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Carbene-Catalyzed Direct Functionalization of β -sp³-Carbons of α -Chloroaldehydes

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Abstract: A direct functionalization of the β -sp³ carbon of α -chloro aldehyde is developed. The reaction starts with the addition of a carbene catalyst to α -chloroaldehyde to eventually form homoenolate intermediate. This overall redox-neutral process successfully converts the otherwise inert β -sp³-carbon of the aldehyde substrate to a nucleophilic carbon for asymmetric reactions. This study constitutes the first success in activating α -chloroaldehydes to generate homoenolate intermediates via carbene organic catalysis, and shall encourage further explorations in using organic catalysis for transforming inert chemical bonds.

Carbonyl compounds are among the most common substrates involved in organic synthesis. Numerous methods have been developed to functionalize the α -carbons of saturated carbonyl compounds or β -sp²-carbons of α,β -unsaturated carbonyl molecules.^[1] In contrast, strategies for direct functionalization of β -sp³-carbons of saturated carbonyl substrates are less developed. Much progress in catalytic direct functionalization on the β -sp³-carbons of carbonyl compounds comes from transition metal-mediated carbon-hydrogen bond activations.^[2] The use of organic catalysts (such as amines) in combination with transition metal photo catalysts^[3] or oxidants^[4] have also shown impressive success in activating otherwise inert β -sp³ carbons of saturated carbonyl compounds. In 2013, our laboratory showed that with N-heterocyclic carbene (NHC) used as the organic catalysts,^[5] saturated carboxylic esters can be activated to generate homoenolate intermediates via an overall redox-neutral process (Figure 1a).^[6] This unusual activation catalytically converts the β -sp³ carbon of ester to a reactive nucleophilic carbon of asymmetric reactions.^[7] As an important note, these homoenolate intermediates were traditionally generated by using enals as the substrates under NHC catalysis, as pioneered by Bode, Glorius, and others (Figure 1a).^[8]

Here we disclose a new approach for the generation of homoenolate intermediates by using α -chloroaldehydes as the

substrates (Figure 1a). Our reaction starts with the formation of an azolium ester enolate intermediate **I** from α -chloroaldehyde (**1a**) and NHC catalyst (Figure 1b), this process first reported by Rovis and Bode.^[9] In those previous reports,^[9c] the azolium ester enolate intermediates underwent further reactions with the α -carbons as the nucleophilic reaction centres. In our present study, the β -carbon of enolate intermediate **I** undergoes a deprotonation to form homoenolate intermediate **II** for further asymmetric reactions. The overall process converts the otherwise inert β -sp³ carbon of α -chloroaldehyde to a nucleophilic carbon. Bases and acidic additives were found to have dramatic influences on chemo-selectivity of the reactions (selection between α - and β -carbon of the aldehyde substrates). Control experiments revealed that α -chloroaldehydes were not converted to enals under our conditions and ruled out the possibilities for the involvement of enals as substrates in our reactions.

(a) Approaches to generate homoenolate intermediates via NHC organic catalysis

(b) NHC-catalyzed direct activation and functionalization of β -sp³-carbon of α -chloro aldehydes

Figure 1. NHC-catalyzed direct β -sp³ carbon functionalization of α -chloro aldehydes via homoenolate intermediates

Key results of condition optimization by using α -chloro aldehyde **1a** and isatin **2a** as the model substrates are summarized in Table 1. The amino indanol-derived triazolium NHC pre-catalyst, first reported by Bode,^[10] was found as a suitable catalyst. When the reaction was carried out with DIEA as the base and THF as the solvent, the β -carbon reaction product was obtained in low while encouraging 10% yield and the α -carbon reaction product **3a'** was afforded as the main adduct in 42% yield (entry 1). Replacing DIEA with DMAP as the base improved the chemo-selectivity of the β - over α -carbon reactions, with the β -carbon reaction product **3a** obtained in 68% yield (entry

