Research Article

NHCs Catalyzed Hydrophosphonylation of α -Ketoesters and α -Trifluoromethyl Ketones

Lin He, Zhi-Hua Cai, Ji-Xin Pian, and Guang-Fen Du

Key Laboratory for Green Processing of Chemical Engineering of Xinjiang Bingtuan and School of Chemistry and Chemical Engineering, Shihezi University, Xinjiang 832000, China

Correspondence should be addressed to Lin He; helin@shzu.edu.cn and Guang-Fen Du; duguangfen@shzu.edu.cn

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N-Heterocyclic carbenes catalyzed hydrophosphonylation reaction of α -ketoesters and α -trifluoromethyl ketones was developed. Under the catalysis of 10 mol% IPr, α -ketoesters or α -trifluoromethyl ketones reacted with dialkyl phosphites to provide quaternary α -hydroxyphosphonates in good to excellent yield.

1. Introduction

α -Hydroxyphosphonates and phosphonic acids are ubiquitous synthons in the synthesis of pharmaceutically and biologically active molecules [1–3]. Hydrophosphonylation of carbonyl compounds catalyzed by base, metal catalysts, or organocatalysts, which is also named as Pudovik reaction, provides facile access to this vital class of compounds [4–7]. However, in contrast to the hydrophosphonylation reaction of aldehydes [8–14], the similar coupling reaction of ketones was scarcely developed [15–22], which may be attributed to the relatively low reactivity of ketones. Therefore, the development of highly efficient catalysts for ketone that participated in Pudovik reaction is still desirable, which will provide α -hydroxyphosphonates with a quaternary carbon center.

As an important type of organocatalyst, N-heterocyclic carbenes (NHCs) have been used widely in a series of organic transformations [23–26], such as umpolung and extended umpolung reaction based on ambiphilicity of NHCs [27–30] and transesterification [31–34], formal cycloadditions [35, 36], and other reactions based on nucleophilicity of NHCs. On the other hand, NHCs are organocatalysts that possess strong basicities, and based on this property, only very limited reactions were reported [37, 38]. Recently, we found that NHCs can catalyze the coupling reaction between phosphites and imines (or aldehydes) [39, 40], which inspired us to

explore the hydrophosphonylation reaction of ketones with NHCs catalysis.

The study commenced with the reaction of methyl phenylglyoxylate **6a** and dimethyl phosphite **7a** (Table 1). To our delight, under the catalysis of 10 mol% NHC **1** (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene, IPr) [41], the reaction proceeded very smoothly in CH_2Cl_2 to give the desired quaternary α -hydroxyphosphonate **8a** quantitatively (Table 1, entry 1). And after the screening of catalysts, base, solvent, and catalyst loading, the optimal reaction conditions were established: using 10 mol% IPr as catalyst, conducted the reaction in dichloromethane at room temperature (Table 1, entry 1).

The reaction scope was then investigated under the optimized reaction conditions and the results were summarized in Table 2. Methyl or ethyl phenylglyoxylate reacted with dimethyl phosphite smoothly to furnish the corresponding α -hydroxyphosphonates in high yield. Both electron-withdrawing ($-\text{F}$, $-\text{Cl}$, and $-\text{Br}$) and electron-donating ($-\text{OMe}$) groups that substituted ethyl phenylglyoxylates were all suitable reactants for the coupling reaction, providing the desired products in high yield (Table 2, entries 3–6). Ethyl pyruvate was also good candidate for the addition, affording alkyl-substituted α -hydroxyphosphonate **8g** in 90% yield (Table 2, entry 7). Trifluoromethyl ketones, another important type of carbonyl compounds that was used widely in the synthesis of fluorinated molecules, were also tested for the reaction.

TABLE 1: Screening of reaction conditions^a.

Entry	NHC	Solvent	Yield (%) ^b
1	1	DCM	99
2	2 , Cs ₂ CO ₃ (10 mol%)	DCM	72
3	2 , DBU (10 mol%)	DCM	78
4	3 , DBU (10 mol%)	DCM	67
5	4a , Et ₃ N (10 mol%)	DCM	79
6	4b , Et ₃ N (10 mol%)	DCM	52
7	5 , Et ₃ N (10 mol%)	DCM	75
8	1	toluene	77
9	1	THF	85
10	1	Et ₂ O	78
11 ^c	1	DCM	65
12	No catalyst	DCM	/

^a Reaction condition: **6a** (1.5 equiv), **7a** (1.0 equiv), NHC (10 mol%), 0.15 mol L⁻¹ of **7a**, and room temperature.

