Rasta Resin-PPh$_3$BnCl and Its Use in Chromatography-Free Carbonyl Cyanosilylation Reactions

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Abstract: Rasta resin-PPh$_3$BnCl, a new heterogeneous polystyrene-based phosphonium salt, has been synthesized and used to catalyze cyanosilylation reactions of aldehydes and ketones. It was found to be more efficient as a catalyst than a similar heterogeneous phosphonium salt anchored onto a polystyrene based on the Merrifield resin architecture of 2% divinylbenzene cross-linking. In these reactions rasta resin-PPh$_3$BnCl was separated from the desired reaction product simply by filtration, and it could be reused without significant loss of catalytic activity numerous times.

**Key words:** polymer-supported catalyst, polystyrene, phosphonium salt, organocatalysis, cyanosilylation

The use of phosphonium salts to catalyze reactions is an emerging aspect of organocatalysis.[1] For example, they have recently been reported to efficiently convert various aldehydes[2] and ketones[3] into the corresponding silylated cyanohydrins in the presence of trimethylsilyl cyanide under mild reaction conditions (Scheme 1). There has also been a report of a polymer-supported phosphonium salt catalyzing both the conversion of alcohols to the corresponding THP, THF and EE acetals, and the hydrolysis of such protected alcohols.[4]
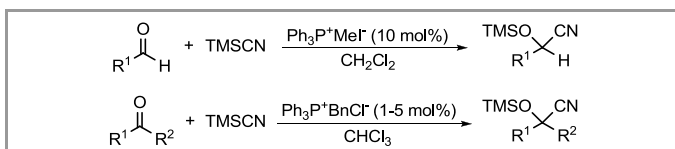

Scheme 1 Cyanosilylation of aldehydes and ketones catalyzed by phosphonium salts

We have been examining the use of various organic polymers as supports for organic chemistry,[5] especially in the context of polymer-supported phosphine reagents and catalysts,[6-8] and have recently reported the use of JandaJel[9] as a core for the rasta resin architecture (Figure 1)[10] in the synthesis of rasta resin-PPh$_3$ (1, Scheme 2).[11] This reagent was found to be superior in Wittig reactions to other polymer-supported phosphine reagents anchored onto the more common Merrifield resin architecture of divinylbenzene cross-linked polystyrene, and we attributed this observation to the fact that the phosphine groups of 1 were located on the flexible polystyrene grafts rather than on the rigid, heterogeneous core. Thus, the phosphine groups of 1 were readily accessible to the reacting substrates even when the polymer swelled poorly in the reaction solvent. For example, some of the one-pot Wittig reactions we reported were performed in 1-PrOH, a solvent that does not swell cross-linked polystyrene. As a follow up to this work, we wanted to see if 1 would also represent an improved platform for phospho-

nium salt organocatalysis compared to polymers related to Merrifield resin. Herein we report the reaction of 1 with benzyl chloride to form 2 (Scheme 2), and its use as a catalyst in carbonyl group cyanosilylation reactions.
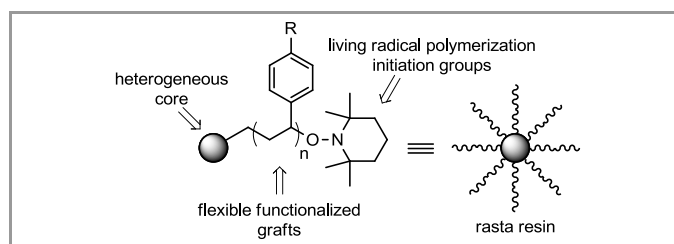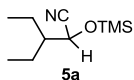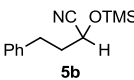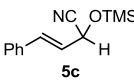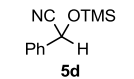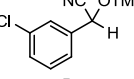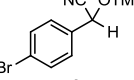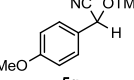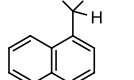

