Synthesis of 6,7-Dihydro-5*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazines by a C–C Ring Cyclization under Mild Conditions

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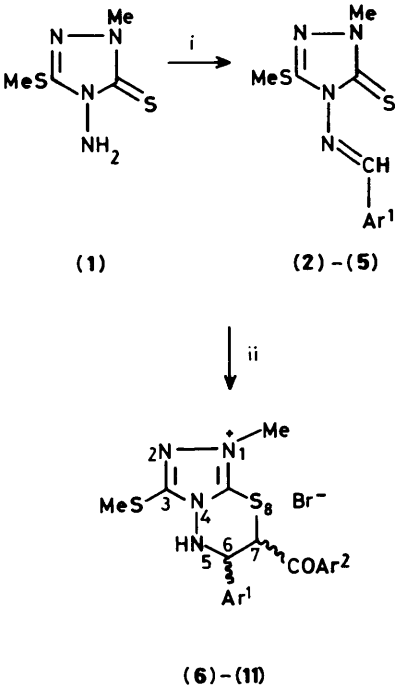
The reaction between Schiff bases derived from 4-amino-2-methyl-5-methylthio-2*H*-1,2,4-triazole-3(4*H*)-thione and phenacyl bromides yields 7-aroyl-6-aryl-6,7-dihydro-1-methyl-3-methylthio-5*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazinium bromides [(**6**)—(**11**)]. The structure of one of these compounds, (**6**) (in which both aryl groups are phenyl), has been determined by *X*-ray crystallography. It incorporates dioxane molecules and the bromide ion is sandwiched between two units. In the 1,3,4-thiadiazinium ring the consecutive hydrogen atoms –N(5)H–C(6)H–C(7)H– are *trans* to each other, the ring showing an E^{C6} conformation. The crystalline *trans* derivatives equilibrate to a 60:40 mixture of *trans* and *cis* 7-aroyl-6-aryl isomers, which have been analysed by ^1H and ^{13}C n.m.r. spectroscopy.

Schiff bases have been shown to be highly useful as synthetic intermediates in preparative heterocyclic chemistry. Addition reactions of Schiff bases with acylating agents lead to the synthesis of penicillins and β-lactams; condensations of homophthalic anhydrides with Schiff bases have been the key steps for synthesizing isoquinolines and indole alkaloids;[1] however, reactions of Schiff bases with active methylene compounds remain almost unexplored in synthetic heterocyclic chemistry; it has only been briefly mentioned that cyclization of α-and β-alkylthio substituted amines possessing a positively charged carbon linked to the nitrogen leads to thiazolidines, thiomorpholines and dihydro-1,4-benzothiazines.[2]

On the other hand, no generally useful procedure for the preparation of the 6,7-dihydro-5*H*-1,2,4-triazolo[3,4-*b*][1,3,4]-thiadiazine ring system has hitherto been reported. The only two examples described are based on the reduction of the C=N double bond of the pre-formed 7*H*-1,2,4-triazolo[3,4-*b*][1,3,4]-thiadiazine ring,[3] available from thiono derivatives of 4-amino-1,2,4-triazole and α-halogenocarbonyl compounds.[4,5] The present paper describes a new and non-reductive general method for the synthesis of 6,7-dihydro-5*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazines, compounds hitherto difficult to obtain, based on the formation of the C(6)–C(7) bond. This type of reaction has not previously been reported in the literature.



Scheme 1. *Reagents:* i, Ar^1CHO; ii, Ar^2COCH_2Br

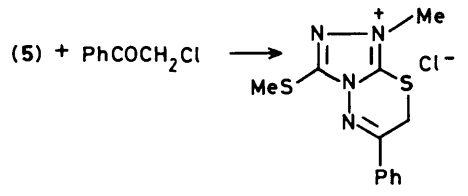
Results and Discussion

Synthesis.—The *N*-aminoheterocycle (**1**) reacted with aromatic aldehydes in the presence of hydrochloric acid to give the corresponding aldimines (**2**)—(**5**) in good yields (Scheme 1). Compounds (**2**)—(**5**) reacted with phenacyl bromides in methanol or ethanol at reflux temperature for 20 h to give the corresponding 7-aroyl-6-aryl- 6,7-dihydro-1-methyl-3-methylthio-5*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazinium bromides (**6**)—(**11**) as crystalline solids in moderate to good yields (Table 1).

The i.r. spectra of compounds (**6**)—(**11**) show absorptions due to the stretching vibration of the NH group at 3 415—3 340 cm^{-1} and to the CO group at 1 687—1 670 cm^{-1}. Mass spectra do not show the molecular ion, the most characteristic fragments being those appearing at *m/z* (*M* − MeBr), (*M* − HBr − S), (Ar^2CO), (Ar^1CN), and ($Ar^1CH{=}CHCOAr^2$).

We also found that compound (**5**) reacted with phenacyl chloride under similar reaction conditions to give a mixture which contained equimolecular amounts of starting material and 6-phenyl-7*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazinium chloride (**12**).

We believe that the conversion (**2**)—(**5**) ⟶ (**6**)—(**11**) involves the initial formation of a triazolium salt which through



(12)

