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Base Mediated Synthesis of Alkyl-aryl Ethers from the Reaction of Aliphatic Alcohols and Unsymmetric Diaryliodonium Salts

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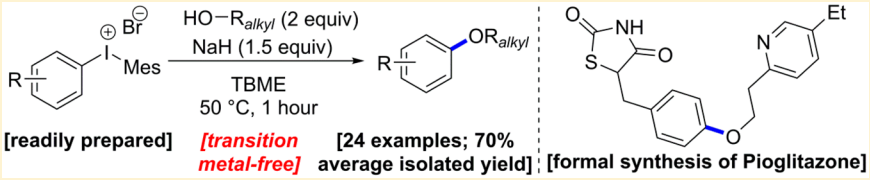
Supporting Information



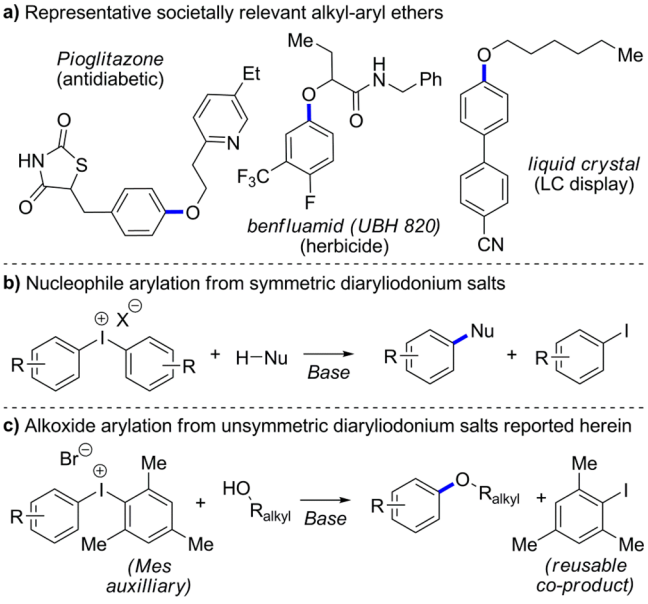
ABSTRACT: The base mediated coupling of aliphatic alcohol pronucleophiles with unsymmetric diaryliodonium salt electrophiles is described. This metal-free reaction is operationally simple, proceeds at mild temperature, and displays broad substrate scope to generate industrially important alkyl-aryl ethers in moderate to excellent yield. The synthetic utility of these reactions is demonstrated, and aspects of sustainability are highlighted by the use of unsymmetric aryl(mesityl)iodonium arylating reagents.

INTRODUCTION

Alkyl-aryl ethers are prevalent motifs in molecules essential to diverse industries including pharmaceutical, agrochemical, and high-tech. Indeed, innovative strategies to access these moieties have continued to evolve in order to accommodate the structurally elaborate alkyl and aryl components of these molecules (Scheme 1a). Convergent approaches that couple an aryl fragment with an alkyl fragment to form a new C−O bond are efficient and synthetically attractive. The alkylation of phenols ($O-C_{alkyl}$ bond) via the Williamson ether synthesis,[1] related condensation reactions,[2] and Mitsunobu reaction[3] are classic methods. However, the synthetic utility of this traditional strategy is often restricted by limited substrate scope, toxic reagents (i.e., alkylating agents), and harsh reaction conditions (i.e., high temperature and strong acid). The alternative strategy of forming the C_{aryl}-O bond (highlighted blue in Scheme 1a) has traditionally been accomplished by nucleophilic aromatic substitution (S_NAr) with aryl halides and alkali metal alkoxides.[4] While this reaction continues to find widespread use,[5] it is limited by very specific aryl substitution patterns and the requirement for highly electron-withdrawing functional groups. Recent advances in O-arylation methodology with aliphatic alcohols have focused on transition metal catalysis and ligand development studies.[6−9] However, novel transition metal-free reactions have a potential environmental and economic benefit as they avoid precious metal catalyst systems and metal-remediation steps in synthesis.

Symmetric diaryliodonium salts are well-known to participate in base mediated arylation reactions under relatively mild conditions, and this underpins a general strategy to metal-free arylation of diverse nucleophiles (Scheme 1b).[10−12] Given the utility of the products, heteroatom nucleophiles have been an active area of research particularly with nitrogen,[13−16] oxygen,[17−26] and sulfur[27−31] nucleophiles. Phenols, carboxylic acid, sulfonate, and oxime derived reactants are representative of the most successful O-nucleophiles recently reported. Importantly, a common structural feature of these coupling partners is the absence of α-C-H bonds that are susceptible to oxidative cleavage. This side reaction represents the most significant challenge to the development of a general alkoxide arylation

Scheme 1. Important Alkyl-aryl Ethers and Approaches from Diaryliodonium Salts



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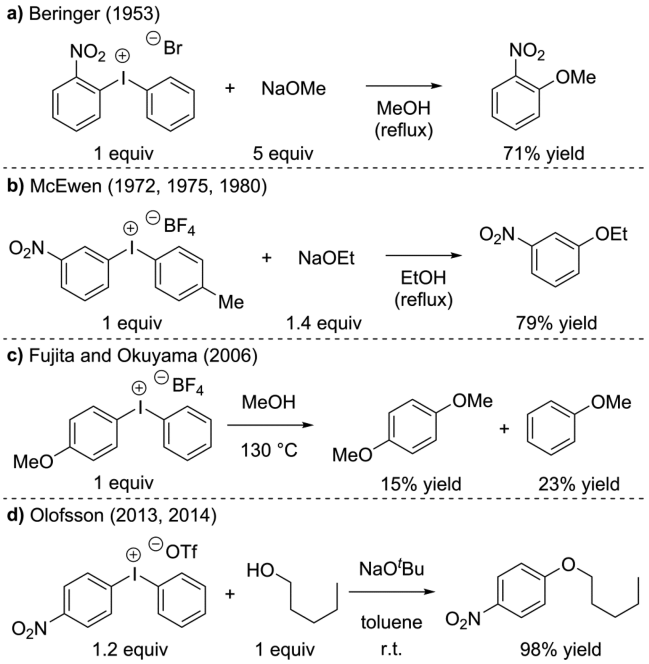
reaction, and synthetically useful protocols have only recently begun to emerge.[32,33] Herein, we describe our contribution to alkyl-aryl ether synthesis and report the discovery and development of a metal-free coupling reaction between aliphatic alcohols and *unsymmetric* aryl(mesityl)iodonium salts (Scheme 1c).

Despite the potential synthetic utility of a metal-free coupling reaction between diaryliodonium salts and aliphatic alcohols, to the best of our knowledge, there are only seven reports of such a reaction in the chemical literature. Representative examples are provided from the contributions of Beringer,[34] McEwen,[35−37] Fujita and Okuyama,[38] and Olofsson[32,33] to the discovery and development of this class of reaction (Scheme 2).

Scheme 2. History of Innovation in the Synthesis of Alkyl-aryl Ethers from Diaryliodonium Salts



Beringer provided the seminal contribution in 1953 for the foundational reactivity of diaryliodonium salts with methoxide nucleophile generated in methanol (Scheme 2a). Two examples were described in this work and one featured an unsymmetric diaryliodonium salt in which aryl transfer selectivity of the electron-deficient aryl group to the alkoxide nucleophile was observed (Scheme 2a). McEwen and co-workers studied the mechanism of this reaction for alkoxide nucleophiles derived from methanol, ethanol, and 2-propanol in the respective alcohols (Scheme 2b). Importantly, it was found that a radical decomposition side-reaction leading to alcohol oxidation was minimized by the addition of the radical inhibitor diphenylethylene (DPE) or by solvent modulation to include nonpolar solvents such as toluene or *n*-hexane. Fujita and Okuyama have recently found that solvolysis of diaryliodonium salts occurred in alcohol solvent at elevated temperature (130 °C) in the absence of base (Scheme 2c). Despite the low yields, preference for the solvolysis of the more electron-deficient aryl groups was observed, and mechanistic experiments were inconsistent with the intermediacy of an aryl cation. Olofsson and co-workers have provided the latest innovation to this class of metal-free coupling reaction and have developed synthetically useful methods that tolerate a range of aliphatic alcohols. Benzylic and allylic alcohols were specifically demonstrated to couple with a range of symmetric diaryliodonium salts under aqueous conditions in the presence of hydroxide base.[32] It was noted, however, that other aliphatic alcohols were not compatible under these conditions, and significant alcohol oxidation was observed. Subsequently, mild reaction conditions that are compatible with nonbenzylic and nonallylic aliphatic alcohols were described by Olofsson in which the alkoxide nucleophile is generated by deprotonation with sodium *tert*-butoxide in toluene as a nonpolar solvent at room temperature (Scheme 2d). Collectively, in all applicable cases within these reports the electron-deficient aryl group transfers from unsymmetric diaryliodonium salts to the alkoxide nucleophile. This selectivity is consistent with other metal-free arylation reactions of unsymmetric diaryliodonium salts and contrasts the selectivity that is observed in metal-catalyzed reactions with these reagents.[39] Despite these advances, the use of a general auxiliary that facilitates alkoxide arylation from a wide variety of unsymmetric aryl(auxiliary)iodonium salts has not been described in the literature and would constitute a practical advance to alkyl-aryl ether synthesis.

We are cognizant of the inherently poor atom economy[40] associated with symmetric diaryliodonium salts as an equivalent of aryl iodide is generated as a coproduct when these reagents are employed (Scheme 1b). Moreover, the synthesis of symmetric diaryliodonium salts that incorporate elaborate aryl groups can be challenging. Unsymmetric aryl(auxiliary)-iodonium salts provide several practical advantages in the preparation and use of these reactants in metal-free arylation reactions.

