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Apart from the previous report, the reaction of 3-(4-nitrobenzoylformamido)-4-(4-nitrophenyl)-1,2,5-thiadiazole (**2a**) with *m*-chloroperbenzoic acid in chloroform at room temperature did not proceed, whereas at reflux temperature the same reaction gave 4-nitrobenzoic acid (**5**) (86%) and a minute amount of a mixture of 4-nitrobenzoylformamide (**6**) and 3-amino-4-(4-nitrophenyl)-1,2,5-thiadiazole (**7a**). On the other hand the same reaction in a mixture of ethanol and chloroform (1:4) at room temperature gave 3-ethoxycarbamoyl-4-(4-nitrophenyl)-1,2,5-thiadiazole (**8a**) (24%) as an isolable product. When 3-aroylformamido-4-aryl-1,2,5-thiadiazoles **2** in tetrahydrofuran were treated with various alkoxides in the corresponding alcohols at room temperature, 3-amino-4-aryl- **7**, 3-alkoxycarbamoyl-4-aryl- **8**, and 3-aryl-4-(aryl)(hydroxy)acetamido-1,2,5-thiadiazoles **9** were isolated. The ratios of which were dependent on the kind of bases and the solvent employed. Selected compounds **2** were allowed to react with phosphorus pentasulfide in the presence of pyridine at reflux to give 3-aryl-4-arylacetamido-1,2,5-thiadiazoles **17** (55-64%), which were also produced by the reaction of **2** with either Lawesson's reagent or hydrogen sulfide gas in the presence of pyridine at reflux.

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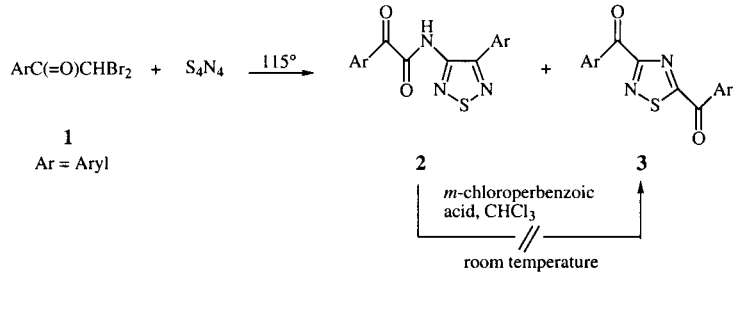
Some years ago we reported that heating of aryl dibromomethyl ketones **1** with tetrasulfur tetranitride (S_4N_4) at 115° without a solvent gave the title compounds **2** as major products and 3,5-diaroyl-1,2,4-thiadiazoles **3** as minor products in certain cases [1] (Scheme 1). For the structural information on compounds **2**, selected compounds **2** were treated with *m*-chloroperbenzoic acid in chloroform at room temperature. When the aryl groups of **2** were phenyl, 3- and 4-nitrophenyl, 4-cyanophenyl, and 2-naphthyl, the corresponding 3,5-diaroyl-1,2,4-thiadiazoles **3** were reported to be produced in 39%, 59%, 63%, 66%, and 43% yields, respectively.

Scheme 1



It was not possible to determine out how compounds **3** could be formed from **2**. We carefully reexamined this strange reaction. Our results are described herein.

Results.

Preparation of Compounds **2**.

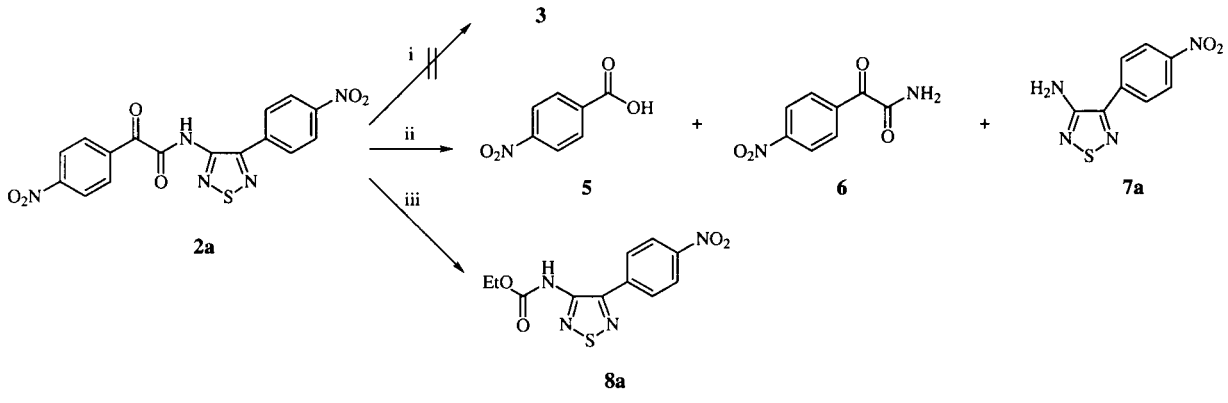
Compound **2a** (Ar = 4-$O_2NC_6NH_4$), **2b** (Ar = 4-NCC_6H_4), **2c** (Ar = 4-ClC_6H_4), **2d** (Ar = 4-BrC_6H_4), **2e** (Ar = C_6H_5), and **2f** (Ar = 4-$MeOC_6H_4$) were prepared according to the literature procedure [1] and purified by recrystallization from carbon tetrachloride.

Reactions of Compounds **2a** with *m*-Chloroperbenzoic Acid.

Treatment of **2a** (0.276 mmole) with *m*-chloroperbenzoic acid (1.09 mmoles) in chloroform at room temperature for 9 hours gave no 1,2,4-thiadiazole **3** (Ar = 4-$O_2NC_6H_4$); **2a** was recovered quantitatively. However, when the same reaction was carried out at reflux temperature for 23 hours, 4-nitrobenzoic acid (**5**) (86%), a mixture (trace amount) of 4-nitrobenzoylformamide (**6**) and 3-amino-4-(4-nitrophenyl)-1,2,5-thiadiazole (**7a**), along with unreacted *m*-chloroperbenzoic acid were obtained (Scheme 2).