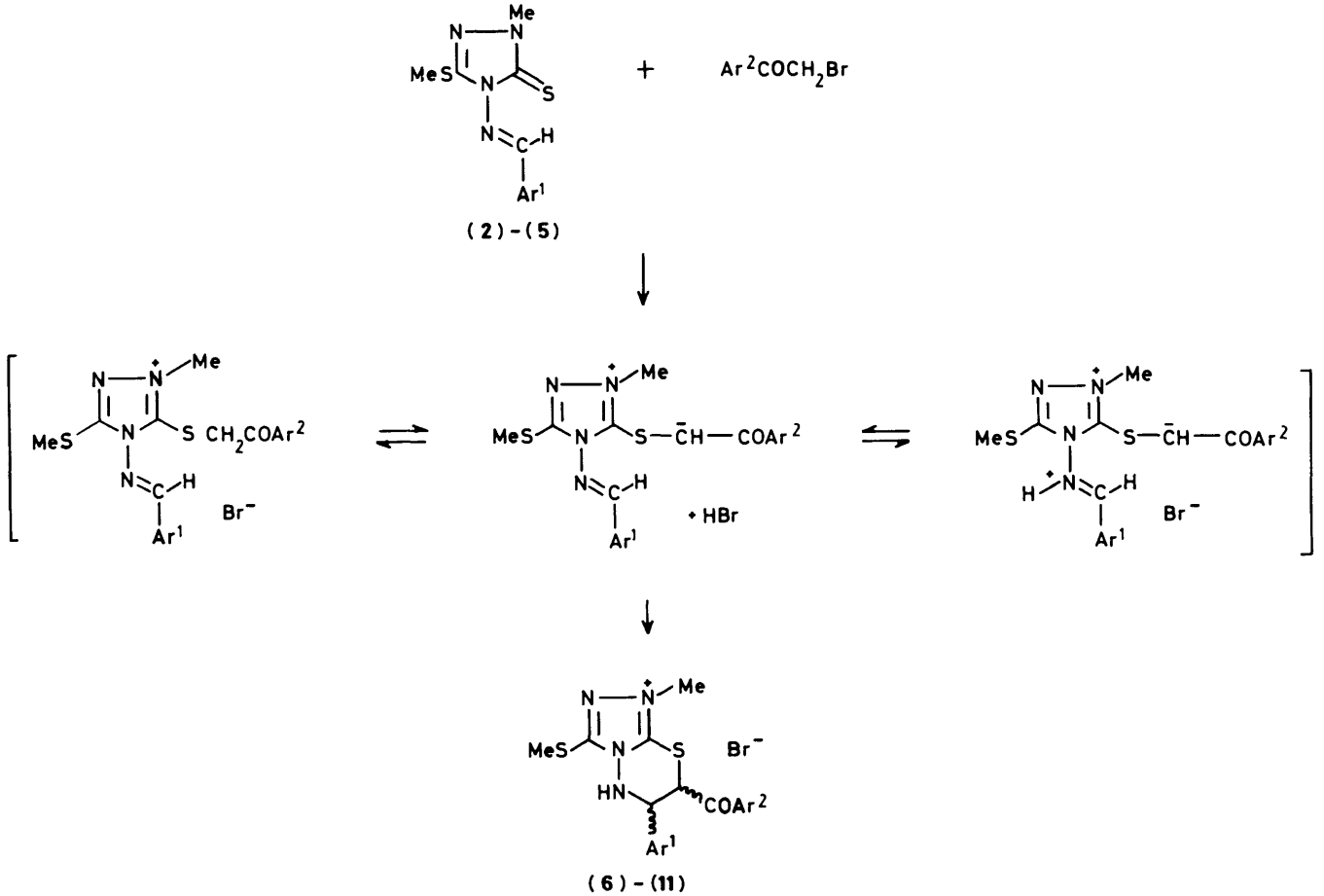
attack of the bromide ion could give a zwitterionic compound as intermediate. The zwitterion undergoes protonation on the aldimine group and subsequent cyclization by intramolecular nucleophilic attack of the carbon atom of the phenacylthio group on the iminium function to give the corresponding 7-aroyl-6-aryl- 6,7-dihydro-1-methyl-3-methylthio-5*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazinium bromides (**6**)—(**11**) (Scheme 2).

The key points of this mechanism are: (i) the presence of an activated methylene group and (ii) the presence of the aldimine group which undergoes protonation to give an iminium salt highly reactive towards nucleophilic attack. This mechanism is similar to that suggested[6] for the reaction of 2-amino-3-phenacyl-1,3,4-thiadiazolium bromides with dimethylformamide dimethyl acetal to give imidazo[2,1-*b*][1,3,4]thiadiazoles.

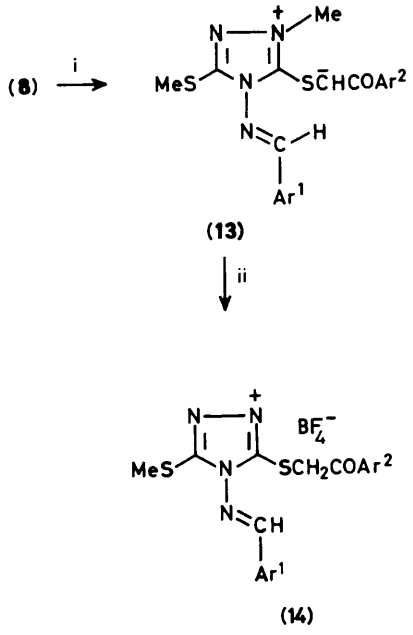
On the other hand, when (**8**; Ar^1 = *p*-MeC_6H_4; Ar^2 = *p*-BrC_6H_4) was treated with potassium carbonate in dichloromethane–water (1:1) solution at room temperature, the

Table 1. Data for aldimines (**2**)—(**5**) and 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazinium bromides (**6**)—(**11**)

Compd.	Crystal form	Yield (%)	M.p. (°C)	Solvent	Found (%) C	H	N	Formula	Required (%) C	H	N
(**2**)	White needles	97	149—150	EtOH	49.85	4.45	21.30	$C_{11}H_{12}N_4S_2$	49.97	4.57	21.19
(**3**)	White prisms	98	158—159	EtOH	44.15	3.80	18.65	$C_{11}H_{11}ClN_4S_2$	44.21	3.71	18.75
(**4**)	White needles	98	156—157	EtOH	48.85	4.85	18.90	$C_{12}H_{14}N_4OS_2$	48.96	4.79	19.03
(**5**)	White prisms	99	138—139	EtOH	51.70	4.95	20.25	$C_{12}H_{14}N_4S_2$	51.77	5.07	20.12
(**6**)	White needles	69	139—140	MeOH	49.30	4.05	12.15	$C_{19}H_{19}BrN_4OS_2$	49.24	4.07	12.09
(**7**)	White needles	57	183—185	MeOH	48.75	4.20	11.25	$C_{20}H_{21}BrN_4O_2S_2$	48.68	4.29	11.35
(**8**)	White prisms	79	162—163	MeOH	43.05	3.55	10.10	$C_{20}H_{20}Br_2N_4OS_2$	43.18	3.62	10.07
(**9**)	White needles	55	100—102	MeOH	48.60	4.25	11.25	$C_{20}H_{21}BrN_4O_2S_2$	48.68	4.29	11.35
(**10**)	White needles	45	160—163	MeOH	45.75	3.50	11.35	$C_{19}H_{18}BrClN_4OS_2$	45.84	3.64	11.25
(**11**)	White needles	55	156—158	MeOH	45.70	3.55	11.20	$C_{19}H_{18}BrClN_4OS_2$	45.84	3.64	11.25



Scheme 2.



