

Accepted Article

Title: Palladium-Catalyzed One-Pot Four-Component Synthesis of β-Cyano-α,β-unsaturated Ketones Using Calcium Carbide as an Acetylene Source and Potassium Hexacyanoferrate(II) as an Eco-Friendly Cyanide Source

Authors: Hao Lu and Zheng Li

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Adv. Synth. Catal. 10.1002/adsc.201900733

Link to VoR: http://dx.doi.org/10.1002/adsc.201900733

10.1002/adsc.201900733

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Palladium-Catalyzed One-Pot Four-Component Synthesis of β -Cyano- α , β -unsaturated Ketones Using Calcium Carbide as an Acetylene Source and Potassium Hexacyanoferrate(II) as an Eco-Friendly Cyanide Source

Hao Lu^a, Zheng Li^a*

^a Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou, Gansu, 730070, P. R. China. E-mail: lizheng@nwnu.edu.cn.

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201#######.((Please delete if not appropriate))

Abstract: Palladium-catalyzed one-pot four-component synthesis of β -cyano- α , β -unsaturated ketones by the reactions of aryl halides, calcium carbide, potassium hexacyanoferrate(II) and aroyl chlorides is described. The salient features of this protocol are the direct use of easy-to-handle acetylene source and eco-friendly cyanide source, wide scope of substrates with good functional group tolerance, and simple work-up procedure.

Keywords: calcium carbide; potassium hexacyanoferrate(II); one-pot procedure; four-component synthesis; β -cyano- α , β -unsaturated ketone

β-Cyano-α,β-unsaturated ketones contain important functional groups, such as cyano, carbonyl and alkenyl, which are significant intermediates for the synthesis of fine chemicals, such as pharmaceuticals, pesticides and perfumes.^[1-3] At the same time, the substances containing β-cyano-α,β-unsaturated ketone moieties also have great potential application value.^[4] Figure 1 shows two structures which can separately be used as a calciumchannel blocker (treating hypertension, cerebral artery occlusion^[5] and Alzheimer's disease^[6]) and a new type of nearinfrared dye.^[7]



Figure 1. Representative examples containing β -cyano- α , β -unsaturated ketone moiety.

In the past years, a few synthetic methods for β cyano- α , β -unsaturated ketones were reported (Scheme 1), which included i) the reactions of (phenacylidene)triphenylphosphorane with benzoyl cyanide;^[8] ii) the palladium-catalyzed reactions of arylacetylenes with aroyl cyanides;^[9] iii) the nickelcatalyzed conjugate addition of trimethylsilyl cyanide to ynones;^[10] and iv) the reactions of cyclic bromo imidates with triethylamine.^[11] However, there are a number of problems with these synthetic methods, such as environment-unfriendly reagents, limited sources of raw materials, limited functional group compatibility, lengthy synthetic steps and unsafe cyanide sources, etc. Therefore, it is the focus of research in this field to develop a more efficient, green and practical method for the synthesis of β cyano- α , β -unsaturated ketones and to expand their application range.

Previous work



Scheme 1. Preparation of β -cyano- α , β -unsaturated ketones

Calcium carbide, CaC₂, is commercial available solid, which is stable and inexpensive, and extensively used as a raw material of acetylene gas by hydrolysis in chemical industry. The recent reports have revealed that calcium carbide can be directly used as a sustainable, easy-to-handle, and low-cost feedstock, and an efficient source of acetylene for *in situ* chemical transformations.^[12]

Potassium hexacyanoferrate(II), $K_4[Fe(CN)_6]$, is a byproduct of the coal chemical industry and commercially available on a ton scale. It is also used in the food industry for metal precipitation. In addition, it has been described as an antiagglutinating auxiliary for table salt (NaCl). Recently, $K_4[Fe(CN)_6]$ has been used as an eco-friendly cyanide source for some organic reactions to synthesize important compounds bearing cyano groups.^[13]

Our recent research interests focused on the use of CaC_2 and $K_4[Fe(CN)_6]$ in the organic synthesis, respectively, and reported the synthesis of 2-methylbenzofurans,^[14] diarylacetylenes,^[15] triarylacrylonitriles^[16] and 1,3,5-triaroylcyclohexanes^[17] direct using CaC_2 as an acetylene source, and the cyanation of unsaturated compounds including C=O, C=N and/or C=C bonds by nucleophilic addition reactions using $K_4[Fe(CN)_6]$ as an eco-friendly cyanide source.^[18]

In this work, we report a more efficient and green method for the combined use of two cheap and safe inorganic chemicals, CaC_2 as an easy-to-handle acetylene source and $K_4[Fe(CN)_6]$ as an eco-friendly cyanide source, in one reaction to synthesize β -cyano- α , β -unsaturated ketones by one-pot four-component procedure using commercial available aryl halides and aroyl chlorides as substrates.