^b Isolated yield.

^c Using 5 mol% NHC **1** (IPr).

Experiment results indicated that dimethyl phosphite can add to trifluoromethyl ketones smoothly to give trifluoromethyl-substituted α -hydroxyphosphonates in good yields (Table 2, entries 8–10). However, when acetophenone was used instead of α -ketoesters or trifluoromethyl ketones, no desired product was obtained and the starting substrates were recovered completely; these results may be attributed to the low reactivity of acetophenone (Table 2, entry 11).

Based on the previous study of NHCs catalyzed hydrophosphonylation reaction [39, 40], a possible mechanism is proposed in Scheme 1. A complex **I** is formed via the deprotonation of dialkyl phosphite by the basic NHCs catalyst, which might trigger the subsequent coupling of carbonyl compounds and after proton transfer, the desired product will be obtained.

In summary, we have demonstrated an efficient NHCs-promoted hydrophosphonylation of α -ketoesters and α -trifluoromethyl ketones, which provide a valuable approach for the preparation of quaternary α -hydroxyphosphonates.

2. Experimental

Unless otherwise indicated, all reactions were conducted under nitrogen atmosphere in oven-dried glassware with magnetic stirring bar. Column chromatograph was performed with silica gel (200–300 mesh) and analytical TLC on silica gel 60-F254. ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were recorded on a Bruker-DMX 400 spectrometer in CDCl₃, with tetramethylsilane as an internal standard and reported in ppm (δ). Infrared spectra were

TABLE 2: NHC-catalyzed hydrophosphonylation of phosphites with active ketones^a.

$ \begin{array}{c} \text{RO}-\text{P}(=\text{O})-\text{H} \\ \text{RO} \end{array} + \text{R}^1-\text{C}(=\text{O})-\text{R}^2 \xrightarrow[\text{CH}_2\text{Cl}_2, 0^\circ\text{C}-\text{rt}]{10\text{ mol\% IPr}} \begin{array}{c} \text{OH} \\ \\ \text{R}^1-\text{C}-\text{P}(=\text{O})(\text{OR})_2 \\ \\ \text{R}^2 \end{array} $ 6 (1.5 equiv) 7 (1.0 equiv) 8				
Entry	Ketones	Time (h)	Products	Yield (%) ^b
1		24	8a	99
2		24	8b	89
3		24	8c	84
4		24	8d	96
5		24	8e	85
6		24	8f	93
7		24	8g	90
8		48	8h	57
9		24	8i	64
10		48	8j	63
11 ^c		48	8k	—

^a Reaction conditions: **7** (1.5 equiv), **6** (1.0 equiv), IPr (10 mol%), and 0.15 mol L⁻¹ of **6**.^b Isolated yield.^c Recovered yield of acetophenone: 95%.

SCHEME 1: Proposed reaction mechanism.

recorded on a Nicolet FT/IR-360 spectrophotometer and reported as wave number (cm^{-1}). Other starting materials were obtained from commercial supplies and used as received. Anhydrous THF, toluene, Et_2O , and DCM were distilled from sodium or calcium hydride. Petroleum ether (PE), where used for flash column chromatography, has a boiling range of 60–90°C.

General Procedure for Preparing of α -Hydroxyphosphonates 8. To an oven-dried Schlenk tube were added aldehyde 7 (0.3 mmol), dry dichloromethane (2.0 mL), and phosphite 6 (0.45 mmol), then cooled to 0°C. IPr (10 mol %) was subsequently added under nitrogen and the mixture was stirred at room temperature until completion of the reaction as indicated by TLC. After completion of the reaction, the mixture was extracted by dichloromethane (3 $\times$ 20 mL). The combined organic phase was dried by anhydrous sodium sulfate and concentrated under vacuum. The residue was subjected to flash column chromatography (silica-gel and petroleum/ethyl acetate 2 : 1~1 : 1) to obtain α -hydroxyphosphonates.

