Pergamon

Tetrahedron Letters 42 (2001) 2293–2295

TETRAHEDRON
LETTERS

# Efficient catalytic methods for the Baeyer–Villiger oxidation and epoxidation with hydrogen peroxide

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Received 19 September 2000; revised 16 December 2000; accepted 24 January 2001

**Abstract**—We have found that the Baeyer–Villiger oxidation of cyclohexanone with hydrogen peroxide in 1,1,1,3,3,3-hexafluoro-2-propanol as solvent is catalyzed by Brønsted acids: in the presence of 1 mol% of *p*-TsOH, transformation to ε-caprolactone occurs rapidly and under mild conditions. Epoxidation of 1-octene can be performed just as efficiently in the presence of 1 mol% of benzenearsonic acid. Since Brønsted acids do not effect epoxidation under these conditions, the formation of perarsonic acid appears to be the crucial feature of the latter catalyst. © 2001 Elsevier Science Ltd. All rights reserved.

Hydrogen peroxide is a highly attractive oxidant for a number of reasons: it is a cheap, mild and an environmentally benign reagent with a high content of 'active' oxygen, and water is formed as the only by-product. However, catalysts are normally required to effect oxygen transfer from hydrogen peroxide to the substrate. From a synthetic point of view, the most attractive oxygenations of organic compounds are the epoxidation of olefins and the Baeyer–Villiger oxidation of ketones. Particularly with regard to the epoxidation of olefins, much effort has been spent on the development of metal containing catalysts. Without going into detail, complexes of Mo, W, Re and Mn have proven particularly useful for the latter purpose.[1–5] Furthermore, arsonic acids were shown to catalyze the epoxidation of olefins such as 1-octene with hydrogen peroxide.[6] With regard to the Baeyer–Villiger oxidation of ketones, the use of hydrogen peroxide has mainly been restricted to strained substrates such as cyclobutanones.[7] For unactivated ketones like cyclohexanone, it was shown that again arsonic acids are capable of catalyzing lactone formation.[8] Furthermore, certain Pt complexes effect the Baeyer–Villiger oxidation of unstrained ketones with hydrogen peroxide.[9]

Very recently, fluorinated alcohols have attracted considerable attention as solvents for epoxidations with hydrogen peroxide. For example, it was shown by Sheldon et al. that the epoxidation of a number of olefins, effected by $HReO_4$ and $Ph_2AsMe$ as co-catalyst, works best in 2,2,2-trifluoroethanol as solvent.[10,11] Furthermore, Neimann and Neumann recently reported that in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), the epoxidation of olefins and the Baeyer–Villiger oxidation of ketones proceed efficiently in the *absence* of catalysts.[12] Their report prompts us to disclose our own results in this area which can be summarized as follows: (i) the Baeyer–Villiger oxidation of e.g. cyclohexanone in HFIP is an acid-catalyzed process. Quite remarkable acceleration can be effected by addition of as little as 1 mol% of Brønsted acids, such as *p*-toluenesulfonic acid. (ii) the epoxidation of e.g. 1-octene is not significantly accelerated by simple Brønsted acids. However, clean and rapid epoxide formation is effected by addition of 1 mol% of arsonic acids, such as benzenearsonic acid.

*Epoxidation:* In a typical run, 144 mg (1.28 mmol) of 1-octene were mixed with 2 ml of HFIP in a 10 ml flask equipped with a magnetic stir bar and a reflux condenser. Then, 12.8 μmol of the acid catalyst (1 mol% rel. to the substrate olefin) was added. No precautions were taken to exclude air or moisture. The reaction was started by the addition of 94 μl (1.66 mmol, 1.3 equiv.) of 50% aqueous hydrogen peroxide.[13] The reaction mixture was then heated to 60°C and stirred continuously. The course of the epoxidation was followed by capillary GC.[14] The results for various acid additives are summarized in Table 1.

