Halogenation of Alkyl *p*-Tolyl Sulfones with Carbon Tetrahalides. Application to the Synthesis of Aromatic Ketones

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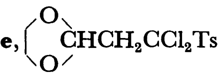
Synopsis. Carbanions of alkyl *p*-tolyl sulfones reacted with carbon tetrahalides to give the corresponding polyhalogenated products in good yields. Some chlorinated sulfones were converted to unsymmetrical ketones by treatment with silver perchlorate in trifluoroacetic acid.

Arnold and Kulenovic have reported that carbanions of esters reacted with carbon tetrahalides to give the corresponding α-monohalo esters.[1]

TABLE 1. CHLORINATION OF ALKYL *p*-TOLYL SULFONES WITH CCl_4[a]

$$\underset{\textbf{1a—f}}{\text{RTs}} \xrightarrow[\text{ii) } CCl_4\ (-78\ ^\circ C\text{—r.t.})]{\text{i) BuLi } (-78\ ^\circ C,\ 15\ \text{min})} \underset{\textbf{2a—f}}{\text{Chlorinated product}}$$

RTs	Product	Mp(°C)	Yield[b] (%)
1a, CH_3Ts	**2a**, CCl_3Ts	143—144	62
1b, CH_3CH_2Ts	**2b**, CH_3CCl_2Ts	106.5—108	91
1c, $PhCH_2Ts$	**2c**, $PhCCl_2Ts$	142—143	57
1d, $PhCH_2CH_2Ts$	**2d**, $PhCH_2CCl_2Ts$	184—185	81
1e, 	**2e**, 	109—110.5	85
1f, $(CH_3)_2CHTs$	**2f**, $(CH_3)_2CClTs$	105—106.5	93

a) Tenfold molar quantity of CCl_4 was used. b) Isolated yields by preparative TLC.

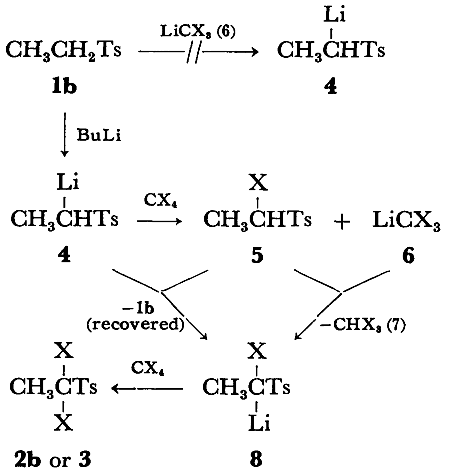
In connection with our continuing interest to extend the synthetic utility of sulfones,[2] we have tried a similar halogenation reaction to sulfones. When an alkyl *p*-tolyl sulfone (**1**) was lithiated with an equimolar amount of butyllithium in THF at −78 °C followed by addition of tenfold molar quantity of carbon tetrachloride, the corresponding polychlorinated sulfone (**2**) was obtained (Table 1), being in contrast with the report mentioned above.[1]

TABLE 2. HALOGENATION OF **1b** UNDER THE VARIOUS CONDITIONS

$$\underset{\textbf{1b}}{CH_3CH_2Ts} \xrightarrow[\text{ii) } CX_4]{\text{i) BuLi}} \begin{array}{l} CH_3CX_2Ts \\ X{=}Cl,\ \textbf{2b} \\ X{=}Br,\ \textbf{3} \end{array}$$

Molar ratio			Yield(%)	
1b	BuLi	CX_4	Product	Recovered **1b**
1	1	10 (X=Cl)	**2b**, 91	—
1	*ca.* 0.1	10 (X=Cl)	**2b**, 12	82
1	1	1 (X=Cl)	**2b**, 51	38
1	1	10 (X=Br)	**3**, 54	41

The result of halogenation of ethyl *p*-tolyl sulfone (**1b**) under the various conditions (Table 2) suggested that the polyhalogenation proceeds through the following scheme[3] and that the order of acidities are $CH_3CHClTs$ (**5**)>$HCCl_3$ (**7**)>CH_3CH_2Ts (**1b**).



