



Novel preparation of ion-supported triphenylphosphines and their synthetic utility

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ABSTRACT

Novel ion-supported Ph_3P compounds, 4-(diphenylphosphino)-benzyltrimethylammonium bromide (**A**) and *N*-methyl-*N*-[4-(diphenylphosphino)-benzyl]pyrrolidinium bromide (**B**), were prepared. Because of their stability in air, ion-supported Ph_3P **A** and **B** could be used for the halogenation of alcohols, the esterification of carboxylic acid with the Mitsunobu reaction, the Mizoroki–Heck reaction, and the Sonogashira reaction. The advantages of using these ion-supported Ph_3P **A** and **B** are the simple isolation of the products by ether extraction due to their poor solubility in ether, and the easy recovery of the co-product, ion-supported Ph_3PO , by filtration in high yields (>90%), which could be regenerated and reused for the same reactions, in the halogenation of alcohols and the esterification of carboxylic acid with the Mitsunobu reaction. On the other hand, ionic liquid reaction media containing $\text{Pd}(\text{OAc})_2$ or PdCl_2 and ion-supported Ph_3P **A** or **B** as catalysts could be reused for the same Mizoroki–Heck reaction and the Sonogashira reaction maintaining high yields, using iodotoluene with methyl acrylate and phenylacetylene, respectively.

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1. Introduction

Triphenylphosphine (Ph_3P) is one of the most important reagents for the bromination, iodination, and chlorination of alcohols with carbon tetrabromide, molecular iodine-imidazole, and carbon tetrachloride (the Appel reaction), respectively, and the esterification of carboxylic acids with alcohols in the presence of diethyl azodicarboxylate (DEAD) (the Mitsunobu reaction).^{1,2} Moreover, it can be used as a ligand for Pd-catalyzed C–C bond formation (the Mizoroki–Heck reaction,^{3a,3b} the Sonogashira reaction,^{3c} the Stille reaction,^{3d,3e} and the Suzuki–Miyaura reaction^{3f,3g}). However, in the halogenation of alcohols with $\text{Ph}_3\text{P}/\text{CBr}_4$, $\text{Ph}_3\text{P}/\text{I}_2/\text{imidazole}$, or $\text{Ph}_3\text{P}/\text{CCl}_4$, and the esterification and amidation of carboxylic acids with $\text{Ph}_3\text{P}/\text{DEAD}$ or $\text{Ph}_3\text{P}/\text{di}(2\text{-pyridyl})\text{disulfide}$, Ph_3PO is formed as a co-product and it must be removed carefully by troublesome column chromatography to obtain the product in the pure state. To the best of our knowledge, no study of ion-supported Ph_3P has been reported so far.

Here, as part of our study of novel ion-supported reagents,⁴ we would like to report the preparation of novel ion-supported Ph_3P compounds, 4-(diphenylphosphino)benzyltrimethylammonium bromide (**A**) and *N*-methyl-*N*-[4-(diphenylphosphino)benzyl]pyrrolidinium bromide (**B**). Then, their synthetic utility in the halogenation of

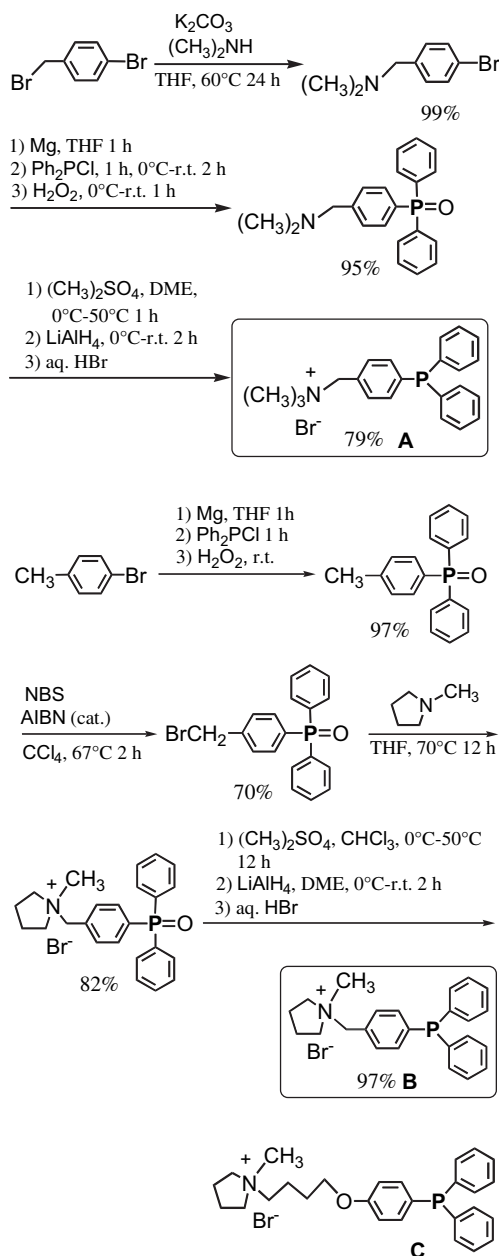
alcohols and the esterification of carboxylic acid as an equivalent required reagent, and the Mizoroki–Heck reaction and the Sonogashira reaction as a catalytic amount of ligand with $\text{Pd}(\text{OAc})_2$ or PdCl_2 was studied.

2. Results and discussion

Ion-supported Ph_3P **A** and **B** were prepared from 4-bromobenzyl bromide in three steps and 4-bromotoluene in four steps, respectively, as shown in Scheme 1. Both ion-supported Ph_3P **A** and **B** are solids and stable in air. Therefore, they can be stored under argon atmosphere at room temperature. Meanwhile, ion-supported Ph_3P **C** is highly viscous oil, that is, smoothly oxidized in air because it bears electron-rich aromatics on the phosphorus atom.

