Acknowledgment. We acknowledge generous support from the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Registry No. 5, 69631-77-2; 7, 19214-00-7; 8, 86729-16-0; 9, 22607-75-6; 10, 79499-77-7; 11, 86729-17-1; 12, 32456-48-7; 13, 32456-49-8; 14, 86729-18-2; 15, 56781-86-3; 16, 56781-85-2; HCl, 7647-01-0; HBr, 10035-10-6; HI, 10034-85-2.

Facile Syntheses of Aldehydes and β-Dialdehyde Monoacetals

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During recent research on the synthesis of β-lactam antibiotics, our synthetic strategy required the preparation of 2,2-dimethyl-1,3-propanedial (1 Chart I) with one of the aldehydes suitably masked. Either the β-dialdehyde monoacetal **2a**, β-dialdehyde monothioacetal **2b**, or the other masked aldehyde **2c** where Y could be readily converted to the aldehyde function would serve the synthetic purpose.

The unsubstituted β-dialdehyde monothioacetal **3** has been prepared by the displacement of bromoacetaldehyde diethyl acetal by 2-lithio-1,3-dithiane followed by acid hydrolysis.[1] We anticipated that this would not be preparatively useful to synthesize **2b** since it involved an S_N2 substitution reaction of a tertiary bromide. Trimethylsilyl enol ethers, in the presence of $TiCl_4$ and orthoformate, are known to generate β-keto acetals.[2] However, no example has been given for the preparation of a β-dialdehyde monoacetal. Reaction of the trimethylsilyl enol ether **4** with trimethyl orthoformate in the presence of $TiCl_4$ gave the desired β-dialdehyde derivative **2d** in less than 5% yield.[3]

Methyl Phenyl Sulfides as Masked Aldehydes. Methyl phenyl sulfides have been used as aldehyde synthons.[4] However, the experimental procedure for the generation of the aldehyde requires strong base or mercury-mediated cleavage over a lengthy period. This procedure precludes their use as aldehyde equivalents in sensitive molecules such as β-lactams. This problem obviously limits the usefulness of utilizing methyl phenyl sulfides as an aldehyde synthon.

In searching for a practical synthesis of the β-dialdehyde derivative, we discovered a mild and convenient procedure for converting methyl phenyl sulfide to the aldehyde group. In this paper we report this procedure that may extend the synthetic utility of this group in the preparation of aldehydes of sensitive molecules and other β-dialdehyde derivatives.

The rationale which led to this procedure was based on the hypothesis that sulfuryl chloride readily α chlorinates methyl phenyl sulfide to yield the chloromethyl phenyl sulfide derivative **6**, which upon treatment with water in the presence of silica gel would give hydroxy intermediate

Chart I[a]

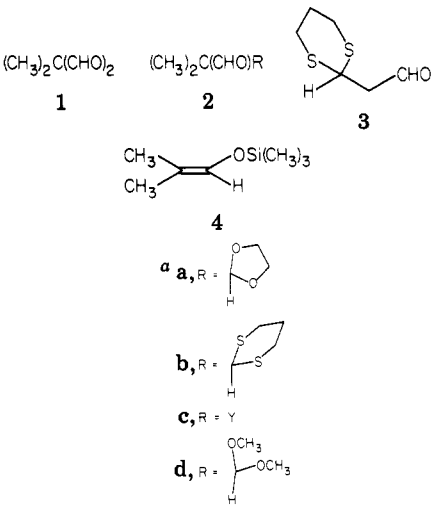
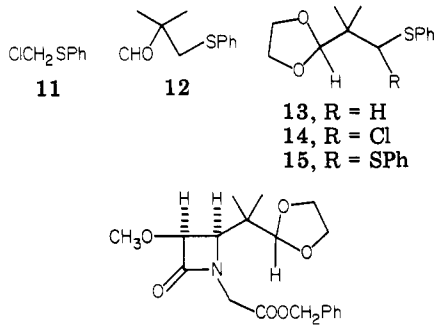
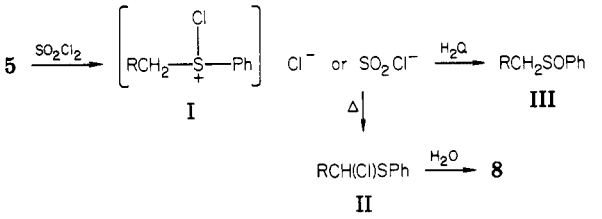


