Reaction of *N*-Aryl- and Imidoyl-sulphimides with Diphenylcyclopropenone; Synthesis of 4-Pyrimidones [1]

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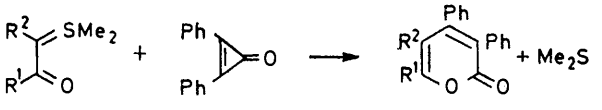
SS-Dimethylsulphimides have been prepared from aniline, 4-chloroaniline, 2-aminopyridine, 2-aminopyrimidine and its 3,5-dimethyl derivative, *N*-phenylbenzamidine, and 2-aminobenzoxazole. The sulphimides all react readily with diphenylcyclopropenone, with elimination of dimethyl sulphide. The products from the *N*-arylsulphimides are amides [(2) and (3)] : the other sulphimides give 4-pyrimidone derivatives [(6a), (8), (11), and (12)]. The assignment of structure (6a) to the adduct from *SS*-dimethyl-*N*-2-pyridylsulphimide and diphenylcyclopropenone is supported by a study of the effect of added shift reagent [Eu(fod)$_3$] on the n.m.r. spectrum. An analogous adduct (6b) is formed by the reaction of this sulphide with diphenylcyclopropenethione.

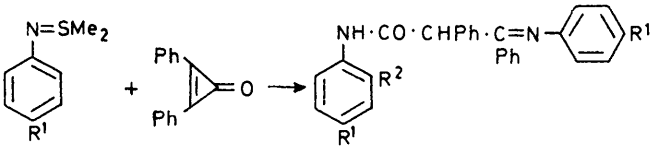
SULPHONIUM ylides are known to act as nucleophiles and are readily acylated by a wide variety of reagents. With diphenylcyclopropenone, carbonyl-substituted sulphonium ylides have been shown to be acylated on carbon, the products being 2-pyrones formed by the



SCHEME 1

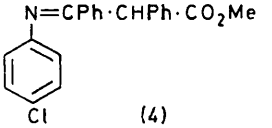
elimination of dimethyl sulphide (Scheme 1).[2] Analogous reactions have been observed with carbonyl-substituted pyridinium ylides [3] and imides.[4] We have investigated the reactions of several sulphur–nitrogen ylides with diphenylcyclopropenone and find that they are also readily acylated in an analogous way.

SS-Dimethyl-*N*-phenylsulphimide (1a) and diphenylcyclopropenone reacted in dichloromethane at room temperature to give a mixture of the amides (2a) and (3a) in a total yield of 66%. The *N*-*p*-chlorophenyl-



(1) a; R^1 = H
b; R^1 = Cl

(2) a; R^1 = R^2 = H
b; R^1 = Cl, R^2 = H
(3) a; R^1 = H, R^2 = CH$_2$SMe
b; R^1 = Cl, R^2 = CH$_2$·SMe

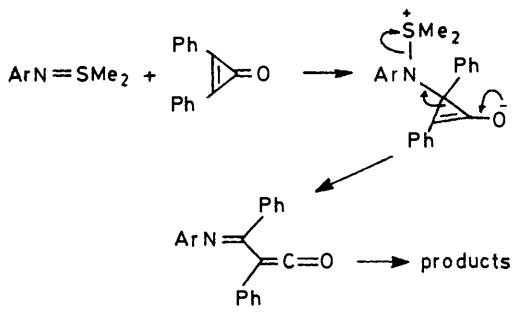


(4)

sulphimide (1b) gave a similar mixture of the amides (2b) (57%) and (3b) (17%). These amides are probably

[1] Preliminary communication, T. L. Gilchrist, C. J. Harris, and C. W. Rees, *J.C.S. Chem. Comm.*, 1974, 487.
[2] Y. Hayashi and H. Nozaki, *Tetrahedron*, 1971, **27**, 3085.
[3] Th. Eicher, E. von Angerer, and A.-M. Hansen, *Annalen*, 1971, **746**, 102; Th. Eicher and E. von Angerer, *ibid.*, p. 120.
[4] T. Sasaki, K. Kanematsu, and A. Kakehi, *J. Org. Chem.*, 1971, **36**, 2451.

