REACTION OF ARYL BROMOMETHYL KETONE PHENYLSULFONYLHYDRAZONES WITH BENZYLIDENEANILINE[1]

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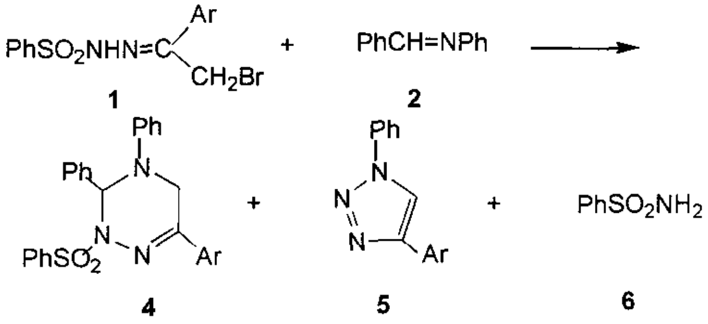
Abstract — 6-Aryl-3,4-diphenyl-2-phenylsulfonyl-2,3,4,5-tetrahydro-1,2,4-triazines and 4-aryl-1-phenyl-1,2,3-triazoles were obtained in moderate yields by the reaction of aryl bromomethyl ketone phenylsulfonylhydrazones with benzylideneaniline.

Arylsulfonylhydrazones of α-halo ketones are known to undergo the 1,4-elimination of hydrogen halides affording arylsulfonylazoethylenes[2] by the action of base: some nucleophilic reagents function as a base to give the same result. However, appropriate nucleophiles such as quinoline and isoquinoline[3] react with the hydrazones in a substitution mode to give the corresponding sulfonylhydrazones of α-substitututed acetophenones as intermediates which serve potentially useful precursors for the synthesis of nitrogen-containing heterocycles.[4]

In the present paper, we would like to describe the reaction of aryl bromomethyl ketone phenylsulfonyhydrazones (**1**) with benzylideneaniline (**2**) forming 6-aryl-3,4-diphenyl-2-phenylsulfonyl-2,3,4,5-tetrahydro-1,2,4-triazines (**4**) and 4-aryl-1-phenyl-1,2,3-triazoles (**5**) together with benzenesulfonamide (**6**).

The reaction of **1** with **2** was carried on at room temperature. When an equimolar quantity of **2** was added to a THF solution of **1**, the precipitation of benzylidene-*N*-phenyliminium salts (**3**) was observed. Without isolation of **3**, the reaction mixture was stirred with a small excess amount of triethylamine for half a day. Removal of the solvent from the reaction mixture and chromatographic treatment of the residue gave 6-aryl-3,4-diphenyl-2-phenylsulfonyl-2,3,4,5-tetrahydro-1,2,4- triazines (**4**) and 4-aryl-1-phenyl-1,2,3-triazoles (**5**) along with benzenesulfonamide (**6**). (Scheme 1.)

Without using triethylamine, the reaction of **1** with **2** in twice the molar quantity of **1** afforded similar results, while that of **1** with **2** in an equimolar ratio gave also **4**, **5**, and **6** in lower yields except a few examples. The results are summarized in Table 1.



1a, **4a**, **5a** : Ar = Ph
1b, **4b**, **5b** : Ar = *p*-BrC_6H_4
1c, **4c**, **5c** : Ar = *p*-ClC_6H_4
1d, **4d**, **5d** : Ar = *p*-MeC_6H_4
1e, **4e**, **5e** : Ar = *p*-$NO_2C_6H_4$

Scheme 1.

Table 1. Reactions of Hydrazones (**1**) with Benzylideneaniline (**2**)

Hydrazones	Products and Their Yields[a]		
	4	**5**	**6**[b]
1a	25 (16)	22 (20)	32 (39)
1b	30 (13)	18 (21)	34 (36)
1c	40 (10)	13 (19)	24 (20)
1d	20 (11)	25 (24)	27 (25)
1e	45 (15)	14 (19)	27 (30)

a) Isolated yields as mole per cent based on **1**. Data in parenthese are those obtained from the reactions between **1** and **2** in 1:1 molar ratio without triethylamine.

b) mp 153—154℃ (lit., mp 153℃: N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," 2nd ed., Interscience, New York(1957), p. 690). Spectroscopically identical with an authentic sample prepared from benzenesulfonyl chloride and aqueous ammonia.

