Synthesis of 1-Aryl-5-chloro-3-(phenylsulfonyl)pyrazol-4-ols from 1,1-Dichloro-3-phenylsulfonyl-2-propanone

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1,1-Dichloro-3-phenylsulfonyl-2-propanone was treated with arenediazonium chlorides to give 1-arylhydrazono-3,3-dichloro-1-phenylsulfonyl-2-propanones, which were cyclized to 1-aryl-5-chloro-3-(phenylsulfonyl)pyrazol-4-ols on treatmemt with base.

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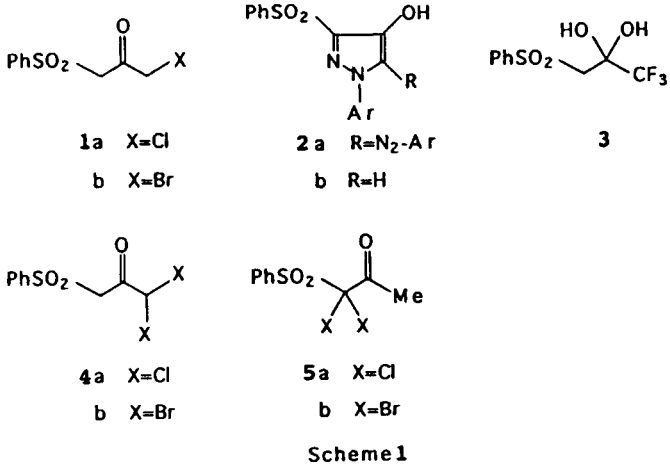
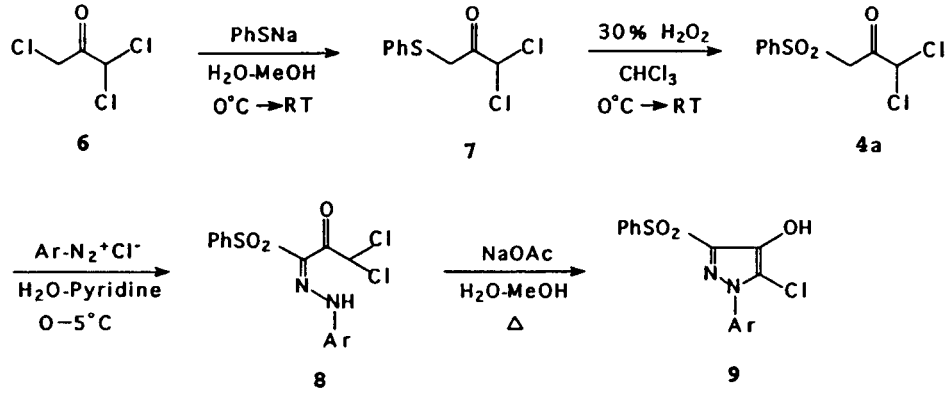
It has been of interest to us to develop multifunctionalized sulfones useful for heterocyclic synthesis. As compared with β-keto sulfones which are often used in heterocyclic synthesis [1], γ -halo-β-keto sulfones are a little known class of sulfones. We have shown already that 1-bromo-3-phenylsulfonyl-2-propanone (**1b**) was cyclized in one step to 1-aryl-5-arylazo-3-(phenylsulfonyl)pyrazol-4-ols **2a** on treatment with arenediazonium chlorides [2] (Scheme 1). On the other hand, when 1-chloro-3-phenylsulfonyl-2-propanone (**1a**) was treated similarly, the corresponding intermediate 5-unsubstituted 1-aryl-3-(phenylsulfonyl)pyrazol-4-ols **2b** were isolated [3]. The related sulfone, 1,1,1-trifluoro-3-phenylsulfonyl-2-propanone hydrate (**3**), was also shown to be a useful starting material for the synthesis of trifluoromethylated heterocycles such as pyrazoles and pyridazines [4]. As an extension of these works, we have examined the reactivity of 1,1-dichloro-3-phenylsulfonyl-2-propanone (**4a**), which seems also to be a useful building block for heterocycles. Although 1,1-dibromo-3-phenylsulfonyl-2-propanone (**4b**) was reported earlier [5], the preparation and reaction of the dichlorinated analogue **4a** has not been described in the literature in spite of increasing interest in sulfones in organic synthesis recently [6].



