



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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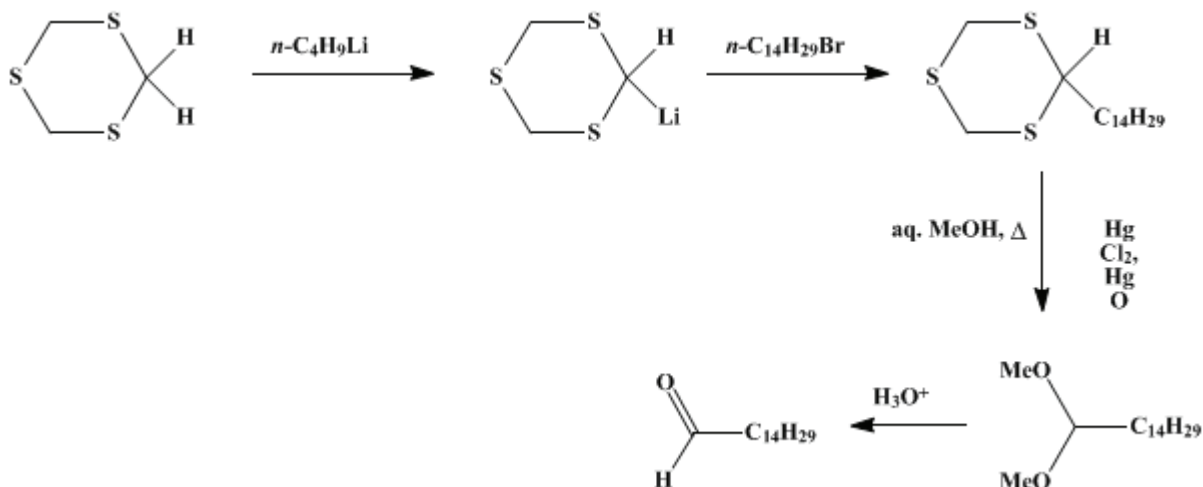
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.869 (1988); Vol. 51, p.39 (1971).

ALDEHYDES FROM *sym*-TRITHIANE: *n*-PENTADECANAL

[Pentadecanal]



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1. Procedure

A. *2-Tetradecyl-sym-trithiane*. A 1-l., round-bottomed, side-armed flask containing a magnetic stirring bar is charged with 25.0 g. (0.180 mole) of finely ground, pure, *sym*-trithiane (Note 1). The flask is equipped with a three-way stopcock and a rubber septum on the side arm. The air in the flask is replaced with dry nitrogen (Note 2). Tetrahydrofuran (Note 3) (350 ml.) is added by syringe, and the resulting slurry is stirred vigorously in a cooling bath at -30° (Note 4). After the addition of 0.190 mole of *n*-butyllithium (1.5–2.5 molar in *n*-hexane) (Note 5), the mixture is stirred for 1.5–2.5 hours, keeping the bath temperature between -25° and -15° . After this period of time the trithiane is dissolved (Note 6), and dry ice is added (no excess!) to the bath until the temperature is about -70° . To this cooled solution is rapidly added 50.0 g. (49.5 ml., 0.180 mole) of 1-bromotetradecane (myristyl bromide) (Note 7) by syringe, and the resulting mixture is stirred overnight, during which time the bath temperature rises to 0 – 25° and a heavy, colorless precipitate separates. Stirring is continued for 1 hour at room temperature before the mixture is poured into a 2-l. separatory funnel containing 800 ml. of water and 500 ml. of carbon tetrachloride. After shaking, the layers are separated and the aqueous layer is shaken with two additional 500-ml. portions of carbon tetrachloride. Some undissolved trithiane is filtered from the combined organic layers, which are washed with water and dried over anhydrous potassium carbonate. The solvent is removed by evaporation, yielding 54–59 g. of crude, solid 2-tetradecyl-*sym*-trithiane, after drying under reduced pressure (Note 8).