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2). In NHC-catalyzed reaction of enals, earlier studies from Bode^[11] and us^[12] found that bases could influence the β -carbon protonation process and thus converted homoenolate to enolate intermediates. In this present study, it appears that the bases can have profound impacts on the β -carbon deprotonation process and thus convert enolate to homoenolate intermediates (intermediates **I** to **II**, Figure 1). We next studied the effects of additives and found that HOBt could dramatically improve the β -carbon reaction yield and product dr (entries 3–8). For example, the yield of β -carbon reaction product (**3a**) could be improved from 68% to 95% when HOBt additive was added to the reaction with DMAP as the base (entries 2–3). This beneficial effect of HOBt is quite general when different bases were used (entries 3–8). Inorganic bases (such as K_2CO_3) and other solvent (such as EtOAc) could be used as well to afford **3a** with excellent yield and dr and er values. It is worth noting that in the absence of HOBt the β -carbon reaction product (**3a**) was obtained in a low yield under otherwise identical conditions (e.g., entry 9; also see SI). In all cases with HOBt as an additive, the α -carbon reaction product was dramatically suppressed. The exact roles of HOBt remain unclear. It appears HOBt can have hydrogen bonding interactions with the isatin substrate (**2a**)^[7d] to facilitate the β -carbon reactions. The use of HOBt also led to small while consistent improvements on reaction diastereo- and enantio-selectivities.^[4e,7b,13]

Table 1. Optimization of reaction conditions.^[a]

Entry	Base, Solvent	additive	3a (3a')	3a	3a
			Yield [%] ^[b]	dr ^[c]	er ^[d]
1	DIEA, THF	-	~10 (42)	--	--
2	DMAP, THF	-	68 (11)	3:1	94:6
3	DMAP, THF	HOBt	95 (trace)	6:1	97:3
4	DIEA, THF	HOBt	92 (trace)	13:1	97:3
5	K_2CO_3 , THF	HOBt	84 (trace)	13:1	96:4
6	DIEA, EtOAc	HOBt	86 (trace)	15:1	98:2
7	K_2CO_3 , EtOAc	HOBt	92 (trace)	17:1	99:1
8	DMAP, EtOAc	HOBt	78 (trace)	8:1	99:1
9	K_2CO_3 , EtOAc	-	29 (trace)	8:1	83:17

[a] General conditions (unless otherwise specified): **1a** (0.10 mmol), **2a** (0.05 mmol), NHC (0.01 mmol), base (0.15 mmol), solvent (1.0 mL), HOBt (0.01 mmol), RT, 24 h. [b] Isolated yield. [c] The dr values were determined via ¹H NMR analysis. [d] Er values were determined via HPLC on chiral stationary phase. Trt = Triphenylmethyl, DIEA = N,N-diisopropyl-ethylamine, DMAP = 4-dimethylaminopyridine.

Table 2. Scope of reactions.^[a]

[a] General conditions (unless otherwise specified): **1** (0.20 mmol), **2** (0.10 mmol), NHC (0.02 mmol), K_2CO_3 (0.30 mmol), HOBt (0.02 mmol), EA (2.0 mL), RT, 24 h. [b] Isolated yield of **3**. [c] The dr values were estimated via ¹H NMR analysis. [d] Er was determined via HPLC on chiral stationary phase.

With an optimized reaction condition in hand (Table 1, entry 7), we next examined the generality of our β -sp³ carbon reaction strategy with different α -chloroaldehydes (**1**) and isatins (**2**) (Scheme 2). Placing substituents (e.g. halogens, methyl or methoxy groups) on the para-carbons of the β -phenyl rings of the α -chloroaldehydes were well tolerated (**3b-f**). These substituents could also be installed on the meta-carbon of the β -phenyl rings of the aldehydes (**3g-j**). Variations on the isatin substrates were all well tolerated, as exemplified in products **3k-v**. As a technical note, when α -chloroaldehyde with a β -alkyl substituent was used, the corresponding β -carbon reaction product (**3w**) was not observed likely due to the low acidity of the β -CH.

Scheme 1. Control experiments to understand reaction mechanism.

To understand the reaction pathway and the role of HOBT, multiple control experiments were performed. Under the current optimized reaction condition, elimination of α -chloroaldehyde **1a** to form α,β -unsaturated aldehyde **5a** was not observed. We then used a mixture of α -chloroaldehyde and saturated ester (**4a**) from HOBT (1:1 molar ratio) to react with isatin (**1a**) under the optimal condition (Scheme 1b and 1c). Our results showed that the β -carbon reaction products (e.g., **3a** or **3f**) mainly came from the α -chloroaldehydes. These experiments support that the β -carbon activation and homoenolate intermediate formation are directly resulted from α -chloroaldehydes (not via the saturated esters with HOBT),^[9d,9e] as proposed in Figure 1b. We also ruled out the possibility for the involvement of α,β -unsaturated aldehydes (e.g., **5a** or **5b**) as key intermediates in our reaction (Scheme 1d and 1e). Specifically, when the corresponding α,β -unsaturated aldehydes were used as substrates under the present conditions (optimized for the α -chloroaldehyde reactions), the corresponding γ -lactam products (e.g., **3a** or **3f**) were not formed.

