

CrossMark
click for updatesCite this: *Chem. Sci.*, 2017, 8, 2431Received 14th November 2016
Accepted 19th December 2016

DOI: 10.1039/c6sc05026c

www.rsc.org/chemicalscience

Cobalt catalyzed carbonylation of unactivated C(sp³)-H bonds†

Nagaraju Barsu, Shyam Kumar Bolli and Basker Sundararaju*

A general efficient regioselective cobalt catalyzed carbonylation of unactivated C(sp³)-H bonds of aliphatic amides was demonstrated using atmospheric (1–2 atm) carbon monoxide as a C1 source. This straightforward approach provides access to α -spiral succinimide regioselectively in a good yield. Cobalt catalyzed sp³ C-H bond carbonylation is reported for the first time including the functionalization of (β)-C-H bonds of α -1°, 2°, 3° carbons and even internal (β)-C-H bonds. Our initial mechanistic investigation reveals that the C-H activation step is irreversible and will possibly be the rate determining step.

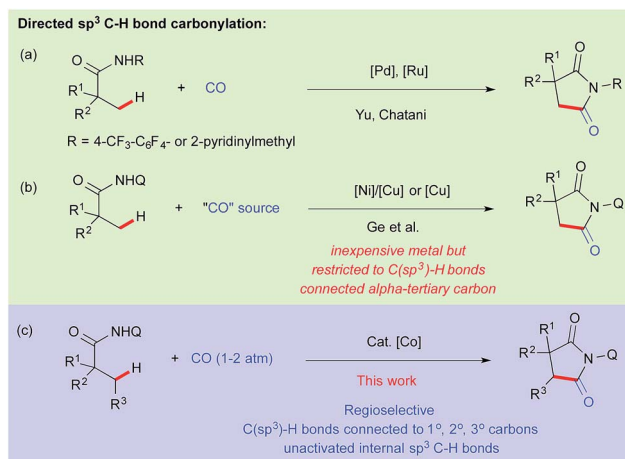
Introduction

Catalytic carbonylation is one of the most straightforward processes for the production of carbonyl compounds both in academia and industry.¹ Insertion of CO into carbon-hydrogen bonds has become even more interesting provided that the catalyst has the ability to activate both inert C-H bonds and to bind π -acidic carbon monoxide.² In this regard, Shunsuke Murahashi reported the first effective catalytic C-H carbonylation of benzaldimine in 1955 using a low valent cobalt(0) complex.³ Since then, several reports have been documented for catalytic C(sp²)-H bond carbonylation.⁴ However the corresponding extension to carbonylation of C(sp³)-H bonds is rare and only a handful of examples have been reported in the literature.⁵ After the pioneering work of Tanaka *et al.* for photocatalytic carbonylation of alkanes,⁶ Chatani reported the directing group assisted C-H carbonylation of α -C(sp³)-H bonds adjacent to nitrogen.⁷ In 2010–11, Yu and Chatani independently reported the site-selective C(sp³)-H carbonylation of aliphatic amide using Pd and Ru based catalysts, while the former used oxidative conditions, the latter proceeded through a metal-hydride pathway (Scheme 1a).^{8–10} We assumed that it would be more rational to choose a metal abundantly present in nature compared to precious metals in terms of cost effectiveness and the unexploited inherent properties exhibited by them.¹¹ Utilization of 8-aminoquinoline as a bidentate auxiliary for C-H bond functionalization was first reported by Daugulis,¹² and later developed by Chatani¹³ and others¹⁴ for several profitable applications using first row late transition metal precursors.

