ACS Catalysis

Subscriber access provided by READING UNIV

Letter

Palladium-Catalyzed Cyclization Reaction of o-Iodoanilines, CO2 and CO: Access to Isatoic Anhydrides

Wen-Zhen Zhang, Ning Zhang, Yu-Qian Sun, Yu-Wei Ding, and Xiao-Bing Lu

ACS Catal., **Just Accepted Manuscript** • Publication Date (Web): 23 Oct 2017

Downloaded from http://pubs.acs.org on October 23, 2017

Just Accepted

“Just Accepted” manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides “Just Accepted” as a free service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. “Just Accepted” manuscripts appear in full in PDF format accompanied by an HTML abstract. “Just Accepted” manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are accessible to all readers and citable by the Digital Object Identifier (DOI®). “Just Accepted” is an optional service offered to authors. Therefore, the “Just Accepted” Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the “Just Accepted” Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these “Just Accepted” manuscripts.

ACS Catalysis is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

Palladium-Catalyzed Cyclization Reaction of *o*-Iodoanilines, CO_2 and CO: Access to Isatoic Anhydrides

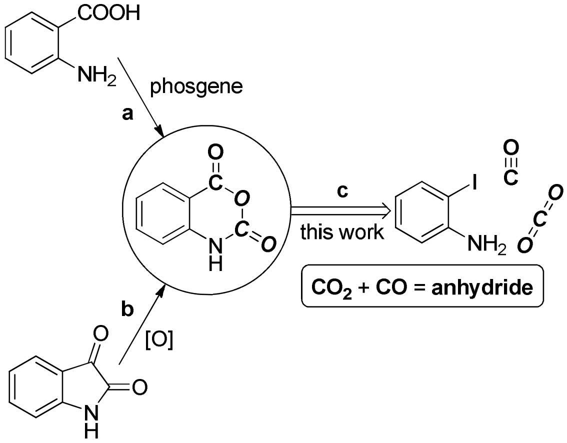
Wen-Zhen Zhang,* Ning Zhang, Yu-Qian Sun, Yu-Wei Ding, and Xiao-Bing Lu

State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian, 116024, P. R. China

ABSTRACT: Isatoic anhydrides, a class of valuable synthetic intermediates and RNA structure probing reagents, are usually prepared with highly toxic phosgene or stoichiometric oxidants. Herein we report a highly selective palladium-catalyzed cyclization reaction for the efficient synthesis of isatoic anhydrides from readily available *o*-iodoanilines, CO_2 and CO. The reaction proceeds under mild conditions and is redox-neutral. Both CO_2 and CO are indispensable C1 building blocks for this catalytic reaction.

KEYWORDS: carbon dioxide, carbonylation, palladium, homogeneous catalysis, anhydrides

Isatoic anhydrides are valuable synthetic intermediates in the preparation of biologically important compounds in medicinal chemistry.[1,2] They have also been well-validated as SHAPE (selective 2'-hydroxyl acylation analyzed by primer extension) reagent in RNA structure probing chemistry.[3] In general, isatoic anhydrides are synthesized by cyclization reactions of anthranilic acids using phosgene or its substitutes (Scheme 1, **a**),[1a,1h,1j,4] or oxidative reactions of indoles or isatins (Scheme 1, **b**).[5] Despite their practicality, these approaches involve the use of highly toxic phosgene reagents/stoichiometric oxidants and require the multi-step synthesis of starting materials. Therefore, a transition-metal-catalyzed method for the synthesis of isatoic anhydrides from readily available starting materials in a redox-neutral and step-economical way is highly desirable.

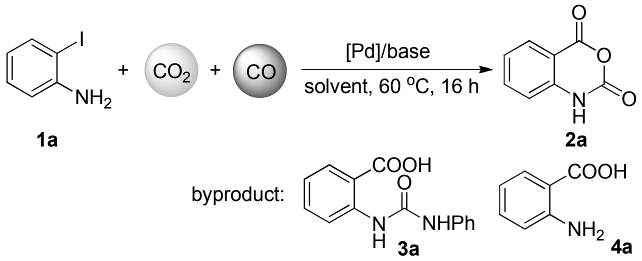


Scheme 1. Approaches to synthesize isatoic anhydrides.

