Sulphonyl Derivatives of Succindianilide and Glutardianilide

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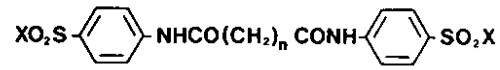
Summary: Succin - and glutar - dianilides reacted with chlorosulphonic acid to give the sulphonyl chlorides (I,XVII). These were condensed with amines, azide ion and hydrazine to give 20 derivatives. The succindianilide sulphonyl derivatives usually gave poor microanalyses, but were identified by the spectral data which are discussed.

The work described forms part of our general programme on the chemistry and biocidal properties of aromatic sulphonyl compounds [1-4], and extends previous studies of the chlorosulphonation of carboxylic acid acid anilides [5].

We showed [6] that oxalic and malonic acid dianilides by warming with a large excess of chlorosulphonic acid gave good yields of the corresponding 4,4'-bis-sulphonyl chlorides.

Succinic and glutaric acids were converted into the dianilides by successive treatment with thionyl chloride and aniline. The products, by reaction with excess (12 moles) of chlorosulphonic acid, gave excellent yields of the corresponding sulphonyl chlorides (I,XVII). The direct chlorosulphonation of these dianilides has not been previously reported. However, Irani [7] claimed that fusion of glutaric acid with sulphanilamide afforded 4,4'-bis-sulphamoyl glutardianilide, while under similar conditions succinic acid afforded N-(p-sulphamoylphenyl) succinimide; this difference presumably reflects the greater ease of formation of the 5- as compared with the 6-membered ring system.

(I, XVII) by condensation with dimethylamine, ammonia, azide ion and hydrazine afforded the derivatives (II,XVIII,III,VIII and XXI respectively) (Chart 1). Acetylation of the sulphonamide, following the procedure of Vogel [8], gave the sulphonacetamide (IV). Unsuccessful attempts were made to convert (IV) into the N-trichloromethylthio derivative with trichloromethylsulphenyl chloride in the presence of a sodium hydroxide or triethylamine. The failure is probably due to the low solubility of (IV) rather than lack of chemical reactivity, since many sulphonacetamides have been condensed with trichloromethylsulphenyl chloride [9]. The azides (V,XIX) reacted with triethylphosphite and norbornene to give (VI,XX,VII) (Chart 1). The PMR spectra of the phosphinimines (VI,XX) showed the ethyl resonances as multiplets due to interaction with the phosphorus atom. In the PMR spectrum of the aziridine (VII), the H_aH_b protons appear as sharp singlets implying that these protons are in the endo configuration with respect to the aziridine ring [10]. The aziridine ring must therefore be exo, which is surprising because this configuration



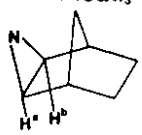
n=2	n=3	X
(I)	(XVII)	Cl
(II)	(XVIII)	NMe_2
(III)	–	NH_2
(IV)	–	NHCOMe
(V)	(XIX)	N_3
(VI)	(XX)	$N=P(OEt)_3$
(VII)	–	
(VIII)	(XXI)	$NHNH_2$
(IX)	(XXII)	$NHN=CMe_2$
(X)	–	
(XI)	–	NHN=CHPh
(XII)	–	$NHN=CHC_6H_4NO_2$-p
(XIII)	–	$NHN=CHC_6H_4OMe$-p
(XIV)	–	
(XV)	–	NHNHCONHPh
(XVI)	–	NHNHCSNHPh

Chart 1

would be expected to be less stable on steric grounds; however the results agree with those previously observed for malondianilide 4,4'-bis-sulphonylaziridine [6]. The hydrazides (VIII, XXI) were condensed with aldehydes and ketones to give the hydrazones (IX-XIII,XXII). (VIII) by refluxing with acetylacetone afforded the 3,5-dimethylpyrazole (XIV) and with phenylisocyanate and phenylisothiocyanate (VIII) gave (XV, XVI).

