

University of Groningen

Ionic liquids for enhancing the enantioselectivity of isolated BVMO-catalysed oxidations

Rodriguez, Cristina; de Gonzalo, Gonzalo; Fraaije, Marco W.; Gotor, Vicente

Published in:
Green Chemistry

DOI:
[10.1039/c0gc00560f](https://doi.org/10.1039/c0gc00560f)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2010

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Rodriguez, C., de Gonzalo, G., Fraaije, M. W., & Gotor, V. (2010). Ionic liquids for enhancing the enantioselectivity of isolated BVMO-catalysed oxidations. *Green Chemistry*, 12(12), 2255-2260. <https://doi.org/10.1039/c0gc00560f>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Ionic liquids containing media for isolated BVMO-catalysed oxidations

Cristina Rodríguez,^a Gonzalo de Gonzalo,^a Marco W. Fraaije^b and Vicente Gotor^{*,a}

^a Departamento de Química Orgánica e Inorgánica, Instituto de Biotecnología de Asturias, Universidad de Oviedo, c/ Julián Clavería 8, 33006, Oviedo, Spain.

e-mail: ygs@fq.uniovi.es

^b Laboratory of Biochemistry, Groningen Biomolecular Sciences and Biotechnology Institute, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands.

Supporting Information

Contents

1. Experimental data.....	S2
2. Chromatographic data.....	S5

1. Experimental data.

1.1. Effect of different ILs in PAMO activity

The enzymatic activity was determined spectrophotometrically by monitoring NADPH consumption at 340 nm ($\epsilon_{340} = 6.22 \text{ mM}^{-1} \text{ cm}^{-1}$) using as the assay media Tris/HCl 50 mM pH 8.0 (pH 9.0 for [thma]MeSO₄) buffer / ionic liquid mixtures (1.0 mL), containing 1.0 mM phenylacetone **1a** (1% DMSO), 0.1 mM NADPH and 0.05 μM PAMO.

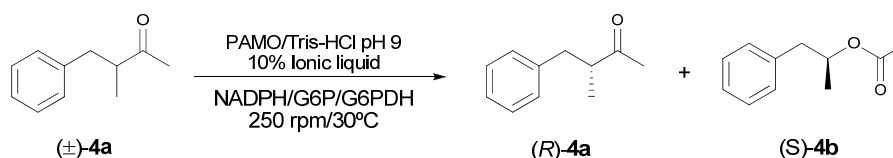
Table S1. Effect of ionic liquids in PAMO initial activity with **1a** as substrate.

Entry	Ionic Liquid	% IL	k_{obs} (s ⁻¹)	Rel. activity (%)
1	None	--	2.17	100
2	[thma]MeSO ₄	10	0.92	42
3	[thma]MeSO ₄	30	0.36	17
4	[tbma]MeSO ₄	10	0.87	40
5	[tbma]MeSO ₄	30	0.28	13
6	[bdmim]OTf	10	0.78	36
7	[bdmim]OTf	30	0.24	11
8	Ammonoeng TM 100	10	1.01	46
9	Ammonoeng TM 102	10	1.21	56
10	Ammonoeng TM 102	30	0.97	45

1.2. Effect of ILs in the enantioselectivity of PAMO.

In order to investigate the effect of the IL-containing media in the enantioselectivity of PAMO, the oxidations of (\pm)-3-methyl-4-phenylbutan-2-one [(\pm)-**4a**] (Table S1) and benzylketones aryl-substituted [(\pm)-**5a-7a**] (Table S2) were studied. Conversions and enantiomeric excesses of (*R*)-ketones and (*S*)-esters were determined by GC analysis.

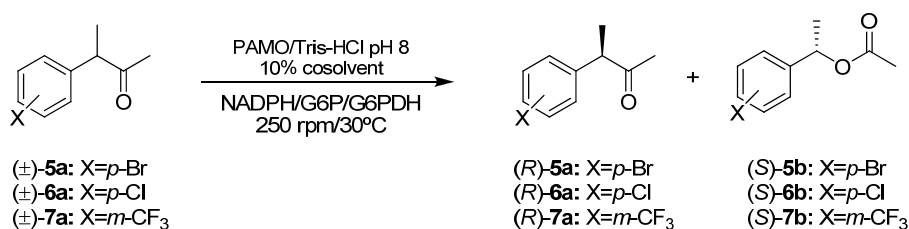
Table S2. Oxidation of (\pm)-**4a** catalysed by PAMO in presence of 10% (v v⁻¹) ILs.



