NJC



View Article Online

LETTER



Cite this: DOI: 10.1039/c4nj02076f

Received (in Porto Alegre, Brazil) 18th November 2014, Accepted 15th January 2015

DOI: 10.1039/c4nj02076f

www.rsc.org/njc

Versatile O- and S-functionalized 1,2,3triazoliums: ionic liquids for the Baylis–Hillman reaction and ligand precursors for stable MIC-transition metal complexes[†]

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The efficient synthesis of O- and S-functionalized 1,2,3-triazoliums is reported. Owing to their physical properties, these cations are efficient ionic liquids for Baylis–Hillman addition under mild reaction conditions. Simultaneously, the functionalization of the triazolium rings allows for the *in situ* C-5 metallation providing air stable triazol-5-ylidene Rh(I) Au(I), and Pd(II) complexes. The present work constitutes a rare example of versatile triazolium salts capable of serving in two unrelated synthetic procedures.

1,2,3-Triazolium salts are an important class of frameworks in organic chemistry. The convenient access to 1,2,3-triazole precursors via the Cu(1)-catalyzed azide-alkyne process (CuAAC) and their relatively easy N-alkylation has resulted in the modular synthesis of a wide library of functionalized triazolium cations.¹ Although the most recognized uses of these derivatives include organocatalysis,² molecular machines and supramolecular chemistry,³ their application as ionic liquids (ILs),^{1,4} and as ligand precursors for mesoionic carbene (MIC) complexes has been recently discovered.⁵ According to a specific process, the triazolium moiety can be designed to feature key characteristics such as flexibility, hydrophilicity, aromaticity, acidity, etc. For instance, asymmetric organocatalysts based on triazoliums require a chiral moiety,^{1b,c,6} whilst MIC precursors in most cases contain rigid structures with voluminous substituents next to the carbene center.⁵ Despite all the advantages in the design of triazolium cations, once their functionalization has been directed to a specific process, their possible use in another non-related practice is deterred. Interested in the design and preparation of multifunctional triazole based molecules, we report

^b Departamento de Química, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Apartado Postal 14-740, 07000 México D.F., Mexico herein the synthesis of *O*- and *S*-functionalized 1,2,3-triazoliums which are efficient ionic liquids for the Baylis–Hillman reaction and additionally tolerate the selective metallation at the C-5 position providing highly stable triazol-5-ylidene rhodium(i), gold(i) and palladium(ii) complexes. To our knowledge, this work represents a rare demonstration of single triazolium salts successfully applied in two unrelated synthetic procedures.

The synthesis of triazoliums I and II comprises two main steps namely the CuAAC of the benzyloxy- and thiophenoxyalkynes with sodium azide (in the presence of 4-chlorobenzyl chloride) to produce the respective 1,2,3-triazoles,⁷ followed by *N*-alkylation with methyl iodide (Scheme 1). After column chromatography purification, the triazolium salts I and II were obtained as air and moisture stable yellow liquids in high yields (90–94%). Interestingly, I and II slowly (one week) solidified as waxy materials and melted at 35 and 53 °C, respectively. After they melted, they remained as liquids for several days.⁸ The new cations are highly soluble in most halogenated solvents, acetonitrile and THF, and they are immiscible in aliphatic derivatives and water.

The application of ILs as "green" solvents has increased interest in both academia and industry. Their unique properties such as low melting points, viscosity and solubility, open a great deal of opportunities in many synthetic procedures with great potential of substituting the commonly used volatile organic solvents.⁹ During the last decade, most of the research



Scheme 1 Synthesis of triazolium salts I and II.

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[†] Electronic supplementary information (ESI) available: Details of experimental procedures, spectroscopic characterization, and ¹H and ¹³C NMR spectra of new compounds. See DOI: 10.1039/c4nj02076f



Fig. 1 Ionic liquids based on 1,2,3-triazole scaffolds

in ionic liquids has been conquered by imidazolium salts with successful application in several fields.¹⁰ However, in basic media, the acidic C-2 proton of the imidazolium cation can be removed and the so obtained carbene derivative inhibits transformations such as Claisen–Schmidth and Knoevenagel condensations, and the Baylis–Hillman reaction.¹¹