Methyl 2-(Dimethoxyphosphoryl)-2-hydroxy-2-phenylacetate 8a [15]. Colorless oil, yield 99%; ^1H NMR (400 MHz, CDCl_3) δ : 7.49–7.38 (m, 5H), 5.77 (d, $^2J_{\text{PH}} = 8.2$ Hz, 1H), 3.85 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H), 3.74 (s, 3H), 3.60 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 169.2 (d, $J_{\text{CP}} = 6.0$ Hz), 134.8 (d, $J_{\text{CP}} = 6.0$ Hz), 129.4, 128.8, 127.2, 76.9 (d, $^1J_{\text{CP}} = 4.0$ Hz), 54.8 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.4 (d, $^2J_{\text{CP}} = 6.0$ Hz), 52.8, 29.7.

Ethyl 2-(Dimethoxyphosphoryl)-2-hydroxy-2-phenylacetate 8b [15]. Colorless oil, yield 89%; ^1H NMR (400 MHz, CDCl_3) δ : 7.50–7.45 (m, 2H), 7.41–7.36 (m, 3H), 5.75 (d, $^2J_{\text{PH}} = 8.2$ Hz, 1H), 4.28–4.16 (m, 2H), 3.85 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H), 3.61 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H), 1.22 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.7 (d, $J_{\text{CP}} = 5.0$ Hz), 134.9 (d,

$J_{\text{CP}} = 6.0$ Hz), 129.3, 128.8, 127.2, 76.8 (d, $^1J_{\text{CP}} = 11.0$ Hz), 61.9, 54.7 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.3 (d, $^2J_{\text{CP}} = 6.0$ Hz), 14.0.

Ethyl 2-(Dimethoxyphosphoryl)-2-(4-fluorophenyl)-2-hydroxyacetate 8c. Colorless oil, yield 84%; ^1H NMR (400 MHz, CDCl_3) δ : 7.50–7.44 (m, 2H), 7.08 (t, $J = 8.7$ Hz, 2H), 5.73 (d, $^2J_{\text{PH}} = 8.3$ Hz, 1H), 4.30–4.16 (m, 2H), 3.86 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H), 3.63 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H), 1.23 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.6 (d, $J = 5.0$ Hz), 163.2 (d, $^1J_{\text{CF}} = 248.0$ Hz), 130.9 (dd, $J = 6.0, 3.0$ Hz), 129.2 (d, $J = 8.0$ Hz), 115.8 (d, $J = 22.0$ Hz), 76.2 (d, $^1J_{\text{CP}} = 4.0$ Hz), 62.0, 54.8 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.4 (d, $^2J_{\text{CP}} = 6.0$ Hz), 14.0; HRMS(ESI) Calcd for ($\text{C}_{12}\text{H}_{16}\text{FO}_6\text{P} + \text{Na}$) 329.0566, found: 329.0569.

Ethyl 2-(4-Chlorophenyl)-2-(dimethoxyphosphoryl)-2-hydroxyacetate 8d. Colorless oil, yield 96%; ^1H NMR (400 MHz, CDCl_3) δ : 7.39 (q, $J = 8.6$ Hz, 4H), 5.72 (d, $^2J_{\text{PH}} = 8.4$ Hz, 1H), 4.27–4.15 (m, 2H), 3.86 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H), 3.64 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H), 1.23 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.4 (d, $J = 5.0$ Hz), 135.4, 133.5 (d, $J = 6.0$ Hz), 129.0, 128.5, 76.2 (d, $^1J_{\text{CP}} = 5.0$ Hz), 62.1, 54.8 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.4 (d, $^2J_{\text{CP}} = 7.0$ Hz), 14.0. HRMS(ESI) Calcd for ($\text{C}_{12}\text{H}_{16}\text{ClO}_6\text{P} + \text{Na}$) 345.0271, found: 345.0282.

