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Skeletal Reorganization of Enynes into 1-Vinylcycloalkenes in Ionic Liquids

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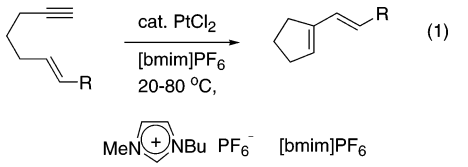
Abstract: The skeletal reorganization of enynes catalyzed by transition metal chlorides, such as $PtCl_2$, $[RuCl_2(CO)_3]_2$, $[RhCl(CO)_2]_2$, and $AuCl_3$, in ionic liquids proceeds under milder conditions (at lower reaction temperatures and for shorter reaction times) than those needed for ordinary solvents. The products produced by the skeletal reorganization of enynes were easily removed from the catalyst by a simple extraction with Et_2O or distillation. The $PtCl_2$ can be reused up to five times.

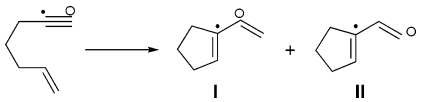
The skeletal reorganization of enynes leading to 1-vinylcycloalkenes[1] has been of interest because of the possibility of producing cyclic flameworks from relatively simple acyclic starting materials.[2,3] A variety of simple metal halides or cation complexes, including $[RuCl_2(CO)_2]_2$,[4] $Pt(PPh_3)_2(OAc)_2/CF_3COOH$,[5] $PtCl_2$,[6−8] $PtCl_4$,[6,9] $[Pt(dppp)(PhCN)_2](BF_4)_2$,[10] $[IrCl(CO)_3]_n$,[11] $[Rh(OAc)_2]_2$,[7] $AuCl_3$,[6] $Au(PPh_3)Cl/AgSbF_6$,[12] $ZnCl_2$,[13] and $GaCl_3$,[14] have been reported to be active for the skeletal reorganization of enynes. The skeletal reorganization of enynes has also been used in the synthesis of natural compounds, indicating its potential utility in organic synthesis.[15] Of the available catalysts, $PtCl_2$ represents one of the most effective catalysts with respect to substrate availability and catalyst activity. However, the reaction requires higher reaction temperatures (80 °C), probably due to its low solubility in toluene, the solvent of choice. On the other hand, the reaction proceeds under milder reaction conditions (rt to 40 °C) when $[Pt(dppp)(PhCN)_2](BF_4)_2$ or $PtCl_4$ is used as the catalyst.[9,10] This is probably due to their good miscibility to toluene.

Recently, interest in developing organic reactions in environmentally friendly media, such as ionic liquids, water, and fluorous liquids, has grown. Ionic liquids are known to solubilize organometalic compounds and to have a stabilizing effect on transition metal complexes.[16] We concluded that the reaction might well proceed under milder reaction conditions when the reaction is carried out in an ionic liquid. In addition, the products can often be readily separated from ionic liquids by a simple separation procedure, such as extraction. We wish to report herein on the skeletal reorganization of enynes in ionic liquids (eq 1). The reaction occurs under milder reaction conditions than have been previously reported, when toluene is used as the solvent.



Results and Discussion. The reaction of **1** in toluene at 80 °C was complete within 3 h, giving **2** in 86% isolated yield.[6] The reaction of **1** (0.5 mmol) in the presence of $PtCl_2$ (0.02 mmol) in [bmim]Cl (0.7 mL) as a solvent at 80 °C resulted in no reaction. However, the efficiency was found to be markedly influenced by the structure of the anion. Thus, the use of $[bmim]PF_6$ as a solvent gave **2** in 79% yield even after only 15 min. The reaction at 40 °C gave **2** in 81% isolated yield. Further experiments indicated that the reaction takes place at ambient temperature. Thus, **2** was obtained in 92% yield when the reaction was carried out at 23 °C for 20 h. In contrast, no reaction took place in toluene at 40 °C. The use of the $PtCl_2$−$[bmim]PF_6$ system resulted in much higher reaction rates than those performed with common organic solvents. In all cases, the product was isolated by extraction with Et_2O followed by column chromatography. On the other hand, we found that the product also can be removed directly from the reaction system by distillation (78% yield, at 40 °C for 5 h).

(1) The conversion of enynes into 1-vinylcycloalkenes can be classified into two types, enyne-metathesis and skeletal reorganization, although two reactions are not strictly distinguished. The two reactions differ based on their mechanism and product distributions. Skeletal reorganization gives two possible isomers **I** and **II**, although the selectivity depends on the structure of the enynes and the nature of the catalysts. In many cases, either of the two products are obtained. The enyne-metathesis is typically catalyzed by Grubbs-type catalysts and the reaction gives only **I**.



