Green photochemistry: photo-Friedel–Crafts acylations of 1,4-naphthoquinone in room temperature ionic liquids

Brian Murphy,[a] Peter Goodrich,[b] Christopher Hardacre[b] and Michael Oelgemöller*[a,c]

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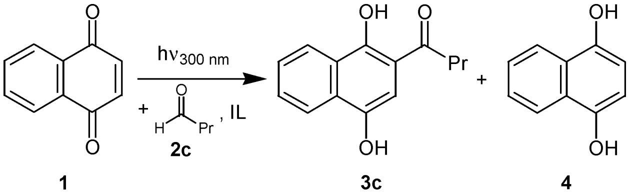
The photo-Friedel–Crafts acylation of 1,4-naphthoquinone with various aldehydes was investigated in a series of room temperature ionic liquids. High conversions and selectivities were achieved in $[C_2mim]^+$-based ionic liquids with the highest isolated yields found in $[C_2mim][NTf_2]$. The developed procedure allowed for a replacement of hazardous solvents such as benzene and acetonitrile which are commonly used for this transformation.

Introduction

Ionic liquids (ILs) have been intensively studied over the last decade as non-flammable and replacement solvents for molecular systems.[1] The ease of product removal allows an efficient reuse of the ILs and this property, coupled with the lack of vapour pressure, has the potential to result in materials which are much less environmentally intrusive than conventional organic solvents. However, recent studies on the toxicity of ionic liquids have raised some concerns regarding their broader use.[2] In addition to their physical properties, ionic liquids can stabilise a wide range of highly reactive species and through the ionic solvent–solute interactions can direct the chemistry.[3] For example, ionic liquids have been shown to stabilize radicals and radical ions in solution more efficiently than many conventional organic solvents.[4,5] This coupled with their weak or missing absorption of light above 300 nm makes them an ideal solvent for photochemical reactions.[6] Despite these advantages, photochemical transformations in ionic liquids are rare.[7] This is surprising since photochemistry itself is regarded as a 'green technology',[8] especially if conducted with sunlight.[9] However, photochemical transformations conventionally use solvents that are toxic and/or flammable.

Over the last years we have intensively studied the photochemical acylation of 1,4-quinones with aldehydes as a mild and atom efficient alternative to Friedel–Crafts acylations or (photo-)Fries-rearrangements.[10,11] The original procedure developed by Kraus and Kirihara involved the use of hazardous benzene or acetonitrile as solvents.[12] Supercritical carbon dioxide ($SC\text{-}CO_2$) has recently been reported as an alternative medium,[13] but this technique suffers from technical limitations, *e.g.* high pressure or small reactor volume, especially for a large-scale application. We have, therefore, investigated the photochemical acylation of 1,4-naphthoquinone in benzene and various room temperature ionic liquids, the latter either commercially available or readily synthesised by standard procedures.[1]

The photoacylation of 1,4-naphthoquinone (**1**) with butyraldehyde (**2c**) was initially chosen as a model reaction to determine the optimum cation/anion combination for the ionic liquid (Scheme 1). A mixture of 1,4-naphthoquinone and excess of butyraldehyde dissolved in the IL was irradiated for 16 h while stirring. After work-up the crude product was analyzed by ^{1}H-NMR spectroscopy.[14] The crude mixture generally consisted of unreacted 1,4-naphthoquinone (**1**), the desired photoacylation product (**3c**) and the reduction product 1,4-dihydroxynaphthalene (**4**). The ratio of these components critically depended on the structure of the ionic liquid employed (Table 1).



Scheme 1 Photoacylation of 1,4-naphthoquinone with butyraldehyde.

In many of the chosen ionic liquids the photoacylation product **3c** was formed in larger amounts than in the conventional solvent benzene. The best result was achieved in $[C_2mim][OTf]$ and **3c** was obtained in 91% yield without any photoreduction product (**4**) present. The photoreaction in $[C_2mim][NTf_2]$ also resulted in a high yield of **3c** at 81%; however, in this case, 1% of the photoreduction product (**4**) was formed as well. In both cases, the desired product **3c** was isolated by column chromatography.