B. *Pentadecanal dimethyl acetal*. The crude material obtained from Part A is placed in a 2-l., three-necked flask fitted with an overhead stirrer, a reflux condenser with drying tube, and a stopper. Methanol (1 l., reagent grade) is added, the stirrer is started, and 40 g. (0.18 mole) of mercury(II) oxide and 100 g. (0.368 mole) of mercury(II) chloride are introduced. The mixture is heated under reflux for 4.5 hours and filtered through a Büchner funnel after cooling. The residue is washed with 300 ml. of pentane (Note 9), and the combined organic solutions are poured into 1 l. of water. The layers are separated, and the lower aqueous layer is shaken with two 500-ml. portions of pentane. The combined organic layers are quickly washed with 10% ammonium acetate solution (Note 10) and water and dried over sodium sulfate. The pentane is evaporated under reduced pressure, giving 30.0–32.5 g. of the crude acetal as a mobile, slightly yellow oil.

C. *n*-Pentadecanal. The crude acetal from Part B is dissolved in 600 ml. of tetrahydrofuran, and 150

ml. of water containing 2 g. of *p*-toluenesulfonic acid monohydrate is added. The resulting pale mixture is heated at reflux for 1 hour and cooled. The hydrolysate is poured into 600 ml. of water and extracted with three 300-ml. portions of pentane (Note 9). The colorless pentane extracts are combined, washed three times with saturated sodium hydrogen carbonate solution and once with water, and dried over sodium sulfate. Evaporation of the solvent furnishes an oil which upon distillation under reduced pressure (Note 11) yields 18.7–22.5 g. of *n*-pentadecanal, b.p. 103–106° (0.2 mm.). The overall yield from 1-bromotetradecane is 47–55%. The product solidifies eventually and should be kept under an inert atmosphere in the refrigerator.

2. Notes

1. It is essential that the *sym*-trithiane be of good purity. Commercial *sym*-trithiane can be purified by extraction from a thimble in a hot extractor using 300 ml. of toluene for 30 g. of trithiane. After cooling the extract to 0°, *sym*-trithiane is recovered by filtration and recrystallized from toluene. In one run the checkers used *sym*-trithiane as obtained from Eastman Organic Chemicals and observed a 10% decrease in yield of *n*-pentadecanal.
2. This is done by evaporating and filling with dry nitrogen three times; during the reaction a pressure of about 50 mm. is maintained against the atmosphere using a mercury bubbler.
3. Tetrahydrofuran is distilled from a blue solution of benzophenone ketyl, obtained by refluxing tetrahydrofuran in the presence of sodium wire, some potassium, and benzophenone. See *Org. Synth., Coll. Vol. 5*, 976 (1973) for a warning note regarding the purification of tetrahydrofuran.
4. A 2-l. Dewar cylinder was used.
5. The checkers used 120 ml. of 1.6 *M* *n*-butyllithium in hexane, obtained from Foote Mineral Company.
6. If the trithiane, apart from a few crystals, does not dissolve entirely, the workup procedure is complicated. The crude tetradecyltrithiane must then be purified (by dissolving in 500 ml. of carbon tetrachloride at 30°, filtering, and precipitating with 1.5 l. of methanol) before conversion to the acetal.
7. A commercial product (Aldrich Chemical Company, Inc., or Matheson, Coleman and Bell) proved satisfactory without further purification. The purity should be checked by refractive index and/or GC.
8. The crude tetradecyltrithiane contains 4–6% of *sym*-trithiane, m.p. 69–71°; recrystallization (Note 6) gives pure product, m.p. 76.3–76.6°.
9. Low-boiling ligroin can be used as well.
10. A white precipitate is formed during the first and second washing.
11. A short-path distillation apparatus with a cold finger, but no condenser, should be used since the product may crystallize. The distillation is carried out under nitrogen or argon (balloon at capillary).

3. Discussion

The procedure described here provides a convenient route to aldehydes, with trithiane serving as an inexpensive, “masked” carbonyl group.^{2,3,4} The reaction is limited, however, to the use of primary alkyl halides, aldehydes, and ketones for elaboration of the carbon chain through attack on the metallated trithiane. Examples of aldehydes synthesized by this method are given in Table I.

