

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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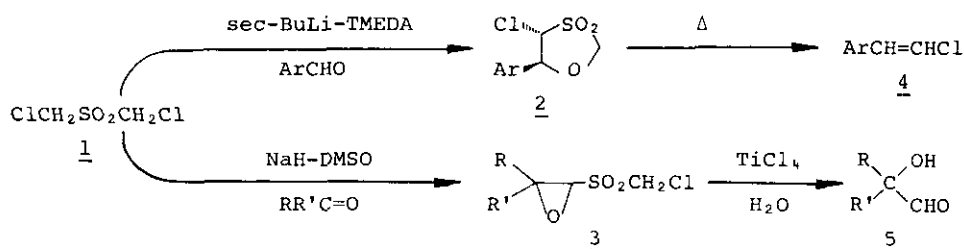
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Abstract — Bis(chloromethyl)sulfone (1) has been proved to be a useful reagent for the synthesis of aromatic 2-chlorovinyl compounds (4) from aromatic aldehydes and of α -hydroxyaldehydes (5) from aliphatic carbonyl compounds with one carbon prolongation. 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 known¹ to react with carbonyl compounds to give 2-sulfonyl-substituted oxiranes. However, chemical behavior of bis(chloromethyl)sulfone² (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 ¹H-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 reported³ 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)

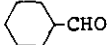
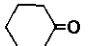
| Entry No | ArCHO | Yield (%) ^a of 2a-k (Compd. No) | mp (°C) | React. Temp. (°C) | Yield (%) ^a of 4a-j ^b (Compd. No) [ratio of E:Z ^c] |
|----------|--|--|---------|-------------------|--|
| 1 | C ₆ H ₅ CHO | 59 (2a) | 117-119 | 200 | 60 (4a) [100:0] |
| 2 | p-MeOC ₆ H ₄ CHO | 33 (2b) | 132-133 | 220 | 48 (4b) [55:45] |
| 3 | p-ClC ₆ H ₄ CHO | 19 (2c) | 81-82 | 220 | 75 (4c) [100:0] |
| 4 | p-MeC ₆ H ₄ CHO | 40 (2d) | 90-91 | 210 | 86 (4d) [100:0] |
| 5 | o-MeOC ₆ H ₄ CHO | 34 (2e) | 107-108 | 180 | 18 (4e) [100:0] |
| 6 | m-MeOC ₆ H ₄ CHO | 39 (2f) | 77-78 | 220 | 69 (4f) [100:0] |
| 7 | m-ClC ₆ H ₄ CHO | 11 (2g) | 93-94 | 220 | 51 (4g) [100:0] |
| 8 | C ₆ H ₅ CH=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 reported⁴ except 4e and 4j.

c. Ratio of E- and Z-isomers was determined by ¹H-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 |  -CHO | 51 (3a) | 103-106 | 63 (5a) | 150-155 (28) ^c |
| 2 | C ₅ H ₁₁ CHO | 45 (3b) | liquid ^d | 52 (5b) | 155-160 (25) ^e |
| 3 |  =O | 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. Kazinilova, *Zh. Obsch. Khim.*, **18**, 1816 (1948); *C. A.*, **43**, 3790i (1949)].

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

g. R. Dworzark and J. Pierri, *Monatsh. Chem.*, **52**, 141 (1927) [*C. A.*, **23**, 4670 (1929)].