Figure 1 The rasta resin concept
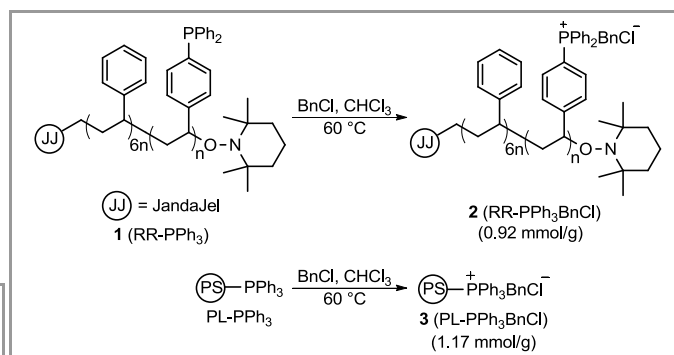
Scheme 2 Synthesis of 2 and 3

As outlined in Scheme 2, 1 (RR-PPh$_3$)[11] was reacted with benzyl chloride in hot CHCl$_3$ to afford 2 (RR-PPh$_3$BnCl).[12] Analysis of 2 by ^{31}P-NMR spectroscopy indicated complete conversion of the phosphine groups of 1 to the corresponding phosphonium salts. Elemental analysis was used to determine the loading level of 2 to be 0.92 mmol PPh$_3$BnCl/g. For the sake of comparison, a commercially available polystyrene-supported phosphine reagent based on the Merrifield resin architecture (PL-PPh$_3$ from Polymer Laboratories) was also converted to the corresponding phosphonium salt 3 (PL-PPh$_3$BnCl) using a similar procedure. The loading level of 3 was determined by elemental analysis to be 1.17 mmol PPh$_3$BnCl/g and its ^{31}P-NMR spectrum was similar to that of 2.

We next set out to compare the performance of 2 and 3 as catalysts in the cyanosilylation of various aldehydes using TMSCN. It should be noted that in the original report of using PPh$_3$BnCl to catalyze such reactions by Wang and Tian, only ketones were studied as starting materials.[3] However, Córdoba and Plumet had previously described the use of PPh$_3$MeI as the catalyst in cyano-

silylation reactions of aldehydes substrates. The reactions with **2** were performed on a 0.5 mmol scale at 50 °C in CHCl₃ until TLC analysis indicated the complete disappearance of starting material. As can be seen in Table 1, all of the 8 aldehydes studied (**4a-h**) afforded nearly quantitative yield of the desired product (**5a-h**) in 2.5 hours or less.[13] In these reactions, the product was obtained simply after filtration of the reaction mixture to remove **2** and concentration to remove the excess TMSCN and the solvent. All products **5a-h** were essentially pure according to ¹H-NMR spectroscopy. We next used **3** as the catalyst with two randomly chosen aldehydes, **4b** and **4d** (Table 1, entries 2 and 4). While **3** also afforded high yield in these reactions, they took much longer to proceed to completion than did the reactions using **2** as the catalyst.

When ketones **6a-h** were used in cyanosilylation reactions with TMSCN and **2** as the catalyst on a 0.5 mmol scale, the desired products **7a-h** were obtained in excellent yields in reactions that were somewhat slower than the reactions with aldehydes (Table 2). In these reactions of ketones, 1.5 to 12 hours were required for complete consumption of the starting material. Nevertheless, **2** was a more efficient catalyst than **3** when they were compared side by side with the substrates **6b** and **6h** (Table 2, entries 2 and 8). Just as before, essentially pure products **7a-h** were isolated from the reactions after only filtration and concentration. It should be noted that our results using **2** as catalyst are comparable to what Wang and Tian reported.[3] When they used PPh₃BnCl as the catalyst, they obtained 86-99% isolated yield of the desired product from 18 different ketone starting materials, using 0.01 or 0.05 equivalents of catalyst, 1.2 or 1.5 equivalents of TMSCN, at 25 or 50 °C, after 4-48 h in CHCl₃.
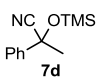
Table 1 Cyanosilylation of aldehydes using **2** or **3**
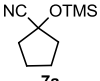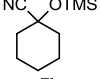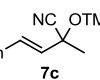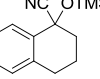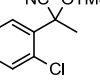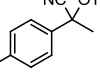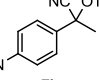
Entry	Substrate	Product	Time (h)	Yield (%)[a]
1	**4a**	**5a**	0.5	97
2	**4b**	**5b**	1 (4)[b]	99 (96)[b]
3	**4c**	**5c**	1	99
4	**4d**	**5d**	0.5 (2)[b]	99 (94)[b]
5	**4e**	**5e**	0.5	99
6	**4f**	**5f**	0.5	99
7	**4g**	**5g**	2.5	99
8	**4h**	**5h**	0.5	99

[a] Isolated yield of reactions using 0.5 mmol **4a-h**, 0.75 mmol TMSCN and 0.025 mmol **2** in 0.3 ml CHCl₃ stirring at 50 °C.