Initially, the reaction of iodobenzene (1a), CaC_2 , $K_4[Fe(CN)_6]$ with benzoyl chloride (2a) was selected as a model reaction to optimize the reaction

conditions. The different ligands, catalysts, bases and solvents were attempted to synthesize β -cyano- α , β unsaturated ketone. The results are shown in Table 1. The reaction was first conducted in DMF using $Pd(OAc)_2$ as a catalyst, Cs_2CO_3 as a base in the absence of a ligand. The product (Z)-4-oxo-2,4diphenylbut-2-enenitrile (3a) was obtained in 45% yield (Table 1, entry 1). Only Z-type structure was observed, which was determined by comparison with literature data.^[9a, 10] The reaction yield could be improved in the presence of some ligands such as PPh₃, dppe, dppp and dppb (entries 2–5). Among them, dppb exhibited the best ligand effect (entry 5). In addition, it was found that Pd(II) catalysts, such as Pd(OAc)₂, PdCl₂ and Pd(PPh₃)₂Cl₂, could catalyze the reaction to give **3a** in moderate to good yield (entries 5–7). $Pd(OAc)_2$ as a catalyst could give best yield (entry 5). However, Pd(0) complex, for example Pd(PPh₃)₄, did not exhibit catalytic effect on the reaction (entry 8). Bases played a prominent role in the reaction. Some inorganic bases, such as Cs₂CO₃, K₂CO₃, Na₂CO₃, KOAc and NaOH, exhibited moderate to good activities for the reaction (entries 5, 9–12). In contrast, organic bases, such as Et₃N, DBU, DMAP and DABCO, could not give the desired product (entries 13–16). The best yield for **3a** was obtained by using K_2CO_3 as a base (entry 9). Solvents also had certain effect on the yield of **3a**. Besides DMF, the reaction in DMAc, DMSO, MeCN, PhMe and 1,4-dioxane were also attempted (entries 17–21), but no better yield for **3a** was observed in comparison with DMF (entry 9).

On the basis of the optimized reaction conditions, the four-component reactions of various aryl iodides with CaC_2 , $K_4[Fe(CN)_6]$ and aroyl chloride were used to synthesize β-cyano α,β -unsaturated ketones. The results are summarized in Table 2. It was found that aryl iodides containing electron-donating groups, such as Me, n-Pr, n-Bu, n-pentyl and MeO, on aromatic rings afforded the corresponding products in good yield (3b-3g). Aryl iodides containing electron-withdrawing groups, such as F, Cl, Br, NO₂ and CF₃ on the ortho-, meta-, or para-positions of phenyl group could also give satisfactory yield (3h-3n). The reactions were also suitable to different substituted aroyl chlorides, and the corresponding products could be obtained in moderate to good yield (30-3z). In heteroaryl iodides, such addition. 2as iodopyridine and 2-iodothiophene, could also be suitable to this kind of reactions, and gave the corresponding products in moderate to good yield $(3\alpha, 3\beta).$