Regarding the syntheses of anhydride compounds using carbon dioxide (CO_2)[6,7] or carbon monoxide (CO)[8] as a sole C1 building block, several reactions have been documented. Maleic anhydrides can be accessed by nickel-catalyzed double carboxylation of internal alkynes with CO_2 using excess metal powder as reductive agents,[9] or palladium-catalyzed double carbonylation of terminal alkynes using CO with external oxidants.[10] In addition, double carbonylation of epoxides with CO using an Al-Co bimetallic catalyst afforded succinic anhydrides.[11] Recently, Guan group reported carbonylation of *N*-alkyl anilines or anthranilic acids using CO to yield isatoic anhydrides with stoichiometric amounts of copper(II) oxidants.[12] CO_2 is an abundant, renewable C1 feedstock and can serve as an alternative for the combined use of CO and oxidants.[13] Inspired by the precedented formation of anhydride moiety via reductive elimination of an acyl metal carboxylate complex,[14,15] we proposed that anhydride compounds could be constructed more economically by the combined use of CO_2 and CO as building blocks. Given that *o*-haloanilines were used as substrates for CO insertion and CO_2 capture to form aryl acyl and carbamate[16] intermediates respectively, isatoic anhydrides could be accessed via a redox-neutral transition-metal catalyzed reaction (Scheme 1, **c**). Herein, we describe a highly selective and efficient synthesis of isatoic anhydrides by palladium-catalyzed cyclization of easily available *o*-iodoanilines, CO_2 and CO under mild conditions.

The initial reaction of *o*-iodoaniline (**1a**) under 1 MPa of CO_2 and 0.5 MPa of CO with 5 mol% $Pd(PPh_3)_4$ as catalyst and 2 equivalent Cs_2CO_3 as base in THF at 60 °C furnished 86% yield of the desired isatoic anhydride **2a**, along with 6% yield of urea **3a** and 1% yield of anthranilic acid **4a** (Table 1, entry 1, and see Supporting Information). Variation of the palladium source and ligand led to decreased yields of **2a** and/or increased yields of byproducts (entries 2-5, see SI). The reaction at an elevated temperature (80 °C) gave lower selectivity for the anhydride product while a significantly lower conversion of **1a** was observed when the temperature was decreased to 40 °C (see SI).

Table 1. Optimization of the reaction conditions[a]

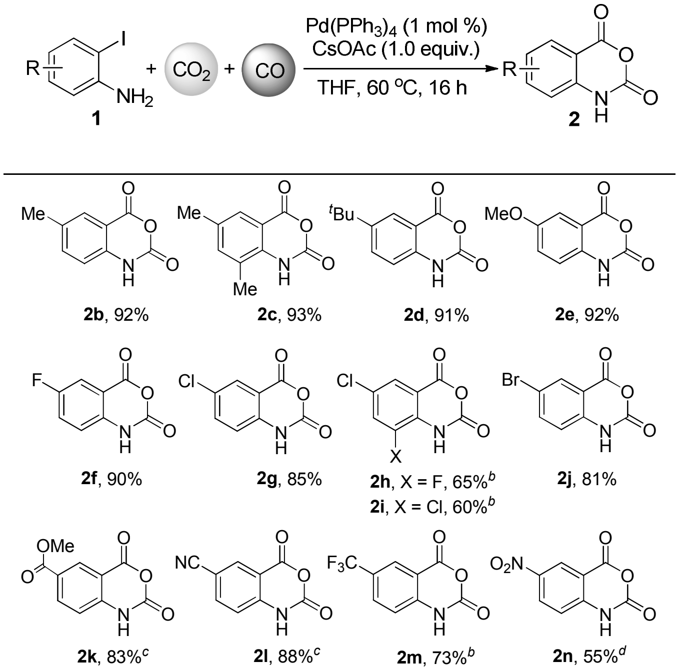


Entry	Catalyst (mol%)	Base (equiv.)	Yield[b] (%)
1	$Pd(PPh_3)_4$ (5)	Cs_2CO_3 (2.0)	86
2	$Pd(CH_3CN)_2Cl_2/PPh_3$ (5/20)	Cs_2CO_3 (2.0)	69
3	$Pd(CH_3CN)_2Cl_2$/dppf (5/10)	Cs_2CO_3 (2.0)	82
4	$Pd(CH_3CN)_2Cl_2$/DPEPhos (5/10)	Cs_2CO_3 (2.0)	86
5	$Pd(CH_3CN)_2Cl_2$/S-Phos (5/10)	Cs_2CO_3 (2.0)	77
6	$Pd(PPh_3)_4$ (5)	CsOAc (2.0)	96
7	$Pd(PPh_3)_4$ (5)	KOAc (2.0)	94
8	$Pd(PPh_3)_4$ (5)	NaOAc (2.0)	46
9	$Pd(PPh_3)_4$ (5)	NEt_3 (2.0)	92
10	$Pd(PPh_3)_4$ (1)	CsOAc (2.0)	99
11	$Pd(PPh_3)_4$ (0.1)	CsOAc (2.0)	99(90)
12	$Pd(PPh_3)_4$ (1)	**CsOAc (1.0)**	**99(90)**
13	$Pd(PPh_3)_4$ (1)	CsOAc (0.5)	55
14	$Pd(PPh_3)_4$ (1)	-	-
15	-	CsOAc (1.0)	-
16[c]	$Pd(PPh_3)_4$	CsOAc (1.0)	-
17[d]	$Pd(PPh_3)_4$	CsOAc (1.0)	86

