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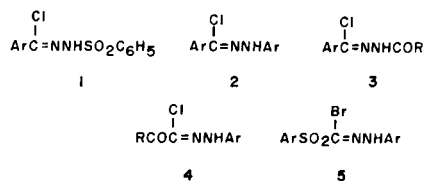
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Bromination of 1-arylsulfonyl-1,2-propanedione-1-aryl-hydrazones **7** in a mixture of acetic acid and acetic anhydride in the presence of sodium acetate gave *N*-aryl-*C*-arylsulfonylformohydrazidoyl bromides **5**. Treatment of **5** with dibenzoylmethane, acetylacetone, ethyl acetoacetate and ethyl benzoylacetate in ethanol in the presence of sodium ethoxide yielded the pyrazole derivatives **8-11**, respectively. Reaction of **5** with potassium thiocyanate afforded the thiadiazoline derivative **14**. The bromides **5** also react with nucleophiles such as morpholine, piperidine, phenoxide, thiophenoxide and benzenesulfinate anions to give the corresponding substitution products **19-23**, respectively. The structures of the products **8-23** were assigned and confirmed on the basis of their spectral and elemental analyses, their chemical behaviour and alternate synthesis wherever possible.

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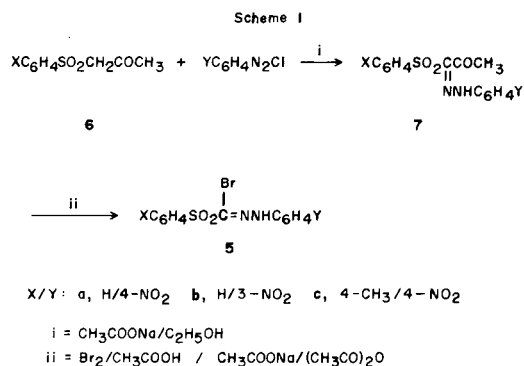
Introduction.

Hydrazidoyl halides **1** carrying an *N*-phenylsulfonyl group were reported to exhibit chemical behaviour different from their *N*-aryl or *N*-acyl analogs **2** and **3**, respectively [2,4]. This difference was rationalized in terms of the ease with which an arylsulfonyl group can be eliminated as a cation [5]. Also, the presence of an electron-withdrawing group at the *C*-atom of hydrazidoyl molecule as in **4** was reported to destabilize the corresponding intermediates involved in the reactions studied and thus render their reactivity to be different from *C*-aryl counterparts **2** [5]. These facts prompted us to investigate the reactions of *C*-arylsulfonylhydrazidoyl halides in order to examine the effect of the presence of arylsulfonyl group at the *C*-atom of the hydrazidoyl molecule on its reactivity. To our knowledge, there has been no published information concerning the synthesis and the reactions of such halides until recently. In this paper, we wish to report the synthesis of a series of three of *N*-aryl-*C*-arylsulfonylformohydrazidoyl bromides **5a-c** and the results of their reactions with selected dipolarophiles and nucleophiles.



Results and Discussion.

Bromination of hydrazones **7a-c**, prepared by coupling of arylsulfonylacetones **6a-b** with diazotized *p*-nitro- and *m*-nitroanilines, afforded the corresponding hydrazidoyl bromides **5a-c** respectively (Scheme 1). The reaction was carried out at room temperature in anhydrous conditions



using sodium acetate in a mixture of glacial acetic acid and acetic anhydride. Structural assignments for these novel hydrazidoyl bromides are based on their elemental analyses and spectra. For example, pmr spectra of **5a-c** revealed the presence of NH singlet near 11.4 ppm. Infrared spectra showed the following characteristic bands: 3290-3260 (NH), 1610-1590 (C=N), 1320 and 1135 (SO₂) cm⁻¹.

