Ring-substituted Derivatives of 5,6,11,12-Tetrahydrodibenzo[*b,f*][1,4]-diazocine

By **A. Saunders** and **J. M. Sprake,*** School of Pharmacy, The Polytechnic, Sunderland, Co. Durham

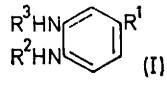
Ring-substituted derivatives of 5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine (IIb) have been prepared by the interaction of substituted *NN'*-bis-*p*-tolylsulphonyl-*o*-phenylenediamines (Ib—e) and αα'-dibromo-*o*-xylene, and hydrolysis of the products (IIc—f). In general, hydrolysis gives either the free base (IIg—j) or a mixture of this and the 5-*p*-tolylsulphonyl derivative (IVa—c), depending on the reaction time. The free bases (IIg—i) reacted with paraformaldehyde and with 5-nitro-2-furaldehyde to give bridged-ring compounds (III).

THE interaction of *NN'*-bis-*p*-tolylsulphonyl-*o*-phenylenediamine (Ia) and αα'-dibromo-*o*-xylene affords 5,6,11,12-tetrahydro-5,12-bis-*p*-tolylsulphonyldibenzo-[*b,f*][1,4]diazocine (IIa), which can be hydrolysed to the free base (IIb).[1] The base reacts with paraformaldehyde and with aromatic aldehydes to give bridged-ring compounds (III; R^1 = H).[1b] Ring-substituted derivatives of the compounds (IIb) and (III; R^1 = H) have now been synthesised.

4-Chloro- and 4-methoxy-*o*-phenylenediamine reacted with toluene-*p*-sulphonyl chloride in pyridine below 60° to give the *NN'*-bis-*p*-tolylsulphonyl derivatives (Ib and c), but it was necessary to heat the mixture at 100° to obtain the bis-*p*-tolylsulphonyl derivatives of 4-trifluoromethyl- and 4-nitro-*o*-phenylenediamine (Id and e).

TABLE 1

Substituted *o*-phenylenediamines



(I)

(I)	R^1	R^2	R^3	Solvent for cryst.	Form	M.p.	Yield (%)	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
a	H	Tosyl	Tosyl											
b	Cl	Tosyl	Tosyl	AcOH	Prisms	198—200°	84	$C_{20}H_{19}ClN_2O_4S_2$	53·55	4·45	6·25	53·3	4·25	6·2
c	MeO	Tosyl	Tosyl	AcOH	Plates	164—166	70	$C_{21}H_{22}N_2O_5S_2$	56·6	5·2	5·85	56·5	5·0	6·3
d	CF_3	Tosyl	Tosyl	EtOH aq.	Needles	144—146	36	$C_{21}H_{19}F_3N_2O_4S_2$	52·2	3·9	6·0	52·05	3·95	5·8
e	NO_2	Tosyl	Tosyl	AcOH	Needles [a]	220—221	36	$C_{20}H_{19}N_3O_6S_2$	51·85	4·2	9·05	52·05	4·15	9·1
f	CF_3	H	Tosyl	PhMe	Prisms	173—174	73	$C_{14}H_{13}F_3N_2O_2S$			8·65			8·5
g	Cl	Tosyl	H	PhH	Needles	133—134	40	$C_{13}H_{13}ClN_2O_2S$	52·9	4·6	9·25	52·6	4·4	9·45
h	Cl	$PhSO_2$	H	PhH	Needles	156—157	64	$C_{12}H_{11}ClN_2O_2S$	51·2	4·15	10·05	50·95	3·95	9·9
i	MeO	Tosyl	H	PhH	Prisms	87—88	84	$C_{14}H_{16}N_2O_3S$	57·75	5·65	9·35	57·5	5·55	9·6
j	MeO	$PhSO_2$	H	PhH	Prisms	123—125 [b]	70	$C_{13}H_{14}N_2O_3S$						
k	CF_3	Tosyl	H	PhH	Needles	136—137	69	$C_{14}H_{13}F_3N_2O_2S$	50·9	4·35	8·65	50·9	4·0	8·5
l	CF_3	$PhSO_2$	H	CCl_4	Needles	169	73	$C_{13}H_{11}F_3N_2O_2S$	49·45	3·85	9·0	49·35	3·5	8·85
m	Cl	Tosyl	$PhSO_2$	EtOH	Prisms	159—160	65	$C_{19}H_{17}ClN_2O_4S_2$	52·2	3·85	6·65	52·2	3·95	6·4
n	Cl	$PhSO_2$	Tosyl	EtOH	Needles	210—211	58	$C_{19}H_{17}ClN_2O_4S_2$	52·1	3·9	6·45	52·2	3·95	6·4
o	MeO	Tosyl	$PhSO_2$	PhH	Prisms	169—170	63	$C_{20}H_{20}N_2O_5S$	55·8	4·8	6·8	55·55	4·65	6·5
p	MeO	$PhSO_2$	Tosyl	PhH	Prisms	146—147	77	$C_{20}H_{20}N_2O_5S$	55·8	4·4	6·6	55·55	4·65	6·5
q	CF_3	Tosyl	$PhSO_2$	EtOH	Prisms	177—178	65	$C_{20}H_{17}F_3N_2O_4S_2$	51·25	3·65	6·2	51·4	3·65	5·95
r	CF_3	$PhSO_2$	Tosyl	EtOH aq.	Needles	133—134	80	$C_{20}H_{17}F_3N_2O_4S_2$	51·65	3·9	6·15	51·4	3·65	5·95