The structure assignment of **4** and **5** was made on the basis of their analytical and spectral data (Tables 2 and 3). In the IR spectra, products **4** exhibit characteristic absorption bands near 1350 (asym. ν SO_2) and 1170 cm^{-1} (sym. ν SO_2).
In the ^{1}H-NMR spectra, compounds **4** have an AB quartet-type methylene signal near δ 4.00 ppm, which should imply the tetrahydrotriazine ring to be nonplanar.
The EI mass spectrum of **4a** (ionization energy: 70 eV) has the $M^{+\cdot}$ ion peak (m/z 453,

Table 2. 2,3,4,5-Tetrahydro-1,2,4-triazines (**4**)

Compd	mp(decomp)^a °C	Formula	Found(Calcd)/% C	H	N
4a	185—187	$C_{27}H_{23}N_3O_2S$	71.49(71.50)	5.05(5.11)	9.14(9.26)
4b	203—205	$C_{27}H_{22}N_3O_2BrS$	60.90(60.91)	4.16(4.16)	7.63(7.89)
4c	205—206	$C_{27}H_{22}N_3O_2ClS$	66.49(66.45)	4.61(4.54)	8.51(8.61)
4d	205—206	$C_{28}H_{25}N_3O_2S$	71.89(71.92)	5.42(5.39)	9.00(8.99)
4e	206—207	$C_{27}H_{22}N_4O_4S$	64.92(65.05)	4.51(4.45)	11.31(11.24)

a) Recrystallized from benzene – hexane.

Table 3. Spectral Data of 2,3,4,5-Tetrahydro-1,2,4-triazines (**4**)

Compd.	IR (KBr, υ, cm^{-1}) SO$_2$		^{1}H-NMR (CDCl$_3$, δ, ppm)^a CH$_3$(s)	C^{5}H$_2$(dd)	C^{3}H and Aromatic(m)
4a	1344	1169		3.75, 4.20 (*J*=18 Hz)	6.8 — 7.9
4b	1352	1168		3.59, 4.13 (*J*=18 Hz)	6.7 — 7.8
4c	1352	1169		3.70, 4.14 (*J*=18 Hz)	6.7 — 7.8
4d	1348	1169	2.39	3.75, 4.21 (*J*=18 Hz)	6.8 — 7.8
4e	1344	1169		3.74, 4.17 (*J*=18 Hz)	6.8 — 8.5