Treatment of **5** with equimolecular amounts of the sodi-

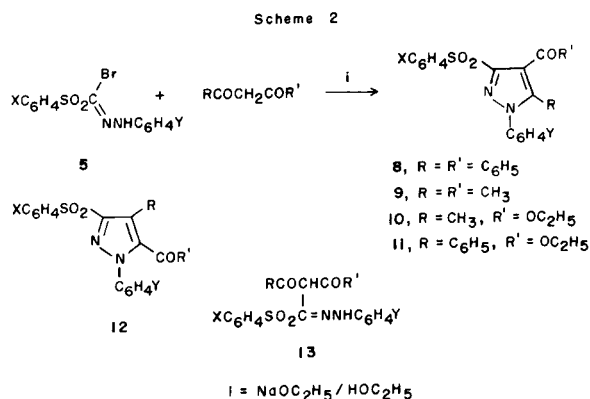


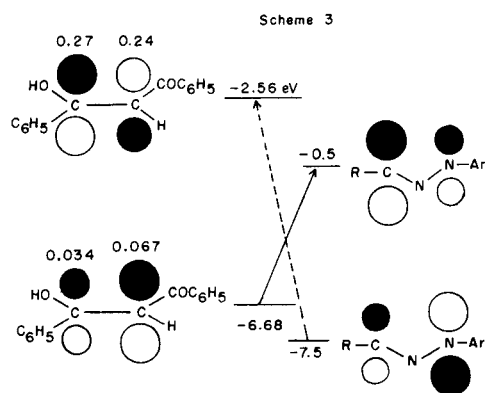
Table 1

Compound No.	Mp °C	Molecular Formula	Analysis %		
			C	Calcd. (Found) H	N
5a	176	C ₁₃ H ₁₀ BrN ₃ O ₄ S	40.64 (40.42)	2.62 (2.91)	10.93 (10.71)
5b	154	C ₁₃ H ₁₀ BrN ₃ O ₄ S	40.64 (40.51)	2.62 (2.81)	10.93 (10.87)
5c	173	C ₁₄ H ₁₂ BrN ₃ O ₄ S	42.22 (42.01)	3.04 (2.89)	10.55 (10.31)
7a	220	C ₁₅ H ₁₃ N ₃ O ₅ S	51.87 (51.78)	3.77 (3.70)	12.09 (12.10)
7b	207	C ₁₅ H ₁₃ N ₃ O ₅ S	51.87 (51.72)	3.77 (3.72)	12.09 (12.01)
7c	216	C ₁₆ H ₁₅ N ₃ O ₅ S	53.18 (53.20)	4.18 (4.20)	11.63 (11.58)
8a	220	C ₂₈ H ₁₉ N ₃ O ₅ S	66.00 (66.20)	3.76 (3.61)	8.28 (8.30)
8c	214	C ₂₉ H ₂₁ N ₃ O ₅ S	66.53 (66.41)	4.04 (4.12)	8.02 (8.24)
9a	196	C ₁₈ H ₁₅ N ₃ O ₅ S	56.10 (55.98)	3.92 (3.71)	10.90 (10.81)
9b	159	C ₁₈ H ₁₅ N ₃ O ₅ S	56.10 (56.21)	3.92 (3.72)	10.90 (10.85)
9c	167	C ₁₉ H ₁₇ N ₃ O ₅ S	57.13 (57.21)	4.29 (4.31)	10.52 (10.37)
10a	200	C ₁₉ H ₁₇ N ₃ O ₆ S	54.93 (54.91)	4.12 (4.21)	10.12 (10.11)
10c	160	C ₂₀ H ₁₉ N ₃ O ₆ S	55.94 (55.67)	4.46 (4.38)	9.78 (9.51)
11a	196	C ₂₄ H ₁₉ N ₃ O ₆ S	60.37 (60.01)	4.01 (4.00)	8.80 (8.92)

