

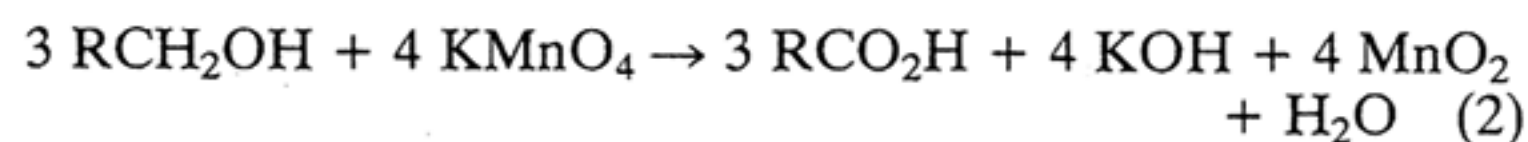
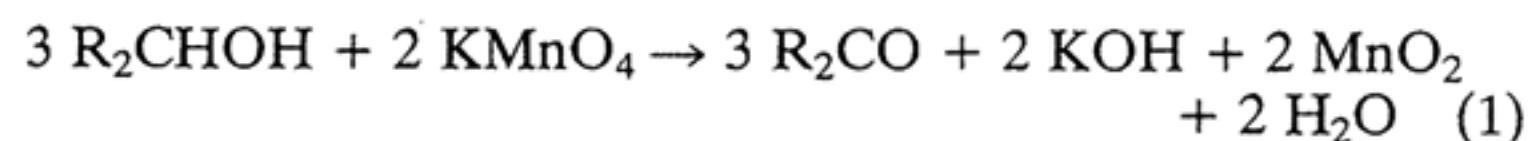
Selective, Heterogeneous Oxidation of Alcohols and Diols with Potassium Permanganate

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Primary alcohols can be conveniently oxidized to carboxylic acids using solid $\text{KMnO}_4/\text{CuSO}_4 \cdot 5\text{H}_2\text{O}/\text{KOH}$ in an organic solvent; 1,4- and 1,5-diols can be selectively oxidized to the corresponding lactones using appropriate mixtures of $\text{KMnO}_4/\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ without added base.

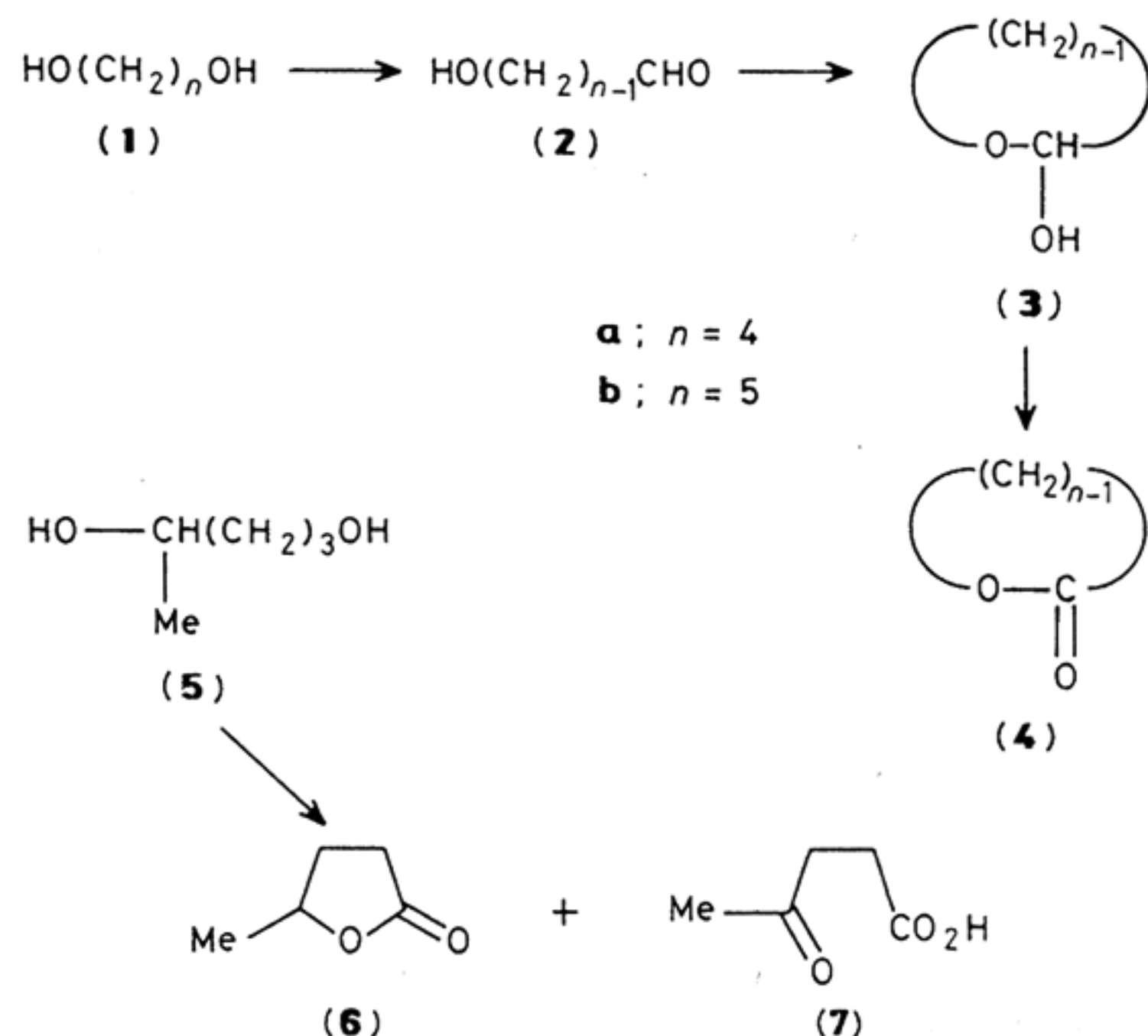
Potassium permanganate can be used for the heterogeneous oxidation of secondary alcohols to their ketones.¹ Mixtures of KMnO_4 and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ ² and hydrated $\text{Cu}(\text{MnO}_4)_2$ ³ have been reported to be useful reagents. Paradoxically, primary alcohols are slowly oxidized, giving the corresponding carboxylic acids in low yields.² It occurred to us that the remarkable disparity in behaviour between secondary and primary alcohols may be due to the different stoichiometries. Secondary alcohols are oxidized forming potassium hydroxide and ketone (equation 1), whereas primary alcohols give rise to two events, generation of carboxylic acid (equation 2) and its neutralization by the excess of potassium hydroxide formed (equation 3). As the potassium carboxylate is likely to be poorly soluble in organic solvents, it could deposit on the surface of the oxidant so inhibiting further reaction. Consequently, if another base were intermixed with KMnO_4 then alternative salt formation might keep the oxidizing sites free. This expectation is confirmed by the results obtained when $\text{KMnO}_4/\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ is mixed with $\text{Cu}(\text{OH})_2 \cdot \text{CuCO}_3$ or KOH .

