did form. The reaction was completed by heating the mixture for one hour. Acidification with dilute hydrochloric acid, and filtration afforded the desired product (VII) which, after washing with water and drying *in vacuo*, weighed 0.18 g. (90%) and melted at 139–139.8°.

In essentially the same way, the iodide of VI could be converted in high yield to the styrene derivative (VII), m.p. 139.8–140.3°.

**The Volatile Amine Derived from the Direct Conversion of the Dihydroisoquinoline** (I) **to Vinyl Ketone** (VII).—The gases evolved on heating a mixture of 3.50 g. (0.0102 mole) of 1-(3′,4′,5′-trimethoxyphenyl)-6,7-methylenedioxy-3,4-dihydroisoquinoline (I), 8 ml. of methyl sulfate, 50 ml. of 40% sodium hydroxide solution, and 50 ml. of water for six hours were passed into dilute hydrochloric acid. Removal of all solvent from the acid solution left 0.85 g. (89%) of residual white solid, m.p. 265–266.7° dec. Shaking a portion of this solid with benzoyl chloride and cold aqueous alkali furnished no trace of an N-benzoyl derivative. One crystallization of the solid from absolute alcohol yielded trimethylamine hydrochloride, m.p. 272–273° dec.[11]

The 2-(3′,4′,5′-trimethoxyphenyl)-4,5-methylenedioxy styrene (VII) isolated from this reaction weighed 3.5 g. (100%), and melted at 139–139.8°. After crystallization from benzene–petroleum ether, the material weighed 3.4 g. and showed m.p. 139.4–139.9°.

**Reaction of Dimethylamine and Methyl Sulfate under Conditions Similar to those Employed in the Direct Conversion of I to VII.**—A solution of 0.82 g. (0.01 mole) of dimethylamine hydrochloride (m.p. 172.4–173.4°) in 40 ml. of water was added slowly over a period of 4 hours under the surface of a stirred and heated mixture of 85 ml. of 20% sodium hydroxide solution and 7 ml. of methyl sulfate. The evolved gases were passed into dilute hydrochloric acid. After the addition, stirring and heating were continued for another two hours. Evaporation of the hydrochloric acid solution left 0.62 g. of solid amine hydrochloride, m.p. 142–164°. Treatment of 0.26 g. of this salt with benzenesulfonyl chloride in the usual manner afforded 0.30 g. (54%) of N-benzenesulfonyldimethylamine. The melting point of the derivative alone or admixed with an authentic sample (m.p. 45.5–46.5°) was 45.5–46.5°.

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[11] Melting points of 271–272° and 271–275° dec. have been observed [E. Winterstein and A. Guyer, *Z. physiol. Chem.*, **128**, 175 (1923); M. Delépine, *Ann. chim. phys.*, [7] **8**, 439 (1896)] although trimethylamine hydrochloride has been reported to melt as high as 280–282° [G. S. Hiers and R. Adams, *Ber.*, **59**, 162 (1926)]. The melting point of dimethylamine hydrochloride is 171° [M. Delépine, above] while that of methylamine hydrochloride is 232–233.5° [M. Sommelet, *Compt. rend.*, **178**, 217 (1924)].

BOSTON, MASSACHUSETTS

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[COMMUNICATION FROM THE DEPARTAMENTO DE QUIMICA DA FACULDADE DE FILOSOFIA, CIENCIAS E LETRAS DA UNIVERSIDADE DE SAO PAULO, BRASIL]

# Interchange Reactions of Mercaptals and Mercaptols with Thiols[1,2]

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The action of four thiols (ethanethiol, thiophenol, benzylmercaptan and propanedithiol-1,3) upon benzaldehyde mercaptals is studied. Interchange reactions are observed, which are analogous to those between alcohols and acetals. The cyclic mercaptals are obtained in highest yields and do not react with monovalent mercaptals. Steroid mercaptols and thioenolethers are able to undergo the same reactions.

