The Oxidative Coupling of Aliphatic Aldehydes

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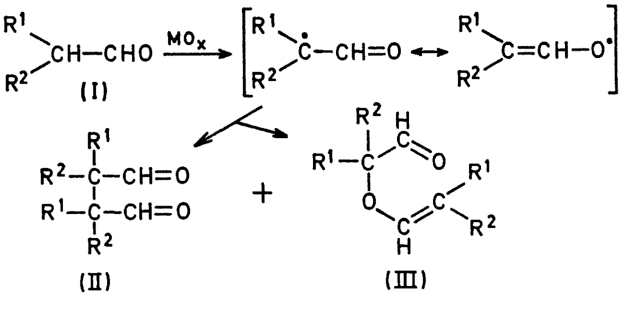
Summary The C–C and C–O oxidative coupling of aliphatic aldehydes is reported.

Manganese dioxide and nickel peroxide are classical mild oxidants for the conversion of allylic and benzylic alcohols into $\alpha\beta$-unsaturated aldehydes and ketones.[1–3] Recently we reported the oxidative dehydrogenation of various cyclohexene aldehydes with active manganese dioxide as a convenient preparative procedure for the production of aromatic aldehydes.[4] We now report that α-substituted aliphatic aldehydes readily undergo α-hydrogen abstraction and subsequent C–C and C–O dimerization without further oxidation of the –CHO functionality or appreciable formation of $\alpha\beta$-unsaturation.[5] Although the oxidative coupling of phenolic materials[6] and aromatic amines[7] has been widely reported, only a few examples of the C–C and C–O coupling of ketones[8] or β-diketones[9] have appeared, and no previous reports of aldehyde couplings are available. The results of our preliminary work indicate that certain aldehydes are in fact easily dimerized by a number of common oxidizing agents, and the products are stable, easily isolable materials of considerable synthetic interest. Among the reagents which are effective for such oxidative aldehyde couplings are activated manganese dioxide, nickel peroxide, and lead dioxide.

For example, when isobutyraldehyde (I; $R^1 = R^2 =$ Me) (18 g) in THF (150 g) was continuously refluxed through a modified Soxhelet cup containing activated manganese dioxide (50 g) for 48 hr. *ca.* 80% of a dimeric mixture of 2,2,3,3-tetramethylsuccinaldehyde (II; $R^1 = R^2 =$ Me) [I.r. absorptions at 3·59 and 5·76 μm (saturated aldehyde); n.m.r. (CDCl$_3$): gem dimethyls at τ 8·84 and aldehydic proton resonance at 0·53 in a ratio of 6 : 1; mass spectrum: molecular ion at *m/e* 142] and 2-methyl-2-(2′-methyl-1′-propenoxy)propionaldehyde (III; $R^1 = R^2 =$ Me) [I.r.: 3·66 and 5·75 (saturated aldehyde) and 5·93 μm (vinyl ether); n.m.r. (CDCl$_3$): gem dimethyls at τ 8·75 (6H), allylic methyls centred at 8·45 (6H), olefinic proton at 4·34 (1H), and aldehyde proton at 0·55 (1H); mass spectrum: molecular ion at *m/e* 142] was produced. The resultant mixture (see Table) was conveniently separated by steam distillation in that the enol ether-aldehyde was rapidly distilled while the tetramethylsuccinaldehyde formed a hydrate obtained by solvent extraction of the steam pot. Approximate ratios of C–C and C–O coupling products for some representative systems are in the Table. Product ratios are virtually identical using nickel peroxide as



Aldehyde	Reagent	Solvent	Coupling product ratios C–C(%)		C–O(%)
Isobutyraldehyde	MnO_2	THF	43	:	57
2-Methylbutyraldehyde	MnO_2	THF	44	:	56
2-Ethylbutyraldehyde	MnO_2	Dioxan–pyridine	12	:	88
Cyclohexanecarboxaldehyde	PbO_2	Dioxan	45	:	55

oxidant; however, low yields are generally obtained with this oxidant.

The C–O dimerization product (III; $R^1 = R^2 = Me$) from isobutyraldehyde which formally appears to meet the requirements for a potential thermally degenerate system was examined by n.m.r. over a varying temperature range up to 150° without any indication of valence isomerism.

Finally, our experiments in which C–O coupling products of α-substituted aldehydes are actually isolated offer an alternative explanation for the formation of α-hydroxy-aldehydes in aqueous acid media by one electron oxidants.[10]

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