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Tetrahedron
Tetrahedron 63 (2007) 1435–1439

Heterogeneous Baeyer–Villiger oxidation of ketones with H_2O_2/nitrile, using Mg/Al hydrotalcite as catalyst

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Received 31 October 2006; revised 21 November 2006; accepted 24 November 2006
Available online 19 December 2006

Abstract—We synthesized a magnesium–aluminium hydrotalcite and used it as a catalyst in the Baeyer–Villiger (BV) oxidation of cyclohexanone with a mixture of 30% aqueous hydrogen peroxide and benzonitrile as oxidant. The hydrotalcite proved an excellent catalyst for the process. The influence of experimental variables was examined in depth in order to bring the working conditions as close as possible to those usable on an industrial scale. We optimized the cyclohexanone/hydrogen peroxide/benzonitrile proportion and used various nitriles, solvents and amounts of catalyst, benzonitrile and methanol proving the most effective nitrile and solvent, respectively, for the intended purpose. The reaction was found to occur to an acceptable extent with other carbonyl compounds as substrates; by exception, α,β-unsaturated carbonyl compounds provided poor results by effect of their undergoing competitive epoxidation of their double bonds.

1. Introduction

The oxidation of cyclic and linear ketones to their respective lactones and esters with oxidants such as organic peroxides or peroxyoxides, alkyl hydroperoxides or hydrogen peroxide is known as the Baeyer–Villiger (BV) reaction.[1] The BV reaction also includes the oxidation of aldehydes to formate esters. The currently accepted general mechanism for this reaction with organic peroxides involves two steps (see Scheme 1), namely, addition of the peroxyacid to the carbonyl compound to form a Criegee adduct (**1**) and rearrangement of the adduct to the reaction end-product (**2**),[2] which retains the stereochemistry of the migrating site.[3] The BV reaction requires the presence of a catalyst to occur; such a catalyst can be of the acid–base or enzyme type and is usually employed in a homogeneous phase with the reaction ingredients.[4,5] The oxidants used are almost invariably organic peroxides, which can produce large amounts of environmentally hazardous by-products. The environmental concern they have raised and the advantages of heterogeneous catalysts over homogeneous catalysis have propitiated the development of effective heterogeneous catalysts for the BV oxidation with hydrogen peroxide in recent years. Hydrogen peroxide as an oxidant has some advantages such as its ease of use, the large amount of active oxygen it can supply and the decreased production of the sole by-product it generates (water).

The use of heterogeneous catalysts in oxidation processes has been dramatically revolutionized by the discovery of Ti-silicalite (TS-1).[6] This solid consists of a zeolite structure (silicalite) into which titanium is incorporated. It possesses a high oxidizing power, which lies in the ability of titanium metal sites to form Ti-peroxide species that can activate hydrogen peroxide in various oxidation reactions including epoxidation, ammonoxidation and CH oxidation.[7,8] The original catalyst has been refined by inserting other oxidizing metals into the zeolite structure, albeit with poorer results than those obtained with titanium. Corma et al. developed a catalyst consisting of Sn incorporated into a beta zeolite.[9] In subsequent work,[10–15] Corma and co-workers conducted extensive research into Baeyer–Villiger oxidation reactions using their Sn–beta zeolite catalysts. Recently, they proposed a mechanism for the underlying process from a combination of theoretical and experimental data;[16] based on it, tin, which acts as an oxygen transfer agent, activates the carbonyl group in the ketone.

Various other catalysts have been successfully used in BV oxidation reactions. Some are based on hydrotalcite-like structures that are used in combination with other oxidants such as benzaldehyde/O_2 mixtures[17–19] or peroxyacids.[20] Also, a hydrotalcite-supported SnO_2 catalyst was found to effect BV oxidations with hydrogen peroxide[21] in the presence of a nitrile as oxygen transfer reagent. Hydrotalcites constitute a family of natural or synthetic materials, also named layered double hydroxides (LDH), the structure of which derives from hydrotalcite[24] [a magnesium–aluminium hydroxycarbonate of formula $MgAl_2(OH)_{16}CO_3 \cdot 4H_2O$

Keywords: Hydrotalcite; LDH; Baeyer–Villiger oxidation; Nitrile.

