Accepted Manuscript

Mechanistic studies of thiourea-catalyzed cross-dehydrogenative C-P and C-C coupling reactions and their further applications

Zhiguo Zhang, Kai Gu, Zongbi Bao, Huabin Xing, Qiwei Yang, Qilong Rena

PII: S0040-4020(17)30405-2

DOI: 10.1016/j.tet.2017.04.033

Reference: TET 28634

To appear in: *Tetrahedron*

Received Date: 17 March 2017

Revised Date: 11 April 2017

Accepted Date: 13 April 2017

Please cite this article as: Zhang Z, Gu K, Bao Z, Xing H, Yang Q, Rena Q, Mechanistic studies of thiourea-catalyzed cross-dehydrogenative C-P and C-C coupling reactions and their further applications, *Tetrahedron* (2017), doi: 10.1016/j.tet.2017.04.033.

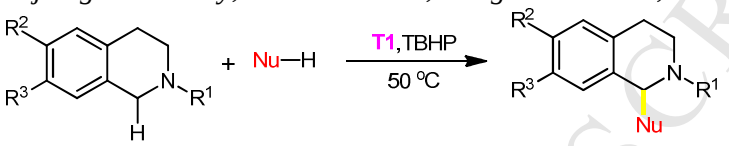
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

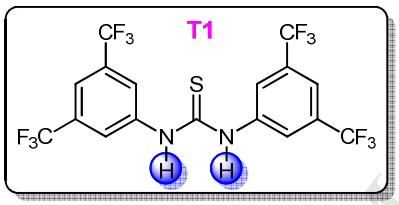
Type the title of your article here
Mechanistic studies of thiourea-catalyzed cross-dehydrogenative C-P and C-C coupling reactions and their further applications

Thiourea-based hydrogen bond donor has been recently disclosed by our group to be an efficient organocatalyst for cross-dehydrogenative coupling (CDC) reactions. Here we present a detailed mechanistic study of this reaction using NMR spectroscopy and kinetic isotope effect experiment. The results revealed that α-amino peroxide is the true intermediate within the catalytic cycle, formed via a thiourea-catalyzed rate-determining hydrogen atom transfer (HAT) process. These experimental investigations not only provide somewhat insight into the mechanism of thiourea-catalyzed CDC reactions but also promote their further applications.

Zhiguo Zhang,[a,*] Kai Gu,[a] Zongbi Bao,[a] Huabin Xing,[a] Qiwei Yang,[a] and Qilong Ren[a]
Key Laboratory of Biomass Chemical Engineering of Ministry of Education, College of Chemical and Biological Engineering, Zhejiang University, Zheda Road 38, Hangzhou 310027, China.



NuH = nitroalkanes, dimethyl malonate, diethyl phosphite, etc.



#mild reaction condition

#broad substrate scope

#good to excellent yield

Tetrahedron
journal homepage: www.elsevier.com

Mechanistic studies of thiourea-catalyzed cross-dehydrogenative C-P and C-C coupling reactions and their further applications

Zhiguo Zhang,[a, *] Kai Gu,[a] Zongbi Bao,[a] Huabin Xing,[a] Qiwei Yang,[a] and Qilong Ren[a]

[a] *Key Laboratory of Biomass Chemical Engineering of Ministry of Education, College of Chemical and Biological Engineering, Zhejiang University, Zheda Road 38, Hangzhou 310027, China.*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

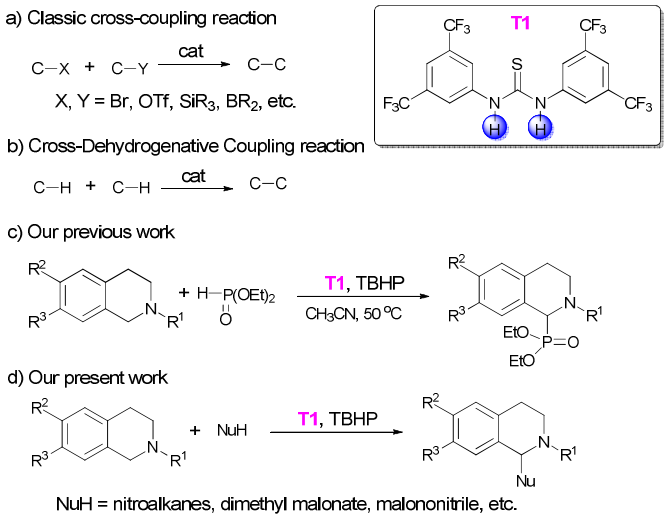
Keywords:
C-C coupling
organocatalysis
C-H activation
cross-dehydrogenative coupling
thiourea

ABSTRACT

Thiourea-based hydrogen bond donor has been recently disclosed by our group to be an efficient organocatalyst for cross-dehydrogenative coupling (CDC) reactions. Here we present a detailed mechanistic study of this reaction using NMR spectroscopy and kinetic isotope effect experiment. The results revealed that α-amino peroxide is the true intermediate within the catalytic cycle, formed via a thiourea-catalyzed rate-determining hydrogen atom transfer (HAT) process. These experimental investigations not only provide somewhat insight into the mechanism of thiourea-catalyzed CDC reactions but also promote their further applications.

1. Introduction

The selective transformation of C(sp^3)-H bonds to other functional groups represents an active and vibrant research area over the past decades, as C(sp^3)-H bonds are ubiquitous in organic molecules.[1] Among these reactions, the cross-dehydrogenative-coupling (CDC) reaction of two C(sp^3)-H or heteroatom-bonds[2] has been recognized as an elegant and promising strategy in modern synthetic chemistry, mainly because it can directly form a new bond without prior activation of substrates (Scheme 1, a and b). Pioneered by the studies of Murahashi and Li,[3] the direct activation of C(sp^3)-H bonds adjacent to tertiary amines, in particular *N*-aryl tetrahydroisoquinolines, has seen an explosion of interest. Currently, these reactions are often dominated by the use of transition metals as catalysts[4] or visible-light mediated photocatalysis[5]. Although examples of metal free systems (SO_2Cl_2[6], AcOH[7], 2-Chloroanthra-9,10-quinone[8], I_2[9], Eosin Y[10], KI[11], DDQ[12], (Diacetoxyiodo)benzene[13]) have progressed considerably, profitable practical organocatalyzed CDC reactions have not yet been developed. We recently reported for the first time an efficient thiourea-catalyzed cross-dehydrogenative coupling of C(sp^3)-H with diethyl phosphite using *N*,*N*'-bis(3,5-bis(tri-fluoromethyl)-phenyl)thiourea (**T1**), also known as Schreiner's catalyst,[14] as the catalyst and *tert*-butyl peroxide as a terminal oxidant (Scheme 1, c).[15] However, our understanding of how these thiourea-catalyzed CDC reactions occur, and what their inherent advantages and limitations for practical C(sp^3)-H



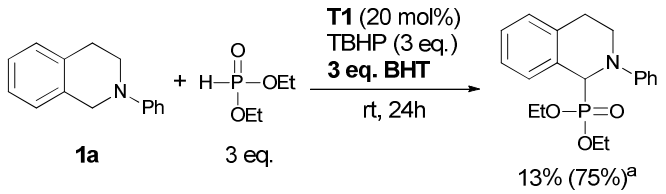
Scheme 1. Cross-coupling reactions

conversion are lacking. Here, we present in situ probes of **T1**-catalyzed oxidative coupling of *N*-phenyl tetrahydroisoquinolines with different nucleophiles such as diethyl phosphite and nitroalkanes using NMR spectroscopy and kinetic isotope effect experiment, with an attempt to reveal the mechanism and further expand the generality of substrates (Scheme 1, d).

