Chlorosulphonation of Some Anilides

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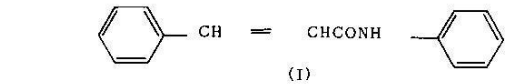
Summary: Cinnamanilide (I), the N(p-chloro) (XVI) and 4-chloro (XXVII) derivatives by reaction with chlorosulphonic acid gave the sulphonyl chlorides (II,XVII,XXVIII); these were reacted with nucleophiles, e.g. amines, azide ion and hydrazine to give 28 compounds. Oxalanilide (XXXV), the 4, 4'-dichloro derivative (XLV) and malonanilide (LIV; X=H) similarly afforded the sulphonyl chlorides (XXXVI, XLVI and LV) which were characterized as 30 derivatives. In contrast, 4, 4'-dichloromalonanilide (LIV; X=Cl) failed to give the sulphonyl chloride with chlorosulphonic acid. The spectral data of selected compounds are briefly discussed.

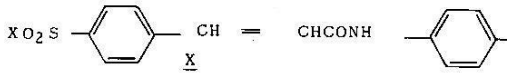
Results and Discussion

The work described here forms part of our general programme on the chemistry and biological activity of aromatic sulphonyl compounds [1-5] and forms an extension of previous studies [6] on the chlorosulphonation of carboxylic acid anilides. The cinnamanilides and oxalanilides were obtained from the corresponding acids by conversion to the acid chlorides and condensation with aniline or p-chloroaniline. Cinnamic acid reacts [7] easily with chlorosulphonic acid to give the p-sulphonyl chloride; the relative ease of sulphonation is due to electron donation by the π -electrons of the α,β -double bond into the phenyl ring. Cinnamanilide (I) reacted at room temperature with chlorosulphonic acid (10 moles) to give an excellent yield (98%) of the 4, 4' -bis-sulphonyl chloride (II). A similar yield of II was obtained by heating I with chlorosulphonic acid (12 moles) at 60° for 2 hr. Attempts to obtain the monosulphonyl chloride, by reaction with less reagent (3 moles) at room temperature, were unsuccessful.

The bis-sulphonyl chloride (II) by treatment with dimethylamine, ammonia and sodium azide gave III, IV and VI respectively (Chart 1). The amide (IV) by heating with acetyl chloride - acetic acid afforded the sulphonylacetamide (V), and the azide (VI) with triethylphosphite and norbornene was converted into the derivatives (VII and VIII). II by condensation with hydrazine hydrate gave the bis-hydrazide (IX) which condensed with aldehydes and ketones to give the hydrazones (X-XIV) Table 1). IX, by refluxing with acetylacetone, was converted into the 3, 5-dimethylpyrazole (XV). N(p-chlorophenyl)-cinnamide (XVI) with warm chlorosulphonic acid (12 moles) gave the 4-sulphonyl chloride (XVII, 90%) (Chart 2). Here the monosulphonyl chloride was obtained, because sulphonation occurred selectively in the monosubstituted ring A and not in ring B which is deactivated by the electron-withdrawing chlorine atom. The sulphonyl chloride (XVII) was reacted with dimethylamine,ammonia, sodium azide and hydrazine to give



(I)



X

(II) Cl

(III) NMe_2

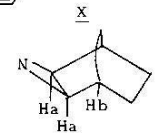
(IV) NH_2

(V) NHCOMe

(VI) N_3

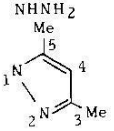
(VII) $N=P(OEt)_3$

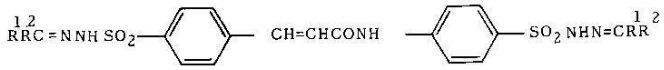
(VIII)



(IX) $NHNH_2$

(XV)

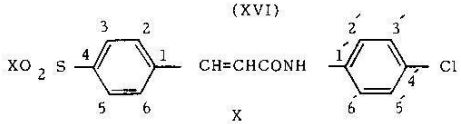




	R^1	R^2
(X)	Me	Me
(XI)	H	Ph
(XII)	H	C_6H_4OMe-p
(XIII)	H	$C_6H_4NO_2$-p
(XIV)	$-(CH_2)_5-$	

Chart 1

(XVI)



