



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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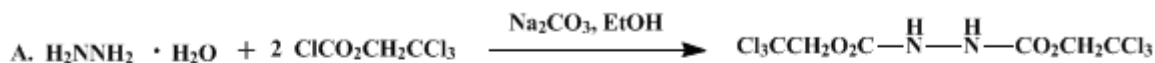
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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BIS(2,2,2-TRICHLOROETHYL) AZODICARBOXYLATE

[Diazenedicarboxylic acid, bis(2,2,2-trichloroethyl) ester]



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Checked by Sandy Banks and Orville L. Chapman.

1. Procedure

A. *Bis (2,2,2-trichloroethyl)hydrazodicarboxylate*. In a 500-mL, three-necked flask equipped with mechanical stirrer, thermometer, and 250-mL and 125-mL dropping funnels (Note 1) is placed a solution of 13.34 g (0.23 mol) of 64% hydrazine hydrate (Note 2) in 60 mL of 95% ethanol. The reaction flask is cooled in an ice bath and 96 g (0.46 mol) of 2,2,2-trichloroethyl chloroformate (Note 3) is added dropwise so that the temperature is kept below 20°C. During the addition of 1 equiv of the chloroformate, a white precipitate is formed. After exactly one-half of the chloroformate has been added, a solution of 25 g (0.24 mol) of sodium carbonate in 100 mL of water is added dropwise along with the remaining chloroformate. The rate of addition of these two reagents is such that the flow of the chloroformate is faster than that of the sodium carbonate so that there is always an excess of chloroformate present; the temperature is kept below 20°C during the addition. As the second equivalent of chloroformate is added the white precipitate dissolves.

After the addition of the reactants is complete, the reaction is allowed to stir for an additional 30 min while the solution warms to room temperature. The reaction mixture is then transferred to a separatory funnel. The viscous organic bottom layer is separated from the aqueous layer and is dissolved in 200 mL of ether. The reaction vessel is washed with 100 mL of ether, and this ether portion is used to extract further the aqueous layer. The ether layers are combined, dried over magnesium sulfate, and filtered, and the solvent is removed under reduced pressure. The viscous oil is allowed to crystallize in an ice bath (0°C). The crystals are collected on a Büchner funnel, washed with 500 mL of water, and dried in a vacuum desiccator at 0.5 mm for 48 hr. 80.8 g (93%) of white crystalline bis(2,2,2-trichloroethyl) hydrazodicarboxylate (mp 85–89°C) is obtained. This material is sufficiently pure for the next preparation. However, further purification can be achieved using an Abderhalden drying apparatus (refluxing 95% EtOH for 12 hr at 0.05 mm; MgSO₄ desiccant). Material purified in this way melted at 96.5–97.5°C (Note 4) and (Note 5).

B. *Bis (2,2,2-trichloroethyl) azodicarboxylate*. *Caution! Large amounts of nitrogen oxides are evolved during the oxidation with fuming nitric acid. Therefore, operations should be conducted in an efficient fume hood.*

In a 500-mL, three-necked flask equipped with mechanical stirrer, thermometer, pressure-equalizing dropping funnel, and gas outlet tube is added 78.55 g (0.21 mol) of bis(2,2,2-trichloroethyl) hydrazodicarboxylate dissolved in 180 mL of chloroform (Note 6). The solution is cooled to 0°C and 53.2 mL (1.26 mol) of fuming nitric acid (Note 7) and (Note 8) is added so that the temperature of the solution does not rise above 5°C. The reaction mixture is then allowed to warm slowly to room temperature over 4 hr (Note 9). After an additional 2 hr at room temperature, the material is transferred to and shaken in a 1-L separatory funnel half-filled with ice chips. The two layers are allowed to separate and the bottom organic layer is removed. The aqueous layer is extracted with 250 mL of chloroform. The organic layers are combined and washed with 300 mL of water, 300 mL of aqueous 5% sodium bicarbonate, and again with 300 mL of water. The organic layer is dried with magnesium sulfate, filtered, and the solvent is removed under reduced pressure. The yellow crystals that form are

collected on a Büchner funnel and washed with more [pentane](#). The [pentane](#) filtrate is concentrated under reduced pressure to afford more crystalline material which is again collected on a Büchner funnel and washed with more [pentane](#). The cycle is repeated until no more crystals appear after removal of [pentane](#). The yellow crystals so obtained are air dried for 1 hr to afford 59.2 g (75.8%) of [bis\(2,2,2-trichloroethyl\) azodicarboxylate](#) which melts at 108–110°C. Further drying using an Abderhalden drying apparatus (refluxing 95% [EtOH](#) for 12 hr at 0.5 mm; MgSO_4 desiccant) affords a compound that melts at 109–110.5°C ([Note 10](#)),([Note 11](#)),([Note 12](#)).

