Base-induced Dehydrosulfinatocyclization of *N*-Alkyl-*N*-phenylsulfonyl-*N''*-arylbenzamidrazones to 3,4-Diaryl-4*H*-1,2,4-triazoles

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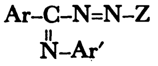
3,4-Diaryl-4*H*-1,2,4-triazoles were obtained in good to comparable yields by the reaction of *N*-alkyl-*N*-phenylsulfonyl-*N''*-arylbenzamidrazones with sodium hydride. The reaction probably proceeds *via* the elimination of benzenesulfinic acid and the oxidative cyclization of *N*-alkylidene-*N''*-arylbenzamidrazones generated by the base-catalyzed isomerization of azo intermediates.

As the McFadyen-Stevens[1)] and the Bamford-Stevens reactions,[2)] such reactions of arylsulfonylhydrazine derivatives involving the elimination of arenesulfonyl group as arenesulfinate anion may be attractive from synthetic aspects.

In a previous paper,[3)] we reported a preparative method of 3-aryl-1,2,4-benzotriazines by the mercury(II) oxide-oxidation of *N*-phenylsulfonyl-*N''*-arylbenzamidrazones (**1**). This reaction has been postulated to proceed *via* diazonium benzenesulfinates generaed from intermediate azo sulfones (**2**), the oxidizing producs of the benzamidrazones.



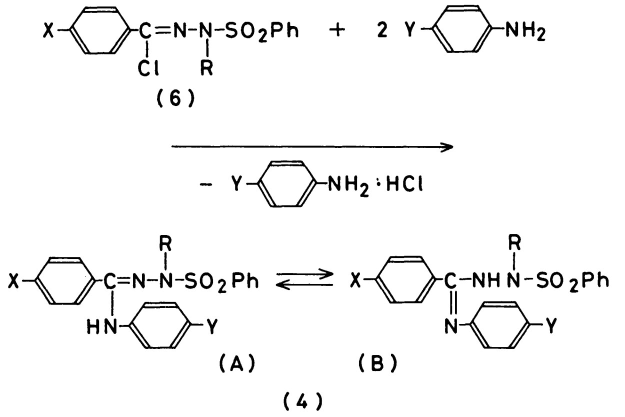
$$\begin{array}{l}\mathrm{Ar{-}C{-}N{=}N{-}Z}\\ \quad\ \ \|\\ \quad\ \ \mathrm{N{-}Ar'}\end{array}$$

2 ($\mathrm{Z{=}PhSO_2}$)
3 (Z=Alkyl)

N,*N*-Disubstituted amidrazones such as the title amidrazones (**4**) cannot undergo this type of oxidation leading to the formation of **2**, as a matter of course. However, as has been seen in some reactions of arylsulfonylhydrazines (carrying a free hydrogen at the 2-position) with a base,[4)] the base-induced 1,2- (or 1,4-) elimintion of arenesulfinic acid can be expected for the title amidrazones, which would result in the formation of 1,2,4-triazabutadiene intermediates (**3**). The present paper deals with the formation of 3,4-diaryl-4*H*-1,2,4-triazoles (**5**) from *N*-alkyl-*N*-phenylsulfonyl-*N''*-arylbenzamidrazones (**4**) *via* the elimination of benzenesulfinic acid by the action of sodium hydride.

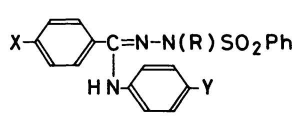
Results and Discussion

Preparation of N-*Alkyl*-N-*phenylsulfonyl*-N''-*arylbenzamidrazones (4).* Amidrazones **4** were prepared by the reaction of anilines with *N*-alkyl-*N*-(phenylsulfonyl)benzohydrazonoyl chlorides (**6**), readily obtainable from *N*-(phenylsulfonyl)benzohydrazonoyl chlorides or *N*-alkyl-*N*-(phenylsulfonyl)benzohydrazides[5)] (Scheme 1).



Scheme 1.