Ionic liquid	t (h)	ee (<i>R</i>)- 4a (%) ^a	ee (<i>S</i>)- 4b (%) ^a	c (%) ^b	E ^b
None	3.5	99	79	56	42
[bmp]PF ₆	6	76	88	46	36
[bmim]PF ₆	6	17	95	14	48
[hmim] PF ₆	6	11	96	10	48
[bmim]BF ₄	6	10	94	10	35
[bmp]BF ₄	6	n.d.	n.d.	≤3	n.d.
[bdmim]OTf	6	16	96	14	52
[tbma]MeSO ₄	3.5	82	88	48	38
[thma]MeSO ₄	3.5	99	71	58	38
[tbmp]MeSO ₄	3.5	60	90	40	35
[bmim]MeSO ₄	3.5	49	98	33	129
[bmim]MeSO ₄	6	60	97	38	121
Ammoeng TM 100	6	16	98	14	105
Ammoeng TM 101	6	55	97	36	96
Ammoeng TM 102	6	31	98	24	111

n.d. not determined. ^a Measured by GC. ^b Conversion, $c = ee_s / (ee_s + ee_p)$. ^c Enantiomeric ratio, $E = \ln[ee_p(1 - ee_s) / (ee_s + ee_p)] / \ln[ee_p(1 + ee_s) / (ee_s + ee_p)]$.

Table S3. Oxidation of (±)-**5a-7a** catalysed by PAMO in presence of 10% (v v⁻¹) cosolvent.^a



Substrate	Cosolvent	t (h)	ee (<i>R</i>)-ketone (%) ^b	ee (<i>S</i>)-ester (%) ^b	c (%)	E
(±)- 5a	None	1	17	48	26	3
(±)- 5a	MeOH	1	22	73	23	8
(±)- 5a	Ammoeng TM 102	6	96	79	55	34
(±)- 6a	None	1	39	82	32	15
(±)- 6a	MeOH	1	31	88	26	21
(±)- 6a	Ammoeng TM 102	1	46	97	32	107
(±)- 7a	None	1	47	43	52	4
(±)- 7a	MeOH	1	42	52	45	5
(±)- 7a	Ammoeng TM 102	1	94	94	50	111

^a Reactions without the cosolvent were carried out at pH 8.0 and 20°C. ^b Measured by GC.

1.3. PAMO-biocatalysed oxidation in 10% AmmoengTM 102 at increasing concentrations of (±)-3-(*m*-trifluoromethylphenyl)-butan-2-one.

Increasing concentrations of racemic ketone (±)-**7a** (10-240 mM) were dissolved in 50 mM Tris/HCl pH 8.0 in the presence of 10% (v v⁻¹) AmmoengTM 102 (1.0 mL), containing glucose-6-phosphate, glucose-6-phosphate dehydrogenase, NADPH and PAMO. In order to compare the activity of the enzyme, the reaction rate (expressed as mmol of ketone per L of solution h⁻¹) was defined (Table S3).

Table S4. Oxidation of (±)-**7a** catalysed by PAMO in presence 10% (v/v) of AmmoengTM 102.

(±)- 7a (mM)	t (h)	<i>ee</i> (<i>R</i>)-ketone (%) ^a	<i>ee</i> (<i>S</i>)-ester (%) ^a	<i>c</i> (%) ^a	<i>E</i>	<i>v</i> (mmol L ⁻¹ h ⁻¹)
10	1	94	94	50	111	5.00
20	1.5	96	94	51	127	6.80
40	2	44	96	31	77	6.20
80	4	48	96	33	63	6.60
120	4	40	94	30	51	9.00
200	4	14	94	13	38	6.50
240	4	n.d.	n.d.	10	n.d.	6.00

n.d. not determined. ^a Measured by GC.

2. Chromatographic data

GC analyses were performed on a Hewlett Packard 6890 Series II chromatograph equipped with the following columns: Restek Rt β DEXse (30 m x 0.25 mm x 0.25 μ m, 1.0 bar N₂) for chiral determinations or a HP-1 cross-linked methyl siloxane (30 m x 0.32 mm x 0.25 μ m, 1.0 bar N₂) for measuring the conversion values (Table S4). For all the analyses, the injector temperature is 225°C and the FID temperature is 250°C.

Table S4. Determination of conversion and *ee* values by GC.

Compound	Program ^a	Column ^b	Retention times (min)
1a	70/7/10/90/0	A	6.0
1b	70/7/10/90/0	A	7.7
2a	140/0/2/200/0	B	14.0
2b	140/0/2/200/0	B	11.6 (<i>R</i>); 12.7 (<i>S</i>)
3	140/0/2/200/0	B	3.7
4a	90/30/5/120/10	B	46.9 (<i>R</i>); 48.5 (<i>S</i>)
4b	90/30/5/120/10	B	42.7 (<i>S</i>); 45.8 (<i>R</i>)
5a	100/5/1/150/5	B	56.6 (<i>R</i>); 58.2 (<i>S</i>)
5b	100/5/1/150/5	B	54.1 (<i>S</i>); 57.6 (<i>R</i>)
6a	110/10/1/140/0	B	37.4 (<i>R</i>); 39.0 (<i>S</i>)
6b	110/10/1/140/0	B	34.6 (<i>S</i>); 38.5 (<i>R</i>)
7a	100/20/2/150/0	B	21.7 (<i>R</i>); 23.7 (<i>S</i>)
7b	100/20/2/150/0	B	18.3 (<i>S</i>); 22.8 (<i>R</i>)

^a Program: initial T (°C)/ time (min)/ slope (°C/min)/ T (°C)/ time (min). ^b Column: A=> HP-1; B=> Restek Rt β DEXse.