# Organic Sulfur Compounds; II[1]. Sulfur Dioxide as Catalyst in the Synthesis of Thioacetals from Aldehydes or Ketones and Alkanethiols, Alkanedithiols, or Hydroxyalkanethiols[2]

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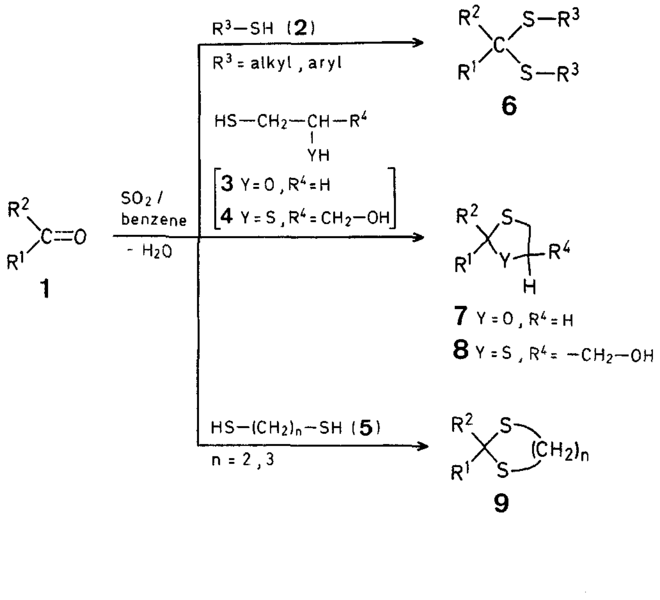
The usual preparation of thioacetals from aldehydes or ketones and thiols, dithiols, or hydroxythiols is carried out in the presence of acidic catalysts such as dry hydrogen chloride or hydrochloric acid, zinc chloride, tin(IV) chloride, boron trifluoride, *p*-toluenesulfonic acid, and ion-exchange resins[3-6].

We recently reported the possibility of using gaseous sulfur dioxide as a catalyst in the direct condensation of carbonyl compounds with alcohols and diols[7]. We have now extended these studies to the preparation of linear and cyclic thioacetals although it has been reported that thiols react with sulfur dioxide to give di- and polysulfides[8]. We have found that sulfur dioxide conveniently catalyzes the formation of open-chain and cyclic dithioacetals (**6**, **8**, **9**) as well as cyclic *O,S*-acetals (**7**) from aldehydes or ketones (**1**) and alkanethiols (**2**), alkanedithiols (**5**), hydroxyalkanethiols (**3**), or hydroxyalkanedithiols (**4**), respectively.



$R^1$ = alkyl, aryl
$R^2$ = H, alkyl

The yields of compounds **6**–**9** thus obtained are comparable to the yields obtained using conventional catalysts, and in certain cases are even better (see Table 1). The condensation of two 4-dimethylaminobenzaldehydes with 2-mercaptoethanol or 2,3-dithioglycerol according to our method proceeded with distinctly better yields than the same condensations in the presence of hydrogen chloride. The reaction times required are in the range of several hours. The acetalization can be performed either by passing sulfur dioxide through a mixture of the components in benzene (Method A) or by saturating benzene with sulfur dioxide and then adding the components. Method B is more time-consuming, the yields being almost the same as with Method A.

Our method is applicable to both aliphatic and aromatic aldehydes and ketones. A hydroxy group in the alkanedithiol (**4**) does not interfere with the reaction whereas it may be replaced by chlorine when hydrogen chloride is used as catalyst[4].

When the reaction mixture is cooled after performance of the reaction it becomes turbid and a small quantity of precipitate appears which probably is a polysulfide. Further, G.L.C. analysis of the reaction mixtures obtained from the reaction of carbonyl compounds with 2-mercaptoethanol showed the presence of small amounts of bis[2-hydroxyethyl] disulfide; the formation of this by-product suggests that thiol oxidation occurs as a side reaction to some degree.

Known products were identified by comparison with authentic samples. The structure of the new compounds were confirmed by element analyses, I.R.-, and $^1$H-N.M.R. spectra. I.R. spectra were obtained on a Perkin-Elmer 621 spectrophotometer. $^1$H-N.M.R. spectra were recorded using an 80 MHz Tesla BS 487 instrument. The purity of the products (>97%) was checked by G.L.C. analysis using a GCHF 18.3 gas chromatograph equipped with a column filled with SE-30 or XE-60 on Chromosorb G/AW DMCS.