TABLE 1. *N*-ALKYL-*N*-PHENYLSULFONYL-*N''*-ARYLBENZAMIDRAZONES (**4**),



	Amidrazone			Yield/%[a)]	Mp	Formula	Found (%)			Calcd (%)		
	X	Y	R		θ_m/°C		C	H	N	C	H	N
4a	H	H	Me	70	154—156	$C_{20}H_{19}N_3O_2S$	65.70	5.24	11.50	65.78	5.25	11.63
4b	H	Me	Me	56	165—167	$C_{21}H_{21}N_3O_2S$	66.14	5.68	11.06	66.47	5.58	11.07
4c	H	MeO	Me	50	172—174	$C_{21}H_{21}N_3O_3S$	63.82	5.56	10.21	63.82	5.35	10.63
4d	H	Cl	Me	62	161—162	$C_{20}H_{18}N_3O_2SCl$	59.45	4.63	10.70	60.07	4.54	10.51
4e	Me	H	Me	79	152—154	$C_{21}H_{21}N_3O_2S$	66.41	5.54	10.86	66.47	5.58	11.07
4f	Me	Me	Me	61	167—168	$C_{22}H_{23}N_3O_2S$	67.07	5.81	10.64	67.15	5.89	10.68
4g	Me	Cl	Me	69	172—173	$C_{21}H_{20}N_3O_2SCl$	60.97	4.85	10.05	60.94	4.87	10.15
4h	Cl	H	Me	71	148—150	$C_{20}H_{18}N_3O_2SCl$	59.89	4.50	10.40	60.07	4.54	10.51
4i	Cl	Me	Me	68	173—175	$C_{21}H_{20}N_3O_2SCl$	60.70	4.86	10.25	60.94	4.87	10.15
4j	Cl	Cl	Me	77	194—196	$C_{20}H_{17}N_3O_2SCl_2$	55.23	3.93	9.65	55.31	3.95	9.67
4k	H	H	Et	76	140—142	$C_{21}H_{21}N_3O_2S$	66.29	5.51	10.71	66.47	5.58	11.07
4l	H	Cl	Et	87	146—148	$C_{21}H_{20}N_3O_2SCl$	61.15	4.76	10.03	60.94	4.87	11.15

a) Isolated yield.

Table 2. Spectral data of amidrazones (**4**)

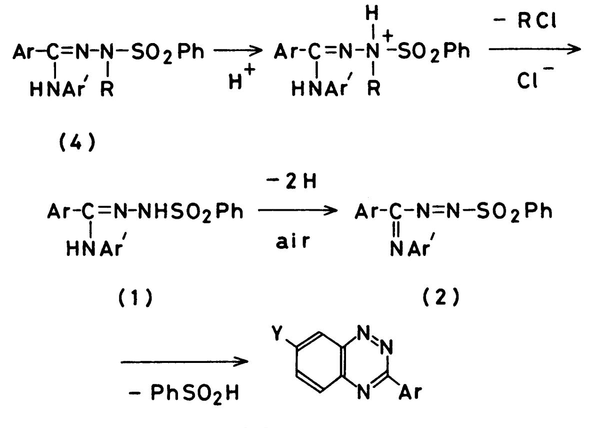
Amidrazone	IR (KBr)[a)]				NMR ($CDCl_3$) δ[b,c)]		
	ν_{NH} cm^{-1}	$\nu_{C=N}$ cm^{-1}	as. ν_{SO_2} cm^{-1}	sym. ν_{SO_2} cm^{-1}	N-H	N-CH_3 (-CH_2CH_3)	Aromatic H
4a	3300	1590s	1390m 1343s	1167m 1158s	8.23brs	2.92s	6.60—8.12m
4b	3280	1598s	1383m 1348s	1170w 1165s	7.98brs	2.92s	6.50—8.20m
4c	3280	1595s	1390m 1335s	1175m 1156s	8.08brs	2.91s	6.40—8.20m
4d	3295	1590s	1375m 1344s	1175w 1157s	8.19brs	2.91s	6.50—8.10m
4e	3350	1598s	1395m 1350s	1185m 1163s	8.47brs	2.90s	6.55—8.40m
4f	3295	1600s	1391m 1339s	1184m 1162s	8.07brs	2.90s	6.50—8.30m
4g	3285	1605s	1388m 1340s	1180m 1160s	8.15brs	2.90s	6.50—8.30m
4h	3260	1582s	1362m 1330s	1163sh 1147s	7.93brs	2.90s	6.65—8.08m
4i	3265	1583s	1361w 1330s	1162w 1150s	8.18brs	2.90s	6.50—8.10m
4j	3260	1600s	1360w 1332s	1172w 1148s	8.47brs	2.90s	6.50—8.10m
4k	3290	1595s	1382m 1340s	1154m 1167s	8.30brs	3.23q, 1.18t (J=7.2, 7.2 Hz)	6.60—8.15m
4l	3290	1590s	1382m 1340s	1155sh 1166s	8.23brs	3.24q, 1.15t (J=7.2, 7.2 Hz)	6.55—8.10m

