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CRYSTALLINE ANHYDROUS TRIMETHYLAMINE N-OXIDE

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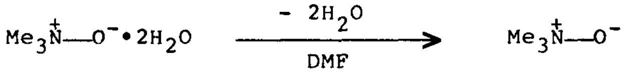
Abstract: A rapid, efficient procedure for the preparation of pure, crystalline anhydrous trimethylamine N-oxide from the commercially available dihydrate form of the reagent is described. DMF serves to both allow the distillative removal of water as well as to provide an excellent medium for obtaining large crystals of the pure (mp 225-7°C (dec)), anhydrous material in excellent (94%) yield.



$$Me_3\overset{+}{N}—O^-\cdot 2H_2O \xrightarrow[DMF]{-\ 2H_2O} Me_3\overset{+}{N}—O^-$$

Trimethylamine N-oxide (TMANO) is an important natural oxidant which is involved in many of the metabolic processes of bacteria that are contained in fish and marine animals.[2] In chemical systems, its uses include: (1) oxidative decarbonylation of transition metal carbonyl compounds,[3] (2) versatile preparative routes to aldehydes,[4] pyrrolidines,[5] and vicinal diols,[6] and (3) selective oxidations of organo- aluminum,[7] boron[8] and silicon[9] compounds.

Many of the above applications require the conversion of the commercially available TMANO dihydrate into the anhydrous reagent employing one of several procedures which culminate routinely in a tedious sublimation process.[10] We wish to report a convenient, efficient method for preparing the crystalline, anhydrous TMANO which not only avoids the need for sublimation, but also, combines the dehydration and recrystallization aspects of the problem into a single, simple process. Moreover, the method gives a pure product which melts ca. 15° higher than previously-reported values.

Our procedure[11] is described as follows: To TMANO·$2H_2O$ (9.80 g, 88.2 mmol) is added DMF (bp 153° from CaH_2) (130 mL). The solution is distilled to reach a distillation temperature of 153° and a final volume of ca. 35 mL. Slow cooling to 0° gives large, colorless crystals. Removal of the supernatant followed by washing (2 x 10 mL dry C_5H_{12}) and in vacuo (3h @ rt, 0.1 torr) drying provides 4.90 g (74%) of TMANO (mp 225-7°(dec)). The supernatant is concentrated at 30 torr and fresh, dry DMF (7 mL) is added, and the mixture warmed to effect dissolution of the residue. After cooling and workup as above, an additional 1.32 g of TMANO (mp 224-6°(dec)) is obtained, resulting in an overall yield of 94%. This material is spectroscopically and analytically pure and, in our hands, gives excellent results for several of the reported[8] oxidative organoborane conversions which use anhydrous TMANO.

Repeated recrystallizations from dry DMF give material which consistently maintains its 225-7° melting range. Thus, while lower values in the 208-212° range are routinely reported with sublimation methods, our product appears to be of higher purity than has previously been achieved.[10] However, we find that even our crystalline material is very hygroscopic, absorbing ca 1% water/min at 28° @ 80% relative humidity. Despite this inherent property of the reagent, we find that the crystals can be stored indefinitely without decomposition and its free-flowing nature greatly enhances the ease of its handling when compared to the sublimed material.

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10. The dihydrate (cf. Dunstan, W. R.; Goulding, E. J. Chem. Soc. **1899**, 1004 and Riley, D. P.; Correa, P. E. J. Org. Chem. **1985**, 50, 1563.) was originally dehydrated and sublimed (cf. Meisenheimer, J.; Bratring, K. Ann. **1913**, 397, 286 and Hickinbottom, W. J., "Reactions of Organic Compounds" Longmans Green and Co.: New York, 1936, p. 227.) to give mp 208°C. See also ref. 3, 5, 7 and 8. This material melts without noticeable decomposition. The pure, anhydrous reagent decomposes at its higher melting temperature. Distillation of DMF solutions of the dihydrate form followed by vacuum drying has previously been used to prepare anhydrous TMANO.[4] However, in this case, the crude material was utilized directly without further purification.

11. All experiments were carried out in predried (4 h @ 110°C) glassware under a nitrogen atmosphere employing standard handling techniques for air-sensitive compounds (cf. Brown, H. C.; Midland, M. M.; Levy, A. B.; Kramer, G. W. "Organic Synthesis via Boranes", Wiley-Interscience: New York, 1975).

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