To date, very few examples of the application of 1,2,3triazolium salts as ionic liquids have been known. For instance, Ryu and coworkers reported that C-4 and C-5 unsubstituted ionic liquid (**A**) were efficient solvent media for the Baylis– Hillman reaction showing improved yields when compared to ILs based on imidazolium systems.¹² This positive effect on the conversion to Baylis–Hillman products has been attributed to the stabilization of zwitterionic intermediates generated from the Michael addition of a nucleophilic Lewis base to an activated alkene.¹³ As the intermediate can be maintained in high concentration in the IL, the attack on the aldehyde can be accelerated.¹⁴ In addition to (**A**), bicyclic (**B**)¹⁵ and spiro triazolium cations (**C**)¹⁶ showed their potential as inert media for natural product synthesis and asymmetric catalysis, respectively (Fig. 1).

Driven by the physical nature of **I** and **II** and their structural similitude to ionic liquid **A**, we decided to test the efficiency of our new triazolium salts in the addition of benzaldehyde to methyl acrylate (MA) in the presence of DABCO. To ensure the liquid state of the triazolium salts in the Baylis–Hillman reaction, we exclusively used freshly prepared (or just melted) **I** and **II** in the reaction tests. The initial results displayed in Table 1 indicate that the yields of the addition product are similar to those obtained under the same reaction conditions employed by Ryu¹² and coworkers (entries 1–3). Encouraged by

Table 1	able 1 Screening trials of ILs in the Baylis-Hillman reaction				
ĺ		H + 0-	- DABCO	OH	<u>й</u> о-
Entry	IL	MA (eq.)	DABCO (eq.)	Yield ^a (%)	Temp. (°C)
1	Α	2.0	2.0	81	25
2	Ι	2.0	2.0	87	25
3	Π	2.0	2.0	83	25
4	Ι	1.5	1.5	85	25
5	II	1.5	1.5	80	25
6	I	1.2	1.2	85	25
7	II	1.2	1.2	79	25
8	Α	2.0	2.0	83	40
9	Ι	1.2	1.2	87	40
10	II	1.2	1.2	80	40
11	Ι	1.2	1.2	89	60
12	Π	1.2	1.2	83	60

Reaction conditions: benzaldehyde (1.0 mmol), IL (100 mg), 24 h. a Isolated yields.

Table 2	Baylis-Hillman reaction of various aldehydes with methyl acrylate in
the prese	ence of IL (I)

	R H + 0−			-
Entry	RCHO	Product	Yield ^a (%)	Time (h)
1	H (a)	1a	85	20
2	CI H (b)	1b	98	20
3	O ₂ N (C)	1c	85	0.3
4	Ph (d)	1d	81	12
5	H (e)	1e	77	16
6	MeO MeO MeO OMe (f)	1f	83	60
7) H (g)	1g	95	1.5

Reaction conditions: aldehyde (1.0 mmol), MA (1.2 mmol), DABCO (1.2 mmol), I (100 mg), room temperature. Reaction times assigned as maximum conversion to the product was reached. ^{*a*} Isolated yields.

these successful results, we further demonstrate that only 1.2 equivalents of MA and DABCO delivered the Baylis–Hillman addition products in high yields without the need of time increase (entries 4–7). As a final screening test, we carried out the addition reaction at 40 and 60 °C (above melting point temperatures for I and II, respectively) observing that no significant improvement in the isolated yields is achieved (entries 8–12). Furthermore, it is noticeable that triazolium salt I which features a more flexible C4-moiety (ArCH₂O–) than II (ArS–) provided the best yields of the series.

Established by the screening data, we extended the reaction scope by treating a series of *p*-substituted benzaldehydes and aliphatic aldehydes in the presence of IL (I). As observed in Table 2, most of the addition reactions proceeded smoothly under mild reaction conditions. Not surprisingly, those substrates containing electron withdrawing groups (*p*-NO₂ and *p*-CN) underwent faster reaction rates providing high yields (95–98%), whilst less activated substrates such as isobutyraldehyde or 3,4,5-trimethoxybenzaldehyde registered the lower performances of the series (yields of 77–83%).