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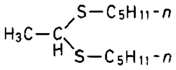
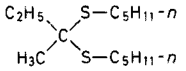
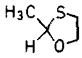
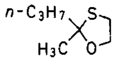
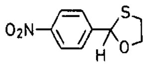
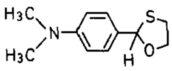
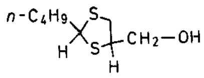
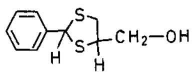
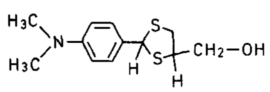
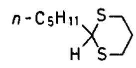
**Table 1.** Thioacetals (6–9) prepared using Sulfur Dioxide as Catalyst

| Product[a] | Yield [%] | | m.p. or b.p./torr [°C] | Molecular formula[b] or Lit. Data [°C] | $n_D^{20}$ | $d_4^{20}$ |
|---|---|---|---|---|---|---|
| | using $SO_2$ | by Other Methods | | | | |
| **6a**  | 64 | | m.p. 113–114° | $C_{12}H_{26}S_2$ (234.3) | 1.4121 | 1.1475 |
| **6b**  | 69 | | b.p. 120–122°/4.5 | $C_{14}H_{30}S_2$ (262.4) | 1.3972 | 1.1267 |
| **7a**  | 83 | 81 (Tos-OH)[5] | b.p. 50.5–51.5°/30 | b.p. 50°/30[5] | 1.4869 | 1.0650 |
| **7b**  | 72 | 78 (Tos-OH)[5] | b.p. 92–93.5°/47 | b.p. 61–62°/18[5] | 1.4749 | 0.9905 |
| **7c**  | 70 | | m.p. 82.5–84°[c] | $C_9H_9NO_3S$ (211.2) | — | — |
| **7d**  | 52 | 41 (HCl)[d] | m.p. 126–128° | $C_{14}H_{19}NOS_2$ (281.3) | — | — |
| **8a**  | 81[e] | 90 (Tos-OH)[4] | b.p. 114–116°/0.2 | —[4] | 1.4346 | 1.1135 |
| **8b**  | 62[e] | 56 (HCl)[4] | m.p. 70–76.5° | m.p. 69–75°[4] | | |
| **8c**  | 54[e] | 47 (HCl)[d] | m.p. 89–95.5°[c] | $C_{12}H_{17}NOS_2$ (255.3) | | |
| **9a**  | 83[f] | 70 (HCl)[9,10] | m.p. 38–40.5° | b.p. 85°/0.3[9]<br>$n_D^{28}$: 1.5209[9] | | |

[a] The products were >97% pure as determined by G.L.C. analysis.

[b] The microanalyses showed the following maximum deviations from the calculated values: C, ±0.41; H, ±0.29; S, ±0.22.

[c] Recrystallized from benzene/petroleum ether (1/1).

[d] Results of our comparative experiments.

[e] Mixture of diastereoisomers.

[f] Colorless crystals isolated by preparative G.L.C. The product readily forms a supercooled liquid; $n_D^{25}$: 1.5210 (Ref.[9], $n_D^{28}$: 1.5209).