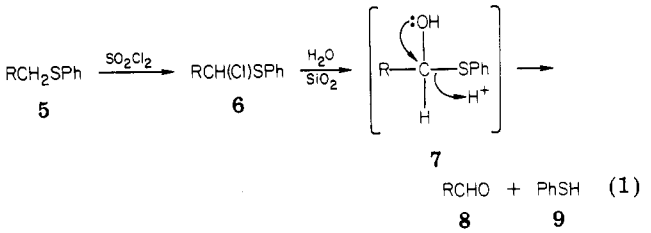
Chart II



Scheme I



7, which would fragment to yield the aldehyde **8** and thiophenyl **9** (eq 1).

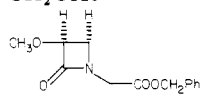


Oxidation of sulfides to sulfoxides by the use of sulfuryl chloride in the presence of wet silica gel had recently been reported by Hojo et al.[5] Our experimental technique, however, has yielded predominantly the aldehyde. Hojo's procedure involved water, SiO_2, sulfuryl chloride, and sulfide in the same reaction medium while our procedure allowed sulfuryl chloride to react with the sulfides to form the α-chloro sulfides first before addition to the water-deactivated silica gel columns. The difference of reaction courses may be explained by the mechanistic consideration

(1) Trost, Barry M.; Kunz, Robert A. *J. Am. Chem. Soc.* **1975**, *97*, 7152.
(2) Mukaiyama, Teruaki; Hayashi, Masatoshi. *Chem. Lett.* **1974**, 15.
(3) The presence of **2d** was detected NMR upon enriching the product by repeated purification on silica gel column.
(4) Paquette, Leo A.; Klobucar, W. D.; Snow, Robert A. *Synth. Commun.* **1976**, *6*, 575.
(5) Hojo, Masaru; Masuda, Ryoichi. *Tetrahedron Lett.* **1976**, 613.

0022-3263/83/1948-3571$01.50/0

Table I. Generation of Aldehydes B from Methyl Phenyl Sulfides A by Method of Eq 1

	A		B		C	
entry	R	compd	isolated yield, %	compd	isolated yield, %	compd
1		13	67	2a	13	15
2		17	72	16	11	26
3	CH_2OAc	18	66	19	8	
4		20	70	21	11	25
5[8]	A = $PhCH_2SPh$	23	58[a]	24	9[b]	

[a] B = Ph-CHO. [b] C = $PhCH(SPh)_2$.

as outlined in Scheme I. Since sulfur–chlorine complexs such as I can be kept at −78 to −40 °C for 24 h or even a short period at 0 °C and since it yielded sufoxide after hydrolysis,[6] a proper time and temperature prior to contact with water are required for the complex to rearrange to II which is subsequently hydrolyzed to 8.

β-Dialdehyde Monoacetal. Phenylthioalkylation[7] of trimethylsilyl enol ether **4** with chloromethyl phenyl sulfide (**11**) in the presence of zinc bromide in dichloromethane yielded 3-(phenylthio)-2,2-dimethylpropanal (**12**) (Chart II). Ketalization of **12** with ethylene glycol in the presence of a catalytic amount of *p*-toluenesulfonic acid in benzene yielded the 1,3-dioxolane **13**. Chlorination of **13** with 1 molar equiv of sulfuryl chloride at 0 °C in dichloromethane for 3 min followed by solvent removal at room temperature yielded the chloro compound **14**. Its structure was confirmed by NMR analysis which showed the disappearance of a singlet at δ 3.02 (corresponding to the two methylene protons in the parent compound) and the presence of a singlet at δ 5.40 (corresponding to the C*H*Cl–SPh proton). Hydrolysis of **14** on a water-deactivated silica gel (dry packed) column yielded the monoacetal **2a** (67% yield) together with the thioacetal **15** (13% yield) as a byproduct.

The generality of this preparative procedure for aldehydes and β-dialdehyde monoacetals is apparent from the results compiled in Table I. We emphasize that the reaction conditions employed were sufficiently mild for acid- and base-sensitive molecules. Selective generation of the aldehyde is possible in the presence of acetate and acetal groups (entries 1–3). Sensitive molecules such as β-lactams (entry 4) are stable under these conditions. In contrast, compound **22** does not afford the desired aldehydes **21** due to cleavage of β-lactam ring during acid hydrolysis of the acetal.