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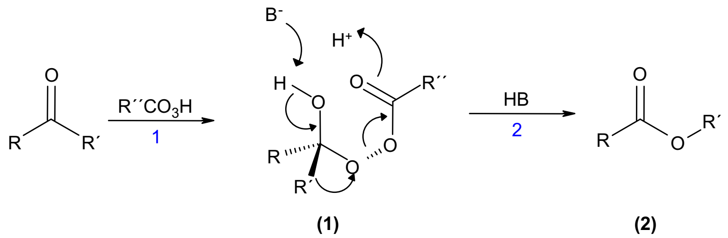
doi:10.1016/j.tet.2006.11.081



Scheme 1. General mechanism for the Baeyer–Villiger oxidation of ketones with organic peracids.

structurally similar to brucite where some Mg^{2+} ions are replaced with Al^{3+} ions in such a way that positively charged layers are formed and their charge neutralized by carbonate ions in the interlayer region]. The structure of hydrotalcite is compatible with variable Mg/Al ratios and also with the exchange of metal cations and anions; this has facilitated the production of a large family of hydrotalcite-like materials of general formula $[M(II)_{1-x}M(III)_x(OH)_2]^{x+}(A^{n-})A\cdot mH_2O$, with x=M(III)/[M(II)+M(III)].

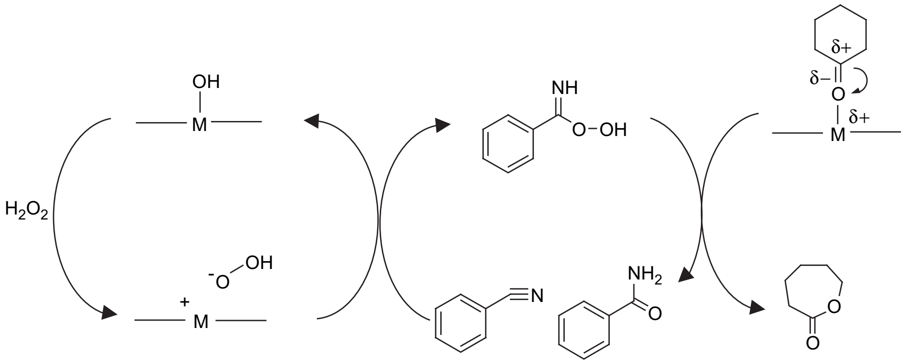
In previous work,[22,23] we used hydrotalcites as effective catalysts for the BV oxidation of cyclohexanone with hydrogen peroxide. Also, we examined the influence of the nature of the catalyst on its activity and proposed a mechanism involving two steps, namely (1) the initial attack of hydrogen peroxide on a Bronsted basic site at the catalyst surface to form a hydroperoxide species, followed by the attack of such a species on benzonitrile to give a peroxycarboximidic acid intermediate and (2) the attack of the previous intermediate on cyclohexanone adsorbed at an acid site of the catalyst to form an intermediate equivalent to the Criegee adduct in homogeneous catalysis processes that undergoes rearrangement to ε-caprolactone, the peroxycarboximidic intermediate being transformed into benzamide (see Scheme 2).

In this work, we expanded the above-described study by examining the influence of some experimental variables including the solvent, nature of the nitrile and amount of catalyst with a view to bringing them as close to those used in large-scale work as possible. All tests were conducted by using an Mg/Al hydrotalcite with a metal ratio of 4, which was previously found to be the best choice for the intended purpose.[22]

2. Results and discussion

In previous work,[22,23] we found hydrotalcites to be effective catalysts for the BV oxidation of cyclic ketones with hydrogen peroxide/benzonitrile mixtures in a large excess with respect to the carbonyl compound. Also, we found the reaction rate to be substantially increased by the addition of a surfactant such as sodium dodecylsulfate. As noted in Section 1, we proposed a mechanism for the reaction based on the results.

