The Formation of Vinyl Sulfides by the Cleavage of the Carbon-Sulfur Bond in Dithioacetals with $CuCl_2$

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Synopsis. The elimination of arene- and alkanethiol from diaryl and dialkyl dithioacetals, in the presence of copper(I) or copper(II) salt plus tertiary amine, to produce the corresponding aryl and alkyl vinyl sulfides, respectively, has been studied. The employment of a combination of 2 mol equiv. of $CuCl_2$ and 2 mol equiv. of *N,N*-diisopropylethylamine is most favorable.

Cohen and co-workers have reported that, in the presence of *N,N*-diisopropylethylamine, the benzene complex of copper(I) trifluoromethanesulfonate promotes the removal of benzenethiol from the unsaturated or vinylogous diphenyl dithioacetals to produce 1,3-butadienes substituted with a phenylthio group.[1,2] Prior to this work, Mukaiyama and co-workers have found that, in the presence of 2,6-lutidine, the $CuCl_2$-induced reaction of benzaldehyde diethyl dithioacetal with malononitrile in tetrahydrofuran proceeds smoothly to afford the condensation product, benzylidenemalononitrile.[3] They have also found that $CuCl_2$ together with CuO can convert a wide variety of 1,3-dithiane derivatives into the corresponding carbonyl compounds.[4] Since all of these reactions appear to involve a reaction mechanism in which the alkylthio or arylthio group is liberated from the dithioacetal molecule, it can be concluded that, in the presence or absence of tertiary amine, copper(I) or copper(II) salt effects the cleavage of one or two carbon-sulfur bonds in dithioacetals. With these considerations in mind, we have studied the elimination of arene- and alkanethiol from several diaryl and dialkyl dithioacetals, in the presence of copper(I) or copper(II) salt plus tertiary amine, to produce the corresponding aryl and alkyl vinyl sulfides.

In preliminary experiments, phenylacetaldehyde diphenyl dithioacetal (**1a**) and two molar amounts of *N,N*-diisopropylethylamine in benzene[5] were heated at reflux temperature with stirring for 24 h without any reaction occurring. When copper(I) or copper(II) salt was added to the mixture, the expected reaction took place to afford phenyl styryl sulfide (**2a**) and phenyl disulfide (**3a**).

$$\underset{\mathbf{1}}{(RS)_2CHCHR'R''} \xrightarrow[\text{benzene}]{CuX_n,\ \text{tertiary amine}} \underset{\mathbf{2}}{RSCH{=}CR'R''} + \underset{\mathbf{3}}{1/2\,RSSR}$$

a: $R=R'=C_6H_5$, $R''=H$
b: $R=C_6H_5$, $R'=n\text{-}C_3H_7$, $R''=H$
c: $R=C_6H_5$, $R'=R''=CH_3$
d: $R=C_6H_5$, $R'=CH_2{=}CH\text{-}$, $R''=H$
e: $R=C_6H_5$, $R'=CH_2{=}C(CH_3)\text{-}$, $R''=H$
f: $R=C_6H_5CH_2$, $R'=C_6H_5$, $R''=H$
g: $R=CH_3$, $R'=C_6H_5$, $R''=H$
h: $R=C_2H_5$, $R'=C_6H_5$, $R''=H$

Table 1 shows that, among these copper(I) and copper(II) salts, only anhydrous $CuCl_2$ is available for the elimination and that even in the case with $CuCl_2$ the use of an excess or a deficiency of this salt causes a significant decrease in the yield.

We then examined the possibility of substituting the other tertiary amines for the *N,N*-diisopropylethylamine employed in the above experiments. Thus when **1a** and two molar amounts of $CuCl_2$ in benzene were heated at reflux temperature with stirring for 24 h, in the presence of a variety of tertiary amines, **2a** and **3a** were obtained in the yields shown in Table 2, together with unchanged **1a**.

As can be seen from Table 2, the addition of tertiary amine is unessential to promote the formation of **2a**, since the yield of **2a** in the absence of any tertiary amine is nearly equal to that obtained in the cases where 2 mol equiv. of *N,N*-diisopropylethylamine or 2,6-lutidine was used. However, it is noteworthy that

TABLE 1. REACTION OF PHENYLACETALDEHYDE DIPHENYL DITHIOACETAL (**1a**) WITH VARIOUS COPPER(I) AND COPPER(II) SALTS IN THE PRESENCE OF *N,N*-DIISOPROPYLETHYLAMINE

1a 0.2 mmol, *N,N*-diisopropylethylamine 0.4 mml, benzene 20 ml. Reaction conditions: 24 h reflux.

