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Cyclopropanation of olefins using a silica gel anchored palladium phosphine complex

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A silica gel anchored palladium phosphine complex is synthesized and used as a catalyst for the first time in the cyclopropanation of several olefins using ethyl diazoacetate as a carbene source.

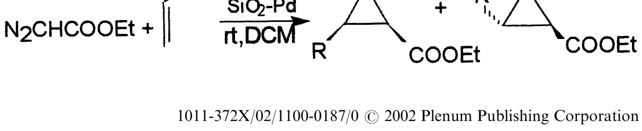
KEY WORDS: anchored palladium catalyst; cyclopropanation; olefins; *trans*-selectivity; reusability.

1. Introduction

The cyclopropanation reaction is of great interest and is employed to generate cyclopropanes, which are the building blocks of several biologically active compounds [1,2], with activity ranging from antibiotic, antiviral, antifungal, insecticidal, hormonal etc. to plant growth and fruit-ripening controls and enzyme and gluconeogenesis inhibitions [3]. The transfer of carbenes sourced from diazo compounds to the olefins is generally catalyzed by several transition metal complexes [4–7]. In most cases, *trans*-isomers are preferably obtained, but the selectivity depends on the nature of the complex used in the chemical reaction. In the reactions of olefins with diazo esters, copper catalysts generally provide a high *trans*-selectivity while the selectivity is reduced with rhodium and palladium catalysts. On the other hand, in the reaction of ethyl diazoacetate (EDA) with styrene catalyzed by RhTPPI and $[(\eta^5\text{-}C_5H_5)Fe(CO)_2(THF)]BF_4$, *cis*-isomer is preferentially formed [8,9]. $Pd(OAc)_2$ [10], $PdCl_2$ [11], $PdCl_2{\cdot}2PhCN$ [12], $Pd(PPh_3)_4$ [12,13] and platinum complexes [14] efficiently catalyze the reaction of diazomethane and EDA with both electron-rich and electron-deficient olefins, including α,β-unsaturated ketones and esters in homogeneous phase.

Although many of the transition metal compounds (metal salts, metal complexes or organometallic compounds) are active homogeneous catalysts for many reactions, heterogeneous solid catalysts [15] are preferred industrially in view of the inherent advantages of easy adaptability, handling and simple separation of the catalysts from the reaction. In search of an ideal catalyst, the "hybrid" or heterogenization of a homogeneous catalyst was conceived, aimed at retaining the higher activity and selectivity characteristics of the homogeneous catalyst and simple separation, an inherent feature of a heterogeneous catalyst. A heterogenized catalyst in which an analog of a homogeneous transition metal catalyst is attached, usually through covalent bonding to a solid support, thus manifests the advantages of both the heterogeneous and homogeneous systems. The active site is a definable, discrete complex, whose mechanism of action is similar to that of its truly homogeneous counterpart. At the same time, the ease of separation and recovery which is characteristic of heterogeneous catalysts is retained. In recent years, many methodologies involving functionalization on organic resins [16] like polystyrene, polyethylene glycol [17] or ligands bound to inorganic oxides like silica [18] have been reported. The former suffers from the disadvantages of solvent dependency, swelling and porosity, while the latter lacks the secured ligand attachment and possesses relatively low concentrations of ligand groups.

There are few reports on the cyclopropanation reaction catalyzed by heterogeneous catalysts, copper bronze, Cu-exchanged clays and zeolites [19]. The catalytic activity of the recovered Cu-exchanged catalyst is low. Silica support has high thermal stability over polymers, and economically it is cheaper than any other polymers. In view of these advantages we herein report the synthesis and activity of silica gel anchored palladium phosphine complex (SiO_2–Pd) through covalent attachment of the phosphine group *via* chloropropyl as a spacer and subsequent complexation with palladium benzyl cyanide complex for catalytic cyclopropanation of olefins for the first time (scheme 1).