[a] Reaction conditions: **1a** (0.4 mmol), CO_2 (1.0 MPa), CO (0.5 MPa), THF (4 mL), 60 °C, 16 h. [b] Yields of **2a** were determined by NMR using 1,1,2,2-tetrachloroethane as internal standard. Yields of **2a** in parentheses are isolated yields. [c] In the absence of CO_2 or CO. [d] Using CO_2 and CO balloons.

Gratifyingly, it is found that the switching base to CsOAc, CsF, KOAc or NEt_3 gave rise to enhanced yields and selectivity for **2a** (entries 6-9). CH_3CN, 1,4-dioxane, DME, and DMF also proved to be suitable solvent for this reaction, while toluene and DMSO gave the inferior results (see SI). Notably, a lower catalyst loading (1 mol%) improved the yield of the anhydride product (entry 10). The reaction with 0.1 mol% $Pd(PPh_3)_4$ still proceeded smoothly (entry 11). The use of 1 equivalent CsOAc gave excellent isolated yield of **2a** (entry 12). Only 55% yield of **2a** was obtained when the reaction was conducted with 0.5 equivalent CsOAc (entry 13). No product was observed in the absence of a base (entry 14), implicating its necessity. The Reaction without the catalyst gave no product, which conformed the catalytic role of the palladium complex (entry 15). It is noteworthy that no anhydride product was detected when the reactions were conducted in the absence of either CO_2 or CO (entry 16), indicating that both C1 building blocks were indispensable. The excellent selectivity of the reaction could be maintained with CO_2 and CO balloons, though a decreased yield (86%) of **2a** was obtained (entry 17).

Table 2. Substrate scope for iodoanilines[a]



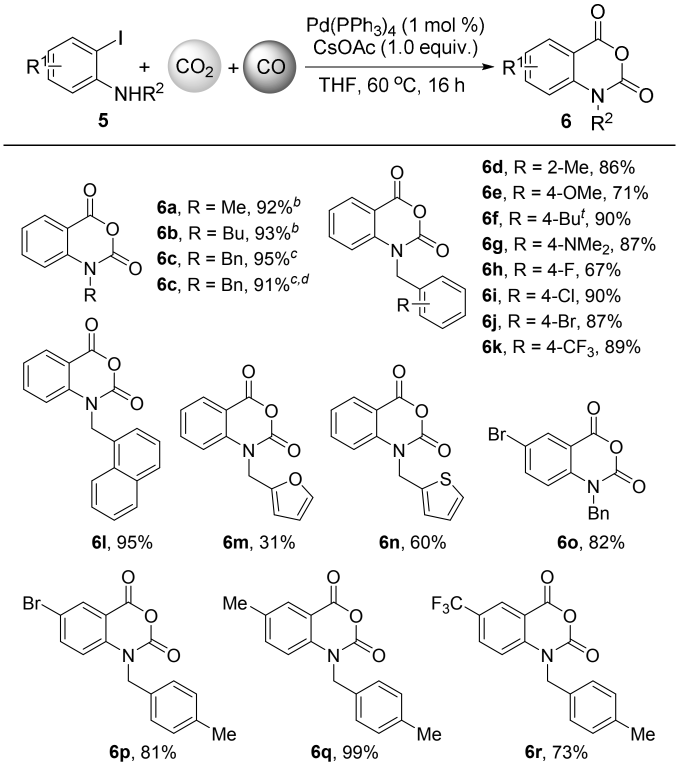
[a] Reaction conditions: **1** (0.2-0.4 mmol), $Pd(PPh_3)_4$ (1 mol%), CsOAc (1.0 equivalent), CO_2 (1.0 MPa), CO (0.5 MPa), THF (0.1 M), 60 °C, 16 h. Isolated yiled. [b] With 2.5 mol% $Pd(PPh_3)_4$. [c] 36 h. [d] With 5.0 mol% $Pd(PPh_3)_4$.

With the optimized reaction conditions in hand, the cyclization reactions of various *o*-iodoanilines (**1**) with CO_2 and CO were investigated with 1 mol% $Pd(PPh_3)_4$ and 1 equivalent CsOAc in THF at 60 °C (Table 2). Alkyl-, methoxy-, fluoro-, chloro-, and bromo-substituted *o*-iodoanilines participated in the reaction to afford the corresponding isatoic anhydrides (**2b-g**, **2j**) in good to excellent yields. Substrates bearing electron-withdrawing group such as **1k** and **1l** furnished the desired products with a prolonged reaction time in 83% and 88% yield respectively. Trifluoromethyl- and nitro-contained *o*-iodoanilines also reacted to provide the corresponding products in moderate to good yields using 2.5-5.0 mol% catalyst. Unfortunately, *o*-bromoaniline was inert under these reaction conditions.

