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I+/TBHP Catalysis For Tandem Oxidative Cyclization To Indolo[2,3-*b*]quinolines

Muhammet Uyanik, Hiroki Tanaka, and Kazuaki Ishihara*

[*] Prof. Dr. M. Uyanik, H. Tanaka, Prof. Dr. K. Ishihara
Graduate School of Engineering
Nagoya University
Chikusa, Nagoya, 464-8603 Japan
E-mail: ishihara@cc.nagoya-u.ac.jp

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Abstract: We report a chemoselective tandem oxidative cyclization/aromatization of indole derivatives tethered to aniline sulfonamides using catalytic amount of tetrabutylammonium iodide in the presence of *tert*-butyl hydroperoxide (TBHP) as an oxidant under nearly neutral conditions at room temperature. The corresponding indolo[2,3-*b*]quinolines were obtained as sulfonate salts, which could be easily isolated in analytically pure form *via* only a simple filtration of the crude reaction mixture. The natural product quinindoline could be easily obtained after basic work-up of the sulfonate salt. Control experiments revealed that both ionic and radical active species could be generated *in situ* under mild conditions for the corresponding oxidative transformations to proceed in a chemoselective manner.

Indole is a scaffold that is widely found in many natural products and bioactive compounds; more than 4000 indole-derived alkaloids have been found in nature.[1] Indoloquinolines, which have fused indole and quinoline rings, are a family of relatively rare and unique natural alkaloids (Figure 1).[2] These compounds show a wide range of biological activities such as antibacterial, antiviral, antifungal, antimuscarinic, antihyperglycemic and antitumor activity.[2] Cryptolepine, 5-methyl-5*H*-indolo[3,2-*b*]quinoline, was isolated in 1951 as the first example of these alkaloids.[3] However, due to the strong toxicity of cryptolepine,[2,4] more recently, neocryptolepine (cryptotackieine), 5-methyl-5*H*-indolo[2,3-*b*]quinoline, has been a focus of attention as a promising natural alkaloid that displays interesting and varied biological activities with low toxicity.[2] Neocryptolepine was isolated in 1996 from the bark of the roots of *Cryptolepis sanguinolenta*, albeit in small quantities.[5] Neocryptolepine could also be easily synthesized[2,6] from quinindoline (norcryptotackieine, **1a**),[7] which is also a natural product that exhibits many of the same bioactivities as neocryptolepine including antiproliferative, cytotoxic, and antitumor properties.[2] In addition, several studies revealed that introduction of an appropriate substituent at certain positions of the indoloquinoline mother skeleton could lead to better biological activity.[2,8]

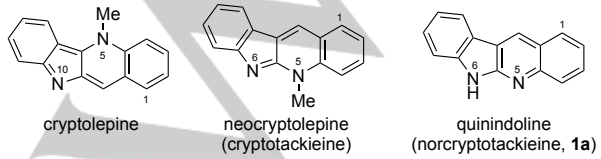
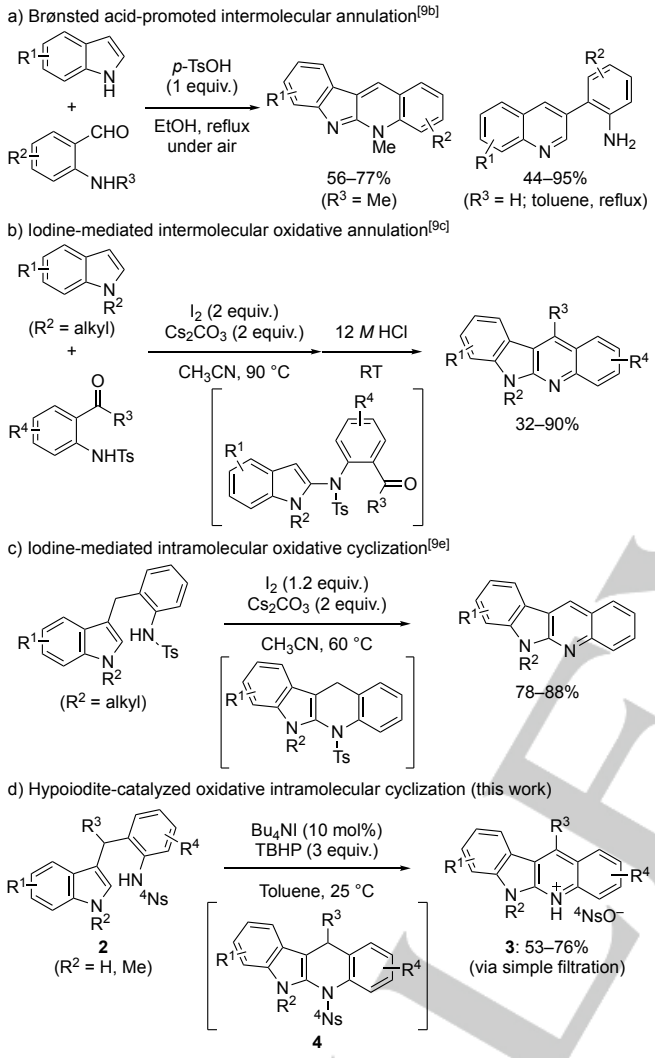


Figure 1. Representative examples of indoloquinoline alkaloids.