2. Notes

1. The thermometer is fitted into one of the necks of the flask so that when it is immersed in the solution, the range between 10 and 20°C is easily visible. A two-necked adapter is used for the dropping funnels.
2. [Hydrazine hydrate](#), 64%, practical grade, was obtained from MCB, Inc.
3. [2,2,2-Trichloroethyl chloroformate](#) (96%) is commercially available from Aldrich Chemical Company, Inc., and is used without further purification.
4. The average yield obtained for five runs performed by three different people was 83%.
5. The spectral properties of [bis \(2,2,2-trichloroethyl\) hydrazodicarboxylate](#) are as follows: ^1H NMR (CDCl_3) δ : 4.80 (s, 4 H, CH_2CCl_3), 7.0–7.6 (s, br, 2 H, -NH, the position is concentration-dependent).
6. The solution can be warmed gently without harm to facilitate solution of the hydrazo compound.
7. Mallinckrodt fuming [nitric acid](#) (90–95%, *d* 1.5) was used.
8. The reaction seems to be surprisingly dependent on the amount of [nitric acid](#) used. A run with 78.6 g of hydrazo compound and a sixfold excess of [nitric acid](#) was quenched after 22 hr and afforded 100% conversion to the desired azo compound (NMR analysis). Another run with 80.0 g of hydrazo compound and a fivefold excess of [nitric acid](#) gave only 92% conversion after 25 hr. In another run with 2.0 g of hydrazo compound and a sixfold excess of [nitric acid](#) the reaction was complete after 4 hr. In addition, the oxidation was found to be temperature dependent. For example, in a run in which the temperature was maintained between 0 and 5°C for 3 hr and the solution was not allowed to warm to room temperature, only 18% yield was obtained (NMR analysis).
9. The evolution of large amounts of nitrogen oxides was noticed after approximately 1.5 hr (the temperature had reached 13°C).
10. Yields ranged from 76 to 94% (six runs performed by three different people).
11. The NMR spectrum (CDCl_3) for [bis\(2,2,2-trichloroethyl\) azodicarboxylate](#) shows only a singlet at δ 5.05.
12. The title compound is now commercially available from Aldrich Chemical Co., Inc.

3. Discussion

[Bis \(2,2,2-trichloroethyl\) azodicarboxylate](#) has been prepared by oxidation of [bis\(2,2,2-trichloroethyl\) hydrazodicarboxylate](#) with dinitrogen tetroxide.³

[Bis\(2,2,2-trichloroethyl\) azodicarboxylate](#) is a yellow crystalline material that is stable indefinitely in a vacuum desiccator stored in the dark. This compound offers a number of important advantages over diethyl and dimethyl azodicarboxylate for the synthesis of azo compounds. Probably the most important advantage is that in contrast to the ethyl and methyl esters, the trichloroethyl ester grouping can be removed under neutral conditions—a requirement when the product of the transformation is acid- or base-labile.^{4 5 6 7 8 9} Furthermore, in contrast to [dimethyl azodicarboxylate](#) and [diethyl azodicarboxylate](#), which have been known to explode when heated and require distillation for purification, [\(2,2,2-trichloroethyl\) azodicarboxylate](#) is isolated as a crystalline solid requiring no heating whatsoever. Another advantage is that Diels–Alder cycloadducts with [bis\(2,2,2-trichloroethyl\) azodicarboxylate](#) are often crystalline solids that can be purified by recrystallization. This is in marked contrast to the viscous oils that are often obtained when the commercially available [diethyl azodicarboxylate](#) is used. Finally, we have found that Diels–Alder cycloadditions using [bis\(2,2,2-trichloroethyl\) azodicarboxylate](#) often proceed faster and at a temperature lower than that required for the dimethyl and diethyl analogues (e.g., reaction with [6,6-dimethylfulvene](#) and [6-acetoxyfulvene](#)).

This preparation is referenced from:

References and Notes

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 2. The authors wish to thank Ahmed Bukhari for the data that he supplied for this publication.
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

nitrogen oxides

dinitrogen tetroxide

diethyl and dimethyl azodicarboxylate

ethanol,
EtOH (64-17-5)

ether (60-29-7)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

nitric acid (7697-37-2)

sodium carbonate (497-19-8)

hydrazine hydrate (7803-57-8)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

diethyl azodicarboxylate (1972-28-7)

Bis(2,2,2-trichloroethyl) azodicarboxylate,
Diazenedicarboxylic acid, bis(2,2,2-trichloroethyl) ester,
Bis (2,2,2-trichloroethyl) azodicarboxylate (38857-88-4)

2,2,2-trichloroethyl chloroformate (17341-93-4)

Bis(2,2,2-trichloroethyl) hydrazodicarboxylate,
bis (2,2,2-trichloroethyl) hydrazodicarboxylate (38858-02-5)

dimethyl azodicarboxylate (2446-84-6)

(2,2,2-trichloroethyl) azodicarboxylate

6,6-dimethylfulvene

6-acetoxyfulvene

Bis (2,2,2-trichloroethyl)hydrazodicarboxylate