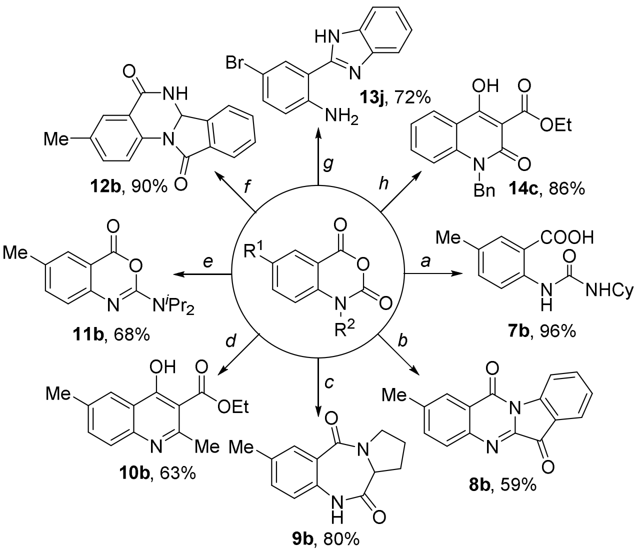
The substrate scope with regard to *N*-substituted *o*-iodoanilines (**5**) was evaluated (Table 3). The use of *N*-methyl, *N*-butyl and *N*-benzyl iodoanilines (**5a-c**) required an enhanced catalyst loading to achieve full conversion. A wide range of functional groups including electron-donating alkoxy and dimethyl amino and electron-withdrawing trifluoromethyl group, on *N*-benzyl *o*-iodoanilines are tolerated. Electronic modulations of the

N-benzyl substituents had no substantial effect on the yields of the cyclization reaction. Substrates containing furan and thiophene gave the desired product **6m** and **6n**. Single-crystal X-ray analyses of **6c**, **6g**, and **6l** confirmed the structural assignment of these products (See SI).[17] This catalytic approach is scalable, as highlighted by the synthesis of **6c** (91% yield) with 2 mol % palladium catalyst on 1.5 mmol scale. Since *N*-substituted *o*-iodoanilines **5** could be readily prepared from *o*-iodoanilines **1**, this reaction provided a more convenient way to access *N*-substituted isatoic anhydrides **6** than post-modification of isatoic anhydrides **2**. Taking advantage of the highly reactive anhydride group, the isatoic anhydride obtained could be easily converted into urea-substituted benzoic acid[1a] and many biologically important heterocyclic compounds[1,18] (Scheme 2).

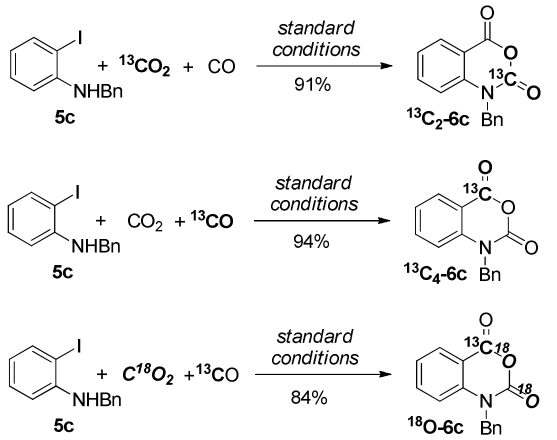
Table 3. Substrate scope for *N*-substituted iodoanilines [a]



[a] Reaction conditions: **5** (0.2-0.4 mmol), $Pd(PPh_3)_4$ (1 mol%), CsOAc (1.0 equivalent), CO_2 (1.0 MPa), CO (0.5 MPa), THF (0.1 M), 60 °C, 16 h. Isolated yiled. [b] With 5 mol% $Pd(PPh_3)_4$. [c] With 2 mol% $Pd(PPh_3)_4$. [d] 1.5 mmol **5c** was used.