Table 3. Spectral Data of 2a-k

| Compd. No | IR $\nu_{\text{SO}_2 \text{ max}}$ (cm ⁻¹) | H_A -2(d) [J = Hz] | H_B -2(d) [J = Hz] | NMR δ (ppm in CDCl ₃) | | C-2(t) | C-4(d) | C-5(d) |
|-----------|--|-------------------------|-------------------------|--|--------|--------|--------|--------|
| | | | | H-4(d) [J = Hz] | H-5(d) | | | |
| <u>2a</u> | 1340 1170 | 5.05 [9.6] | 4.48 | 4.91 [9.0] | 4.56 | 82.79 | 70.54 | 87.23 |
| <u>2b</u> | 1330 1165 | 5.09 [9.5] | 4.51 | 4.89 [9.0] | 4.69 | 82.95 | 70.60 | 87.18 |
| <u>2c</u> | 1345 1330 1170 | 5.11 [9.8] | 4.53 | 4.93 [9.0] | 4.60 | 82.79 | 70.33 | 82.26 |
| <u>2d</u> | 1335 1160 1120 | 5.04 [9.5] | 4.46 | 4.78 [9.0] | 4.55 | 82.90 | 70.60 | 87.28 |
| <u>2e</u> | 1323 1172 1129 | 4.99 [9.5] | 4.48 | 5.35 [8.5] | 4.88 | 82.36 | 69.08 | 83.17 |
| <u>2f</u> | 1332 1168 1130 | 5.06 [9.6] | 4.46 | 4.88 [9.0] | 4.57 | 82.46 | 70.38 | 89.96 |
| <u>2g</u> | 1332 1171 1125 | 5.09 [9.5] | 4.50 | 4.92 [9.0] | 4.54 | 82.64 | 70.27 | 86.31 |
| <u>2h</u> | 1329 1173 1134 | 4.98 [9.7] | 4.42 | 4.50-4.60 2H, m | | 82.57 | 69.42 | 86.53 |
| <u>2i</u> | 1320 1140 1120 | 4.99 [9.5] | 4.51 | 5.03, 2H, s | | 82.52 | 66.97 | 80.24 |
| <u>2j</u> | 1339 1127 | 5.03 [9.8] | 4.50 | 5.20 [8.8] | 4.69 | 82.79 | 70.44 | 83.17 |
| <u>2k</u> | 1320 1150 | 5.01 [9.4] | 4.58 | 5.31 [7.9] | 5.15 | 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 literature¹ 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 reported⁵ by means of tert-BuOK-H₂O. 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 CH₂Cl₂, TiCl₄ (10 mmol) was added at room temperature. After stirring

Table 4. Spectral Data of 4a-j

| Compd. | IR $\nu_{\text{max}}^{\text{C=C}}$ (cm^{-1}) | $^1\text{H-NMR } \delta$ (ppm in CDCl_3 , $J = \text{Hz}$) | |
|-----------|--|--|--|
| | | -CH= | =CHCl |
| <u>4a</u> | 1605 | 6.82 (d, $J=13.7$) [E] | 6.57 (d, $J=13.7$) [E] |
| <u>4b</u> | 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] |
| <u>4c</u> | 1605 | 6.76 (d, $J=13.7$) [E] | 6.55 (d, $J=13.7$) [E] |
| <u>4d</u> | 1610 | 6.76 (d, $J=13.4$) [E] | 6.49 (d, $J=13.4$) [E] |
| <u>4e</u> | 1607 | 7.03 (d, $J=13.6$) [E] | 6.77 (d, $J=13.6$) [E] |
| <u>4f</u> | 1610 | 6.75 (d, $J=13.4$) [E] | 6.55 (d, $J=13.4$) [E] |
| <u>4g</u> | 1615 | 6.79 (d, $J=13.7$) [E] | 6.59 (d, $J=13.7$) [E] |
| <u>4h</u> | 1630 | 5.96-6.74 (4H, m, -CH=CH-CH=CH-) [EE] | |
| <u>4i</u> | 1610 | 6.55 (2H, s, -CH=CHCl) [E] 6.57 (d, $J= 7.9$) [Z] | _____ a |
| <u>4j</u> | 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