X

(XVII) Cl

(XVIII) NMe_2

(XIX) NH_2

(XX) N_3

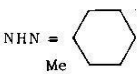
(XXI) $N=P(OEt)_3$

(XXII) $NHNH_2$

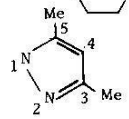
(XXIII) $NHN=CMe_2$

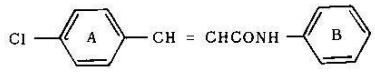
(XXIV) NHN = CHPh

(XXV) NHN =

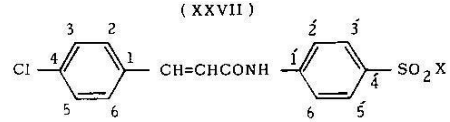


(XXVI)





(XXVII)



X

(XXVIII) Cl

(XXIX) NMe

(XXX) NH_2

(XXXI) N_3

(XXXII) $N=P(OEt)_3$

(XXXIII) $NHNH_2$

(XXXIV) $NHN=CMe_2$

Chart 3

Chart 2

the derivatives (XVIII-XXVI) (Chart 2). 4-Chlorocinnamanilide (XXVII) was warmed (50°) with chlorosulphonic acid (12 mols) to give the 4′-sulphonyl chloride (XXVIII) (92%); again selective sulphonation occurred in the monosubstituted ring B. XXVIII was characterized by reaction with nucleophilic reagents to give the derivatives (XXIX-XXXIV) (Chart 3).

Oxalanilide (XXXV) was heated with chlorosulphonic acid (12 moles) at 80 - 85° (3 hr) to give the 4,4′-bis-sulphonyl chloride (XXXVI, 60%). XXXVI was reacted with nucleophilic reagents to give the derivatives (XXXVII-XLIV) (Chart 4 and Table 2). 4, 4′-Dichloro-oxalanilide (XLV) with chlorosulphonic acid (12 moles) at 80-85°(4 hr) gave the 3, 3′-bis-sulphonyl chloride (XLVI) (84%); this was characterized as the derivatives (XLVII-LIII) (Chart 4).

Malonanilide (LIV; X=H) was prepared by refluxing diethyl malonate with aniline. When the reaction was performed in the dark and under nitrogen, the yield of (LIV; X=H) increased from 17 to 71%; these conditions minimized the oxidative decomposition of aniline. The reaction of malonanilide with chlorosulphonic acid was investigated under various conditions: the yield of the 4, 4′-bis-sulphonyl chloride (LV), increased from 60 to 99% as the molar ratio of chlorosulphonic acid was increased from 8 to 12 moles. The optimum conditions used a large excess (12 moles) of the reagent at 50° (5 minutes), the bis-sulphonyl chloride (LV) was converted to the derivatives (LVI-LXX I) (Chart 5 and Table 3). The direct chlorosulphonation of these anilides has not been previously reported. 4, 4′-Dichloromalonanilide (LIV; X=Cl), was prepared by heating p-chloroaniline and diethyl malonate. The reaction of (LIV; X=Cl) with chlorosulphonic acid (12 moles) under the conditions used for malonanilide (LIV; X=H) (50°, 5 min) was unsuccessful. This is not surprising since the introduction of the 4, 4′-chlorine atoms should reduce the ease of chlorosulphonation by a combination of steric and electronic effects. However repetition of the reaction under more drastic conditions (80°, 4 hr) also failed to yield any solid product. This is difficult to explain since these conditions were successfully used for the chlorosulphonation of 4,4′-dichloro-oxalanilide (XLV).

The IR spectra of the various anilide sulphonyl derivatives showed the normal stretching absorptions associated with the NH, N_3, C=O and SO_2 groups [8].

The PMR spectra of the cinnamanilide derivatives (Charts 1-3) indicated p-sulphonation; thus in the dimethylamide (III) (Table 1), the 8 aromatic protons resonated as a multiplet (δ 8.1-7.5) showing the AA'BB' pattern together with one of the olefinic protons; the other olefinic proton appeared as doublet (δ 7.0, $J_{H,H}$16Hz), the value of the coupling constant (J_{HH}) confirms the trans orientation of these protons. The PMR spectra of the malonanilide sulphonyl derivatives (Chart 5) similarly showed that p-sulphonation had occurred, e.g. LXIII (Table 3). On the other hand, the PMR spectra of the 4, 4′-dichloro-oxalanilide sulphonyl derivatives, e.g. X-LVII (Table 2) did not show the AA' BB' pattern in the aromatic proton resonances.

