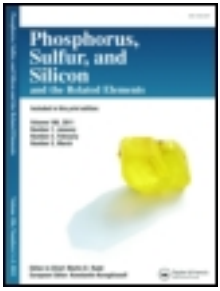

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

CHLOROSULFONATION OF SOME CRISSCROSS CYCLOADDUCTS FROM ISOCYANATES AND DIARYL AZINES

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Published online: 04 Oct 2006.

To cite this article: Richard J. Cremlyn , Richard M. Ellam & Sultan Farouk (2000) CHLOROSULFONATION OF SOME CRISSCROSS CYCLOADDUCTS FROM ISOCYANATES AND DIARYL AZINES, Phosphorus, Sulfur, and Silicon and the Related Elements, 161:1, 213-238, DOI: 10.1080/10426500008042109

To link to this article: http://dx.doi.org/10.1080/10426500008042109

Phosphorus, Sulfur and Silicon, 2000, Vol. 161, pp. 213-238
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CHLOROSULFONATION OF SOME CRISSCROSS CYCLOADDUCTS FROM ISOCYANATES AND DIARYL AZINES

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(Received June 17, 1999; In final form September 14, 1999)

Reaction of chlorosulfonyl isocyanate (**1**) with arylaldehyde azines (**7**) gave the 2:1 crisscross adducts (**8**); attempts to prepare a disulphonamide of **8a** gave only a mixture of the monosulfamide **9** and the diureide **10**. The latter with trichloromethanesulfenyl chloride afforded the derivative **12a**, and with chlorosulfonic acid hydrazinodicarbonamide (**11**). The azine **7a** with benzoyl isocyanate (**2**) gave the expected crisscross adduct **13**. With thiobenzoyl isocyanate (**3**) however, both **7a** and **7d** gave the 1:1 adducts (**14**), whereas **7c** gave a different 2:1 adduct (**15**). Treatment of **14a** with **1** gave the ureide **16**. With both methyl isocyanate (**4**) and phenyl isocyanate (**5**), **7a** gave the expected crisscross adducts (**17a** and **b**), and **7c** with **5** similarly gave **17c**. When **7a** was treated with **1** followed by aqueous potassium iodide, the diureide (**10**) was formed; concentrated nitric acid converted **10** into the triazolenone (**18**). Treatment of **18** with chlorosulfonic acid-thionyl chloride gave the sulfonyl chloride (**19**) which was characterised as the sulfonamides (**20 a-d**).

Diarylsulfamoyl azines (**21 a-f**) with **1** and potassium iodide, gave the diureides **22 a-f**. 4-Methoxy-3-sulfamoylbenzaldehyde azines (**23 a-c**) reacted with **3** to give the 1:1 adducts **24 a-c**, while 4-chlorosulfonylphenyl isocyanate (**6**) with benzaldehyde azine (**7a**) gave the *bis*-chlorosulfonyl adduct (**25a**), characterised as the diethylsulfonamide **25b**. Attempted chlorosulfonation of the tetraphenyl cycloadduct **17b** did not give the tetrasulfonyl chloride (although the reaction was successful with the more reactive methoxy adduct **17c**); the tetrasulfonyl chloride (**26a**) was converted into 3 sulfonamides (**26 b-d**). The unsymmetrically-substituted diaryl azines (**27**) reacted with **1** and potassium iodide to yield the diureides **28 a-f**. Analogous cycloadditions of **1** with several keto azines were unsuccessful. Selected compounds will be screened for medicinal and pesticidal activity; compounds **9, 10** and **12a** showed fungicidal activity against barley powdery mildew.

Keywords: crisscross isocyanate-diaryl azine cycloadducts; chlorosulfonation; sulfonamides

* Corresponding Author.

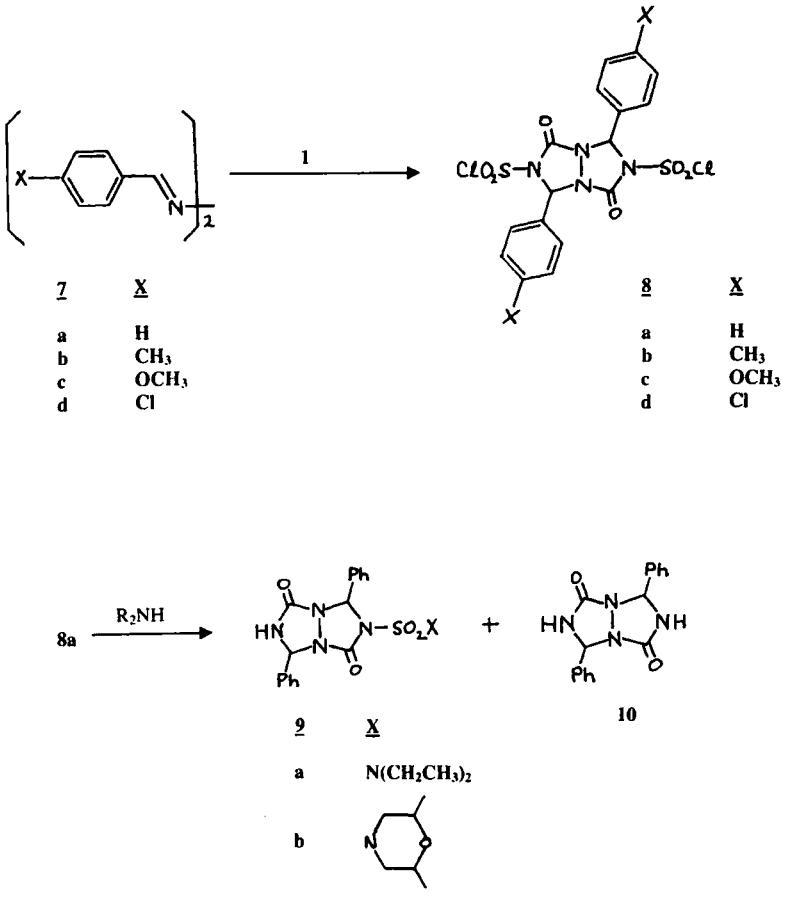
INTRODUCTION

The work described in this paper forms part of our general research programme on the chemistry and biological activity of aromatic sulfonyl derivatives[1,2]. In particular, it extends previous studies of the chlorosulfonation of some crisscross adducts derived from the reaction of maleic anhydrides and maleimides with diaryl azines[3]. Biological screening of these sulfonyl derivatives indicated that sulfonation enhanced the initial fungicidal activity against barley powdery mildew by 30–50%[8]. These results suggested that the synthesis of the sulfonyl derivatives of selected cycloadducts from arylaldehyde azines and isocyanates should be prepared for biological evaluation. In the current work, the cycloadducts from the reaction of isocyanates with diaryl azines were treated with chlorosulfonic acid to synthesise the sulfonyl derivatives as candidate medicinal and pesticidal agents.

DISCUSSION

The formation of crisscross cycloadducts from the reaction of cyanic acid or isocyanates with benzaldehyde azine was first reported in 1917 by Bailey and co-workers[4]. We have extended the scope of these reactions by investigating the reactions of arylaldehyde azines with a range of isocyanates. The cycloaddition of chlorosulfonyl isocyanate (**1**), the most reactive isocyanate known[5] occurs with the arylaldehyde azines (**7 a-d**) in 1 hour at room temperature to yield the dichlorosulfonyl adducts (**8 a-d**) as reported by Suschitzky and co-workers[6,7] (Scheme 1). They also reported the preparation (in low yields) of the disulfamide derivatives of the crisscross adduct **8a**.

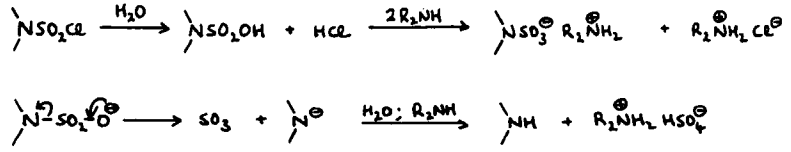
However, in our hands, treatment of compound **8a** with diethylamine did not afford the expected disulfamide, but a mixture of the monosulfamide (**9a**) and the bicyclic diureide (**10**). A similar result was obtained by reaction of **8a** with morpholine to give a mixture of **10** and the monomorpholidate **9b** as shown in Scheme 1. This failure to convert the disulfonyl chloride (**8a**) into a disulfamide is probably due to a competing hydrolysis in the presence of trace amounts of water. The chlorosulfonyl group would be converted into the corresponding sulfamic acid group, which in the



SCHEME 1

presence of the base would rapidly lose sulfur trioxide to yield a ureide group, as outlined in Scheme 2. This is supported by the fact that treatment of **8a** with aqueous dimethylamine yielded only the diureide **10**.