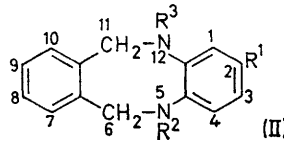
[a] Pale yellow. [b] Lit.,[4] m.p. 116·5—117·5°.

[1] (*a*) W. Schroth and B. Streckenbach, *Z. Chem.*, 1963, **3**, 465; (*b*) N. J. Harper and J. M. Sprake, *J. Chem. Soc.* (*C*), 1969, 882.

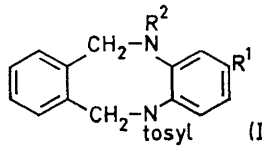
Below 60°, 4-trifluoromethyl-*o*-phenylenediamine gave a compound which was identified as the mono-*p*-tolylsulphonyl derivative (If), since it reacted with benzenesulphonyl chloride at 100° to give the bisarylsulphonyl (IIc—f). However, no reaction occurred between 3,4,5,6-tetrachloro-*NN'*-bis-*p*-tolylsulphonyl-*o*-phenylenediamine [2] and αα'-dibromo-*o*-xylene in boiling toluene or xylene.

TABLE 2

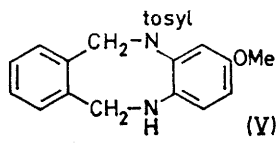
Substituted 5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,4]diazocines



(II)



(IV)



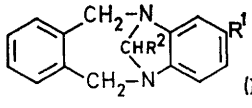
(V)