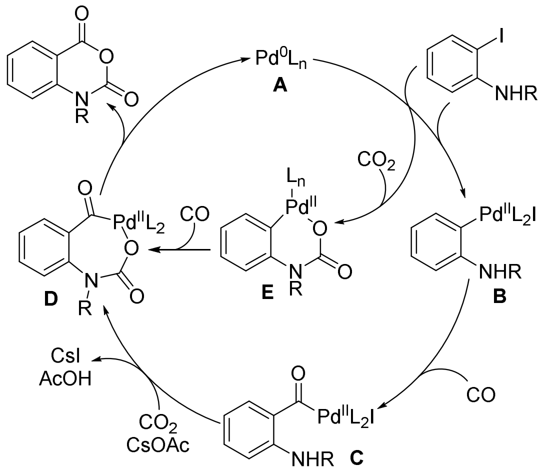


Scheme 2. Synthesis of urea-substituted benzoic acid and other heterocycles using obtained anhydrides products. [a] **2b**, $CyNH_2$, H_2O, rt, 15 min. [b] **2b**, isatin, NEt_3, toluene, reflux, 4 h. [c] **2b**, proline, DMSO, reflux, 3 h. [d] **2b**, ethyl acetoacetate, NaH, DMAc, 120 °C, 0.5 h. [e] **2b**, $^iPr_2NH$, rt, 48 h. [f] **2b**, 2-carboxybenzaldehyde, NH_4OAc, AcOH, 110 °C, 1 h. [g] **2j**, o-phenyldiamine, AcOH, 100 °C, 3 h. [h] **6c**, diethyl malonate, NaH, DMF, reflux, 5 h.



Scheme 3. Cyclization reaction using labeled CO_2 and CO.

To verify whether the anhydride group in the product originated from CO_2 and CO, the cyclization reactions using isotopically-labeled reactants were carried out (Scheme 3). The ^{13}C NMR and mass spectra of the obtained product indicated that labeled CO_2 or CO were incorporated into the anhydride molecules (see SI). The ^1H-^{13}C COSY spectra of **$^{13}C_2$-6c** and **$^{13}C_4$-6c**showed that the carbonyl group in the carbamate moiety came from CO_2, while the carbonyl group linked to the aryl ring derived from CO (see SI).



Scheme 4. Possible mechanism.

Based on the labeling experiments in Scheme 3, a possible mechanism was proposed (Scheme 4). The oxidative addition of Pd^0 catalyst **A** into iodoaniline afforded Pd^{II} species **B**. CO insertion gave acyl palladium intermediate **C** which underwent reaction with CO_2 to form seven-membered acyl palladium carbamate **D**. Subsequent reductive elimination provided isatoic anhydride product and regenerated the Pd^0 catalyst. Another pathway first involved the formation of six-membered palladium carbamate **E** from Pd^0 catalyst **A**, *o*-iodoaniline, and CO_2. Subsequent CO insertion gave intermediate **D**. Although intermediate **B**, but not **E**, was detected by MS in the reaction system of *o*-iodoaniline, stoichiometric $Pd(PPh_3)_4$, CsOAc, and CO_2 in the absence of CO, the possibility of latter route could not be excluded at this stage.

In summary, we have developed a highly selective palladium-catalyzed cyclization reaction for the preparation of a broad range of substituted isatoic anhydrides from *o*-iodoaniline, CO_2, and CO. The reaction takes place under mild conditions and can be carried out even at atmospheric pressure. With the combined use of CO_2 and CO as C1 feedstocks, this reaction is redox-neutral. Further investigations of the mechanism and the combined use of CO_2 and CO as an anhydride source for other transition-metal-catalyzed reactions are in progress in our laboratory.

ASSOCIATED CONTENT

The Supporting Information is available free of charge via the Internet at http://pubs.acs.org.

X-ray crystallographic data for compound **6c**, **6g**, and **6l** (CIF)
Experimental details, optimization of reaction conditions, characterization of products, copies of ^{1}H and ^{13}C NMR spectra of all products.

AUTHOR INFORMATION

Corresponding Author

* E-mail: zhangwz@dlut.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was supported by the Natural Science Foundation of Liaoning Province (20170540156), and the Fundamental Research Funds for the Central Universities (DUT17ZD210). X.-B Lu acknowledges the Program for Changjiang Scholars and Innovative Research Team in University (IRT13008, IRT_17R14). We thank John C. K. Chu for the proofreading of this manuscript.