First, the halogenation of alcohols was carried out as follows: a mixture of alcohol (2-phenylethanol, 3-phenyl-1-propanol, and 4-phenyl-1-butanol: 2.0 mmol) and **A** (2.4 mmol) with CBr_4 (2.2 mmol) in 1,2-dichloroethane was warmed at 60 °C for 2 h, or a mixture of alcohol (2-phenylethanol, 3-phenyl-1-propanol, and 4-phenyl-1-butanol: 2.0 mmol), and **B** (3.0 mmol) with CBr_4 (2.2 mmol) in dichloromethane was warmed at 40 °C for 2 h. Then, ether was added to the reaction mixture to separate the ion-supported Ph_3PO and the oil. After filtration and removal of ether solvent, the corresponding bromides were obtained in high yields with moderate purities, due to the presence of co-product CHBr_3 only (Table 1). On the other hand, ion-supported Ph_3PO was

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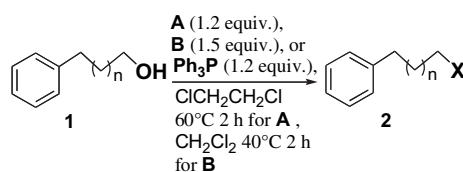


Scheme 1. Preparation of ion-supported Ph_3P **A** and **B**.

recovered in over 90% yield. After the O-methylation of the recovered ion-supported Ph_3PO with dimethyl sulfate and the subsequent reduction with LiAlH_4 , ion-supported Ph_3P **A** and **B** could be regenerated easily, based on the reduction method of Ph_3PO in the literature,⁵ and the recovered **A** and **B** could be reused for the same bromination of 3-phenyl-1-propanol in good yields up to the second time, as shown in Table 1. For the iodination of alcohols with **A**, a mixture of alcohol (2 mmol), **A** (2.4 mmol), I_2 (3.0 mmol), imidazole (3.0 mmol), and KI (10 mmol) in 1,2-dichloroethane was warmed at 60 °C for 2 h to provide the corresponding iodides in high yields with high purities, as shown in Table 1.

Similarly, for the iodination of alcohols with **B**, a mixture of alcohol (2 mmol), **B** (3.0 mmol), I_2 (3.0 mmol), imidazole (3.0 mmol), and KI (10 mmol) in dichloromethane was warmed at 40 °C for 2 h to provide the corresponding iodides in high yields with high purities, as shown in Table 1. Here, ion-supported Ph_3PO co-products, 4-(diphenylphosphono)benzyltrimethylammonium bromide and N-methyl-N-[4-(diphenylphosphono)benzyl]pyrrolidinium bromide,

Table 1
Halogenation of alcohols with **A** and **B**



For bromination: CBr_4 (1.1 equiv) with Ph_3P , **A** or **B**
For iodination: I_2 (1.5 equiv), imidazole (1.5 equiv), KI (5 equiv)

	Yields of 2 /%		
	$n=0$	$n=1$	$n=2$
A			
X=Br	86 ^a	95, ^a 88, ^{a,c} 76 ^{a,d}	91 ^a
X=I	85 ^b	80 ^b	80 ^b
B			
X=Br	89 ^a	95, ^a 93, ^{a,c} 87 ^{a,d}	97 ^a
X=I	83 ^b	85 ^b	83 ^b
Ph_3P			
X=Br	72 ^e	68 ^e	53 ^e

^a Yield of purified **2**. Purity of the product **2** after removal of ether from the extracts was 70%–75%.

^b Yield of purified **2**. Purity of the product **2** after removal of ether from the extracts was 85%–93%.

^c Yield of purified **2** with the first regenerated **A** or **B**.

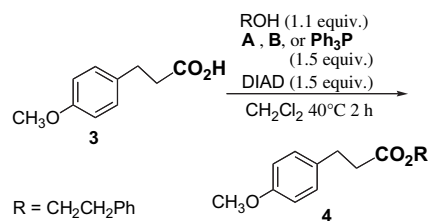
^d Yield of purified **2** with the second regenerated **A** or **B**.

^e Yield of purified **2**. Purity of the product **2** after removal of ether from the extracts was 14%–43%. Ph_3PO was recovered in 42–44% yield.

were recovered in high yields. When Ph_3P was used for the conversion of the alcohols with CBr_4 in 1,2-dichloroethane at 60 °C for 2 h under the same conditions and procedure, Ph_3PO was recovered only in the range of 42–44% yields, together with the corresponding bromides in 72%–53% yields, and the purity of the bromides after removal of ether was in the range of 14%–43%, as shown in Table 1. This result indicates ion-supported Ph_3P **A** and **B** are efficiently recyclable reagents for the halogenation of alcohols and the purity of ether extracts from the reaction mixture is enough high.

The present ion-supported Ph_3P **A** and **B** could be also used for esterification of 3-(4'-methoxyphenyl)propanoic acid with 2-phenylethanol and diisopropyl azodicarboxylate (DIAD) in dichloromethane to provide the corresponding 2-phenylethyl 3-(4'-methoxyphenyl)propanoate (the Mitsunobu reaction) in good yields, as shown in Table 2.

Table 2
Mitsunobu reaction with **A** and **B**



Reuse	Yields of 4 /%		
	0	1	2
A	84 ^a	79 ^{a,b}	70 ^{a,c}
B	87 ^a	80 ^{a,b}	77 ^{a,c}
Ph_3P	87 ^d	—	—

^a Yield of purified **4**. Purity of the product **4** after removal of ether from the extracts was >90%.

