



Accepted Article

Title: Radical Carbonylation Under Low CO Pressure: Synthesis of Esters from Activated Alkylamines at Transition Metal-Free Conditions

Authors: Fengqian Zhao, Han-Jun Ai, and Xiao-Feng Wu*

This manuscript has been accepted and appears as an Accepted Article online.

This work may now be cited as: *Chin. J. Chem.* **2020**, *38*, 10.1002/cjoc.202000624.

The final Version of Record (VoR) of it with formal page numbers will soon be published online in Early View: http://dx.doi.org/10.1002/cjoc.202000624.

WILEY-VCH SIOC CCS

ISSN 1001-604X • CN 31-1547/O6 mc.manuscriptcentral.com/cjoc www.cjc.wiley-vch.de Cite this paper: Chin. J. Chem. 2021, 39, XXX-XXX. DOI: 10.1002/cjoc.202100XXX

Radical Carbonylation Under Low CO Pressure: Synthesis of Esters from Activated Alkylamines at Transition Metal-Free Conditions

Fengqian Zhao,^a Han-Jun Ai,^a and Xiao-Feng Wu*^{a,b}

Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Straße 29a, 18059 Rostock, Germany, E-mail: ´´ao-Feng.Wu@catalysis.de

^a Dalian National Laboratory for Clean Energy, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, Liaoning, 116023, China, E-mail: xwu2020@dicp.ac.cn

Keywords

Accepte

Carbonylation | Radical | Ester | Alkylamine | Katritzky salt

Main observation and conclusion

High CO pressure (> 40 bar) usually needed in radical carbonylation reactions in the absence of metal catalyst. In this communication, we developed a transition-metal-free radical carbonylation of activated alkylamines with phenols and alcohols under low CO pressure (1-6 bar). Various esters were obtained in moderate to excellent yields under simple reaction conditions with good functional group compatibility.

Comprehensive Graphic Content



*E-mail:	View HTML Articl	e Supporting Information
Chin. J. Chem. 2021 , 39, XXX—XXX	© 2021 SIOC, CAS, Shanghai, & WILEY-VCH GmbH	
This article has been accept through the copyediting, ty differences between this v 10.1002/cjoc.202000624	ed for publication and undergone full peer r pesetting, pagination and proofreading pro- ersion and the Version of Record. Please	eview but has not been cess which may lead to cite this article as doi:

This article is protected by copyright. All rights reserved.

Background and Originality Content

Carbonyl-containing compounds (esters, amides, aldehydes, ketones) are widely found in pharmaceuticals, functional materials, and biologically active molecules. Carbonyl structures are also important building blocks in organic transformations.^[1] Hence the synthesis of carbonyl-containing compounds is an attractive subject. Since the first example of the highly efficient trapping of CO by radicals was reported by Ryu et al. in 1990,^[2] radical carbonylation with CO as a cheap carbonyl source has gained considerable a tention. Nowadays, this strategy represents one of the most powerful tools, and has been widely used in the construction of methods, including transition-metal catalyzed, oxidant-induced and photoinitiated carbonylation, have been developed to obtain lue-added carbonylated products.^[4]

In general, there are two accepted pathways for the radical rbonylative transformations: 1) One is trapping the radical by (noble)metal center to form an organometallic intermediate and en followed by CO insertion (Scheme 1a, path a).^[5] However, this process is usually limited by the slow oxidative addition and/or rapid β -hydride elimination.^[6] 2) The other pathway is pture the CO by radicals to generate acyl radicals directly (Scheme 1a, path b). This acyl radical generation process is rersible (the reversed decarbonylation step is even more favored), thus require high CO pressure (> 40 bar)^[7] or metal catalyst^[8] to stabilize the acyl radical intermediates. Therefore, there is still an unmet need for low CO pressure strategy that can be applied in transition-metal-free radical carbonylation. Notably, Ryu and co-workers reported their achievement on black-light-induced dical carbonylation of alkyl iodides in 2010. The reaction proceeds under 1 bar of CO in the presence of tetrabutylammonium orohydride, the corresponding hydroxymethylated products were formed in moderate to good yields.^[7f]

cheme 1 The strategies for radical carbonylation a) General strategies for radical carbonylation

