

Phthalimidobenzenesulphonyl Derivatives

By R.J. Cremlyn, F.J. Swinbourne and R.J. Nunes
Division of Chemical Sciences, Hatfield
Polytechnic, Hatfield, Herts., England.

Recebido em 12/11/84

Abstract

Treatment of N-phenyl-, and 2- and 4-chloro-N-phenylphthalimide with chlorosulphonic acid gave the sulphonyl chlorides, which were then reacted with nucleophilic reagents. Ring-fission occurred with Me₂NH. Replacement of the N-H hydrogen atom took place with perchloromethylmercaptan. Preliminary *in vitro* studies suggest enhanced fungicidal activity on introduction of the sulphonyl group.

Certain phthalimides show fungicidal activity.^{1,2} The mode of action of these compounds may depend upon their ability to acylate enzymes.³

In a search for candidate pesticides, and as an extension of previous work,⁴ we report the synthesis of sulphonyl derivatives of N-phenyl-, and 2- and 4-chloro-N-phenylphthalimide. Many N-trichloromethylthio derivatives are fungitoxic,⁵ and we have prepared some derivatives from the sulphonamides.

The reaction of N-phenyl-, 2- and 4-chloro-N-phenylphthalimide with chlorosulphonic acid (6 mols) at 80-90° (2h) gave the corresponding sulphonyl chlorides (1-3), which were characterised by reaction with amines, azide ion and hydrazines (Table 1), giving the derivatives (4-31).

The sulphonyl chlorides (1-3) with amines (2 moles) in methanol at room temperature gave the sulphonamides (4-13). However, when the sulphonyl chloride (1) was treated with dimethylamine (4 mols) in methanol (50°), the ring-opened product (m.p. 197-8°) (32) was obtained. Under the same conditions, morpholine did not cause ring-fission, presumably due to lower nucleophilicity and greater steric size. Confirmation of this was obtained under more forcing conditions (boiling acetonitrile), which gave the ring-opened product (m.p. 142-3°) (33).

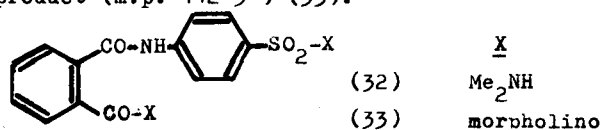
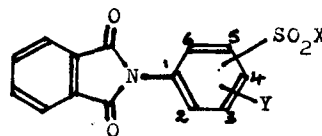


Table 1. Phthalimidobenzenesulphonyl Derivatives.



Compd. No.	X	Y	mp °C	Yield (%)
1	4-Cl	H	235-6*	85
2	4-Cl	2-Cl	118-20	70
3	3-Cl	4-Cl	183-4	70
4	4-NMe ₂	H	237-8	75
5	4-NHCH ₂ Ph	H	190-1	70
6	4-morpholino	H	213-4	80
7	4-NHPh	H	218-9*	95
8	4-NHC ₆ H ₄ OMe-p	H	166-7	85
9	4-NHC ₆ H ₄ Cl-p	H	195-6	75
10	4-NMe ₂	2-Cl	178-80	90
11	4-NHPh	2-Cl	95-6	84
12	3-NMe ₂	4-Cl	139-40	68
13	3-morpholino	4-Cl	176-7	70
14	4-NHNH ₂	H	171-2	60
15	4-NHNMe ₂	H	158-9	50
16	3-NHNMe ₂	4-Cl	129-30	50

* reference 6

Table 1. (continued)

Compd. No.	X	Y	mp °C	Yield (%)
17	4-NHN=CMe ₂	H	180-1	73
18	4-NHN=CHPh	H	196-7	88
19	4-NHN=CHC ₆ H ₄ NO ₂ -p	H	166-7	80
20	4-NHN=CHC ₆ H ₄ OMe-p	H	180-1	70
21	4-NHN=C(CH ₂) ₄	H	198-9	80
22	4-(3,5-dimethyl-1-pyrazolyl)	H	185-6	70
23	4-N ₃	H	156-7**	95
24	4-N ₃	2-Cl	118-20	76
25	3-N ₃	4-Cl	147-8	90
26	4-N=P(OEt) ₃	H	168-9	95
27	4-N=P(OEt) ₃	2-Cl	104-6	98
28	3-N=P(OEt) ₃	4-Cl	114-5	70
29	4-(3-aza-tri-cyclo[3.2.1.0 ^{2,4}]oct-3-yl)	H	241-2	80
30	4-N(SCCl ₃)Ph	H	198-9	63
31	4-N(SCCl ₃)C ₆ H ₄ Cl-p	H	185-6	60

** reference 4

With hydrazine hydrate (1 mol) and N,N-dimethylhydrazine (1 mol) in the presence of triethylamine (1 mol), the sulphonohydrazides (14-16) were obtained. The sulphonohydrazide (14) was characterised by reaction with aldehydes and ketones, with the formation of sulphonohydrazones (17-21). In the case of acetylacetone (1 mol), ring-closure occurred to give the dimethylpyrazole (22).

The sulphonyl azides (23-25) were obtained by the condensation of the sulphonyl chlorides (1-3) with sodium azide (3 mols) in aqueous acetone at room temperature. The sulphonyl azides (23-25) gave the corresponding phosphinimines (26-28) with triethylphosphite, and the aziridine (29) was obtained from (23) with norbornene.

The N-phenylsulphonamide (7) was condensed with perchloromethylmercaptan in the presence of triethylamine in acetone-ether to give (30). However, condensation with N-p-chlorophenyl-sulphonamide (9) required the use of a stronger base (sodium hydroxide) to provide the derivative (31). This is expected on the basis of the lower polarity of the N-H bond.

Preliminary *in vitro* fungicidal screening of the phthalimidobenzenesulphonyl derivatives against Aspergillus niger, Chaetomium globosum, Fusarium culmorum, Mucor mucedo and Trichoderma viride shows that the activity of N-phenyl-phthalimide is enhanced by the introduction of the sulphonyl group.

The products were fully characterised by microanalytical (C,H,N), and p.m.r., i.r. and m. spectral data. The purity of each product was determined by t.l.c.

I.r. spectroscopy was used to distinguish ring-closed and ring-opened products in the carbonyl region.⁷ These compounds each gave two absorptions, but the frequency range was not the same, (closed : 1780-70, 1720-15 cm⁻¹; opened : 1680-70, 1630-20 cm⁻¹).

The sulphonyl chlorides (1-3) were characterised by the p.m.r. spectra (DMSO-d₆) of the dimethylamides, δ 8.00-7.70, m, 4H (aromatic), 2.70, s, 6H (NMe₂).

Acknowledgment : Thanks are due to the British Council and CAPES for a research award to one of us (R.J. Nunes).

References

1. A. Fujinami, T. Ozaki, K. Nodera and K. Tanaka, Agr. Bid. Chem., **36**(2), 318 (1972), Chem. Abstr., **77**, 29591u (1972).
2. G.T. Bottger and S.I. Gerther, Plant Quarantine, E-777 (1949), Chem. Abstr., **43**, 7182c (1949).
3. R.J. Cremlyn, Pesticides : Preparation and Mode of Action, Wiley, Chichester, 1978, 136.
4. R.J. Cremlyn, D. Leonard and R. Motwani, J. Chem. Soc. Perkin I, 500 (1973).
5. R.J. Cremlyn, Int. Pest Control, **8**(4), 20 (1966).
6. M.J.S. Dewar and F.E. King, J. Chem. Soc., 114 (1945).
7. M.K. Hargreaves, J.G. Pritchard and H.R. Dave, Chemical Reviews, **70**(4), 439 (1970).