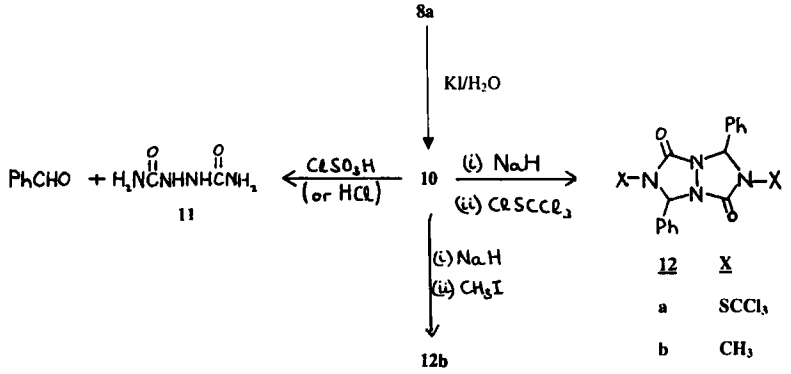
The various disulfonyl chlorides (**8**) were characterised as the corresponding bicyclic diureides by warming them with aqueous methanolic potassium iodide solution[8]; thus **8a** was converted into the diureide **10**. The latter, after treatment with sodium hydride, reacted with trichloromethanesulfenyl chloride to give the *bis*-N-(trichloromethanesulfenyl) derivative (**12a**), and with methyl iodide to give the *bis*-N-methyl deriva-



SCHEME 2

tive (**12b**) (Scheme 3). This affords an alternative to the direct synthesis of **12b** from the azine (**7**) and methyl isocyanate (**4**), with the advantage of avoiding the use of the latter, highly toxic, reagent.

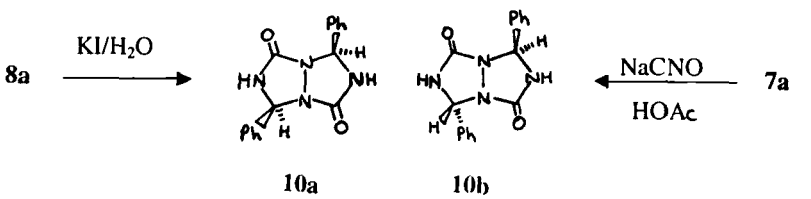
The attempted chlorosulfonation of the diureide (**10**) to the corresponding 4,4[1]-disulfonyl chloride, with either chlorosulfonic acid alone or in the presence of thionyl chloride, led to hydrazinodicarbonamide (**11**) (Scheme 3). The latter was also formed when diureide (**10**) reacted with concentrated hydrochloric acid, and presumably results from acid-catalysed scission of the heterocyclic ring system, with liberation of benzaldehyde. The identity of **11** was confirmed by comparison with an authentic sample prepared from urea and hydrazine hydrate[9], while the formation of benzaldehyde was detectable by its odour and confirmed by the formation of its 2,4-dinitrophenylhydrazone.



SCHEME 3

The bicyclic diureide (**10**) obtained by either of the two-step routes described above had a melting point of 229 – 230°C (in good agreement

with the literature value of 232°C[7]), and was shown by TLC to be the same single substance in each case. However when **10** was synthesised directly from the azine (**7a**) using sodium cyanate in acetic acid, it had a melting point of 195 – 197°C. TLC analysis showed this latter product to be a two component mixture. On the basis of the ^{1}H NMR spectral evidence, it would appear that both the *cis*-(**10a**) and *trans*-(**10b**) isomers are being formed in this case, while the two-step methods produce a single isomer (tentatively assigned the *trans*-configuration (**10b**) (Scheme 4).

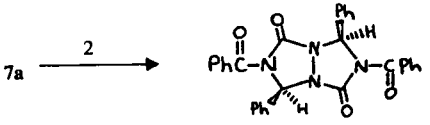


10a **10b**

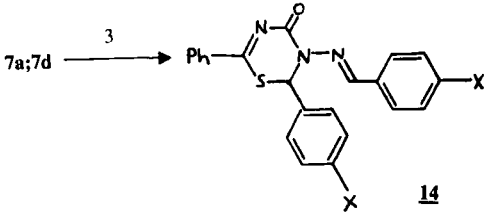
SCHEME 4

The other isocyanates (**2–6**) were found to be much less reactive than **1** towards the diarylazines (**7**). The type of adduct formed (**13, 14**, or **15**) (Scheme 5) was also influenced by the nature of the substituent present in the azine. Thus although benzaldehyde azine (**7a**) reacted with benzoyl isocyanate (**2**) under reflux in xylene for 22 hours to give the expected 2:1 crisscross adduct **13**, with thiobenzoyl isocyanate (**3**) (prepared *in situ* from 2-phenylthiazoline-4,5-dione[10]) both benzaldehyde azine **7a** and 4-chlorobenzaldehyde azine (**7d**) yielded the 1:1 adducts **14a** and **14b** respectively (in agreement with previous work[11]). 4-Methoxybenzaldehyde azine (**7c**) however, under the same conditions with **3** yielded a quite different type of 2:1 adduct (**15**). Treatment of the adduct **14a** with chlorosulfonyl isocyanate (**1**) gave the expected N-sulfonyl chloride **16**[6]. Reaction of the crisscross adduct (**13**) with chlorosulfonic acid (20 molar equivalents) alone or with thionyl chloride gave only hydrazinodicarbonamide (**11**). The attempted chlorosulfonation of the 1:1 adduct **14b** under various conditions also failed.

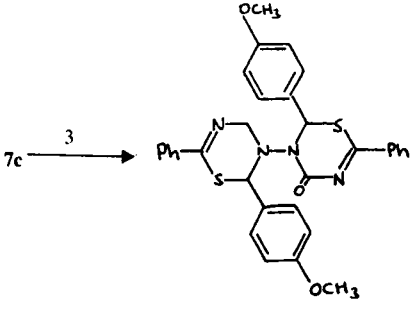
When benzaldehyde azine (**7a**) was heated under reflux with phenyl isocyanate (**5**) in xylene for 18 hours, the expected 2:1 crisscross cycloadduct (**17b**) was obtained, and its structure as shown in Scheme 6 was consistent with the ^{1}H and ^{13}C NMR data and was confirmed by X-ray crystallo-



13



14	X
a	H
b	Cl



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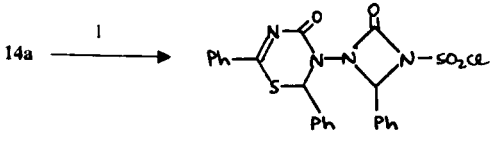
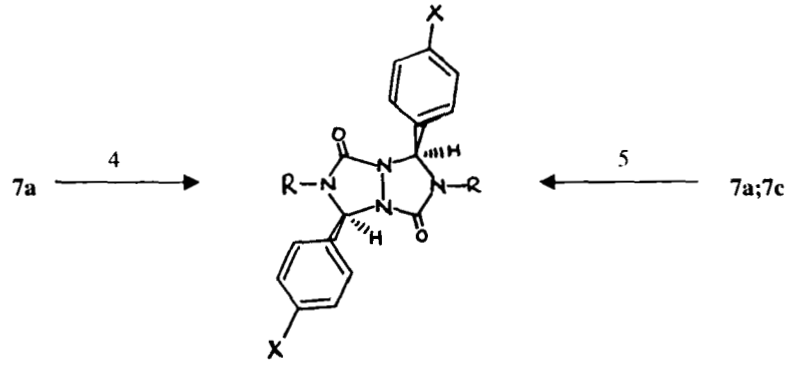


16

SCHEME 5

graphic analysis[8]. The adducts **17a** and **17c** were similarly obtained by reaction of the azines **7a** and **7c** with methyl isoscyanate (**4**) and phenyl isocyanate (**5**) respectively. Their TLCs, and ^{1}H and ^{13}C NMR spectra were consistent with the formation of a single symmetrical adduct in each case. Their proposed structures are as shown in Scheme 6, by analogy with (**17b**).