The oxalanilide sulphonyl derivatives (Chart 4) were not sufficiently soluble to measure their PMR spectra. The PMR spectra of the aziridines (VIII, LXI) showed the Ha, Hb proton resonances as sharp singlets which

indicates that the Ha protons are in the endo configuration with respect to the aziridine ring. Since this would lead to a dihedral angle between the Ha and Hb protons of approximately 90° so no appreciable coupling occurs. If however the Ha protons were exo, coupling with the Hb proton would broaden the Ha proton resonance.

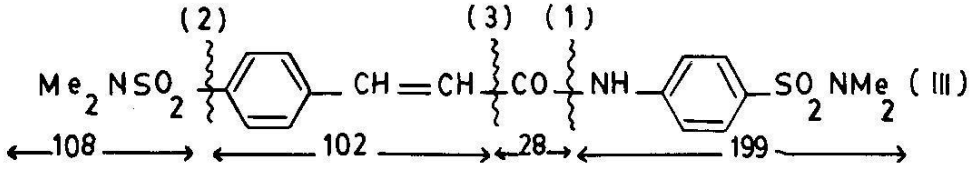
In the mass spectra, some of the compounds showed the molecular ions (M^+) (Tables 1-3), notable exceptions were the hydrazides and hydrazones which suffered extensive fragmentation. The general pattern of fragmentation shown by the cinnamanilide sulphonyl derivatives (Charts 1-3) is illustrated by the behaviour of the dimethylamides (III,XVIII,XXIX) in which cleavage occurs in the order 1→2→3:

The oxalanilide (Chart 4) and the majority of the malonanilide (Chart 5) sulphonyl derivatives were not sufficiently volatile to obtain their mass spectra. The few compounds, e.g. the dimethylamide (LVI, Table 3), which gave mass spectra showed extensive fragmentation.

The various compounds reported are being screened for biological activity by ICI Ltd (Pharmaceuticals and Plant Protection Divisions).

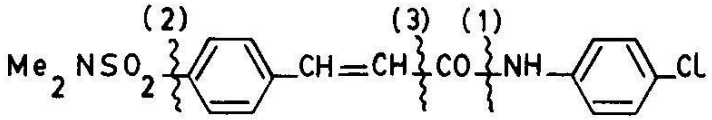
Experimental

Melting points were measured with a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded as nujol mulls with a Unicam SP 100 spectrophotometer. PMR spectra were determined with a Varian HA 80 spectrometer using TMS as internal stan-



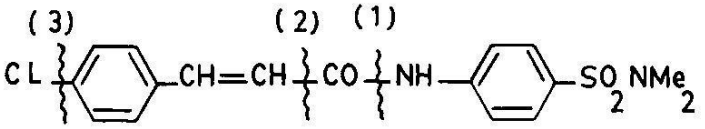
(III)

MS: 437 (M^+), 238, 199, 130, 108, 102



(XVIII)

MS: 364 (M^+), 238, 126,102

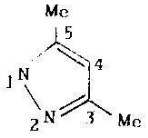


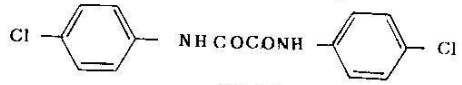
(XXIX)

MS: 364 (M^+), 199 165, 137, 102

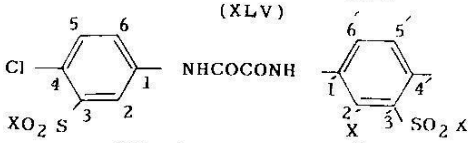
PhNHCOCONHPh

(XXXV)

(XXXVI)	Cl
(XXXVII)	NMe_2
(XXXVIII)	NH_2
(XXXIX)	N_3
(XL)	$N{=}P(OEt)_3$
(XLI)	$NHNH_2$
(XLII)	$NHN{=}CMe_2$
(XLIII)	NHN=CHPh
(XLIV)	



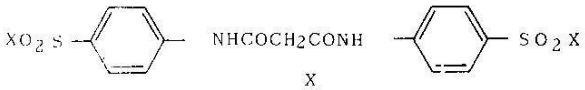
(XLV)



(XLVI)	Cl
(XLVII)	NMe_2
(XLVIII)	NH_2
(XLIX)	N_3
(L)	$N{=}P(OEt)_3$
(LI)	$NHNH_2$
(LII)	$NHN{=}CMe_2$
(LIII)	NHN=CHPh

Chart 4

(LIV)