For $[C_2mim][OTf]$, the isolated yield of **3c** was low with only 10% obtained following work-up. This low yield may be associated with the strong hydrogen bonding interaction of the substrate with the ionic liquid anion. On changing the anion from $[OTf]^-$ to $[NTf_2]^-$ the isolated yield of **3c** improved to 40% (49% based on the amount of **1** consumed). This is still only modest and reflects the strong affinity of aromatics and carbonyl

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[a] *School of Chemical Sciences and NCSR, Dublin City University, Glasnevin, Dublin 9, Ireland*
[b] *School of Chemistry and Chemical Engineering/QUILL, Queen's University, Belfast, Northern Ireland, UK BT9 5AG*
[c] *School of Pharmacy and Molecular Sciences, James Cook University, Townsville, Queensland, 4811, Australia.*
E-mail: oelgemoeller@jcu.edu.au; Fax: +61-7-4781-6078; Tel: +61-7-4781-4535

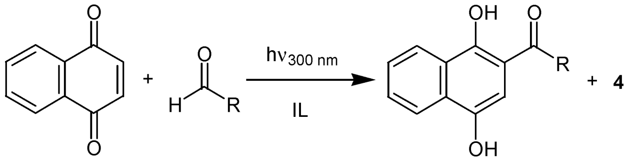
Table 1 Product compositions for photoacylations of **1** with **2c**

	Composition [%][b]		
Solvent[a]	**1**	**3c**	**4**
Benzene	49	44 (23[c]/45[d])	7
$[C_2mim][OTf]$	9	91 (10[c]/11[d])	—
$[C_2mim][NTf_2]$	18	81 (40[c]/49[d])	1
$[C_2mim][BF_4]$	58	42	—
$[C_4mim][NTf_2]$	29	25	46
$[C_6mim][PF_6]$	44	13	43
$[C_8mim][PF_6]$	39	10	51
$[C_4Py][NTf_2]$	24	75	1
$[C_4mPyrr][NTf_2]$	12	83	5

[a] $[C_nmim]^+$ = 1-alkyl-3-methylimidazolium, $[C_4Py]^+$ = 1-butyl-pyridinium, $[C_4mPyrr]^+$ = 1-butyl-1-methylpyrrolidinium, $[NTf_2]^-$ = bis-{(trifluoromethyl)sulfonyl}imide, $[OTf]^-$ = trifluoromethane sulfonate. [b] As determined by integration of characteristic peaks in the ^{1}H-NMR of the crude product. [c] Isolated yield. [d] Isolated yield based on conversion.

species in ionic liquids. Similarly poor isolation was found for other Friedel–Crafts processes.[15] On extending the alkyl length of the imidazolium side-chain, photoreduction to **4** increased with the largest yield of **4** (51%) found in $[C_8mim][PF_6]$. The influence of the anion on the photoacylation was studied using $[C_2mim]^+$-derived ionic liquids. The chemoselectivity remained high in all three cases studied; however, the conversion was significantly reduced in $[C_2mim][BF_4]$. This finding may be associated with the higher viscosity of the $[BF_4]^-$ based ionic liquid.[1c,16] The higher viscosity, and thus the reduced diffusion, hinders the necessary approach of the two reactants during the irradiation. It was also noticed that the $[PF_6]^-$ based ionic liquid was less favourable for the photoreaction and large amounts of the reduction product **4** were produced.

The photoacylation protocol was further applied to a range of aldehydes (Scheme 2). Due to the high selectivity obtained for the **1**/**2c** model pair in combination with the good isolated yield of **3c**, $[C_2mim][NTf_2]$ was selected as the ionic liquid for this study. For comparison, selected transformations were also studied in $[C_2mim][OTf]$.



1 **2** **3**

Scheme 2 Photoreaction of 1,4-naphthoquinone with various aldehydes.

The conversion rate was lower for long chain aldehydes (Table 2). With increasing chain-length of aliphatic aldehydes, a general increase in the photoreduction product **4** was also noticed.† This tendency may be best explained by the reduced solubility of long-chained aldehydes in the selected ionic liquids hence favouring hydrogen abstraction from the ionic liquid instead. A similar dependency of the outcome of a photoreaction on the solubility of the starting material in an ionic liquid has been reported for the attempted triplet-sensitised photolysis of myrcene.[17] Likewise, benzaldehyde and crotonaldehyde gave the desired acylated hydroquinones **3k** and **l** in moderate yields and selectivities.

