Iron(III)-induced Cleavage of Cyclic Allylic Hydroperoxides to Dicarbonyl Compounds under Aprotic Conditions

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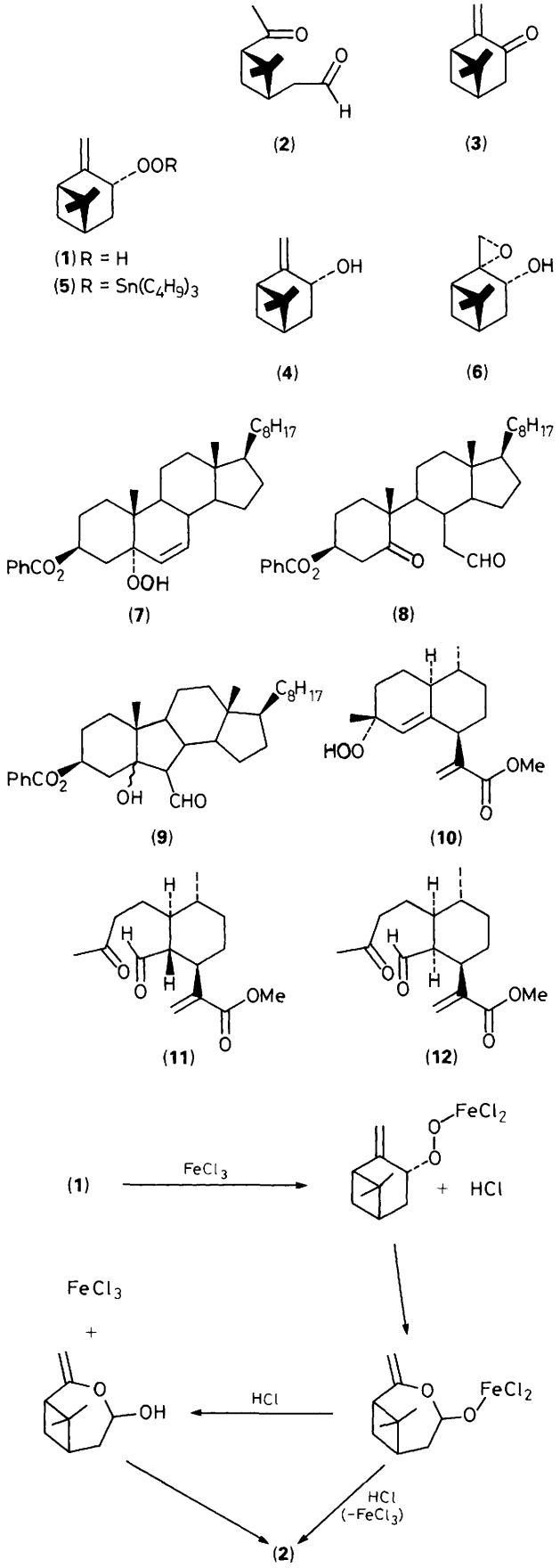
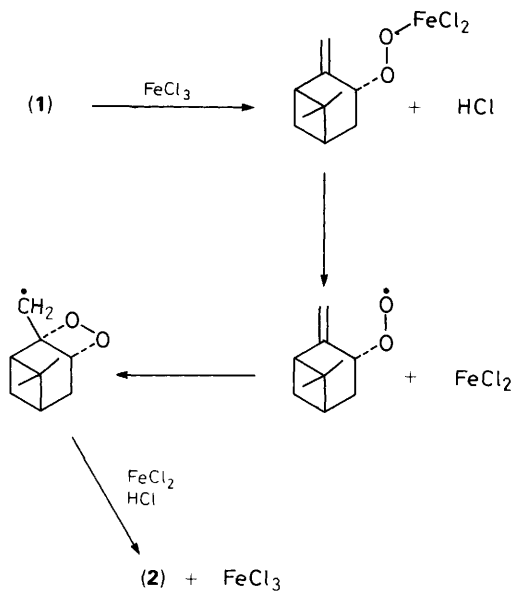
Secondary and tertiary cyclic allylic hydroperoxides are rapidly cleaved by iron(III) catalysts in dichloromethane into dicarbonyl compounds.

Oxygen transfer reactions from alkyl hydroperoxides to alkenes induced by main group and transition metal Lewis acids proceed by hetereolytic or free radical mechanisms and generally provide epoxides as the major products.[1—3] Allylic hydroperoxides generated either as intermediates in the autoxidation of alkenes, or by the action of singlet oxygen on alkenes, also act as epoxidizing agents in the presence of Lewis acid catalysts.[1,3] We have now found that cyclic allylic hydroperoxides do not conform to this well-studied pattern of reactivity, but rather undergo cleavage, in the presence of iron(III) catalysts in dichloromethane.