Some years ago it was reported that mercaptols and alcohols undergo interchange reactions in the presence of catalysts of the "Friedel–Crafts type" such as hydrochloric acid, zinc chloride or *p*-toluenesulfonic acid.[3] The reaction is of practical value for the preparation of ketals.[4] No indication could be found about reactions of mercaptals or mercaptols with thiols.[5] In order to find out whether such interchange reactions take place we allowed several benzaldehydemercaptals to react with thiols in the presence of hydrochloric acid and other similar catalysts. The results gathered in Table I show that interchange reactions of mercaptals with thiols: $H_5C_6\underset{H}{C}(SR)_2 + 2R'SH \longrightarrow H_5C_6\underset{H}{C}(SR')_2 + 2RSH$ do indeed exist. Thus benzaldehyde diethylmercaptal (I) reacted with thiophenol, benzylmercaptan and propanedithiol-1,3 and the mercaptals of these thiols (II, III, IV) could be isolated from the reaction mixtures. Benzaldehyde diphenylmercaptal (II) in an analogous manner interchanged with benzylmercaptan and propanedithiol-1,3, whereas from benzaldehyde dibenzylmercaptal (III) the trimethylene mercaptal (IV) could be obtained by reaction with propanedithiol-1,3. Besides benzaldehyde diphenylmercaptal (II) the mixed ethyl phenylmercaptal (V) was formed in the reaction of benzaldehyde diethylmercaptal (I) with thiophenol as could be proved by isolation of its disulfone of m.p. 178–181.5 after oxidation with hydrogen peroxide.[6]

When benzaldehyde trimethylenemercaptal (IV) was allowed to react with either benzylmercaptan or thiophenol or ethanethiol it could be recovered in high yield and no other mercaptal could be isolated from the reaction mixture. The same is true for the reaction of benzaldehyde dibenzylmercaptal (III) with ethanethiol. However, when thiophenol was allowed to react with benzaldehyde dibenzylmercaptal (III) only about a third of this substance could be recovered and from the oily residue the disulfone of benzaldehyde benzylphenylmercaptal (VI) was isolated after oxidation with hydrogen peroxide. In the reaction between benzaldehyde diphenylmercaptal (II) and ethanethiol the presence of the mixed benzaldehyde ethylphenylmercaptal (V) was demonstrated by the isolation of its disulfone after oxidation with hydrogen peroxide.

The reactions were carried out with catalysts of

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[1] Presented to the XIIth International Chemical Congress, New York City, September, 1951.

[2] Extracted from a thesis submitted by M. Moura Campos to the Faculdade de Filosofia, Ciencias e Letras da Universidade de Sao Paulo in partial fulfillment of the requirements for the degree of Doutor em Ciencias.

[3] W. E. Mochel, C. L. Agre and W. E. Hanford, THIS JOURNAL, **70**, 2268 (1948).

[4] W. E. Hanford and W. E. Mochel, U. S. Patent 2,229,651 (1941); W. E. Mochel, U. S. Patent 2,229,665 (1941).

[5] Mochel and co-workers state in a footnote that thiol esters give interchange reactions with thiols, but less readily than with alcohols.

[6] Th. Posner, *Ber.*, **36**, 300 (1903). The m.p. indicated by Posner is 155–156°. From the analysis there can, however, be no doubt that we had the benzaldehyde ethylphenyldisulfone in hand.

TABLE I

| No. | Benzaldehyde mercaptal | Solvent | Benzaldehyde mercaptal formed in reaction with— Ethanethiol | Thiophenol | Benzylmercaptan | Propanedithiol |
|---|---|---|---|---|---|---|
| I | Diethyl mercaptal | None | ..... | ..... | 77% III | 98.7% IV |
| | | Gl. acetic acid | ..... | 44% II<br>27% II + 12.5% V[a] | 56% III | 84% IV |
| II | Diphenyl mercaptal | None | 32.6% II + 27% V[a] | ..... | 40.8% III + 10% VI[a] | ..... |
| | | Gl. acetic acid | ..... | ..... | 37% III | 60% IV |
| III | Dibenzyl mercaptal | None | ..... | 37% III + 6.5% VI[a] | ..... | 74% IV |
| | | Gl. acetic acid | 90% III | 35% III | ..... | 73% IV |
| IV | Trimethylene mercaptal | None | ..... | ..... | ..... | ..... |
| | | Gl. acetic acid | 90% IV | 83% IV | 84.5% IV | ..... |

V Benzaldehyde ethyl phenylmercaptal. VI Benzaldehyde benzyl phenylmercaptal.