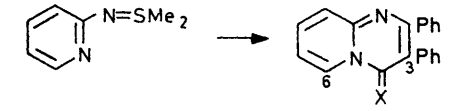
formed by the mechanism shown in Scheme 2: when the reaction of the sulphimide (1b) and diphenylcyclopropenone was carried out in methanol, the ester (4) was isolated. The amides (2) and (3) can be formed from the intermediate keten shown in Scheme 2 by reaction



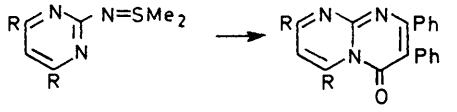
SCHEME 2

either with another mole of the sulphimide or with the products of its Sommelet–Hauser rearrangement, this rearrangement being a ready reaction of these *N*-arylsulphimides.

A similar mechanistic rationale can be applied to the reaction of acylsulphonium ylides with diphenylcyclopropenone shown in Scheme 1, but in these reactions, the carbonyl group of the ylide acts as an intramolecular nucleophile to intercept the keten. By using sulphimides derived from 2-aminopyridine, 2-aminopyrimidines, *N*-phenylbenzamidine, and 2-aminobenzoxazole, we were also able to intercept the keten intermediate in a reaction which provides an efficient synthesis of a variety of 4-pyrimidone derivatives. Thus, the sulphimide (5) gave 2,3-diphenylpyrido[1,2-*a*]pyrimidin-4-one (6a) (93%). The pyrimidine derivatives (7) gave



(5) (6) a; X=O
b; X=S

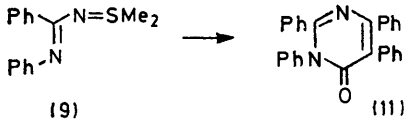


(7) a; R=H
b; R=Me
(8) a; R=H
b; R=Me

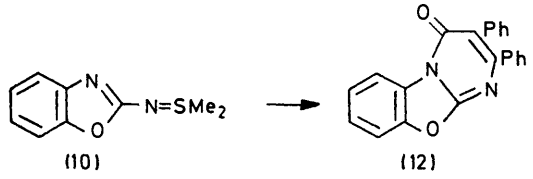
the corresponding adducts (8) in good yields; the amidines (9) and (10) gave the pyrimidones (11) (25%) and (12) (66%).

The structure assigned to the pyrimidone (6a) was supported by a study of the effect of added $Eu(fod)_3$ on the n.m.r. spectrum of the substance. The signal at τ 0.97, assigned to H-6, showed a rapid linear downfield shift when successive amounts of $Eu(fod)_3$ were added to the solution; the molar shift was 9.1 p.p.m. The signal assigned to the *ortho*-hydrogen atoms of the phenyl group on C-3 also showed a large molar downfield shift (8.6 p.p.m.). There is good evidence that $Eu(fod)_3$ complexes to the carbonyl oxygen atom in these pyrimidones,[5] and the effect is therefore expected to be most marked on the groups attached to C-3 and C-6, as observed. This would not be true of the other possible structure (13). Similar results have been obtained in a study of the effect of added $Eu(fod)_3$ on the n.m.r. spectrum of another pyrido[1,2-*a*]pyrimidin-4-one derivative.[6] Basic hydrolysis of (6a) gave deoxybenzoin.

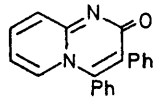
The standard method of preparing derivatives of this ring system involves condensation of 2-aminopyridine with a β-oxo-ester at high temperature. Attempts to synthesise (6a) by reaction of 2-aminopyridine with



(9) (11)



(10) (12)



(13)

methyl 2-benzoyl-2-phenylacetate in the presence of acidic catalysts were unsuccessful; the sulphimide and diphenylcyclopropenone reaction is a better route to the 2,3-diphenyl derivatives.

The reaction can also be used to synthesise pyrimidine-4-thione derivatives: diphenylcyclopropenethione and *SS*-dimethyl-*N*-2-pyridylsulphimide gave the thione (6b) (80%). The thione (6b) was readily oxidised to the pyrimidone (6a) but could not be formed from (6a) by reaction with phosphorus pentasulphide.

EXPERIMENTAL

N.m.r. spectra were recorded at 60 MHz with a Perkin-Elmer R12 instrument, or (for the lanthanide-induced shift studies) at 100 MHz on a Varian HA-100 spectrometer. I.r. spectra were recorded for Nujol mulls, except where indicated otherwise. Petroleum refers to the fraction of b.p. 60—80°.