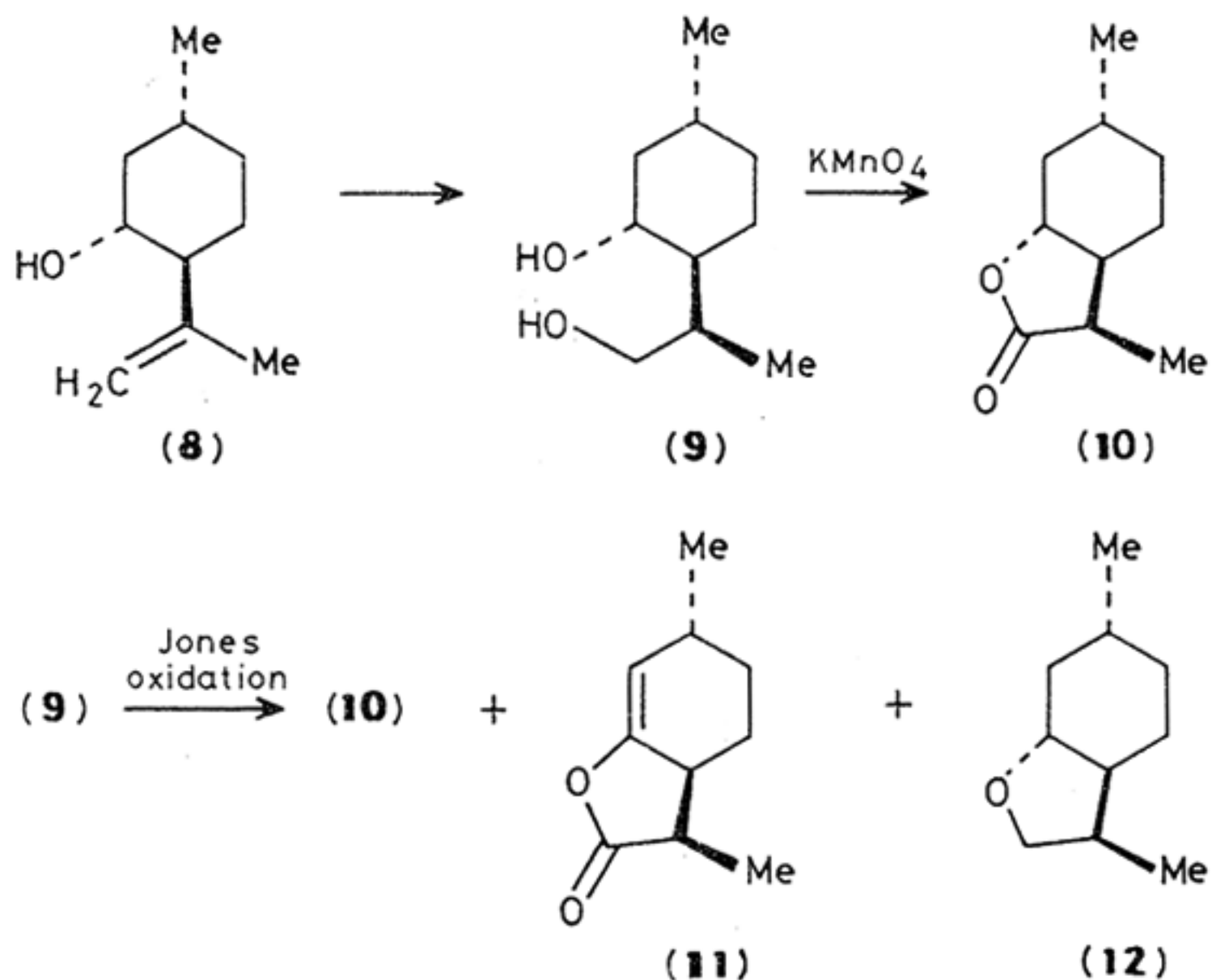


The conventional reagent $\text{KMnO}_4/\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ in benzene, as expected, converts octan-1-ol inefficiently to octanoic acid and octanal. In contrast, mixing basic copper carbonate with the conventional reagent improves oxidation. In ethyl acetate, dichloromethane, and *t*-butyl alcohol, octanoic acid is obtained cleanly in 50–78% yields. Admixture of KOH with

$\text{KMnO}_4/\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ has a similar effect. Oxidation of octan-1-ol is efficient in benzene, ether, and dichloromethane, affording octanoic acid in yields of 82–94%.

This new basic reagent is equally effective for oxidizing alcohols with straight-chain, branched, cyclic, bulky, and aromatic substituents. For example, decan-1-ol, 2-methylbutanol, and the cyclohexyl, cyclopropyl, *t*-butyl, and phenyl derivatives of methanol in benzene are all smoothly transformed into their corresponding acids in 80–96% yields. The action of the basic reagent on mixtures of octan-1- and





-2-ol is selective, with a preference for the primary alcohol at shorter reaction times.†

This last observation provides a basis for a novel synthetic application. The oxidation of α,ω -diols (**1**) should be interrupted at the aldehyde stage (**2**) by intramolecular capture so that the resulting hemi-acetal (**3**) would finally give the lactone (**4**). Since no acid is produced, base would be unnecessary. In fact, $KMnO_4/CuSO_4 \cdot 5H_2O$ alone converts butane-1,4- (**1a**) and pentane-1,5-diol (**1b**) to the γ - and δ -lactones (**4a**) and (**4b**) in 58 and 85% yields respectively. Pentane-1,4-diol (**5**), in which

