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RUTHENIUM-CATALYZED [2 + 2] CYCLIZATION OF 1,7-ALLENYNES IN IONIC LIQUID AND CATALYST RECYCLING

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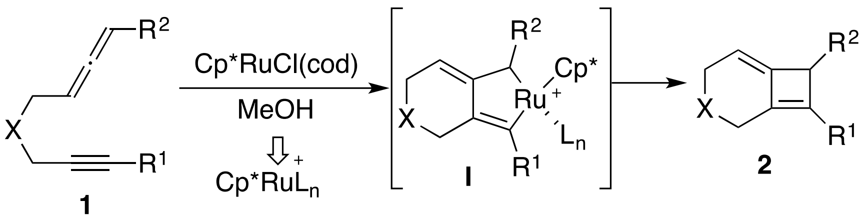
Abstract – Ruthenium-catalyzed [2 + 2] cyclization of 1,7-allenynes in ionic liquid ([BDMI]PF_6) as a reaction medium proceeded to give the corresponding bicyclo[4.2.0]octa-1(8),5-diene derivative in high yield. Furthermore, the recovered catalyst immobilized in the ionic liquid could be recycled up to 10 times.

This paper is dedicated to Professor Kiyoshi Tomioka on the occasion of his 70th birthday.

Ionic liquids (ILs) have attracted much attention as useful reaction media in recent synthetic organic chemistry due to their favorable properties such as high polarity, non-volatility, thermal stability, and high dissolution activity.[1] Furthermore, it is well known that ILs can dissolve and immobilize various transition metal complexes, especially a cationic metal complex. Due to these unique characteristics of ILs, separation of the product and the catalyst in an IL can be easily conducted by simple phase separation after the end of the chemical reaction, and the catalyst immobilized in the IL can be re-used for another reaction. Therefore, many examples of transition metal catalysis in an IL and re-use of the catalyst immobilized in the IL have been reported,[2] and we previously demonstrated rhodium(I)-catalyzed intramolecular hydroacylation of 4-alkenals and cycloisomerizatin of ene-diene in an IL and recycling of the rhodium catalyst immobilized in the IL.[3]

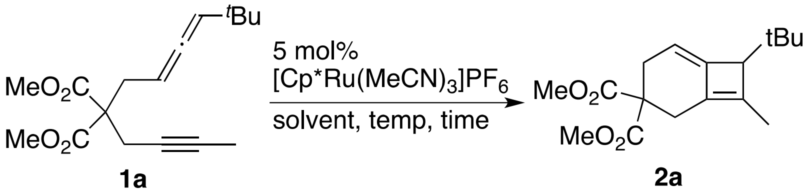
On the other hand, we have reported ruthenium-catalyzed [2 + 2] cyclization of 1,7-allenynes (Scheme 1).[4,5] Reaction of the allenyne **1** in the presence of Cp*RuCl(cod) in methanol proceeded to give bicyclo[4.2.0]octa-1(8),5-diene derivative **2** via ruthenacyclopentene intermediate **I**. We also demonstrated that the real active species in the [2 + 2] cyclization was a cationic ruthenium complex generated from Cp*RuCl(cod) and methanol *in situ*.[4]



Scheme 1. Ruthenium-catalyzed [2 + 2] cyclization of 1,7-allenyne in methanol

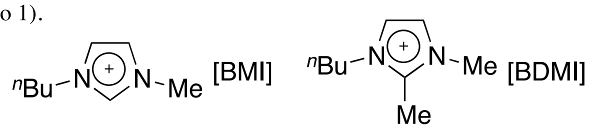
With this as a background, we planned ruthenium-catalyzed [2 + 2] cyclization of 1,7-allenyne in an IL recycling of the ruthenium catalyst immobilized in the IL.[6] First of all, [2 + 2] cyclization of allenyne with 5 mol% of $[Cp^*Ru(MeCN)_3]PF_6$[7] in THF was carried out as a control experiment (Table 1, run 1). The reaction proceeded smoothly at room temperature to give bicyclic compound **2a** in 96% yield. Cyclization of **1a** in various imidazolium cation-based ILs (BMI = 1-butyl-3-methylimidazolium, BDMI 1-butyl-2,3-dimethylimidazolium) were examined (runs 2-7), and $[BDMI][PF_6]$ was found to be a reaction medium (run 7). Next, the effects of co-solvents were investigated using $[BDMI][PF_6]$ (runs 8-11). When toluene was used as a co-solvent, cyclized product **2a** was obtained in only 11% yield (run On the other hand, the use of polar solvents gave good results, and the reaction of **1a** in a mixed solvent $[BDMI][PF_6]$ and acetonitrile proceeded to afford **2a** in quantitative yield (run 11).