Table 2

Compound No.	Mp °C	Molecular Formula	Analysis %		
			C	Calcd. (Found) H	N
14a	147	C ₁₄ H ₁₀ N ₄ O ₄ S ₂	46.41 (46.30)	2.78 (2.61)	15.46 (15.31)
14b	151	C ₁₄ H ₁₀ N ₄ O ₄ S ₂	46.41 (46.35)	2.78 (2.61)	15.46 (15.22)
15a	110	C ₁₄ H ₉ N ₅ O ₅ S ₂	42.96 (42.77)	2.32 (2.29)	17.89 (17.70)
15b	112	C ₁₄ H ₉ N ₅ O ₅ S ₂	42.96 (42.85)	2.32 (2.19)	17.89 (17.81)
16a	74	C ₁₄ H ₉ N ₅ O ₅ S ₂	46.28 (46.11)	2.49 (2.33)	11.56 (11.41)
16b	136	C ₁₄ H ₉ N ₅ O ₅ S ₂	46.28 (46.14)	2.49 (2.41)	11.56 (11.31)
17a	204	C ₁₆ H ₁₂ N ₄ O ₅ S ₂	47.52 (47.41)	2.99 (2.77)	13.85 (13.75)
17b	196	C ₁₆ H ₁₂ N ₄ O ₅ S ₂	47.52 (47.81)	2.99 (3.01)	13.85 (13.92)
18a	206	C ₂₁ H ₁₄ N ₄ O ₅ S ₂	54.06 (53.91)	3.03 (3.05)	12.01 (12.20)
18b	181	C ₂₁ H ₁₄ N ₄ O ₅ S ₂	54.06 (54.32)	3.03 (3.12)	12.01 (12.11)

um salts of dibenzoylmethane, acetylacetone, ethyl acetoacetate and ethyl benzoylacetate in ethanol at room temperature yielded the pyrazole derivatives **8-11**, respectively (Scheme 2). The structures of these products followed their spectral and elemental analyses (Tables 1 and 4). Although the exact course of this reaction was not explored, it probably involved the cycloaddition of the corresponding *N*-aryl-*C*-arylsulfonylformonitrile imine, generated *in situ* from **5** by the action of sodium ethoxide or sodium enolate, to the carbon-carbon double bond of the enol tautomer of the active methylene compound used. The cycloadduct formed seems to lose the elements of water as it is formed to give the corresponding pyrazole derivative. In all cases examined, neither the other regioisomeric products of type **12**, nor the acyclic hydrazone derivatives of type **13** have been identified in the reaction mixture as evidenced by tlc analysis.

