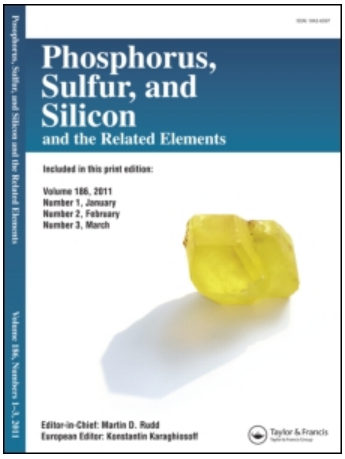


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis of Di- and Tetra-Sulfonated Heterocyclic Compounds by Crisscross Cycloaddition Reactions

Augusto C. Tomé[a]; José A. S. Cavaleiro[a]; Fernando M. J. Domingues[a]; Richard J. Cremlyn[b]
[a] Department of Chemistry, University of Aveiro, Aveiro, Portugal [b] Division of Biosciences, University of Hertfordshire, Hatfield, Hertfordshire, England

To cite this Article Tomé, Augusto C. , Cavaleiro, José A. S. , Domingues, Fernando M. J. and Cremlyn, Richard J.(2005) 'Synthesis of Di- and Tetra-Sulfonated Heterocyclic Compounds by Crisscross Cycloaddition Reactions', Phosphorus, Sulfur, and Silicon and the Related Elements, 180: 12, 2617 — 2634
To link to this Article: DOI: 10.1080/104265090930362
URL: http://dx.doi.org/10.1080/104265090930362

Phosphorus, Sulfur, and Silicon, 180:2617–2634, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090930362

Taylor & Francis
Taylor & Francis Group

Synthesis of Di- and Tetra-Sulfonated Heterocyclic Compounds by Crisscross Cycloaddition Reactions

Augusto C. Tomé
José A. S. Cavaleiro
Fernando M. J. Domingues
Department of Chemistry, University of Aveiro, Aveiro, Portugal

Richard J. Cremlyn
Division of Biosciences, University of Hertfordshire, Hatfield, Hertfordshire, England

Using sulfonated diaryl azines and sulfonated N*-arylmaleimides as starting reagents, a range of di- and tetra-sulfonated crisscross cycloadducts were selectively prepared. While the di-sulfonated adducts were obtained by carrying out the cycloaddition reaction in solution, the tetra-sulfonated adducts could be obtained only by fusion of the two reagents in the absence of solvent. The stereoisomers of the sulfonated cycloadducts were separated by preparative TLC.*

Keywords Crisscross cycloadducts; sulfonamides; sulfonates

INTRODUCTION

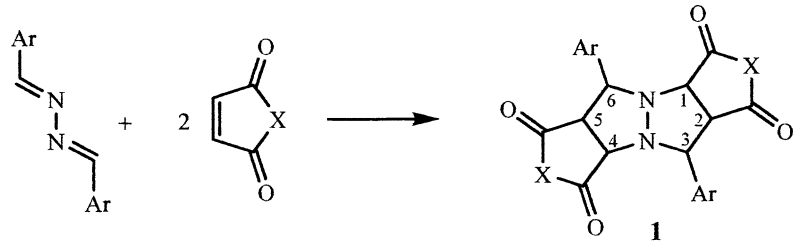
Diaryl azines are versatile intermediates in the synthesis of a wide range of heterocydic compounds.[1] One of the most interesting reactions of the diaryl azines is their transformation into pyrazolo[1,2-a]pyrazole derivatives by (1,3:2,4)-dipolar cycloadditions (also known as crisscross cycloadditions).[2] After the initial work of Bailey and Moore in 1917,[3] several studies on the reaction of diaryl azines with different dipolarophiles were published. The reaction of diaryl azines with maleic acid derivatives, such as maleic anhydride,[4] maleimide, and *N*-alkyl

Received December 9, 2004; accepted December 9, 2004.

Thanks are due to the University of Aveiro and Fundação para a Ciência e a Tecnologia (FCT, Portugal) and FEDER for funding the Organic Chemistry Research Unit. The authors thank Prof. A. M. S. Silva (University of Aveiro) for his invaluable assistance in the NMR experiments.

Address correspondence to Augusto C. Tomé, University of Aveiro, Department of Chemistry, Aveiro 3810-193, Portugal. E-mail: actome@sq.un.pt

and *N*-arylmaleimides[5–8] gives the structurally interesting adducts **1** (see Scheme 1).



SCHEME 1

During our search for new compounds with potential biological and pharmacological activities, or both, we have produced a number of different sulfonated compounds. The synthesis has involved the use of chlorosulfonic acid, a valuable sulfonating and chlorosulfonating reagent.[9] Our interest in this type of compound is based on the well-established antibacterial,[10,11] antifungal,[12] and herbicidal[13] activities of the sulfonyl derivatives (namely sulfonamides, sulfonylureas, and sulfonylhydrazides). As part of that project, we prepared several sulfonated derivatives of diaryl azines[14] and *N*-arylmaleimides.[15] We decided to use these compounds to prepare new sulfonated heteropolycyclic compounds of the types **4**, **7**, and **8** by crisscross cycloadditions (Schemes 2–4). In this article, we describe the regioselective synthesis of a range of di- and tetra-sulfonated adducts of these types. This work extends previous studies on crisscross sulfonyl adducts.[16]

RESULTS AND DISCUSSION

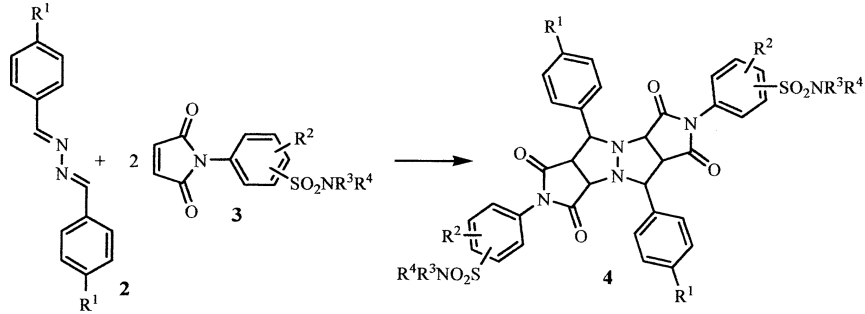
Reaction of *N*-(Sulfamoylaryl)maleimides with Diaryl Azines

Compound **4** was obtained by the crisscross cycloaddition reactions of *N*-(sulfamoylaryl)maleimides **3** with several diaryl azines (Scheme 2). The versatility of this reaction was demonstrated by the synthesis of several adducts. *N*,*N*-Diethyl and *N*-phenyl sulfonamide derivatives of three different *N*-arylmaleimides were used as starting reagents. The reaction of these maleimides occurs irrespectively of the electron-donating or electron-withdrawing character of the substituents in the diaryl azine. All adducts were obtained in moderate to good yields (Table I) after refluxing a chlorobenzene solution of the reagents, under nitrogen atmosphere, for 20–24 h.

TABLE I Disulfonated Adducts 4

Comp.	R^1	R^2	$SO_2NR^3R^4$	Yield (%)
4.1	MeO	H	4-SO_2NEt_2	62
4.2	MeO	4-Me	3-SO_2NHPh	74
4.3	MeO	4-MeO	3-SO_2NEt_2	75
4.4	MeO	4-MeO	3-SO_2NHPh	49
4.5	Cl	4-MeO	3-SO_2NEt_2	53
4.6	H	4-MeO	3-SO_2NHPh	93

As expected, several stereoisomers were formed in all these reactions. In all cases, the most abundant isomer is the one with the higher R_f value on silica gel TLC.