Preparation of Sulphimides.—*SS*-Dimethyl-*N*-phenylsulphimide and *N*-4-chlorophenyl-*SS*-dimethylsulphimide

[5] G. A. Neville, *Canad. J. Chem.*, 1972, **50**, 1253.
[6] H. L. Yale, B. Toeplitz, J. Z. Gougoutas, and M. Puar, *J. Heterocyclic Chem.*, 1973, **10**, 123.

were prepared from the corresponding aniline, dimethyl sulphide, and phosphorus pentoxide by the method of Claus and Vycudilik.[7] †

SS-Dimethyl-*N*-2-pyridylsulphimide, *SS*-dimethyl-*N*-pyrimidin-2-ylsulphimide, and *N*-3,5-dimethylpyrimidin-2-yl-*SS*-dimethylsulphimide were prepared from the corresponding amines with t-butyl hypochlorite and dimethyl sulphide, according to the general method of Gassman and Huang.[8] These sulphimides were all generated and used directly, without further purification. *SS*-Dimethyl-*N*-(*N*-phenylbenzimidoyl)sulphimide was prepared as described earlier.[9]

N-Benzoxazol-2-yl-SS-dimethylsulphimide was prepared (67%) from 2-aminobenzoxazole, t-butyl hypochlorite, and dimethyl sulphide, according to the procedure described earlier,[9] and had m.p. 139—141° (Found: C, 55.2; H, 5.1; N, 14.5. $C_9H_{10}N_2O_2S$ requires C, 55.6; H, 5.2; N, 14.3%); τ ($CDCl_3$) 7.18 (6 H) and 2.6—3.2 (4 H, m); *m/e* 194 (M^+) and 134 (base).

Reaction of Diphenylcyclopropenone with N-Arylsulphimides.—(a) *With* N-4-*chlorophenyl*-SS-*dimethylsulphimide*. The sulphimide (390 mg, 2.1 mmol) and diphenylcyclopropenone (472 mg, 2.3 mmol) were dissolved in dichloromethane (25 ml) and kept at 20 °C under nitrogen for 18 h. Layer chromatography (silica; chloroform–petroleum, 1 : 1) gave N-4-*chlorophenyl*-3-(4-*chlorophenylimino*)-2,3-*diphenylpropionamide* (2b) (290 mg, 57%), m.p. 174—176° (Found: C, 69.9; H, 4.5; N, 6.1. $C_{27}H_{20}Cl_2N_2O$ requires C, 70.6; H, 4.4; N, 6.1%); $\nu_{max.}$ 3 400 (NH) and 1 618 cm^{-1} (C=O); *m/e* 458 (M^+) and 332 (base). A second fraction from the plate gave N-[4-*chloro*-2-(*methylthiomethyl*)*phenyl*]-3-(4-*chlorophenylimino*)-2,3-*diphenylpropionamide* (3b) (95 mg, 17%), m.p. 173—175° (Found: C, 67.1; H, 4.85; N, 5.1. $C_{29}H_{24}Cl_2N_2OS$ requires C, 67.05; H, 4.6; N, 5.4%); $\nu_{max.}$ 3 350 (NH) and 1 630 cm^{-1} (C=O); τ ($CDCl_3$) 8.30 (3 H), 6.74 (2 H), 3.45 (1 H), and 1.8—3.1 (17 H, m); *m/e* 518 (M^+) and 332 (base).

(b) *With* SS-*dimethyl*-N-*phenylsulphimide*. The sulphimide (510 mg, 3.3 mmol) and diphenylcyclopropenone (660 mg, 3.2 mmol) in dichloromethane similarly gave 2-phenyl-2-(*N*-phenylbenzimidoyl)acetanilide (2a) (100 mg, 22%), m.p. 156—158° (lit.,[10] 158—160°) (Found: C, 82.9; H, 5.8; N, 7.3. Calc. for $C_{27}H_{22}N_2O$: C, 83.05; H, 5.7; N, 7.2%); *m/e* 390 (M^+) and 298 (base); and N-[2-(*methylthiomethyl*)*phenyl*]-2,3-*diphenyl*-3-(*phenylimino*)*propionamide* (3a) (240 mg, 44%), m.p. 159—160° (Found: C, 76.8; H, 5.9; N, 6.0. $C_{29}H_{26}N_2OS$ requires C, 77.3; H, 5.8; N, 6.2%); τ ($CDCl_3$) 8.30 (3 H), 6.66 (2 H), 3.32 (1 H), and 1.8—3.0 (19 H, m); *m/e* 450 (M^+) and 298 (base).

