

Interchange Reactions of Diphenyl Acetals and Alkyl Dialkylaminomethyl Ethers with Thiols

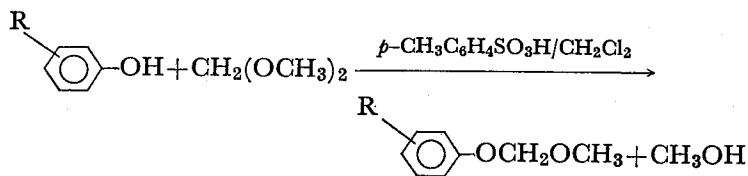
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Sulfur-for-oxygen interchange in diphenyl acetals, which may be generally applicable to the preparation of mercaptals of aldehydes other than formaldehyde, has been studied. The related interchange in the case of alkyl dialkylaminomethyl ethers has also been demonstrated. A possible explanation for the reaction of diphenyl acetals has been given.

KEY WORDS: Sulfur-for-oxygen interchange / Mercaptals / Aryl dialkylaminomethyl sulfides /

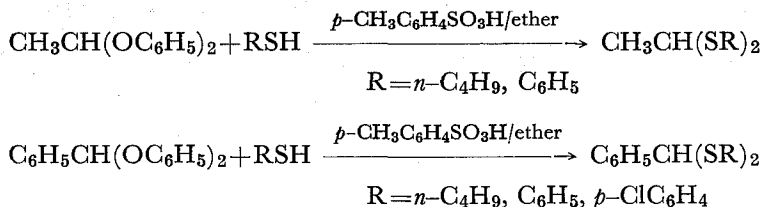
Some interchange reactions of carboxylic esters¹⁾ with alcohols and of thiol esters²⁾ with alcohols were demonstrated long ago. The related interchanges in the cases of orthoesters³⁾ and acetals⁴⁾ have also been known for a long time. Moreover, it has been shown that oxygen-for-sulfur interchanges in orthothioformates^{2,5)} and mercaptoles^{2,6)} can be readily carried out in the presence of a catalyst such as ZnCl₂, furnishing an alternative means of preparation of orthoformates and acetals. The reported preparation of 2-ethoxy-1,3-dithiolane from ethyl orthoformate and 1,2-ethanedithiol with the liberation of ethyl alcohol is a kind of sulfur-for-oxygen interchange.⁷⁾ Shostakovskii and co-workers have reported the formation of acetaldehyde mercaptals in the interchange reaction of 2-methyl-1,3-dioxolane with thiophenol or aliphatic thiols.^{8,9)} Recently, in the presence of *p*-toluenesulfonic acid the interchange reaction indicated below was achieved using dichloromethane as solvent with which methyl alcohol forms an azeotropic mixture.¹⁰⁾



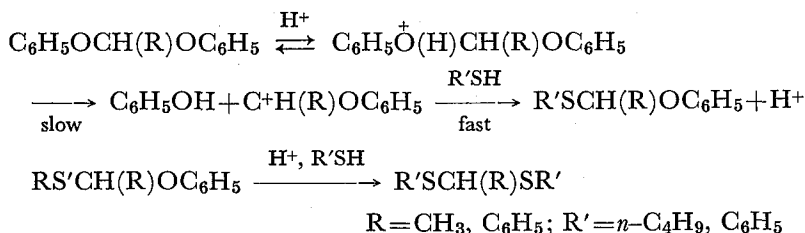
We now report sulfur-for-oxygen interchanges in diphenyl acetals of acetaldehyde and of benzaldehyde under mild conditions, which may be generally applicable to the preparation of mercaptals of aldehydes other than formaldehyde. Thus, in the

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presence of a catalytic amount of *p*-toluenesulfonic acid the following reactions take place.




Though more evidence has to be collected to clarify the detailed scheme of the reactions, from the type of catalyst employed it seems reasonable to propose a stepwise substitution mechanism in analogy with that postulated for the acid-catalyzed interchange reaction of ethyl orthothioformate with an alcohol.²⁾



When diphenoxymethane was allowed to react with either thiophenol or *p*-chlorothiophenol under the same conditions, it was recovered in high yield and no formaldehyde mercaptal could be isolated from the reaction mixture. The same was true for the reaction of bis(*p*-chlorophenoxy)methane with thiophenol or *p*-chlorothiophenol.