Run	Additive (CuX_n) (equiv.)	Yield/%		Recovered **1a** (%)[a]
		2a[a]	**3a**[a]	
1	None	0	0	
2	$CuCl_2$ (0.5)	7	2	82
3	$CuCl_2$ (1)	9	10	81
4	$CuCl_2$ (2)	49	42	47
5	$CuCl_2$ (4)	2	92	0
6	$CuCl_2$ (1)+CuCl (1)	17	17	72
7	CuCl (2)	12	20	78
8	$Cu(OAc)_2$ (2)	8	7	82
9	$CuBr_2$ (2)	11	95	0
10	$Cu(CN)_2$ (2)	0	0	
11	$CuCl_2\cdot 2H_2O$	0	0	

a) Determined by GLC using *p*-terphenyl as internal standard.

TABLE 2. REACTION OF PHENYLACETALDEHYDE DIPHENYL DITHIOACETAL (**1a**) WITH $CuCl_2$ IN THE PRESENCE OF A VARIETY OF TERTIARY AMINES

1a 0.2 mmol, $CuCl_2$ 0.4 mmol, benzene 20 ml. Reaction conditions: 24 h reflux.

Run	Additive (tertiary amine) (equiv.)	Yield/%		Recovered **1a** (%)[a]
		2a[a]	**3a**[a]	
1	None	46	66	25
2	*N,N*-Diisopropylethylamine (1)	40	54	44
3	*N,N*-Diisopropylethylamine (2)	49[b]	42[b]	47[b]
4	*N,N*-Diisopropylethylamine (4)	25	31	64
5	*N,N*-Diisopropylethylamine (8)	5	12	87
6	Triethylamine (2)	6	12	88
7	Pyridine (2)	3	4	95
8	2,6-Lutidine (2)	48	32	47
9	DBU[c] (2)	12	73	0
10	$CuCl_2\cdot(pyridine)_2$ (2)	0	0	

a) Determined by GLC using *p*-terphenyl as internal standard. b) These valuesare identical to those for Run 4 given in Table 1. c) 1,8-Diazabicyclo[5.4.0]undec-7-ene,

TABLE 3. REACTION OF SEVERAL DITHIOACETALS (**1a**—**h**) WITH $CuCl_2$ IN THE PRESENCE OF *N*,*N*-DIISOPROPYLETHYLAMINE

Dithioacetal 0.2 mmol, $CuCl_2$ 0.4 mmol; *N*,*N*-diisopropylethylamine 0.4 mmol, benzene 20 ml. Reaction conditions: 36 h reflux.

Run	Starting dithio-acetal	Products (yield/%)[b]	Recovered dithio-acetal (%)	Analytical data of product Found (Calcd) (%) C	H	MS(40 eV) *m/e* M^+
1	**1a**	**2a** (79)	14	78.95(79.20)	5.51(5.70)	212
2	**1b**	**2b** (63)	20	73.96(74.10)	8.05(7.91)	178
3	**1c**	**2c** (77)	10	73.01(73.12)	7.08(7.36)	164
4	**1d**	**2d** (30)	<2	73.88(74.03)	6.04(6.21)	162
5	**1e**	**2e** (36)	<2	75.21(74.95)	6.84(6.86)	176
6	**1f**	**2f** (90)	4	79.40(79.60)	6.09(6.23)	226
7	**1g**	**2g** (54)	26	71.83(71.95)	6.53(6.71)	150
8	**1h**	**2h** (79)	9	73.06(73.12)	7.21(7.36)	164

a) Except **2c**, these products seem to be a mixture of *trans*-isomer and *cis*-isomer in small amounts. The isolation of **3**, which was produced together with **2**, was omitted because of its minor importance. The ^{1}H-NMR spectra (60 MHz, δ, in CCl_4) are as follows: **2a**: 6.41(d, 1H, *J*=17 Hz), 6.68(d, 1H, *J*=17 Hz), 7.0—7.7(m, 10H). **2b**: 0.96(t, 3H, *J*=6 Hz), 1.0—1.8(m, 2H), 1.9—2.4(m, 2H), 5.5—6.3(m, 2H), 7.1—7.3(m, 5H). **2c**: 1.86(s, 6H), 5.86(s, 1H), 7.0—7.3(m, 5H). **2d**: 4.7—5.2 (m, 2H), 6.1—6.7(m, 3H), 7.1—7.5(m, 5H). **2e**: 1.83(s, 3H), 5.86(d, 1H, *J*=1 Hz), 6.35(d, 1H, *J*=1 Hz), 6.60(d, 1H, *J*=10 Hz), 7.17(d, 1H, *J*=10 Hz), 7.0—7.5(m, 5H). **2f**: 3.70(s, 2H), 6.16(d, 1H, *J*=15 Hz), 6.48(d, 1H, *J*=15 Hz), 7.0—7.3(m, 10H). **2g**: 2.22(s, 3H), 6.18(d, 1H, *J*=17 Hz), 6.69(d, 1H, *J*=17 Hz), 7.1—7.4(m, 5H). **2h**: 1.23(t, 3H, *J*=7 Hz), 2.4—2.9(m, 2H), 6.18(d, 1H, *J*=17 Hz), 6.45(d, 1H, *J*=17 Hz), 7.0—7.5(m, 5H). b) Yield of isolated product based on **1**.