Because quinindoline, neocryptolepine and their analogues have received great interest in the fields of synthetic and medicinal chemistry, many synthetic approaches have been developed to construct the basic 6*H*-indolo[2,3-*b*]quinoline framework.[2,9,10] Among these, indole derivatives are often used as a starting material, from which the quinoline moiety is formed *via* cyclization.[9] Recent representative methods are shown in Scheme 1. Seidel and colleagues reported a practical Brønsted acid-promoted reaction of indole with aminobenzaldehydes under reflux conditions in ethanol to give neocryptolepine and analogues *via* annulation/aerobic oxidation cascades (Scheme 1a).[9b] However, this reaction was limited to secondary aminobenzaldehydes to give the corresponding *N*-substituted quinolines. Primary aminobenzaldehydes afforded 3-(2-aminophenyl)quinolines instead of indoloquinolines *via* an indole ring-opening process. On the other hand, iodine-mediated oxidative coupling of indole derivatives to construct indoloquinolines was also reported. For example, Liang and colleagues reported an intermolecular coupling of *N*-alkyl indoles with 1-(2-tosylaminophenyl)-ketones to give indolo[2,3-*b*]quinolines (Scheme 1b).[9c] The reaction sequence was proposed to proceed *via* an iodine-mediated amination of indoles with sulfonamides at the C2-position followed by intramolecular cyclization of the 2-amino indole intermediates, subsequent detosylation gave the corresponding indoloquinolines. However, no reaction was observed for *N*-unsubstituted indoles. In addition, concentrated HCl was required to achieve the second step and tosyl chloride was generated as a side product of detosylation. On the other hand, Sekar and colleagues reported an intramolecular tandem cyclization of indole derivatives tethered to aniline sulfonamide followed by detosylation and aromatization to give the corresponding indolo[2,3-*b*]quinolines (Scheme 1c).[9e] However, similar to the intermolecular coupling reaction shown in Scheme 1b,[9c] the substrate scope of this intramolecular reaction was also limited to *N*-alkyl substituted indoles. In addition, both the inter- and intramolecular coupling methods required a stoichiometric amount of molecular iodine in the presence of cesium carbonate under heating conditions.[9c,e]

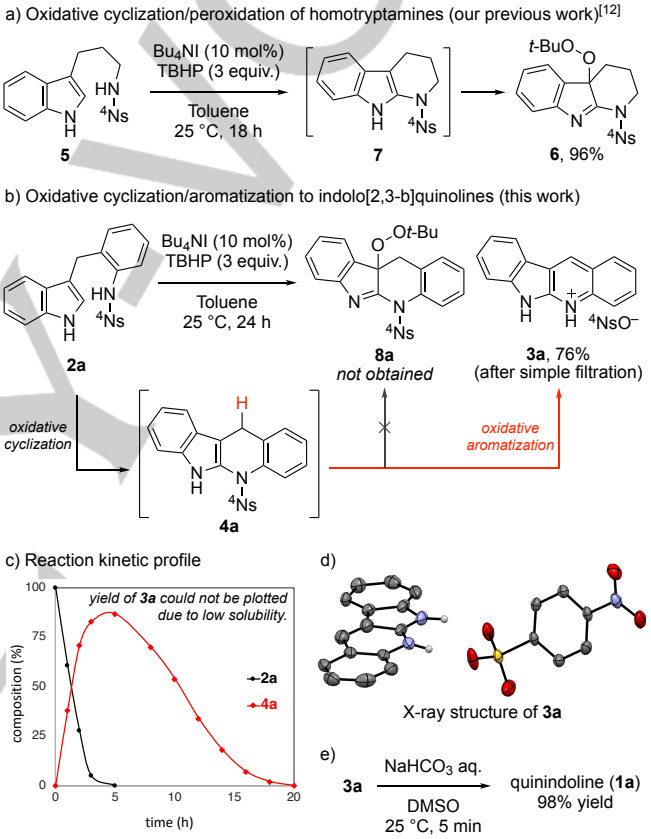
Based on our recent findings regarding the tandem oxidative dearomative[11] cyclization of homotryptamines,[12] we report here the hypoiodite-catalyzed[13,14] chemoselective tandem oxidative cyclization of indole derivatives **2** tethered to aniline sulfonamides to give indolo[2,3-*b*]quinolin-5-ium sulfonates **3** under mild conditions using catalytic amount of tetrabutylammonium iodide and TBHP as an oxidant at room temperature (Scheme 1d). Although, similar to previous iodine-mediated intramolecular coupling reactions under basic conditions,[9e] our catalytic

oxidative coupling proceeded under nearly neutral conditions *via* a similar intermediate dihydroindolo[2,3-*b*]-quinoline **4**, but to give the products **3** as a salt, which could be easily isolated in analytically pure form via only a simple filtration of the crude reaction mixture. In addition, both *N*-unsubstituted and *N*-Me indole derivatives **2** could be used under our catalytic conditions to give the corresponding indolo[2,3-*b*]quinolin-5-ium salts **3** in good to high yields.



Scheme 1. Representative examples of the synthesis of indolo[2,3-*b*]quinolines from indole derivatives. ^{4}Ns, 4-nitrobenzenesulfonyl.