^b Yield of purified **4** with the first regenerated **A** or **B**.

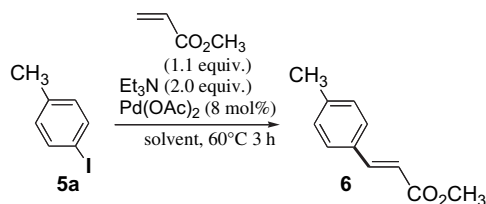
^c Yield of purified **4** with the second regenerated **A** or **B**.

^d Yield of purified **4**. Ph_3PO was recovered in 30% yield.

After the reaction, ether was added to the reaction mixture to separate the ion-supported Ph_3PO and the oil. After filtration and removal of ether solvent, the corresponding ester was obtained in high yields with high purity (>90%) in both ion-supported Ph_3P **A** and **B**, respectively, without chromatography. Ion-supported Ph_3PO co-products, 4-(diphenylphosphono)benzyltrimethylammonium bromide and *N*-methyl-*N*-[4-(diphenylphosphono)benzyl]pyrrolidinium bromide, were recovered in over 90% yield. Again, after the *O*-methylation of the recovered ion-supported Ph_3PO with dimethyl sulfate and the subsequent reduction with LiAlH_4 , ion-supported Ph_3P **A** and **B** could be regenerated and reused for the same esterification reaction, maintaining good yield with high purity. On the other hand, when Ph_3P was used for the same esterification of 3-(4'-methoxyphenyl)propanoic acid under the same conditions, Ph_3PO was recovered only in 30% yield, together with the ester in 87% yield after purification from ether extracts, as shown in Table 2. This result indicates again ion-supported Ph_3P **A** and **B** are efficiently recyclable reagents for the esterification of carboxylic acids and the purity of ether extracts from the reaction mixture is enough high.

Then, to evaluate the catalytic activity of ion-supported Ph_3P **A** and **B** as a ligand on palladium, the Mizoroki–Heck reaction and the Sonogashira reaction were studied. First, mixtures of *p*-iodotoluene (1 mmol), methyl acrylate (1.1 mmol), $\text{Pd}(\text{OAc})_2$ (8 mol%), and Et_3N (2 mmol) without ion-supported Ph_3P **A** or **B** in DMF, acetonitrile, THF, and toluene were warmed at 60 °C for 3 h to provide methyl *p*-methylcinnamate in 38%, 20%, 7%, and 16% yields, respectively, as shown in Table 3 (entries 1–4). Surprisingly, the same reaction without ion-supported Ph_3P **A** or **B** in typical ionic liquids (ILs), such as [bmim]PF₆ (butylmethylimidazolium phosphorus hexafluoride), [bmpy]NTf₂ (butylmethylpyrrolidinium bis(trifluoromethanesulfonyl)imide), gave methyl *p*-methylcinnamate in good yields (entries 5 and 8). The reaction promotion of the Mizoroki–Heck reaction by using iodobenzene (40 °C–80 °C, 24 h) or bromoanisole (100 °C, 72 h) with ethyl cinnamate without Ph_3P in ILs, such as [C₆Py]Cl, [C₆Py]PF₆, and [C₆Py]BF₄, was previously reported.⁶ Thus, the same reaction promotion of the Mizoroki–Heck reaction with *p*-iodotoluene (1 mmol), methyl acrylate (2.4 mmol), $\text{Pd}(\text{OAc})_2$ (8 mol%), and Et_3N (2 mmol) without ion-supported Ph_3P **A** or **B** in [bmim]PF₆ and [bmpy]NTf₂ was observed to provide methyl *p*-methylcinnamate in good yields. However, ILs containing $\text{Pd}(\text{OAc})_2$ could not be reused efficiently, and the yields of methyl *p*-methylcinnamate for the second reuse and the third reuse were

Table 3
Mizoroki–Heck reaction without **A** or **B** in DMF and IL



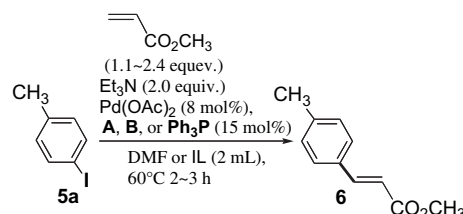
Entry	Solvent	Reuse	Yield ^a (%)	Purity (%)
1	DMF		38 (54) ^a	<40
2	CH ₃ CN		20 (68) ^a	<20
3	THF		7 (82) ^a	<7
4	Toluene		16 (70) ^a	<15
5	[bmim]PF ₆	0	88 (10) ^a	<80
6 ^b		1	50 (45) ^a	<55
7 ^b		2	14 (80) ^a	<10
8	[bmpy]NTf ₂	0	92 (7) ^a	<90
9 ^b		1	50 (48) ^a	<50
10 ^b		2	27 (60)	<25

^a Yield of recovered iodotoluene.