In these formaldehyde acetals, *2p-2p* π -bond resonance between the phenyl group and the oxygen would operate against the formation of the protonated intermediate. While, such resonance in acetaldehyde diphenyl acetal or benzaldehyde diphenyl acetal, because of a greater twist of the phenyl groups, would be hindered and would thus permit the easy formation of protonated intermediate in assisting in the rate-

Table I. Interchange Reaction of Diphenyl Acetals with Thiols

Run ^{a)}	Diphenyl acetal	Thiol	Reaction time (hr)	Product ^{b)}	Yield ^{c)} (%)
1	CH ₃ CH(OC ₆ H ₅) ₂	<i>n</i> -C ₄ H ₉ SH	4	CH ₃ CH(S- <i>n</i> -C ₄ H ₉) ₂ ^{d)}	89
2	CH ₃ CH(OC ₆ H ₅) ₂	C ₆ H ₅ SH	8	CH ₃ CH(SC ₆ H ₅) ₂ ^{e)}	95
3	C ₆ H ₅ CH(OC ₆ H ₅) ₂	<i>n</i> -C ₄ H ₉ SH	2	C ₆ H ₅ CH(S- <i>n</i> -C ₄ H ₉) ₂ ^{d)}	97
4	C ₆ H ₅ CH(OC ₆ H ₅) ₂	C ₆ H ₅ SH	2	C ₆ H ₅ CH(SC ₆ H ₅) ₂ ^{e)}	96
5	C ₆ H ₅ CH(OC ₆ H ₅) ₂	<i>p</i> -ClC ₆ H ₄ SH	2	C ₆ H ₅ CH(S-  -Cl) ₂ ^{h)}	65

a) All runs were conducted in boiling ether. b) All spectral data (NMR and IR) of the isolated products were consistent with the assigned structures. c) Yield of isolated, pure product. d) Bp 82–84°C/1 mmHg (lit,⁹⁾ 92°C/2 mmHg). e) Bp 159–163°C/1 mmHg (lit,¹²⁾ 166–171°C/1.2 mmHg). f) Bp 147–151°C/1 mmHg (lit,¹³⁾ 133–135°C/0.3 mmHg). g) Mp 51–52°C (from ethyl alcohol) (lit,¹¹⁾ 49.5–51°C). h) Mp 59–61°C (from ethyl alcohol) (lit,¹⁴⁾ 60–61°C).

Some Interchange Reactions

Table II. Interchange Reaction of Diethylaminomethyl Methyl Ether with Aromatic Thiols

Run ^{a)}	Aromatic thiol	Reaction time (hr)	Product ^{b)}	Yield ^{c)} (%)
1	C ₆ H ₅ SH	5	C ₆ H ₅ SCH ₂ N(C ₂ H ₅) ₂	81
2	<i>p</i> -CH ₃ C ₆ H ₄ SH	8	<i>p</i> -CH ₃ C ₆ H ₄ SCH ₂ N(C ₂ H ₅) ₂	80
3	<i>m</i> -CH ₃ C ₆ H ₄ SH	8	<i>m</i> -CH ₃ C ₆ H ₄ SCH ₂ N(C ₂ H ₅) ₂	67
4	<i>o</i> -CH ₃ C ₆ H ₄ SH	9	<i>o</i> -CH ₃ C ₆ H ₄ SCH ₂ N(C ₂ H ₅) ₂	84
5	<i>p</i> -ClC ₆ H ₄ SH	8	<i>p</i> -ClC ₆ H ₄ SCH ₂ N(C ₂ H ₅) ₂	58
6	C ₆ H ₅ CH ₂ SH	8	C ₆ H ₅ CH ₂ SCH ₂ N(C ₂ H ₅) ₂ ^{d)}	67

a) All runs were conducted in boiling dichloromethane. b) The first five products were identified by direct comparison with samples synthesized according to ref. 16; the remainder is a new compound. c) Yield of isolated, pure product. d) Bp 149–151°C/17 mmHg. Found: C, 68.58; H, 9.42%. Calcd for C₁₂H₁₉NS: C, 68.84; H, 9.15%. NMR(CCl₄) δ 0.97 (t, 6H), 2.55 (q, 4H), 3.68 (s, 2H), 3.95 (s, 2H), 7.03–7.38 (m, aromatic 5H).

determining unimolecular decomposition to phenol and a resonance-stabilized carbonium ion.

The attempted interchange reactions of several diaryl mercaptals such as formaldehyde diaryl mercaptals, acetaldehyde diaryl mercaptals or benzaldehyde diaryl mercaptals with phenols were futile under the same conditions, supporting the concept that sulfur is considerably less basic than oxygen. It may be said that the cleavage of the carbon-sulfur bond in diaryl mercaptals would generally be more difficult than that of the carbon-oxygen bond in diaryl acetals. However, there is an example involving such a carbon-sulfur bond cleavage, *i.e.*, in the presence of HCl benzaldehyde diphenyl mercaptal interchanged with a large excess of ethanethiol in poor yield.¹¹⁾ On the other hand, it has been shown that the Lewis acid-catalyzed oxygen-for-sulfur interchange in aliphatic mercaptoles proceeds smoothly, and that it is an equilibrium reaction and can be shifted to give the desired acetals by removal of the produced low-boiling aliphatic thiols.²⁾

The results of sulfur-for-oxygen interchange in diphenyl acetals of acetaldehyde and of benzaldehyde are given in Table I.