simply by adding 2 mol equiv. of the tertiary amine to the reaction mixture the proportion of recovered **1a** can be increased to 47% from 25%. An advantage of the employment of the tertiary amine lies in that it suppresses the occurrence of undesirable side reaction. Presumably, an obvious difference in yields of **2a** between the former case and the latter case using 2 mol equiv. of the tertiary amine should be observed if the reaction time is extended over 24 h. On the other hand, the use of a large excess of *N*,*N*-diisopropylethylamine results in a significant decrease in yield of **2a**. The addition of 2 mol equiv. of triethylamine or pyridine also diminished the yield of **2a**, presumably due to the complex formation between the amine and $CuCl_2$. The inactivity of such a complex is easily understandable if we consider the finding that the pre-formed 1:2 complex between $CuCl_2$ and pyridine does not promote the reaction.

This information concerning the elimination of benzenethiol from **1a** in benzene to produce **2a** could help in accomplishing the conversion of the other dithioacetals (**1**) into the corresponding vinyl sulfides (**2**). Thus, when diaryl and dialkyl dithioacetals in benzene were heated at reflex temperature with stirring for 36 h in the presence of 2 mol equiv. of $CuCl_2$ and 2 mol equiv. of *N*,*N*-diisopropylethylamine, the moderately good yields of the corresponding aryl and alkyl vinyl sulfides were obtained toegther with disulfides (**3**), suggesting that our procedure is fairly general for this type of elimination reaction. Table 3 shows the results obtained with **1b**—**h**, including **1a**, as the starting substrate.

Experimental

1a, **1b**, **1c**, **1d**, and **1e** were synthesized in yields of 99, 93, 88, 99, and 91%, respectively, by the reaction of lithiated formaldehyde diphenyl dithioacetal in tetrahydrofuran with each of benzyl bromide, butyl bromide, isopropyl bromide, allyl bromide, and 2-methylallyl chloride.[6] **1g** was prepared in yield of 60%, by the same procedure, from lithiated formaldehyde dimethyl dithioacetal and benzyl bromide. **1f** and **1h** were synthesized in yields of 96 and 90%, respectively, by the *p*-toluenesulfonic acid-promoted interchange reaction of phenylacetaldehyde dimethyl acetal in benzene with α-toluenethiol and with ethanethiol.

Reactions Summarized in Table 1. The copper(I) or copper(II) salt used for each run is listed in Table 1. To a suspension of the salt in 20 ml of benzene were added 0.2 mmol of phenylacetaldehyde diphenyl dithioacetal (**1a**) and 0.4 mmol of *N*,*N*-diisopropylethylamine under nitrogen. The mixture was heated at reflux temperature with stirring for 24 h. Thirty ml of water was added and the organic layer was separated and subjected to GLC.

Reactions Summarized in Table 2. The tertiary amines used were noted in Table 2. To a suspension of 0.4 mmol of $CuCl_2$ in 20 ml of benzene were added 0.2 mmol of phenylacetaldehyde diphenyl dithioacetal (**1a**) and the tertiary amine under nitrogen. The mixture was heated as above, and similarly worked up. The obtained organic layer was subjected to GLC.

Reactions Summarized in Table 3. To a suspension of 0.4 mmol of $CuCl_2$ in 20 ml of benzene were added 0.2 mmol of a dithioacetal (**1**) and 0.4 mmol of *N*,*N*-diisopropylethylamine under nitrogen. After the addition was complete, the mixture was heated at reflux temperature with stirring for 36 h. Thirty ml of water and 50 ml of saturated aqueous solution of NH_4Cl were added, and the mixture was extracted with several portions of ether. The combined ethereal extracts were dried, filtered, and concentrated *in vacuo* to give a residue. The products were isolated by column chromatography on silica gel, using 20% benzene-hexane or 10% chloroform-hexane as the eluent.

References

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5) In preliminary experiments, it was found that benzene is the most suitable solvent for this reaction.

6) Fröling and Arens found that formaldehyde dialkyl dithioacetal can be metallated easily with $NaNH_2$ or $LiNH_2$ in liquid ammonia and subsequently converted to dialkyl dithioacetals of higher aldehydes by trapping the metallated compound with alkyl halides: A. Fröling and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **81**, 1009 (1962).