Heterogeneous Permanganate Oxidations; Part 6: Selective Oxidation of Arenes

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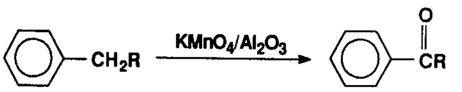
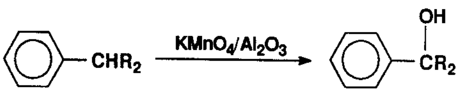
Potassium permanganate adsorbed on alumina selectively oxidizes arenes at the benzylic position. If the benzyl carbon is secondary, ketones are obtained in good yields; alcohols are produced if the benzylic position is tertiary. Benzopyranoid and benzofuranoid systems exhibit highly selective oxidation patterns. Decarboxylation occurs when phenylacetic acid is oxidized, but not when the corresponding ester, ethyl phenylacetate, is oxidized to ethyl benzoylformate.

The use of solid supports in synthetic reactions is a well established technique.[1] Oxidation of organic compounds by permanganate adsorbed on a solid support has two major advantages over the corresponding reactions that take place in homogeneous solutions: (a), the products can be easily isolated by filtration, followed by flash evaporation or distillation of the solvent; and (b), heterogeneous permanganate oxidations often exhibit greater selectivity. For example, although permanganate dissolved in water or methylene dichloride (with the aid of a phase-transfer agent) reacts most rapidly with carbon–carbon double bonds,[2] the heterogeneous reagent can be used to oxidize alcohols selectively in the presence of double bonds.[3] As a consequence, permanganate adsorbed on a solid support can be used to convert α,β-unsaturated alcohols into the corresponding unsaturated ketones without oxidation of the double bond.[3] Also, when conditions are adjusted to promote carbon–carbon bond cleavage under heterogeneous conditions, the products are aldehydes[4] and not carboxylic acids, which are the usual cleavage products obtained under homogeneous conditions.[5]

In this paper we wish to report a procedure in which permanganate adsorbed on alumina[6] can be used to selectively oxidize arenes at the benzylic position. As the results summarized in Table 1 indicate, ketones are obtained if the α-carbon is secondary (Equation 1), while alcohols are produced when the α-carbon is tertiary (Equation 2).



(1)



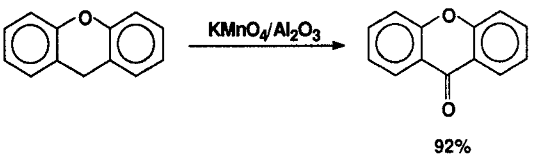
(2)

The remarkable selectivity of this reagent is illustrated by a consideration of the oxidation of benzopyranoid and benzofuranoid systems. Some of these compounds such as xanthene and phthalan are very readily oxidized to the corresponding carbonyl compounds (Equations 3 and 4), while others such as 2,3-dihydrobenzofuran and dihydrocoumarin are completely resistant to oxidation (Equations 5 and 6).

Table. Heterogeneous Permanganate Oxidations

Reactant	Time (h)	Product (Yield)[a]
fluorene	118	9-fluorenone (100)
9,10-dihydroanthracene	121	anthraquinone (98)
tetrahydronaphthalene	240	α-tetralone (86)
indan	256	1-indanone (70)
5-methoxyindan	85	5-methoxyindanone (54) 6-methoxyindanone (16)
9,10-dihydrophenanthrene	240	9-phenanthrol (59)
toluene	328	benzaldehyde (30)
p-nitrotoluene	138	no reaction
ethylbenzene	141	acetophenone (58)
propylbenzene	167	propiophenone (69)
diphenylmethane	282	benzophenone (91)
cumene	136	2-phenyl-2-propanol (78)
s-butylbenzene	234	2-phenyl-2-butanol (79)
anthrone	75	anthraquinone (100)
xanthene	67	xanthone (92)
phthalan	66	phthalide (91)
2,3-dihydrobenzofuran	217	no reaction
dihydrocoumarin	214	no reaction
phenylacetic acid	24	benzaldehyde (54) benzoylformic acid (5)
ethyl phenylacetate	161	ethyl benzoyl formate (94)
cyclohexane	209	cyclohexanone (24) 1,2-cyclohexanedione (4)
cyclohexanol	45	cyclohexanone (97)
cyclohexanone	120	1,2-cyclohexanedione (59)

[a] Isolated yields, expressed as a percentage of the hydrocarbon initially added to the oxidant. The products were identified by comparing melting points and NMR and IR spectra with authentic compounds.