[M], [O] or h R = alkyl, aryı X = I. Br, N₂BF₄, Limitation High CO pressure catalvs Transition-metal-free radical carbonylation under low CO pressure (this work) CO (6 bar) R³OF DBU R1 ⊖ BF DBL k2 $R^{3} =$ aryl, benzyl, alkyl, ally Low CO pressure Organic base as promotor Transition-metal-free 🧳 Broad substrates scope

As an effective strategy for the formation of alkyl radicals, deamination of Katritzky salts, which are easily obtained from amines, has been used in various transformations^[9] as well as in carbonylation reactions.^[10] However, as above discussed, high pressure of CO and/or metal catalyst was still required in deaminative carbonylation of Katritzky salts. In order to solve these challenges, and also as our continuing interest in deaminative carbonylative coupling of activated amines and phenols. This new transformation proceeds under low CO pressure (1-6 bar) in the

absence of transition-metal catalysts.

Results and Discussion

Our initial research started with deaminative carbonylation of Katritzky salts 1a and 4-methoxyphenol 2a in the presence of DBU under CO pressure, 5% yield of alkylphenol ester 3 was detected (Table 1, entry 1). The yield of 3 was greatly improved when Cs₂CO₃ was added to the reaction (Table 1, entry 2). DBU was proved to be indispensable through control experiment (Table 1, entry 3). Subsequently, other promoters, such as DBN, TBD, and DABCO were used to replace DBU, and DBN gave the best result and two equivalents of it is necessary (Table 1, entries 4-5, see the Supporting Information for more details). Various bases were submitted to the transformation and K₃PO₄ gave a significant improvement in the yield (Table 1, entries 6-10, see the Supporting Information for more details). In addition, other solvents were also used, and DMAc led to a great increase in the reaction efficiency (Table 1, entries 11-12, see the Supporting Information for more details). It is worthy to mention that good yield can be still obtained when 6 bar of CO was used. Notably, this transformation can also be achieved under 1 bar CO with 54% yield of 3 was obtained (Table 1, entry 13). Furthermore, the yield was improved slightly by increasing the reaction concentration (Table 1, entry 14). Decreasing the temperature led to reduced yield of ester (Table 1, entry 15).

Table 1 Optimization of the reaction conditions^a

$\begin{array}{c} Ph \\ & & \\ & & \\ Ph \\ & & \\ & & \\ Ph \end{array} \xrightarrow{Ph} + \\ & & $						
1a 2a			3			
Entry	Promoter	Base	Solvent	CO (bar)	Yield (%) ^b	
1	DBU	/	THF	20	5	
2	DBU	Cs_2CO_3	THF	20	25	
3	/	Cs_2CO_3	THF	20	trace	
4	DBN	Cs_2CO_3	THF	20	47	
5	TBD	Cs_2CO_3	THF	20	14	
6	DBN	K ₂ CO ₃	THF	20	32	
7	DBN	Na_2CO_3	THF	20	32	
8	DBN	K ₃ PO ₄	THF	20	72	
9	DBN	t-BuOK	THF	20	20	
10	DBN	K ₃ PO ₄	MeCN	20	42	
11	DBN	K_3PO_4	DMAc	20	87	
12	DBN	K ₃ PO ₄	DMAc	6	90	
13	DBN	K ₃ PO ₄	DMAc	1	54	
14 ^c	DBN	K ₃ PO ₄	DMAc	6	92 (91) ^e	
15 ^{<i>c,d</i>}	DBN	K ₃ PO ₄	DMAc	6	60	

