Reaction of Sulphimides with Electrophilic Acetylenes

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Stable sulphonium imidoylides (2) have been isolated from the reaction of N-aryl-SS-dimethylsulphimides (1) with electrophilic acetylenes at room temperature. Similar ylides (2) are also formed from SS-dimethyl-Nphthalimidosulphimide. The ylides (2a, c, and e) give the pyrroles (3) when heated with a further mol. equiv. of dimethyl acetylenedicarboxylate or dibenzoylacetylene. The ylide (2c) reacts with other electrophiles, including hydrogen chloride, iodomethane, benzoyl chloride, and cyanogen bromide; these reactions (Scheme 5) involve electrophilic attack at the nitrogen atom of the ylide followed by nucleophilic attack at sulphur or at an S-methyl group.

SULPHONIUM acylides have proved versatile synthetic intermediates, particularly in the preparation of furans and of pyrones.^{1,2} In order to develop similar routes to nitrogen heterocyclic systems we have investigated various methods of preparing sulphonium imidoylides. Winterfeldt discovered one preparation of sulphonium acylides which involves the reaction of acetylenic esters with dimethyl sulphoxide (Scheme 1).^{2a} We find that

$$Me_2S=0 + RC \equiv C \cdot CO_2Me \xrightarrow{R} CO_2Me \xrightarrow{CO_2Me}_{O-SMe_2} \xrightarrow{R} CO_2Me \xrightarrow{CO_2Me}_{SMe_2}$$

analogous reactions take place between some sulphimides (1) and electrophilic acetylenes; the reaction has been used to prepare a series of sulphonium imidoylides (2), and some reactions of these with electrophiles have been investigated.

The ylides (2) were readily prepared by mixing the sulphimide and the acetylene in a dry solvent at room temperature. With the highly electrophilic acetylenes dimethyl acetylenedicarboxylate and dibenzoylacetylene, and with phenylprop-2-ynal compounds (2) were isolated in good yields from their reaction with N-arylsulphimides and with SS-dimethyl-N-phthalimidosulphimide (Scheme 2). Pure products could not be obtained with

$$Me_{2}S = NR^{1} + R^{2}C \equiv CR^{3} \xrightarrow{R^{2}}_{R^{1}N} \xrightarrow{R^{3}}_{SMe_{2}} \xrightarrow{R^{2}}_{R^{1}N} \xrightarrow{R^{3}}_{SMe_{2}} \xrightarrow{R^{2}}_{R^{1}N} \xrightarrow{R^{3}}_{SMe_{2}}$$
(1)
(2)

a;
$$R^{L} p - CIC_{6}H_{L}$$
, $R^{L} R^{2} CO_{2}Me$ f; $R^{L} = N \cdot \dot{C}O \cdot C_{6}H_{L} \dot{C}O$, $R^{2} R^{3} COPh$
b; $R^{1} = N \cdot \dot{C}O \cdot C_{6}H_{L} \cdot CO$, $R^{2} R^{3} = CO_{2}Me$ g; $R^{1} = \rho - C_{5}H_{L}N$, $R^{2} R^{3} = COPh$
c; $R^{1} = \rho - CIC_{6}H_{L}$, $R^{2} R^{3} = COPh$ h; $R^{1} = \rho - CIC_{6}H_{L}$, $R^{2} = Ph$, $R^{3} = CHO$
d; $R^{1} = \rho - NO_{2}C_{6}H_{L}$, $R^{2} = R^{3} = COPh$ j; $R^{1} = N \cdot \dot{C}O \cdot C_{6}H_{L} \cdot CO$, $R^{2} = Ph$, $R^{3} = CHO$
e; $R^{1} = m - CIC_{6}H_{L}$, $R^{2} = R^{3} = COPh$

SCHEME 2

methyl propiolate; less activated acetylenes, including ethyl phenylpropiolate and phenylacetylene, failed to react. It was unnecessary to isolate the N-arylsulphimides before reaction with the acetylenes: an

¹ For reviews of the chemistry of sulphonium acylides see A. W. Johnson, 'Ylid Chemistry,' Academic Press, New York, 1966, p. 310; A. W. Johnson, in 'Organic Compounds of Sulphur, Selenium, and Tellurium,' senior reporter D. H. Reid, The Chemical Society, London, vol. 1, 1970, p. 248; vol. 2, 1973, p. 288.

alternative method of preparation of the ylides was investigated in which the sulphimides were generated in situ from the corresponding anilines. The sulphimides were then treated directly with the acetylenes; this also gave good yields. The products (2) are all air-stable crystalline solids.