Compd.	R¹	R²	R³	Solvent for cryst.[a]	Form	M.p.	Yield (%)	Formula	Found (%) C	H	N	Required (%) C	H	N
(IIa)	H	Tosyl	Tosyl											
(IIb)	H	H	H											
(IIc)	Cl	Tosyl	Tosyl	AcOH	Prisms	172—173°	73	$C_{28}H_{25}ClN_2O_4S_2$	60·65	4·7	5·05	60·85	4·55	5·05
(IId)	MeO	Tosyl	Tosyl	AcOH	Prisms	159—161	59	$C_{29}H_{28}N_2O_5S_2$	63·1	5·1	4·95	63·5	5·15	5·1
(IIe)	CF_3	Tosyl	Tosyl	PhH–Cycl	Prisms	161—162	61	$C_{29}H_{25}F_3N_2O_4S_2$	59·1	4·55	4·75	59·35	4·3	4·8
(IIf)	NO_2	Tosyl	Tosyl	AcOH	Prisms	194—195	65	$C_{28}H_{25}N_3O_6S_2$	59·4	4·65	7·6	59·65	4·5	7·45
(IIg)	Cl	H	H	EtOH	Prisms	180—181	*b*	$C_{14}H_{13}ClN_2$	68·45	5·6	11·45	68·75	5·35	11·45
(IIh)	MeO	H	H	EtOH	Plates	160—162	*b*	$C_{15}H_{16}N_2O$	74·6	6·7	11·9	75·0	6·7	11·65
(IIi)	CF_3	H	H	MeOH	Prisms	160—161	*b*	$C_{15}H_{13}F_3N_2$	64·5	5·0	9·75	64·75	4·7	10·05
(IIj)	NO_2	H	H	EtOH	Prisms[c]	206—208	44	$C_{14}H_{13}N_3O_2$	65·8	5·05	16·6	65·9	5·15	16·45
(IIk)	Cl	Ac	Ac	PhMe	Prisms	178—179	87	$C_{18}H_{17}ClN_2O_2$	65·95	5·3	8·45	65·8	5·2	8·5
(III)	MeO	Ac	Ac	PhMe	Prisms	155—156	94	$C_{19}H_{20}N_2O_3$	70·3	6·2	8·7	70·35	6·25	8·65
(IIm)	CF_3	Ac	Ac	PhH–Cycl	Needles	158—159	75	$C_{19}H_{17}F_3N_2O_2$	63·35	5·0	7·85	62·95	4·75	7·75
(IIn)	Cl	Tosyl	$PhSO_2$	AcOH	Needles	199—201	46[d]	$C_{27}H_{23}ClN_2O_4S_2$	59·75	4·5	5·35	60·15	4·3	5·2
(IIo)	Cl	$PhSO_2$	Tosyl	AcOH	Prisms	194—195	38	$C_{27}H_{23}ClN_2O_4S_2$	59·9	4·5	5·35	60·15	4·3	5·2
(IIp)	MeO	Tosyl	$PhSO_2$	AcOH	Needles	229—231	35[d]	$C_{28}H_{26}N_2O_5S_2$	62·65	4·9	5·5	62·9	4·9	5·25
(IIq)	MeO	$PhSO_2$	Tosyl	AcOH	Prisms	184—186	59[d]	$C_{28}H_{26}N_2O_5S_2$	62·6	4·7	5·5	62·9	4·9	5·25
(IIr)	CF_3	Tosyl	$PhSO_2$	Cycl	Prisms	155—156	22[d]	$C_{28}H_{23}F_3N_2O_4S_2$	58·5	4·2	5·1	58·7	4·05	4·9
(IIs)	CF_3	$PhSO_2$	Tosyl	PhH–Cycl	Prisms	191—192	24	$C_{28}H_{23}F_3N_2O_4S_2$	58·5	4·2	5·05	58·7	4·05	4·9
(IVa)	Cl	H		Cel	Prisms	195—197	*b*	$C_{21}H_{19}ClN_2O_2S$	63·3	4·85	7·3	63·2	4·8	7·0
(IVb)	MeO	H		Cel	Prisms	202—206	*b*	$C_{22}H_{22}N_2O_3S$	67·1	6·0	7·0	66·95	5·65	7·1
(IVc)	CF_3	H		Cel	Needles	223—225	*b*	$C_{22}H_{19}F_3N_2O_2S$	61·1	4·7	6·75	61·05	4·45	6·5
(IVd)	Cl	NO		CCl_4	Prisms	188—190	63	$C_{21}H_{18}ClN_3O_3S$	59·2	4·4	9·7	58·9	4·25	9·8
(IVe)	MeO	NO		PhMe	Prisms	202—203	88	$C_{22}H_{21}N_3O_4S$	62·6	5·15	10·0	62·4	5·0	9·9
(IVf)	CF_3	NO		CCl_4	Needles	173—174	62	$C_{22}H_{15}F_3N_3O_3S$	57·0	4·15	9·4	57·25	3·95	9·1
(V)				EtOH	Needles	192—194	3	$C_{22}H_{22}N_2O_3S$	67·0	5·6	7·3	66·95	5·65	7·1

[a] Cycl = cyclohexane; Cel = 2-ethoxyethanol. [b] See Table 4. [c] Orange. [d] When prepared from the appropriate substituted *o*-phenylenediamine and αα'-dibromo-*o*-xylene.

TABLE 3

2-Substituted 5,12-*endo*-substituted 5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,4]diazocines



(III)

(III)	R¹	R²	Solvent for cryst.*	Form	M.p.	Yield (%)	Formula	Found (%) C	H	N	Required (%) C	H	N
a	Cl	H	Pet	Prisms	123—124°	45	$C_{15}H_{13}ClN_2$	70·5	5·25	11·2	70·2	5·1	10·9
b	MeO	H	Cycl	Needles	135—136	61	$C_{16}H_{16}N_2O$	75·75	6·6	11·0	76·15	6·4	11·1
c	CF_3	H	Cycl	Prisms	92—93	46	$C_{16}H_{13}F_3N_2$	65·9	4·8	9·5	66·2	4·5	9·65
d	Cl	O·C(NO₂):CH·CH:C·	EtOH	Prisms	184—186	76	$C_{19}H_{14}ClN_3O_3$	61·9	3·7	11·4	62·05	3·85	11·4
e	MeO	O·C(NO₂):CH·CH:C·	EtOH	Needles †	182—184	58	$C_{20}H_{17}N_3O_4$	66·0	4·9	11·8	66·1	4·7	11·55
f	CF_3	O·C(NO₂):CH·CH:C·	EtOH	Needles	175—176	60	$C_{20}H_{14}F_3N_3O_3$	59·75	3·75	10·55	59·85	3·5	10·45

