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A Versatile C−H Functionalization of Tetrahydroisoquinolines Catalyzed by Iodine at Aerobic Conditions†

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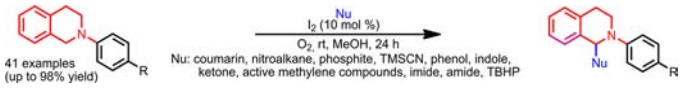
ABSTRACT



A versatile aerobic catalytic system (I_2 and O_2/TBHP) for C−H functionalization is reported. This CDC (cross-dehydrogentive coupling) reaction is compatible with a large number of nucleophiles and is performed under ambient reaction conditions. The scope of the metal-free CDC is illustrated by synthesizing a variety of functionalized tetrahydroisoquinolines and *N,N*-dimethylaniline. The highlight of the method is a Friedel−Crafts reaction of phenols and indole with tertiary amines.

Iodine catalyzed reactions are of great interest since iodine is an inexpensive, nontoxic, and environmentally benign reagent.[1] The utility of iodine, particularly in organic chemistry, is more emphasized in the use of hypervalent iodine derivatives.[2] Despite these facts, efforts to use iodine in C−H activation for C−C bond formation is limited. C−H functionalization is a rapidly growing area in organic synthesis as it provides shorter routes for synthesizing biologically and pharmaceutically active natural products.[3] A variety of metal catalysts[4] are used for C−H bond activation of tertiary amines such as THIQ (tetrahydroisoquinoline), *N,N*-dialkyl anilines, etc.[5] to form C−C bonds and C−hetero bonds. The C−H functionalization of tertiary amines has been poineered by Murahashi,[5a−c] Li,[5e,f] and others.[6−10] However, functionalization of tertiary amines was documented by Reinhoudt[10d] and recently by others.[10e−g] The sp^3-C center adjacent to a tertiary N-atom is functionalized with a variety of nucleophiles,[5−10] using metal catalysts, organocatalysts, photocatalysts, etc.[4−11] Among these, Cu-catalysts[5f] and

† In memories of Prof. A. Srikrishna (1955−2013).

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(1) (a) Parvatkar, P. T.; Parameswaran, P. S.; Tilve, S. G. *Chem.—Eur. J.* **2012**, *18*, 5460–5489. (b) Tago, H.; Iida, S. *Synlett* **2006**, 2159–2175. (c) Deuri, S.; Phukan, P. *J. Phys. Org. Chem.* **2012**, *2* (5), 1228–1235.

(2) (a) Wirth, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3656–3665. (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299–5358.

(3) Arend, M.; Westermann, B.; Risch, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 1044–1070 and references therein.

(4) (a) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215–1292. (b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624–655. (c) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293–1394. (d) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788–802. (e) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147–1169. (f) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879–2932. (g) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068–5083.

(5) (a) Murahashi, S.-I.; Zhang, D. *Chem. Soc. Rev.* **2008**, *37*, 1490–1501. (b) Murahashi, S.; Naota, T.; Miyaguchi, N.; Nakato, T. *Tetrahedron Lett.* **1992**, *33*, 6991–6994. (c) Murahashi, S.-I.; Komiya, N.; Terai, H.; Nakae, T. *J. Am. Chem. Soc.* **2003**, *125*, 15312–15313. (d) North, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4126–4128. (e) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 11810–11811. (f) Li, Z.; Bohle, D. C.; Li, C.-J. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 8928–8933.

(6) (a) Li, Z.; Li, C.-J. *Eur. J. Org. Chem.* **2005**, 3173–3176. (b) Mu-rahashi, S.-I.; Nakae, T.; Terai, H.; Komiya, N. *J. Am. Chem. Soc.* **2008**, *130*, 11005–11012 and references therein. (c) Singhal, S.; Jain, S. L.; Sain, B. *Chem. Commun.* **2009**, 2371–272. (d) Han, W.; Ofial, A. R. *Chem. Commun.* **2009**, 5024–5026. (e) Allen, J. M.; Lambert, T. H. *J. Am. Chem. Soc.* **2011**, *133*, 1260–1262. (f) Alagiri, K.; Prabhu, K. R. *Org. Biomol. Chem.* **2012**, *10*, 835–842. (g) Maxim, O. R.; Michael, P. D. *J. Am. Chem. Soc.* **2013**, *135*, 1549–1557.

