CARBON-CARBON BOND FORMING REACTION OF BIS(CHLOROMETHYL)SULFONE WITH CARBONYL COMPOUNDS: GENERAL ROUTE TO AROMATIC 2-CHLOROVINYL COMPOUNDS AND α-HYDROXYALDEHYDES

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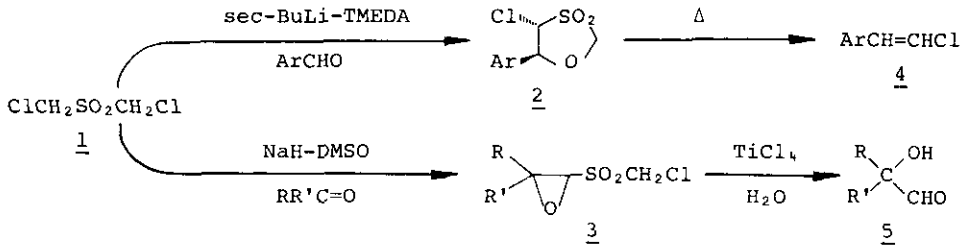
Abstract —— Bis(chloromethyl)sulfone (1) has been proved to be a useful reagent for the synthesis of aromatic 2-chlorovinyl compounds (4) from aromatic aldehydes and of α-hydroxyaldehydes (5) from aliphatic carbonyl compounds with one carbon prolongation. The sec-butyllithium-aided reaction of 1 with aromatic aldehydes gives 1,3-oxathiolane-3,3-dioxides (2) which are converted to 4 in good yields by thermolysis. On the other hand, the sodium hydride-aided reaction of 1 with aliphatic carbonyl compounds is favorable to the formation of chloromethylsulfonyloxiranes (3). *Titanium tetrachloride has been found to be an efficient reagent* for hydrolysis of 3 to 5.

α-Chlorosulfonyl carbanions formed from α-chlorosulfones have been known[1] to react with carbonyl compounds to give 2-sulfonyl-substituted oxiranes. However, chemical behavior of bis(chloromethyl)sulfone[2] (1) toward carbonyl compounds in basic media has not been known in the literature. In this case, there are considered two possibilities of the release of chlorine anion from the adduct of 1 to carbonyl compounds leading to 1,3-oxathiolane-3,3-dioxide (2) or to oxirane (3) by ring closure. We now wish to describe our finding that in the case of aromatic aldehydes the reaction exclusively proceeded to give 2, whereas in the case of aliphatic aldehydes and ketones the reaction was favorable to the formation of 3 (Scheme 1).

Further investigation was conducted to develop the useful application of the products 2 and 3. Thus, thermolysis of 2 was found to give aromatic 2-chlorovinyl compounds (4) with the release of sulfur dioxide and formaldehyde. On the other

hand, hydrolysis of 3 to α-hydroxyaldehydes (5) was found easily to proceed with the aid of titanium tetrachloride.



Scheme 1

THE REACTION WITH AROMATIC ALDEHYDES

Preliminary experiments included examination of efficiencies of bases, tert-BuOK, LDA, sec-BuLi and NaH, in the reaction of 1 with benzaldehyde in THF. Among them sec-BuLi and NaH gave 4-chloro-5-phenyl-1,3-oxathiolane-3,3-dioxide (2a) in 18% and 5% yield, but in the presence of tetramethylethylenediamine (TMEDA) and DMSO, gave 59% and 47% yield, respectively. Typical procedures are as follows: to a solution of 1(20 mmol) and TMEDA(30 mmol) in THF, sec-BuLi(30 mmol) was added with stirring at -70°C and then a THF solution of benzaldehyde(20 mmol) was added at the same temperature. Stirring was continued for overnight at room temperature. Usual work-up and purification with a silica gel column(eluent, benzene) gave pure 2a as crystals. In these experiments, the formation of 2-chloromethylsulfonyl-3-phenyloxirane was not detected.