TABLE I
ALDEHYDES FROM 2-LITHIO-1,3,5-TRITHIANE AND ALKYL HALIDES

Halide	2-Alkyl-1,3,5-Trithiane % ^{a,b,c}	Aldehyde Dimethyl		Aldehyde Product	Yield, % ^{a,e,f}
		Acetal Yield, % ^{a,b}	Yield, %		
1-Bromopentane	96		66 ^d	Hexanal	43
(S)-(+)-1-Iodo-2-methylbutane	98		67 ^{d,g}	(S)-(-)-3-Methylpentanal	41
1-Bromoheptane	100		60 ^d	Octanal	45
1-Bromodecane	100		99 ^c	Undecanal	65

1-Bromohexadecane	100	60 ^c	Heptadecanal	32
Benzyl Bromide	100	32 ^d	Phenylacetaldehyde	20

^a Based on halide.

^b Reaction conducted on 100 mmoles scale.

^c Crude product.

^d Distilled product.

^e Reaction conducted on 5–10 mmoles scale.

^f Yield of distilled or recrystallized product.

^g (+)-Iodide with optical purity of 89% gave acetal with $\alpha_D + 7.6^\circ$ (neat, $l = 100$ mm.).

The *S*-acetal is converted to the *O*-acetal in anhydrous methanol because hydrolysis of monosubstituted trithianes in aqueous methanol furnishes a mixture of the free aldehyde and its *O*-acetal derivative. It is advantageous to store aldehydes as the *O*-acetal derivatives since free aldehydes are susceptible to polymerization and oxidation.

This method has several common features with the dithiane method⁵ that is useful for the synthesis of aldehydes and ketones.⁴ This latter method is illustrated by the synthesis of cyclobutanone [*Org. Synth.*, **Coll. Vol. 6**, 316 (1988)].

n-Pentadecanal has also been prepared by pyrolysis of α -hydroxy-⁶ and α -methoxypalmitic acid,⁷ from α -bromopalmitic acid chloride and sodium azide,⁸ and from α -hydroxypalmitic acid and lead tetraacetate.⁹

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 6*, 542
- *Org. Syn. Coll. Vol. 7*, 290
- *Org. Syn. Coll. Vol. 7*, 447
- *Org. Syn. Coll. Vol. 8*, 444

References and Notes

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 6. See literature cited in *Beilstein*, **1**, p. 716, 2nd Suppl., **1**, p. 770.
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 8. M. S. Newman, *J. Am. Chem. Soc.*, **57**, 732 (1935).
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Appendix

Chemical Abstracts Nomenclature (Collective Index Number);

(Registry Number)

ligroin

benzophenone ketyl

(S)-(-)-3-Methylpentanal

potassium carbonate (584-08-7)

methanol (67-56-1)

ammonium acetate (631-61-8)

sodium hydrogen carbonate (144-55-8)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

nitrogen (7727-37-9)

mercury(II) oxide (21908-53-2)

toluene (108-88-3)

Benzophenone (119-61-9)

mercury(II) chloride (7487-94-7)

potassium (7440-09-7)

Pentane (109-66-0)

sodium azide (26628-22-8)

1-bromoheptane (629-04-9)

benzyl bromide (100-39-0)

phenylacetaldehyde (122-78-1)

butyllithium,
n-butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

hexane,
n-hexane (110-54-3)

1-bromohexadecane (112-82-3)

argon (7440-37-1)

Cyclobutanone (1191-95-3)

OCTANAL (124-13-0)

1-bromopentane (110-53-2)

1-Bromodecane (112-29-8)

Pentadecanal,
n-PENTADECANAL (2765-11-9)

trithiane (3325-33-5)

1-bromotetradecane,
myristyl bromide (112-71-0)

Hexanal (66-25-1)

(S)-(+)-1-Iodo-2-methylbutane (29394-58-9)

Undecanal (112-44-7)

Heptadecanal

tetradecyltrithiane

α -methoxypalmitic acid

α -bromopalmitic acid chloride

α -hydroxypalmitic acid (764-67-0)

p-toluenesulfonic acid monohydrate (6192-52-5)

sym-Trithiane (291-21-4)

2-Tetradecyl-sym-trithiane (24644-07-3)

Pentadecanal dimethyl acetal (52517-73-4)