In summary, we have developed the first carbene-catalyzed direct β -sp³-carbon functionalization of α -chloroaldehydes. Key steps in this catalytic process include azoium ester enolate formation followed by β -CH deprotonation to form homoenolate intermediate for direct β -carbon reactions. The use of HOBT additive significantly alters the chemo-selectivity between α - and

β -carbons of α -chloroaldehydes. Chloroaldehydes exhibit high reactivities with carbene catalysts, and therefore we expect this approach to offer complimentary and, in some cases, better solutions for homoenolate reactions. Further studies for direct activation of other inert chemical bonds via carbene organic catalysis are in progress in our laboratory.

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- [1] For selected reviews, see: a) K. Zeitler, *Angew. Chem. Int. Ed.* **2005**, *44*, 7506; *Angew. Chem.* **2005**, *117*, 7674; b) B. List, J. W. Yang, *Science* **2006**, *313*, 1584; c) M. Marigo, K. A. Jørgensen, *Chem. Commun.* **2006**, 2001; d) C. Palomo, A. Mielgo, *Angew. Chem. Int. Ed.* **2006**, *45*, 7876; *Angew. Chem.* **2006**, *118*, 8042; e) D. W. C. MacMillan, *Nature* **2008**, *455*, 304; f) V. Nair, S. Vellalath, B. P. Babu, *Chem. Soc. Rev.* **2008**, *37*, 2691; g) A. Moyano, R. Rios, *Chem. Rev.* **2011**, *111*, 4703; h) F. Giacalone, M. Gruttadauria, P. Agrigento, R. Noto, *Chem. Soc. Rev.* **2012**, *41*, 2406; i) J. L. Li, T.-Y. Liu, Y. C. Chen, *Acc. Chem. Res.* **2012**, *45*, 1491; j) J. Izquierdo, G. E. Hutson, D. T. Cohen, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2012**, *51*, 11686; *Angew. Chem.* **2012**, *124*, 11854; k) J. Mahatthananchai, J. W. Bode, *Acc. Chem. Res.* **2014**, *47*, 696; l) J. Burés, A. Armstrong, D. G. Blackmond, *Acc. Chem. Res.* **2016**, *49*, 214.
- [2] For selected reviews, see: a) O. Daugulis, H. Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074; b) X. Chen, K. M. Engle, D. H. Wang, J. Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094; *Angew. Chem.* **2009**, *121*, 5196; c) R. Jazzar, J. Hitce, A. Renaudat, J. Sofack-Kreutzer, O. Baudoin, *Chem. Eur. J.* **2010**, *16*, 2654; d) T. W. Lyons, S. M. Sanford, *Chem. Rev.* **2010**, *110*, 1147; e) M. Wasa, K. M. Engle, J. Q. Yu, *Isr. J. Chem.* **2010**, *50*, 605; f) O. Baudoin, *Chem. Soc. Rev.* **2011**, *40*, 4902; for selected examples, see: g) A. Nickon, L. James, S. J. Lambert, *J. Am. Chem. Soc.* **1962**, *84*, 4604; h) E. Nakamura, I. Kuwajima, *J. Am. Chem. Soc.* **1983**, *105*, 651; i) V. G. Zaitsev, D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2005**, *127*, 13154; j) M. Wasa, K. S.-L. Chan, X.-G. Zhang, J. He, M. Miura, J. Q. Yu, *J. Am. Chem. Soc.* **2012**, *134*, 18570; k) J. He, M. Wasa, K. S. L. Chan, J. Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 3387; l) G. Chen, W. Gong, Z. Zhuang, M. S. Andra, Y. Q. Chen, X. Hong, Y. F. Yang, T. Liu, K. N. Houk, J. Q. Yu, *Science* **2016**, *353*, 1023; m) T. Liu, J. X. Qiao, M. A. Poss, J. Q. Yu, *Angew. Chem. Int. Ed.* **2017**, *56*, 10924; *Angew. Chem.* **2017**, *129*, 11064; n) Z. Zhuang, C. B. Yu, G. Chen, Q. F. Wu, Y. Hsiao, C. L. Joe, J. X. Qiao, M. A. Poss, J. Q. Yu, *J. Am. Chem. Soc.* **2018**, *140*, 10363.