Scheme 3. *Reagents:* i, Na_2CO_3, CH_2Cl_2, H_2O; ii, HBF_4

zwitterionic compound (**13**) was isolated as a yellow crystalline solid in 25% yield (Scheme 3).

By acidification of the ethanolic solution of (**13**) with fluoroboric acid at room temperature, the triazolium fluoroborate (**14**) was isolated as a colourless solid in nearly quantitative yield. Attempts to cyclize (**14**) by heating in ethanol failed to give (**8**). This corroborates the role of the bromide ion as the base in the proposed mechanism.

The structural elucidation of compounds (**13**) and (**14**) was accomplished on the basis of spectral and microanalytical data. The i.r. spectrum of compound (**14**) shows a carbonyl band at 1 687 cm^{-1} while this band is absent in (**13**). In addition, (**14**) shows the characteristic bands of the fluoroborate anion. The ^1H n.m.r. spectra of compounds (**13**) and (**14**) show the signals due to the SMe, NMe and aldiminic protons; in compound (**14**) the methylene group appears at δ 5.10, while in (**13**) the methine proton is included within the aromatic multiplet.

When compound (**6**; $Ar^1 = Ar^2 = Ph$) was heated at 200 °C under reduced pressure for 0.5 h, the collected distillate was found to be a mixture of benzaldehyde, benzonitrile, and benzylideneacetophenone.

Physical Properties of Compounds (**6**)—(**11**).—*X-Ray Crystallography of* (**6**). The compound was crystallized from dioxane and two molecules of the solvent are included in the unit cell. The incorporated dioxane molecule, situated at symmetry centres, presents a chair conformation. The bromide ion is sandwiched between two molecules of the compound (see Figure 1); more specifically it is positioned in such a way that Br···H(5) = 2.81(5), Br···H(7) = 2.75(4), Br···N(1) (x, $\frac{1}{2} - y$, $-\frac{1}{2} + z$) = 3.479(2), Br···C(9) (x, $\frac{1}{2} - y$, $-\frac{1}{2} + z$) = 3.442(3) Å and 3.347(1) Å from the least-squares plane through the triazole ring. The double bond character distribution in this ring N(2)–C(3) = 1.315(4), N(1)–C(9) = 1.316(4) Å suggest that the charge is localized around N(1). Then N(5) nitrogen has its hydrogen tetrahedrically bonded angles around N(5) being 110(3), 111(3), and 108.7(2)°. This hydrogen atom is situated *cis* with respect to H(7) and *trans* to H(6), torsion angles being: H(6), C(6), C(7), H(7) = −171(3) and H(5), N(5), C(6), H(6) = +174(4)°. The 1,3,4-thiadiazine ring conforms as an envelope flapping at C(6), the endocyclic torsion angles at the C(9)–S(8), S(8)–C(7), and so on, being −4.5(3), −26.6(2), 63.8(3), −65.3(3), 32.8(4), and 2.1(4)° (Table 2).

N.m.r. Spectroscopy of Compounds (**6**)—(**11**).—The n.m.r. spectra were determined on a Varian XL-300 superconducting spectrometer (^1H n.m.r. at 300 MHz, ^{13}C n.m.r. at 75 MHz). The proton n.m.r. spectra of the recently dissolved crystalline compounds corresponded to a single product, whose stereochemistry, *trans*, agreed with that of the *X*-ray structure. Very slowly in deuteriochloroform and quite rapidly when deuterium oxide was added, the signals of a second diastereoisomer appeared, corresponding to the epimerization of C(7). A 60:40 mixture of *trans* and *cis* isomers was present at equilibrium. The chemical shifts and coupling constants are given in Table 3.

The NH signals appeared as narrow doublets, and were as equally well resolved as those of the CH signals. They dis-

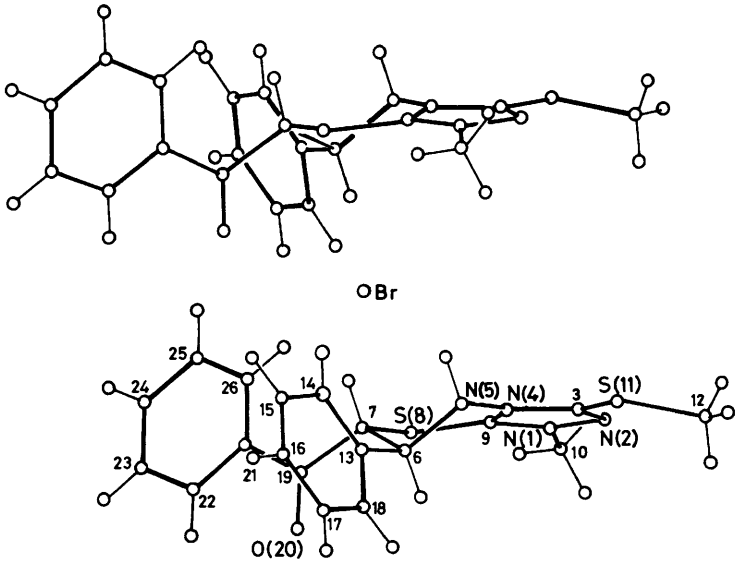


Figure. The structure of compound (**6**)[12] showing the numbering scheme and the sandwiching of the Br ion between the (x, y, z) molecule (below) and the (x, $\frac{1}{2} - y$, $-\frac{1}{2} + z$) molecule (above)

Table 2. Selected geometrical parameters for compound (**6**) (Å and °). ′ Stands for the centrosymmetrical related dioxane atoms ($1-x, -y, -z$), and ″ for the atoms related through ($x, \frac{1}{2}-y, -\frac{1}{2}+z$)