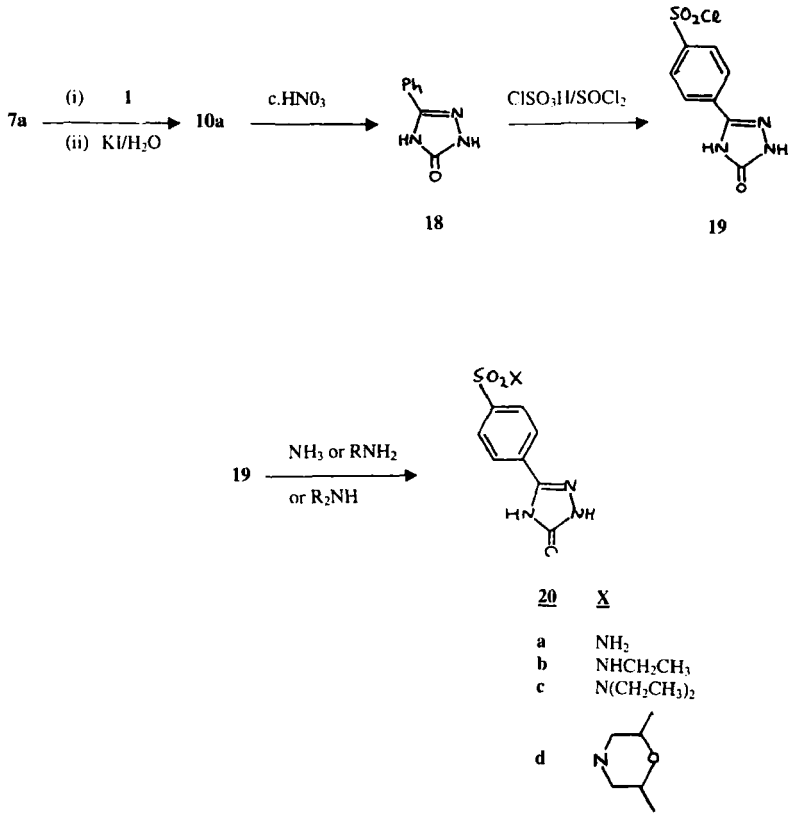


17	X	R
a	H	CH_3
b	H	Ph
c	OCH_3	Ph

SCHEME 6

The bicyclic diureide (**10a**) with concentrated nitric acid afforded the triazolenone **18** as previously reported[4] (Scheme 7) and its ^{1}H NMR spectrum was consistent with the proposed structure. Attempted chlorosulfonation of **18** with chlorosulfonic acid (8 equivalents) in thionyl chloride at room temperature failed. However, reaction at 80°C afforded the sulfonyl chloride (**19**) which by condensation with ammonia and amines afforded the sulfonamides (**20 a-d**) (Scheme 7).

An alternative synthetic route to sulfonyl crisscross adducts involved starting with sulfonyl azines, which were prepared by chlorosulfonation of the appropriate diaryl azine as previously described[12]. Thus the six diarylsulfamoyl azines (**21a – f**) on sequential treatment with chlorosulfonyl iso-

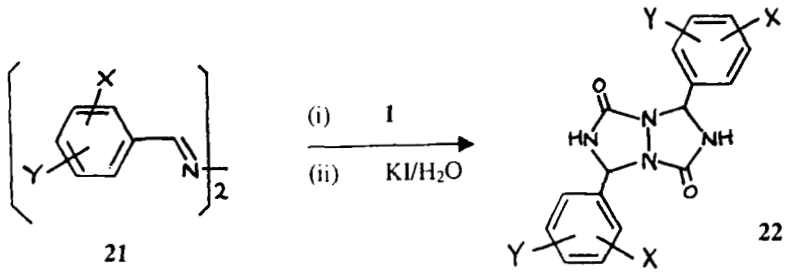


SCHEME 7

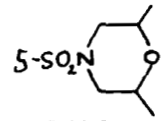
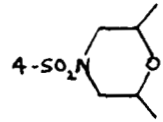
cyanate (**1**) and potassium iodide yielded the *bis*-sulfamoyl cycloadducts (**22a – f**) (Scheme 8).

Previous studies[11] indicated that arylaldehyde azines containing electron-withdrawing groups afforded 1:1 adducts with thiobenzoyl isocyanate (**3**). In agreement, the analogous reactions with the sulfamoyl azines (**23a-c**) in dichloromethane gave the 1:1 cycloadducts (**24a-c**) since the sulfamoyl group is an electron-withdrawing substituent (Scheme 9).

However when the electron-withdrawing sulfamoyl group is present only in the isocyanate reactant, then 2:1 crisscross cycloadducts are formed. Thus, 4-chlorosulfonylphenyl isocyanate (**6**) reacted with benzal-



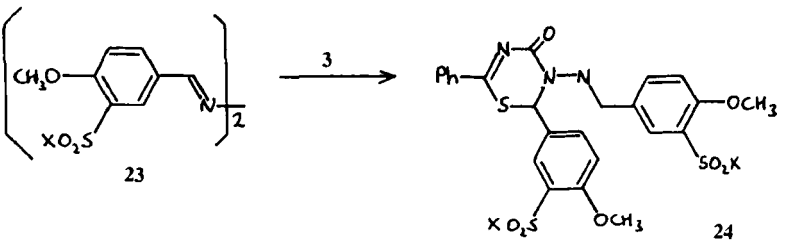
21 22

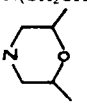
21	X	Y	22
a	2-CH_3	5-$SO_2N(CH_3)_2$	a
b	2-CH_3		b
c	2-OCH_3	5-$SO_2N(CH_3)_2$	c
d	3-OCH_3	4-$SO_2N(CH_3)_2$	d
e	3-OCH_3	4-$SO_2N(CH_2CH_3)_2$	e
f	3-OCH_3		f

SCHEME 8

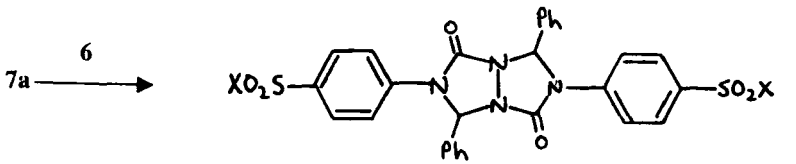
dehyde azine (**7a**) to give the bis-chlorosulfonyl adduct (**25a**) which was characterized by formation of the diethylsulfonamide derivative (**25b**) (Scheme 10). The ^1H NMR spectrum was consistent with the proposed structure and its mass spectrum showed the required molecular ion.

The synthesis of tetrasulfonyl derivatives of the crisscross cycloadducts was attempted by several methods. 4-Chlorosulfonylphenyl isocyanate (**6**) was reacted with 3-chlorosulfonyl-4-methoxybenzaldehyde azine under various conditions, but did not yield the desired tetrachlorosulfonylcycloadduct, possibly due to the poor solubility of the sulfonyl azine in the



23	X	24
a	$N(CH_3)_2$	a
b	$N(CH_2CH_3)_2$	b
c		c

SCHEME 9

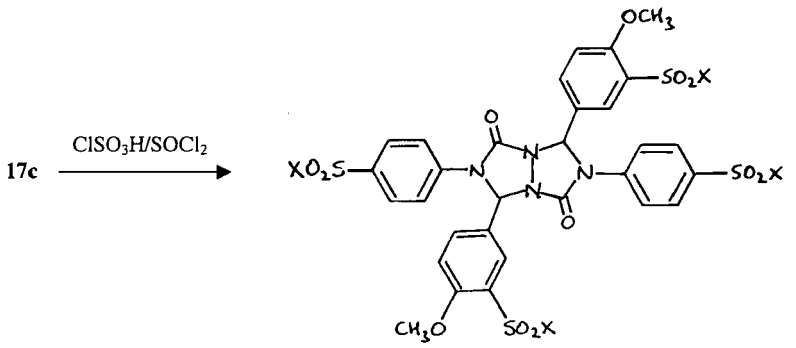


25	X
a	Cl
b	$N(CH_2CH_3)_2$

SCHEME 10

non-polar solvent. Treatment of the cycloadduct **(17b)** (derived from the reaction of benzaldehyde azine **(7)** and phenyl isocyanate **(5)**) with a large excess of chlorosulfonic acid (24 equivalents) in thionyl chloride at room temperature or at 80°C afforded a complex mixture of products (multiple spots on TLC), which after reaction with excess dimethylamine failed to yield a pure product. On the other hand, when the more reactive

4,4′-dimethoxycycloadduct (**17c**) was treated with chlorosulfonic acid (25 equivalents) in thionyl chloride at room temperature for 1 week, the desired tetrachlorosulfonyl derivative (**26a**) was isolated (Scheme 11). The tetrasulfonyl chloride (**26a**) was condensed with ethylamine, dimethylamine, and diethylamine to yield the tetrasulfonamides **26 b,c** and **d** respectively.