(7) (a) Shen, Y.; Li, M.; Wang, S.; Zhan, T.; Tan, Z.; Guo, C.-C. *Chem. Commun.* **2009**, 953–955. (b) Sud, A.; Sureshkumar, D.; Klussmann, M. *Chem. Commun.* **2009**, 3169–3971. (c) Pinter, A.; Sud, A.; Sureshkumar, D.; Klussmann, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 5004–5007. (d) Rueping, M.; Vila, C.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C. *Chem. Commun.* **2011**, 2360–2362. (e) Boess, E.; Schmitz, C.; Klussmann, M. *J. Am. Chem. Soc.* **2012**, *134*, 5317.

(8) (a) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, *127*, 3672–3673. (b) Basle, O.; Li, C.-J. *Green Chem.* **2007**, *9*, 1047–1050. (c) Tsang, A. S.-K.; Todd, M. H. *Tetrahedron Lett.* **2009**, *50*, 1199–1202. (d) Shu, X.-Z.; Xia, X.-F.; Yang, Y.-F.; Ji, K.-G.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2009**, *74*, 7464–7469. (e) Zeng, T.; Song, G.; Moores, A.; Li, C.-J. *Synlett* **2010**, 2002–2008. (f) Condie, A. G.; González-Gómez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464–1465. (g) Hari, D. P.; Konig, B. *Org. Lett.* **2011**, *13*, 3852–3855 and references therein.

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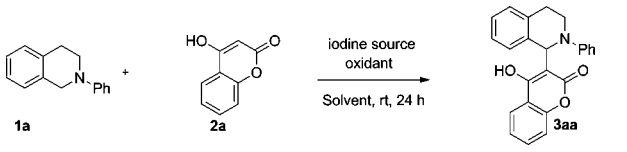
photocatalysts[8g] have shown wide application for C−H activation, while most of the other metal catalysts have shown limited scope. Due to the increasing demand for sustainable methods in organic synthesis, it is imperative to design metal-free reactions under aerobic conditions. Apart from reports by Konig[8g] (eosin Y) and our group (DDQ),[11a] to the best of our knowledge, functionalization of THIQ and coupling with nucleophiles using metal-free conditions are scarce.[8c,g,11a] In light of the environmental benefits of metal-free reactions and continuation of our work on C−H activation,[6f,9f,11] we envisioned using I_2 for C−H functionalization to form C−C bonds.[12,13] Herein we report an iodine catalyzed CDC (cross-dehydrogentive coupling) reaction of a wide variety of nucleophiles with THIQs using O_2 as an oxidant under ambient conditions.

Extensive screening with THIQ (**1a**) and 4-hydroxycoumarin (**2a**) revealed that I_2 (10 mol %) and O_2 or aq TBHP or NaOCl are effective combinations for the C−H bond functionalization of THIQ followed by C−C bond formation to form **3aa** (entries 1−3, Table 1). The reactions in the absence of oxidants did not proceed to completion (entry 4). To find out whether iodine is necessary for the CDC, **1a** was reacted with **2a** in the absence of iodine, and in the presence of oxidants such as aq. TBHP or O_2 (entry 5). However, this reaction did not furnish the coupled product **3aa** (entry 5). Lowering the amount of iodine to 5 mol % furnished a low yield of **3aa** (entry 6, Table 1). Other iodine sources such as TBAI, NaI, KI, and NIS with aq. TBHP, H_2O_2, or O_2 furnished low yields (entries 7−14, Table 1). Further, it was found that CuI and I_2 in the presence of air produced low yields of **3aa** (entries 15−16, Table 1). Solvent screening studies revealed that MeOH is the most suitable solvent as other solvents furnished low yields of the product (entries 17−23).