Hayashi and his co-workers have reported briefly the preparation of two ylides of this type by the same method as we employed.³

Sulphonium acylides are known to react further with electrophilic acetylenes: such a reaction was observed by Winterfeldt, who found that the ylide from dimethyl sulphoxide and dimethyl acetylenedicarboxylate reacted when heated with another mol. equiv. of the acetylene to give tetramethyl furantetracarboxylate (Scheme 3).^{2a}



Several other furan syntheses of this type have since been reported, although the reaction is by no means universally observed: other types of reaction may involve proton transfer or acyl transfer to give new, extended ylides, and the nature of the products is solvent-dependent.¹ We investigated the further reaction of the sulphonium imidoylides (2) with acetylenes in order to discover whether it would be a useful route to pyrroles. The imidoylides (2) reacted readily with dimethyl acetylenedicarboxylate or with dibenzoylacetylene, but not with less activated acetylenes, when heated under reflux in benzene or toluene. Pyrroles (3) were isolated in good yields from the reactions of the ylides (2a, c, and e) with these acetylenes (Scheme 4). The reaction thus appears to have some limited use as a route to pyrroles.

The reactions of the dibenzoyl imidoylide (2c) with several other electrophiles were investigated. With hydrogen chloride the sulphonium group was lost, the product being the enamine (4), isolated in good yield.

² (a) E. Winterfeldt, Chem. Ber., 1965, 98, 1581; E. Winter-feldt and H. J. Dillinger, *ibid.*, 1966, 99, 1558; (b) M. Takaku, Y. Hayasi, and H. Nozaki, *Tetrahedron Letters*, 1969, 2053; M. Higo and T. Mukaiyama, *ibid.*, 1970, 2565; Y. Hayasi, M. Kobayashi, and H. Nozaki, *Tetrahedron*, 1970, **26**, 4353; Y. Hayasi and H. Nozaki, *ibid.*, 1971, **27**, 3085. ⁵ Y. Hayashi, Y. Iwagami, A. Kadoi, T. Shono, and D.

Swern, Tetrahedron Letters, 1974, 1071.

The structure was confirmed by an independent synthesis from 4-chloroaniline and dibenzoylacetylene.



The same product was isolated in low yield when the ylide (2c) was treated with iodomethane. Benzoyl chloride reacted with the imidoylide by acylation on



nitrogen, followed by demethylation of the resulting sulphonium salt (Scheme 5), the major product isolated



being the amide (5a). A similar sequence of reactions is observed in the acylation of dimethylsulphonium phenacylide with benzoyl chloride.⁴ Cyanogen bromide also reacted with the ylide (2c) in this way, cyanation on nitrogen being followed by demethylation to give the cyanamide (5b). With succinic anhydride the product of acylation could not be isolated; the enamine (5c) was obtained instead. This is probably formed by hydrolysis of the acylation product: the same compound (5c) was isolated in low yield as a by-product of the reaction of (2c) with benzoyl chloride.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were recorded for KBr discs with a Perkin-Elmer 125 spectrometer. N.m.r. spectra were recorded with a Varian HA-100 instrument and mass spectra with an A.E.I. MS12 or MS902 spectrometer operating at 70 eV. Preparative layer chromatography was carried out with Kieselgel PF254 (Merck) as stationary phase.