2. Results and discussion

We have previously observed that **T1** facilitates the formation

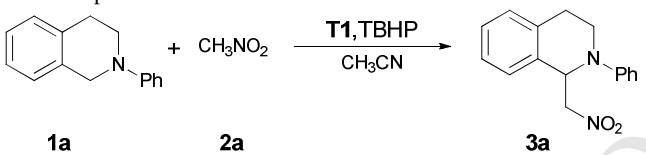
* Fax: +86-571-87952375; Tel: +86-571-87951224; E-mail: zhiguo.zhang@zju.edu.cn.



Scheme 2. Coupling of diethyl phosphite with 1a in the presence of the radical inhibitor BHT. [a] Isolated yield. Number in parentheses is the isolated yield of the reaction without BHT.

of α-amino peroxide, a possible reactive intermediate for the oxidative coupling of *N*-aryl tetrahydroisoquinolines with diethyl phosphite,[15] but it is still unclear how this intermediate formed. Based on the literature reports, there are two possible CDC mechanisms: either a radical mechanism or an ionic mechanism.[3d] To gain insight into the mechanism of our **T1**/TBHP system for C-P coupling, we first added 3.0 eq. of 2,6-di-tert-butyl-4-methyl phenol (BHT) as radical scavenger in the coupling reaction between *N*-phenyltetrahydroisoquinolines and diethyl phosphite, a significant drop in yield was observed (Scheme 2). This result suggested that a radical process involves in the present reaction. Then we tried to monitor the reaction process in situ by means of NMR spectroscopy, unfortunately, no peaks of the intermediate have been successfully intercepted, presumably because diethyl phosphite reacts extremely fast with the intermediate. To address the above questions, we selected nitromethane as a new nucleophile to investigate substrate scope for **T1**/TBHP-catalyzed CDC reactions and detailed mechanism.

Table 1. Optimization of reaction conditions



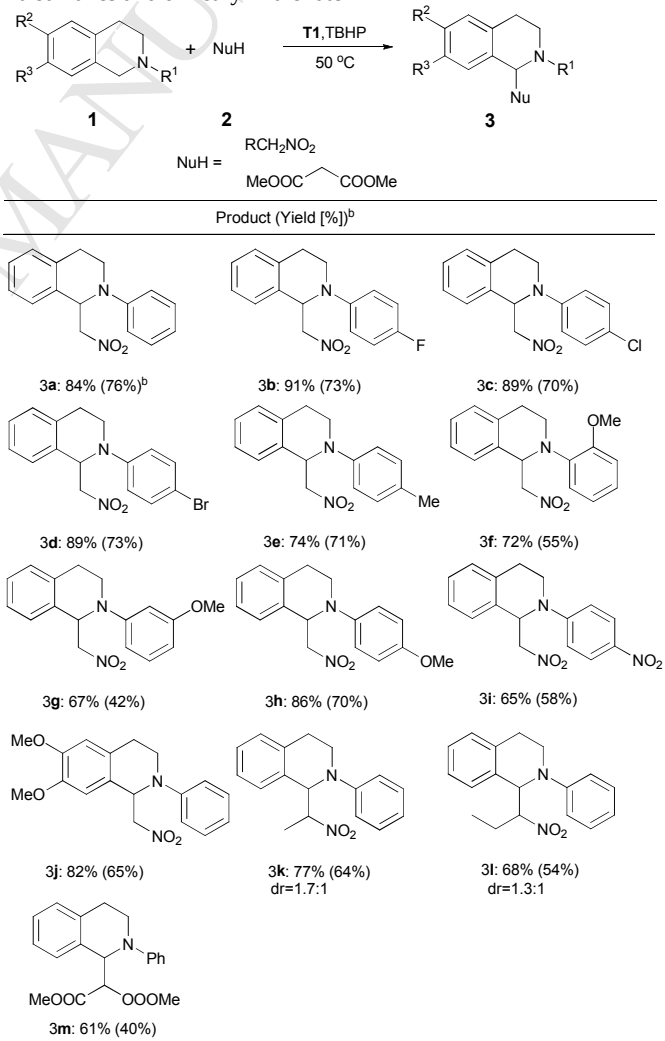
Entry[a]	2a [equiv.]	TBHP [equiv.]	T1 [mol%]	Temp [°C]	Time [h]	Yield [%][b]
1	2	2	20	15	48	55
2	2	2	20	30	32	61
3	2	2	20	50	10	64
4	2	2	20	70	5	59
5	2	2	0	50	48	trace
6	2	2	1	50	48	45
7	2	2	5	50	36	51
8	2	2	10	50	24	61
9	2	2	15	50	12	65
10	2	1	15	50	12	48
11	2	1.5	15	50	12	66
12	2	2.5	15	50	12	67
13[c]	2	1.5	15	50	12	66
14[d]	2	1.5	15	50	12	67
15[d]	5	1.5	15	50	12	74
16[d]	10	1.5	15	50	12	84
17[d]	20	1.5	15	50	12	82

[a] Reaction conditions: amine **1a** (0.2 mmol), CH_3CN (200 μL). [b] Yields determined by ^{1}H NMR using mesitylene as an internal standard. [c] with 4Å molecular sieve. [d] without CH_3CN.

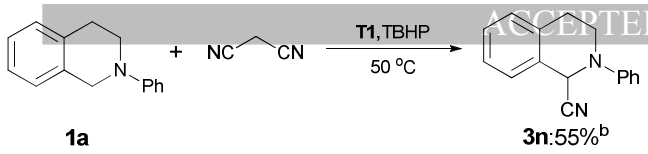
To our delight, the oxidative C-C coupling reaction couldoccur under the catalysis of **T1** (20 mol%) with CH_3CN as solvent at 50 °C, to afford **3a** in 64% yield. (Table 1, entry 3). Intrigued by these results, we performed a detailed optimization study on the **T1** promoted cross-dehydrogenative coupling (CDC) of *N*-phenyl tetrahydroisoquinoline (**1a**) with nitromethane (**2a**). First, **1a** was treated with 20 mol% of **T1** in a mixture of nitromethane and TBHP at different temperatures, using CH_3CN as the solvent (entries 1−4). The reaction temperature at 50 °C proved to be optimal.

Next, we assessed the effect of other reaction parameters including catalyst loadings, substrate/oxidant ratios, etc. on this CDC reaction. Starting from 20 mol% of **T1**, the catalyst loading can decrease to 1.0 mol% albeit at the expense of prolonged reaction time. 15 mol% of **T1** seems optimal for completion of the reaction within reasonable reaction time (entry 9). The yield of product can be improved as the ratio of TBHP to substrate increases but no continuously beneficial effect was observed when the amount of TBHP was more than 1.5 equivalents (entries 9–12). The addition of 4Å molecular sieve was not beneficial for the improvement of the product yield (entry 13).