Many of the succindianilide sulphonyl derivatives (Table 1) failed to give good microanalytical data, even on repeated examination. On the other hand, the analogous glutardianilide derivatives afforded satisfactory results. Spectroscopy was therefore of special importance in confirming the structures. The IR spectra of the compounds showed the normal stretching absorption bands associated with NH, N_3, C=O, SO_2 and P-O-alkyl groups [11]. The mass spectra of the compounds did not show the molecular ions (M^+), and extensive fragmentation was observed in agreement with previous results obtained with the analogous malondianilide bis-sulphonyl derivatives [6]. PMR spectra were especially valuable in structural elucidation; for instance, the bis-dimethylamides (II,XVII) showed the correct aliphatic-aromatic proton ratios of 2:1 and 9:4 respectively, while the aromatic protons appeared as a multiplet with a well-defined AA'BB' pattern indicative of p-disulphonation. However, in the spectra of (III), (IV), (VI), (VII) and (XXII) surprisingly, the 8 aromatic protons resonated as a singlet indicating that all the aromatic protons are magnetically equivalent.

Experimental

Melting points were determined with a Gallenkemp electric apparatus and are uncorrected. IR spectra were recorded as nujol mulls with a Perkin Elmer 197 spectrophotometer. PMR spectra were measured with a Varian HA 80 spectrometer using TMS as internal standard. Mass spectra were determined with a VG micromass spectrometer at 80 ev, an asterisk indicates signals that were removed by D_2O treatment. TLC was carried out using Camlab silica gel plates sinsitized to UV 254 nm, with ethyl acetate - cyclohexane 3:2 as eluant unless otherwise stated.

Table-1: Physical Data of the Sulphonyldianilide Derivatives

Compound No.	M.P. °C	Yield %	Formula	ANALYSIS Found % C	H	N	Calc % C	H	N
(II)	228	40	$C_{20}H_{26}N_4O_6S_2$	48.0	4.0	10.8	49.8	5.4	11.6
(III)	271	54	$C_{16}H_{18}N_4O_6S_2$	43.5	4.0	11.9	45.0	4.2	13.1
(IV)	213-215	83	$C_{20}H_{22}N_4O_8S_2$	43.8	4.3	9.8	47.1	4.3	11.0
(V)	193-195	65	$C_{16}H_{14}N_8O_6S_2$	38.7	2.6	20.6	40.2	2.9	23.4
(VI)	209-211	91	$C_{28}H_{44}N_4O_{12}P_2S_2$	43.7	6.0	6.0	44.6	5.8	7.4
(VII)	205-207	66	$C_{30}H_{34}N_4O_6S_2$	58.1	5.7	8.0	59.0	5.6	9.2
(VIII)	213-215	75	$C_{16}H_{20}N_6O_6S_2$	38.2	4.1	15.8	42.1	4.4	18.4
(IX)	155	90	$C_{22}H_{28}N_6O_6S_2$	43.8	4.9	13.5	49.3	5.2	15.7
(X)	199	84	$C_{28}H_{36}N_6O_6S_2$	54.2	5.7	13.7	54.5	5.8	13.6
(XI)	225	86	$C_{30}H_{28}N_6O_6S_2$	56.0	4.4	13.6	57.0	4.4	13.3
(XII)	226-228	80	$C_{30}H_{26}N_8O_{10}S_2$	45.8	3.7	16.1	49.9	3.6	15.5
(XIII)	228	85	$C_{32}H_{32}N_6O_8S_2$	54.8	4.6	12.0	55.5	4.6	12.1
(XIV)	230	75	$C_{26}H_{28}N_6O_6S_2$	53.5	4.6	14.2	53.4	4.8	14.4
(XV)	216-220	66	$C_{30}H_{30}N_8O_8S_2$	47.0	4.6	16.7	51.9	4.3	16.1
(XVI)	222	61	$C_{30}H_{30}N_8O_6S_4$	46.2	4.5	16.0	49.6	4.1	15.4
(XVIII)	248-249	65	$C_{21}H_{28}N_4O_6S_2$	50.5	5.9 (S, 12.5)	10.9	50.8	5.6 (S, 12.9)	11.3
(XIX)	170-171	60	$C_{17}H_{16}N_8O_6S_2$	41.2	3.3	22.6	41.5	3.25	22.75
(XX)	149-150	71	$C_{29}H_{46}N_4O_{12}P_2S_2$	45.2	5.9	7.1	45.3	6.0	7.3
(XXI)	185-186	66	$C_{17}H_{22}N_6O_6S_2$	43.1	4.9	17.6	43.4	4.7	17.9
(XXII)	198-199	77	$C_{23}H_{30}N_6O_6S_6$	49.9	5.6	15.1	50.2	5.5	15.3