Dichloromethane and acetonitrile were dried by distillation from calcium hydride and were stored over molecular sieves (type 4A). Triethylamine was distilled from, and stored over, sodium hydroxide. Benzene and toluene were sodium-dried. The *N*-aryl-*SS*-dimethylsulphimides and *N*-2-pyridyl-*SS*-dimethylsulphimide were prepared by published procedures.⁵

SS-Dimethyl-N-phthalimidosulphimide.— N-Aminophthalimide (1.62 g, 0.01 mol) and dimethyl sulphide (0.7 g, 0.011 mol) dissolved in dichloromethane (150 cm³) were cooled to -25 °C; some N-aminophthalimide came out of solution at this temperature. The mixture was stirred and N-chlorosuccinimide (1.33 g, 0.01 mol) in dichloromethane (50 cm³) was added during 0.5 h; stirring was continued at -25 °C for 1 h, at 0 °C for 0.5 h, and at room temperature for 0.5 h. The mixture was washed with saturated aqueous sodium hydrogen carbonate $(3 \times 50 \text{ cm}^3)$, then with water. The aqueous solutions were shaken with dichloromethane until no yellow colouration of the organic phase was observed. The combined organic solutions were dried and evaporated to give the crude sulphimide, which was crystallised; yield 1.55-2.0 g (70-90%), m.p. 133-134° (decomp.) (from dichloromethane-petroleum) (Found: C, 54.0; H, 4.6; N, 12.3. $C_{10}H_{10}N_2O_2S$ requires C, 54.05; H, 4.5; N, 12.6%); $\delta(CDCl_3)$ 2.67 (6 H) and 7.81 (4 H, m); m/e 222 (M^+), 179, 162, 147, and 104 (base).

Preparation of Betaines.—Method A. To a stirred solution of the sulphimide (4.0 mmol) in dry benzene (10 cm^3) was added a solution of the alkyne (4.0 mmol) in dry benzene. The mixture was stirred at room temperature for the time indicated and the product was isolated either by filtration or by layer chromatography.

The following betaines were obtained in this way: dimethylsulphonium 2-(4-chlorophenylimino)-1,2-bismethoxycarbonylethylide (2a) (61%), m.p. 134-135° (from benzenehexane) (Found: C, 51.0; H, 4.9; N, 4.0. C14H16CINO4S requires C, 51.0; H, 4.9; N, 4.25%); δ(CDCl_a) 3.10 (6 H), 3.62 (3 H), 3.71 (3 H), 6.85 (2 H, d, J 10 Hz), and 7.30 (2 H, d, J 10 Hz); m/e 331 and 329 (M⁺); dimethylsulphonium 1,2-bismethoxycarbonyl-2-(phthalimidoimino)ethylide (40%), m.p. 252° (decomp.) (from dichloromethane-chloroform) (Found: C, 52.4; H, 4.5; N, 7.4; S, 9.1. C16N16-N₂O₆S requires C, 52.75; H, 4.4; N, 7.7; S, 8.8%); δ(CDCl₃) 3.17 (6 H), 3.65 (3 H), 3.69 (3 H), and 7.6-7.9 (4 H, m); m/e 364 (M⁺); dimethylsulphonium 1,2-dibenzoyl-2-(4-chlorophenylimino)ethylide (2c) (80%), m.p. 216-217° (from dichloromethane-hexane), isolated after 2 h by filtration (Found: C, 68.2; H, 4.7; N, 3.3. $C_{24}H_{20}CINO_2S$ requires C, 68.4; H, 4.75; N, 3.3%); ν_{max} 1 665 cm⁻¹ (C=O); $\delta(CDCl_3)$ 3.15 (6 H), 6.62 (2 H, d, \tilde{J} 9 Hz), 6.96 (2 H, d, J 9 Hz), 7.2–7.4 (8 H, m), and 7.74 (2 H, m); m/e 423 and 421 (M^+); dimethylsulphonium 1,2-dibenzoyl-2-(4-nitrophenylimino)ethylide (2d) (85%), m.p. 245-246° (from ethanol), isolated after 16 h by filtration (Found: C, 66.1; H, 4.5; N, 6.45. C₂₄H₂₀N₂O₄S requires C, 66.7; H, 4.7; N, 6.5%); v_{max} 1 668 cm⁻¹ (C=O); δ (CDCl₃) 3.22 (6 H), 6.76 (2 H, d, J 9 Hz), 7.25–7.43 (8 H, m), 7.74 (2 H, m), and 7.92 (2 H, d, J 9 Hz); m/e 432 (M⁺); ⁵ P. K. Claus, W. Rieder, P. Hofbauer, and E. Vilsmaier, Tetrahedron, 1975, 31, 505.