Table 2. T1-catalyzed CDC of *N*-aryl tetrahydroisoquinolines with nitroalkanes and dimethyl malonate[a]



[a] Reaction conditions: amine **1a** (0.2 mmol), pronucleophiles **2** (10.0 equiv.), **T1** (15 mol%), TBHP (0.3 mmol, 5.5 M in decane), 12 h. [b] Yields determined by ^{1}H NMR using mesitylene as an internal standard; isolated yields are given in parentheses. dr was determined by ^{1}H NMR.



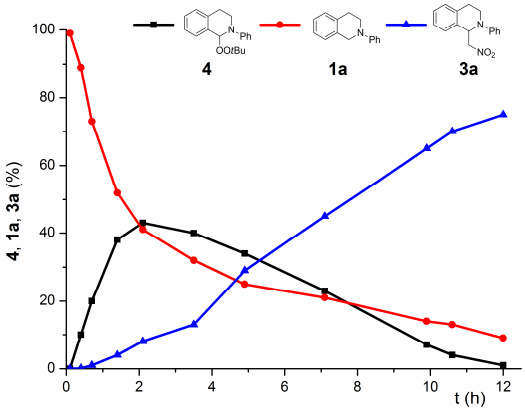
Scheme 3. T1-catalyzed CDC of N-phenyl tetrahydroisoquinolines with malononitrile.[a a] Reaction conditions: amine **1a** (0.2 mmol), malononitrile (10.0 equiv.), **T1** (15 mol%), TBHP (0.3 mmol, 5.5 M in decane), 12 h. [b] isolated yields.

Gratifyingly, when the C-C coupling reaction was performed without a solvent, the yield can be dramatically improved with the increase of the amount of nitromethane (entries 14–17) and 10 equivalents of nitromethane gives the best yield of **3a** (entry 16). A control experiment demonstrated that when the oxidative C-C coupling reaction was carried out in the absence of **T1**, only trace amount of product was observed (entry 5).

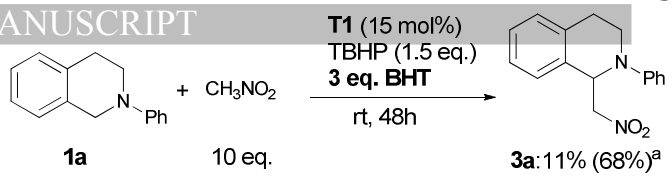
After the optimized reaction conditions were established, the substrate scope of this **T1**-catalyzed C-C coupling reaction was investigated by treatment with various *N*-aryl tetrahydroisoquinoline derivatives. As shown in Table 2, all the substrates with diverse substituents on *N*-aryl tetrahydroisoquinolines proceeded smoothly to give the corresponding products **3a-l** in good to excellent yields (65−91%).

In addition, when nitroethane or 1-nitropropane was used both as solvent and reactant, the coupling products were obtained in good yields and slight diastereoselectivities, respectively (Table 2, **3k** and **3l**). It should be noted that this protocol was also compatible with dimethyl malonate, affording the product in 61% yield (**3m**).

In addition to nitroalkanes and dimethyl malonate, the catalytic system was also applied to malononitrile. Surprisingly, no expected β-dicyano substituted derivative was obtained, but providing the α-amino nitriles as the sole product in good yield (Scheme 3, 55%). Although those data are similar with the results using Eosin Y[5d] as the catalyst, when CuBr[3d] was employed as the catalyst, both β-dicyano coupling product and α-amino nitriles were afforded. In this context, amino nitriles are synthetically useful intermediates, upon which the nitrile functionality can be elaborated into α-amino acids, α-amino aldehydes or α-amino alcohols. The developed procedure demonstrates the potential of this organocatalytic coupling reaction in the synthesis of α-amino nitriles without the use of toxic cyanides and expensive metals.[16]



Scheme 4. In situ probes of the formation of products **3a** (triangles, solid line) and intermediate **4** (squares, solid line) in the **T1**/TBHP system with nitromethane[a a] Reaction conditions: amine **1a** (0.1 mmol), nitromethane (10.0 equiv.), **T1** (15 mol%), TBHP (0.15 mmol, 5.5 M in decane), $CDCl_3$ (0.5 ml) in NMR tube.

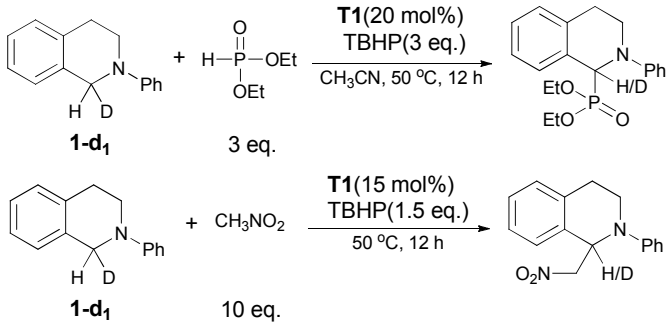


Scheme 5. Coupling of nitromethane with **1a** in the presence of the radical inhibitor BHT. [a] Isolated yield. Number in parentheses are the isolated yields of the reaction without BHT.

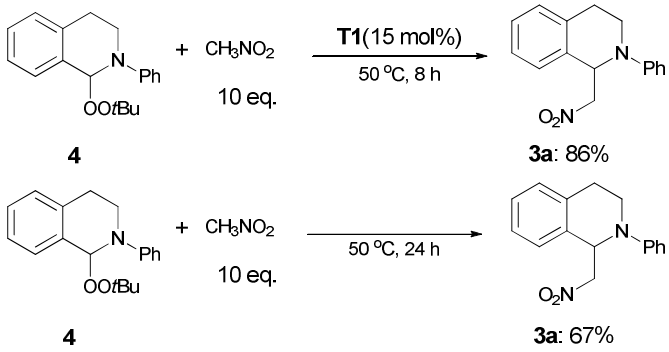
To our delight, we can intercept the characteristic peak of the intermediate **4** during the CDC reaction of *N*-phenyl tetrahydroisoquinolines with nitroalkanes with NMR spectroscopy, which brings us great convenience to further reveal the role of **4**. Then, we investigated oxidative coupling reactions of **1a** with nitromethane using the **T1**/TBHP method by means of NMR to monitor changes of reactants, products and active intermediate during the reaction process. (Scheme 4) The curves shown in Scheme 4 suggest that the intermediate **4** may be the direct precursor of **3a**.

In line with the role of radical inhibitor 2,6-di-tert-butyl-4-methylphenol (BHT) in the CuBr/TBHP catalyzed CDC reactions,[17] 3.0 equiv of BHT was added into the CDC reaction of *N*-phenyl tetrahydroisoquinolines with nitromethane catalyzed by our **T1**/TBHP catalyst system to check whether the reaction proceeds via a radical mechanism or not. As observed in **T1**-catalyzed C-P coupling, adding the radical inhibitor BHT to the reaction dramatically decreased the reaction yield (Scheme 5, from 68% to 11%), thus suggesting that a radical mechanism could be involved.

Further information on radical mechanism was illustrated from a kinetic isotope effect (KIE) experiment (Scheme 6). When monodeuterated substrate **1-d$_1$** was used as the subsrate, a KIE value k_H/k_D with diethyl phosphite and nitromethane of 2.6 and 3.3 was obtained through NMR spectra, respectively. Based on the KIE results as well as previous reports,[18] the reaction pathway was in agreement with a hydrogen atom transfer (HAT) rate-determining C-H bond cleavage.