Table 1. Optimization of the reaction conditions^a

$ \begin{array}{c} & & \\ & & $					
1a			2a		3a
Entry	Catalyst	Ligand	Base	Solvent	Yield
					$(\%)^{\nu}$
1	$Pd(OAc)_2$	-	Cs_2CO_3	DMF	45
2	Pd(OAc) ₂	PPh ₃	Cs ₂ CO ₃	DMF	46
3	Pd(OAc) ₂	dppe	Cs_2CO_3	DMF	48
4	$Pd(OAc)_2$	dppp	Cs_2CO_3	DMF	55
5	Pd(OAc) ₂	dppb	Cs_2CO_3	DMF	66
6	PdCl ₂	dppb	Cs_2CO_3	DMF	43
7	PdCl ₂ (PPh ₃) ₂	dppb	Cs_2CO_3	DMF	51
8	Pd(PPh ₃) ₄	dppb	Cs ₂ CO ₃	DMF	NR
9	Pd(OAc) ₂	dppb	K ₂ CO ₃	DMF	72
10	Pd(OAc) ₂	dppb	Na ₂ CO ₃	DMF	57
11	Pd(OAc) ₂	dppb	KOAc	DMF	32
12	Pd(OAc) ₂	dppb	NaOH	DMF	39
13	Pd(OAc) ₂	dppb	Et ₃ N	DMF	NR
14	Pd(OAc) ₂	dppb	DBU	DMF	NR
15	Pd(OAc) ₂	dppb	DMAP	DMF	NR
16	Pd(OAc) ₂	dppb	DABCO	DMF	NR
17	Pd(OAc) ₂	dppb	K ₂ CO ₃	DMAc	66
18	Pd(OAc) ₂	dppb	K ₂ CO ₃	DMSO	33
19	Pd(OAc) ₂	dppb	K ₂ CO ₃	MeCN	NR
20	Pd(OAc) ₂	dppb	K ₂ CO ₃	PhMe	Trace
21	Pd(OAc) ₂	dppb	K ₂ CO ₃	1,4-Dioxane	NR



^{*a*} Reaction condition: K₄[Fe(CN)₆] (0.1 mmol), benzoyl chloride (**2a**) (0.5 mmol) and catalyst (0.05 mmol) stirred first at 150 °C for 4 h, then iodobenzene (**1a**) (0.5 mmol), CaC₂ (1.25 mmol), H₂O (2.50 mmol), base (0.25 mmol) and ligand (0.05 mmol) in 4 mL of degassed and dried solvent were added under nitrogen atmosphere and stirred at 80 °C for 28 h. ^{*b*}Isolated yield.

Table 2. Synthesis of β -cyano- α , β -unsaturated ketones from aryl iodides^{*a*}



^{*a*} Reaction condition: $K_4[Fe(CN)_6]$ (0.1 mmol), aroyl chloride (0.5 mmol) and Pd(OAc)₂ (0.05 mmol) stirred first at 150 °C for 4 h, then aryl iodide (0.5 mmol), CaC₂ (1.25 mmol), H₂O (2.50 mmol), K₂CO₃ (0.25 mmol) and dppb (0.05 mmol) in 4 mL of degassed and dried DMF were added under nitrogen atmosphere and stirred at 80 °C for 28 h.

In addition, various aryl bromides, instead of aryl iodides, could also be used in fourcomponent synthesis under optimized reaction conditions. The results are summarized in Table 3. Fifteen examples of β -cyano- α , β -unsaturated ketones could be obtained in satisfactory yield. However, the yield of the corresponding products was slightly lower than that of aryl iodides. **Table 3.** Synthesis of β -cyano- α , β -unsaturated ketones from aryl bromides^{*a*}



^{*a*} Reaction condition: $K_4[Fe(CN)_6]$ (0.1 mmol), aroyl chloride (0.5 mmol) and Pd(OAc)₂ (0.05 mmol) stirred first at 150 °C for 4 h, then aryl bromide (0.5 mmol), CaC₂ (1.25 mmol), H₂O (2.50 mmol), K₂CO₃ (0.25 mmol) and dppb (0.05 mmol) in 4 mL of degassed and dried DMF were added under nitrogen atmosphere and stirred at 80 °C for 28 h.

It is noteworthy to mention that reaction substrates and reagents could also be extended. When Fe(III) complex, K_3 [Fe(CN)₆], was used to replace Fe(II) complex, K_4 [Fe(CN)₆], in the reaction, the product **3a** could also be obtained in 35% yield (Scheme 2).



Scheme 2. Synthesis of 3a using $K_3[Fe(CN)_6]$ instead of $K_4[Fe(CN)_6]$. Reaction condition: $K_3[Fe(CN)_6]$ (0.1 mmol), 2a (0.5 mmol) and Pd(OAc)₂ (0.05 mmol) stirred first at 150 °C for 8 h, then 1a (0.5 mmol), CaC₂ (1.25 mmol), H₂O (2.50 mmol), K₂CO₃ (0.25 mmol) and dppb (0.05 mmol) in 4 mL of degassed and dried DMF were added under nitrogen atmosphere and stirred at 80 °C for 28 h.

