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# READY OXIDATION OF HALIDES TO ALDEHYDES USING TRIMETHYLAMINE N-OXIDE IN DIMETHYLSULFOXIDE

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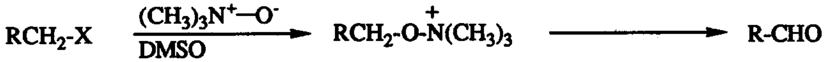
*Abstract* -- The combination of anhydrous trimethylamine N-oxide in dimethylsulfoxide rapidly oxidizes a variety of alkyl and allylic halides to aldehydes in very good yield at or below room temperature.

The nucleophilicity of heteroatom oxides makes them good chemical oxidants. In studying new reactions of amines based on N-nitrosation,[1] we discovered that anhydrous trimethylamine N-oxide (TMANO) transforms nitrosamides to aldehydes under mild conditions.[2] Knowing that dimethylsulfoxide (DMSO) enhances bimolecular nucleophilic displacements,[3] we tested anhydrous TMANO in DMSO and found it superior to other reagent-solvent pairs. Here we report that another application of nucleophilic N-oxide chemistry, the slow oxidation of aliphatic halides **1** to aldehydes **3** in $CHCl_3$ at reflux,[4] can likewise be improved using DMSO solvent.



$$\underset{\mathbf{1}}{RCH_2\text{-}X} \xrightarrow[\text{DMSO}]{(CH_3)_3N^+\!-\!O^-} \underset{\mathbf{2}}{RCH_2\text{-}O\text{-}\overset{+}{N}(CH_3)_3} \longrightarrow \underset{\mathbf{3}}{R\text{-}CHO}$$

Crystalline anhydrous TMANO, easily prepared by the method of Soderquist,[5] is only moderately soluble in DMSO, however the mixture reacts smoothly at rt with primary bromides (Table, Entries 1-2) to afford aldehydes upon simple extractive workup. Alkyl chlorides are not oxidized (Entry 3), whereas secondary or otherwise elimination-prone halides like phenethylbromide (Entry 4) tend to form alkenes. With more reactive allylic or benzylic halides (Entries 5-8), both chlorides and bromides rapidly give aldehydes at 0°C. In these cases a mixed solvent system helps keep the DMSO from freezing. Oxidation of geranyl bromide at low temperature is required to prevent alkene isomerization (Compare Entries 6 and 7). The method is also compatible with esters (Entry 9). With its shorter reaction times and lower temperatures, this improved procedure should find more widespread use in synthetic organic chemistry.[6,7]

**Table**

*Oxidation of Halides to Aldehydes Using TMANO-DMSO*

| Entry | Halide | Conditions[a] | Product (Yield)[b] |
|---|---|---|---|
| 1 | $C_{11}H_{23}CH_2Br$ | DMSO, rt, 5 h | $C_{11}H_{23}CHO$ (83%) |
| 2 | $C_9H_{19}CH_2Br$ | DMSO, rt, 5 h | $C_9H_{19}CHO$ (81%) |
| 3 | $C_9H_{19}CH_2Cl$ | DMSO, rt, 24 h | $C_9H_{19}CH_2Cl$ (95%) |
| 4 | $PhCH_2CH_2Br$ | DMSO, rt, 1 h | $PhCH{=}CH_2$ (83%)<br>$PhCH_2CHO$ (17%) |
| 5 | $Ph\text{-}CH{=}CH\text{-}CH_2Cl$ | 1:1 DMSO:$CH_2Cl_2$<br>-20° to rt, 6 h | Ph-CH=CH-CHO (60%) |
| 6 | geranyl bromide | DMSO, rt, 40 min | geranial (92%) 2:1 E:Z[c] |
| 7 | geranyl bromide | 1:1 DMSO:$CH_2Cl_2$<br>-20° to 0°, 30 min | geranial (71%) 100% E[c] |
| 8 | $PhCH_2Br$ | 3:1 DMSO:$CH_2Cl_2$<br>0° to rt, 30 min | PhCHO (88%)[c] |
| 9 | $AcO(CH_2)_3CH_2Br$ | DMSO, rt, 3 h | $AcO(CH_2)_3CHO$ (47%) |

(a) All oxidations were performed using 4 equiv of TMANO. (b) Reported yields are for distilled or chromatographed samples of aldehyde. (c) No purification necessary.

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6. *Representative procedure:* To a mixture of anhydrous TMANO (0.588 g, 7.83 mmol, 4 equiv) in DMSO (4 mL) was added neat dodecyl bromide (0.484 g, 1.94 mmol) at rt under Ar. After stirring 5 h at rt, the reaction mixture was poured into ice-cold, half-saturated aqueous NaCl (10 mL) and extracted 4 x 10 mL with ether. The combined organic layers were washed once with brine, dried ($Na_2SO_4$) and concentrated *in vacuo*. Kugelrohr distillation afforded pure dodecanal (0.298 g, 83%).

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