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REACTION OF 1-CHLORO-2,4-DINITROBENZENE WITH THIOLS IN THE PRESENCE OF A CROWN ETHER

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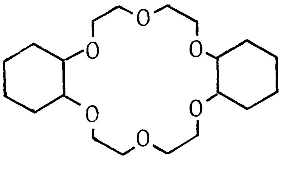
The title reaction was carried out and the corresponding 2,4-dinitrophenyl sulfides were obtained. The scope of the reaction was examined, and visible and NMR spectra of the reaction mixtures were measured.

The marked chelating ability of crown ethers with metal ions has been revealed.[1,2] Furthermore, the formation of complexes of crown ethers with various cationic species[1-3] and compounds having positively charged center[2,4,5] has been reported. For protons which are the most simple cationic species, powerful solvation between crown ethers with hydrogen bromide has been demonstrated.[6] It is likely from the fact that crown ethers would act as a solvating agent for thiols. To confirm this, we have chosen the reaction of 1-chloro-2,4-dinitrobenzene with thiols.

It is known that the reaction proceeds easily in the presence of alkalis in aqueous alcoholic solution to provide the corresponding 2,4-dinitrophenyl sulfides.[7,8] Thus, if any *naked* thiolate ion is formed by use of crown ethers in place of alkalis, nucleophilic attack of the ion would still take place.

As a typical example, the reaction with 4-bromobenzenethiol will be mentioned. A mixture of 0.13 g (0.64 mmol) of 1-chloro-2,4-dinitrobenzene, 0.12 g (0.64 mmol) of 4-bromobenzenethiol, 0.22 g (0.59 mmol) of 2,5,8,15,18,21-hexaoxatricyclo[20.4.0.0^{9,14}]hexacosane (CR), and 2 ml of acetonitrile was heated at 77-80°C for about 6 hr. The resulting solution was washed with ca. 5 ml of 1 M aqueous sodium chloride two times after addition of 5 ml of benzene, and then with water two times. The benzene solution obtained was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The residue was recrystallized from alcohol-benzene, giving 0.096 g (42%) of yellow crystals of 4-bromophenyl



CR

2,4-dinitrophenyl sulfide with mp 140.5-141.5°C.

Other reactions with 4-nitro-, 4-chloro-, and 4-methoxybenzenethiols and benzenethiol were carried out. The results are listed in Table 1. The reactions with 4-cyanobenzenethiol and phenylmethanethiol were also attempted. However, in the case of the former, only a water soluble material was obtained, and in the latter, the desired sulfide was not produced on heating for 4.5 hr. In addition, the reaction of 1-chloro-4-nitrobenzene with 4-nitrobenzenethiol in the presence of CR was tested. In this case, only bis(4-nitrophenyl) disulfide was obtained.

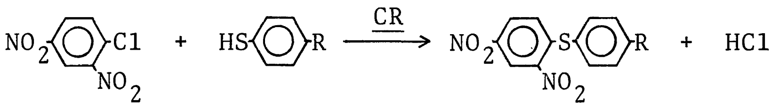


Table 1. Reaction of 1-Chloro-2,4-dinitrobenzene with Thiols (4-RC_6H_4SH) in the Presence of CR in Acetonitrile*

R in 4-RC_6H_4SH	[CR]/[Thiol]**	Temp. (°C)	Time (hr)	Product Yield (%)	Mp (°C)	Mp, Lit. (°C)
NO_2	0.88	80	1.5	17	163-165	155,160[9)]
Br	0.92	77-80	5.8	42	140.5-141.5	140-141[10)]
Cl	0.88	79-80	6	31	124-125	123-124[10)]
H	0.88	79-80	7	7.9	120-121	117,120.5,121[9)]
CH_3O	0.88	69-70	7	13	116-117 116-117***	116-117[7)]

* Each reaction mixture contains 0.64 mmol of 1-chloro-2,4-dinitrobenzene and 0.64 mmol of thiol; acetonitrile 2 ml. ** Molar ratio. *** Mixture melting point.

4-Substituted phenyl 2,4-dinitrophenyl sulfides in Table 1 were identified by comparison of melting points with literature data, and by mixture melting point with an authentic sample (the 4-methoxyphenyl sulfide). Elemental analyses gave satisfactory results (for four sulfides except the 4-methoxyphenyl sulfide), which coincided with calculated values within 0.3% for the three elements.[11)] Another product, *viz.,* hydrogen chloride was also detected (pH 2-3) in washings of the reaction mixtures.