Recently, we reported the quaternary ammonium hypoiodite-catalyzed oxidative cyclization/peroxidation of homotryptamine derivatives **5** with TBHP to give the corresponding peroxyindolenines **6** under mild conditions (Scheme 2a).[12] The tandem process would proceed *via* intramolecular oxidative aminocyclization of **5** to give tetrahydropyridoindole **7** as an isolable intermediate. Oxidative coupling of **7** with TBHP at the C-3 position would then would afford peroxyindolenines **6**. To expand the substrate scope, we examined indole **2a**, an aniline analogue of homotryptamine, as a substrate under the identical reaction conditions (Scheme 2b). The reaction proceeded with a similar efficiency, however, initially expected peroxide adduct **8a** was not obtained. Instead, a hardly soluble salt, which was determined to be quinindolin-5-ium nosylate **3a** by X-ray analysis (Scheme 2d), was obtained in 76% isolated yield after simple filtration. A reaction kinetic profile analysis using in situ ^{1}H NMR monitoring of the reaction progress revealed the rapid consumption of **2a** to give dihydroindolo[2,3-*b*]quinoline **4a**, an analogue of **7**,[12] as an intermediate, which was then converted to **3a** (Scheme 2c). We speculated that the enhanced acidity of benzylic protons in **4a** might lead to aromatization/denosylation to give **3a** rather than intermolecular oxidative coupling with TBHP. The natural product quinindoline (**1a**) could be obtained quantitatively as a free base by treatment of **3a** with aqueous $NaHCO_3$ solution (Scheme 2e).

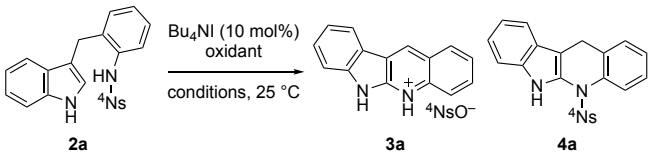


Scheme 2. Tandem oxidation of indole derivatives **2a** and **5**, and initial findings of this work.

We investigated the reaction parameters for the tandem oxidative cyclization/aromatization of **2a** using 10 mol% of Bu_4NI as a catalyst (Table 1). A brief screening of common organic solvents revealed that toluene was the most suitable reaction medium (entries 1–5). Interestingly, the use of diethyl ether or ethyl acetate gave only intermediate **4a** in moderate yield (entries 2 and 3). On the other hand, almost no reaction occurred in polar medium such as acetonitrile or *N*,*N*-dimethylformamide (entries 4 and 5). Next, we investigated common oxidants that have been used in several hypoiodite catalysis (entries 6–9).[13] A reduction in the amount of TBHP (3 to 2.5 equiv.) led a similar yield, albeit after a longer reaction time (entry 6 versus entry 1). On the other hand, a faster reaction proceeded with the use of cumene hydroperoxide (CHP) as an oxidant to give **3a** in lower yield along

with several unidentified byproducts (entry 7). Interestingly, a clean reaction was observed with the use of hydrogen peroxide, albeit to give only intermediate **4a** in good yield (entry 8), suggesting that alkyl hydroperoxides plays a crucial role in the oxidation of **4a** to **3a**. Finally, no reaction proceeded in the absence of iodide catalyst (entry 9).

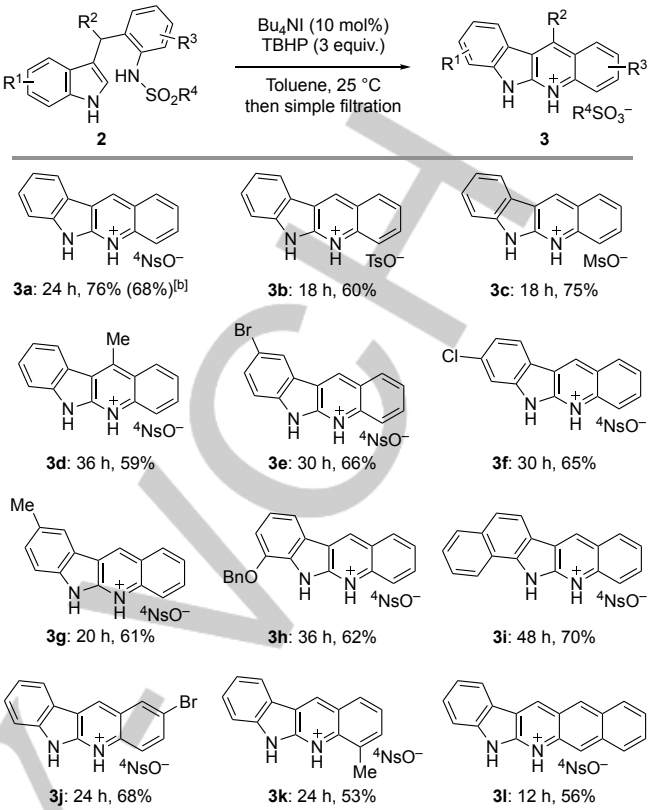
Table 1. Investigation of conditions for the oxidation of **2a**.[a]



Entry	Oxidant (equiv.)	Solvent	Time [h]	Yield, **3a**, **4a** [%][b]
1	TBHP (3)	Toluene	24	86 (76)[c], <1
2	TBHP (3)	Et_2O	24	<1, 21
3	TBHP (3)	EtOAc	24	<1, 52
4	TBHP (3)	CH_3CN	24	<1, <5
5	TBHP (3)	DMF	24	n.r.[d]
6	TBHP (2.5)	Toluene	36	85, <1
7	CHP (3)	Toluene	10	65, <1[e]
8	30% H_2O_2 (3)	Toluene	24	<1, 75
9[f]	TBHP (3)	Toluene	24	n.r.[d]

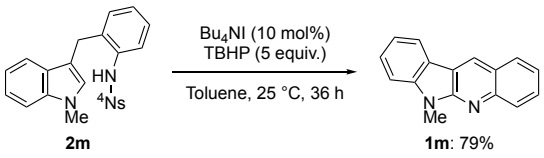
[a] A solution of **2a** (0.1 mmol), Bu_4NI (10 mol%) and oxidant (1.5–3 equiv.) in solvent (0.02 *M*) was stirred at 25 °C. [b] Determined by ^1H NMR analysis of the crude mixture dissolved completely in DMSO. [c] Isolated yield after filtration of the crude mixture (another batch). [d] No reaction. [e] Several unidentified by-products were also observed. [f] In the absence of Bu_4NI. n.r., no reaction.

