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Highly Efficient Heterogeneous Aqueous Kharasch Reaction with an Amphiphilic Resin-Supported Ruthenium Catalyst

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Abstract: An amphiphilic polystyrene-polyethylene glycol (PS-PEG) resin-supported ruthenium complex was designed and prepared. The polymeric Ru complex was found to promote the transition metal-catalyzed atom transfer radical addition of halogenated compounds to olefins, the Kharasch reaction, in water under heterogeneous as well as AIBN-free conditions with a high level of atom economy to meet green chemical requirements.

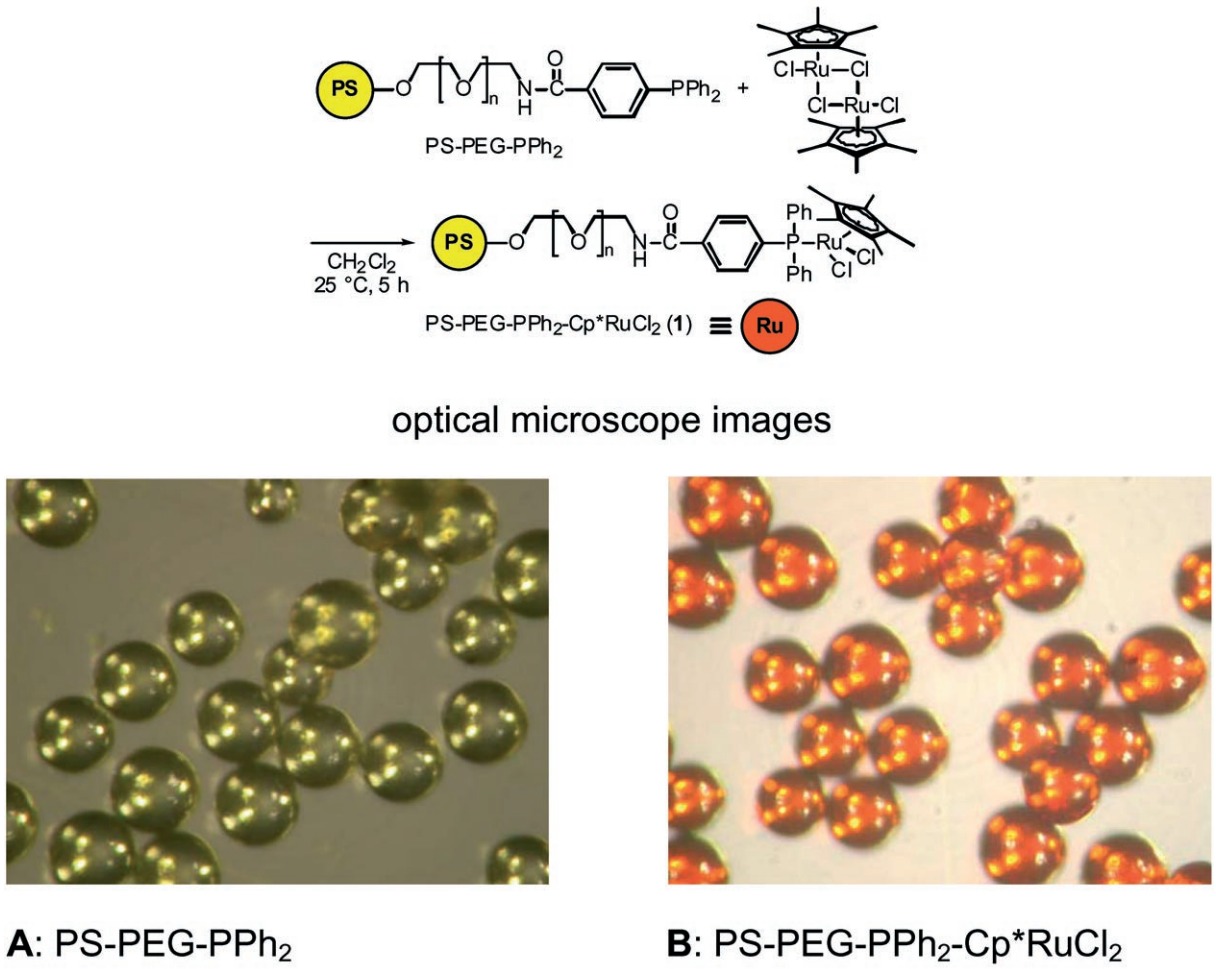
Keywords: allylic substitution; aqueous media; asymmetric catalysis; combinatorial chemistry; palladium; polymer-supported catalyst