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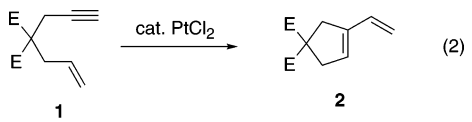
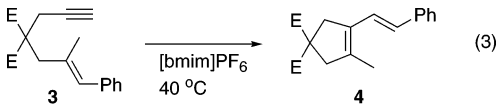


toluene	80 °C	3 h	86%
[bmim]$^+$Cl$^-$	80 °C	20 h	no reaction
[bmim]$^+$BF$_4^-$	80 °C	5 h	28%
[bmim]$^+$NTf$_2^-$	80 °C	20 h	17%
[bmim]$^+$PF$_6^-$	80 °C	15 min	79%
[bmim]$^+$PF$_6^-$	40 °C	5 h	81%
[bmim]$^+$PF$_6^-$	23°C	20 h	92%

The reaction was carried out in [bmim]$^+$PF$_6^-$ with several transition metal halides, which are known to be active for skeletal reorganization in toluene. Among the catalysts examined, $PtCl_2$ showed the highest activity, as shown in Table 1. Although $AuCl_3$ showed a catalytic activity comparable to that of $PtCl_2$, it gradually decomposed during the reaction.[17]

It was found that the skeletal reorganization of **1** proceeds in [bmim]PF$_6$ even at ambient temperature, as shown in eq 1. However, $PtCl_2$ was not completely miscible in [bmim]PF$_6$ at 25−80 °C. As a result, $PtCl_2$ was heated to 115 °C in [bmim]PF$_6$ to give a nearly homogeneous solution, and was then reacted with **1** at 40 °C. Using this protocol, **2** was obtained in 99% crude yield (80% isolated yield) after 2 h by extraction with Et_2O from the ionic liquids. Encouraged by the success of this procedure (method B), several enynes were produced by using the new protocol and the results are shown in Table 2. The reaction of the ester-substituted enyne **5** gave **6** (type II),[1] in which both the C−C triple bond and double bonds are cleaved.[1,6] While the reaction of **7** in toluene gave **8** in 35% (at 80 °C for 24 h), the yield was 58% in the ionic liquid after a 1 h reaction.

It was found that preheating is not always necessary for the reaction to proceed when the catalyst was changed. The reaction of **3** in the presence of $[RuCl_2(CO)_3]_2$ following method B (with preheating) gave **4** in 76% yield after 12 h, while method A (without preheating) gave **2** in 90% yield after only 2 h. These results indicate that catalyst decomposition takes place during the preheating. In fact, the color of the catalyst changes to a pale green during the reaction. This is probably due to the loss of the CO ligand from the catalyst, since the presence of such a ligand on ruthenium is known to be essential for the skeletal reorganization to proceed.[4]



$[RuCl_2(CO)_3]_2$	method A	2 h	90%
$[RuCl_2(CO)_3]_2$	method B	12 h	76%
$[RhCl(CO)_2]_2$	method A	1 h	90%

The reaction of **9** did not result in skeletal reorganization, but instead cycloisomerizatioin took place to give **10**, similar to the case when toluene is used as a solvent. The ionic liquid was again a better solvent than common solvents. In toluene, the reaction proceeded at 80 °C for 7 h to give **10** in 88% yield.[18]

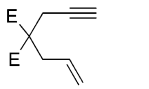
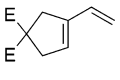
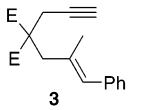
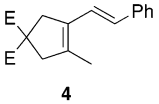
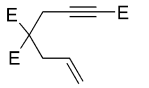
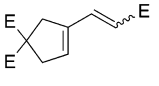
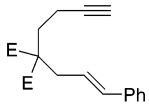
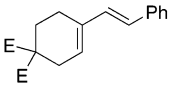
(17) Gold mirror was observed on the wall of the reaction vessel after the reaction.

TABLE 1. Screening of Catalysts in [bmim]PF$_6$

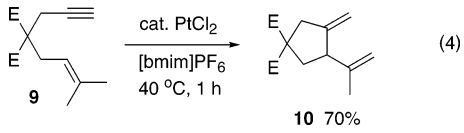
catalyst	time, h	crude yield, %
$PtCl_2$	5	81
$[RuCl_2(CO)_3]_2$	6	53
$[RhCl(CO)_2]_2$	20	no reaction
$[Rh(OAc))_2$	20	no reaction
$[IrCl(CO)_3]_n$	20	79[a]
$AuCl_3$	3	82
$InCl_3$	20	no reaction
$GaCl_3$	20	no reaction

[a] NMR yield.

TABLE 2. PtCl$_2$-Skeletal Reorganization of Enynes[a]

enyne	product	reaction time isolated yield [b]
		2 h 80%
1	2	
		1 h 90%
3	4	
		8 h 53% (*E*:*Z* = 3:1)
5	6	
		1 h [c] 58%
7	8	

[a] Reaction conditions (method B): The $PtCl_2$ (0.02 mmol) was stirred in [bmim]PF$_6$ (0.7 mL) at 115 °C for 5 min, and cooled to 40 °C. The mixture was then treated with enyne (0.5 mmol) at the same temperature. [b] Isolated yield. [c] At 80 °C.