⁴ A. W. Johnson and R. T. Amel, J. Org. Chem., 1969, 34, 1240; H. Nozaki, M. Takaku, and K. Kondo, Tetrahedron, 1966, 22, 2145.

dimethylsulphonium 1,2-dibenzoyl-2-(3-chlorophenylimino)ethylide (2e) (65%), m.p. 228-230° (from dichloromethanehexane), isolated after 2 h by filtration (Found: C, 68.55; H, 4.7; N, 3.45. C24H20CINO2S requires C, 68.4; H, 4.75; N, 3.3%); v_{max} 1670 cm⁻¹ (C=O); δ (CDCl₃) 3.20 (6 H), 6.5-7.0 (4 H, m), 7.2-7.4 (8 H, m), and 7.75 (2 H, m); m/e 423 and 421 (M^+); dimethylsulphonium 1,2dibenzoyl-2-(phthalimidoimino)ethylide (2f) (30%), m.p. 168-170° (from chloroform), isolated after 12 h by layer chromatography (Found: C, 68.7; H, 4.2; N, 6.3. $C_{26}H_{20}N_2O_4S$ requires C, 68.4; H, 4.4; N, 6.1%); ν_{max} 1785, 1726, and 1676 cm⁻¹ (C=O); m/e 456 (M^+); dimethylsulphonium 1,2-dibenzoyl-2-(2-pyridylimino)ethylide (2 g) (60%), m.p. 207-208° (from ethanol), isolated after 12 h by filtration (Found: C, 71.0; H, 5.3; N, 7.1. $C_{23}H_{20}N_2O_2S$ requires C, 71.1; H, 5.2; N, 7.2%); ν_{max} . 1.675 cm^{-1} (C=O); δ (CDCl₃) 3.07 (6 H) and 6.48-7.90 $(14 \text{ H}, \text{m}); m/e 388 (M^+); dimethylsulphonium 2-(4-chloro$ phenylimino)-1-formyl-2-phenylethylide (2 h) (75%), m.p. 165-167° (from dichloromethane-hexane), isolated after 2 h by layer chromatography (chloroform-acetone, 9:1) (Found: C, 64.0; H, 5.1; N, 4.2. C17H16CINOS requires C, 64.2; H, 5.05; N, 4.4%); ν_{max} 1 590 and 1 535br cm⁻¹; δ(CDCl₃) 3.10 (6 H), 6.42 (2 H, d, J 9 Hz), 6.93 (2 H, d, J 9 Hz), 7.08–7.24 (5 H, m), and 8.70 (1 H); m/e 319 and 317 (M^+) , and 254 (base); and dimethylsulphonium 1-formyl-2-phenyl-2-(phthalimidoimino)ethylide (2j) (55%), m.p. 189-191° (from chloroform), isolated after 24 h by layer chromatography (chloroform-acetone, 4:1) (Found: C, 65.0; H, 4.2; N, 8.1. C₁₉H₁₆N₂O₃S requires C, 64.8; H, 4.6; N, 8.0%); ν_{max} 1778, 1760, 1712, and 1611 cm⁻¹; δ (CDCl₃) 3.20 (6 H), 7.3—7.6 (9 H, m), and 8.57 (1 H); m/e 352 (M^+) .

Method B. To a solution of N-chlorosuccinimide (1.34 g,10 mmol) in dry dichloromethane (25 ml) was added a solution of dimethyl sulphide (0.7 g, 11 mmol) in dichloromethane (5 ml) during 5 min at 0 °C. A colourless precipitate appeared. The aniline (10 mmol) in dichloromethane (5 ml) was added to the stirred mixture during 5 min; the mixture was then stirred at 0 °C for 10 min and at room temperature for 20 min. A clear solution resulted. The acetylene (7 mmol) in dichloromethane (5m l) was added, followed by a solution of triethylamine (7 mmol) in dichloromethane (5 ml). The mixture was stirred for 12 h, and washed with aqueous sodium hydroxide. The solvent was removed from the organic phase to yield the crude betaine (80-100%), which was crystallised from dichloromethane-hexane. The betaines (2a) (85%), (2c) (95%), and (2h) (75%) were prepared by this method.