Preparation of the dicarboxylic acid dianilides:

Succinic or glutaric acid (0.1 mole) was heated with thionyl chloride (0.25 mole) and dimethylformamide (2 drops) until complete solution was attained (ca. 1½ hr). Thionyl chloride was evaporated in vacuo, the residue dissolved in toluene (50 ml) and treated with aniline (0.4 mole). After 4 hr, the white precipitate was collected, extracted with water and recrystallized (ethanol) to give succindianilide (85%), m.p. 231° (lit.[12] 230°), or glutardianilide (80%), m.p. 228-229° (lit.[13] 225°).

Chlorosulphonation of succindianilide:

The dianilide (5g) was added gradually to chlorosulphonic acid (16.6 ml.) at room temperature and the mixture was heated at 50° until effervescence ceased. The solution was left at room temperature for 1½ hr and was poured onto ice (200g) to give the bis-sulphonyl chloride (I), m.p. 185-187°; yield 90%. IR : ν_{max} 3380 (NH), 1700(C=O), 1585 (arom C=C), 1335, 1160(SO_2)cm^{-1}. MS : no M^+, 175($PhSO_2Cl$), 93($PhNH_2$), 64(SO_2), 36(HCl). TLC showed one spot, R_F 0.17. When chlorosulphonation was carried out at a higher temperature (80-90°, 1hr), the yield of (I) was substantially lower (29%).

Chlorosulphonation of glutardianilide:

Chlorosulphonic acid (50g) was added to the dianilide (10g) and the mixture was warmed on the steam bath for 15 min. After 3 hr at room temperature, the solution was added to ice (300 ml) to give (XVII), m.p. 300°; yield 85%. IR : ν_{max} 3300(NH), 1700 (C=O), 1600(arom C=C), 1340, 1150 (SO_2)cm^{-1}.

General procedures for the preparation of derivatives of the bis-sulphonyl chlorides (I,XVII):

(a) with dimethylamine:

The bis-sulphonyl chloride (0.01 mole) was reacted with dimethylamine (0.04 mole) in methanol for 3 hr. The solution was added to ice (50g) and the product purified by recrystallization from methanol to give the dimethylamides (II,XVIII).

Compound (II) TLC showed one spot, R_F 0.10. IR: ν_{max} 3380, 3100 (NH), 1700 (C=O), 1590 (arom C=C), 1330, 1155 (SO_2)cm^{-1}.

PMR (DMSO-d_6) δ : 10.50* (2H,s, CONH), 8.10-7.10(8H,m,ArH), 3.45 (4H,s,CH_2), 2.50(12H,s,Me). MS: no M^+, 200 ($NH_2C_4SO_2NMe_2$),156($NH_2C_6H_4SO_2H$),93(PhNH).

Compound (XVIII) TLC (ethyl acetate) showed one spot, R_F 0.29.

PMR(DMSO-d_6) δ : 10.40*(2H,s,CONH) ,8.00-7.50(8H,m,ArH), 3.35(4H,s, CH_2CO),2.20-1.80(14H,m,Me,CH_2). MS:no M^+, 296(M-$NH_2C_6H_4SO_2NMe_2$), 252(m-$NH_2C_6H_4SO_2NMe_2$, -NMe_2), 188(M-$NH_2C_6H_4SO_2NMe_2$,-NMe_2, -SO_2).