Table 2 Product compositions for photoacylations of **1** with various aldehydes **2**

		Composition [%][a]					
		$[C_2mim][OTf]$			$[C_2mim][NTf_2]$		
Entry	R	**1**	**3**	**4**	**1**	**3**	**4**
a	CH_3	—[b]			25	70	5
b	C_2H_5	55	45	—	26	74	—
c	C_3H_7	9	91	—	18	81	1
d	C_4H_9	27	73	—	37	48	15
e	C_5H_{11}	—[b]			26	66	8
f	C_6H_{13}	30	70	—	35	47	18
g	C_7H_{15}	50	50	—	20	70	10
h	C_8H_{17}	39	56	5	69	23	8
i	$C_{10}H_{21}$	62	32	6	36	51	13
j	$C_{11}H_{23}$	—[b]			40	41	19
k	Ph	50	50	—	38	52	10
l	MeCH=CH	38	52	10	46	43	11

[a] As determined by integration of characteristic peaks in the ^{1}H-NMR spectrum of the crude product. [b] Not studied.

For recycling purposes, the purity of the ILs was investigated by NMR spectroscopy after irradiation and work-up.‡ Although the ^{1}H-NMR spectra of the recovered ILs did not reveal any significant changes, a strong yellow or brown colour often remained. Decolourisation was easily achieved by diluting the ionic liquid with methanol and stirring with activated charcoal. Subsequent filtration and removal of methanol gave almost entirely colourless ionic liquids. Experiments performed with recycled solvent showed no discernible loss in efficiency even after 3 cycles.

The mechanism of the photoacylation has been extensively studied by Bruce and Maruyama and both *in-cage* and *out-of-cage* scenarios have been described. Both mechanisms operate essentially simultaneously depending on the specific reaction conditions of the irradiation experiment, *i.e.* temperature, solvent, quinone/aldehyde applied.[10a] The photoaddition is initiated by hydrogen-abstraction from the aldehyde function to the triplet excited quinone (Scheme 3, path **A**). The higher viscosity of ionic liquids compared with conventional solvents may prevent separation of the intermediary radical pair by diffusion, thus favouring the *in-cage* mechanism. A similar assumption was also made for the photoreduction of benzophenones in ionic liquids.[18] Addition of the acyl radical to the delocalised semiquinone radical and subsequent tautomerisation yields the acylated hydroquinones **3**. For long alkyl-chain containing ionic liquids, which are highly viscous, hydrogen abstraction from the ionic liquid can operate the alternative pathway (path **B**) thus yielding the photoreduction product **4**. It is known that the triplet excited states of some molecules are capable

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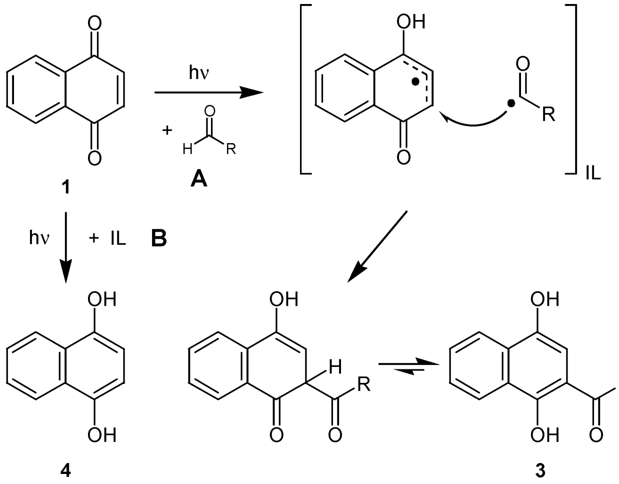
† In contrast, photoacylations in benzene give similar yields independent from the aldehyde.[11]

‡ For some common organic solvents, solvent recovery can be environmentally and economically harmful because of the large cumulative energy demand (CED) for the process.[22] However, the relatively high price for common ionic liquids may justify recovery and reuse.



Scheme 3 Mechanistic scenario for the photoacylation and -reduction.

of abstracting hydrogen atoms from the side-chains of ionic liquids.[19] The improved efficiency, *i.e.* higher conversion rates, of the photoacylation process in most ionic liquids may be best explained by an enhanced lifetime of the triplet exited state of the quinone as, for example, known for xanthone.[4]

In conclusion, the photoacylation of 1,4-naphthoquinone with a series of aldehydes has been carried out in ionic liquids. High conversions and chemoselectivities have been achieved in [C$_2$mim][OTf] and [C$_2$mim][NTf$_2$], respectively. The isolated yield of model compound **3c** was, however, better in [C$_2$mim][NTf$_2$]. The ionic liquids replaced previously used toxic solvents (benzene and acetonitrile) and, in comparison, showed increased activity and selectivity. In addition, the ionic liquid could be recovered and reused. Hence, this transformation can be regarded as a model reaction for 'Green Photochemistry'.[20] The simple protocol is currently being transferred to 'microphotochemistry', *i.e.* photochemical transformations in microstructured devices.[21]

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