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Highly active phosphine-free carbene ruthenium catalyst for cross-metathesis of acrylonitrile with functionalized olefins

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Abstract—The carbene ruthenium complex [1,3-bis(2,6-dimethylphenyl)-4,5-dihydroimidazol-2-ylidene](C$_5$H$_5$N)$_2$(Cl)$_2$Ru=CHPh (**8**) was prepared by the reaction of [1,3-bis (2,6-dimethylphenyl)-4,5-dihydroimidazol-2-ylidene](PPh$_3$)(Cl)$_2$Ru=CHPh (**7**) with pyridine and used as a highly effective catalyst for the cross-metathesis of acrylonitrile with various functionalized olefins.

In the last decade, olefin metathesis has emerged as a powerful tool for C–C bond formation.[1] The commercial availability of well-defined transition metal catalysts (Fig. 1), such as molybdenum alkoxyimido alkylidene **1**,[2] ruthenium benzylidene catalysts **2**, **3**[3] and ether-tethered ruthenium alkylidene derivative catalyst **4**,[4] have made olefin metathesis practical for application to synthetic organic chemistry. However, cross-metathesis (CM), a method for the intermolecular formation of carbon–carbon double bonds, has been underutilized in comparison with other metathesis reactions. This is primarily due to the lack of reaction selectivity and olefin stereoselectivity.[5] The discovery of the highly active and stable ruthenium-based 'second generation' Grubbs' catalyst **3**, (H_2IMes) (PCy_3)(Cl)$_2$Ru=CHPh (H_2IMes = 1,3-dimesityl-4,5-dihydroimi-dazol-2-ylidene),[6] has dramatically advanced the utility of CM.

Although the advances have been significant, the cross-metathesis (CM) between functionalized olefins has remained a synthetic challenge.[7] Several examples of selective Mo- and Ru-catalyzed acrylonitrile CM have appeared in the literature.[8]

However, molybdenum alkoxyimido alkylidene **1** is very air- and moisture-sensitive and shows a restricted tolerance of several heteroatom functionalities. The presence of acids, reactive carbonyl groups, and alcohols significantly leads to the catalyst inactive.[9] Most of phosphine-ligated ruthenium catalysts have given poor results for this transformation.[10] Recently, a new member of the family of catalysts, (H_2IMes)(3-bromopyridine)$_2$(Cl)$_2$Ru=CHPh, was found to initiate more rapidly than **3**.[11] In this letter, we have developed an inexpensive and highly efficient ruthenium complex **8** to perform acrylonitrile CM with different functionalized olefins.

Indeed, the original synthetic route of complex **3** and **4**, suitable for small scale laboratory syntheses, was not

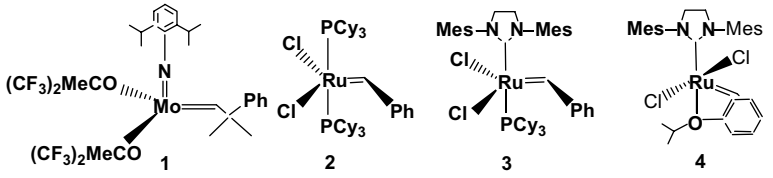

Figure 1. Olefin metathesis catalysts. Mes = 2,4,6-trimethylphenyl.

Keywords: Acrylonitrile; Ruthenium; Metathesis.
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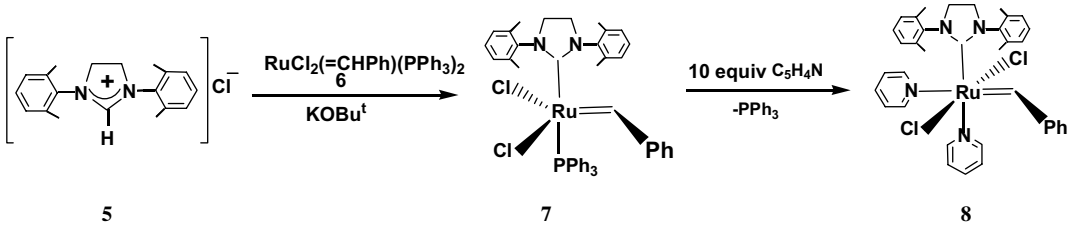
practical for large scale operations, because it was heavily relied on column chromatography purification steps and the use of expensive PCy_3. For example, the synthesis of **4** was considerably less efficient and more time consuming, especially because chromatography was required for purification and not all reagents were commercially available.[4] And expensive and sensitive PCy_3 was used for the synthesis of **3**.[11]