To get more insight in the potential of IL (I) in the Baylis– Hillman reaction, we explored next effects such as sterics and electronics in the Michael acceptor. Thus, we carried out the addition of aldehydes to the bulkier *tert*-butyl acrylate (${}^{t}BuA$)

Table 3 Baylis–Hillman reaction of various aldehydes with tert-butyl acrylate ('BuA) in the presence of IL (I)

	R H +			∞-{
Entry	RCHO	Product	Yield ^a (%)	Time (h)
1	a	2a	83	24
2	b	2b	93	24
3	с	2c	86	2.5
4	d	2d	86	18
5	e	2e	72	20
6	f	2f	80	72
7	g	2g	84	3.5

Reaction conditions: aldehyde (1.0 mmol), ^{*t*}BuA (2.0 mmol), DABCO (2.0 mmol), **I** (100 mg), room temperature. Reaction times assigned as maximum conversion to the product was reached. ^{*a*} Isolated yields.

Table 4 Baylis–Hillman reaction of various aldehydes with acrylonitrile (AN) in the presence of IL (I)

	RH +	CN DAB		
Entry	RCHO	Product	Yield ^a (%)	Time (h)
1	a	3a	96	12
2	b	3b	99	2.5
3	с	3c	94	0.2
4	d	3d	92	6
5	e	3e	86	10
6	f	3f	81	4
7	g	3g	98	0.1

Reaction conditions: aldehyde (1.0 mmol), AN (1.2 mmol), DABCO (1.2 mmol), I (100 mg), room temperature. Reaction times assigned as maximum conversion to the product was reached. ^a Isolated yields.

and then to acrylonitrile (AN). The results are presented in Tables 3 and 4, respectively.

Compared to methyl acrylate, the formation of the respective adducts with the *tert*-butyl analogue requires two equivalents of DABCO, two equivalents of the Michael acceptor, and longer reaction times in most cases. Although the yields under these optimized conditions are not low, the hindrance effect of the bulky *tert*-butyl group is easily noticeable. In contrast, reaction with the smaller and highly activated acrylonitrile delivers products in high yields (81–99%) and shorter reaction times, regardless of the substrate (Table 4).

Acknowledging their chemical stability, negligible vapor pressure, and high polarity, ionic liquids are prone to be reused after an appropriate recovery process. Consequently, we tested the recyclability of IL (I) in the addition of *p*-cyanobenzaldehyde to acrylonitrile. After the first run under the optimal reaction conditions and product isolation (Table 4, entry 7), the ionic liquid was easily recovered by column chromatography using a DCM/ethanol (97:3) eluent mixture. The recovered IL (I) displayed high purity by ¹H and ¹³C NMR spectroscopy and conserved its original appearance. A second batch of *p*-cyanobenzaldehyde with acrylonitrile in the presence of DABCO was added to the recovered IL (I) and after work up and isolation, no change in the yield or reaction time was observed. The process could be repeated for at least three more times with no significant loss in the yield (96–98%).

Overall, the results displayed by IL (I) in the Baylis–Hillman reaction are comparable to those observed with the previously reported ionic liquid **A**. However, it is important to remark that in contrast to IL (I) (which contains an iodine counter ion), IL **A** required previous exchange from iodine to a bigger counter ion (NTf₂ or PF₆) to execute the addition under optimal conditions. Additionally, the fact that only 1.2 equivalents of DABCO are enough for optimal reaction conditions makes the recyclability of (I) an easy task as the contamination with base excess is avoided.

Interested in the further application of the new ILs, we noticed that I and II possessed a single acidic proton at position C-5. The latter feature, which is observed in most MIC precursors together with the presence of aromatic rings at N-1 and the heteroatom availability at C-4, provided a suitable environment for the selective deprotonation and the subsequent generation of 1,2,3-triazol-5-ylidene ligands. To test the suitability of I and II as precursors for 1,2,3-triazol-5-ylidenes, the treatment of the cationic salts with equimolar amounts of KHMDS was carried out in THF at -78 °C. After work up, the expected mesoionic carbenes were not isolated due to their fast decomposition in solution.