^{*a*} Reaction conditions: **1a** (0.12 mmol, 1.2 equiv), **2a** (0.1 mmol, 1.0 equiv), promoter (0.2 mmol, 2.0 equiv), base (0.1 mmol, 1.0 equiv), solvent (2.0 mL), CO, 80 °C, 15 h. ^{*b*} Determined by GC using hexadecane as the internal standard. ^{*c*} DMAc (1.5 mL). ^{*d*} 60 °C. ^{*e*} Isolated yield. DBN = 1,5-Diazabicyclo[4.3.0]non-5-ene. DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene. TBD =

1,3,4,6,7,8-Hexahydro-2*H*-pyrimido [1,2-*a*] pyrimidine.

Scheme 2 Scope of radical carbonylation



Reaction conditions: Katritzky salts (0.24 mmol, 1.2 equiv), phenols or alcohols (0.2 mmol, 1.0 equiv), DBN (0.4 mmol, 2.0 equiv), K₃PO₄ (0.2 mmol, 1.0 equiv), DMAc (3.0 mL), CO (6 bar), 80 °C, 15 h, isolated yield. ^{*a*} 2.0 equiv of Katritzky salts were uesd. ^{*b*} 0.1 mmol 2,2'-biphenol was uesd. ^{*c*} 5.0 equiv of alcohols and 0.2 mmol Katritzky salts were uesd.

With the optimized reaction conditions in hand, the substrate scope of this transformation was examined. A variety of Katritzky salts derived from amines were tested firstly and led to the corresponding esters in moderate to excellent yields (Scheme 2, **3-13**). Cyclic, chain, and phenyl-containing amine derivatives were well-tolerated in this transformation (**3-11**). When the derivative of indan-2-amine was used, moderate yield was obtained because of the fast θ -hydride elimination of the alkyl radical intermediate (**8**). Remarkably, *N*- and *O*-heterocyclic amines were successfully converted into the corresponding esters in good yields (**12-13**). It is important to mention that primary alkyl Katritzky salts can not be activated in the current reaction system.

Subsequently, the scope with respect to phenols were exammed. Various phenols were all tolerated and delivered the desired esters smoothly (Scheme 2, 14-34). Versatile functional groups appended to the phenols, such as alkyl (15-17, 19), phenyl (18), alkoxy (20), allyl (21), dimethylamino (22), amide (23), fluorine (4), ketone (28), and pyrrolyl (30) were all efficiently transformed into the desired products in moderate to excellent yields. Rearkably, the corresponding esters also can be obtained in moderate yields with electron-withdrawing groups substituted phenols, ir cluding bromine (25), ester (26), and acetyl (27). Meanwhile, the influence of steric hindrance was tested as well, 2-tert-butyl (31), 2-phenyl (32), 2,6-dimethyl (33), and 2,6-diphenyl (34) were all rell-tolerated, the yields of the wished esters had no decrease or even got better. When 2-hydroxycarbazol was used, the desired enter was obtained in good yield, and no amide was detected (35). me reaction occurs selectively at the -OH site when benzene rings contain both -OH and -NH. Additionally, 2,2'-biphenol can be transformed into the corresponding diester in good yield (36). In addition to phenols, 3-hydroxypyridine was also applied in this transformation smoothly and the corresponding ester was obtrined in moderate yield (37). To expand the scope of substrates, benzyl alcohols were also tested. As shown in Scheme 2, the corsponding esters were obtained smoothly when various benzyl alcohols were tested instead of phenols (38-50). Methoxy (38-39) and phenyl (40) substituted benzyl alcohols gave the desired esrs in excellent yields. Other synthetically valuable groups, such as dimethylamino (41), amide (42), halogen (43), trifluoromethyl 5), and cyclopropyl (46) were also well-tolerated in this transformation, the presence of benzylic substituent had no obvious ffect on the reaction. In addition to this, 1-indanol (47), 1-(1-naphthyl) ethanol (48), thienyl (49), and pyridyl methanol (50) b give the corresponding products in good yields as well.