* Pet = light petroleum (b.p. 60—80°); Cycl = cyclohexane. † Pale yellow.

compound (Ir); this was prepared unequivocally as described later.

The *NN'*-bis-*p*-tolylsulphonyl-*o*-phenylenediamines (Ib—e) reacted with αα'-dibromo-*o*-xylene in boiling toluene to give the 2-substituted 5,6,11,12-tetrahydro-5,12-bis-*p*-tolylsulphonyldibenzo[*b*,*f*][1,4]diazocines

When the 5,12-bis-*p*-tolylsulphonyl compound (IIa) is hydrolysed with hydrogen bromide in glacial acetic acid the base (IIb) separates from the mixture in the form of a salt,[1b] now shown to be a (mono)hydrobromide. Of the

[2] D. E. Burton, A. J. Lambie, D. W. J. Lane, G. T. Newbold, and A. Percival, *J. Chem. Soc.* (*C*), 1968, 1268.

ring-substituted bases (IIg—j) only the nitro-derivative (IIj) separated as a salt; the chloro-, methoxy-, and trifluoromethyl derivatives (IIg—i) were isolated by pouring the reaction mixture into an excess of aqueous sodium hydroxide solution, and extracting the base from the precipitate with dilute hydrochloric acid.

When the methoxy-bis-*p*-tolylsulphonyldibenzodiazocine (IId) was stirred with hydrogen bromide in glacial acetic acid for 7 days, the free base (IIh) was obtained in 63% yield (Table 4). After 1 day only 32% of the base (IIh) was obtained, but in addition there was considerably more acid-insoluble material which, on recrystallisation, afforded the methoxy-5-*p*-tolylsulphonyldibenzodiazocine (IVb) (37%). A higher yield of the 5-*p*-tolylsulphonyl derivative was obtained after only 1 hr.; extraction of the crude product with dilute hydrochloric acid furnished not the free base (IIh) but a small quantity of the isomeric 12-*p*-tolylsulphonyl derivative (V) (3%). The structure of the 5-*p*-tolylsulphonyl compound (IVb) was determined by conversion with benzenesulphonyl chloride into the bisarylsulphonyl compound (IIp), which was identical with an authentic sample. The latter was prepared by interaction of 4-methoxy-2-nitroaniline and toluene-*p*-sulphonyl chloride, reduction of the product (VIc) to the substituted *o*-phenylenediamine (Ii), and subsequent acylation with benzenesulphonyl chloride to give the bisarylsulphonyl-*o*-phenylenediamine (Io); interaction of this compound and αα′-dibromo-*o*-xylene gave the required dibenzodiazocine (IIp). The isomer (IIq) was prepared similarly from 4-methoxy-2-nitroaniline, and proved identical with the product of the reaction between the 12-*p*-tolylsulphonyl compound (V) and benzenesulphonyl chloride.

TABLE 4

Hydrolysis products of 2-substituted 5,6,11,12-tetrahydro-5,12-bis-*p*-tolylsulphonyldibenzo[*b*,*f*][1,4]diazocines (IIc—e)

R¹	Time	Free base (IIg—i) (%)	5-*p*-Tolylsulphonyl derivative (IVa—c) (%)
MeO	1 hr.	*	63
MeO	1 day	32	37
MeO	7 days	63	
Cl	2·5 hr.	5	50
Cl	1 day	35	17
CF_3	2 hr.	16	29
CF_3	1 day	50	

* The acid-soluble material in this experiment proved to be the 12-*p*-tolylsulphonyl derivative (V) (3%).