^b Only iodotoluene, methyl acrylate, and Et_3N were added.

dramatically decreased (entries 6,7,9, and 10). On the other hand, when the same Mizoroki–Heck reaction with *p*-iodotoluene (1 mmol), methyl acrylate (1.1 mmol), $\text{Pd}(\text{OAc})_2$ (8 mol%), and Et_3N (2 mmol) with ion-supported Ph_3P **A** or **B** (15 mol%) in DMF and ILs, such as [bmim]PF₆ (2 mL), [emim]OTs (2 mL, ethylmethylimidazolium tosylate),^{4a} and [bmpy]NTf₂ (2 mL), was carried out at 60 °C for 2 h, methyl *p*-methylcinnamate was obtained in good yields. After the reaction in ILs, ether was added to the reaction mixtures to extract the reaction products, and methyl *p*-methylcinnamate was obtained in good yield with high purity for each reaction with **A** or **B** by removal of ether solvent, as shown in Table 4. In addition, after ether extraction and drying by a vacuum pump, ILs containing $\text{Pd}(\text{OAc})_2$ and ion-supported Ph_3P **A** or **B** could be repeatedly used for the same reaction, maintaining the high yield and the high purity of methyl *p*-methylcinnamate up to the second or third reuse (Table 4). When the same reaction was carried out using Ph_3P instead of ion-supported Ph_3P **A** or **B**, methyl *p*-methylcinnamate was obtained in good yields in the first time. However, the yield was gradually decreased as in the first reuse, the second reuse, and the third reuse, as shown in Table 4, and each ether extract contains 2–3% of Ph_3P together with methyl *p*-methylcinnamate. Thus, ion-supported Ph_3P **A** or **B** in ILs can be used as a recyclable reaction media for the Mizoroki–Heck reaction, and each ether extract does not contain ion-supported Ph_3P **A** or **B** at all.

Table 4
Mizoroki–Heck reaction with **A** or **B** in IL



DMF or IL		Yields of 6 /%				
		Reuse	0	1 ^c	2 ^c	3 ^c
DMF	A		99 ^a			
	B		94 ^a			
[bmim]PF ₆	A		90 ^b	91 ^b	76 ^b	63
	B		95 ^b	83 ^b	81 ^b	48
[emim]OTs	A		92 ^b	88 ^b	89 ^b	85 ^b
	B		93 ^b	76 ^b	60 ^b	55
[bmpy]NTf ₂	A		95 ^b	96 ^b	90 ^b	63
	B		96 ^b	96 ^b	95 ^b	62
	Ph₃P		97 ^d	63 ^d	58 ^d	33 ^d

^a Yield of purified **6**. Purity of the product **6** after removal of DMF and ether from the extracts was ~99%.

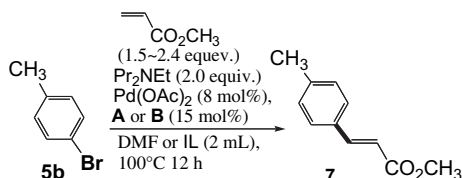
^b Yield of purified **6**. Purity of the product **6** after removal of ether from the extracts was 86%–99%.

^c Only iodotoluene, methyl acrylate, and Et_3N were added.

^d Yield of purified **6**. Each ether extract contains 2–3% of Ph_3P .

The Mizoroki–Heck reaction with bromotoluene (1 mmol), methyl acrylate (1.5–2.4 mmol), Pr_2NEt (2.0 mmol), and $\text{Pd}(\text{OAc})_2$ (8 mol%) without ion-supported Ph_3P **A** or **B** in DMF, [bmim]PF₆, and [bmpy]NTf₂ was carried out at 100 °C for 12 h to give methyl *p*-methylcinnamate in 0%, 7%, and <1% yields, respectively. On the other hand, the same reaction in the presence of ion-supported Ph_3P **A** in DMF, [bmim]PF₆, and [bmpy]NTf₂ provided methyl *p*-methylcinnamate in 100%, 77%, and 77% yields, respectively, as shown in Table 5. The same reaction promotion in the presence of ion-supported Ph_3P **B** in DMF, [bmim]PF₆, and [bmpy]NTf₂ was also observed. Thus, the Mizoroki–Heck reaction with bromotoluene in

Table 5
Mizoroki–Heck reaction with **A** or **B** in IL



DMF of IL	Yields of 7 /%				
	Reuse	0	1	2	3
DMF	— ^a	0			
	A	100			
	B	45			
[bmim]PF ₆	— ^a	7			
	A	77 ^b	65 ^b	25	16
	B	71 ^b	65 ^b	73 ^b	40
[bmpy]NTf ₂	— ^a	<1			
	A	77 ^b	60 ^b	7	<1
	B	85 ^b	84 ^b	60 ^b	55

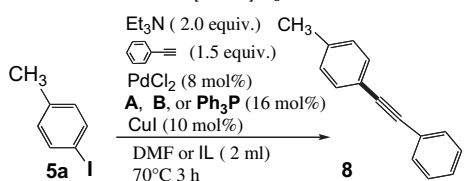
^a Without **A** or **B**.

^b Yield of purified **7**. Purity of the product **7** after removal of ether from the extracts was 80–70%.

the presence of ion-supported Ph₃P **A** or **B** was dramatically accelerated, and ILs containing Pd(OAc)₂ and ion-supported Ph₃P **A** or **B** could be reused for the same reaction, especially for ion-supported Ph₃P **B**.

