



The Baeyer–Villiger oxidation of ketones with Oxone[®] in the presence of ionic liquids as solvents

Anna Chrobok

Department of Chemical Organic Technology and Petrochemistry, Silesian University of Technology, ul. Krzywoustego 4, Gliwice 44-100, Poland

ARTICLE INFO

Article history:

Received 1 March 2010

Received in revised form 2 May 2010

Accepted 24 May 2010

Available online 1 June 2010

Keywords:

Baeyer–Villiger oxidation

Ionic liquids

Oxone[®]

Lactones

Esters

ABSTRACT

Cyclic and linear ketones were readily oxidised with Oxone[®] at 40 °C in ionic liquids as solvents and short times (2.5–20 h), affording their corresponding lactones and esters in high yields (65–95%). Both, aprotic and protic ionic liquids were used. The best conversion of ketones and the highest yields of products were obtained with 1-buty-3-methylimidazolium tetrafluoroborate and 1-methylimidazolium acetate as solvents. These ionic liquids were also efficiently recycled in the Baeyer–Villiger reaction without significant loss of activity. Several factors, such as the partial solubility of KHSO₅ in the ionic liquid, its viscosity and the presence of a proton in protic ionic liquids, have an influence on the course of the reaction.

© 2010 Elsevier Ltd. All rights reserved.

1. Introduction

The Baeyer–Villiger (BV) reaction was first reported by Adolf von Baeyer and Victor Villiger in 1899.¹ The reaction is based on the oxidation of cyclic and linear ketones to lactones or esters with peroxide derivatives. A large range of possible applications for this reaction in organic synthesis can be found, e.g., the synthesis of antibiotics, steroids, pheromones and monomers for polymerization.² For this reason, new and more environmentally friendly synthetic methods, using non-toxic reagents, oxidants and solvents are constantly under investigation.³

The most commonly used oxidants in the BV process are organic peroxyacids and hydrogen peroxide. However, Baeyer and Villiger used Caro's acid (H₂SO₅) in their pioneering work. This oxidizing agent is only used occasionally as a potassium salt.⁴

Currently, the use of a commercially available source of KHSO₅ (Oxone[®]) in fine chemicals synthesis has increased rapidly. Oxone[®] is a stable oxidising agent, which is easy to handle, is non-toxic, generates non-polluting by-products and is relatively inexpensive. Oxone[®] has been widely studied as a routine reagent for epoxidation reactions, oxidation of aldehydes to carboxylic acids and in many other oxidation processes.⁵

Extensive studies of green solutions for organic oxidation processes are focused on minimizing the environmental impact

resulting from the use of oxidizing agents and solvents. From this point of view, a marriage of ionic liquids with Oxone[®] would be an effective combination.

Recently, ionic liquids (ILs), possessing negligible vapour pressures, having the ability to dissolve many organic and inorganic substances, and being readily recyclable, have been described as one of the most promising new reaction mediums and alternatives to volatile organic solvents.⁶ Additionally, ionic liquids can be tunable to specific chemical tasks. The task-specific acidic ionic liquids have been widely used, as both solvents and catalysts, e.g., in esterifications, etherifications and Friedel–Crafts alkylation processes.⁷ We have also reported the catalytic influence of ionic liquids on BV reactions before.⁸

Herein, a new approach to lactone synthesis involving the application of Oxone[®] as an oxidant and using ionic liquids as solvents, affording a clean oxidation and providing additional efficiency to the reaction is presented.

2. Results and discussion

Potassium peroxomonosulfate triple salt (2KHSO₅·KH SO₄·K₂SO₄) was chosen as a good alternative to organic peroxyacids in the Baeyer–Villiger reaction. It is known from a few reports in the literature, that Oxone[®] is an efficient oxidizing agent in the BV oxidation that requires an aqueous reaction medium,⁹ which leads to extensive hydrolysis of the reaction products. An alternative application is possible using anhydrous potassium peroxomonosulfate supported on silica (SiO₂·KHSO₅).⁴

E-mail address: anna.chrobok@polsl.pl (A. Chrobok).

This work focused on the application of the versatile ionic liquids solvents due to their great potential for dissolving both organic and inorganic substances. Furthermore, acids and bases are catalysts for the BV reaction,² thus the application of Brønsted acidic ionic liquids was interesting.