Alkyl alcohols can also be used in this transformation. Both p imary and secondary alcohols can deliver the desired esters uccessfully (**51-59**), but tertiary alcohols were not applicable under our conditions. Unsaturated alcohols were also able to be t ansformed in moderate to good yields and the triple bond (**57**) or double bond (**58**) were retained in products. Meanwhile, 2-chloroethanol was well-tolerated (**59**). These functional groups r ovide the possibility for subsequent transformations and utilizauons. Remarkably, compared with phenols, most alkyl alcohols provided their esters in moderated yields, this might due to the ecreased acidity of the -OH group.

To prove the application values of our transformation, bioactive molecules were also tested. Estrone, which was usually used as pharmaceutical intermediates and common raw materials, provided the corresponding ester in 83% yield (Scheme 2, 60). Naturally occurring steroids, such as epiandrosterone (61) and cholestanol (62), could be easily transformed and provided the target esters in 41% and 64% yields, respectively. Nerol with multiple unsaturated bonds delivered the desired ester smoothly as well (63). These results proved the application potential of this transition-metal-free transformation in the synthesis and modification of pharmaceutical molecules.

To gain some insight into the mechanism of this reaction, mechanistic experiments were performed (Scheme 3). When TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) was added into the

system under the standard conditions, the reaction was inhibited completely, meanwhile the adduct of radical with TEMPO 64 was detected by GC-MS (See the Supporting Information for GC-MS). In contrast, when the reaction was carried out in the absence of DBN or at room temperature, neither 3 nor 64 was detected. Subsequently, the product was obtained in 24% yield when BHT (butylated hydroxytoluene) was added to the reaction. We also detected the cyclohexyl radicals through EPR spectra (See the Supporting Information for more details). And the addition of 1,1-diphenylethylene lead to 18% yield of 3 and 35% yield of 65. These results suggest that the alkyl radical and acyl radical were probably generated in this transformation and the key to promote the formation of alkyl radicals is DBN and heat. Finally, when PhONa replaced PhOH and K₃PO₄, the corresponding ester was isolated in 36% yield (52% yield, when PhOH and K₃PO₄ were used). It proven that phenols were deprotonated to form PhO⁻ in the presence of bases.

Scheme 3 Mechanistic experiments



On the basis of above results and previous literatures,^[10,11] a possible mechanism was proposed (Scheme 4). Firstly, radical I was formed from 1 through a SET process with DBN, and DBN radical was produced at the same time. Then, CO trapped by the alkyl radical I form an acyl radical II which will be oxidized by the DBN radical to give the corresponding acyl cation III. Finally, the terminal ester product IV will be formed after reacting with alcohols in the presence of base.

Scheme 4 Proposed mechanism



Conclusions

In conclusion, under low CO pressure (1-6 bar), a transition-metal-free radical carbonylation of activated alkylamines with phenols and alcohols has been developed. Various target esters were obtained in moderate to excellent yields under modest reaction conditions. The involvement of radical intermediates was proven by our preliminary mechanistic studies. From synthetic point of view, this transformation can be more meaningful in the pharmaceutical fields which need to avoid the use of metals.

Experimental

A 4 mL screw-cap vial was charged with Katritzky salts (0.24 mol), phenols or alcohols (if solid, 0.2 mmol, 1.0 equiv), K₃PO₄ (0.2 mmol, 1.0 equiv) and an oven-dried stirring bar. The vial was c osed by Teflon septum and phenolic cap and connected with mosphere with a needle. After flashed the vials with argon and vacuum three times, DBN (0.4 mmol, 2.0 equiv), phenols or alcobls (if liquid, 0.2 mmol, 1.0 equiv) and dry DMAc (3.0 mL) were injected by syringe. The vial was fixed in an alloy plate and put into urr 4560 series autoclave (500 mL) under argon atmosphere. At room temperature, the autoclave was flushed with carbon monoxide for three times and 6 bar of carbon monoxide was charged. he autoclave was reacted at 80 °C for 15 h. Afterwards, the autoclave was cooled to room temperature and the pressure was refully released. The mixture was diluted with water (15 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layer was removed under reduced pressure and the residue was purified by silica gel chromatography (n-Pentane/EtOAc) to afford the corresponding esters.

Jupporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2021xxxxx.

Acknowledgement

The authors thank the Chinese Scholarship Council (CSC) for "nancial support. We also thank the analytical team of LIKAT for their excellent analytic support.

References

- (a) Goossen, L. J.; Rodriguez, N.; Goossen, K. Carboxylic Acids as Substrates in Homogeneous Catalysis. *Angew. Chem. Int. Ed.* 2008, 47, 3100-3120; (b) Otera, J. *Esterification: Methods, Reactions, and Applications*; Wiley-VCH: Weinheim, Germany, 2003; pp. 1–303.
- [2] Ryu, I.; Kusano, K.; Ogawa, A.; Kambe, N.; Sonoda, N. Free Radical Carbonylation. Efficient Trapping of Carbon Monoxide by Carbon Radicals. J. Am. Chem. Soc. **1990**, *112*, 1295-1297.
- [3] (a) Ryu, I.; Sonoda, N. Free-Radical Carbonylations: Then and Now. Angew. Chem. Int. Ed. 1996, 35, 1050-1066; (b) Matsubara, H.; Kawamoto, T.; Fukuyama, T.; Ryu, I. Applications of Radical Carbonylation and Amine Addition Chemistry: 1,4-Hydrogen Transfer of 1-Hydroxylallyl Radicals. Acc. Chem. Res. 2018, 51, 2023-2035; (c) Lang, R.; Xia, C.; Li, F. Carbonylative Diversification of Unactivated Heteroaromatic Compounds. New J. Chem. 2014, 38, 2732-2738; (d) Liu, Q.; Zhang, H.; Lei, A. Oxidative Carbonylation Reactions: Organometallic Compounds (R-M) or Hydrocarbons (R-H) as Nucleophiles. Angew. Chem. Int. Ed. 2011, 50, 10788-10799; (e) Hu, X. Q.; Liu, Z. K.; Xiao, W. J. Radical Carbonylative Synthesis of Heterocycles by Visible Light Photoredox Catalysis. Catalysts 2020, 10, 1054; (f) Zhu, C.; Liu, J.; Li, M.-B.; Bäckvall, J.-E. Palladium-catalyzed oxidative dehydrogenative carbonylation reactions using carbon monoxide and mechanistic overviews. Chem. Soc. Rev., 2020, 49, 341-353; (g) Cai, B.; Cheo, H.

W.; Liu, T.; Wu, J. Light-Promoted Organic Transformations Utilizing Carbon-Based Gas Molecules as Feedstocks. *Angew. Chem. Int. Ed.* **2021**, 10.1002/anie.202010710.