The most significant challenge to the use of unsymmetric aryl(auxiliary)iodonium salts is selective transfer of the aryl moiety to the nucleophilic coupling partner while the auxiliary remains inert. The inherent electronic and steric effects that control the selectivity of aryl group transfer are summarized by several examples. In metal-free reactions, the electron-deficient aryl group is transferred (as demonstrated in Scheme 2), and therefore, electron-rich auxiliaries, such as 2-thienyl,[41] have been studied. The steric effects on aryl group transfer in metal-free reactions depend on the nature of the nucleophile.[42] When the electronic effects are relatively close (i.e., phenyl vs mesityl), transfer of the sterically bulky aryl group (mesityl) is favored with phenol as an *O*-nucleophile.[42] However, when the electronic effects are disparate (i.e., phenyl vs 2,4,6-trimethoxyphenyl), electronic effects override the steric effects, and transfer of the more electron-deficient phenyl group to phenol is observed.[42] In the context of alkoxide arylation, only very disparate electronic effects of the aryl groups (nitrophenyl vs phenyl) have been tested, and the interplay between electronic and steric effects are currently unknown. The mesityl group is well-known as a general auxiliary for unsymmetric diaryliodonium salts in metal-catalyzed reactions[43] and in some metal-free reactions;[42,44] however, to the best of our knowledge, the use of the mesityl auxiliary in metal-free alkoxide arylation has not been reported. This sterically bulky auxiliary is unique among several recognized auxiliaries (i.e., 2-thienyl and 2,4,6-trimethoxyphenyl) as it is commercially available (and relatively inexpensive) as the simple arene (mesitylene), the aryl iodide (iodomesitylene), and a hypervalent iodine reagent (iodomesitylene diacetate). This confers significant preparative advantages with this auxiliary over other potential auxiliaries. The mesityl auxiliary also offers fertile ground to test the limits of electronic and steric effect control on aryl group transfer

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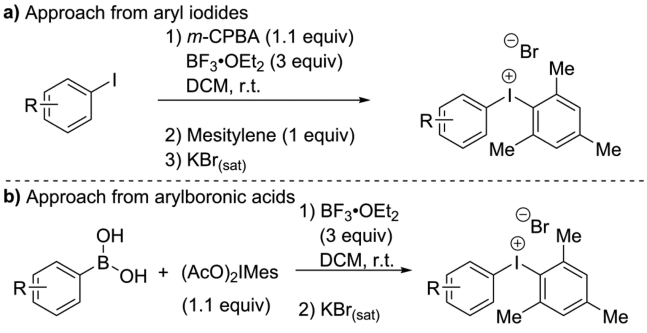
selectivity. Taken together, these attractive features have prompted our exploration of the mesityl group as the first general auxiliary in metal-free alkoxide arylation with aryliodonium electrophiles (Scheme 1c).

In this article, we describe a metal-free, base mediated approach to alkyl-aryl ethers from aliphatic alcohols and diaryliodonium salts in which we specifically address atom economy by using *unsymmetric* aryl(mesityl)iodonium salts. Moreover, we have built sustainability into this strategy by the selection of a recoverable and reusable mesityl-derived auxiliary, and this approach has enabled the synthesis of a broad range of alkyl-aryl ethers by this method. Additionally, we have demonstrated the utility of this transformation in the formal synthesis of pioglitazone, the active ingredient of the antidiabetic drug Actos.

RESULTS AND DISCUSSION

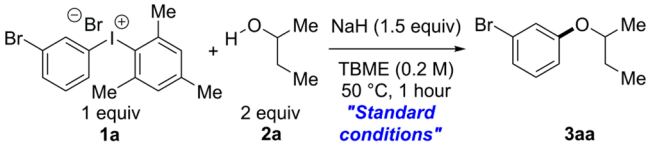
Reaction Development. In order to access a diverse array of unsymmetric aryl(mesityl)iodonium bromides, we have adapted two known routes to this general class of compound (Scheme 3).[45−47] These approaches are complementary from the stand-point of aryl group genesis. In the first approach (Scheme 3a), the iodo-moiety of an aryl iodide is oxidized, and the mesityl group is introduced as inexpensive and readily available mesitylene. In the second approach (Scheme 3b), an arylboronic acid reacts with a commercially available iodine(III) reagent, mesitylene iododiacetate, under nonoxidizing conditions to yield the unsymmetric aryl(mesityl)iodonium salt. In both cases, the bromide counterion is introduced with inexpensive potassium bromide (KBr), and we have generally found that the aryliodonium bromides are easier to purify and have more robust bench stability than the corresponding triflate or tetrafluoroborate salts. Both of these reactions exhibit the general properties of diaryliodonium salt synthesis: operationally simple to set up ("one-pot"), scalable (~10 mmol), employ inexpensive, and commercially available reagents, and, most importantly, do not require chromatographic purification of the iodonium salts. These attractive features will facilitate the use of this chemistry and promote the development of other metal-free arylation reactions with these reagents.

Scheme 3. One-Pot Approaches to Aryl(mesityl)iodonium Bromide Electrophiles

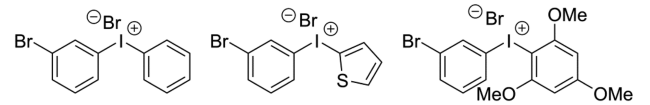


Substrate selection was a key feature of our reaction discovery and development. 3-Bromophenyl derived iodonium salt (**1a**) and 2-butanol (**2a**) were selected as test substrates. The *meta*-bromo substituent is moderately inductively withdrawing, provides opportunities for further functionalization, and has not been previously explored in the context of this class of reaction with unsymmetric diaryliodonium salts. The secondary alcohol was chosen as a substrate that currently represents a challenge in transition metal-catalyzed alkyl-aryl ether bond forming reactions due to competitive oxidation to ketone byproducts.[6,7] Therefore, success using this class of alcohol would constitute a general advance in strategy for assembling these molecules. Empirical screening of reaction conditions led to the "standard conditions" in Table 1, entry 1.

Table 1. Influence of Reaction Parameters on the Yield of 3aa



Entry	Deviation from "Standard Conditions"[a]	Yield of **3aa**[b]
1	*none*	81%
	Structure of 1a	
2	3-bromoiodobenzene instead of **1a**	—[c]
3	**1a-Ph** instead of **1a**	27%
4	**1a-Th** instead of **1a**	51%
5	**1a-TMB** instead of **1a**	68%[d]
6	OTf instead of Br counterion on **1a**	81%
	Identity of base	
7	Na_2CO_3 instead of NaH	—[c]
8	NaO^{t}Bu instead of NaH	70%
9	NaHMDS instead of NaH	22%
	Reaction solvent	
10	toluene instead of TBME	72%
11	DCE instead of TBME	30%
12	DMF instead of TBME	—[c]
	Reaction temperature	
13	30 °C instead of 50 °C	76%
14	70 °C instead of 50 °C	70%



[a]Conditions: **1a** (0.1 mmol, 0.2 M, 1 equiv), **2a** (0.2 mmol, 2 equiv), NaH (0.15 mmol, 1.5 equiv), TBME (0.5 mL), 50 °C, and 1 h (unless otherwise stated above). [b]Yield determined by ^{1}H NMR spectroscopy from the crude reaction mixture against 1,3,5-trimethoxybenzene as an internal standard. [c]**3aa** not detected in the crude ^{1}H NMR spectrum. [d]4-Fluoro-2-nitro-1-iodobenzene as internal standard.

Under these conditions, complete consumption of **1a** and 81% yield of **3aa** were observed in the crude ^{1}H NMR spectrum versus 1,3,5-trimethoxybenzene as an internal standard. During the preparation of this manuscript, Olofsson and co-workers reported a method to access alkyl-aryl ethers from diaryliodonium salts.[33] Importantly, when we used Olofsson's conditions in the reaction of **1a** and **2a**, a substantially lower yield of 56% **3aa** was observed in the crude ^{1}H NMR spectrum (compare to 81% from Table 1, entry 1).

Several other features of our reaction development warrant comment (Table 1). With regard to the structure of **1a**, no product **3aa** was observed when the monovalent aryl iodide, 3-bromoiodobenzene, was used as the aryl electrophile (Table 1, entry 2). The preparative advantages of the mesityl auxiliary have been emphasized (*vide supra*), and this auxiliary also provided the highest yield of **3aa** relative to other aryl auxiliaries including phenyl (**1a-Ph**), 2-thienyl (**1a-Th**), and trimethoxybenzene (**1a-TMB**) (Table 1 compare entry 1 with