SCHEME 2

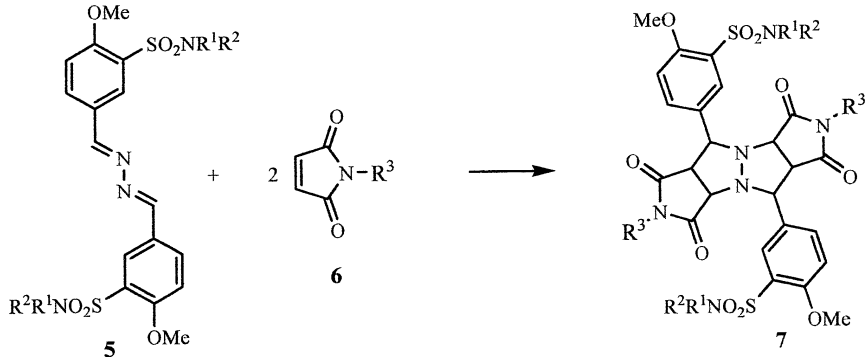
Reaction of Bis-Sulfamoylaryl Azines with Maleimides

A range of adduct **7** was prepared by reacting 3,3′-bis(sulfamoyl)-4,4′-dimethoxybenzaldazines **5** with maleimide, *N*-alkyl, *N*-arylalkyl, and *N*-arylmaleimides (Scheme 3). The reaction of 3,3′-bis(*N*,*N*-diethylsulfamoyl)-4,4′-dimethoxybenzaldazine with maleimides occurred in solution (chlorobenzene at reflux), and all the adducts were obtained in good yields (Table II). However, the reactions with 3,3′-bis(*N*-isopropylsulfamoyl)-4,4′-dimethoxybenzaldazine and 3,3′-bis(*N*-phenylsulfamoyl)-4,4′-dimethoxybenzaldazine were carried out by melting a mixture of these reagents with the maleimide derivative. This modification was required because of the low solubility of these azines in chlorobenzene, even at the boiling point. In these reactions, the low yields are mainly due to the tendency of the sulfonated azines to decompose at high temperatures.

TABLE II Disulfonated Adducts 7

Comp.	NR^1R^2	R^3	Yield (%)
7.1	NEt_2	H	55
7.2	NEt_2	Me	57
7.3	NEt_2	Et	62
7.4	NEt_2	CH_2CH_2Ph	60
7.5	NEt_2	Ph	58
7.6	NEt_2	3-ClC_6H_4	77
7.7	NEt_2	4-ClC_6H_4	75
7.8	NEt_2	4-IC_6H_4	94
7.9	NEt_2	4-MeC_6H_4	49
7.10	NEt_2	4-$NO_2C_6H_4$	92
7.11	$NHPr^i$	4-$NO_2C_6H_4$	42
7.12	NHPh	4-$NO_2C_6H_4$	25
7.13	NHPh	4-$MeOC_6H_4$	35
7.14	NHPh	4-MeC_6H_4	40

The wide range of disulfonated adducts of type **7** obtained by this route shows the versatility of this method for the regioselective synthesis of these di-sulfonated crisscross adducts.



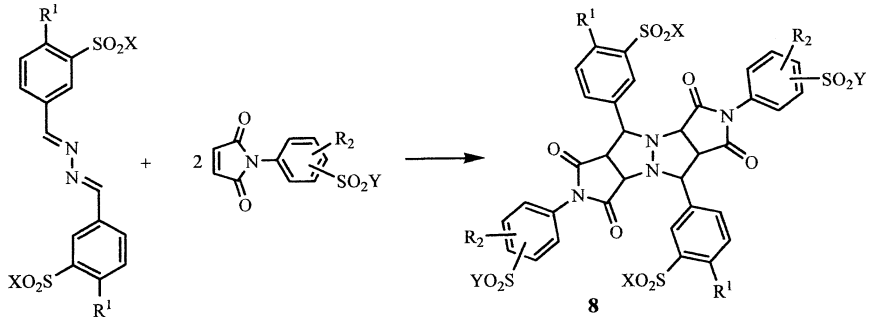
SCHEME 3

Reaction of Bis-Sulfamoylaryl Azines with *N*-(sulfamoylaryl)-maleimides

The tetra-sulfonated adducts **8.1–8.5** were prepared regioselectively by reacting sulfonated diaryl azines (di-sulfonamides or di-sulfonates) with sulfonated *N*-arylmaleimides (sulfonamides or sulfonates). The use of sulfonated reagents allowed us to prepare tetra-sulfonated adducts with the following diaryl azine/maleimide combinations: sul-

fonamide/sulfonamide (adduct **8.1**), sulfonate/sulfonate (adduct **8.2**), sulfonamide/sulfonate (adducts **8.3** and **8.4**) and sulfonate/sulfonamide (adduct **8.5**). By this synthetic route, it is possible to prepare, selectively, regioisomers such as adducts **8.4** and **8.5**. The versatility of this synthetic route allows the synthesis of a large number of compounds in order to establish fungicidal or pharmacological structure/activity relationships for these types of compounds.

All the adducts of **8** were prepared by melting mixtures of the reagents under a nitrogen atmosphere. Some of the adducts were obtained in low yields; in some cases, this is not an indication of the low reactivity of the reagents, but it can be attributed to the difficulties found in the separation of the adducts from the unreacted starting reagents.



SCHEME 4

Characterization of the Adducts

As previously mentioned, several diastereoisomers are formed in these crisscross cycloadditions. In some cases, the main isomer can be obtained in pure form only by crystallization. The minor isomers can be purified by chromatography. Particularly in the reactions with the less reactive azines, where significant amounts of starting reagents remain

TABLE III Tetrasulfonated Adducts 8

Comp.	R^1	X	R^2	SO_2Y	Yield (%)
8.1	OMe	NEt_2	H	4-SO_2NHPh	58
8.2	OMe	OC_6H_4Cl-4	H	4-$SO_2OC_6H_4NO_2$-4	20
8.3	Me	NEt_2	H	4-$SO_2OC_6H_4NO_2$-4	45
8.4	OMe	NEt_2	4-OMe	3-$SO_2OC_6H_4NO_2$-4	75
8.5	OMe	$OC_6H_4NO_2$-4	4-OMe	3-SO_2NEt_2	72

in the reaction mixture, purification by crystallization is not practicable. In those cases, small portions of the reaction mixture were purified by preparative TLC. The three major fractions were isolated for characterization while the minor fractions generally were not examined in detail. In some cases, the most abundant stereoisomer is not the easiest one to get in pure form. In those cases, the isomers with lower R_f values were the ones spectroscopically analyzed.

For each reaction, at least one isomer was characterized by ^{1}H NMR and MS. For some compounds, the ^{13}C NMR spectrum also was recorded. For simplicity, the numbering system used for the assignment of the NMR signals is indicated in Scheme 1. For all reactions, the cycloadduct with the lower R_f displays C_2 symmetric ^{1}H and ^{13}C NMR spectra: the ^{1}H NMR spectrum shows only one set of signals for protons H^1/H^4, H^2/H^5, and H^3/H^6, and the ^{13}C NMR spectrum shows only two signals corresponding to the four carbonyl carbons. In contrast, the other isomers show two sets of signals for the protons H^1-H^6 in their ^{1}H NMR spectra and four signals for the carbonyl carbon atoms in the ^{13}C NMR spectra. The FAB mass spectra of all adducts show the expected peaks corresponding to $m/z = (M + H)^+$ except for compounds 8.3, 8.4, and 8.5, were the observed peaks correspond to $m/z = M^+$.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 300 spectrometer. Deuteriochloroform was used as solvent (except were otherwise indicated) and TMS was used as an internal reference. The chemical shifts are expressed in δ (ppm) and the coupling constants (J) in Hertz (Hz). Mass spectra were recorded on a VG AutoSpec-Q instrument. Elemental analyses were performed in a Leco 932 CHNS analyzer. Melting points were measured on a Reichert Thermovar apparatus fitted with a microscope and are uncorrected.