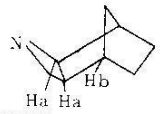
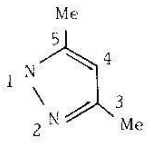
(LV)	Cl
(LVI)	NMe_2
(LVII)	NH_2
(LVIII)	NHCOMe
(LIX)	N_3
(LX)	$N{=}P(OEt)_3$
(LXI)	
(LXII)	$NHNH_2$
(LXIII)	$NHN{=}CMe_2$
(LXIV)	
(LXV)	NHN=CHPh
(LXVI)	$NHN{=}C_6H_4NO_2$-p
(LXVII)	$NHN{=}C_6H_4OMe$-p
(LXVIII)	
(LXIX)	NHNHCONHPh
(LXX)	NHNHCSNHPh
(LXXI)	

Chart 5

Table-1: Physical data of sulphonylcinnamanilide derivatives.

Compd No	M.P. °C	Yield %	Formula	Analysis % Calc (Found) C	H	N	MS M^+
IIIa	268-270	81	$C_{19}H_{23}N_3O_5S_2$	52.2	5.3	9.6	437
				(51.9)	(5.3)	(9.6)	
IV	266-268	69	$C_{15}H_{15}N_3O_5S_2$	47.2	3.9	11.0	381
				(47.0)	(4.0)	(10.7)	
V	258	70	$C_{19}H_{19}N_3O_5S_2$	49.0	4.1	9.0	465
				(48.8)	(3.9)	(9.1)	
VI	172	56	$C_{15}H_{11}N_7O_5S_2$	41.6	2.5	22.6	433
				(41.3)	(2.3)	(22.9)	
VII	137-138	27	$C_{27}H_{41}N_3O_{11}P_2S_2$	(45.7)	5.8	5.9	565
				(45.8)	(5.9)	(5.8)	
VIII	167	74	$C_{29}H_{31}N_3O_5S_2$	61.6	5.5	7.4	565
				(61.3)	(5.7)	(7.2)	
IX	228	89	$C_{15}H_{17}N_5O_5S_2$	43.8	4.1	17.1	
				(43.8)	(4.2)	(17.1)	
Xb	220-222	33	$C_{21}H_{25}N_5O_5S_2$	51.3	5.1	14.3	
				(51.1)	(5.1)	(14.1)	
XI	255-256	56	$C_{29}H_{25}N_5O_5S_2$	59.3	4.3	11.9	
				(59.0)	(4.4)	(11.7)	
XII	210	62	$C_{31}H_{29}N_5O_7S_2$	57.5	4.5	10.8	
				(57.3)	(4.5)	(10.7)	
XIII	216-217	61	$C_{29}H_{23}N_7O_9S_2$	51.4	3.4	14.5	
				(51.2)	(3.6)	(14.3)	
XIV	190	15	$C_{27}H_{33}N_5O_5S_2$	56.7	5.8	12.3	
				(56.5	(5.9)	(12.1)	

Table-1: (Continued)

Compd No	M.P. °C	Yield %	Formula	Analysis % Calc C	H	N	MS M^+
XV	245	25	$C_{25}H_{25}N_5O_5S_2$	55.6 (55.4)	4.6 (4.8)	13.0 (12.8)	539
XVIII	225	49	$C_{17}H_{17}ClN_2O_3S$	56.0 (56.0)	4.7 (4.8)	7.7 (7.8)	364
XIX	293	64	$C_{15}H_{13}ClN_2O_3S$	53.5 (53.4)	3.9 (3.9)	8.3 (8.1)	336
XX	180	26	$C_{15}H_{11}ClN_4O_3S$	49.7 (49.6)	3.0 (2.8)	15.4 (15.3)	362
XXI	148-150	56	$C_{21}H_{26}ClN_2O_6PS$	50.3 (50.1)	5.2 (5.2)	5.6 (5.5)	500
XXII	172-173	71	$C_{15}H_{14}ClN_3O_3S$	49.8 (49.6)	3.9 (4.0)	11.6 (11.5)	
XXIII	196	60	$C_{18}H_{18}ClN_3O_3S$	55.2 (55.1)	4.6 (4.6)	10.7 (10.8)	
XXIV	212	65	$C_{22}H_{18}ClN_3O_3S$	60.1 (60.0)	4.1 (4.1)	9.6 (9.6)	
XXV	195	51	$C_{20}H_{20}ClN_3O_3S$	57.5 (57.3)	4.8 (4.7)	10.1 (10.3)	
XXVI	196-197	37	$C_{20}H_{18}ClN_3O_3S$	57.8 (57.7)	4.3 (4.3)	10.1 (10.0)	415
XXIX	180-182	63	$C_{17}H_{17}ClN_2O_3S$	56.0 (55.8)	4.7 (4.7)	7.7 (7.6)	364
XXX	170	57	$C_{15}H_{13}ClN_2O_3S$	53.5 (53.3)	3.9 (3.8)	8.3 (8.2)	336

