A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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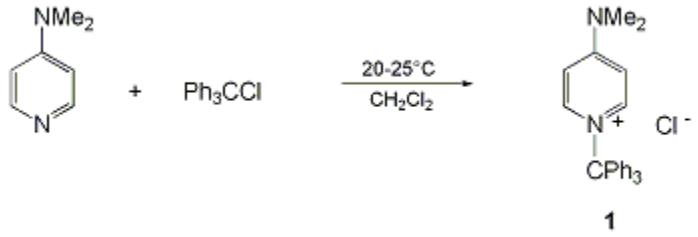
4-DIMETHYLAMINO-N-TRIPHENYLMETHYLPYRIDINIUM CHLORIDE

[Pyridinium, 4-(dimethylamino)-1-(triphenylmethyl)-, chloride]



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1. Procedure

A mixture of 30.6 g (0.1 mol) of pure chlorotriphenylmethane (Note 1) and 12.2 g (0.1 mol) of 4-dimethylaminopyridine (Note 2) is placed in a 2-L, three-necked, round-bottomed flask equipped with a dropping funnel and a Y-tube holding a thermometer and a nitrogen (N_2) inlet adapter. To the mixture is added, with continuous stirring, 200 mL of dry dichloromethane (CH_2Cl_2, (Note 3)) through the dropping funnel. After the addition, stirring is continued for an additional 3 hr at 20-25°C under N_2.

To the clear solution is gradually added 1 L of ethyl acetate (Note 4) over 1 hr with continual stirring. The product slowly crystallizes during the addition of ethyl acetate. At the end of the addition, the product slurry is cooled to 5°C by immersing the reaction flask in an ice bath. The product is filtered and washed twice with 100 mL of cold ethyl acetate . Upon drying under vacuum at 50°C for 24 hr, 38.6 g of the product is recovered as a white solid (96% yield, mp 128-131°C) (Note 5).

2. Notes

1. Chlorotriphenylmethane was purchased from Aldrich Chemical Company, Inc. , and crystallized from toluene/petroleum ether.
2. 4-Dimethylaminopyridine was purchased from Aldrich Chemical Company, Inc. , and recrystallized from ethyl acetate/cyclohexane.
3. Dichloromethane was placed over 3 Å molecular sieves for 24 hr prior to use. The checkers used dichloromethane freshly distilled over calcium hydride (CaH_2).
4. HPLC grade ethyl acetate was washed with aqueous 5% sodium carbonate solution, followed by brine. After drying the organic phase over anhydrous potassium carbonate, ethyl acetate was recovered after distillation over CaH_2.
5. Because of the hygroscopic nature of the product, the melting point is somewhat broad and varies with the amount of moisture present in the product. Anal. Calcd for $C_{26}H_{25}N_2Cl \cdot 0.9H_2O$: C, 74.85; H, 6.48; N, 6.72; Cl, 8.50; O, 3.45. Found: C, 75.16; H, 6.61; N, 6.66; Cl, 8.82; O, 3.64. The sample has the following spectral characteristics: ^{1}H NMR (300 MHz, CD_2Cl_2) δ: 3.2 (s, 6 H), 6.7 (d, 2 H, J = 7), 7.2-7.3 (m, 15 H), 8.0-8.1 (m, 2 H) ; ^{13}C NMR (75 MHz, CD_2Cl_2) δ: 40.3, 106.9, 127.4, 128.0, 128.1, 128.3, 139.1, 147.5 . The checkers dried the product under vacuum at 50°C for 72 hr; shorter drying times resulted in a different, more complex ^{1}H NMR spectrum. In addition, significant shifts were observed in the ^{13}C NMR spectrum depending upon the state of dryness.

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

Selective protection of a primary alcohol functionality in a molecule has considerable utility in contemporary organic synthesis. Protection of alcohol groups as triphenylmethyl ethers has found applications in the syntheses of a variety of molecules, particularly in the carbohydrate and nucleoside chemistry areas.[4 5 6 7,8 9 10 11] The authors have shown that tritylation may be accomplished in a facile manner by treating an alcohol with chlorotriphenylmethane and 4-dimethylaminopyridine in a suitable solvent.[12] A postulated intermediate in such a tritylation reaction is 4-dimethylamino-N-triphenylmethylpyridinium chloride.[13] The proposal was based on our knowledge of the mechanism of the tritylation reaction and on the enhanced nucleophilic properties of 4-dimethylaminopyridine, which would favor formation of a salt such as **1**. The use of **1** for tritylation of alcohols and amines offers distinct advantages over traditional tritylation methods using pyridine as solvent. For example, **1** may be used in combination with solvents such as dimethylformamide and dichloromethane to accommodate a variety of starting materials. Moreover, with the use of **1**, stoichiometry is better controlled, which in turn enhances selectivity.

A practical, large scale preparation of **1** further enhances the usefulness of the authors tritylation procedure.[8,9,10,11] The preparation involves N-tritylation of 4-dimethylaminopyridine under mild conditions. Isolation of the product is straightforward and the product may be stored at ambient temperature for extended periods, without degradation.

References and Notes

1. Chemical Development Department, D-54Z, Abbott Laboratories, North Chicago, IL 60064;
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

4-Dimethylamino-N-triphenylmethylpyridinium chloride:
Pyridinium, 4-(dimethylamino)-1-(triphenylmethyl)-, chloride (10); (78646-25-0)

4-Dimethylaminopyridine: HIGHLY TOXIC:
4-Pyridinamine, N,N-dimethyl- (9); (1122-58-3)

Chlorotriphenylmethane:
Methane, chlorotriphenyl- (8);
Benzene, 1,1',1"-(chloromethylidyne)tris- (9); (76-83-5)