Reaction of *N*-(sulfamoylaryl)maleimides with Diaryl Azines

General Procedure

A solution (or suspension) of a *N*-(sulfamoylaryl)maleimide (4 mmol) and a diaryl azine (2 mmol) in chlorobenzene (20 mL) was refluxed, with stirring and under a nitrogen atmosphere, for 20–24 h. If the adduct precipitated on cooling, it was filtered and washed with petroleum ether. Otherwise, it was precipitated by the addition of petroleum ether and filtered, and the isomers then were separated by preparative TLC using adequate mixtures of chloroform/acetone as eluent.

5,10-Bis(4-Methoxyphenyl)-2,7-Bis(4-(*N*,*N*-Diethylsulfamoyl)-phenyl)-3a,5a,8a,10a-Tetrahydro(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-c]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (4.1)

The isomer with lower R_f, m.p. 259–261°C. (Found: C, 59.33; H, 5.52; N, 9.74; $C_{44}H_{48}N_6O_{10}S_2$ requires C, 59.71; H, 5.47; N, 9.50%). ^{1}H NMR δ: 1.13 (t, 12H, 4 × CH_2 $\underline{CH_3}$), 3.22 (q, 8H, 4 × $\underline{CH_2}CH_3$), 3.77–3.85 (m, 8H, 2 × OCH_3, H^2 and H^5), 4.23 (d, 2H, H^1 and H^4, $J = 7.6$ Hz), 4.75 (d, 2H, H^3 and H^6, $J = 8.7$ Hz), 6.95-6.99 and 7.50–7.54 (m, 8H, 2 × C_6H_4OMe), 7.30–7.37 and 7.78–7.84 (m, 8H, 2 × $C_6H_4SO_2NR_2$). MS (FAB): 885 $(M + H)^+$.

5,10-Bis(4-Methoxyphenyl)-2,7-Bis(3-*N*-Phenylsulfamoyl-4-Methylphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (4.2)

The isomer with lower R_f, m.p. 260–263°C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 2.60 (s, 6H, 2 × CH_3), 3.80 (s, 6H, 2 × OCH_3), 3.98 (t, 2H, H^2 and H^5), 4.30 (d, 2H, H^1 and H^4, $J = 7.4$ Hz), 4.83 (d, 2H, H^3 and H^6, $J = 9.1$ Hz), 6.95–7.39 (m, 8H, ArH), 7.39–7.49 (m, 4H, ArH), 7.83 (m, 2H, ArH), 10.35 (broad s, 2H, 2 × NH). MS (FAB): 953 $(M + H)^+$.

5,10-Bis(4-Methoxyphenyl)-2,7-Bis(3-*N*,*N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (4.3)

The isomer with higher R_f, m.p. 186–189°C. (Found: C, 58.31; H, 5.53; N, 8.84; $C_{46}H_{52}N_6O_{12}S_2$ requires C, 58.46; H, 5.55; N, 8.89%). ^{1}H NMR δ: 1.10 (2 overlapping t, 12H, 4 × $CH_2\underline{CH_3}$), 3.30 (2 overlapping q, 8H, 4 × $\underline{CH_2}CH_3$), 3.80 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.80–3.95 (m, 2H, H^2 and H^5), 4.10 (d, 1H, H^1, $J = 8.2$ Hz), 4.73 (overlapping d, 2H, H^3 and H^4), 5.18 (d, 1H, H^6, $J = 9.0$ Hz), 6.67–7.13 (m, 7H, ArH), 7.30–7.67 (m, 7H, ArH). MS (FAB): 945 $(M + H)^+$.

The isomer with lower R_f, m.p. 271–273°C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 1.08 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.28 (q, 8H, 4 × $\underline{CH_2}CH_3$), 3.83 (s, 6H, 2 × $ArOCH_3$), 3.94 (s, 6H, 2 × $Ar'OCH_3$), 3.90–3.95 (m, 2H, H^2 and H^5), 4.35 (d, 2H, H^1 and H^4, $J = 8.2$ Hz), 4.80 (d, 2H, H^3 and H^6, $J = 9.0$ Hz), 6.94–6.98 and 7.51–7.55 (m, 8H, 2 × C_6H_4OMe), 7.09 (d, 2H, ArH, $J = 8.9$ Hz), 7.30–7.35 (dd, 2H, ArH, $J = 8.9$ Hz and $J = 2.5$ Hz), 7.71 (d, 2H, ArH, $J = 2.5$ Hz). MS (FAB): 945 $(M + H)^+$.

5,10-Bis(4-Methoxyphenyl)-2,7-Bis(3-*N*-Phenylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]Pyrazolo[1,2-A]pyrazole-1,3,6,8tetrone (4.4)

The isomer with lower R_f, m.p. 220–223°C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 3.82 (s, 6H, 2 × Ar-OCH_3), 3.84 (s, 6H, 2 × Ar′-OCH_3), 3.91 (m, 2H, H^2 and H^5), 4.26 (d, 2H, H^1 and H^4, $J = 7.3$ Hz), 4.74 (d, 2H, H^3 and H^6, $J = 9.0$ Hz), 6.93–7.15 (m, 16H, ArH), 7.26–7.31 (dd, 2H, ArH, $J = 8.8$ Hz and $J = 2.5$ Hz), 7.50 (m, 4H, ArH), 7.73 (d, 2H, ArH, $J = 2.5$ Hz), 9.59 (broad s, 2H, 2 × NH). MS (FAB): 985 $(M + H)^+$.

5,10-Bis(4-Chorophenyl)-2,7-Bis(3-*N*,*N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (4.5)

The isomer with higher R_f, m.p. 215–218°C. ^{1}H NMR δ: 1.10 (m, 12H, 4 × $CH_2\underline{CH_3}$), 3.23–3.37 (m, 8H, 4 × $\underline{CH_2}CH_3$), 3.75–3.80 (dd, 1H, H^2, $J = 8.3$ Hz and $J = 5.2$ Hz), 3.87 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 4.03 (t, 1H, H^5), 4.15 (d, 1H, H^4, $J = 8.3$ Hz), 4.76 (d, 1H, H^1, $J = 8.3$ Hz), 4.82 (d, 1H, H^3, $J = 5.2$ Hz), 5.28 (d, 1H, H^6, $J = 9.4$ Hz), 7.09–7.31 (m, 5H, ArH), 7.39–7.46 (m, 6H, ArH), 7.63–7.71 (m, 3H, ArH). MS (FAB): 954 $(M + H)^+$.

The isomer with lower R_f, m.p. 288–291°C. ^{1}H NMR δ: 1.10 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.30 (q, 8H, 4 × $\underline{CH_2}CH_3$), 3.84 (t, 2H, H^2 and H^5), 3.92 (s, 6H, 2 × OCH_3), 4.10 (d, 2H, H^1 and H^4, $J = 7.7$ Hz), 4.73 (d, 2H, H^3 and H^6, $J = 9.0$ Hz), 7.00 (d, 2H, ArH, $J = 8.9$ Hz), 7.23–7.29 (dd, 2H, ArH, $J = 8.9$ Hz and $J = 2.5$ Hz), 7.32–7.37 and 7.47–7.51 (m, 8H, 2 × C_6H_4Cl), 7.70 (d, 2H, ArH, $J = 2.5$ Hz). MS (FAB): 954 $(M + H)^+$.