† Products were isolated or assayed by one of the following procedures. (i) The reaction mixture was treated dropwise with formic acid with stirring at 20°C. The solution was filtered and analysed by g.l.c. Evaporation gave the carboxylic acid. (ii) Saturated aq. $NaHSO_3$ was added to the reaction mixture at 0°C. Extraction with Et_2O , followed by drying (Na_2SO_4), and evaporation furnished the acid. (iii) The reaction mixture was filtered (Celite); the crude product obtained by evaporation was purified by short-path distillation or chromatography [lactones (**4**), (**6**), and (**10**)]. Procedure (ii) was used for separation of acidic by-products.

primary and secondary alcohol functions might compete, gives the γ -lactone (**6**) and the keto-acid (**7**) in yields of 32 and 21%. Nevertheless, on decreasing the hydrated salt content of the oxidant, the intramolecular reaction course prevails and (**6**) is formed in 87% yield.‡

This selective oxidation is further illustrated by an economical synthesis of the insect repellent 3-hydroxy-*p*-menthan-10-oic acid lactone (**10**).⁴ The preparation of (**10**) usually requires at least four steps from precursors such as menthol and gives yields of 12–14%.^{4,5} However, by using the hydrate-deficient $KMnO_4$ reagent, lactone (**10**) can be exclusively obtained from the diol (**9**) derived from (–)-isopulegol (**8**) in an overall yield of 83%. Such discrimination is worth comparing with that observed for the Jones oxidation. Although (**9**) is reported to give (**10**) in 89% yield,⁶ repetition of the experiment shows that (**10**) (38%) is actually accompanied by the unsaturated lactone (**11**) (29%) and the cyclic ether (**12**) (15%).

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‡ The composition of the oxidant is critical to ensure complete lactonization. For (**1b**), the amounts of $KMnO_4$ and $CuSO_4 \cdot 5H_2O$ needed are 1.0 g each; for (**1a**) and (**5**), 1.0 and 0.2 g respectively. Best results for (**9**) are procured with 2.0 and 0.2 g. All alcohols (1 mmol) are dissolved in CH_2Cl_2 (5, 50, 15, and 5 ml respectively).