Table 1. Screening Studies[a]



entry	iodine source	oxidant	solvent	conversion[b]
1	**I_2 (10 mol %)**	**O_2**	**MeOH**	**98**
2	I_2 (10 mol %)	aqTBHP	MeOH	95
3	I_2 (10 mol %)	NaOCl	MeOH	93
4	I_2 (10 mol %)	none	MeOH	23
5	none	aqTBHP or O_2	MeOH	NR
6	I_2 (5 mol %)	aqTBHP	MeOH	70
7	TBAI (10 mol %)	aqTBHP	MeOH	77
8	TBAI (10 mol %)	H_2O_2	MeOH	29
9	TBAI (10 mol %)	O_2	MeOH	13
10	NaI (10 mol %)	aqTBHP	MeOH	67
11	NaI (10 mol %)	O_2	MeOH	8
12	KI (10 mol %)	aqTBHP	MeOH	72
13	KI (10 mol %)	O_2	MeOH	10
14	NIS (10 mol %)	O_2	MeOH	72
15	CuI (10 mol %)	air	MeOH	78
16	I_2 (10 mol %)	air	MeOH	75
17	I_2 (10 mol %)	O_2	H_2O	NR
18	I_2 (10 mol %)	O_2	CH_2Cl_2	88
19	I_2 (10 mol %)	O_2	EtOAc	52
20	I_2 (10 mol %)	O_2	DMF	23
21	I_2 (10 mol %)	O_2	THF	65
22	I_2 (10 mol %)	O_2	toluene	44
23	I_2 (10 mol %)	O_2	CH_3CN	51

[a] Reaction conditions: **1a** (0.24 mmol), **2a** (0.29 mmol), solvent (1 mL), I_2 (10 mol %), O_2 atmosphere. [b] Based on ^1H NMR data.

As O_2 is environmentally benign and readily available, further studies were conducted using a variety of nucleophiles and various THIQ derivatives using a catalytic amount of I_2 (10 mol %) and O_2 under ambient reaction conditions.

The scope of the coupling reaction was studied using a variety of THIQ derivatives and coumarin derivatives. Thus, *N*-phenyltetrahydroisoquinoline (**1a**), *N*-(4-methylphenyl)tetrahydroisoquinoline (**1b**), *N*-(4-methoxyphenyl)-tetrahydroisoquinoline (**1c**), and *N*-(4-bromophenyl)tetrahydroisoquinoline (**1d**) reacted well with coumarin nucleophiles such as 4-hydroxycoumarin (**2a**) and 4-hydroxy-6-methylcoumarin (**2b**) to furnish coupled products **3aa**, **3ab**, **3ba**, **3bb**, **3ca**, **3cb**, **3da**, and **3db** in good to excellent yields (Scheme 1). It is noteworthy that this is the second report of coupling 4-hydroxycoumarins with THIQ derivatives.[11a]

Further exploration revealed that nitroalkanes are also good nucleophiles for this reaction (Scheme 2). The initial reaction of THIQ **1a** with nitromethane (**4a**) was very sluggish and resulted in low yields of coupled product **5aa**.[14] However, addition of silica gel, as an additive, circumvented this problem by bringing a spectacular change in product yields. As can be seen, nitromethane (**4a**) and nitroethane (**4b**) coupled readily with THIQs **1a**, **1b**, and **1d** to furnish products **5aa**, **5ab**, **5ba**, **5bb**, **5da**, and **5db** in excellent yields (Scheme 2).

(9) (a) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, *127*, 6968–6969. (b) Ghobrial, M.; Harhammer, K.; Mihovilovic, M. D.; Schnürch, M. *Chem. Commun.* **2010**, 8836–8838. (c) Liu, P.; Zhou, C.-Y.; Xiang, S.; Che, C.-M. *Chem. Commun.* **2010**, *46*, 2739–2741. (d) Yang, F.; Li, J.; Xie, J.; Huang, Z.-Z. *Org. Lett.* **2010**, *12*, 5214–5217. (e) Wang, M.-Z.; Zhou, C.-Y.; Wong, M.-K.; Che, C.-M. *Chem.—Eur. J.* **2010**, *16*, 5723–5735. (f) Alagiri, K.; Kumara, G. S. R.; Prabhu, K. R. *Chem. Commun.* **2011**, *47*, 11787–11789.