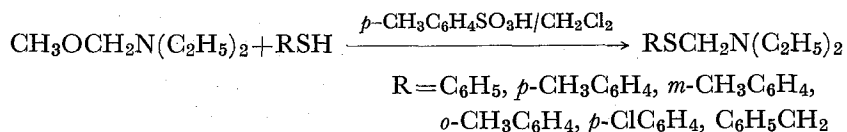
Sulfur-for-oxygen interchange reaction of several alkyl dialkylaminomethyl ethers with higher aliphatic thiols such as 1-octanethiol or 1-decanethiols has previously been observed,¹⁵⁾ where the reaction was carried out in absence of any catalyst. We have

Table III. Reaction of Dimethyl(methylene)ammonium Chloride with Aromatic Thiols

Run ^{a)}	Aromatic thiol	Reaction time (hr)	Product	Yield ^{b)} (%)
1	C ₆ H ₅ SH	20	C ₆ H ₅ SCH ₂ N(CH ₃) ₂ ^{c)}	64
2	<i>p</i> -CH ₃ C ₆ H ₄ SH	24	<i>p</i> -CH ₃ C ₆ H ₄ SCH ₂ N(CH ₃) ₂ ^{d)}	70

a) Both runs were conducted in dimethylformamide at room temperature. b) Yield of isolated, pure product. c) Bp 118–120°C/16 mmHg. Found: C, 64.30; H, 7.64%. Calcd for C₉H₁₃NS: C, 64.62; H, 7.83%. NMR (CCl₄) δ 2.27 (s, 6H), 4.35 (s, 2H), 7.00–7.53 (m, aromatic 5H). d) Bp 79–81°C/1 mmHg. Found: C, 66.27; H, 8.05%. Calcd for C₁₀H₁₅NS: C, 66.25; H, 8.34%. NMR (CCl₄) δ 2.21 (s, 6H), 2.27 (s, 3H), 4.31 (s, 2H), 6.84–7.42 (m, aromatic 4H).

now found that in the presence of *p*-toluenesulfonic acid several aromatic thiols behave like the higher aliphatic thiols, furnishing an alternative means of preparation of aryl dialkylaminomethyl sulfides.¹⁶⁾ For instance, the results in the case of diethylaminomethyl methyl ether are gathered in Table II.



This kind of compounds are also derived from dialkyl(methylene)ammonium chlorides.¹⁷⁾ Two examples from dimethyl(methylene)ammonium chloride are given in Table III.

EXPERIMENTAL

Illustrative examples of the reactions will be given below.

Reaction of Benzaldehyde Diphenyl Acetal with Thiophenol. To a solution containing 2.76 g (10 mmol) of benzaldehyde diphenyl acetal and 2.2 g (20 mmol) of thiophenol in 40 ml of ether is added 0.17 g (1 mmol) of *p*-toluenesulfonic acid and the resulting mixture is refluxed for 2 hr. The mixture is cooled, washed repeatedly with dilute aqueous NaOH, then with water, dried (MgSO₄) and the solvent is removed to afford a crystalline solid. The crude product is recrystallized from ethyl alcohol.

Reaction of Diethylaminomethyl Methyl Ether with Thiophenol. To a solution containing 23.4 g (0.2 mol) of diethylaminomethyl methyl ether and 11.0 g (0.1 mol) of thiophenol in 120 ml of dichloromethane is added 0.26 g (1.5 mmol) of *p*-toluenesulfonic acid and the resulting mixture is refluxed for 5 hr. The mixture is poured into twice its volume of ether, and the ether solution is washed repeatedly with dilute aqueous NaOH, then with water, dried (MgSO₄) and evaporating the solvents gives a light yellow oil which is distilled.

Reaction of Dimethyl(methylene)ammonium Chloride with Thiophenol. A solution containing 6.0 g (64 mmol) of dimethyl(methylene)ammonium chloride and 7.0 g (64 mmol) of thiophenol in 100 ml of dimethylformamide is allowed to stir for 20 hr at room temperature. The mixture is poured into a large quantity of cold brine, made basic with K₂CO₃, and then extracted with several portions of ether. The ether solution is washed with water, dried (Na₂SO₄) and evaporating the solvent gives a light yellow oil which is distilled.

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