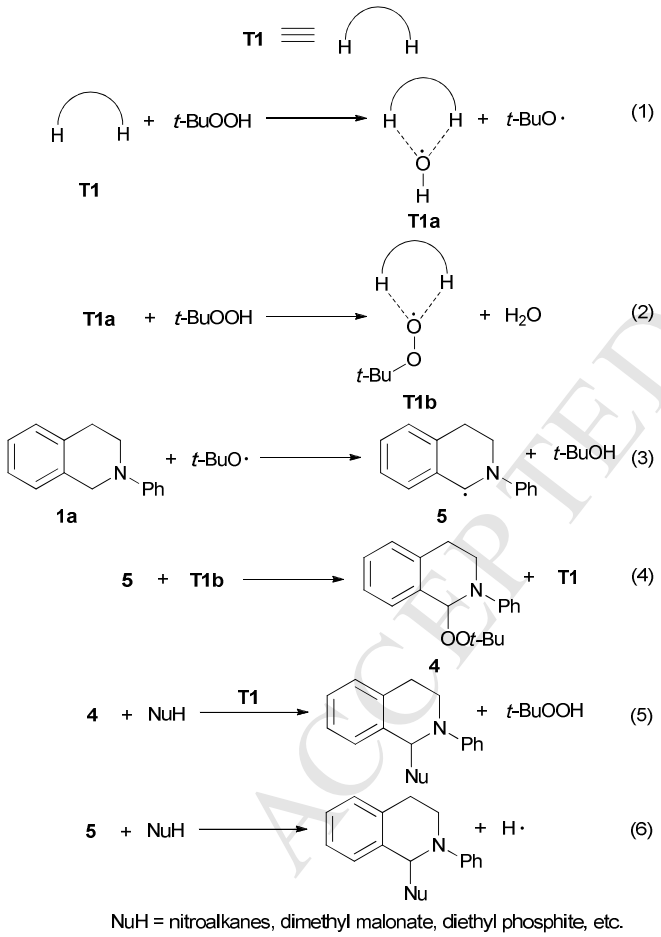
Scheme 6. Kinetic isotope effect (KIE) experiment with monodeuterated **1-d$_1$**



Scheme 7. The effect of **T1** in coupling nitromethane with intermediate **4**

In order to clarify whether **T1** is also involvement in promoting the substitution of intermediate **4** with a nucleophile,the reaction of nitromethane with **4** was evaluated (scheme 7). The reaction with **T1** proceeds much faster (a yield of 86% over 8 h) than the control experiment (a yield of 67% over 24 h), suggesting that **T1** has a strong ability to promote this reaction.

The detailed mechanistic investigations reveal apparent similarities of **T1**/TBHP and CuBr/TBHP systems for catalytic CDC reactions. Based on previous studies[19] and our experimental results, a plausible mechanism for the present reaction system, is proposed and depicted in Scheme 8. **T1** first interacts with TBHP through double hydrogen bonding, generating a hydroxyl complex **T1a** and a *tert*-butyloxy radical (eq 1). Then, a hydrogen atom was transferred from TBHP to **T1a**, forming a radical complex **T1b** and one molecular of water (eq 2). The *tert*-butyloxy radical in eq. 1 can abstrat a hydrogen atom from **1a**, giving rise to the radical species **5** (eq 3), which reacts with **T1b** to afford the intermediate **4** (eq 4). Aided by **T1**, the intermediate **4** will be subsequently intercepted with a nucleophile to generate the corresponding coupling product (eq 5). Nevertheless, the direct coupling of benzylic radical **5** with NuH can not be ruled out either (eq 6).



Scheme 8. Proposed reaction mechanism

3. Conclusion

In summary, mechanistic investigations using a combination of NMR, KIE, as well as other experimental techniques reveal for the first time the apparent similarities of **T1**/TBHP and CuBr/TBHP systems for catalytic CDC reactions. Furthermore, we were also able to extend this valuable methodology to C–C bonds formation between *N*-aryltetraisoquinolines with various C-nucleophiles such as nitroalkanes, dialkyl malonates and malononitrile. *N*-aryltetrahydroisoquinolines bearing either electron-withdrawing or -donating groups were well tolerated with this method, and the corresponding α-functionalized amines were delivered in good yields. The present method not only expands the application of **T1** further but also paves a new avenue for thiourea-based organocatalysts. Asymmetric CDC reaction catalyzed by chiral thiourea derivatives are underway in our laboratory and will be reported in due course.

4. Experimental section

4.1. General information

All commercially available materials were used as provided without further purification unless otherwise noted. Reactions were monitored by TLC on silica gel plates (GF254). Column chromatography was conducted on Silica gel 200-300 and the solvent mixtures are understood as volume/volume. The NMR spectra were recorded on a BRUKER-AV400 spectrometer in $CDCl_3$, Tetramethylsilane (TMS; δ = 0.00 ppm) served as internal standards for ^{1}H NMR and $CDCl_3$ was used as the internal standard (δ = 77.0 ppm) for ^{13}C NMR. The HRMS were measured with Waters GCT Premier. IR spectra were measured using a Nicolet 6700 FT-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). The 1,2,3,4-tetrahydroisoquinoline derivatives were prepared according to reported procedures.[20] The catalyst 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea (**T1**) was prepared according to reported procedures.[21]

4.2. General procedure of the CDC reaction

Nitroalkanes **2** (2.0 mmol) and TBHP (0.3 mmol, 5.5 M in decane) were successively added to a mixture of *N*-aryl-1,2,3,4-tetrahydroisoquinolines **1** (0.2 mmol) and *N*,*N*-bis[3,5-bis-(trifluoromethyl) phenyl]thiourea **T1** (15 mol%, 15 mg). Then the reaction mixture was stirred at 50 ^{o}C for 12 hours. After the reaction was completed monitoring by TLC analysis under UV, the reaction mixture was directed purified by column chromatography on silica gel with a mixture of *n*-hexane and ethyl acetate as the eluent (*n*-hexane/ethyl acetate = 10:1) to afford the desired coupling products **3**.

*4.2.1. 1-(nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**3a**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.10 (m, 6H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.88 – 6.80 (m, 1H), 5.54 (t, *J* = 7.2 Hz, 1H), 4.87 (dd, *J* = 11.8, 7.8 Hz, 1H), 4.56 (dd, *J* = 11.8, 6.6 Hz, 1H), 3.73 – 3.54 (m, 2H), 3.15 – 3.01 (m, 1H), 2.79 (dt, *J* = 16.3, 4.9 Hz, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ 148.38, 135.24, 132.87, 129.48, 129.16, 128.09, 126.96, 126.67, 119.39, 115.05, 78.74, 58.16, 42.02, 26.40.IR (neat): ν = 3033, 1982, 1914, 1596, 1548, 1495, 1383, 1330, 1292, 1211, 1006, 757. HRMS (GC-TOF) m/z calcd for $C_{16}H_{16}N_2O_2$ [M]+: 268.1212; found: 268.1211.

