



Catalytic Pauson–Khand reaction in ionic liquids

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Received 31 July 2003; accepted 17 November 2003

Abstract

Ionic liquids (ILs) are suitable media for the $\text{Co}_2(\text{CO})_8$ -catalysed intramolecular and intermolecular Pauson–Khand (PK) annelation, provided that the reaction is carried out under a CO pressure of 10 bar. Two diethyl allyl propargyl malonates were quantitatively converted into the relevant cyclopentenones, whereas heteroatom tethered enynes gave lower yields in their cyclocarbonylation products. A moderate yield in the corresponding Pauson–Khand product was obtained reacting phenylacetylene with norbornene.

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Keywords: Pauson–Khand reaction; Cyclocarbonylation; Ionic liquids; Cobalt

1. Introduction

The cyclization of an alkene and an alkyne with carbon monoxide, better known as the Pauson–Khand reaction (PKR) is one of the most powerful tools for the synthesis of cyclopentenones [1–3]. Since its serendipitous discovery in 1971 [4], several approaches have been developed to make the reaction more viable. A first milestone in this perspective has been posed by the discovery that the annelation, which in its first applications required stoichiometric amounts of dicobalt octacarbonyl, could be carried out under catalytic conditions [5]. Since then, a number of promoters (hard [6] and soft donors [7–10]) has been successfully employed aiming at carrying out the reaction under ambient conditions. Among the recent developments in this field we acknowledge the binding of the catalyst onto organic [11] or inorganic matrices [12,13] and the replacement of carbon monoxide by suitable aldehydes [14,15]. Notably, throughout the recent literature there is a rising interest for the use of alternative solvents such as water [16] and supercritical fluids [17] for stoichiometric and catalytic PKR.

Ionic liquids (ILs) have been emerging as a versatile class of solvents with many projected advantages compared with conventional media. Their non-volatility, for instance,

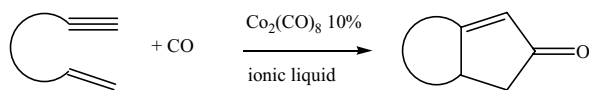
makes their use an intriguing alternative to volatile organic solvents. ILs are now being tested as solvents for a wide range of catalytic reactions [18–23]. Interesting results have been obtained especially in carbon–carbon bond forming reactions. Very recent studies include use of ILs as media for palladium-catalysed reactions [24–26], for radical C–C coupling promoted by Mn(III) [27] or Ce(IV) [28] reactions, as well as for radical copolymerization [29] and metal catalysed olefin oligomerization [30]. Intrigued by the interesting properties of ILs we have investigated C–C bond forming reactions in ILs focussing on the Rh(I) catalysed polymerization of phenylacetylene [31] and on the Michael addition reaction [32,33]. In this framework, we deemed it worthwhile to consider the catalytic PKR for its synthetic relevance. In the course of our investigation, the stoichiometric use of $\text{Co}_2(\text{CO})_8$ for the intermolecular thermal or amine oxide promoted PKR in the IL 1-butyl-2,3-dimethylimidazolium hexafluorophosphate ([bmim]PF₆) was reported [34]. Here, we describe the results of our studies on imidazolium-based ionic liquids as media for the $\text{Co}_2(\text{CO})_8$ catalysed PKR focusing our attention mainly on bifunctional enynes as substrates (Scheme 1).

