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A Powerful Combination: Recent Achievements on Using TBAI and TBHP as Oxidation System

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Xiao-Feng Wu,[a,b*] Jin-Long Gong,[a] and Xinxin Qi[a]

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The recent achievements on using TBAI (tetrabutylammonium iodide) and TBHP (*tert*-butyl hydroperoxide) as oxidation system have been summarized and discussed.

Introduction

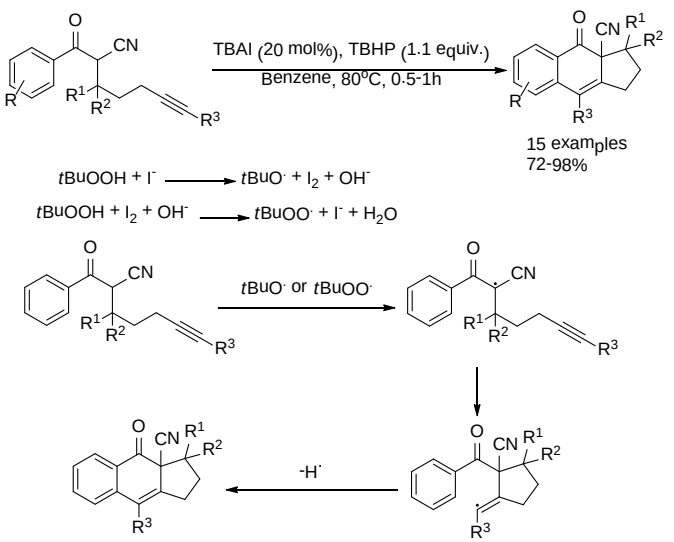
Oxidative transformation is one of the fundamental reactions in modern organic synthesis, which have experienced impressive progress during the last decades.[1] Among the numerous achievements, epoxidation reactions are representative example from academic point of view[2] while *p*-xylene oxidation is vital from the point of industrial importance.[3] Epoxidation have been verified by the Nobel Prize of Chemistry in 2001; while terephthalic acid is an aromatic carboxylic acid core to polyester fibers production which mainly produced by *p*-xylene oxidation. However, large percentage of the known procedures demands the presence of transition metals as catalysts.

Since the end of 20th century, sustainable development has been taken as one of the main targets of our society development. Under this background, 'Green Chemistry' started to be considered more and more by chemists in developing new synthetic methodologies.[4] In the respect of oxidation reactions, catalytic systems without the need of metal catalysts are more appealing than the traditional transition metal relied oxidative transformations. Recently, iodide or hypervalent iodine-promoted organic reactions have received considerable attentions which have already experienced impressive advancements during the past few years.[5] Although these reactions can avoid the usage of metal salts, the stability and toxicity of these compounds lead those transformations have to be paid special attentions. More recently, the using of tetrabutylammonium iodide (TBAI) as catalyst with the combination of *tert*-butyl hydroperoxide (TBHP) as a powerful oxidation system has received unique attentions. In the light of the advantages of TBAI, such as inexpensive, stable and etc., increasing efforts are being put on this topic. Even though the populating of TBAI catalyst in organic synthesis, a general review on this topic is still absent.[6] Taking all these points into consideration and our own interests on TBAI-catalyzed oxidations, we started to prepare a review on this topic. The main achievements on this topic will be discussed and catalogued by the bonds formed (C-C, C-N, C-O, C-S, N-N). The reaction mechanisms will be discussed and compared. Selected examples of substrates will be listed as well and a personal outlook will be given at the end.

TBAI-catalyzed C-C bonds formation

The group of Shia reported an intramolecular radical cascade of the α-cyano-TMS (TMS- = Me_3Si-)/aryl-capped alkynyl aryl alkyl ketones in 2012.[7] The reaction using TBAI as their catalyst and TBHP as the oxidant, a variety of [6,6,5] tricyclic frameworks were constructed which containing a high level of functionalization efficiently (Scheme 1). One main issue is the reaction should be performed in benzene. Regarding the reaction mechanism, this cascade process was proposed to be initiated with abstracting H-atom, α to both cyano and carbonyl groups, by the free radical species *t*-BuO$^{\bullet}$ or *t*-BuOO$^{\bullet}$ generated by a catalytic cycle of oxidants TBHP and I_2.

Scheme 1. Intramolecular radical cyclization.

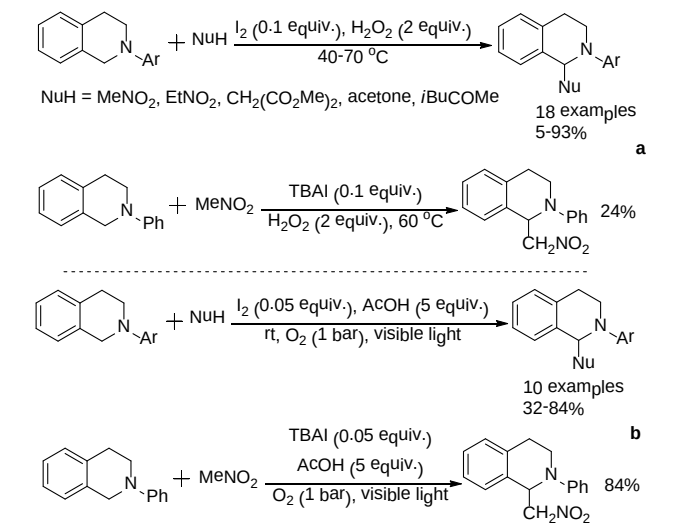


Nachtsheim and co-workers developed an iodocyclization reaction of *o*-alkynylphenyl carboxaldehydes.[8] Highly

substituted 1-naphthalenones were prepared in high yields (up to 91%). In their catalyst system, tetrabutylammonium iodide (TBAI) was applied as the electrophilic iodine source, Oxone was used as a non-nucleophilic co-oxidant, and HFIP (1,1,1,3,3,3-hexafluoro-2-propanol) as a fluorinated protic solvent. TBHP, which was intensively used as co-oxidant in previous (hypo)iodite-catalyzed reactions, seemed to be a nonsuitable co-oxidant due to the nucleophilic properties of the emerging *t*-BuO$^-$ anion which could undergo undesired nucleophilic addition to the reaction intermediate.

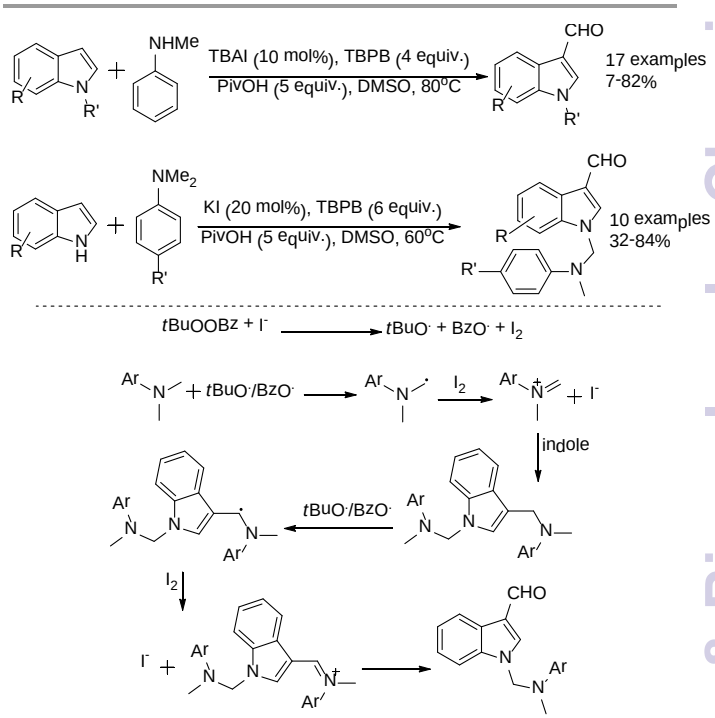
At the beginning of 2013, Itoh and co-workers reported a molecular iodine-catalyzed cross-dehydrogenative coupling (CDC) reaction between tertiary amine and a carbon nucleophile using hydrogen peroxide as the terminal oxidant.[9] The corresponding aza-Henry products were formed in good yields using 0.1 equiv. of molecular iodine and 2 equiv. of H_2O_2 at 40 ^oC (Scheme 2a). TBAI was tested as catalyst under the standard conditions as well, 24% of the desired product was formed. However, when the authors tested their model system with 1 equiv. of molecular iodine in the absence of aq. hydrogen peroxide, only 16% yield of the desired produced was formed and recovered 75% of their starting material. This result suggested that the oxidation of amines requires both molecular iodine and hydrogen peroxide. NaI/H_2O_2/acid as a known system for generated HOI could gave the desired products in 65% yield as well. Additionally, BHT [2,6-bis(1,1-dimethylethyl)-4-methylphenol] as a radical inhibitor was added in their reaction system as well, the reaction was scarcely suppressed and gave 71% of the desired product. Based on these observations, they proposed a HOI catalyzed reaction mechanism. In the same year, the same group reported an improved reaction system (Scheme 2b).[10] They succeed to avoid the usage of H_2O_2 and further decreased the loading of iodine. Molecular oxygen was applied as the terminal oxidant, and visible light from a general-purpose fluorescent lamp was necessary. In this new system, TBAI, CaI_2, KI, MgI_2 and etc. can all be applied as the catalyst and gave the corresponding product in good yield. In the case when one equivalent of molecular iodine was used in the absence of molecular oxygen and visible light irradiation, only a trace amount of the corresponding product was obtained. The same as their precious system, BHT did not inhibit the reaction, which exclude the radical mechanism.