The transition metal-catalyzed atom transfer radical addition of halogenated compounds to olefins, the Kharasch reaction, offers a powerful tool to functionalize olefins with a high level of atom economy. Ruthenium complexes are among the most active catalysts for the Kharasch reaction, where AIBN, a radical initiator, is often used as a co-catalyst to promote the reaction with synthetically useful efficiency. While only homogeneous transition metal catalysts have been developed thus far,[1] the aqueous[2] and heterogeneous switching[3] of this catalysis still remains a major challenge in terms of chemical safety and green chemistry.[4] If it took place in water with a readily recyclable immobilized catalyst[5] without any additional radical initiator, the Kharasch reaction would represent an ideal olefin functionalization.

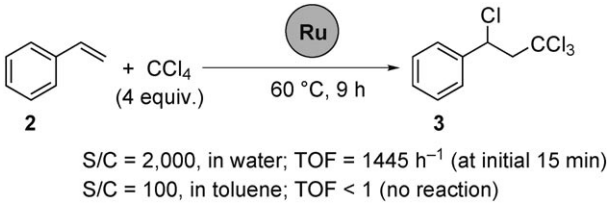
We have previously developed amphiphilic polymer resin-supported transition metal complexes (Pd, Rh) and nanoparticles (Pd, Pt) that catalyze various organic transformations in water under heterogeneous conditions.[6] Very recently, Severin et al. have reported that $RuCp^*Cl_2PPh_3$-AIBN (Cp^* = pentamethylcyclopentadienyl) acts as a highly efficient catalyst system to promote the Kharasch reaction.[7] Their results prompted us to develop an amphiphilic resin-supported phosphine-ruthenium complex[8] to realize a heterogeneous aquacatalytic Kharasch reaction. Here we report the amphiphilic polystyrene-poly(ethylene glycol) (PS-PEG) resin-supported ruthenium complex PS-PEG-$NHCOC_6H_4PPh_2$-$RuCp^*Cl_2$ (**1**) which exhibited high aquacatalytic activity and recyclability for the Kharasch reaction without radical initiators (Scheme 1).

A polymeric ruthenium complex was readily prepared by mixing PS-PEG resin-supported triarylphosphine and $[RuCp^*Cl_2]_2$ (Scheme 1) according to the preparation of $RuCp^*Cl_2PPh_3$.[9] Thus, a ruthenium-monophosphine complex PS-PEG-$NHCOC_6H_4PPh_2$-$RuCp^*Cl_2$ (**1**)[10] was obtained by treatment of PS-PEG-phosphine (phosphorus loading = 0.26 mmol g^{-1}; average diameter of polymeric beads = 100 μm; 1% DVB cross-linking) with an excess amount of $[RuCp^*Cl_2]_2$ (1.4 mol equiv to phosphorus) in dichloromethane at room temperature for 5 h followed by removal of non-immobilized ruthenium species by washing several times with dichloromethane to give the polymeric ruthenium complex **1** as reddish beads. The ICP-AES analysis of the resulting polymeric beads exhibited the loading values of ruthenium and phosphorus to be 0.23 mmol Ru/g and 0.24 mmol P/g, respectively, demonstrating that its structure is $RuCp^*Cl_2$(phosphine).

The aquacatalytic potential of the novel polymeric ruthenium complex **1** was examined for the Kharasch reaction of styrene with carbon tetrachloride (Scheme 2). Thus, the reaction of styrene (**2**) and CCl_4 (**2**/CCl_4 = 1/4) was carried out in water as a single reaction medium in the presence of 0.05 mol% ruthenium of the polymeric complex **1** (S/C = 2,000) at 60 °C to give 1,1,1,3-tetrachloro-3-phenylpropane **3**. We were pleased to find that a high TOF value of 1450 h^{-1} (during the initial 15 min period) was achieved even without any radical initiators, such as AIBN, and was comparable to the highest TOF value hitherto reported under homogeneous AIBN-free



Scheme 1. Preparation of an amphiphilic resin-supported Ru complex.