5,10-Diphenyl-2,7-Bis(3-*N*-Phenylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10A-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo [3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (4.6)

The isomer with higher R_f, m.p. 226–228°C. (Found: C, 61.97; H, 4.67; N, 9.34; $C_{48}H_{40}N_6O_{10}S_2$ requires C, 62.33; H, 4.36; N, 9.09%). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 3.82 (s, 3H, OCH_3), 3.84–3.88 (m, 1H, H^2), 3.90 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 4.07 (t, 1H, H^5), 4.25 (d, 1H, H^4, $J = 8.0$ Hz), 4.76 (d, 1H, H^3, $J = 5.9$ Hz), 4.84 (d, 1H, H^1, $J = 8.3$ Hz), 5.24 (d, 1H, H^6, $J = 9.5$ Hz), 6.83–7.72 (m, 25H, ArH), 7.86 (d, 1H, ArH, $J = 2.6$ Hz), 9.52 (s, 1H, NH), 9.65 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ: 52.2, 56.2 (C-2, C-5), 55.7, 55.8 (2 × OCH_3), 64.5, 65.2 (C-1,

C-4), 66.2, 68.5 (C-3, C-6), 112.0, 112.1, 119.5, 119.6, 119.7, 123.2, 123.3, 123.4, 123.5, 126.7, 127.1, 127.6, 127.8, 128.2, 128.3, 128.4, 131.8, 131.9, 136.1, 137.0, 138.9, 155.6, 155.8 (Ar—C), 170.6, 171.4, 172.7, 174.4 (4 × C=O). MS (FAB): 925 $(M + H)^+$.

Reaction of Bis-Sulfamoylaryl Azines with Maleimides

General Procedure 1 (Soluble Azines)

A stirred suspension of the sulfonated azine (2.5 mmol) and a maleimide (5.4 mmol) in chlorobenzene (20 mL) was refluxed under nitrogen atmosphere for 20–24 h. After cooling to room temperature, petroleum ether was added to the reaction mixture and the solid (adduct + azine) was filtered and washed with petroleum ether. The solid was dissolved in hot acetone and, on cooling, the adduct (main isomer) crystallized. After filtration, the minor isomers of the adduct were obtained from the "mother liquor" by preparative TLC using chloroform: acetone (95:5) as an eluent.

General Procedure 2 (Insoluble Azines)

A mixture of the bis-sulfamoylaryl azine (1 mmol) and the maleimide (2.1 mmol) was triturated in a mortar and the solid was heated, under a nitrogen atmosphere, in an oil bath at 200–210°C. The mixture melted and was left at this temperature for 30 min. After cooling, the solid was dissolved in acetone and purified by preparative TLC.

5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.1)

The isomer with a higher R_f, m.p. 227–230°C. (Found: C, 51.02; H, 6.38; N, 10.93; $C_{32}H_{40}N_6O_{10}S_2.H_2O$ requires C, 51.19; H, 6.64; N, 11.19%). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 1.06–1.14 (m, 12H, 4 × $CH_2\underline{CH_3}$), 3.25–3.38 (m, 8H, 4 × $\underline{CH_2}CH_3$), 3.58–3.62 (dd, 1H, H^2, $J = 8.2$ Hz and $J = 5.5$ Hz), 3.89–3.97 (m, 7H, 2 × OCH_3 and H^5), 4.04 (d, 1H, H^4, $J = 8.1$ Hz), 4.56 (d, 1H, H^1, $J = 8.2$ Hz), 4.70 (d, 1H, H^3, $J = 5.5$ Hz), 5.11 (d, 1H, H^6, $J = 9.4$ Hz), 6.96 (d, 1H, ArH, $J = 8.7$ Hz), 7.10 (d, 1H, ArH, $J = 8.7$ Hz), 7.55–7.59 (dd, 1H, ArH, $J = 8.6$ Hz and $J = 2.1$ Hz), 7.84–7.87 (dd, 1H, ArH, $J = 8.6$ Hz and $J = 2.3$ Hz), 7.92 (d, 1H, ArH, $J = 2.1$ Hz), 8.07 (d, 1H, ArH, $J = 2.2$ Hz). ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ: 13.6, 13.8 (2 × $CH_2\underline{C}H_3$), 41.0, 41.3 (2 × $\underline{C}H_2CH_3$), 53.0, 56.9 (C-2, C-5), 55.2, 55.4 (2 × OCH_3), 63.6, 65.5 (C-1, C-4), 66.6, 67.4 (C-3, C-6), 111.2, 112.2, 127.4, 128.3, 128.5, 129.3, 129.9, 130.7, 132.3, 132.6,

155.4, 155.6 (Ar—C), 173.2, 173.5, 174.7, 176.5 (4 × C=O). MS (FAB): 733 $(M + H)^+$.

2,7-Dimethyl-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.2)

The isomer with a higher R_f, m.p. 230–233°C. ^{1}H NMR δ: 1.13 (overlapping t, 12H, 4 × $CH_2\underline{CH_3}$) 2.78 (s, 3H, CH_3), 2.96 (s, 3H, CH_3), 3.28–3.43 (overlapping q, 8H, 4 × $\underline{CH_2}CH_3$), 3.57–3.64 (dd, 1H, H^2, $J = 7.7$ Hz and $J = 6.1$ Hz), 3.69 (t, 1H, H^5), 3.88 (d, 1H, H^4, $J = 7.7$ Hz), 3.92 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.52 (d, 1H, H^1, $J = 7.7$ Hz), 4.61 (d, 1H, H^3, $J = 6.1$ Hz), 5.02 (d, 1H, H^6, $J = 9.3$ Hz), 6.92 (d, 1H, ArH, $J = 8.8$ Hz), 7.08 (d, 1H, ArH, $J = 8.8$ Hz), 7.37–7.42 (dd, 1H, ArH), 7.81–7.83 (dd, 1H, ArH), 7.92 (d, 1H, ArH, $J = 2.2$ Hz), 8.09 (d, 1H, ArH, $J = 2.2$ Hz). MS (FAB): 761 $(M + H)^+$.

2,7-Diethyl-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.3)

The isomer with a higher R_f, m.p. 238–240°C. (Found: C, 54.62; H, 6.15; N, 10.58. $C_{36}H_{48}N_6O_{10}S_2$ requires C, 54.81; H, 6.13; N, 10.65%). ^{1}H NMR δ: 0.83–1.18 (m, 18H, 6 × $CH_2\underline{CH_3}$), 3.27–3.40 (m, 12H, 6 × $\underline{CH_2}CH_3$), 3.48–3.85 (m, 3H, H^2, H^4 and H^5), 3.89 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.52 (d, 1H, H^1, $J = 8.2$ Hz), 4.67 (d, 1H, H^3, $J = 5.0$ Hz), 5.01 (d, 1H, H^6, $J = 9.4$ Hz), 6.90 (d, 1H, ArH, $J = 8.2$ Hz), 7.06 (d, 1H, ArH, $J = 8.8$ Hz), 7.43–7.48 (dd, 1H, ArH), 7.82–7.87 (dd, 1H, ArH), 7.93 (d, 1H, ArH, $J = 2.2$ Hz), 8.08 (d, 1H, ArH, $J = 2.2$ Hz). MS (FAB): 789 $(M + H)^+$.

Isomer with a lower R_f, m.p. 280–283°C. MS (FAB): 789 $(M + H)^+$.