Tetramethyl 1-(4-Chlorophenyl)pyrrole-2,3,4,5-tetracarboxylate (3a).—The betaine (2a) (36 mg, 0.011 mmol) and dimethyl acetylenedicarboxylate (50 mg, 0.35 mmol) were heated in dry benzene (20 cm³) under reflux for 22 h. Layer chromatography gave the title pyrrole (31 mg, 67%), m.p. 100—101° (from aqueous methanol) (Found: C, 52.5; H, 4.0; N, 3.4. C₁₈H₁₆ClNO₈ requires C, 52.7; H, 3.9; N, 3.4%); ν_{max} .(KBr) 1 730 cm⁻¹; δ (CDCl₃) 3.66 (6 H), 3.86 (6 H), 7.18 (2 H, d, J 9 Hz), and 7.40 (2 H, d, J 9 Hz); m/e 411 and 409 (M⁺), 380, and 379.

Dimethyl 4,5-Dibenzoyl-1-(4-chlorophenyl)pyrrole-2,3-dicarboxylate (3b).—The betaine (2a) (165 mg, 0.5 mmol) and dibenzoylacetylene (210 mg, 0.9 mmol) were dissolved in toluene (75 cm³) and the solution was heated under reflux for 18 h. Layer chromatography (chloroform) gave the

title pyrrole (126 mg, 50%), m.p. 281–283° (from dichloromethane-hexane) (Found: C, 66.8; H, 3.85; N, 2.6. $C_{28}H_{20}ClNO_6$ requires C, 67.0; H, 4.0; N, 2.8%); v_{max} . 1730sh, 1718, and 1665 cm⁻¹ (C=O); $\delta(CDCl_3)$ 3.60 (3 H), 3.70 (3 H), and 7.0–7.5 (14 H, m); m/e 503 and 501 (M^+).

2,3,4,5-*Tetrabenzoyl*-1-(4-*chlorophenyl*)*pyrrole* (3c).—The betaine (2c) (210 mg, 0.5 mmol) and dibenzoylacetylene (210 mg, 0.9 mmol) were dissolved in benzene (75 cm³) and the solution was heated under reflux for 18 h. Layer chromatography (chloroform-acetone, 12:1) gave the title *pyrrole* (175 mg, 60%), m.p. 257—259° (from dichloromethane-hexane) (Found: C, 76.5; H, 4.1; N, 2.2. $C_{38}H_{24}CINO_4$ requires C, 76.8; H, 4.1; N, 2.4%); v_{max} . 1 650 cm⁻¹ (C=O); *m/e* 595 and 593 (*M*⁺).

2,3,4,5-*Tetrabenzoyl*-1-(3-*chlorophenyl*)*pyrrole* (3d).—The betaine (2e) (100 mg, 0.24 mmol) and dibenzoylacetylene (56 mg, 0.24 mmol) were dissolved in acetonitrile (5 ml) and the solution was heated under reflux for 14 h. Layer chromatography (chloroform) gave the title *pyrrole* (71 mg, 50%), m.p. 198—200° (from dichloromethane-hexane) (Found: C, 76.5; H, 4.2; N, 2.2%); ν_{max} 1 665 cm⁻¹ (C=O); *m/e* 595 and 593 (*M*⁺).

Reactions of the Betaine (2c) with Other Electrophiles.— (a) With hydrogen chloride. Dry hydrogen chloride was passed through a solution of the betaine (2c) (210 mg, 0.5 mmol) in dichloromethane (20 cm³) at room temperature for 10 min. The solution was purged with nitrogen and evaporated to leave a yellow solid. Crystallisation of the solid gave (Z)-2-(4-chlorophenylamino)-1,4-diphenylbut-2-ene-1,4-dione (4) (160 mg, 90%), m.p. 150—151° (from ethanol) (Found: C, 72.8; H, 4.5; N, 3.8. C₂₂H₁₆ClNO₃ requires C, 73.0; H, 4.4; N, 3.9%); v_{max} (KBr) 1 665, 1 597, 1 583, 1 571, and 1 550 cm⁻¹; δ (CDCl₃) 6.09 (1 H), 6.85 (2 H, d, J 9 Hz), 7.07 (2 H, d, J 7 Hz), 7.3—7.6 (6 H, m), and 7.8—8.0 (4 H, m). An authentic specimen was obtained (90%) by dropwise addition of 4-chloroaniline (128 mg, 1 mmol) in ether (10 ml) to dibenzoylacetylene (246 mg, 1 mmol) in ether (25 ml) at room temperature.