Scheme 1

Dihalogenation of 1-phenylsulfonyl-2-propanone by sulfuryl chloride or by pyridinium bromide perbromide gave 1,1-dichloro-, **5a**, or 1,1-dibromo-1-phenylsulfonyl-2-propanone **5b**, respectively [7], whereas bromination by bromine was reported to give 1,1-dibromo-3-phenylsulfonyl-2-propanone (**4b**) [5]. We prepared **4a** from commercially available 1,1,3-trichloroacetone (**6**) (Scheme 2). The substitution reaction of **6** with sodium thiophenolate occurred at the 3-position selectively to give 1,1-dichloro-3-phenylthio-2-propanone (**7**), which was oxidized without further purification by hydrogen peroxide to yield **4a** in 45% yield. Arylhydrazones **8a-h** of **4a** were prepared in 24-64% yields on addition of arenediazonium chlorides to a solution of **4a** in pyridine (Table 1). The hydrazones



Scheme 2

Table 1

Pysical Properties of Compounds **8** and **9**

	Ar	Yield %	Mp °C	Molecular Formula (Molecular Weight)	Found/Calcd. C%	H%	N%
8a	C_6H_5	57	159-161 (MeOH)	$C_{15}H_{12}Cl_2N_2O_3S$ (371.24)	48.70 48.53	3.32 3.26	7.36 7.55
8b	4-MeC_6H_4	29	177-179 (MeOH-$CHCl_3$)	$C_{16}H_{14}Cl_2N_2O_3S$ (385.26)	50.36 49.88	3.83 3.66	7.06 7.27
8c	4-$MeOC_6H_4$	35	182-184 (MeOH-$CHCl_3$)	$C_{16}H_{14}Cl_2N_2O_4S$ (401.26)	48.05 47.89	3.63 3.52	6.69 6.98
8d	4-FC_6H_4	24	173-175 (MeOH-$CHCl_3$)	$C_{15}H_{11}Cl_2FN_2O_3S$ (389.23)	46.52 46.28	2.92 2.85	7.07 7.20
8e	4-ClC_6H_4	43	198-200 (EtOH)	$C_{15}HC_{11}Cl_3N_2O_3S$ (405.68)	44.69 44.41	2.79 2.73	6.93 6.91
8f	2-ClC_6H_4	49	153-155 (MeOH-$CHCl_3$)	$C_{15}H_{11}Cl_3N_2O_3S$ (405.68)	44.53 44.41	2.77 2.73	6.76 6.91
8g	3,4-$Cl_2C_6H_3$	64	187-189 (MeOH-$CHCl_3$)	$C_{15}H_{10}Cl_4N_2O_3S$ (440.12)	40.97 40.93	2.42 2.29	6.29 6.37
8h	4-BrC_6H_4	50	208-210 (MeOH-$CHCl_3$)	$C_{15}H_{11}BrCl_2N_2O_3S$ (450.11)	40.43 40.02	2.69 2.46	6.01 6.22
9a	C_6H_5	28	155-156 (C_6H_6)	$C_{15}H_{11}ClN_2O_3S$ (334.78)	53.93 53.82	3.27 3.31	8.22 8.37
9b	4-MeC_6H_4	60	147-149 (iso-PrOH)	$C_{16}H_{13}ClN_2O_3S$ (348.81)	55.26 55.09	3.77 3.76	7.85 8.03
9c	4-$MeOC_6H_4$	30	133-135 (iso-PrOH)	$C_{16}H_{13}ClN_2O_4S$ (364.80)	52.67 52.67	3.60 3.59	7.55 7.68
9d	4-FC_6H_4	54	148-150 (iso-PrOH-$CHCl_3$)	$C_{15}H_{10}ClFN_2O_3S$ (352.77)	51.23 51.07	2.91 2.86	7.83 7.94
9e	4-ClC_6H_4	43	163-164 (C_6H_6)	$C_{15}H_{10}Cl_2N_2O_3S$ (369.22)	48.92 48.80	2.79 2.73	7.52 7.59
9f	2-ClC_6H_4	50	185-187 (iso-PrOH-$CHCl_3$)	$C_{15}H_{10}Cl_2N_2O_3S$ (369.22)	48.71 48.80	2.81 2.73	7.51 7.59
9g	3,4-$Cl_2C_6H_3$	82	196-197 (iso-PrOH-$CHCl_3$)	$C_{15}H_9Cl_3N_2O_3S$ (403.66)	44.75 44.63	2.36 2.25	6.68 6.94
9h	4-BrC_6H_4	54	168-170 (iso-PrOH-$CHCl_3$)	$C_{15}H_{10}BrClN_2O_3S$ (413.65)	43.69 43.55	2.52 2.44	6.65 6.77