Fine Chemical Laboratory, Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur, Uttar Pradesh, India. E-mail: basker@iitk.ac.in

† Electronic supplementary information (ESI) available. CCDC 1507203 (2t) & 1507204 (2a). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6sc05026c

Using this approach, Ge *et al.* reported recently the carbonylation of unactivated C(sp³)-H bonds with Ni-Cu/Cu as a catalyst using DMF and nitromethane as a carbonyl sources.¹⁵ But the presented nickel-copper/copper catalyzed carbonylation was limited to β -C(sp³)-H bonds connected to α -tertiary carbon (Scheme 1b). On the other hand, cobalt seems to be a very promising alternative metal catalyst for various C(sp²)-H bond functionalizations.^{11a,b,16} Very recently Ge and Zhang independently reported cobalt catalyzed intramolecular cyclization through activation of directed C(sp³)-H bonds.¹⁷ Daugulis reported lately, cobalt catalyzed *o*-C(sp²)-H bond carbonylation of benzamides at room temperature.¹⁶ⁿ We have previously demonstrated the activation of C(sp³)-H bonds using Cp*Co(III) for C-H alkenation with alkynes and C-H amidation with oxazolone.¹⁸ Inspired by these results and based on our continuous efforts on the development of cobalt catalyzed C-H bond functionalization,¹⁹ we report herein the first regio- and site-

Scheme 1 Carbonylation of unactivated C(sp³)-H bonds.

selective cobalt catalyzed carbonylation of unactivated C(sp³)-H bonds including terminal and internal C-H bond connected α -1°, 2° and 3° carbons (Scheme 1c).

Results and discussion

We began our investigation using aliphatic amide **1a**, 2 atm CO gas as a C1 source with a catalytic amount of simple Co(OAc)₂, metal carboxylate and silver carbonate as an oxidant at 150 °C for 36 h in chlorobenzene (0.5 mL). The optimization results are summarized in Table 1. Initial screening of different metal carboxylates revealed that a good yield of **2a** was obtained with sodium benzoate (50 mol%) as an additive, which is also an optimal reaction parameter for intramolecular β -sp³ C-H bond amidation^{17a} (Table 1, entry 1–4). Lowering the reaction concentration did not provide any further improvement (entry 5). A small amount of sodium benzoate turned out to be crucial for high product formation with cobalt(II) (entry 6 and 7).

There was no significant change in yield when the reaction time was reduced to 24 h or by increasing the catalyst loading to 20 mol% (entries 8 and 9). To our delight, a small increment in the silver carbonate gave excellent product formation after 24 h (entry 10). Next, we examined various cobalt sources from different oxidations states. It was revealed that Co(II) and Co(III) gave excellent yields whereas Co(0) and Co(II)Br₂ gave moderate

yields (entries 11–14). After a brief solvent screening,²⁰ we found out that α,α,α -trifluorotoluene (TFT) was the best solvent, which provided 95% of the succinimide **2a** under our optimized reaction parameters (entry 15). A well-defined, isolated cobalt-pivalate dimer²¹ was used as a catalyst without any additive and this resulted in a 55% yield (entry 16). We further confirmed that the direct use of the Co(III) precursor in the absence of the sodium benzoate provides **2a** in 92% yield and the structure of **2a** was confirmed by X-ray crystallography (entry 17).²²

Prior to the scope of the reaction, we examined the scalability of the reaction. A gram scale reaction was performed with **1a** using atmospheric CO gas and provides succinimide **2a** in 71% yield after 36 h (Scheme 2) and silver carbonate was regenerated from the residue in 69% (2.5 g) yield using the known literature procedure.^{16e,23} The recycled silver carbonate was used for C-H carbonylation and resulted in 83% of **2a** under standard conditions (Scheme 2).