The halogenation of alkyl *p*-tolyl sulfone with carbon tetrahalide was successfully applied to the synthesis of unsymmetrical aromatic ketones as illustrated in the following scheme: the alkylated intermediate (**9**), without isolation, was lithiated again with butyllithium followed by the addition of carbon tetrachloride to give the chlorinated sulfone (**10**) in good yield (Table 3). The chloro sulfone (**10**) was treated with silver perchlorate in refluxing trifluoroacetic acid containing a small amount of water to afford the corresponding aromatic ketone (**11**) in good yield (Table 3).[5]

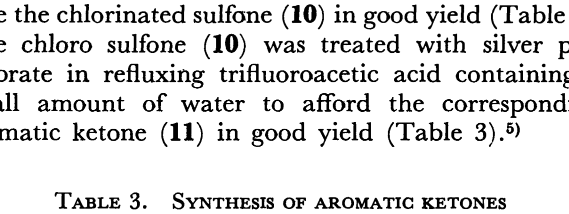


TABLE 3. SYNTHESIS OF AROMATIC KETONES

RX	Isolated yield/(%)	
	10	**11**
$PhCH_2Br$	87	85
$PhCH_2CH_2Br$	98	79
$CH_3(CH_2)_4I$	quant.	88

Experimental

All the melting points are uncorrected. The NMR and IR spectra were recorded on JEOL JNM/MH-60 and JASCO IRA-1 spectrometers, respectively.

Materials. Freshly distilled THF with lithium aluminum hydride under nitrogen was used. Thin-layer chromatography (TLC) was performed on Merck's Silicagel 60 PF_{254} (Type 7749).

Alkyl p-*Tolyl Sulfones (1a—f).* All of them were readily prepared from equimolar amounts of alkyl halides and sodium *p*-toluenesulfinate tetrahydrate by refluxing in methanol for 8—19 h except **1e** previously described.[4] 2-Phenylethyl *p*-tolyl sulfone (**1d**) is an only new compound. Mp 73.0—73.5 °C. Found: C, 69.23; H, 6.14%. Calcd for $C_{15}H_{16}O_2S$: C, 69.23; H, 6.15%.

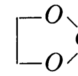
1,1-Dichloroethyl p-*Tolyl Sulfone (2b).* Ethyl *p*-tolyl sulfone (**1b**, 184 mg, 1 mmol) was lithiated by stirring with an equimolar amount of butyllithium in THF (10 ml) at −78 °C for 15 min under nitrogen. After addition of carbon tetrachloride (1.538 g, 10 mmol), the reaction mixture was allowed to warm to room temperature and then stirred for 15 min at room temperature. After evaporation of the solvent, the resulting residue was treated with pH 7 buffer solution followed by extraction with ethyl acetate. The crude residue obtained by concentration of the extract was subjected to preparative TLC (hexane–ether 5 : 4 v/v) to give **2b** (229 mg, 91%, mp 100—105 °C). NMR ($CDCl_3$) δ 2.39 (s, 3H), 2.45 (s, 3H), 7.29 (d, 2H, J=9 Hz), 7.82 (d, 2H, J=9 Hz). Recrystallization from heptane gave the pure substance (187 mg, 74%, mp 106—108.0 °C) for elemental analysis. Found: C, 42.81; H, 3.92%. Calcd for $C_9H_{10}Cl_2O_2S$: C, 42.69; H, 3.95%.

In a silmilar manner, **2a**,**c**—**f** and **3** were prepared from the corresponding alkyl *p*-tolyl sulfones (Tables 1 and 2).

CCl_3Ts (2a): Found: C, 35.40; H, 2.54%. Calcd for $C_8H_7Cl_3O_2S$: C, 35.10; H, 2.56%.

$PhCCl_2Ts$ (2c): Found: C, 53.39; H, 3.73%. Calcd for $C_{14}H_{12}Cl_2O_2S$: C, 53.33; H, 3.81%.

$PhCH_2CCl_2Ts$ (2d): NMR ($CDCl_3$) δ 2.44 (s, 3H), 3.71 (s, 2H), 7.25 (s, 5H), 7.30 (d, 2H, J=9 Hz), 7.83 (d, 2H, J=9 Hz). Found: C, 54.90; H, 4.24%. Calcd for $C_{15}H_{14}Cl_2O_2S$: C, 54.71; H, 4.26%.



$CHCH_2CCl_2Ts$ (2e): NMR ($CDCl_3$) δ 2.45 (s, 3H), 2.82 (d, 2H, J=4 Hz), 3.91 (broad, 4H), 5.32 (t, 1H, J=4 Hz), 7.34 (d, 2H, J=9 Hz), 7.87 (d, 2H, J=9 Hz). Found: C, 44.41; H, 4.39%. Calcd for $C_{12}H_{14}Cl_2O_4S$: C, 44.31; H, 4.31%.