Scheme 2. I_2-catalyzed CDC reaction.



Wang and co-workers developed an interesting TBAI-catalyzed C3-formylation of indoles with *N*-methylaniline as the source.[11] This method can be applied to N-H and *N*-substituted indoles without using toxic phosphorus oxychloride and transition metal catalyst. Good yields of formylated indoles were produced (Scheme 3). *tert*-Butyl peroxybenzoate (TBPB) was used as the oxidant. Notably, under the optimized reaction conditions, TBHP was completely ineffective at 80 ^oC, and only a trace product was obtained at 100 ^oC. The use of H_2O_2 led to no product formation either at 80 ^oC or 100 ^oC. The yield dropped from 82% to 15% in the absence of nBu_4NI, which indicated that the use of nBu_4NI was critical for the success of this reaction. When a radical inhibitor, TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl), was added into the reaction system, the yield of the desired product decreased dramatically to 30% under the optimized conditions. Taking all these into consideration, the author proposed the reaction started with the reaction between an iodide (I^-) ion and TBPB which provide a benzoyloxy radical (or *tert*-butyloxy radical) and iodine (I_2). Soon later, the same group found that replace *N*-methylaniline with 4-substituted-*N*,*N*-dimethylanilines, a C3-formylation and *N*-aminomethylation of indoles occurred using potassium iodide as the best catalyst (Scheme 3).[12] TBAI could gave moderate yield of the desired product in model study. In this two methodologies, pivalic acid was used as the additive as it has been shown to suppress decomposition of indoles under oxidative conditions.[13]

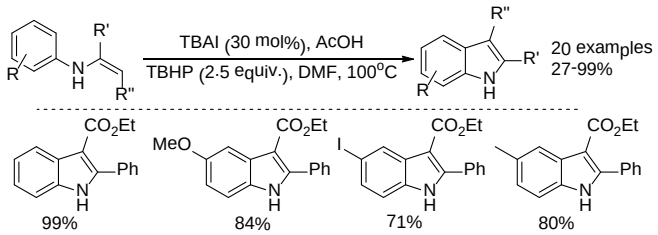
Scheme 3. TBAI-catalyzed formylation of indoles.



Li et al. reported a TBAI-catalyzed intramolecular cross-dehydrogenative coupling (CDC) reaction for the synthesis of 1*H*-indole derivatives.[14] Intramolecular oxidative coupling of *N*-arylenamines proceeded in the presence of a catalytic amount of nBu_4NI and *tert*-butyl hydroperoxide (TBHP) to afford the corresponding 1*H*-indole derivatives in good to excellent yields (Scheme 4). The addition of TEMPO did not suppress the reaction completely, which suggests that a radical pathway does

not predominate in this system. The other iodide salts like LiI, NaI, NH_4I gave worse results.

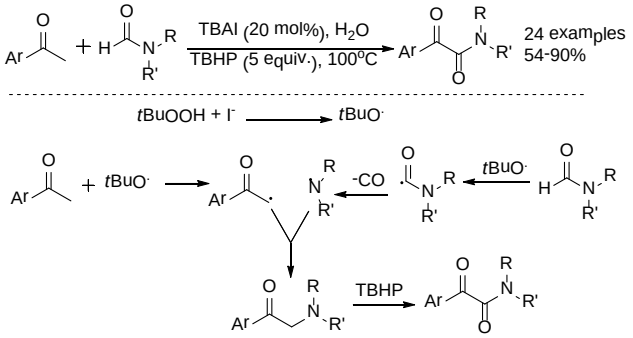
Scheme 4. TBAI-catalyzed indoles synthesis.



TBAI-catalyzed C-N bonds formation

In 2012, a novel and easy practical direct synthesis of α-ketoamides from aryl methyl ketones and dialkylformamides was developed.[15] The procedure based on using TBAI as the catalyst, TBHP as the oxidant and water was required as the reaction media. The desired products were isolated in good yields (Scheme 5). DTBP and BPO (benzoyl peroxide) were examined as the oxidant as well, but none of the two showed activation under the standard condition. In respect of the substrates scope, in addition to the ketones, different dialkylformamides including *N*,*N*-diethylformamide, piperidine-1-carbaldehyde, morpholine-4-carbaldehyde, 4-methylpiperazine-1-carbaldehyde were tested instead of DMF and the corresponding products were obtained in moderate to high yields. Notably, no desired product was observed when piperidine was used instead of piperidine-1-carbaldehyde in their catalyst system. Additionally, 1-arylethanols can be applied as substrates and give access to α-ketoamides in satisfactory yields while 2-oxo-2-phenylacetic acid failed to coupling with DMF under the standard conditions. Regarding the reaction mechanism, the authors proposed the reaction beginning with the *tert*-butoxyl radical generation under the assistance of the iodide anion. This radical traps H from the aryl methyl ketone and DMF respectively to form the corresponding radicals and starts the reaction (Scheme 5). In this article, the author demonstrated that iodine was not effective for this transformation under the same conditions. Wang and co-workers later reported that by the addition of benzoic acid as additive, this transformation can be achieved with iodine as the catalyst in toluene at 80 °C.[16] Moderate to good yields of the desired products were isolated.

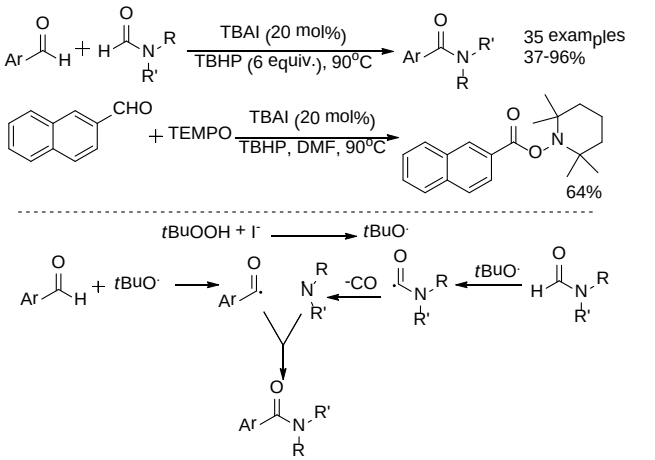
Scheme 5. TBAI-catalyzed synthesis of α-ketoamides.



As indicated in Scheme 5, they failed in the reaction between acetophenone with piperidine under their conditions. In another report, Prabhu and co-workers succeeded in this transformation by using *N*-iodosuccinamide as the catalyst in MeCN at room temperature.[17] In this report, NaI was found to effective as catalyst as well. The combination of TBAI with TBHP was not tested here; only trance of product was formed in the case of using TBAI and H_2O_2 as the oxidation system. TEMPO as a radical scavenger was tested in this system as well, good yield was formed which exclude the possibility of radical process. The authors proposed the corresponding α-iodo compound as the intermediate and followed by reaction with amine and further oxidation.

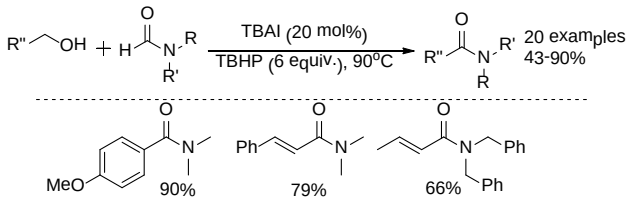
In 2012, Wan and co-workers developed a TBAI-catalyzed oxidative coupling of aldehydes and dialkylformamides.[18] TBHP was applied as the terminal oxidant, all the desired amides were isolated in good yields (Scheme 6). Interestingly, when dimethylamine was tested under the optimized conditions, only less than 5% of the desired product was formed.

Scheme 6. TBAI-catalyzed synthesis of amides from aldehydes.