A series of indoles **2** were examined for the tandem oxidative cyclization/aromatization reaction under optimized conditions (Scheme 3). Products **3** were obtained in good yield as sulfonate salts in analytically pure form after a simple filtration of the crude reaction mixture. Beside the 4-nosyl group as a protecting group for aniline tether, other sulfonyl groups such as tosyl (Ts) and methanesulfonyl (Ms) groups could also be used to afford the desired products **3b** and **3c**, respectively. Notably, substitution (R^2 = Me) at the methylene tether was tolerated under our conditions to give **3d** in good yield. Electron-donating or -withdrawing substituents at both the indole and aniline moieties were also tolerated to give the corresponding **3e**–**l** in good yields.



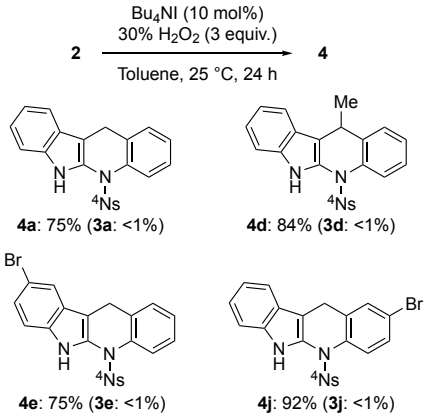
Scheme 3. Tandem oxidation of **2** to **3**. [a] Unless otherwise noted, reactions were performed using 0.2 mmol of **2**. [b] 4.9 mmol (2.0 gram) of **2a** was used.

Interestingly, in sharp contrast to a previous oxidative peroxycyclization of homotryptamines in which *N*-substituted indoles were inert to oxidation,[12] *N*-Me-indole derivative **2m** could be used for this oxidative cyclization/aromatization reaction (Scheme 4). Notably, compared to **3a**–**l**, due to the higher solubility of the corresponding sulfonate salt **3m**, we obtained *N*-Me indoloquinoline **1m** as a free base in good yield after a basic work-up and column chromatography.



Scheme 4. Tandem oxidative cyclization/aromatization of *N*-Me-indole **2m**.

On the other hand, a chemoselective oxidative cyclization of indoles **2a**, **2d**, **2e** and **2j** with the use of aqueous hydrogen peroxide as an oxidant under otherwise identical conditions gave the corresponding dihydroindolo[2,3-*b*]-quinolines **4** in high yield (Scheme 5). Notably, re-aromatized products **3** were not observed under these conditions.



Scheme 5. Chemoselective oxidative cyclization of **2** to **4**.

To probe the active species, several control experiments were performed using **2a** as a model substrate (Scheme 6). No reaction of **2a** was observed with stoichiometric amounts of various iodine-based oxidants such as molecular iodine (I_2), triiodide (I_3^-), and high-valence iodines (IO_3^- and IO_4^-) (Scheme 6a, entry 3). On the other hand, rapid oxidation of **2a** proceeded with the use of triiodide under basic conditions to afford intermediate **4a** in 52% yield along with several unidentified side products (Scheme 6a, entry 4), suggesting that, as in our previous oxidative coupling reactions,[13] hypoiodite might be a catalytic active species for the oxidative cyclization of **2a** to **4a**. However, no oxidative aromatization product **3a** (or **1a**) was obtained in the absence of TBHP, suggesting that TBHP should be required for the oxidation of **4a** (Scheme 6a, entry 4 versus entries 1 and 2). Next, we investigated the oxidative aromatization of **4a** to **3a** in detail (Scheme 6b). Again, oxidation of **4a** with a stoichiometric amount of triiodide (I_3^-) or high-valence iodines (IO_3^- and IO_4^-) did not give **3a** (or **1a**), and most of the unreacted **4a** was recovered (Scheme 6b, entry 2). On the other hand, oxidation of **4a** with the use of I_2 proceeded to give **3a** in 67% yield (Scheme 6b, entry 3). However, no reaction was observed under dark conditions (Scheme 6b, entry 4), suggesting that a radical species (i.e., I·) generated *in situ*[15] rather than I_2 itself might be the active species for the oxidation. Interestingly, the oxidation of **4a** also proceeded with the use of only TBHP (Scheme 6b, entry 5). In contrast with the use of I_2, the oxidation reaction still proceeded under dark conditions with the use of TBHP, albeit with a decrease in the chemical yield (Scheme 6b, entry 6 versus entry 4). Contrarily, the use of TEMPO as an additive hampered the reaction, suggesting that radical species might be generated from TBHP (Scheme 6b, entry 7). Obviously, oxidation of **4a** with TBHP proceeded much faster in the presence of a catalytic amount of Bu_4NI regardless of the presence of light (Scheme 6b, entries 1 and 8), which suggests that the I^-/I^+ couple might catalyze the generation of radical species such as *tert*-butylperoxy (*t*-BuOO·) or *tert*-butoxy radicals (*t*-BuO·) from TBHP.[14] Interestingly, similar to the oxidation of **2a** (Scheme 6a, entry 4), **4a** was consumed smoothly with the use of a stoichiometric amount I^+ species generated *in situ* from I_3^- under alkaline conditions. However, **3a** was obtained in less than 20% yield along with several unidentified products (Scheme 6a, entry 9). These results suggest that the low concentration of I^+ species generated *in situ* under catalytic conditions might be crucial to induce high chemoselectivity. Finally, we may be able to rule out the possibility of aerobic oxidative aromatization since no reaction was observed in the absence of reagents under air (Scheme 6b, entry 10).