Then, the Sonogashira reaction with iodotoluene and phenylacetylene in the absence and presence of ion-supported Ph₃P **A** or **B** was studied. First, the reaction of iodotoluene (1 mmol), phenylacetylene (1.5 mmol), PdCl₂ (8 mol%), and CuI (10 mol%) without ion-supported Ph₃P **A** or **B** in [bmim]PF₆ was conducted to provide phenyl(*p*-tolyl)acetylene in 75% yield, as shown in Table 6 (entry 10). However, IL containing PdCl₂ and CuI could not be reused efficiently, and the yields of phenyl(*p*-tolyl)acetylene for the second reuse and

Table 6
Sonogashira reaction with **A** or **B** in [bmim]PF₆



Entry	DMF or IL	Reuse	Yields of 8 (%)		
			A	B	Ph₃P
1	DMF	0	41	98	99
2	[bmim]PF ₆	0	100 ^c	100 ^c	91 ^e
3		1 ^b	100 ^c	100 ^c	92 ^e
4		2 ^b	97 ^c	100 ^c	99 ^e
5		3 ^b	100 ^c	100 ^c	76 ^e
6		4 ^b	100 ^c	100 ^c	41
7		5 ^b	96 ^c	90 ^c	18
8		6 ^b	96 ^c	95 ^c	—
9		7 ^b	100 ^c	94 ^c	—
10 ^a		[bmim]PF ₆	0	75	
11 ^a	1 ^b		68 (4) ^d		
12 ^a	2 ^b		40 (28) ^d		

^a Without **A**, **B**, or **Ph₃P**.

^b Only iodotoluene, phenylacetylene, and Et₃N were added.

^c Yield of purified **8**. Purity of the product **8** after removal of ether from the extracts was 95–85%.

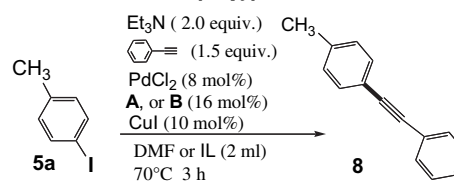
^d Yield of recovered iodotoluene.

^e Yield of purified **8**. Each ether extract contains 2–3% of Ph₃P.

the third reuse were decreased (entries 10–12). On the other hand, the same reaction in the presence of ion-supported Ph₃P **A** or **B** (16 mol%) in [bmim]PF₆ under the same conditions generated phenyl(*p*-tolyl)acetylene in 100% yield. After the reaction, ether was added to the reaction mixture to extract the reaction products, and phenyl(*p*-tolyl)acetylene was obtained in good yield with high purity for each reaction with **A** or **B**, by removal of ether solvent, as shown in Table 6 (entry 2). Moreover, after ether extraction and drying by a vacuum pump, IL containing PdCl₂, CuI, and ion-supported Ph₃P **A** or **B** could be repeatedly used for the same reaction, maintaining the high yield and the high purity of phenyl(*p*-tolyl)acetylene up to the seventh reuse (entries 2–9).

When Ph₃P was used instead of ion-supported Ph₃P **A** or **B**, in [bmim]PF₆ under the same conditions, phenyl(*p*-tolyl)acetylene was surprisingly obtained in good yields up to the third reuse. However, from the fourth reuse of the reaction media, the yield of phenyl(*p*-tolyl)acetylene was dramatically decreased, and each ether extract contains 2–3% of Ph₃P. Thus, ion-supported Ph₃P **A** or **B** can be also used for the Sonogashira reaction in ionic liquid as a recyclable reaction media and each ether extract does not contain ion-supported Ph₃P **A** or **B** at all. The same reactivity of ion-supported Ph₃P **A** or **B** was also observed in [bmpy]NTf₂. When [bmpy]NTf₂ was used for the same reaction, IL containing PdCl₂, CuI, and ion-supported Ph₃P **A** or **B**, especially the former one, could be repeatedly used for the same reaction, maintaining the high yield and the high purity of phenyl(*p*-tolyl)acetylene up to the fifth reuse, as shown in Table 7 (entries 1–6). However, reuse of the same Sonogashira reaction without ion-supported Ph₃P **A** or **B** in [bmpy]NTf₂ gave it in moderate yields (entries 7–9).

Table 7
Sonogashira reaction with **A** or **B** in [bmpy]NTf₂



Entry	IL	Reuse	Yields of 8 (%)	
			A	B
1	[bmpy]NTf ₂	0	97 ^c	100 ^c
2		1 ^b	100 ^c	95 ^c
3		2 ^b	100 ^c	90 ^c
4		3 ^b	100 ^c	51
5		4 ^b	100 ^c	50
6		5 ^b	100 ^c	40
7 ^a	[bmpy]NTf ₂	0	75 (19) ^d	
8 ^a		1 ^b	73 (32) ^d	
9 ^a		2 ^b	52 (47) ^d	

^a Without **A**, **B**, or **Ph₃P**.

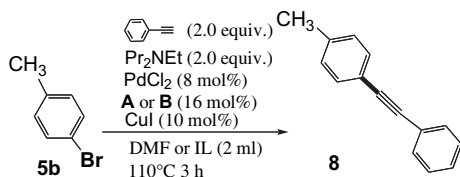
^b Only iodotoluene, phenylacetylene, and Et₃N were added.

^c Yield of purified **8**. Purity of the product **8** after removal of ether from the extracts was 95–85%.

^d Yield of recovered iodotoluene.

Finally, the Sonogashira reaction with bromotoluene (1 mmol), phenylacetylene (2.0 mmol), Pr₂NEt (2.0 mmol), PdCl₂ (8 mol%), and CuI (10 mol%) without ion-supported Ph₃P **A** or **B** in DMF and [bmim]PF₆ was carried out at 110 °C for 3 h to give phenyl(*p*-tolyl)acetylene in 0% and 3% yields, respectively, as shown in Table 8 (entries 2 and 11). On the other hand, the same reaction in the presence of ion-supported Ph₃P **A** in [bmim]PF₆ and [bmpy]NTf₂ provided phenyl(*p*-tolyl)acetylene in 76% and 97% yields, respectively (entries 3 and 7), although the reuse of the reaction media containing PdCl₂, CuI, and ion-supported Ph₃P **A** gave it in moderate yields. The similar

Table 8
Sonogashira reaction with **A** or **B** in [bmim]PF₆



Entry	DMF or IL	Reuse	Yields of 8 (%)	
			A	B
1	DMF	—	30 (26) ^c	42 (21) ^c
2 ^a		—	0	
3	[bmim]PF ₆	0	76	72
4		1 ^b	73	68
5		2 ^b	30	60
6		3 ^b	14 (28) ^c	41
7	[bmpy]NTf ₂	0	97	82
8		1 ^b	71	75
9		2 ^b	27 (47) ^c	35
10		3 ^b	32 (39) ^c	31
11 ^a	[bmim]PF ₆	0	3 (26) ^b	
12 ^a		1 ^b	3 (49) ^b	
13 ^a		2 ^b	2 (36) ^b	

^a Without **A** or **B**.