$(CH_3)_2CClTs$ (2f): Found: C, 51.76; H, 5.53%. Calcd for $C_{10}H_{13}ClO_2S$: C, 51.61; H, 5.59%.

CH_3CBr_2Ts (3): Mp 121—122 °C (recrystallized from heptane). NMR ($CDCl_3$) δ 2.45 (s, 3H), 2.65 (s, 3H), 7.31 (d, 2H, J=9 Hz), 7.87 (d, 2H, J=9 Hz). Found: C, 31.78; H, 2.88%. Calcd for $C_9H_{10}Br_2O_2S$: C, 31.58; H, 2.92%.

1-Chloro-1,2-diphenylethyl p-*Tolyl Sulfone (10, R=CH_2Ph).* Benzyl *p*-tolyl sulfone (**1c**, 246 mg, 1 mmol) was lithiated by stirring with an equimolar amount of butyllithium in THF (20 ml) at −78 °C for 20 min and then at room temperature for 20 min under nitrogen. After cooling to −78 °C, a THF (2 ml) solution of benzyl bromide (171 mg, 1 mmol) was added. The reaction mixture was allowed to warm to room temperature to complete the alkylation and then cooled again to −78 °C followed by the addition of carbon tetrachloride (1.538 g, 10 mmol). After stirring for 20 min, the mixture was treated with 1 mol dm^{-3} HCl–MeOH at −78 °C and partitioned between ether and water. The organic layer was dried over Na_2SO_4 followed by evaporation of the solvent under reduced pressure. The resulting residue was subjected to preparative TLC (hexane–ethyl acetate 5 : 1 v/v) to give **10** (322 mg, 87%, mp 133 °C). NMR ($CDCl_3$) δ 2.35 (s, 3H), 3.82 (d, 1H, J=15 Hz), 4.30 (d, 1H, J=15 Hz), 6.85—7.65 (m, 14H). Recrystallization from heptane gave the pure substance (mp 136—137 °C) for elemental analysis. Found: C, 67.89; H, 5.00%. Calcd for $C_{21}H_{19}ClO_2S$: C, 68.01; H, 5.16%.

In a similar manner, other chlorinated sulfones (**10**, R=CH_2CH_2Ph, $(CH_2)_4CH_3$ and **12**) were prepared.

$PhCH_2CH_2CPhClTs$: Mp 114—115 °C (recrystallized from cyclohexane). NMR ($CDCl_3$) δ 2.32 (s, 3H), 2.4—3.2 (m, 4H), 6.8—7.6 (m, 14H). Found: C, 68.51; H, 5.44%. Calcd for $C_{22}H_{21}ClO_2S$: C, 68.66; H, 5.46%.

$CH_3(CH_2)_4CPhClTs$: Mp 66—67 °C (recrystallized from hexane). NMR ($CDCl_3$) δ 0.6—1.6 (m, 9H), 2.36 (s, 3H), 2.15—3.20 (m, 2H), 7.07 (d, 2H, J=9 Hz), 7.1—7.5 (m, 5H), 7.35 (d, 2H, J=9 Hz). Found: C, 65.09; H, 6.57%. Calcd for $C_{19}H_{23}ClO_2S$: C, 65.05; H, 6.56%.

$CH_3(CH_2)_4(CH_2Ph)ClTs$: Oil. NMR ($CDCl_3$) δ 0.82 (t, 3H, J=5 Hz), 0.95—2.25 (m, 8H), 2.39 (s, 3H), 3.17 (d, 1H, J=14 Hz), 3.53 (d, 1H, J=14 Hz), 7.14 (s, 5H), 7.23 (d, 2H, J=8 Hz), 7.77 (d, 2H, J=8 Hz).

1,2-Diphenylethanone (11, R=CH_2Ph). To a solution of **10** (100 mg, 0.27 mmol) in trifluoroacetic acid (2 ml) were added silver perchlorate (112 mg, 0.54 mmol) and water (0.5 ml). After refluxing for 1 h, the reaction mixture was diluted with ether, neutralized with a saturated $NaHCO_3$ solution, washed with water, and dried over Na_2SO_4. The crude residue obtained by evaporation of ether was subjected to preparative TLC (hexane–ethyl acetate 5 : 1 v/v) to give **11** (45 mg, 85%, mp 50—54 °C (lit, 55—56 °C)). IR and NMR spectra were in accordance with those of authentic sample.

In a similar way, other aromatic ketones (**11**, R=CH_2CH_2Ph, $(CH_2)_4CH_3$) were obtained as shown in Table 3.

References

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