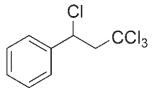
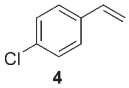
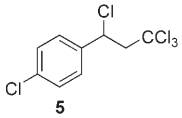
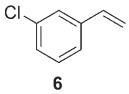
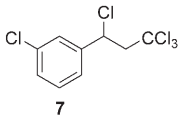
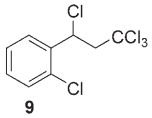
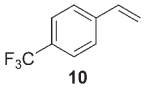
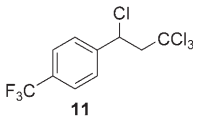
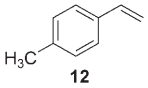
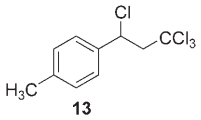
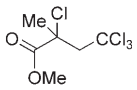
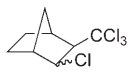
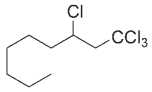
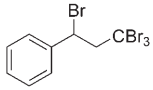
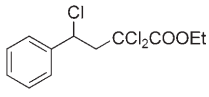
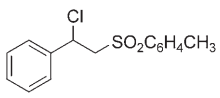
Scheme 2. Amphiphilic polymeric Ru-catalyzed Kharasch reaction (water *vs.* toluene).

conditions.[11] It is noteworthy that the reaction did not proceed at all in toluene even with 1 mol% of ruthenium under similar conditions. The hydrophobic organic substrates must diffuse into the hydrophobic polystyrene matrix in water to provide a highly *self-concentrated* reaction sphere where the addition-type reaction is significantly accelerated to reduce the initial molar concentration.

With the efficient catalytic system in hand, we next examined the Kharasch reaction of various olefins and chlorinated compounds in an exact equimolar ratio. The Kharasch reaction generally is carried out with an excess amount of a chlorinated compound.[1] Considering the high toxicity of chlorinated organic materials, a highly efficient, heterogeneous aquacatalytic Kharasch reaction with an equimolar mixing ratio would offer a safe, clean, and highly atom-economical alternative to more conventional Kharasch reaction systems.

A mixture of an equimolar ratio of styrene and CCl_4 and 0.33 mol% ruthenium of the PS-PEG resin-supported ruthenium complex **1** in water was shaken at 60 °C for 9 h, and the Kharasch adduct **3** was obtained in 91% isolated yield (Table 1, entry 1). Representative results are summarized in Table 1. Styrenes bearing *ortho*-, *meta*- and *para*-chloro groups, **4**, **6**, and **8**, underwent the Kharasch reaction with CCl_4 under similar conditions to give the corresponding 1,1,1,3-tetrachloro-3-arylpropanes **5**, **7**, and **9** in 92%, 87% and 86% isolated yield, respectively (entries 5, 6 and 7). The reaction of *para*-trifluoromethylstyrene (**10**) gave an 80% isolated yield of **11** (entry 8). *para*-Methylstyrene (**12**) bearing an electron-rich aromatic ring required a higher reaction temperature (70 °C) to

Table 1. The Kharasch reaction of various olefins with PS-PEG-PPh_2-Cp*$RuCl_2$ (**1**).[a]

Entry	Substrate	Chlorine Species	Product	Yield [%][b]
1	 **2**	CCl_4	 **3**	91
2	Recycling experiment: 1st run			94
3	2nd run			96[c]
4	3rd run			98[c]
5	 **4**	CCl_4	 **5**	92
6	 **6**	CCl_4	 **7**	87
7	 **8**	CCl_4	 **9**	86
8	 **10**	CCl_4	 **11**	80
9	 **12**	CCl_4	 **13**	84
10	 **14**	CCl_4	 **15**	83[c]
11	 **16**	CCl_4	 **17**	72
12	 **18**	CCl_4	 **19**	36
13	**2**	CBr_4	 **20**	89
14	**2**	$Cl_3CCOOEt$	 **21**	89
15	**2**	TsCl	 **22**	92

