Functional transformation of aldehydes and ketones *via* homolytic induced decomposition of unsaturated peroxy acetals and peroxy ketals

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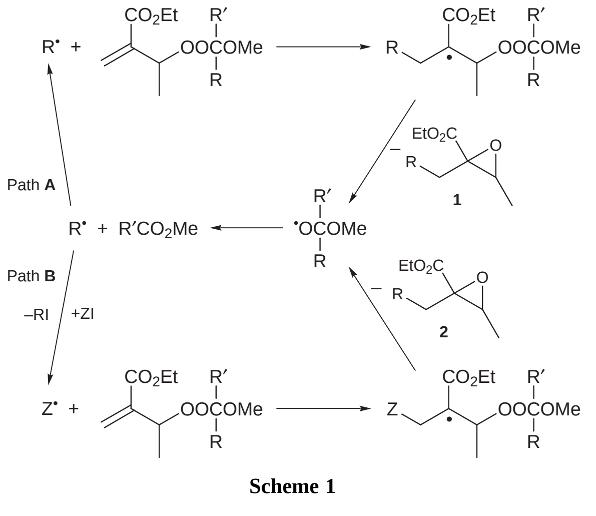
Induced decomposition of unsaturated peroxy acetals prepared from trimethyl orthoformate, dodecanal or 2-methylundecanal and 2,3-dimethyl-2-hydroperoxybut-3-ene, in the presence of ethyl iodoacetate, CCl_4 or dodecanethiol, allowed respectively their iodo-, chloro- and hydrodecarbonylation with yields of over 70%; the same reaction applied to the monoperoxy ketal or diperoxy ketal of cyclohexanone in the presence of ethyl iodoacetate resulted in its functional transformation in methyl 6-iodohexanoate or 1,5-diiodopentane with respective yields of 65 and 40%.

In the last decades, reactions involving free radicals have been increasingly used[1] in synthesis for the creation of carbon–carbon and carbon–heteroatom bonds. Another important field of interest for free radical reactions is the functional transformations one, pioneered by Barton and his group[2] with the development of the chemistry related to *O*-acyl thiohydroxamates. This allows the reductive decarboxylation of an acid or its decarboxylative transformation into a halide, sulfone, nitrile, alcohol *etc*. This methodology is based on a free radical chain reaction, in which the decarboxylation step is the classical generation of an alkyl radical from an acyloxy one.

In the last few years, our attention turned to the reactivity of unsaturated peroxy acetals and peroxy ketals, *via* polymer chemistry,[3] since it was shown that their corresponding alkoxy radicals undergo a very rapid β-scission reaction[4] to generate an alkyl radical. Thus, the homolytic induced decomposition of unsaturated peroxy acetals and peroxy ketals, derived from the ethyl 2-(1-hydroperoxyethyl)propenoate, was applied for the preparation of glycidic esters[5] (Scheme 1, path **A**). As this method of producing glycidic esters requires the preparation of a specific unsaturated peroxy derivative for each application, we developed a more general method[6] using ethyl 2-[1-(1-methoxy-1-methylethylperoxy)ethyl]propenoate (Scheme 1, path **B**, R = R′ = Me). In the light of these results and taking into account the fact that no general method for the decarbonylative functionalization of aldehydes has been described,[7] we decided to approach these transformations using the induced decomposition of unsaturated peroxy acetals. Indeed, applying the type of methodology that we have just described (Scheme 1, path **B**, R′ = H), it appeared possible to generate an alkyl iodide from the aldehyde, as it could be obtained from the hemiacetal *via* Suarez's method.[8]