Bond lengths					
S(8)–C(7)	1.842(3)	C(19)–C(21)	1.489(4)	N(1)–C(9)	1.316(4)
S(8)–C(9)	1.710(3)	N(1)–N(2)	1.381(4)	N(2)–C(3)	1.315(4)
S(11)–C(12)	1.787(7)	N(5)–N(4)	1.409(3)	N(4)–C(9)	1.347(4)
S(11)–C(3)	1.725(3)	C(19)–O(20)	1.208(4)	N(4)–C(3)	1.375(4)
C(6)–C(13)	1.511(4)	O(31)–C(30)	1.398(7)	N(5)–C(6)	1.483(4)
C(6)–C(7)	1.536(4)	O(31)–C(32)	1.440(6)	N(1)–C(10)	1.448(5)
C(7)–C(19)	1.526(4)	C(32)–C(30′)	1.480(8)		
Bond angles					
C(12)–S(11)–C(3)	99.2(2)	C(3)–N(4)–N(5)	124.5(2)	S(8)–C(7)–C(19)	104.4(2)
N(2)–C(3)–S(11)	129.6(2)	N(1)–C(9)–S(8)	127.4(2)	C(6)–C(7)–C(19)	113.6(2)
N(4)–C(3)–S(11)	120.7(2)	C(9)–N(4)–N(5)	127.1(2)	C(7)–C(19)–C(21)	117.5(2)
N(2)–N(1)–C(10)	120.8(3)	N(4)–N(5)–C(6)	108.7(2)	C(7)–C(19)–O(20)	120.4(3)
C(9)–N(1)–C(10)	126.8(3)	N(5)–C(6)–C(7)	110.9(2)	C(21)–C(19)–O(20)	122.1(3)
C(9)–N(1)–N(2)	111.8(3)	C(6)–C(7)–S(8)	112.6(2)	C(19)–C(21)–C(26)	122.6(3)
N(1)–N(2)–C(3)	104.6(2)	C(7)–S(8)–C(9)	98.9(1)	C(19)–C(21)–C(22)	118.3(3)
N(2)–C(3)–N(4)	109.6(3)	S(8)–C(9)–N(4)	126.6(2)	C(30)–O(31)–C(32)	108.6(4)
C(3)–N(4)–C(9)	108.0(2)	N(5)–C(6)–C(13)	107.2(2)	O(31)–C(32)–C(30′)	110.2(4)
N(4)–C(9)–N(1)	105.9(2)	C(7)–C(6)–C(13)	111.6(2)	C(32′)–C(30)–O(31)	112.2(4)
N(4)–N(5)–H(5)	110(3)	C(6)–N(5)–H(5)	111(3)		
Torsion angles					
N(2)–C(3)–S(11)–C(12)	−6.3(4)	N(4)–C(9)–S(8)–C(7)	−4.5(3)	C(7)–C(19)–C(21)–C(22)	171.8(3)
S(11)–C(3)–N(4)–N(5)	−2.6(4)	C(9)–S(8)–C(7)–C(6)	−26.6(2)	O(20)–C(19)–C(21)–C(22)	−7.0(4)
C(10)–N(1)–C(9)–S(8)	−4.8(5)	S(8)–C(7)–C(6)–N(5)	63.8(3)	C(13)–C(6)–C(7)–C(19)	−58.4(3)
N(5)–C(6)–C(13)–C(14)	72.1(4)	C(7)–C(6)–N(5)–N(4)	−65.3(3)	C(32′)–C(30)–O(31)–C(32)	−58.0(5)
S(8)–C(7)–C(19)–O(20)	104.4(3)	C(6)–N(5)–N(4)–C(9)	32.8(4)	C(30)–O(31)–C(32)–C(30′)	56.7(5)
S(8)–C(7)–C(19)–C(21)	−74.5(3)	N(5)–N(4)–C(9)–S(8)	2.1(4)	O(31)–C(32)–C(30′)–O(31′)	58.8(6)
H(6)–C(6)–C(7)–H(7)	−171(3)	H(5)–N(5)–C(6)–H(6)	174(4)		
Bond lengths					
Br···N(4)	3.790(2)	Br···C(6)	4.005(3)	Br···C(9)	3.968(3)
Br···N(5)	3.486(3)	Br···C(7)	3.469(3)	Br···S(8)	3.914(1)
Br···H(5)	2.81(5)	N(5)–H(5)···Br	144(4)		
Br···N(1″)	3.439(3)	Br···N(2″)	3.633(3)	Br···C(3″)	3.686(3)
Br···N(4″)	3.617(2)	Br···C(9″)	3.442(3)	Br···C(6″)	3.992(3)

appeared on addition of D_2O, and simultaneously the CH(7) protons exchanged. Addition of trifluoroacetic acid broadened the ABX [H(7)H(6)H(5)] signals, the NH(7) (X) signal being the most sensitive. The most remarkable difference between the diastereoisomers concerns the ABX coupling constants. It is known[7] that the ratio between vicinal coupling constants for different conformers or isomers of the same molecular structure depends only on the torsion angles:

$$\frac{^3J[\mathrm{H(5)H(6)}]\ trans}{^3J[\mathrm{H(5)H(6)}]\ cis} = \frac{11.6}{3.3} = 3.5$$

$$\frac{^3J[\mathrm{H(6)H(7)}]\ trans}{^3J[\mathrm{H(6)H(7)}]\ cis} = \frac{9.2}{2.6} = 3.5$$

According to the Karplus equation[7] these ratios correspond to:

$$trans \longrightarrow = 173.5° \longrightarrow J = 9.10\,J\ trans$$
$$cis \longrightarrow = 53.5° \longrightarrow J = 2.61\,J\ cis \qquad \frac{}{} = 3.5$$

The value for the *trans* isomer is in good agreement with the *X*-ray data (175 and 170°). The value for the *cis* isomer corresponds to a conformation where Ar^1 and **H(6)** are permuted with regard to the *trans* derivative.

Comparison of the chemical shifts of the *cis–trans* pairs (mean values) shows the following effects (δ_{cis}–δ_{trans}).

These effects are difficult to rationalize since there are two free rotating aromatic rings and a carbonyl function that can shield or deshield the protons depending on their conformation.

The ^{13}C n.m.r. chemical shifts are given in Table 4. Some aromatic signals of Ar^1 and Ar^2, separated by less than 1 p.p.m. where only tentatively assigned. The *cis–trans* isomers are very similar; when split, the *trans* isomer signals are always the more intense, even on reaching equilibrium.

Experimental

Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were recorded on a Nicolet FT-5DX spectrometer. ^1H N.m.r. spectra were recorded on a Varian EM-360 A (60 MHz) or on a Varian XL-300 spectrometer (300 MHz) with Me_4Si as internal standard for compounds (**6**)—(**11**). ^{13}C N.m.r. spectra were measured on a Varian XL-300 (75.4 MHz). Electro-impact mass spectra were carried out on a Hewlett-Packard 5993 C spectrometer at an ionization potential of 70 eV. Elemental analyses were performed with a Perkin-Elmer 240 C instrument (the samples were dried *in vacuo* at 100 °C for 36 h).

