

## Das Reagenz • The Reagent

## Trimethylamine N-Oxide – A Useful Oxidizing Reagent

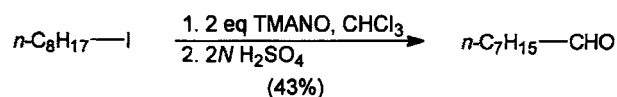
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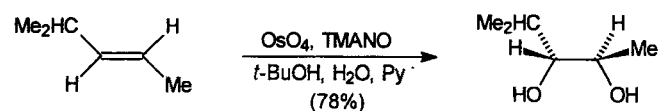
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Trimethylamine N-oxide (TMANO) plays a pivotal role as natural oxidant in many metabolic processes of bacteria in fish and marine animals [1]. TMANO has also proven to be a very useful oxidizing reagent in synthetic organic chemistry and is applied either in its dihydrate or in its anhydrous solid form [2], which are both commercially available [3].

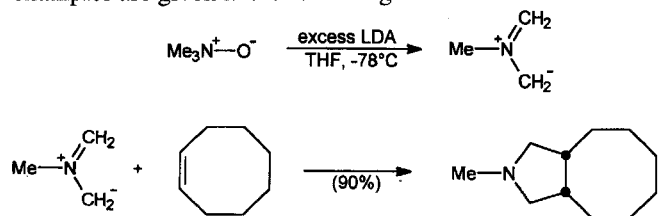
The conversion of alkyl halides into aldehydes and ketones is a synthetically important transformation and easily achieved using anhydrous TMANO [4]. This procedure gives less side reactions than previous methods and is applicable to ordinary aliphatic halides and sulfonates.



The osmium tetroxide catalyzed *cis*-dihydroxylation of sterically hindered olefins proceeds very efficient if TMANO in the presence of pyridine is used as the oxidizing reagent. This procedure proved to be highly successful for olefins bearing bulky substituents (e.g. an *iso*-propyl group) as well as for trisubstituted and tetrasubstituted double bonds [5].

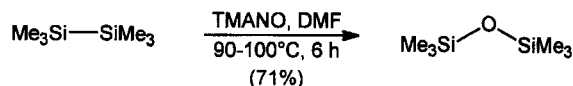


Double deprotonation of TMANO with an excess of lithium diisopropylamide (LDA) affords an ylide, which undergoes remarkable [3+2] cycloadditions with various unactivated olefins, thus providing an efficient access to pyrrolidines [6]. Many useful applications of TMANO as an oxidizing reagent have been described for organometallic compounds. Some examples are given in the following.



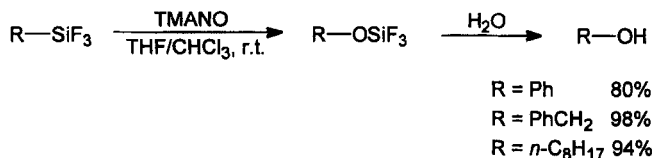
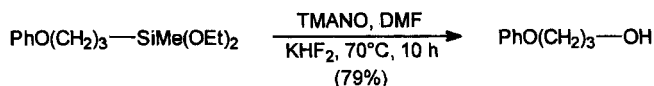
## Organosilicon compounds

The remarkable oxygen insertion into the silicon-silicon bond of organodisilanes on reaction with TMANO provides a simple access to disiloxanes. Thus, hexamethyldisilane is converted to hexamethyldisiloxane in 71% yield [7].



Pyridine N-oxide is less reactive than TMANO and does not react with the same substrate. Using TMANO vinylpentamethylsilyl silane is chemoselectively oxidized to vinylpentamethylsilyloxane in contrast to the reaction with perbenzoic acid, which occurs with concomitant epoxidation of the C=C double bond [7].