(10) (a) Basle, O.; Li, C.-J. *Chem. Commun.* **2009**, 4124–4126. (b) Rueping, M.; Zhu, S.; Koenigs, R. M. *Chem. Commun.* **2011**, *47*, 8679–8681. (c) Leonard, N. J.; Leubner, G. H. *J. Am. Chem. Soc.* **1949**, *71*, 3408. (d) Verboom, W.; Reinhoudt, D. N.; Visser, R.; Harkema, S. *J. Org. Chem.* **1984**, *49*, 269–276. (e) Vadola, P. A.; Sames, D. *J. Am. Chem. Soc.* **2009**, *131*, 16525. (f) Zhang, C.; Kanta, De, C.; Mal, R.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 416. (g) Mori, K.; Sueoka, S.; Akiyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 2424.

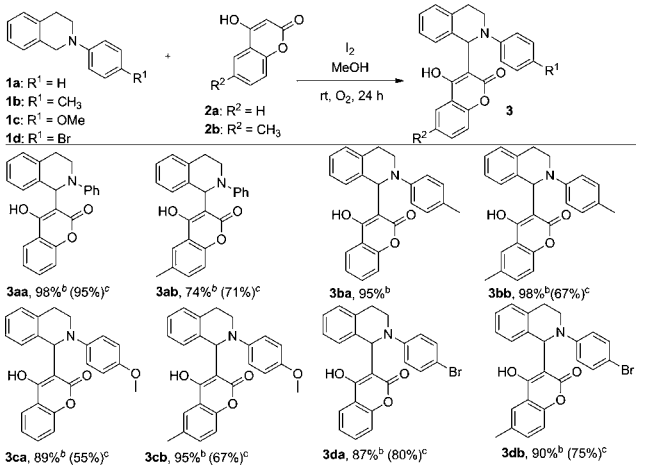
(11) (a) Alagiri, K.; Devadig, P.; Prabhu, K. R. *Chem.—Eur. J.* **2012**, *18*, 5160–5164. (b) Alagiri, K.; Devadig, P.; Prabhu, K. R. *Tetrahedron Lett.* **2012**, *53*, 1456–1459.

(12) (a) Uyanik, M.; Okamoto, H.; Yasui, T.; Ishihara, K. *Science* **2010**, *328*, 1376–1379. (b) Uyanik, M.; Suzuki, D.; Yasui, T.; Ishihara, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 5331–5334. (c) Froehr, T.; Sindlinger, C. P.; Kloeckner, U.; Finkbeiner, P.; Nachtsheim, B. J. *Org. Lett.* **2011**, *13*, 3754–3757. (d) Wei, W.; Zhang, C.; Xu, Y.; Wan, X. *Chem. Commun.* **2011**, *47*, 10827–10829. (e) Ma, L.; Wang, X.; Yu, W.; Han, B. *Chem. Commun.* **2011**, *47*, 11333–11335. (f) Jiang, H.; Huang, H.; Cao, H.; Qi, C. *Org. Lett.* **2010**, *12*, 5561–5563. (g) Zhang, J.; Zhu, D.; Yu, C.; Wan, C.; Wang, Z. *Org. Lett.* **2010**, *12*, 2841–2843. (h) He, T.; Yu, L.; Zhang, L.; Wang, L.; Wang, M. *Org. Lett.* **2011**, *13*, 5016–5019. (i) Kumar, A.; Gupta, G.; Srivastava, S. *Org. Lett.* **2011**, *13*, 6366–6369.

(13) (a) Lamani, M.; Prabhu, K. R. *J. Org. Chem.* **2011**, *76*, 7938–7944. (b) Lamani, M.; Devadig, P.; Prabhu, K. R. *Org. Biomol. Chem.* **2012**, *10*, 2753–2579. (c) Lamani, M.; Prabhu, K. R. *Chem.—Eur. J.* **2012**, *18*, 14638–14642.

(14) The reaction of **1a** and **5a** in I_2/O_2 conditions (48 h) at rt yielded 40% of **5aa**.