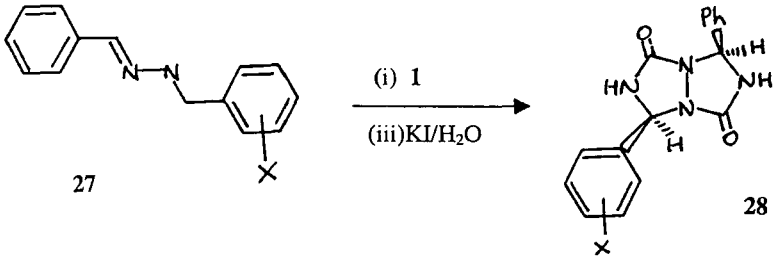


26	X
a	Cl
b	$NHCH_2CH_3$
c	$N(CH_3)_2$
d	$N(CH_2CH_3)_2$

SCHEME 11

The crisscross cycloaddition was extended to the unsymmetrically-substituted diarylazines (**27 a – f**) which were reacted with chlorosulfonyl isocyanate (**1**), (Scheme 12). The crude 3,7-disulfonyl chlorides were immediately treated with aqueous potassium iodide to give rather low yields of the corresponding 3,7-dihydrocycloadducts (**28a – f**), each showing a single spot on TLC. Their ^1H NMR spectra show the presence in each case of a single isomer, tentatively assigned the configuration shown in Scheme 12. The presence of the electron-donor substituents (X = NMe_2 and Me) enhanced the yields of **28e** and **28f** respectively. Attempts to synthesise the crisscross adduct of phenyl-4-nitrobenzaldehyde azine (**28a**) by

reaction of **27a** with sodium cyanate and acetic acid failed to give a pure product.



27 28

27	X	28
a	4-NO_2	a
b	4-Cl	b
c	2,4-Cl_2	c
d	2,6-Cl_2	d
e	4-$N(CH_3)_2$	e
f	4-CH_3	f

SCHEME 12

Attempted cycloaddition reactions of camphor 3,4-dimethoxybenzaldehyde azine with chlorosulfonyl isocyanate (**1**) and sodium cyanate-acetic acid were unsuccessful. The analogous reactions with acetone and acetophenone azines also failed, possibly due to steric hindrance.

In screening tests against barley powdery mildew *(Erysiphe graminis)*, the 1:1 mixture of the N,N- diethylsulfonamide (**9a**) and the diureide (**10**) showed good initial activity (68%) which decreased to 12% 12 days after inoculation. **10** alone had moderate activity (48%) and the N-trichloromethanesulfenimide (**12a**) had 55% activity (40% after 12 days)[8]. The screening procedures used were described in our paper in *Pesticide Science*[3].

EXPERIMENTAL

Melting points were determined with a Gallenkamp electric apparatus and are uncorrected. IR spectra were recorded as KBr discs with a Perkin Elmer 237 spectrophotometer. NMR spectra were obtained using a Brucker AC250 spectrometer and tetramethylsilane as internal standard and DMSO-d_6 as solvent unless otherwise stated. Resonances reduced by D_2O are indicated by an asterisk. EI mass spectra were measured with a VG Micromass 16F spectrometer operating at 70 eV. TLC was carried out using Camlab silica gel plates sensitised to UV 256 nm and 1:1:1-petroleum ether (30 – 40°C), ethyl acetate, cyclohexane mixture as eluant unless otherwise stated.

2,6-Diphenyl-1,3,5,7-tetraazabicyclo[3,3.0]octane-4,8-dione-3,7-disulfonyl chloride (8a)

Chlorosulfonyl isocyanate (**1**) (33.8 g, 0.24 mole) was gradually added to dichloromethane (80 ml) at 10°C with stirring. Benzaldehyde azine (**7a**) (20 g, 0.096 mole) was added portionwise and the mixture stirred for 1 hour. After dilution with ether (40 ml) and cooling (0°C), the solid was filtered off under suction, washed with ether (2 × 10 ml), dried in a vacuum desiccator over phosphorus pentoxide to give (**8a**) (33.7 g, 71%), m.p. 144 – 145°C (lit.[7] 150°C). IR: ν_{max} 1770, 1730 (C = 0), 1600 (Ar C = C), 1350, 1180 (SO_2) cm^{-1}. ^{1}HNMR: δ 7.6- 7.1 (m, 10H, ArH, 6.1 (s, 2H, CH). MS: 490 (M^+)

2,6-Di(4-methylphenyl)-1,3,5,7-tetraazabicyclo[3,3.0]octane-4,8-dione-3,7-disulfonyl chloride (8b)

A similar procedure using 4-methylbenzaldehyde azine (**7b**) afforded (**8b**) (89%), m.p. 150–151°C (lit.[7] 160°C). I.R.: ν_{max} 1760, 1740 (C = O), 1600 (Ar C = C), 1350, 1180 (SO_2) cm^{-1}. ^{1}HNMR: δ 7.6 – 7.4 (m, 8H, ArH, AA^1BB^1 pattern), 6.2 (s, 2H, CH), 2.4 (s, 6H, Me). MS: 518 (M^+).

2,6-Di(4-methoxyphenyl)-1,3,5,7-tetraazabicyclo[3,3.0]octane-4,8-dione-3,7-disulfonyl chloride (8c)

A similar procedure using 4-methoxybenzaldehyde azine (**7c**) gave (**8c**) (78%), m.p. 76–78°C (lit.[7] 80°C). IR: ν_{max} 1760, 1735 (C=0, 1600

(ArC=C), 1350, 1180 (SO_2) cm^{-1}. ^{1}HNMR: δ 7.4 – 7.2 (m, 8H, ArH, AA^1BB^1), 6.0 (s, 2H, CH), 3.5 (s, 6H, OMe). MS: 451 (M^+-SO_2Cl).

2,6-Di(4-chlorophenyl)-1,3,5,7-tetraazabicyclo[3,3.0]octane-4,8-dione-3,7-disulfonyl chloride (8d)

Prepared from 4-chlorobenzaldehyde azine (**7d**) (63%), m.p. 159–160°C (lit.[7] 160°C). IR (KBr): ν_{max} 1755, 1725 (C=O), 1600 (ArC=C), 1180, 1360 (SO_2) cm^{-1}. ^{1}HNMR: δ 7.3 – 7.2 (m, 8H, ArH, AA^1BB^1), 6.05 (s, 2H, CH). MS: 558 (M^+).

Attempted synthesis of 2,6-diphenyl-1,3,5,7-tetraazabicyclo[3,3.0] octane-4,8-dione-3,7-N,N-bis-diethylsulfonamide

The disulfonyl chloride (**8a**) (2 g, 0.0041 mole) was dissolved in dichloromethane (10 ml) at 0°C and diethylamine (1.5 g, 0.02 mole) was added dropwise with stirring. After 30 minutes, the solvent was evaporated off under vacuum and the resultant solid recrystallized from aqueous ethanol to give a mixture of (**9a**) and (**10**) (0.64 g), m.p. 203–208°C. IR (KBr: ν_{max} 3250 (NH), 1770, 1735 (C=O), 1605 (ArC=C), 1360, 1180 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.6, 9.2 (2xs, 2H, NH), 7.7 – 7.1 (m, 10H, ArH), 6.2, 6.3 (2xs, 2H, CH), 3.1 (q, 4H, CH_2Me), 1.05 (t, 6H, $CH_2\underline{Me}$).

3,7-Dihydro-2,6-diphenyl-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (10) (Method 1)

The disulfonyl chloride (**8a**) (20 g, 0.096 mole) was gradually added to a solution of 4% aqueous potassium iodide (15ml) in methanol (40ml). The pH of the reaction was maintained at 1–3 by addition of 20% aqueous potassium hydroxide solution. When all the sulfonyl chloride had been added, the pH was brought to neutrality. The solid was filtered off and recrystallized from methanol to give (**10**) (15.7 g, 55%), m.p. 229–230°C (lit[7] 232°C).

(Found: C, 65.1; H, 4.5; N, 19.2. $C_{16}H_{14}N_4O_2$ requires C, 65.3; H, 4.8; N, 19.0%). IR: ν_{max} 3300(NH), 1740, 1725 (C=0), 1600(ArC=C), cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.1* (s, 2H, NH), 7.4–7.2(m, 10H, ArH), 6.0(s, 2H, CH). MS: 294 (M^+).

Reaction of the diureide (10) with (a) methyl iodide

The diureide (**10**) (5 g, 0.017 mole) was gradually added with stirring to dry DMF (10 ml) containing sodium hydride (1.2 g, 0.05 mole). The mixture was warmed on a water bath until a clear solution formed. Methyl iodide (5.8 g, 0.04 mole) was introduced, the solution left for 1 hour and poured onto ice-water (100ml). The precipitate was filtered off, the solid washed with water and recrystallised from ethanol to yield the 3,7-dimethyl derivative (**12b**) (2.57 g, 46%) m.p. 142–144°C. (Found: C, 66.9; H, 5.5; N, 17.2. $C_{18}H_{18}N_4O_2$ requires C, 67.1; H, 5.6; N, 17.4%). IR: ν_{max} 1765, 1730 (C=O), 1600 (ArC=C) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 7.4–7.3 (m, 10H, ArH), 6.1 (s, 2H, CH) 2.6 (s, 6H, Me).