2,7-Bis(2-Phenylethyl)-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.4)

The isomer with a higher R_f, m.p. 217–220°C. (Found: C, 60.95; H, 5.97; N, 8.88; $C_{48}H_{56}N_6O_{10}S_2$ requires C, 61.26; H, 6.00; N, 8.93%). ^{1}H NMR δ: 1.04–1.15 (m, 12H, 4 × $CH_2\underline{CH_3}$), 2.40–3.44 (m, 16H, 4 × $\underline{CH_2}CH_3$ and 2 × $N\underline{CH_2}\underline{CH_2}Ph$), 3.56–3.60 (dd, 1H, H^2, $J = 8.3$ Hz and J= 4.0 Hz), 3.74–3.83 (m, 1H, H^5), 3.86 (s, 3H, OCH_3), 3.93 (s, 3H,

OCH_3), 3.96 (m, 1H, H^4), 4.35 (d, 1H, H^1, $J = 8.3$ Hz), 4.64 (d, 1H, H^3, $J = 4.0$ Hz), 5.13 (d, 1H, H^6, $J = 9.5$ Hz), 6.86 (d, 1H, ArH, $J = 8.6$ Hz), 7.05 (d, 1H, ArH, $J = 8.7$ Hz), 7.10–7.30 (m, 10H, 2 × C_6H_5), 7.42–7.45 (dd, 1H, ArH, $J = 8.6$ Hz and $J = 2.3$ Hz), 7.76–7.80 (dd, 1H, ArH, $J = 8.7$ Hz and $J = 2.3$ Hz), 7.93 (d, 1H, ArH, $J = 2.3$ Hz), 8.02 (d, 1H, ArH, $J = 2.3$ Hz). ^{13}C NMR δ: 14.3, 14.4 (2 × $CH_2\underline{C}H_3$), 32.4, 33.3 (2 × $NCH_2\underline{C}H_2Ph$), 39.4, 39.8 (2 × $N\underline{C}H_2CH_2Ph$), 41.7, 41.9 (2 × $\underline{C}H_2CH_3$), 52.6, 55.6 (C-2, C-5), 55.9, 56.0 (2 × OCH_3), 63.6, 64.5 (C-1, C-4), 67.0, 69.1 (C-3, C-6), 111.8, 112.9, 126.6, 127.1, 128.4, 128.5, 128.6, 128.7, 128.9, 129.0, 129.1, 129.6, 130.9, 131.5, 132.6, 133.0, 137.1, 137.4, 156.1, 156.3 (Ar—C), 172.4, 173.1, 174.0, 175.6 (4 × C═O). MS (FAB): 941 $(M + H)^+$.

2,7-Diphenyl-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.5)

The isomer with a higher R_f, m.p. 248–251°C. ^{1}H NMR δ: 0.91 (t, 6H, 2 × $CH_2\underline{CH_3}$), 1.13 (t, 6H, 2 × $CH_2\underline{CH_3}$), 3.06–3.43 (m, 9H, 4 × $\underline{CH_2}CH_3$ + H^2), 3.85 (t, 1H, H^5), 3.87 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.01 (d, 1H, H^4, $J = 8.2$ Hz), 4.73 (d, 1H, H^1, $J = 8.8$ Hz), 4.87 (d, 1H, H^3, $J = 5.5$ Hz), 5.44 (d, 1H, H^6, $J = 9.3$ Hz), 6.89–6.93 (m, 2H, ArH), 7.09 (d, 1H, ArH, $J = 8.2$ Hz), 7.24–7.49 (m, 6H, ArH), 7.57–7.62 (dd, 1H, ArH, $J = 8.3$ Hz and $J = 2.2$ Hz), 7.90–7.96 (dd, 1H, ArH, $J = 8.3$ Hz and $J = 2.2$ Hz), 8.6 (m, 2H, ArH). MS (FAB): 885 $(M + H)^+$.

The isomer with a lower R_f, m.p. 258–261°C; MS (FAB): 885 $(M + H)^+$.

2,7-Bis(3-Chlorophenyl)-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.6)

The isomer with a higher R_f, m.p. 192–195°C. ^{1}H NMR δ: 0.92 (t, 6H, 2 × $CH_2\underline{CH_3}$), 1.16 (t, 6H, 2 × $CH_2\underline{CH_3}$), 3.03–3.53 (m, 8H, 4 × $\underline{CH_2}CH_3$), 3.67 (m, 1H, H^5), 3.80–3.85 (dd, 1H, H^2, $J = 6.6$ Hz and $J = 8.3$ Hz), 3.92 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 4.07 (d, 1H, H^4, $J = 8.0$ Hz), 4.76–4.82 (m, 2H, H^1 and H^3), 5.40 (d, 1H, H^6, $J = 9.5$ Hz), 6.75 (d, 1H, ArH, $J = 7.5$ Hz), 6.83 (s, 1H, ArH), 6.94 (d, 1H, ArH, $J = 8.7$ Hz), 7.07–7.17 (m, 3H, ArH), 7.32–7.46 (m, 4H, ArH), 7.55–7.58 (dd, 1H, ArH, $J = 8.6$ Hz and $J = 2.0$ Hz), 7.91–7.94 (dd, 1H, ArH, $J = 8.6$ Hz and $J = 2.1$ Hz), 8.15 (d, 1H, ArH, $J = 1.6$ Hz), 8.19 (d, 1H, ArH, $J = 2.0$ Hz). MS (FAB): 953 $(M + H)^+$.

2,7-Bis(4-Chlorophenyl)-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.7)

The isomer with a higher R_f, m.p. 270–273°C. (Found: C, 55.31; H, 4.83; N, 8.78; $C_{44}H_{46}Cl_2N_6O_{10}S_2$ requires C, 55.40; H, 4.86; N, 8.81%). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 0.97 (t, 6H, 2 × $CH_2\underline{CH_3}$), 1.14 (t, 6H, 2 × $CH_2\underline{CH_3}$), 2.98–3.20 (m, 4H, 2 × $\underline{CH_2}CH_3$), 3.31–3.42 (m, 4H, 2 × $\underline{CH_2}CH_3$), 3.84–3.90 (dd, 1H, H^2, $J = 8.4$ Hz and $J = 6.5$ Hz), 3.90 (s, 3H, OCH_3), 3.95–3.98 (m, 1H, H^5), 3.98 (s, 3H, OCH_3), 4.22 (d, 1H, H^4, $J = 7.9$ Hz), 4.82 (d, 1H, H^1, $J = 6.5$ Hz), 4.87 (d, 1H, H^3, $J = 8.4$ Hz), 5.32 (d, 1H, H^6, $J = 9.5$ Hz), 6.93–6.99 (m, 3H, ArH), 7.15 (d, 1H, ArH, $J = 8.7$ Hz), 7.28–7.31 (m, 4H, ArH), 7.43–7.57 (m, 4H, ArH), 7.92–7.96 (dd, 1H, ArH, $J = 8.6$ Hz and $J = 2.0$ Hz), 8.07 (d, 1H, ArH, $J = 2.0$ Hz), 8.17 (d, 1H, ArH, $J = 2.2$ Hz). ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ: 13.4, 13.7 (2 × $CH_2\underline{C}H_3$), 40.8, 41.3 (2 × $\underline{C}H_2CH_3$), 51.9, 55.9 (C-2, C-5), 55.2, 55.4 (2 × OCH_3), 64.2, 64.3 (C-1, C-4), 64.9, 67.2 (C-3, C-6), 111.3, 112.4, 126.9, 127.3, 127.9, 128.4, 128.5, 129.2, 129.3, 129.7, 130.0, 132.4, 132.5, 133.4, 133.7, 155.7, 155.9 (Ar—C), 169.6, 171.5, 172.4, 173.4 (4 × C═O). MS (FAB): 953 $(M + H)^+$.

2,7-Bis(4-Iodophenyl)-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.8)

The isomer with a lower R_f, m.p. 295–297°C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 1.08 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.29 (q, 8H, 4 × $\underline{CH_2}CH_3$), 3.90 (m, 2H, H^2 and H^5), 3.94 (s, 6H, 2 × OCH_3), 4.18 (d, 2H, H^1 and H^4, $J = 7.6$ Hz), 4.89 (d, 2H, H^3 and H^6, $J = 8.9$ Hz), 6.94–6.97 and 7.71–7.73 (m, 8H, 2 × C_6H_4I), 7.07 (d, 2H, ArH, $J = 8.7$ Hz), 7.74 (m, 2H, ArH), 8.10 (broad s, 2H, ArH). MS (FAB): 1137 $(M + H)^+$.

