Heterogeneous Olefin Aziridination Reactions Catalyzed by Polymer-Bound Tris(triazolyl)methane Copper Complexes

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Efficient olefin aziridination has been achieved with a tris(triazolyl)methane copper catalyst supported onto polystyrene.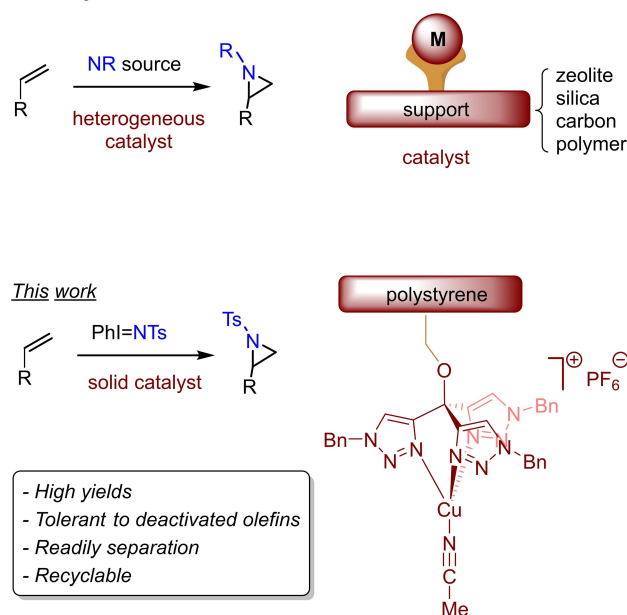 Aryl, alkyl and methoxycarbonyl-substituted olefins are converted into N-tosylaziridines in good to high yields. The solid catalyst is readily separated by filtration and recycled, allowing its reuse with no significant loss of the catalytic activity.

Introduction

Catalytic olefin aziridination constitutes a powerful tool for the generation of carbon-nitrogen bonds from an array of available alkenes, the reported catalytic systems allowing the achievement of quantitative yields as well as excellent diastereo- and/or enantioselectivities.[1] First developed as soluble catalysts, the need of a readily separation from reactants/products led to the use of their heterogeneous counterparts, with a significant degree of success. Several supports have been employed to anchor the molecular catalysts (Scheme 1), such as zeolites,[2] silica[3] or carbon, either amorphous[4] or as nanotubes.[5] Interestingly, the fixation of such catalysts onto polymeric materials is rare. To the best of our knowledge, the use of polymeric supports for the olefin aziridination reaction is limited to a ruthenium-based system reported by Gallo[6] and a copper-based system previously described by Albeniz and our group.[7]

We have previously described[8] the use of polystyrene-linked tris(triazolyl)methane copper(I) cationic catalysts for the transfer of

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Scheme 1. The heterogeneous olefin aziridination reaction.

carbene units from diazo compounds to several saturated and unsaturated substrates in batch and flow. Herein we report that a Cu(I) complex attached to polystyrene catalyzes the transfer of the NTs (Ts=p-toluenesulfonyl) group from PhI=NTs to olefins bearing aryl, alkyl or carboxyl substituents, in good to high yields and with acceptable ratios of recovery and recycling.

Results and Discussion

The soluble catalyst

In our previous work on carbene transfer reactions[8] we employed a polystyrene-supported copper complex bearing a tris(triazolyl)methane (TTM) ligand.[9] The metal complex was cationic in nature, an acetonitrile ligand completing the coordination sphere, and PF_6 acting as the counterion (Scheme 1). Since we have now targeted

