$^+$).

Treatment of (7) *with Raney Nickel*.—A solution of (7) (1.0 g, 3.4 mmol) in dioxan (30 ml) containing an excess of Raney nickel was refluxed for 18 h. The organic layer was separated and concentrated to give 2-*ethoxyquinolin-4-ol* (10) in 50% (0.32 g) yield, m.p. 179—181 °C (Found: M$^+$, 189.0773. C$_{11}$H$_{11}$NO$_2$ requires M, 189.0788); δ ([^{2}H$_6$]Me$_2$-SO) 1.40 (t, 3 H, MeCH$_2$), 4.43 (q, 2 H, MeC*H$_2$*), 6.14 (s, 1 H, 3-H), 7.20—7.55 (m, 1 H, 6-H), 7.55—7.80 (m, 2 H, 5-H and 7-H), and 8.17 (m, 1 H, 8-H).

Reactions of (3e) *and* (3f) *with* CN-*Diphenylnitrone*.—A mixture of (3e) (0.9 g, 5 mmol) and CN-diphenylnitrone (1.0 g, 5 mmol) in benzene (30 ml) was refluxed for 6 h. After removal of solvent the residue was chromatographed on silica gel eluting with benzene containing increasing amounts of ethanol. The last eluting solution (ethanol) gave 3-*methyl-3-methylthioindol-2-one* (10a) in 40% yield, m.p. 146—147 °C (from benzene–hexane) (lit.,^{7} 150—151 °C) (Found: M$^+$, 193.0540. C$_{10}$H$_{11}$NOS requires M, 193.0561); δ (CDCl$_3$) 1.70 (s, 3 H, Me), 1.91 (s, 3 H, MeS), 7.08—7.50 (m, 4 H, ArH), and 9.64 (br, 1 H, NH).

Similarly 3-*ethyl-3-methylthioindol-2-one* (10b) was obtained in 22% yield from (3f) (2.41 g, 13 mmol) and CN-diphenylnitrone (2.56 g, 13 mmol), m.p. 154—155 °C (Found: M$^+$, 207.0749. C$_{11}$H$_{13}$NOS requires M, 207.0719); δ (CDCl$_3$) 0.74 (t, 3 H, MeCH$_2$), 1.87 (s, 3 H, MeS), 1.77—2.30 (m, 2 H, MeC*H$_2$*, overlapping signal), 6.80—7.40 (m, 4 H, ArH), and 9.23 (br, 1 H, NH).

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