With (b) trichloromethanesulfenyl chloride

A similar procedure using trichloromethanesulfenyl chloride afforded the 3,7-di (trichloromethanesulfenyl) derivative (**12a**) (2.7 g, 67%, m.p. 178–179°C (recrystallised from aqueous ethanol). (Found: C, 36.2; H, 1.9; N, 9.5, $C_{18}H_{12}Cl_6N_4O_2S_2$ requires C, 36.6; H, 2.0; N, 9.5%).

Attempted chlorosulfonation of 3,7-dihydro-2,6-diphenyl-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (10)

The substrate (**10**, 2.9 g, 0.01 mole) was gradually added to chlorosulfonic acid (12 ml, 0.20 moles) at O°C and left at room temperature for one week. The solution was added to ice-water (50 ml) to give hydrazinodicarbonamide (**11**) (1.2 g), m.p. 242–244°C (after trituration with ether). (Found: C, 19.8; H, 5.3; N, 47.0. $C_2H_6N_4O_2$ requires C, 20.3; H, 5.1; N, 47.45%). IR: ν_{max} 3300 (d, NH_2), 3200 (NH), 1680 (CONH) cm^{-1}.

Experiments using a large excess of chlorosulfonic acid in thionyl chloride at room temperature or at 80°C gave similar results.

Reaction of the diureide (10) with hydrochloric acid

The diureide (**10**) (2 g) was added to methanol (20 ml) containing concentrated hydrochloric acid (5 ml). The mixture was warmed on the water bath for 30 minutes; the yellow solution was evaporated under vacuum and the residual solid was washed with a little water, and triturated with

ether (2 × 10 ml) to yield hydrazinodicarbonamide (**11**) (0.85 g), m.p. 242–245 (decomp) (lit.[9] 244–245°C) (m.m.p. with an authentic sample of (**11**) prepared from urea and hydrazine hydrate was 246–250°C). Evaporation of the ethereal washings afforded a liquid with an almond odour which was confirmed to be benzaldehyde by formation of the 2,4-dinitrobenzaldehyde hydrazone derivative.

3,7-Dibenzoyl-2,6-diphenyl-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (13)

Benzoyl isocyanate (**2**) (7.7 g, 0.052 mole) and benzaldehyde azine (**7a**) (5 g, 0.0024 mole) were heated under reflux in dry xylene (20 ml) in an atmosphere of nitrogen for 22 hours. The solution was evporated under reduced pressure to yield an oil, which solidified after trituration with petroleum ether to yield (**13**) (7.1 g, 58%), m.p. 130–132°C (lit.[11] 130.5–131°C). (Found: C, 71.5; H, 4.6; N, 10.9. $C_{30}H_{22}N_4O_4$ requires C, 71.7; H, 4.4; N, 11.15%). I.R.: ν_{max} 1760, 1680 (C=O), 1600 (ArC=C) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 7.6–7.1 (m, 20H, ArH), 6.1 (s, 2H, CH). MS: 502 (M^+).

5,5^1-bis[2-phenyl-6-(4-methoxyphenyl)-1-thia-3,5-diazacyclohex-2-en-4-one] (15)

2-Phenylthiazoline-4,5-dione[10] (3 g, 0.018 mole) was dissolved in xylene (30 ml) and 4-methoxybenzaldehyde azine (**7c**) (1.5 g, 0.0092 mole) added. The mixture was heated on the water bath for 30 minutes. The precipitated solid was filtered off, washed with methanol and dried in a vacuum desiccator (P_2O_5) to give (**15**) (3.05 g, 58%), m.p. 174–175°C (lit.[11] 181°C decomp.). TLC showed one spot, R_F0.18. (Found: C, 64.9; H, 4.4; N, 9.2. $C_{32}H_{26}N_4O_4S_2$ requires C, 64.6; H, 4.4; N, 9.4%). IR (Nujol): ν_{max} 1686, 1670 (C=O), 1645 (C=N), 1605 (ArC=C) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 8.0–7.2 (m, 10H, C_6H_5), 7.0–6.9 (m, 4H, $C_6\underline{H}_4OMe$, AA^1BB^1), 6.6–6.5 (m, 4H, C_6H_4OMe, AA^1BB^1), 6.2 (s, 2H, CH), 3.7 (s, 6H, OMe).

2,6-Diphenyl-5-(benzylideneamino)-1-thia-3,5-diazacyclohex-2-en-4-one (14a)

2-Phenylthiazoline-4,5-dione (8.6 g, 0.05 mole) was similarly reacted with benzaldehyde azine (**7a**) (5 g, 0.024 mole) to give (**14a**) (4.45 g, 35%),

m.p. 145–146°C (lit.[11] 148–149°C) (Found: C, 71.1; H, 4.5; N, 11.2. $C_{22}H_{17}N_3OS$ requires C, 71.15; H, 4.6; N, 11.3%). IR (Nujol): ν_{max} 1690, 1670 (C=O) 1650 (C=N), 1600 (ArC=C) cm^{-1}.

2-Phenyl-5-(4-chlorobenzylideneamino)-6-(4-chlorophenyl)-1-thia-3,5-diazacyclohex-2-en-4-one (14b)

2-Phenylthiazoline-4,5-dione (8.6 g, 0.05 mole) was similarly reacted with 4-chlorobenzaldehyde azine (**7d**) (5 g, 0.018 mole) to give (**14b**) (4.16 g, 53%), m.p. 162–164°C (lit.[11] 165–168°C). (Found: C, 59.8; H, 3.35; N, 9.4. $C_{22}H_{15}Cl_2N_3OS$ requires C, 60.0; H, 3.4; N, 9.5%). IR (Nujol): ν_{max} 1690, 1670 (C=O), 1650 (C=N), 1600 (ArC=C) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 8.6 (s, 1H, N=C<u>H</u>), 8.0–6.9 (m, 13H, ArH), 6.3 (s, 1H, CH).

Reaction of the cycloadduct (14a) with chlorosulfonyl isocynate (1)

The cycloadduct (**14a**) (2 g, 0.0054 mole) was reacted with chlorosulfonyl isocyanate (**1**) (1.8ml, 0.02 mole) in dichloromethane (15ml) for 1 hour. Addition of ether (20ml) and cooling afforded the sulfonyl chloride (**16**) (1.5 g, 59%), m.p. 91–93°C. (Found: C, 53.6; H, 3.1; N, 11.2. $C_{23}H_{17}ClN_4O_4S_2$ requires C, 53.8; H, 3.3; N, 10.9%). IR: ν_{max} 1680, 1675 (C=O), 1350, 1180 (SO_2)cm^{-1}.

3,7-Dimethyl-2,6-diphenyl-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione(17a)

Benzaldehyde azine (**7a**) (10 g, 0.004 mole) and methyl isocyanate (**4**) (6 g, 0.1 mole) were heated under reflux in xylene (50 ml) for 18 hours under nitrogen. The solution was allowed to cool to room temperature and then to 0°C. The solid was filtered off under suction, washed with cold xylene (10 ml), ethanol (20ml) and dried under the IR lamp to yield (**17a**) (8.1 g, 52%), m.p. 172–173°C (lit.[13] 174–5°C). (Found: C, 66.8; H, 5.9; N, 17.5. $C_{18}H_{18}N_4O_2$ requires C, 67.1; H, 5.6; N, 17.4%). IR (nujol): ν_{max} 1728 (C=O), 1605 (ArC=C) cm^{-1}. ^{1}HNMR: δ 7.51–7.25 (m, 10H, ArH), 6.1 (s, 2H, CH), 2.79 (s, 6H, Me). MS: 322 (M^+).

2,3,6,7-Tetraphenyl-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (17b)

Benzaldehyde azine (**7a**) (10 g, 0.004 mole) and phenyl isocyanate (**5**) (13.1 g, 0.11 mole) similarly gave **17b** (17.9 g, 84%), m.p. 256–260°C (lit.[13]257–258°C). TLC showed one spot, R_F 0.66. IR (nujol): ν_{max}1725 (C=O), 1600 (ArC=C) cm^{-1}. ^{1}HNMR: δ 7.6–7.0 (m, 20H, ArH), 6.6 (s, 2H, CH). MS: 446 (M^+).

