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Synthetic Methods

Scalable, Transition-Metal-Free Direct Oxime *O*-Arylation: Rapid Access to *O*-Arylhydroxylamines and Substituted Benzo[*b*]furans

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Abstract: *O*-Aryloximes, generated from readily available and inexpensive oximes through transition-metal-free *O*-arylation, can either be hydrolyzed to *O*-arylhydroxylamines or conveniently converted to structurally diverse benzo[*b*]furans through an environmentally benign, one-pot [3,3]-sigmatropic rearrangement/cyclization sequence.

The benzofuran[1] structural motif, in particular the benzo[*b*]furan motif, appears widely in many biologically active natural products,[2] active pharmaceutical ingredients[1a] (APIs), and intermediates/building blocks for the synthesis of complex molecules, as well as in functional materials such as dyes, polymers, and film-forming compounds (Figure 1).

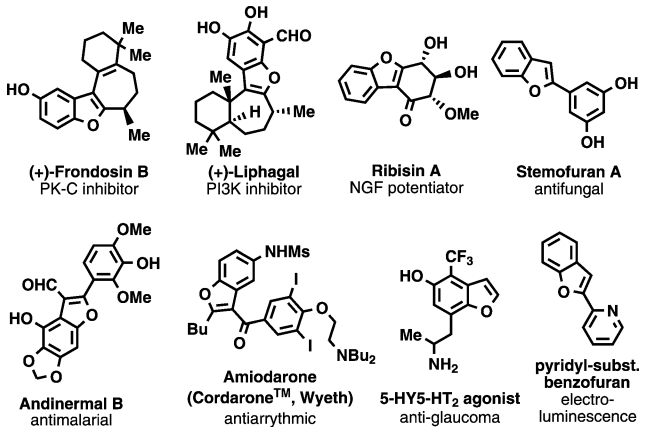
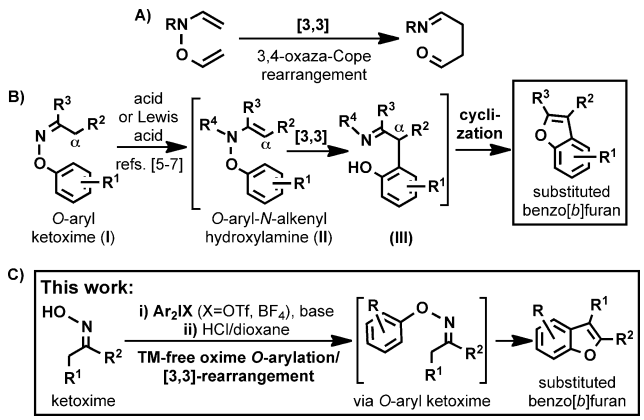


Figure 1. Important benzo[*b*]furan motifs.

Given the importance of functionalized benzo[*b*]furans and their derivatives across several key scientific fields, there is great demand for versatile synthetic methods that allow their rapid, efficient, and readily scalable preparation. Thus, it is not surprising that during the past few decades a number of synthetic approaches have been developed to access these heterocycles from acyclic precursors.[3] The overwhelming majority of these methods utilize transition-metal (TM) catalysts (e.g., Cu, Pd, Pt)[3a,b,d–f] to form the required C–C and C–O bonds of the benzo[*b*]furan substructure; most commonly the furan nucleus is assembled on a prefunctionalized benzenoid scaffold (i.e., through cycloisomerization[3e]). Even though TM-catalyzed syntheses of benzofurans are currently the most widely used, they often suffer from certain drawbacks such as the necessity to employ harsh conditions (e.g., elevated temperatures for extended periods of time) and the generation of toxic heavy metal waste that is expensive to remove, especially during the production of APIs in which residual metal contamination needs to meet stringent specifications.[4] In light of the above, there is a clear need for the development of versatile TM-free approaches to functionalized benzo[*b*]furans that utilize structurally diverse, readily available, and inexpensive starting materials and/or reagents (Scheme 1 C).



Scheme 1. 3,4-Oxaza-Cope rearrangement approach to benzo[*b*]furans.

In this regard, we considered the [3,3]-sigmatropic rearrangement of *O*-aryl-*N*-alkenyl hydroxylamines (e.g., a 3,4-oxaza-Cope rearrangement; Scheme 1 A and B) to be synthetically attractive, because the cleavage of the weak N–O bond drives the formation of the much stronger C–C bond under mild reaction conditions.[5] The subsequent intramolecular cyclization/elimination sequence then furnishes the substituted benzo[*b*]furan product (Scheme 1 B).