In summary, a facile synthesis of aldehyde and β-dialdehyde monoacetal has been achieved by converting methyl phenyl sulfide group into an aldehyde function via a direct hydrolysis of α-chloro sulfide on a wet column of silica gel. Sensitive molecules such as β-lactams are stable under such hydrolysis conditions. With this mild and convenient procedure, the use of methyl phenyl sulfide as an aldehyde equivalent should prove to be of value in a wide variety of synthetic processes, since not only does the moiety serve as a potential aldehyde group but also it is stable under various acidic, basic, and reductive reaction conditions.

Experimental Section

The IR spectra were recorded on a Perkin-Elmer Model 710A infrared spectrophotometer. The NMR spectra were recorded on a Varian Associates A-60 spectrometer in deuterated solvents; resonance positions are given on the δ scale (parts per million) relative to internal tetramethylsilane. The NMR peaks were designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiple; b, broad. The high-resolution mass spectra were determined on an Associated Electrical Industries MS-902 double-focusing mass spectrometer and were processed on an IBM 1800 computer. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

Generation of Aldehydes from Methyl Phenyl Sulfides. The conditions used for the generation of aldehydes from methyl phenyl sulfides were identical with those illustrated in the preparation of **16**. Yields of all the products are compiled in Table I. Satisfactory spectral data have been obtained for all new compounds. The syntheses and physical data of various β-lactam derivatives will be reported in a subsequent paper. Proton magnetic resonance data (δ values) taken in $CDCl_3$ and high-resolution mass spectra data include the follwing. **12**: 1.20 (s, 6, $2CH_3$), 3.12 (s, 2, CH_2–S), 7.31 (m, 5, C_6H_5), 9.51 (s, 1, CHO). **13**: 1.04 (s, 6, $2CH_3$), 3.02 (s, 2, CH_2–S), 3.85 (m, 4, OCH_2CH_2O), 4.70 (s, 1, CH), 7.25 (m, 5, C_6H_5). **14**: 1.20 (s, 3, CH_3), 1.23 (s, 3, CH_3), 3.88 (s, 4, OCH_2CH_2O), 5.13 (s, 1, CHO_2), 5.41 (s, 1, CHCl), 7.40 (m, 5, C_6H_5). **16**: 0.70 (s, 3, CH_3), 1.10 (s, 6, $2CH_3$), 1.15 (s, 3, CH_3), 3.47 (d, J = 11, 2 Hz, CH_2), 3.71 (d, J = 11, 2 Hz, CH_2), 4.44 (s, 1, CHO_2), 9.73 (s, 1, CHO). **19**: 1.04 (s, 6, 2 CH_3), 2.01 (s, 3, $OCOCH_3$), 4.14 (s, 2, CH_2), 9.61 (s, 1, CHO). **4**: 0.05 (s, 9, $3SiCH_3$), 1.47 (m, 6, $2CH_3$), 5.97 (m 1, H). **20**: Calcd for $C_{23}H_{27}NO_4S$ m/e 413.1661, found 413.1669. **25**: calcd for $C_{29}H_{31}NO_4S_2$ m/e 521.1694, found 521.1675.

Preparation of the Aldehyde 16. Sulfuryl chloride (8.9 mL, 110 mmol) was added to a solution of the acetal **17** (30.5 g, 109 mmol) in dry dichloromethane (300 mL) at 0 °C. After the mixture was stirred for 3 min, the solvent was evaporated at 10 mm at room temperature. The residue was purified through a 2% water-deactivated silica gel (900 g) dry packed column. After elution with dichloromethane, 15 g (72%) of the β-dialdehyde monoacetal **16** together with 4.6 g (11%) of the thioacetal **26** were isolated.

(6) Traynelis, Vincent J.; Yoshikawa, Yoichiro; Tarka, Stanley M.; Livingston, Joel R., Jr. *J. Org. Chem.* **1973**, *38*, 3976.
(7) Paterson, Ian; Fleming, Ian. *Tetrahedron Lett.* **1979**, 2179.
(8) This experiment was performed by D. Lester. The low yield of the product was due to difficulty in purification with a substantial amount lost as mixture.