2,7-Bis(4-Methylphenyl)-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.9)

The isomer with a lower R_f, m.p. 285–288°C. (Found: C, 60.30; H, 5.70; N, 9.17; $C_{46}H_{52}N_6O_{10}S_2$ requires C, 60.51; H, 5.74; N, 9.20%). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 1.06 (t, 12H, 4 × $CH_2\underline{CH_3}$), 2.35 (s, 6H, 2 × CH_3), 3.29 (q, 8H, 4 × $\underline{CH_2}CH_3$), 3.95 (s, 6H, 2 × OCH_3), 4.00 (t, 2H,

H^2 and H^5), 4.22 (d, 2H, H^1 and H^4, $J = 7.6$ Hz), 4.91 (d, 2H, H^3 and H^6, $J = 8.6$ Hz), 7.04–7.22 (m, 10H, ArH), 7.80–8.09 (m, 4H, ArH). MS (FAB): 913 $(M + H)^+$.

2,7-Bis(4-Nitrophenyl)-5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.10)

The isomer with a lower R_f, m.p. 228–231°C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 1.08 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.30 (q, 8H, 4 × $\underline{CH_2}CH_3$), 3.96 (s, 6H, 2 × OCH_3), 4.06 (t, 2H, H^2 and H^5), 4.28 (d, 2H, H^1 and H^4, $J = 7.6$ Hz), 4.95 (d, 2H, H^3 and H^6, $J = 9.2$ Hz), 7.10 (d, 2H, ArH, $J = 8.7$ Hz), 7.48–7.51 and 8.23–8.27 (m, 8H, 2 × $C_6H_4NO_2$), 7.78 (broad m, 2H, ArH), 8.12 (broad s, 2H, ArH). MS (FAB): 975 $(M + H)^+$.

2,7-Bis(4-Nitrophenyl)-5,10-Bis(3-*N*-Isopropylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.11)

The isomer with a higher R_f, m.p. 227–230°C. (Found: C, 53.18; H, 4.45; N, 11.83; $C_{42}H_{42}N_8O_{14}S_2$ requires C, 53.27; H, 4.47; N, 11.83%). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 0.85–0.95 (m, 6H, $CH(\underline{CH_3})_2$), 1.08–1.11 (m, 6H, $CH(\underline{CH_3})_2$), 3.10 (m, 1H, $\underline{CH}(CH_3)_2$), 3.47 (m, 1H, $\underline{CH}(CH_3)_2$), 3.90–3.95 (dd, 1H, H^2, $J = 8.4$ Hz and $J = 6.2$ Hz), 3.97 (s, 3H, OCH_3), 4.03–4.09 (m, 1H, H^5), 4.04 (s, 3H, OCH_3), 4.25 (d, 1H, H^4, $J = 8.1$ Hz), 4.85 (d, 1H, H^1, $J = 8.4$ Hz), 4.88 (d, 1H, H^3, $J = 6.2$ Hz), 5.31 (d, 1H, NH, $J = 7.7$ Hz), 5.36 (d, 1H, H^6, $J = 9.6$ Hz), 5.47 (d, 1H, NH, $J = 7.0$ Hz), 6.99 (d, 1H, ArH, $J = 8.6$ Hz), 7.18 (d, 1H, ArH, $J = 8.7$ Hz), 7.24–7.27 and 8.13–8.16 (m, 4H, $C_6H_4NO_2$), 7.56–7.60 (dd, 1H, ArH, $J = 8.7$ Hz and $J = 2.0$ Hz), 7.60–7.63 and 8.33–8.36 (m, 4H, $C_6H_4NO_2$), 7.96–8.00 (dd, 1H, ArH, $J = 8.6$ Hz and $J = 2.2$ Hz), 8.09 (d, 1H, ArH, $J = 2.0$ Hz), 8.17 (d, 1H, ArH, $J = 2.2$ Hz). MS (FAB): 947 $(M + H)^+$.

The isomer with a lower R_f, m.p. 257–260°C. MS (FAB): 947 $(M + H)^+$.

2,7-Bis(4-Nitrophenyl)-5,10-Bis(3-*N*-Phenylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.12)

The isomer with a lower R_f, m.p. 255–259°C. ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 3.95 (s, 6H, 2 × OCH_3), 4.08 (t, 2H, H^2 and H^5), 4.22 (d, 2H, H^1

and H^4, $J = 7.8$ Hz), 4.95 (d, 2H, H^3 and H^6, $J = 9.0$ Hz), 6.88 (broad m, 2H, ArH), 7.09–7.19 (m, 10H, 2 × C_6H_5), 7.48–7.51 and 8.26–8.29 (m, 8H, 2 × $C_6H_4NO_2$), 7.73 (broad m, 2H, ArH), 8.13 (broad s, 2H, ArH), 10.0 (s, 2H, 2 × NH). MS (FAB): 1015 $(M + H)^+$.

2,7-Bis(4-Methoxyphenyl)-5,10-Bis(3-*N*-Phenylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.13)

The isomer with a lower R_f, m.p. 283–286°C. (Found: C, 60.62; H, 4.22; N, 8.37; $C_{50}H_{44}N_6O_{12}S_2$ requires C, 60.97; H, 4.50; N, 8.53%). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 3.78 (s, 6H, 2 × ArO$\underline{CH_3}$), 3.91 (s, 6H, 2 × Ar′O$\underline{CH_3}$), 3.97 (t, 2H, H^2 and H^5), 4.13 (d, 2H, H^1 and H^4, $J = 7.3$ Hz), 4.86 (d, 2H, H^3 and H^6, $J = 8.7$ Hz), 6.66–7.11 (m, 20H, ArH), 7.69 (m, 2H, ArH), 8.13 (m, 2H, ArH), 9.87 (s, 1H, NH). MS (FAB): 985 $(M + H)^+$.

2,7-Bis(4-Methylphenyl)-5,10-Bis(3-*N*-Phenylsulfamoyl-4-Methoxyphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (7.14)

The isomer with a higher R_f, m.p. 254–257°C. (Found: C, 62.84; H, 4.92; N, 8.80; $C_{50}H_{44}N_6O_{10}S_2$ requires C, 63.01; H, 4.65; N, 8.82%). ^{1}H NMR ($CDCl_3$ + DMSO-d_6) δ: 2.33 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.79–3.83 (dd, 1H, H^2), 3.85 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.15 (t, 1H, H^5), 4.21 (d, 1H, H^4, $J = 8.3$ Hz), 4.75 (d, 1H, H^1, $J = 8.2$ Hz), 4.88 (d, 1H, H^3, $J = 5.3$ Hz), 5.34 (d, 1H, H^6, $J = 9.6$ Hz), 6.77–7.31 (m, 18H, ArH), 7.57 (dd, 1H, ArH, $J = 8.1$ Hz and $J = 2.0$ Hz), 7.86–7.90 (dd, 1H, ArH, $J = 8.8$ Hz and $J = 2.2$ Hz), 8.08 (d, 1H, ArH, $J = 2.0$ Hz), 8.12 (d, 1H, ArH, $J = 2.1$ Hz), 9.63 (s, 1H, NH), 9.71 (s, 1H, NH). MS (FAB): 953 $(M + H)^+$.

Reaction of Bis-Sulfamoylaryl Azines with *N*-(Sulfamoylaryl)maleimides

General Procedure

The sulfonated diaryl azine (2.5 mmol) and the sulfonated maleimide (5.4 mmol) were triturated in a mortar until an homogeneous powder was obtained. The solid was transferred to a round-bottomed flask and was purged with nitrogen gas. It then was heated, under a nitrogen

atmosphere, in an oil bath at 185–190°C. When all the solid had melted, the mixture was heated for a further 15 minutes. After cooling to room temperature, the solid was dissolved in acetone and purified by column chromatography.