*4.2.2. 2-(4-fluorophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**3b**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.08 (m, 4H), 7.01 – 6.81 (m, 4H), 5.42 (dd, *J* = 8.6, 5.9 Hz, 1H), 4.83 (dd, *J* = 12.0, 8.7 Hz, 1H), 4.57 (dd, *J* = 12.0, 5.9 Hz, 1H), 3.69 – 3.47 (m, 2H), 3.12 – 2.90 (m, 1H), 2.72 (dt, *J* = 16.5, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.09 (d, *J* = 239.1 Hz), 145.26 (d, *J* = 2.2 Hz), 135.20,

132.47, 129.41, 128.05, 126.90, 126.71, 117.86 (d, *J* = 7.6 Hz), 115.81 (d, *J* = 22.2 Hz), 78.79, 58.67, 42.75, 25.69. IR (neat): ν = 3045, 2965, 2922, 1610, 1556, 1509, 1369, 1265, 1219, 1111, 1032, 950, 747. HRMS (GC-TOF) m/z calcd for $C_{16}H_{15}FN_2O_2$ [M]+: 286.1118; found: 286.1122

*4.2.3. 2-(4-chlorophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**3c**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.09 (m, 6H), 6.95 – 6.81 (m, 2H), 5.57 – 5.39 (m, 1H), 4.83 (dd, *J* = 12.0, 8.2 Hz, 1H), 4.56 (dd, *J* = 12.0, 6.3 Hz, 1H), 3.68 – 3.49 (m, 2H), 3.12 – 2.97 (m, 1H), 2.77 (dt, *J* = 16.4, 4.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.06, 135.03, 132.39, 129.26, 128.22, 126.85 (d, *J* = 14.5 Hz), 124.32, 116.43, 78.61, 58.17, 42.11, 26.07. IR (neat): ν = 3104, 3045, 2950, 1592, 1548, 1495, 1377, 1332, 1279, 1219, 1134, 744. HRMS (GC-TOF) m/z calcd for $C_{16}H_{15}ClN_2O_2$ [M]+: 302.0822; found: 302.0821

*4.2.4. 2-(4-bromophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**3d**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 2H), 7.28 – 7.07 (m, 4H), 6.91 – 6.76 (m, 2H), 5.60 – 5.36 (m, 1H), 4.84 (dd, *J* = 12.0, 8.1 Hz, 1H), 4.56 (dd, *J* = 12.0, 6.4 Hz, 1H), 3.71 – 3.42 (m, 2H), 3.02 (ddd, *J* = 42.1, 24.4, 12.1 Hz, 1H), 2.78 (dt, *J* = 16.4, 4.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.45, 135.01, 132.39, 132.18, 129.25, 128.25, 126.93, 126.80, 116.72, 111.51, 78.57, 58.07, 42.03, 26.13. IR (neat): ν = 3110, 3045, 2950, 1588, 1547, 1491, 1376, 1280, 1219, 1129, 1000, 947, 743. HRMS (GC-TOF) m/z calcd for $C_{16}H_{15}BrN_2O_2$ [M]+: 346.0317; found: 346.0324

*4.2.5. 1-(nitromethyl)-2-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline (**3e**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.10 (m, 4H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.93 – 6.81 (m, 2H), 5.58 – 5.40 (m, 1H), 4.84 (dd, *J* = 11.8, 8.1 Hz, 1H), 4.54 (dd, *J* = 11.8, 6.3 Hz, 1H), 3.73 – 3.37 (m, 2H), 3.12 – 2.95 (m, 1H), 2.74 (dt, *J* = 16.4, 4.5 Hz, 1H), 2.26 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.33, 135.31, 132.88, 129.93, 129.24, 129.06, 127.96, 126.93, 126.58, 115.84, 78.78, 58.35, 42.24, 26.15, 20.32. IR (neat): ν = 3105, 3045, 2949, 1612, 1590, 1552, 1518, 1281, 1220, 1147, 1068, 1004, 949, 836. HRMS (GC-TOF) m/z calcd for $C_{17}H_{18}N_2O_2$ [M]+: 282.1368; found: 282.1376

*4.2.6. 2-(2-methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**3f**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (ddd, *J* = 23.3, 8.3, 3.5 Hz, 4H), 7.03 (dd, *J* = 11.6, 4.9 Hz, 1H), 6.86 (dt, *J* = 15.1, 6.8 Hz, 3H), 5.50 (dd, *J* = 8.2, 5.1 Hz, 1H), 4.82 (dd, *J* = 12.0, 8.5 Hz, 1H), 4.53 (dd, *J* = 12.1, 5.0 Hz, 1H), 3.82 (s, 3H), 3.60 (dd, *J* = 13.3, 4.8 Hz, 1H), 3.54 – 3.42 (m, 1H), 2.99 (ddd, *J* = 17.1, 11.4, 6.2 Hz, 1H), 2.71 (d, *J* = 16.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.04, 138.82, 135.32, 133.59, 129.51, 127.53, 126.79, 126.40, 124.08, 121.89, 120.98, 112.42, 79.13, 58.13, 55.75, 42.91, 26.79. IR (neat): ν = 2953, 2843, 1609, 1590, 1550, 1498, 1378, 1283, 1220, 1027, 910, 745. HRMS (GC-TOF) m/z calcd for $C_{17}H_{18}N_2O_3$ [M]+: 298.1317; found: 298.1314

*4.2.7. 2-(3-methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**3g**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 67%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.15 (m, 4H), 7.14 – 7.09 (m, 1H), 6.59 (dd, *J* = 8.2, 2.3 Hz,1H), 6.53 (t, *J* = 2.3 Hz, 1H), 6.41 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.53 (t, *J* = 7.2 Hz, 1H), 4.87 (dd, *J* = 11.8, 7.6 Hz, 1H), 4.55 (dd, *J* = 11.8, 6.8 Hz, 1H), 3.81 (d, *J* = 11.3 Hz, 3H), 3.66 – 3.55 (m, 2H), 3.15 – 3.03 (m, 1H), 2.79 (dt, *J* = 16.3, 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.81, 149.69, 135.19, 132.85, 130.20, 129.10, 128.13, 126.96, 126.68, 107.49, 104.03, 101.39, 78.74, 58.21, 55.17, 42.09, 26.56. IR (neat): ν = 2950, 2834, 1609, 1548, 1496, 1378, 1280, 1219, 1166, 1040, 835, 758. HRMS (GC-TOF) m/z calcd for $C_{17}H_{18}N_2O_3$ [M]+: 298.1317; found: 298.1317

*4.2.8. 2-(4-methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (**3h**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.07 (m, 4H), 6.95 – 6.86 (m, 2H), 6.85 – 6.76 (m, 2H), 5.38 (dd, *J* = 8.5, 5.9 Hz, 1H), 4.82 (dd, *J* = 11.9, 8.7 Hz, 1H), 4.55 (dd, *J* = 11.9, 5.8 Hz, 1H), 3.73 (s, 3H), 3.62 – 3.48 (m, 2H), 3.00 (m, *J* = 16.2, 9.2, 6.8 Hz, 1H), 2.68 (dt, *J* = 16.5, 3.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.89, 142.99, 135.39, 132.77, 129.42, 127.85, 126.86, 126.56, 118.78, 114.62, 78.89, 58.86, 55.51, 43.03, 25.68. IR (neat): ν = 2949, 2840, 1661, 1610, 1548, 1508, 1471, 1378, 1242, 1131, 1034, 833. HRMS (GC-TOF) m/z calcd for $C_{17}H_{18}N_2O_3$ [M]+: 298.1317; found: 298.1320