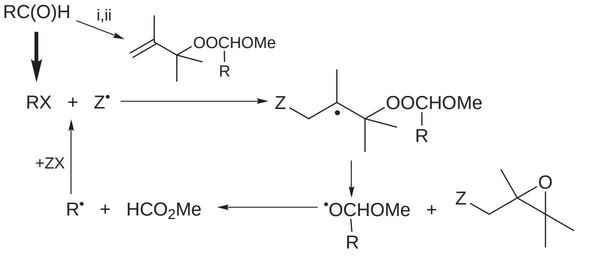


Scheme 1

The decomposition of benzoyl peroxide in a cyclohexane solution of peroxy acetal, obtained from dodecanal, in the presence of a stoichiometric amount of ethyl iodoacetate (relative ratios 0.1:5:1:1.1) afforded the desired 1-iodoundecane (Scheme 1, path **B**, R = $C_{11}H_{23}$, R′ = H) in a 60% yield. In order to check the general character of this reaction, ethyl iodoacetate was replaced by CCl_4: 1-chloroundecane was obtained but with a much lower yield than the corresponding iodide, even when operating in neat perhalogeno solvent (25%). Moreover, in addition to the expected epoxide **2** (Z = CCl_3), the formation of epoxide **1** (R = $C_{11}H_{23}$) with a 46% yield was observed, showing that competition occurred for the alkyl radical between chlorine atom abstraction and addition to the activated double bond of the peroxy acetal. Thus, in order to achieve an effective decarbonylative functionalization of the aldehyde, it appears that the double bond of the peroxy acetal should not be too reactive towards the produced alkyl radical, but very reactive towards the radical $Z^{\cdot}$, formed in the atom transfer with ZX.

Allylic hydroperoxides, possessing a terminal double bond with no electron-withdrawing substituent on it, appeared to be attractive candidates as starting materials for the synthesis of the desired unsaturated peroxy acetals. The easy preparation of allylic hydroperoxides by reaction of singlet oxygen with alkenes[9] prompted us to test the ones produced from the photooxygenation of 2,3-dimethylbut-2-ene (2,3-dimethyl-2-hydro-peroxybut-3-ene), 2-methylbut-2-ene (a mixture of 2-methyl-2-hydroperoxybut-3-ene and 3-methyl-2-hydroperoxybut-3-ene) and 6,7,7-trimethylbicyclo[3.1.1]hept-5-ene (7,7-dimethyl-5-hydroperoxy-6-methylenebicyclo[3.1.1]heptane). The thermolysis of benzoyl peroxide in mixtures of the corresponding peroxy acetals of dodecanal and CCl_4 (relative molar ratios: 0.1:1:5) afforded the 1-chloroundecane in 72, 62 and 42% yield, respectively. These results led us to replace ethyl 2-(1-hydroperoxyethyl)propenoate with 2,3-dimethyl-2-hydroperoxybut-3-ene. The general method for achieving decarbonylative functionalization of the aldehyde is summarized in Scheme 2.

Having determined the appropriate nature of the unsaturated peroxide, it was necessary to optimize the temperature of the reaction. Indeed, in addition to the expected 1-chloroundecane, methyl dodecanoate was obtained (with a yield of about 5% relative to the peroxy ketal). The formation of this compound could be attributed to the disproportionation, in the solvent cage, of the oxyl radicals formed by the spontaneous decomposition of the unsaturated peroxy acetal.[10] Performing the same reaction at room temperature with initiation by BEt_3–O_2 (a BEt_3 solution in hexane was added slowly to the mixture of the other reactants prepared under air, the needle of the syringe being in the liquid) confirmed this origin since no methyl dodecanoate was detected under these conditions and 1-chloro-



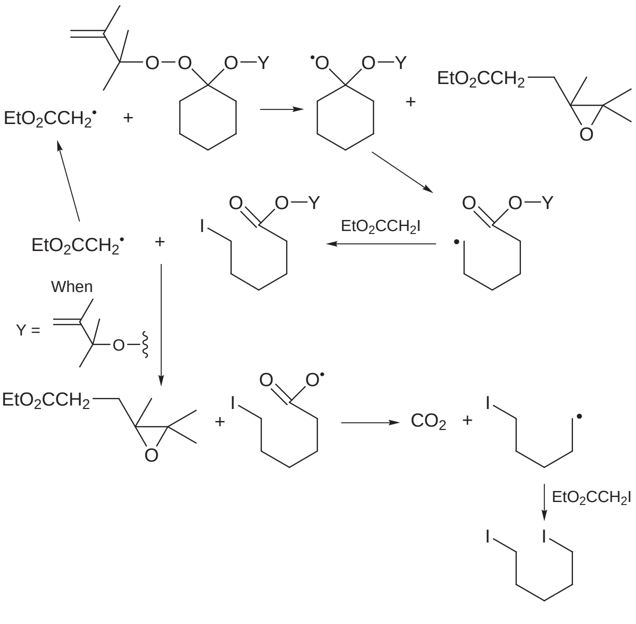
Scheme 2 *Reagents and conditions*: i, HC(OMe)$_3$, TsOH; ii, 2,3-dimethyl-2-hydroperoxybut-3-ene, TsOH.