With the ubiquitous success of this protocol, the synthesis of **3a** by four-component reaction of iodobenzene, CaC_2 , $K_4[Fe(CN)_6]$ and benzoyl chloride could also be carried out on a gram scale. Under optimized conditions, the reaction of 1.12 mL

of iodobenzene, 1.60 g of CaC_2 , 0.74 g of $K_4[Fe(CN)_6]$ and 1.15 mL of benzoyl chloride in 50 mL of degassed and dried DMF was performed to give 1.45 g of **3a** in 62% isolated yield. The success of this gram-reaction further demonstrated the effectiveness of the optimized condition of the process (Scheme 3).



Scheme 3. Gram-scale synthesis of 3a. Reaction Conditions: $K_4[Fe(CN)_6]$ (2 mmol), benzoyl chloride (10 mmol) and Pd(OAc)₂ (1 mmol) stirred first at 150 °C for 4 h, then iodobenzene (10 mmol), CaC₂ (25 mmol), H₂O (50 mmol), K₂CO₃ (5 mmol) and dppb (1 mmol) in 50 mL of degassed and dried DMF were added under nitrogen atmosphere and stirred at 80 °C for 28 h.

In experimental process, it was observed that (*Z*)- β -cyano- α , β -unsaturated ketones could partially convert into (*E*)- β -cyano- α , β -unsaturated ketones at room temperature. For example, **3a** in CHCl₃ placed at room temperature for 24 h could transform into its *E* isomer in 9% isolated yield. Similarly, **3l** could transform into its *E* isomer in 72% isolated yield (Scheme 4).



Scheme 4. Transformation of *Z*-type to *E*-type of β -cyano- α , β -unsaturated ketones. Conditions: β -cyano- α , β -unsaturated ketones in CHCl₃ (2 mL) placed at room temperature for 24 h.

In order to investigate the reaction mechanism, several control experiments were carried out (Scheme 5). i) The two-component mixture of benzoyl chloride (2a) with $K_4[Fe(CN)_6]$ was heated at 150 °C to give benzoyl cyanide as a product in 91% yield. This indicated that benzoyl cyanide possibly is an intermediate of the four-component reaction. Ne reaction was observed at 80 °C; ii) The twocomponent reaction of 0.5 mmol of iodobenzene (1a) with 1.25 mmol of calcium carbide catalyzed by Pd(OAc)₂ afforded phenylacetylene in 79% yield. This result implied that phenylacetylene possibly is also an intermediate of four-component reaction; iii) The reaction of the resulting benzoyl cyanide and phenylacetylene under the standard condition produced β -cyano- α , β -unsaturated ketone **3a** in 66% yield. This result further demonstrated that both benzoyl cyanide and phenylacetylene might be the intermediates of the four-component reaction.



Scheme 5. Control experiments

Based on the above control experiments, a plausible mechanism is proposed for the fourcomponent synthesis of β -cyano- α , β -unsaturated ketones (Scheme 6). Oxidative addition of aryl iodide (ArI) to a palladium(0) species, PdL₂, which is generated most commonly from palladium diacetate and dppb,^[19] forms an arylpalladium iodide complex A. Complex A reacts with acetylene calcium hydroxide **B**, which formed *in situ* by the reaction of calcium carbide with water,^[12f,12g] in the presence of potassium carbonate to obtain palladium complex C. Complex C undergoes reductive elimination to obtain arylacetylene calcium hydroxide **D**. **D** hydrolyzes in the presence of water to give arylacetylene E. At the same time, potassium hexacyanoferrate(II) reacts with aroyl chlorides to give aroyl cyanide F.^[18b] F further reacts with PdL₂ through oxidative addition to form aroyl palladium cyanide \mathbf{G} .^[9a] The addition of \mathbf{G} to E gives vinyl palladium intermediate H.^[9a] H undergoes reductive elimination to give the final product, β -cyano- α , β -unsaturated ketone.