Scheme 1. CDC with Coumarins[a]

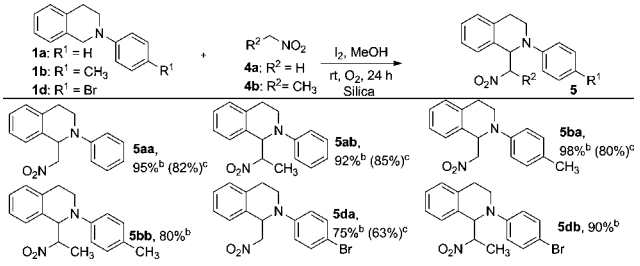


[a] Reaction conditions: **1a**−**1d** (0.24 mmol), **2a**−**2b** (0.29 mmol), MeOH (1 mL), I_2 (10 mol %), O_2 atmosphere. [b] Conversions based on ^{1}H NMR. [c] Isolated yields.

After successfully establishing CDC reactions of coumarins and nitroalkanes, we attempted C−P bond formation by employing alkyl phosphites as nucleophiles to obtain the corresponding α-aminophosphonates (Scheme 3). Generally, metal catalysts are used for the synthesis of α-aminophosphonates under strenuous reaction conditions and need a large excess of phosphite.[8g] Under optimized reaction conditions, tertiary amines **1a**−**d** underwent a smooth coupling with a variety of dialkyl phosphites such as dimethyl phosphite (**6a**), diethyl phosphite (**6b**), diisopropyl phosphite (**6c**), and dibenzyl phosphite (**6d**) to afford corresponding α-aminophosphonates **7ab**, **7ac**, **7ad**, **7ba**, **7bb**, **7ca**, **7cb**, and **7cc** in good to excellent yields (Scheme 3).

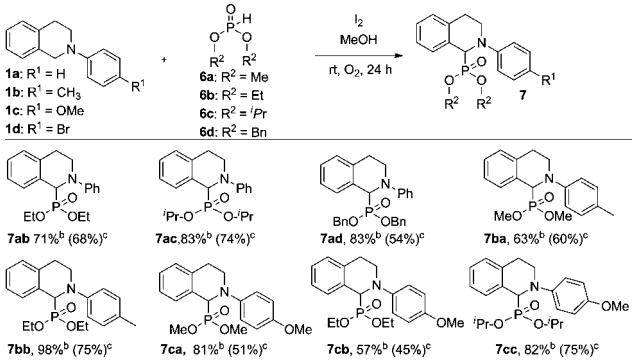
α-Functionalization of tertiary amines provides access to a variety of intermediates that are useful in natural products synthesis.[6b] For example, α-amino nitriles are useful intermediates,[6b,8g] which are synthesized using toxic metal cyanides and halides.[6b] As the CDC methods are a good alternative to obtain α-amino nitriles, we attempted the reaction of TMSCN (**8a**) with THIQs **1a** and **1c** under optimized conditions. As expected, the reaction furnished corresponding cyano derivatives **9aa** and **9ca** in good to excellent yields (Scheme 4). The compatibility of the I_2/O_2 system for CDCs is exploited in the functionalization of THIQs with nucleophiles such as phenol and indole (Scheme 4). Thus, phenol (**8b**) with THIQs **1a** and **1d** furnished Friedel−Crafts products **9ab** and **9db** in good yields. In these examples, THIQs are coupled to phenol selectively at the *para*-position, while the phenolic-OH is unaffected. To the best of our knowledge, this is the first report using phenol as a pronucleophile in CDCs. Further, we found that *N*-methylindole (**8c**) is a good nucleophile for CDCs, which reacted with **1a** and **1d** to give Friedel−Crafts products **9ac** and **9dc** (Scheme 4). The reaction of amide and imide with **1a** resulted in moderate yields of coupled products **9ad** and **9ae** (Scheme 4). Finally, the reaction of TBHP (**8f**)

Scheme 2. CDC with Nitroalkanes[a]



[a] Reaction conditions: **1a**−**1d** (0.24 mmol), **4a**−**4b** (0.1 mL), Silica gel (100 mg), MeOH (1 mL), I_2 (10 mol %), O_2 atmosphere. [b] Conversions, based on ^{1}H NMR. [c]Isolated yields.