We subsequently set to optimize the process with a view to its transfer to a more ‘realistic’ operating scale. We used cyclohexanone as substrate in all tests in order to reduce the amount of benzonitrile and hydrogen peroxide needed, and also that of catalyst. To this end, we used variable benzonitrile/cyclohexanone and hydrogen peroxide/cyclohexanone ratios in order to bring the operating conditions closer to the industrial case and render the process feasible. This additionally involved performing some tests with variable amounts of catalyst that revealed 0.1 g to be appropriate for our purpose. The optimum benzonitrile/cyclohexanone ratio was found to be 4. In order to ensure that the reaction would not be affected by the volume loss resulting from a decreased nitrile/ketone ratio, the reaction vessel was filled with methanol to the volume used in the previous tests. Then, the optimum amount of hydrogen peroxide was determined under the new conditions. As before, the reaction vessel was filled with water as the hydrogen peroxide/cyclohexanone ratio was lowered in order to ensure that the final volume coincided with that used until then. Based on the results obtained with variable hydrogen peroxide/cyclohexanone ratios, an amount of 2 equiv of hydrogen peroxide proved optimal.



Scheme 2. Mechanism for the Baeyer–Villiger oxidation of cyclohexanone with H_2O_2 over HT as catalyst.

As noted earlier, the reaction medium was supplied with an amount of methanol identical with that by which the volume of benzonitrile used was reduced in order to ensure constancy in the total volume of the reaction medium in all tests. We then examined the influence of variably polar solvents on the reaction. As can be seen from Table 1, the best conversion values were obtained with methanol, the other three solvents performing more or less similarly in this respect. This is consistent with the proposed mechanism, based on which the reaction takes place at the interface between the organic and aqueous phases in the reaction medium, so the presence of a surfactant must increase the contact area between the two phases and favour the reaction—as was indeed the case. A solvent such as methanol, which can further increase the contact area between the two phases as it is miscible with both, therefore provided better results than other, water-immiscible solvents, as reflected in the experimental results. Because the other three solvents were immiscible with water, their results should be relatively similar—as they actually were in practice.

Table 1. Influence of the solvent on the Baeyer–Villiger oxidation of cyclohexanone with hydrotalcite as catalyst[a]

Entry	Solvent	Conversion (%)[b]
1	Benzonitrile	100
2	Toluene	65 (85)
3	Dioxane	53 (86)
4	1-Butanol	58 (78)
5	Methanol	73 (96)
6	Methanol[c]	0

[a] Reaction conditions: cyclohexanone: 12 mmol; benzonitrile: 48 mmol; hydrogen peroxide: 2 equiv (30% v/v aqueous solution); catalyst: 0.1 g; T=70 °C; surfactant (DBS): 0.6 mmol.

[b] Conversion to ε-caprolactone after 6 h (in brackets conversion after 24 h).

[c] Reaction without benzonitrile.

While the primary aim of this work was to render the reaction feasible for ε-caprolactone production in a large scale, it would be more economical to use acetonitrile instead of benzonitrile. We therefore examined the influence of using acetonitrile and other nitriles, with and without acid protons in α-position with respect to the nitrile group, as co-oxidants on the BV oxidation of cyclohexanone. The epoxidation of limonene with hydrogen peroxide and benzonitrile[24,25] takes place via a mechanism similar to that for the BV oxidation in the first step (both involve the formation of a peroxycarboximidic intermediate that acts as the actual oxidant). The epoxidation of limonene was found to provide better results in the presence of a nitrile with no acid protons in α-position than that of a nitrile possessing such protons or a catalyst based on an Mg/Al layered double hydroxide or metal hydroxide.[24,25] This can be ascribed to the formation of carbanionic species through the loss of acid protons from the α carbon of the nitrile by effect of the basic character of the catalyst, which decreased the final conversion. In order to check whether this effect was also present in our reaction, we conducted it in the presence of various nitriles with and without α protons. Table 2 shows the results. As with the epoxidation of limonene, the use of a nitrile with