O-Arylketoximes bearing acidic α-hydrogen atoms (**I**, Scheme 1 B) arguably are the most convenient precursors for the required *O*-aryl-*N*-alkenyl hydroxylamines (**II**), which are short-lived intermediates en route to the benzo[*b*]furan prod-

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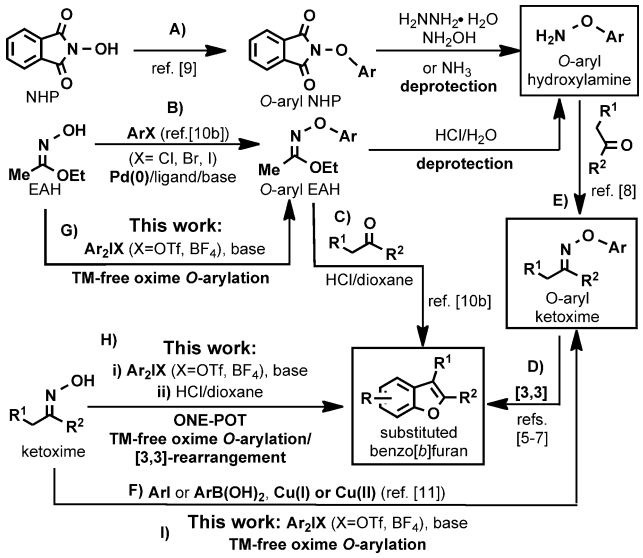


Scheme 2. Transition-metal (TM)-free direct synthesis of *O*-aryl ketoximes and their subsequent [3,3]-rearrangement to benzo[*b*]furans.

ucts. The in situ tautomerization of *O*-arylketoximes (**I**→**II**, Scheme 1 B) and the subsequent [3,3]-rearrangement (**II**→**III**) can be readily achieved either by the use of protic or Lewis acids[6,5a] at elevated temperatures or by *N*-acylation[7,3c] at ambient temperature or below (Scheme 2 D). *O*-Arylketoximes are generally prepared by the spontaneous condensation of *O*-arylhydroxylamines with the corresponding ketones (Scheme 2 E).[8] However, the lack of commercially available structurally diverse *O*-arylhydroxylamines is a major limitation of this approach, a fact that can be attributed primarily to the sensitivity of these compounds.

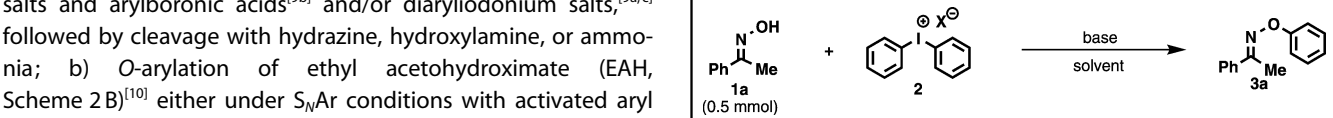
Currently, synthetic access to *O*-arylhydroxylamines (Scheme 2 A and B) invariably requires an *O*-arylation/deprotection sequence: a) *O*-arylation of *N*-hydroxyphthalimide (NHP, Scheme 2 A)[9] by using either stoichiometric amounts of Cu salts and arylboronic acids[9b] and/or diaryliodonium salts,[9a,c] followed by cleavage with hydrazine, hydroxylamine, or ammonia; b) *O*-arylation of ethyl acetohydroximate (EAH, Scheme 2 B)[10] either under S_NAr conditions with activated aryl fluorides[10a] or by using aryl bromides and iodides under Pd catalysis[10b] in the presence of a biarylphosphine ligand, followed by acid hydrolysis. In the latter case, the often volatile *O*-arylated ethyl acetoxihydroximate products must be heated with ketones in the presence of HCl, which facilitates a transoximation/[3,3]-rearrangement sequence to afford the corresponding benzo[*b*]furans (Scheme 2 C).[10b] *O*-Arylketoximes can also be synthesized, albeit generally only on a small scale and in moderate yields, directly from ketoximes through a Cu-mediated cross-coupling reaction (Scheme 2 F)[11] by using aryl iodides and Cu^{I} salts at elevated temperatures[11a] or by utilizing arylboronic acids and Cu^{II} salts.[11b–e] Unfortunately, the majority of the above approaches also suffer from additional shortcomings that include but are not limited to a) long reaction times, b) the use of excess coupling partners ($\geq$2 equiv) and stoichiometric amounts of transition metal salts, c) incompatibility of substrates with multiple Br and I substituents, d) a generally narrow substrate scope, e) the necessity to employ expensive TM catalysts (e.g., Pd) and/or sensitive ligands, and f) the lack of reasonable scalability (i.e., generally only up to $\leq$1 mmol).