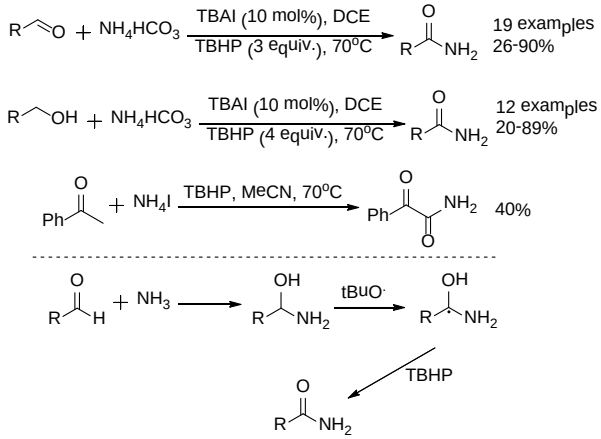
In the same year, Zhu and co-workers described a TBAI-catalyzed synthesis of amides from alcohols and dialkylformamides.[19] Using TBHP as the oxidant, various amides were formed in good yields (Scheme 7). In their optimization process, reaction temperature was found to be critical as no product could be observed at 60 °C while 88% of the desired product was formed at 90 °C. When the reaction was carried out in 1,4-dioxane or THF, unsatisfactory yields were resulted. Further studies indicated that else catalysts including nBu_4NCl, NaI, and CuI showed a lower catalytic activity. No reaction occurred with I_2 as catalyst for this system. Interestingly, the report from Wang's group shown that this transformation can be achieved with I_2 by adding catalytic amount of NaOH as additive.[20]

Scheme 7. TBAI-catalyzed synthesis of amides from alcohols.



In the report of Wan,[18] they demonstrated the reaction of aldehyde with dimethylamine was failed under their conditions. This challenge can be resolved by using ammonium as amine source.[21] Various primary amides were produced from the corresponding benzylic alcohols and aldehydes (Scheme 8). The oxidative amidation of acetophenone was achieved as well using ammonium iodide as both amine source and catalyst. The undesired nitriles were detected in all the cases. Especially when using ammonia as amine source, 25% of benzonitrile was formed. In the mechanistic study, they found benzonitrile could not be transformed into benzamide under the standard conditions. The author proposed the attack of ammonia to aldehydes generating hemiaminals was the first step of this procedure, which can then be converted into the corresponding primary amides *via* dehydrogenation.

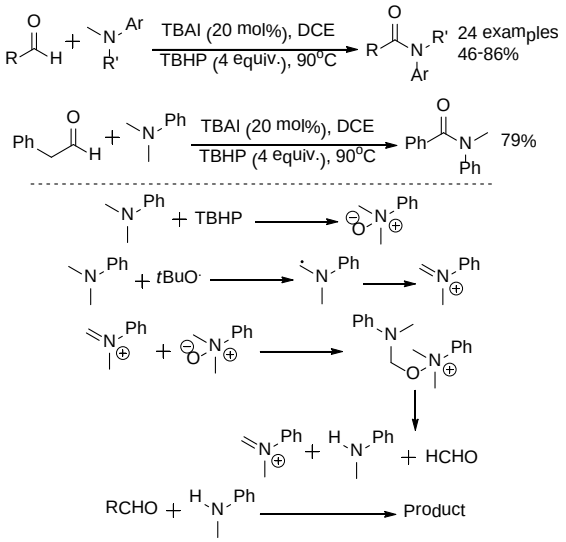
Scheme 8. TBAI-catalyzed synthesis of primary amides.



At the beginning of 2013, a TBAI-catalyzed oxidative synthesis of amides from aldehydes and aromatic tertiary amines was developed.[22] Various amides were isolated in good yields by using TBAI and TBHP as the catalytic system (Scheme 9). I_2 was found to be non-effective for this transformation. Additionally, neither H_2O_2 nor DTBP showed any activation in this transformation. Notably, this reaction could also proceed to afford the desired amides under the optimal conditions by reacting *N*-alkylaniline with aldehydes. For example, *N*-methylaniline or *N*-ethylaniline reacted with benzaldehyde to obtain the corresponding products in 53% and 75% yields, respectively. Interestingly, when 2-phenylacetaldehyde was investigated with *N*,*N*-dimethylaniline under the optimal conditions, *N*-methyl-*N*-phenylbenzamide was produced in 79% yield. Meanwhile, a similar system with lower loading of TBAI in refluxing ethyl acetate was reported [TBAI (2.5 mol %), TBHP (2 equiv.), EtOAc (ethyl acetate), refluxing].[23] In this report, aliphatic amines such as triethylamine and tributylamine can be applied as the coupling partners as well. In both studies, the oxidation of tertiary amines to give secondary amines was proposed to be the first step, and then followed by the reaction of secondary amines with aldehydes to give amides.

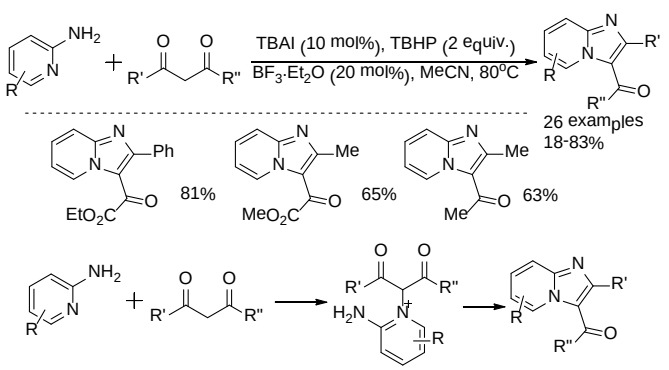
In 2012, TBAI as a reagent for *in situ* generation of hypoiodite for aziridination of alkenes was reported.[24] *m*CPBA (3-chloroperbenzoic acid) was the oxidant needed, TBHP was not effective at all in this case. Based on mechanistic study, they proposed the *in situ* generated hypoiodous acid, HOI, may be the active species in this reaction.

Scheme 9. TBAI-catalyzed synthesis of amides from tertiary amines.



In 2011, TBAI was reported has the ability to catalyze the direct oxidative C-N coupling of 2-aminopyridines with *β*-keto esters and 1,3-diones to give imidazo[1,2-*α*]pyridines (Scheme 10).[25] *tert*-Butyl hydroperoxide (TBHP) was applied as the oxidant and reaction temperature was found has significant effect in this procedure (no product was detected at 60 °C while good yield was formed at 80 °C). Additionally, it is noteworthy to demonstrate that using a catalytic amount of TBAI ensures a good result, while higher loading of TBAI has negative effect on the reaction. The reaction also took place in the absence of $BF_3.Et_2O$, but the yield of product was lower. On the other hand, using 1.0 equiv. of $BF_3.Et_2O$ was less favorable for the reaction. Besides TBAI, NaI and KI were also capable to catalyze this reaction which indicates the not necessaricity of ammonium counterion during the reaction.

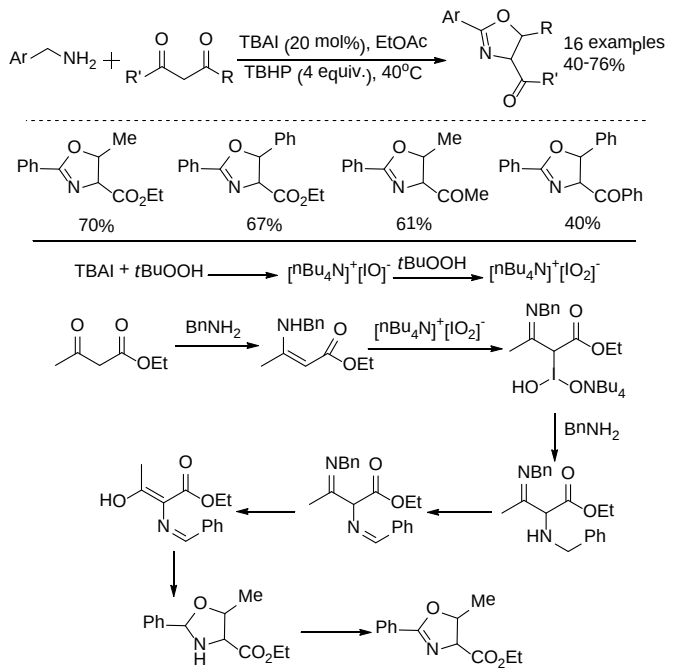
Scheme 10. TBAI-catalyzed synthesis of imidazo[1,2-α]pyridines.