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2. Experimental

2.1. Preparation of the catalyst

The catalyst was prepared similarly to the procedure adopted for montmorillonite [20]. The (3-chloropropyl)-trimethoxysilane functionalized silica was prepared by refluxing silica (1 g) with a spacer (3-chloropropyl)trimethoxysilane (0.219 ml, 1.2 mequiv./g) for 48 h, followed by Soxhlet extraction, and vacuum dried. The reaction of chlorodiphenyl phosphine (0.56 ml, 3 mmol) in dry tetrahydrofuran (THF) with an excess of Li-metal (63 mg, 9 mmol) under reflux gave the orange $LiPPh_2$, which was then added to the vacuum-dried (3-chloropropyl)trimethoxysilane functionalized silica and the mixture was refluxed under stirring for 24 h and filtered. The residue was washed until the washings were free of chloride ions. The functionalized silica was dried in vacuo at 70 °C for 12 h. This was taken suspended in a solution of $PdCl_2(PhCH_2CN)_2$ (0.154 g) in dry benzene at room temperature, under nitrogen and agitated in a flask shaker until the color of the Pd complex disappeared (3–4 h) and subsequently filtered to give the brown silica gel anchored palladium phosphine complex (SiO_2–Pd). The chemical analysis (SEM) of the catalyst indicates that 0.37 mmol/g of Pd was incorporated.

2.2. A typical experimental procedure for cyclopropanation of olefins

To a mixture containing catalyst (0.037 mmol, 100 mg) and styrene (2.5 mmol, 0.29 ml) in dry dichloromethane (DCM) (5 ml), ethyl diazoacetate (2.5 mmol, 0.25 ml) in dry dichloromethane (5 ml) was added dropwise over a period of 4 h, under nitrogen atmosphere and stirred at room temperature. After completion (as monitored by TLC) of the reaction, the reaction mixture was filtered, washed and concentrated to get the crude product. The crude product was column chromatographed on silica gel using hexane/ethyl acetate as eluent to afford the ethyl 2-phenylcyclopropanecarboxylate (yield: 62%, 0.117 g). ^{1}H NMR (200 MHz $CDCl_3$) of ethyl-*cis*-2-phenylcyclopropanecarboxylate: δ 1.00–2.83 (m, 4H, cyclopropyl ring protons), 0.9–1.1 (t, 3H, CH_3), 3.8–4.0 (q, 2H, CO_2CH_2), 7.1–7.5 (5H, C_6H_5); ethyl-*trans*-2-phenylcyclopropanecarboxylate: δ 1.00–2.83 (m, 4H, cyclopropyl ring protons), 1.2–1.5 (t, 3H, CH_3), 4.1–4.4 (q, 2H, CO_2CH_2), 7.1–7.5 (5H, C_6H_5).

3. Results and discussion

Silica gel anchored palladium phosphine (SiO_2–Pd) catalyzed the cyclopropanation of a wide range of alkenes in addition to styrene with EDA (table 1). Good yields were obtained with styrene, norbornene and allylbenzene (entry 1, 7 and 8), while the yield with α-methyl styrene (entry 6) was poor due to steric factors using SiO_2–Pd catalyst. The yield and the selectivity mostly depend on the reaction conditions and the nature of the catalyst, respectively. It was also found that the yield of the product varies with the change in addition time of the EDA because accelerated addition of the diazoacetate results in decomposition of the diazoacetate to higher amounts of carbene dimers (diethyl maleate and diethyl fumarate). In order to keep the low concentration of EDA in the reaction mixture, the reagent was added slowly over a longer period. The solvent also has a noticeable influence on the reaction and it was observed that when co-ordinating solvents like ether and acetonitrile were used, the reaction did not proceed. The SiO_2–Pd catalyst showed *trans*-preference and the products can be easily separated by simple filtration. The percentage of isomers was estimated from the ^{1}H NMR spectra. In general, the less sterically hindered cyclopropane (*trans* or *exo*) is the major product, as is the case with homogeneous palladium catalysts.

Table 1
Cyclopropanation of olefins using a silica gel anchored palladium phosphine complex.