- [3] For selected examples, see: a) M. T. Pirnot, D. A. Rankic, D. B. C. Martin, D. W. C. MacMillan, *Science* **2013**, *339*, 1593; b) F. R. Petronijević, M. Nappi, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2013**, *135*, 18323; c) J. A. Terrett, M. D. Clift, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2014**, *136*, 6858; d) J. L. Jeffrey, F. R. Petronijević, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2015**, *137*, 8404.
- [4] a) Y. Hayashi, T. Itoh, H. Ishikawa, *Angew. Chem. Int. Ed.* **2011**, *50*, 3920; *Angew. Chem.* **2011**, *123*, 4006; b) S. L. Zhang, H. X. Xie, J. Zhu, H. Li, X. S. Zhang, J. Li, W. Wang, *Nature Commun.* **2011**, *2*, 211; c) X. Zeng, Q. Ni, G. Raabe, D. Enders, *Angew. Chem. Int. Ed.* **2013**, *52*, 2977; *Angew. Chem.* **2013**, *125*, 3050; d) J. Mo, L. Shen, Y. R. Chi, *Angew. Chem. Int. Ed.* **2013**, *52*, 8588; *Angew. Chem.* **2013**, *125*, 8750; e) B. Liu, W. Wang, R. Huang, J. Yan, J. Wu, W. Xue, S. Yang, Z. Jing, Y. R. Chi, *Org. Lett.* **2018**, *20*, 260-263.
- [5] For reviews on NHC catalysis, see: a) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606; b) N. Marion, S. Díez-González, S. P. Nolan, *Angew. Chem. Int. Ed.* **2007**, *46*, 2988; *Angew. Chem.* **2007**, *119*, 3046; c) A. T. Biju, N. Kuhl, F. Glorius, *Acc. Chem. Res.* **2011**, *44*, 1182; d) J. Douglas, G. Churchill, A. D. Smith, *Synthesis* **2012**, *44*, 2295; e) X. Bugaut, F. Glorius, *Chem. Soc. Rev.* **2012**, *41*, 3511; f) H. U. Vora, P. Wheeler, T. Rovis, *Adv. Synth. Catal.* **2012**, *354*, 1617; g) J. Izquierdo, G. E. Hutson, D. T. Cohen, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2012**, *51*, 11686; *Angew. Chem.* **2012**, *124*, 11854; h) D. T. Cohen, K. A. Scheidt, *Chem. Sci.* **2012**, *3*, 53; i) S. J. Ryan, L. Candish, D. W. Lupton, *Chem. Soc. Rev.* **2013**, *42*, 4906; j) M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485; k) R. S. Menon, A. T. Biju, V. Nair, *Chem. Soc. Rev.* **2015**, *44*, 5040; l) D. M. Flanagan, F. Romanov-Michailidis, N. A. White, T. Rovis, *Chem. Rev.* **2015**, *115*, 9307; m) M. H. Wang, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2016**, *55*, 14912; *Angew. Chem.* **2016**, *128*, 15134; n) S. Mondal, S. R. Yetra, S. Mukherjee, A. T. Biju, *Acc. Chem. Res.* **2019**, *52*, 425.
- [6] Z. Fu, J. Xu, T. Zhu, W. W. Y. Leong, Y. R. Chi, *Nature Chem.* **2013**, *5*, 835.
- [7] a) Z. Fu, K. Jiang, T. Zhu, J. Torres, Y. R. Chi, *Angew. Chem. Int. Ed.* **2014**, *53*, 6506; *Angew. Chem.* **2014**, *126*, 6624; b) Z. Jin, S. Chen, Y. Wang, P. Zheng, S. Yang, Y. R. Chi, *Angew. Chem. Int. Ed.* **2014**, *53*, 13506; *Angew. Chem.* **2014**, *126*, 13724; c) Z. Jin, K. Jiang, Z. Fu, J. Torres, P. Zheng, S. Yang, B.-A. Song, Y. R. Chi, *Chem. Eur. J.* **2015**, *21*, 9360; d) J. Xu, S. Yuan, M. Miao, Z. Chen, *J. Org. Chem.* **2016**, *81*, 11454.