a) **2a** → (Toluene, 25 °C) → **3a** or **4a**

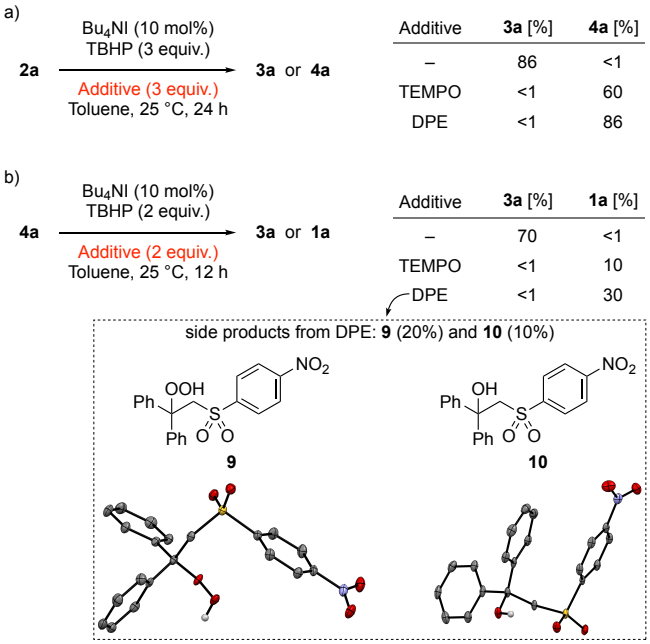
Entry	Reagent (equiv.)	Time [h]	Conv. [%] **2a**	Yield [%] **3a**	Yield [%] **4a**
1	Bu_4NI (0.1), TBHP (3)	24	>95	86	<1
2	Bu_4NI (0.1), TBHP (1)	24	60	10	46
3	I_2, Bu_4NI_3, $NaIO_3$ or Bu_4NIO_4 (2)	24	<1	<1	<1
4	Bu_4NI_3 (1), Bu_4NOH (2)	0.1	>95	<1	52

b) **4a** → (Toluene, 25 °C) → **3a**

Entry	Reagent (equiv.)	Time [h]	Conv. [%] **4a**	Yield [%] **3a**
1	Bu_4NI (0.1), TBHP (2)	10	>95	71
2	Bu_4NI_3, $NaIO_3$ or Bu_4NIO_4 (2)	24	<5	<5
3	I_2 (1)	4	>95	67
4	I_2 (1) *(under dark)*	24	<5	<5
5	TBHP (2)	24	70	60
6	TBHP (2) *(under dark)*	24	60	50
7	TBHP (2) + TEMPO (2)	24	<5	<5
8	Bu_4NI (0.1), TBHP (3) *(under dark)*	10	>95	70
9	Bu_4NI_3 (1), Bu_4NOH (2)	0.1	>95	<20
10	none *(under air)*	24	<5	<5

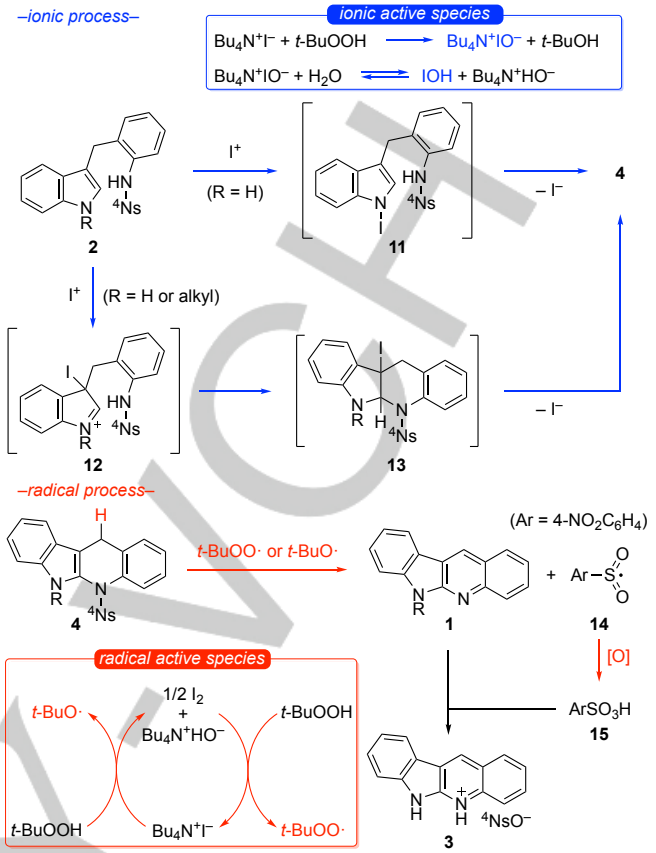
Scheme 6. Control experiments to probe active species.