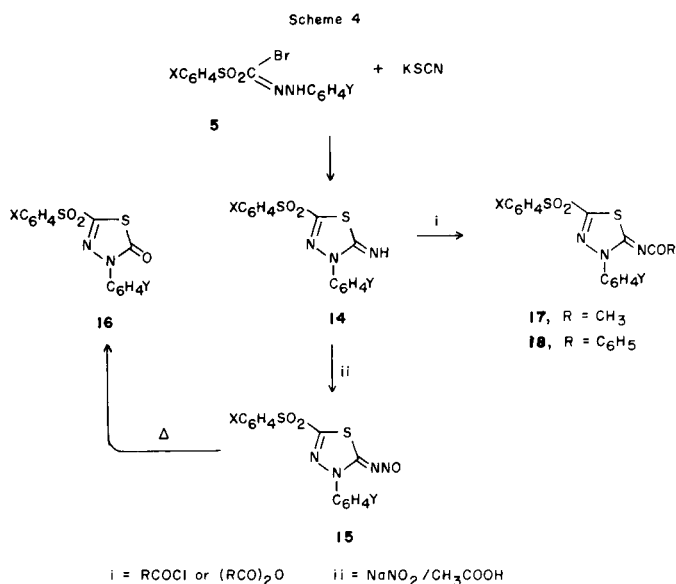


The unique regioselectivity observed in these reactions may be explained as follows. The FMO coefficients and energies of the enol tautomer of dibenzoylmethane, taken as a typical example of the studied series of active methylene compounds, were calculated by the Extended HMO method. The results are summarized in Scheme 3. Such results, by considering the data reported for benzalacetophenone [6], are in agreement with the qualitative prediction that an electron donating substituent (OH group in this case) tends to raise the HOMO energy and decrease the HOMO orbital coefficient at the site of attachment [7,8]. Furthermore, the introduction of electron-withdrawing groups on the termini of a nitrile imine is reported to lower the LUMO energy and decrease the LUMO orbital coefficients at the sites of attachment [7]. Accordingly, the relative order of magnitude of the LUMO orbital coefficients at the cationic and anionic centers of *e.g.* *N*-(*p*-nitrophenyl)-*C*-arylsulfonylformonitrile imine will be qualitatively similar to that in formonitrile imine [8]. Consequently, as shown in Scheme 3, the energetically favourable LUMO(Dipole)-HOMO(Dipolarophile) interaction gives the regioisomer **8** as the predominant product.

The reaction of **5a,b** with thiocyanate anion in boiling ethanol gave 2-phenylsulfonyl-4-aryl-5-imino- Δ^2 -1,3,4-thiadiazolines **14a,b** respectively (Scheme 4). The structures of the latter products were deduced from their spectra and elemental analyses. For example, the infrared spectra of **14** revealed no bands in the 2200-2000 cm^{-1} region due to a free thiocyanato group. However, they exhibit bands at 3320 (imino NH), 1620 (C=N), 1320 and 1135 (SO_2) cm^{-1} .

Table 3

Compound No.	Mp, °C	Molecular Formula	Analysis %		
			C	H	N
19a	160	$\text{C}_{17}\text{H}_{18}\text{N}_4\text{O}_5\text{S}$	52.29	4.65	14.35
			(52.44)	(4.55)	(14.45)
19b	157	$\text{C}_{17}\text{H}_{18}\text{N}_4\text{O}_5\text{S}$	52.29	4.65	14.35
			(52.30)	(4.70)	(14.41)
20a	161	$\text{C}_{18}\text{H}_{20}\text{N}_4\text{O}_4\text{S}$	55.66	5.19	14.42
			(55.70)	(5.20)	(14.19)
20c	160	$\text{C}_{19}\text{H}_{22}\text{N}_4\text{O}_4\text{S}$	56.70	5.51	13.92
			(56.41)	(5.38)	(13.59)
21a	145	$\text{C}_{19}\text{H}_{18}\text{N}_3\text{O}_5\text{S}$	57.42	3.80	10.57
			(57.31)	(3.77)	(10.32)
22a	174	$\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_4\text{S}_2$	56.19	4.01	9.83
			(55.97)	(3.97)	(9.61)
22b	137	$\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_4\text{S}_2$	55.19	3.66	10.16
			(55.22)	(3.53)	(10.14)
22c	171	$\text{C}_{21}\text{H}_{19}\text{N}_3\text{O}_4\text{S}_2$	57.12	4.34	9.52
			(57.21)	(4.31)	(9.21)
23a	182	$\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_6\text{S}_2$	52.28	3.73	9.14
			(52.17)	(3.62)	(9.31)
23b	201	$\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_6\text{S}_2$	51.23	3.29	9.43
			(51.40)	(3.29)	(9.60)
23c	182	$\text{C}_{21}\text{H}_{19}\text{N}_3\text{O}_6\text{S}_2$	53.26	4.04	8.87
			(53.12)	(4.00)	(8.78)



The chemical reactions of **14** outlined in Scheme 4 also substantiate the assigned structures and exclude the possibility of the isomeric 5-mercapto-1,2,4-triazoles. Thus, nitrosation of **14** with sodium nitrite in acetic acid gave the *N*-nitroso derivatives **15** which yield the corresponding thiadiazolin-5-one derivatives **16** upon thermolysis in xylene. The products **14** undergo also acylation with acetic anhydride or with benzoyl chloride in pyridine and gave the *N*-acetyl and *N*-benzoyl derivatives **17** and **18**, respectively.