The same reaction of **2a** in a mixture of chloroform and ethanol (4:1) for 48 hours at room temperature afforded 3-ethoxycarbamoyl-4-(4-nitrophenyl)-1,2,5-thiadiazole (**8a**). In contrast, the same reactions of **2a** in a different

Scheme 2



i, *m*-chloroperbenzoic acid, $CHCl_3$, room temperature. ii, *m*-chloroperbenzoic acid, $CHCl_3$, reflux. iii, *m*-chloroperbenzoic acid, $C_2H_5OH/CHCl_3$ (1:4), room temperature.

solvent mixture, *i.e.*, chloroform-methanol (4:1), chloroform-2-propanol (4:1), and chloroform-*t*-butyl alcohol (4:1), at room temperature for 48 hours did not give any product analogous to **8a, 2a** was almost quantitatively recovered.

Reactions of Compounds **2** with Alkoxides.

When a solution of **2a** (0.23 mmole) in tetrahydrofuran was treated with sodium ethoxide *in situ* prepared from sodium and absolute ethanol, at room temperature for 5 hours, compound **8a** (38%) together with unreacted **2a** (22%) were isolated. Similarly other compounds **2** were treated with various alkoxides under similar conditions. From the reactions were isolated 3-amino-4-aryl-**7**, 3-aryl-4- (aryl)(hydroxy)acetamido-1,2,5-thiadiazoles **9**, and/or **8**. The ratios of the products vary with the structures **2** and the reaction conditions (Scheme 3). The reaction conditions and yields of compounds **7-9** are summarized in Table 1. The analytical, ir, and ^1H nmr spectroscopic data of compounds **8** and **9** are summarized in Tables 2 and 3, respectively.

Scheme 3

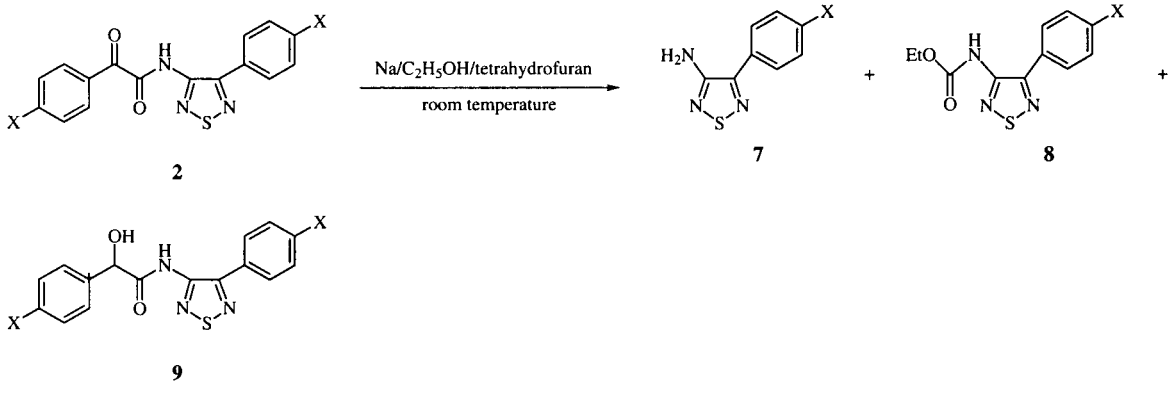


Table 1

Reaction Conditions, and Yields of 3-Amino-4-aryl-**7**, 3-Aryl-4-ethoxycarbamoyl- **8**, and 3-Aryl-4-(aryl)(hydroxy)acetamido-1,2,5-thiadiazoles **9**

Entry	Compound (mmole)	Tetrahydrofuran ml	Base [a] Na (mg)/ROH (ml)	Time (hours)		Yield [b] %
1	**2a** X = NO_2 0.23	8	60/9, R = Et	5		**8a** 38
2	**2a** X = NO_2 0.10	10	30/1, R = Me	24		**8f** 62
3	**2a** X = NO_2 0.24	8	150/2, R = *n*-Pr	24	**7a** 37 [c]	**8g** 16 [c]
4	**2a** X = NO_2 0.19	6	$H_2N(CH_2)_2OH$ (110 mg)	24	**7a** 53	
5	**2b** X = CN 0.27	8	123/2, R = Et	18		**8c** 66

Table 1 (continued)

Reaction Conditions, and Yields of 3-Amino-4-aryl-**7**, 3-Aryl-4-ethoxycarbamoyl- **8**, and 3-Aryl-4-(aryl)(hydroxy)acetamido-1,2,5-thiadiazoles **9**

Entry	Compound (mmole)		Tetrahydrofuran ml	Base [a] Na (mg)/ROH (ml)	Time (hours)	Yield [b] %		
6	**2c** X= Cl	0.21	8	100/2, R = Et	4			**9a** 40
7	**2d** X = Br	0.18	8	100/2, R = Et	22		**8b** 22	**9b** 57
8	**2d** X = Br	0.21	8	NaH (25 mg)/2, R = Et	22	**7c** 61		**9b** 16
9	**2d** X = Br	0.11	6	50/1, R = Me	47	**7c** 75		
10	**2d** X = Br	0.11	6	57/2, R = *i*-Pr	12	**7c** 28		**9b** 54
11	**2d** X = Br	0.21	8	NaOH (45 mg)/2, R = Et	15	**7c** 13		**9b** 39
12	**2e** X = H	0.17	8	80/2, R = Et	17		**8d** 47	**9c** 27
13	**2f** X = OMe	0.09	5	50/1, R = Et	20		**8e** 55	**9d** 15

[a] Sodium alkoxide was prepared *in situ* by the addition of sodium to the alcohol. [b] Isolated yields. [c] Yields are calculated based on ^{1}H nmr spectroscopic data.