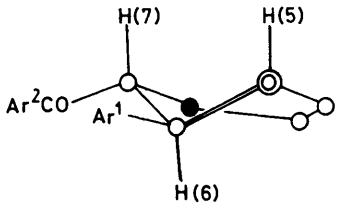
Reagents. All solvents were dried according to standard procedures, distilled and stored over activated molecular sieves

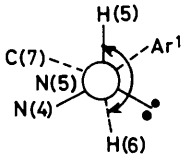
Table 3. ^{1}H N.m.r. data of compounds (**6**)—(**11**) (solvent: $CDCl_3$)

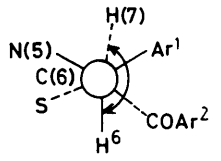
	trans Isomer, δ, *J* (Hz)								*cis* Isomer, δ, *J* (Hz)							
Compound	1-Me	3-MeS	5-H	6-H	7-H	Ar^1		Ar^2	1-Me	3-MeS	5-H	6-H	7-H	Ar^1		Ar^2	
(**6**)	3.90	2.64	8.42(d)	4.53(q)	7.00(d)	H_o	7.68	H_o 7.89	3.85	2.65	9.64(d)	5.63(q)	7.38(d)	H_o	7.14	H_o	8.45
			$J_{5,6}$ 11.6		$J_{6,7}$ 9.2	H_m	7.24	H_m 7.35			$J_{5,6}$ 3.3		$J_{6,7}$ 2.7	H_m	7.18	H_m	7.55
						H_p	7.22	H_p 7.56						H_p	7.24	H_p	7.67
(**7**)	3.89	2.65	8.37(d)	4.55(q)	6.92(d)	H_o	7.67	H_o 7.89	3.84	2.67	9.59(d)	5.66(q)	7.35(d)	H_o	7.14	H_o	8.38
			$J_{5,6}$ 11.5		$J_{6,7}$ 9.3	H_m	7.25	H_m 6.87			$J_{5,6}$ 3.2		$J_{6,7}$ 2.5	H_m	7.19	H_m	7.07
						H_p	7.23	*p*-MeO 3.82						H_p	7.25	*p*-MeO	3.76
(**8**)	3.90	2.65	8.31(d)	4.49(q)	6.98(d)	H_o	7.54	H_o 7.76	3.84	2.66	9.56(d)	5.59(q)	7.36(d)	H_o	7.05	H_o	8.35
			$J_{5,6}$ 11.7		$J_{6,7}$ 9.4	H_m	7.05	H_m 7.52			$J_{5,6}$ 3.2		$J_{6,7}$ 2.7	H_m	6.92	H_m	7.75
						p-Me	2.21							*p*-Me	2.21		
(**9**)	3.89	2.64	8.32(d)	4.52(q)	6.96(d)	H_o	7.62	H_o 7.92	3.84	2.65	9.59(d)	5.63(q)	7.38(d)	H_o	7.02	H_o	8.42
			$J_{5,6}$ 11.6		$J_{6,7}$ 9.1	H_m	6.76	H_m 7.40			$J_{5,6}$ 3.3		$J_{6,7}$ 2.5	H_m	6.74	H_m	7.60
						p-MeO	3.68	H_p 7.55						*p*-MeO	3.72	H_p	7.67
(**10**)	3.90	2.65	8.47(d)	4.57(q)	7.02(d)	H_o	7.68	H_o 7.93	3.85	2.66	9.61(d)	5.65(q)	7.38(d)	H_o	7.06	H_o	8.43
			$J_{5,6}$ 11.5		$J_{6,7}$ 9.2	H_m	7.22	H_m 7.42			$J_{5,6}$ 3.4		$J_{6,7}$ 2.6	H_m	7.20	H_m	7.60
								H_p 7.58								H_p	7.65
(**11**)	3.90	2.65	8.43(d)	4.53(q)	7.04(d)	H_o	7.66	H_o 7.83	3.84	2.66	9.65(d)	5.64(q)	7.39(d)	H_o	7.14	H_o	8.46
			$J_{5,6}$ 11.6		$J_{6,7}$ 9.1	H_m	7.25	H_m 7.33			$J_{5,6}$ 3.3		$J_{6,7}$ 2.6	H_m	7.18	H_m	7.58
						H_p	7.22							H_p	7.24		

Table 4. ^{13}C N.m.r. data for compounds **(6)**—**(11)** (solvent: $CDCl_3$)

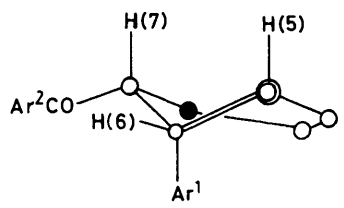
	trans Isomer									*cis* Isomer								
Compd.	1-Me	5-MeS	3-C	6-C	7-C	8a-C	Ar^1	CO	Ar^2	1-Me	5-MeS	3-C	6-C	7-C	8a-C	Ar^1	CO	Ar^2
(6)	37.9	13.7	146.6	62.2	45.1	155.8	133.4 (*i*)	193.4	134.6 (*i*)	37.3	13.8	146.8	62.2	45.1	155.6	134.0 (*i*)		134.0 (*i*)
							129.0 (*o*)		128.0 (*o*)							128.4 (*o*)		128.1 (*o*)
							129.2 (*m*)		129.6 (*m*)							129.0 (*m*)		129.6 (*m*)
							129.6 (*p*)		134.9 (*p*)							129.0 (*p*)		135.0 (*p*)
(7)	37.8	13.4	146.8	62.2	44.7	155.8	133.6 (*i*)	191.3	127.7 (*i*)	37.2	13.8	146.9	62.2	44.7	157.7	134.2 (*i*)		127.1 (*i*)
							128.8 (*o*)		132.0 (*o*)							128.2 (*o*)		131.9 (*o*)
							129.2 (*m*)		114.4 (*m*)							129.0 (*m*)		114.4 (*m*)
							129.3 (*p*)		165.1 (*p*)							128.7 (*p*)		165.2 (*p*)
									55.7 (MeO)									55.7 (MeO)
(8)	37.9	13.6	146.3	61.9	45.1	155.9	130.0 (*i*)	192.9	133.3 (*i*)	37.4	13.6	147.5	61.9	45.1	155.5	130.5 (*i*)	193.3	132.4 (*i*)
							128.6 (*o*)		130.7 (*o*)							126.5 (*o*)		131.2 (*o*)
							129.9 (*m*)		133.0 (*m*)							129.7 (*m*)		132.3 (*m*)
							139.6 (*p*)		130.0 (*p*)							138.9 (*p*)		130.1 (*p*)
							21.1 (Me)									21.0 (Me)		
(9)	37.9	13.6	146.4	61.5	44.7	155.8	125.3 (*i*)	193.5	134.5 (*i*)	37.3	13.7	146.4	61.5	44.7	155.5	125.3 (*i*)	194.2	134.5 (*i*)
							130.1 (*o*)		129.0 (*o*)							129.6 (*o*)		128.0 (*o*)
							114.5 (*m*)		129.3 (*m*)							114.3 (*m*)		129.3 (*m*)
							160.1 (*p*)		134.9 (*p*)							159.6 (*p*)		135.0 (*p*)
							55.2 (MeO)									55.4 (MeO)		
(10)	38.0	13.6	146.3	61.3	44.6	155.9	132.0 (*i*)	193.0	134.2 (*i*)	37.5	13.7	146.3	61.3	44.6	155.9	133.4 (*i*)	194.0	133.5 (*i*)
							130.3 (*o*)		129.2 (*o*)							129.7 (*o*)		129.2 (*o*)
							129.3 (*m*)		129.4 (*m*)							129.6 (*m*)		129.4 (*m*)
							134.2 (*p*)		135.2 (*p*)							133.5 (*p*)		135.4 (*p*)
(11)	37.8	13.6	146.3	62.4	45.2	155.9	132.9 (*i*)	192.6	133.0 (*i*)	37.2	13.6	146.5	62.4	45.2	155.6	133.3 (*i*)	193.0	132.4 (*i*)
							130.7 (*o*)		128.7 (*o*)							130.4 (*o*)		128.6 (*o*)
							129.3 (*m*)		129.3 (*m*)							129.1 (*m*)		129.3 (*m*)
							129.6 (*p*)		141.7 (*p*)							129.0 (*p*)		141.8 (*p*)