To gain further insight into the reaction mechanism, we investigated the effect of radical scavengers (Scheme 7). Oxidation of **2a** proceeded with similar efficiency in the presence of radical scavengers such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 1,1-diphenylethylene (DPE) to give intermediate **4a** in good yield; no formation of **3a** was observed (Scheme 7a). These results suggest that while a free-radical pathway might be unlikely for the oxidative cyclization of **2a** to **4a**, radical species might play a role in the oxidative aromatization/denosylation of **4a** to **3a**. Indeed, the reaction of **4a** in the presence of TEMPO or DPE under otherwise identical conditions was sluggish and more than half of the unreacted **4a** was recovered (Scheme 7b). Interestingly, however, a free base **1a** was obtained instead of sulfonate salt **3a** in low yield, suggesting that the generation of 4-nitrobenzenesulfonic acid might be inhibited in the presence of radical scavengers. The clue to understand this particular aromatization/denosylation process came from a careful investigation of the side products of the radical trapping experiments. From the control experiment using DPE, we obtained two major side products, which were unambiguously determined to be nosyl hydroperoxide **9** and its reduced form **10** by X-ray analysis (Scheme 7b). These results clearly indicated the generation of nosyl radical species[16] that would be trapped by DPE to give a Markovnikov adduct, which was further captured by O_2 to give nosyl hydroperoxide **9** under air.



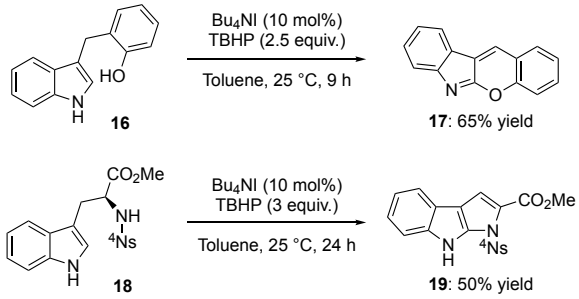
Scheme 7. Control experiments with radical scavengers.

Based on the above observations and previous findings,[12-14] a proposed mechanism is depicted in Scheme 8. Control experiments in Scheme 6 revealed that both ionic (i.e., hypoiodite) and radical (i.e., *t*-BuO· and/or *t*-BuOO·) species might be generated *in situ* and worked in synergy under our catalytic oxidation conditions to proceed a chemoselective tandem oxidation.[14] While the hypoiodite-catalyzed oxidative cyclization of **2** gave dihydroindoloquinoline intermediates **4** *via* an ionic process, denosylative aromatization of **4** to indoloquinolines **1** might involve a free-radical species. In the ionic process, a reversible *N*-iodination of *N*-unsubstituted indoles **2** with I^+ active species might afford indolyl hypoiodite **11**, which might then give **4** *via* intramolecular aminocyclization at the C-2 position.[12,17] Alternatively, iodination of *N*-substituted indoles (i.e., **2m**) at the C-3 position might give iminium cations **12**. Intramolecular trapping with a sulfonamide tether (**12** to **13**) followed by elimination might also afford **4**. We could not completely rule out the possibility of a C-3-iodination pathway for *N*-unsubstituted indoles. On the other hand, in the radical process,[14e] abstraction of benzylic hydrogen of **4** with a free-radical species such as *t*-BuOO· or *t*-BuO· might trigger denosylative aromatization to give the indoloquinoline **1** and nosyl radical **14**, which could be oxidized to the 4-nitrobenzenesulfonic acid (**15**). *In situ* protonation of free base **1** with **15** would give indoloquinoline sulfonate salts **3**.



Scheme 8. Proposed mechanism.

Finally, we investigated the tandem oxidative cyclization of other two types of indole derivatives (Scheme 9). A chemoselective oxidation of indole derivative **16** tethered to phenol gave chromeno[2,3-*b*]indole **17**, which is a core structure of the alkaloids hyrtimomine A and hyrtimomine B.[18] On the other hand, oxidative cyclization of tryptophane derivative **18** afforded pyrrolo[2,3-*b*]indole **19**, which is found in many natural alkaloids.[1]



Scheme 9. Chemoselective tandem oxidative cyclization to chromenoindole **17** and pyrroloindole **19**.

In conclusion, we have developed a chemoselective tandem oxidative cyclization of indole derivatives tethered to aniline sulfonamides using catalytic amount of tetrabutylammonium iodide and TBHP as an oxidant. Catalytic tandem oxidations proceeded under nearly neutral conditions at room temperature via dihydroindolo[2,3-*b*]-quinolines as isolable intermediates to

give the corresponding indolo[2,3-*b*]quinolines as sulfonate salts, which could be easily isolated in analytically pure form via only a simple filtration of the crude reaction mixture. The natural product quinindoline could be easily obtained after basic work-up of the sulfonate salt. Interestingly, control experiments revealed that while oxidative cyclization of indole derivatives proceeded with hypoiodite as a catalytic active species via an ionic process, radical species might play a role in oxidative aromatization/desulfonylation of intermediate to give indoloquinoline sulfonate salts. Importantly, both ionic and radical active species would be generated *in situ* under these mild conditions for the corresponding oxidative transformation to proceed in a chemoselective manner.

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Keywords: indole • indoloquinoline • hypoiodite catalysis • oxidation • radical

[1] a) D. S. Seigler, *Plant Secondary Metabolism, Ch. 34–Indole Alkaloids,* Springer, Boston, MA, **1998**; pp. 628-654; b) R. L. Riggs, D. M. Smith in *Comprehensive Heterocyclic Chemistry III, Vol.12* (Eds. A. R. Katritzky, C. A. Ramsden, E. E. V. Scriven, R. J. K. Taylor), Elsevier, Oxford, **2008**, pp. 857-973; c) M. Ishikura, T. Abe, T. Choshi, S. Hibino, *Nat. Prod. Rep.* **2015**, *32*, 1389-1471.