Entry	Substrate	Temp. (°C)	Time (h)	Yield (%)[a]	Cis/trans[b]
1	Styrene	RT	4	69 (62) 64[c]	30/70
2	*p*-Chlorostyrene	RT	16	59 (53)	26/74
3	*p*-Methoxystyrene	50	16	41	28/72
4	*p*-Methylstyrene	RT	4	74 (70)	21/79
5	*p*-Acetoxystyrene	RT	16	34	28/72
6	α-Methylstyrene	50	16	10	28/72
7	Norbornene	RT	5	70	–
8	Allylbenzene	RT	8	83	–

[a] ^{1}H NMR yields; yields in the parentheses refer to isolated yields.

[b] cis/trans ratio based on ^{1}H NMR of crude compounds.

[c] Third recycle.

Table 2
Comparison with various homogeneous catalysts using styrene as an example.

Catalyst	Yield (%)	Trans/cis
SiO_2–Pd	69.0	2.3
$PdCl_2$ [a]	91.3	1.5
$Na_2(PdCl_4)$ [a]	83.3	1.1
$Pd(PhCH_2CN)_2Cl_2$	62.6	1.3
$Pd(OAc)_2$	70.6	1.6
$Pd(PPh_3)_2Cl_2$	56.0	1.4

Reaction conditions: [a] RT; styrene 2.5 mmol; catalyst: 0.037 mmol of Pd; diazo ester 2.5 mmol; DCM solvent.

The activity and the selectivity of the catalyst SiO_2–Pd was compared with the precursors $PdCl_2$, $Pd(PhCH_2CN)_2Cl_2$ and the analog, $Pd(PPh_3)_2Cl_2$, in the cyclopropanation of styrene conducted under identical conditions, and the results are summarized in table 2. It is found that the heterogenized SiO_2–Pd catalyst displayed higher trans-selectivity than the homogeneous Pd precursors and the analog, which may be ascribed to steric factors that allow the formation of *trans*-isomer. Although the yields obtained with SiO_2–Pd are not as impressive as homogeneous precursors composed of free $PdCl_2$, the SiO_2–Pd shows better performance over the homogeneous analog, $Pd(PPh_3)_2Cl_2$.

Further, the activity and selectivity of the heterogeneous SiO_2–Pd is compared with the reported Cu-exchanged heterogeneous catalysts in the cyclopropanation of styrene (table 3), since there are no reports found using Pd-heterogeneous catalysts. As can be seen, the SiO_2–Pd catalyst displayed 5–46 manifold activity over the heterogeneous Cu-exchanged catalysts in the cyclopropanation reaction. The higher activity may be due to the nature of the metal, palladium. Thus, our catalyst displayed higher activity in the insertion of carbene into olefin over the other catalysts.

In heterogeneity and recyclability of the catalyst, the SiO_2–Pd catalyst was recovered after the reaction by a simple filtration and recycled three times in the cyclopropanation of styrene, which shows almost consistent activity and selectivity (table 1, entry 1). We then examined the residual activity of the filtrate of the first cycle after the addition of fresh amounts of styrene and the ethyl diazoacetate, but the formation of no additional product was noticed. There is no Pd detected in the filtrate of the catalyst by AAS analysis. These results demonstrate the heterogeneity of the catalyst in the cyclopropanation of the styrene.

Table 3
Comparison of the yields of cyclopropane with various heterogeneous catalysts taking styrene as an example.

Catalyst	Temp. (°C)	Time (min.)	Yield (%)	Specific activity [a]	Trans/cis
SiO_2–Pd	25	240	69	46	2.33
Cu-bentonite	25	40	23	1	1.8
Cu-zeolite	50	40	19	1	2.0
Cu-laponite	25	40	20	1	1.4
Cu–K10	25	40	22	8	0.8

[a] Moles of product obtained per mole of catalyst.

The insertion of carbene into the olefins to yield cyclopropanes using ethyl diazoacetate as a carbene source is achieved using the silica gel anchored palladium phosphine catalyst with high throughput. Easy separation of the catalyst from the reaction mixture by the simple filtration and reusability for several cycles without any further reactivation are the additional advantages.

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