3,7-Diphenyl-2,6-di(4-methoxyphenyl)-1,3,5,7-tetraazabicyclo[3,3,0] octane-4,8-dione (17c)

4-Methoxybenzaldehyde azine (**7c**) (30 g, 0.11 mole) and phenyl isocyanate (**5**) (31.9 g, 0.2 mole) similarly gave (**17c**) (50.2 g, 88%), m.p. 235 – 237°C (lit[13]. 238 – 239°C). TLC showed one spot, RF 0.66. (Found: C, 71.4; H, 5.0; N, 11.0. $C_{30}H_{26}N_4O_4$requires C, 71.3; H, 5.15; N, 11.1%).

3,7-Dihydro-2,6-diphenyl-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (10) (method 2)

Benzaldehyde azine (**7a**) (4.5 g, 0.022 mole) was reacted with sodium cyanate (5.25 g, 0.08 mole) in acetic acid (30 ml). The mixture was stirred with cooling (ice-bath) for 1 hour and acetic acid was evaporated off under reduced pressure. The solid residue was washed with water and ethanol (20 ml) and filtered off to give (**10**) (4.45 g, 70%), m.p. 195 – 197°C (lit[7]. 232°C). IR (nujol): 1725 (C=O), 1600 (ArC=C) cm^{-1} ^{1}HNMR: δ 9.3* (br s, 1H, NH), 8.8* (br s, 1H, NH), 6.1, 6.0 (2 × s, 2H, CH). MS: 294 (M^+).

3-Phenyl-1,2,4-triazolen-5-one (18)

3,7-Dihydro-2,6-diphenyl-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (**10**) (2 g, 0.007 mole) was added portionwise to stirred concentrated nitric acid (10 ml) at 0°C; stirring was continued until all the substrate had dissolved. The solution was poured onto ice-water (100 ml), and the solid filtered off under suction, and dried under the IR lamp to yield the triazolenone (**18**) (0.86 g, 79%), m.p. 322 –324°C (lit.[4] 321 – 322°C). (Found: C, 59.9; H, 4.4; N, 26.1. $C_8H_7N_3O$ requires C, 59.6; H, 4.3; N, 26.1%). IR (nujol): ν_{max} 3300 (NH), 1680 (C=O), 1600 (ArC=C), cm^{-1}. ^{1}HNMR: δ 11.9*, 11.7* (2 × s, 2H, NH), 7.8 – 7.4 (m, 5H, ArH).

^{13}CNMR: δ 156.6, 145.1 (C=O), 129.1, 128.8, 126.6, 124.2. (Ar-C). MS: 161 (M^+).

Chlorosulfonation of 3-phenyl-1,2,4-triazolen-5-one (18)

The triazolenone (**18**) (2 g, 0.012 mole) was gradually added to a mixture of chlorosulfonic acid (6 ml, 0.093 mole) in thionyl chloride (5 ml) at 0°C. The solution was allowed to attain room temperature and was heated on the water-bath (80°C) for 2 hours and was added to ice-water (50 ml) with stirring. The solid was filtered off under suction and dried in a vacuum desiccator (P_2O_5) to give the sulfonyl chloride (**19**) (2.2 g, 68%), m.p. 203 – 204°C. IR (nujol): ν_{max} 3300 (NH), 1690 (CO),, 1600 (ArC=C), 1350, 1160 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 11.0*, 10.8* (2 × s, 2H, NH), 7.8 – 7.6 (m, 4H, ArH, AA^1BB^1) MS: 250 (M^+).

3-(4-Sulfamoylphenyl)-1,2,4-triazolen-5-one (20a)

The sulfonyl chloride (**19**) (2 g) was stirred with 0.88 aqueous ammonia (10 ml) in acetone (20 ml) to yield **20a** (1.3 g, 72%), m.p. 330 – 331°C. IR ν_{max} 3350, 3330 (NH), 1670 (C=O), 1600 (ArC=C), 1340, 1160 (SO_2) cm^{-1}. ^{1}HNMR: δ 11.9* (br s, 1H, NH), 11.7* (br s, 1H, NH), 7.8 – 7.6 (m, 4H, ArH, AA^1BB^1), 7.2* (s, 2H, NH_2). MS: 240 (M^+).

3-(4-N-Ethylsulfamoylphenyl)-1,2,4-triazolen-5-one-(20b)

The sulfonyl chloride (**19**) (2 g, 0.0067 mole) was reacted with ethylamine (0.015 mole) in methanol (20 ml) at 0°C. The mixture was stirred at room temperature for 3 hours; the solid precipitate was collected, washed with water (25 ml) and recrystallized from ethanol to give **20b** (0.78 g, 51%), m.p. 310 – 312°C. (Found: C, 44.6; H, 4.8; N, 20.8. $C_{10}H_{12}N_4O_3S$ requires C, 44.8; H, 4.5; N, 20.9%). IR (nujol): ν_{max} 3280 (NH), 1680 (C=O), 1605 (ArC=C), 1340, 1160 (SO_2) cm^{-1}. ^{1}HNMR: δ 10.9* (s, 1H, NH), 10.3* (s, 1H, NH), 7.8 – 7.6 (m, 4H, ArH, AA^1BB^1), 7.2* (s, 1H, NH), 2.7 (q, 2H, $C\underline{H}_2Me$), 1.0 (t, 3H, Me).

The diethylsulfonamide (20c)

A similar procedure using N,N-diethylamine afforded **20c** (60%), m.p. 324–328°C (Found: C, 48.4; H, 5.7; N, 21.5. $C_{12}H_{16}N_4O_3S$ requires C,

48.6; H, 5.4; N, 21.6%). ^{1}HNMR: δ 11.9* (br s, 2H, NH), 8.0–7.8) (m, 4H, ArH, AA^{1}BB^1), 3.1 (q, 8H, C$\underline{H_2}$Me), 1.0 (t, 12H, $CH_2\underline{Me}$). MS: 296 (M^+).

The 2,6-dimethylmorpholidate (20d)

A similar method using 2,6-dimethylmorpholine gave **20d** (62%), m.p. 345 – 347°C. IR (nujol): ν_{max} 1670 (C=O), 1600 (ArC=C), 1340, 1155 (SO_2)cm^{-1}. ^{1}HNMR: δ 11.9*, 11.6* (brs, 2H, NH), 7.8 – 7.6 (m, 4. H, ArH, AA^{1}BB^1), 3.4 (m, 4H, CH_2), 2.2 (t, 2H, CH), 1.05 (s, 6H, Me).

3,7-Dihydro-2,6-di(2-methyl-5-N,N-dimethylsulfamoylphenyl)-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (22a)

2-Methyl-5-N,N-dimethylsulfamoylbenzaldehyde azine (**21a**) (1 g, 0.0022 mole) was gradually added to a cold (10°C) stirred solution of chlorosulfonyl isocyanate (**1**) (12.3 ml, 0.14 mole) and stirring was continued for 1 hour. The mixture was diluted with ether (40 ml), cooled in an ice-bath and the oil separated off. The oil was treated dropwise with 4% potassium iodide solution (10 ml) in methanol (20 ml), keeping the pH of the mixture at 1–3 by addition of 20% potassium hydroxide solution. After all the iodide had been added, the reaction mixture was neutralized, the solid precipitate was collected and washed with ether to give (**22a**) (0.84 g, 71%). m.p. 226 – 228°C. (Found: C, 48.8; H, 5.8; N, 15.4.

$C_{22}H_{30}N_6O_6S_2$requires C, 49.1; H, 5.6; N, 15.6%). I.R. (nujol): ν_{max}3250 (NH), 1725 (C=O), 1600 (ArC=C), 1340, 1160 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.4* (br s, 2H, NH), 7.6 - 7.4 (m, 6H, ArH), 6.4 (s, 2H, CH), 2.5 (s, 12H, NMe_2), 2.4 (s, 6H, Ar-Me). MS: 538 (M^+).

The 2-methyl-5-(2,6-dimethylmorpholinosulfonyl) adduct (22b)

2-Methyl-5-(2,6-dimethylmorpholinosulfonyl)benzaldehyde azine (**21b**) (4 g, 0.0074 mole) was similarly reacted with chlorosulfonyl isocyanate (**1**) (2.15 g, 0.018 mole) to give the corresponding cycloadduct (**22b**) (0.32 g, 52%), m.p. 210 – 212°C. (Found: C, 53.1; H, 5.5; N, 12.6. $C_{30}H_{40}N_6O_8S_2$ requires C, 53.6; H, 5.9; N, 12.6%). I.R. (nujol): ν_{max} 3360 (NH), 1725 (C=O), 1600 (ArC=C), 1340, 1160 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.4* (br s, 2H, NH), 7.6 – 7.4 (m, 6H, ArH), 6.8, 6.2 (2 × s, 6H,

CH), 3.5 (q, 8H, CH_2) 2.5 (s, 6H, Ar-Me), 1.1 (s, 12H, morpholino-Me). FAB (+) MS: 677 ($M^+ + 1$).