Scheme 3. CDC Reactions with Phosphites[a]



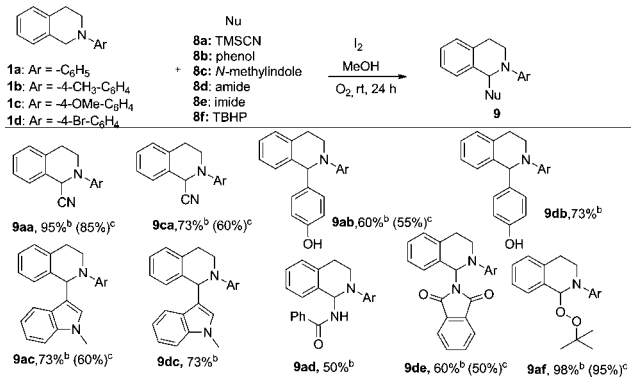
[a] Reaction conditions: **1a**−**1d** (0.24 mmol), **6a**−**6d** (0.29 mmol), MeOH (1 mL), I_2 (10 mol %), O_2 atmosphere. [b] Conversions based on ^{1}H NMR. [c] Isolated yields.

with **1a** under the reaction condition produced the coupled product **9af** in excellent yield (Scheme 4).

The success of CDCs with several nucleophiles led us to explore the coupling of ketones with THIQs under optimal conditions. Disappointingly, the reaction of THIQ **1a** with acetone (**10a**) did not furnish the coupled product even under forcing conditions. As the same reaction can be accomplished using I_2 and TBHP as an oxidant (entry 2, Table 1), the coupling of **1a** with acetone using I_2 and aq. TBHP as an oxidant was attempted.[15] The initial reaction of **1a** with acetone in the presence of I_2 and aq TBHP has resulted in the formation of coupled products in lower yields (20−30%). However, the reaction of **1a** with acetone proceeded successfully with I_2 and aq. TBHP in the presence of L-proline (30 mol %) to furnish the coupled product **11aa** in 95% yield (Scheme 5). This observation was found to be general as THIQs **1b** and **1c** coupled with acetone to afford products **11ba** and **11da** in excellent yields (Scheme 5). Next, active methylene compounds such

(15) While preparing this manuscript, a paper appeared on the synthesis of THIQ derivatives through a CDC reaction, employing KI as the catalyst and aq. TBHP as an external oxidant at 50 °C; Kumar, R. A.; Saidulu, G.; Prasad, K. R.; Kumar, G. S.; Sridhar, B.; Reddy, K. R. *Adv. Synth. Catal.* **2012**, *354*, 2985–2991.

Scheme 4. CDC Reactions with Other Nucleophiles[a]



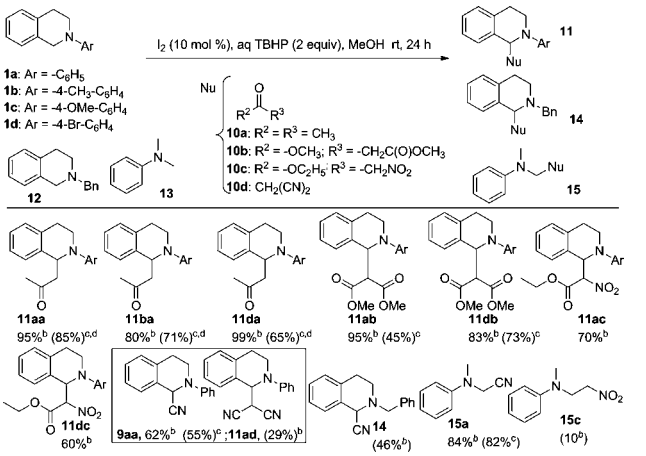
[a] Reaction conditions: **1a**–**1d** (0.24 mmol), **8a**–**8f** (0.29 mmol), MeOH (1 mL), I_2 (10 mol %), O_2 atmosphere. [b] Conversions based on ^{1}H NMR. [c] Isolated yields.

as dimethyl malonate (**10b**) and ethyl-2-nitroacetate (**10c**) underwent a smooth coupling to afford products **11db**, **11ab**, **11ac**, and **11dc** in good yields (Scheme 5). However, malononitrile (**10d**) reacted with **1a** under the stabilized conditions, furnishing a mixture of α-amino nitrile (**9aa**) as the major product along with a minor quantity of coupled product **11ad** (Scheme 5).