*4.2.9. 1-(nitromethyl)-2-(4-nitrophenyl)-1,2,3,4-tetrahydroisoquinoline (**3i**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 – 8.12 (m, 2H), 7.35 – 7.29 (m, 1H), 7.29 – 7.23 (m, 2H), 7.17 (dd, *J* = 6.0, 2.6 Hz, 1H), 7.01 – 6.92 (m, 2H), 5.71 (t, *J* = 7.2 Hz, 1H), 4.88 (dd, *J* = 12.0, 7.2 Hz, 1H), 4.63 (dd, *J* = 12.0, 7.2 Hz, 1H), 3.88 – 3.61 (m, 2H), 3.23 – 3.08 (m, 1H), 2.97 (dt, *J* = 16.2, 6.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.53, 138.94, 134.41, 131.92, 129.06, 128.86, 127.23, 127.04, 126.21, 111.92, 78.09, 57.49, 42.21, 26.99. IR (neat): ν = 2947, 2840, 1662, 1591, 1551, 1506, 1406, 1318, 1221, 1113, 835, 754. HRMS (GC-TOF) m/z calcd for $C_{16}H_{15}N_3O_4$ [M]+: 313.1063; found: 313.1059

*4.2.10. 6,7-dimethoxy-1-(nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**3j**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=2:1, R_f=0.4); Yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 2H), 7.02 – 6.90 (m, 2H), 6.89 – 6.79 (m, 1H), 6.65 (s, 1H), 6.60 (s, 1H), 5.51 – 5.41 (m, 1H), 4.85 (dd, *J* = 11.8, 8.1 Hz, 1H), 4.57 (dd, *J* = 11.8, 6.4 Hz, 1H), 3.85 (d, *J* = 3.0 Hz, 5H), 3.68 (dt, *J* = 13.2, 5.1 Hz, 1H), 3.62 – 3.53 (m, 1H), 3.05 – 2.94 (m, 1H), 2.73 – 2.60 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.71, 148.56, 147.66, 129.41, 127.38, 124.50, 119.53, 115.48, 111.66, 109.54, 78.75, 57.95, 56.03, 55.86, 42.01, 25.76. IR (neat): ν = 2946, 2834, 1598, 1547, 1514, 1375, 1245, 1109, 1031, 753. HRMS (GC-TOF) m/z calcd for $C_{18}H_{20}N_2O_4$ [M]+: 328.1423; found: 328.1418

*4.2.11. 1-(1-nitroethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**3k**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 77%; dr=1.7:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.00 (m, 6H), 6.96 – 6.88 (m, 2H), 6.81 – 6.70 (m, 1H), 5.17 (t, *J* = 8.6 Hz, 1H), 5.03 – 4.93 (m, 0.6H, major isomer), 4.82 (m, *J* = 8.9, 6.8 Hz, 0.4H, minor isomer), 3.76 (m, *J* = 13.5, 8.2, 5.6 Hz, 0.6H, minor isomer), 3.60

– 3.40 (m, 1.4H, major isomer), 2.98 (m, *J* = 14.4, 7.1 Hz, 1H), 2.82 (m, *J* = 20.8, 13.5, 6.0 Hz, 1H), 1.63 (d, *J* = 6.8 Hz, 1H, minor isomer), 1.47 (d, *J* = 6.6 Hz, 2H, major isomer). ^{13}C NMR (101 MHz, $CDCl_3$, minor isomer marked*) δ 149.10*, 148.82, 135.58, 134.74*, 133.76*, 131.97, 129.41*, 129.29 (major and minor isomers), 129.08*, 128.69*, 128.33 (*J* = 14.5 Hz), 128.18, 127.22*, 126.58*, 126.11, 119.31, 118.76*, 115.38, 114.44*, 88.93*, 85.39, 62.72, 61.12*, 43.54*, 42.65, 26.72*, 26.35, 17.41*, 16.36. IR (neat): ν = 2923, 2834, 1667, 1599, 1549, 1504, 1360, 1220, 949, 760. HRMS (GC-TOF) m/z calcd for $C_{17}H_{18}N_2O_2$ [M]+: 282.1368; found: 282.1369

*4.2.12. 1-(1-nitropropyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**3l**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=10:1, R_f=0.4); Yield: 68%; dr=1.3:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.00 (m, 6H), 6.92 – 6.84 (m, 2H), 6.79 – 6.65 (m, 1H), 5.16 (d, *J* = 9.3 Hz, 0.4H), 5.05 (d, *J* = 9.6 Hz, 0.6H), 4.85 – 4.71 (m, 0.6H), 4.67 – 4.51 (m, 0.4H), 3.82 – 3.71 (m, 0.6H), 3.63 – 3.39 (m, 1.4H), 3.04 – 2.92 (m, 1H), 2.87 – 2.73 (m, 1H), 2.19 – 1.94 (m, 1.5H), 1.75 (dqd, *J* = 14.7, 7.4, 3.0 Hz, 0.5H), 0.85 (tt, *J* = 6.9, 3.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, minor isomer marked*) δ 149.02, 148.94*, 135.52, 134.66*, 133.87*, 132.50, 129.39, 129.31 (major and minor isomers), 129.15, 128.66, 128.56*,128.20*, 128.15, 127.18*, 126.60*, 125.86 (s,major and minor isomers), 119.35, 118.51*, 115.77, 114.04*, 96.13*, 93.01, 62.14, 60.66*, 43.49*, 42.24, 26.80*, 25.66, 24.97*, 24.60, 10.66 (d, *J* = 1.2 Hz,major and minor isomers). IR (neat): ν = 2971, 2914, 2360, 1598, 1546, 1493, 1370, 1319, 1269, 1212, 933, 809, 749. HRMS (GC-TOF) m/z calcd for $C_{18}H_{20}N_2O_2$ [M]+: 296.1525; found: 296.1526

*4.2.13. Dimethyl 2-(2-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)malonate (**3m**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=20:1, R_f=0.4); Yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.07 (m, 6H), 6.99 (t, *J* = 8.3 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 5.70 (d, *J* = 9.4 Hz, 1H), 3.95 (d, *J* = 9.4 Hz, 1H), 3.73 – 3.59 (m, 5H), 3.55 (s, 3H), 3.07 (ddd, *J* = 15.6, 8.9, 6.4 Hz, 1H), 2.87 (dt, *J* = 16.5, 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 167.38, 148.73, 135.61, 134.74, 129.07, 128.94, 127.59, 127.01, 126.00, 118.59, 115.16, 59.07, 58.14, 52.51 (d, *J* = 1.4 Hz), 42.14, 26.00. IR (neat): ν = 2951, 2362, 1731, 1597, 1504, 1434, 1267, 1208, 1140, 750, 693. HRMS (GC-TOF) m/z calcd for $C_{20}H_{21}NO_4$ [M]+: 339.1471; found: 339.1468

*4.2.14. 2-phenyl-1,2,3,4-tetrahydronaphthalene-1-carbonitrile (**3n**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=20:1, R_f=0.4); Yield: 82%;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (ddd, *J* = 7.7, 6.6, 2.3 Hz, 2H), 7.32 – 7.22 (m, 4H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 1H), 5.52 (s, 1H), 3.78 (dddd, *J* = 12.3, 5.8, 2.9, 1.0 Hz, 1H), 3.49 (ddd, *J* = 12.4, 10.8, 4.1 Hz, 1H), 3.16 (ddd, *J* = 16.5, 10.7, 6.0 Hz, 1H), 2.97 (dt, *J* = 16.3, 3.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.35, 134.59, 129.56, 129.34, 128.75, 127.04, 126.84, 121.89, 117.72, 117.60, 53.22, 44.16, 28.52. IR (neat): ν = 3100, 2925, 2832, 2223, 1597, 1495, 1377, 1260, 1201, 1030, 937, 753, 694. HRMS (GC-TOF) m/z calcd for $C_{16}H_{14}N_2$ [M]+: 234.1157; found: 234.1155