2. Results and discussion

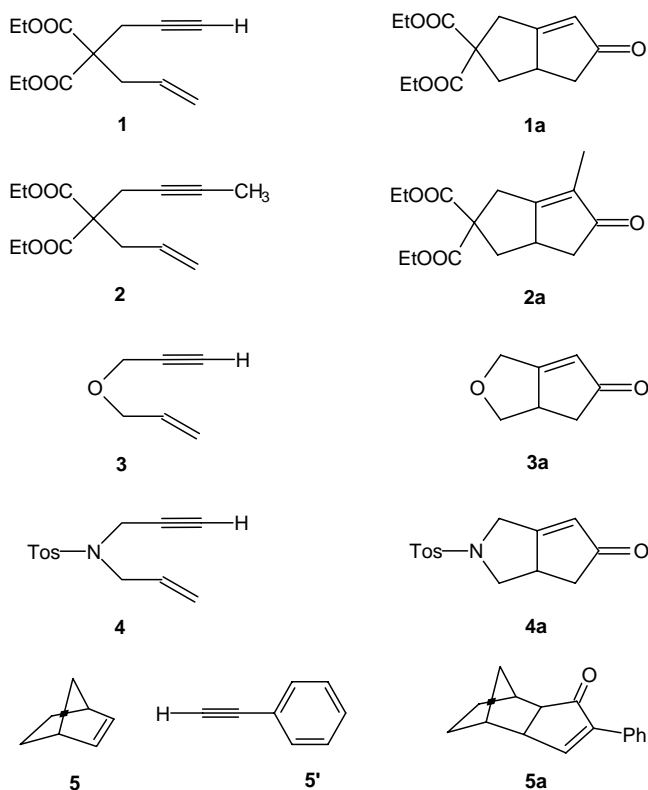
The results obtained in the PKR of substrate **1** in [bmim]PF₆ (Scheme 2) are reported in Table 1. Under the

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Scheme 1.



Scheme 2. Substrates chosen for catalytic PKR and relevant products.

specified conditions the substrate conversion was always quantitative.

In order to test the effect of the partial pressure of CO, two experiments were carried out on **1** using a substrate/ $\text{Co}_2(\text{CO})_8$ ratio of 1.0. The first test (entry 1) was carried out under 1 bar nitrogen, as is common for stoichiometric PKR. This resulted in a low selectivity towards the product (23% yield). The same reaction carried out under

Table 1
Pauson–Khand reaction of substrate **1** in [bmim]PF₆

Entry	$\text{Co}_2(\text{CO})_8/\text{substrate}$ (mol/mol)	P_{CO} (bar)	Time (h)	Yield (%)
1 ^a	1.0	–	1.0	23
2	1.0	1	1.0	45
3	1.0	10	1.5	85
4	0.10	1	24	25
5 ^b	0.10	1	24	37
6 ^c	0.10	1	2.5	34
7	0.10	3	1.5	43
8	0.10	10	1.5	90

Reaction conditions: $T = 80^\circ\text{C}$; $[\text{Co}_2(\text{CO})_8] = 0.025 \text{ mol/kg}$.

^a Reaction carried out under nitrogen.

^b Reaction carried out in [bmim]BF₄.

^c Reaction carried out in [bdmim]PF₆.

1 bar CO yielded 45% of **1a** pointing out the effect exerted by carbon monoxide in preventing catalyst deactivation [1]. This result prompted us to investigate the effect of CO pressure on the reaction course. Carrying out the stoichiometric reaction under 10 bar CO, a sensible increase in selectivity was observed as a 85% yield in **1a** was registered (entry 3).

Next, the reaction under catalytic conditions was investigated. Using a substrate/ $\text{Co}_2(\text{CO})_8$ ratio of 0.10 and a concentration of $[\text{Co}_2(\text{CO})_8]$ of 0.025 mol/kg under an atmosphere of carbon monoxide the reaction was slow and rather unselective, yielding 25% of **1a** after 24 h (entry 4). Using [bmim]BF₄ instead of [bmim]PF₆ had only a minor effect on the reaction course, leading to an isolated yield of 37% in **1a** (entry 5).

The reaction was carried out also in the IL 1-butyl-2,3-dimethylimidazolium hexafluorophosphate ([bdmim]PF₆), the analogous of [bmim]PF₆ in which the acidic proton on carbon 2 of the imidazolium ring is replaced by a methyl group. In this solvent the reaction was complete in only 2.5 h, although with unsatisfactory yield (34%, entry 6). The possible interaction of the acidic proton of the [bmim]⁺ with the catalyst can therefore be excluded as the cause of the low selectivity of the reaction at ambient CO pressure [35–37].