Table 2

Melting Points, Ir, and ^{1}H nmr Spectral Data of Compounds **8**

Product	Mp [a] °C	IR [b] (cm^{-1})	^{1}H NMR (deuteriochloroform) δ (ppm)	Molecular Formula	Analyses % Calcd./Found C	H	N	S
8a	146-148	3248, 1696, 1590, 1507, 1338, 1242 1085, 858	120 (t, 3H, J = 7.2 Hz, CH_3), 4.14 (q, 2H, J = 7.2 Hz, CH_2), 7.44 (s, 1H, NH), 7.96 (d, 2H, J = 8.4 Hz, ArH), 8.34 (d, 2H, J = 8.4 Hz, ArH)	$C_{11}H_{10}N_4O_4S$	44.89 44.79	3.43 3.41	19.04 19.20	10.90 10.78
8b	166-168	3248, 1718, 1580, 1504, 1459, 1219, 1068, 1001, 825	1.22 (t, 3H, J = 7.2 Hz, CH_3), 4.19 (q, 2H, J = 7.2 Hz, CH_2), 7.19 (s, 1H, NH), 7.63 (s,4H, ArH)	$C_{11}H_{10}BrN_3O_2S$	40.26 40.02	3.07 3.03	12.80 13.01	9.77 9.54
8c	123-125	3280, 2208, 1702, 1606, 1516, 1424, 1283, 1228, 1081, 1008, 854	1.15 (t, 3H, J = 7.2 Hz, CH_3), 4.16 (q, 2H, J = 7.2 Hz, CH_2), 7.4 (s, 1H, NH), 7.68-8.02 (m, 4H, ArH)	$C_{12}H_{10}N_4O_2S$	52.54 52.38	3.67 3.64	20.43 20.58	11.69 11.58
8d	liquid	3248, 1721, 1606, 1516, 1433, 1308, 1212, 1072, 774	1.21 (t, 3H, J = 7.2 Hz, CH_3), 4.22 (q, 2H, J = 7.2 Hz, CH_2), 7.23 (s, 1H, NH) 7.41-7.78 (m, 5H, ArH)	$C_{11}H_{11}N_3O_2S$	53.00 52.84	4.45 4.36	16.86 17.01	12.86 12.72
8e	83-85	3184, 1718, 1600, 1539, 1507, 1404, 1248, 1174, 1030, 835	1.26 (t, 3H, J = 7.1 Hz, CH_3), 3.86 (s, 3H, OCH_3), 4.21 (q, 2H, J = 7.1 Hz, CH_2), 7.01 (d, 2H, J = 8.8 Hz, ArH), 7.64 (d, 2H, J = 8.8 Hz, ArH), 7.70 (s, 1H, NH)	$C_{12}H_{13}N_3O_3S$	51.60 51.43	4.69 4.61	15.04 15.23	11.48 11.32
8f	143-145	3264, 1705, 1593, 1507, 1337, 1238, 1078, 848	3.71 (s, 3H, CH_3), 7.30 (s, 1H, NH), 7.92 (d, 2H, J = 8.4 Hz, ArH), 8.34 (d, 2H, J = 8.4 Hz, ArH)	$C_{10}H_8N_4O_4S$	42.86 42.76	2.88 2.87	19.99 20.04	11.44 11.32
8g	149-151	3264, 1693, 1590, 1510, 1337, 1235, 1078, 848	0.88 (t, 3H, J = 7.1 Hz,CH_3), 1.41-1.81 (m, 2H, CH_2), 4.04 (t, 2H, J = 7.1 Hz, CH_2), 7.33 (s, 1H, NH), 7.98 (d, 2H, J = 8.4 Hz, ArH), 8.34 (d, 2H, J = 8.4 Hz, ArH)	$C_{12}H_{12}N_4O_4S$	46.75 46.58	3.92 3.90	18.17 18.24	10.40 10.29

[a] From a mixture of dichloromethane and *n*-hexane. [b] The ir were recorded in a potassium bromide pellet except for **8d**.

Table 3

Melting Points, IR, and ^{1}H NMR Spectroscopic Data of Compounds **9**

Product	Mp [a] °C	IR [b] (cm^{-1})	^{1}H NMR (deuteriochloroform) δ (ppm)	Molecular Formula	Analyses % Calcd./Found C	H	N	S
9a	138-140	3328, 3232, 1680, 1587 1507, 1481 1401, 1084 822	5.2 (d, 1H, J = 4.5 Hz, CH), 6.83 (d, 1H, J = 4.5 Hz, OH), 7.22-7.66 (m, 8H, ArH), 9.61 (s, 1H, NH)	$C_{16}H_{11}Cl_2N_3O_2S$	50.54 50.23	2.92 2.96	11.05 10.84	8.43 8.62

Table 3 (continued)
Melting Points, IR, and ^{1}H NMR Spectroscopic Data of Compounds **9**

Product	Mp [a]	IR [b]	^{1}H NMR (deuteriochloroform)	Molecular Formula	Analyses % Calcd./Found			
	°C	(cm^{-1})	δ (ppm)		C	H	N	S
9b	169-171	3344, 3248, 1683, 1580, 1478, 1401, 1065, 1004, 819	5.19 (d, 1H, J = 4.5 Hz, CH), 6.30 (d, 1H, J = 4.5 Hz, OH), 7.37-7.48 (m, 8H, ArH), 9.83 (s, 1H, NH)	$C_{16}H_{11}Br_2N_3O_2S$	40.96 40.53	2.36 2.38	8.96 8.61	6.83 7.16
9c	126-129	3344, 1689, 1516, 1491, 1440, 1408, 1056, 1017, 774	3.86 (br s, 1H, OH), 5.22 (s, 1H, CH), 7.16-7.68 (m, 10H, ArH), 8.96 (s, 1H, NH)	$C_{16}H_{13}N_3O_2S$	61.72 61.50	4.21 4.28	13.50 13.24	10.30 10.62
9d	108-110	3424, 3376 1723, 1600, 1505, 1451, 1078, 1019, 936, 662	3.79 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 5.22 (d, 1H, J = 3.7 Hz, CH), 5.29 (d, 1H, J = 3.7 Hz, OH), 6.87-6.93 (m, 4H, ArH), 7.42 (d, 2H, J = 8.7 Hz, ArH), 7.52 (d, 2H, J = 8.7 Hz, ArH), 9.47 (s, 1H, NH)	$C_{18}H_{17}N_3O_4S$	58.21 58.02	4.61 4.65	11.31 11.02	8.63 8.89

[a] From a mixture of dichloromethane and *n*-hexane. [b] The ir were recorded in a potassium bromide pellet.

Discussion.