Heating 2a at 200°C and purification of the resulting oily material by preparative TLC (silica gel-benzene) gave (E)-β-chlorostyrene (4a) in 60% yield. The 1,3-oxathiolane formation and the thermolysis were extended to a number of aromatic aldehydes and the results are summarized in Table 1. The trans configuration of 2a-k was assigned on the bases of ^{1}H-NMR parameters. The magnitude of vicinal, $J_{4,5}$ coupling constants, 7.9-9.0, of 2a-k (see Table 3) is well consistent with the reported[3] values, 6.4-9.3, for trans isomers of 4,5-substituted 1,3-oxathiolanes and is apparently distinguishable from those of the coupling constants, $J_{4,5}$ = 4.4-4.9, for the corresponding cis isomers. The spectral data of 2a-k and 4a-j are given in Tables 3 and 4, respectively. It is demonstrated that the reaction of 1 with aromatic aldehydes and successive thermolysis are a convenient route to aromatic 2-chlorovinyl compounds (4a-j) from aromatic aldehydes with one carbon prolongation.

Table 1. Syntheses of 1,3-Oxathiolane-3,3-dioxides (2a-k) and 2-Chlorovinyl Compounds (4a-j)

Entry No	ArCHO	Yield(%)[a] of 2a-k (Compd. No)	mp(°C)	React. Temp. (°C)	Yield(%)[a] of 4a-j[b] (Compd. No) [ratio of E:Z[c]]
1	C_6H_5CHO	59(2a)	117-119	200	60(4a) [100:0]
2	p-$MeOC_6H_4CHO$	33(2b)	132-133	220	48(4b) [55:45]
3	p-ClC_6H_4CHO	19(2c)	81-82	220	75(4c) [100:0]
4	p-MeC_6H_4CHO	40(2d)	90-91	210	86(4d) [100:0]
5	o-$MeOC_6H_4CHO$	34(2e)	107-108	180	18(4e) [100:0]
6	m-$MeOC_6H_4CHO$	39(2f)	77-78	220	69(4f) [100:0]
7	m-ClC_6H_4CHO	11(2g)	93-94	220	51(4g) [100:0]
8	$C_6H_5CH=CHCHO$	8(2h)	110-111	220	31(4h) [100:0]
9	Furfural	15(2i)	100-101	150	16(4i) [45:55]
10	2-Thiophene-carboxaldehyde	27(2j)	82-83	150	7(4j) [50:50]
11	2-Pyridine-carboxaldehyde	15(2k)	88-89	150	0

a. Isolated yield.

b. These compounds have been reported[4] except 4e and 4j.

c. Ratio of E- and Z-isomers was determined by ^{1}H-NMR.

Table 2. Syntheses of 2-Chloromethylsulfonyloxiranes (3a-d) and α-Hydroxyaldehydes (5a-d)

Entry No	RR'C=O	Yield(%)[a] of 3a-d (Compd. No)	mp(°C)	Yield(%)[a] of 5a-d (Compd. No)	bp(°C/mmHg)
1		51(3a)	103-106	63(5a)	150-155(28)[c]
2	$C_5H_{11}CHO$	45(3b)	liquid[d]	52(5b)	155-160(25)[e]
3		67(3c)	liquid[d]	45(5c)	145-150(35)[f]
4	MeCOMe	28(3d)	liquid[d]	20(5d)	120-125(40)[g]

a. Isolated yield.

b. The bath temperature of "Kugelröhr" short path distillation apparatus.

c. Lit. bp 100°C(bath temp.)/0.0015 mmHg [H. Mohrle, D. Schitenbelm and E. Federolf, Arch. Pharm., 305, 578 (1972)].

d. Liquid products are thermally unstable and nondistillable. Purification of these products was conducted by silica gel column chromatography.

e. Lit. bp 103-105°C/4 mmHg[E. D. Venus-Danilova and V. F. Kazinilowa, Zh. Obsch. Khim., 18, 1816 (1948); C. A., 43, 3790i (1949)].

f. Lit. bp 80-82°C/12 mmHg[O. H. Oldenziel and A. M. Leusen, Tetrahedron Letters, 1974, 167].

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Table 3. Spectral Data of 2a-k

