Click type Polycycloadditions in Ionic Liquids

Synthesis of Poly(triazole)s from Diacetylenes and Diazides

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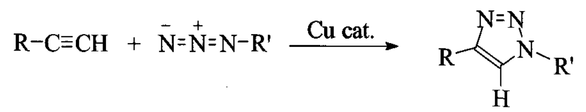
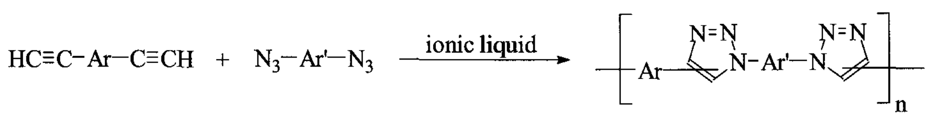
Introduction

1,3-Dipolar cycloaddition reactions have been systematically studied by Huisgen in the 1980s.[1] Since then, the area of research had remained silent until Sharpless and co-workers have found that Cu(I) species could effectively catalyze the 1,3-dipolar cycloaddition of alkynes with azides in a 1,4-regioselective fashion, defined as "click chemistry" (scheme 1).[2]



(1)

Click type synthetic procedures have attracted much attention by many researchers, because of their remarkable features such as high yield, mild reaction condition, and simple product isolation.[3] In the field of polymer and material chemistry, some click type reactions have been successfully used to synthesize dendritic and linear macromolecules.[4,5]
Recently the chemistry of ionic liquids (ILs), which are low melting salts and consist of organic cations and inorganic anions, has grown exponentially, because of their unique chemical and physical properties such as low vapor pressure, highly thermal and chemical stability, high polarity, and so on.[6,7] So far, ILs are employed as media for a wide variety of reactions and polymerizations such as radical polymerizations,[8] cationic polymerizations,[9] polycondensations,[10] and polyaddition. However, click chemistry in ionic liquids has been rarely investigated.
In this work, the synthesis of polytriazoles using both of click chemistry and ionic liquids as reaction medium from diacetylenes and diazides was studied in detail (Scheme 2).



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Results and Discussion

Model reaction

In an initial approach, the reactions of phenylacetylene and azidobenzene in ionic liquids as well as water with or without Cu catalyst were carried out as the model reaction (scheme 3). The results are shown in Table 1.

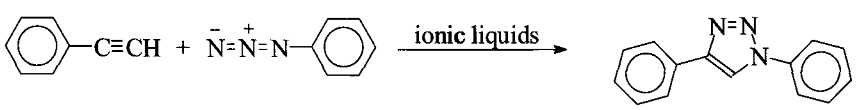

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Table 1. Synthesis of diphenyl-1,2,3-triazole in ionic liquids and water [a)]

Solvent	Yield (%)	
	With Cu catalyst [b)]	Without Cu catalyst
[bmim][Br]	51	35
[bmim][BF_4]	76	10
H_2O	88	49

a) Condition. Phenylacetylene : 0.25 mmol/L, azidobenzene : 0.25 mmol/L, ionic liquids: 5mL or water : 20mL at 85°C for 24h. b) $CuSO_4$: 12.5 mmol/L, sodium ascorbate : 25mmol/L.

In imidazolium type ionic liquids such as 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]), the cycloaddition reaction proceed in the presence of Cu catalyst to provide only 1,4-diphenyl-1,2,3-triazole in high yields as well as in water. In the absence of Cu catalyst, the reaction of phenylacetylene and azidobenzene in ionic liquids didn't smoothly proceed, compared with the use of water, and the products were the mixture of 1,4- and 1,5-regioisomers of dipheny-1,2,3-triazole.

Polycycloaddition

After confirming that click reaction could proceed in ionic liquids, the polymerization of 4,4'-diethynyldiphenyl ether and 4,4'-diazidodiphenyl ether was carried out in [bmim][BF_4] with various Cu catalysts, as shown in Table 2. Among three Cu catalysts which were used in ordinary click reaction, $Cu(PPh_3)_3Br$ was most effective for the polycycloaddition to give polytriazole with the highest inherent viscosity in high yield. Even in the absence of Cu catalysts, the polymerization could proceed to give polytriazoles in moderate yield. So further studies were carried out both in the presence of $Cu(PPh_3)_3Br$ and in the absence of Cu catalysts to investigate the click type polycycloadditions.

Table 2. Synthesis of polytriazoles with various Cu catalysts [a)]

Cu Catalyst	Yield (%)	η inh (dL/g) [b)]
$CuSO_4 \cdot 5H_2O$ + sodium ascorbate	48	0.27
$Cu(PPh_3)_3Br$	94	0.40
CH_3COOCu	27	0.32
none	43	0.37

a) Condition. Diacetylene : 0.5mmol, diazide : 0.5mmol, Cu catalyst : 0.025 mmol, [bmim][BF_4] : 5mL at 100℃ for 18h under N_2.
b) Measured at a concentration of 0.5 g/dL in H_2SO_4 at 30℃.