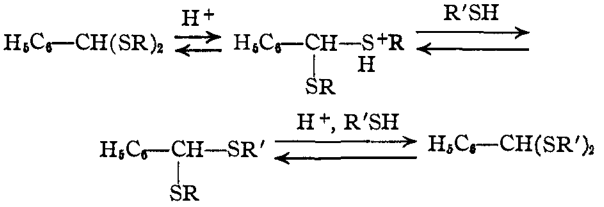
[a] Calculated from the amount of disulfone isolated.

gaseous hydrogen chloride either in absence of any solvent or in a mixture of glacial acetic acid and concentrated hydrochloric acid. Generally higher yields were obtained under the former conditions. It should, however, be noted that mixed mercaptals might have been formed even in cases where their presence could not be proved up to now. When the reaction between benzaldehyde diethyl mercaptal (I) and propanedithiol-1,3 was performed in a closed system, so that no ethylmercaptane could escape, yields were lower. The same is true for reactions between the same substances under catalysis of *p*-toluenesulfonic acid in an open system.

A comparison of the yields obtained under comparable conditions shows that they are highest when trimethylenemercaptals are formed. The analogous reaction of acetals of aliphatic aldehydes with alcohols has been observed long ago[7] and thoroughly studied by Délépine.[8] It is interesting to note that in the case of the oxygenated compounds the best yields are also obtained with glycols, which lead to the formation of cyclic acetals substituting "almost completely" for the monovalent alkoxyl groups of the original acetals. The only phenol studied is $\beta$-naphthol. Here, however, the main reaction consists in the condensation of one molecule of the acetals with the $\alpha$-position of two molecules of $\beta$-naphthol under formation of dinaphtholylmethane derivatives, and only some $\beta$-dinaphthylmercaptal is obtained. In our experiment involving thiophenol no reaction product of this kind could be isolated.

Délépine reports the formation of mixed acetals in the interchange reaction of aliphatic acetals with aliphatic alcohols. In some cases the mixed acetals are even the main reaction products. This finding is noteworthy since these compounds disproportionate easily in the presence of acids into the two simple acetals.[9]

As already mentioned formation of mixed mercaptals was observed also in some of the reactions described in this paper. Therefore, it seems reasonable to admit them as intermediates and to propose a stepwise substitution mechanism as a working hypothesis in analogy to that postulated for the interchange reactions of mercaptols and alcohols, whose equilibrium nature has been established.



$$H_5C_6\text{—}CH(SR)_2 \overset{H^+}{\rightleftarrows} H_5C_6\text{—}\underset{SR}{CH}\text{—}\underset{H}{S^+}R \overset{R'SH}{\rightleftarrows}$$

$$H_5C_6\text{—}\underset{SR}{CH}\text{—}SR' \overset{H^+,\ R'SH}{\rightleftarrows} H_5C_6\text{—}CH(SR')_2$$

The formation of benzaldehyde benzylphenylmercaptal (VI) in the reaction of benzaldehyde dibenzylmercaptal (III) with thiophenol and of benzaldehyde ethyl phenylmercaptal (V) in that of benzaldehyde diphenylmercaptal (III) with ethanethiol shows that interchange may occur in both directions. More evidence has to be collected, however, in order to decide whether or not this is the case in any combination of mercaptals and thiols and also in order to prove beyond doubt the equilibrium nature of the reactions.

Finally, it should be mentioned that mercaptols and thioenol ethers too are able to undergo interchange reactions with thiols. When ethyl 3,3-dimercapto-7,12-diketocholanate was allowed to react with propanedithiol-1,3 the 3,7,12-tris-(trimethylene)-mercaptol of ethyl dehydrocholate was formed. This compound, hitherto unknown, was synthesized by the reaction of ethyl dehydrocholate and propanedithiol-1,3 in presence of gaseous hydrogen chloride. On the other hand, 3-ethylmercaptocholestadiene-3,5 yielded either the correspondent benzyl derivative, 3-benzylmercaptocholestadiene-3,5, or the dibenzylmercaptol of cholestene, 3,5-dibenzylmercaptocholestene-4. The former was obtained when equimolar amounts of thioenolether and thiol were used in the reaction, the latter when an excess of thiol was present.