Next, the scope of the reaction of 1-chloro-2,4-dinitrobenzene with thiols was examined. 1-Chloro-2,4-dinitrobenzene was allowed to react with 4-bromobenzenethiol under the same conditions as described above except the amount of CR. When the molar ratio of CR was changed against 4-bromobenzenethiol (0.05, 0.2, 0.5, 0.92, and 1.5), the yield of the sulfide reached to a maximum near the molar ratio of 1.0 as shown in Fig. 1. On the other hand, to a stirred mixture of 0.13 g (0.64 mmol) of 1-chloro-2,4-dinitrobenzene, 0.12 g (0.64 mmol) of 4-bromobenzenethiol, and 2 ml

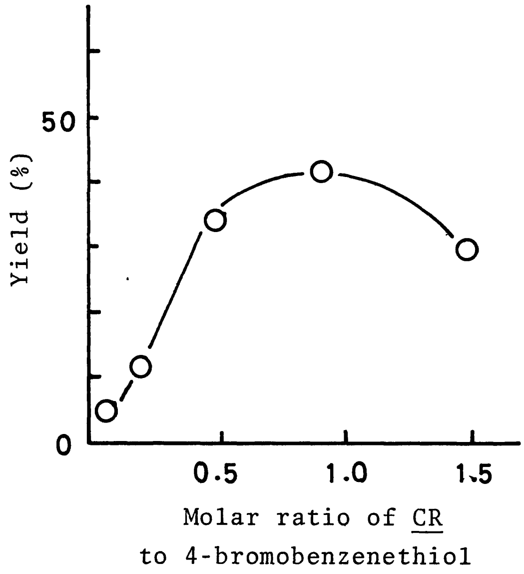


Fig. 1 Relation between Yield and Molar Ratio of CR in the Reaction with 4-BrC_6H_4SH.
1-Cl-2,4-$(NO_2)_2C_6H_3$ 0.64 mmol, 4-BrC_6H_4SH 0.64 mmol, CH_3CN 2 ml; 77-80°C, 6 hr.

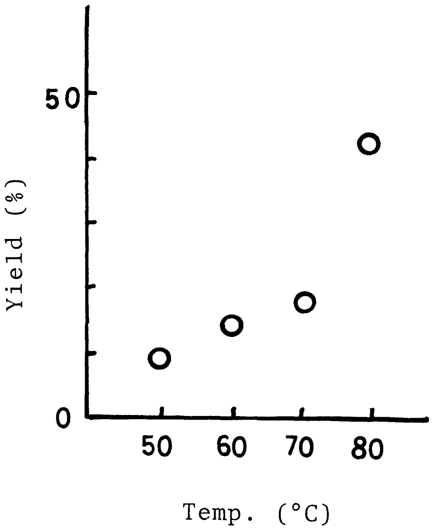


Fig. 2 Temperature Dependence of Yield in the Reaction with 4-BrC_6H_4SH in the Presence of CR.
1-Cl-2,4-$(NO_2)_2C_6H_3$ 0.64 mmol, 4-BrC_6H_4SH 0.64 mmol, CR 0.59 mmol, CH_3CN 2 ml; 6 hr.

of acetonitrile, was added 0.7 ml of 1 M aqueous sodium hydroxide for 5 min at room temperature. The crystals formed were recrystallized from alcohol-benzene to give 0.19 g (84%) of the sulfide. Therefore, the formation of the sulfide in the alkali-catalyzed reaction is much favorable than that in CR-catalyzed. When the reaction temperature was raised, the yields of the sulfide increased as shown in Fig. 2.

When the reaction of 1-chloro-2,4-dinitrobenzene with 4-bromobenzenethiol was carried out under the same conditions as described in Table 1, except that CR was *absent*, the starting materials were recovered unchanged. In the case of the reaction with 4-nitrobenzenethiol under the same conditions, bis(4-nitrophenyl) disulfide was obtained (mp 173-181°C; lit.[12] 181°C). The reaction of 1-chloro-2,4-dinitrobenzene (0.64 mmol) with 4-bromobenzenethiol (0.64 mmol) in *dioxane* in the absence of CR at 77-80°C for 6 hr gave no sulfide but the starting materials were recovered. From the reaction with 4-nitrobenzenethiol under the same conditions, 13% of the disulfide (mp 181-182°C) was obtained, and the remaining was the starting materials.

Consequently, if CR is not involved in the reaction mixtures, the reaction to form sulfides does not occur, and dioxane has no catalytic ability to advance the reaction.

All the above results may be interpreted from the viewpoint that the deprotonation of thiols by CR occurs to make possible the nucleophilic attack by thiolate anions. Visible spectrum of the mixture of 4-nitrobenzenethiol and CR was measured

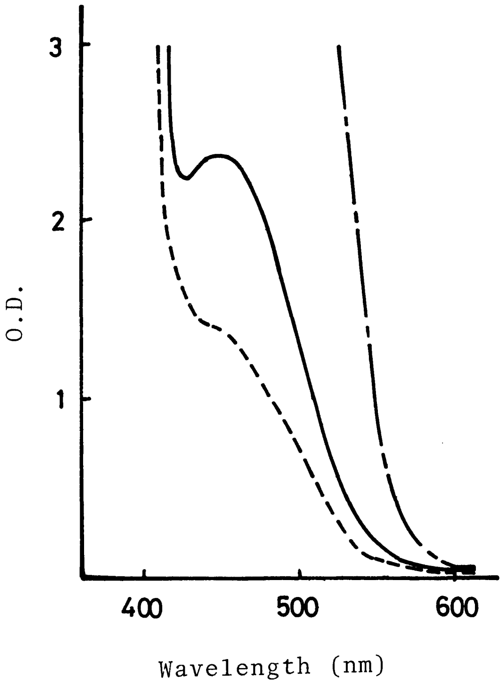


Fig. 3 Visible Spectra of $4\text{-}NO_2C_6H_4SH$ in Acetonitrile.