[2] a) P. T. Parvatkar, P. S. Parameswaran, S. G. Tilve, *Curr. Org. Chem.* **2011**, *15*, 1036-1057; b) A. B. J. Bracca, D. A. Heredia, E. L. Larghi, T. S. Kaufman, *Eur. J. Org. Chem.* **2014**, 7979-8003; c) E. L. Larghi, A. B. J. Bracca, A. A. A. Aguilar, D. A. Heredia, J. L. Pergomet, S. O. Simonetti, T. S. Kaufman, *Curr. Top. Med. Chem*. **2015**, *15*, 1683-1707.

[3] E. Gellert, R. Hamet, E. Schlitter, *Helv. Chim. Acta* **1951**, *34*, 642-651.

[4] a) K. Bonjean, M. P. D. Pauw-Gillet, P. Colson, C. Houssier, L. Dassoneville, C. Bailly, R. Greimers, C. Wright, M. Quetin-Leclercq, M. Tits, L. Angenot, *Biochemistry* **1998**, *37*, 5136-5146; b) C. W. Wright, J. Addae-Kyereme, A. G. Breen, J. E. Brown, M. F. Cox, S. L. Croft, Y. Gökçek, H. Kendrick, R. M. Phillips, P. L. Pollet, *J. Med. Chem.* **2001**, *44*, 3187-3194.

[5] a) M. H. M. Sharaf, P. L. Schiff Jr., A. N. Tackie, C. H. Phoebe Jr., G. E. Martin, *J. Heterocycl. Chem.* **1996**, *33*, 239-243; b) K. Cimanga, T. De Bruyne, L. Pieters, M. Claeys, A. Vlietnick, *Tetrahedron Lett.* **1996**, *37*, 1703-1706.

[6] W. Peczynska-Czoch, F. Pognan, L. Kaczmarek, J. Boratynski, *J. Med. Chem.* **1994**, *37*, 3503-3510.

[7] G. V. Subbaraju, J. Kavitha, D. Rajasekhar, J. I. Jimenez, *J. Nat. Prod*. **2004**, *67*, 461-462.

[8] a) J. Lavrado, R. Moreira, A. Paulo, *Curr. Med. Chem.* **2010**, *17*, 2348-2370; b) N. Wang, M. Switalska, L. Wang, E. Shaban, M. Hossain, I. E. T. El Sayed, J. Wietrzyk, T. Inokuchi, *Molecules* **2019**, *24*, 2121.

[9] Selected examples using indoles as starting materials: a) P. T. Parvatkar, P. S. Parameswaran, S. G. Tilve, *J. Org. Chem*. **2009**, *74*, 8369-8372; b) M. K. Vecchione, A. X. Sun, D. Seidel, *Chem. Sci.* **2011**, *2*, 2178-2181; c) S. Ali, Y.-X. Li, S. Anwar, F. Yang, Z.-S. Chen, Y.-M. Liang, *J. Org. Chem.* **2012**, *77*, 424-431; d) R. Ghorbani-Vaghei, S. M. Malaekehpoor, *Tetrahedron Lett.* **2012**, *53*, 4751-4753; e) S. Badigenchala, V. Rajeshkumar, G. Sekar, *Org. Biomol. Chem.* **2016**, *14*, 2297-2305; f) Z. Yan, C. Wan, J. Wan, Z. Wang, *Org. Biomol. Chem.* **2016**, *14*, 4405-4408; g) L. Shi, B. Wang, *Org. Lett.* **2016**, *18*, 2820-2823; h) S. Yu, Y. Li; X. Zhou, H. Wang, L. Kong, X. Li, *Org. Lett.* **2016**, *18*, 2812-2815; i) C. Challa, J. Ravindran, M. M. Konai, S. Varughese, J. Jacob, B. S. D. Kumar, J. Haldar, R. S. Lankalapalli, *ACS Omega* **2017**, *2*, 5187-5195; j) P. T. Parvatkar, P. S. Parameswaran, D. Bandyopadhyay, S. Mukherjee, B. K. Banik, *Tetrahedron Lett.* **2017**, *58*, 2948-2951.

[10] Other approaches: a) M. Alajarín, P. Molina, A. Vidal, *J. Nat. Prod.* **1997**, *60*, 747-748; b) P. Vera-Luque, R. Alajarín, J. Alvarez-Builla, J. J. Vaquero, *Org. Lett.* **2006**, *8*, 415-418; c) M. J. Haddadin, R. M. B. Zerdan, M. J. Kurth, J. C. Fettinger, *Org. Lett.* **2010**, *12*, 5502-5505; d) Y. Tokimizu, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2014**, *16*, 3138-3141; e) L. Fan, M. Liu, Y. Ye, G. Yin, *Org. Lett.* **2017**, *19*, 186-189; f) B. Akkachairin, J. Tummatorn, N. Khamsuwan, C. Thongsornkleeb, S. Ruchirawat, *J. Org. Chem.* **2018**, *83*, 11254-11268; g) S. Kundal, B. Chakraborty, K. Paul, U. Jana, *Org. Biomol. Chem.* **2019**, *17*, 2321-2325; h) L.-H. Yeh, H.-K. Wang, G. Pallikonda, Y.-L. Ciou, J-C. Hsieh, *Org. Lett.* **2019**, *21*, 1730-1734; i) K. M. Medas, R. W. Lesch, F. B. Edioma, S. P. Wrenn, V. Ndahayo, S. P. Mulcahy, *Org. Lett.* **2020**, *22*, 3135-3139.

