# KORNBLUM OXIDATION

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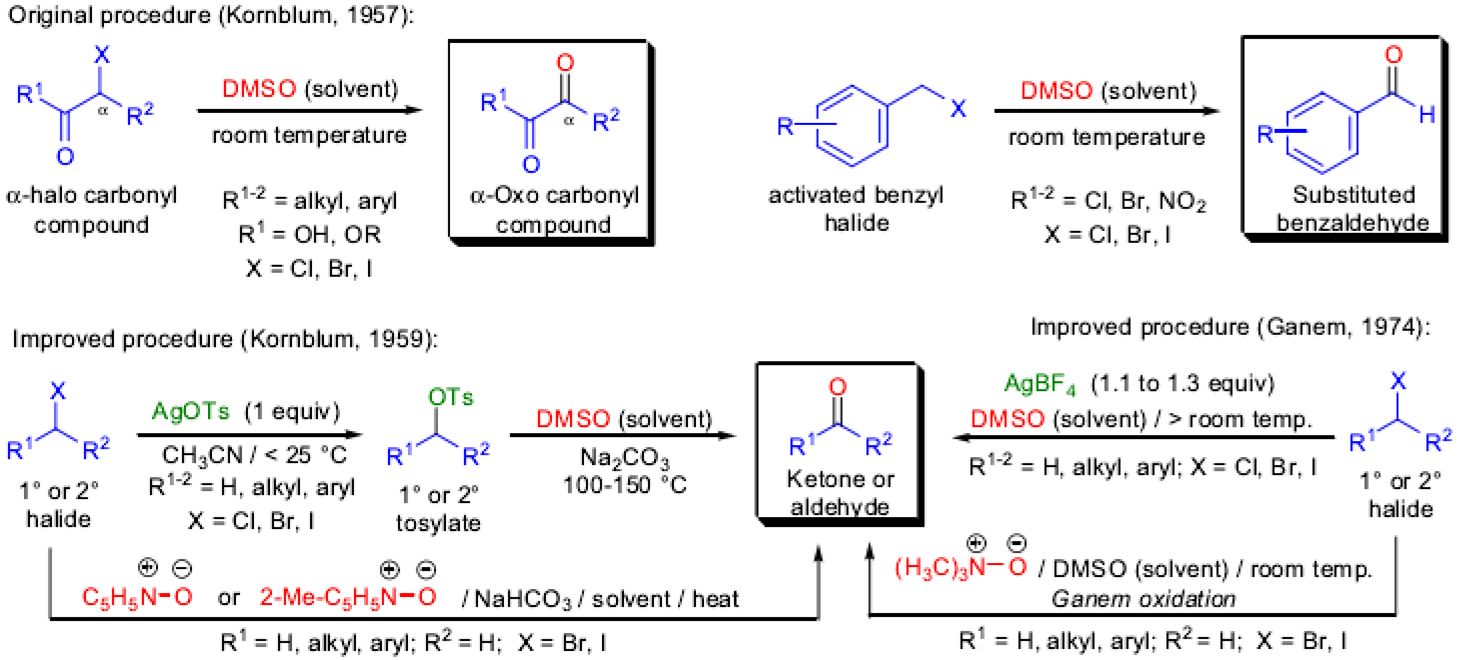
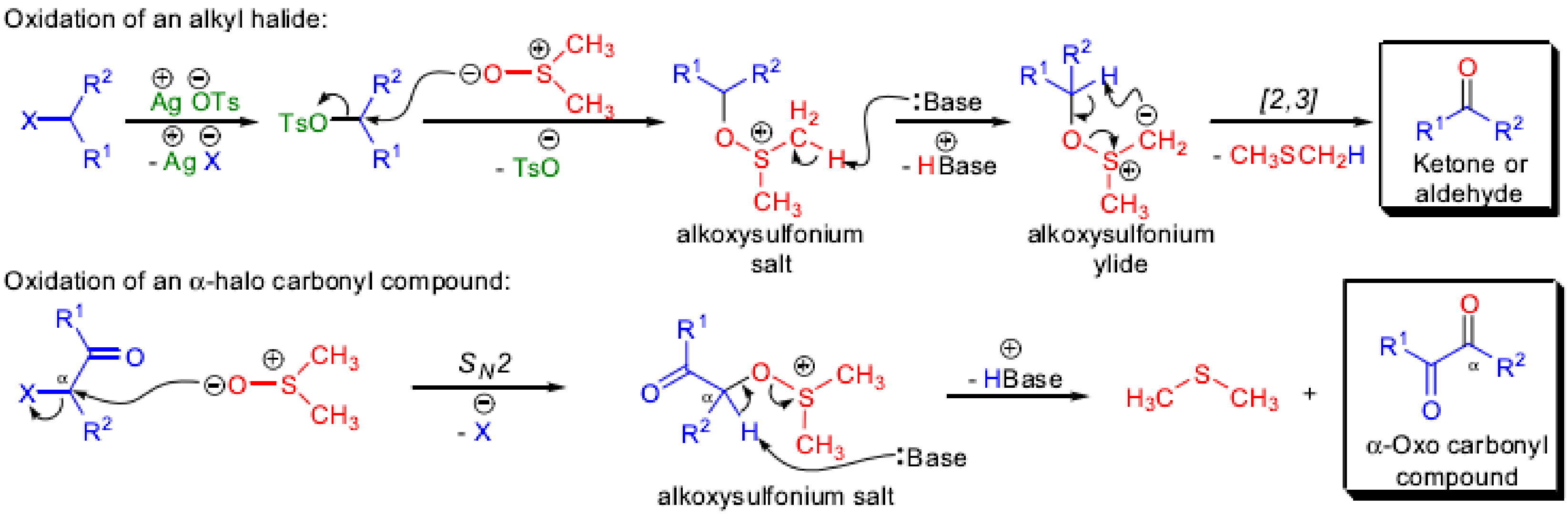
In 1957, N. Kornblum and co-workers discovered that activated primary benzyl bromides and α-bromo aromatic ketones are efficiently oxidized to the corresponding aldehydes and phenylglyoxals by simply dissolving the substrates in dimethyl sulfoxide (DMSO).The drawback of this procedure was that it gave low yields for benzyl bromides having no electron-withdrawing groups, and less reactive halides, such as aliphatic alkyl halides, did not get oxidized at all. It was quickly recognized that the unreactive alkyl halides first had to be converted to the more reactive tosylates, which were oxidized readily in hot DMSO in the presence of a base (e.g., Na2CO3).The oxidation of alkyl halides to the corresponding carbonyl compounds using DMSO as the oxidant is known as the Kornblum oxidation.