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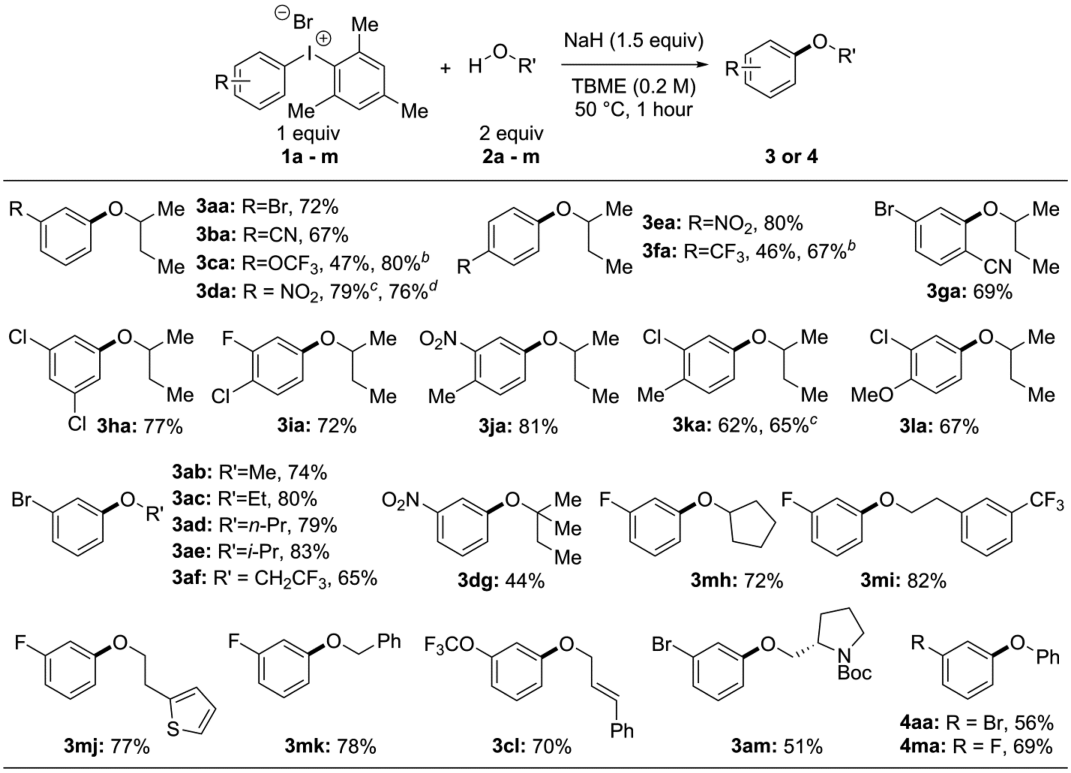
Table 2. Reaction Scope[a]



[a]Conditions: **1** (0.5 mmol, 0.2 M, 1 equiv), **2** (1 mmol, 2 equiv), NaH (0.75 mmol, 1.5 equiv), TBME (2.5 mL), 50 °C, and 1 h (yields are reported for isolated material after chromatography). [b]Yield determined from the crude ^{1}H NMR spectrum against 1,3,5-trimethoxybenzene as an internal standard (0.1 mmol scale reaction). [c]Reaction scale: 1 mmol of **1**. [d]Reaction scale: 5 mmol of **1**.

3−5). The counterion of the iodonium salt had less influence on reaction yield than auxiliary and the triflate salt of **1a** provided the same yield of **3aa** relative to the bromide salt (Table 1, compare entry 1 and 6). A variety of bases were tested in the reaction, and sodium hydride provided the highest yield of **3aa** (Table 1, entry 7−9). The use of neutral organic amine bases, such as triethylamine, did not provide any evidence of **3aa** in the crude ^{1}H NMR spectrum. Under our "standard conditions," the ethereal solvent *tert*-butyl methyl ether (TBME) provided the highest yield (Table 1, entry 1). Toluene also provided synthetically useful yields, whereas 1,2-dichloroethane (DCE) resulted in low yield (30%), and dimethylformamide (DMF) resulted in no product observed (Table 1, entries 10−12). Notably, the effective temperature range for this reaction was relatively narrow. Both lower (30 °C) and higher (70 °C) reaction temperatures resulted in lower yields of **3aa** (Table 1, entries 13 and 14).

Reaction Scope. The scope of the transformation described here is presented in Table 2. In total, 13 different aryl groups and 13 different aliphatic alcohols demonstrate aspects of steric and electronic compatibility in this reaction. With respect to aryl groups, *ortho*-, *meta*-, and *para*-substitutions are tolerated, and a variety of different functional groups including halides (bromo, chloro, fluoro), nitro, nitrile, trifluoromethyl, trifluoromethoxy, methoxy, and methyl are compatible as substituents on the aromatic ring of the electrophile under the reaction conditions. The use of this broad range of substrates aptly differentiates this work from traditional S_NAr reactions. Primary, secondary, and tertiary aliphatic alcohols all react with aryl(mesityl)iodonium salts in this reaction to provide alkyl-aryl ethers with primary, secondary, and tertiary alkyl groups. This attribute distinguishes this work from phenol alkylation methods that are most general with methyl or primary alkyl electrophiles. Additionally, allylic, benzylic and phenolic alcohols are compatible nucleophiles in the coupling reaction.

Several important aspects of the scope of this reaction are facilitated by the use of aryliodonium electrophiles, specifically unsymmetric aryl(mesityl)iodonium bromides, and warrant additional comment. First, fluoro-substituents are well tolerated on the aromatic ring of the electrophile in this reaction (**3ia**, **3mh**, **3 mi**, **3mj**, **3mk**, and **4ma**; Table 2). Aryl fluorides are broadly compatible with hypervalent iodine chemistry, and the chemoselective substitution at the iodonium group is a result of the highly electrophilic nature of this moiety. This is in contrast to S_NAr reactions where fluoride is the optimal leaving group, and selective substitution of polyfluorinated aromatic rings can be challenging. As such, active ingredients of pharmaceuticals and agrochemicals that contain alkyl-aryl ethers with fluoro-substituents may be chemoselectively accessed with this method. Second, the potential for the synthesis of more elaborate and highly substituted aromatic compounds is presented here. The synthesis of unsymmetrical aryl(mesityl)-iodonium salt electrophiles is more straightforward than that of the corresponding symmetric diaryliodonium salts and the use of a common auxiliary (mesityl) allows for sustainable synthesis (*vide infra*). The synthesis of alkyl-aryl ethers with polysubstituted aromatic rings (**3ga**, **3ha**, **3ia**, **3ja**, **3ka**, and **3la**, Table 2) is achieved here as a result of this strategy. To the best of our knowledge, products with more the two aryl substituents have not been produced by previous alkyl-aryl ether syntheses from diaryliodonium salts and aliphatic alcohols. Third, only trace

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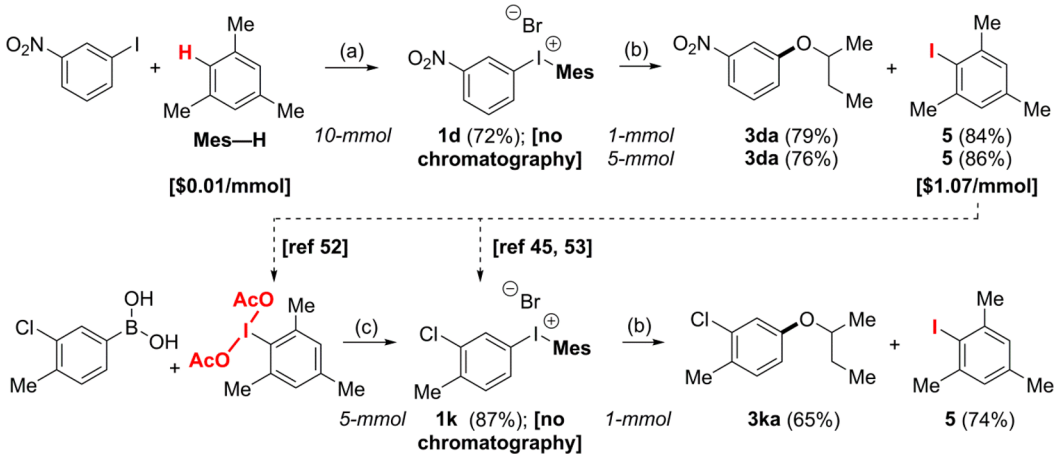
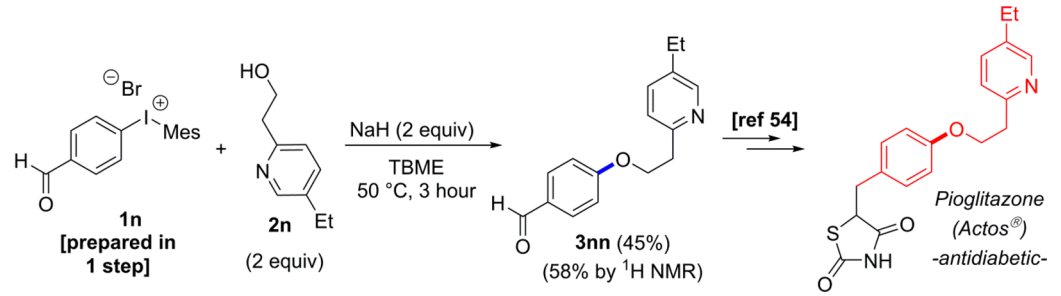
Scheme 4. Recovery of Iodomesitylene Co-product[a]



[a]Conditions: (a) (*i*) 3-nitroiodobenzene (10 mmol), *m*-CPBA (11 mmol), BF_3•OEt_2 (30 mmol), DCM (50 mL), 0 °C to room temperature, 2 h; (*ii*) mesitylene (**Mes**) (10 mmol), 0 °C to room temperature, 12 h; (*iii*) $KBr_{(sat,\ aq)}$, room temperature, 30 min. (b) **1** (0.2 M, 1 equiv), **2a** (2 equiv), NaH (1.5 equiv), TBME, 50 °C, 1 h. (c) (*i*) 3-chloro-4-methylphenyl boronic acid (5 mmol), BF_3•OEt_2 (15 mmol), mesitylene iododiacetate (5.5 mmol), DCM (50 mL), 0 °C to room temperature, 12 h; (*ii*) $KBr_{(sat.\ aq)}$, room temperature, 30 min.