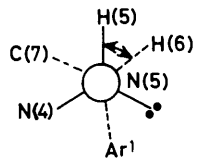


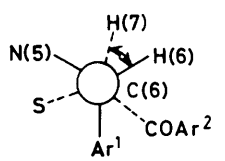




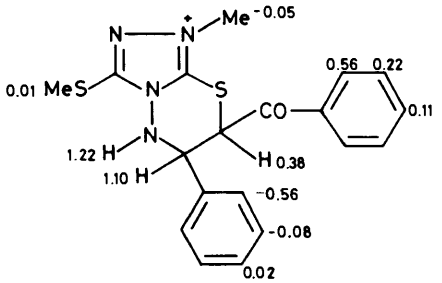
φ[H(5)N(5)C(6)H(6)] ~175° φ[H(6)C(6)C(7)H(7)] ~170°







φ[H(5)N(5)C(6)H(6)] ~55° φ[H(6)C(6)C(7)H(7)] ~50°



4Å. The 4-amino-2-methyl-5-methylthio-2*H*-1,2,4-triazole-3-(4*H*)-thione (**1**) was prepared by the previously reported procedure.[8] Aldehydes and phenacyl bromides were commercially obtained.

X-*Ray Analysis of Compound* (**6**).—*Crystal data.* $C_{19}H_{19}BrN_4OS_2\cdot\frac{1}{2}C_4H_8O_2$, M = 507.46, Monoclinic, $P2_1/c$, a = 17.269 5(15), b = 9.506 7(6), c = 14.221 6(9) Å, β = 90.761(6)°, U = 2 334.6(3) Å^3, D_c = 1.444 g cm^{-3}, Z = 4, μ = 42.60 cm^{-1} (empirical absorption correction[9] applied).

Collection mode. The compound incorporates two molecules of solvent $C_4H_8O_2$, per unit cell. A transparent colourless prismatic sample of dimensions 0.33 × 0.33 × 0.20 mm was used to give the spectra on a Philips PW1100 diffractometer, with Cu-K_α radiation, graphite monochromated with ω/2θ scans and 1.5° of width. No instabilities were observed during collection. Cell parameters were obtained from least-squares fit of the angular positions of 92 reflections with θ up to 45°. Among the 3 967 collected independent reflexions, 3 615 were observed within a 3σ(I) criterion.

Solution and refinement. The structure was solved by means of the Patterson function and refined by least-squares methods on $F_{obs.}$.[10,11] All hydrogen atoms were found in a difference synthesis. Weights were chosen empirically to even the dependence of $\langle\omega\Delta^2F\rangle$ *vs.* $\langle F_o\rangle$ and $\langle\sin\theta/\lambda\rangle$. The final R and R_w factors were 0.042, 0.050 and the final difference synthesis showed no peaks above 0.33 e Å^{-3}. The final atomic co-ordinates are given in Table 5. Anisotropic thermal parameters, hydrogen parameters and other supplementary data are available on request from the Cambridge Crystallographic Data Centre.*

General Procedure for the Preparation of 4-Arylideneamino-2-methyl-5-methylthio-2H-1,2,4-triazole-3(4H)-thiones (**2**)—(**5**).—The appropriate aldehyde (50 mmol) and a catalytic amount of hydrochloric acid were added to a solution of the *N*-aminotriazole (**1**) (8.8 g, 50 mmol) in methanol (10 ml). The resultant solution was heated at reflux temperature for 30 min after which it was cooled. The precipitated solid was filtered off, washed with cold methanol, dried, and crystallized from methanol.

The following compounds were obtained (yields, m.p.s and analyses are given in Table 1). 4-*Benzylideneaminotriazolethione* (**2**) $\nu_{max.}$(Nujol) 1 510, 1 410, 1 315, 760, and 695 cm^{-1}; δ($CDCl_3$) 10.90 (1 H, s, ylidene H), 8.0—7.7 (5 H, m, ArH), 3.85 (3 H, s, NMe), and 2.60 (3 H, s, SMe); *m/z* (%) 264 (M^+, 100), 161 (42), 160 (20), and 103 (10). 4-(p-*Chlorobenzylidene*)-*aminotriazolethione* (**3**) $\nu_{max.}$(Nujol) 1 500, 1 410, 1 327, 1 315, 1 302, 835, and 827 cm^{-1}; δ($CDCl_3$) 10.40 (1 H, s, ylidene H), 7.7—7.1 (4 H, dd, ArH), 3.80 (3 H, s, NMe), and 2.60 (3 H, s, SMe); *m/z* (%) 300 (M^+ + 2, 11), 298 (M^+, 27), 161 (100), 160 (37), 128 (54), and 102 (53). 4-(p-*Methoxybenzylidene*)-*aminotriazolethione* (**4**) $\nu_{max.}$(Nujol) 1 512, 1 465, 1 308, 1 275,