REFERENCES

(1) (a) Tedesco, R.; Shaw, A. N.; Bambal, R.; Chai, D.; Concha, N. O.; Darcy, M. G.; Dhanak, D.; Fitch, D. M.; Gates, A.; Gerhardt, W. G.; Halegoua, D. L.; Han, C.; Hofmann, G. A.; Johnston, V. K.; Kaura, A. C.; Liu, N.; Keenan, R. M.; Lin-Goerke, J.; Sarisky, R. T.; Wiggall, K. J.; Zimmerman, M. N.; Duffy, K. J. *J. Med. Chem.* **2006**, *49*, 971–983. (b) Hacker, H.-G.; Leyers, S.; Wiendlocha, J.; Gutschow, M.; Wiese, M. *J. Med. Chem.* **2009**, *52*, 4586–4595. (c) Tseng, M.-C.; Chu, Y.-W.; Tsai, H.-P.; Lin, C.-M.; Hwang, J.; Chu, Y.-H. *Org. Lett.* **2011**, *13*, 920–923. (d) Araujo, A. C.; Rauter, A. P.; Nicotra, F.; Airoldi, C.; Costa, B.; Cipolla, L. *J. Med. Chem.* **2011**, *54*, 1266–1275. (e) Goncalves, V.; Brannigan, J. A.; Whalley, D.; Ansell, K. H.; Saxty, B.; Holder, A. A.; Wilkinson, A. J.; Tate, E. W.; Leatherbarrow, R. J. *J. Med. Chem.* **2012**, *55*, 3578–3582. (f) Clark, R. L.; Clements, C. J.; Barrett, M. P.; Mackay, S. P.; Rathnam, R. P.; Owusu-Dapaah, G.; Spencer, J.; Huggan, J. K. *Bioorg. Med. Chem.* **2012**, *20*, 6019–6033. (g) Yang, S.; Li, X.; Hu, F.; Li, Y.; Yang, Y.; Yan, J.; Kuang, C.; Yang, Q. *J. Med. Chem.* **2013**, *56*, 8321–8331. (h) Wang, G.; Chen, X.; Deng, Y.; Li, Z.; Xu, X. *J. Agric. Food Chem.* **2015**, *63*, 6883–6889. (i) Polishchuk, P. G.; Samoylenko, G. V.; Khristova, T. M.; Krysko, O. L.; Kabanova, T. A.; Kabanov, V. M.; Kornylov, A. Y.; Klimchuk, O.; Langer, T.; Andronati, S. A.; Kuzmin, V. E.; Krysko, A. A.; Varnek, A. *J. Med. Chem.* **2015**, *58*, 7681–7694. (j) Yang, Y.; Yu, Y.; Li, X.; Li, J.; Wu, Y.; Yu, J.; Ge, J.; Huang, Z.; Jiang, L.; Rao, Y.; Yang, M. *J. Med. Chem.* **2017**, **60**, 1994–2005.

(2) (a) D'Souza, A. M.; Spiccia, N.; Basutto, J.; Jokisz, P.; Wong, L. S.-M.; Meyer, A. G.; Holmes, A. B.; White, J. M.; Ryan, J. H. *Org. Lett.* **2011**, *13*, 486–489. (b) Lu, W.; Chen, J.; Liu, M.; Ding, J.; Gao, W.; Wu, H. *Org. Lett.* **2011**, *13*, 6114–6117. (c) Beutner, G. L.; Hsiao, Y.; Razler, T.; Simmons, E. M.; Wertjes, W. *Org. Lett.* **2017**, *19*, 1052–1055.

(3) (a) Weeks, K. M.; Mauger, D. M. *Acc. Chem. Res.* **2011**, *44*, 1280–1291. (b) Steen, K.-A.; Rice, G. M.; Weeks, K. M. *J. Am. Chem. Soc.* **2012**, *134*, 13160–13163. (c) Spitale, R. C.; Crisalli, P.; Flynn, R. A.; Torre, E. A.; Kool, E. T.; Chang, H. Y. *Nat. Chem. Biol.* **2013**, *9*, 18–20. (d) Ursuegui, S.; Yougnia, R.; Moutin, S.; Burr, A.; Fossey, C.; Cailly, T.; Laayoun, A.; Laurent, A.; Fabis, F. *Org. Biomol. Chem.* **2015**, *13*, 3625–3632.

(4) (a) Lygin, A. V.; de Meijere, A. *J. Org. Chem.* **2009**, *74*, 4554–4559. (b) Huang, G.; Roos, D.; Stadtmuller, P.; Decker, M. *Tetrahedron Lett.* **2014**, 55, 3607–3609. (c) Jamali, H.; Khan, H. A.; Stringer, J. R.; Chowdhury, S.; Ellman, J. A. *J. Am. Chem. Soc.* **2015**, *137*, 3616–3621. (d) Kim, H.; Park, G.; Park, J.; Chang, S. *ACS Catal.* **2016**, *6*, 5922–5929. (e) Tang, Q.; Zhai, X.; Tu, Y.; Wang, P.; Wang, L.; Wu, C.; Wang, W.; Xie, H.; Gong, P.; Zheng, P. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 1794–1798. (f) Gibbs, A. C.; Abad, M. C.; Zhang, X.; Tounge, B. A.; Lewandowski, F. A.; Struble, G. T.; Sun, W.; Sui, Z.; Kuo, L. C. *J. Med. Chem.* **2010**, *53*, 7979–7991. (g) Lee, A. H. F.; Kool, E. T. *J. Am. Chem. Soc.* **2006**, *128*, 9219–9230. (h) Verma, C.; Sharma, S.; Pathak, A. *Tetrahedron Lett.* **2013**, *54*, 6897–6899. (i) Callingham, M.; Blum, F.; Pave, G. *Org. Lett.* **2015**, *17*, 4930–4932.