With the optimized conditions in hand, we next investigated the scope of the aliphatic amides and the results are depicted in Scheme 3. Architecturally interesting spiral succinimides possessing a 4-, 5-, 6-membered ring on the backbone were achieved in good yields (**2b–d**). Replacing one of the methyl groups from **1a** with a benzyl, 4-OMe-benzyl, cyclopentyl, isopropyl or alkyl chain at the α -tertiary center gave the desired succinimides in high yields (**2e–j**). Phenyl, ester, and -Br substituents on the backbone were tolerated (**2k–m**). Next, the reactivity difference between C(sp²)-H and C(sp³)-H bonds was investigated for cyclocarbonylation. It was found out that carbonylation of unactivated C(sp³)-H bonds was favoured over C(sp²)-H bonds (**2n–o**) and only **2o'** was obtained in 15% yield in addition to **2o** (50%). This may be due to the fact that the former proceeds *via* facile 5-membered cyclocobaltation while the latter proceeds through a 6-membered metalocycle. Furthermore, we explore the possibility of activating β -C(sp³)-H bonds next to an α -secondary and primary carbon center, which is much more challenging (this has not been explored before for carbonylation using first row transition metals) than a C-H bond next to an α -tertiary carbon. Gratifyingly, propanamide (**1p**) and α -methylpropanamide (**1q**) underwent cyclocarbonylation albeit in a moderate yield (**2p**, **2q**) but the mass of the product can be improved if we prolong the reaction to 36 h with a 20 mol% cobalt catalyst.

Systematic increase of bulkiness by incorporating a -Et and -*t*-Bu group did not significantly alter the isomeric ratio (**2r–s**). Furthermore, to our delight, an internal C(sp³)-H bond was carbonylated in the case of **1t** and **1u**, and it resulted in the formation of substituted and structurally strained succinimides (**2t** & **2u**) and X-ray crystallography further confirmed the structure of **2t**.²² The reactivity of **1u** was documented for the

Table 1 Optimization studies and control experiments^a

Entry	[Co]	MCO ₂ R (mol%)	Oxidant	Yield ^b
1	Co(OAc) ₂	NaOPiv (50)	Ag ₂ CO ₃	27
2	Co(OAc) ₂	Mn(OAc) ₃ (50)	Ag ₂ CO ₃	n.r.
3	Co(OAc) ₂	NaO ₂ CPh (50)	Ag ₂ CO ₃	67
4	Co(OAc) ₂	NaO ₂ CMes (50)	Ag ₂ CO ₃	49
5	Co(OAc) ₂	NaO ₂ CPh (50)	Ag ₂ CO ₃	53 ^c
6	Co(OAc) ₂	NaO ₂ CPh (100)	Ag ₂ CO ₃	43
7	Co(OAc) ₂	NaO ₂ CPh (20)	Ag ₂ CO ₃	76
8	Co(OAc) ₂	NaO ₂ CPh (20)	Ag ₂ CO ₃	70 ^d
9	Co(OAc) ₂	NaO ₂ CPh (20)	Ag ₂ CO ₃	79 ^{d,e}
10	Co(OAc) ₂	NaO ₂ CPh (20)	Ag ₂ CO ₃	87 ^{d,f}
11	Co(acac) ₂	NaO ₂ CPh (20)	Ag ₂ CO ₃	86 ^{d,f}
12	Co(acac) ₃	NaO ₂ CPh (20)	Ag ₂ CO ₃	87 ^{d,f}
13	Co ₂ (CO) ₈	NaO ₂ CPh (20)	Ag ₂ CO ₃	68 ^{d,f}
14	CoBr ₂	NaO ₂ CPh (20)	Ag ₂ CO ₃	61 ^d
15	Co(acac) ₂	NaO ₂ CPh (20)	Ag ₂ CO ₃	95 ^{d,g}
16	[Co(Piv) ₂] ₂	—	Ag ₂ CO ₃	55 ^{d,g}
17	Co(acac) ₃	—	Ag ₂ CO ₃	92 ^{d,g}

^a All reactions reagents were added under argon atmosphere unless otherwise stated using **1a**/[Co]/NaO₂CR/Ag₂CO₃ in 0.2/0.02/0.02–0.05/0.5 mmol using chlorobenzene (0.5 mL) as a solvent at room temperature and then pressurized with CO (2 atm) at 150 °C for 36 h. ^b Isolated yield. ^c 1 mL of PhCl was used. ^d Reaction performed for 24 h. ^e 20 mol% of [Co] was used. ^f 3 equiv. of Ag₂CO₃ was used. ^g TFT (0.5 mL) was used as a solvent.