Ionic liquids can be classified as protic or aprotic depending on whether they possess an available proton on the cation moiety. Among the aprotic ionic liquids (AILs) the following ILs were chosen: 1-butyl-3-methylimidazolium tetrafluoroborate (bmimBF₄), 1-butyl-3-methylimidazolium acetate (bmimOAc), 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide (bmimNTf₂), 1-ethyl-3-methylimidazolium ethylsulfate (ECOENG212), PEG-5 cocomonium methylsulfate (ECONG500). From the big class of protic ionic liquids (PILs), which are easily

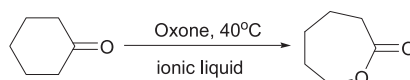
produced through the combination of a Brønsted acid and Brønsted base, those that are liquid at room temperature were selected: 1-methylimidazolium acetate (HmimOAc), 2-methylpyridinium acetate (H2mpyrOAc) and 1-methylimidazolium tetrafluoroborate (HmimBF₄).

HmimBF₄ is actually a solid at room temperature (mp=35.8 °C), but at the reaction temperature (40 °C) it is a rather non viscous liquid. However, the PILs are classified as ‘poor’ ionic liquids, according to the classification scheme devised by Angell et al.,¹⁰ with the salts of the tetrafluoroborate anion, being an exception, having particularly good ionicity. Some of the PILs can be distilled, e.g., HmimOAc and H2mpyrOAc.¹¹

It is known that peroxy compounds are relatively unstable and easily decompose in the presence of various reagents. For this

Table 1

Oxidation of cyclohexanone (4 mmol) with Oxone[®] (4 mmol) in ionic liquids (3 g) as the solvent at 40 °C



Entry	Ionic liquid	Solubility of Oxone [®] at rt [g/mL]	Viscosity of ILs at rt [mPas]	Reaction time [h]	Conversion ^a [%]	Yield ^b [%]
1	 bmimBF₄^c	0.13	154 ¹²	4	95	93 (88)
2	 HmimBF₄^c	—	Solid (mp=35.8 °C) ¹¹	8	63	55
3	 HmimOAc^c	0.03	5.6 ¹¹	6	96	93 (87)
4	 bmimOAc^d	0	646 ¹³	10	23	9
5	 H2mpyrOAc^c	0.04	Not determined	8	81	76 (71)
6	 bmimNTf₂^c	0	52 ¹⁴	10	40	21
7	 ECOENG212^e	0.01	97 ¹⁵	10	10	3
8	 ECONG500^e	0.10	2780 ¹³	10	80	75 (71)
9	CH ₂ Cl ₂	0	0.437	6	24	11

^a Conversion determined by GC.

^b Yields determined by GC; in parenthesis isolated yields by the extraction with ethyl acetate (entry 1), diethyl ether (entry 8) or dibutyl ether (entry 3 and 5).

^c ILs synthesized in lab.

^d IL from Fluka.

^e ILs from Merck.

reason, it was important to test the stability of potassium peroxomonosulfate by stirring Oxone[®] at 40 °C in the ionic liquids to be studied. After 5 h, the amount of KHSO₅ in these test samples, as checked by iodometric titration, had not changed.

In additional preliminary studies, the solubility of potassium peroxomonosulfate in the ionic liquids studied was checked by stirring the Oxone[®] for 1 h at room temperature. As shown in Table 1, a level of KHSO₅ in bmimBF₄ and ECOENG500 of 0.1 g per mL was detected. For other ionic liquids studied either solubility levels of KHSO₅ of 0.01–0.04 g per 1 mL was observed or any trace of KHSO₅ was not observed. The question to answer was: would ILs be efficient solvents for the BV reaction if the solubility of Oxone[®] in ILs is low?

For the optimisation of the BV reaction conditions, the oxidation of cyclohexanone as a model was used, because this process is important to the industry. In Table 1, the influence of the structure of the ILs on the oxidation of cyclohexanone at 40 °C with a 1:1 ketone/Oxone[®] ratio (which is an actual 1:2 ketone/KHSO₅ ratio) is illustrated. In most instances of using ionic liquids as solvents, relatively high conversions and yields of ϵ -caprolactone were observed. The best results were obtained using bmimBF₄, in which the reaction was completed after 4 h (Table 1, entry 1). All other ionic liquids studied required longer reaction times (6–10 h), and are sometimes not sufficient to achieve high conversion. The highest conversions of ketone and yields of ϵ -caprolactone were observed when the reaction was carried out in bmimBF₄, HmimOAc, H2mpyrOAc and ECOENG500 (Table 1, entry 1, 3, 5 and 8). For comparison, the same reaction was carried out in dichloromethane. Oxone[®] is completely insoluble in dichloromethane, which may be a reason for the low conversion of ketone to lactone (Table 1, entry 9).