The oxidative cleavage of the carbon-silicon bond is an important transformation in organosilicon chemistry [8]. The cleavage of various organodialkoxymethylsilanes and organotrifluorosilanes with TMANO provides the corresponding alcohols in high yields [9, 10].

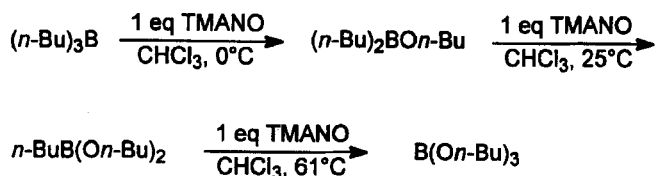


The first procedure requires KHF<sub>2</sub> as an additive and uses rather drastic reaction conditions, while the cleavage of organotrifluorosilanes with TMANO proceeds without any additives smoothly at room temperature.

## Organoborane compounds

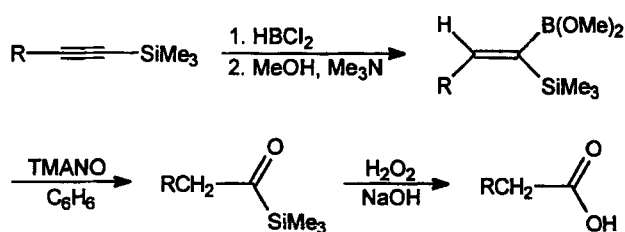
Trialkylboranes are important and versatile intermediates for organic synthesis. The usual alkaline hydrogen peroxide oxidation affords only the corresponding carbinols by

hydrolysis of the intermediate alkoxyboranes. The utility of anhydrous TMANO for the controlled oxidation of trialkylboranes has been demonstrated by the pioneering work of Köster [11]. The oxidation of the three B-C bonds in trialkylboranes with anhydrous TMANO occurs at significantly different reaction rates [11]. Thus, using stoichiometric amounts of the reagent, sequential oxidation of acyclic trialkylboranes provides selectively first borinate, then boronate, and finally borate esters [12].



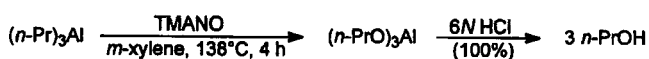
The hydroboration of alkenes followed by oxidation of the resulting alkylboranes with three equivalents of TMANO dihydrate is a mild and convenient procedure for the conversion of alkenes to the corresponding alcohols. In comparison with the standard oxidation procedure ( $\text{H}_2\text{O}_2/\text{NaOH}$ ) the oxidation using TMANO provides better yields and tolerates a series of functional groups in the organoborane [13]. The oxidation of unsymmetrical organoboranes with TMANO is chemoselective. It was found, that bulkier groups are oxidized in preference to smaller groups ( $3^\circ$  alkyl  $>$   $2^\circ$  alkyl  $>$   $1^\circ$  alkyl) [12, 14]. Selective oxidations of boranes to borinates, boronates, and borates using TMANO have been frequently applied in organic synthesis [15].

Acylsilanes are versatile synthetic intermediates and useful for a variety of chemical transformations. However, syntheses of acylsilanes are limited because of their sensitivity towards acids and bases. A simple two-step procedure for the preparation of acylsilanes involves regioselective monohydroboration of trimethylsilylacetylenes using dichloroborane followed by methanolysis and subsequent oxidation of the intermediate dimethyl vinylboronates with TMANO dihydrate. The acylsilanes can be isolated in high yields. Oxidation of acylsilanes with alkaline hydroperoxide provides carboxylic acids [16].



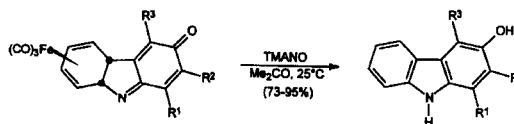
#### Organoaluminum compounds

TMANO is also a convenient reagent for the oxidation of organoaluminum compounds and provides in many cases quantitative yields of the corresponding alcohols [17].