^b Only iodotoluene, phenylacetylene, and Pr₂NEt were added.

^c Yield of recovered bromotoluene.

results in the same reactions with ion-supported Ph₃P **B** in [bmim]PF₆ and [bmpy]NTf₂ were also obtained.

3. Conclusion

In summary, novel ion-supported Ph₃P, 4-(diphenylphosphino)benzyltrimethylammonium bromide (**A**) and *N*-methyl-*N*-[4-(diphenylphosphino)benzyl]pyrrolidinium bromide (**B**), were prepared. Because of their stability in air, ion-supported Ph₃P **A** and **B** could be used for the halogenation of alcohols, the esterification of carboxylic acid with the Mitsunobu reaction as an equivalent required reagent, and the Mizoroki–Heck reaction and the Sonogashira reaction as a catalytic ligand with Pd(OAc)₂ or PdCl₂. The advantages of using these ion-supported Ph₃P **A** or **B** are the simple isolation of the products by extraction due to their poor solubility in ether, and the easy recovery of the co-product, ion-supported Ph₃P, by filtration in high yields (over 90%), which could be regenerated and reused for the same reactions. For the Mizoroki–Heck reaction and the Sonogashira reaction, the ionic liquid reaction media containing Pd(OAc)₂ or PdCl₂ and ion-supported Ph₃P **A** or **B** could be reused for the same reactions, maintaining the high yield and the high purity of the products.

4. Experimental

4.1. General

¹H NMR and ¹³C NMR spectra were obtained with JEOL-JNM-GSX-400, JEOL-JNM-LA-400, and JEOL-JNM-LA-500 spectrometers. Chemical shifts are expressed in parts per million downfield from TMS in δ units. Mass spectra were recorded on JEOL-HX-110 and JEOL-JMS-AT115 spectrometers. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel 60 (Kanto Kagaku Co.) was used for column chromatography and Wakogel B-5F was used for preparative TLC.

4.1.1. Compound A. Mp 168–170 °C; IR (neat) 1477, 1433, 822, 745, 697 cm⁻¹; ¹H NMR (CDCl₃, TMS) δ =3.39 (s, 9H), 5.02 (s, 2H), 7.27–

7.30 (m, 2H), 7.32–7.40 (m, 12H); ¹³C NMR (CDCl₃, TMS) δ =52.78 (p), 68.51 (s), 127.48 (q), 128.71 (t), 128.77 (t), 129.23 (t), 132.98 (t), 133.80 (t), 133.88 (t), 133.95 (t), 134.03 (t), 135.90 (q); ³¹P-NMR (CDCl₃, H₃PO₄) δ = -4.98; Elemental analysis: calcd for C₂₂H₂₅BrNP·1/2CH₃OH: C, 62.80%; H, 6.32%; N, 3.25%. Found: C, 62.77%; H, 6.09%; N, 3.16%.

4.1.2. Compound B. Mp 207–209 °C; IR (neat) 1433, 742, 696 cm⁻¹; ¹H NMR (CDCl₃, TMS) δ =2.22 (m, 2H), 2.35 (m, 2H), 3.21 (s, 3H), 3.68 (m, 2H), 4.03 (m, 2H), 5.08 (s, 2H), 7.26–7.40 (m, 12H), 7.62 (d, *J*=2.8 Hz, 2H); ¹³C NMR (CDCl₃, TMS) δ =21.33 (s), 47.82 (p), 63.12 (s), 65.71 (s), 128.21 (q), 128.69 (t), 128.75 (t), 129.22 (t), 132.54 (t), 132.59 (t), 133.79 (t), 133.95 (t), 133.96 (t), 134.12 (t), 135.95 (q); ³¹P-NMR (CDCl₃, H₃PO₄) δ = -5.00; Elemental analysis: calcd for C₂₄H₂₇BrNP·1/2H₂O: C, 64.15%; H, 6.28%; N, 3.12%. Found: C, 64.09%; H, 6.11%; N, 2.96%.

4.1.3. Compound C. Viscous oil; IR (neat) 1435, 746, 696 cm⁻¹; ¹H NMR (CDCl₃, TMS) δ =1.95–2.04 (m, 4H), 2.29–2.32 (m, 2H), 3.27 (s, 3H), 3.76–3.86 (m, 6H), 4.05 (t, 2H, *J*=5.8 Hz), 6.87 (m, 2H), 7.25–7.33 (m, 12H); ¹³C NMR (CDCl₃, TMS) δ =20.98 (s), 21.10 (2s), 25.77 (s), 49.04 (p), 59.02 (s), 64.72 (2s), 71.73 (s), 114.73 (2t), 128.36–128.54 (6t), 128.87 (q), 132.19 (2q), 133.35 (4t), 135.60 (2t), 159.31 (q); ³¹P-NMR (CDCl₃, H₃PO₄) δ = -6.43; Elemental analysis: calcd for C₂₇H₃₃BrNOP·H₂O·1/2CH₂Cl₂: C, 59.10%; H, 6.49%; N, 2.51%. Found: C, 59.28%; H, 6.05%; N, 2.39%.