Scheme 5. Formal Synthesis of Pioglitazone, the Active Ingredient of Actos



benzaldehyde is observed in the crude ^{1}H NMR spectrum of the reaction of **1m** and **2k** (benzyl alcohol). Alcohol oxidation is a current challenge in other reactions to access alkyl-aryl ethers, and the nominal amount aldehyde side-product observed here is likely due to a medium-effect of the nonpolar reaction solvent (TBME), consistent with McEwen's[36] observations.[48]

The chemoselectivity of aryl group transfer from aryl(mesityl)iodonium bromides to alkoxide nucleophiles in all cases presented in Table 2 is consistent with electronically controlled transfer of the more electron-deficient[49] aryl group. Moreover, several examples highlight the extent to which electronic control overrides the established *ortho*-effect[50] that has been observed with phenol *O*-nucleophiles.[42] Specifically, the aryl(mesityl)iodonium bromides **1j**, **1k**, and **1l** each contain aryl groups with an electron-donating group in the *para*-position and a mitigating electron-withdrawing group in the *meta*-position. The aryl group in **1l** is mildly electron-deficient[51] but sufficient enough to chemoselectively transfer in good yield (**3la**, 67%, Table 2). Notably, the mass balance in this case is not a result of poor chemoselectivity, and a mesityl-coupled alkyl-aryl ether product is not observed in the crude ^{1}H NMR spectrum of **3la**. To the best of our knowledge, the diarylethers **4aa** and **4ma** have not been prepared from symmetric or unsymmetric diaryliodonium salts and phenols. While the yields for these products are moderate relative to typical yields described by Olofsson,[20,22,32] for related diarylethers, they have been prepared from readily accessible unsymmetric aryl(mesityl)iodonium bromides in this case. Moreover, these products provide two additional examples where electronic control overrides the *ortho*-effect (specifically with phenol *O*-nucleophiles) and highlights the utility of the mesityl auxiliary. Electron-rich aryl groups are noticeably absent from Table 2, and arylation of alkoxide nucleophiles with symmetric or unsymmetric diaryliodonium salts with electron-rich arenes constitutes the most significant current challenge in this general class of reaction.[33] Attempts to transfer an electron-rich tolyl group were unsuccessful even with more electron-rich thienyl and trimethoxybenzene auxiliaries, and we are continuing to investigate this aspect of the reaction.

Sustainability. The development of metal-free arylation reactions with unsymmetric diaryliodonium electrophiles provides a platform to incorporate sustainability into method development. To demonstrate, **1d** is readily prepared in a "one-pot" reaction from 1-iodo-3-nitrobenzene on 10 mmol scale in 72% isolated yield with no chromatographic purification necessary (Scheme 4, step a). Compound **1d** reacts with **2a** under our "standard conditions" to yield alkyl-aryl ether **3da** and iodomesitylene **5** in good isolated yield on both 1- and 5 mmol scales (Scheme 4, step b). Notably, compound **5** is readily recovered in high yield and has a 100-fold increase in commercial value relative to the mesitylene starting material. The iodomesitylene coproduct may be converted into hypervalent iodomesitylene diacetate therefore linking the two synthetic methods used here to access aryl(mesityl)iodonium bromides (Scheme 3).[52] Alternatively, **5** may be used directly in

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combination with specific arenes and an oxidant for the synthesis of aryl(mesityl)iodonium triflates.[45,53] Compound **1k** is prepared from 3-chloro-4-methylphenyl boronic acid and iodomesitylene diacetate in excellent yield (87%) with no chromatographic purification. The reaction of **1k** and **2a** under our "standard conditions" yields **3ka** and **5** in good yield (Scheme 4, 65% and 74%, respectively). The use of a common mesityl-derived, recoverable, and reusable auxiliary highlights the sustainability of this approach and enables the synthesis of diverse unsymmetric aryl(mesityl)iodonium bromides and therefore alkyl-aryl ethers.

Synthetic Applications. The alkyl-aryl ether framework of pioglitazone, the active ingredient of the antidiabetic Actos, was prepared by our method to demonstrate the general utility of this protocol (Scheme 5). The unsymmetric aryl(mesityl)-iodonium salt **1n** was prepared in a one-pot reaction from the corresponding and commercially available arylboronic acid. Under only slightly modified reaction conditions, **1n** couples to the commercially available alcohol **2n** to yield the alkyl-aryl ether scaffold of pioglitazone in synthetically useful yield. Notably, the reaction is compatible with the electrophilic aldehyde moiety and the azine heterocycle. The aldehyde **3nn** has previously been converted into pioglitazone in two synthetic steps.[54]

CONCLUSIONS

In summary, this reaction provides access to industrially important compounds in a sustainable manner. A broad scope of alkyl-aryl ethers has been produced by using easily assembled unsymmetric diaryliodonium salts in combination with primary, secondary, tertiary, allylic, and benzylic aliphatic alcohols. The utilization of an inexpensive, broadly useable, and recoverable auxiliary renders this strategy sustainable and practically attractive. The formal synthesis of pioglitazone further demonstrates the synthetic utility of this method. We are continuing to explore mechanistic profiles and develop novel auxiliaries that will promote chemoselective aryl transfer from unsymmetric diaryliodonium salts to alkoxide and other heteroatom nucleophiles.

EXPERIMENTAL SECTION

General Considerations. Commercially available reagents and solvents were used without further purification unless otherwise stated. The triflate salt of **1a** was prepared by known literature methods.[37] The preparation of all other materials is described in detail below. Crude reaction mixtures were analyzed by ^{1}H NMR or ^{19}F NMR spectroscopy and thin-layer chromatography (TLC) on silica gel (60 Å F-254) TLC plates and visualized by UV irradiation. Crude material was purified by flash column chromatography on silica gel unless otherwise stated. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 (referenced to tetramethylsilane) on a 400 MHz spectrometer at 298 K unless otherwise stated. The following notation is used: br—broad, s—singlet, d—doublet, t—triplet, q—quartet, m—multiplet, and dd—doublet of doublets. FTIR spectra were obtained from solutions in DCM or $CDCl_3$. High resolution mass spectrometry (HRMS) data were recorded on an instrument by electrospray ionization (ESI) with an ion trap mass analyzer or electron impact (EI, 70 eV). Melting points are reported as uncorrected.

General Procedure for the Synthesis of Aryl(mesityl)-iodonium Bromides (1d) from Aryl Iodides (Scheme 3a).[38,39] To a stirred solution of aryl iodide (1.0 equiv) in DCM (0.1 M) was added *m*-CPBA (1.1 equiv. based on ∼70 wt % active oxidant). The resulting solution was cooled to 0 °C. BF_3•OEt_2 (3.0 equiv) was added slowly via syringe to the above solution, and the reaction mixture was stirred for 2 h at 0 °C. Mesitylene (1.0 equiv) was added via syringe, and the reaction mixture was allowed to warm to ambient room temperature and stirred overnight. The septum was removed, and an aqueous saturated solution of KBr (2 × volume of DCM) was added with vigorous stirring for ∼30 min. The biphasic mixture was added to a separatory funnel and the DCM/water layers separated. The water layer was extracted with DCM (3 × 50 mL). The combined DCM layers were dried over $MgSO_4$, filtered, and the DCM removed on a rotary evaporator. The crude residue was triturated with diethyl ether to yield analytically pure aryl(mesityl)iodonium bromide. See below for the specific scale of reactions and characterization data of individual compounds.

General Procedure for the Synthesis of Aryl(mesityl)-iodonium Bromides (1a, 1a-Ph, 1b, 1c, 1g, 1h, 1i, 1j, 1k, 1l, 1m, and 1n) from Aryl Boronic Acids (Scheme 3b).[40] Aryl boronic acid (1.0 equiv) was weighed and transferred to a pear-shaped flask equipped with a magnetic stir bar and rubber septum. The flask was flushed with nitrogen and left under a static nitrogen atmosphere. DCM (0.1 M) was added via syringe to the aryl boronic acid, and the solution was cooled to ∼0 °C in an ice—water bath with stirring. BF_3•OEt_2 (3.0 equiv) is added via syringe to the aryl boronic acid solution and the reaction mixture was stirred for 10 min at 0 °C. Mesitylene iododiacetate (1.1 equiv) was weighed and transferred to a separate pear-shaped flask equipped with rubber septum. The flask was flushed with nitrogen and left under a static nitrogen atmosphere. DCM (0.33 M) was added to the mesitylene iododiacetate. The mesitylene iododiacetate solution was added to the aryl boronic acid/BF_3•OEt_2 solution dropwise via syringe at ∼0 °C. The reaction mixture was allowed to warm to ambient room temperature and stirred overnight. The septum was removed, and an aqueous saturated solution of KBr (1.25 × total volume of DCM) was added with vigorous stirring for ∼30 min. The biphasic mixture was added to a separatory funnel, and the DCM/water layers separated. The water layer was extracted with DCM (3 × 30 mL). The combined DCM layers were dried over $MgSO_4$, filtered, and the DCM removed on a rotovap. The crude residue was triturated with diethyl ether to yield analytically pure aryl(mesityl)iodonium bromide. See below for the specific scale of reactions and characterization data of individual compounds.

General Procedure for Triflate (or Tosylate) to Bromide Ion Exchange Reactions from Aryl(mesityl)iodonium Triflates (or Tosylate) (1a-Th, 1a-TMB, 1e, and 1f). Crude aryl(mesityl)-iodonium triflate (or tosylate) (1 equiv) was dissolved in DCM (0.1 M), and a saturated solution of KBr was added with vigorous stirring for 30 min at room temperature. The organic layer was separated, and the aqueous layer was extracted with DCM (3 × 30 mL). The combined organic layer is dried over $MgSO_4$ and evaporated on a rotary evaporator. The resulting solid was triturated with diethyl ether and isolated by filtration to give analytically pure aryl(mesityl)-iodonium bromide. See below for specific scale of reactions and characterization data of individual compounds.