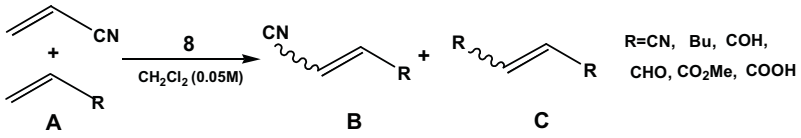
We were thus encouraged to develop a straightforward and convenient method ideal for preparing this ligand efficiently on a large scale, replacing PCy_3 with PPh_3. The compounds $(PPh_3)_2Cl_2Ru{=}CHPh$ (**6**)[12] and 1,3-bis-(2,6-dimethylphenyl)-4,5-dihydroimidazolinium chloride (**5**)[13] were prepared according to the literature procedures. The ruthenium complex **7** was prepared by treatment of complex **6** and **5** with potassium *tert*-butoxide in toluene followed by stirring for 30 min at 70 °C (Scheme 1). The resulting clear dark-brown solution was transferred into cold (−10 °C) hexane to give the desired complex **7** as a precipitate.

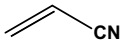
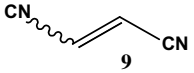
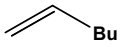
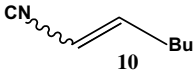
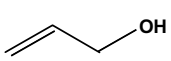
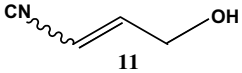
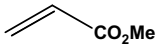
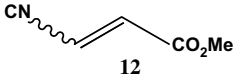
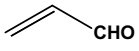
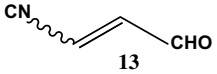
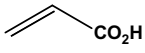
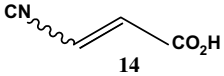
Complex **7** was purified by several washes with hexane as a brown microcrystalline solid in 77% yield (Scheme 1). A bispyridine ruthenium complex **8** was prepared by adding excess pyridine to **7**. These reactions were completed within minutes, in the absence of any solvent. Product **8** was isolated in 91% yield simply by precipitation in hexane and without further purification.[14] The resulted complex **8** not only retained air and moisture insensitivity characteristic, but also showed better catalytic characteristic than Grubbs catalyst **3** for acrylo-



Scheme 1. Synthesis of bispyridine complex **8**.

Table 1. Result of the CM with acrylonitrile and catalyst **8**



Entry	Substrate **A**	Products **B**	Yield [%][a]	(*Z*/*E*)[b]	RCH=CHR C Yield [%][c]
1		 **9**	12[d]	3:1	—
2			36[e]	3:1	—
3		 **10**	37[d]	3:1	7
4			51[e]	3:1	5
5		 **11**	56[d]	3:1	5
6			68[e]	3:1	3
7		 **12**	60[d]	4:1	0
8			71[e]	4:1	0
9		 **13**	61[d]	4:1	0
10			77[e]	4:1	0
11		 **14**	35[d]	3:1	11
12			55[e]	3:1	7

Reaction: CH_2Cl_2 ($c = 0.05$ M), 2 equiv acrylonitrile, 45 °C, 12 h.
[a] Isolated yield.
[b] Ratios determined by means of ^1H NMR spectroscopy.
[c] Determined by GC.
[d] Catalyst **8** = 2 mol %.
[e] Catalyst **8** = 10 mol %.