Raising the CO pressure to 3 bar in [bmim]PF₆ resulted in a selectivity enhancement (43%, entry 7) that was even higher when the reaction was carried out under 10 bar CO. In the latter conditions 90% yield in **1a** could be obtained (entry 8).

The attempts to lower the temperature and to reduce the amount of catalyst and/or of IL used were unsuccessful. At 50 °C the reaction proceeded more sluggishly yielding 25% of **1a** at 67% conversion after 18 h. At lower catalyst to substrate ratio (0.05) and 80 °C the yield and the conversion were both 20% after 1.5 h. The reaction was also carried out at a higher catalyst concentration (0.050 mol/kg) but, notwithstanding a 83% selectivity in **1a**, the conversion was only 40%.

To extend the scope of the reaction, other substrates (Scheme 2) were submitted to PKR under the conditions of entry 8. The relevant results are reported in Table 2.

The internal enyne **2** could be quantitatively converted into the corresponding PK product **2a** in 1.5 h (entry 1). Unfortunately under the conditions optimised for **1** and **2** the heteroatom bridged enynes bearing an ether (**3**) or an amide (**4**) tether gave less satisfactory yields in the relevant PK products (23% **3a** and 45% **4a**, entries 2 and 3).

Table 2
Catalytic Pauson–Khand reaction of substrates **2–5** in [bmim]PF₆

Entry	Substrate	Time (h)	Yield (%)
1	2	1.5	99
2	3	1.5	23
3	4	1.5	45
4	5 + 5'	39	47

Conditions: $[\text{Co}_2(\text{CO})_8] = 0.025 \text{ mol/kg}$; $\text{Co}_2(\text{CO})_8/\text{substrate} = 0.10 \text{ mol/mol}$; $T = 80^\circ\text{C}$; $P_{\text{CO}} = 10 \text{ bar}$.

Intermolecular PKR has also been investigated under these conditions: norbornene reacted with phenylacetylene under 10 bar CO yielding 47% of its PK product 2-phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methano-inden-1-one (**5a**) after 39 h (entry 4).

3. Experimental

Unless otherwise stated all manipulations were carried out under an inert atmosphere (dinitrogen) using standard Schlenk techniques. $\text{Co}_2(\text{CO})_8$ (stabilised with 1–5% hexane) was purchased from Strem Chemicals and used without further purification. The solvents were purified according to literature procedures [38]. Flash-chromatography was performed on silica gel MN Kieselgel 60 M. Gas chromatographic analyses were carried out on a HP-5890 instrument equipped with a SPB-1 dimethylpolysiloxane capillary column (30 m \times 320 μm \times 0.25 μm). The chloride residues of the ionic liquids were determined by potentiometric titration on water–IL mixtures using a Metrohm 716 DMS Titrimo instrument. The water content of the ionic liquids was determined by Karl–Fischer titration with Composite 5 solution as the titrant and anhydrous methanol as the solvent using a Metrohm 716 DMS Titrimo-703 stand instrument (instrumental detection limit = 0.018 mg/l).

3.1. Synthesis of solvents and substrates

1-*n*-Butyl-3-methylimidazolium chloride ([bmim]Cl) was synthesised according to the procedure of Rogers and co-workers [39] while 1-*n*-butyl-2,3-dimethylimidazolium chloride ([bdmim]Cl) was synthesised according to the procedure of Welton and co-workers [40] using *n*-butylchloride and 1-methylimidazole or 1,2-dimethylimidazole as reagents. Both salts were isolated as white solids by triple crystallisation from acetonitrile/ethyl acetate. The halogen metathesis leading to [bmim]BF₄ [33], [bmim]PF₆ and [bdmim]PF₆ [40] was performed according to literature procedures. Chlorides were removed from ILs by washing with water until the aqueous phase was found negative to the chloride test (AgNO₃). Water traces were eliminated by drying in vacuo at 60 °C for 10 h in the case of [bdmim]PF₆ or by azeotropic distillation with light petroleum ether and subsequent solvent evaporation. All ILs used for this study were obtained as colourless liquids; their IR and ¹H NMR spectra are in agreement with literature data. The solvents contained amounts of residual water ranging from 80 to 180 ppm for [bmim]PF₆ and [bdmim]PF₆, of about 460 ppm for [bmim]BF₄; potentiometric titration confirmed that residual chlorine amount in the ILs was below the detection limit of 0.38 mg/l.