The 2-methoxy-5-(N,N-dimethylsulfamoyl) adduct (22c)

2-Methoxy-5-(N,N-dimethylsulfamoyl) benzaldehyde azine (**21c**) (0.5 g, 0.001 mole) was similarly reacted with chlorosulfonyl isocyanate (**1**) (0.35 g), 0.0025 mole) to yield (**22c**) (0.22 g, 66%), m.p 293 – 295°C: I.R. (nujol): ν_{max} 3300 (NH), 1725 (C=O), 1600 (ArC=C), 1350, 1160 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.0* (br s, 2H, NH), 7.9–7.2 (m, 6H, ArH), 6.3 (s, 2H, CH), 3.9 (s, 6H, OMe), 2.4 (s, 12H, NMe_2). FAB (+) MS: 569 ($M^+ + 1$).

The 3-methoxy-4-(N,N-dimethylsulfamoyl) adduct (22d)

3-Methoxy-4-(N,N-dimethylsulfamoyl)benzaldehyde azine (**21d**) (0.4 g, 0.0082 mole) was reacted with chlorosulfonyl isocyanate (**1**) (2.4 g, 0.02 mole) to give (**22d**) (0.62 g, 54%), m.p. 255 – 256°C. I.R. (nujol): ν_{max} 3300 (NH), 1725 (C=O), 1600 (ArC=C), 1350, 1160 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.1* (br s, 2H, NH), 7.6–7.4 (m, 6H, ArH), 6.9 (s, 2H, CH), 4.0 (s, 6H, OMe), 2.8 (s, 2H, NMe_2). FAB (+) MS: 569 ($M^+ + 1$).

The 3-methoxy-4-(N,N-diethylsulfamoyl) adduct (22e)

3-Methoxy-4-(N,N-diethylsulfamoyl)benzaldehyde azine (**21e**) (0.4 g, 0.0074 mole) and chlorosulfonyl isocyanate (**1**) (2.15 g, 0.018 mole) reacted to give **22e** (0.39 g, 65%), m.p. 204 – 207°C. ^{1}HNMR ($CDCl_3$): δ 8.6* (s, 2H, NH), 7.8 – 7.0 (m, 6H, ArH), 6.8 (s, 2H, CH), 3.9 (s, 6H, OMe), 3.3 (q, 8H, $\underline{CH_2}Me$), 1.1 (t, 12H, $CH_2\underline{Me}$). FAB (+) MS: 625 ($M^+ + 1$).

The 3-methoxy-4-(2,6-dimethylmorpholinosulfonyl) adduct (22f)

3-Methyl-4-(2,6-dimethylmorpholinosulfonyl)benzaldehyde azine (**21f**) (0.4 g, 0.0078 mole) reacted with chlorosulfonyl isocyanate (**1**) to give (**22f**) (0.38 g), 72%, m.p. 235 – 236°C. I.R. (nujol): ν_{max}3350 (NH), 1725 (C=O), 1605 (ArC=C), 1340, 1160 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ

8.6*(s, 2H, NH), 8.3 – 7.0 (m, 6H, ArH), 6.8, 6.4 (2 × s, 6H, CH), 4.1 (s, 6H, OMe), 3.4 (q, 8H, CH_2), 1.1 (t, s, 12H, morpholino-Me).

2-Phenyl-5-(4-methoxy-3-N,N-dimethylsulfamoylbenzydideneamino)-6-(4-methoxy-3-N,N-dimethylsulfamoylphenyl)-1-thia-3,5-diazacyclohex-2-en-4-one (24a)

4-Methoxy-3-(N,N-dimethylsulfamoyl)benzaldehyde azine (**23a**) (0.75 g, 0.0015 mole) was warmed with 2-phenylthiazoline-4,5-dione (0.62 g, 0.003 mole) to yield (**24a**) (0.86 g, 85%), m.p. 155 – 156°C. (Found: C, 51.9; H, 4.5; N, 10.8, $C_{28}H_{31}N_5O_7S_3$ requires C, 52.1; H, 4.8; N, 10.85%). I.R. (nujol): ν_{max} 1680 (C=O), 1600 (ArC=C), 1340, 1160 (SO_2), 1180 C-O-C) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.4 (s, 1H, N=CH), 8.7 (s, 1H, CH), 8.2 – 7.2 (m, 11H, ArH), 4.0 (s, 6H, OMe), 2.8, 2.7 (2 × s, 12H, NMe_2).

Cycloadduct (24b)

4-Methoxy-3-(N,N-diethylsulfamoyl)benzaldehyde azine (**24a**) (0.56 g), 0.010 mole) and 2-phenylthiazoline-4,5-dione (0.41 g, 0.002 mole) were similarly reacted to give (**24b**) (0.63 g, 86%), m.p. 167 – 168°C. (Found: C, 57.5; H, 5.3; N, 10.3. $C_{32}H_{39}N_5O_7S_3$ requires C, 57.8; H, 5.6; N, 10.0%). ^{1}HNMR ($CDCl_3$): δ 9.3 (s, 1H, N=CH), 8.8 (s, 1H, CH), 8.1 – 7.1 (m, 11H, ArH), 3.8 (s, 6H, OMe), 3.0, 2.8 (2 × q, 8H, $C\underline{H}_2Me$) 1.1, 1.0 (2 × t, 12H, $CH_2C\underline{H}_3$).

Cycloadduct (24c)

4-Methoxy-3-(2,6-dimethylmorpholinosulfonyl)benzaldehyde azine (**23c**) (0.60 g, 0.0096 mole) and 2-phenylthazoline-4,5-dione (0.41, 0.002 mole) similarly gave (**24c**) (0.4 g, 53%), m.p. 192 – 194°C. (Found: C, 55.3; H, 5.4; N, 8.8. $C_{36}H_{43}N_5O_9S_3$ requires C, 55.0; H, 5.5; N, 8.9%).

2,6-(Diphenyl)-3,7-di(4-chlorosulfonylphenyl)-1,3,5,7-tetraazabicyclo [3.3.0]octane-4,8-dione (25a)

Benzaldehyde azine (**7a**) (0.8 g, 0.038 mole) and 4-chlorosulfonylphenyl isocyanate (**6**) (1.47 g, 0.006 mole) were reacted in dichloromethane

(20 ml) for 1 hour. Addition of ether (20 ml) and cooling (0°C) afforded the dichlorosulfonyl cycloadduct (**25a**) (1.67 g, 64%), m.p. 135 – 137°). I.R. (nujol): ν_{max} 1700 (C=O), 1600 (ArC=C), 1350, 1160 (SO_2) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 7.6 – 7.3 (m, 18H, ArH), 6.5 (s, 2H, CH). MS: 445 (M^+- $2SO_2Cl$)..

The bis-N,N-diethylsulfonamide (25b)

The disulfonyl chloride (**25a**) (1 g, 0.0015 mole) was reacted with diethylamine (0.44 g, 0.006 mole) in ethanol (15 ml) to give (**25b**) (0.72 g, 67%), m.p. 175 – 178°C. (Found: C, 60.4; H, 5.4; N, 11.7. $C_{36}H_{40}N_6O_6S_2$ requires C, 60.3; H, 5.6; N, 11.7%). ^{1}HNMR ($CDCl_3$): δ 7.8 – 7.2 (m, 18H, ArH), 6.6 (s, 2H, CH), 3.2 (q, 8H, $C\underline{H}_2Me$), 1.1 (t, 12H, $CH_2\underline{Me}$).

Chlorosulfonation of 2,6-(diphenyl)-3,4-di(4-methoxyphenyl)-1,3,5,7-tetraazabicyclo[3.3.0.]octane (17c)

The cycloadduct (**17c**) (6 g, 0.011 mole) was added portionwise to a mixture of chlorosulfonic acid (3.5 g, 0.3 mole) in thionyl choride at 0°C, and was left at room temperature for 1 week. The solution was poured onto ice-water (50 ml); the precipitate was collected, washed with cold water and dried in a vacuum desiccator over P_2O_5 to give the tetrasulfonyl chloride (**26a**) (8.14 g, 82%), m.p. 228 – 230°C. ^{1}HNMR ($CDCl_3$): δ 8.9 (s, 2H, CH), 8.2 – 6.0 (m, 14H, ArH), 2.9 (s, 6H, OMe). MS: 505 (M^+ – $4SO_2Cl$)

The tetra (N-ethylsulfonamide) (26b)

The sulfonyl chloride ((**26a**) (2 g, 0.0023 mole) was reacted with ethylamine (0.5 g, 0.01 mole) to give (**26b**) (0.72 g, m.p. 244 – 246°C). (Found: C, 48.7; H, 4.5; N, 12.2. $C_{38}H_{46}N_8O_{12}S_4$ requires C, 48.8; H, 4.9; N, 12.0%). I.R. (nujol): ν_{max}3250 (NH), 1725 (C=O), 1600 (ArC=C), 1340, 1160 (SO_2), 1200 (C-O-C) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.8* (br s, 2H, NH), 8.8 (s, 2H, CH), 8.3 – 7.0 (m, 14H, ArH), 3.3 (s, 6H, OMe), 2.8 (q, 8H $NC\underline{H}_2CH_3$), 0.9 (t, 12H, $NCH_2\underline{Me}$).