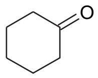
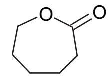
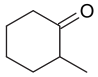
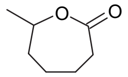
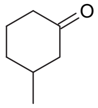
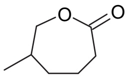
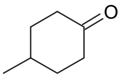
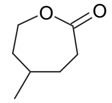
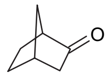
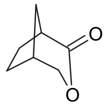
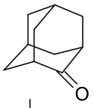
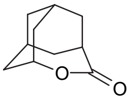
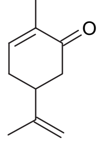
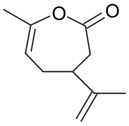
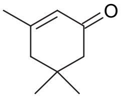
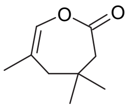
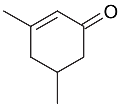
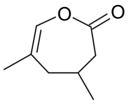
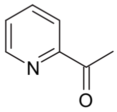
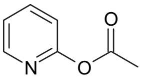
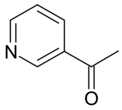
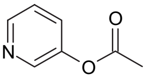
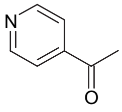
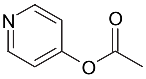
Table 2. Conversion to ε-caprolactone in the Baeyer–Villiger oxidation of cyclohexanone over HT–Mg/Al with hydrogen peroxide and different nitriles as oxidants[a]

Entry	Nitrile	Conversion (%)[b]
1	Acetonitrile	28 (57)
2	Phenylacetonitrile	43 (63)
3	Acrylonitrile	51 (74)
4	Benzonitrile	73 (99)

[a] Reaction conditions: cyclohexanone: 12 mmol; nitrile: 48 mmol; hydrogen peroxide: 2 equiv (30% v/v aqueous solution); catalyst: 0.1 g; T=70 °C; surfactant (DBS): 0.6 mmol.

[b] Conversion to ε-caprolactone after 6 h (in brackets conversion after 24 h).

Table 3. Conversion and selectivity obtained in the Baeyer–Villiger oxidation of various ketones with hydrogen peroxide over Mg/Al hydrotalcite as catalyst[a]

Entry	Substrate	Product	Conversion (%)[b]	Selectivity (%)[c]
1			100	100
2			100	90
3			100	54
4			100	100
5			100	100
6			100	100
7			64	32
8			70	26
9			71	29
10			70	100
11			96	100
12			100	100

[a] Reaction conditions: ketone: 12 mmol; benzonitrile: 48 mmol; hydrogen peroxide: 2 equiv (30% v/v aqueous solution); catalyst: 0.1 g; T=70 °C; surfactant (DBS): 0.6 mmol.

[b] Conversion to lactone after 6 h.

[c] Selectivity to lactone.

acid α protons such as acetonitrile or phenylacetonitrile had an adverse effect and resulted in considerably decreased conversion relative to benzonitrile. As expected, acrylonitrile provided better results than did the previous two nitriles—it possesses no α protons—and matched those of benzonitrile. Therefore, benzonitrile was the most effective nitrile among those tested for the intended purpose.

Once the reaction variables were optimized, we tested other cyclic ketones and acetylpyridines as substrates for the BV reaction. As can be seen, all cyclic ketones exhibited 100% conversion after 24 h of reaction; by exception, 2-methyl- and 3-methylcyclohexanone fell short of complete conversion by effect of the disparate migrating ability of the methylene and methine groups observed in previous work.[23] Also, the presence of an ethylene bond conjugated with the carbonyl group was found to decrease conversion and selectivity towards the lactone by effect of competition from the epoxidation reaction. Finally, acetylpyridines must involve some kind of interaction between the electron pair on the nitrogen atom in the ring and the catalyst surface as 2-acetylpyridine exhibited lower conversion values than did 3- and 4-acetylpyridine—where the nitrogen atom lies farther from the catalyst surface (see Table 3).

