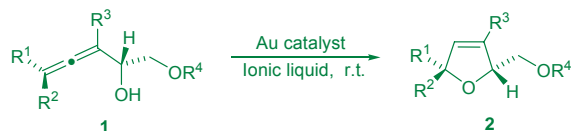


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PURPOSE

Development of **inexpensive**, **recyclable** gold catalysts and **environmentally benign systems** for the synthesis of heterocycles via cyclization of α -heteroallenes.



Scheme 1. Gold-catalyzed cycloisomerization of functionalized α -hydroxyallenes **1** to 2,5-dihydrofurans **2**.

INTRODUCTION

2,5-Dihydrofurans...

are structural subunits that are frequent in a wide variety of natural products which find application as pharmaceuticals, flavor and fragrance compounds.¹

can be synthesized by gold-catalyzed cycloisomerization of α -hydroxyallenes, a method that was extended to the cyclization of α -thioallenes, β -hydroxyallenes and α -/ β -aminoallenes to the corresponding 5- or 6-membered S-, O- or N- heterocycles.²

Ionic liquids...

are salts with ions are poorly coordinated, which are being liquid <100°C, or even at RT (room temperature ionic liquids, RTIL's).

Cations can be imidazolium, pyridinium, ammonium or phosphonium ions. Anions can be halide, inorganic (BF₄⁻, PF₆⁻) or organic anions (tosylate, triflate, formate, alkylsulfate, alkylphosphate).

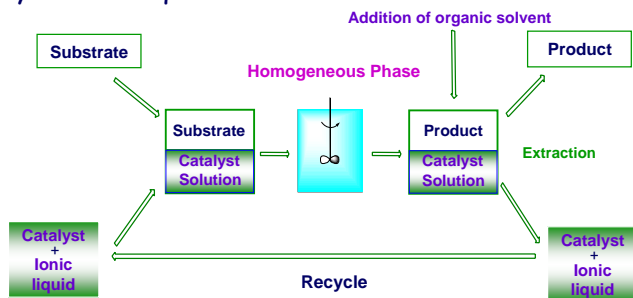
Ionic liquids are an alternative solvent for recyclable and sustainable catalyst systems.^{3,4}

Why Ionic Liquids?

- Due to their peculiar characteristics:
 - High electrochemical stability,
 - Repeated use of the metal catalyst solution and negligible metal contamination of the product,
 - High thermal stability,
 - Extremely low volatility,
 - Remarkable dissolution properties for organic and inorganic materials.

EXPERIMENTAL STRATEGY

Catalysis in Ionic liquids



RESULTS AND DISCUSSION

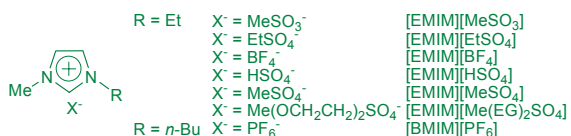


Figure 1. Imidazolium-based ionic liquids employed as solvent.

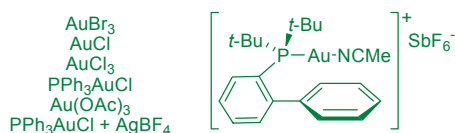
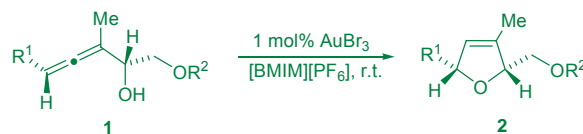


Figure 2. Gold sources employed as catalyst.

In all cases, complete conversion of the allene was achieved. Generally, alkyl-substituted α -hydroxyallenes (Table 1, entries 1-12, 17-20) react faster and afford higher yields than aryl-substituted substrates (entries 13-16).⁵

Table 1. Cycloisomerization of α -hydroxyallenes **1** with AuBr₃ in [BMIM][PF₆].^[a]



Entry	Run	R ¹	R ²	Time	Isolated Yield [%]
1	1	Me	TBS	10 min	84
2	2	Me	TBS	3 h	74
3	3	Me	TBS	3 h	81
4	4	Me	TBS	3 h	84
5	5	Me	TBS	3 h	84
6	1	<i>n</i> -Bu	TBS	10 min	75
7	2	<i>n</i> -Bu	TBS	18 h	76
8	1	<i>i</i> -Pr	TBS	10 min	75
9	2	<i>i</i> -Pr	TBS	22 h	77
10	3	<i>i</i> -Pr	TBS	22 h	78
11	1	<i>t</i> -Bu	TBS	10 min	79
12	2	<i>t</i> -Bu	TBS	24 h	65
13 ^[b,c]	1	Ph	TBS	4 h	50
14 ^[b,c]	2	Ph	TBS	6 h	45
15 ^[b,c]	1	2-MeOC ₆ H ₄	TBS	3 h	65
16 ^[b,c]	2	2-MeOC ₆ H ₄	TBS	8 h	54
17	1	Me	Bn	30 min	88
18	2	Me	Bn	30 min	89
19	1	Me	Bn	30 min	87
20	2	Me	Bn	30 min	86

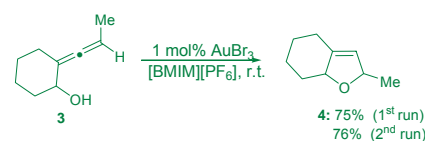
^[a] The reaction was carried out using 0.5 mmol of **1** and 1 mol% of the precatalyst in 1.0 mL of [BMIM][PF₆] at r.t. under argon. The yield was determined after extraction of the reaction mixture with dry hexane. All reactions took place with complete axis-to-center chirality transfer.

^[b] 0.25 mmol allene and 2.5 mol% AuBr₃ were used.

^[c] The bis-TBS ether formed by silyl transfer to the hydroxy group of substrate **1** was isolated as side product.

Interestingly, changing the TBS protecting group to a benzyl group resulted in high product yields without the drop in reactivity after the first run that is typical for TBS ethers (entries 17-20 vs. 1-5). The catalyst system is so stable that high yields and reactivities are observed even after exposure to air for several days (entries 19 and 20).

The reliability of the gold-catalyzed cycloisomerization using the AuBr₃/[BMIM][PF₆] system was also demonstrated for the exocyclic α -hydroxyallene **3** (Scheme 2). This difficult-to-cyclize substrate afforded the desired bicyclic 2,5-dihydrofuran **4**.



Scheme 2. Cycloisomerization of α -hydroxyallene **3** catalyzed by AuBr₃ in [BMIM][PF₆].

Finally, we tested our system for metal leaching which is one of the most important criteria for recyclable catalysts. Analysis of the hexane extracts obtained in the cyclization (Table 1, entries 1-5) by ICP-MS revealed gold contents ranging from 31-318 ppb over five runs. The highest gold loss was determined in the first run; together with the decrease of reactivity after the first run (entry 2 vs. 1), this indicates a partial removal of catalytically gold species by the extraction.

CONCLUSION

We have demonstrated that ionic liquids are highly suitable reaction media for the gold-catalyzed cycloisomerization of α -hydroxyallenes to 2,5-dihydrofurans. Nine α -hydroxyallenes **1/3** were cyclized to the corresponding 2,5-dihydrofurans **2/4** with complete axis-to-center chirality transfer in the presence of 1 mol% of AuBr₃ using [BMIM][PF₆] as solvent at room temperature. The gold catalyst/ionic liquid system is air-stable and recyclable. The leaching of the gold catalyst upon extraction of the product is extremely low (0.03% after five runs).

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