Ethyl 2-(4-Bromophenyl)-2-(dimethoxyphosphoryl)-2-hydroxyacetate 8e. Colorless oil, yield 85%; ^1H NMR (400 MHz, CDCl_3) δ : 7.53 (d, $J = 8.6$ Hz, 2H), 7.36 (d, $J = 8.3$ Hz, 2H), 5.70 (d, $^2J_{\text{PH}} = 8.4$ Hz, 1H), 4.32–4.14 (m, 2H), 3.86 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H), 3.64 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H), 1.23 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.3 (d, $J = 5.0$ Hz), 134.0 (d, $J = 6.0$ Hz), 132.0, 128.8, 123.6, 76.2 (d, $^1J_{\text{CP}} = 5.0$ Hz), 62.1, 54.8 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.5 (d, $^2J_{\text{CP}} = 6.0$ Hz), 14.0. HRMS(ESI) Calcd for ($\text{C}_{12}\text{H}_{16}\text{BrO}_6\text{P} + \text{Na}$) 388.9766, found: 388.9770.

Ethyl 2-(Diethoxyphosphoryl)-2-hydroxy-2-(4-methoxyphenyl) Acetate 8f. Colorless oil, yield 93%; ^1H NMR (400 MHz, CDCl_3) δ : 7.33 (d, $J = 8.7$ Hz, 2H), 6.84 (d, $J = 8.8$ Hz, 2H), 5.63 (d, $^2J_{\text{PH}} = 8.4$ Hz, 1H), 4.22–4.00 (m, 4H), 3.97–3.82 (m, 2H), 3.74 (s, 3H), 1.28 (td, $J = 7.1, 1.0$ Hz, 3H), 1.19–1.09 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 168.0 (d, $J_{\text{CP}} = 6.0$ Hz), 159.3, 127.7, 126.3, 113.1, 75.4 (d, $^1J_{\text{CP}} = 5.0$ Hz), 63.2 (d, $^2J_{\text{CP}} = 6.0$ Hz), 62.9 (d, $^2J_{\text{CP}} = 6.0$ Hz), 60.7, 54.2, 15.0 (d, $J_{\text{CP}} = 7.0$ Hz), 14.9 (d, $J_{\text{CP}} = 7.0$ Hz), 13.0. HRMS(ESI) Calcd for ($\text{C}_{15}\text{H}_{23}\text{O}_7\text{P} + \text{Na}$) 369.1079, found: 369.1075.

Ethyl 2-(Dimethoxyphosphoryl)-2-hydroxypropanoate 8g [42]. Colorless oil, yield 90%; ^1H NMR (400 MHz, CDCl_3) δ : 8.64 (br s, OH), 4.95–4.87 (m, 1H), 4.27–4.20 (m, 2H), 3.84 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H), 3.79 (d, $^3J_{\text{PH}} = 11.3$ Hz, 3H), 1.57 (dd, $^3J_{\text{PH}} = 6.9, 0.7$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 170.5 (d, $J_{\text{CP}} = 5.0$ Hz), 72.0 (d, $^1J_{\text{CP}} = 5.0$ Hz), 61.7, 54.7 (d, $^2J_{\text{CP}} = 7.0$ Hz), 54.5 (d, $^2J_{\text{CP}} = 6.0$ Hz), 19.2 (d, $^2J_{\text{CP}} = 6.0$ Hz), 14.1.

Dimethyl 2,2,2-Trifluoro-1-hydroxy-1-phenylethylphosphonate 8h [17]. Colorless oil, yield 57%; ^1H NMR (400 MHz, CDCl_3) δ : 7.53–7.48 (m, 2H), 7.47–7.41 (m, 3H), 5.61 (dd, $^2J_{\text{PH}} = 10.2$,

6.4 Hz, 1H), 3.78 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H), 3.57 (d, $^3J_{\text{PH}} = 11.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 131.2, 130.3, 128.8, 127.9, 76.3 (dd, $^1J_{\text{CP}} = 34.0$, 5.0 Hz), 54.7 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.5 (d, $^2J_{\text{CP}} = 6.0$ Hz), 29.7.

Dimethyl 1-(4-Bromophenyl)-2,2,2-trifluoro-1-hydroxyethylphosphonate 8i [17]. Colorless oil, yield 64%; ^1H NMR (400 MHz, CDCl_3) δ : 7.58 (d, $J = 8.6$ Hz, 2H), 7.37 (d, $J = 8.6$ Hz, 2H), 5.69–5.42 (m, 1H), 3.80 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H), 3.61 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 132.0, 130.2, 129.5, 124.7, 75.6 (dd, $^1J_{\text{CP}} = 34.0$, 5.0 Hz), 54.7 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.5 (d, $^2J_{\text{CP}} = 6.0$ Hz), 29.7.