a) Abbreviations are as follows: m, medium; s, strong; w, weak; sh, shoulder. b) Abbreviations are as follows: brs, broad singlet; s, singlet; q, quartet; t, triplet. c) Other signals are as follows: **4b**, 2.24s, *p*-CH_3 (Y); **4c**, 3.71s, *p*-OCH_3 (Y); **4e**, 2.31s, *p*-CH_3 (X), **4f**, 2.31s, *p*-CH_3 (X) and 2.25s, *p*-CH_3 (Y); **4g**, 2.33s, *p*-CH_3 (X); **4i**, 2.27s, *p*-CH_3 (Y).

On heating in refluxing dioxane, hydrazonoyl chlorides **6** and anilines afforded amidrazones **4** only in poor yields (for example, *N*-methyl-*N*-(phenylsulfonyl)-benzohydrazonoyl chloride and aniline gave the corresponding amidrazone in an 18% yield after refluxing for 24 h). However, when chlorides **6** were fused with anilines at 105—110 °C for 3—4 h under an atmosphere of nitrogen, compounds **4** were obtained in good yields. Small amounts of *N*-methyl-*N*-(phenylsulfonyl)benzohydrazide, hydrolyzed products of **6**, were also obtained. The results are summarized in Tables 1 and 2.

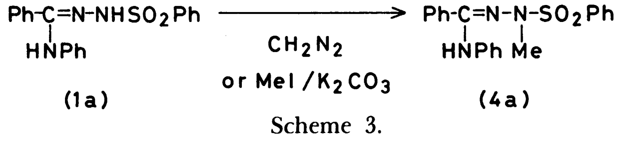
Interestingly, when a fusion of compounds **6** with anilines was conducted at higher temperature, the yields of amidrazones decreased remarkably and the formation of 3-aryl-1,2,4-benzotriazines was observed. For example, *N*-methyl-*N*-(phenylsulfony)-*p*-methylbenzohydrazonoyl chloride gave **4g** in a 19% yield and 7-chloro-3-*p*-tolyl-1,2,4-benzotriazine in a 17% yield on heating with *p*-chloroaniline at 120 °C for 1.5 h, and 7-chloro-3-phenyl-1,2,4-benzotriazine (21%) was obtained by the fusion of *N*-methyl-*N*-(phenylsulfonyl)benzohydrazonoyl chloride with *p*-chloroaniline at 150 °C for 1.5 h. In the latter case, no amidrazone could be detected.

For these benzotriazine formations, the *N*-alkyl group of **4** must be eliminated. Since hydrogen chloride exists in the reaction medium, the reaction may proceed *via* a route which involves the protonation of initially formed amidrazones and the subsequent nucleophilic attack of chloride ion. The resulting *N*-dealkylated amidrazones (**1**) probably undergo air oxidation leading to the formation of benzotriazines *via* **2** (Scheme 2).



Scheme 2.

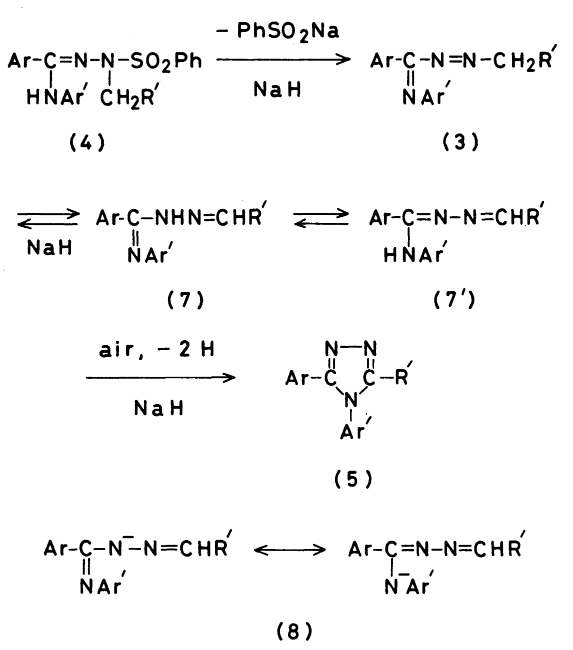
N-Alkylaion of *N*-phenylsulfonyl-*N''*-arylbenzamidrazone (**1**) with diazoalkane or alkyl iodide may be available for preparing **4**. For example, **4a** was obtained in a good yield by these methods (Scheme 3).