Table-1: (Continued)

Compd No	M.P. °C	Yield %	Formula	Analysis % Calc (Found) C	H	N	MS M^+
XXXI	182	22	$C_{15}H_{11}ClN_4O_3S$	49.7	3.0	15.4	362
				(49.7)	(3.0)	(15.2)	
XXXIIc	150-151	45	$C_{21}H_{26}ClN_2O_6PS$	50.3	5.2	5.6	500
				(50.0)	(5.1)	(5.4)	
XXXIII	164-166	25	$C_{15}H_{14}ClN_3O_3S$	49.8	3.9	11.6	
				(49.7)	(4.0)	(11.8)	
XXXIV	219	54	$C_{18}H_{18}ClN_3O_3S$	55.2	4.6	10.7	
				(55.0)	(4.8)	(10.6)	

a) PMR (DMSO-d_6) : δ 10.77* (1H, s, CONH), 8.10 - 6.80 (10H, m, 8ArH, CH=CH), 2.63 (12H, d, $CONMe_2$)

b) PMR ($CDCl_3$) : δ 10.43*, 10.0* (2H, s, SO_2NH), 8.30 - 6.80 (10H, m, 8ArH, HC=CH), 1.90 (12H, s, $N=CMe_2$)

c) PMR (DMSO-d_6) : δ 10.57* (1H, s, CONH), 8.20 - 6.70 (10H, 8ArH, CH=CH), 4.43 - 3.67 (6H, m, $POCH_2CH_3$), 1.10 (9H, t, $POCH_2CH_3$).

dard; an asterisk indicates signals removed by treatment with D_2O. Mass spectra were obtained with a VG micromass spectrometer at 60 eV.

Chlorosulphonation of cinnamanilide (I)

I (4.5 g) was added portion-wise to chlorosulphonic acid (12 ml) at 0° with stirring, and the solution was left at room temperature for 1 week. Addition of crushed ice (150 g) gave the 4, 4′-bis-sulphonyl chloride (II) m.p. 148°; yield 98%. IR: ν max 3350 (NH), 1680(C=0), 1590(arom C=C), 1335, 1170(SO_2)cm^{-1}. MS: 64(SO_2). TLC (EtOAc-cyclohexane 1:1) showed one spot, R_f 0.35.

Chlorosulphonation of N(4′-chlorophenyl) cinnamide (XVI)

XVI (12 g) was gradually added to chlorosulphonic acid (40.7 ml) at room temperature. The solution was warmed (50°) until effervescence ceased and the mixture was poured onto crushed ice (250 g). The precipitate was filtered off, washed with water and dried to give the 4-sulphonyl chloride (XVII) m.p. 172°; yield 90%. IR: ν_{max} 3300(NH), 1700(C=O), 1600(arom C=C), 1335, 1170(SO_2) cm^{-1}. MS: 356(M^+), 289, 229 (M-NH.C_6H_4Cl), 162, 127, 102, 91. TLC (EtOAc-cyclohexane 1:1) showed one major spot, R_f 0.68.

Table-2: Physical data of sulphonyloxalanilide derivatives.