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such material as catalyst for olefin aziridination reactions, the catalytic capabilities of the molecular catalyst, i.e., [(TTM)Cu(NCMe)]PF$_6$ (**1**) are needed for further comparison with the heterogeneous counterpart. This yet unreported compound has been prepared by reaction of tris(triazolyl)methane ligand with [Cu(NCMe)$_4$]PF$_6$ at room temperature (Scheme 2) in acetonitrile. After workup, solid material was obtained for which NMR spectra showed somewhat broad resonances for three equivalent azolyl rings, as well as coordinated acetonitrile, as expected for complex **1**. Interestingly, HRMS studies showed the presence of two species in acetonitrile solutions, with masses corresponding to (TTM)Cu-(NCMe) (621, M-PF$_6$) and (TTM)Cu (580, M-PF$_6$). A plausible association-dissociation equilibrium of the acetonitrile ligand would explain such finding. The generation of the [(TTM)CuPF$_6$] units was assessed when attempting to crystallize the copper complex **1** from dichloromethane-hexane solutions at room temperature. Colorless crystals of a new dinuclear complex **2** (Scheme 2) were formed, its structure being determined by X-ray

studies (Figure 1). Its formation is explained straightforwardly due to the lability of the acetonitrile ligand in **1** and the association of two (TTM)CuPF$_6$ units.

The molecules of complex **2** consist of two (TTM)Cu units in which each copper center is bonded to two azolyl groups of one TTM ligand and a third azolyl group from the other TTM fragment. This pattern is identical to that previously described for the [Tp^{Me2}Cu]$_2$ complex,[10] the main distances and angles being in the expected ranges. The intermetallic Cu–Cu distance of 2.7091(11) Å is very close to the sum of two van der Waals radii for copper (2× 1.40 Å = 2.80 Å), and therefore the copper-copper interaction is, at best, very weak.

The availability of complex **1** led us to explore its use as catalyst in the olefin aziridination reaction. A dichloromethane solution of **1** and styrene was prepared, and PhI=NTs was then added to the stirred solution in one portion. The nitrene precursor slowly dissolved, the final reaction time being marked by the complete disappearance of solid PhI=NTs in the mixture. Several [Cu]:[PhI=NTs]:[styrene] ratios were screened, with NMR analysis of the reaction crude providing the data shown in Table 1. With 2–5% catalyst loading, referred to the nitrene precursor, very high yields of the aziridine were obtained (entries 3, 4), and a remarkable 90% yield was found employing equimolar amounts of PhI=NTs and styrene (entry 5). On the other hand, lower catalyst loadings were not that productive (entries 1, 2). The remaining of the initial nitrene precursor PhI=NTs not converted into aziridines was consumed upon forming TsNH$_2$, a common byproduct in these transformations. Furthermore, the use of **2** instead of **1** showed no difference in the catalytic outcome.