4.2. Typical procedure for halogenation of alcohols with ion-supported Ph₃P **A** or **B**

N-Methyl-*N*-[4-(diphenylphosphino)benzyl]pyrrolidinium bromide **B** (1320 mg, 3.0 mmol) was dried by a vacuum pump for 2 h at 70 °C. To the flask containing compound **B** was added a solution of 3-phenyl-1-propanol (272 mg, 2.0 mmol) and CBr₄ (729 mg, 2.2 mmol) in dichloromethane (6 mL). The obtained mixture was stirred for 2 h at 40 °C under an argon atmosphere. After the reaction, ether (10 mL) was added and the obtained mixture was stirred for 40 min at room temperature. Then, the mixture was filtered and washed with ether. Removal of the solvent from the filtrates gave 3-phenyl-1-bromopropane as a crude state. The purity was in the range of 70–75%, due to containing a co-product, CHBr₃. Pure 3-phenyl-1-bromopropane was obtained by short column chromatography on silica gel (eluent: CHCl₃). The another co-product, *N*-methyl-*N*-[4-(diphenylphosphino)benzyl]pyrrolidinium bromide was recovered by the above filtration in 93% yield.

2-Phenylbromoethane, 3-phenyl-1-bromopropane, 4-phenyl-1-bromobutane, 2-phenyliodoethane, and 3-phenyl-1-iodopropane were identified with commercially available authentic compounds. 4-Phenyl-1-iodobutane: bp 100–105 °C/1 mm Hg (lit.⁷) bp 148–151 °C/15 mm Hg).

4.3. Typical regeneration of ion-supported Ph₃P **A** or **B**

(CH₃)₂SO₄ (3.3 mmol) was added to a flask containing *N*-methyl-*N*-[4-(diphenylphosphino)benzyl]pyrrolidinium bromide (3 mmol) in chloroform (6 mL) at 0 °C. The obtained mixture was stirred for 12 h at 50 °C under an argon atmosphere. Then, the solvent was removed and 1,2-dimethoxyethane (6 mL) was added to the residue. LiAlH₄ (12 mmol) was added to the solution at 0 °C and the obtained mixture was stirred for 2 h at rt.⁵ The reaction mixture was quenched with ice in the usual manner, 1 N aq HBr (10 mL) was added to the aqueous solution, and the obtained solution was washed with ether twice. Then, the aqueous solution was extracted with CH₂Cl₂ (10 mL×5), and the combined organic layer was dried over Na₂SO₄. After removal of the solvent,

N-methyl-*N*-[4-(diphenylphosphino)benzyl]pyrrolidinium bromide **B** was obtained in 93% yield.

4.4. Typical procedure for the Mitsunobu reaction with ion-supported Ph₃P

1-Methyl-3-[4'-(diphenylphosphino)benzyl]pyrrolidinium bromide **B** (660 mg, 1.5 mmol) was dried by a vacuum pump for 2 h at 70 °C. To the flask containing 1-methyl-3-[4'-(diphenylphosphino)benzyl]pyrrolidinium bromide **B** was added a solution of 3-(4'-methoxyphenyl)propanoic acid (180 mg, 1.0 mmol) and 2-phenylethanol (1.1 mmol) in dichloromethane (6 mL). Then, 40% diisopropyl azodicarboxylate in a toluene solution (0.758 mL, 1.5 mmol) was added dropwise to the mixture, and the obtained mixture was stirred for 2 h at 40 °C under an argon atmosphere. After the reaction, ether (10 mL) was added and the mixture was stirred for 10 min at 0 °C. Then, the mixture was filtered and washed with ether. Removal of the solvent from the filtrates gave 2-phenylethyl 3-(4'-methoxyphenyl)propanoate in >90% purity. It was purified by short column chromatography on silica gel (eluent: AcOEt and hexane=5:1) to give 2-phenylethyl 3-(4'-methoxyphenyl)propanoate in 87% yield. The co-product, 1-methyl-3-[4'-(diphenylphosphino)benzyl]pyrrolidinium bromide was recovered by the above filtration in 99% yield.

4.4.1. *2-Phenylethyl 3-(4'-methoxyphenyl)propanoate*. Oil; IR(neat): 1734, 1514, 1248, 1177, 1036, 701 cm⁻¹; ¹H NMR (CDCl₃, TMS) δ=2.58 (t, *J*=7.9 Hz, 2H), 2.86 (t, *J*=7.7 Hz, 2H), 2.91 (t, *J*=7.0 Hz, 2H), 3.78 (s, 3H), 4.28 (t, *J*=7.1 Hz, 2H), 6.82 (d, *J*=8.7 Hz, 2H), 7.07 (d, *J*=8.7 Hz, 2H), 7.17–7.32 (m, 5H); ¹³C NMR (CDCl₃, TMS): δ=30.15 (s), 35.18 (s), 36.28 (s), 55.34 (p), 64.98 (s), 113.96 (t), 126.63 (t), 128.57 (t), 128.99 (t), 129.32 (t), 132.64 (q), 137.91 (q), 158.13 (q), 172.98 (q); HRMS (EI) Calcd for C₁₈H₂₀O₃ M⁺: 284.1412. Found M: 284.1412.