3. Conclusions

The results obtained in this work confirm that catalysts consisting of Mg/Al hydrotalcites provide excellent conversion and selectivity in the Baeyer–Villiger reaction under operating conditions that can be transferred to large-scale work. The optimum benzonitrile/carbonyl substrate and carbonyl substrate/hydrogen peroxide ratios are 4 and 2, respectively. Under these conditions, conversion is also affected by the nature of the solvent, methanol being the best choice for the intended purpose. Also, benzonitrile is the most suitable nitrile among those tested. Finally, tests with alternative carbonyl compounds including cyclic ketones and methyl ketones provided results that were also consistent with the proposed mechanism. Only α,β-unsaturated carbonyl compounds exhibited considerably decreased conversion (a result of competition from epoxidation of their double bonds).

4. Experimental

4.1. General

$Mg(NO_3)_2\cdot 6H_2O$, $Al(NO_3)_3\cdot 9H_2O$ and H_2O_2 (about 30%) were purchased from Panreac. Ketones, solvents, nitriles and surfactants were supplied by Aldrich and used without further purification. All oxidation products were identified by mass spectrometry.

4.2. General procedure for preparing the Mg/Al hydrotalcite

Hydrotalcite (HT) was prepared by mixing solutions of $Mg(NO_3)_2\cdot 6H_2O$ and $Al(NO_3)_3\cdot 9H_2O$ in an Mg(II)/Al(III) ratio of 4, using a previously reported coprecipitation method.[26] In a typical synthetic run, a solution containing 0.4 mol of $Mg(NO_3)_2\cdot 6H_2O$ and 0.1 mol of $Al(NO_3)_3\cdot 9H_2O$ in 250 mL of deionized water was used. This solution was slowly dropped over 500 mL of an Na_2CO_3 solution at pH 10 at 60 °C under vigorous stirring. The pH was kept constant by adding appropriate volumes of 1 M NaOH during precipitation. The suspension thus obtained was kept at 80 °C for 24 h, after which the solid was filtered and washed with 2 mL of deionized water. The resulting hydrotalcite was ion-exchanged with carbonate to remove intercalated ions between layers. The procedure involved suspending the solid in a solution containing 0.345 g of Na_2CO_3 in 50 mL of bidistilled, deionized water per gram of HT at 100 °C for 2 h. Then, the solid was filtered off in vacuo and washed with 200 mL of bidistilled, deionized water. The HT thus obtained was subjected to a second ion-exchange operation under identical conditions as the first.

4.3. Characterization of the hydrotalcite

Our HT was characterized from its X-ray diffraction pattern, which exhibited the typical signals for hydrotalcite.[27] Its empirical formula as established by elemental analysis was $Mg_{0.80}Al_{0.20}(OH)_2(CO_3)_{0.10}\cdot 0.72H_2O$.

4.4. General procedure for the Baeyer–Villiger oxidation

Baeyer–Villiger oxidation runs were performed at 70 °C in a two-neck flask containing 0.012 mol of carbonyl compound, different amounts of nitrile, hydrogen peroxide, catalyst and 0.6 mol of surfactant. One of the neck mouths was fitted with a reflux condenser and the other was used for sampling at regular intervals. The system was stirred throughout the process. Products were identified from their retention times as measured by GC–MS analysis on an HP 5890 GC instrument furnished with a Supelcowax 30 m×0.32 mm column and an HP 5971 MSD instrument.

4.5. Optimized procedure for the Baeyer–Villiger oxidation

Optimized Baeyer–Villiger reaction runs were performed at 70 °C in a two-neck flask containing 0.012 mol of carbonyl compound, 0.048 mol of benzonitrile, 2 equiv of hydrogen peroxide, 0.1 g of catalyst (hydrotalcite), 0.6 mmol of sodium dodecylbenzenesulfonate and 5.2 mL of methanol.

Acknowledgements

The authors gratefully acknowledge funding by Spain's Ministerio de Educación y Ciencia (Project MAT-2006-04847), Feder Funds and the Consejería de Innovación, Ciencia y Empresa de la Junta de Andalucía.

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