- [4] For selected recent examples on transition-metal, oxidant-induced and photoinitiated radical carbonylation, see: (a) Peng, J.-B.; Geng, H.-Q.; Wu, X.-F. The Chemistry of CO: Carbonylation. Chem. 2019, 5, 526-552; (b) Zhao, S.; Mankad, N. P. Metal-Catalysed Radical Carbonylation Reactions. Catal. Sci. Technol. 2019, 9, 3603-3613; (c) Yang, L.; Shi, L.; Xing, Q.; Huang, K.-W.; Xia, C.; Li, F. Enabling CO Insertion into o-Nitrostyrenes beyond Reduction for Selective Access to Indolin-2-one and Dihydroquinolin-2-one Derivatives. ACS Catal. 2018, 8, 10340-10348; (d) Zhang, W.; Zhao, M.-N.; Chen, M.; Ren, Z.-H.; Guan, Z. Palladium-Catalyzed Regioselective Cyclocarbonylation of N-(3-Phenylprop-2-ynyl)anilines with Carbon Monoxide and Alcohols for the Synthesis of Quinoline-3-carboxylic Esters. Asian J. Org. Chem. 2018, 7, 1605-1608; (e) Cheng, J.; Qi, X.; Li, M.; Chen, P.; Liu, G. Palladium-Catalvzed Intermolecular Aminocarbonvlation of Alkenes: Efficient Access of B-Amino Acid Derivatives. J. Am. Chem. Soc. 2015, 137, 2480-2483; (f) Qi, X.; Yu, F.; Chen, P.; Liu, G. Intermolecular Palladium-Catalyzed Oxidative Fluorocarbonylation of Unactivated Alkenes: Efficient Access to *B*-Fluorocarboxylic Esters. Angew. Chem. Int. Ed. 2017, 56, 12692-12696; (g) Hu, Y.; Shen, Z.; Huang, H. Palladium-Catalyzed Intramolecular Hydroaminocarbonylation to Lactams: Additive-Free Protocol Initiated by Palladium Hydride. ACS Catal. 2016, 6, 6785-6789; (h) Yu, H.; Zhang, G.; Huang, H. Palladium-catalyzed Dearomative Cyclocarbonylation by C-N Bond Activation. Angew. Chem. Int. Ed. 2015, 54, 10912-10916; (i) Zhang, G.; Gao, B.; Huang, H. Palladium-Catalyzed Hydroaminocarbonylation of Alkenes with Amines: A Strategy to Overcome the Basicity Barrier Imparted by Aliphatic Amines. Angew. Chem. Int. Ed. 2015, 54, 7657-7661; (j) Lu, Y.; Leow, D.; Wang, X.; Engle, K. M.; Yu, J.-Q. Hydroxyl-Directed C-H Carbonylation Enabled by mono-N-Protected Amino Acidligands: An Expedient Route to 1-Isochromanones. Chem. Sci. 2011, 2, 967-971; (k) Zeng, L.; Li, H.; Hu, J.; Zhang, D.; Hu, J.; Peng, P.; Wang, S.; Shi, R.; Peng, J.; Pao, C.-W.; Chen, J.-L.; Lee, J.-F.; Zhang, H.; Chen, Y.-H.; Lei, A. Electrochemical Oxidative Aminocarbonylation of Terminal Alkynes. Nat. Catal. 2020, 3, 438-445; (I) Zhang, H.; Shi, R.; Ding, A.; Lu, L.; Chen, B.; Lei, A. Transition-Metal-Free Alkoxycarbonylation of Aryl Halides. Angew. Chem. Int. Ed. 2012, 51, 12542-12545; (m) Guo, W.; Lu, L. Q.; Wang, Y.; Wang, Y. N.; Chen, J. R.; Xiao, W.-J. Metal-Free, Room-Temperature, Radical Alkoxycarbonylation of Aryldiazonium Salts through Visible-Light Photoredox Catalysis. Angew. Chem. Int. Ed. 2015, 54, 2265-2269; (n) Lu, B.; Cheng, Y.; Chen, L.-Y.; Chen, J.-R.; Xiao, W.-J. Photoinduced Copper-Catalyzed Radical Aminocarbonylation of Cycloketone Oxime Esters. ACS Catal. 2019, 9, 8159-8164.
- [5] For selected recent examples on radical carbonylation involving the formation of metal alkyl intermediates, see: (a) Yin, H.; Kumke, J. J.; Domino, K.; Skrydstrup, T. Palladium Catalyzed Carbonylative Coupling of Alkyl Boron Reagents with Bromodifluoroacetamides. *ACS Catal.* 2018, *8*, 3853-3858; (b) Sargent, B. T.; Alexanian, E. J. Palladium-Catalyzed Alkoxycarbonylation of Unactivated Secondary Alkyl Bromides at Low Pressure. *J. Am. Chem. Soc.* 2016, *138*, 7520-7523; (c) Xie, P.; Xie, Y.; Qian, B.; Zhou, H.; Xia, C.; Huang, H. Palladium-Catalyzed Oxidative of Benzylic C-H Bonds via Nondirected C(sp³)-H Activation. *J. Am. Chem. Soc.* 2012, *134*, 9902-9905; (d) Ai, H. J.; Wang, H.; Li, C. L.; Wu, X.-F. Rhodium-Catalyzed Carbonylative Coupling of Alkyl Halides with Phenols under Low CO Pressure. *ACS Catal.* 2020, *10*, 5147-5152.
- [6] (a) Zanti, G.; Peeters, D. DFT Study of Small Palladium Clusters Pdn and Their Interaction with a CO Ligand (n = 1-9). *Eur. J. Inorg. Chem.* **2009**, *26*, 3904-3911; (b) Bissember, A. C.; Levina, A.; Fu, G. C. A Mild, Palladium-Catalyzed Method for the Dehydrohalogenation of Alkyl Bromides: Synthetic and Mechanistic Studies. *J. Am. Chem. Soc.* **2012**, *134*, 14232-14237.
- [7] For selected recent examples on radical carbonylation involving acyl radicals directly attacked by nucleophiles, see: (a) Cartier, A.; Lever-