Unexpectedly, the reaction of **2a** with *m*-chloroperbenzoic acid in chloroform at room temperature did not give 1,2,4-thiadiazole **3** (Ar = 4-$O_2NC_6H_4$) and only the starting material **2a** was quantitatively recovered. However, it decomposed to give 4-nitrobenzoic acid (**5**), trace amounts of 4-nitrobenzoylformamide (**6**) and 3-amino-4-(4-nitrophenyl)-1,2,5-thiadiazole (**7a**) at reflux. The structure of compound **5** was identified based on spectroscopic data (^{1}H nmr, ir), by comparison of its melting point with that of an authentic sample [2], and by transformation into methyl 4-nitrobenzoate [2] by treatment with iodomethane. On the other hand, it was difficult to separate a mixture of trace amounts of two compounds **6** and **7a**, exhibiting two spots on tlc (R_f = 0.49 for **6**, R_f = 0.50 for **7a**, ethyl acetate/*n*-hexane = 1:4), by column chromatography. The structure of **7a** was assigned based on gc-ms data [3], which was compared with that of an authentic sample [1]. However, compound **6** did not give a fragment corresponding to molecular ion. The structure of **6** was determined based on spectroscopic data (^{1}H nmr, ir) and elemental analysis. Although the structures of the products **5-7a** have been determined, the mechanism for the formation of the products **5-7a** is uncertain. More information is needed to delineate the mechanistic obsecurity. Futhermore, it is difficult, at present moment, to explain the reason why the same reaction carried out in a mixture of chloroform and ethanol gave compound **8a**, whereas the same reaction did not occur in a mixture of chloroform and various alcohols such as methanol, 2-propanol, and *t*-butyl alcohol under the same conditions. We realized that the previous report on the rearrangement of **2** leading to **3** in the presence of *m*-chloroperbenzoic acid in chloroform at room temperature was faulty and the isolated compounds **3** originated from incompletely purified **2** contaminated with **3** which had been formed by the reaction of tetrasulfur tetranitride with aryl monobromomethyl ketones by the disproportionation of **1** [4].

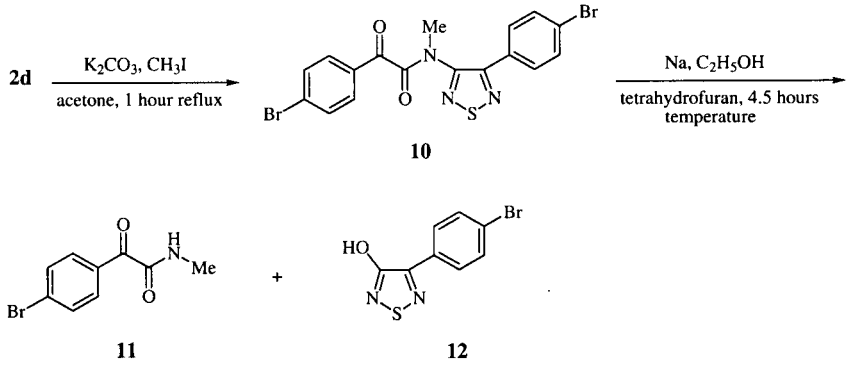
In Table 1 is shown that treatment of **2a** in tetrahydrofuran with sodium alkoxides, *i.e.*, sodium ethoxide, sodium methoxide, sodium propoxide, in the corresponding alcohols at room temperature gives 3-alkoxycarbamoyl-1,2,5-thiadiazoles **8a**, **8f**, and **8g**, respectively (entries 1-3). Similarly from the reactions of **2b**, **2d-f** in tetrahydrofuran with sodium ethoxide in ethanol under the same conditions were isolated 3-alkoxycarbamoyl-4-aryl-1,2,5-thiadiazoles **8b-e** (entries 5, 7, 12, 13) along with 3-aryl-4-(aryl)(hydroxy)acetamido-1,2,5-thiadiazoles **9**. The formation of **8** suggests cleavage of a bond between the two carbonyl carbons of compound **2**.

Interestingly, treatment of **2a** in tetrahydrofuran with ethanolamine gave 3-amino-4-aryl-1,2,5-thiadiazole **7a** in 53% yield (Table 1, entry 4), which suggests cleavage of a bond between an amide nitrogen and a carbonyl carbon. It is noteworthy that treatment of **2c** in tetrahydrofuran with sodium ethoxide in ethanol gave a reduced compound, 3-aryl-4-(aryl)(hydroxy)acetamido-1,2,5-thiadiazole **9a** in 40% yield (Table 1, entry 6). Analogous types of compounds **9b-d** were obtained from **2d**, **2e**, and **2f** in 57%, 27%, and 15% yields, respectively (entries 7, 12, 13).

When compound **2d** was treated with different bases such as sodium hydride and sodium hydroxide, compounds **9b** and **7c** were isolated in 16% and 61% from the former base (entry 8), and 39% and 13% from the latter base (Table 1, entry 11), respectively. The results indicate that the formation of **9** is achieved regardless of an electron transfer mechanism which might be involved in the presence of sodium metal.

In order to see the role of the NH proton of **2**, 3-(4-bromophenyl)-4-(*N*-methyl-4-bromobenzoylformamido)-1,2,5-thiadiazole (**10**) was prepared and subjected under the same reaction conditions as for the reaction of **2d** (Table 1, entry 7). From the reaction were isolated *N*-methylaroylformamide **11** and 3-aryl-4-hydroxy-1,2,5-thiadiazole **12** in 26% and 70% yields, respectively (Scheme 4).

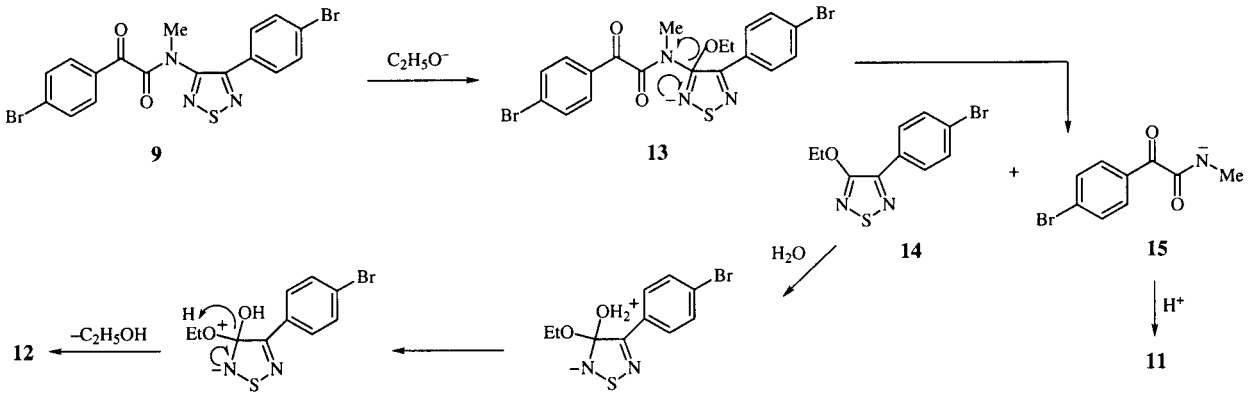
Scheme 4



Compounds **9b** and **7c** were also obtained in 54% and 28% yields, respectively by treatment of **2d** in tetrahydrofuran with sodium in 2-propanol (Table 1, entry 10). However, only **7c** was isolated in 75% yield by treatment with sodium in methanol (Table 1, entry 9). When compound **2d** in tetrahydrofuran was treated with sodium ethoxide (Table 1, entry 7) and sodium hydride (Table 1, entry 8) in ethanol, different sets of compounds, *i.e.*, **8b** and **9b**, **7c** and **9b** were isolated. The results coupled with different ratio of two compounds, *i.e.*, **7c** and **9b** (Table 1, entries 9-11) indicate that the reduction leading to **9** is competitive with the nucleophilic substitution leading to **7** and **8**, which may be attributable to solvation effects.