< with Cu catalysts >

In the presence of $Cu(PPh_3)_3Br$, the polymerizations were carried out in various imidazolium-type ionic liquids and DMF (Table 3). While the polymerization in [bmim][Cl] and [bmim][Br] proceeded homogenously, the yields and inherent viscosities of obtained polymers were low values. In the use of [bmim][BF_4] and [bmim][PF_6], the yields and the molecular weight of obtained polytriazoles were higher, even thought the precipitations of the polymers were observed. DMF also gave the polytriazloe with high viscosity in high yield.

Table 3. Synthesis of polytriazoles with $Cu(PPh_3)_3Br$ in various ionic liquids and DMF [a)]

Solvent	Yield (%)	η inh (dL/g)[b)]
[bmim][Cl]	46	0.12
[bmim][Br]	43	0.18
[bmim][BF_4]	90	0.26
[bmim][PF_6]	94	0.40
DMF	86	0.34

a) Condition. Diacetylene : 0.5mmol, diazide : 0.5mmol, ionic liquid : 5mL, $Cu(PPh_3)_3Br$: 0.25mmol at 100℃ for 24h under N_2.
b) Measured at a concentration of 0.5 g/dL in H_2SO_4 at 30℃.

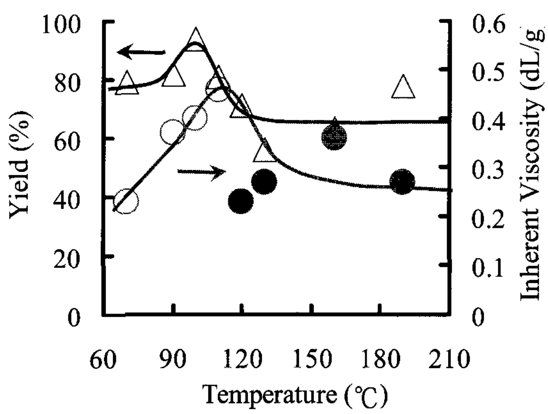
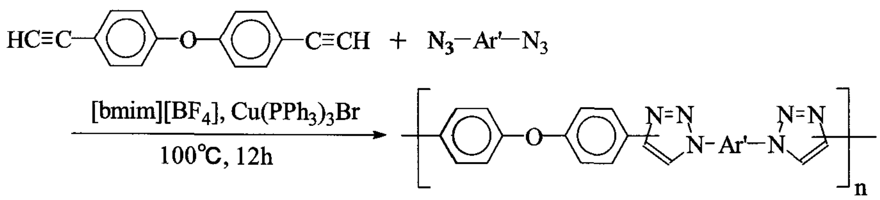


Figure 1. Effect of temperature on polycycloaddition with $Cu(PPh_3)_3Br$ in [bmim][BF_4] for 18h under N_2

The effect of temperature on the polycycloaddition in [bmim][BF_4] with $Cu(PPh_3)_3Br$ was investigated. The increase of temperature caused the increase of the molecular weight of obtained polymers as shown in Figure 1. However higher temperature than 120℃ gave insoluble polymers in any solvents. Therefore, further polymerization were carried out at 100℃

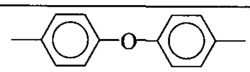
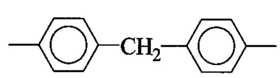
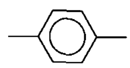
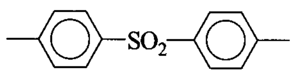
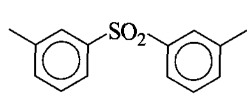
Under the optimum condition obtained above, five aromatic diazides reacted with 4,4'-diethynyldiphenyl ether in [bmim][BF_4] at 100℃ for 12h (Scheme 4). Aromatic diazides such as 4,4'-diazidodiphenyl ether, 4,4'-diazidodiphenylmethane, p-phenylenediazide, 4,4'-diazidodiphenyl sulfone, and 3,3'-diazidodiphenyl sulfone were readily prepared in high yields from corresponding aromatic diamines with sodium nitrite, followed by sodium azide.