- [8] a) S. S. Sohn, E. L. Rosen, J. W. Bode, *J. Am. Chem. Soc.* **2004**, *126*, 14370; b) C. Burstein, F. Glorius, *Angew. Chem. Int. Ed.* **2004**, *43*, 6205; *Angew. Chem.* **2004**, *116*, 6331; c) C. Burstein, S. Tschan, X. Xie, F. Glorius, *Synthesis* **2006**, 2418; d) V. Nair, S. Vellalath, M. Poonoth, R. Mohan, E. Suresh, *Org. Lett.* **2006**, *8*, 507; e) M. Rommel, T. Fukuzumi, J. W. Bode, *J. Am. Chem. Soc.* **2008**, *130*, 17266; f) M. He, J. W. Bode, *J. Am. Chem. Soc.* **2008**, *130*, 418; g) A. Chan, K. A. Scheidt, *J. Am. Chem. Soc.* **2008**, *130*, 2740; h) V. Nair, C. R. Sinu, B. P. Babu, V. Varghese, A. Jose, E. Suresh, *Org. Lett.* **2009**, *11*, 5570; i) X. Zhao, D. A. DiRocco, T. Rovis, *J. Am. Chem. Soc.* **2011**, *133*, 12466; j) B. Maji, L. Ji, S. Wang, S. Vedachalam, R. Ganguly, X. W. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 8276; *Angew. Chem.* **2012**, *124*, 8401; k) H. Lv, W. Q. Jia, L. H. Sun, S. Ye, *Angew. Chem. Int. Ed.* **2013**, *52*, 8607; *Angew. Chem.* **2013**, *125*, 8769; l) N. A. White, D. A. DiRocco, T. Rovis, *J. Am. Chem. Soc.* **2013**, *135*, 8504; m) K. P. Jang, G. E. Hutson, R. C. Johnston, E. O. McCusker, P. H. Y. Cheong, K. A. Scheidt, *J. Am. Chem. Soc.* **2014**, *136*, 76; n) J. L. Li, B. Sahoo, C. G. Daniluc, F. Glorius, *Angew. Chem. Int. Ed.* **2014**, *53*, 10515; *Angew. Chem.* **2014**, *126*, 10683; o) L. Wang, S. Li, M. Blümel, A. R. Philipps, A. Wang, R. Puttreddy, K. Rissanen, D. Enders, *Angew. Chem. Int. Ed.* **2016**, *55*, 11110; *Angew. Chem.* **2016**, *128*, 11276.
- [9] a) N. T. Reynolds, J. R. Alaniz, T. Rovis, *J. Am. Chem. Soc.* **2004**, *126*, 9518; b) N. T. Reynold, T. Rovis, *J. Am. Chem. Soc.* **2005**, *127*, 16406; c) M. He, G. J. Uc, J. W. Bode, *J. Am. Chem. Soc.* **2006**, *128*, 15088; d) H. U. Vora, T. Rovis, *J. Am. Chem. Soc.* **2007**, *129*, 13796; e) H. U. Vora, T. Rovis, *J. Am. Chem. Soc.* **2010**, *132*, 2860; f) P. Wheeler, H. U. Vora, T. Rovis, *Chem. Sci.* **2013**, *4*, 1674.
- [10] M. He, J. R. Struble, J. W. Bode, *J. Am. Chem. Soc.* **2006**, *128*, 8418.
- [11] J. Kaebamrungs, M. C. Kozłowski, J. W. Bode, *Pro. Nat. Acad. Sci. U. S. A.* **2010**, *107*, 20661.
- [12] Z. Fu, H. Sun, S. Chen, B. Tiwari, G. Li, Y. R. Chi, *Chem. Commun.* **2013**, *49*, 261.
- [13] Z. Fu, X. Wu, Y. R. Chi, *Org. Chem. Front.* **2016**, *3*, 145.

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Layout 2:

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**Carbene-Catalyzed Direct
Functionalization of β -sp³-Carbons of
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Inert carbon activation: direct functionalization of the β -sp³ carbons of α -chloro aldehydes under the influence of NHC organic catalyst is realized.