The exclusive formation of **14** in the reaction of **5** with potassium thiocyanate substantiates the foregoing conclusion that the larger coefficient in the LUMO of *N*-(*p*-nitrophenyl)-*C*-arylsulfonylformonitrile imine is at the *C*-atom.

This is because of the following. As the thiocyanate anion is an electron-rich dipolarophile, its reaction with the electrophilic *N*-aryl-*C*-arylsulfonylformonitrile imine derived from **5** is expected to be LUMO(Dipole)-HOMO(-SCN) controlled. Furthermore, as the HOMO(SCN⁻) has the larger orbital coefficient on the sulfur atom [9], the formation of **14** indicates that the larger orbital coefficient in the LUMO of the nitrile imine derived from **5** is at the cationic center, *i.e.* the carbon atom carrying the arylsulfonyl group, in agreement with the foregoing conclusion.

The hydrazidoyl bromides **5a-c** undergo readily nucleophilic substitutions at room temperature when treated with nucleophiles. For example, treatment of **5a,b** with equivalent amounts of morpholine and piperidine in ethanol yielded the corresponding amidrazones **19** and **20** respectively in 80-90%. Also, **5a-c** reacted with phenoxide, thiophenoxide and benzenesulfinate anions in ethanol to

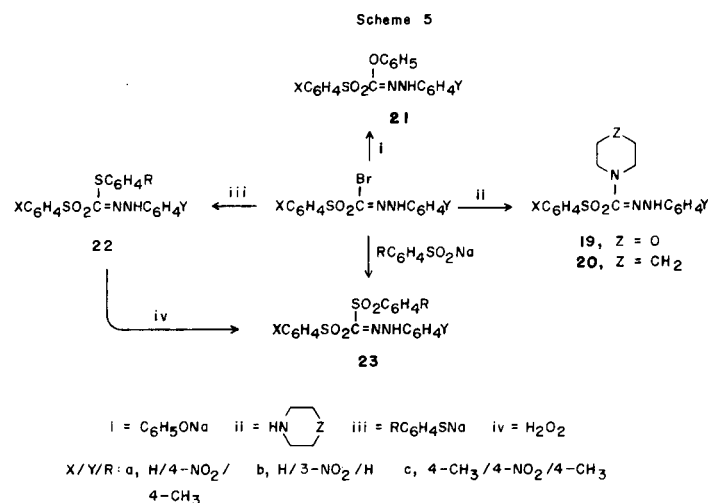


Table 4

Characteristic IR Bands and PMR Signals of Some of the Products Studied

Compound	¹ H NMR (deuteriochloroform), ppm	IR (potassium bromide) cm ⁻¹
8c	2.6 (s, 3H), 7.4-8.4 (m, 8H)	1680, 1620, 1600, 1315, 1135
9a	2.6 (s, 3H), 2.82 (s, 3H), 7.3-8.4 (m, 9H)	1680, 1600, 1318, 1140
9b	2.45 (s, 3H), 2.81 (s, 3H), 7.0-8.3 (m, 9H)	1677, 1605, 1317, 1145
9c	2.5 (s, 3H), 2.65 (s, 3H), 7.1-8.4 (m, 8H)	1680, 1615, 1600, 1320, 1135
10a	2.65 (s, 3H), 1.4 (t, 3H, J = 7 Hz), 4.5 (q, 2H, J = 7 Hz), 7.6-8.6 (m, 9H)	1720, 1620, 1600, 1318, 1137
10c	2.5 (s, 3H), 2.65 (s, 3H), 1.4 (t, 3H, J = 7 Hz), 4.5 (q, 2H, J = 7 Hz), 7.4-8.4 (m, 8H)	1715, 1620, 1600, 1315, 1140
14a	7.2-8.4 (m)	3320, 1625, 1600, 1320, 1135
15a	7.0-8.4 (m)	1620, 1600, 1320, 1140
16a	7.1-8.3 (m)	1710, 1615, 1600, 1325, 1145
17a	2.2 (s, 3H), 7.0-8.2 (m, 9H)	1645, 1615, 1600, 1319, 1137
18a	7.4-8.4 (m)	1635, 1615, 1600, 1320, 1135
19a	3.4 (two d, 4H), 3.85 (two d, 4H), 6.8-8.2 (m, 10H)	3240, 1615, 1600, 1315, 1140
21a	11.2 (s, 1H), 7.2-8.3 (m, 14H)	3250, 1600, 1320, 1220, 1135
22a	2.54 (s, 3H), 7.3-8.2 (m, 13H) 11.1 (s, 1H)	3230, 1618, 1600, 1330, 1140
22c	2.60 (s, 3H), 2.5 (s, 3H), 7.1-8.3 (m, 12H), 11.0 (s, 1H)	3210, 1600, 1320, 1140
23a	2.65 (s, 3H), 7.3-8.4 (m, 13H), 11.5 (s, 1H)	3240, 1600, 1317, 1134
23c	2.6 (s, 6H), 7.5-8.4 (m, 12H), 11.6 (s, 1H)	3250, 1600, 1320, 1140