Therefore, a new TM-free direct oxime *O*-arylation approach would be highly advantageous, because it a) does not require the use and removal of protecting groups (compare Scheme 2 A), b) obviates the storage and handling of sensitive *O*-arylhydroxylamines and their separate condensation with ketones (compare Scheme 2 E), c) offers an alternative to surrogate *O*-aryloximes (compare Scheme 2 B) that are often volatile and can only be converted to benzo[*b*]furans after an acidic transoximation (compare Scheme 2 C), and d) allows the use of readily available/inexpensive ketone oximes.

We envisioned that diaryliodonium salts might be well-suited for the direct *O*-arylation of ketoximes under mild conditions. During the past decade, diaryliodonium salts have been widely used owing to their relatively high reactivity and tolerance to a wide range of functional groups.[12] Recently, diaryliodonium salts were utilized as inexpensive electrophilic reagents in *C*-arylations,[13], *O*-arylations,[14] *N*-arylations,[15] and for a variety of other functionalizations.[16] Herein, we report a scalable, transition-metal-free direct *O*-arylation of ketone oximes with diaryliodonium salts at ambient temperature.

After extensive optimization of the reaction conditions, we selected DMF/*t*BuOK as the optimal solvent/base pair for the *O*-arylation of ketoximes (Table 1; see a detailed discussion of these studies and an expanded Table 1 in the Supporting Information). During the final round of optimization, we were delighted to find that lowering the reaction temperature from 60 °C to RT affected neither the isolated yield of **3a** nor the overall reaction time (Table 1, entry 8). It was also gratifying to observe that decreasing both the amounts of **2a** and *t*BuOK

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



Entry	X	2	Base	Solvent	Temp.	Time	Yield 3 [%][b]
1	OTf	**2a**	N/A	THF	RT to 70 °C	10 h	n.r.
2	OTf	**2a**	*t*BuOK	THF	RT	10 h	70
3	OTf	**2a**	*t*BuOK	dioxane	60 °C	30 min	77
4	OTf	**2a**	*t*BuOK	DMF	60 °C	30 min	89
5	OTf	**2a**	*t*BuOK	DMSO	60 °C	30 min	78
6	OTf	**2a**	*t*BuOK	DMA	60 °C	30 min	78
7	OTf	**2a**	*t*BuOK	NMP	60 °C	30 min	72
8	OTf	**2a**	^{t}BuOK	DMF	RT	1 h	90
9[c]	OTf	**2a**	*t*BuOK	DMF	RT	1 h	83
10[d]	OTf	**2a**	*t*BuOK	DMF	RT	1 h	76

[a] Reactions were performed on a 0.5 mmol scale (0.1 M solution) by using **2** (1.5 equiv) and base (1.5 equiv), unless indicated otherwise. [b] Yield of isolated product after column chromatography. [c] 1.3 equiv of **2a** and 1.3 equiv of base were used. [d] 1.1 equiv of **2a** and 1.1 equiv of base were used. n.r. = no reaction; DMA = dimethylacetamide; NMP = *N*-methylpyrrolidone.

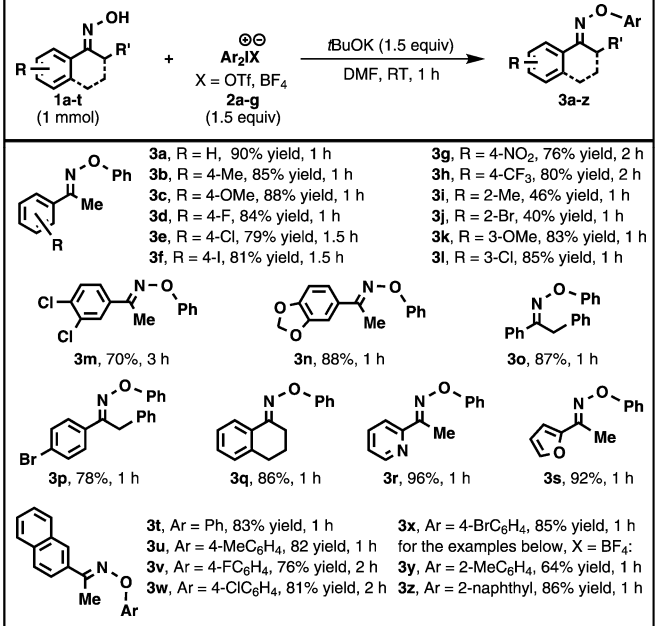
from the optimal 1.5 equivalents to 1.3 and then 1.1 equivalents dropped the isolated yield of **3a** only slightly from 90% to synthetically still valuable levels of 83 and 76%, respectively (Table 1, entries 9 and 10). Employing more than 1.5 equivalents of base and arylating agent did not improve the yield beyond 90%.