Mechanism:

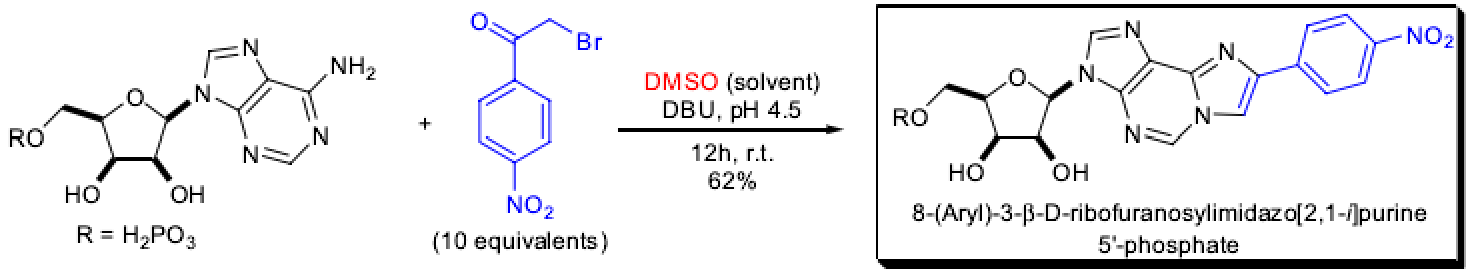
With alkyl halide substrates, the first step of the oxidation is the SN2 displacement of the halide with tosylate anion. Next the alkyl tosylate undergoes a second SN2 reaction with the nucleophilic oxygen atom of the DMSO to form the alkoxysulfonium salt that undergoes deprotonation to give the alkoxysulfonium ylide, which upon a [2,3]-sigma tropic shift affords the carbonyl compound. In the case of α-halo carbonyl substrates, the deprotonation takes place at the more acidic α-carbon instead of the methyl group attached to the sulfur atom of the alkoxysulfonium salt.