Several factors may influence the BV reaction in ionic liquids. The first one is the partial solubility of KHSO₅ in ionic liquids, that is, observed with bmimBF₄ and ECOENG500. The viscosity of ionic liquids is also crucial for the reaction rate, and can explain the longer reaction time when using the most viscous ECOENG500. On the other hand, this task-specific ionic liquid is a powerful reaction medium because it possesses a cation structure with several ethoxy

groups bound to the nitrogen atom. Complexation of the potassium cation causes the solubility of KHSO₅ to be higher and the contact of reagents to be better.

The availability of a proton in the cation structure (PILs) also has an influence on the reaction course. Very efficient reaction in HmimOAc and H2mpyrOAc is caused by the possibility of acid catalysis of PILs. The free proton on the nitrogen atom may catalyse the BV reaction in the same way that potassium hydrogen sulfate does, described previously by Asensio et al.⁴

All of the ionic liquids studied, with the exception of bmimNTf₂, are hydrophilic. After the reaction, for the isolation of the remaining salts from Oxone[®] the post reaction mixture was dissolved in CH₂Cl₂, filtered and concentrated. The isolation of the product was accomplished in two ways. The first one was simple extraction of the product from ionic liquid with an appropriate solvent. The second one was the possibility of distillation of the product or ionic liquid from the reaction mixture because some of the PILs can be distilled, e.g., HmimOAc (bp=70 °C/1.2 mbar) and H2mpyrOAc (bp=90 °C/1.2 mbar).¹¹ The distillation process seems to be a more environmentally friendly solution than extraction.

It was found that the most effective ionic liquids for BV reactions are bmimBF₄ and HmimOAc. For this reason, the oxidation of other cyclic and linear ketones with Oxone[®] as an oxidising agent at 40 °C was demonstrated as shown in Table 2. High yields of lactone and ester formation were observed, and within relatively short reaction time as compared to literature results. The yield of the BV reaction depends of the reactivity of the applied ketones, on the ring size of cyclic ketones and on the migration ability of the substituents. In the case of less reactive ketones, such as 1-indanone, hexan-2-one, acetophenone and metoxyacetophenone (Table 2, entry 6, 8–11) the reactions were carried out with molar ratios of ketone/Oxone[®] of 1:1.5.

At the end of study, the possibility of recycling the ILs was checked. The ionic liquids were recovered and reused for further BV reactions. In Table 3, four cycles of the oxidation of 2-adamantanone in bmimBF₄ and HmimOAc, recycled each time is shown. A significant loss of activity of these solvents was not observed.

Table 2
Oxidation of ketones (4 mmol) with Oxone[®] (4 mmol) in the presence of ionic liquids (3 g) as the solvent at 40 °C


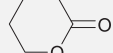

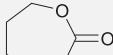

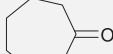

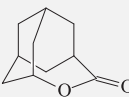


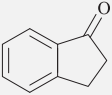
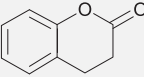

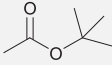

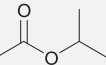
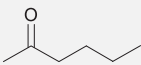
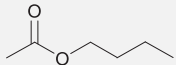
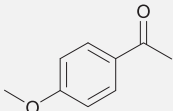
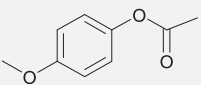
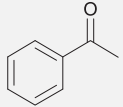
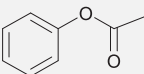
Entry	Ketone	BV product	Molar ratio ketone/Oxone [®]	bmimBF ₄			HmimOAc		
				Time [h]	Conversion [%]	Yield ^a [%]	Time [h]	Conversion [%]	Yield ^a [%]
1			1:1	3	100	88 (82)	5	100	90 (85)
2			1:1	4	95	93 (88)	6	96	93 (87)
3			1:1	2.5	100	93 (88)	5	100	90 (86)
4			1:1	3	100	99 (95)	5.5	100	99 (97)
5			1:1	7	100	98 (95)	10	100	97 (93)

Table 2 (continued)

Entry	Ketone	BV product	Molar ratio ketone/Oxone [®]	bmimBF ₄			HmimOAc		
				Time [h]	Conversion [%]	Yield ^a [%]	Time [h]	Conversion [%]	Yield ^a [%]
6			1:1.5	20	77	77 ^b (70)	20	56	50 ^b
7			1:1	8	99	95 (88)	12	99	92 (88)
8			1:1.5	12	99	90 (84)	15	99	89 (82)
9			1:1.5	15	29	25	20	25	21
10			1:1.5	12	80	79 ^b (72)	16	75	72 ^b (65)
11			1:1.5	12	33	30	12	22	18 ^b

^a Yields determined by GC; in parenthesis isolated yields.