5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-2,7-Bis(4-*N*-Phenylsulfamoylphenyl)-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (8.1)

The isomer with a lower R_f, m.p. 231–233°C. ^{1}H NMR (DMSO-d_6) δ: 0.90 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.05–3.25 (m, 8H, 4 × $\underline{CH_2}CH_3$), 3.87 (s, 6H, 2 × OCH_3), 4.03 (t, 2H, H^2 and H^5), 4.15 (d, 2H, H^1 and H^4, $J = 6.9$ Hz), 4.87 (d, 2H, H^3 and H^6, $J = 8.2$ Hz), 6.97–7.36 (m, 16H, ArH), 7.65 (dd, 2H, ArH), 7.80 (d, 4H, ArH), 7.92 (d, 1H, ArH), 10.30 (s, 2H, NH). ^{13}C NMR (DMSO-d_6) δ: 14.0 ($CH_2\underline{C}H_3$), 41.3 ($\underline{C}H_2CH_3$), 51.3 (C-2, C-5), 56.0 (OCH_3), 65.6 (C-1, C-4), 67.4 (C-3, C-6), 120.3, 124.3, 127.1, 127.2, 127.3, 128.4, 129.1, 135.4, 137.3, 139.3, 156.3 (Ar—C), 172.8, 173.4 (C=O). MS (FAB): 1195 $(M + H)^+$.

5,10-Bis[3-(4-Chlorophenoxysulfonyl)-4-Methoxyphenyl]-2,7-Bis[4-(4-Nitrophenoxysulfonyl) phenyl]-3a,5a,8a,10A-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]Pyrazolo [1,2-a]pyrazole-1,3,6,8-Tetrone (8.2)

The isomer with a lower R_f, m.p. 168–171°C. ^{1}H NMR (acetone-d_6) δ: 4.05 (s, 6H, 2 × OCH_3), 4.27 (dd, 2H, H^2 and H^5), 4.51 (d, 2H, H^1 and H^4, $J = 7.6$ Hz), 5.23 (d, 2H, H^3 and H^6, $J = 9.0$ Hz), 13–7.17 and 7.31–7.33 (m, 8H, 2 × OC_6H_4Cl), 7.36–7.41 and 8.26–8.31 (m, 8H, 2 × $OC_6H_4NO_2$), 7.43 (d, 2H, ArH, $J = 8.8$ Hz), 7.52–7.55 and 7.97–8.00 (m, 8H, 2 × $NC_6H_4SO_3Ar$), 8.15 (broad s, 2H, ArH). ^{13}C NMR (acetone-d_6) δ: 52.7 (C-2, C-5), 57.0 (OCH_3), 66.5 (C-1, C-4), 68.8 (C-3, C-6), 114.3, 124.0, 124.3, 124.5, 126.5, 128.2, 128.6, 130.1, 130.7, 132.7, 134.8, 138.7, 147.4, 149.4, 154.5, 158.8 (Ar—C), 173.3, 173.8 (C=O). MS (FAB): 1397 $(M + H)^+$.

5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-2,7-Bis[4-(4-Nitrophenoxysulfonyl) Phenyl]-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5]pyrazolo [1,2-A]pyrazole-1,3,6,8-Tetrone (8.3)

The isomer with a lower R_f, m.p. 169–172°C. ^{1}H NMR (acetone-d_6) δ: 1.03 (t, 12H, 4 × $CH_2\underline{CH_3}$), 2.60 (s, 6H, 2 × CH_3), 3.27–3.36 (m, 8H, 4 ×

$\underline{CH_2}CH_3$), 4.34 (dd, 2H, H^2 and H^5), 4.57 (d, 2H, H^1 and H^4, $J = 7.6$ Hz), 5.29 (d, 2H, H^3 and H^6, $J = 9.1$ Hz), 7.38–7.42 and 8.28–8.31 (m, 8H, 2 × $OC_6H_4NO_2$), 7.48 (d, 2H, ArH, $J = 7.9$ Hz), 7.57–7.60 and 7.98–8.02 (m, 8H, 2 × $NC_6H_4SO_3Ar$), 7.75–7.81 (broad dd, 2H, ArH), 8.20 (broad d, 2H, ArH). ^{13}C NMR (acetone-d_6) δ: 14.1 ($CH_2\underline{C}H_3$), 20.3 (Ar—CH_3), 41.6 ($\underline{C}H_2CH_3$), 52.7 (C-2, C-5), 66.8 (C-1, C-4), 69.4 (C-3, C-6), 124.3, 126.5, 128.4, 130.0, 133.8, 134.6, 134.8, 138.5, 138.8, 140.0, 147.4, 154.5 (Ar—C), 173.2, 173.9 (C=O). MS (FAB): 1254 ($M^{+\cdot}$).

5,10-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-2,7-Bis[3-(4-Nitrophenoxysulfonyl)-4-Methoxyphenyl]-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5] Pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (8.4)

The isomer with lower R_f, m.p. 232–235°C; ^{1}H NMR (acetone-d_6) δ: 1.02 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.24–3.36 (m, 8H, 4 × $\underline{CH_2}CH_3$), 3.97 (s, 6H, 2 × $ArOCH_3$), 4.05 (s, 6H, 2 × $Ar'OCH_3$), 4.20 (t, 2H, H^2 and H^5), 4.44 (d, 2H, H^1 and H^4, $J = 7.5$ Hz), 5.11 (d, 2H, H^3 and H^6, $J = 9.2$ Hz), 7.22 (d, 2H, ArH, $J = 8.6$ Hz), 7.41 (d, 2H, ArH, $J = 9.2$ Hz), 7.42–7.46 and 8.24–8.29 (m, 8H, 2 × $OC_6H_4NO_2$), 7.63 (d, 2H, ArH, $J = 2.4$ Hz), 7.66–8.06 (m, 6H, ArH). ^{13}C NMR (acetone-d_6) δ: 14.7 ($CH_2\underline{C}H_3$), 42.6 ($\underline{C}H_2CH_3$), 52.5 (C-2, C-5), 56.4 ($ArOCH_3$), 57.4 ($Ar'OCH_3$), 66.8 (C-1, C-4), 69.1 (C-3, C-6), 113.3, 114.7, 123.5, 124.0, 125.5, 126.4, 128.1, 130.1, 130.2, 132.6, 136.4, 147.2, 154.9, 157.7, 158.2 (Ar—C), 173.6, 174.2 (C=O). MS (FAB): 1346 ($M^{+\cdot}$).

2,7-Bis(3-*N,N*-Diethylsulfamoyl-4-Methoxyphenyl)-5,10-Bis[3-(4-Nitrophenoxysulfonyl)-4-Methoxyphenyl]-3a,5a,8a,10a-Tetrahydro-(2*H*,5*H*,7*H*,10*H*)-Pyrrolo[3,4-C]pyrrolo[3′,4′:4,5] Pyrazolo[1,2-A]pyrazole-1,3,6,8-Tetrone (8.5)

The isomer with a higher R_f, m.p. 169–173°C. ^{1}H NMR (acetone-d_6) δ: 1.05 (overlapping t, 12H, 4 × $CH_2\underline{CH_3}$), 3.32 (overlapping q, 8H, 4 × $\underline{CH_2}CH_3$), 3.92 (dd, 1H, H^2, $J = 8.4$ Hz and $J = 7.3$ Hz), 3.98 (s, 3H, $ArOCH_3$), 3.99 (s, 3H, $ArOCH_3$), 4.04 (s, 3H, $Ar'OCH_3$), 4.06 (s, 3H, $Ar'OCH_3$), 4.25 (dd, 1H, H^5, $J = 9.5$ Hz and $J = 7.9$ Hz), 4.46 (d, 1H, H^4, $J = 7.9$ Hz), 4.87 (d, 1H, H^1, $J = 7.3$ Hz), 4.97 (d, 1H, H^3, $J = 8.4$ Hz), 5.43 (d, 1H, H^6, $J = 9.5$ Hz), 7.20 (d, 1H, ArH, $J = 8.9$ Hz), 7.24 (d, 1H, ArH, $J = 9.0$ Hz), 7.27–7.30 and 8.05–8.08 (m, 4H, $OC_6H_4NO_2$), 7.40–7.44 (dd, 1H, ArH, $J = 8.8$ Hz and $J = 2.6$ Hz), 7.56 (d, 1H, ArH, $J = 2.5$ Hz), 7.75 (d, 1H, ArH, $J = 2.6$ Hz), 7.88–7.91 (m, 2H, ArH), 8.10 (d, 1H, ArH, $J = 2.3$ Hz), 8.15 (d, 1H, ArH, $J = 2.2$ Hz), 7.46–7.49 and 8.23–