Table 5. Final atomic co-ordinates

Atom	*x/a*	*y/b*	*z/c*
Br	0.140 96(2)	0.220 22(5)	0.063 11(3)
N(1)	0.057 9(1)	0.420 4(3)	0.363 1(2)
N(2)	−0.006 1(1)	0.338 7(3)	0.382 4(2)
C(3)	0.014 1(2)	0.210 6(3)	0.357 8(2)
N(4)	0.087 2(1)	0.212 9(3)	0.320 6(2)
N(5)	0.128 3(1)	0.092 5(3)	0.292 2(2)
C(6)	0.210 4(2)	0.108 1(3)	0.322 3(2)
C(7)	0.248 9(2)	0.230 8(3)	0.270 4(2)
S(8)	0.205 00(4)	0.401 97(7)	0.298 55(6)
C(9)	0.114 2(2)	0.345 5(3)	0.326 9(2)
C(10)	0.061 9(2)	0.565 6(4)	0.393 5(3)
S(11)	−0.035 94(5)	0.054 53(10)	0.368 61(6)
C(12)	−0.116 7(3)	0.116 0(7)	0.434 3(6)
C(13)	0.250 3(2)	−0.029 9(3)	0.302 5(2)
C(14)	0.266 5(2)	−0.072 6(4)	0.211 6(3)
C(15)	0.305 3(3)	−0.200 0(4)	0.196 8(3)
C(16)	0.327 1(2)	−0.281 8(4)	0.271 5(4)
C(17)	0.310 5(3)	−0.241 5(4)	0.361 6(4)
C(18)	0.272 1(2)	−0.115 3(4)	0.376 8(3)
C(19)	0.334 5(2)	0.249 2(3)	0.295 5(2)
O(20)	0.361 2(1)	0.197 3(3)	0.366 4(2)
C(21)	0.382 3(2)	0.334 8(3)	0.230 6(2)
C(22)	0.457 7(2)	0.368 0(3)	0.258 3(2)
C(23)	0.503 2(2)	0.454 8(4)	0.204 0(3)
C(24)	0.472 9(2)	0.509 5(4)	0.120 8(3)
C(25)	0.399 4(2)	0.474 9(4)	0.091 4(3)
C(26)	0.353 4(2)	0.387 6(3)	0.145 3(2)
O(31)	0.551 5(2)	0.106 9(3)	−0.028 2(2)
C(30)	0.495 6(4)	0.129 4(5)	0.040 5(4)
C(32)	0.573 4(3)	−0.039 2(5)	−0.026 4(4)

* See Instructions for Authors (1987), para. 5.6.3., *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1.

1 166, 832, and 668 cm^{-1}; δ($CDCl_3$) 10.80 (1 H, s, ylidene H), 8.2—7.1 (4 H, dd, ArH), 4.00 (3 H, s, OMe), 3.90 (3 H, s, NMe), and 2.60 (3 H, s, SMe); *m/z* (%) 294 (M^+, 26), 161 (100), 160 (27), 134 (13), 133 (59), 128 (37), and 102 (28). 4-(p-*Methylbenzylidene*)*aminotriazolethione* (**5**) $\nu_{max.}$(Nujol) 1 506, 1 308, 1 178, 1 039, 815, and 770 cm^{-1}; δ($CDCl_3$) 10.80 (1 H, s, ylidene H), 8.1—7.3 (4 H, dd, ArH), 3.90 (3 H, s, NMe), 2.60 (3 H, s, SMe), and 2.45 (3 H, s, ArMe); *m/z* (%) 278 (M^+, 100), 161 (27), 160 (11), 117 (10), and 102 (8).

General Procedure for the Preparation of 7-*Aroyl*-6-*aryl*-6,7-*dihydro*-1-*methyl*-3-*methylthio*-5H-1,2,4-*triazolo*[3,4-b]-[1,3,4]*thiadiazinium Bromides* (**6**)—(**11**).—The appropriate phenacyl bromide (10 mmol) was added to a solution of the corresponding aldimine (**2**)—(**5**) (10 mmol) in hot methanol (25 ml) and the reaction mixture refluxed for 20 h. The solution was cooled to room temperature, diethyl ether (10 ml) was added, and the mixture was left at 0 °C overnight. The precipitated solid was filtered off, dried, and recrystallized.

The following compounds were obtained (yields, m.p.s and analyses are given in Table 1): *Compound* (**6**; Ar^1 = Ph, Ar^2 = Ph) $\nu_{max.}$(Nujol) 3 347, 1 687, 1 483, 1 200, 1 036, 764, and 676 cm^{-1}; *m/z* (%) 368 (*M* − MeBr, 5), 350 (*M* − HBr − S, 5), 264 (25), 208 (PhCH=CHCOPh, 17), 161 (41), 105 (PhCO, 100), 103 (PhCN, 32), and 77 (62); *Compound* (**7**; Ar^1 = Ph, Ar^2 = *p*-$MeOC_6H_4$) $\nu_{max.}$(Nujol) 3 370, 1 670, 1 596, 1 278, 1 172, 719, and 702 cm^{-1}; *m/z* (%) 398 (*M* − MeBr, 10), 380 (*M* − HBr − S, 7), 292 (5), 238 ($PhCH{=}CHCOC_6H_4OMe$, 10), 135 ($MeOC_6H_4CO$, 100), 103 (PhCN, 22), and 77 (26); *Compound* (**8**; Ar^1 = *p*-MeC_6H_4, Ar^2 = *p*-BrC_6H_4) $\nu_{max.}$(Nujol) 3 381, 1 682, 1 585, 1 206, 1 030, 1 002, 889, and 809 cm^{-1}; *m/z* (%) 462 (17), 460 (*M* − MeBr, 19), 444 (100), 442 (*M* − HBr − S, 94), 342 (71), 340 (64), 302 (5), 300 ($MeC_6H_4CH{=}CHCOC_6H_4Br$, 10), 185 (44), 183 ($BrC_6H_4CO$, 51), 155 (11), 117 ($MeC_6H_4CN$, 12), and 91 (5); *Compound* (**9**; Ar^1 = *p*-$MeOC_6H_4$, Ar^2 = Ph) $\nu_{max.}$(Nujol) 3 415, 1 670, 1 518, 1 251, 883, 838, and 725 cm^{-1}; *m/z* (%) 398 (*M* − MeBr, 22), 380 (*M* − HBr − S, 30), 262 (20), 238 ($MeOC_6H_4CH{=}CHCOPh$, 7), 161 (28), 133 ($MeOC_6H_4CN$, 25), 105 (PhCO, 100), and 77 (32); *Compound* (**10**; Ar^1 = *p*-ClC_6H_4, Ar^2 = Ph) $\nu_{max.}$(Nujol) 3 370, 1 687, 1 484, 1 291, 1 093, 826, 766, and 694 cm^{-1}; *m/z* (%) 404 (4), 402 (*M* − MeBr, 13), 386 (10), 384 (*M* − HBr − S, 30), 242 ($ClC_6H_4CH{=}CHCOPh$, 5), 162 (5), 160 (17), 139 (4), 137 (ClC_6H_4CN, 11), 105 (PhCO, 100), and 77 (46). *Compound* (**11**; Ar^1 = Ph, Ar^2 = *p*-ClC_6H_4) $\nu_{max.}$(Nujol) 3 341, 1 682, 1 591, 1 483, 1 291, 1 093, 883, 792, 707, and 702 cm^{-1}; *m/z* (%) 404 (3), 402 (*M* − MeBr, 10), 386 (5), 384 (*M* − HBr − S, 15), 298 (7), 296 (20), 244 (8), 242 ($PhCH{=}CHCOC_6H_4Cl$, 24), 163 (17), 161 (52), 141 (33), 139 (ClC_6H_4CO, 100), 111 (41), 103 (PhCN, 28), and 77 (18).