^b Yield determined by HPLC.

Table 3

Recycling of ionic liquids (6 g) in the oxidation of adamantanone (8 mmol) in the presence of Oxone[®] (8 mmol) at 40 °C

Recycle of IL	bmimBF ₄		HmimOAc	
	Yield [%] ^a	Recovery of IL [%]	Yield [%] ^b	Recovery of IL [%]
Fresh, non-recycled IL	95	92	97	91
First	94	90	97	91
Second	93	91	97	90
Third	93	89	97	89

^a The reaction time 3 h.

^b The reaction time 5.5 h.

3. Conclusion

In summary, an efficient method for the synthesis of lactones and esters from the corresponding ketones was reported that utilizes Oxone[®] as the oxidant along with environmentally attractive ionic liquids. The use of Oxone[®]/ionic liquid system eliminates currently used solvents in BV reactions, such as dichloromethane, chloroform and acetonitrile.

Ionic liquids were selected and tested in the oxidation of cyclohexanone with Oxone[®] at 40 °C. Protic and aprotic ionic liquids were applied, that were mainly hydrophilic, with the exception of bmimNTf₂.

Several factors may influence the BV reaction using ionic liquids as the solvent, such as the partial solubility of KHSO₅ in ionic liquids and the possibility of acid catalysis of PILs. The viscosity of AILs ionic liquids can also influence the reaction rate. The most effective ionic liquids were bmimBF₄ and HmimOAc. These ionic liquids were then used for other lactone and ester synthesis, in which high yields (65–95%) were obtained. Additionally, ionic liquids were recycled three times in a model reaction without significant loss of

activity. In conclusion, the application of Oxone[®] and ionic liquids provide a novel way for Baeyer–Villiger reactions.

4. Experimental section

4.1. Materials

Ionic liquids: ECOENG500 (Merck), ECOENG212 (Merck), bmimOAc (Fluka), ketones and Oxone[®] (Acros Organics) were commercial materials; bmimBF₄¹⁶, bmimNTf₂¹⁴, HmimOAc, HmimBF₄, H2mpyrOAc¹¹ were prepared according to known procedures.

4.2. Typical procedure for BV oxidation with Oxone[®] in ionic liquid as the solvent

Oxone[®] (4.0 mmol) was added to a solution of ketone (4.0 mmol) in ionic liquid (3.0 g) and stirred at 40 °C for 2.5–20 h (depending on the reaction rate). The progress of the reaction was monitored by GC or HPLC. After this time, the post reaction mixture was dissolved in CH₂Cl₂ and filtered. Next, the filtrate was concentrated and extracted with the appropriate solvent of: ethyl acetate, diethyl or dibutyl ether (6×5 mL) and concentrated. The yields of lactones after the purification by column chromatography with hexane/ethyl acetate (4:1) as the eluent were 65–95%.

For HmimOAc (bp=240 °C; 70 °C/1.2 mbar) and H2mpyrOAc (bp=255 °C; 90 °C/1.2 mbar) distillation of the product or ionic liquid from the reaction mixture was performed.

4.3. Recycling of bmimBF₄ and HmimOAc

ILs were purified for recycling tests. After the filtration of post reaction mixture, and the extraction of the product with ethyl

acetate (bmimBF₄) or dibutyl ether (HmimOAc), ILs were concentrated, dried under vacuum (60 °C, 5 h) and reused.

4.4. Stability of Oxone[®]

A solution of Oxone[®] (0.63 g) in 0.7 g of IL was stirred for 5 h at 40 °C. After this time the content of KHSO₅ was determined by iodometric titration.

4.5. Solubility of Oxone[®]

Oxone[®] (4 g) was mixed with 5 g of IL and stirred for 1 h at room temperature. Next, CH₂Cl₂ was added to isolate the insoluble parts of Oxone[®] and to lower the viscosity. The mixture was filtered and the amount of KHSO₅ in the filtrate was determined by iodometric titration.

4.6. Analysis

All products were characterized by comparing their NMR spectra with these of authentic samples: δ-valerolactone, ε-caprolactone, 2-oxabicyclo[3.2.1]octan-3-one, 4-oxatricyclo [4.3.1.1^{3,8}]undecan-5-one, phenyl acetate, butyl acetate,^{4b} 6-methylcaprolactone,^{17a} 3,4-dihydrocoumarin,^{17b} 4-methoxyphenyl acetate, *tert*-butyl acetate, isopropyl acetate.^{17c}

¹H NMR and ¹³C NMR spectra were recorded at 300 MHz in CDCl₃ (Varian Unity Inova plus, internal TMS). GC analysis was performed using a Perkin–Elmer chromatograph and decane as the external standard. HPLC (Alliance, Waters 2690 system) was performed using a 2×150 mm column (Nova-Pak Silica, 60A, 4 μm) and a solvent system of hexane/2-propanol (95/5 v/v, flow rate 0.25 ml/min).