The tetra (N,N-dimethylsulfonamide) (26c)

A similar reaction of (**26a**) with dimethylamine gave (**26c**), (46%), m.p. 222 – 224°C. ^{1}HNMR ($CDCl_3$): δ 8.7 (s, 2H, CH), 7.7 – 6.9 (m, 14H, ArH), 3.5 (s, 6H, OMe), 2.6 (s, 24H, NMe_2).

The tetra (N,N-diethylsulfonamide) (26d)

Treatment of **26a** with diethylamine afforded **26d** (35%), m.p. 234 – 236°C. (Found: C, 52.5; H, 5.6; N, 10.4). $C_{46}H_{62}N_8O_{12}S_4$ requires C, 52.8; H, 5.9; N, 10.7%) ^{1}HNMR ($CDCl_3$): δ 8.7 (s, 2H, CH), 8.0 – 7.2 (m, 14H, ArH), 3.8 (s, 6H, OMe), 3.1 (q, 16H, $NC\underline{H_2}Me$), 1.0 (t, 24H, $NCH_2\underline{Me}$).

3,7-Dihydro-2-phenyl-6-(4-nitrophenyl)-1,3,5,7-tetraazabicyclo[3.3.0] octane-4,8-dione (28a)

Chlorosulfonyl isocyanate (**1**) (33.8 g, 0.24 mole) was added dropwise to stirred solution of phenyl-4-nitrobenzaldehyde azine (**27a**) (4 g, 0.015 mole) in dichloromethane (80 ml) at 10°C. After 1 hour the mixture was diluted with ether (40 ml) and cooled (0°C) to give the crude 3,7-disulfonyl chloride contaminated with unreacted azine. The solid was added gradually to methanol (40 ml) and 4% aqueous potassium iodide (15 ml). During the addition, the pH was kept at 1 – 3 by adding 20% potassium hydroxide solution. When addition was complete, the reaction mixture was neutralized and the solid recrystallized from ethanol to give the cycloadduct (**28a**) (1.4 g, 27%), m.p. 186 – 188°C. (Found: C, 56.2; H, 3.7; N, 20.6. $C_{16}H_{13}N_5O_4$ requires C, 56.6; H, 3.8; N, 20.6%). TLC showed one spot, R_F 0.43. I.R. (KBr): ν_{max} 1730, 1680 (C=O) 3300 (NH), 1600 (ArC=C) cm^{-1}. ^{1}HNMR ($CDCl_3$): δ 9.3* (s, 2H, NH), 8.1 – 7.7 (m, 4H, $C_6H_4NO_2$, AA^1BB^1), 7.5 (m, 5H, Ph), 6.3, 6.1, (s, 2H, CH). MS: 339 (M^+).

3,7-Dihydro-2-phenyl-6-(4-chlorophenyl)-1,3,5,7-tetraazabicyclo [3.3.0]octane-4,8-dione (28b)

Reaction of phenyl-4-chlorobenzaldehyde azine (**27b**) (2 g, 0.0083 mole) and chlorosulfonyl isocyanate (**1**) (2.4 g, 0.017 mole) similarly gave (**28b**) (0.85 g, 31%), m.p. 210 – 212°C. (Found: C, 58.1; H, 3.8; N, 16.9. $C_{16}H_{13}ClN_4O_2$ requires C, 58.4; H, 3.95; N, 17.0%). ^{1}HNMR ($CDCl_3$): δ

9.3* (br s, 2H, NH), 7.8–7.6 (m, 4H, C_6H_4Cl, AA^1BB^1), 7.5 (m, 5H, Ph), 6.4, 6.1 (2 × s, 2H, CH). MS: 330,328, (M^+).

3,7-Dihydro-2-phenyl-6-(2,4-dichlorophenyl)-1,3,5,7-tetraazabicyclo [3.3.0]octane-4,8-dione (28c)

Phenyl-2,4-dichlorobenzaldehyde azine (**27c**) (2 g, 0.0072 mole) and chlorosulfonyl isocyanate (**1**) (3 g, 0.021 mole) gave (**28c**) (0.64 g, 24%), m.p. 214 – 216°C. (Found: C, 52.8; H, 3.2; N, 15.4. $C_{16}H_{12}Cl_2N_4O_2$ requires C, 52.9; H, 3.3; N, 15.4%).

^{1}HNMR ($CDCl_3$): δ 9.4* (br s, 2H, NH), 8.2–7.6 (m, 3H, $C_6H_3Cl_2$), 7.5 (m, 5H, Ph), 6.3, 6.1 (2 × s, 2H, CH). MS: 362 (M^+, ion cluster).

3,7-Dihydro-2-phenyl-6-(2,6-dichlorophenyl)-1,3,5,7-tetraazabicyclo [3.3.0]octane-4,8-dione (28d)

Phenyl-2,6-dichlorobenzaldehyde azine (**27d**) (2 g, 0.0072 mole) and chlorosulfonyl isocyanate (**1**) (3 g, 0.021 mole) gave (**28d**) (1.15 g, 36%), m.p. 238 – 240°C. (Found: C, 52.7; H, 3.0; N, 15.2. $C_{16}H_{12}Cl_2N_4O_2$ requires C, 52.9; H, 3.3; N, 15.4%). ^{1}HNMR ($CDCl_3$): δ 9.4* (br s, 2H, NH), 7.8–7.6 (m, 3H, $C_6H_3Cl_2$), 7.5 (m, 5H, Ph), 6.3, 6.1 (2 × s, 2H, CH). MS: 362, (M^+ ion cluster).

3,7-Dihydro-2-phenyl-6-(4-dimethylaminophenyl)-1,3,5,7-tetraazabicyclo[3.3.0]octane-4,8-dione (28e)

Phenyl-4-dimethylaminobenzaldehyde azine (**27e**) (3 g, 0.012 mole) and chlorosulfonyl isocyanate (**1**) (3 g, 0.021 mole) gave (**28e**) (2.36 g, 52%), m.p. 143 – 144°C. IR (KBr): ν_{max} 3300 (NH), 1730 (C=O), 1600 (ArC=C), cm^{-1}. ^{1}HNMR ($CDCl_3$) δ: 9.3* (br s, 2H, NH), 8.0–7.7 (m, 4H, $C_6\underline{H}_4NMe_2$, AA^1BB^1), 7.5 (m, 5H, Ph), 6.3, 6.1 (2 × s, 2H, CH). 3.3 (s, 6H, NMe_2). MS: 333, (M^+).

3,7-Dihydro-2-phenyl-6-(4-methylphenyl)-1,3,5,7-tetraazabicyclo [3.3.0]octane-4,8-dione (28f)

Phenyl-4-methylphenylbenzaldehyde azine (**27f**) (2 g, 0.009 mole) and chlorosulfonyl isocyanate (**1**) (3 g, 0.021 mole) gave (**28f**) (1.3 g, 46%),

m.p. 220 – 221°C. (Found: C, 66.0; H, 5.1; N, 18.5. $C_{17}H_{16}N_4O_2$ requires C, 66.2; H, 5.2; N, 18.2%). ^{1}HNMR ($CDCl_3$): δ 9.3* (br s, 2H, NH), 8.1–7.7 (m, 4H, C_6H_4Me, AA^1BB^1), 7.5 (m, 5H, Ph), 6.3, 6.1 (s, 2H, CH). MS: 308 (M^+).

Acknowledgements

Thanks are due to: the British Technology Group (BTG, Biosciences Division) for the award of a research grant (SF); Dr. Richard A'Court (BTG) for his support and interest in the project; Glaxo Group Research for the microanalyses; SmithKline Beecham for the FAB mass spectra; the Scottish Agricultural College, Ayr for fungicidal screening, and Professor M.B. Hursthouse (University of Wales, Cardiff) for X-ray crystallography.

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