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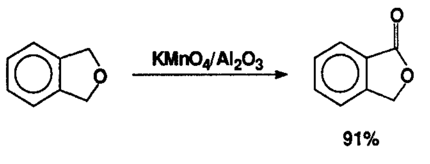

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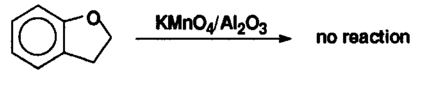
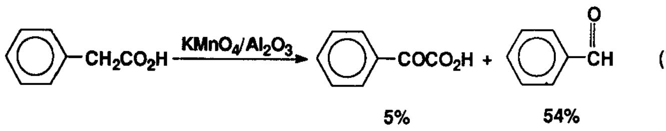


(5)

(6)

The oxidation of 5-methoxyindan results in a larger yield of 5-methoxyindanone (54%) than 6-methoxyindanone (16%), thereby indicating that the methoxy group activates side chains in the *para*-position to a greater extent than those in a *meta*-position. On the other hand, the unreactivity of *p*-nitrotoluene suggests that electron-withdrawing groups in the *para*-position are deactivating.

The observation that decarboxylation accompanies the oxidation of phenylacetic acid (Equation 7), but not the corresponding oxidation of ethyl phenylacetate (Equation 8) may have implications for the preparation of α-keto carboxylates.



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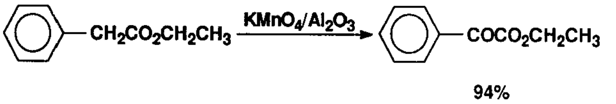
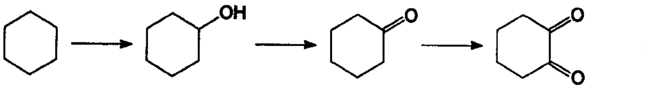


(8)

Cyclohexyl derivatives were used for comparison with saturated systems. As expected, cyclohexanol was rapidly oxidized to cyclohexanone. More suprisingly, cyclohexanone was oxidized to 1,2-cyclohexanedione in over 50 % yield, while the oxidation of cyclohexane gave cyclohexanone along with smaller amounts of 1,2-cyclohexanedione. This suggests that the reaction must proceed according to Equation 9.



(9)

Preparation of Oxidant; Typical Procedure:

Finely ground $KMn0_4$ (2.2 g, 14.0 mmol), dissolved in H_2O (5 mL) was added to alumina (acid, Brockmann activity 1, 8.8 g) with continued stirring to give a permanganate/alumina mixture. The mixture was dried in an uncovered 100 x 20 mm Petri dish overnight at r.t.

9-Fluorenone:

Fluorene (0.54 g, 3.2 mmol), dissolved in 1,2-dichloroethane (120 mL), was placed in a round-bottomed flask with a magnetic stirrer and the permanganate/alumina mixture added in small portions over 10 min. The mixture was stirred at r.t. and the reaction monitored by TLC. After 118 h, analysis of the liquid phase by TLC indicated complete conversion to 9-fluorenone. The product was filtered through a fritted glass funnel and the residue washed with portions of CH_2Cl_2 (3 x 50 mL). The solvent was then removed by flash evaporation to give the product (0.59 g, 3.2 mmol, 100 %) which produced only one TLC spot. Mp, 82.5–85 °C (lit.[7] 82–85 °C). The infrared and NMR spectra were identical with those of an authentic sample.

Benzophenone:

Diphenylmethane (0.61 g, 3.6 mmol) was dissolved in 1,2-dichloroethane (120 mL) and placed in a round-bottomed flask. $KMn0_4/Al_2O_3$ reagent (11.5 g), prepared as described above, was added in small portions over 15 min. The mixture was stirred at r.t. for 282 h. The spent oxidant and solid support were removed by filtration through a fritted glass funnel and the residue was washed with CH_2Cl_2 (3 x 50 mL). Evaporation of the solvent gave impure product (0.62 g) which was purified by elution chromatography to yield benzophenone (0.59 g, 3.3 mmol, 91 %). Mp (2,4-DNP derivative) 235.5–237.5 °C (lit.[8] 239 °C). The infrared and NMR spectra were identical to those of an authentic sample.

The yields obtained from other compounds are reported in Table 1.

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