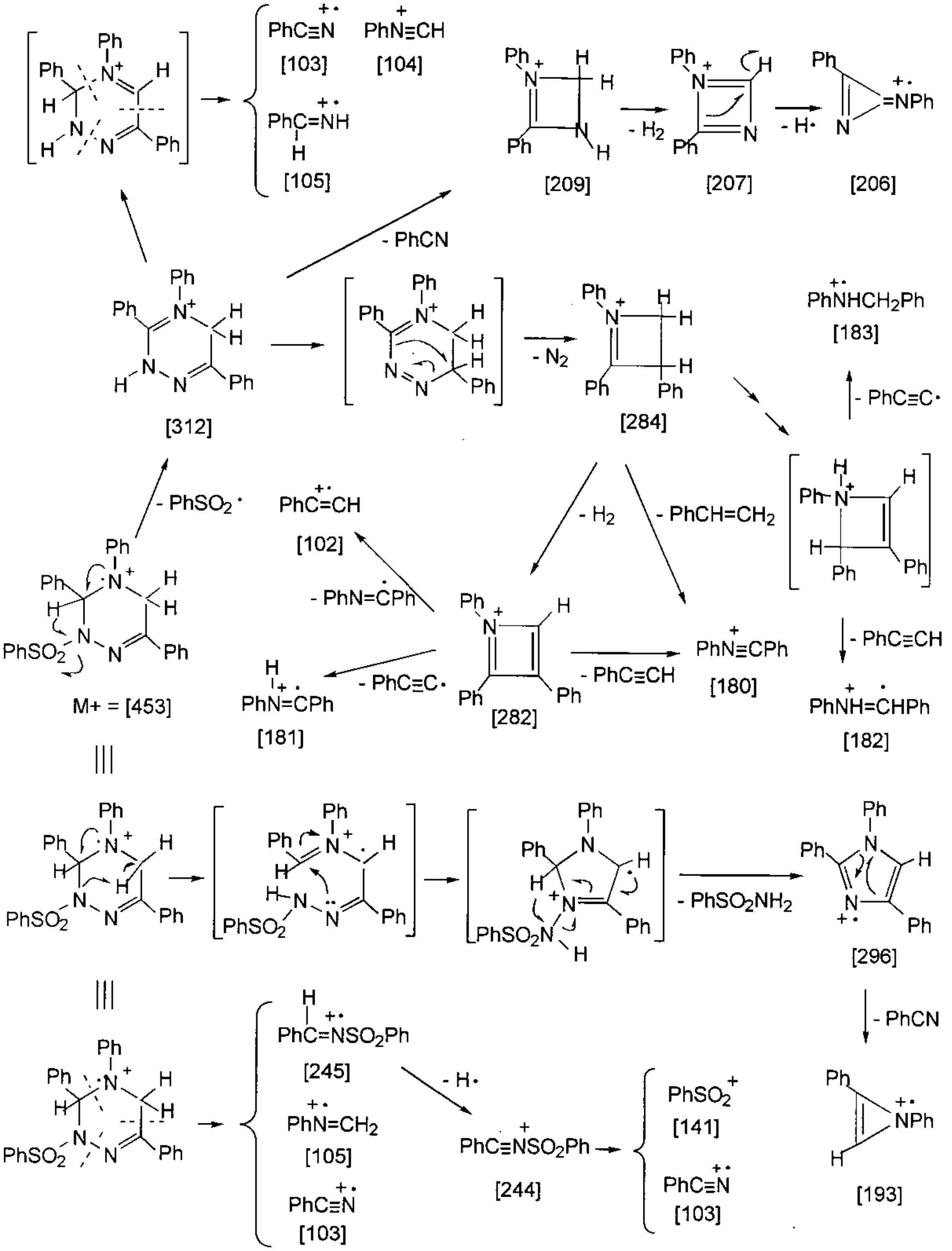
a) Abbreviations are as follows: dd, double doublet; m, multiplet; s, singlet.

12%) along with the following fragment ion peaks: m/z 312 (30%), 296 (14%), 284 (22%), 282 (26%), 245 (4.2%), 244 (9.3%), 209 (12%), 207 (12%), 206 (11%), 193 (13%), 183 (44%), 182 (99%), 181 (99%), 180 (99%), 142 (15%), 141 (13%), 125 (17%), 105 (30%), 104 (99%), 103 (100%), 102 (86%), 91 (13%), 78 (99%), 77 (99%), 51 (99%), 28 (54%), and other minor peaks. These ions can be reasonably interpreted by fragmentations represented in Scheme 2.

The analytical and physical data of **5** are shown in Tables 4 and 5. Compounds **5** exhibit a pair of absorption bands due to 1,2,3-triazole ring vibrations near 1040 and 995 cm^{-1} in the IR spectra.[5] In the ^{1}H-NMR spectra, **5** show a singlet near 8.3 ppm along with an aromatic multiplet at δ 7.1 — 8.5 ppm.

For the fragmentation in the EI-mass spectroscopy of **5a**, m/z 221 (M$^{+\cdot}$, 15%), 193 (100%), 192 (40%), 165 (96%), 116 (73%), 90 (72%), 89 (68%), 77 (99%), 51 (72%), and 28 (75%), a reasonable interpretation is given in Scheme 3.