*4.2.15. 1-Deutero-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**1-d$_1$**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.8 Hz, 2H), 7.23 – 7.10 (m, 4H), 6.98 (d, *J* = 8.6 Hz, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 4.39 (s, 1H), 3.57 (dd, *J* = 11.7, 5.7 Hz, 2H), 2.99 (t, *J* = 5.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.52, 134.88, 134.38, 129.18, 128.50, 126.52, 126.32, 126.00, 118.62, 115.09, 50.63 – 50.00 (m), 46.46, 29.07. HRMS (GC-TOF) m/z calcd for $C_{15}H_{14}DN$ [M]+: 210.1267; found: 210.1263

*4.2.16. 1-(tert-butylperoxy)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (**4**)*

Purified by column chromatography on silica gel (eluting with hexane/ethyl acetate=20:1, R_f=0.4); Yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ=7.33 – 7.25 (m, 1H), 7.22 – 7.16 (m, 3H), 7.16 – 7.08 (m, 2H), 7.05 (d, *J* = 7.9 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.10 (s, 1H), 3.64 (ddd, *J* = 11.7, 7.0, 4.9 Hz, 1H), 3.53 – 3.41 (m, 1H), 3.06 – 2.82 (m, 2H), 1.05 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ=147.83, 135.59, 131.91, 128.07, 127.95, 127.53, 126.67, 124.94, 117.84, 113.80, 89.66, 79.01, 41.50, 27.08, 25.49; IR (neat): ν =2975,2923,2359,1599,1504,1402,1362, 1196,947,924,880,754; HRMS (GC-TOF) m/z calcd for $C_{19}H_{23}NO_2$ [M]+: 297.1729; found: 297.1734.

Acknowledgements

We are grateful for financial support from the MOST (2016YFA0202900), the National Natural Science Foundation of China (21376212, 21436010), the Fundamental Research Funds for the Central Universities (2016FZA4019) and the Natural Science Foundation of Zhejiang Province, China (LY13B060001).

References:

1. (a) W. Yoo, C. Li, in *Topics in Current Chemistry, Vol. 292* (Eds.: J. Q. Yu, Z. Shi), **2010**, pp. 281.; (b) C. J. Scheuermann, *Chem. Asian J.* **2010**, *5*, 436; (c) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem., Int. Ed.* **2011**, *50*, 11062; (d) J. Xuan, W. Xiao, *Angew. Chem., Int. Ed.* **2012**, *51*, 6828; (e) C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3464; (f) L. Shi, W. Xia, *Chem. Soc. Rev.* **2012**, *41*, 7687; (g) J. W. Beatty, C. R. J. Stephenson, *Accounts Chem. Res.* **2015**, *48*, 1474; (h) R. Narayan, K. Matcha, A. P. Antonchick, *Chem. Eur. J.* **2015**, *21*, 14678
2. (a) S. Murahashi, D. Zhang, *Chem. Soc. Rev.* **2008**, *37*, 1490; (b) C. Li, *Accounts Chem. Res.* **2009**, *42*, 335; (c) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; (d) M. Klussmann, D. Sureshkumar, *Synthesis* **2011**, *2011*, 353; (e) S. A. Girard, T. Knauber, C. Li, *Angew. Chem., Int. Ed.* **2014**, *53*, 74
3. (a) N. Chatani, T. Asaumi, S. Yorimitsu, T. Ikeda, F. Kakiuchi, S. Murai, *J. Am. Chem. Soc.* **2001**, *123*, 10935; (b) S. Murahashi, N. Komiya, H. Terai, T. Nakae, *J. Am. Chem. Soc.* **2003**, *125*, 15312; (c) Z. Li, C. Li, *J. Am. Chem. Soc.* **2005**, *127*, 6968; (d) Z. P. Li, D. S. Bohle, C. J. Li, *P. Natl. Acad. Sci. Usa.* **2006**, *103*, 8928; (e) O. Baslé, C. Li, *Chem. Commun.* **2009**, 4124
4. (a) A. Yu, Z. Gu, D. Chen, W. He, P. Tan, J. Xiang, *Catal. Commun.* **2009**, *11*, 162; (b) X. Shu, Y. Yang, X. Xia, K. Ji, X. Liu, Y. Liang, *Org. Biomol. Chem.* **2010**, *8*, 4077; (c) T. Zeng, G. Song, A. Moores, C. Li, *Synlett* **2010**, *2010*, 2002; (d) E. Shirakawa, T. Yoneda, K. Moriya, K. Ota, N. Uchiyama, R. Nishikawa, T. Hayashi, *Chem. Lett.* **2011**, *40*, 1041; (e) K. Alagiri, K. R. Prabhu, *Org. Biomol. Chem.* **2012**, *10*, 835; (f) J. Wang, C. Wang, K. E. Dekrafft, W. Lin, *ACS Catal.* **2012**, *2*, 417; (g) E. Boess, C. Schmitz, M. Klussmann, *J. Am. Chem. Soc.* **2012**, *134*, 5317; (h) Q. Meng, Q. Liu, J. Zhong, H. Zhang, Z. Li, B. Chen, C. Tung, L. Wu, *Org. Lett.* **2012**, *14*, 5992; (i) J. Xie, H. Li, J. Zhou, Y. Cheng, C. Zhu, *Angew. Chem., Int. Ed.* **2012**, *51*, 1252; (j) M. O. Ratnikov, X. Xu, M. P. Doyle, *J. Am. Chem. Soc.* **2013**, *135*, 9475; (k) R. Hudson, S. Ishikawa, C. Li, A. Moores, *Synlett* **2013**, *24*, 1637; (l) A. Tanoue, W. Yoo, S. Kobayashi, *Adv. Synth. Catal.* **2013**, n/a-n/a; (m) X. Yang, C. Zou, Y. He, M. Zhao, B. Chen, S. Xiang, M. O'Keeffe, C. Wu, *Chem. Eur. J.* **2014**, *20*, 1447; (n) B. Wang, D. P. Shelar, X. Han, T. Li, X. Guan, W. Lu, K. Liu, Y. Chen, W. Fu, C. Che, *Chem. Eur. J.* **2015**, *21*, 1184; (o) M. Brzozowski, J. A. Forni, G. Paul Savage, A. Polyzos, *Chem. Commun.* **2015**, *51*, 334; (p) S. Zhu, S. Ou, M. Zhao, H. Shen, C. Wu, *Dalton T.* **2015**, *44*, 2038
5. (a) A. G. Condie, J. C. Gonza· lez-Go· mez, C. R. J. Stephenson, *J. Am.*