3-Bromophenyl(mesityl)iodonium Bromide (1a). Prepared from the corresponding aryl boronic acid on a 9.998 mmol-scale and obtained in 71% isolated yield as a white powder (3.426 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.15 (t, J = 1.6 Hz, 1H), 7.74 (m, 2H), 7.36 (t, J = 8.0 Hz, 1H), 7.17 (s, 2H), 2.60 (s, 6H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 142.4, 140.9, 135.4, 133.8, 133.1, 132.2, 129.5, 125.4, 123.1, 119.3, 26.1, 20.4. FTIR: 2976, 2936, 1587, 1474 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^{+}$ calculated for $C_{15}H_{15}BrI^{+}$ 400.9396; found 400.9418. Melting point (DCM/Et_2O): 145.4—146.8 °C.

3-Bromophenyl(phenyl)iodonium Bromide (1a-Ph). Prepared from the corresponding aryl boronic acid (1.03 mmol-scale) and phenyl iododiacetate and obtained in 83% isolated yield as a white powder (0.381 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.59 (t, J = 1.6 Hz, 1H), 8.28 (t, J = 8.5 Hz, 3H), 7.87 (dd, J = 8.1, 1.0 Hz, 1H), 7.69 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.49 (dd, J = 14.9, 6.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 136.8, 135.1, 134.9, 133.9, 133.3, 132.1, 131.7, 123.1, 116.9, 116.7. FTIR: 1238, 11673, 1026, 769 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^{+}$ calculated for

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$C_{12}H_9BrI^+$ 358.8926; found 358.8935. Melting point (DCM/Et_2O): 166 °C−169 °C.

3-Bromophenyl(thienyl)iodonium Bromide (1a-Th). The tosylate salt was prepared by known procedures,[35,55] and the bromide salt was obtained in 53% isolated yield as a light brown powder (0.561 g) via ion-exchange. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.50 (t, J = 1.8 Hz, 1H), 8.26−8.17 (m, 1H), 8.03−7.93 (m, 1H), 7.89 (dd, J = 5.3, 1.3 Hz, 1H), 7.84−7.76 (m, 1H), 7.48−7.38 (m, 1H), 7.18−7.08 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 139.1, 136.2, 136.0, 134.1, 133.2, 132.9, 129.1, 122.6, 122.6, 106.3. FTIR: 1224, 777 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{10}H_7BrIS^+$ 364.8491; found 364.8495. Melting point (DCM/Et_2O): 149 °C−159 °C.

3-Bromophenyl(2′,4′,6′-trimethoxyphenyl)iodonium Bromide (1a-TMB). The tosylate salt was prepared by known procedures,[35,50] and the bromide salt was obtained in 17% isolated yield as a pale yellow powder (0.152 g) via ion-exchange. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.11 (t, J = 1.8 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.76 (dd, J = 8.0, 0.9 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 6.44 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 165.7, 159.1, 135.7, 133.7, 132.9, 132.6, 122.6, 119.0, 91.9, 90.4, 57.1, 55.9. FTIR: 2948, 2839, 1581, 1453, 1221, 1122, 769 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{15}H_{15}BrIO_3^+$ 448.9243; found 448.9234. Melting point (DCM/Et_2O): 175 °C−179 °C.

3-Cyanophenyl(mesityl)iodonium Bromide (1b). Prepared from the corresponding aryl boronic acid on a 6.0 mmol-scale and obtained in 20% isolated yield as a yellow powder (0.51 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.49 (s, 1H), 8.14 (d, J = 8.2 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.62 (t, J = 8.3 Hz, 1H), 7.19 (s, 2H), 2.58 (s, 6H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 142.4, 140.9, 138.1, 137.0, 134.6, 131.9, 129.5, 125.6, 119.1, 117.0, 113.5, 26.2, 20.4. FTIR: 3020, 2226, 1457 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{16}H_{15}IN^+$ 348.0244; found 348.0259. Melting point (DCM/Et_2O): 138.8−140.0 °C.

3-Trifluoromethoxyphenyl(mesityl)iodonium Bromide (1c). Prepared from the corresponding aryl boronic acid on a 4.8 mmol-scale and obtained in 51% isolated yield as a pale yellow powder (1.2 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.00 (s, 1H), 7.77−7.74 (m, 1H), 7.59 (m, 2H), 7.18 (s, 2H), 2.59 (s, 6H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 148.6, 142.4, 140.8, 132.9, 132.2, 129.5, 126.2, 125.8, 123.5, 119.8 (q, J_{C-F} = 254.7 Hz), 119.2, 26.1, 20.4. ^{19}F NMR (377 MHz, DMSO-d_6): δ (ppm) −57.02. FTIR: 2924, 1579, 1468, 1257, 1218, 1202, 1163 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{16}H_{15}F_3IO^+$ 407.0114; found 407.0130. Melting point (DCM/Et_2O): 155.5−158.0 °C.

3-Nitrophenyl(mesityl)iodonium Bromide (1d). Prepared from the corresponding aryl iodide on a 10.1 mmol-scale and obtained in 72% isolated yield as a pale yellow powder (3.24 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.70 (t, J = 1.8 Hz, 1H) 8.35−8.33 (m, 1H), 8.10−8.08 (m, 1H), 7.68 (t, J = 8.8 Hz, 1H), 7.20 (s, 2H), 2.60 (s, 6H) 2.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 148.3, 142.6, 140.9, 138.9, 132.3, 129.5, 128.0, 125.7, 125.5, 119.2, 26.2, 20.4. FTIR: 3106, 2223, 1524, 1346, 1293 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{15}H_{15}INO_2^+$ 368.0142; found 368.0157(4). Melting point (DCM/Et_2O): 140.5−142.2 °C.

4-Nitrophenyl(mesityl)iodonium Bromide (1e). The triflate salt was prepared by a known procedure.[37] Prepared by ion exchange from the corresponding crude aryl(mesityl)iodonium triflate on a 4.091 mmol-scale and obtained in 79% isolated yield as a white powder (1.448 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.21 (d, J = 9.2 Hz, 2H), 8.10 (d, J = 9.1 Hz, 2H), 7.20 (s, 2H), 2.59 (s, 6H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 148.7, 142.6, 140.9, 134.8, 129.6, 125.7, 125.4, 125.1, 26.1, 20.4. FTIR: 3084, 3047, 1532, 1354 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{15}H_{15}INO_2^+$ 368.0142; found 368.0156(8). Melting point (DCM/Et_2O): 144.0−145.0 °C.

4-Trifluoromethylphenyl(mesityl)iodonium Bromide (1f). The triflate salt was prepared by a known procedure.[37] Prepared by ion-exchange from the corresponding crude aryl(mesityl)iodinonium triflate on 3.731 mmol-scale and obtained in 81% isolated yield as a pale yellow powder (1.416 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.07 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.5 Hz, 2H), 7.20 (s, 2H), 2.59 (s, 6H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 142.5, 140.9, 134.4, 130.8 (q, J_{C-F} = 31.7 Hz), 129.5, 127.8 (q, J_{C-F} = 3.7 Hz), 125.5, 123.6 (q, J_{C-F} = 270.5 Hz), 123.1, 26.1, 20.4. ^{19}F NMR (377 MHz, DMSO-d_6): δ (ppm) −61.61. FTIR: 2920, 1593, 1329, 1127, 1066, 1002 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{16}H_{15}F_3I^+$ 391.0165; found 391.0183. Melting point (DCM/Et_2O): 162.0−162.5 °C.

5-Bromo-2-cyanophenyl(mesityl)iodonium Bromide (1g). Prepared from the corresponding aryl boronic acid on a 3.0 mmol-scale and obtained in 16% isolated yield as a pale yellow powder (0.25 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.39 (d, J = 0.8 Hz, 1H), 8.05−7.95 (m, 2H), 7.17 (s, 2H), 3.32 (s, 1H), 2.67 (s, 6H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 142.5, 141.1, 138.4, 136.4, 134.9, 129.7, 128.6, 126.2, 125.3, 117.6, 115.1, 26.2, 20.3. FTIR: 2976, 2947, 2288, 1444 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{16}H_{14}BrIN^+$ 425.9348; found 425.9347. Melting point (DCM/Et_2O): 161.0−164.0 °C.

3,5-Dichlorophenyl(mesityl)iodonium Bromide (1h). Prepared from the corresponding aryl boronic acid on a 3.23 mmol-scale and obtained in 40% isolated yield as a white powder (0.604 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.86 (d, J = 1.8 Hz, 2H), 7.8 (t, J = 1.2 Hz, 1H), 7.18 (s, 2H), 2.60 (s, 6H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 142.5, 140.9, 135.5, 131.4, 130.8, 129.5, 125.8, 120.7, 26.2, 20.4. FTIR: 3042 1577, 1574, 1404 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{15}H_{14}Cl_2I^+$ 390.9512; found 390.9533. Melting point (DCM/Et_2O): 143.0−147.0 °C.