After the initial screening with styrene, we employed less activated olefins as substrates (Scheme 3). Thus, 1-hexene, cis-cyclooctene and methyl methacrylate were tested in their reactions with PhI=NTs catalyzed by **1**. The linear, non-activated alkene was converted into the corresponding aziridine in 66% yield, whereas for the cyclic olefin a 93% yield was found. The olefin bearing the electron-withdrawing methoxycarbonyl group was also aziridinated in 80% yield. It is worth mentioning that the latter transformation is challenging, and that only few copper catalysts for aziridination reaction are also active for deactivated olefins.[11]
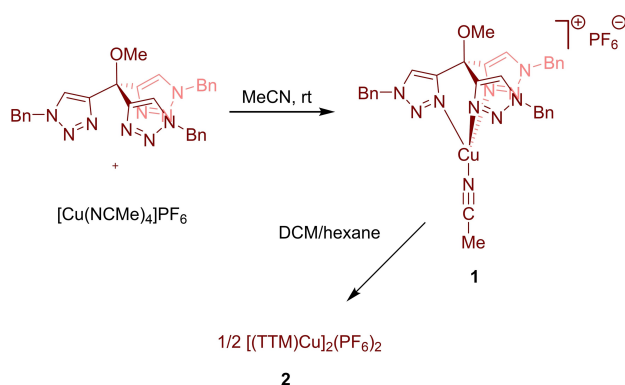
Scheme 2. Synthetic routes to complexes **1** and **2**.
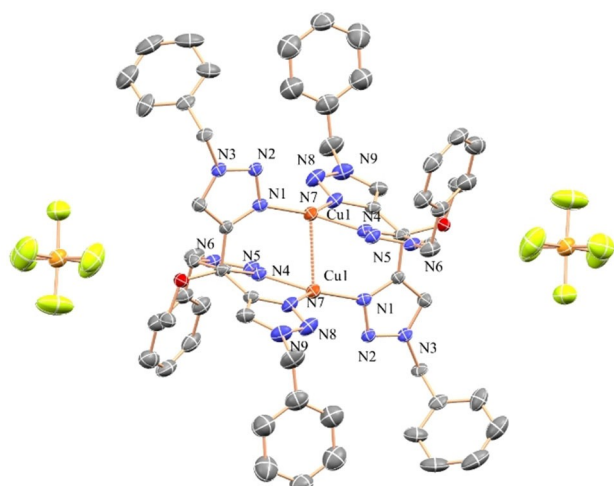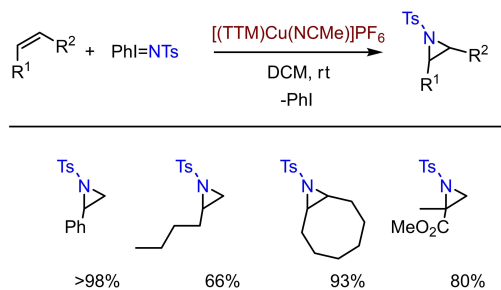
Figure 1. Molecular structure for the molecules of **2**. Hydrogen atoms have been omitted. Relevant distances (Å) and angles (°) (see Supporting Information for full data): Cu(1)-Cu(1) 2.7091(11); Cu(1)-N(1), 1.926(4); Cu(1)-N(4), 2.014(4); Cu(1)-N(7), 1.986(4); N(1)-Cu(1)-Cu(1), 109.04(11); N(1)-Cu(1)-N(4), 129.71(15).

Table 1. Aziridination of styrene using **1** as catalyst.[a]

Entry	[%] [Cu]	[Cu]:[PhI=NTs]:[Styrene]	[%] Aziridine
1	0.5	1:200:200	57
2	1	1:100:200	75
3	2	1:50:200	96
4	5	1:20:200	>98
5	5	1:20:20	90
6	20	1:5:50	>98

[a] Conditions: 0.0075 mmol of **1**, 0.15 mmol (20 equiv) of PhI=NTs, 4 mL dichloromethane. Yields determined by ¹H NMR of the reaction crude using 1,3,5-trimethoxybenzene as internal standard. TsNH$_2$ accounted for 100% of initial PhI=NTs not converted into aziridine.

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Scheme 3. Aziridination of alkyl-, aryl- and methoxycarbonyl-substituted olefins. Reaction conditions as in Table 1 with 200 equiv. of olefin.
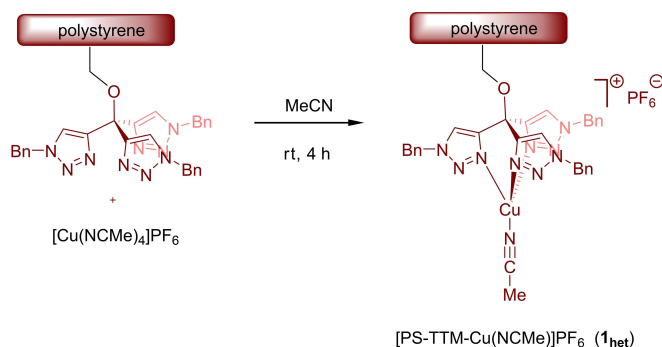
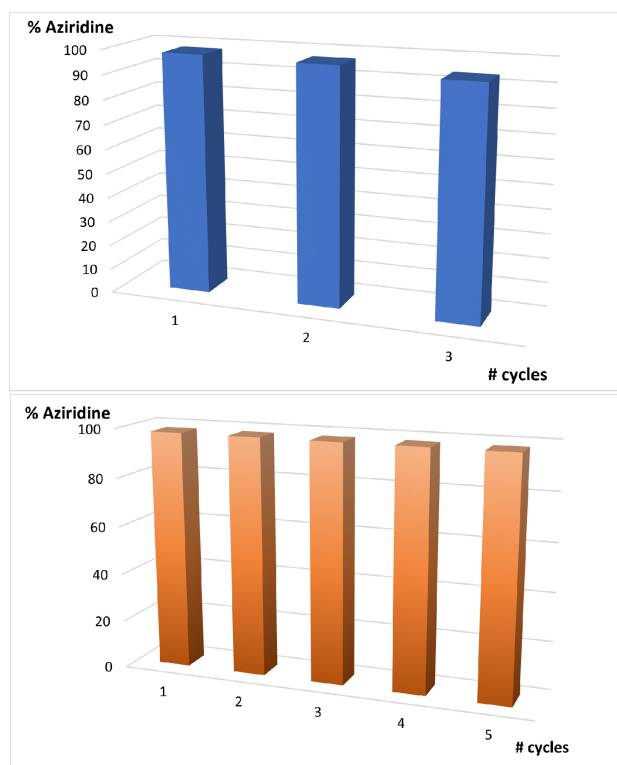**Scheme 4.** Preparation of the heterogeneous catalyst 1_{het}.