Acknowledgements

This work was financially supported by the Ministry of Science and Higher Education (Grant no N N209 149236).

Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.05.091.

References and notes

- Baeyer, A.; Villiger, V. *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3625–3633.
- (a) Krow, G. *Org. React.* **1993**, *43*, 251–798; (b) Renz, M.; Meunier, B. *Eur. J. Org. Chem.* **1999**, 737–750.
- (a) Strukul, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 1198–1209; (b) Brink, G.; Arends, I.; Sheldon, R. A. *Chem. Rev.* **2004**, *104*, 4105–4123.
- (a) Gonzalez-Nunez, M. E.; Mello, R.; Olmos, A.; Asensio, G. *J. Org. Chem.* **2005**, *70*, 10879–10882; (b) Gonzalez-Nunez, M. E.; Mello, R.; Olmos, A.; Asensio, G. *J. Org. Chem.* **2006**, *71*, 6432–6436.
- (a) Yang, D. *Acc. Chem. Res.* **2004**, *37*, 497–505; (b) Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031–1034.
- Wasserscheid, P.; Welton, T. *Ionic Liquids in Synthesis*; Wiley-VCH: Weinheim, 2007.
- (a) Gupta, N.; Sonu, K. G. L.; Singh, J. *Catal. Commun.* **2007**, *8*, 1323–1328; (b) Hajipour, A. R.; Rajaei, A.; Ruocho, A. E. *Tetrahedron Lett.* **2009**, *50*, 708–711; (c) Khosropour, A. R. *Can. J. Chem.* **2008**, *86*, 264–269; (d) Xu, D. Q.; Yang, W. L.; Luo, S. P.; Wang, B. T.; Wu, M.; Xu, Z. Y. *Eur. J. Org. Chem.* **2007**, 1007–1012; (e) Wang, W.; Cheng, W.; Shao, L.; Yang, J. *Catal. Lett.* **2008**, *121*, 77–80; (f) Du, Y.; Tian, F.; Zhao, W. *Synth. Commun.* **2006**, *36*, 1661–1669.
- (a) Baj, S.; Chrobok, A. *Synth. Commun.* **2008**, *38*, 1–7; (b) Baj, S.; Chrobok, A.; Stupska, R. *Green Chem.* **2009**, *11*, 279–282; (c) Chrobok, A.; Baj, S.; Pudlo, W.; Jarzebski, A. *Appl. Catal., A* **2009**, *366*, 22–28.
- Kennedy, R. J.; Stock, A. M. *J. Org. Chem.* **1960**, *25*, 1901–1906.
- Xu, W.; Cooper, E. I.; Angell, C. A. *J. Phys. Chem. B* **2003**, *107*, 6170–6178.
- Greaves, T. L.; Drummond, C. *J. Chem. Rev.* **2008**, *108*, 206–237.
- Kosmulski, M.; Marczewska-Boczkowska, K.; Zukowski, P.; Subocz, J.; Saneluta, C. *Croat. Chem. Acta* **2007**, *80*, 461–466.
- Crosthwaite, J. M.; Muldoon, M. J.; Dixon, J. K.; Anderson, J. L.; Brennecke, J. F. *J. Chem. Thermodyn.* **2005**, *37*, 559–568.
- Bonhote, P.; Dias, A. P.; Papageorgiou, N.; Kalyanasundaram, K.; Graetzel, M. *Inorg. Chem.* **1996**, *35*, 1168–1178.
- Gomez, E.; Gonzalez, B.; Calvar, N.; Tojo, E.; Dominguez, A. *J. Chem. Eng. Data* **2006**, *51*, 2096–2102.
- Shang, H.; Wu, J.; Zhou, Q.; Wang, L. *J. Chem. Eng. Data* **2006**, *51*, 1286–1288.
- (a) Jacobson, S. E.; Mares, F.; Zambri, P. M. *J. Am. Chem. Soc.* **1979**, *101*, 6938–6946; (b) Zeitler, K.; Rose, C. A. *J. Org. Chem.* **2009**, *74*, 1759–1762; (c) Spectral Database for Organic Compounds—internet site organized by National Institute of Advanced Industrial Science and Technology, Japan.