The products produced by the skeletal reorganization of enynes were easily removed from the catalyst by a simple extraction with Et_2O. Extraction with hexane gave **2** in 50% crude yield and the extract was colorless. The use of cyclohexane in place of hexane improved the yield of **2** to a 70% crude yield, and the extract was slightly colored. Although Et_2O extraction was the most effective (99% crude yield), the extract was a pale yellow color, indicating that traces of catalyst were present in the extract.

In ionic liquids, the catalyst can be reused up to five times with some loss in activity, as shown in eq 5. This

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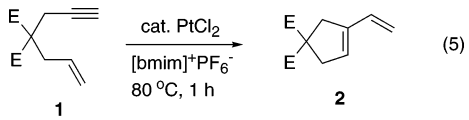
is due to the extraction of the catalyst from the ionic liquids, as described above. However, extending the reaction times led to a quantitative yield.



1 2 (5)

cycle	1	2	3	4	5[b]
crude yield	>99 %	>99 %	>99 %	72 %[a]	>99 %

[a] NMR yield
[b] reaction time : 5 h

In summary, we demonstrated herein that a $PtCl_2$–ionic liquid system can be used in the skeletal reorganization of enynes under milder conditions than those needed for ordinary solvents. The reaction proceeds effectively even at lower reaction temperatures than for toluene reported previously.[6] The $PtCl_2$ can be reused repeatedly.

Experimental Section

2-(3-Butynyl)-2-(3-phenyl-2-propenyl)propandionic Acid Diethyl Ester (7). ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 6H), 1.96 (t, J = 2.3 Hz, 1H), 2.22 (m, 4H), 2.82 (dd, J = 7.5, 1.3 Hz, 2H), 4.20 (dq, J = 7.2, 1.3 Hz, 4H), 6.04 (dt, J = 15.5, 7.5 Hz, 1H), 6.46 (d, J = 15.5 Hz, 1H), 7.23 (tt, J = 6.2, 2.7 Hz, 1H), 7.29 (t, J = 6.2 Hz, 2H), 7.30 (d, J = 6.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0, 14.1, 31.7, 36.6, 57.3, 61.5, 68.8, 83.3, 123.6, 126.2, 127.5, 128.5, 134.1, 137.0, 170.7; IR (neat) 3026 (w), 2981 (m), 2937 (w), 2908 (w), 2119 (w), 1730 s, 1599 (w), 1496 (w), 1466 (w), 1446 (m), 1389 (w), 1367 (m), 1298 (m), 1265 (m), 1240 (m), 1196 (s), 1095 (m), 1043 (w), 1026 (m), 970 (w), 862 (w), 744 (m), 694 (m), 644 (w); mass 328 (M^+, 26), 255 (23), 254 (100), 181 (47), 165 (12), 141 (17), 91 (13). Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H 7.37. Found: C, 72.93; H, 7.34.

Representative Procedure. $PtCl_2$ (5.3 mg, 0.02 mmol) was placed in a 8-mL screw vial, and [bmim]PF_6 (0.7 mL) was then added. The mixture was heated to 115 °C for 5 min and then cooled to 80 °C. To the homogeneous mixture was added **7** (164 mg, 0.5 mmol), followed by stirring for 1 h. The reaction mixture was extracted with Et_2O and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, R_f 0.26, hexane/Et_2O 5/1) to give 4-(2-phenyl-1-ethenyl)-3-cyclohexene-1,1-dicarboxylic acid diethyl ester (**8**) (98 mg, 58% yield) as a white solid; mp 86 °C; ^{1}H NMR ($CDCl_3$) δ 1.25 (t, J = 7.1 Hz, 6H), 2.26 (t, J = 5.9 Hz, 2H), 2.37 (t, J = 5.9 Hz, 2H), 2.74 (s, 2H), 4.19 (q, J = 7.0 Hz, 4H), 5.85 (s, 1H), 6.47 (d, J = 16.1 Hz, 1H), 6.75 (d, J = 16.5 Hz, 1H), 7.19 (tt, J = 7.2, 1.3 Hz, 1H), 7.30 (t, J = 7.2 Hz, 2H), 7.38 (d, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 21.7, 27.4, 31.3, 53.2, 61.4, 125.9, 126.2, 126.6, 127.1, 128.6, 131.2, 137.6, 171.4; IR (KBr) 2983 (m), 1736 (s), 1593 (w), 1493 (w), 1446 (m), 1387 (w), 1331 (w), 1286 (m), 1242 (s), 1217 (m), 1176 (s), 1161 (s), 1142 (m), 1085 (m), 1070 (s), 1038 (m), 1016 (m), 970 (m), 958 (m), 865 (w), 800 (w), 782 (w), 746 (m), 694 (m); mass 328 (M^+, 3), 254 (48), 215 (14), 181 (27), 169 (61), 141 (37), 128 (14), 117 (100), 115 (32), 91 (23). Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H 7.37. Found: C, 73.07; H, 7.23.

Products **2**,[4] **4**,[4] **6**,[4] and **10**[18] are known compounds.

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