Compd No	M.P. °C	Yield %	Formula	Analysis % Calc (Found) C	H	N	MS M^+
XXXVII	270-272	80	$C_{18}H_{22}N_4O_6S_2$	47.5	4.8	12.3	
				(47.0)	(4.3)	(11.6)	
XXXVIII	331 (lit[9] >330)	63	$C_{14}H_{14}N_4O_6S_2$	42.2	3.5	14.1	
				(40.4)	(3.8)	(14.9)	
XXXIX	365	58	$C_{14}H_{10}N_8O_6S_2$	37.3	2.2	24.9	
				(36.9)	(2.3)	(25.5)	
XL	212-215	82	$C_{26}H_{40}N_4O_{12}P_2S_2$	43.0	5.5	7.7	
				(43.6)	(5.9)	(7.2)	
XLI	323-325	91	$C_{14}H_{16}N_6O_6S_2$	39.2	3.7	19.6	
				(38.8)	(3.8)	(20.0)	
XLII	>360	82	$C_{20}H_{24}N_6O_6S_2$	47.2	4.7	16.5	
				(47.6)	(4.7)	(15.8)	
XLIII	>360	75	$C_{28}H_{24}N_6O_6S_2$	55.6	4.0	13.9	
				(55.2)	(3.8)	(13.6)	
XLIV	>380	36	$C_{24}H_{24}N_6O_6S_2$	51.8	4.3	15.1	
				(51.4)	(4.5)	(15.5)	
XLVIIa	320	81	$C_{18}H_{20}N_4O_6S_2 .2\frac{1}{2}H_2O$	38.0	4.4	9.9	
				(38.2)	(4.3)	(9.8)	
XLVIII	328-330	82	$C_{14}H_{12}Cl_2N_4O_6S_2$	32.8	3.3	10.9	
				(32.9)	(3.3)	(10.7)	
XLIX	265	97	$C_{14}H_8Cl_2N_8O_6S$	32.4	1.5	21.6	
				(32.5)	(1.5)	(21.4)	

Table-2: (Continued)

L	110-111	36	$C_{26}H_{38}Cl_2N_4O_{12}P_2S_2$	39.2	4.8	7.0
				(39.0)	(5.0)	(7.0)
LI	340	74	$C_{14}H_{14}Cl_2N_6O_6S_2$	39.4	3.3	19.7
				(39.2)	(3.4)	(19.8)
LII	134	73	$C_{20}H_{22}Cl_2N_6O_6S_2$	36.9	3.4	12.9
				(37.0)	(3.2)	(12.8)
LIII	250-252	64	$C_{28}H_{22}Cl_2N_6O_6S_2$	49.9	3.3	12.5
				(49.9)	(3.1)	(12.7)

a) PMR(DMSO-d^6) δ : 11.90* (2H, s, COHN), 8.62 - 7.30 (6H, s, ArH), 2.60 (12H, s, NMe_2).

Table-3: Physical data of sulphonylmalonanilides.

Compd No	M.P. °C	Yield %	Formula	Analysis % Calc (Found) C	H	N
LVIa	188	59	$C_{19}H_{24}N_4O_6S_2$	48.7	5.1	12.0
				(48.6)	(4.9)	(11.8)
LVII	272 (lit[9] 272)	83	$C_{15}H_{16}N_4O_6S_2$	43.7	3.9	13.6
				(43.6)	(3.8)	(13.8)
LVIII	237-238	83	$C_{19}H_{20}N_4O_8S_2$	46.3	4.1	11.4
				(46.0)	(4.0)	(11.2)
LIX	178	75	$C_{15}H_{12}N_8O_6S_2$	38.8	2.6	24.1
				(38.9)	(2.7)	(23.9)
LX	163-164	70	$C_{27}H_{42}N_4O_{12}P_2S_2$	43.8	5.7	7.6
				(43.6)	(5.7)	(7.4)
LXIb	139-140	62	$C_{29}H_{32}N_4O_6S_2$	58.4	5.4	9.4
				(58.5)	(5.4)	(9.6)

Table-3: (Continued)

LXII	200	64	$C_{15}H_{18}N_6O_6S_2$	40.7	4.1	19.0
				(40.8)	(4.2)	(18.9)
LXIIIc	140	84	$C_{21}H_{26}N_6O_6S_2$	48.3	5.0	16.1
				(48.2)	(4.9)	(16.1)
LXIV	160	73	$C_{27}H_{34}N_6O_6S_2$	53.8	5.6	13.9
				(53.5)	(5.8)	(13.6)
LXV	180	91	$C_{29}H_{26}N_6O_6S_2$	56.3	4.2	13.6
				(56.6)	(4.6)	(13.3)
LXVI	215	93	$C_{29}H_{24}N_6O_6S_2$	49.2	3.4	15.8
				(49.0)	(3.5)	(15.5)
LXVII	152-154	95	$C_{31}H_{30}N_6O_8S_2$	54.9	4.4	12.4
				(55.1)	(4.4)	(12.2)
LXVIIId	85	63	$C_{25}H_{26}N_6O_6S_2$	52.6	4.6	14.7
				(52.4)	(4.6)	(14.5)
LXIX	218	98	$C_{29}H_{28}N_8O_8S_2$	51.2	4.1	16.5
				(51.8)	(4.2)	(16.5)
LXX	208	73	$C_{29}H_{28}N_8O_6S_4$	48.9	3.9	15.7
				(48.6)	(4.0)	(16.0)
LXXI	136-137	51	$C_{23}H_{28}N_4O_8S_2$	50.0	5.1	10.1
				(49.8)	(5.1)	(10.2)

a) MS: no M^+ (468), 200, 156, 92

b) PMR ($CDCl_3$) δ: 10.7* (2H, s, CONH), 7.87 - 7.80 (8H, m, ArH), 2.93 (2H, s, CH_2CO), 2.40 (4H, s, Ha), 2.10 (4H, s, Hb), 1.50 - 1.0 (12H, m, alip H).