## Experimental[10]

**Reaction of Benzaldehyde Diethylmercaptal with Thiophenol in Glacial Acetic Acid Solution.**—To 1.6 g. of benzaldehyde diethylmercaptal (7 mmoles) and 2 ml. of thiophenol (19 mmoles) dissolved in about 3 ml. of glacial acetic acid a few drops of concd. hydrochloric acid was added and the mixture kept in the ice-box for three hours. Under continuous cooling a stream of gaseous hydrogen chloride was passed through the mixture for two hours and the mix-

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[7] A. Geuther and A. Bachmann, *Ann.*, **218**, 44 (1883).

[8] N. Délépine, *Compt. rend.*, **132**, 968 (1901): *Chem. Zentr.*, **22**, I, 1146 (1901).

[9] R. Leinu and R. Vuorinen, *Ann. Acad. Sci. Fennicae Ser. A II. Chem. n.* 19; *C. A.*, **42**, 3316 (1948).

[10] All melting points were taken with a Kofler melting point apparatus. The method of A. Schoeberl, R. Jaczynski and P. Rambacher, *Angew. Chem.*, **50**, 334 (1937), was used for sulfur analyses.

TABLE II

| Benzaldehydemercaptal | g. | Thiol | g. | Benzaldehydemercaptal formed | g. | M.p.,[a] °C. | Disulfone m.p.,[a] °C. |
|---|---|---|---|---|---|---|---|
| Diethylmercaptal | 0.45 | $H_7C_7SH$ | 1.07 | Dibenzylmercaptal | 0.4 | 58.5–60 | 215.5–217.5 |
| Diethylmercaptal | 0.9 | $H_6C_3(SH)_2$ | 0.5 | Trimethylenemercaptal | 0.7 | 70.5–72 | 269–270 |
| Diethylmercaptal | 3.7 | $H_5C_6SH$ | 4.5 | Diphenylmercaptal + | 1.3 | 49.5–51 | ......... |
| | | | | Ethyl phenylmercaptal | .. | | 178–181.5[b] |
| Diphenylmercaptal | 1 | $H_7C_7SH$ | 0.82 | Dibenzylmercaptal | 0.4 | 59–60 | 215–217 |
| Diphenylmercaptal | 1 | $H_6C_3(SH)_2$ | .4 | Trimethylenemercaptal | .38 | 70–72 | 269–270.5 |
| Dibenzylmercaptal | 1 | $H_6C_3(SH)_2$ | .33 | Trimethylenemercaptal | .4 | 70.5–72 | 268.5–270 |
| Dibenzylmercaptal | 0.26 | $H_5C_6SH$ | .16 | Dibenzylmercaptal | .09 | 59–60 | ......... |
| Dibenzylmercaptal | .5 | $H_5C_2SH$ | .42 | Dibenzylmercaptal | .45 | 58–60 | ......... |
| Trimethylenemercaptal | .15 | $H_7C_7SH$ | .17 | Trimethylenemercaptal | .13 | 70–72 | ......... |
| Trimethylenemercaptal | .6 | $H_5C_6SH$ | 1 | Trimethylenemercaptal | .5 | 70–72 | ......... |

[a] All crystallized substances were identified by mixed melting points except those which were analyzed. [b] 0.71 g. (12.5%) was obtained. *Anal.* Calcd. for $C_{15}H_{16}S_2O_4$: S, 19.77. Found: S, 19.60.

TABLE III

| Benzaldehydemercaptal | g. | Thiol | g. | Benzaldehydemercaptal formed | g. | M.p.,[a] °C. | Disulfone, m.p.,[a] °C. | g. |
|---|---|---|---|---|---|---|---|---|
| Diethylmercaptal | 1 | $H_6C_3(SH)_2$ | 0.5 | Trimethylenemercaptal | 0.9 | 70–72 | ...... | .. |
| Diphenylmercaptal | 1.96 | $H_5C_2SH$ | 3.35 | Diphenylmercaptal + | .64 | 48.5–51 | ...... | .. |
| | | | | Ethylphenylmercaptal | .. | ....... | 180–182 | 0.54 |
| Diphenylmercaptal | 1.8 | $H_7C_7SH$ | 1.93 | Dibenzylmercaptal + | .8 | 59.5–61 | ...... | .. |
| | | | | Benzyl phenylmercaptal | .. | ....... | 245–248[b] | 0.91 |
| Dibenzylmercaptal | 2 | $H_6C_3(SH)_2$ | 0.7 | Trimethylenemercaptal | .82 | 70–72 | ...... | .. |
| Dibenzylmercaptal | 2 | $H_5C_6SH$ | 1.5 | Dibenzylmercaptal + | .7 | 58–61 | ...... | .. |
| | | | | Benzyl phenylmercaptal | .. | ....... | 245–248 | 0.15 |
| Trimethylenemercaptal | 1 | $H_5C_2SH$ | 1 | Trimethylenemercaptal | .9 | 69.5–71.5 | ...... | .. |