(5) (a) Reissenweber, G.; Mangold, D. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 222–223. (b) Deligeorgiev, T.; Vasilev, A.; Vaquero, J. J.; Alvarez-Builla, J.; *Ultrason. Sonochem.* **2007**, *14*, 497–501. (c)

Nelson, A. C.; Kalinowski, E. S.; Czerniecki, N. J.; Jacobson, T. L.; Grundt, P. *Org. Biomol. Chem.* **2013**, *11*, 7455–7457. (d) Yu, L.; Ye, J.; Zhang, X.; Ding, Y.; Xu, Q. *Catal. Sci. Technol.* **2015**, *5*, 4830–4838.

(6) For the recent reviews on the transformation of CO_2, see: (a) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365–2387. (b) Riduan, S. N.; Zhang, Y. *Dalton Trans.* **2010**, *39*, 3347–3357. (c) Huang, K.; Sun, C.-L.; Shi, Z.-J. *Chem. Soc. Rev.* **2011**, *40*, 2435–2452. (d) Peters, M.; Kohler, B.; Kuckshinrichs, W.; Leitner, W.; Markewitz, P.; Muller, T. E. *ChemSusChem* **2011**, *4*, 1216–1240. (e) Cokoja, M.; Bruckmeier, C.; Rieger, B.; Herrmann, W. A.; Kuhn, F. E. *Angew. Chem. Int. Ed.* **2011**, *50*, 8510–8537. (f) Zhang, W.-Z.; Lu, X.-B. *Chin. J. Catal.* **2012**, *33*, 745–756. (g) Tsuji, Y.; Fujihara, T. *Chem. Commun.* **2012**, *48*, 9956–9964. (h) Zhang, L.; Hou, Z. *Chem. Sci.* **2013**, *4*, 3395–3403. (i) Aresta, M.; Dibenedetto, A.; Angelini, A. *Chem. Rev.* **2014**, *114*, 1709–1742. (j) Yu, B.; He, L.-N. *ChemSusChem* **2015**, *8*, 52–62. (k) Fiorani, G.; Guo, W.; Kleij, A. W. *Green Chem.* **2015**, *17*, 1375–1389. (l) Liu, Q.; Wu, L.; Jackstell, R.; Beller, M. *Nat. Commun.* **2015**, *6*, 5933–5948. (m) Borjesson, M.; Moragas, T.; Gallego, D.; Martin, R. *ACS Catal.* **2016**, *6*, 6739–6749. (n) Zhang, W.-Z.; Zhang, N.; Lu, X.-B. *Chin. J. Org. Chem.* **2017**, *37*, 1309–1321.

(7) For the synthesis of anhydride using CO_2 under electrochemical conditions, see: (a) Yuan, G.-Q.; Jiang, H.-F.; Lin, C. *Tetrahedron* **2008**, *64*, 5866–5872. (b) Li, C.; Yuan, G.-Q.; Jiang, H.-F. *Chin. J. Chem.* **2010**, *28*, 1685–1689.

(8) For the recent reviews on the carbonylation reaction using CO, see: (a) Brennfuhrer, A.; Neumann, H.; Beller, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 4114–4133. (b) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Soc. Rev.* **2011**, *40*, 4986–5009. (c) Liu, Q.; Zhang, H.; Lei, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 10788–10799. (d) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Rev.* **2013**, *113*, 1–35. (e) Sumino, S.; Fusano, A.; Fukuyama, T.; Ryu, I. *Acc. Chem. Res.* **2014**, *47*, 1563–1574. (f) Wu, X.-F.; Fang, X.; Wu, L.; Jackstell, R.; Neumann, H.; Beller, M. *Acc. Chem. Res.* **2014**, *47*,1041–1053.

(9) Fujihara, T.; Horimoto, Y.; Mizoe, T.; Sayyed, F. B.; Tani, Y.; Terao, J.; Sakaki, S.; Tsuji, Y. *Org. Lett.* **2014**, *16*, 4960–4963.

(10) (a) Zargarian, D.; Alper, H. *Organometallics* **1991**, *10*, 2914–2921. (b) Sakurai, Y.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **1999**, *40*, 1701–1704. (c) Gabriele, B.; Salerno, G.; Costa, M.; Chiusoli, G. P. *Chem. Commun.* **1999**, 1381–1382. (d) Li, J.; Li, G.; Jiang, H.; Chen, M. *Tetrahedron Lett.* **2001**, *42*, 6923–6924. (e) Gabriele, B.; Veltri, L.; Salerno, G.; Costa, M.; Chiusoli, G. P. *Eur. J. Org. Chem.* **2003**, 1722–1728.