4.5. Typical procedure for the Mizoroki–Heck reaction with ion-supported Ph₃P A or B in ionic liquid

A mixture of [bmim]PF₆ (2 mL) and *N*-methyl-*N*-[4-(diphenylphosphino)benzyl]pyrrolidinium bromide **B** (66 mg, 15 mol %) was dried by a vacuum pump for 2 h at 60 °C. Then, Pd(OAc)₂ (18 mg, 8 mol %), *p*-iodotoluene (218 mg, 1.0 mmol), methyl acrylate (95 mg, 1.1 mmol), and Et₃N (202 mg, 2 mmol) were added to the mixture, and the obtained mixture was stirred for 2 h at 60 °C under an argon atmosphere. After the reaction, the products were extracted by ether (5 mL×6). Removal of the solvent from the extracts gave methyl *p*-methylcinnamate in 95% (167 mg) with >95% purity.

4.5.1. *Methyl p-methylcinnamate*. Mp 58–58 °C (lit.⁸ mp 57–58 °C). Recyclic use of ionic liquid containing **B** was carried out as follows. After extraction with ether as above, the recovered ionic liquid containing Pd(OAc)₂ and **B** was dried by a vacuum pump for 2 h at 60 °C. Then, *p*-iodotoluene (218 mmol, 1.0 mmol), methyl acrylate (95 mg, 1.1 mmol), and Et₃N (202 mg, 2 mmol) were added to the mixture, and the obtained mixture was again stirred for 2 h at 60 °C

under an argon atmosphere. The products were extracted by ether mentioned as above.

4.6. Typical procedure for the Sonogashira reaction with ion-supported Ph₃P A or B in ionic liquid

A mixture of [bmim]PF₆ (2 mL) and 4-(diphenylphosphino)benzyltrimethylammonium bromide **A** (66 mg, 16 mol %) was dried by a vacuum pump for 2 h at 60 °C. Then, PdCl₂ (14 mg, 8 mol %), CuI (19 mg, 10 mol %), *p*-iodotoluene (218 mg, 1.0 mmol), phenylacetylene (157 mg, 1.5 mmol), and Et₃N (202 mg, 2.0 mmol) were added to the mixture, and the obtained mixture was stirred for 3 h at 70 °C under an argon atmosphere. After the reaction, the products were extracted by ether (5 mL×6). Removal of the solvent from the extracts gave phenyl(*p*-tolyl)acetylene in 100% yield with >95% purity.

Recyclic use of ionic liquid containing **A** was carried out as follows. The ionic liquid reaction media containing PdCl₂, CuI, and **A** was dried by vacuum pump for 2 h at 60 °C. Then, *p*-iodotoluene (218 mg, 1.0 mmol), phenylacetylene (157 mg, 1.5 mmol), and Et₃N (202 mg, 2.0 mmol) were added to the mixture, and the obtained mixture was again stirred for 2 h at 70 °C under an argon atmosphere. The products were extracted by ether mentioned as above.

4.6.1. *Phenyl(p-tolyl)acetylene*. Mp 69–70 °C (lit.⁹ mp 69–71 °C); IR (KBr) 2218 cm⁻¹; ¹H NMR: δ=2.37 (s, 3H), 7.16 (d, *J*=7.8 Hz, 2H), 7.32–7.36 (m, 3H), 7.43 (d, *J*=7.8 Hz, 2H), 7.51–7.53 (m, 2H); ¹³C NMR: δ=21.5, 88.7, 89.6, 120.2, 123.5, 128.0, 128.3, 129.1, 131.5, 131.6, 138.3.

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References and notes

- Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley & Sons: New York, NY, 1967; Vol. 1; p 1247; **1969**, Vol 2, p 445; **1972**, Vol 3, p 320; **1974**, Vol 4, p 549; **1975**, Vol 5, p 725; **1977**, Vol 6, p 643; **1979**, Vol 7, p 404; **1980**, Vol 8, p 516; **1981**, Vol 9, p 503; **1982**, Vol 10, p 448; **1984**, Vol 11, p 588; **1986**, Vol 12, p 550; **1988**, Vol 13, p 331; **1989**, Vol 14, p 336; **1990**, Vol 15, p 352; **1992**, Vol 16, p 366.
- Comprehensive Organic Transformations*; Larock, R. C., Ed.; VCH: New York, NY, 1989; p 353 and 849.
- (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, 44, 581; (b) Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, 37, 2320; (c) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 16, 4467; (d) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, 106, 4630; (e) Stille, J. K. *Pure Appl. Chem.* **1985**, 57, 1771; (f) Miyaura, N.; Yanagi, T.; Suzuki, A. *Tetrahedron Lett.* **1979**, 3437; (g) Suzuki, A. *Acc. Chem. Res.* **1982**, 15, 178.
- Ion-supported PhI: (a) Akiike, J.; Yamamoto, Y.; Togo, H. *Synlett* **2007**, 2168; (b) Kawano, Y.; Togo, H. *Synlett* **2008**, 217; (c) Moroda, A.; Togo, H. *Synthesis* **2008**, 1257; (d) Kawano, Y.; Togo, H. *Tetrahedron* **2009**, 65, 6251; (e) Ishiwata, Y.; Togo, H. *Tetrahedron Lett.* **2009**, 50, 5354.
- Imamoto, T.; Kikuchi, S.; Miura, T.; Wada, Y. *Org. Lett.* **2001**, 3, 87.
- Carmichael, A. J.; Earle, M. J.; Holbrey, J. D.; McCormac, P. B.; Seddon, K. R. *Org. Lett.* **1999**, 1, 997.
- Braun, V. *Ber.* **1911**, 43, 2837.
- Myrbohn, B. *J. Org. Chem.* **1983**, 48, 5327.
- Kakusawa, N.; Yamaguchi, K.; Kurita, J. *J. Organomet. Chem.* **2005**, 690, 2956.