(c) *With* N-4-*chlorophenyl*-SS-*dimethylsulphimide in the presence of methanol*. The sulphimide (206 mg, 1.1 mmol) and diphenylcyclopropenone (248 mg, 1.2 mmol) were mixed in dichloromethane (13 ml) containing methanol (0.2 ml). After 17 h the solvent was removed. Layer chromatography gave the amide (2b) (126 mg, 50%) and *methyl* 3-(4-*chlorophenylimino*)-2,3-*diphenylpropionate* (4) (105 mg, 25%), m.p. 153—154° (from ether–pentane) (Found: C, 71.8; H, 5.0; N, 3.8. $C_{22}H_{18}ClNO_2$ requires C, 71.7; H, 5.1; N, 4.0%); $\nu_{max.}$ 1 648 cm^{-1} (C=O); *m/e* 363 (M^+), 332, 331, and 214 (base).

(d) *With* SS-*dimethyl*-N-2-*pyridylsulphimide*. A solution of the sulphimide (320 mg, 2.1 mmol) and diphenylcyclopropenone (412 mg, 2.0 mmol) in dichloromethane (20 ml) gave, after 20 h at room temperature, 2,3-*diphenylpyrido*[1,2-a]*pyrimidin-4-one* (6a) (566 mg, 93%), m.p. 191—192° (from ethanol) (Found: C, 80.8; H, 4.8; N, 9.6. $C_{20}H_{14}N_2O$ requires C, 80.5; H, 4.7; N, 9.4%); $\nu_{max.}$ 1 658 and 1 633 cm^{-1}; $\lambda_{max.}$ (Pr^iOH) 245, 260sh, and 355 nm; τ ($CDCl_3$) 2.25—3.0 (13 H, m, H on C-7, C-8, and C-9, and 2 × Ph), and 0.97 (1 H, dd, *J* 7.5 and 1.5 Hz, H on C-6) [addition of $Eu(fod)_3$ to the specimen produced a molar shift of 9.1 p.p.m. (910 Hz at 100 MHz) in the signal initially at τ 0.97, and a molar shift of 8.6 p.p.m. in the part of the signal initially at 2.25—3.0 which is assigned to the *ortho*-hydrogen atoms of the phenyl at C-3]; *m/e* 298 (M^+, base) and 270. The pyridopyrimidinone (100 mg) was hydrolysed by heating in ethanol (5 ml) with aqueous potassium hydroxide (10%; 10 ml) for 24 h and gave deoxybenzoin (44 mg, 67%), m.p. 52°.

(e) *With* SS-*dimethyl*-N-*pyrimidin-2-ylsulphimide*. The sulphimide (365 mg, 2.4 mmol) and diphenylcyclopropenone (412 mg, 2.0 mmol) gave 2,3-*diphenylpyrimido*[1,2-a]*pyrimidin-4-one* (8a) (420 mg, 71%), m.p. 205—207° (yellow prisms from ethanol) (Found: C, 76.0; H, 4.5; N, 14.2. $C_{19}H_{13}N_3O$ requires C, 76.2; H, 4.4; N, 14.0%); $\nu_{max.}$ 1 665 cm^{-1} (C=O); *m/e* 299 (M^+), 271, and 270.

(f) *With* N-3,5-*dimethylpyrimidin-2-yl*-SS-*dimethylsulphimide*. The sulphimide (830 mg, 4.5 mmol) and diphenylcyclopropenone (618 mg, 3.0 mmol) gave 6,8-*dimethyl*-2,3-*diphenylpyrimido*[1,2-a]*pyrimidin-4-one* (8b) (712 mg, 72%), m.p. 207—208° (from ethanol) (Found: C, 77.0; H, 5.25; N, 13.05. $C_{21}H_{17}N_3O$ requires C, 77.0; H, 5.2; N, 12.8%); $\nu_{max.}$ 1 675 cm^{-1} (C=O); τ ($CDCl_3$) 7.40 (3 H), 6.92 (3 H), 3.36 (1 H), and 2.3—2.8 (10 H, m); *m/e* 327 (M^+), 299, and 298.