Compd. No	IR $\nu^{SO_2}_{max}$ (cm^{-1})	NMR δ (ppm in $CDCl_3$) H_A-2(d)	H_B-2(d) [J = Hz]	H-4(d)	H-5(d) [J = Hz]	C-2(t)	C-4(d)	C-5(d)
2a	1340 1170	5.05	4.48 [9.6]	4.91	4.56 [9.0]	82.79	70.54	87.23
2b	1330 1165	5.09	4.51 [9.5]	4.89	4.69 [9.0]	82.95	70.60	87.18
2c	1345 1330 1170	5.11	4.53 [9.8]	4.93	4.60 [9.0]	82.79	70.33	82.26
2d	1335 1160 1120	5.04	4.46 [9.5]	4.78	4.55 [9.0]	82.90	70.60	87.28
2e	1323 1172 1129	4.99	4.48 [9.5]	5.35	4.88 [8.5]	82.36	69.08	83.17
2f	1332 1168 1130	5.06	4.46 [9.6]	4.88	4.57 [9.0]	82.46	70.38	89.96
2g	1332 1171 1125	5.09	4.50 [9.5]	4.92	4.54 [9.0]	82.64	70.27	86.31
2h	1329 1173 1134	4.98	4.42 [9.7]	4.50-4.60 2H, m		82.57	69.42	86.53
2i	1320 1140 1120	4.99	4.51 [9.5]	5.03, 2H, s		82.52	66.97	80.24
2j	1339 1127	5.03	4.50 [9.8]	5.20	4.69 [8.8]	82.79	70.44	83.17
2k	1320 1150	5.01	4.58 [9.4]	5.31	5.15 [7.9]	82.08	67.89	87.50

THE REACTION WITH ALIPHATIC ALDEHYDES AND KETONES

The base-aided reaction of 1 with aliphatic aldehydes and ketones was distinguished from that with aromatic aldehydes resulting in the predominant formation of 2-chloromethylsulfonyloxiranes (3a-d) in a similar fashion to the literature[1] of the reaction of α-chlorosulfones. Among several bases examined, the combination of NaH-DMSO gave the best yields of oxiranes and the experimental results of a number of aliphatic carbonyl compounds are summarized in Table 2. In Table 5, the spectral data of 3a-d are given.

In view of the affinity of 3 toward nucleophiles, the conversion to α-hydroxyaldehydes is a useful transformation that was very recently reported[5] by means of tert-BuOK-H_2O. We have found titanium tetrachloride as a specifically efficient reagent for this hydrolysis. Typical procedures are as follows: to a stirred solution of 3(5 mmol) in CH_2Cl_2, $TiCl_4$(10 mmol) was added at room temperature. After stirring

Table 4. Spectral Data of 4a-j

Compd.	IR $\nu_{max}^{C=C}$ (cm^{-1})	^{1}H-NMR δ (ppm in $CDCl_3$, J = Hz) -CH=	=CHCl
4a	1605	6.82(d, J=13.7)[E]	6.57(d, J=13.7)[E]
4b	1610	6.78(d, J=13.7)[E] 6.55(d, J= 8.1)[Z]	6.47(d, J=13.7)[E] 6.09(d, J= 8.1)[Z]
4c	1605	6.76(d, J=13.7)[E]	6.55(d, J=13.7)[E]
4d	1610	6.76(d, J=13.4)[E]	6.49(d, J=13.4)[E]
4e	1607	7.03(d, J=13.6)[E]	6.77(d, J=13.6)[E]
4f	1610	6.75(d, J=13.4)[E]	6.55(d, J=13.4)[E]
4g	1615	6.79(d, J=13.7)[E]	6.59(d, J=13.7)[E]
4h	1630	5.96-6.74(4H, m, -CH=CH-CH=CH-)[EE]	
4i	1610	6.55(2H, s, -CH=CHCl)[E] 6.57(d, J= 7.9)[Z]	——[a]
4j	1600	6.85(d, J=13.5)[E] 6.80(d, J= 7.3)[Z]	6.40(d, J=13.5)[E] 6.10(d, J= 7.3)[Z]

a. Proton signal of =CHCl (Z-isomer) is overlapped with those of furfuryl ring protons and can not be assigned.