4-Chloro-3-fluorophenyl(mesityl)iodonium Bromide (1i). Prepared from the corresponding aryl boronic acid on a 4.0 mmol-scale and obtained in 79% isolated yield as a white powder (1.4 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.22−8.20 (dd, J = 4.7 Hz, 2.3 Hz, 1H), 7.78−7.75 (m, 1H), 7.47 (t, J = 9.0 Hz, 1H), 7.16 (s, 2H), 2.59 (s, 6H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 158.5 (d, J = 251.1 Hz), 142.4, 140.8, 135.5, 134.5 (d, J_{C-F} = 8.11 Hz), 129.4, 125.9, 121.8 (d, J_{C-F} = 18.54 Hz), 119.6 (d, J_{C-F} = 22.0 Hz), 113.7, 26.1, 20.4. ^{19}F NMR (377 MHz, DMSO-d_6): δ (ppm) −111.31. FTIR: 3011, 1474, 1263, 1063 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{15}H_{14}ClFI^+$ 374.9807; found 374.9826. Melting point (DCM/Et_2O): 142.5−146.8 °C.

4-Methyl-3-nitrophenyl(mesityl)iodonium Bromide (1j). Prepared from the corresponding aryl boronic acid on a 5.0 mmol-scale and obtained in 46% isolated yield as a pale yellow powder (1.1 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.5 (d, J = 1.9 Hz, 1H), 7.97−7.94 (dd, J = 6.4 Hz, 2.0 Hz, 1H), 7.53 (d, J = 8.8 Hz, 1H), 7.18 (s, 2H), 2.60 (s, 6H), 2.48 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 149.5, 142.4, 140.9, 137.4, 135.7, 135.2, 129.5, 129.1, 125.6, 115.6, 26.18, 20.4, 19.1. FTIR: 3028, 2365, 1524, 1340 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{16}H_{17}INO_2^+$ 382.0299; found 382.0316. Melting point (DCM/Et_2O): 135.8−138.8 °C.

3-Chloro-4-methylphenyl(mesityl)iodonium bromide (1k). Prepared from the corresponding aryl boronic acid on a 5.0 mmol-scale and obtained in 87% isolated yield as a white powder (2.0 g). ^{1}H NMR (400 MHz, DMSO-d_6): 8.01 (d, J = 1.93 Hz, 1H), 7.65−7.63 (dd, J = 6.5 Hz, 1.6 Hz, 1H), 7.39 (d, J = 8.34 Hz, 1H), 7.16 (s, 2H) 2.58 (s, 6H), 2.31 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 142.3, 140.8, 139.1, 134.9, 133.5, 133.2, 132.1, 129.4, 125.4, 115.3, 26.1, 20.4, 19.3. FTIR: 2950, 2920, 1465, 1055 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{16}H_{17}ClI^+$ 371.0058; found 371.0075. Melting point (DCM/Et_2O): 151.3−153.9 °C.

3-Chloro-4-methoxyphenyl(mesityl)iodonium Bromide (1l). Prepared from the corresponding aryl boronic acid on a 5.0 mmol-scale and obtained in 82% isolated yield as a yellow powder (1.9 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.00 (t, J = 2.0 Hz, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.19−7.15 (m, 3H), 3.87 (s, 3H), 2.59 (s, 6H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 156.6, 142.3, 140.8, 134.6, 134.4, 129.4, 125.3, 122.9, 115.3, 106.4, 56.4, 26.1, 20.3. FTIR: 3014, 1568, 1304, 1279, 1063 cm^{-1}. HRMS (ESI) m/z: [M −

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Br]$^+$ calculated for $C_{16}H_{17}ClIO^+$ 387.0007; found 387.0025. Melting point (DCM/Et2O): 151.0−156.0 °C.

3-Fluorophenyl(mesityl)iodonium Bromide (1m). Prepared from the corresponding aryl boronic acid on a 10 mmol-scale and obtained in 49% isolated yield as a pale yellow powder (2.1 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.86−7.83 (m, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.50−7.38 (m, 2H), 7.16 (s, 2H), 2.58 (s, 6H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 161.9 (d, J_{C-F} = 252.9 Hz), 142.3, 140.8, 132.9 (d, J_{C-F} = 7.9 Hz), 129.5 (d, J_{C-F} = 3.0 Hz), 129.4, 125.8 120.7 (d, J_{C-F} = 24.8 Hz), 118.9 (d, J_{C-F} = 7.2 Hz), 118.1 (d, J_{C-F} = 21.1 Hz), 26.1, 20.4. ^{19}F NMR (377 MHz, DMSO-d_6): δ (ppm) −108.38. FTIR: 3061, 1585, 1468, 1213 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{15}H_{15}FI^+$ 341.0197; found 341.0214. Melting point (DCM/Et_2O): 126.6−128.8 °C.

4-Formylphenyl(mesityl)iodonium Bromide (1n). Prepared from the corresponding aryl boronic acid on a 5.0 mmol-scale and obtained in 81% isolated yield as a white powder (1.7 g). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.99 (s, 1H), 8.08 (d, J = 8.3 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 7.18 (s, 2H), 2.59 (s, 6H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 192.4, 142.1, 140.7, 137.0, 134.2, 131.4, 129.4, 126.3, 125.8, 26.1, 20.4. FTIR: 3102, 1699, 1264, 728 cm^{-1}. HRMS (ESI) m/z: [M − Br]$^+$ calculated for $C_{16}H_{16}IO^+$ 351.0240; found 351.0255. Melting point (DCM/Et_2O): 173−177 °C.

General Procedure for the Synthesis of Alkyl-aryl Ethers. Sodium hydride (0.75 mmol, 1.5 equiv. based on 60 wt % dispersion in mineral oil) was weighed out to air and transferred to an oven-dried vial equipped with a magnetic stir bar. The vial was sealed with a cap and Teflon-lined septum and purged with nitrogen. A solution of the alcohol (1 mmol, 2 equiv) in TBME (2.5 mL) was added dropwise to the sodium hydride and the cloudy white mixture stirred at ambient room temperature for at least 15 min. Compound **1** (0.5 mmol, 1 equiv) was powdered into the reaction vial. The vial was sealed with a solid cap and placed into a preheated (50 °C) aluminum block for 1 h. The reaction was then removed from the heat and quenched with 5 mL of a saturated solution of ammonium chloride. The biphasic mixture was transferred to a separatory funnel and the aqueous layer extracted with DCM (3 × 10 mL). The combined DCM layers were dried over $MgSO_4$, filtered, and the DCM removed on a rotary evaporator. The crude residue was purified by flash column chromatography on silica gel (see below for specific eluent composition). In cases where duplicate experiments were performed on the same mmol-scale, the range of yields and average yield are reported; the average yield is reported in Table 2.

1-Bromo-3-s-butoxybenzene (3aa). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.50 mmol-scale and obtained in 78% (0.090 g) and 67% (0.077 g) isolated yields, respectively, as a colorless oil (72% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.13 (t, J = 8.1 Hz, 1H), 7.05−7.03 (m, 2H), 6.83−6.80 (m, 1H), 4.30−4.23 (m, 1H), 1.79−1.56 (m, 2H), 1.28 (d, J = 6.3 Hz, 3H), 0.97 (t, J = 8.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.1, 130.5, 123.4, 122.7, 119.0, 114.7, 75.4, 29.1, 19.1, 9.7. FTIR: 2974, 2934, 1587, 1282, 1241 cm^{-1}. HRMS (EI) m/z: [M]$^+$ calculated for $C_{10}H_{13}BrO^+$ 228.0150; found 228.0138. R_f: 0.42 in 100% hexane.

3-(*sec*-Butoxy)benzonitrile (3ba). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.46 mmol scale and obtained in 70% (0.061 g) and 65% (0.057 g) isolated yields, respectively, as a light yellow oil (67% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 (t, J = 8.1 Hz, 1H), 7.20−7.18 (m, 1H), 7.12−7.08 (m, 2H), 4.34−4.26 (m, 1H), 1.80−1.58 (m, 2H), 1.30 (d, J = 6.1 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.1, 130.5, 123.4, 122.7, 119.0, 114.7, 75.4, 29.1, 19.1, 9.7 (one signal missing due to overlapping peaks). FTIR: 2974, 2935, 2230, 1577, 1288, 1261 cm^{-1}. HRMS (EI) m/z: [M]$^+$ calculated for $C_{11}H_{13}NO^+$ 175.0997; found 175.0992. R_f: 0.25 in 5% diethyl ether/hexane.

1-(*sec*-Butoxy)-3-(trifluoromethoxy)benzene (3ca). Prepared according to the general procedure above on a 0.50 mmol-scale and obtained in 47% (0.053 g) isolated yield as a colorless oil. Because of the volatility of this compound, the yield was also obtained from the crude ^{1}H NMR spectra versus 1,3,5-trimethoxybenzene as an internal standard in 82% and 79% (80% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.24 (t, J = 16.5 Hz, 1H), 6.81−6.73 (m, 3H), 4.31−4.24 (m, 1H), 1.79−1.57 (m, 2H) 1.29 (d, J = 6.2 Hz, 3H) 0.97 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.3, 150.2, 130.1, 120.1 (q, J_{C-F} = 260.8 Hz) 114.0, 112.5, 108.8, 75.4, 29.0, 19.0, 9.7. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −57.75. FTIR: 2976, 2936, 1589, 1260, 1008 cm^{-1}. HRMS (EI) m/z: [M]$^+$ calculated for $C_{11}H_{13}F_3O_2^+$ 234.0868; found 234.0876. R_f: 0.42 in 100% hexane.

1-(*sec*-Butoxy)-3-nitrobenzene (3da). Prepared according to the general procedure above on a 1.00 mmol-scale and obtained in 79% (0.154 g) and on a 5.04 mmol-scale and obtained in 76% (0.782 g) isolated yields as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.78−7.75 (m, 1H), 7.70 (t, J = 2.3 Hz, 1H), 7.39 (t, J = 7.7 Hz, 1H), 7.20−7.17 (m, 1H), 4.42−4.34 (m, 1H), 1.82−1.60 (m, 2H), 1.32 (d, J = 6.2 Hz, 3H), 0.98 (t, J = 5.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 158.8, 149.2, 129.9, 122.6, 115.3, 109.9, 75.9, 29.0, 18.9, 9.6. FTIR: 2976, 2936, 1529, 1349, 1150 cm^{-1}. HRMS (EI) m/z: [M]$^+$ calculated for $C_{10}H_{13}NO_3^+$ 195.0895; found 195.0903. R_f: 0.41 in 50% diethyl ether/hexane.