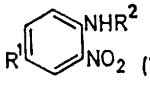
When the chloro- and trifluoromethyl-bis-*p*-tolylsulphonyldibenzodiazocines (IIc and e) were stirred with hydrogen bromide in glacial acetic acid for a short time, mixtures of the base and the 5-*p*-tolylsulphonyl derivative were obtained (Table 4); after 1 day the yield of the base had increased, and that of the 5-*p*-tolylsulphonyl derivative had diminished. The position of the *p*-tolylsulphonyl group in the chloro- and trifluoromethyldibenzodiazocines (IVa and c) was again determined by acylation with benzenesulphonyl chloride and comparison of the products with authentic samples of the bisarylsulphonyl compounds (IIn and o, and r and s); the products were identical with the compounds (IIn) and (IIr) respectively. The authentic samples were prepared by the route described for the methoxy-compounds (IIp and q), from 4-chloro-2-nitroaniline or 4-amino-3-nitrobenzylidyne trifluoride.

Thus hydrolysis of 5,6,11,12-tetrahydro-2-methoxy-*NN*′-bis-*p*-tolylsulphonyldibenzo[*b*,*f*][1,4]diazocine (IId) to the free base (IIh) occurs in two steps, and in the major route loss of the 12-*p*-tolylsulphonyl group occurs first, and is followed by a slower hydrolysis of the second sulphonamide group. The initial loss of the 5-*p*-tolylsulphonyl group occurs only to a minor extent. The 5-*p*-tolylsulphonyl derivatives (IVa and c) are similarly the major intermediates in the hydrolysis of the chloro- and trifluoromethyl compounds (IIc and e) to the free bases (IIg and i).

On the assumption that in the hydrolysis of the sulphonamide groups in the bis-*p*-tolylsulphonyl compounds (IIc—e) the first step is protonation of the nitrogen, an electron-withdrawing group in the 2-position would make the cation resulting from protonation of the nitrogen in the 5-position less stable than that resulting from protonation in the 12-position. Protonation in the 12-position would be favoured, and the 12-*p*-tolylsulphonyl group should be lost first. An electron-donating group, in contrast, would promote initial loss of the 5-*p*-tolylsulphonyl group. In the chloro- and trifluoromethyl-bis-*p*-tolylsulphonyl compounds (IIc and e)

TABLE 5

5-Substituted 2-arylsulphonylaminonitrobenzenes



(VI)

(VI)	R¹	R²	Method	Solvent for cryst.[a]	Form	M.p.	Yield (%)	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
a	Cl	Tosyl	*B*	EtOH	Needles[b]	108—110°[c]	41	$C_{13}H_{11}ClN_2O_4S$						
b	Cl	$PhSO_2$	*B*	EtOH	Prisms[b]	116—117	44	$C_{12}H_9ClN_2O_4S$	46·25	3·1	9·05	46·1	2·95	8·95
c	MeO	Tosyl	*A*	EtOH	Needles[b]	105—106[d]	87	$C_{14}H_{14}N_2O_5S$						
d	MeO	$PhSO_2$	*A*	EtOH aq.	Needles[b]	82—83[e]	89	$C_{13}H_{12}N_2O_5S$						
e	CF_3	Tosyl	*B*[f]	Cycl	Needles	143—144	44	$C_{14}H_{11}F_3N_2O_4S$	47·0	3·4	7·8	46·65	3·1	7·8
f	CF_3	$PhSO_2$	*B*[f]	Cycl	Plates	86—87	51	$C_{13}H_9F_3N_2O_4S$	45·4	2·85	7·85	45·05	2·6	8·1

[a] Cycl = cyclohexane. [b] Yellow. [c] Lit.,[3c] m.p. 110°. [d] Lit.,[3a] m.p. 105°. [e] Lit.,[3b] m.p. 87°. [f] Heated for 12 hr.

the 2-substituent has a $-I$ effect, and the isolation of the 5-*p*-tolylsulphonyl derivatives (IVa and c) as intermediates during hydrolysis therefore supports this hypothesis. On the other hand, the formation of the methoxy-5-*p*-tolylsulphonyl derivative (IVb) as the major intermediate in the hydrolysis of the compound (IId) appears contradictory, since a methoxy-group is normally electron-donating. However, under the strongly acidic reaction conditions the methoxy-group may well be protonated, and may thus be acting as an electron-withdrawing group.

The 2-substituted dibenzodiazocines (IIg—i) show differences in basic strength, as determined in aqueous ethanol, corresponding to the electronic effect of the 2-substituent; as expected the unsubstituted compound (IIb) (pK_a 5·17) is a stronger base than the 2-chloro- or 2-trifluoromethyl derivatives (IIg or i) (pK_a values 4·20 and 4·06), but weaker than the 2-methoxy-derivative (IIh) (pK_a 5·29).