Table 5. Spectral Data of 3a-d

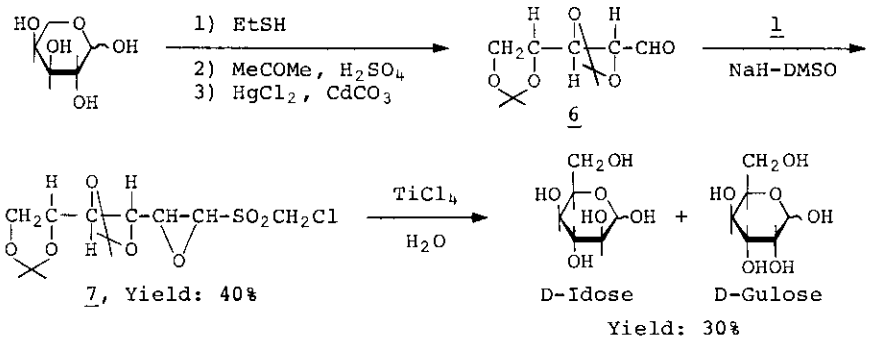
Compd. No	IR $\nu_{max}^{SO_2}$ (cm^{-1})	NMR δ (ppm in $CDCl_3$, J = Hz) C_2-H/C_3-H/CH_2Cl	C-2/C-3/CH_2Cl
3a	1340 1135	4.28(d, J=1.7) 3.49(dd, J=1.7 & 5.9) 4.54(ABq, J=12.6 & 22.3)	63.28(d) 61.22(d) 54.29(t)
3b	1315 1140	4.24(d, J=1.2) 3.62(dt, J=1.2 & 5.4) 4.65(ABq, J=12.7 & 19.5)	64.37(d) 57.43(d) 54.40(t)
3c	1340 1155	4.16(s) —— 4.65(ABq, J=7.8 & 10.5)	70.71(d) 68.27(s) 56.19(t)
3d	1320 1155	4.15(s) —— 4.57(ABq, J=9.3 & 17.1)	70.00(d) 63.77(s) 55.86(t)

Table 6. Spectral Data of 5a-d

Compd.	IR $\nu_{max}^{liq.}$ cm^{-1} OH	CHO	NMR δ (ppm in $CDCl_3$, J = Hz) CHO	C-2/C-3/CH_2Cl	-C-OH
5a	3440	1735	9.46(d, J=3.2)	195.32	69.35(d)
5b	3420	1730	9.48(d, J=2.4)	195.10	64.04(d)
5c	3420	1725	9.39(s)	194.94	52.32(s)
5d	3430	1730	9.22(s)	194.12	52.08(s)

for 1 h, the reaction mixture was treated with H_2O. Usual work-up and bulb-to-bulb distillation under reduced pressure gave 5. The results are summarized in Table 2 and the spectral data of the products, 5a-d, in Table 6. Thus, an alternative method convenient for the synthesis of α-hydroxyaldehydes has been provided.

The reaction was applied to synthesis of a mixture of D-idose and D-gulose from D-xylose. Diisopropylidenealdehyde-D-xylose (6), obtained from D-xylose according to the reported method[6], was allowed to react with 1 in the presence of NaH-DMSO



7, Yield: 40%

Yield: 30%

and the corresponding oxirane 7 was obtained in 40% yield. 7: Colorless liquid, IR $\nu_{max}^{SO_2}$ (cm^{-1}): 1330, 1150. NMR δ(ppm in $CDCl_3$): ^1H; 4.55(1H, d, J = 1.5 Hz), 4.56 (2H, ABq, J = 12.6 & 20.2 Hz), 3.70-4.55(6H, m), 1.40(6H, s), 1.35(6H, s). ^{13}C; 26.12(q), 26.19(q), 26.77(q), 26.97(q), 54.39(t), 55.79(d), 62.26(d), 65.32(t), 74.17(d), 77.42(d), 77.62(d), 105.33(s), 111.02(s). Hydrolysis of 7 by the use of $TiCl_4$ gave a mixture of D-idose and D-gulose as a syrup insoluble in CH_2Cl_2 which was purified by passing through an anion exchange resin (Amberlite A-400). Combined yield, 30%. ^{13}C-NMR δ[ppm in D_2O, internal standard: sodium 3-(trimethylsilyl)-1-propanesulfonate]: for D-idose; 96.1, 94.5, 74.6, 74.2, 73.5, 72.4, 72.1, 71.4, 70.5, 70.1, 61.4 and 61.4. for D-gulose; 99.0, 94.6, 78.3, 76.5, 75.3, 73.9, 72.0, 71.7, 70.4, 70.1, 63.5 and 62.8.

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2. Bis(chloromethyl)sulfone was prepared by $KMnO_4$ oxidation of bis(chloromethyl)-sulfide [J. S. Grossert and R. F. Langler, Can. J. Chem., 55, 407 (1977)] in AcOH at room temperature. Yield, 48%. Mp 67-9°C (recrystallized from iso-Pr_2O).

IR $\nu_{max}^{SO_2}$(cm^{-1}): 1350, 1155, 1120. ^{1}H-NMR δ(ppm in $CDCl_3$): 4.67(4H, s).

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Received, 6th March, 1985