Zhu and co-workers reported a TBAI-catalyzed oxidative synthesis of oxazoles at the beginning of 2012.[26] The corresponding products were formed in good yields in their

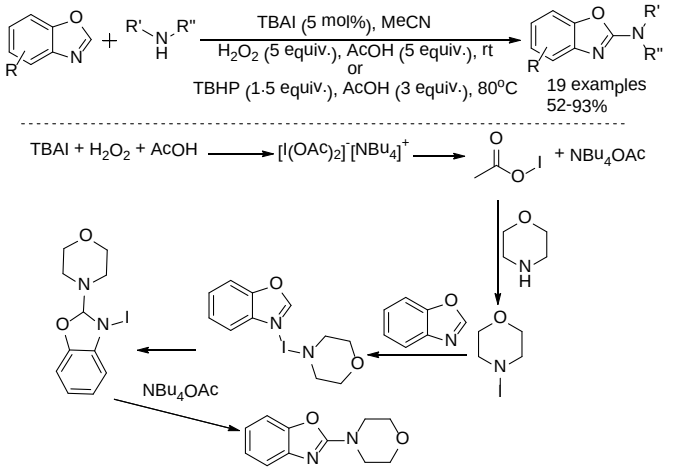
system (Scheme 11). It should be noted that the cascade reaction did not occur in place of nBu_4NI with nBu_4NCl or nBu_4NBr. Additionally, TBHP in water gave better results than the TBHP in decane which suggested that a small amount of water was beneficial to the reaction. Surprisingly, when HOAc or $BF_3.Et_2O$ was used as an additive, a less satisfactory yield was obtained. In the solvents testing, EtOAc afforded the best result, DCE, DMF or MeCN led to lower yield. Adding a radical inhibitor BHT (2,6-di-*tert*-butyl-4-methylphenol) to the reaction system of ethyl acetoacetate with benzylamine, no significant influence was found. Moreover, no radical intermediate was trapped by radical scavenger TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl). These results ruled out the possibility of a radical mechanism. The authors suggested the active iodine species ammonium hypoiodite ([n-$Bu_4N]^+[IO]^-$) or iodite (n-$[Bu_4N]^+[IO_2]^-$) plays an important role in this reaction

Scheme 11. TBAI-catalyzed synthesis of oxazoles.

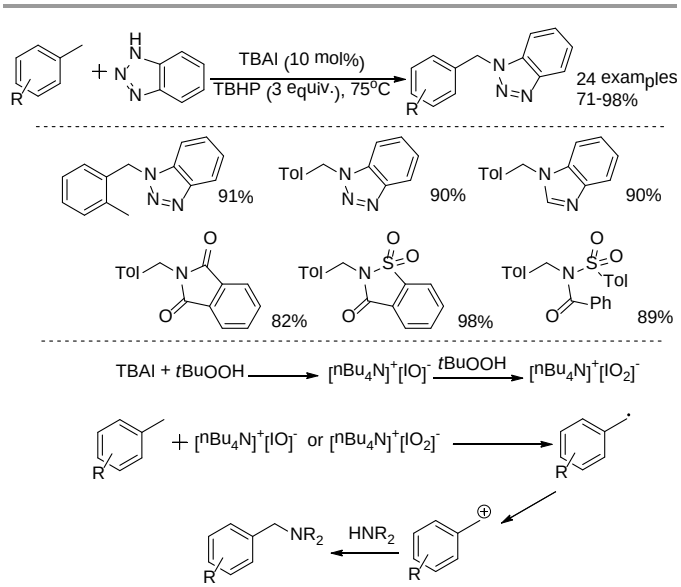


In 2011, an efficient procedure for amination of benzoxazoles based on the use of catalytic amount of TBAI and aqueous solutions of H_2O_2 or TBHP as co-oxidant was developed.[27] Highly desirable 2-aminobenzoxazoles were isolated in excellent yields (Scheme 12). In their optimization process, tetrabutylammoniumbromide and -chloride showed no catalytic activity at all. Addition of a base such as K_2CO_3 or NEt_3 resulted in the complete loss of reactivity. In contrast, when carboxylic acids, in particular acetic acid or benzoic acid, were added to the reaction mixture, the yields of the desired product increased significantly to 68% and 70% respectively. Regarding the reaction mechanism, addition of radical scavenger TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl) had only a slight impact on the yield of the desired product. Furthermore no TEMPO-bound intermediate could be observed. Thus a radical mechanism can be ruled out. Since catalytic amounts of I_2 (without co-oxidant) did not yield the desired product, the *in situ* generation of I_2 and its subsequent function as a mild Lewis acid can be excluded as well. Then the author proposed +I should be the active catalyst. Thus *N*-iodomorpholine hydroiodide was synthesized and further investigated. The reaction of hydroiodide with benzoxazole gave the corresponding product in 33% yield. A two-fold excess of hydroiodide did not increase the yield. Nevertheless, when catalytic amount of hydroiodide (10 mol%) was used, the corresponding product was isolated in 92% yield. Based on all these observations, the authors stated that the activation of the amine via *in situ* formation of a highly reactive N-I bond from TBAI and the co-oxidant seems to be the reaction pathway which could also explain the effect of carboxylic acids.

Scheme 12. TBAI-catalyzed synthesis of amination of benzoxazoles.



Scheme 13. TBAI-catalyzed amination of toluenes.

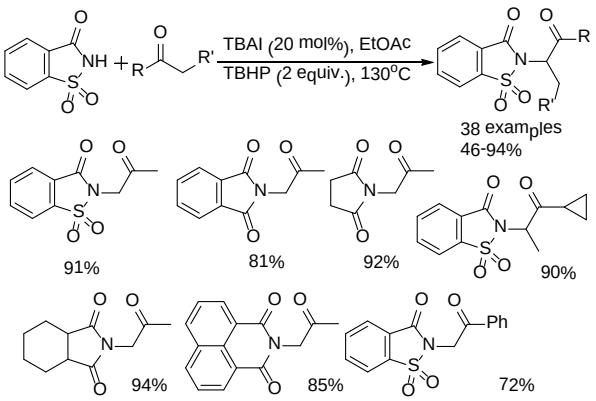


In 2013, Zhu and co-workers reported a novel n-Bu_4NI-catalyzed method for the oxidative coupling of benzylic C-H substrates with unmodified amines.[28] Various amination products were obtained in good to excellent yields by using TBHP (70% in water) as an environmentally benign oxidant (Scheme 13). This method affords a facile metal-free approach for the synthesis of imidazole and purine nucleoside derivatives and has also been easily scaled-up to the gram scale. In the mechanism studies, when a radical inhibitor, BHT, was

introduced into the reaction mixture, the formation of the desired product was completely suppressed. Furthermore, replacing n-Bu_4NI with I_2 led to no product. Interestingly, the reaction proceeded smoothly by the combined use of n-Bu_4NOH and I_2, which could afford the desired product in 76% yield. The authors proposed that the active hypoiodite [n-$Bu_4N]^+[IO]^-$ or iodite [n-$Bu_4N]^+[IO_2]^-$ plays an important role in the sp^3 C-H amine reactions. Additionally, the benzyl radical intermediate was trapped by a radical scavenger, TEMPO, and the oxyamination product was isolated in 62% yield.

More recently, Zhang and co-workers developed a TBAI-catalyzed oxidative imidation of ketones and imides.[29] α-Amino ketones were produced in good yields (Scheme 14). In this reaction, the use of some other catalysts, such as NaI, NH_4I, nBu_4NBr, nBu_4NCl, I_2, and NIS, the yields of the desired product decreased dramatically, or no product was observed. In all the tested oxidants, TBHP was the most effective peroxide in the process, other peroxides such as $K_2S_2O_8$, di-*tert*-butylperoxide (TBP), O_2 and 30% H_2O_2 did not perform well. Regarding the amines, amines like pyrrolidine and morpholine did not give the desired aminated products. In respect of the reaction mechanism, when TEMPO was added to the imidation reaction of pentan-3-one under the optimal condition, after 3 h, trace amount of the desired product was observed. The authors proposed the radical addition of enol to provide the α-functionalized ketone as a possible reaction pathway.

Scheme 14. TBAI-catalyzed amination of ketones.

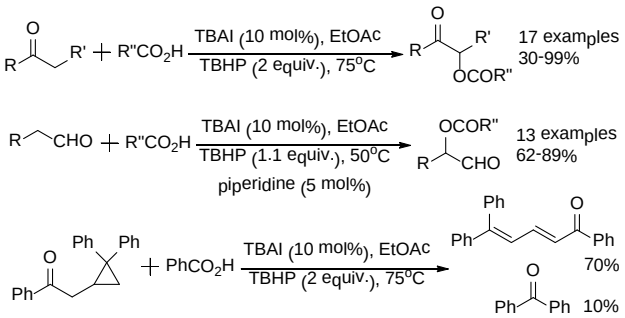


In 2011, Wan and co-workers described an efficient synthetic methodology for C-N bond formation based upon *in situ* generation of TsN·NaI.[30] *N*-Sulfonyl formamidines were produced from sulfonamides and formamides in good yields. NaI was used as the catalyst and TBHP as the oxidant. As the authors pointed out, TBAI was as effective as NaI for this transformation.