With the optimized reaction conditions in hand, we next investigated the scope of the TM-free direct *O*-arylation of ketoximes **1** with symmetrical diaryliodonium salts **2** (Table 2). First, a wide range of aryl-alkyl ketoximes with diverse substitution patterns were evaluated. *Para*- and *meta*-substituted acetophenone oximes (Table 2, **1a**–**n**) gave rise to the corresponding *O*-arylated oximes products **3a**–**n** in good to excellent yields when reacted with diphenyliodonium triflate (**2a**) as the arylating agent. Both electron-donating and electron-withdrawing groups on the aromatic ring of these substrates are well-tolerated, resulting only in minor variation of the isolated yields. However, *ortho*-substituted acetophenone oximes (**3i** and **3j**) could only be *O*-arylated in moderate yields under a variety of conditions (including our standard conditions), presumably owing to steric hindrance. It is worth noting that halogen substituents, especially bromine and iodine (**3f**, **3j**, and **3p**), behaved well in this transformation (i.e., no side reactions at these halogenated positions were observed); aryl bromides and iodides are generally incompatible with TM-catalyzed/-mediated *O*-arylation conditions.[11] α-Substituted acetophenone oximes (**2o** and **2p**) and a cyclic aryl-alkyl oxime (**2q**) were also smoothly coupled with diphenyliodonium triflate (**2a**) to furnish the *O*-arylated derivatives (Table 2, **3o**–**q**) in good to excellent isolated yields. In addition, we were delighted to find that heteroaryl-alkyl oximes such as 2-pyridinyl and 2-furanyl ethanone oximes (Table 2, **2r** and **2s**) were suitable coupling partners, affording the *O*-arylated products (**3r** and **3s**) in excellent yield.

Next, we turned our attention to explore the impact of the structural variation in the diaryliodonium salt coupling partner (Table 2, **2b**–**g**) on the efficiency of the *O*-arylation process under the optimized reaction conditions. Notably, symmetrical diaryliodonium salts that bear *para*- and *ortho*- substituents, including methyl and halogen atoms, reacted well with 1-(naphthalen-2-yl)ethanone oxime (**1t**) to give the desired *O*-arylketoxime products in good yields (Table 2, **3t**–**3y**). Symmetrical di(2-napthyl)-iodonium tetrafluoroborate (**2g**) was prepared and used in our laboratory for the first time (see the Supporting Information), and it performed efficiently during the *O*-arylation of oxime **1t**. It is important to note that when a number of unsymmetrical diaryliodonium salts (**2h**–**l**, Figure 2) were tested as arylating agents, only complex reaction mixtures were obtained under our optimized *O*-arylation conditions; the desired *O*-arylated ketoximes could not be isolated in synthetically useful amounts.

To demonstrate the synthetic utility of this direct oxime *O*-arylation process on a multi-gram scale, we chose (*E*)-1,2-diphenylethanone oxime (**1o**) and diphenyliodonium triflate (**2a**) as substrates (Scheme 3). To our delight, we found that this reaction could be easily scaled-up to a 40 mmol scale. The *O*-arylated product **3o** was isolated in 82% yield (9.4 g). Moreover, the by-product iodobenzene (PhI) could be recovered in a synthetically useful yield of 78%; subsequently, PhI was reused in the preparation of diphenyliodonium triflate (**2a**; Scheme 3). This facile recovery of aryl iodides improves the atom economy, reduces costs, and decreases the overall environmental impact of the reaction. All other substituted iodoarenes could be recovered from the various *O*-arylation reactions (Table 2) in 70–80% isolated yield and were recycled for the preparation of new batches of the corresponding symmetrical diaryliodonium salts (**2b**–**g**).

Table 2. Scope of the *O*-arylation of oximes **1** with diaryliodonium salts **2**.[a,b]



[a] Reaction conditions: **1** (1 mmol), **2** (1.5 mmol), *t*BuOK (1.5 mmol), DMF (10 mL) at RT. [b] Yield of isolated product after column chromatography.