Scheme 2 Gram scale synthesis of succinimide.





Scheme 5 Proposed mechanism.

intermediate **C**, which may either undergo reductive elimination to Co(I) and reoxidized by silver to active Co(III) species as depicted in path a.^{16a-g} Alternatively, intermediate **C** will undergo one electron oxidation to Co(IV), which will undergo reductive elimination to **2a** and regenerate Co(II) (path b). At the same time, one may also consider that intermediate **B** will undergo one electron oxidation to **C'** which then subsequently insert CO between Co-C and lead to **D** (path c), which further undergoes reductive elimination. Although the final solution cannot be given for the mechanism at this stage, control experiments suggest that path b or c may be favoured over path a.

To validate the synthetic utility of this method, we have performed a two ring opening reaction with **1a** to obtain 1,4-dicarbonyl compound **3** and 1,4-dicarboxylic acid **4** in good yields under the standard reaction conditions (Scheme 6).

Conclusions

We have developed a new protocol for cobalt catalyzed site-selective carbonylation of unactivated C(sp³)-H bonds under atmospheric CO pressure to access various succinimide derivatives that are active against seizures (anticonvulsant ethosuximide). Our initial mechanistic investigation reveals that the involvement of a one electron process operated in the catalytic cycle and the reaction may proceed through Co(IV) to Co(II) (Scheme 5, path b or c). Studies to further extend this new reactivity to develop new medicinal compounds and materials are



Scheme 6 Synthetic applications.

currently underway. Further understanding of the mechanism including the SET process, isolation of stoichiometric intermediates is presently on going in our laboratory.

Acknowledgements

Financial support provided by SERB (EMR2016/000136) to support this research work is gratefully acknowledged. NB thanks to CSIR for his fellowship.

Notes and references

- M. Beller, *Catalytic carbonylation reactions, topic in organometallic Chemistry*, Springer, 2006, pp. 1–283.
- S. T. Gadge, P. Gautam and B. M. Bhanage, *Chem. Rev.*, 2016, **16**, 835–856 and references therein.
- S. Murahashi, *J. Am. Chem. Soc.*, 1955, **77**, 6403–6404.
- Selected recent reviews see: (a) R.-Y. Zhu, M. E. Farmer, Y.-Q. Chen and J. Q. Yu, *Angew. Chem., Int. Ed.*, 2016, **55**, 10578–10599; (b) K. Gao and N. Yoshikai, *Acc. Chem. Res.*, 2014, **47**, 1208; (c) X.-F. Wu, H. Neumann and M. Beller, *ChemSusChem*, 2013, **6**, 229–241; (d) X.-F. Wu, H. Neumann and M. Beller, *Chem. Rev.*, 2013, **113**, 1–35; (e) D. A. Colby, R. G. Bergmann and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 624–655; (f) A. Brennfuhrer, H. Neumann and M. Beller, *ChemCatChem*, 2009, **1**, 28–41.
- (a) H. Li, B.-J. Li and Z.-J. Shi, *Catal. Sci. Technol.*, 2011, **1**, 191–206; (b) R. H. Crabtree, *J. Organomet. Chem.*, 2004, **689**, 4083–4091.
- T. Sakakura, T. Sodeyama, K. Sasaki, K. Wada and M. Tanaka, *J. Am. Chem. Soc.*, 1990, **112**, 7221–7229.
- N. Chatani, T. Asaumi, T. Ikeda, S. Yorimitsu, Y. Ishii, F. Kakiuchi and S. Murai, *J. Am. Chem. Soc.*, 2000, **122**, 12882–12883.
- E. J. Yoo, M. Wasa and J.-Q. Yu, *J. Am. Chem. Soc.*, 2010, **132**, 17378–17380.
- (a) N. Hasegawa, V. Charra, S. Inoue, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2011, **133**, 8070–8073; (b) N. Hasegawa, K. Shibata, V. Charra, S. Inoue, Y. Fukumoto and N. Chatani, *Tetrahedron*, 2013, **69**, 4466–4472.
- Selected other recent reports on Pd Catalyzed sp³ C-H bond carbonylation, see: (a) P.-L. Wang, Y. Li, Y. Wu, C. Li, Q. Lan and X.-S. Wang, *Org. Lett.*, 2015, **17**, 3698–3701; (b) C. Wang, L. Zhang, C. Chen, J. Han, Y. Yao and Y. Zhao, *Chem. Sci.*, 2015, **6**, 4610–4614; (c) A. McNally, B. Haffemayer, B. S. L. Collings and M. J. Gaunt, *Nature*, 2014, **510**, 129–133; (d) P. Xie, Y. Xie, B. Qian, H. Zhou, C. Xia and H. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 9902–9905; (e) S. S. Stahl, J. A. Labinger and J. E. Bercaw, *Angew. Chem., Int. Ed.*, 1998, **37**, 2180–2192; (f) M. Asadullah, T. Kitamura and Y. Fujiwara, *Chem. Lett.*, 1999, **28**, 449–450.
- Selected recent reviews on first row transition metal catalysed C-H bond functionalization see: (a) D. Wei, X. Zhu, J.-L. Niu and M.-P. Song, *ChemCatChem*, 2016, **8**, 1242–1263; (b) N. Moselage, J. Li and L. Ackermann, *ACS Catal.*, 2016, **6**, 498–525; (c) N. Yoshikai, *ChemCatChem*, 2015, **7**, 732–734; (d) T. Hyster, *Catal. Lett.*, 2015, **145**, 458–