The formation of tetrahydro-1,2,4-triazines (**4**) can be formulated by the intramolecular nuclephilic process of intermediate benzylideneanilinium salts (**3**) accompanied with the elimination of hydrogen bromide (Scheme 4). For a related reaction, the conden-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PhN≡CH [104]
PhC=NH [105]
[209]
- H₂
[207]
- H·
=NPh
[206]
- PhCN
[312]
- N₂
[284]
PhNHCH₂Ph [183]
- PhC≡C·
- PhSO₂·
PhC=CH [102]
- H₂
- PhCH=CH₂
- PhN=CPh
M+ = [453]
- PhC≡C·
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- PhC≡CH
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- PhC≡CH
PhNH=CHPh [182]
- PhSO₂NH₂
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- PhCN
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PhN=CH₂ [105]
PhC≡N [103]
- H·
PhC≡NSO₂Ph [244]
PhSO₂ [141]
PhC≡N [103]
NPh
[193]

Scheme 2.

Table 4. 4-Aryl-1-phenyl-1,2,3-triazoles (**5**)

Compd	mp[a] ℃	Formula	Found(Calcd)/% C	 H	 N
5a	186—187[b]	$C_{14}H_{11}N_3$	76.16(76.00)	5.08(5.01)	18.76(18.99)
5b	226—227[c]	$C_{14}H_{10}N_3Br$	56.21(56.02)	3.45(3.36)	13.72(14.00)
5c	222—224[d]	$C_{14}H_{10}N_3Cl$	65.99(65.76)	3.97(3.94)	16.18(16.43)
5d	154—155	$C_{15}H_{13}N_3$	76.65(76.57)	5.66(5.57)	17.69(17.86)
5e	247—249	$C_{14}H_{10}N_4O_2$	63.36(63.15)	3.79(3.79)	20.83(21.04)

a) Recrystallized from benzene.

b) lit., mp 185℃: G. Rembarz, B. Kirchhoff, and G. Dongowski, *J. prakt. Chem.*[4], 1966, **33**, 199.

c) lit., mp 224℃: *idem, ibid.*

d) lit., mp 221℃: *idem, ibid.*

Table 5. Spectral Data of 4-Aryl-1-phenyl-1,2,3-triazoles (**5**)

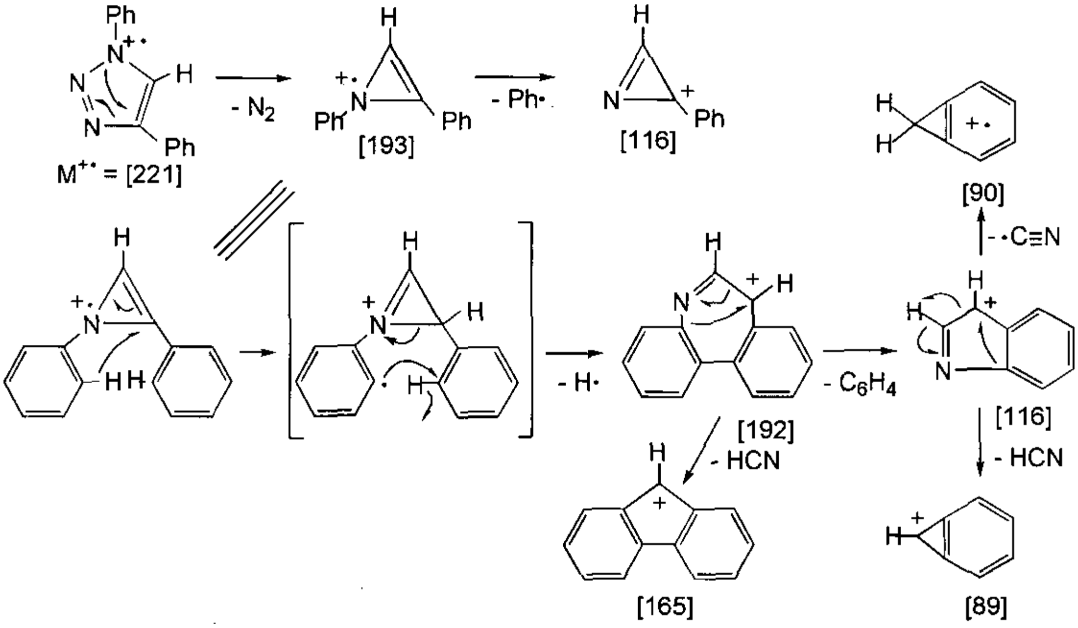
Compd.	IR (KBr, υ, cm^{-1})[a]		^{1}H-Nmr ($CDCl_3$, δ, ppm)[b]		
	Triazole ring		CH_3	C^5H	Aromatic
5a	1042m	995w		8.32s	7.4 — 8.2m
5b	1043m	999w		8.25s	7.4 — 8.0m
5c	1046m	997w		8.27s	7.4 — 8.1m
5d	1042m	997w	2.39s	8.23s	7.1 — 8.1m
5e	1044m	995w		8.23s	7.5 — 8.4m