TBAI-catalyzed C-O bonds formation

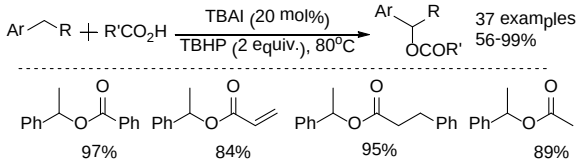
In 2010, Ishihara and co-workers reported a cycloetherification of ketophenols.[31] 2-Acyl-2,3-dihydrobenzofuran derivatives were isolated in excellent yields by using TBAI as the catalyst and H_2O_2 as the oxidant. When chiral quaternary ammonium iodide was applied as the catalyst, this oxidative transformation can be achieved in an enantioselective manner. In situ generated hypoiodite ($[R_4N]^+[IO]^-$) or iodite ($[R_4N]^+[IO_2]^-$ was proposed to be the active catalyst. Later on, they reported their achievements on the intermolecular version.[32] In the presence of TBAI and TBHP, ketones, aldehydes, and 1,3-dicarbonyl compounds were reacted with carboxylic acids and gave the corresponding α-acyloxycarbonyl compounds in good to excellent yields (Scheme 15). In the case of α-oxyacylation of aldehydes, piperidine was needed as an additive and leads the reaction under milder conditions. In the mechanism study, they confirmed the existence of hypoiodite or iodite. By the reaction of diphenylcyclopropyl ketone, they confirmed the reaction included a radical intermediate.

Scheme 15. TBAI-catalyzed α-oxyacylation of ketones and aldehydes.



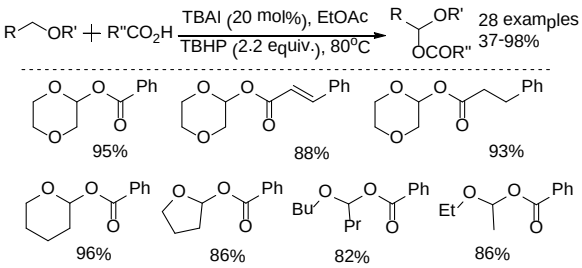
In 2012, the direct esterification of a benzyl C-H bond using TBAI as catalyst and TBHP as co-oxidant was reported.[33] Benzylic substrates were reacted smoothly with various carboxylic acids to give the desired esters with good to excellent yields (Scheme 16). This method was also suitable for the *O*-protection of *N*-Boc amino acids (Boc = *tert*-butoxycarbonyl). Interestingly, the other iodides such as NaI and CuI showed no catalytic activity for this transformation. Several mechanistic studies were performed. In the competitive esterifications involving toluene and its deuterated derivative toluene-d^8, obvious kinetic isotope effects (k_H/k_D=9/1) was observed, which indicating that the cleavage of benzyl C-H bond was involved in the rate-determining step. The yield of the reaction decreased when addition of the radical scavenger TEMPO or BHT to the reaction mixture. In the reaction with TEMPO, the oxyamination product, which was formed through the trapping of the benzyl radical by TEMPO, was separated in 58% yield. This result indicates that the benzyl radical was involved in the catalytic cycle of this esterification. Based on those observations, they proposed a reasonable reaction mechanism which is similar as shown in Scheme 13. The reaction started with the oxidation of TBAI to form the {$[Bu_4N]^+[IO]^-$} or {$[Bu_4N]^+[IO_2]^-$} species, which is going to induce the homolysis of a benzyl C-H bond to give a benzyl radical which is the rate-determining step in the whole reaction. The single electron of hydrogen is captured by hypoiodite which is subsequently reduced to Bu_4NI and the benzyl radical is liable to be oxidized by the hypoiodite species to form the benzyl cation. In this redox process, the excess oxygen atom of hypoiodite captures the proton of benzoic acid to give the benzoate anion and a water molecule. The final coupling between the benzoate anion and benzyl cation gives the ester product.

Scheme 16. TBAI-catalyzed esterification of benzyl C-H bonds.

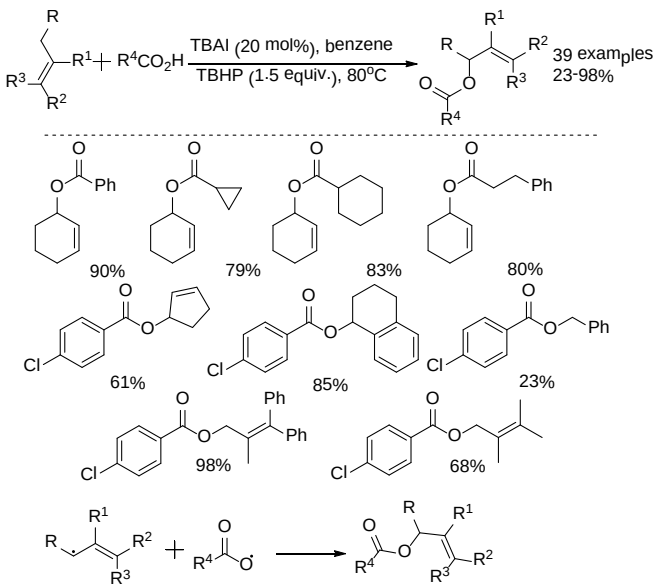


In 2011, Wan and co-workers reported a TBAI-catalyzed oxidative coupling of carboxylic acids with ethers.[34] Various α-oxyacylated ethers were isolated in good yields (Scheme 17). In their model study on the coupling of benzoic acid with 1,4-dioxane, all the other oxidant like oxone, H_2O_2, O_2 and etc. were found to be ineffective when combined with TBAI. The using of metal catalysts like $Pd(OAc)_2$, CuI, CuCl, and $RuCl_3$ instead of TBAI did not gave any of the desired product. In mechanistic study, TEMPO was found suppressed the reaction. No coupling occurred when TBAI was replaced with iodine and the desired product can be formed in low yield by switching the catalyst to KI. Hence, the author proposed TBAI promoted decomposition of TBHP to the *tert*-butoxyl radical and a hydroxyl anion started the transformation.

Scheme 17. TBAI-catalyzed oxidative C-O bond formation.

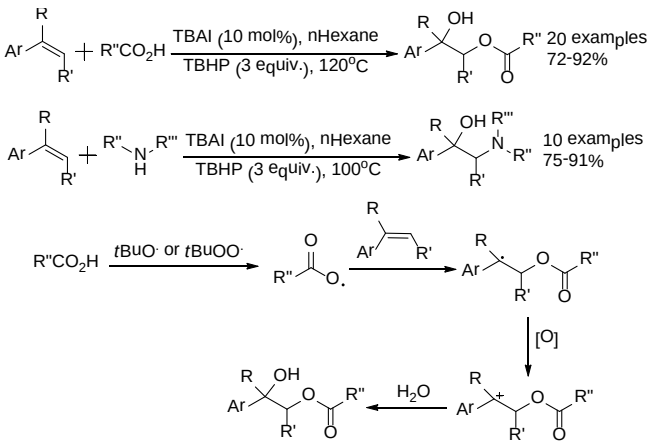


Scheme 18. TBAI-catalyzed coupling of carboxylic acids with allylic compounds.