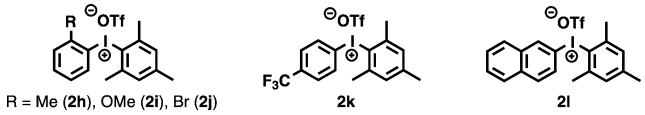
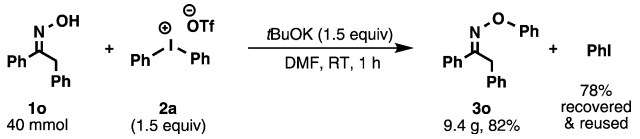
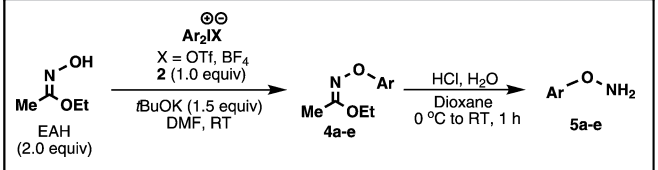


Figure 2. Unsymmetrical diaryliodonium salts that were also tested in the *O*-arylation process.



Scheme 3. Direct *O*-arylation of oxime **1o** on a 40 mmol scale.

Table 3. *O*-Arylation of ethyl *N*-hydroxyacetimidate (EAH), followed by hydrolysis.[a,b,c]



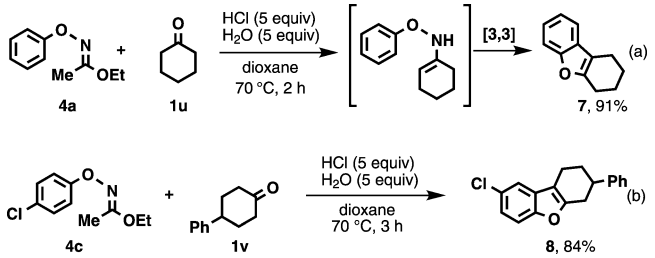
4a, Ar = Ph, 74% yield, 2 h (**20 mmol scale**)
4b, Ar = 4-FC_6H_4, 58% yield, 2 h
4c, Ar = 4-ClC_6H_4, 72% yield, 2 h
4d, Ar = 4-BrC_6H_4, 78% yield, 2 h
4e, Ar = 2-naphthyl, 63% yield, 1 h

5a, Ar = Ph, 89% yield, 1 h
5b, Ar = 4-FC_6H_4,88% yield, 1 h
5c, Ar = 4-ClC_6H_4, 92% yield, 1 h
5d, Ar = 4-BrC_6H_4, 93% yield, 1 h
5e, Ar = 2-naphthyl, 87% yield, 1 h

[a] Reaction conditions of **2**→**4**: diaryliodonium salt (1 mmol, 1 equiv), ethyl *N*-hydroxy-acetimidate (2 equiv), *t*BuOK (1.5 mmol), DMF (0.1 M) at RT [b] Reaction conditions of **4**→**5**: *O*-aryl oxime (1 equiv), H_2O (5 equiv), HCl (4 M in dioxane, 5 equiv), 1,4-dioxane (0.1 M), 0 °C. [c] Yield of isolated product after column chromatography.

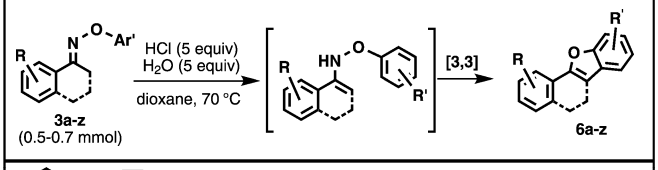
Since the use of surrogate *O*-aryloximes (Scheme 2C) can be advantageous in certain situations, we were eager to extend our optimized protocol for the direct TM-free *O*-arylation of ethyl *N*-hydroxyacetimidate (EAH) to a variety of diaryliodonium salts (Table 3). The *O*-arylated products (Table 3, **4a**–**e**) could be obtained in good isolated yields at room temperature, albeit the volatile nature of these compounds necessarily results in some loss of material during isolation and purification. The yields for compounds **4a**–**e** are comparable to those reported by Buchwald[10b] who used aryl halides as coupling partners at elevated temperatures with Pd catalysis (compare Scheme 2B). Thus, one now has the option to avoid the use of TM catalysts if circumstances demand (i.e., during late-stage syntheses of APIs[4]) in addition to running the *O*-arylation of EAH at ambient temperature. The *O*-arylated products could either be readily hydrolyzed to the free *O*-aryloxyamines in the presence of aqueous HCl (Table 3, **5a**–**e**) or converted to the corresponding benzo[*b*]furans in the presence of ketones through an acid-mediated transoximation/tautomerization/[3,3]-rearrangement sequence (Scheme 4).[10b]

The more than two dozen *O*-arylated ketoximes that were prepared by using our new TM-free *O*-arylation protocol (Table 4, **3a**–**z**) were then successfully transformed into the corresponding 2-substituted benzo[*b*]furans (Table 4, **6a**–**z**) under acid-mediated conditions in good to excellent yields.