(b) With cyanogen bromide. A solution of the betaine (2c) (160 mg, 0.38 mmol) and cyanogen bromide (320 mg, 3.0 mmol) in dichloromethane (20 cm³) was heated under reflux for 16 h. Layer chromatography (chloroformacetone, 9:1) gave (Z)-2-(N-cyano-4-chlorophenylamino)-3methylthio-1,4-diphenylbut-2-ene-1,4-dione (5b) (99 mg, 60%), m.p. 120—122° (from dichloromethane-hexane) (Found: C, 66.5; H, 4.1; N, 6.3. $C_{24}H_{17}ClN_2O_2S$ requires C, 66.6; H, 3.9; N, 6.5%); v_{max} .(KBr) 2 220, 1 675, and 1 643 cm⁻¹; δ (CDCl₃) 2.19 (3 H), 6.75 (2 H, d, J 9 Hz), 7.08 (2 H, d, J 9 Hz), 7.2—7.7 (8 H, m), and 8.00 (2 H, m).

(c) With succinic anhydride. A solution of the betaine (2c) (210 mg, 0.5 mmol) and succinic anhydride (50 mg, 0.5 mmol) in acetonitrile (25 cm³) was heated under reflux for 16 h. Layer chromatography (chloroform) gave (Z)-2-(4-chlorophenylamino)-3-methylthio-1,4-diphenylbut-2-ene-

1,4-dione (5c) (40 mg, 20%), m.p. 132–133° (from ethanol) (Found: C, 67.7; H, 4.4; N, 3.4. $C_{23}H_{18}ClNO_2$ requires C, 67.7; H, 4.4; N, 3.4%); $v_{max.}$ (KBr) 1 660, 1 580, and 1 535br cm⁻¹; δ (CDCl₃) 1.76 (3 H), 6.97 (2 H, d, J 9 Hz), 7.14 (2 H, d, J 9 Hz), 7.3–7.6 (6 H, m), 7.75 (2 H, m), and 7.95 (2 H, m).

(d) With benzoyl chloride. To a solution of the betaine (2c) (210 mg, 0.5 mmol) in dichloromethane (10 cm³) was added a solution of benzoyl chloride (70 mg, 0.5 mmol) in

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dichloromethane (5 cm³) during 5 min. The solution was evaporated and the residue was triturated with hexaneether (10:1) to give a yellow solid (215 mg). Layer chromatography of the solid (chloroform) gave (i) (Z)-2-(N-4-chlorophenylbenzamido)-3-methylthio-1,4-diphenylbut-2-ene-1,4-dione (5a) (190 mg, 75%), m.p. 187–188° (from ethanol) (Found: C, 70.1; H, 4.3; N, 2.7. C₃₀H₂₂ClNO₃S requires C, 70.4; H, 4.3; N, 2.7%); ν_{max} (KBr) 3 060, 1 650, 1 590, and 1 575 cm⁻¹; δ (CDCl₃) 1.93 (3 H), 6.70 (2 H, d, J 9 Hz), 6.89 (2 H, d, J 9 Hz), 7.0–7.7 (11 H, m), and 7.9–8.2 (4 H, m); m/e 513 and 511 (M^+), and 464 and 462 (M^+ – SMe); (ii) the enamine (4) (9 mg, 5%), m.p. 150–151°; and (iii) the enamine (5c) (20 mg, 10%), m.p. 132–133°.

We thank Professor C. W. Rees for discussion, and the S.R.C. for a Research Studentship (to M. E.).

[5/1396 Received, 15th July, 1975]