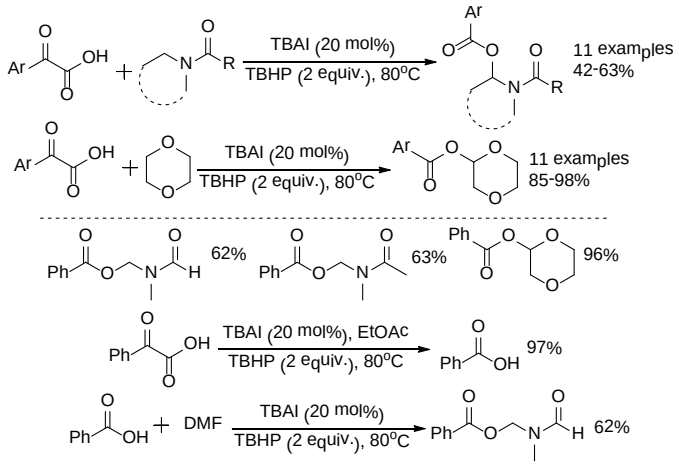
Wan and co-workers developed a TBAI-catalyzed oxidative coupling of carboxylic acids with allylic compounds.[35] Allylic esters were synthesized by the selective coupling of acyloxy and allylic radicals in good yields with TBHP as the oxidant (Scheme 18). In control experiments, no reaction occurred by the combination of sodium benzoate and cyclohexene. 3-Chloroperoxybenzoic acid, a known acyloxy radical donor, was also a suitable reaction partner for the transformation. Notably, a *tert*-butyl perester, from the coupling of the acyloxy and *tert*-butoxyl radicals, was detected by LC-MS in the reaction mixture of 4-bromobenzoic acid with cyclohexene. When hippuric acid was used as a reactant, both the *tert*-butyl perester and decarboxylation product were observed as by-products. The formation of the desired allylic ester was completely suppressed by introducing TEMPO to the reaction mixture. The compound from the reaction of TEMPO and the allylic radical was isolated in 31% yield. Hence, proposed the *tert*-butoxyl and *tert*-butylperoxy radicals from TBHP abstract hydrogen atoms from the substrates then giving the product.

Scheme 19. TBAI-catalyzed difunctionalization of alkenes.



More recently, Zhu and co-workers reported a nBu_4NI-catalyzed regioselective difunctionalization of unactivated alkenes.[36] Various carboxylic acids and amines could react smoothly with alkenes to give the corresponding dioxygenation and oxyamidation products, respectively (Scheme 19). The substrate was rapidly consumed with only a trace amount of the product was detected when $K_2S_2O_4$ was used as an oxidant. Other oxidants such as O_2, H_2O_2, and DTBP gave unsatisfactory results. Additionally, control experiments demonstrated that no desired product could be identified when either nBu_4NI or TBHP was absent. And the best result was afforded in n-hexane.

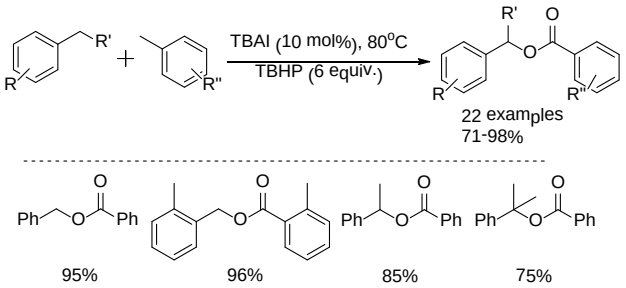
Scheme 20. TBAI-catalyzed decarboxylative acyloxylation of sp^3 C-H bond.



In 2013, TBAI was applied as catalyst in the decarboxylative acyloxylation of an sp^3 C-H bond in formamides and ethers.[37] A variety of *N*-acyloxymethylamides and *α*-acyloxy ethers were easily synthesized in good yields (Scheme 20). For the reaction pathway, the authors proposed the corresponding carboxylic acid as the intermediate, as benzoic acid was isolated in 97% yield from phenylglyoxylic acid when the reaction was performed in ethyl acetate under the same conditions. On the other hand, the reaction of benzoic acid with DMF also gave the *N*-acyloxymethylamide in 62% isolated yield. Furthermore, the reaction was suppressed by addition of a radical scavenger, such as TEMPO. Hence, a radical pathway was anticipated.

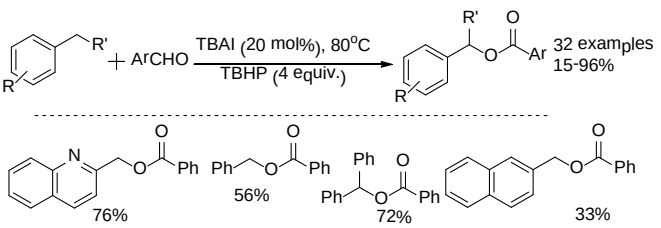
Patel and co-workers developed for the first time a TBAI-catalyzed oxidation of alkylbenzenes to benzylic esters.[38] This method gives a self-coupled product for mono or poly methylatedbenzenes (Scheme 21). The cross-coupled product can be prepared from ethylbenzene and methylbenzene where the acid part is derived from methylbenzene and the benzyl cation is derived from ethylbenzene. Various functional groups are tolerated under the present reaction conditions. In their optimization process, no desired product could be obtained when oxidants H_2O_2, DDQ (2,3-dichloro-5,6-dicyanobenzoquinone), $PhI(OAc)_2$ were used instead of TBHP. Other halogen species such as Bu_4NBr, KI and I_2 were found to be completely ineffective. In the absence of either the catalyst (TBAI) or the oxidant (TBHP) failed to bring about the desired transformation. Regarding the reaction mechanism, they proposed the active hypoiodite $[Bu_4N^+][IO]^-$ species would initiate a homolytic cleavage at the benzylic C-H bond of the toluene to give a benzyl radical. Formation of a benzyl radical could be the rate determining step in the entire reaction. The benzylic radical was further oxidized by the hypoiodite species $[Bu_4N^+][IO]^-$ to a benzyl cation. Alternatively, some of the alkylbenzene could be converted to its alcohol via a radical oxidation path and subsequently to corresponding acid via an aldehyde intermediate. After the formation of the acid, the oxygen atom of the hypoiodite species $[IO]^-$ removes the acidic proton from the benzoic acid, giving a benzoate ion. Finally, the coupling between the in situ generated benzoate ion and the benzyl cation would give the desired ester.

Scheme 21. TBAI-catalyzed oxidative transformation of alkylbenzenes.



Wang and co-workers reported a TBAI-catalyzed benzylic C-H acyloxylation of 2-methylquinolines with readily available aromatic aldehydes in 2012.[39] The corresponding products were produced in good to excellent yields under mild and clean reaction conditions using *tert*-butyl hydroperoxide as the green terminal oxidant (Scheme 22). This reaction could be inhibited by the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as well. Detailly, firstly, TBHP and TBPB (*tert*-butyl peroxybenzoate) was decomposed by the iodide ion to generate a *tert*-butoxyl radical and benzoic acid. The iodide ion is oxidized to the corresponding (hypo)iodites ($[IO]^-$ or $[IO_2]^-$). Subsequently, the *tert*-butoxyl radical or (hypo)iodites abstract a hydrogen atom from the benzylic C-H bond of alkylarene to afford benzylic radical, which was re-oxidized quickly by (hypo)iodites to provide benzyl cation. Finally, the reaction of benzyl cation with the benzoate anion affords the ester. Notably, it has been reported that the reaction of 2-picoline *N*-oxide with acetic anhydride yields the 2-pyridylcarbinol acetate, together with some sp^2 C-H acyloxylation products. In the case of 2-methylquinolines, neither 2-methylquinoline *N*-oxide nor the sp^2 C-H acyloxylation product was detected.

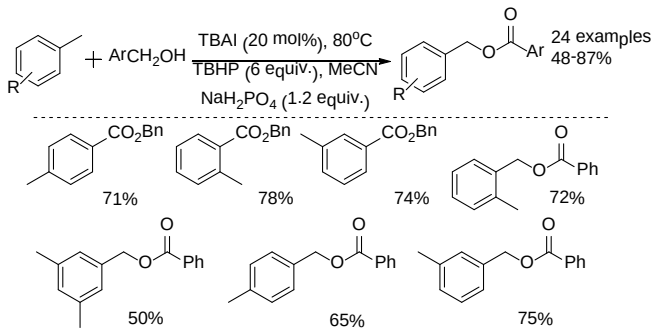
Scheme 22. TBAI-catalyzed reaction of alkylbenzenes with aldehydes.



Fu's group found direct esterification of alcohols with toluene derivatives could be achieved by using nBu_4NI as the catalyst and *tert*-butyl hydroperoxide as the oxidant (Scheme 23).[40] In this process, the addition of NaH_2PO_4 can improve the yield in some distance and applying BHT as a radical inhibitor can completely inhibited the reaction. 60% of 2,2,6,6-tetramethylpiperidin-1-yl 1-naphthoate was isolated by adding two equivalents of TEMPO to the reaction mixture. These observations suggested that the esterification reaction occurred through a sequential oxidation involving: (1) radical initiated oxidation of alcohol to aldehyde; (2) oxidation of aldehyde to carboxylic acid via a carbonyl radical intermediate; (3) oxidative coupling of carboxylic acid and toluene to form benzyl ester. Additionally, for this system, when Bu_4NI was replaced by KI, the yield of benzyl 1-naphthoate dropped to 11%. However, addition of a phase transfer reagent (benzo-18-crown-6) can improve the yield of the desired product to 74%. Although no ester product was observed using I_2 as the catalyst, 84% yield of the ester was formed by adding additionally a catalytic amount of Bu_4NBr. On the other hand, employ

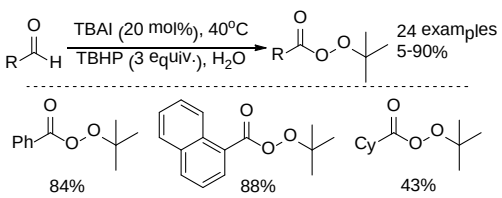
Bu_4NBr only led to a dramatic decrease of the yield of the desired ester.