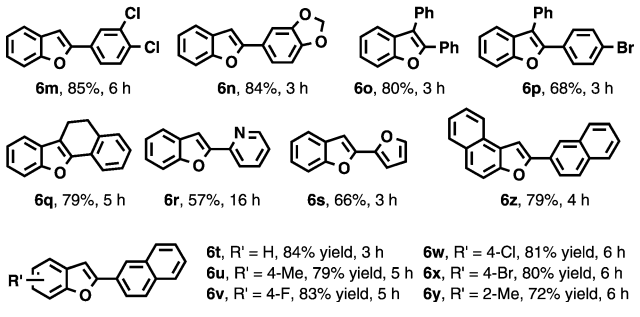


Scheme 4. One-pot transoximation approach to benzo[*b*]furans.

Table 4. Preparation of benzo[*b*]furans starting from *O*-aryl oximes.[a,b]



6a, R = H, 86% yield, 2 h
6b, R = 4-Me, 83% yield, 3 h
6c, R = 4-OMe, 81% yield, 3 h
6d, R = 4-F, 89% yield, 4 h
6e, R = 4-Cl, 84% yield, 4 h
6f, R = 4-I, 83% yield, 5 h
6g, R = 4-NO_2, 73% yield, 6 h
6h, R = 4-CF_3, 83% yield, 6 h
6i, R = 2-Me, 73% yield, 6 h
6j, R = 2-Br, 69% yield, 6 h
6k, R = 3-OMe, 92% yield, 3 h
6l, R = 3-Cl, 80% yield, 3 h



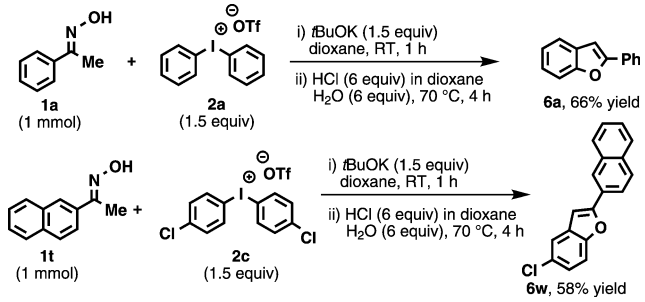
6m, 85%, 6 h
6n, 84%, 3 h
6o, 80%, 3 h
6p, 68%, 3 h
6q, 79%, 5 h
6r, 57%, 16 h
6s, 66%, 3 h
6z, 79%, 4 h

6t, R' = H, 84% yield, 3 h
6u, R' = 4-Me, 79% yield, 5 h
6v, R' = 4-F, 83% yield, 5 h
6w, R' = 4-Cl, 81% yield, 6 h
6x, R' = 4-Br, 80% yield, 6 h
6y, R' = 2-Me, 72% yield, 6 h

[a] Reaction conditions: *O*-aryl oxime (1 equiv), H_2O (5 equiv), HCl (4 M in dioxane, 5 equiv), 1,4-dioxane (0.1 M), 70 °C, 3–16 h. [b] Yield of isolated product after column chromatography.

The *O*-arylketoximes (**3a**–**z**) can also be rearranged through *N*-acylation[7,3c] at ambient temperature or below if acid-sensitive functional groups are present.

Finally, a one-pot TM-free ketoxime *O*-arylation/[3,3]-rearrangement process was successfully developed, utilizing dioxane as the solvent (Scheme 5). The *O*-arylated ketoximes **3a** and **3w** could be treated with HCl with subsequent [3,3]-rearrangement at 70 °C. The yields of the benzo[*b*]furan products (**6a** and **6w**) obtained in the one-pot process were nearly identical to the yields of the two-step process (compare Tables 2 and 4).



Scheme 5. Convenient one-pot preparation of benzo[*b*]furans from oximes.

In conclusion, we have developed a scalable, transition-metal-free direct *O*-arylation of ketone oximes utilizing structurally diverse and readily available diaryliodonium salts as electrophilic arylating agents. The *O*-arylation proceeds under mild conditions at ambient temperature and furnishes the corresponding *O*-aryl oximes in high yields while tolerating both

electron-rich and electron-poor substituents on both reactants. The *O*-arylated ketoxime products can be efficiently converted into substituted benzo[*b*]furans either under acid-mediated or *N*-acylation conditions if acid-sensitive functionalities are present. We have also developed a one-pot TM-free *O*-arylation/[3,3]-rearrangement sequence that conveniently affords benzo[*b*]furans in a streamlined fashion in good isolated yields, while avoiding the preparation and handling of sensitive *O*-aryloxyamines. We anticipate that this transformation will serve as a prototype for related transformations that build molecular complexity rapidly under mild conditions in a step-economical and environmentally friendly fashion.