Scheme 6. Proposed mechanism for four-component synthesis of β -cyano- α , β -unsaturated ketones

In conclusion, a palladium-catalyzed one-pot fourcomponent synthetic method for β -cyano- α , β unsaturated ketones has developed. The salient features of this protocol are the use of calcium carbide as an easy-to-handle acetylene source, potassium hexacyanoferrate(II) as an eco-friendly cyanide source, good substrate scope for aryl halides and aroyl chlorides, inexpensive and commercial available raw materials, high functional tolerance, satisfactory yield and simple work-up procedure. A gram-scale reaction further demonstrates the efficacy of this synthetic method. This will be a good alternative to the synthesis of wide range of β -cyano- α , β -unsaturated ketones.

Experimental Section

General procedure: The mixture of $K_4[Fe(CN)_6]$ (0.1 mmol), aroyl chlorides (0.5 mmol) and Pd(OAc)₂ (0.05 mmol) was first stirred at 150 °C for 4 h, then aryl halides (0.5 mmol), CaC₂ (1.25 mmol), H₂O (2.50 mmol), K₂CO (0.25 mmol) and dppb (0.05 mmol) in 4 mL of degassed and dried DMF were added under nitrogen atmosphere and stirred at 80 °C for 28 h. The reaction was monitored by TLC. After the completion, the resulting mixture was filtered to remove the solid, and the liquor was extracted with ethyl acetate (3×10 mL), and washed with saturated brine (3×10 mL). The resulting organic phase was dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 7:1) as eluent to give pure (Z)-4-oxo-2,4-diarylbut-2enenitriles 3a-z and $3\alpha-\beta$.

Acknowledgements

The authors thank the National Natural Science Foundation of China (21462038) for the financial support of this work.

Conflict of Interest

The authors declare no conflict of interest.

References

- M. Ohoka, S. Yanagida, S. Komori, J. Org. Chem. 1972, 37, 3030–3032.
- [2] T. Kurihara, M. Miki, R. Yoneda, S. Harusawa, *Chem. Pharm. Bull.* **1986**, *34*, 2747–2753.
- [3] E. Brenna, F. G. Gatti, A. Manfredi, D. Monti, F. Parmeggiani, *Catal. Sci. Technol.* 2013, *3*, 1136–1146.
- [4] G. W. Coates, P. D. Hustad, S. Reinartz, Angew. Chem. Int. Ed. 2002, 41, 2236–2257.
- [5] F. F. Fleming, L. Yao, P. C. Ravikumar, L. Funk, B. C. Shook, J. Med. Chem. 2010, 53, 7902–7917.
- [6] F. F. Fleming, Nat. Prod. Rep. 1999, 16, 597–606.
- [7] Y. Matsuda, H. Gotou, K. Katou, H. Matsumoto, M. Yamashita, S. Maeda, *Dyes Pigm.* 1990, 14, 225–238.
- [8] Z. C. Litman, Y. Wang, H. Zhao, J. F. Hartwig, *Nature* 2018, 560, 355–359.
- [9] a) K. Nozaki, N. Sato, H. Takaya, J. Org. Chem. 1994, 59, 2679–2681; b) M. Murai, K. Miki, K. Ohe, J. Org. Chem. 2008, 73, 9174–9176; c) K. Nozaki, N. Sato, H. Takaya, Bull. Chem. Soc. Jpn. 1996, 69, 1629–1637.