Table 1. Investigation of Ru(II)-catalyzed [2 + 2] cyclization of **1a** in various ILs



run	solvent	co-solvent	temp (°C)	yield (%)[a]
1	THF	-	rt	96
2	$[BMI][NTf_2]$	-	50	- (91)
3	$[BMI][BF_4]$	-	50	11 (75)
4	$[BMI][PF_6]$	-	50	- (79)
5	$[BDMI][NTf_2]$	-	50	5 (84)
6	$[BDMI][BF_4]$	-	50	5 (87)
7	$[BDMI][PF_6]$	-	50	18 (80)
8[b]	$[BDMI][PF_6]$	tolunene	rt	11 (75)
9[b]	$[BDMI][PF_6]$	THF	rt	95
10[b]	$[BDMI][PF_6]$	$ClCH_2CH_2Cl$	rt	93
11[b]	$[BDMI][PF_6]$	MeCN	rt	quant

[a] The values in parentheses are the yields of recovered allenyne **1a**.
[b] The reaction was carried out in a mixed solvent of $[BDMI][PF_6]$ and co-solvent (ratio of 1 to 1).



Encouraged by these results, the recyclability of the ruthenium catalyst remaining in the IL after the reaction was evaluated for [2 + 2] cyclization of **1a** in mixed solvents of the IL and polar co-solvents 2). When THF was used as a co-solvent, the second cycle showed a drop in the yield of **2a** (run 1). On the other hand, three consecutive cycles were realized in reactions using 1,2-dichloroethane and as a co-solvent, though a small amount of starting allenyne was recovered in the third run (runs 2 and 3). Since the yield of **2a** obtained by the reaction using acetonitrile as a co-solvent was better than that by the reaction in [BDMI][PF_6]/1,2-dichloroethane, we next investigated the effect of temperature using a [BDMI][PF_6]/acetonitrile mixed solvent system. When the reaction was carried out at 50 °C in the presence of 5 mol% of the ruthenium complex, cyclized product **2a** was obtained in high yield for each of five consecutive cycles (run 4). Finally, the use of 10 mol% of the ruthenium catalyst enabled recycling the catalyst 10 times without loss of yield of **2a** (run 5).[8]

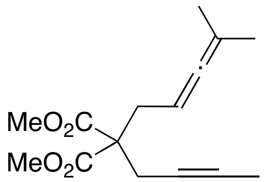
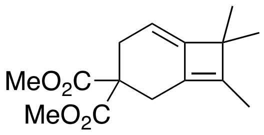
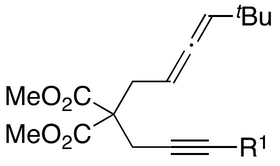
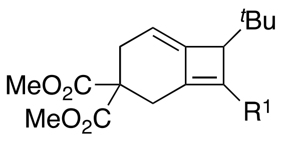
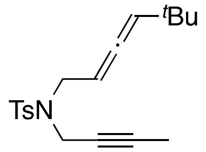
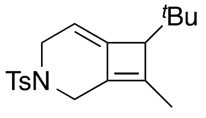
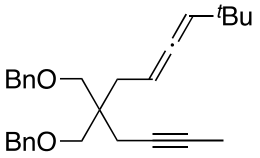
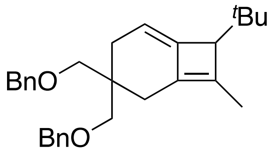
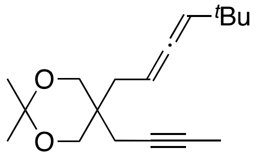
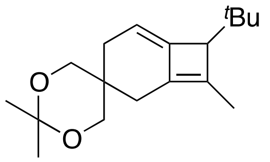
Table 2. Effects of co-solvent, temperature and catalyst loading on recyclability of the catalyst[a]