Dimethyl 1-(4-Chlorophenyl)-2,2,2-trifluoro-1-hydroxyethylphosphonate 8j [17]. Colorless oil, yield 63%; ^1H NMR (400 MHz, CDCl_3) δ : 7.46–7.40 (m, 4H), 5.59 (dd, $^2J_{\text{PH}} = 10.2$, 6.3 Hz, 1H), 3.80 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H), 3.61 (d, $^3J_{\text{PH}} = 11.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 136.5, 129.8, 129.3, 129.1, 75.7 (dd, $^1J_{\text{CP}} = 34.0$, 5.0 Hz), 54.8 (d, $^2J_{\text{CP}} = 6.0$ Hz), 54.5 (d, $^2J_{\text{CP}} = 6.0$ Hz), 29.7.

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References

- [1] H. Gröger and B. Hammer, "Catalytic concepts for the enantioselective synthesis of α -amino and α -hydroxy phosphonates," *Chemistry*, vol. 6, no. 6, pp. 943–948, 2000.
- [2] O. I. Kolodiazny, "Asymmetric synthesis of hydroxyphosphonates," *Tetrahedron Asymmetry*, vol. 16, no. 20, pp. 3295–3340, 2005.
- [3] O. I. Kolodiazny, "Chiral hydroxy phosphonates: synthesis, configuration and biological properties," *Russian Chemical Reviews*, vol. 75, no. 3, pp. 227–253, 2006.
- [4] P. Merino, E. M. López, and R. P. Herrera, "Catalytic enantioselective hydrophosphonylation of aldehydes and imines," *Advanced Synthesis and Catalysis*, vol. 350, no. 9, pp. 1195–1208, 2008.
- [5] J. A. Ma, "Catalytic asymmetric synthesis of α - and β -amino phosphonic acid derivatives," *Chemical Society Reviews*, vol. 35, no. 7, pp. 630–636, 2006.
- [6] O. I. Kolodiazny, "Asymmetric synthesis of organophosphorus compounds," *Tetrahedron Asymmetry*, vol. 9, no. 8, pp. 1279–1332, 1998.
- [7] A. N. Pudovik and I. V. Kononova, "Addition reactions of esters of phosphorus(III) acids with unsaturated systems," *Synthesis*, vol. 2, pp. 81–96, 1979.
- [8] B. Saito and T. Katsuki, "Synthesis of an optically active Cl-symmetric Al(salalen) complex and its application to the catalytic hydrophosphonylation of aldehydes," *Angewandte Chemie—International Edition*, vol. 44, no. 29, pp. 4600–4602, 2005.
- [9] X. Zhou, X. Liu, X. Yang, D. Shang, J. Xin, and X. Feng, "Highly enantioselective hydrophosphonylation of aldehydes catalyzed by tridentate schiff base aluminum(III) complexes," *Angewandte Chemie—International Edition*, vol. 47, no. 2, pp. 392–394, 2008.
- [10] G. D. Joly and E. N. Jacobsen, "Thiourea-catalyzed enantioselective hydrophosphonylation of imines: practical access to enantiomerically enriched α -amino phosphonic acids," *Journal of the American Chemical Society*, vol. 126, no. 13, pp. 4102–4103, 2004.
- [11] F. Yang, D. Zhao, J. Lan et al., "Self-assembled bifunctional catalysis induced by metal coordination interactions: an exceptionally efficient approach to enantioselective hydrophosphonylation," *Angewandte Chemie—International Edition*, vol. 47, no. 30, pp. 5646–5649, 2008.