1-*Methyl*-3-*methylthio*-6-*phenyl*-7H-1,2,4-*triazolo*[3,4-b]-[1,3,4]*thiadiazinium Chloride* (**12**).—Phenacyl chloride (0.55 g, 3.59 mmol) was added to a solution of (**5**) (1.0 g, 3.59 mmol) in hot methanol (50 ml), and the reaction mixture refluxed for 20 h. The solution was cooled and the precipitated solid filtered off, dried, and recrystallized from methanol to give starting material (0.4 g, 40%). To the mother liquors of the original solution, diethyl ether (10 ml) was added and the resultant solution left at 0 °C overnight; the precipitated solid was filtered off, dried, and crystallized from methanol–ether to give (**12**) (0.45 g, 40%) as white needles, m.p. 202—204 °C (Found: C, 45.95; H, 4.1; N, 18.05. $C_{12}H_{13}ClN_4S_2$ requires C, 46.07; H, 4.19; N, 17.91%); $\nu_{max.}$(Nujol) 1 550, 1 480, 1 365, 1 320, 1 290, 1 195, 1 170, 920, 868, 800, 770, 690, 680, and 670 cm^{-1}; δ[$(CD_3)_2SO$] 8.5—7.4 (5 H, m, ArH), 4.80 (2 H, s, CH_2), 4.15 (3 H, s, NMe), and 2.80 (3 H, s, SMe); *m/z* (%) 276 (*M* − HCl, 22), 275 (13), 262 (14), 244 (31), 243 (10), 175 (11), 174 (8), 173 (21), 172 (50), 161 (15), 159 (10), 142 (18), 129 (25), 128 (15), 127 (17), 126 (13), 119 (10), 118 (13), 117 (15), 104 (35), 103 (43), 102 (63), 101 (18), 98 (13), 96 (100), 94 (99), 82 (67), 80 (62), and 77 (73).

Treatment of Compound (**8**) *with Potassium Carbonate.*—Potassium carbonate (0.27 g, 20 mmol) in water (25 ml) was added to a well stirred solution of (**8**) (1.10 g, 20 mmol) in dichloromethane (25 ml). The reaction mixture was stirred at room temperature for 4 h after which the organic layer was separated, washed with water (3 × 20 ml), and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude product was crystallized from dichloromethane–diethyl ether (1:3) (20 ml) to give (**13**) (0.20 g, 25%) as yellow prisms, m.p. 143—146 °C (Found: C, 50.4; H, 3.95; N, 11.7. $C_{20}H_{19}BrN_4OS_2$ requires C, 50.53; H, 4.03; N, 11.78%); $\nu_{max.}$(Nujol) 1 585, 1 557, 1 494, 1 319, 1 092, 1 007, 871, 837, 815, 770, 747, 724, 696, and 667 cm^{-1}; δ($CDCl_3$) 8.60 (1 H, s, ylidene H), 8.1—7.2 (9 H, m, ArH and SCH=), 4.00 (3 H, s, NMe), 2.60 (3 H, s, SMe), and 2.45 (3 H, s, ArMe); *m/z* (%) 442 (12), 440 (11), 327 (42), 325 (43), 299 (33), 297 (33), 185 (100), 183 (100), 157 (31), 155 (30), 117 (28), 116 (19), 91 (5), and 89 (6).

Protonation of (**13**) *with Fluoroboric Acid.*—A slight excess of fluoroboric acid was added to a solution of (**13**) (1.13 g, 2 mmol) in ethanol (10 ml), and the mixture refluxed for 5 min. The solution was cooled to room temperature, ether (5 ml) was added and the precipitated solid was filtered off, dried, and recrystallized from ethanol–ether to give (**14**) (1.20 g, 90%) as colourless prisms, m.p. 185—186 °C (Found: C, 42.54; H, 3.63; N, 9.88. $C_{20}H_{20}BBrF_4N_4OS_2$ requires C, 42.65; H, 3.58; N, 9.95%); $\nu_{max.}$(Nujol) 1 687, 1 602, 1 585, 1 325, 1 059, 991, 855, 821, 787, 758, and 725 cm^{-1}; δ($CDCl_3$) 9.10 (1 H, s, ylidene H), 8.3—7.3 (8 H, m, ArH), 5.20 (2 H, s, $-SCH_2CO-$), 4.20 (3 H, s, NMe), 2.80 (3 H, s, SMe), and 2.50 (3 H, s, ArMe); *m/z* (%) 442 (12), 440 (12), 357 (24), 356 (19), 326 (45), 324 (100), 322 (70), 299 (47), 297 (5), 185 (62), 183 (73), 155 (15), 119 (31), 117 (66), and 91 (22).

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