Figure 2. Styrene aziridination using 1_{het} as catalyst: Top: 5% catalyst loading. Bottom: 20% catalyst loading.

The heterogeneous system

Once demonstrated that complex **1** promotes the transfer of nitrene units from PhI=NTs to olefins, we moved onto the heterogeneous system. The preparation of the solid catalyst has been previously reported,[8,9] and it is briefly commented of the sake of clarity. A polystyrene material bearing TTM ligand was reacted with the copper source at room temperature in acetonitrile (Scheme 4). After workup, all the TTM sites are covered by Cu(I) ions, (31.4 mg Cu/g polymer) and the catalyst 1_{het} is ready to be used.

We first investigated the use of 1_{het} as catalyst for the benchmark reaction, *i.e.*, the aziridination of styrene. Figure 2 shows the results from a series of experiments carried out with $[1_{het}]$:[PhI=NTs]:[styrene] ratio of 1:20:200, and for three consecutive recyclings. The first cycle originated aziridines in ca. 98% yield. After filtration, washing of the solid and the addition of fresh solvent and reactants, the next two cycles gave nearly identical results (97 and 94%), values also indistinguishable from that obtained with the soluble catalyst. Considering those two steps of filtering and washing, it is reasonable assuming that the activity loss is due to the workup. When employing a larger catalyst loading (20%) to disfavor the effect of the workup, five consecutive runs provided the exclusive formation of the aziridine in >98% yield (Figure 2), as inferred from NMR studies of the reaction crude after each run. Therefore, the anchoring of the soluble catalysts onto the polymeric material does not affect to its catalytic behavior, while allowing easy recycling and reuse.

Given the activated nature of the olefinic bond in styrene, we wondered if the observed behavior of 1_{het} could be extended to the less activated olefins already tested in solution. Toward that end, we run experiments with the three olefins 1-hexene, *cis*-cyclooctene and methyl methacrylate with the results shown in Table 2, which also contains those achieved under homogeneous conditions for a direct comparison. There is no doubt that the copper center promotes the aziridination reaction with similar efficiencies no matter the reaction occurs in solution or under heterogeneous conditions. Only the less activated olefin methyl methacrylate shows a slight decrease in aziridination yield, whereas the others verify the conversion into aziridines without any effect of the nature (homogeneous or heterogeneous) of the catalyst employed.

Table 2. Comparison of the catalytic activity of **1** and 1_{het} in the olefin aziridination reaction.[a]

Entry	Olefin	[%] Aziridines	
		Catalyst **1**	Catalyst 1_{het}
1	styrene	>98	>98
2	1-hexene	63	61
3	*cis*-cyclooctene	93	96
4	Methyl methacrylate	80	70

[a] See experimental for details.