c) PMR (DMSO-d_6) δ: 9.61* (2H, s, SO_2NH), 8.97* (2H, s, CONH), 7.20 - 6.82 (8H, m, ArH), 3.3 (2H, CH_2CO), 2.60 (12H, s, $N{=}CMe_2$).

d) PMR ($CDCl_3$) δ: 9.0* (2H, s, CONH), 6.80 - 6.50 (8H, m, ArH), 4.90 (2H, s, pyrazole-4H), 3.3 (2H, s, CH_2CO), 2.63 (2H, s, $COCH_2$), 1.47 (6H, s, pyrazole-5Me), 1.13 (6H, s, pyrazole-3Me).

Chlorosulphonation of 4-chlorocinnamanilide (XXVII)

XXVII (10 g) was heated with chlorosulphonic acid (34 ml) at 50° for 5 min and the solution poured onto ice to give the 4′-sulphonyl chloride (XXVIII) m.p. 199°; yield 92%. IR: ν_{max} 3400(NH), 1700(C=O), 1595(arom C=C),1335, 1160(SO_2)cm^{-1}. MS: 200, 165 (M-$NHC_6H_4SO_2Cl$), 137, 101. TLC (EtOAC-cyclohexane 1:1) showed one spot, R_f 0.76.

General procedures for the reactions of the chlorosulphonylanilides with:

(a) dimethylamine

The chlorosulphonylanilide (0.01 mole) was heated with dimethylamine (0.06 mole) in methanol at 60° for ½ hr. The solution was poured onto ice and the product purified by recrystallization from methanol to give the dimethylamines (III, XVIII, XXIX, XXXVII, XLVII, LVI).

(b) ammonia

The chlorosulphonylanilide (0.01 mole) was treated with 0.88 ammonium hydroxide (10 ml) in acetone (30 ml) at room temperature (6 hr). The solid product was recrystallized from aqueous acetone to give the sulphonamides (IV, XIX, XXX, XXXVIII, XLVIII, LVII).

(c) Sodium azide

The chlorosulphonylanilide (0.01 mole) was condensed with sodium azide (0.06 mol) in aqueous acetone (30 ml). Addition of ice (200 g) and recrystallization from acetone gave the azides (VI, XX, XXXI, XXXIX, XLIX, LIX). The azides (0.002 mole) were refluxed with triethylphosphite (0.002 mole) in toluene (15 ml) for 2 hr and left at room temperature (1 hr) to give the triethoxyphosphinimines (VII, XXI, XXXII, XL, L, LX). The azide (0.002 mole) by reaction with norbornene (0.002 mole) in boiling THF (6 hr) afforded the aziridines (VIII, LXI).

(d) Hydrazine

The chlorosulphonanilide (0.01 mole) was stirred with hydrazine hydrate (98%) (0.06 mole) in methanol (30 ml) for 3 hr to give the hydrazides (IV, XXII, XXXIII, XLI, LI, LXII). These were characterized as hydrazones obtained by heating the hydrazide (0.004 mole) with an aldehyde or ketone (0.005 mole) in ethanol (15 ml) at 50° for 1/4 hr. With cyclohexanone and cyclopentanone the solution was refluxed for 4 hr; while formation of the 3, 5-dimethylpyrazoles (XXVI, XLIV, LXVIII) required boiling the hydrazide with acetylacetone in ethanol for 6 hr.

Chlorosulphonation of Oxalanilide (XXXV)

XXXV (5 g) was added to chlorosulphonic acid (28 g) at room temperature and the solution was heated at 80-85° for 3 hr. Addition of ice (100 g) afforded (XXXVI), m.p. 350°; yield 60%. IR: ν_{max} 3300 (NH), 1705 (C=O), 1600 (arom C=C), 1365, 1160 (SO_2)cm^{-1}.