run	co-solvent	temp	cycle	time (h)	yield (%)[b]
1	THF	rt	1	0.5	95
			2	21	31 (68)
2	$ClCH_2CH_2Cl$	rt	1	0.5	93
			2	1	87
			3	14	86 (14)
3	MeCN	rt	1	2	quant
			2	4	97
			3	42	92 (8)
4	MeCN	50 °C	1	0.5	quant
			2	0.5	quant
			3	0.5	quant
			4	14	quant
			5	47	93
			6	50	75 (25)
5	MeCN	50 °C	1	0.5	quant
			2	0.5	quant
			3	0.5	quant
			4	0.5	quant
			5	0.5	95
			6	1	quant
			7	4	quant
			8	4	quant
			9	19	quant
			10	48	78 (17)

[a] Reaction conditions: [Cp*Ru$(MeCN)_3$]PF_6 (5 mol%: runs 1-4, 10 mol%: run 5), [BDMI][PF_6]/co-solvent = 1/1.
[b] The values in parentheses are the yields of recovered allenyne **1a**.

With the optimal conditions in hand, we investigated [2 + 2] cyclization of various allenynes in the combined solvent of [BDMI][PF_6] and acetonitrile and catalyst recycling (Table 3). It was found that the yield of the product and recyclability of the ruthenium catalyst were affected by the structure of the substrate. When the reaction of **1h** was carried out, the corresponding cyclized product **2h** was obtained in high yield (run 6). Moreover, the ruthenium catalyst immobilized in the IL could be re-used at least 9 times without significant loss of yield of **2h** (run 6).

Table 3. [2+2] Cyclization of various allenyne in IL and catalyst recycling[a]

run	allenyne	product	cycle	time (h)	yield (%)
1[b]	 **1c**	 **2c**	1 2 3 4	0.5 1 22 50	89 91 92 17 (55)
					
2	**1d** (R^1 = Ph)	**2d** (R^1 = Ph)	1 2 3	0.5 2 18	55 77 34 (33)
3	**1e** (R^1 = CH_2OTBS)	**2e** (R^1 = CH_2OTBS)	1 2	2 21	95 47 (5)
4	 **1f**	 **2f**	1 2 3	0.5 21 54	71 74 complex mixture
5[c]	 **1g**	 **2g**	1 2	0.5 22	82 31 (57)
6	 **1h**	 **2h**	1 2 3 4 5 6 7 8 9 10	0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 1 2	quant quant quant 91 97 92 93 93 quant quant

[a] Reaction conditions : 10 mol% [Cp*Ru(MeCN)$_3$]PF$_6$, [BDMI][PF$_6$]:MeCN = 1;1, 50 °C. [b] The reaction was carried out in the mixed solvent of [BDMI][PF$_6$] and $ClCH_2CH_2Cl$ (1:1). [c] The reaction was carried out in the mixed solvent of BDMI][PF$_6$] and MeCN (1:2).

In summary, we demonstrated that cationic ruthenium-catalyzed [2 + 2] cycloaddition of 1,7-allenynes in [BDMI]PF_6/co-solvent proceeded to give the corresponding bicyclo[4.2.0]octa-1(8),5-diene derivatives in high yield. We also revealed that the ruthenium catalyst immobilized in the IL could be recycled up to ten times without loss of catalytic activity. Further studies along this line are in progress.

ACKNOWLEDGEMENTS

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8. Typical procedure for recycling of the ruthenium catalyst in [BDMI]PF_6/MeCN (Table 2, run 5). 1-Butyl-2,3-dimethylimidazolium hexafluorophosphate ([BDMI]PF_6, 1.0 mL) was put into a test tube, and [BDMI]PF_6 was dried at 70 °C under vacuum over 0.5 h. A solution of **1a** (57.5g, 0.19 mmol) in MeCN (1 mL) and $[Cp^{*}Ru(MeCN)_3]PF_6$ (10.2 mg, 0.020 mmol) were added to the test tube, and the mixture was stirred at 50 °C for 0.5 h under an argon atmosphere. The ionic liquid layer was extracted with Et_2O (5 mL, 3 times) via a cannula under an argon atmosphere, and the

combined Et_2O solution was concentrated. The crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 15/1) to give **2a** (57.5 mg, quant) as a colorless oil. The remaining $[BDMI]PF_6$ layer was dried under vacuum at room temperature for 0.5 h and reused for the next cycle.