undecane was obtained with a yield of 86% relative to the starting aldehyde. The iododecarbonylation of dodecanal realized using the same conditions (ethyl iodoacetate–peroxyacetal–cyclohexane: 1.1:1:5; BEt$_3$–O$_2$; room temperature) led to 1-iodoundecane with a yield of 75% relative to aldehyde.

The halodecarbonylation of 2-methylundecanal confirmed the general character of this approach since 2-chloroundecane and 2-iodoundecane were also isolated with yields of about 75%.[11] Peroxy acetals formed from aldehydes bearing a tertiary alkyl group have not been studied as a consequence of their lower stability.[12] Moreover, since the decarbonylation of the corresponding acyl radical is a much faster process[13] than that for the one bearing primary and secondary alkyl groups, there is less synthetic need for the setting of such a reaction.

In order to identify possible extensions of this induced decomposition of unsaturated peroxy acetals we decided, on the first hand, to perform the same reaction with both aldehyde derivatives, replacing ethyl iodoacetate by dodecanethiol to achieve the reductive decarbonylations. In each case, undecane was obtained with a yield of about 75%. Thus, this reaction appears to be an attractive alternative, under less drastic conditions, to the direct one designed from the aldehyde by Berman *et al.*[14]

On the other hand, the efficiency of this reaction prompted us to check a possible extension of this methodology to ketones. We therefore tried to achieve the iododeacylation of cyclohexanone. The peroxy ketal was prepared by addition of the hydroperoxide to 1-methoxycyclohexene, with acid catalysis by TsOH, since the reaction of the hydroperoxide with the corresponding acetal leads to a mixture of monoperoxy ketal and diperoxy ketal. The addition of BEt$_3$ to a non-degassed solution of ethyl iodoacetate and 1-(1,1,2-trimethylprop-2-enylperoxy)-1-methoxycyclohexane in cyclohexane, under the conditions previously described, afforded the desired methyl 6-iodohexanoate (65%) (Scheme 3, Y = Me). The homolytic induced decomposition of cyclohexanone diperoxy ketal, obtained from the corresponding acetal, under the same conditions, but using 2.2 equiv. of ethyl iodoacetate, produced 1,5-diiodopentane in a 40% yield (Scheme 3, Y = $CH_2{=}CMeCMe_2O$).



Scheme 3

In conclusion, homolytic induced decomposition of unsaturated peroxy acetals and mono- and di-peroxyketals appears to be a promising way of achieving decarbonylative functionalization of aldehydes and deacylative functionalization of ketones. The search for new X–Z molecules able to generate other useful transformations is in progress in our laboratory.

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11 Reaction of the aldehyde with trimethyl orthoformate in presence of TsOH yielded, after elimination of methyl formate and excess orthoformate, the raw acetal. Addition of 2,3-dimethyl-2-hydroperoxybut-3-ene (ref. 6) to the acetal, with continuous distillation of MeOH under vacuum (ref. 5), produced the peroxy acetal. After elimination of TsOH by washing the ethereal solution with sodium carbonate and water, followed by drying over magnesium sulfate, the solvent was removed under vacuum. BEt$_3$ in hexane was added to a solution of the peroxy acetal and the required atom transfer agent in the reaction solvent (cyclohexane, CHCl$_3$ or CCl$_4$) until total disappearance of the peroxy acetal as determined by ^{1}H NMR spectroscopy. After elimination of the solvent and the low boiling reaction products, the expected product was separated by column chromatography (SiO$_2$).

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