afford the corresponding substitution products **21-23** respectively. Oxidation of the thiohydrazidate ester, obtained from **5** and thiophenoxide anion, with hydrogen peroxide in acetic acid yielded the hydrazone derivatives **23** (Scheme 5). Structural assignments for the products **19-23** were based on their elemental and spectral analyses (Tables 3 and 4).

The present work establishes that C-arylsulfonylformohydrazidoyl halides are eminantly suitable intermediates for synthesis of heterocyclic and acyclic compounds.

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. The ir (potassium bromide) and nmr (deuteriochloroform): spectra were recorded with Perkin Elmer 257 spectrophotometer and a Varian T60-A spectrometer, respectively. The microanalyses were performed by Galbraith Laboratory, Knoxville, Tennessee 37916, USA. Phenylsulfonylacetone and *p*-tolylsulfonylacetone were prepared as previously described [10].

Preparation of 3-Arylsulfonyl-2,3-propanedione-3-arylhyazones **7a-c**.

To a solution of the appropriate arylsulfonylacetone (0.01 mole) in ethanol (50 ml) were added sodium acetate (2 g) and aqueous sodium hydroxide solution (1 *M*, 10 ml). The mixture was chilled to 0-5°, vigorously stirred and treated dropwise over a period of 20 minutes with a cold (0-5°) solution of diazonium salt, prepared in the usual way by diazotizing arylamine (0.01 mole) in hydrochloric acid solution (6 *M*, 6 ml) with sodium nitrite (0.7 g, 0.01 mole) solution in water (10 ml). After addition, the mixture was stirred for 15 minutes and left in the ice chest for 3 hours. The precipitated solid was collected, washed with water, and finally crystallized from acetic acid. The compounds **7a-c** prepared are listed together with their physical constants in Table 1.

Preparation of N-Aryl-C-arylsulfonylformohydrazidoyl Bromides **5a-c**.

To a stirred suspension of the appropriate hydrazone **7** (0.01 mole) and sodium acetate (1.3 g) in glacial acetic acid (80 ml) and acetic anhydride (20 ml), a solution of bromide (5.4 ml, 0.01 mole) in acetic acid (20 ml) was added dropwise over a period of 1 hour during which the hydrazone **7** dissolved and the corresponding crude hydrazidoyl bromide precipitated. Stirring was continued for 2 hours at room temperature. The solid that precipitated was collected, washed with acetic acid, and finally crystallized from acetic acid. The compounds **5a-c** prepared together with their physical constants are given in Table 1.

Preparation of Pyrazoles **8-11**.

To an ethanolic sodium ethoxide solution, prepared from sodium metal (0.11 g, 0.005 g-atom) and absolute ethanol (20 ml), was added the appropriate β -diketone or β -ketoester (0.005 mole). After stirring the mixture for 15 minutes at room temperature, the appropriate hydrazidoyl bromide **5** (0.005 mole) was added and stirring continued for 4 hours. The reaction mixture was then left overnight at room temperature. The solid that precipitated was collected, washed with water and crystallized from ethanol to give the pyrazoles **8-11** in 60-80% yields. Table 1 lists the compounds prepared together with their physical constants.