Scheme 23. TBAI-catalyzed reaction of alkylbenzenes with alcohols.



In 2011, Wan and co-workers developed a Bu_4NI-catalyzed C-H oxidation of aldehydes with TBHP to produce *tert*-butyl peresters.[41] This process represents the first synthesis of *tert*-butyl peresters directly from aldehydes and TBHP, all the desired products were formed in good yields (Scheme 24). When TEMPO was added to the reaction, the product, adduct of acyl radical and TEMPO, was obtained in nearly quantitative yield. The combination of Bu_4NOH and iodine (*in situ* generation of $[Bu_4N]^+[IO]^-$) did not give any desired product. Based on the control experiments, a radical process was proposed. Initially, the *tert*-butoxyl and *tert*-butylperoxy radicals were generated in the catalytic system. The resulting *tert*-butoxyl radical traps H from aldehyde to form the acyl radical. The coupling of the acyl radical and the *tert*-butylperoxy radical affords the desired perester

Scheme 24. TBAI-catalyzed synthesis of peresters.



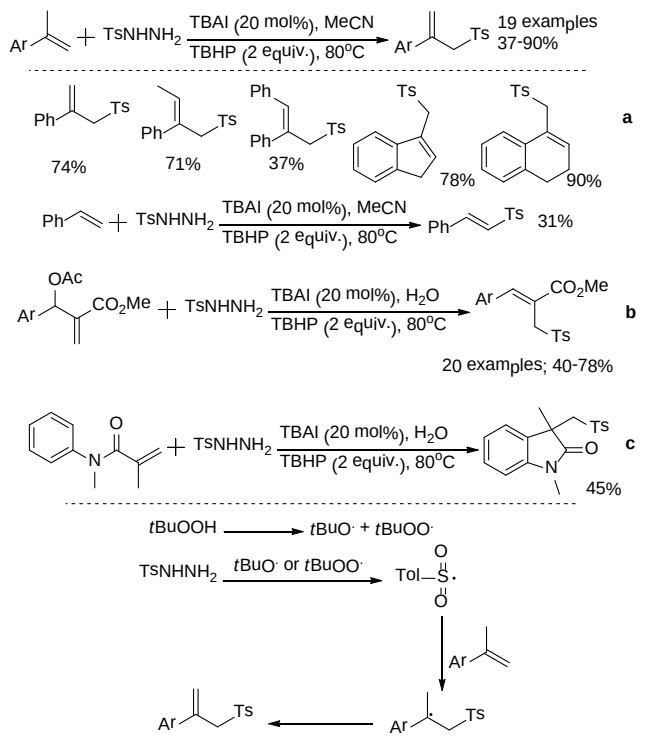
Barbas' group developed a TBAI-catalyzed cross coupling reaction of aldehydes with *N*-hydroxyimides, hexafluoroisopropyl alcohol, and sulfonimides in 2012.[42] This method succeed to provide active esters and imides in moderate to excellent yields. The resulting active intermediates can be directly converted into amides or esters in one-pot manner. A possible reaction mechanism was proposed. Initially, nBu_4NI was oxidized by TBHP to generate the active intermediate iodide and the *tert*-butoxyl and *tert*-butylperoxyl radicals. These radicals subsequently abstract a hydrogen atom from the acetal or aminal species, which formed from the reaction of the nucleophiles with the aldehyde, and the resulting radical species were then further oxidized to the product esters or imides.

TBAI-catalyzed C-S bonds formation

In 2013, Li and co-workers described the allylic sulfonylation of α-methyl styrenes by using TBAI as the catalyst.[43] Sulfonyl radicals generated from sulfonylhydrazides by the Bu_4NI-TBHP catalysis system underwent addition to a variety of α-methyl styrene derivatives to give the corresponding allylic sulfones in moderate to good yields. A variety of substituted groups, such as methyl, methoxyl, fluoro, chloro, bromo, trifluoromethyl and naphthyl, were well tolerated and the desired sulfones were produced selectively (Scheme 25a). In the control experiments, TEMPO, a radical-trapping reagent, was introduced into the reaction mixture and the formation of the desired sulfone was found been completely suppressed. Then, α-methyl styrene alone was treated with TEMPO under the standard conditions, but no adduct of TEMPO and the allylic radical was isolated. At last, the coupling of styrene with $TsNHNH_2$ was found could take place as well and gave the corresponding sulfone in 31% yield. Later on, this catalytic system was applied in the synthesis of allyl aryl sulfone derivatives from Baylis-Hillman acetates and sulfonylhydrazides (Scheme 25b).[44] In the tested solvents, water gave the best results and moderate yields were isolated in most of the cases. More recently, a catalytic system consisting of KI, 18-crown-6, and TBHP for the synthesis of sulfonated oxindoles was reported. They using activated alkenes and sulfonylhydrazides as substrates and water as solvent, the desired oxindoles were formed in moderate to good yields. The combination of TBAI and TBHP were tested as catalyst under the same conditions as well, and 45% of the desired product was formed (Scheme 25c).[45] For the reaction mechanisms in the latter two cases, they are similar with the previous one. They all started with formation of sulfonyl radical.

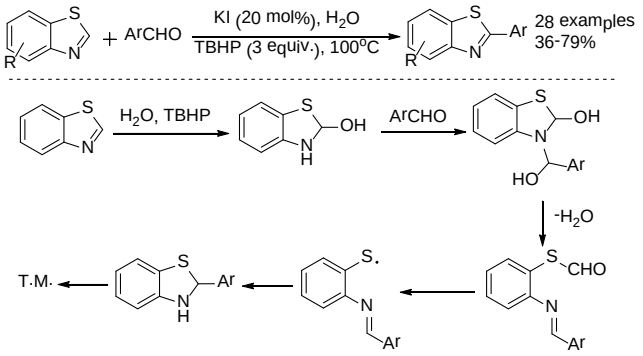
More recently, Deng and co-workers found that sulfonyl radical can be generated from sodium sulfinates in acidic media in the presence of TBHP and TBAI as well. The generated sulfonyl radical was applied in the 2-sulfonylation of indoles.[46]

Scheme 25. TBAI-catalyzed sulfonylation of alkenes.



At the end of 2013, Cui and co-workers developed a KI-catalyzed oxidative coupling of benzothiazoles with aryl aldehydes.[47] They using TBHP as an oxidant in neat water, various 2-aryl benzothiazoles were prepared in 36-79% yields (Scheme 26). TBAI showed the same reactivity as KI under the same conditions and the authors proved this transformation proceeded via a radical process. Notably, not the acyl radical as normally estimated but thio radical.

Scheme 26. TBAI-catalyzed synthesis of 2-aryl benzothiazoles.



In addition, Wan and co-workers developed a procedure for the synthesis of *N*-nitrosamines using nitromethane as the source of the nitroso group under catalytic conditions *via* C-N cleavage.[48] TBAI was found to be as effective as KI, could gave the desired product in excellent yields. For the reaction mechanism, firstly, iodide is oxidized to hypoiodite by TBHP, followed by the formation of iodo(nitro)methane. The iodo(nitro)methane formed rearranged and decomposed into formaldehyde and NO^+ go through 2-oxo-1,2-oxaziridin-2-ium as the intermediate. Finally, nucleophilic attack of the amine on NO^+ gave the desired product. Tertiary amines can be transformed as well via oxidative C-N cleavage with higher loading of oxidant.

Summery

The contributions on TBAI-catalyzed oxidative transformations with TBHP as oxidant have been collected and discussed. The combination of TBAI and TBHP as a powerful green catalyst system, make the reactions which usually need metal catalysts come to "metal-free". The reaction conditions are generally mild and the functional group tolerance is excellent. Additionally, as the advantages of TBAI and TBHP, we are expecting a boom in this topic.

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Notes and references

[a] Department of Chemistry, Zhejiang Sci-Tech University, Xiasha Campus, Hangzhou, Zhejiang Province, 310018, People's Republic of China.
E-mail: xiao-feng.wu@catalysis.de

[b] Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Strasse 29a, 18059 Rostock (Germany).