- [12] J. P. Abell and H. Yamamoto, "Catalytic enantioselective Pudovik reaction of aldehydes and aldimines with tethered bis(8-quinolino) (TBOx) aluminum complex," *Journal of the American Chemical Society*, vol. 130, no. 32, pp. 10521–10523, 2008.
- [13] D. Uruguchi, T. Ito, and T. Ooi, "Generation of chiral phosphonium dialkyl phosphite as a highly reactive P-nucleophile: application to asymmetric hydrophosphonylation of aldehydes," *Journal of the American Chemical Society*, vol. 131, no. 11, pp. 3836–3837, 2009.
- [14] K. Suyama, Y. Sakai, K. Matsumoto, B. Saito, and T. Katsuki, "Highly enantioselective hydrophosphonylation of aldehydes: base-enhanced aluminum-salalen catalysis," *Angewandte Chemie—International Edition*, vol. 49, no. 4, pp. 797–799, 2010.
- [15] F. Wang, X. Liu, X. Cui, Y. Xiong, X. Zhou, and X. Feng, "Asymmetric hydrophosphonylation of α -ketoesters catalyzed by cinchona-derived thiourea organocatalysts," *Chemistry—A European Journal*, vol. 15, no. 3, p. 589, 2009.
- [16] X. Zhou, Y. Liu, L. Chang et al., "Highly efficient synthesis of quaternary α -hydroxy phosphonates via lewis acid-catalyzed hydrophosphonylation of ketones," *Advanced Synthesis and Catalysis*, vol. 351, no. 16, pp. 2567–2572, 2009.
- [17] X. Zhou, Q. Zhang, Y. Hui et al., "Catalytic asymmetric synthesis of quaternary α -hydroxy trifluoromethyl phosphonate via chiral aluminum(III) catalyzed hydrophosphonylation of trifluoromethyl ketones," *Organic Letters*, vol. 12, no. 19, pp. 4296–4299, 2010.
- [18] D. Uruguchi, T. Ito, S. Nakamura, and T. Ooi, "Catalytic asymmetric hydrophosphonylation of ynones," *Chemical Science*, vol. 1, no. 4, pp. 488–490, 2010.
- [19] S. Zhou, Z. Wu, J. Rong et al., "Highly efficient hydrophosphonylation of aldehydes and unactivated ketones catalyzed by methylene-linked pyrrolyl rare earth metal amido complexes," *Chemistry—A European Journal*, vol. 18, no. 9, pp. 2653–2659, 2012.
- [20] F. Jahania, B. Zameniana, S. Khaksarb, and M. Tajbakhsh, "Pyridine 2,6-dicarboxylic acid as a bifunctional organocatalyst for hydrophosphonylation of aldehydes and ketones in water," *Chemistry—A European Journal*, vol. 19, pp. 3315–3318, 2010.
- [21] Bo. Liu, J. F. Carpentier, and Y. Sarazin, "Highly effective alkaline earth catalysts for the sterically governed hydrophosphonylation of aldehydes and nonactivated ketones," *Chemistry*, vol. 18, no. 42, pp. 13259–13264, 2012.
- [22] M. Hatano, T. Horibe, and K. Ishihara, "Chiral magnesium(II) binaphtholates as cooperative Brønsted/Lewis acid-base catalysts for the highly enantioselective addition of phosphorus nucleophiles to α,β -unsaturated esters and ketones," *Angewandte Chemie—International Edition*, vol. 52, no. 17, pp. 4549–4553, 2013.
- [23] A. Grossmann and D. Enders, "N-heterocyclic carbene catalyzed domino reactions," *Angewandte Chemie—International Edition*, vol. 51, no. 2, pp. 314–325, 2012.