Diethyl 6-hepten-1-yne-4,4-dicarboxylate (**1**), diethyl 7-octen-2-yne-5,5-dicarboxylate (**2**), allyl propargyl ether (**3**), *N*-allyl-*N*-propargyl-4-methylphenylsulfonamide (**4**) were synthesised according to literature procedures [41,42].

3.2. Catalytic runs

For experiments at ambient pressure, a 100 ml flask equipped with a rubber septum was charged with $\text{Co}_2(\text{CO})_8$ (18.52 mg, 0.054 mmol), diethyl 6-hepten-1-yne-4,4-dicarboxylate (**1**) (128 mg, 0.54 mmol) and the relevant IL (2.162 g). The resulting suspension¹ was quickly purged with CO, then heated to the desired temperature and stirred vigorously. Substrate consumption was monitored by GLC after sampling 200 μl of the reaction mixture with a syringe and extracting the organic phase with diethylether. Upon completion of the reaction the organic products were extracted with diethyl ether (20 \times 5 ml)² and filtered through a short column of silica gel to remove traces of the IL; the solvent was removed in vacuo and the yield determined by GLC on the crude mixture using *n*-dodecane as internal standard. Comparison of MS, ¹H and ¹³C{¹H} NMR spectra with those of authentic samples confirmed the obtainment of the product diethyl 7-oxobicyclo[3.3.0]oct-1(8)-ene-3,3-dicarboxylate (**1a**) after flash-chromatography purification (vide infra).

For reactions carried out at higher CO pressures, analogous quantities of $\text{Co}_2(\text{CO})_8$, substrate, and ionic liquid were added to a glass inlet which was transferred to a stainless steel autoclave under nitrogen stream; the autoclave was quickly purged with CO, pressurised with CO, heated to the desired temperature and the reaction mixture vigorously stirred. Upon reaction completion the organic products were extracted as previously specified and the yield assigned either by GLC (internal standard method, *n*-dodecane) or by flash-chromatography purification.

3.3. Details for product isolation

Diethyl 7-oxobicyclo[3.3.0]oct-1(8)-ene-3,3-dicarboxylate (**1a**) and diethyl 8-methyl-7-oxobicyclo[3.3.0]oct-1(8)-ene-3,3-dicarboxylate (**2a**): flash-chromatography on silica gel, diethyl ether/petroleum ether 40–60 °C = 3/4; 3a,4-dihydro-1H,3H-cyclopenta[c]furan-5-one (**3a**) and 2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**4a**): preparative TLC (silica) ethyl acetate/*n*-hexane = 1/4; 2-phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methano-inden-1-one (**5a**): preparative TLC (silica), ethyl acetate/*n*-hexane = 1/9.

Acknowledgements

Dr. Giuseppe Romanazzi, Dr. Vito Gallo and Dr. Nicola Taccardi are gratefully acknowledged for kind help. The

¹ The attempts to solubilise $\text{Co}_2(\text{CO})_8$ by stirring the reaction mixture at room temperature for up to 24 h led to unreproducibility of the results, probably due to partial deactivation of the catalyst.

² Recycling of the catalytic system was not performed because severe cobalt leaching occurs during product isolation from the IL phase.

Polytechnic of Bari is gratefully acknowledged for financial support (Fondi di Ricerca di Ateneo).

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