Scheme 3.

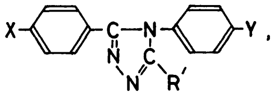
For the amidrazones, two tautomeric structures, **4**(A) and **4**(B), are possible. The IR spectra of **4** are far simple in the N-H absorption region (>3000 cm^{-1}) as compared with those of *N*-phenylsulfonyl-*N*''-arylbenzamidrazones. According to Walter and Weiss,[6] *N,N*-disubstituted *N*''-arylbenzamidrazones prefer to an amide hydrazone form which is stabilized by intramolecular hydrogen bonding. Thus, amidrazones **4** also may take the amide hydrazone structure, **4**(A). The duality of as. ν_{SO_2} and sym. ν_{SO_2} absorptions may be due to Fermi resonance.

*Reactions of Amidrazones **4** with Sodium Hydride.* Amidrazones **4** were allowed to react with small excess amounts of sodium hydride dispersion in dioxane under reflux.[7] With the progress of reaction, precipitation of sodium benzenesulfinate was observed. The reaction went essentially to completion after about 20 h of refluxing. After removal of the precipitated sodium benzenesulfinate, the reaction mixtures were chromatographed to give 3,4-diaryl-4*H*-1,2,4-triazoles in good to comparable yields along with small amounts of undeterminable oils. The results are summarized in Tables 3 and 4.



Scheme 4.

TABLE 3. 3,4-DIARYL-4*H*-1,2,4-TRIAZOLES (**5**) FROM AMIDRAZONES **4**



	Triazole			Yield/%[a)]	Mp	Formula	Found (%)			Calcd (%)		
	X	Y	R′		θ_m/°C		C	H	N	C	H	N
5a	H	H	H	78	139—140[b)]	$C_{14}H_{11}N_3$	75.79	5.12	18.42	75.60	5.01	18.99
5b	H	Me	H	57	149—151	$C_{15}H_{13}N_3$	76.47	5.67	18.07	76.57	5.57	17.86
5c	H	MeO	H	63	121—122	$C_{15}H_{13}N_3O$	71.65	5.16	16.88	71.70	5.21	16.72
5d	H	Cl	H	80	189—190	$C_{14}H_{10}N_3Cl$	65.31	3.90	16.49	65.76	3.94	16.43
5e	Me	H	H	46	165—166	$C_{15}H_{13}N_3$	76.41	5.58	17.64	76.57	5.57	17.86
5f	Me	Me	H	34	192—194	$C_{16}H_{15}N_3$	77.10	6.02	17.02	77.08	6.06	16.85
5g	Me	Cl	H	57	201—203	$C_{15}H_{12}N_3Cl$	66.93	4.53	15.71	66.79	4.48	15.58
5h	Cl	H	H	36	174—175	$C_{14}H_{10}N_3Cl$	65.98	3.95	16.20	65.76	3.94	16.43
5i	Cl	Me	H	40	174—176	$C_{15}H_{12}N_3Cl$	66.76	4.43	15.67	66.79	4.48	15.58
5j	Cl	Cl	H	40	184—186	$C_{14}H_{10}N_3Cl_2$	57.66	3.07	14.38	57.95	3.13	14.48
5k	H	H	Me	90	161—163[c)]	$C_{15}H_{13}N_3$	76.72	5.64	17.90	76.57	5.57	17.86
5l	H	Cl	Me	63	160—162	$C_{15}H_{12}N_3Cl$	66.88	4.57	15.75	66.79	4.48	15.58

a) Isolated yield. b) Lit, mp 140 °C: R. Fusco and S. Rossi, *Ann. Chim.*, **50**, 277 (1960). c) Lit, mp 158.0—160.5 °C: Ref. 11.