Report

nier, E.; Corcé, V.; Fukuyama, T.; Dhimane, A.-L.; Ollivier, C.; Ryu, I.; Fensterbank, L. Carbonylation of Alkyl Radicals Derived from Organosilicates through Visible-Light Photoredox Catalysis. Angew. Chem. Int. Ed. 2019, 58, 1789-1793; (b) Cartier, A.; Levernier, E.; Dhimane, A. L.; Fukuyama, T.; Ollivier, C.; Ryu, I.; Fensterbank, L. Synthesis of Aliphatic Amides through a Photoredox Catalyzed Radical Carbonylation Involving Organosilicates as Alkyl Radical Precursors. Adv. Synth. Catal. 2020, 362, 2254-2259; (c) Lu, L.; Cheng, D.; Zhan, Y.; Shi, R.; Chiang, C.-W.: Lei, A. Metal-Free Radical Oxidative Alkoxycarbonylation and Imidation of Alkanes. Chem. Commun. 2017, 53, 6852-6855; (d) Ryu, I.; Tani, A.; Fukuyama, T.; Ravelli, D.; Fagnoni, M.; Albini, A. Atom-Economical Synthesis of Unsymmetrical Ketones through Photocatalyzed C-H Activation of Alkanes and Coupling with CO and Electrophilic Alkenes. Angew. Chem. Int. Ed. 2011, 50, 1869-1872; (e) Majek, M.; Jacobi von Wangelin, A. Metal-Free Carbonylations by Photoredox Catalysis. Angew. Chem. Int. Ed. 2015, 54, 2270-2274. (f) Kobayashi, S.; Kawamoto, T.; Uehara, S.; Fukuyama, T.; Ryu, I. Black-Light-Induced Radical/Ionic Hydroxymethylation of Alkyl Iodides with Atmospheric CO in the Presence of Tetrabutylammonium Borohydride. Org. Lett. 2010, 12, 1548-1551; (g) Zhou, Q.-Q.; Guo, W.; Ding, W.: Wu, X.: Chen, X.: Lu, L.-Q.: Xiao, W.-J. Decarboxylative Alkynylation and Carbonylative Alkynylation of Carboxylic Acids Enabled by Visible-Light Photoredox Catalysis. Angew. Chem. Int. Ed. 2015. 54. 11196-11199.

