



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

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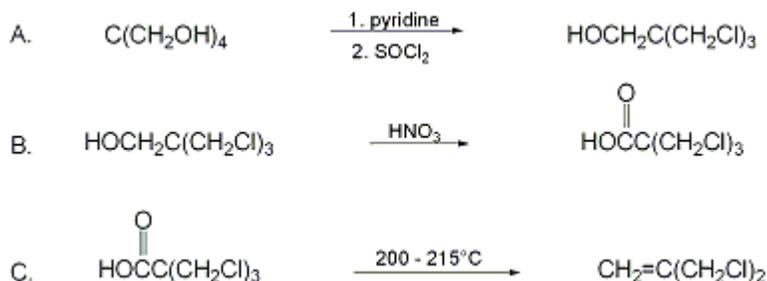
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*September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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### 3-CHLORO-2-(CHLOROMETHYL)-1-PROPENE

#### [ 1-Propene, 3-chloro-2-(chloromethyl)- ]



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#### 1. Procedure

*A. Pentaerythrityl trichlorohydrin: 3-Chloro-2,2-bis(chloromethyl)propan-1-ol*. A dry, 5-L, four-necked, round-bottomed flask equipped with an efficient mechanical stirrer, addition funnel, thermometer adapter, and a condenser is charged with 417 g (3.06 mol) of [pentaerythritol](#) (Note 1) and 730 g (9.24 mol) of [pyridine](#) (Note 2). A Drierite drying tube is attached to the condenser, and the addition funnel is closed with a glass stopper after being charged with 1.134 kg (9.53 mol) of [thionyl chloride](#) (Note 3). The reaction flask is placed inside a bucket to which an ice/water mixture may be added in the event that the reaction becomes too exothermic. [Thionyl chloride](#) is added dropwise with vigorous stirring to the slurry so that the white mist that appears in the flask does not rise up into the condenser. [Thionyl chloride](#) is added as rapidly as possible over 4-5 hr so that the temperature of the yellow-orange reaction mixture is maintained between 65-95°C (Note 4). When the addition is complete, the drying tube is removed, and the ice bucket is replaced with a heating mantle. The resulting orange-yellow reaction mixture is heated to 120-130°C until no more [sulfur dioxide](#) is evolved (Note 5). As the heating continues, the reaction mixture turns from dark orange to brown, and gas evolution becomes evident. After gas evolution ceases, the flask is cooled slightly and 2 L of cold water is added with stirring. The brown-yellow product precipitates, is filtered, and washed with 2-3 L of water. The dried, crude product (461 g) is approximately a 1:2.8 mixture of [pentaerythrityl tetrachloride](#) (131 g) and [pentaerythrityl trichlorohydrin](#) (330 g, 57% yield) (Note 6). This crude material may be used directly in the next step (Note 7).

*B. Tris(chloromethyl)acetic acid: 3-Chloro-2,2-bis(chloromethyl)propanoic acid*. (*Caution: Nitrogen oxides are highly toxic. This procedure should be carried out in a well-ventilated hood!*) The crude mixture (461 g) of [pentaerythrityl tetrachloride](#) and [pentaerythrityl trichlorohydrin](#) obtained from the above reaction is transferred to a 3-L, four-necked, round-bottomed flask that is equipped with an efficient mechanical stirrer, reflux condenser, thermometer adapter, and an addition funnel. The transfer is most easily accomplished by melting the solid over a steam bath and pouring the mixture through a funnel directly into the reaction flask. The flask and its contents are heated to 70-80°C with a heating mantle (Note 8), and a small portion (10-15 mL) of concentrated [nitric acid](#) (Note 9) is added with vigorous stirring to initiate the reaction (Note 10). As the reaction begins, a large amount of dark orange-brown vapors appears. Stirring is continued, and the addition of [nitric acid](#) is resumed after the initial exothermic reaction subsides (usually within 15 min). The remaining [nitric acid](#) (660-680 mL) is added in 20-30-mL aliquots over 30 to 60 min so that nitrogen oxides are continually evolved but the reaction does not become violent. After the addition is complete, the addition funnel is carefully removed and left in the hood to air out and is replaced by a glass stopper. The reaction mixture is heated at 70-80°C until the evolution of nitrogen oxides is no longer evident (Note 11). At this point, the biphasic reaction mixture is a cloudy yellow or white liquid. The warm reaction mixture is poured into a 4-L beaker and 2 L of cold water is added to precipitate the tetrachloride/carboxylic acid product