- 467; (e) I. Bauer and H. J. Knölker, *Chem. Rev.*, 2015, **115**, 3170–3387; (f) S. Z. Tasker, E. A. Standley and T. F. Jamison, *Nature*, 2014, **509**, 299–309; (g) A. A. Kulkarni and O. Daugulis, *Synthesis*, 2009, 4087–4109.
- 12 V. G. Zaitsev, D. Shabashov and O. Daugulis, *J. Am. Chem. Soc.*, 2005, **127**, 13154–13155.
- 13 (a) Y. Aihara and N. Chatani, *J. Am. Chem. Soc.*, 2014, **136**, 898–901; (b) Y. Aihara, M. Tobisu, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2014, **136**, 15509–15512; (c) T. Kubo, Y. Aihara and N. Chatani, *Chem. Lett.*, 2015, **44**, 1365–1367.
- 14 Selected recent reviews on the use of 8-aminoquinoline as a directing group, see: (a) L. C. Misal Castro and N. Chatani, *Chem. Lett.*, 2015, **44**, 410–421; (b) G. Rouquet and N. Chatani, *Angew. Chem., Int. Ed.*, 2013, **52**, 11726–11743; (c) M. Corbet and F. Decampo, *Angew. Chem., Int. Ed.*, 2013, **52**, 9896–9898; see also (d) T. Matsubara, S. Asako, E. Iiies and E. Nakamura, *J. Am. Chem. Soc.*, 2014, **136**, 646–649.
- 15 (a) X. Wu, J. Miao, Y. Li, G. Li and H. Ge, *Chem. Sci.*, 2016, **7**, 5260–5264; (b) X. Wu, Y. Zhao and H. Ge, *J. Am. Chem. Soc.*, 2015, **137**, 4924–4927.
- 16 Selected references high valent in cobalt catalyzed C(sp²)-H bond functionalization see: (a) S. Prakash, K. Muralirajan and C.-H. Cheng, *Angew. Chem., Int. Ed.*, 2016, **55**, 1844–1848; (b) C. Du, P.-X. Li, X. Zhu, J.-F. Suo, J.-L. Niu and M.-P. Song, *Angew. Chem., Int. Ed.*, 2016, **55**, 13571–13575; (c) S. Maity, R. Kancherla, U. Dhawa, E. Hoque, S. Pimparkar and D. Maiti, *ACS Catal.*, 2016, **6**, 5493–5499; (d) A. Lerchen, S. Vásquez-Céspedes and F. Glorius, *Angew. Chem., Int. Ed.*, 2016, **55**, 3208–3211; (e) G. Tan, S. He, X. Huang, X. Liao, Y. Cheng and J. You, *Angew. Chem., Int. Ed.*, 2016, **55**, 10414–10418; (f) R. Manoharan, G. Sivakumar and M. Jeganmohan, *Chem. Commun.*, 2016, **52**, 10533–10536; (g) T. Yamaguchi, Y. Kommagalla, Y. Aihara and N. Chatani, *Chem. Commun.