TABLE 4. SPECTRAL DATA OF TRIAZOLES (**5**)

Triazole	IR (KBr) ν/cm^{-1}			NMR ($CDCl_3$) δ				
	1,2,4-triazole ring			5-H	5-CH_3	*p*-CH_3	(-OCH_3)	Aromatic H
5a	1598	1070	1016	8.35s				7.00—7.70m
5b	1600	1070	1010	8.31s		2.45s	(Y=Me)	7.00—7.70m
5c	1610	1070	1017	8.29s		3.87s	(Y=OMe)	6.80—7.68m
5d	1575	1073	1013	8.32s				6.80—7.68m
5e	1596	1090	1012	8.32s		2.34s	(X=Me)	6.90—7.70m
5f	1612	1089	1010	8.29s		2.35s 2.43s	(X=Me) (Y=Me)	6.85—7.53m
5g	1620	1089	1018	8.28s		2.33s	(X=Me)	6.95—7.67m
5h	1584	1073	1007	8.36s				7.00—7.60m
5i	1599	1082	1003	8.32s		2.46	(Y=Me)	7.00—7.60m
5j	1595	1080	1004	8.33s				7.00—7.60m
5k	1596	1073	1012		2.34s			7.00—7.70m
5l	1597	1075	1010		2.37s			7.00—7.70m

The triazoles obtained were confirmed by their analytical and spectral data, and the idetification of known compounds was made by direct comparison with authentic specimens. The absorptions at near 1600, 1080, and 1010 cm^{-1} in the IR spectra can be attributed to the 1,2,4-triazole ring vibrations.[8]

The present triazole formation can be explained by the following route, which involves the 1,4-elimination of benzenesulfinic acid[9] and the base-catalyzed tautomerization[10] of **3** to *N*-alkylidene-*N''*-arylbenzamidrazones (**7** or **7'**) followed by oxidative cyclization to 1,2,4-triazoles (Scheme 4).

In view of the acidity of the amino hydrogen of **4**, **4** should generae initially **3**, from which **7** or **7'** may be formed. The cyclization of *N*-arylmethylene-*N''*-arylbenzamidrazones to 3,4,5-trisubstituted 4-*H*-triazoles by mercury(II) oxide-oxidation has been reported by Spassov *et al.*[11] For the oxidative cyclization step, **7** or **7'** to **5**, the anionic 6π-electrocyclic process or intramolecular nucleophilic process of **8** and the subsequent aromatization to **5** may be conceivable.

Experimental

Melting points were determined with a Yanagimoto MP-S3 micromelting point apparatus, and are uncorrected. The microanalysis was performed on a Perkin-Elmer 240 elemental analyzer. The IR and NMR spectra were recorded with a Hitachi 260-10 and a Varian EM-360A spectrometers, respectively. *N*-Methyl-*N*-(phenylsulfonyl)benzohydrazonoyl chlorides were prepared by the method previously reported.[5]

Preparation of N-*Ethyl*-N-*(phenylsulfonyl)benzohydrazonoyl Chloride.* To a solution of 1-benzoyl-2-phenylsulfonylhydrazine (5.52 g, 20 mmol) in DMF (50 ml), a 0.58 g-portion (net 24 mmol) of sodium hydride dispersion (70% in liquid paraffin) was added under external cooling. After the cease of gas evolution (a few minutes), ethyl iodide (3.43 g, 22 mmol) was added to the mixture. After stirring for 1 h at room temperature, the DMF solution was poured into water to separate 1-benzoyl-2-ethyl-2-phenylsulfonylhydrazine, which was purified by crystallization from ethanol (yield: 4.95 g, 82%). Mp 162—164 °C; IR(KBr, cm^{-1}): 3210 (NH), 1673 (C=O), 1353, and 1163, (SO$_2$); NMR (CDCl$_3$), δ=3.73 (2H q, N-C$\underline{\text{H}}_2$CH$_3$, J=7.2 Hz), 1.25 (3H t, N-CH$_2$C$\underline{\text{H}}_3$, J=7.2 Hz), and 7.20—8.20 (11H m, 2Ph and NH). Found: C, 59.35; H, 5.46; N, 9.18%. Calcd for $C_{15}H_{16}N_2O_3S$: C, 59.19; H, 5.30; N, 9.20%.