(b) Ammonia:

(I) was reacted with ammonia as previously described [6] to give the bis-sulphonamide (III). TLC showed one spot, R_F 0.40. IR: ν_{max} 3350, 3230(NH_2),3120(NH),1670(C=O),1595 (arom C=C), 1310,1155(SO_2)cm^{-1}.

PMR(DMSO-d_6) δ : 10.37*(2H,s, CONH), 7.80(8H,s,ArH), 7.23*(4H, s,SO_2NH_2), 2.73(4H,s,CH_2). The amide(III) was boiled with acetyl chloride-acetic acid as described by Vogel [8] to give the acetyl derivative (IV). TLC showed one spot, R_F 0.31 IR: ν_{max} 3260(NH), 1700,1680(C=O), 1590(arom C=C), 1340,1155(SO_2)cm^{-1}.

PMR($CDCl_3$) δ: 12.00*(2H,s,SO_2NH), 10.58*(2H,s,CONH),7.88(8H,s,ArH), 2.78(4H,s,CH_2),1.96(6H,s,CH_3).

(c) With sodium azide:

The sulphonyl chlorides (I,XVII) were reacted with sodium azide as previously detailed [6] to give the azides (V,XIX):

Compound (V) IR: ν_{max} 3390(NH), 2180(N_3),1700(C=O), 1590(arom C=C), 1530(C-N),1365,1160(SO_2)cm^{-1}.

MS:no molecular ion (M^+) obtained by electron impact or chemical ionization methods.

Compound (XIX) IR: ν_{max} 3400(NH), 2030(N_3),1705(C=C), 1600(arom C=C), 1340,1150(SO_2)cm^{-1}. The azides (V,XIX) by refluxing with triethylphosphite (2hr) gave the triethoxyphosphinimines (VI,XX):

Compound (VI) IR: ν_{max} 3330(NH), 1700(C=O),1590(arom C=C),1530 (C-N),1335,1145(SO_2),1030 (P-O-Me). PMR ($CDCl_3$) δ : 10.07*(2H,s, CONH),7.7(8H,s,ArH), 4.38-4.00 (12H,m,P-O-$\underline{CH_2}CH_3$),2.80(4H,s, CH_2),1.43-1.25(18H,m,P-O-$CH_2\underline{CH_3}$).

Compound (XX) IR: ν_{max} 3300(NH), 1700(C=O),1595(arom C=C),1340,1150 (SO_2)cm^{-1}.

PMR($CDCl_3$) δ : 9.50*(2H,s,CONH), 7.90-7.60(8H,m,ArH),4.40(12H,m, P-O-$\underline{CH_2}CH_3$), 2.50-1.90(6H,m,CH_2), 1.45-1.20(18H,m,P-O-$CH_2\underline{CH_3}$).

The azide (V)(0.005 mole) was refluxed with norbornene (0.01 mole) in THF for 10hr to give the aziridine (VII). IR: ν_{max} 3380(NH),1680(C=O), 1600(arom C=C),1320,1160(SO_2)cm^{-1}.

PMR(DMSO-d_6) δ :10.50*(2H,s, CONH),7.83(8H,s,ArH),2.93(4H,s, CH_2CO),2.77(2H,s,C<u>H</u>N),2.40-10.06 (16H,m,alicyclic H).

(d) With Hydrazine Hydrate:

The reactions were performed by the standard procedure [6], and the hydrazides (VIII,XXI) were characterized as the hydrazones (IX-XIII,XXII) (Chart 1). Typical spectral data are illustrated by the acetone derivatives (IX,XXII):

Compound (IX) IR: ,$_{max}$ 3360,3430 (NH),1690(C=O),1590(arom C=C), 1520(C-N),1320,1150(SO_2)cm^{-1}.