[3] For selected recent examples on radical carbonylation involving acyl radicals react with metals, see: (a) Sumino, S.; Fusano, A.; Fukuyama, T.; Ryu, I. Carbonylation Reactions of Alkyl Iodides through the Interplay of Carbon Radicals and Pd Catalysts. Acc. Chem. Res. 2014, 47, 1563-1574; (b) Cheng, L.-J.; Mankad, N. P. Copper-Catalyzed Borocarbonylative Coupling of Internal Alkynes with Unactivated Alkyl Halides: Modular Synthesis of Tetrasubstituted β-Borylenones. Angew. Chem. Int. Ed. 2018, 57, 10328-10332; (c) Cheng, L.-J.; Islam, S. M.; Mankad, N. P. Synthesis of Allylic Alcohols via Cu-Catalyzed Hydrocarbonylative of Alkynes with Alkyl Halides. J. Am. Chem. Soc. 2018, 140, 1159-1164; (d) Zhao, S.; Mankad, N. P. Cu-Catalyzed Hydroxymethylation of Unactivated Alkyl Iodides with CO to Provide One-Carbon-Extended Alcohols. *Angew. Chem. Int. Ed.* **2018**, *57*, 5867-5870.

- [9] For selected recent reviews on deaminative transformations of Katritzky salts, see: (a) Rössler, S. L.; Jelier, B. J.; Magnier, E.; Dagousset, G.; Carreira, E. M.; Togni, A. Pyridinium Salts as Redox-Active Functional Group Transfer Reagents. *Angew. Chem. Int. Ed.* 2020, *59*, 9264-9280; (b) He, F.-S.; Ye, S.; Wu, J. Recent Advances in Pyridinium Salts as Radical Reservoirs in Organic Synthesis. *ACS Catal.* 2020, *9*, 8943-8960; (c) Kong, D.; Moon, P. J.; Lundgren, R. J. Radical Coupling from Alkyl Amines. *Nat. Catal.* 2019, *2*, 473-476; (d) Pang, Y.; Moser, D.; Cornella, J. Pyrylium Salts: Selective Reagents for the Activation of Primary Amino Groups in Organic Synthesis. *Synthesis*, 2020, *52*, 489-503.
- [10] For selected recent examples on deaminative carbonylation of Katritzky salts, see: (a) Zhao, F.; Li, C.-L.; Wu, X.-F. Deaminative Carbonylative Coupling of Alkylamines with Styrenes under Transition-Metal-Free Conditions. *Chem. Commun.* 2020, *56*, 9182-9185; (b) Li, C.-L.; Jiang, X.; Lu, L.-Q.; Xiao, W.-J.; Wu, X.-F. Cobalt(II)-Catalyzed Alkoxycarbonylation of Aliphatic Amines via C-N Bond Activation. *Org. Lett.* 2019, *21*, 6919-6923; (c) Jiang, X.; Zhang, M.-M.; Xiong, W.; Lu, L.-Q.; Xiao, W.-J. Deaminative (Carbonylative) Alkyl-Heck-type Reactions Enabled by Photocatalytic C-N Bond Activation. *Angew. Chem. Int. Ed.* 2019, *58*, 2402-2406.
- [11] Hu, J.; Cheng, B.; Yang, X.; Loh, T.-P. Transition-Metal-Free Deaminative Vinylation of Alkylamines. *Adv. Synth. Catal.* **2019**, *361*, 4902-4908.

(The following will be filled in by the editorial staff) Manuscript received: XXXX, 2021 Manuscript revised: XXXX, 2021 Manuscript accepted: XXXX, 2021 Accepted manuscript online: XXXX, 2021 Version of record online: XXXX, 2021

Entry for the Table of Contents

Radical Carbonylation Under Low CO Pressure: Synthesis of Esters from Activated Alkylamines at Transition Metal-Free Conditions Fengqian Zhao, Han-Jun Ai, and Xiao-Feng Wu* *Chin. J. Chem.* **2021**, *39*, XXX—XXX. **DOI: 10.1002/cjoc.202100XXX**

Accepted A



Transition-metal-free radical carbonylation of activated alkylamines with phenols and alcohols has been successful developed. This radical carbonylative strategy can be carried out under low CO pressure (1-6 bar). Esters with various functional groups were obtained in moderate to good yields.