Table 2

Spectral Data of Compounds **8** and **9**

	MS m/z (M^+)	IR cm^{-1} (KBr)					^{1}H-NMR δ ppm
8a	370	3200	1680	1530	1460	1420	6.75 (s, 1H), 7.33-8.13 (m, 10H), 12.63 (br s, 1H) ($CDCl_3$)
8b	384	3200	1670	1520	1420	1305	2.38 (s, 3H), 6.80 (s, 1H), 6.23-8.15 (m, 9H), 12.63 (br s, 1H) ($CDCl_3$)
8c	400	3200	1680	1595	1530	1440	3.84 (s, 3H), 6.77 (s, 1H), 6.87-8.11.(m, 9H), 12.69 (br s, 1H) ($CDCl_3$)
8d	388	3200	1680	1525	1475	1440	6.74 (s, 1H), 7.13-8.13 (m, 9H), 12.66 (br s, 1H) ($CDCl_3$)
8e	404	3200	1695	1520	1475	1300	7.43-8.13 (m, 10H), 12.60 (br s, 1H) (DMSO-d_6)
8f	404	3180	1700	1580	1520	1440	6.76 (s, 1H), 7.23-8.18 (m, 9H), 13.04 (br s, 1H) ($CDCl_3$)
8g	438	3160	1680	1575	1520	1440	6.70 (s, 1H), 7.07-8.10 (m, 8H), 12.57 (br s, 1H) ($CDCl_3$)
8h	448	3200	1690	1585	1520	1470	6.73 (s, 1H), 7.13-8.14 (m, 9H), 12.61 (br s, 1H) ($CDCl_3$)
9a	334	3450	1600	1500	1440	1405	7.54-8.11 (m, 10H). 10.16 (br s, 1H) (DMSO-d_6)
9b	348	3400	1590	1510	1440	1400	2.37 (s, 3H), 6.90 (br s, 1H), 7.25-8.08 (m, 9H) ($CDCl_3$)
9c	364	3050	1580	1510	1440	1320	3.81 (s, 3H), 6.87 (s, 1H), 6.82-8.11 (m, 9H) ($CDCl_3$)
9d	352	3430	1600	1515	1445	1410	6.90 (s, 1H), 7.10-8.10 (m, 9H) ($CDCl_3$)
9e	368	3440	1600	1500	1440	1410	6.91 (s, 1H), 7.40-8.10 (m 9H) ($CDCl_3$)
9f	368	3420	1590	1480	1440	1395	6.88 (br s, 1H), 7.32-8.11 (m, 9H) ($CDCl_3$)
9g	402	3450	1600	1475	1450	1370	7.41-8.12 (m, 9H) ($CDCl_3$)
9h	412	3440	1590	1485	1440	1320	6.90 (br s, 1H), 7.19-8.07 (m, 9H) ($CDCl_3$)

8a-h were cyclized readily to 1-aryl-5-chloro-3-(phenylsulfonyl)pyrazol-4-ols **9a-h** in 28-82% yields on refluxing of a mixture of **8a-h** in aqueous methanol in the presence of sodium acetate (Table 1). The structures of **8a-h** and **9a-h** were established by analytical and spectral data (Table 1 and 2). Common features of **8a-h** are the ir bands at *ca.* 3200 and 1690 cm^{-1} due to the NH and C=O groups, respectively. The methine resonances at *ca.* δ 6.7 observed in the ^{1}H-nmr spectra of **8a-h** disappeared in those of **9a-h**. Instead, the presence of hydroxyl group in **9a-h** is clearly indicated by ir bands at *ca.* 3400 cm^{-1} and broad singlets at *ca.* δ 6.9 in the ^{1}H-nmr spectra.