Preparation of Trimethylsilyl Enol Ether 4. Triethylamine (377 mL, 2.7 mol) was added to a solution of isobutyraldehyde (180 mL, 2 mol) and chlorotrimethylsilane (372 mL, 2.6 mol) in dimethylformamide (650 mL). The mixture was refluxed at 95 °C for 20 h. After filtration, the solid was washed with pentane. The combined organic solution (2.5 L) was washed with saturated sodium bicarbonate solution (4 × 2 L). The organic layer was dried and fractionally distilled to give 178 g (61.5%) trimethylsilyl enol ether **4**; bp 108–120 °C.

Preparation of 3-(Phenylthio)-2,2-dimethylpropanal (12). To a solution of trimethylsilyl enol ether **4** (30 g, 20.8 mmol) and chloromethyl phenyl sulfide (**11**; 30 g, 18.9 mmol) in dry dichloromethane (200 mL) was added anhydrous zinc bromide (500 mg). After being stirred for 30 min, the solution was poured into an ice cold sodium chloride solution (500 mL) and extracted once more with dichloromethane (200 mL). The organic layer was dried over magnesium sulfate. Evaporation to dryness and distillation gave **12**: 33 g (82%); bp 115 °C (1.7 mm).

Registry No. **2a**, 67213-30-3; **4**, 6651-34-9; **11**, 7205-91-6; **12**, 20967-51-5; **13**, 86767-55-7; **14**, 80689-69-6; **15**, 86767-56-8; **16**, 86767-57-9; **17**, 86767-58-0; **18**, 86767-59-1; **19**, 16184-79-5; **20**, 86767-60-4; **21**, 86767-61-5; **23**, 831-91-4; **24**, 100-52-7; **25**, 86767-62-6; **26**, 86767-63-7; isobutyraldehyde, 78-84-2.

Practical Procedure for the Isolation of Emodin and Chrysophanol

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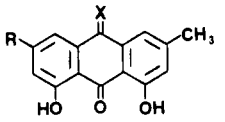
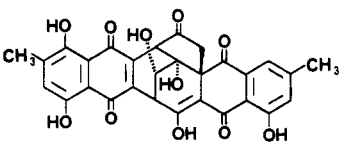
Received January 20, 1983

The presence of the functionalized tricyclic skeleton of emodin (**1**)[2a] and its derived anthrone (**2**)[3] in a diverse array of complex natural products (e.g., **4–6**, Chart I) suggests that **1** might serve as a useful synthetic starting material if adequate supplies could be procured. Emodin is available commerically, but the price it commands (>$50/g) would daunt all but the most intrepid investigator. Emodin occurs widely in nature,[2a] and various procedures have been reported for its isolation, but all require prior collection of plant materials.[7] We now describe a simple procedure for the isolation of emodin from readily available[8] Indian rhubarb root extract. The process also provides abundant quantities of chrysophanol (**3**).[2b]

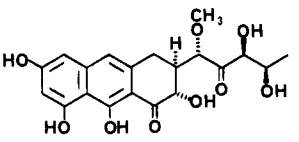
Chart I



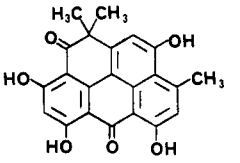
1, R=OH, X=O
2, R=OH, X=H_2
3, R=H, X=O



4, Purpurogenone[4]



5, Olivin[5]



6, Resistomycin[6]

Experimental Section

To a 5-L round-bottomed flask containing 1.5 L each of concentrated HCl and water and equipped with a mechanical stirrer and condenser is added 1 kg of "1-2 Indian Rhubarb Root Solid Extract".[8,9] The stirred mixture is refluxed overnight, cooled, and vacuum filtered. The solid is washed with water and air-dried to constant weight, giving ca. 350 g of fine black powder. The black powder is continuously extracted with ether until <1 g of additional crude extract is obtained in a 24-h period (usually 3–4 days). The crude extract is stripped of volatiles at aspirator pressure (rotary evaporator) to give 40–45 g of gummy solid which is boiled for 0.5 h with 250 mL of ether and vacuum filtered to give 27–28 g of yellow solid A. An additional 1 g of A is obtained by partially concentrating the filtrate.