The formation of **11** can be explained by nucleophilic attack of ethoxide ion to C-3 of the 1,2,5-thiadiazole moiety to give an intermediate **13**, which then undergoes bond cleavage, leading to 3-(4-bromophenyl)-4-ethoxy-1,2,5-thiadiazole (**14**) and an intermediate **15**, a conjugate base of **11**. Hydrolysis of **14** would give **12** and protonation of **15** gives **11** (Scheme 5).

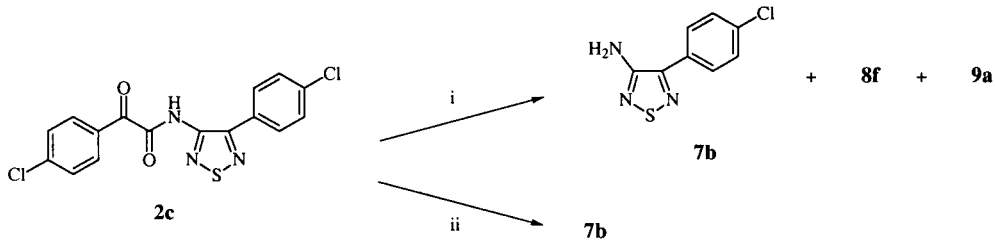
Scheme 5



Apart from the formation of **8b** and **9b** from **2d** (Table 1, entry 7), the formation of **12** as a major product might be attributable to the difficulty to access of ethoxide ions to the carbonyl carbon α to the *N*-methyl group because of steric hindrance. For an independent synthesis of the reducing products **9a**, sodium borohydride in ethanol was added to a

solution of **2c** in a mixture of ethanol and chloroform (1:1) at room temperature, which gave **9a** (34%) and a mixture of 3-amino-4-(4-chlorophenyl)-1,2,5-thiadiazole (**7b**) and **8f** (Scheme 6). However, the addition of the solvent mixture (ethanol/chloroform = 1:1) to the mixture of **2c** and sodium borohydride (2 molar equivalents) led to only **7b** in 72% yield. The formation of **7b** in preference to both **9a** and **8f** may be attributable to the predominant hydride attack on amide carbonyl carbon prior to the formation of ethoxide ions. The formation of **9a** is consistent with the results in which *N,N*-dimethyl-α-hydroxybenzylamide is formed by treatment of α-oxo-*N,N*-dimethylphenylacetamide with sodium borohydride in ethanol [5]. In view of the fact that amide **16** was inert even for a prolonged time under the conditions where **2** was treated with sodium ethoxide to give **8a** (Table 1, entry 1) (Scheme 7), a vicinal carbonyl group as shown in **2** is necessary for the reactions.

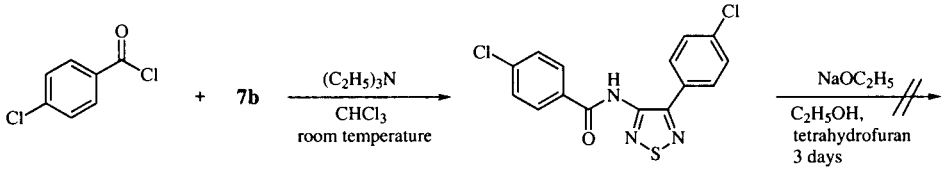
Scheme 6



i, Sodium borohydride in ethanol was added to **2c** in a mixture of chloroform and ethanol.
ii, A mixture of ethanol and chloroform was added to a mixture of sodium borohydride and **2c**.

by phosphorus pentasulfide and Lawesson's reagent made the investigation on the reactions of **2** with hydrogen sulfide intriguing. Bubbling hydrogen sulfide gas into the solution of **2c** in pyridine at reflux temperature gave rise to **17b** (67%) together with sulfur (Scheme 9). Since compound **9a** is not converted to **17b** by treatment with either hydrogen sulfide or phosphorus pentasulfide at reflux, **17b** is envisaged to be formed directly from **2c**. The result is consistent with the report in which one of the two carbonyl groups of 1,2-diketones is reduced selectively to either a methylene group or to a secondary alcohol by treatment with hydrogen sulfide in the presence of an amine base [6]. So our finding in which **9a** is not converted to **17b** is a new example for the selective

Scheme 7



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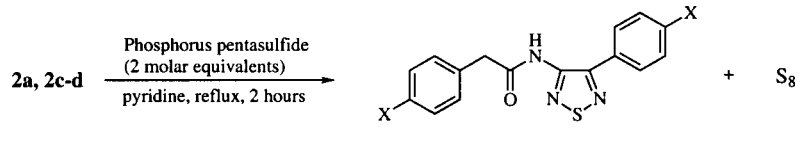
For the preparation of sulfur analogs of **2**, selected compounds **2a**, **2c-d** were treated with 2 molar equivalents of phosphorus pentasulfide in the presence of pyridine for 2 hours at reflux. From the reactions were obtained deoxy- reduction of an aroyl carbonyl group of an aroylformamide utilizing either hydrogen sulfide or phosphorus pentasulfide. Interestingly reduction of **2c** with aluminum isopropoxide in 2-propanol at reflux gave **9a** in 79% yield.