8.27 (m, 8H, 2 × $OC_6H_4NO_2$). ^{13}C NMR (acetone-d_6) δ: 14.7 ($CH_2\underline{C}H_3$), 42.7 ($\underline{C}H_2CH_3$), 53.5, 57.9 (C-2, C-5), 56.67, 56.70, 56.9, 57.2 ($ArOCH_3$ and $Ar'OCH_3$), 65.7, 66.3 (C-1, C-4), 66.6, 68.3 (C-3, C-6), 113.7, 113.8, 114.2, 115.0, 123.3, 123.6, 123.7, 123.8, 124.8, 124.9, 126.3, 129.9, 130.1, 130.5, 130.6, 130.8, 131.5, 131.8, 132.3, 133.0, 133.1, 137.0, 137.2, 146.8, 147.0, 155.1, 155.2, 157.3, 157.4, 158.4, 158.7 (Ar—C), 171.2, 173.4, 174.2, 175.3 (C=O). MS (FAB): 1346 ($M^{+\cdot}$).

The isomer with an intermediate R_f, m.p. 162–167°C. ^{1}H NMR (acetone-d_6) δ: 1.04 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.29 (overlapping q, 8H, 4 × $\underline{CH_2}CH_3$), 3.97 (s, 3H, $ArOCH_3$), 3.98 (s, 3H, $ArOCH_3$), 4.05 (s, 3H, $Ar'OCH_3$), 4.06 (s, 3H, $Ar'OCH_3$), 4.00–4.32 (m, 3H, H^2, H^4 and H^5), 4.40 (d, 1H, H^1, $J = 8.0$ Hz), 4.83 (d, 1H, H^6, $J = 9.2$ Hz), 5.05 (d, 1H, H^3, $J = 6.5$ Hz), 7.16–7.50 (m, ArH), 7.28–7.31 and 8.05–8.08 (m, 4H, $OC_6H_4NO_2$), 7.77 (d, 1H, ArH, $J = 2.5$ Hz), 7.89 (d, 1H, ArH, $J = 2.2$ Hz), 7.95 (dd, 1H, ArH), 8.14 (dd, 1H, ArH), 8.19 (d, 1H, ArH, $J = 2.2$ Hz), 7.46–7.49 and 8.23–8.26 (m, 8H, 2 × $OC_6H_4NO_2$). ^{13}C NMR (acetone-d_6): 14.7 ($CH_2\underline{C}H_3$), 42.7 ($\underline{C}H_2CH_3$), 55.6, 56.9 (C-2, C-5), 56.7 ($ArOCH_3$ and $Ar'OCH_3$), 57.1, 60.5 (C-1, C-4), 65.5, 68.3 (C-3, C-6), 113.6, 113.9, 114.7, 122.9, 123.7, 123.8, 123.9, 125.0, 126.3, 129.3, 129.8, 130.0, 130.5, 132.7, 133.0, 133.2, 137.8, 138.8, 146.8, 147.1, 155.1, 157.2, 158.8 (Ar—C), 172.8, 173.3, 173.9, 175.2 (C=O). MS (FAB): 1346 ($M^{+\cdot}$).

The isomer with a lower R_f, m.p. 188–191°C. ^{1}H NMR (acetone-d_6) δ: 1.06 (t, 12H, 4 × $CH_2\underline{CH_3}$), 3.32 (q, 8H, 4 × CH_2CH_3), 3.99 (s, 6H, 2 × $ArOCH_3$), 4.08 (s, 6H, 2 × $ArOCH_3$), 4.16–4.22 (m, 2H, H^2 and H^5), 4.50 (d, 2H, H^1 and H^4, $J = 7.5$ Hz), 5.14 (d, 2H, H^3 and H^6, $J = 9.2$ Hz), 7.22 (d, 2H, ArH, $J = 8.9$ Hz), 7.34 (d, 2H, ArH, $J = 2.6$ Hz), 7.37–7.41 and 8.13–8.19 (m, 8H, 2 × $OC_6H_4NO_2$), 7.46 (d, 2H, ArH, $J = 8.7$ Hz), 7.60 (d, 2H, ArH, $J = 2.3$ Hz), 7.98 (m, 2H, ArH). ^{13}C NMR (acetone-d_6) δ: 14.7 ($CH_2\underline{C}H_3$), 42.7 ($\underline{C}H_2CH_3$), 52.4 (C-2, C-5), 56.7, 57.0 ($ArOCH_3$ and $Ar'OCH_3$), 66.9 (C-1, C-4), 68.7 (C-3, C-6), 113.7, 114.0, 123.5, 123.8, 125.0, 126.4, 129.1, 129.8, 130.5, 132.9, 147.0, 155.1, 157.2, 158.7 (Ar—C), 173.7, 174.3 (C=O). MS (FAB): 1346 ($M^{+\cdot}$).

REFERENCES

[1] T. Wagner-Jauregg, *Synthesis*, **349** (1976).
[2] S. Rádl, *Aldrichim. Acta*, **30,** 97 (1997).
[3] (a) J. Bailey and N. Moore, *J. Am. Chem. Soc.*, **39**, 279 (1917); (b) J. Bailey and A. McPherson, *J. Am. Chem. Soc.*, **39,** 1322 (1917).
[4] M. Haring and T. Wagner-Jauregg, *Helv. Chim. Acta*, **40,** 852 (1957).
[5] T. Wagner-Jauregg and L. Zirngibl, *Chimia,* **19,** 393 (1965).
[6] S. Abdou, A. Habashy, G. Aziz, and F. Khalifa, *Indian J. Chem.*, **21B,** 522 (1982).
[7] S. Abdou, H. Zaher, S. Selim, and Y. Ibrahim, *Egypt. J. Pharm. Sci.*, **22,** 289 (1981).

[8] A. El-Eman, M. Moustafa, H. Eisa, and M. El-Kerdawy, *Heterocycles*, **24,** 1025 (1986).
[9] R. J. Cremlyn, Chlorosulfonic Acid: A Versatile Reagent (Royal Society of Chemistry, Cambridge, 2002).
[10] L. Weinstein, Sulfonamides in the Pharmacological Basis of Therapeutics (S. L. Goodman and A. Goodman, Ed.) (Macmillan, New York, 1975) 5th ed., p. 113.
[11] N. Anand (Burger's Medicinal Chemistry and Drug Discovery, M. E. Wolff, Ed. (Wiley, New York, 1996) 5th ed., Vol. 2, pp. 527–573.
[12] R. Cremlyn, K. Goulding, K. Yung, and A. Hall, *Pestic. Sci.*, **14,** 158 (1983).
[13] (a) J. Hay, *Pestic. Sci.*, **29,** 247 (1990); (b) H. Brown, *Pestic. Sci.*, **29,** 263 (1990).
[14] R. Cremlyn, F. S. Swinbourn, S. Graham, J. Cavaleiro, F. Domingues, and M. Dias, *Phosphorus, Sulfur and Silicon*, **60,** 57 (1991).
[15] A. Tomé, J. Cavaleiro, F. Domingues, and R. Cremlyn, *Phosphorus, Sulfur, and Silicon*, **79,** 187 (1993).
[16] R. J. Cremlyn, R. M. Ellam, S. Farouk, S. Graham, and A. Williams, *Phosphorus, Sulfur, and Silicon*, **122,** 87 (1997).