(4)

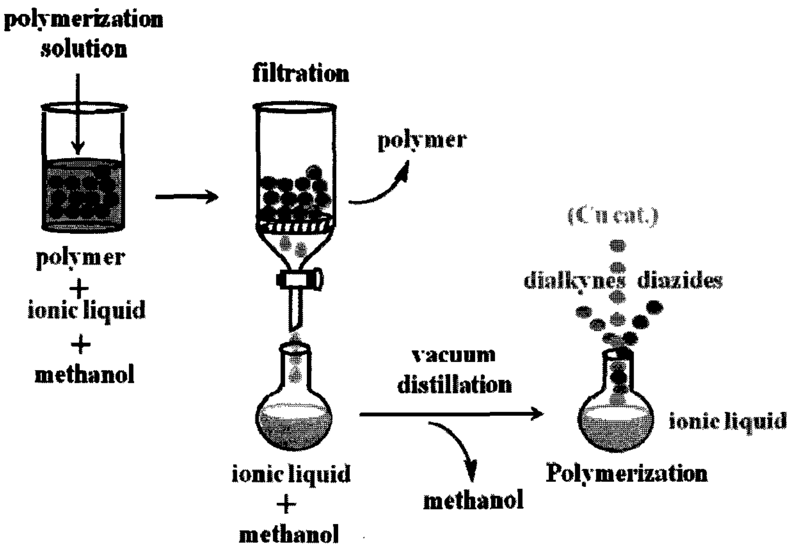
Four diazides except for 1,4-phenylenediazide provided the polytriazoles in high yield, as shown in Table 4. Especially, 4,4'-diazidodiphenylmethane gave the polymer with the highest inherent viscosity of 0.83dL/g.

Table 4. Synthesis of polytriazoles from 4,4'-diacetyldiphenyl ether and various diazides with $Cu(PPh_3)_3Br$ in [bmim][BF_4] [a)]

Diazides	Yield (%)	η inh (dL/g) [b)]
	87	0.42
	78	0.83
	29	0.34
	88	0.27
	86	0.35

a) Condition. Diacetylene : 0.5mmol, diazide : 0.5mmol, [bmim][BF_4] : 5mL, $Cu(PPh_3)_3Br$: 0.25mmol at 100℃ for 12h under N_2.
b) Measured at a concentration of 0.5 g/dL in H_2SO_4 at 30℃.

As ionic liquids are generally very thermal stable solvents, the recovery of [bmim][BF_4] was performed as the following procedure (Scheme 5). After the polymerization mixture was poured into methanol, the precipitated polymers were removed by filtration. The filtrate was evaporated to remove methanol and dried *in vacuo*. The polycycloaddition of bis(acetylene)s and diazides was carried out in recovered [bmim][BF_4] with the introduce of monomers and Cu catalyst.
As shown in Table5, [bmim][BF_4] could be reused several times to provide the polymer in high yields. However the molecular weights of obtained polymers were lower than that of the polymers prepared in new [bmim][BF_4]. No addition of $Cu(PPh_3)_3Br$ caused drastic decrease of the yields and the molecular weight, because of the deactivation of Cu catalysts during the recovery.



Scheme 5. Illustration of the recycling process

Table 5. Recycle use of [bmim][BF_4] for synthesis of polytriazoles with $Cu(PPh_3)_3Br$ [a)]

Run	Yield (%)	η inh (dL/g) [b)]
New	87	0.42
1st recycle	85 (10[c)])	0.33 (0.22[c)])
2nd recycle	79	0.32
3rd recycle	95	0.25

a) Condition. Diacetylene : 0.5mmol, diazide : 0.5mmol, [bmim][BF_4] : 5mL, $Cu(PPh_3)_3Br$: 0.25mmol at 100℃ for 12h under N_2.
b) Measured at a concentration of 0.5 g/dL in H_2SO_4 at 30℃.
c) Without the addition of $Cu(PPh_3)_3Br$.

< without catalysts>

The thermal polycycloaddition of 4,4'-diethynyldiphenyl ether with 4,4'-diazidodiphenyl ether without Cu catalysts were studied in an effort to optimize the process.

Table 6. Synthesis of polytriazoles without Cu catalysts in various ionic liquids and DMF [a)]

Solvent	Yield (%)	η inh (dL/g)[b)]
[bmim][Cl]	49	0.14
[bmim][Br]	69	0.19
[bmim][BF_4]	37	0.34
[bmim][PF_6]	34	0.35
DMF	26	0.11

a) Condition. Diacetylene : 0.5mmol, diazide : 0.5mmol, ionic liquid : 5mL at 100℃ for 24h under N_2.
b) Measured at a concentration of 0.5 g/dL in H_2SO_4 at 30℃.