Preparation of Thiadiazoline Derivatives **14a,b**.

A solution of potassium thiocyanate (0.68 g, 0.006 mole) in water (5 ml) was added to a warm solution of the appropriate bromide **5** (0.005 mole) in ethanol (30 ml). The mixture was refluxed for 3 hours and then cooled. The crude product that precipitated was collected, washed with water and crystallized from ethanol to give the corresponding thiadiazoline derivatives **14a,b** in 70-80% yields. The compounds prepared are listed in Table 2.

Nitrosation of **14**.

To a stirred solution of **14** (3 mmoles) in acetic acid (15 ml) was added sodium nitrite (0.21 g, 0.004 mole) solution in water (10 ml) dropwise at room temperature. The crude reddish nitroso derivative that precipitated was collected and crystallized from ethanol. The compounds **15a,b** prepared are given in Table 2.

Thermolysis of **15**.

The appropriate nitroso derivative **15** (0.5 g) was refluxed in xylene (20 ml) for 4 hours and solvent was then distilled under reduced pressure. Trituration of the oil residue with petroleum ether (40/60°) afforded the crude thiadiazolone derivative **16**. The latter was collected and crystallized from ethanol. Table 2 lists the compounds **16a,b** prepared together with their physical constants.

Acylation of **14**.

Compound **14** (0.003 mole) was refluxed in acetic anhydride (15 ml) for 20 minutes, and the reaction mixture was poured onto ice cooled water. The crude product that precipitated was collected and crystallized from acetic acid to give the *N*-acetyl derivatives **17a,b** in almost quantitative yields. The latter are listed in Table 2 together with their physical constants.

The *N*-benzoyl derivatives **18a,b** were obtained by refluxing equimolecular amounts of **14** and benzoyl chloride (0.003 mole each) in pyridine (25 ml) for 30 minutes. Work up of the reaction mixture in the usual way and crystallization of the crude product from acetic acid gave **18a,b** in 65-75% yields (Table 2).

Preparation of Amidrazones **19** and **20**.

Morpholine (or piperidine) (0.006 mole) was added to a stirred solution of the appropriate hydrazidoyl bromide **5** (0.005 mole) in ethanol (20 ml). Immediately the solution turned red and the mixture was refluxed for 3 hours, cooled, and the solid that precipitated was collected and crystallized from ethanol to give the corresponding amidrazones **19** and **20** (Table 3).

Preparation of the Hydrazidate Esters **21** and **22**.

Equimolecular quantities (0.005 mole, each) of **5** and sodium phenolate (or thiophenolate) were dissolved in ethanol (50 ml) and the mixture was stirred for 24 hours at room temperature. The solid that precipitated was collected, washed with water, dried and then crystallized from ethanol to give the corresponding esters **21a** and **22a-c** (Table 3).

Preparation of bis(Arylsulfonyl)formaldehyde Arylhyazones **23a-c**. Method A.

To the appropriate hydrazidoyl bromide **5** (0.005 mole) in ethanol (40 ml) was added sodium benzenesulfinate (0.005 mole) and the mixture was stirred for 24 hours at room temperature. The mixture was diluted with water and the crude precipitate was collected, washed with water, dried and then crystallized from acetic acid to give **23a-c** in 60-80% yields (Table 3).

Method B.

To a solution of the appropriate thiohydrazidate **22** (0.002 mole) in acetic acid (20 ml) was added hydrogen peroxide solution (33%, 2 ml). The mixture was stirred for 1 hour and left at room temperature for 2 days, then poured on water with stirring. The solid that precipitated was collected, washed with water, dried and crystallized from acetic acid to give the corresponding hydrazone derivatives **23a-c** in 80% yield. The compounds prepared by this method were identical in all respects (mp, mixed mp, spectra) with those prepared by method A above.

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