- [10] T. Arai, Y. Suemitsu, Y. Ikematsu, Org. Lett. 2009, 11, 333–335.
- [11] H. Trabulsi, G. Rousseau, Synth. Commun. 2011, 41, 2123–2134.
- [12] a) W. Zhang, H. Wu, Z. Liu, P. Zhong, L. Zhang, X. Huang, J. Cheng, Chem. Commun. 2006, 4826-4828; b) Y. Jiang, C. Kuang, Q. Yang, Synlett 2009, 3163-3166; c) P. Chuentragool, K. Vongnam, Ρ. Rashatasakhon, M. Sukwattanasinitt, S. Wacharasindhu, Tetrahedron 2011, 67, 8177-8182; d) Q. Yang, Y. Jiang, C. Kuang, Helv. Chim. Acta 2012, 95, 448-454; e) Z. Lin, D. Yu, Y. N. Sum, Y. Zhang, ChemSusChem 2012, 5, 625-628; f) D. Yu, Y. N. Sum, A. C. C. Ean, M. Chin, Y. Zhang, Angew. Chem. Int. Ed. 2013, 52, 5125-5128; g) Y. N. Sum, D. Yu, Y. Zhang, Green Chem. 2013, 15, 2718-2721; h) N. Thavornsin, M. Sukwattanasinitt, S. Wacharasindhu, Polym. Chem. 2014, 5, 48-52; i) A. Hosseini, D. Seidel, A. Miska, P. R. Schreiner, Org. Lett. 2015, 17, 2808-2811; j) N. Kaewchangwat, R. Sukato, V. Vchirawongkwin, T. Vilaivan, M. Sukwattanasinitt, S. Wacharasindhu, Green Chem. 2015, 17, 460-465; k) K. S. Rodygin, V. P. Ananikov, Green Chem. 2016, 18, 482–486; l) K. S. Rodygin, G. Werner, F. A. Kucherov, V. P. Ananikov, *Chem. Asian J.* **2016**, *11*, 965–976; m) S. P. Teong, D. Yu, Y. N. Sum, Y. Zhang, Green Chem. 2016, 18, 3499–3502; n) E. Rattanangkool, T. Vilaivan, M. Sukwattanasinitt, S. Wacharasindhu, Eur. J. Org. Chem. 2016, 4347-4353; o) Y. Yu, Y. Chen, W. Huang, W. Wu, H. Jiang, J. Org. Chem. 2017, 82, 9479–9486; p) A. Samzadeh-Kermani, Synlett 2017, 28, 2126-2130; q) A. Hosseini, A. Pilevar, E. Hogan, B. Mogwitz, A. S. Schulze, P. R. Schreiner, Org. Biomol. Chem. 2017, 15, 6800-6807; r) G. Werner, K. S. Rodygin, A. A. Kostin, E. G. Gordeev, A. S. Kashin, V. P. Ananikov, Green Chem. 2017, 19, 3032-3041; s) W. E. Van Beek, K. Gadde, K. A. Tehrani, Chem. Eur. J. 2018, 24, 16645-16651; t) M. Turberg, K. J. Ardila-Fierro, C. Bolm, J. G. Hernandez, Angew. Chem. Int. Ed. 2018, 57, 10718-10722; u) V. V. Voronin, M. S. Ledovskaya, E. G. Gordeev, K. S. Rodygin, V. P. Ananikov, J. Org. Chem. 2018, 83, 3819-3828; v) M. S. Ledovskaya, K. S. Rodygin, V. P. Ananikov, Org. Chem. Front. 2018, 5, 226–231; w) D. Wang, Z. Liu, Q. Liu, Ind. Eng. Chem. Res. 2019, 58, 6226–6234; x) K. S. Rodygin, Y. A. Vikenteva, V. P. Ananikov, ChemSusChem 2019, 12, 1483-1516; y) A. Hosseini, P. R. Schreiner, Org. Lett. 2019, 21, 3746-3749.
- [13] a) T. Schareina, A. Zapf, M. Beller, J. Organomet. Chem. 2004, 689, 4576–4583; b) T. Schareina, A. Zapf, M. Beller, Chem. Commun. 2004, 1388–1389; c) T. Schareina, A. Zapf, M. Beller, Tetrahedron Lett. 2005, 46, 2585–2588; d) S. A. Weissman, D. Zewge, C. Chen, J. Org. Chem. 2005, 70, 1508–1510; e) O. Grossman,