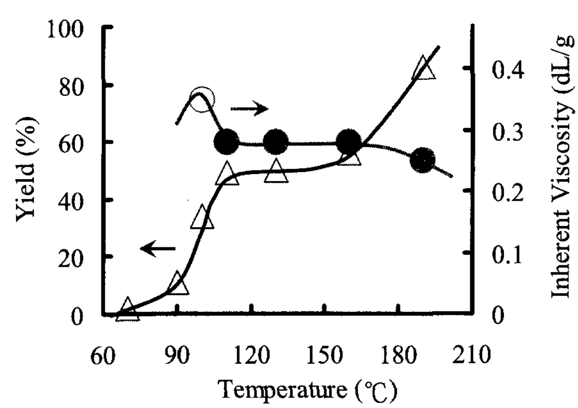
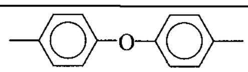
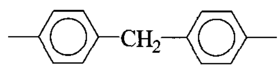
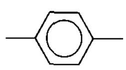
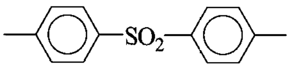
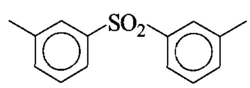


Figure 2. Effect of temperature on polycycloaddition in [bmim][BF_4] for 24h under N_2

Table 6 shows the polycycloadditions in various ionic liquids and DMF as reaction medium at 100℃ for 24h under nitrogen. While the polymerization in DMF provided the polymer with low viscosity in lower yield, the polycycloadditions using ionic liquids gave the polymers with higher molecular weights in higher yields. Especially [bmim][BF_4] and [bmim][PF_6] provided the polymers with the inherent viscosities of 0.35dL/g, which were similar to that prepared with Cu catalysts. It was thought that ionic liquids act as Cu catalysts in this polycycloaddition. Further polymerizations were carried out in [bmim][BF_4] as reaction medium.
Figure 2 shows the effect of temperature on the thermal polymerization in [bmim][BF_4] under nitrogen. Higher temperature than 110℃ gave only insoluble polytriazoles in about 60%. At only 100℃ the polymerization proceed smoothly and gave soluble polymers.
Under the optimum condition obtained above, five diazides reacted with 4,4'-diethynyldiphenyl ether in [bmim][BF_4] at 100 ℃ for 12h (Table 7). When 4,4'-diazidodiphenylmethane and p-phenylenediazide gave the polytriazoles with high inherent viscosities (1.01 and 0.51 dL/g), even though their yields were still low. Other diazides provided only the polymers with moderate or lower molecular weighs (0.13~0.37 dL/g).

Table 7. Synthesis of polytriazoles from 4,4'-diacetyldiphenyl ether and various diazides in [bmim][BF_4] [a)]

Diazides	Yield (%)	η inh (dL/g) [b)]
	71	0.37
	27	1.01
	17	0.51
	49	0.17
	53	0.13

a) Condition. Diacetylene : 0.5mmol, diazide : 0.5mmol, [bmim][BF_4] : 5mL at 100℃ for 12h under N_2.
b) Measured at a concentration of 0.5 g/dL in H_2SO_4 at 30℃.

The possibility of reuse of ionic liquids was also investigated for the thermal polycycloaddition. [bmim][BF_4] was recovered by the same procedure mentioned above and used as polymerization medium without the addition of new $Cu(PPh_3)_3Br$. As shown in Table 8, recovered [bmim][BF_4] could be used 6 times without any decrease of yields and molecular weighs of polytriazoles obtained.

Table 8. Recycle use of [bmim][BF_4] for synthesis of polytriazoles [a)]

Run	Yield (%)	η inh (dL/g) [b)]
New	39	0.27
1st recycle	48	0.30
2nd recycle	41	0.24
3rd recycle	66	0.27
4th recycle	55	0.26
5th recycle	44	0.23
6th recycle	71	0.29

a) Condition. Diacetylene : 0.5mmol, diazide : 0.5mmol, [bmim][BF_4] : 5mL at 100℃ for 12h under N_2.
b) Measured at a concentration of 0.5 g/dL in H_2SO_4 at 30℃.

Conclusions

1,3-Dipolar cycloaddition reactions of acetylenes and azides have proceeded in ionic liquids such as [bmim][Br] and [bmim][BF_4] as well as in water to give 1,2,3-triazole derivatives in high yields, when the Cu catalysts were used. However, no introduce of Cu catalysts disturbed drastically the cycloaddition. Polycycloaddition of diacetylenes and diazides in [bmim][BF_4] with $Cu(PPh_3)_3Br$ proceeded at 100℃ to provide the polytriazoles with the inherent viscosities of 0.27～0.83 dL/g in high yields. Even though no Cu catalysts were used, the polycycloaddition could proceed in [bmim][BF_4] to give the polytriazoles with inherent viscosities of 0.13～1.01 dL/g. In this polycycloadditions both with and without CU catalysts, ionic liquids could be reused several times without any decrease of activity of monomers.

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