The 5-*p*-tolylsulphonyldibenzodiazocines (IVa—c) afforded nitroso-derivatives (IVd—f) with nitrous acid. Attempted reduction of the methoxynitroso-derivative (IVe) to the *N*-amino-compound with zinc dust and acetic acid [1b] was unsuccessful.

The ring-substituted dibenzodiazocines (IIg—i) were characterised as diacetyl derivatives. The chloro-, methoxy-, and trifluoromethyl-dibenzodiazocines (IIg—i) reacted with paraformaldehyde and with 5-nitro-2-furaldehyde to give the corresponding bridged-ring compounds (IIIa—f), but the nitrodibenzodiazocine (IIj) did not react.

EXPERIMENTAL

I.r. spectra were determined for Nujol mulls, with a Unicam SP 200G spectrophotometer. U.v. spectra were determined for ethanolic solutions. pK_a Values were determined by titration of a 0·001M-solution of the base in 50% aqueous ethanol with 0·001N-hydrochloric acid, with use of a Beckman Research pH meter, model 1019.

*General Methods for Acylations with Benzenesulphonyl and Toluene-*p*-sulphonyl Chlorides.*—(*A*) The amine (1 mol.) was dissolved in dry pyridine (*ca.* 3 ml./g.). A solution of the arenesulphonyl chloride (1·1 or 2·2 mol., as appropriate) in dry pyridine (1·8 ml./g.) was added slowly with stirring while the mixture was kept below 60°. After 3 hr. the product was poured into an excess of hydrochloric acid (5N). The mixture was stirred vigorously until the oil which separated solidified, and the solid was crystallised from a suitable solvent.

(*B*) The amine in dry pyridine (5 ml./g.) was heated with the arenesulphonyl chloride on a steam-bath for 2 hr. The mixture was worked up as in method (*A*).

4-Substituted NN′-*Bis*-p-*tolylsulphonyl*-o-*phenylenediamines* (Ib—e) (Table 1).—The 4-*chloro-* and 4-*methoxy*-NN′-*bis*-p-*tolylsulphonyl*-o-*phenylenediamines* (Ib and c) were prepared by method (*A*); the 4-*trifluoromethyl* and 4-*nitro-compounds* (Id and e) by method (*B*).

4-Amino-3-p-*tolylsulphonylaminobenzylidyne trifluoride* (If) (Table 1) was obtained when 3,4-diaminobenzylidyne trifluoride was treated with toluene-*p*-sulphonyl chloride by method (*A*); $\nu_{max.}$ 3600, 3500 (NH_2), 3330 (NH), and 1645 (NH_2) cm.$^{-1}$.

When treated with toluene-*p*-sulphonyl chloride by method (*B*) the compound (If) gave the bis-*p*-tolylsulphonyl-*o*-phenylenediamine (Id), m.p. and mixed m.p. 144—146°.

The compound (If) and benzenesulphonyl chloride [method (*B*)] gave the bisarylsulphonyl compound (Ir), m.p. and mixed m.p. 133—134°. The preparation of an authentic sample is described later.

2-Substituted 5,6,11,12-*Tetrahydro*-5,12-*bis*-p-*tolylsulphonyldibenzo*[b,f][1,4]*diazocines* (IIc—f).—A mixture of the bis-*p*-tolylsulphonyl-*o*-phenylenediamine (Ib—e) (50 g., 1 mol.), αα′-dibromo-*o*-xylene (1·1 mol.), and anhydrous potassium carbonate (2 mol.) was heated under reflux in dry toluene (500 ml.) for 4 hr. in an oil-bath. The hot solution was filtered and the filtrate was evaporated to dryness under reduced pressure. Crystallisation of the residue afforded the *substituted dibenzodiazocine* (Table 2).

When 3,4,5,6-tetrachloro-*NN′*-bis-*p*-tolylsulphonyl-*o*-phenylenediamine [2] was heated under reflux with αα′-dibromo-*o*-xylene and anhydrous potassium carbonate in toluene or in xylene for 12 hr., no reaction occurred.