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Keywords: benzofurans · cyclization · diaryliodonium salts · *O*-arylation · oximes · sigmatropic rearrangement · transition-metal free

[1] a) B. A. Keay, J. M. Hopkins, P. W. Dibble, in *Compehensive. Heterocyclic Chemistry, Vol. 3* (Ed.: A. R. Katritzky), Elsevier, Oxford, **2008**, pp. 571 – 623; b) A. Boto, L. Alvarez, *Heterocycl. Nat. Prod. Synth.* **2011**, 99 – 152.

[2] a) A. D. Patil, A. J. Freyer, L. Killmer, P. Offen, B. Carte, A. J. Jurewicz, R. K. Johnson, *Tetrahedron* **1997**, *53*, 5047 – 5060; b) R. S. Ward, *Nat. Prod. Rep.* **1997**, *14*, 43 – 74; c) G. D. McCallion, *Curr. Org. Chem.* **1999**, *3*, 67 – 76; d) F. Marion, D. E. Williams, B. O. Patrick, I. Hollander, R. Mallon, S. C. Kim, D. M. Roll, L. Feldberg, R. Van Soest, R. J. Andersen, *Org. Lett.* **2006**, *8*, 321 – 324.

[3] a) S. Cacchi, G. Fabrizi, A. Goggiomani, *Heterocycles* **2002**, *56*, 613 – 632; b) S. Cacchi, G. Fabrizi, A. Goggiamani, *Curr. Org. Chem.* **2006**, *10*, 1423 – 1455; c) O. Miyata, N. Takeda, T. Naito, *Heterocycles* **2009**, *78*, 843 – 871; d) S. Cacchi, G. Fabrizi, A. Goggiamani, *Org. Biomol. Chem.* **2011**, *9*, 641 – 652; e) A. S. Dudnik, V. Gevorgyan, *Catal. Carbon-Heteroat. Bond Form.* **2011**, 317 – 410; f) J. Wu, in *Modern Heterocyclic Chemistry, Vol. 1* (Eds.: J. Alvarez-Builla, J. J. Vaquero, J. Barluenga), Wiley-VCH, Weinheim, **2011**, pp. 593 – 633.

[4] C. J. Welch, J. Albaneze-Walker, W. R. Leonard, M. Biba, J. DaSilva, D. Henderson, B. Laing, D. J. Mathre, S. Spencer, X. Bu, T. Wang, *Org. Process Res. Dev.* **2005**, *9*, 198 – 205.

[5] a) M. M. A. Pereira, in *The Chemistry of Hydroxylamines, Oximes and Hydroxamic Acids* (Eds.: Z. Rappoport, J. F. Liebman), Wiley, Chichester, **2009**, pp. 343 – 498; b) A. A. Tabolin, S. L. Ioffe, *Chem. Rev.* **2014**, *114*, 5426 – 5476.

[6] a) T. Sheradsky, *Tetrahedron Lett.* **1966**, *7*, 5225 – 5227; b) T. Sheradsky, *J. Heterocycl. Chem.* **1967**, *4*, 413 – 414; c) A. J. Castellino, H. Rapoport, *J. Org. Chem.* **1984**, *49*, 4399 – 4404.

[7] N. Takeda, O. Miyata, T. Naito, *Eur. J. Org. Chem.* **2007**, 1491 – 1509.

[8] E. Abele, E. Lukevics, *Org. Prep. Proced. Int.* **2000**, *32*, 235 – 264.

[9] a) J. I. G. Cadogan, A. G. Rowley, *Synth. Commun.* **1977**, *7*, 365 – 366; b) H. M. Petrassi, K. B. Sharpless, J. W. Kelly, *Org. Lett.* **2001**, *3*, 139 – 142; c) R. Ghosh, B. Olofsson, *Org. Lett.* **2014**, *16*, 1830 – 1832.

[10] a) E. Miyazawa, T. Sakamoto, Y. Kikugawa, *Org. Prep. Proced. Int.* **1997**, *29*, 594 – 600; b) T. J. Maimone, S. L. Buchwald, *J. Am. Chem. Soc.* **2010**, *132*, 9990 – 9991.