The pinene hydroperoxide (**1**)[4] (0.37 mmol, 0.05 M solution in CH_2Cl_2) at 0 °C under nitrogen upon treatment with $FeCl_3$ etherate (0.2 equiv., 0.29 M solution in CH_2Cl_2) gave on quenching of the reaction mixture with water after 1 min the ketoaldehyde (**2**)[5] (62% isolated yield) as the sole product. Addition of $Fe(bipyridyl)_3(ClO_4)_3$[6] and $Cu(OSO_2CF_3)_2$ (each 0.2 equiv., 0.03 M solutions in MeCN) to the hydroperoxide in CH_2Cl_2 was also effective. Notably, use of ether as solvent tended to suppress the cleavage reaction in favour of Haber–Weiss disproportionation.[7] Thus, the hydroperoxide (**1**) in ether with $FeCl_3$ (1 equiv.) was converted into the



Scheme 1



Scheme 2

ketoaldehyde (**2**) (17%), the enone (**3**) (17%) and the alcohol (**4**) (14%). The stannyl peroxide (**5**)[9] in CH_2Cl_2 was also rapidly and cleanly converted by $FeCl_3$ etherate into the ketoaldehyde and tributytin chloride, although significantly greater than 1 equiv. of the reagent was required for complete conversion. In contrast, Fe(phenanthroline)$_3$(PF_6)$_3$[8] caused decomposition of the stannyl peroxide to the enone (**3**) (57%) to take place. Use of the corresponding Fe^{II} complex[8] with the free hydroperoxide (**1**) gave the same result. The Ti(O-Pr^i)$_4$ displayed different catalytic activity. The reagent (1 equiv.) induced conversion of the hydroperoxide into the epoxy alcohol (**6**) (60%) and the enone (**3**) (15%) in CH_2Cl_2 or ether. A reaction of this type has been described previously.[3] BF_3 etherate in CH_2Cl_2 was largely ineffective in giving small and variable amounts of the ketoaldehyde (**2**), the enone (**3**), the alcohol (**4**), and other products.

The tertiary hydroperoxide (**7**) in CH_2Cl_2 was cleaved by $FeCl_3$ etherate (1 equiv.) or the iron(III) bipyridyl complex (0.5 equiv.) to give the product (**9**) as a 2.3 : 1 mixture of two epimers corresponding to aldol closure of the cleavage product (**8**) (57—78%). The compound (**8**) could not be isolated, although it is significant that the ketoaldehyde obtained from ozonolysis of cholesteryl acetate is stable to acid for protracted periods.[10] The reaction also succeeded in MeCN. Thus, the iron(III) phenanthroline complex (0.4 equiv.) with the hydroperoxide (**10**)[11] (0.16 mmol) as a 0.03 M solution in MeCN at 0 °C under nitrogen during 1 min gave a 2.5 : 1 mixture of the cleavage products (**11**) and (**12**) in 55% overall yield.

These reactions do not obviously relate to others involving transition metal-catalysed decomposition of hydroperoxides, although they are not entirely without precedent. It was reported that treatment of methyl (9*Z*,11*E*)-13-hydroperoxy-9,11-octadecadienoate (**13**) with BF_3 etherate in ether at room temperature causes cleavage to hexanal and methyl 9-oxononanoate in unspecified yields.[12] Nevertheless, we find that the iron(III) catalysts do not cause cleavage of this and other fatty acid hydroperoxides, and further, under conditions somewhat milder than those reported, the boron catalyst also does not give the cleavage products in significant yields from the hydroperoxide (**14**). For the cleavage of the cyclic allylic hydroperoxides, two possible reaction pathways are pro-

posed. Firstly, a C to O migration analogous to that proposed for cleavage of the linoleate hydroperoxide (**13**)[12] within a discrete iron-peroxy complex can be considered. The intermediate oxonium ion is trapped by the displaced iron-oxy fragment; the resulting iron acetal is decomposed to the free hemiacetal, or directly to the cleavage product, and $FeCl_3$ by the hydrogen chloride produced in the reaction (Scheme 1). In the reaction involving the stannyl peroxide (**5**), the iron(III) is presumably unable to be liberated from the iron acetal, and thus one equivalent of catalyst is required. Nevertheless, the oxidizing nature of the more effective catalysts suggests that oxidative cleavage[1] of the hydroperoxide to generate a peroxy radical is the more likely pathway (Scheme 2). Insertion of the peroxy radical into the double bond to form a dioxetanalkyl radical (or an alkyl-iron equivalent), back electron transfer and cleavage of the dioxetan leads to the dicarbonyl product. The actual sequence of events is unclear at this stage. However, the isolation of the aldol product (**9**) from the steroidal hydroperoxide suggests that after cleavage a precursor is formed which is not the free aldehyde (**8**) and which possesses substantial negative charge density at the site corresponding to the α-carbon atom of the aldehyde. In the case of the stannyl peroxide (**5**) and $FeCl_3$, the catalytic cycle cannot be maintained because of the lack of protolysis of the intermediate alkyl-iron adduct. Steric factors may cause the stannyl peroxide to undergo decomposition by an alternative pathway with the iron(III) phenanthroline complex.

We present in the following communication evidence which is supportive of the second proposal.

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