(g) *With* SS-*dimethyl*-N-(N-*phenylbenzimidoyl*)*sulphimide*. The sulphimide (200 mg, 0.78 mmol) and diphenylcyclopropenone (165 mg, 0.80 mmol) were dissolved in dry toluene (25 ml) and heated under reflux for 20 h. The major component was separated by layer chromatography (silica; chloroform–acetone, 10 : 1) and was crystallised to give 2,3,5,6-tetraphenylpyrimidin-4(3*H*)-one (11) (82 mg, 26%), m.p. 295—296° (lit.,[11] 295°); $\nu_{max.}$ 1 662 cm^{-1} (C=O); *m/e* 400 (M^+), 372, and 180.

(h) *With* N-*benzoxazol-2-yl*-SS-*dimethylsulphimide*. The sulphimide (97 mg, 0.5 mmol) and diphenylcyclopropenone (103 mg, 0.5 mmol) were dissolved in dry toluene (15 ml) and the solution was heated under reflux for 17 h. Preparative layer chromatography gave diphenylcyclopropenone (20 mg) and 2,3-*diphenylpyrimido*[2,1-b]*benzoxazol-4-one* (12) (90 mg, 66%), m.p. 221—222° (from ethanol) (Found: C, 78.1; H, 4.3; N, 8.5. $C_{22}H_{14}N_2O_2$

† A superior method for the preparation of *N*-arylsulphimides has since been developed by ourselves and by other groups. This involves the reaction of *N*-chlorosuccinimide with dimethyl sulphide and treatment of the resulting complex with an aniline (E. Vilsmaier and W. Sprügel, *Tetrahedron Letters*, 1972, 625). This gives an azasulphonium salt, from which the corresponding sulphimide is liberated by reaction with base (*cf.* P. K. Claus, P. Hofbauer, and W. Rieder, *Tetrahedron Letters*, 1974, 3319; T. E. Varkey, G. F. Whitfield, and D. Swern, *J. Org. Chem.*, 1974, **39**, 3365; T. L. Gilchrist, C. J. Moody, and C. W. Rees, preceding paper). See also P. K. Claus, W. Rieder, P. Hofbauer, and E. Vilsmaier, *Tetrahedron*, 1975, **31**, 505.

[7] P. Claus and W. Vycudilik, *Monatsh.*, 1970, **101**, 396.
[8] P. G. Gassman and C. T. Huang, *J. Amer. Chem. Soc.*, 1973, **95**, 4453.
[9] T. L. Gilchrist, C. J. Moody, and C. W. Rees, preceding paper.
[10] W. Bartz and M. Regitz, *Chem. Ber.*, 1970, **103**, 1463.
[11] L. Giammanco and F. P. Invidiata, *Ann. Chim.* (*Italy*), 1970, **60**, 188.

requires C, 78.1; H, 4.2; N, 8.3%); $\nu_{max.}$ 1 675 cm^{-1} (C=O); *m/e* 338, 337, 310, and 309.

Diphenylcyclopropenethione and SS-*Dimethyl*-N-2-*pyridylsulphimide*.—A solution of diphenylcyclopropenethione [12] (444 mg, 2 mmol) and the sulphimide (320 mg, 2.1 mmol) in dichloromethane (20 ml) was left for 22 h in the dark at room temperature, and gave 2,3-*diphenylpyrido*[1,2-a]-*pyrimidine-4-thione* (6b) (525 mg, 80%) as orange needles, m.p. 189—191° (decomp.) (from ethanol) (Found: C, 76.2; H, 4.8; N, 8.7. $C_{20}H_{14}N_2S$ requires C, 76.4; H, 4.5; N, 8.9%); *m/e* 314 (M^+), 313, 270, and 269.

The thione (63 mg, 2 mmol) and mercury(II) acetate (70 mg) in acetic acid (8 ml), heated at 90 °C for 18 h, gave 2,3-diphenylpyrido[1,2-*a*]pyrimidin-4-one (53 mg, 90%), m.p. and mixed m.p. 191—192°.

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[5/727 *Received*, 16*th April*, 1975]

[12] J. W. Lown and T. W. Maloney, *J. Org. Chem.*, 1970, **35**, 1716.