In conclusion, we have shown a new simple sulfone **4a** can serve as a building block for the synthesis of new pyrazoles (**9**) substituted by sulfonyl, hydroxyl, and chloro groups, whose preparation would be difficult in other methods [8].

EXPERIMENTAL

Melting points were determined on Yanagimoto micromelting point apparatus and are uncorrected. The ^{1}H-nmr, ir, and mass spectra were measured with JEOL JNM-PMX 60, JASCO A-102, and JEOL JMS DX-300, respectively. Microanalysis was performed with Yanako CHN Coder MT-5.

1,1-Dichloro-3-phenylsulfonyl-2-propanone (**4a**).

A mixture of sodium thiophenolate in water (240 ml) prepared from thiophenol (60 mmoles, 6.6 ml) and sodium hydroxide (60 mmoles, 2.40 g) was added to a solution of **6** (60 mmoles, 9.7 g) in aqueous methanol (300 ml, methanol:water = 1:3) at 0° with stirring. The stirring was continued at 0° for 10 hours and then at room temperature for 20 hours. After extraction of the mixture with chloroform (60 ml), the extract was washed with water and dried over magnesium sulfate. Removal of the solvent *in vacuo* gave the yellow oil of **7**, which was used for the next step without further purification.

To a solution of **7** obtained above in chloroform (30 ml) was added 30% aqueous hydrogen peroxide (0.48 mole, 54.4 g) with stirring at 0°. The stirring was continued at 0° for 10 hours and then at room temperature until the yellow color disappeared. After extraction of the mixture with chloroform (60 ml) followed by washing of the organic layer with aqueous sodium hydrogen carbonate, the extract was dried over magnesium sulfate and evaporated *in vacuo* to give white solids. Recrystallization of the residue from ethanol gave **4a** (7.2 g, 45% yield), mp 101-103°; ir: 1730, 1445, 1365, 1320, 1305, 1140 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 4.59 (s, 2H), 6.17 (s, 1H), 7.54-8.00 (m, 5H); ms: m/z 183 (M^+ -$CHCl_2$), 141 ($PhSO_2^+$), 77 (100).

Anal. Calcd. for $C_9H_8Cl_2O_3S$: C, 40.46; H, 3.02. Found: C, 40.88; H, 3.09.

1-Arylhydrazono-3,3-dichloro-1-phenylsulfonyl-2-propanone (**8**).

A General Procedure.

A solution of **4a** (270 mg, 1.0 mmole) in pyridine (3 ml) was cooled to 0-5°. To this solution, a solution of arenediazonium chloride (2.0 mmoles) prepared from arylamine (2.0 mmoles), concentrated hydrochloric acid (6 ml), and sodium nitrite (140 mg, 2.0 mmoles) was added dropwise during 20 minutes with stirring. The mixture was stirred at below 5° for 2 hours, the precipitates formed were collected by filtration, washed with water, and air-dried. Recrystallization gave **8**.

1-Aryl-5-chloro-3-(phenylsulfonyl)pyrazol-4-ol (**9**).

A General Procedure.

A mixture of **8** (1.0 mmole) and sodium acetate (250 mg, 3.0 mmoles) in aqueous methanol (1:1, 8 ml) was refluxed for several hours. After evaporation of the solvent *in vacuo* water was added to the residue and the aqueous mixture was extracted with chloroform. After drying the chloroform extract over magnesium sulfate the solvent was removed *in vacuo* to give a solid, which was recrystallized to afford **9**.

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