Scheme 8



17a, X = NO_2, 55%
17b, X = Cl, 60%
17c, X = Br, 64%

Scheme 9

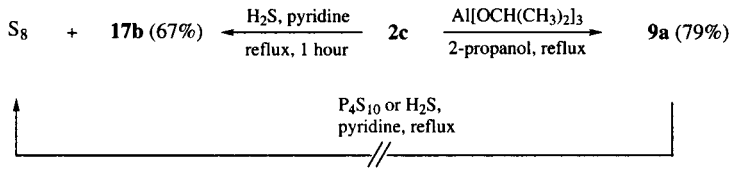


Table 4

Quantities of the Reactants and Analytical and Yields of Compounds **17a-c**

Compound (mmole)	Phosphorus pentasulfide (mmole)	Compound	Yields [a] %	Mp [b] °C	Molecular Formula	Analyses % Calcd./Found C	H	N	S
2a 0.296	0.592	**17a**	55	221-223	$C_{16}H_{11}N_5O_5S$	49.87	2.88	18.17	8.32
						49.75	2.86	18.02	8.41
2c 0.226	0.451	**17b**	60	164-165	$C_{16}H_{11}Cl_2N_3OS$	52.76	3.04	11.54	8.80
						52.68	3.01	11.45	8.92
2d 0.103	0.206	**17c**	64	175-177	$C_{16}H_{11}Br_2N_3OS$	42.41	2.45	9.27	7.08
						42.39	2.40	9.18	7.12

[a] Isolated yields. [b] From a mixture of dichloromethane and *n*-hexane.

Table 5

^{1}H NMR, IR, and Mass Spectroscopic Data of Compounds **17a-c**

Compound	^{1}H NMR (deuteriochloroform-dimethyl-d_6 sulfoxide) δ (ppm)	IR [a] (cm^{-1})	MS (m/z)
17a	3.83 (s, 2H, CH_2), 7.49 (d, 2H, J = 9.0 Hz, ArH), 7.78 (d, 2H, J = 9.0 Hz, ArH), 7.96-8.28 (m, 4H, ArH), 10.96 (s, 1H, NH)	3232, 3056, 1676, 1593, 1510, 1411, 1337, 1260, 1174, 1100, 972, 848	
17b	3.68 (s, 2H, CH_2), 7.28-7.40 (m, 6H, ArH), 7.62-7.65 (m, 2H, ArH), 10.88 (s, 1H, NH)	3248, 3024, 2960, 1660, 1516, 1484, 1411, 1324, 1260, 1088, 1008, 832	363 (M^+, 58), 211 (68) 152 (78), 125 (100), 89 (22)
17c	3.70 (s, 2H, CH_2), 7.19 (d, 2H, J = 8.6 Hz, ArH), 7.46 (m, 6H, ArH), 9.78 (s, 1H, NH)	3264, 3056, 1667, 1584, 1520, 1481, 1417, 1312, 1065, 1004, 848, 822	453 (M^+, 76), 257 (68) 196 (84), 169 (100), 90 (51)

[a] The ir were recorded in a potassium bromide pellet.

EXPERIMENTAL

The proton nuclear magnetic resonance spectra were recorded at 80 MHz and 300 MHz in deuteriochloroform or deuteriochloroform-dimethyl-d_6 sulfoxide containing tetramethylsilane as an internal standard. Infrared spectra were recorded in potassium bromide or a thin film on potassium bromide plates. Mass spectra were obtained using HP 6890 (GC) with HP 5973 (MSD) mass spectrometer. Microanalyses were performed by Perkin-Elmer 240 DS and Carlo Erbra 1106. Column chromatography was performed using silica gel (70-230 mesh, Merck), unless otherwise. Melting points were measured on a Fisher-Johns melting points apparatus and are uncorrected.

Reaction of 3-Aroylformamido-4-aryl-1,2,5-thiadiazoles **2** with *m*-Chloroperbenzoic Acid.

(i) In Chloroform.

To a solution of **2a** (110 mg, 0.276 mmole) in chloroform (14 ml) was added *m*-chloroperbenzoic acid (57-86%, 263 mg, 1.09 mmoles). The mixture was stirred at room temperature for 9 hours. However, the reaction did not proceed. The mixture was heated at reflux for 23 hours and then poured into a saturated aqueous sodium bicarbonate (40 ml), which was extracted with chloroform (30 ml x 3). The combined extracts were washed with water three times and dried over anhydrous magnesium sulfate. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel (230-400 mesh, 2 x 12 cm). Elution with a mixture of benzene and *n*-hexane (1:1) gave *m*-chlorobenzoyl peroxide (18 mg, 8%). Elution with a mixture of ethyl acetate and *n*-hexane (1:3) gave a mixture (14 mg) of 4-nitrobenzoyl for-

mamide (**6**) and 3-amino-4-(4-nitrophenyl)-1,2,5-thiadiazole (**7a**) [1]. Compound **6** was recrystallized from a mixture of ethyl acetate and *n*-hexane, mp 102-104°; ^{1}H nmr (deuteriochloroform, 80 MHz): δ 6.05 (s, 2H, NH_2), 8.30 (s, 4H, ArH); ir (potassium bromide): 3472, 3360, 1686, 1638, 1590, 1545, 1306 cm^{-1}.

Anal. Calcd. for $C_8H_6N_2O_4$: C, 49.49; H, 3.12; N, 14.43. Found: C, 49.32; H, 3.01; N, 14.51.

Treatment of the aqueous layer with concentrated hydrochloric acid gave a white solid, which was filtered and chromatographed on silica gel (2 x 8 cm). Elution with acetone gave unreacted *m*-chloroperbenzoic acid (80 mg, 30%). Elution with ethanol gave 4-nitrobenzoic acid **5** (40 mg, 86%), which was recrystallized from benzene, mp 241-243° (lit [2], mp 242°).

(ii) In a Mixture of Chloroform and Ethanol (4:1).

A solution of **2a** (100 mg, 0.251 mmole) and *m*-chloroperbenzoic acid (387 mg, 1.61 mmoles) in the solvent mixture (15 ml) was stirred for 48 hours at room temperature. The mixture was worked up as described in (i). Chromatography (1 x 10 cm) using a mixture of benzene and *n*-hexane (1:1) as an eluent gave *m*-chlorobenzoyl peroxide (13 mg, 4%). Elution with chloroform gave *m*-chlorobenzoic acid. Subsequent elution with a mixture of ethyl acetate and *n*-hexane (1:2) gave 3-ethoxycarbamoyl-4-(4-nitrophenyl)-1,2,5-thiadiazole (**8a**) (28 mg, 24%) which was recrystallized from a mixture of dichloromethane and *n*-hexane, mp 146-148°; ^{1}H nmr (deuteriochloroform, 80 MHz): δ 1.20 (t, 3H, J = 7.2 Hz, CH_3), 4.14 (q, 2H, J = 7.2 Hz, CH_2), 7.44 (s, 1H, NH), 7.96 (d, 2H, J = 8.4 Hz, ArH), 8.34 (d, 2H, J = 8.4 Hz, ArH); ir (potassium bromide): 3248, 1696, 1590, 1462, 1421, 1338, 1302, 1276, 1242, 1085, 1078, 858, 746, 688, 621, 557 cm^{-1}.