[11] a) W. Zi, Z. Zuo, D. Ma. *Acc. Chem. Res.* **2015**, *48*, 702-711; b) S. P. Roche, J.-J. Y. Tendoung, B. Tréguier, *Tetrahedron* **2015**, *71*, 3549-3591; c) C. Zheng, S.-L. You, *Chem* **2016**, *1*, 830-857; d) H. Abou-Hamdan, C. Kouklovsky, G. Vincent, *Synlett* **2020**, *31*, 1775-1788.

[12] M. Uyanik, H. Tanaka, K. Ishihara, *Org. Lett.* **2020**, *22*, 8049-8054.

[13] a) M. Uyanik, H. Okamoto, T. Yasui, K. Ishihara, *Science* **2010**, *328*, 1376-1379; b) M. Uyanik, H. Hayashi, K. Ishihara, *Science* **2014**, *345*, 291-294; c) M. Uyanik, K. Nishioka, R. Kondo, K. Ishihara, *Nat. Chem.* **2020**, *12*, 353-362; d) M. Uyanik, N. Sahara, M. Tsukahara, Y. Hattori, K. Ishihara, *Angew. Chem.* **2020**, *132*, 17258-17265; *Angew. Chem. Int. Ed.* **2020**, *59*, 17110-17117.

[14] a) M. Uyanik, K. Ishihara, *ChemCatChem* **2012**, *4*, 177-185; b) P. Finkbeiner, B. J. Nachtsheim, *Synthesis* **2013**, *45*, 979-999; c) X.-F. Wu, J.-L. Gong, X. Qi, *Org. Biomol. Chem.* **2014**, *12*, 5807-5817; d) M. S. Yusubov, V. V. Zhdankin, *Resour.-Effic. Technol.* **2015**, *1*, 49-67; e) R. Chen, J. Chen, J. Zhang, X. Wan, *Chem. Rec.* **2018**, *18*, 1292-1305.

[15] a) N. Kanai, H. Nakayama, N. Tada, A. Ito, *Org. Lett*. **2010**, *12*, 1948-1951; b) J. M. Gardner, M. Abrahamsson, B. H. Farnum, G. J. Meyer, *J. Am. Chem. Soc.* **2009**, *131*, 16206-16214.

[16] a) J. Wu, Y. Zhang, X. Gong, Y. Meng, C. Zhu, *Org. Biomol. Chem.* **2019**, *17*, 3507-3513; b) K. S. Kanyiva, D. Hamada, S. Makino, H. Takano, T. Shibata, *Eur. J. Org. Chem.* **2018**, 5905-5909.

[17] a) Y.-X. Li, H.-X. Wang, S. Ali, X.-F. Xia, Y.-M. Liang, *Chem. Commun.* **2012**, *48*, 2343-2345; b) Z.-Y. Yang, T. Tian, Y.-F. Du, S.-Y. Li, C.-C. Chu, L.-Y. Chen, D. Li, J.-Y. Liu, B. Wang, *Chem. Commun.* **2017**, *53*, 8050-8053; c) X. Jiang, W. Zhu, L. Yang, Z. Zheng, C. Yu, *Eur. J. Org. Chem.* **2019**, 2268-2274; d) S.-K. Chen, J.-S. Yang, K.-L. Dai, F.-M. Zhang, X.-M. Zhang, Y.-Q. Tu, *Chem. Commun.* **2020**, *56*, 121-124.

[18] a) R. Momose, N. Tanaka, J. Fromont, J. Kobayashi, *Org. Lett.* **2013**, *15*, 2010-2013; b) E. Gráczol-Fördős, T. Novák, G. Blaskó, I. Fejes, F. Perron-Sierra, M. Nyerges, *Heterocycles* **2013**, *87*, 2053-2069; c) J. Liu, N. Liu, Y. Yue, Y. Wang, K. Chen, J. Zhang, S. Zhao, K. Zhuo, *Chem. Asian J.* **2017**, *12*, 401-404; d) C.-Bao Miao, Y.-F. Sun, H. Wu, X.-Q. Sun, H.-T. Yang, *Adv. Synth. Catal.* **2018**, *360*, 2440-2445; e) G.-Q. Rong, J.-Q. Zhao, X.-M. Zhang, X.-Y. Xu, W.-C. Yuan, M.-Q. Zhou, *Tetrahedron* **2018**, *74*, 2383-2390.

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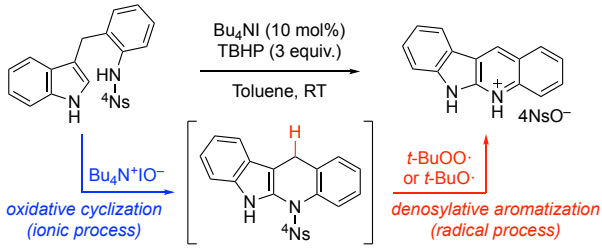

A chemoselective I^+/TBHP catalysis was developed for tandem oxidative cyclization/aromatization of indole derivatives under nearly neutral conditions to give the corresponding indolo[2,3-*b*]quinoline sulfonate salts, which could be easily isolated *via* only simple filtration of the crude reaction mixture. Interestingly both ionic and radical active species would be generated *in situ* for the corresponding oxidative transformations to proceed in a chemoselective manner.

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