As *N*-benzyl substituted THIQs are more attractive substrates for the synthesis of biologically active compounds, the CDC of *N*-benzyltetrahydroisoquonoline with TMSCN in the presence of I_2 and TBHP is attempted, which furnished the coupled cyanated product **14** in moderate yield (46%). Similarly, the CDC of *N,N*-dimethyl aniline with TMSCN resulted in the formation of coupled product **15a** in 82% isolated yield, while a similar reaction with nitromethane resulted in a low yield of the coupled product **15c** (10%, Scheme 5).

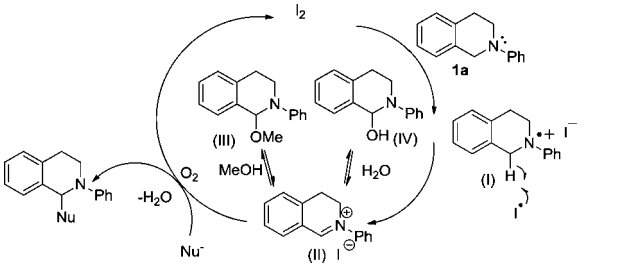
Several control experiments were conducted to gain insight into the mechanism of the I_2 catalyzed CDC reaction. The addition of radical inhibitors such as BHT or TEMPO to the reaction mixture (**1a** and **2a**, I_2 (10 mol %), O_2) has resulted in lowering the yield (40%) of **3aa** even after 48 h, suggesting the possibility of a radical intermediate. The ESI mass spectrometric analysis of the reaction mixture of **1a** with a stoichiometric amount of I_2 and O_2 in MeOH, after 12 h, has shown the formation of the corresponding iminium iodide (**II**) as the major product along with methoxy and hydroxyl substituted products (**III** and **IV**, Scheme 6). After 24 h, the iminium salt was isolated and characterized by ^{1}H NMR, ^{13}C NMR spectroscopic and mass spectrometric analysis, which revealed the formation of iminium iodide (**II**).[16] Based on these experimental observations, we believe that the reaction of tertiary amine **1a** with molecular I_2 (10 mol %) and oxygen

Scheme 5. Coupling Reactions with Carbonyl Derivatives[a]



[a] Reaction conditions: **1a**–**1d** (0.24 mmol), **10a** (0.2 mL), [**10b**–**10d** (0.29 mmol)], MeOH (1 mL), aq TBHP (70%, 0.065 mL, 0.4778 mmol). [b] Conversions based on ^{1}H NMR. [c] Isolated yields. [d] Needed 30 mol % of L-proline.

Scheme 6. A Tentative Reaction Mechanism



generates an iminium iodide (**II**) through a radical intermediate, and the iminium iodide (**II**) thus generated will react with the nucleophile to furnish the coupled product and regenerates I_2 by reacting with molecular O_2 (Scheme 6).[17]

In conclusion, an unprecedented, versatile iodine-catalyzed oxidative CDC reaction of C–H bonds of THIQ under aerobic conditions has been uncovered. This novel catalyst system was found to be very effective and compatible with a wide range of nucleophiles. New and useful nucleophiles such as phenols and indole are employed to accomplish a Friedel–Crafts reaction, and use of ethyl-2-nitroacetate furnished the corresponding nitro compounds. Further studies are ongoing to expand the synthetic utility of this versatile catalytic system.

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Supporting Information Available. Experimental procedures, characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

(16) This intermediate is similar to the one that was observed by Klussmann (see ref 6b and 6e) and Doyle (ref 6g). Leubner (see ref 9c) reported a reaction of *N*-methyl tetrahydroisoquinoline with a stoichiometric amount of I_2. See Supporting Information for a tentative mechanism for I_2/TBHP catalyzed reaction.

(17) Most of the couplings of nucleophiles with tertiary amines discussed here also work with the I_2/TBHP system, which will be presented in due course.