Anal. Calcd. for $C_{11}H_{10}N_4O_4S$: C, 44.89; H, 3.43; N, 19.04; S, 10.90. Found: C, 44.79; H, 3.41; N, 19.20; S, 10.78.

Preparation of Methyl 4-Nitrobenzoate.

To a solution of **5** (25 mg, 0.150 mmole) and potassium carbonate (21 mg, 0.152 mmole) in acetone (5 ml) was added iodomethane (32 mg, 0.225 mmole). The mixture was stirred for 1 hour at reflux and the cooled reaction mixture was neutralized with 10% hydrochloric acid. The acetone was removed under reduced pressure and the residue was extracted with dichloromethane (10 ml x 3). The extracts were dried over magnesium sulfate. Removal of the solvent gave methyl 4-nitrobenzoate (20 mg, 74%), recrystallized from methanol, mp 94-96° (lit [2], mp 96°); ^{1}H nmr (deuteriochloroform, 300 MHz): δ 3.99 (s, 3H, CH_3), 8.22 (d, J = 8.8 Hz, 2H, ArH), 8.31 (d, J = 8.8 Hz, 2H, ArH); ir (potassium bromide): 3056, 2944, 1715, 1596, 1516, 1430, 1340, 1270, 1097, 710 cm^{-1}; ms: m/z 181 (M^+, 31%), 164 (24), 150 (100), 104 (24), 76 (18).

General Procedure for the Reaction of **2** with Sodium Alkoxides.

A solution of **2** (0.1-0.3 mmole) in tetrahydrofuran (5-8 ml) was added dropwise into the sodium alkoxide prepared *in situ* from sodium (1.3-6.5 mmoles) and alcohol (1-9 ml). The mixture was stirred for an appropriate time at room temperature and neutralized with 0.1 *N* hydrochloric acid. Evaporation of tetrahydrofuran *in vacuo* gave a residue, which was extracted with ether (20 ml x 3). The extracts were dried over magnesium sulfate and evaporation of the solvent gave a residue, which was chromatographed on silica gel (2 x 12 cm). Elution with a mixture of ethyl acetate and *n*-hexane (1:4) gave **7**. Elution with the same solvent mixture (1:2) gave **8** and unreacted **2**. Elution with ethyl acetate gave **9**. In each case, consult Table 1 for reaction conditions and yields of compounds **7-9**, and Tables 2 and 3 for physical, analytical, ir, and ^{1}H nmr spectroscopic data of compounds **8** and compounds **9**, respectively.

N-Methyl-3-(4-bromobenzoylformamido)-4-(4-bromophenyl)-1,2,5-thiadiazole (**10**).

To a mixture of 3-(4-bromobenzoylformamido)-4-(4-bromophenyl)-1,2,5-thiadiazole (**2d**) (100 mg, 0.214 mmole) and potassium carbonate (46 mg, 0.333 mmole) in acetone (8 ml) was added iodomethane (46 mg, 0.321 mmole). The mixture was heated for 1 hour at reflux and the cooled reaction mixture was neutralized with 10% hydrochloric acid. The acetone was removed under reduced pressure and the residue was extracted with dichloromethane (30 ml x 3). The extracts were dried over magnesium sulfate. Removal of the solvent gave **10** (77 mg, 75%), recrystallized from a mixture of dichloromethane and *n*-hexane, mp 140-141°; ^{1}H nmr (deuteriochloroform, 80 MHz): δ 3.25 (s, 3H, NCH_3), 7.45-7.89 (m, 8H, ArH); ir (potassium bromide): 1657, 1574, 1472, 1420, 1388, 1360, 1228, 1174, 1142, 1062, 995, 851, 825, 752 cm^{-1}.

Anal. Calcd. for $C_{17}H_{11}Br_2N_3O_2S$: C, 42.44; H, 2.30; N, 8.73; S, 6.66. Found: C, 42.18; H, 2.28; N, 8.90; S, 6.51.

Reaction of **10** with Sodium Ethoxide.

A solution of **10** (75 mg, 0.156 mmole) in tetrahydrofuran (8 ml) was treated with sodium ethoxide prepared *in situ* from sodium (80 mg, 3.48 mmoles) and ethanol (2 ml) for 4.5 hours at room temperature. The mixture was worked up as described in the general procedure for the reactions of **2** with sodium ethoxide. Chromatography (2 x 8 cm) using a mixture of ethyl acetate and *n*-hexane (1:3) as an eluent gave *N*-methyl-4-bromobenzoylformamide (**11**) (10 mg, 26%), recrystallized from a mixture of carbon tetrachloride and *n*-hexane, mp 108-110°; ^{1}H nmr (deuteriochloroform, 80 MHz): δ 2.96 (d, 3H, J = 4.2 Hz, NCH_3), 7.28 (br s, 1H, NH), 7.61 (d, 2H, J = 8.2 Hz, ArH), 8.26 (d, 2H, J = 8.2 Hz, ArH); ir (potassium bromide): 3376, 1683, 1648, 1568, 1529, 1388, 1283, 1059, 1001, 928, 784, 652 cm^{-1}; ms: m/z 241 (M^+, 14%), 183 (100), 155 (34).

Anal. Calcd. for $C_9H_8BrNO_2$: C, 44.66; H, 3.33; N, 5.79. Found: C, 44.42; H, 3.30; N, 5.91.

Elution with the same solvent mixture (1:1) gave 3-(4-bromophenyl)-4-hydroxy-1,2,5-thiadiazole (**12**) (28 mg, 70%), recrystallized from a mixture of dichloromethane and *n*-hexane, mp 247-249° dec; ^{1}H nmr (deuteriochloroform-dimethyl-d_6 sulfoxide, 80 MHz): δ 7.66 (d, 2H, J = 7.8 Hz, ArH), 8.11 (d, 2H, J = 7.8 Hz, ArH), 13.16 (s, 1H, OH); ir (potassium bromide): 3238-2858 (br), 1577, 1555, 1500, 1459, 1395, 1270, 1219, 1065, 1001, 876, 825, 544 cm^{-1}; ms: m/z 256 (M^+, 98%), 213 (12), 182 (30), 75 (32).