D. Gelman, Org. Lett. 2006, 8, 1189-1191; f) L. Li, Z. Pan, X. Duan, Y. Liang, Synlett 2006, 2094–2098; g) T. Schareina, A. Zapf, M. Beller, Tetrahedron Lett. 2007, 48, 1087-1090; h) S. Velmathi, N. E. Leadbeater, Tetrahedron Lett. 2008, 49, 4693–4694; i) G. Chen, J. Weng, Z. Zheng, X. Zhu, Y. Cai, J. Cai, Y. Wan, Eur. J. Org. Chem. 2008, 3524–3528; j) A. W. Franz, L. N. Popa, T. J. J. Muller, Tetrahedron Lett. 2008, 49, 3300-3303; k) Y. Ren, Z. Liu, S. Zhao, J. Wang, W. Yin, S. He, Catal. Commun. 2009, 10, 768-771; 1) Y. Ren, W. Wang, S. Zhao, X. Tian, J. Wang, W. Yin, L. Cheng, Tetrahedron Lett. 2009, 50, 4595-4597; m) Y. Ren, Z. Liu, S. He, S. Zhao, J. Wang, R. Niu, W. Yin, Org. Process Res. Dev. 2009, 13, 764-768; n) P. Yeung, C. Tsang, F. Y. Kwong, Tetrahedron Lett. 2011, 52, 7038-7041; o) P. Anbarasan, H. Neumann, M. Beller, Chem. Eur. J. 2011, 17, 4217-4222; p) P. Y. Yeung, M. S. Chau, P. L. Chak, Org. Lett. 2011, 13, 648-651; q) D. Zhang, H. Sun, L. Zhang, Y. Zhou, C Li, H. Jiang, K. Chen, H. Liu, Chem. Commun. 2012, 48, 2909–2911; r) L. Liu, J. Li, J. Xu, J. Sun, Tetrahedron Lett. 2012, 53, 6954-6956; s) I. A. Azath, P. Suresh, K. Pitchumani, New J. Chem. 2012, 36, 2334–2339; t) X. Tian, Y. Sun, C. Dong, K. Zhang, T. Liang, Y. Zhang, C. Hou, Chem. Lett. 2012, 41, 719-721; u) R. Gerber, M. Oberholzer, C. M. Frech, Chem. Eur. J. 2012, 18, 2978–2986; v) Y. Ren, C. Dong, S. Zhao, Y. Sun, J. Wang, J. Ma, C. Hou, Tetrahedron Lett. 2012, 53, 2825-2827; w) D. Saha, L. Adak, M. Mukherjee, B. C. Ranu, Org. Biomol. Chem. 2012, 10, 952-957; x) W. Yin, R. Liu, G. He, W. Lv, H. Zhu, RSC Adv. 2014, 4, 37773-37778; y) T. Chatterjee, R. Dey, B. C. Ranu, J. Org. Chem. 2014, 79, 5875-5879; z) J. Richardson, S. P. Mutton, J. Org. Chem. 2018, 83, 4922–4931; α) C. Grundke, T. Opatz, Green Chem. **2019**, *21*, 2362–2366.

- [14] R. Fu, Z. Li, Org. Lett. 2018, 20, 2342–2345.
- [15] R. Fu, Z. Li, Eur. J. Org. Chem. 2017, 6648–6651.
- [16] G. Song, Z. Li, *Eur. J. Org. Chem.* 2018, 1326–1332.
 [17] Z. Li, L. He, R. Fu, G. Song, W. Song, D. Xie, J.
- Yang, Tetrahedron 2016, 72, 4321–4328.
 [18] a) Z. Zhao, Z. Li, Eur. J. Org. Chem. 2010, 5460–5463; b) Z. Li, G. Tian, Y. Ma, Synlett 2010, 2164–2168; c) Z. Li, C. Liu, Y. Zhang, R. Li, B. Ma, J. Yang, Synlett 2012, 23, 2567–2571; d) Z. Li, J. Yin, T. Li, G. Wen, X. Shen, J. Yang, Tetrahedron 2014, 70, 5619–5625; e) X. Hu, H. Li, J. Yang, Z. Li, Synlett 2014, 25, 1786–1790; f) Z. Li, F. Wen, J. Yang, Chin. J. Chem. 2014, 32, 1251–1254; g) Z. Li, F. Wen, J. Yang, J. Chem. Sci. 2016, 128, 1849–1853; h) Z. Li, Y. Du, H. Lu, A. Yang, J. Yang, Green Process Syntn. 2019, 8, 93–99.
- [19] T. Havashi, A. Kubo, F. Ozawa, Pure Appl. Chem. 1992, 64, 421–427.

Palladium-Catalyzed One-Pot Four-Component Synthesis of β -Cyano- α , β -unsaturated Ketones Using Calcium Carbide as an Acetylene Source, Potassium Hexacyanoferrate(II) as an Eco-Friendly Cyanide Source

Palladium-Catalyzed One-Pot Four-Component Synthesis of β -Cyano- α , β -unsaturated Ketones Using Calcium Carbide as an Acetylene Source, Potassium Hexacyanoferrate(II) as an Eco-Friendly Cyanide Source

Adv. Synth. Catal. Year, Volume, Page-Page

Hao Lu, Zheng Li*