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Conclusion

We have developed a cationic tris(triazolyl)methane copper(I) catalyst anchored onto a polymeric material (polystyrene) which induces the efficient conversion of aryl-, alkyl or alkoxycarbonyl-substituted olefins into aziridines upon transfer of the NTs moiety from PhI=NTs. This represents the first example of a polymer-immobilized catalyst suitable for the aziridination of olefins covering a range from electron-rich to electron-deficient substrates. Interestingly, the heterogeneous catalyst can be separated by filtration and reused without any reactivation treatment, showing essentially unmodified activity over several (up to five) reaction cycles. Also noteworthy, the catalytic activity of the immobilized catalyst is identical to that observed in solution by the soluble, molecular counterpart.

Experimental Section

General Information: All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen atmosphere or in a glovebox (MBRAUN UNILAB). Solvents were purchased from commercial sources, dried by distillation under nitrogen atmosphere using the suitable drying agent and deoxygenated immediately before their use. Reagents were acquired from suppliers and used without any further purification. The TTM ligand,[9] the supported complex 1_{het}[9] and the nitrene precursor PhI=NTs[12] were synthesized according to literature procedures. NMR spectra were recorded on the Agilent 400MR spectrometer as solutions at 298 K and referenced to residual solvent peaks. High Resolution Mass Spectroscopy (HRMS) experiments were carried out at CITIUS-Universidad de Sevilla.

Synthesis of [(TTM)Cu(NCMe)]PF₆ (1). Tris(triazolyl)methane (TTM) ligand (0.15 mmol, 78 mg), Cu(MeCN)₄PF₆ (0.15 mmol, 56 mg) were dissolved in acetonitrile (3 mL) under nitrogen. After 12 h of stirring, volatiles were removed under reduced pressure and the resulting colorless oil was re-dissolved in dichloromethane (4 mL). Solvent evaporation under vacuum provided a white solid of complex **1** (98 mg, 90%). Crystallization of this solid from a 5:1 mixture of dichloromethane:hexane at room temperature gave colorless crystals of complex **2**.

^{1}H NMR (400 MHz, CD₃CN): δ 7.79 (br s, 3H), 7.31 (m, 15H), 5.51 (br s, 6H), 3.03 (br s, 3H). ^{13}C{^{1}H} NMR (100 MHz, CD₃CN): δ 148.4, 136.0, 130.0, 129.6, 129.1, 126.0, 55.1, 53.3. HRMS (HESI) [M-PF₆]$^+$ (performed in acetonitrile) calculated for C₃₁H₃₀CuN₁₀O: 621.1895. Found: 621.1886. A second peak is observed in the HRMS experiment matching with C₂₉H₂₇CuN₉O: 580.1629. Found: 580.1614.

Catalytic experiments. (a) Homogeneous phase. Complex **1** (5.5 mg, 0.0075 mmol) was dissolved in deoxygenated DCM (4 mL). The olefin was then added in the desired excess, followed by the addition of PhI=NTs (55.8 mg, 0.15 mmol) in one portion. After 4 h of stirring at room temperature, the solvent was removed under reduced pressure and the crude was analyzed by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. The aziridines were identified upon comparison with literature reports.[11] **(b) Heterogeneous phase**. Complex 1_{het} (100 mg of polymer, 0.05 mmol of Cu) was dissolved in deoxygenated DCM (6 mL). Addition of the olefin (10 mmol) was followed by the addition of PhI=NTs (372 mg, 1 mmol) in one portion. After 12 h, the mixture was filtered off. The solid was washed three times with deoxygenated DCM and dried under a N₂ stream before it was charged with solvent and reactants for a next catalytic cycle. The liquid fractions were collected, and volatiles were removed before the crude was investigated by ^{1}H NMR as described above for the homogeneous case.

Deposition Number 2089200 (for **2**) contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

Supporting Information: NMR and HRMS data for complex 1 and crystallograpic data for complex 2.

Conflict of Interest

The authors declare no conflict of interest.

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