[11] a) P. De Nonappa, K. Pandurangan, U. Maitra, S. Wailes, *Org. Lett.* **2007**, *9*, 2767 – 2770; b) A. Ali, A. G. Meyer, K. L. Tuck, *Synlett* **2009**, 955 – 959; c) X.-H. Feng, G.-Z. Zhang, C.-Q. Chen, M.-Y. Yang, X.-Y. Xu, G.-S. Huang, *Synth. Commun.* **2009**, *39*, 1768 – 1780; d) L. Wang, C. Huang, C. Cai, *Catal. Commun.* **2010**, *11*, 532 – 536; e) M. Mondal, G. Sarmah, K. Gogoi, U. Bora, *Tetrahedron Lett.* **2012**, *53*, 6219 – 6222.

[12] a) P. J. Stang, V. V. Zhdankin, *Chem. Rev.* **1996**, *96*, 1123 – 1178; b) E. A. Merritt, B. Olofsson, *Angew. Chem.* **2009**, *121*, 9214 – 9234; *Angew. Chem. Int. Ed.* **2009**, *48*, 9052 – 9070; c) P.-O. Norrby, T. B. Petersen, M. Bielawski, B. Olofsson, *Chem. Eur. J.* **2010**, *16*, 8251 – 8254; d) L. F. Silva, Jr., B. Olofsson, *Nat. Prod. Rep.* **2011**, *28*, 1722 – 1754; e) J. Malmgren, S. Santoro, N. Jalalian, F. Himo, B. Olofsson, *Chem. Eur. J.* **2013**, *19*, 10334 – 10342.

[13] a) N. R. Deprez, M. S. Sanford, *J. Am. Chem. Soc.* **2009**, *131*, 11234 – 11241; b) R. J. Phipps, M. J. Gaunt, *Science* **2009**, *323*, 1593 – 1597; c) A. E. Allen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2011**, *133*, 4260 – 4263; d) R. J. Phipps, L. McMurray, S. Ritter, H. A. Duong, M. J. Gaunt, *J. Am. Chem. Soc.* **2012**, *134*, 10773 – 10776; e) A. M. Wagner, A. J. Hickman, M. S. Sanford, *J. Am. Chem. Soc.* **2013**, *135*, 15710 – 15713.

[14] a) N. Jalalian, E. E. Ishikawa, L. F. Silva, B. Olofsson, *Org. Lett.* **2011**, *13*, 1552 – 1555; b) N. Jalalian, T. B. Petersen, B. Olofsson, *Chem. Eur. J.* **2012**, *18*, 14140 – 14149; c) E. Lindstedt, R. Ghosh, B. Olofsson, *Org. Lett.* **2013**, *15*, 6070 – 6073.

[15] a) F. Guo, L. Wang, P. Wang, J. Yu, J. Han, *Asian J. Org. Chem.* **2012**, *1*, 218 – 221; b) J. D. McKerrow, J. M. Al-Rawi, P. Brooks, *Asian J. Chem.* **2012**, *24*, 1227 – 1236; c) S. Mao, F. Guo, J. Li, X. Geng, J. Yu, J. Han, L. Wang, *Synlett* **2013**, *24*, 1959 – 1962.

[16] a) S. C. Cullen, S. Shekhar, N. K. Nere, *J. Org. Chem.* **2013**, *78*, 12194 – 12201; b) N. Ichiishi, A. J. Canty, B. F. Yates, M. S. Sanford, *Org. Lett.* **2013**, *15*, 5134 – 5137.

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COMMUNICATION

Synthetic Methods

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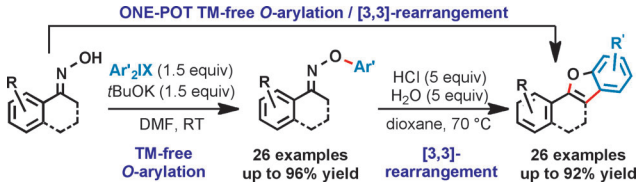
Scalable, Transition-Metal-Free Direct Oxime *O*-Arylation: Rapid Access to *O*-Arylhydroxylamines and Substituted Benzo[*b*]furans



A scalable, transition-metal-free (TM-free) direct *O*-arylation of ketone oximes with a wide range of diaryliodonium salts has been developed. More than two dozen *O*-arylated oximes have been prepared in good to excellent yields at ambient temperature and were converted to the corresponding substituted benzo[*b*]furans through a [3,3]-sigmatropic rearrangement/cyclization sequence. Overall, this operationally simple, environmentally benign, and protecting-group-free approach, including a one-pot variant, allows rapid and convenient synthetic access to substituted benzo[*b*]furans (see scheme).