nitrile CM. Complex **8** was used for the CM reactions of acrylonitrile with a variety of functionalized olefins. All cross-metathesis reactions were performed under N_2 in CH_2Cl_2 at reflux in the presence of 2 or 10 mol % of catalyst **8**, 1 equiv of the acrylonitrile, and 2 equiv of various olefins of type **A** to produce compounds of type **B**. The results are shown in Table 1.[15] Notably, the fair *Z*-selectivity was observed from the CM of acrylonitrile with various functionalized olefins. As in previous cross-metathesis reactions with acrylonitrile, the *Z*-stereoselectivity must be kinetically controlled or related to the presence of the electron-withdrawing properties of the cyano substituent.[8]

No metathesis product was observed spectroscopically (^1H and ^{13}C NMR) at catalyst loadings of less than 2 mol %, employment of higher catalyst concentrations did promote the metathesis, and we observed a maximum 36% conversion of acrylonitrile to 1,4-dicyano-2-butene product with 10 mol % catalyst loading. Though the yield was not high, it was the best result at present. This was due to the moderately strong coordinating of cyano group with the ruthenium center, thus deactivating the catalyst for olefin metathesis.

On the other hand, the highly active ruthenium carbene complex **8** was found to efficiently catalyze the selective CM of 1-hexene and acrylonitrile. Products were obtained in moderate to high yields upon hexene and 2 equiv of acrylonitrile with 10 mol % of catalyst **8** in dry CH_2Cl_2 (0.05 M) for 12 h. The relatively high loading of catalyst was required to ensure a high yield. The yield dropped from 51% to 37% when 2 mol % catalyst was used (entries 3 and 4). Reactions between acrylonitrile with various functionalized olefins, such as allyl alcohol, acrolein, ester, and crylic acid, were performed in good yields (entries 5–12). For example, when allyl alcohol was utilized, product was obtained in 68% yield with 10 mol % catalyst loading (entry 6), however, when crylic acid was selected as the substrate, the yield decreased to around 55% (entry 12).

In conclusion, we have demonstrated that phosphine-free carbene ruthenium complex **8** can efficiently catalyze the cross-metathesis of acrylonitrile with various functionalized olefins. The cross-metathesis can be performed in good yields and fair *Z*-selectivity. Further development of ruthenium metathesis complex having activity in the field of CM is in progress in our laboratory.

Acknowledgments

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14. Spectroscopic data of the new ruthenium carbene complex **7** and **8**: **7**: ^1H NMR (399.9 MHz, $CDCl_3$): $\delta = 19.25$ (s, 1H, Ru–C*H*), 7.69–6.56 (multiple peaks, 24H, PPh_3, *para* C*H*, *meta* C*H*, and 2,6-dimethylphenyl aromatic C*H*), 7.68–7.66 (d, 2H, *ortho* C*H*, $J = 7.2$ Hz), 4.14–4.10 (t, 2H, CH_2CH_2, $J = 7.2$ Hz), 3.98–3.94 (t, 2H, CH_2CH_2, $J = 7.2$ Hz), 2.64 (s, 12H, *ortho* CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 292.3 (d, Ru=CHPh), 219.7, 152.6, 139.7, 138.3, 137.4, 134.2, 132.2, 130.5, 129.4, 129.2, 128.7, 128.6, 128.4, 127.8, 127.6, 125.5, 51.9, 50.2, 21.6, 18.9. ^{31}P NMR (161.9 MHz, $CDCl_3$): $\delta = 37.29$ (s). Q-TOFMS: calcd: 767.1896 $[M-Cl]^+$, found: 767.1916 $[M-Cl]^+$; **8**: ^1H NMR (399.9 MHz, $CDCl_3$): $\delta = 19.10$ (s, 1H, C*H*Ph), 8.63 (br s, 4H, pyridine), 7.80 (br s, 4H, pyridine), 7.64–7.62 (d, 2H, *ortho* C*H*, $J = 7.2$ Hz), 7.46–7.42 (t, 1H, *para* C*H*, $J = 7.8$ Hz), 7.28–7.24 (t, 2H, *meta* C*H*, $J = 7.8$ Hz), 7.17–6.93 (br multiple peaks, 8H,