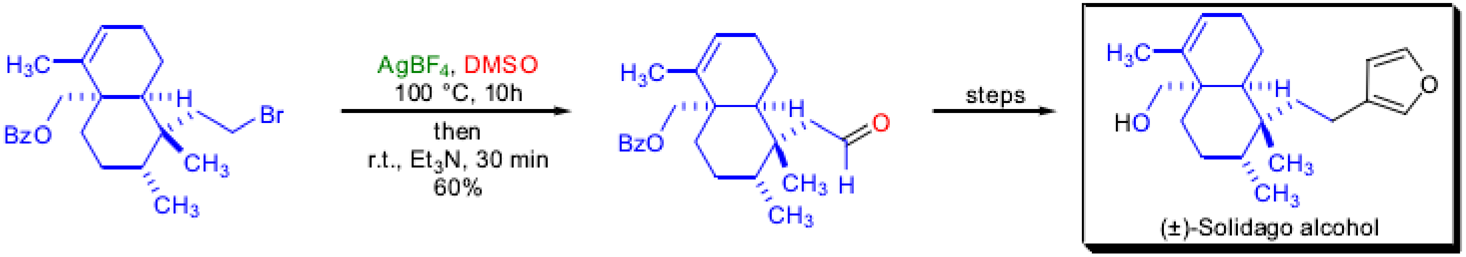
features :

1) the typical procedure calls for the heating of the activated primary or secondary alkyl halide in DMSO in the presence of a base;
2) for unactivated alkyl halides the process requires two steps: first the addition of silver tosylate forms the tosylate, which is heated in DMSO in the presence of a base;
3) for primary alkyl halides the oxidation usually gives high yield of the carbonyl product, but with secondary alkyl halides, elimination of HX to form olefins is often a side reaction;
4) for sterically hindered substrates the yields are only moderate;
5) tertiary alkyl halides do not react;
6) the relative reactivity of the substrates is the following: Ttosylate>iodide>bromide>chloride;
7) the base plays a dual role: it neutralizes the hydrogen halide to avoid the oxidation of HX by DMSO (X2 can lead to side reactions), as well as facilitates the deprotonation of the alkoxysulfonium intermediate; and
8) for substrates that dissolve poorly in DMSO a co-solvent is needed (e.g., DME).

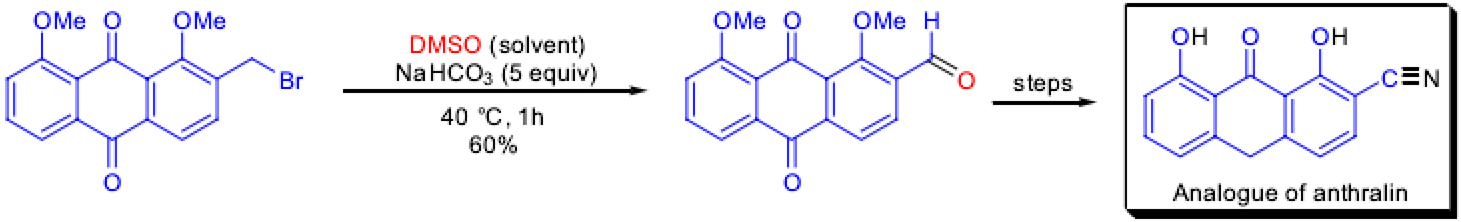
# Synthetic Applications:



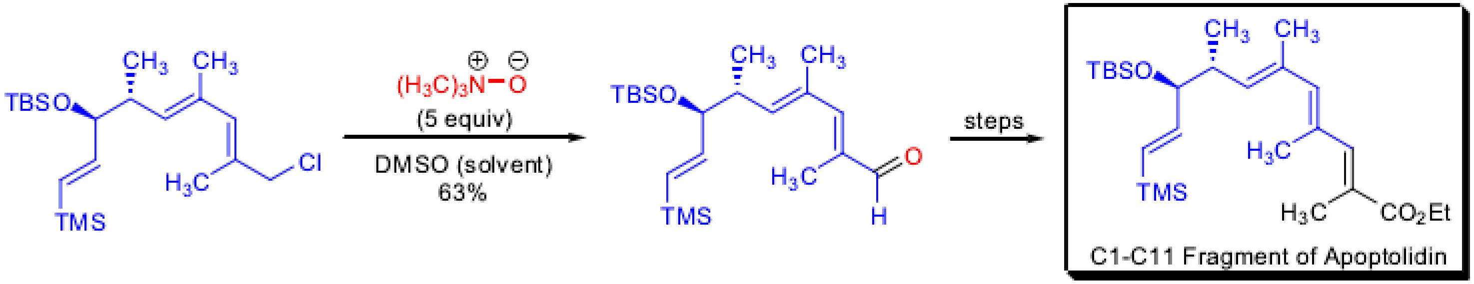
8-(Aryl)-3-β-D-ribofuranosylimidazo[2,1-*i*]purine 5'-phosphate