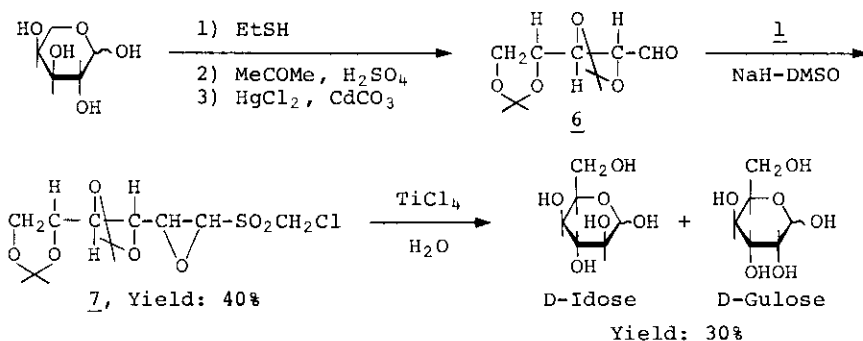
| Compd. No | IR $\nu_{\text{max}}^{\text{SO}_2}$ (cm^{-1}) | NMR δ (ppm in CDCl_3 , $J = \text{Hz}$) | |
|--------------|---|---|--|
| | | $\text{C}_2\text{-H}/\text{C}_3\text{-H}/\text{CH}_2\text{Cl}$ | $\text{C-2}/\text{C-3}/\text{CH}_2\text{Cl}$ |
| <u>3a</u> | 1340 1135 | 4.28 (d, $J=1.7$) 3.49 (dd, $J=1.7$ & 5.9) 4.54 (ABq, $J=12.6$ & 22.3) | 63.28 (d) 61.22 (d) 54.29 (t) |
| <u>3b</u> | 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) |
| <u>3c</u> | 1340 1155 | 4.16 (s) _____ 4.65 (ABq, $J=7.8$ & 10.5) | 70.71 (d) 68.27 (s) 56.19 (t) |
| <u>3d</u> | 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 $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1} | | NMR δ (ppm in CDCl_3 , $J = \text{Hz}$) | | |
|-----------|--|------|--|--------|-----------|
| | OH | CHO | CHO | CHO | -C-OH |
| <u>5a</u> | 3440 | 1735 | 9.46 (d, $J=3.2$) | 195.32 | 69.35 (d) |
| <u>5b</u> | 3420 | 1730 | 9.48 (d, $J=2.4$) | 195.10 | 64.04 (d) |
| <u>5c</u> | 3420 | 1725 | 9.39 (s) | 194.94 | 52.32 (s) |
| <u>5d</u> | 3430 | 1730 | 9.22 (s) | 194.12 | 52.08 (s) |

for 1 h, the reaction mixture was treated with H₂O. 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 method⁶, was allowed to react with 1 in the presence of NaH-DMSO



and the corresponding oxirane 7 was obtained in 40% yield. 7: Colorless liquid, IR $\nu_{\text{max}}^{\text{SO}_2}$ (cm⁻¹): 1330, 1150. NMR δ (ppm in CDCl₃): 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). ¹³C; 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 TiCl₄ gave a mixture of D-idose and D-gulose as a syrup insoluble in CH₂Cl₂ which was purified by passing through an anion exchange resin (Amberlite A-400). Combined yield, 30%. ¹³C-NMR δ [ppm in D₂O, 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.

REFERENCES AND NOTE

1. T. Durst, K. C. Tin, F. Reinach-Hirtzbach, J. M. Desesare and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979) and references cited; F. Reinach-Hirtzbach and T. Durst, *Tetrahedron Letters*, **1976**, 3677.
2. Bis(chloromethyl)sulfone was prepared by KMnO₄ 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-Pr₂O).

IR $\nu_{\text{max}}^{\text{SO}_2}$ (cm⁻¹): 1350, 1155, 1120. ¹H-NMR δ (ppm in CDCl₃): 4.67 (4H, s).

3. R. Keskinen, A. Nikkila and K. Pihlaja, J. Chem. Soc. Perkin Trans. II, 1977, 343.
4. M. Schlosser and V. Landenberger, Chem. Ber., 100, 3901 (1967).
5. A. Adamczyk, E. K. Dolence, D. S. Watt, M. R. Christy, J. H. Reibenspies and O. P. Anderson, J. Org. Chem., 49, 1378 (1984).
6. W. Asbun and S. B. Binkly, J. Org. Chem., 31, 2215 (1966).

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