- - - - The thiol only (0.032 M).
——— In the presence of CR (0.032 M).
—·—·— In the presence of NaOH (0.032 M).

(see Fig. 3). The spectrum indicates the presence of weak interaction between the thiol and CR such as;

$$4\text{-}NO_2C_6H_4SH + \underline{CR} \rightleftharpoons 4\text{-}NO_2C_6H_4S^- + [\underline{CR}\text{-}H^+]$$

NMR spectrum of 4-nitrobenzenethiol (0.64 mmol/2 ml of acetonitrile-d_3) showed a singlet peak of SH proton at δ 4.44 ppm. In the presence of CR (0.64 mmol), the peak shifted to ca. 4.6 ppm and became broad. On the other hand, the peak of SH of 4-bromobenzenethiol did not exhibit such change.

As an application, the reaction of 1-chloro-2,4-dinitrobenzene with benzyl hydrodisulfide was performed. A mixture of 0.13 g (0.64 mmol) of 1-chloro-2,4-dinitrobenzene, 0.10 g (0.64 mmol) of benzyl hydrodisulfide, 0.21 g (0.56 mmol) of CR, and 2 ml of deuterochloroform was heated at 74-79°C for 2.4 hr. After heating, the reaction mixture was treated by the same way as described in the case of the reaction with 4-bromobenzenethiol. The crystals of benzyl 2,4-dinitrophenyl disulfide obtained were purified by recrystallizations from alcohol-benzene and then from alcohol. The identification of benzyl 2,4-dinitrophenyl disulfide was made by melting point, mixture melting point with the authentic specimen, and elemental analysis. The result is presented in Table 2. It is interesting that

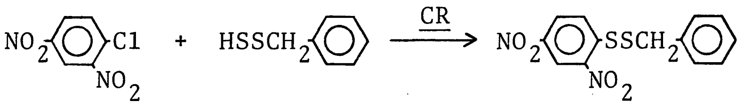


Table 2. Reaction of 1-Chloro-2,4-dinitrobenzene with Benzyl Hydrodisulfide (RSSH) in the Presence of CR in Deuterochloroform*

			Product			
[CR]/[RSSH]	Temp. (°C)	Time (hr)	Yield (%)	Mp (°C)	Mmp (°C)	Mp,Lit. (°C)
0.88	74-79	2.4	8.3	112-112.5	112-113	112-112.5[13]

* 1-Chloro-2,4-dinitrobenzene 0.64 mmol, benzyl hydrodisulfide 0.64 mmol, CR 0.56 mmol; deuterochloroform 2 ml.

the reaction with benzyl hydrodisulfide occured by addition of CR, whereas the reaction with phenylmethanethiol did not proceed under the same conditions. We reported earlier that, when hydrodisulfides are allowed to react with alkali, the hydrodisulfides decompose to hydrogen sulfide, sulfur, and the corresponding disulfides.[14,15] In the present work, it was also confirmed that addition of alkalis to the reaction mixture of 1-chloro-2,4-dinitrobenzene, benzyl hydrodisulfide, and CR gave the same decomposition products without the formation of benzyl 2,4-dinitrophenyl disulfide.

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11) Data of elemental analyses were as follows:
Found for 2,4-dinitrophenyl 4-nitrophenyl sulfide: C, 44.83; H, 2.03; N, 13.03%. Calcd for $C_{12}H_7N_3O_6S$: C, 44.86; H, 2.20; N, 13.08%.
Found for 4-bromophenyl 2,4-dinitrophenyl sulfide: C, 40.61; H, 1.98; N, 7.70%. Calcd for $C_{12}H_7BrN_2O_4S$: C, 40.58; H, 1.99; N, 7.89%.
Found for 4-chlorophenyl 2,4-dinitrophenyl sulfide: C, 46.64; H, 2.15; N, 8.92%. Calcd for $C_{12}H_7ClN_2O_4S$: C, 46.39; H, 2.27; N, 9.02%.

Found for 2,4-dinitrophenyl phenyl sulfide: C, 52.19; H, 2.65; N, 10.03%. Calcd for $C_{12}H_8N_2O_4S$: C, 52.17; H, 2.92; N, 10.14%.

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