Chlorosulphonation of 4, 4′-dichlorooxalanilide (XLIV)

XLIV (40 g) was heated with chlorosulphonic acid (181 g) at 80-86° for 4 hr to give the bis-sulphonyl chloride (XLV), m.p. 300°; yield 84%. IR: ν_{max} 3320 (NH), 1700 (C=O), 1600 (arom C=C), 1520 (C-N), 1370, 1165 (SO_2), 750 (C-Cl)cm^{-1}.

Malonanilide (LIV; X=H)

Aniline (23.4 g) was refluxed with diethyl malonate (13.4 g) for 20 hr. The reaction was carried out in the

dark under nitrogen. Cooling gave a precipitate which was filtered off, washed with 0.1M hydrochloric acid and water to give (LIV; X=H), m.p. 227° (lit[10] 226°): yield 71%. IR: ν_{max} 3280 (NH), 1670(C=O), 1600 (arom C=C). (Found: C, 71.0; H, 5.5; N, 11.0% $C_{15}H_{14}N_2O_2$ requires: C 70.8; H, 5.5; N, 11.0%).

Chlorosulphonation of Malonanilide (LIV, X=H)

(5 g) was heated with chlorosulphonic acid (30 g) at 50° until effervescence ceased; after standing for 3 hr the solution was poured onto ice (150 g) to give the 4, 4′-bis-sulphonyl chloride (LV), m.p. 175°; yield 98%. IR: ν_{max} 3350, 3250 (NH), 1700 (C=O), 1600 (arom C=C), 1520 (C-N), 1340, 1165 $(SO_2)cm^{-1}$. MS: no M^+, 36 (HCl). TLC (EtOAc-cyclohexane 3:2) showed one spot, R_f 0.33. Sodium fusion test was positive for Cl, N, S.

Reaction of 4, 4′-bis-sulphonylhydrazinomalonanilide (LXII) with phenylisocyanate

The hydrazide (LXII) (2 g) was refluxed with phenylisocyanate (1.2 ml) in dry benzene (20 ml) for ½ hr. The solution was left to cool (1 hr) and the precipitate was filtered off. The pale yellow solid was washed with methanol and ether to give the N-phenylureido derivative (LXVIX). IR: ν_{max} 3340 (NH), 1710, 1700 (C=O), 1600 (arom C=C), 1370, 1160 $(SO_2)cm^{-1}$. PMR (DMSO-d_6): δ 10.6* (2H, s, CH_2CONH), 8.27* (2H, s, CONHPh), 7.85-7.40 (18H, m,ArH), 4.07* (2H, s, SO_2NH), 3.60* (2H, s, $NHNHCO$), 3.33 (2H, s, $COCH_2CO$).

LXII reacted similarly with phenylisothiocyanate to give the N-phenylthioureide (LXVX). IR: ν_{max} 3300 (NH), 1700 (C=O), 1600 (arom C=C), 1465 (C=S), 1370, 1150 $(SO_2)cm^{-1}$. PMR (DMSO-d_6): δ 10.58* (2H, s, $CH_2CONHPh$), 8.30* (2H, s, CONHPh), 7.85 7.40 (18H, m, ArH), 3.60* (2H, s, SO_2NH), 3.30 (2H, s, $CO.CH_2CO$), 3.17 (2H, $NHNHCS$).

4, 4′-Dichloromalonanilide (LIV; X=Cl)

A mixture of p-chloroaniline (59.8 g) and diethyl malonate (250 g) was refluxed for 8 hr, the reaction was carried in the dark with an atmosphere of nitrogen. Cooling gave a solid which was filtered off and washed with 0.1M hydrochloric acid and water to give LIV, m.p. 258° (lit[11] 251°); yield 50 g (98%). IR: ν_{max} 3210 (NH), 1680 (C=O), 1600 (arom C=C), 720 (C-Cl cm^{-1}. PMR (DMSO-d_6) δ 10.12* (2H, s, CONH), 7.70 - 7.20 (8H, m, ArH), 3.22 (2H, s, CH_2). TLC (EtOAc-cyclohexane 1:1) showed one spot R_f 0.42.

Attempted chlorosulphonation of 4, 4′-dichloromalonanilide (LIV;X=Cl)

LIV (X=Cl) (0.02 mole) was heated with chlorosulphonic acid (0.24 mole) at 50-60° until effervescence ceased. The solution was poured onto ice but no solid product was obtained. Similar results were obtained by heating the mixture at 80° for 4 hr.

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