A mixture of 2-ethylated hydrazine thus obtained (4.53 g, 15 mmol) and 30 ml of thionyl chloride was refluxed for 3 h. After removal of excess thionyl chloride *in vacuo*, the oily residue was chromatographed on a silica-gel column (2.5 cm-d, 15 cm-h; eluent: benzene) to give *N*-ethyl-*N*-(phenylsulfonyl)benzohydrazonoyl chloride (3.49 g, 72%), which was crystallized from benzene–hexane. Mp 63—65 °C; IR (KBr, cm^{-1}): 1591 (C=O), 1350, and 1168 (SO$_2$); NMR (CDCl$_3$), δ=3.41 (2H q, N-C$\underline{\text{H}}_2$CH$_3$, J=7.0 Hz), 1.07 (3H t, N-CH$_2$C$\underline{\text{H}}_3$, J=7.0 Hz), and 7.30—8.20 (10H m, 2Ph). Found: C, 55.76; H, 4.71; N, 8.70%. Calcd for $C_{15}H_{15}N_2O_2SCl$: C, 55.81; H, 4.68; N, 8.68%.

Preparaton of Amidrazones 4. General Procedure: A mixture of **6** (10 mmol) and aniline (22 mmol) was heated in an oil bath at 105—110 °C for 3—4 h under nitrogen atmosphere. After being cooled, the reaction mixture was extracted with water and chloroform. The chloroform layer was washed and dried, and then concentrated. The chloroform extract was chromatographed on a silica-gel column (2.5 cm-d, 10 cm-h; eluent: benzene–ethanol) to give **4**, which was recrystallized from benzene. The results were summarized in Tables 1 and 2.

*Fusion of **6** with Anilines at a Higher Temperature. A Typical Example*: A mixture of *N*-methyl-*N*-(phenylsulfonyl)-*p*-methylbenzohydrazonoyl chloride (2.582 g, 8 mmol) and *p*-chloroaniline (2.245 g, 17.6 mmol) was heated at 120 °C for 1.5 h in a similar manner. Chloroform extraction followed by chromatography gave amidrazone **4g** (0.569 g, 19%) and 7-chloro-3-*p*-toly-1,2,4-benztoriazine[3] (mp 175—177 °C, 0.342 g, 17%) from the reaction mixture.

N-*Methyltion of* N-*Phenylsulfonyl*-N''-*phenylbenzamidrazone (**1a**). With Methyl Iodide and Potassium Carbonate*: A mixture of **1a** (703 mg, 2 mmol) and methyl iodide (430 mg, 3 mmol) in THF (30 ml) was stirred with potassium carbonate (420 mg, 3 mmol) for 18 h at room temperature. The reaction mixture was poured into water (150 ml) to give precipitates, which were purified by column chromatography to give **4a** (557 mg, 76%).

With diazomethane: To a solution of **1a** (352 mg, 1 mmol) in THF (15 ml), slightly excess amounts of an ethereal solution of diazomethane was added by portions. After removal of solvent, the residue was chromatographed to give **4a** (313 mg, 89%).

The Reaction of Amidrazones 4 with Sodium Hydride. General Procedure: A mixture of **4** (1 mmol) and sodium hydride dispersion (net 1.5 mmol) in dry dioxane (30 ml) was refluxed for 20 h under nitrogen atmosphere. After removal of separated sodium benzenesulfinate by filtration, the reaction mixture was concentrated and chromatographed on a silica-gel column (2.0 cm-d, 10 cm-h; eluent: benzene–ethanol) to give **5**, which was recrystallized from benzene–hexane. The results were summarized in Tables 3 and 4.

The sodium benzenesulfinate above obtained (crude yield: nearly quantitative) was allowed to react with benzyl chloride in ethanol to give phenyl benzyl sulfone, mp 147—148 °C (ethanol), the IR spectrum of which was spectroscopically identical with that of an authentic sample.

References

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4) The McFadyen-Stevens reaction falls within these types of reactions. The formation of diimide by the reaction of *p*-tolylsulfonylhydrazine with sodium hydroxide (R. S. Dewey and E. E. van Tamelen, *J. Am. Chem. Soc.*, **83**, 3729 (1961)) may be the simplest type in these reactions.

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6) W. Walter and H. Weiss, *Justus Liebigs Ann. Chem.*, **758**, 162 (1972).

7) When compounds **4** were stirred with potassium carbonate at room temperature, no reactions were observed.

8) For a reference to IR spectra of 1,2,4-triazoles, see E. Lieber, D. R. Levering, and L. J. Patterson, *Anal. Chem.*, **23**, 1594 (1951).

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