Hydrolysis of 5,6,11,12-*Tetrahydro*-5,12-*bis*-p-*tolylsulphonyldibenzo*[b,f][1,4]*diazocine.*[1b]—The bis-*p*-tolylsulphonyl compound (IIa) (20 g.) and phenol (14·4 g.) were stirred together in 50% (w/w) hydrogen bromide in glacial acetic acid (160 ml.) at 50° for 24 hr. The mixture was set aside at room temperature for 2 days. Crystallisation of the precipitate from water gave 5,6,11,12-*tetrahydrodibenzo*-[b,f][1,4]*diazocine hydrobromide* (7·0 g.) as colourless prisms, m.p. 218—220° (decomp.) (Found: C, 58·2; H, 4·8; Br, 27·8; N, 9·4. $C_{14}H_{15}BrN_2$ requires C, 57·7; H, 5·2; Br, 27·45; N, 9·6%).

Basification of an aqueous solution of the salt gave the free base (IIb), m.p. 190—192° (lit.,[1b] 190—192°).

Hydrolysis of 2-*Substituted* 5,6,11,12-*Tetrahydro*-5,12-*bis*-p-*tolylsulphonyldibenzo*[b,f][1,4]*diazocines.*—(A) 5,6,11,12-*Tetrahydro*-2-*nitrodibenzo*[b,f][1,4]*diazocine* (IIj). A mixture of the bis-*p*-tolylsulphonyl compound (IIf) (1 mol.), 50% (w/w) hydrogen bromide in glacial acetic acid (7·5 ml./g.), and phenol (4 mol.) was stirred at room temperature for 3 days. The precipitate was washed with a little glacial acetic acid and dissolved in boiling water, and the solution was filtered and basified with sodium hydroxide solution. Crystallisation of the precipitate gave the *nitrodibenzodiazocine* (Table 2).

(*B*) The chloro-, methoxy-, and trifluoromethyl-bis-*p*-tolylsulphonyldibenzodiazocines (IIc—e) were hydrolysed by stirring a mixture of the compound (1 mol.), 50% (w/w) hydrogen bromide in glacial acetic acid (7·5 ml./g.), and phenol (4 mol.) at room temperature for various lengths of time (Table 4). The solution was poured into water, and the mixture was basified with sodium hydroxide solution and stirred vigorously until the oil which separated solidified. The solid was extracted three times with hydrochloric acid (1·5%). Crystallisation of the residue gave the 5-p-*tolylsulphonyldibenzodiazocine* (IVa—c) (Table 2). The combined acid extracts were basified and the precipitate was crystallised to give the 2-*substituted dibenzodiazocines* (IIg—i) (Table 2); when the methoxy-bis-*p*-tolylsulphonyl compound (IId) was hydrolysed for 1 hr., the acid-soluble material proved to be the 12-p-*tolylsulphonyl compound* (V) (3%) and not the free base (IIh).

The 2-substituted dibenzodiazocine (IIg) had $\lambda_{max.}$ 228, 266, and 315 mμ (log ε 4·54, 3·78, and 3·69), $\nu_{max.}$ 3380 (NH) cm.$^{-1}$; (IIh) $\lambda_{max.}$ 219 and 310 mμ (log ε 4·50 and 3·65), $\nu_{max.}$ 3340 (NH) cm.$^{-1}$; (IIi) $\lambda_{max.}$ 231, 275, and 313 mμ (log

ε 4·45, 3·76, and 3·69), $\nu_{max.}$ 3455 (NH) cm.$^{-1}$; (IIj) $\lambda_{max.}$ 210, 283, and 413 mμ (log ε 4·39, 4·01, and 3·99), $\nu_{max.}$ 3460 (NH) cm.$^{-1}$.

The bases (IIb and g—i) had pK_a values (aqueous ethanol) of 5·17, 4·20, 5·29, and 4·06 respectively.

Acetylation of the bases (IIg—i) by refluxing in acetic anhydride afforded *diacetyl derivatives* (IIk—m) (Table 2).