mixture. The beaker and its contents are allowed to stand for several hours at room temperature to ensure complete precipitation of the product; then the crude product mixture is filtered, washed with water, and the carboxylic acid is extracted as follows. The solid is pulverized, transferred to a 4-L beaker, and 2.5 L of 1 M sodium hydroxide is added with stirring (Note 12). The liquid reaction mixture instantly becomes bright yellow, and the insoluble, white tetrachloride clumps on the sides of the beaker. Stirring is continued for 30-60 min whereupon the insoluble material is filtered and washed well with water. The combined washings and yellow, aqueous filtrate are acidified to pH 1 with concentrated hydrochloric acid (~250 mL). The carboxylic acid precipitates as a white solid that is easily filtered using two pieces of filter paper. The filtered and dried product thus obtained is a fine white powder (230 g, 65% yield). The aqueous filtrate is extracted with methylene chloride; the extracts are dried with magnesium sulfate and concentrated to provide an additional 50-60 g of the desired acid. The crude, combined product (75% yield) can be used directly in the next step (Note 13). Over several runs, the yield varies from 65-80%.

C. *3-Chloro-2-(chloromethyl)-1-propene*. Tris(chloromethyl)acetic acid (205 g, 1.00 mol) is transferred to a 500-mL, two-necked, round-bottomed flask. On top of the powdery acid, which nearly fills the flask, is placed a football magnetic stir bar (1.25 × 0.5 in.). The neck of the flask to be clamped is wrapped well with aluminum foil and is fitted with a glass stopper. A standard taper 24/40 short path still head, to which is attached a Drierite drying tube, is attached at the second neck. The upper flask and short path column are wrapped with aluminum foil, and the flask is immersed in a high temperature oil bath (Note 14) that has been preheated to a stable 210°C. As the solid melts, the reaction mixture becomes yellow, and the oil bath temperature drops (10-20°C). If after 10-15 min, the temperature does not rise to between 205-215°C, it may be necessary to adjust the heating to maintain the oil bath temperature between 205-215°C (Note 15). Moderate stirring is maintained throughout the reaction (Note 16). Within 30 to 60 min, gas evolution becomes apparent, the reaction mixture turns brown, then black, and the product begins to distill. As the reaction proceeds, a black, tarry residue begins to build up on the bottom and sides of the flask. The product begins to distill, slowly at first, then quite steadily, at which point the head temperature rises to 138°C (Note 17). The reaction time varies (Note 17), but heating is continued until just before dryness. The product (115 g, 92% yield) thus obtained is a clear, colorless liquid (bp 136-138°C) that is > 98% pure by GLC and <sup>1</sup>H NMR analysis (Note 18). Over several runs, the yield varies from 88-99%.