PMR($CDCl_3$) δ :10.48*(2H,s,CONH), 9.84*(2H,s,SO_2NH),7.72(8H,s,ArH), 2.62(4H,s,CH_2),1.72(12H,s,N=CMe_2).

Compound (XXII)

PMR(DMSO-d_6) δ :10.40*(2H,s, CONH),9.80*(2H,s,SO_2NH),7.80(8H, s,ArH),2.60-2.40(4H,m,CH_2CO),2.0 (2H,m,CH_2),1.70(12H,s,N=CMe_2).

The 3,5-dimethylpyrazole(XIV):

(VII)(0.005 mole) was refluxed with acetylacetone (0.01 mole) in methanol for 6 hr to give the 3,5-dimethylpyrazole (XIV): IR: ν_{max} 3300 (NH),1690(C=O),1590(arom C=C), 1520(C-N),1360,1120(SO_2)cm^{-1}.

PMR(DMSO-d_6): δ 10.56*(2H,s, CONH),8.20-7.20(7H,m,ArH),6.16 (2H,s,pyrazole H), 2.76(4H,s,CH_2), 2.48(6H,s,pyrazole 3-Me),2.12(6H, s,pyrazole 5-Me).

Reaction of the hydrazide (VIII) with phenylisocyanate:

The hydrazide (0.03 mole) was refluxed with phenylisocyanate (0.06 mole) in benzene (20 ml) for ½ hr to give the N-phenylureido derivative (XV): IR: ν_{max} 3450, 3150(NH), 1690 (C=O), 1370,1150(SO_2)cm^{-1}. PMR (DMSO-d_6): δ 10.43*(2H,s,CH_2CO), 7.80(18H,m,ArH),4.03*(6H,SO_2 NHNHCONHPh), 2.77(4H,s,CH_2CO).

(VIII) reacted similarly with phenylisothiocyanate to give (XVI) : IR: ν_{max} 3450,3100(NH), 1690(C=O), 1590 (arom C=C),1480(C=S), 1370,1150 (SO_2), 1080(C-N)cm^{-1}.

References

1. R.J.Cremlyn, K.H.Goulding, A.Hall and K.M.Yung, *Pestic.Sci.*, **14**, *158(1983).*
2. R.J.Cremlyn, F.J.Swinbourne, P.Fitzgerald, N.Godfrey, P. Hedges, J.Lapthorne and C. Mizon, *Indian J.Chem.*, **23B**, *962(1984).*
3. R.J.Cremlyn, F.J.Swinbourne and R.J.Nunes, *Quimica Nova*, *7(2)*, *118(1984).*
4. R.J.Cremlyn, F.J.Swinbourne and O.O.Shode, *J.Chinese Chem. Soc.*, **31**, *383 (1984).*
5. R.J.Cremlyn, A.Batchelor, R. Honeyman, D.Nash, O.O.Shode and A.Patel, *Indian J. Chem.*, **22B**, *1029(1983).*
6. R.J.Cremlyn, F.J.Swinbourne, J.G.Bloy, K.Pathak and O.O. Shode, *J.Chem.Soc.Pakistan (in Press, paper No.XIV-210884-454).*
7. R.J.Irani, *Current Sci.*, **14**, *46 (1945); C.A.*, **39**, *4854 (1945).*
8. A.I.Vogel, A Textbook of Practical Organic Chemistry, 3rd edn, Longman, London (1970), p.554.
9. R.J.Cremlyn and R.Brans, *J. Chem. Soc.(C)*, *225 (1970).*
10. J.E.Franz, C.Osuch and M.M. Dietrich, *J. Org. Chem.*, **29**, *2922(1964).*
11. L.J.Bellamy, The Infra-red Spectra of Complex Molecules, 2nd edn., Methuen, London, 1958.
12. G.F.Morrell, *J.Chem.Soc.*, **105**, *1733 (1914).*
13. G.B.Hoey and C.T.Lester, *J.Am.Chem.Soc.*, **73**, *4473(1951).*