a) Abbreviations are as follows: m, medium; w, weak.

b) *Abbreviations are as follows: s, singlet; m, multiplet.*

sation of *N*-*p*-anysylphenacylamine *o*-tolylhydrazone with formaldehyde has been reported.[6] In this reaction, one geometric isomer (the syn or anti isomer of o-tolylhydrazone)[7] gave 4-*p*-anysyl-6-phenyl-2-*o*-tolyl-2,3,4,5-tetrahydro-1,2,4-triazine in preference to the other isomer; *analogously, the cyclization of* **3** *to form* **4** (Scheme 4) probably proceeds *via* the *E*-isomer of hydrazones (**3**).

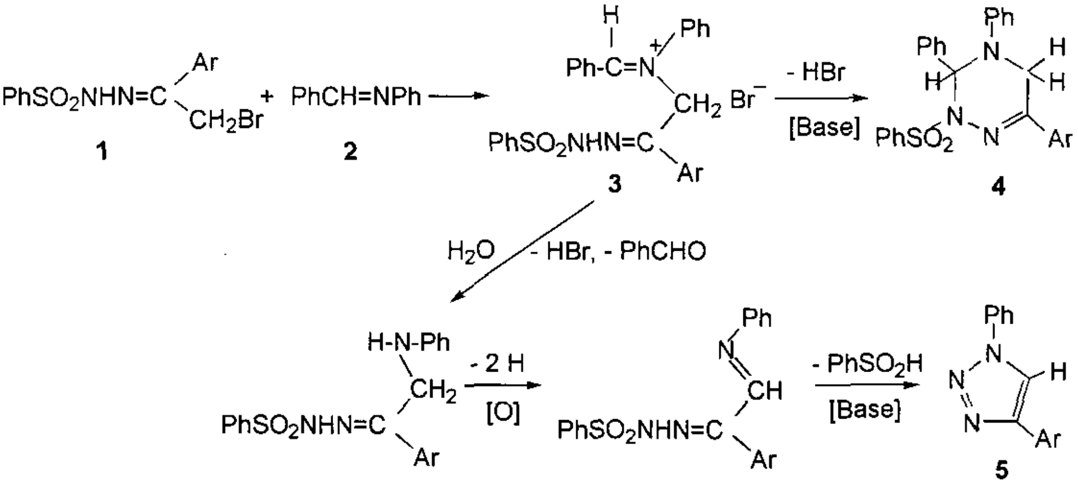
Previously we reported that 1,4-diaryl-1,2,3-triazoles are obtainable from the permanganate oxidation of *N*-arylphenacylamine phenylsulfonylhydrazones prepared *in situ* by the reaction of title hydrazones with arylamines.[8] Thus, *N*-phenylphenacylamine phenylsulfonylhydrazones may be generated by the possible hydrolysis of the intermediates (**3**) with moisture and should undergo air oxidation to result in the formation of 1,2,3-triazoles (**5**) (Scheme 4).