Chem. Soc. **2010**, *132*, 1464; (b) Y. Pan, C. W. Kee, L. Chen, C. Tan, *Green Chem.* **2011**, *13*, 2682; (c) Z. Xie, C. Wang, K. E. Dekrafft, W. Lin, *J. Am. Chem. Soc.* **2011**, *133*, 2056; (d) D. P. Hari, B. Ko¨nig, *Org. Lett.* **2011**, *13*, 3852; (e) M. Rueping, J. Zoller, D. C. Fabry, K. Poscharny, R. M. Koenigs, T. E. Weirich, J. Mayer, *Chem. Eur. J.* **2012**, *18*, 3478; (f) C. Wang, Z. Xie, K. E. Dekrafft, W. Lin, *ACS Appl. Mater. Inter.* **2012**, *4*, 2288; (g) T. Mitkina, C. Stanglmair, W. Setzer, M. Gruber, H. Kisch, B. König, *Org. Biomol. Chem.* **2012**, *10*, 3556; (h) D. B. Freeman, L. Furst, A. G. Condie, C. R. J. Stephenson, *Org. Lett.* **2012**, *14*, 94; (i) M. Neumann, K. Zeitler, *Org. Lett.* **2012**, *14*, 2658; (j) M. Rueping, C. Vila, T. Bootwicha, *ACS Catal.* **2013**, *3*, 1676; (k) J. Jiang, Y. Li, X. Wu, J. Xiao, D. J. Adams, A. I. Cooper, *Macromolecules* **2013**, *46*, 8779; (l) W. To, Y. Liu, T. Lau, C. Che, *Chem. Eur. J.* **2013**, *19*, 5654; (m) J. Zhong, Q. Meng, G. Wang, Q. Liu, B. Chen, K. Feng, C. Tung, L. Wu, *Chem. Eur. J.* **2013**, *19*, 6443; (n) J. Wang, J. Ma, X. Li, Y. Li, G. Zhang, F. Zhang, X. Fan, *Chem. Commun.* **2014**, *50*, 14237; (o) X. Wang, Q. Meng, J. Zhong, X. Gao, T. Lei, L. Zhao, Z. Li, B. Chen, C. Tung, L. Wu, *Chem. Commun.* **2015**, *51*, 11256; (p) C. Wu, J. Zhong, Q. Meng, T. Lei, X. Gao, C. Tung, L. Wu, *Org. Lett.* **2015**, *17*, 884; (q) J. F. Franz, W. B. Kraus, K. Zeitler, *Chem. Commun.* **2015**, *51*, 8280

6. A. Tanoue, W. Yoo, S. Kobayashi, *Org. Lett.* **2014**, *16*, 2346
7. H. Ueda, K. Yoshida, H. Tokuyama, *Org. Lett.* **2014**, *16*, 4194
8. T. Yamaguchi, T. Nobuta, N. Tada, T. Miura, T. Nakayama, B. Uno, A. Itoh, *Synlett* **2014**, *25*, 1453
9. (a) T. Nobuta, N. Tada, A. Fujiya, A. Kariya, T. Miura, A. Itoh, *Org. Lett.* **2013**, *15*, 574; (b) J. Dhineshkumar, M. Lamani, K. Alagiri, K. R. Prabhu, *Org. Lett.* **2013**, *15*, 1092
10. Q. Liu, Y. Li, H. Zhang, B. Chen, C. Tung, L. Wu, *Chem. Eur. J.* **2012**, *18*, 620
11. R. A. Kumar, G. Saidulu, K. R. Prasad, G. S. Kumar, B. Sridhar, K. R. Reddy, *Adv. Synth. Catal.* **2012**, *354*, 2985
12. (a) A. S. K. Tsang, M. H. Todd, *Tetrahedron Lett.* **2009**, *50*, 1199; (b) A. S. K. Tsang, P. Jensen, J. M. Hook, A. S. K. Hashmi, M. H. Todd, *Pure Appl. Chem.* **2011**, *83*; (c) W. Su, J. Yu, Z. Li, Z. Jiang, *The Journal of Organic Chemistry* **2011**, *76*, 9144
13. X. Shu, X. Xia, Y. Yang, K. Ji, X. Liu, Y. Liang, *The Journal of Organic Chemistry* **2009**, *74*, 7464
14. (a) P. R. Schreiner, A. Wittkopp, *Org. Lett.* **2002**, *4*, 217; (b) A. Wittkopp, P. R. Schreiner, *Chem.-Eur. J.* **2003**, *9*, 407; (c) P. R. Schreiner, *Chem. Soc. Rev.* **2003**, *32*, 289; (d) Z. Zhang, P. R. Schreiner, *Chem. Soc. Rev.* **2009**, *38*, 1187; (e) R. Hrdina, C. E. Mu¨ller, R. C. Wende, K. M. Lippert, M. Benassi, B. Spengler, P. R. Schreiner, *J. Am. Chem. Soc.* **2011**, *133*, 7624; (f) Z. Zhang, Z. Bao, H. Xing, *Org. Biomol. Chem.* **2014**, *12*, 3151
15. K. Gu, Z. Zhang, Z. Bao, H. Xing, Q. Yang, Q. Ren, *Eur. J. Org. Chem.* **2016**, 3939
16. (a) D. Enders, J. P. Shilvock, *Chem. Soc. Rev.* **2000**, *29*, 359; (b) S. Murahashi, N. Komiya, H. Terai, T. Nakae, *J. Am. Chem. Soc.* **2003**, *125*, 15312; (c) M. North, *Angew. Chem., Int. Ed.* **2004**, *43*, 4126; (d) S. Murahashi, T. Nakae, H. Terai, N. Komiya, *J. Am. Chem. Soc.* **2008**, *130*, 11005; (e) D. P. Hari, B. Ko¨nig, *Org. Lett.* **2011**, *13*, 3852; (f) A. M. Nauth, N. Otto, T. Opatz, *Adv. Synth. Catal.* **2015**, *357*, 3424
17. E. Boess, C. Schmitz, M. Klussmann, *J. Am. Chem. Soc.* **2012**, *134*, 5317
18. (a) J. Shearer, C. X. Zhang, L. Q. Hatcher, K. D. Karlin, *J. Am. Chem. Soc.* **2003**, *125*, 12670; (b) M. O. Ratnikov, M. P. Doyle, *J. Am. Chem. Soc.* **2013**, *135*, 1549; (c) E. Boess, L. M. Wolf, S. Malakar, M. Salamone, M. Bietti, W. Thiel, M. Klussmann, *ACS Catal.* **2016**, *6*, 3253
19. (a) E. Boess, D. Sureshkumar, A. Sud, C. Wirtz, C. Fare` s, M. Klussmann, *J. Am. Chem. Soc.* **2011**, *133*, 8106; (b) E. Boess, C. Schmitz, M. Klussmann, *J. Am. Chem. Soc.* **2012**, *134*, 5317
20. (a) A. Sud, D. Sureshkumar, M. Klussmann, *Chem. Commun.* **2009**, 3169; (b) J. Zhong, Q. Meng, B. Liu, X. Li, X. Gao, T. Lei, C. Wu, Z. Li, C. Tung, L. Wu, *Org. Lett.* **2014**, *16*, 1988; (c) H. Ueda, K. Yoshida, H. Tokuyama, *Org. Lett.* **2014**, *16*, 4194; (d) M. Brzozowski, J. A. Forni, G. Paul Savage, A. Polyzos, *Chem. Commun.* **2015**, *51*, 334; (e) J. F. Franz, W. B. Kraus, K. Zeitler, *Chem. Commun.* **2015**, *51*, 8280
21. H. Y. Kim, K. Oh, *Org. Lett.* **2011**, *13*, 1306