*Determination of the Structures of the Mono-*p*-tolylsulphonyldibenzodiazocines* (IVa, b, and c) and (V).—The *p*-tolylsulphonyldibenzodiazocines (IVa, b, and c) and (V) showed $\nu_{max.}$ (NH) at 3450, 3430, 3440, and 3380 cm.$^{-1}$ respectively. Interaction of the methoxy-5-*p*-tolylsulphonyldibenzodiazocine (IVb) and benzenesulphonyl chloride by method (*A*) gave the *bisarylsulphonyl compound* (IIp) (69%), m.p. and mixed m.p. 229—231°. The methoxy-12-*p*-tolylsulphonyl compound (V) similarly gave the *bisarylsulphonyl compound* (IIq), m.p. and mixed m.p. 184—186°. The chloro-5-*p*-tolylsulphonyldibenzodiazocine (IVa) reacted with benzenesulphonyl chloride by method (*B*) to give the *bisarylsulphonyl compound* (IIn) (45%), m.p. and mixed m.p. 199—201°. The trifluoromethyl-5-*p*-tolylsulphonyl compound (IVc) was heated on a water-bath with benzenesulphonyl chloride (1·1 mol.) in dry pyridine for 4 hr., after which a further quantity (1·1 mol.) of benzenesulphonyl chloride was added; after a total of 8 hr. heating, the mixture was worked up to give the *bisarylsulphonyl compound* (IIr) (48%), m.p. and mixed m.p. 155—156°.

The preparation of authentic samples of the bisarylsulphonyl compounds (IIn—s) is described later.

2-*Substituted* 5,6,11,12-*Tetrahydro*-12-*nitroso*-5-p-*tolylsulphonyldibenzo*[b,f][1,4]*diazocines* (IVd—f) (Table 2).—A solution of sodium nitrite (1·2 mol.) in water (10 ml.) was added dropwise, with stirring, to a cold solution of the dibenzodiazocine (IVa—c) (1 g.) in hydrochloric acid (5 ml.) and ethanol (20 ml.). Crystallisation of the precipitate gave the 12-*nitroso-derivative*.

Attempted reduction of the methoxynitroso-compound (IVe) to the *N*-amino-compound with zinc dust and acetic acid [1b] was unsuccessful.

[3] (*a*) F. Reverdin, *Ber.*, 1909, **42**, 1524; (*b*) F. Reverdin, *Helv. Chim. Acta*, 1929, **12**, 1057; (*c*) Beilstein, XII, 730.

5-*Substituted* 2-*Arylsulphonylaminonitrobenzenes* (VIa—f) (Table 5).—4-Chloro-, 4-methoxy-, and 4-trifluoromethyl-2-nitroaniline were treated with benzenesulphonyl or toluene-*p*-sulphonyl chloride by method (*A*) or (*B*) (see Table 5) to give the 5-*substituted* 2-*arylsulphonylaminonitrobenzene*.

The methoxy-compounds (VIc and d) and the chloro-compound (VIa) were originally prepared [3] by nitration of the 4′-substituted *N*-phenylarenesulphonamide.

5-*Substituted* 2-*Arylsulphonylaminoanilines* (Ig—l) (Table 1).—The substituted nitrobenzene (VIa—f) was reduced with hydrogen over 10% palladium–charcoal in methanol.

5-Methoxy-2-benzenesulphonamidonitrobenzene (VId) has previously been reduced to the amine with iron filings in dilute acetic acid.[4]

4-*Substituted* NN′-*Bisarylsulphonyl*-o-*phenylenediamines* (Im—r) (Table 1) were prepared from the 5-substituted 2-arylsulphonylaminoanilines (Ig—l) by method (*A*).

2-*Substituted* 5,6,11,12-*Tetrahydro*-5,12-*bisarylsulphonyldibenzo*[b,f][1,4]*diazocines* (IIn—s) (Table 2).—These were prepared from the foregoing *o*-phenylenediamines (Im—r) and αα′-dibromo-*o*-xylene by the method described for the bis-*p*-tolylsulphonyl analogues (IIc—e).

Reaction of 2-*Substituted* 5,6,11,12-*Tetrahydrodibenzo*-[b,f][1,4]*diazocines with Paraformaldehyde and with* 5-*Nitro*-2-*furaldehyde*.—The dibenzodiazocine (IIg—i) (1 g.) was heated under reflux in dry xylene (40 ml.) in an oil-bath with paraformaldehyde (4 mol.) for 16 hr., or with 5-nitro-2-furaldehyde (1·2 mol.) for 1 hr. The mixture was evaporated to dryness under reduced pressure on a steam-bath, and the residue was crystallised from a suitable solvent. The *bridged-ring compounds* so prepared are listed in Table 3.

The nitrodibenzodiazocine (IIj) did not react with paraformaldehyde or with 5-nitro-2-furaldehyde.

We thank the S.R.C. for a research studentship (for A. S.).

[9/1765 *Received, October 17th,* 1969]

[4] V. A. Izmail'skii and A. M. Simonov, *J. Gen. Chem.* (*U.S.S.R.*), 1940 **10** 1580.