- [24] K. Zeitler, "Extending mechanistic routes in heterazolium catalysis-promising concepts for versatile synthetic methods," *Angewandte Chemie—International Edition*, vol. 44, no. 46, pp. 7506–7510, 2005.
- [25] D. Enders, O. Niemeier, and A. Henseler, "Organocatalysis by N-heterocyclic carbenes," *Chemical Reviews*, vol. 107, no. 12, pp. 5606–5655, 2007.
- [26] N. Marion, S. Díez-González, and S. P. Nolan, "N-heterocyclic carbenes as organocatalysts," *Angewandte Chemie—International Edition*, vol. 46, no. 17, pp. 2988–3000, 2007.
- [27] D. Enders, O. Niemeier, and T. Balensiefer, "Asymmetric intramolecular crossed-benzoin reactions by N-heterocyclic carbene catalysis," *Angewandte Chemie—International Edition*, vol. 45, no. 9, pp. 1463–1467, 2006.
- [28] D. A. DiRocco, K. M. Oberg, D. M. Dalton, and T. Rovis, "Catalytic asymmetric intermolecular Stetter reaction of heterocyclic aldehydes with nitroalkenes: backbone fluorination improves selectivity," *Journal of the American Chemical Society*, vol. 131, no. 31, pp. 10872–10874, 2009.
- [29] J. Mo, X. Chen, and Y. Chi, "Oxidative γ -addition of enals to trifluoromethyl ketones: enantioselectivity control via Lewis acid/N-heterocyclic carbene cooperative catalysis," *Journal of the American Chemical Society*, vol. 134, no. 21, pp. 8810–8813, 2012.
- [30] D. E. A. Raup, B. Cardinal-David, D. Holte, and K. A. Scheidt, "Cooperative catalysis by carbenes and Lewis acids in a highly stereoselective route to γ -lactams," *Nature Chemistry*, vol. 2, no. 9, pp. 766–771, 2010.
- [31] G. W. Nyce, J. A. Lamboy, E. F. Connor, R. M. Waymouth, and J. L. Hedrick, "Expanding the catalytic activity of nucleophilic N-heterocyclic carbenes for transesterification reactions," *Organic Letters*, vol. 4, no. 21, pp. 3587–3590, 2002.
- [32] G. A. Grasa, R. M. Kissling, and S. P. Nolan, "N-heterocyclic carbenes as versatile nucleophilic catalysts for transesterification/acylation reactions," *Organic Letters*, vol. 4, no. 21, pp. 3583–3586, 2002.
- [33] G. A. Grasa, R. Singh, and S. P. Nolan, "Transesterification/acylation reactions catalyzed by molecular catalysts," *Synthesis*, no. 7, pp. 971–985, 2004.
- [34] T. Kano, K. Sasaki, and K. Maruoka, "Enantioselective acylation of secondary alcohols catalyzed by chiral N-heterocyclic carbenes," *Organic Letters*, vol. 7, no. 7, pp. 1347–1349, 2005.
- [35] X. L. Huang, L. He, P. L. Shao, and S. Ye, "[4+2] cycloaddition of ketenes with N-benzoyldiazene catalyzed by N-heterocyclic carbenes," *Angewandte Chemie—International Edition*, vol. 48, no. 1, pp. 192–195, 2009.
- [36] T. Y. Jian, L. He, C. Tang, and S. Ye, "N-heterocyclic carbene catalysis: enantioselective formal [2+2] cycloaddition of ketenes and N-sulfinylanilines," *Angewandte Chemie—International Edition*, vol. 50, no. 39, pp. 9104–9107, 2011.
- [37] M. Movassaghi and M. A. Schmidt, "N-heterocyclic carbene-catalyzed amidation of unactivated esters with amino alcohols," *Organic Letters*, vol. 7, no. 12, pp. 2453–2456, 2005.
- [38] E. M. Phillips, M. Risdrich, and K. A. Scheidt, "N-heterocyclic carbene-catalyzed conjugate additions of alcohols," *Journal of the American Chemical Society*, vol. 132, no. 38, pp. 13179–13181, 2010.
- [39] Z. H. Cai, G. F. Du, B. Dai, and L. He, "Nucleophilic carbene-mediated hydrophosphonylation of aldimines," *Synthesis*, vol. 44, no. 5, pp. 694–698, 2012.
- [40] Z. H. Cai, G. F. Du, L. He, C. Z. Gu, and B. Dai, "N-heterocyclic carbene catalyzed hydrophosphonylation of aldehydes," *Synthesis*, no. 13, pp. 2073–2078, 2011.
- [41] A. J. Arduengo III, R. Krafczyk, R. Schmutzler et al., "Imidazolylidenes, imidazolinyliidenes and imidazolidines," *Tetrahedron*, vol. 55, no. 51, pp. 14523–14534, 1999.
- [42] V. S. Abramov, V. I. Barabanov, and L. I. Long, "Reactions of phosphinic acids with aldehydes and ketones, XXXII," *Zhurnal Obshchei Khimii*, vol. 37, no. 3, pp. 714–718, 1967.