## 2. Notes

1. Pentaerythritol (98%) was purchased from Aldrich Chemical Company, Inc., and was used without further purification.
2. Pyridine (> 99%) was purchased from Fisher Scientific Company. Only freshly opened or recently distilled (CaH<sub>2</sub>) pyridine was used.
3. Thionyl chloride (97%, technical) was purchased from Aldrich Chemical Company, Inc. Only freshly opened or recently distilled reagent was used.
4. An addition rate of 2-3 drops per second is adequate to maintain the desired reaction temperature. The submitters have experienced several problems if the reaction temperature is below 60°C. The reaction mixture solidifies, leading to a potentially exothermic situation. In the event that the mixture does become solid, increasing the rate of addition creates enough heat to melt the solid.
5. Gas evolution generally ceases in 8 to 10 hr of heating, but the mixture is allowed to heat overnight.
6. Extraction of the initial filtrate (prior to washing) with toluene provides an additional 94 g of material that is approximately a 1:15 mixture of pentaerythrityl tetrachloride and pentaerythrityl trichlorohydrin. Thus, the yield may be improved by up to 10%. It is important to remove all the toluene prior to oxidation. This may be done by prolonged rotary evaporation or by distillation as described in (Note 7). Some residual pyridine has not been a problem in the oxidation.
7. Pentaerythrityl trichlorohydrin may be separated from pentaerythrityl tetrachloride by fractional distillation under reduced pressure with a heated Vigreux column. The column (6 in. × 1 in.) is preheated to 100°C using a heating tape. Steam is run through the condenser as necessary to prevent the distillate from solidifying. Pentaerythrityl tetrachloride is collected from 95-120°C at 10-12 mm. It may be recrystallized from cyclohexane to yield small white crystals, mp 95-96°C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ: 3.65 (s). Pentaerythrityl trichlorohydrin is collected from 125-130°C at 10-12 mm. It may be recrystallized from cyclohexane to obtain long, fine, white needles, mp 63-65°C; <sup>1</sup>H NMR (500 MHz,

$\text{CDCl}_3$   $\delta$ : 2.0 (br, 1 H), 3.66 (s, 6 H), 3.75 (s, 2 H) . The ratio of [pentaerythrityl tetrachloride](#) to [pentaerythrityl trichlorohydrin](#) was determined by GLC analysis. [Pentaerythrityl tetrachloride](#) has a shorter retention time than the trichlorohydrin.

8. It is important that the starting materials be melted prior to the addition of [nitric acid](#). Heating above  $85^\circ\text{C}$  during the reaction causes the product to sublime on the sides of the flask and in the condenser, potentially clogging it and leading to pressure build-up in the reaction flask. The sublimed acid may be melted back into the reaction mixture with judicious use of a heat gun.

9. Concentrated [nitric acid](#) (specific gravity  $\approx 1.42$ ) was purchased from Fisher Scientific Company and used without further purification.

10. Initiation of the reaction is usually evident within 10 min. More [nitric acid](#) may be added, if necessary, but care should be taken to avoid adding more than 100 mL before the reaction is obviously progressing. The initial reaction may be quite exothermic and large amounts of nitrogen oxides are generated.

11. Heating overnight is usually sufficient, but up to 24 hr may be required. Near the end of the reaction, (i. e., after heating overnight), the condenser and glass stopper may be removed to facilitate escape of the nitrogen oxides.

12. A long magnetic stir bar (2 in.  $\times$  0.25 in.) was found to be useful.

13. The crude product (mp  $107\text{-}109^\circ\text{C}$ ) may be recrystallized from [cyclohexane](#) to yield long white crystals; mp  $111\text{-}112^\circ\text{C}$ , or directly used in the next reaction;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$ : 3.85 (s, 6 H), 10.87 (br 1 H) ;  $^{13}\text{C}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$ : 42.7, 55.3, 175.5 ; IR ( $\text{CDCl}_3$  soln)  $\text{cm}^{-1}$ : 3400-2700 (br), 2990 sharp, 1730, 1445, 1220 . In one run, the checkers isolated the [tris\(chloromethyl\)acetic acid](#) solely by extraction with [dichloromethane](#), rather than by precipitating some and extracting the remainder according to the procedure. In this manner, the amount of water that co-distills with the product in Step C is minimized.

14. Thomas Scientific 6428-R25 Silicone Fluid SF 96/50 was used.

15. Heating to higher temperatures (e.g.,  $>225^\circ\text{C}$ .) leads to a significant decrease in yield as more tar is produced and the carboxylic acid distills. If some acid distills, it may be filtered away from the alkene.