As no free ligand could be obtained, we proceeded then to an in situ metallation process. The one pot reaction of precursors I and II with KHMDS (or KO^tBu) and half 0.5 equivalents of [Pd(allyl)Cl]₂ or [Rh(COD)Cl]₂ in THF provided readily the transition metal complexes 4a-b and 5a-b in high yields (93-95%, Scheme 2). The presence of the MIC complexes was corroborated in ¹H NMR spectroscopy by the disappearance of the acidic proton observed in the triazolium precursors at 9.00 and 9.02 ppm for I and II, respectively. Additionally, when equimolar amounts of KHMDS and AuCl(SMe2) were reacted with precursors I and II, the respective gold(1) complexes 6 and 7 were obtained in 89 and 92% yields (Scheme 2) as white solids. The presence of sharp peaks for all the methylene groups (equivalent protons) in 6 and 7 suggests the lack of coordination through the thio- or ether moieties, and confirms the usual linear geometry around the gold center.¹⁷ The ¹³C NMR chemical shifts of the carbon of Pd^{II} (165.2 and 166.1 ppm), Au^I (169.9 and 170.2 ppm), and Rh^I (doublets at 171.5 and 174.0 ppm)



Scheme 2 Synthesis of metal complexes 4a-b, 5a-b, 6 and 7.



Scheme 3 Synthesis of dicarbonyl rhodium(I) complexes 8 and 9

Table 5 α-Arylation of propiophenone with aryl bromides

	+ Ar-Br	ICat 3%mol] NaO'Bu	Ar
Entry	Ar	Cat.	Yield ^a (%)
1	Ph	4a	87
2	Ph	5a	85
3	$(4-Me)C_6H_4$	4a	82
4	$(4-Me)C_6H_4$	5a	83
5	$(4-CN)C_6CH_4$	4a	90
6	$(4-CN)C_6CH_4$	5a	88
7	$(4-MeO)C_6H_4$	4a	85
8	$(4-MeO)C_6H_4$	5a	86
9	$(4-NO_2)C_6H_4$	4a	81
10	$(4-NO_2)C_6H_4$	5a	83

Reaction conditions: 1 mmol propiophenone, 1.1 mmol arylbromide, 1.5 mmol NaO'Bu, 5 mL THF, 80 $^{\circ}$ C, 3 h. ^{*a*} Isolated yields.

complexes are in the range observed for previously reported metal complexes containing MIC ligands,¹⁷ and as expected, in much higher fields compared to classical NHC analogues.¹⁸

To evaluate the donor properties of the new triazol-5-ylidene ligands, the corresponding rhodium(i) dicarbonyl chloride complexes **8** and **9** were synthesized by the treatment of complexes **4b** and **5b** with an excess of carbon monoxide in dichloromethane (Scheme 3). Complexes **8** and **9** display in ¹³C NMR spectroscopy two new pairs of two doublets in the range of 180.6–186.6 ppm (J = 53 and 79 Hz average), indicating the complete cyclooctadiene removal and the *cis* arrangement of the CO ligands around the tetracoordinated metal center.

The chemical shift of the MIC-rhodium peaks in the carbonylated complexes moved upfield (~160 ppm) in comparison to the cyclooctadiene precursors (~173 ppm), due to the more electron poor nature of the carbonylated metal center. The average CO vibration frequency for 8 and 9 (v_{av} = 2027 cm⁻¹) indicates that the electron donor capacity of the new triazol-5-ylidenes is superior to those of conventional NHCs (v_{av} = 2039–2041 cm⁻¹)¹⁹ and cyclic (alkyl)(amino) carbenes (v_{av} = 2036 cm⁻¹),²⁰ but inferior to those for previously reported MIC ligands (v_{av} = 2016–2025 cm⁻¹).²¹

To preliminary test the catalytic performance of the new MIC complexes, we used the palladium derivatives **4a** and **5a** in the alpha arylation of propiophenone. As observed in Table 5, both complexes display efficient conversions to the coupled products in short periods of time and low catalyst loadings.

In summary, we have provided easy access to 1,2,3-triazolium salts which are efficient ionic liquids for the Baylis–Hillman addition and suitable precursors for transition metal triazol-5ylidene complexes. Remarkably, all new MIC-complexes feature melting points lower than 100 °C, which makes them interesting precursors for processes such as chemical vapor depositions or metallic based ionic liquids. Research on further applications and expansion of the class of bifunctional triazolium cations are underway in our laboratory.

Acknowledgements

We are grateful to Consejo Nacional de Ciencia y Tecnología, CONACyT (project 181448). DME, GNS, RGO, and RS wish to acknowledge the SNI for the distinction and the stipend received.

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