**Table 2.** Spectral Data of the Synthesized Thioacetals

| Product | I.R. $\nu$ [cm$^{-1}$] | | $^1$H-N.M.R. ($CCl_4$/HMDS) $\delta$ [ppm] |
|---|---|---|---|
| | C—S—C | C—O—C | |
| **6a** | 653 | | 0.97 (t, 3H, $CH_3$, $J=7.5$ Hz); 1.12 (t, 6H, $2CH_3$, $J=7$ Hz); 2.24 (m, 12H, $6CH_2$); 2.31 (m, 4H, $2CH_2$); 4.16 (t, 1H, CH); 4.12 (t, 1H, CH) |
| **6b** | 557 | | 1.24 (q, 3H, $CH_3$, $J=7$ Hz); 1.2 (m, 2H, $CH_2$); 2.3 (m, 12H, $6CH_2$); 2.34 (m, 4H, $CH_2$) |
| **7a** | 664 | 1095 | 1.32 (d, 3H, $CH_3$); 2.47 (m, 4H, $2CH_2$); 4.19 (t, 1H, CH, $J=7.5$ Hz); 4.24 (t, 1H, CH, $J=7.5$ Hz) |
| **7b** | 662 | 1063 | 1.37 (m, 3H, $CH_3$); 1.42 (m, 4H, $2CH_2$); 1.53 (m, 3H, $CH_3$); 2.38 (m, 4H, $2CH_2$) |
| **7c** | 680 | 1070 | 2.47 (m, 4H, $2CH_2$); 4.23 (t, 1H, CH, $J=7$ Hz); 4.29 (t, 1H, CH, $J=7$ Hz); 7.85 (m, 4H, $C_6H_4$) |
| **7d** | 660 | 1075 | 1.53 (s, 6H, $2CH_3$); 1.90 (s, 1H, $CH_3$); 2.5 (m, 4H, $2CH_2$); 4.33 (t, 1H, CH, $J=7$ Hz); 4.37 (t, 1H, $J=7$ Hz); 7.63 (m, 3H, $C_6H_3$) |
| **8a** | 712 | | 1.16 (t, 3H, $CH_3$, $J=7$ Hz); 2.6 (m, 6H, $3CH_2$); 2.74 (d, 2H, $CH_2$, $J=7$ Hz); 3.3 (m, 1H, $C\underline{H}—CH_2OH$); 4.2 (m, 2H, $C\underline{H}_2OH$); 4.32 (s, 1H, OH) |
| **8b** | 724 | | 2.4 (m, 2H, $CH_2$); 3.8 (m, 1H, $CH—CH_2OH$); 4.16 (m, 2H, $CH_2OH$); 3.96 (s, 1H, OH); 4.36 (t, 1H, CH, $J=7$ Hz); 4.40 (t, 1H, CH, $J=7$ Hz) |
| **8c** | 718 | | 2.43 (m, 2H, $CH_2$); 3.7 (m, 1H, $CH—CH_2OH$); 3.86 (m, 2H, $CH_2OH$); 4.07 (s, 1H, OH); 4.26 (t, 1H, CH, $J=7$ Hz); 4.34 (t, 1H, CH, $J=7$ Hz) |
| **9a**[a] | 690 | | 1.05 (t, 3H, $CH_3$, $J=7.5$ Hz); 1.13 (m, 8H, $4CH_2$); 2.67 (m, 2H, $CH_2$); 4.46 (m, 4H, $2CH_2$); 4.62 (t, 1H, CH, $J=7$ Hz) |

[a] N.M.R. spectrum recorded on a Varian A-60A instrument, solvent $CDCl_3$.

**General Thioacetalization Procedures:**

Method A: Into a round-bottomed flask equipped with a stirrer, a Dean-Stark trap, and a bubbler for the introduction of gaseous sulfur dioxide are placed dry benzene (250 ml), the carbonyl compound **1** (0.5 mol), and the thiol **2** (1.2 mol) or the mercaptoalkanol **3** (0.6 mol) or the dithiol **4** or **5** (0.6 mol). The mixture is heated at reflux temperature with stirring while a continuous stream of dry sulfur dioxide (Fluka AG) is passed through the mixture. After the reaction is complete (i.e., when the volume of water formed does not increase any more), the mixture is cooled, neutralized with anhydrous potassium carbonate, and filtered. The solvent is evaporated and the residual crude product is purified by fractional distillation or crystallization.

Method B: In a round-bottomed flask equipped with a stirrer, a Dean-Stark trap, and a bubbler, dry benzene (250 ml) is saturated with gaseous sulfur dioxide for 30 min at room temperature. The sulfur dioxide stream is then stopped. The carbonyl compound **1** (0.5 mol) and the thiol **2** (1.2 mol) or the mercaptoalkanol **3** (0.6 mol) or the dithiol **4** or **5** (0.6 mol) are added, the mixture is refluxed, and worked up as in Method A.

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[1] For Part I see: Z. Kortylewicz, B. Burczyk, *Polish J. Chem.*, in press.

[2] Part IX of the Series: Acetals and Ethers. Part VIII: see Ref. 1.

[3] A. Schöberl, A. Wagner, in: Houben-Weyl, Methoden der Organischen Chemie, 4th Edn., E. Müller, Ed., Vol. IX, Georg Thieme Verlag, Stuttgart, 1955, p. 195-205.

[4] R. M. Roberts, C.-C. Chang, *J. Org. Chem.* **23**, 983 (1958).

[5] K. Pihlaja, *Suom. Kemistilehti* [B] **43**, 143 (1970); *C. A.* **73**, 3824 (1970).

[6] M. Anteunis, C. Becu, *Synthesis* **1974**, 23.

[7] B. Burczyk, *Polish Patent* 73725 (1975).
B. Burczyk, S. Witek, A. Bielawska, J. Bielawski, *Polish Patent* 74473 (1977).
B. Burczyk, *J. prakt. Chem.* **322**, 173 (1980).