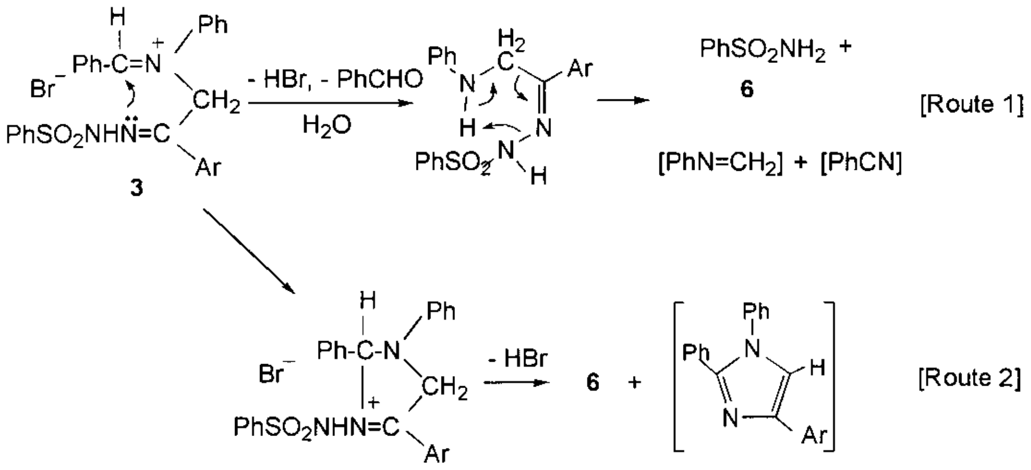
Scheme 3.

An arenesulfonamido group is a good leaving group;[9] the generation of arenesulfonamide from arenesulfonylhydrazone derivatives has been observed also in the reaction of the title hydrazones with quinoline and isoquinoline.[3]

For the present formation of benzenesulfonamide (**6**), two routes may be conceivable (Scheme 5): the 1,4-elimination of **6** *via* a six-membered cyclic transition state from *N*-phenylphenacylamine phenylsulfonylhydrazones, the hydrolysis product from **3** (Route 1); the formation of **6** *via* the intramolecular nucleophilic process of hydrazono



Scheme 4.



Scheme 5.

imino-nitrogen to benzylidene α-cabon followed by the generation of 1,2,4-trisubstituted imidazoles (Route 2).

From the reaction mixture of **1a** and **2**, only a trace amount of benzonitrile (GLC, 1%), and no 1,2,4-triphenylimidazole could be confirmed, thus Routes 1 and 2 are unreasonable; any other information for the sulfonamide formation has not been obtained.

EXPERIMENTAL

Melting points were determined with a Yanagimoto MP-S3 micromelting point apparatus, and are uncorrected. The microanalysis was performed on a Perkin-Elmer 2400 elemental analyzer. The IR, ^{1}H-NMR, and mass spectra were recorded with a JASCO FT/IR-5300S spectrophotometer, a Hitachi R-600 spectrometer, and a Hitachi M-80B mass spectrometer, respectively. Aryl bromomethyl ketone phenylsulfonylhydrazones were prepared from the corresponding bromomethyl ketones and phenylsulfonylhydrazine according to the method described previously.[3]

Reaction of 1 with 2. **General Procedure**: A solution of **2** (10 mmol) in THF (10 mL) was added to a solution of **1** (10 mmol) in THF (10 mL) by portions with stirring at rt. Consumption of **1** was checked by TLC and the resulting reaction mixture was stirred for half a day. After the removal of solvent, the resultant residue was chromatographed on a silica gel column (15 g, 20×20 mm ϕ, eluent: hexane - benzene - ether - ethanol systems) to give **4**, **5**, and **6**. (Table 1.)

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