Inspection of Table 1 reveals that the arsonic acid is a highly efficient catalyst in HFIP as solvent (entries 1 and 2). Neither one of the other acids effects any acceleration beyond background (entries 1 and 3–6). Furthermore, our catalytic system ($Ph\text{-}AsO_3H_2$/HFIP) is far more effective than the combination of benzene-

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PII: S0040-4039(01)00141-1

**Table 1.** Catalytic epoxidation of 1-octene with hydrogen peroxide

| Entry | Solvent | Catalyst | Reaction time (h) | Conversion of 1-octene[a] (%) | Epoxide yield[a] (%) |
|---|---|---|---|---|---|
| 1 | HFIP | None | 4.5 | 9 | 9 |
| 2 | HFIP | Ph-$AsO_3H_2$ | 4.5 | Quant. | 95[b,c] |
| 3 | HFIP | Ph-$PO_3H_2$ | 4.5 | 7 | 7 |
| 4 | HFIP | HCl | 4.5 | 8 | 7 |
| 5 | HFIP | $CF_3CO_2H$ | 4.5 | 9 | 8 |
| 6 | HFIP | *p*-TsOH | 4.5 | 8 | 7 |
| 7 | Dioxane | Ph-$AsO_3H_2$ | 4.5 | <1 | <1 |

[a] GC: HP 5890 Series II Plus; 50 m×0.2 mm HP-1

[b] Up to full conversion of the olefin, no by-products such as 1,2-dihydroxyoctane were observed by GC.

[c] In a small-scale preparative run, 89% of pure 1,2-epoxyoctane was isolated by distillation (see Ref. 17).

arsonic acid and dioxane as solvent, originally described by Jacobson et al. (entries 2 and 7).[6] Although not yet strictly proven, it appears reasonable to assume that the formation of perarsonic acid may account for the effectiveness of Ph-$AsO_3H_2$. It is not clear at the moment by which mechanism HFIP potentiates the activity of this catalyst compared to dioxane as the solvent (entries 2 and 7). Under identical conditions, 1-dodecene was also smoothly and quantitatively epoxidized.

*Baeyer–Villiger oxidation*: In just the same way as described above for the epoxidation of 1-octene, cyclohexanone was treated with 50% hydrogen peroxide in the presence of various additives.[13] The results are summarized in Table 2. Inspection of Table 2 reveals that in the absence of a catalyst, basically no oxygenation of the ketone was observed (entry 1). Furthermore, the known activity of benzenearsonic acid in the Baeyer–Villiger oxidation of ketones is again remarkably increased in HFIP as solvent (entries 2 and 7).[8] Exchanging Ph-$AsO_3H_2$ for the corresponding phosphonic acid led to the interesting observation that the latter material is *even more active* than the arsonic acid (entries 2 and 3). We rapidly realized that, unlike the epoxidation described above, even simple Brønsted acids such as HCl or TFA are catalytically much more active than benzenearsonic acid (entries 2, 4 and 5). In our hands, 1 mol% of *p*-toluenesulfonic acid proved best (entry 6): under these conditions, cyclohexanone is converted to ε-caprolactone in good yield in less than one hour.[15]

The result shown in Table 2, entry 2 leaves open the question of whether the catalytic activity of benzenearsonic acid is based on peracid formation or whether it just acts as a general acid catalyst. On the other hand, the activity of HCl (entry 4) indicates that an alternative non-peracid, but proton-catalyzed process exists that also leads to lactone formation. Since neither Ph-$PO_3H_2$, $CF_3CO_2H$ or *p*-TsOH are active in the epoxidation of 1-octene (Table 1, entries 3, 5 and 6), it is reasonable to assume that they catalyze the Baeyer–Villiger oxidation by acid catalysis. It may be speculated that an acid-catalyzed rearrangement of an initially formed peroxyacetal is involved. This assumption is consistent with the known ionizing power of HFIP and will be the subject of further studies.[16]