(11) Rowley, J. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 4948–4960.

(12) (a) Guan, Z.-H.; Chen, M.; Ren, Z.-H. *J. Am. Chem. Soc.* **2012**, *134*, 17490–17493. (b) Gao, S.; Chen, M.; Zhao, M.-N.; Du, W.; Ren, Z.-H.; Wang; Y.-Y.; Guan, Z.-H. *J. Org. Chem.* **2014**, *79*, 4196–4200.

(13) (a) Sasano, K.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2013**, *135*, 10954–10957. (b) Zhang, Z.; Liao, L.-L.; Yan, S.-S.; Wang, L.; He, Y.-Q.; Ye, J.-H.; Li, J.; Zhi, Y.-G.; Yu, D.-G. *Angew. Chem. Int. Ed.* **2016**, *55*, 7068–7072. (c) Zhang, W.-Z.; Yang, M.-W.; Lu, X.-B. *Green Chem.* **2016**, *18*, 4181–4184. (d) Wang, S.; Shao, P.; Du, G.; Xi, C. *J. Org. Chem.* **2016**, *81*, 6672–6676. (e) Sun, S.; Hu, W.-M.; Gu, N.; Cheng, J. *Chem. Eur. J.* **2016**, *22*, 18729–18732. (f) Zhang, Z.; Ju, T.; Miao, M.; Han, J.-L.; Zhang, Y.-H.; Zhu, X.-Y.; Ye, J.-H.; Yu, D.-G.; Zhi, Y.-G. *Org. Lett.* **2017**, *19*, 396–399. (g) Zhang, Z.; Ju, T.; Ye, J.-H.; Yu, D.-G. *Synlett* **2017**, *28*, 741–750.

(14) (a) Burkhart, G.; Hoberg, H. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 76. (b) Carmona, E.; Gutierrez-Puebla, E.; Marin, J. M.; Monge, A.; Paneque, M.; Poveda, M. L.; Ruiz, C. *J. Am. Chem. Soc.* **1989**, *111*, 2883–2891. (c) Greenburg, Z. R.; Jin, D.; Williard, P. G.; Bernskoetter, W. H. *Dalton Trans.* **2014**, *43*, 15990–15996.

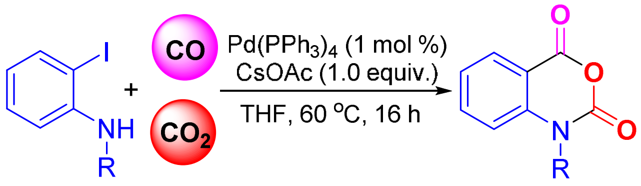
(15) For the combination use of CO_2 and isonitrile, see: (a) Zhao, L.-L.; Wang, S.-Y.; Xu, X.-P.; Ji, S.-J. *Chem. Commun.* **2013**, *49*, 2569–2571. (b) Kaicharla, T.; Thangaraj, M.; Biju, A. T. *Org. Lett.* **2014**, *16*, 1728–1731. (c) Mampuys, P.; Neumann, H.; Sergeyev, S.; Orru, R. V. A.; Jiao, H.; Spannenberg, A.; Maes, B. U. W.; Beller, M. *ACS Catal.* **2017**, *7*, 5549–5556. (d) Xu, P.; Wang, F.; Wei, T.-Q.; Yin, L.; Wang, S.-Y.; Ji, S.-J. *Org. Lett.* **2017**, *19*, 4484–4487.

(16) DellAmico, D. B.; Calderazzo, F.; Labella, L.; Marchetti, F.; Pampaloni, G. *Chem. Rev.* **2003**, *103*, 3857–3898.

(17) CCDC 1549604 (**6c**), 1549606 (**6g**), 1549605 (**6l**).

(18) (a) Reddy, G. R.; Reddy, T. R.; Chary, R. G.; Joseph, S. C.; Mukherjee, S.; Pal, M. *Tetrahedron Lett.* **2013**, *54*, 6744–6746. (b) Pudlo, M.; Luzet, V.; Ismaili, L.; Tomassoli, I.; Lutzeler, A.; Refouvelet, B. *Bioorg. Med. Chem.* **2014**, *22*, 2496–2507. (c) Krantz, A.; Spencer, R. W.; Tam, T. F.; Liak, T. J.; Copp, L. J.; Thomas, E. M.; Rafferty, S. P. *J. Med. Chem.* **1990**, *33*, 464–479.

SYNOPSIS TOC



32 examples
up to 99% yields