[a] All crystallized substances were identified by mixed melting points except those which were analyzed. [b] *Anal.* Calcd. for $C_{20}H_{18}S_2O_4$: S, 16.60. Found: S, 16.40.

ture kept in the ice-box for 12 more hours. The mixture was then dissolved in ether and the ethereal solution washed with water, sodium hydroxide solution (2.5–5%) and again with water, then dried with calcium chloride. After evaporation of the ether an oily residue was left, which crystallized from alcohol; m.p. after several recrystallizations from alcohol 48.5–51° undepressed by benzaldehyde diphenylmercaptal; yield 0.9 g. (44%). Oxidation with hydrogen peroxide in glacial acetic acid and recrystallization from the same solvent yielded crystals, m.p. 205–207.5°, undepressed by the disulfone of benzaldehyde diphenylmercaptal.

In essentially the same way the following experiments and those mentioned in Table II were executed:

One gram of ethyl 3,3-diethylmercapto-7,12-diketocholanate (2 mmoles) and 0.7 g. of propanedithiol-1,3 (7.5 mmoles) gave[11] 1.35 g. (96%) of crystals m.p. 207–209° (from ethyl acetate) undepressed by ethyl 3,7,12-tris-(trimethylenedimercapto)-cholanate. This compound was obtained by reaction of 4 g. (9 mmoles) of ethyl dehydrochlolate and 5 g. (48 mmoles) of propanedithiol-1,3 in a stream of gaseous hydrogen chloride at 0°. After removal of the hydrogen chloride *in vacuo* and of the excess thiol with petroleum ether (50–70°) the residue was recrystallized from ethyl acetate; m.p. 208–209°, yield 3.9 g. (53%).

0.1 g. of 3-ethylmercaptocholestadiene-3,5 (0.2 mmole) and 0.5 ml. of benzylmercaptan (4.2 mmoles) gave[11,12] 0.1 g. (80%) of 3,3-dibenzylmercaptocholestene-4, m.p. 124.5–126°.[13a,b]

0.21 g. of 3-ethylmercaptocholestadiene-3,5 (0.5 mmole) and 0.06 g. of benzylmercaptan (0.5 mmole) gave[11,12] 0.2 g. of 3-benzylmercaptocholestadiene-3,5, m.p. 118–120°.[13b] *Anal.* Calcd. for $C_{34}H_{50}S$: S, 6.53. Found: S, 6.20.

**Reaction of Benzaldehyde Diethylmercaptal with Benzylmercaptan.**—A mixture of 0.9 g. of benzaldehyde diethylmercaptal (4 mmoles) and 2 ml. of benzylmercaptan (17 mmoles) was protected against moisture, cooled in an ice-bath and a stream of gaseous hydrogen chloride was allowed to pass through it for two hours. Then it was left in a vacuum desiccator over potassium hydroxide for several hours. The mixture was dissolved in ether, washed with water, 5% of sodium hydroxide and with water again, and then dried with calcium chloride. After evaporation of the ether, the oily residue was crystallized from alcohol, yielding 1.1 g. (77%) of crystals, m.p. 58–60° undepressed by benzaldehyde dibenzylmercaptal.

In essentially the same manner the experiments mentioned in Table III were executed.

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[11] Without extraction with ether, by direct crystallization.

[12] Without passing a stream of gaseous hydrogen chloride.

[13] (a) H. Hauptmann, THIS JOURNAL, **69**, 562 (1947); (b) Z. Foldi, *C. A.*, **44**, 4047 (1950).