Anal. Calcd. for $C_8H_5BrN_2OS$: C, 37.37; H, 1.96; N, 10.90; S, 12.47. Found: C, 37.15; H, 1.94; N, 11.04; S, 12.28,

Reactions of 3-(4-Chlorobenzoylformamido)-4-(4-chlorophenyl)-1,2,5-thiadiazole (**2c**) with Sodium Borohydride.

(i) To a solution of **2c** (140 mg, 0.370 mmole) in a mixture of chloroform and ethanol (12 ml) was added dropwise sodium borohydride (28 mg, 0.740 mmole) in ethanol (5 ml). The mixture was stirred for 5 minutes at room temperature and then worked up as usual. Chromatography (2 x 8 cm) of the reaction mixture using chloroform and a mixture of ethyl acetate and *n*-hexane (1:1) as eluents gave a mixture of 3-(4-

chlorophenyl)-4-ethoxycarbamoyl-1,2,5-thiadiazole (**8f**) and 3-amino-4-(4-chlorophenyl)-1,2,5-thiadiazole (**7b**) (20 mg) and 3-(4-chlorophenyl)-4-(4-chlorophenyl)(hydroxy)-1,2,5-thiadiazole (**9a**) (48 mg, 34%), respectively.

(ii) A solution of chloroform and ethanol (1:1) (30 ml) was added dropwise to a mixture of sodium borohydride (40 mg, 1.06 mmoles) and **2c** (200 mg, 0.529 mmole). The mixture was stirred for 2 hours at room temperature and worked up as usual. Chromatography as described in (i) gave **7b** (80 mg, 72%).

Preparation of 4-(4-Chlorobenzamido)-3-(4-chlorophenyl)-1,2,5-thiadiazole (**16**).

To a solution of 3-amino-4-(4-chlorophenyl)-1,2,5-thiadiazole (**7b**) (80 mg, 0.378 mmole) and triethylamine (77 mg, 0.762 mmole) in chloroform (5 ml) was added dropwise 4-chlorobenzoyl chloride (266 mg, 1.52 mmoles). The mixture was stirred for 24 hours at room temperature and washed with water. After drying over magnesium sulfate, the solvent was evaporated to give a residue, which was chromatographed on silica gel (2 x 10 cm). Elution with benzene gave unreacted **7b** (15 mg, 7%). Elution with dichloromethane, followed by chloroform gave **16** (40 mg, 30%), recrystallized from carbon tetrachloride, mp 191-193°; ^{1}H nmr (deuteriochloroform, 80 MHz): δ 7.40 (d, J = 7.4 Hz, 4H, ArH), 7.65 (d, J = 7.4 Hz, 2H, ArH), 7.78 (d, J = 7.4 Hz, 2H, ArH), 8.52 (s, 1H, NH); ir (potassium bromide): 3248, 1657, 1584, 1510, 1484, 1414, 1296, 1084, 1004, 908, 838, 822, 745, 649 cm^{-1}; ms: m/z 349 (M^+, 13%), 139 (100), 111 (25), 75 (9).

Anal. Calcd. for $C_{15}H_9Cl_2N_3OS$: C, 51.44; H, 2.59; N, 12.00; S, 9.16. Found: C, 51.28; H, 2.57; N, 11.86; S, 9.24.

Attempted Reaction of **16** with Sodium Ethoxide.

A solution of **16** (37 mg, 0.106 mmole) in tetrahydrofuran (5 ml) was treated with sodium ethoxide prepared *in situ* from sodium (50 mg, 2.17 mmoles) and ethanol (1 ml), for 3 days at room temperature. Work up as usual gave only **16** (37 mg, 100%).

General Procedure for the Reaction of **2** with Phosphorus Pentasulfide.

Pyridine (3-5 ml) was added to a mixture of **2** and phosphorus pentasulfide. The mixture was heated for 2 hours at reflux and then dichloromethane was added to the cooled reaction mixture, which was neutralized with 5% hydrochloric acid. The dichloromethane layer was separated and dried over magnesium sulfate. After removal of the solvent, the residue was chromatographed on silica gel (2 x 5 cm). Sulfur was removed by elution with *n*-hexane. Elution with dichloromethane gave 3-(4-chlorobenzylamido)-4-(4-chlorophenyl)-1,2,5-thiadiazole (**17b**) and 3-(4-bromobenzylamido)-4-(4-bromophenyl)-1,2,5-thiadiazole (**17c**). However, in the case of 3-(4-nitrobenzylamido)-4-(4-nitrophenyl)-1,2,5-thiadiazole (**17a**), ethyl acetate was used as an eluent. For each case, consult Table 4 for quantities of the reactants and yields and analytical data of compounds **17a-c** and Table 5 for their ir, ^{1}H nmr, and ms spectroscopic data of **17a-c.**

Reaction of 4-(4-Bromobenzoylformamido)-3-(4-bromophenyl)-1,2,5-thiadiazole (**2c**) with Lawesson's Reagent.

Pyridine (3 ml) was added to a mixture of **2d** (47 mg, 0.101 mmole) and Lawesson's reagent (162 mg, 0.401 mmole). The mixture was heated for 3.5 hours at reflux. The mixture was worked up as described in the reaction with the phosphorus pentasulfide. Compound **17c** (31 mg) was obtained in 68% yield.

Reaction of **2c** with Hydrogen Sulfide Gas.

Hydrogen sulfide gas was bubbled into the solution of **2c** (40 mg, 0.106 mmole) in pyridine (3 ml) for 1 hour at reflux. Chromatography (2 x 8 cm) of the reaction mixture as described in the reaction with phosphorus pentasulfide gave **17b** (27 mg, 67%) and sulfur (12 mg, 43%).

Reaction of **2c** with Aluminum Isopropoxide.

A mixture of **2c** (30 mg, 0.08 mmole) and aluminum isopropoxide (24 mg, 0.12 mmole) in 2-propanol (4 ml) was heated for 5 hours at 80°. The cooled reaction mixture was neutralized with 10% hydrochloric acid. Evaporation of the solvent *in vacuo* gave a residue, which was extracted with dichloromethane (20 ml x 3). The extracts were dried over magnesium sulfate and evaporation of the solvent gave a residue, which was chromatographed as described for the reaction of **2c** with sodium alkoxide; the yield of **9a** was 24 mg (79%).

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