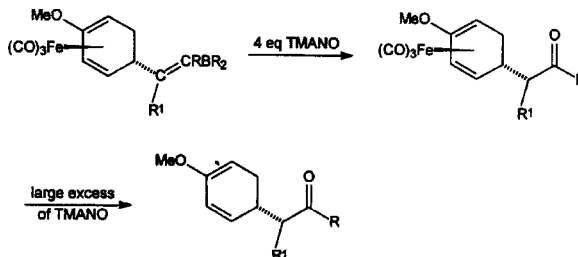


#### Transition Metal Carbonyl Complexes

The demetalation of tricarbonyl( $\eta^4$ -diene)iron complexes using TMANO was reported first by Shvo and Hazum [18] and has been applied to a broad range of tricarbonyliron-diene complexes [19]. More recently this method has been utilized for the demetalation of tricarbonyl[(5-8- $\eta$ )-4b,8a-dihydrocarbazol-3-one]iron complexes under mild conditions [20]. The liberation of the organic ligand occurs with concomitant aromatization and opens up a versatile access to 3-oxygenated carbazole alkaloids [21].

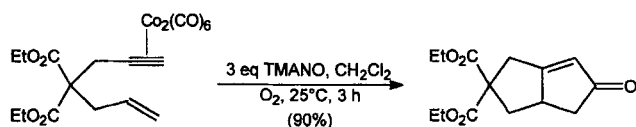
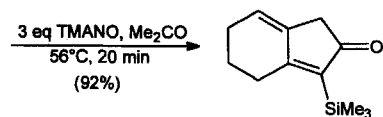
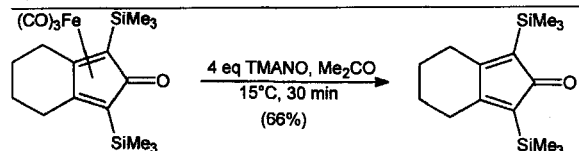


Several examples of sequential chemoselective oxidations of tricarbonyl( $\eta^4$ -diene)iron complexes with TMANO have been described. Based on the method of Köster (see above), Pelter achieved a chemoselective oxidation of a vinylborane to the ketone in presence of a tricarbonyliron-diene moiety on treatment with only four equivalents of TMANO. When using a large excess of TMANO demetalation occurred and the liberated cyclohexadiene was obtained [22].



The oxidative demetalation of tricarbonyliron-complexed annulated 2,5-bis(trimethylsilyl)cyclopentadienones with TMANO at  $15^\circ\text{C}$  afforded the stable corresponding free ligands [23]. These 2,5-bis(trimethylsilyl)cyclopentadienones have been shown to be very useful for consecutive stereoselective cycloadditions leading to cage compounds [24]. Further treatment of the annulated 2,5-bis(trimethylsilyl)cyclopentadienones with TMANO at elevated temperature ( $56^\circ\text{C}$ ) provided the isomerized and monoprotodesilylated dienones in high yields [23].

The mechanism of the oxidative demetalation of tricarbonyl( $\eta^4$ -diene)iron complexes using TMANO is still not clear, although it has been subject of diverse mechanistic investigations [25]. The reduction of amine N-oxides, such as TMANO, with pentacarbonyliron by oxidation of a carbon monoxide ligand to carbon dioxide was originally described by Alper [26]. This reaction can be utilized to promote the complexation of 1,3-dienes with pentacarbonyliron [27] as reported by Shvo and Hazum [28]. TMANO has also been applied to induce the inter- and intramolecular Pauson-Khand reaction [29]. Using this procedure, the Pauson-Khand cycloaddition is dramatically accelerated (reaction in a few hours) and can be performed under mild conditions ( $0^\circ\text{C}$  to room temperature). More recently, the controlled air-oxidation of dinuclear molybdenum carbonyl complexes was achieved in the presence of TMANO [30].



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