1-(*sec*-Butoxy)-4-nitrobenzene (3ea). Prepared according to the general procedure above on a 0.51 mmol-scale and a 0.52 mmol-scale and obtained in 77% (0.075 g) and 83% (0.083 g) isolated yields, respectively, as a light yellow oil (80% average of two runs). Spectroscopic data was consistent with that previously reported.[56] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.17 (d, J = 9.3 Hz, 2H), 6.91 (d, J = 9.3 Hz, 2H), 4.45−4.37 (m, 1H), 1.83−1.61 (m, 2H), 1.33 (d, J = 6.2 Hz, 3H), 0.98 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.4, 135.3, 120.6, 114.6, 75.8, 29.0, 19.0, 9.6. R_f: 0.46 in 5% diethyl ether/hexane.

1-(*sec*-Butoxy)-4-(trifluoromethyl)benzene (3fa). Prepared according to the general procedure above on a 0.50 mmol-scale and obtained in 39% (0.042 g) isolated yield as a colorless oil. Because of the volatility of this compound, the yield was also obtained from the crude ^{1}H NMR spectra versus 1,3,5-trimethoxybenzene as an internal standard in 67% and 68% (67% average of two runs). Spectroscopic data were consistent with those previously reported.[57] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.52 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 4.40−4.32 (m, 1H), 1.82−1.59 (m, 2H), 1.31 (d, J = 6.0 Hz, 3H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 160.8, 129.4, 126.8 (q, J_{C-F} = 3.8 Hz), 122.3 (q, J_{C-F} = 32.3 Hz), 115.4, 75.2, 29.0, 19.0, 9.7. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −61.45. R_f: 0.44 in 100% hexane.

4-Bromo-2-(sec-butoxy)benzonitrile (3ga). Prepared according to the general procedure above on a 0.43 mmol-scale and a 0.50 mmol-scale and obtained in 69% (0.075 g) and 70% (0.088 g) isolated yields, respectively, as a colorless oil (69% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.36 (m, 1H), 7.14−7.12 (m, 1H), 7.12−7.08 (m, 1H), 4.40 (m, 1H), 1.92−1.63 (m, 2H), 1.36 (d, J = 6.1 Hz, 3H), 1.01 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 134.5, 128.5, 123.8, 117.1, 115.9, 101.9, 76.7, 28.9, 18.9, 9.5. FTIR: 2976, 2936, 2278, 1444, 1220, 1070 cm^{-1}. HRMS (EI) m/z: [M]$^+$ calculated for $C_{11}H_{12}BrNO^+$ 253.0102(2); found 253.0102(4). R_f: 0.40 in 5% diethyl ether/hexane.

1-(*sec*-Butoxy)-3,5-dichlorobenzene (3ha). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.50 mmol-scale and obtained in 72% (0.079 g) and 82% (0.090 g) isolated yields, respectively, as a colorless oil (77% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.06 (t, J = 1.2 Hz, 1H), 6.98 (d, J = 1.9 Hz, 2H), 4.50−4.43 (m, 1H), 1.67−1.49 (m, 2H), 1.19 (d, J = 6.0 Hz, 3H), 0.88 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.4, 135.3, 120.6, 114.6, 75.5, 29.0, 19.0, 9.6. FTIR: 2976, 2936, 1588, 1444, 1230, 1090 cm^{-1}. HRMS (EI) m/z: [M]$^+$ calculated for $C_{10}H_{12}Cl_2O^+$ 218.0265; found 218.0270. R_f: 0.48 in 100% hexane.

4-(*sec*-Butoxy)-1-chloro-2-fluorobenzene (3ia). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.50 mmol-scale and obtained in 68% (0.070 g) and 77% (0.078 g) isolated yields, respectively, as a colorless oil (72% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.01 (t, J = 3.7 Hz, 1H), 6.92−6.90 (m, 1H), 6.75−6.71 (m, 1H), 4.22−4.15 (m, 1H), 1.73−

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1.55 (m, 2H), 1.27 (d, J = 6.0 Hz, 3H), 0.96 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 154.4 (d, J_{C-F} = 2.1 Hz), 152.5 (d, J_{C-F} = 241.1 Hz), 121.0 (d, J_{C-F} = 20.4 Hz), 117.7, 116.7 (d, J_{C-F} = 22.1 Hz), 115.6 (d, J_{C-F} = 6.7 Hz), 76.3, 29.0, 19.0, 9.7. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −111.31. FTIR: 2974, 2935, 1589, 1496, 1215, 1201 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{10}H_{12}ClFO^+$ 202.0561; found 202.0564. R_f: 0.26 in 100% hexane.

4-(*sec*-Butoxy)-1-methyl-2-nitrobenzene (3ja). Prepared according to the general procedure above on a 0.51 mmol-scale and a 0.50 mmol-scale and obtained in 79% (0.084 g) and 84% (0.087 g) isolated yields, respectively, as a light yellow oil (81% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45 (d, J = 2.8 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.20−7.18 (dd, J = 7.4 Hz, 2.3 Hz, 1H), 4.48−4.10 (m, 1H), 2.39 (s, 3H), 1.70−1.51 (m, 2H),1.21 (d, J = 6.3 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 156.7, 149.4, 133.4, 125.1, 121.4, 111.1, 75.8, 29.0, 19.7, 19.0, 9.6. FTIR: 2970, 2934, 1710, 1626, 1527, 1243, 1024 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{11}H_{15}NO_3^+$ 209.1051; found 209.1053. R_f: 0.29 in 2.5% diethyl ether/hexane.

4-(*sec*-Butoxy)-2-chloro-1-methylbenzene (3ka). Prepared according to the general procedure above on a 0.50 mmol-scale and a 1.02 mmol-scale and obtained in 70% (0.070 g) and 67% (0.137 g) isolated yield, respectively, as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.09 (d, J = 8.6 Hz, 1H), 6.91 (d, J = 2.6 Hz, 1H), 6.72−6.69 (dd, J = 5.6 Hz, 2.0 Hz, 1H), 4.25−4.21 (m, 1H), 2.29 (s, 3H), 1.76−1.56 (m, 2H), 1.26 (d, J = 6.0 Hz, 3H), 0.97 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 156.9, 134.5, 131.1, 127.6, 116.5, 114.6, 75.5, 29.1, 19.1, 19.0, 9.74. FTIR: 2975, 2935, 1609, 1493, 1240 1040 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{11}H_{15}ClO^+$ 198.0811; found 198.0810. R_f: 0.31 in 100% hexane.

4-(*sec*-Butoxy)-2-chloro-1-methoxybenzene (3la). Prepared according to the general procedure above on a 0.36 mmol-scale and obtained in 67% (0.051 g) isolated yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.02 (d, J = 9.1 Hz 1H), 6.99 (d, J = 3.0 Hz, 1H), 6.87−6.84 (dd, J = 6.0 Hz, 2.1 Hz, 1H), 4.30−4.23 (m, 1H), 3.77 (s, 3H), 1.65−1.46 (m, 2H), 1.17 (d, J = 6.0 Hz, 3H), 0.89 (t, J = 7.8 Hz, 3H). ^{13}C NMR (100 MHz, DMSO): δ (ppm) 156.6, 135.5, 131.5, 126.7, 115.9, 114.6, 74.5, 28.4, 18.3, 18.5, 9.3. FTIR: 2973, 2936, 2838, 1497, 1272, 1211, 1059 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{11}H_{15}ClO_2^+$ 214.0760; found 214.0762. R_f: 0.45 in 10% diethyl ether/hexane.

3-Bromoanisole (3ab). Prepared according to the general procedure above on a 0.51 mmol-scale and a 0.50 mmol-scale and obtained in 77% (0.073 g) and 71% (0.067 g) isolated yields, respectively, as a colorless oil (74% average of two runs). Spectroscopic data were consistent with those previously reported.[58] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.13 (t, J = 5.2 Hz, 1H), 7.08−7.04 (m, 2H) 6.83−6.80 (m, 1H) 3.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 160.3, 130.5, 123.7, 122.8, 117.1, 113.0, 55.4. R_f: 0.24 in 100% hexane.

3-Bromophenetole (3ac). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.50 mmol-scale and obtained in 84% (0.084 g) and 77% (0.077 g) isolated yields, respectively, as a colorless oil (80% average of two runs). Spectroscopic data were consistent with those previously reported.[59] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.11 (t, J = 16.1 Hz, 1H), 7.06−7.03 (m, 2H), 6.82−6.79 (m, 1H) 4.01−3.96 (q, J = 7.0 Hz, 2H) 1.39 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.7, 130.4, 123.5, 122.7, 117.6, 113.5, 63.6, 14.7. R_f: 0.38 in 100% hexane.

1-Bromo-3-propoxybenzene (3ad). Prepared according to the general procedure above on a 0.51 mmol-scale and a 0.50 mmol-scale and obtained in 77% (0.084 g) and 81% (0.088 g) isolated yields, respectively, as a colorless oil (79% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.10 (t, J = 8.3 Hz, 1H), 7.05−7.03 (m, 2H), 6.82−6.80 (m, 1H) 3.87 (t, J = 6.6 Hz, 2H) 1.89−1.73 (m, 2H) 1.01 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.9, 130.4, 123.5, 122.7, 117.7, 113.5, 69.7, 22.4, 10.4. FTIR: 2964, 2936, 1591, 1469, 1244, 1228 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_9H_{11}BrO^+$ 213.9993; found 213.9998. R_f: 0.39 in 100% hexane.