In summary, we have presented two simple but highly efficient protocols for catalytic epoxidation and Baeyer–Villiger oxidation with hydrogen peroxide. We demonstrated the efficiency of the methods on two notoriously difficult-to-oxidize substrates, i.e. 1-octene and cyclohexanone. We believe that our method has great potential for synthetic application: firstly, 50% hydrogen peroxide is employed which is not only safe to handle, but also represents a very economic form of this oxidant. The catalysts used, i.e. *p*-toluenesulfonic acid and benzenearsonic acid, are cheap and commercially available materials. In the course of the distillative work-up procedure, the fluorinated solvent can be recovered basically quantitatively.[17] Furthermore, the reaction times are short and the oxygenation products

**Table 2.** Catalytic Baeyer–Villiger oxidation of cyclohexanone with hydrogen peroxide

| Entry | Solvent | Catalyst | Reaction time (min) | Conversion of cyclohexanone[a] (%) | Lactone yield[a] (%) |
|---|---|---|---|---|---|
| 1 | HFIP | None | 240 | <1 | <1 |
| 2 | HFIP | Ph-$AsO_3H_2$ | 240 | Quant. | 85[b] |
| 3 | HFIP | Ph-$PO_3H_2$ | 75 | 86 | 84[b] |
| 4 | HFIP | HCl | 65 | 90 | 85[b] |
| 5 | HFIP | $CF_3CO_2H$ | 65 | 95 | 90[b] |
| 6 | HFIP | *p*-TsOH | 40 | Quant | 92[b,c] |
| 7 | Dioxane | Ph-$AsO_3H_2$ | 240[c] | <1[d] | <1[d] |

[a] GC: HP 5890 Series II Plus; 50 m×0.2 mm HP-1.

[b] Up to full conversion of the ketone, no by-products were observed by GC.

[c] In a small-scale preparative run, 73% of ε-caprolactone was isolated by distillation (see Ref. 17).

[d] After 24 h, 4% of ε-caprolactone was formed.

are formed in good yields and purities. Finally, the current procedure for the epoxidation of olefins is most suitable for hydrophobic substrate, e.g. long-chain terminal olefins. It is thus complementary to our highly efficient epoxidation method using MnTMTACN/ascorbate as catalyst.[5] For the latter oxidation, more hydrophilic and in particular electron deficient olefins such as acrylates are the best substrates.[5]

## Acknowledgements

This work was supported by the BASF AG and by the Fonds der Chemischen Industrie.

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13. In all experiments, non-stabilized 50% aqueous hydrogen peroxide was used. HFIP was purchased from Aldrich or ABCR, both materials gave the same experimental results. Benzenearsonic acid was purchased from Avocado. All reagents were used without further purification.
14. Samples (100 µl) were withdrawn from the reaction flask and dichloromethane (1 ml) was added. This mixture was filtered through a plug of neutral alumina/MnO$_2$ and analyzed by GC.
15. Similarly, 2-methyl- and 2-phenylcyclohexanone as well as cyclopentanone were cleanly converted to the corresponding lactones.
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17. Small-scale preparative Baeyer–Villiger oxidation of cyclohexanone and epoxidation of 1-octene: 19.3 mmol of cyclohexanone (1.89 g) [1-octene (2.17 g)] were mixed with 24 ml HFIP, and 1 mol% of *p*-toluenesulfonic acid monohydrate (36.7 mg) [benzenearsonic acid (39.0 mg)] was added. Hydrogen peroxide (50%, 1.4 ml, 24.7 mmol, 1.3 equiv.) was added in portions of ca. 100 µl with cooling (CAUTION: significant evolution of heat in the case of the Baeyer–Villiger oxidation). The reaction mixture was stirred at 60°C. Monitoring by GC indicated complete conversion after ca. 1 h in the case of the Baeyer–Villiger reaction, whereas the epoxidation required heating to 60°C for ca. 2–3 h. After removal of the solvent [22 ml (92%) recovered], the crude product was taken up in dichloromethane, washed with aq. NaHCO$_3$, and stirred over anhydrous Na$_2$SO$_4$ and MnO$_2$. Removal of the solvent and fractionating vacuum distillation afforded 1.61 g (73%) of ε-caprolactone and 2.20 g (89%) of 1,2-epoxyoctane, respectively.