[a] All reactions were carried out with **4** at 60–70 °C in water under N_2. The ratio of the alkene (mol)/halo reagent (mol)/Ru (mol) = 1.0/1.0/0.0033–0.01.
[b] Isolated yield.
[c] NMR yield using bibenzyl as an internal standard.

afford a high yield of the Kharasch adduct **13** (84%) (entry 9). The reactions of 1,1- and 1,2-disubstituted alkene substrates took place at 60 °C with 1.0 mol% Ru of the complex **1** (entries 10 and 11). Thus, methyl methacrylate (**14**) reacted with CCl_4 to afford **15** having a quaternary chloride in 83% yield, and norbornene **16** afforded 2-chloro-3-trichloromethylnorbornane (**17**) in 72% yield. It is noteworthy that the Kharasch reaction of the non-activated alkene substrate, *n*-1-octene (**18**) also took place with the polymeric ruthenium complex **1** in water without AIBN to give 1,1,1,3-tetrachlorononane (**19**) with exclusive regioselectivity although the chemical yield was only 36% after 24 h of reaction time (entry 12). The atom transfer addition reaction was also examined with CBr_4, $Cl_3CCOOEt$, and *p*-$ClSO_2C_6H_4CH_3$ under the aquacatalytic conditions. Thus, the reaction of styrene with CBr_4 was smoothly catalyzed in water with the polymeric ruthenium species **1** to give an 89% yield of 1,1,1,3-tetrabromo-3-phenylpropane (**20**) (entry 13). Trichloroacetate and tosyl chloride added to styrene in the atom transfer fashion under similar aquacatalytic conditions to give ethyl 2,2-dichloro-1-chloro-1-phenylbutyrate (**21**) and (2-chloro-2-phenyl)-ethyl tolyl sulfone in 89% and 92% yield, respectively (entries 14 and 15).

The recyclability of the PS-PEG resin supported ruthenium catalyst **1** (1.0 mol% Ru) was examined for the reaction of styrene (**2**) and CCl_4. Thus, after the first reaction, which gave 94% yield of **3** (Table 1, entry 2), the catalyst resin was recovered by filtration and successively subjected to a second and third run of the reaction under the same conditions to afford **3** in 96% and 98% yield, respectively (entries 3 and 4).

In conclusion, an amphiphilic PS-PEG resin-supported ruthenium complex was designed and prepared. The Kharasch reaction was smoothly catalyzed by this PS-PEG Ru complex in water under heterogeneous conditions without any radical initiators, for example, AIBN. Owing to the self-concentration of hydrophobic organic substrates inside the polymer matrix in water, the catalytic efficiency of the PS-PEG Ru in water was comparable to the most efficient homogeneous Ru catalysis reported thus far. A detailed kinetic study and further synthetic applications are currently under investigation in our lab and will be reported in due course.

Experimental Section

PS-PEG Resin-Supported Ruthenium Complex (1)

A reactor was charged with PS-PEG-PPh_2 (340 mg), Cp*$RuCl_2$ (35 mg), and CH_2Cl_2 (10 mL). The reaction mixture was shaken on a wrist action shaker at 25 °C for 5 h. The solvent was removed by filtration, and the collected beads were washed with CH_2Cl_2 (5 times of 5 mL) and dried under reduced pressure overnight to give PS-PEG-PPh_2-Cp*$RuCl_2$ (**1**) as reddish beads (0.23 mmol Ru/g, 0.24 mmol P/g).

General Procedure for Kharasch Reaction with Polymeric 1 in Water

A mixture of PS-PEG-PPh_2-Cp*$RuCl_2$ (**1**) (7.2 mg, 0.0017 mmol Ru), alkene (0.5 mmol), CCl_4 (76 mg, 0.5 mmol) and 1.5 mL of water was shaken at 60 °C for 9 h under nitrogen atmosphere. The reaction mixture was filtered, and the resin was rinsed three times with 5 mL of an appropriate organic solvent or super critical CO_2 (flow extraction system).[12] The crude product was purified by silica gel column chromatography.

Acknowledgements

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