1 J. E. Bäckvall, *Modern Oxidation Methods*, 2nd ed., Wiley-VCH, Weinheim, **2010**.
2 a) G. De Faveri, G. Ilyashenko, M. Watkinson, *Chem. Soc. Rev.* **2011**, *40*, 1722-1760; b) P. Saisaha, J. W. de Boer, W. R. Browne, *Chem. Soc. Rev.* **2013**, *42*, 2059-2074.
3 R. A. F. Tomas, J. C. M. Bordado, J. F. P. Gomes, *Chem. Rev.* **2013**, *113*, 7421-7469.
4 a) N. Winterton, *Chemistry for Sustainable Technologies*, RSC Publishing, **2010**; b) R. A. Sheldon, I. Arends, U. Hanefeld, *Green Chemistry and Catalysis*, Wiley-VCH, **2007**; c) G. Rothenberg, *Catalysis: Concepts and Green Applications*, Wiley-VCH, **2008**.
5 a) H. Togo, S. Iida, *Synlett* **2006**, 2159-2175; b) M. Ochiai, K. Miyamoto, *Eur. J. Org. Chem.* **2008**, 4229-4239; c) M. Uyanik, K. Ishihara, *ChemCatChem* **2012**, *4*, 177-185; d) Z. Zheng, D. Zhang-Negrerie, Y. Du, K. Zhao, *Sci. Chin. Chem.* **2014**, *57*, 189-214.
6 The contributions from Ishihara's group on TBAI-catalyzed oxidation reactions have been mentioned by their own in 2012 in Ref. 5c.
7 Y. -C. Wong, C. -T. Tseng, T. -T. Kao, Y. -C. Yeh, K. -S. Shia, *Org. Lett.* **2012**, *14*, 6024-6027.
8 U. Kloeckner, P. Finkbeiner, B. J. Nachtsheim, *J. Org. Chem.* **2013**, *78*, 2751-2756.
9 T. Nobuta, N. Tada, A. Fujiya, A. Kariya, T. Miura, A. Itoh, *Org. Lett.* **2013**, *15*, 574-577.
10 T. Nobuta, A. Fujiya, T. Yamaguchi, N. Tada, T. Miura, A. Itoh, *RSC Adv.* **2013**, *3*, 10189-10192.
11 L. -T. Li, J. Huang, H. -Y. Li, L. -J. Wen, P. Wang, B. Wang, *Chem. Commun.* **2012**, *48*, 5187-5189.
12 L. -T. Li, H. -Y. Li, L. -J. Xing, L. -J. Wen, P. Wang, B. Wang, *Org. Biomol. Chem.* **2012**, *10*, 9519-9522.
13 a) W. Wu, W. Su, *J. Am. Chem. Soc.* **2011**, *133*, 11924-11927; b) E. M. Ferreira, B. M. Stoltz, *J. Am. Chem. Soc.* **2003**, *125*, 9578-9579.
14 Z. Jia, T. Nagano, X. Li, A. S. C. Chan, *Eur. J. Org. Chem.* **2013**, 858-861.
15 W. -P. Mai, H. -H. Wang, Z. -C. Li, J. -W. Yuan, Y. -M. Xiao, L. -R. Yang, P. Mao, L. -B. Qu, *Chem. Commun.* **2012**, *48*, 10117-10119.
16 Q. Zhao, T. Miao, X. Zhang, W. Zhou, L. Wang, *Org. Biomol. Chem.* **2013**, *11*, 1867-1873.
17 M. Lamani, K. R. Prabhu, *Chem. Eur. J.* **2012**, *18*, 14638-14642.
18 Z. Liu, J. Zhang, S. Chen, E. Shi, Y. Xu, X. Wan, *Angew. Chem. Int. Ed.* **2012**, *51*, 3231-3235.
19 H. Li, J. Xie, Q. Xue, Y. Cheng, C. Zhu, *Tetrahedron Lett.* **2012**, *53*, 6479-6482.
20 K. Xu, Y. Hu, S. Zhang, Z. Zha, Z. Wang, *Chem. Eur. J.* **2012**, *18*, 9793-9797.
21 G. Wang, Q. -Y. Yu, S. -Y. Chen, X. -Q. Yu, *Org. Biomol. Chem.* **2014**, *12*, 414-417.
22 W. -P. Mai, G. Song, J. -W. Yuan, L. -R. Yang, G. -C. Sun, Y. -M. Xiao, P. Mao, L. -B. Qu, *RSC Adv.* **2013**, *3*, 3869-3872.
23 S. Wang, J. Wang, R. Guo, G. Wang, S. -Y. Chen, X. -Q. Yu, *Tetrahedron Lett.* **2013**, *54*, 6233-6236.
24 A. Yoshimura, K. R. Middleton, C. Zhu, V. N. Nemykin, V. V. Zhdankin, *Angew. Chem. Int. Ed.* **2012**, *51*, 8059-8062.

25 L. Ma, X. Wang, W. Yu, B. Han, *Chem. Commun*. **2011**, *47*, 11333-11335.
26 J. Xie, H. Jiang, Y. Cheng, C. Zhu, *Chem. Commun.* **2012**, *48*, 979-981.
27 T. Froehr, C. P. Sindlinger, U. Kloeckner, P. Finkbeiner, B. J. Nachtsheim, *Org. Lett*. **2011**, *13*, 3754-3757.
28 Q. Xue, J. Xie, H. Li, Y. Cheng, C. Zhu, *Chem. Commun.* **2013**, *49*, 3700-3702.
29 Y. Lv, Y. Li, T. Xiong, Y. Lu, Q. Liu, Q. Zhang, *Chem. Commun.* **2014**, *50*, 2367-2369.
30 S. Chen, Y. Xu, X. Wan, *Org. Lett.* **2011**, *13*, 6152-6155.
31 M. Uyanik, H. Okamoto, T. Yasui, K. Ishihara, *Science* **2010**, *328*, 1376-1379.
32 M. Uyanik, D. Suzuki, T. Yasui, K. Ishihara, *Angew. Chem. Int. Ed*. **2011**, *50*, 5331-5334.
33 J. Feng, S. Liang, S. -Y. Chen, J. Zhang, S. -S. Fu, X. -Q. Yu, *Adv. Synth. Catal*. **2012**, *354*, 1287-1292.
34 L. Chen, E. Shi, Z. Liu, S. Chen, W. Wei, H. Li, K. Xu, X. Wan, *Chem. Eur. J*. **2011**, *17*, 4085-4089.
35 E. Shi, Y. Shao, S. Chen, H. Hu, Z. Liu, J. Zhang, X. Wan, *Org. Lett.* **2012**, *14*, 3384-3387.
36 Q. Xue, J. Xie, P. Xu, K. Hu, Y. Cheng, C. Zhu, *ACS Catal.* **2013**, *3*, 1365-1368.
37 S. Zhang, L. -N. Guo, H. Wang, X. -H. Duan, *Org. Biomol. Chem.* **2013**, *11*, 4308-4311.
38 G. Majji, S. Guin, A. Gogoi, S. K. Rout, B. K. Patel, *Chem. Commun*. **2013**, *49*, 3031-3033.
39 J. Huang, L. -T. Li, H. -Y. Li, E. Husan, P. Wang, B. Wang, *Chem. Commun.* **2012**, *48*, 10204-10206.
40 L. Liu, L. Yun, Z. Wang, X. Fu, C. -H. Yan, *Tetrahedron. Lett.* **2013**, *54*, 5383-5386.
41 W. Wei, C. Zhang, Y. Xu, X. Wan, *Chem. Commun.* **2011**, *47*, 10827-10829.
42 B. Tan, N. Toda, C. F. Barbas III, *Angew. Chem. Int. Ed.* **2012**, *51*, 12538-12541.
43 X. Li, X. Xu, C. Zhou, *Chem. Commun*. **2012**, *48*, 12240-12242.
44 X. Li, X. Xu, Y. Tang, *Org. Biomol. Chem.* **2013**, *11*, 1739-1742.
45 X. Li, X. Xu, P. Hu, X. Xiao, C. Zhou, *J. Org. Chem*. **2013**, *78*, 7343-7348.
46 Y. Gao, Q. Song, G. Cheng, X. Cui, *Org. Biomol. Chem.* **2014**, *12*, 1044-1047.
47 F. Xiao, H. Chen, H. Xie, S. Chen, L. Yang, G. -J. Deng, *Org. Lett.* **2014**, *16*, 50-53.
48 J. Zhang, J. Jiang, Y. Li, X. Wan, *J. Org. Chem*. **2013**, *78*, 11366-11372.

1 + 1 > 2

TBAI + TBHP = Powerful Oxidation System

The recent achievements on using TBAI and TBHP as oxidation system have been summarized and discussed.