16. Using a Thermolyne Type 7200 magnetic stir plate, a setting of 5-6 was used to control the stirring.

17. The total reaction time has varied greatly over several runs from 2-6 hr. The head temperature during the reaction rises slowly and appears to depend on how steadily the product distills. Occasionally, the head temperature has reached only  $70^\circ\text{C}$ , but the purity of the product was  $>98\%$  by GC and  $^1\text{H}$  NMR analysis. In three attempts, the checkers found the distillation to be long, in no instance less than 5 hr and once 9 hr. Users should heed the precaution in (Note 15).

18. Occasionally, the product has a pale yellow color. The purity as determined by GLC and  $^1\text{H}$  NMR appears to be unaffected. If desired, the product can be further purified by simple distillation which gives a sharp bp at  $137\text{-}138^\circ\text{C}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$ : 4.18 (s, 4 H), 5.30 (s, 2 H) .

### Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

### 3. Discussion

The present procedure represents a modification of two previously published procedures,<sup>2,3</sup> and results in a safer, more convenient preparation of the title compound. In Step A, the ratio of reagents has been adjusted to allow for the formation of only [pentaerythrityl tetrachloride](#) and trichlorohydrin; none of the dichlorinated product is produced. Thus work up of the reaction is easier: the product can be filtered rather than extracted, so minimal solvent is used, and the crude products are used in Step B, thus avoiding a tedious distillation. Step B has also been modified to make it safer and more convenient. The crude material from Step A is used, and addition of [nitric acid](#) over a longer period reduces the hazards of this step. Previously, it was noted that after the [nitric acid](#) was added in one portion and the mixture was heated, "a reaction became apparent, whereupon the flask was lowered rapidly into a waiting cold bath and the operator withdrew".<sup>2</sup> Step C is a more detailed modification of the procedure reported by the Russian workers<sup>3</sup> as an improvement to the original method of Mooradian and Cloke.<sup>2</sup> The latter used [quinoline](#) to catalyze the conversion of [tris\(chloromethyl\)acetic acid](#) to [3-chloro-2-\(chloromethyl\)propene](#). Gafarov, et al.<sup>3</sup> reported that heating neat [tris\(chloromethyl\)acetic acid](#) to a higher temperature

cleanly affords the final product, 3-chloro-2-(chloromethyl)-1-propene. The present procedure allows for the pyrolysis of the crude material obtained in Step B to be used in Step C, thus eliminating the use of large amounts of solvents for recrystallization.

The best alternative preparation of 3-chloro-2-(chloromethyl)-1-propene involves the direct chlorination of 3-chloro-2-methyl-1-propene using elemental chlorine.<sup>4</sup> This method leads to a mixture of products that must be purified by a tedious spinning band distillation, and only yields 34% of the desired product.

3-Chloro-2-(chloromethyl)-1-propene is commercially available but is very expensive (>\$45/g for 10 g, Aldrich Chemical Company, 1996). It is commonly used in the synthesis of natural products,<sup>5</sup> polymers,<sup>6</sup> cryptands and crown ethers,<sup>7</sup> compounds of biological and medical importance,<sup>8</sup> and is the starting material for the Szeimies synthesis of [1.1.1]propellane.<sup>9</sup>

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 10, 658](#)

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## References and Notes

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## Appendix

### Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

3-Chloro-2-(chloromethyl)-1-propene:  
1-Propene, 3-chloro-2-(chloromethyl)- (8,9); (1871-57-4)

Pentaerythrityl trichlorohydrin:  
1-Propanol, 3-chloro-2,2-bis(chloromethyl)- (8,9) (813-99-0)

Pentaerythritol (8);  
1,3-Propanediol, 2,2-bis(hydroxymethyl)- (9); (115-77-5)

Pyridine (8,9); (110-86-1)

Thionyl chloride (8,9); (7719-09-7)

Pentaerythrityl tetrachloride:  
Propane, 1,3-dichloro-2,2-bis(chloromethyl)- (8,9); (3228-99-7)

Tris(chloromethyl)acetic acid:  
Propionic acid, 3-chloro-2,2-bis(chloromethyl)- (9); (17831-70-8)

Nitric acid (8,9); (7697-37-2)