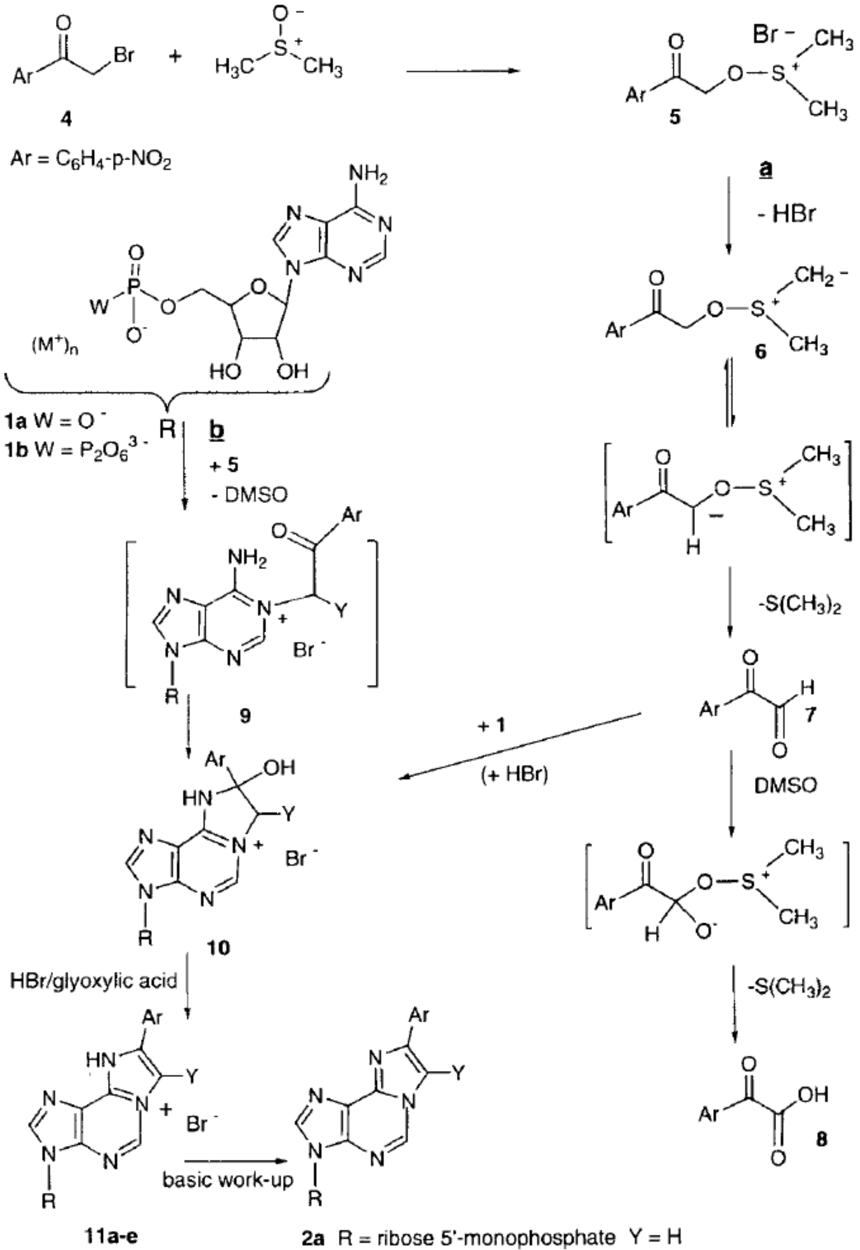
(±)-Solidago alcohol



Analogue of anthralin



C1-C11 Fragment of Apoptolidin



**2a** R = ribose 5'-monophosphate Y = H
**2b** R = ribose 5'-triphosphate Y = H
**2c** R = ribose 5'-diphosphate Y = H
**2d** R = ribose 5'-monophosphate Y = OH
**2e** R = ribose 5'-triphosphate Y = OH