[b] Result using **3** as the catalyst.

Table 2 Cyanosilylation of ketones using **2** or **3**

Entry	Substrate	Product	Time (h)	Yield (%)[a]
1	**6a**	**7a**	4.5	81
2	**6b**	**7b**	1.5 (4)[b]	94 (94)[b]
3	**6c**	**7c**	12	99
4	**6d**	**7d**	10	98
5	**6e**	**7e**	11	95
6	**6f**	**7f**	10	99
7	**6g**	**7g**	10	99
8	**6h**	**7h**	1.5 (4)[b]	99 (93)[b]

a Isolated yield of reactions using 0.5 mmol **6a-h**, 0.75 mmol TMSCN and 0.025 mmol **2** in 0.3 ml CHCl$_3$ stirring at 50 °C.

b Result using **3** as the catalyst.

Lastly, the recyclability of **2** was examined in the conversion of **6h** to **7h**. For these reactions, in order to further establish the practical nature of **2**, we increased the scale from 0.5 mmol of ketone to 3.0 mmol. As can be seen in Table 3, **2** was efficiently recovered and readily reusable. We were able to use it in 8 reaction cycles with no decrease in product yield, and only a slight decrease in reaction efficiency. It should be noted that ^{31}P-NMR analysis of **2** recovered after the 8th reaction cycle afforded a spectrum that was essentially identical to that for freshly prepared **2**.[12]

Table 3 Recycling of **2**
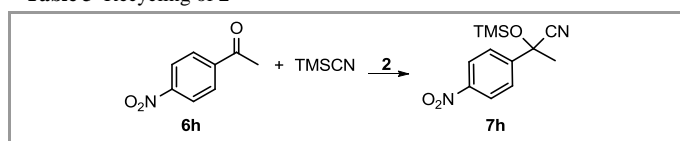
Run	Time	Catalyst Recovery (%)	Yield (%)^a
1	1.5	99	98
2	1.5	92	93
3	1.5	96	99
4	1.5	91	99
5	2.5	97	99
6	3	99	99
7	3	99	98
8	3	99	99

a Isolated yield of reactions using 3 mmol **6h**, 4.5 mmol TMSCN and 0.15 mmol **2** in 1.8 ml CHCl$_3$ stirring at 50 °C.

In conclusion, we have applied the rasta resin architecture as a support for a recyclable phosphonium salt catalyst (**2**), and used this material to catalyze the cyanosilylation of various aldehydes and ketones with TMSCN in reactions that ranged in scale from 0.5 to 3.0 mmol of starting material. Direct comparison of **2** and a Merrifield resin-based analogue (**3**) indicated that the rasta resin architecture allowed **2** to be more efficient as a catalyst. It is believed that this is due to the positioning of the catalytic phosponium groups of **2** on flexible grafts that are more accessible to reagents and substrates than are the catalytic groups of **3**, which are located in the interior of the heterogeneous beads. Additional studies to further demonstrate the utility of the rasta resin architecture are currently underway and the results of these will be reported in due course.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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(12) See Supporting Information for details.
(13) **General Procedure for Cyanosilylation Reactions**
To a solution of the aldehyde or ketone substrate (0.5 mmol) and TMSCN (0.75 mmol) in CHCl$_3$ was added **2** or **3** (0.025 mmol). The reaction mixture was stirred at 50 °C until TLC analysis indicated that the starting material was completely consumed. The reaction mixture was then filtred and the polymer-supported catalyst was washed with CH$_2$Cl$_2$ (2 × 50 mL). The combined filtrate was concentrated *in vacuo* to afford the desired product. All products were characterized by ^{1}H-, and ^{13}C-NMR and mass spectroscopy.

Graphical abstract