[8] J. A. Smythe, A. Foster, *J. Chem. Soc.* **97**, 1195 (1910).

[9] D. Seebach, *Synthesis* **1969**, 17.

[10] E. J. Corey, D. Seebach, *Angew. Chem.* **77**, 1134 (1965); *Angew. Chem. Int. Ed. Engl.* **4**, 1075 (1965).

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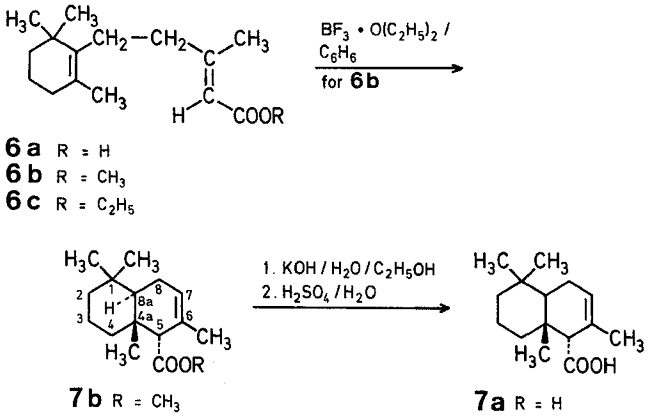
C. Schmidt, N. H. Chishti, T. Breining, *Synthesis* **1982** (5), 391-393:
The formula scheme for the reaction **6**→**7** (p. 391) should be:



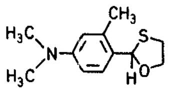
B. A. Arbuzov, N. N. Zobova, *Synthesis* **1982** (6), 433-450:
The correct name for compound **15** (p. 436) is *N*'-benzoyl-*N*,*N*-dimethyl-2-phenyl-2-butenamidine and for compound **30b** (p. 439) is 4-trifluoroacetylimino-2-trifluoromethyl-4*H*, 9a*H*-pyrido[2,1-*b*]-1,3,5-oxadiazine.

Chen-Chu Chan, Xian Huang, *Synthesis* **1982** (6), 452-454:
The last sentence on page 452 should read: However, under the normal conditions [20% aqueous sodium hydroxide in the presence of benzyltriethylammonium chloride (TEBA)] the ring underwent cleavage and the main product was dimethylmalonic acid in the case of methylation.

P. Molina, A. Arques, A. Ferao, *Synthesis* **1982** (8), 645-647:
Compounds **3**,**4**, and **6** are substituted pyrido[2,1-*b*][1,3,4]thiadiazinium salts.

Abstract 6431, *Synthesis* **1982** (9), 801
The correct name for the title compounds **3** is 2-oxoalkanehydroximic chlorides.

B. Burczyk, Z. Kortylewicz, *Synthesis* **1982** (10), 831-832:
In Table 1 (p. 832) the b.p. of product **6a** should be 113-114°C/0.3 torr; the structure and molecular formula of product **7d** should be



and $C_{12}H_{17}NOS$ (223.2); the b.p. and $n_D^{20}$ of product **8a** should be 114-116°C/60 torr and 1.5346, respectively. In Table 2 (p. 832) the second term in the $^1$H-N.M.R. spectrum of product **7b** should be 1.90 (s, 3H, $CH_3$).

K. D. Deodhar, A. D. D'Sa, S. R. Pednekar, D. S. Kanekar, *Synthesis* **1982** (10), 853-854:
The correct name for compounds **4a**,**b** (p. 854) is (*E*)- and (*Z*)-6-benzylidene-3-oxo-2,3,4,6-tetrahydro[1,2,4]triazino[3,4-*a*]isoindoles.

L. Lepage, Y. Lepage, *Synthesis* **1982** (10), 882-884:
The correct name for compound **10** (p. 884) is 2-acetyl-1,4-diphenyl-1,2,3,4-tetrahydro-1,4-epithiopentacene-7,12-quinone.

R. R. Schmidt, A. Wagner, *Synthesis* **1982** (11), 958-962:
It should be noted that the numbers in the products **5**-**16c** in Table 1 refer only to the $^1$H-N.M.R. data in Table 2 and are not identical with the numbering used for the systematic nomenclature of the products.

T. Takajo, S. Kambe, W. Ando, *Synthesis* **1982** (12), 1080-1081:
The compounds **7** should be named 2,4,6,12-tetraaryl-2,5,6,7-tetrahydro-4*H*-3,6a-methanoindeno[1,2-*f*][1,3,5]triazocines.