pyridine, 2,6-dimethylphenyl aromatic C*H*), 4.14 (br s, 4H, NCH_2CH_2N), 2.65 (br s, 6H, *ortho* CH_3), 2.35 (br s, 6H, *ortho* CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 307.3$ (m, Ru=*C*HPh), 220.4 (s, Ru–*C*$(N)_2$), 152.3, 150.0, 136.7, 136.0, 130.6, 130.3, 129.6, 129.0, 128.4, 128.1, 124.0, 123.8, 77.5, 77.2, 76.9, 48.3, 46.5, 22.8, 18.7. Q-TOFMS: calcd: 663.1828 $[M-Cl]^+$, found: 663.1830 $[M-Cl]^+$.

15. General procedure for CM reactions with acrylonitrile: To a mixture of substrate (1.05 mmol) and acrylonitrile (112 mg, 2.10 mmol) in dichloromethane (20 mL) was added **8** (70 mg, 10 mol %). The resulting mixture was stirred at 45 °C for 12 h. The solvent was removed under reduced pressure. Chromatography (4:1 hexane/EtOAc) of the crude residue gave products. All compounds gave satisfactory spectroscopic and analytical data. Selected data for compounds **9**–**14** are included. Compound **9**:^1H NMR (399.9 MHz, $CDCl_3$) $\delta = 6.18$ (s, 1H, *cis*), 6.27 (s, 1H, *trans*). Compound **10**: ^1H NMR (399.9 MHz, $CDCl_3$) $\delta = 6.66$ (dt, $J = 7$ Hz, $J = 17$ Hz, 1H, *trans*), 6.42 (dt, $J = 7$Hz, $J = 11$Hz, 1H, *cis*), 5.28–5.26 (m, 1H), 2.22–2.20 (m, 1H), 2.15–2.12 (m, 1H), 1.39–1.33 (m, 4H), 0.85–0.80 (m, 3H). Compound **11**: ^1H NMR (399.9 MHz, $CDCl_3$) $\delta = 6.81$ (dt, $J = 3$ Hz, $J = 17$ Hz, 1H, *trans*), 6.48 (dt, $J = 7$ Hz, $J = 16$ Hz, 1H, *cis*), 5.72–5.69 (m, 1H), 4.34 (dd, $J = 2$ Hz, $J = 7$ Hz, 2H, *trans*), 4.23 (dd, $J = 2$ Hz, $J = 7$ Hz, 2H, *cis*), 2.11 (s, 1H). Compound **12**: ^1H NMR (399.9 MHz, $CDCl_3$) $\delta = 6.75$ (dt, $J = 7$ Hz, $J = 17$ Hz, 1H, *trans*), 6.64 (dt, $J = 7$ Hz, $J = 11$ Hz, 1H, *cis*), 6.51 (dt, $J = 2$ Hz, $J = 17$ Hz, 1H, *trans*), 6.43 (dt, $J = 7$ Hz, $J = 11$ Hz, 2H, *cis*), 3.84 (s, 3H). Compound **13**: ^1H NMR (399.9 MHz, $CDCl_3$) $\delta = 9.70$ (d, $J = 7$Hz, 1H), 6.90 (dt, $J = 7$ Hz, $J = 17$ Hz, 1H, *trans*), 6.71 (dt, $J = 7$ Hz, $J = 11$ Hz, 1H, *cis*), 6.40 (d, $J = 17$ Hz, 1H, *trans*), 6.37 (d, $J = 11$ Hz, 1H, *cis*). Compound **14**: ^1H NMR (399.9 MHz, $CDCl_3$) $\delta = 11.0$ (d, $J = 7$ Hz, 1H), 6.68 (dt, $J = 7$ Hz, $J = 17$ Hz, 1H, *trans*), 6.45 (dt, $J = 7$ Hz, $J = 11$ Hz, 1H, *cis*), 5.39 (d, $J = 17$ Hz, 1H, *trans*), 5.31 (d, $J = 7$ Hz, 1H, *cis*).