*, 2016, **52**, 10129–10132; (h) L. Kong, S. Yu, X. Zhou and X. Li, *Org. Lett.*, 2016, **18**, 588–591; (i) J. R. Hummel and J. A. Ellman, *J. Am. Chem. Soc.*, 2015, **137**, 490–498; (j) P. Patel and S. Chang, *ACS Catal.*, 2015, **5**, 853–858; (k) H. Wang, J. Koeller, W. Liu and L. Ackermann, *Chem.–Eur. J.*, 2015, **21**, 15525–15528; (l) Z.-Z. Zhang, L. Bin, C.-Y. Wang and B.-F. Shi, *Org. Lett.*, 2015, **17**, 4094–4097; (m) L. Grigorjeva and O. Daugulis, *Angew. Chem., Int. Ed.*, 2014, **53**, 10209–10212; (n) L. Grigorjeva and O. Daugulis, *Org. Lett.*, 2014, **16**, 4688–4690; (o) T. Yoshino, H. Ikemoto, S. Matsunaga and M. Kanai, *Angew. Chem., Int. Ed.*, 2013, **52**, 2207–2211.
- 17 (a) X. Wu, K. Yang, Y. Zhao, H. Sun, G. Li and H. Ge, *Nat. Commun.*, 2015, **6**, 6462–6471; (b) J. Zhang, H. Chen, C. Lin, Z. Liu, C. Wang and Y. Zhang, *J. Am. Chem. Soc.*, 2015, **137**, 12990–12996.
- 18 (a) M. Sen, B. Emayavaramban, N. Barsu, J. R. Premkumar and B. Sundararaju, *ACS Catal.*, 2016, **6**, 2792–2796; (b) N. Barsu, Md. A. Rahman, M. Sen and B. Sundararaju, *Chem.–Eur. J.*, 2016, **22**, 9135–9138.
- 19 (a) D. Kalsi, R. A. Laskar, N. Barsu, J. R. Premkumar and B. Sundararaju, *Org. Lett.*, 2016, **18**, 4198–4201; (b) N. Barsu, M. Sen and B. Sundararaju, *Chem. Commun.*, 2016, **52**, 1338–1341; (c) N. Barsu, D. Kalsi and B. Sundararaju, *Chem.–Eur. J.*, 2015, **21**, 9364–9368; (d) M. Sen, D. Kalsi and B. Sundararaju, *Chem.–Eur. J.*, 2015, **21**, 15529–15533; (e) D. Kalsi and B. Sundararaju, *Org. Lett.*, 2015, **17**, 6118–6121.
- 20 See ESI.†
- 21 G. Aromi, A. S. Batsonov, P. Christian, M. Helliwell, A. Parkin, S. Parsons, A. A. Smith, G. A. Timco and R. E. P. Winpenney, *Chem.–Eur. J.*, 2003, **9**, 5142–5161.
- 22 See notes for more information.†
- 23 Catalytic carbonylation was performed using recycled silver carbonate, which resulted in 83% isolated yield of succinimide **2a** under the standard reaction conditions.