Solid A is boiled for 10 min with 200 mL of 20% aqueous Na_2CO_3 and the mixture filtered under vacuum while hot to give 19–20 g (after air drying) of solid chrysophanol contaminated with a small amount of emodin and tar (see below). The red Na_2CO_3 filtrate is extracted with ether (2 × 100 mL; the extract is discarded) and acidified (**Caution**: foaming) with concentrated HCl. The emodin which precipitates is filtered, washed with water, and dried to give ca. 6.2 g of nearly pure emodin. This emodin is boiled 0.5 h with 70 mL of ether, and the ether phase is removed by vacuum filtration. The solid is then stirred 0.5 h with 60 mL of benzene and the benzene phase removed by vacuum filtration to give 6.0 g of pure emodin, mp 256–257 °C (lit.[2a] mp 255 °C). If desired, recrystallization from 4:1 $CHCl_3$/MeOH (25 mL/g) at 10 °C overnight gives orange needles, mp 256–257 °C (98% recovery), identical with authentic material by direct comparison.

The impure chrysophanol obtained above can be purified as follows. Crude chrysophanol (20 g, vide supra) is washed well with 200 mL of distilled water followed by 50 mL of absolute ethanol, and without being dried it is dissolved in ca. 450 mL of hot benzene and gravity filtered while hot. The filtrate is brought to boiling, 350 mL of boiling absolute ethanol is added, and the resulting solution is allowed to stand overnight at room temperature. Filtration gives 16 g of pure chrysophanol as yellow microcrystalline leaflets, mp 194–195 °C (lit.[2b] mp 196 °C), identical with authentic material by direct comparison. Concentration (at atmospheric pressure) of the mother liquors to ca. 125 mL gives an additional 2.2 g of chrysophanol, mp 180–182

(1) Undergraduate Research Participant.

(2) For a leading reference see: Thomson, R. H. "Naturally Occurring Quinones", 2nd ed.; Academic Press: New York, 1971: (a) p 419, (b) p 388.

(3) Jacobson, R.; Adams, R. *J. Am. Chem. Soc.* **1924**, *46*, 1312.

(4) Roberts, J. C.; Thompson, D. J. *J. Chem. Soc. C* **1971**, 3488.

(5) Bakhaeva, G. P.; Berlin, Yu. A.; Chuprunova, O. A.; Koslov, M. N.; Peck, G. Yu.; Piotrovich, L. A.; Shemyakin, M. M.; Vasina, I. V. *Chem. Commun.* **1967**, 10.

(6) Brockmann, H.; Meyer, E.; Schrempp, K.; Reiners, F.; Reschke, T. *Chem. Ber.* **1968**, *102*, 1224. Rosenbrook, W. *J. Org. Chem.* **1967**, *32*, 2924. Bailey, N. A.; Falshaw, C. P.; Ollis, W. D.; Watanabe, M.; Dhar, M. M.; Khan, A. W.; Vara, C. V. *Chem. Commun.* **1968**, 374. Keay, B. A.; Rodrigo, R. J. *J. Am. Chem. Soc.* **1982**, *104*, 4725.

(7) An unpublished procedure for the isolation of emodin provided by Professor B. Franck (Universität Münster) utilizes chrysarobin (a commerically available complex of anthraquinones) as raw material, but that procedure is more tedious and much more expensive than the one we report herein. Numerous syntheses of emodin have been described,[2a] but with one possible exception (Krohn, K. *Tetrahedron Lett.* **1980**, *21*, 3557) none appears competitive with isolation.

(8) Obtained from Chart Corp., Inc., Glen Rock, NJ. Other sources of rhubarb extract are available. See: "Chem Sources-U.S.A." and "Chem Sources-Europe"; Directories Publishing Co.: Ormond Beach, FL.

(9) The term "Solid Extract" is a misnomer as the material is a syrupy semisolid. The accurately described "Powdered Extract" can also be used, but it is more expensive, and the yield of emodin is not increased.

(10) An extractor similar to that described by Beal [Beal, G. D. In "Organic Syntheses", 2nd ed.; Wiley: New York, 1941; Collect. Vol. I, p 538] was employed.

(11) Coffey, S.; van Alphen, J. In "Chemistry of Carbon Compounds"; Rodd, E. H., Ed.; Elsevier: Amsterdam, 1956; Vol. IIIB, p 1413.

0022-3263/83/1948-3573$01.50/0