1-Bromo-3-isopropoxybenzene (3ae). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.50 mmol-scale and obtained in 81% (0.087 g) and 86% (0.093 g) isolated yields, respectively, as a colorless oil (83% average of two runs). Spectroscopic data were consistent with those previously reported.[60] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.10 (t, J = 8.3 Hz, 1H), 7.05−7.02 (m, 2H) 6.81−6.78 (m, 1H) 4.54−4.45 (septet, J = 6.23 Hz, 1H) 1.31 (d, J = 6.24 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.7, 130.5, 123.5, 122.7, 119.0, 114.7, 70.2, 21.9. R_f: 0.48 in 100% hexane.

1-Bromo-3-(2,2,2-trifluoroethoxy)benzene (3af). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.50 mmol-scale and obtained in 65% (0.083 g) and 65% (0.083 g) isolated yields (65% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.21−7.18 (m, 2H), 7.12−7.11 (m, 1H) 6.91−6.86 (m, 1H), 4.36−4.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 158.0, 130.9, 125.8, 123.7, 123.0 (q, J = 277.8 Hz), 118.4, 113.8, 65.9 (q, J = 35.6 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −73.94. FTIR: 2962, 1591, 1476, 1288, 1166 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_8H_6BrF_3O^+$ 253.9554; found 253.9563. R_f: 0.34 in 100% hexane.

1-Nitro-3-(*tert*-pentyloxy)benzene (3dg). Prepared according to the general procedure above on a 0.50 mmol-scale and a 0.50 mmol-scale and obtained in 44% (0.046 g) and 45% (0.047 g) isolated yields, respectively, as a light yellow oil (44% average of two runs). ^{1}H NMR (400 MHz, CDCl3) δ 7.92 (dd, J = 8.2, 2.2 Hz, 1H), 7.82 (t, J = 2.2 Hz, 1H), 7.41 (t, J = 8.2 Hz, 1H), 7.33−7.27 (m, 1H), 1.79−1.65 (m, 2H), 1.33 (s, 6H), 1.02 (t, J = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, CDCl3): δ 156.5, 148.7, 129.7, 129.4, 118.0, 117.7, 82.6, 34.5, 26.0, 8.5. FTIR: 2970, 2934, 1710, 1243, 1026 m^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{11}H_{15}NO_3^+$ 209.1051; found 209.1048. R_f: 0.32 in 10% diethyl ether/hexane.

1-(Cyclopentyloxy)-3-fluorobenzene (3mh). Prepared according to the general procedure above on a 0.51 mmol-scale and a 0.50 obtained in 69% (0.063 g) and 74% (0.067 g) isolated yields, respectively, as a colorless oil (72% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.20−7.14 (m, 1H), 6.64−6.55 (m, 3H), 4.73−4.68 (m, 1H), 1.93−1.73 (m, 6H) 1.66−1.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 163.6 (d, J_{C-F} = 245.2 Hz), 159.5 (d, J_{C-F}= 10.8 Hz), 130.0 (d, J_{C-F} = 10.3 Hz), 111.3 (d, J_{C-F} = 2.8 Hz), 106.9 (d, J_{C-F} = 21.9), 103.0 (d, J_{C-F} = 24.2 Hz), 79.7, 32.7, 24.0. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −111.98. FTIR: 3014, 2961, 1590, 1221, 1134 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{11}H_{13}FO^+$ 180.0950; found 180.0953. R_f: 0.32 in 100% hexane.

1-Fluoro-3-(3-(trifluoromethyl)phenethoxy)benzene (3 mi). Prepared according to the general procedure above on a 0.510 mmol-scale and a 0.505 mmol-scale and obtained in 78% (0.114 g) and 86% (0.123 g) isolated yields, respectively, as a colorless oil (82% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.57−7.42 (m, 4H), 7.25−7.19 (m, 1H), 6.70−6.60 (m, 3H) 4.18 (t, J = 6.8 Hz, 2H) 13.16 (t, J = 6.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 163.6 (d, J_{C-F} = 245.6 Hz), 159.5 (d, J_{C-F} = 10.3 Hz), 139.1, 132.4 (d, J_{C-F} = 1.4 Hz), 130.8 (q, J = 31.8 Hz), 130.2 (d, J_{C-F} = 9.5 Hz), 128.9, 125.7 (q, J_{C-F} = 3.7 Hz), 124.3 (q, J_{C-F} = 274.3 H), 123.4 (q, J_{C-F} = 3.6 Hz), 110.3 (d, J_{C-F} = 3.1 Hz), 107.6 (d, J_{C-F} = 21.2 Hz), 102.3 (d, J_{C-F} = 24.7 Hz), 68.3, 35.4. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −111.59, −62.60. FTIR: 3086, 2961, 2936, 2867, 1607, 1488, 1124, 1066 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{15}H_{12}F_4O^+$ 284.0824; found 284.0822. R_f: 0.28 in 100% hexane.

2-(2-(3-Fluorophenoxy)ethyl)thiophene (3mj). Prepared according to the general procedure above on a 0.51 mmol-scale and a 0.51 mmol-scale and obtained in 76% (0.086 g) and 78% (0.090 g) isolated yields, respectively, as a colorless oil (77% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.22−7.14 (m, 2H), 6.95−6.89 (m, 2H), 6.69−6.59 (m, 3H), 4.15 (t, J = 6.6 Hz, 2H), 3.29 (t, J = 6.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 163.7 (d, J_{C-F} = 252.8 Hz), 159.9 (d, J_{C-F} = 11.4 Hz), 140.0, 130.2 (d, J_{C-F} =10.3 Hz), 126.8, 125.5, 124.0, 110.3 (d, J_{C-F} = 2.4 Hz), 107.6 (d, J_{C-F} = 21.5 Hz), 102.3 (d, J_{C-F} = 25.0 Hz), 68.6, 29.8. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −111.63. FTIR: 3072, 2928, 1614, 1491, 1277, 1136

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cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{12}H_{11}FOS^+$ 222.0515; found 222.0521. R_f: 0.18 in 100% hexane.

1-(Benzyloxy)-3-fluorobenzene (3mk). Prepared according to the general procedure above on a 0.52 mmol-scale and a 0.50 mmol-scale and obtained in 77% (0.080 g) and 79% (0.080 g) isolated yields, respectively, as a colorless oil (78% average of two runs). Spectroscopic data were consistent with those previously reported.[61] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41−7.28 (m, 5H), 7.22−7.16 (m, 1H), 6.75−6.62 (m, 3H), 5.00 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 163.7 (d, J_{C-F} = 246.4 Hz), 160.1 (d, J_{C-F} = 10.5 Hz), 136.4, 130.2 (d, 1C, J_{C-F} = 10.3 Hz), 128.6, 128.1, 127.4, 110.6 (d, J_{C-F} = 2.8 Hz), 107.7 (d, J_{C-F} = 22.4 Hz), 102.6 (d, J_{C-F} = 24.7 Hz), 70.2. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −111.50. R_f: 0.22 in 100% hexane.

1-(Cinnamyloxy)-3-(trifluoromethoxy)benzene (3cl). Prepared according to the general procedure above on a 0.521 mmol-scale and a 0.50 mmol-scale and obtained in 73% (0.112 g) and 67% (0.099 g) isolated yields, respectively, as a yellow solid (70% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41−7.38 (m, 2H), 7.34−7.23 (m, 4H), 6.89−6.86 (dd, J = 6.4 Hz, 2.1 Hz, 1H) 6.83−6.81(m, 2H), 6.73 (d, J = 15.9 Hz, 1H), 6.41−6.34 (m, 1H), 4.68−4.67 (dd, J = 7.6 Hz, 3.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.6, 150.1 (d, J_{C-F} =1.4 Hz), 136.2, 133.5, 130.2, 128.6, 128.0, 126.6, 123.6, 123.7, 120.5 (q, J = 258.2 Hz), 113.1 (d, J_{C-F}= 7.02 Hz), 107.9, 68.9. ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −57.71. FTIR: 3028, 2936, 1610 1490 1259 1142 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{16}H_{13}F_3O_2^+$ 294.0867; found 294.0862. Melting point (DCM/Et_2O): 38.6−39.8 °C. R_f: 0.27 in 100% hexane.

***tert*-Butyl-(*S*)-2-((3-bromophenoxy)methyl)pyrrolidine-1-carboxylate (3am).** Prepared according to the general procedure above on a 0.48 mmol-scale and a 0.50 mmol-scale and obtained in 50% (0.087 g) and 53% (0.096 g) isolated yields, respectively, as a yellow oil (51% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$, appears as an unresolved mixture of amide bond rotamers): δ (ppm) 7.12−7.06 (m, 3H), 6.85 (br, 1H), 4.13- 4.08 (b, 2H), 3.83 (b, 1H), 3.37 (br, 2H), 1.99−1.82 (m, 4H), 1.469 (s, 1H). ^{1}H NMR (600 MHz, DMSO-d_6, 373 K): δ (ppm) 7.20 (t, J = 8.1 Hz, 1H), 7.13−7.11 (m, 1H), 7.09 (m, 1H), 6.95 (m, 1H), 4.10−4.06 (m, 1H), 4.03−3.95 (m, 2H), 3.36−3.29 (m, 1H), 3.28−3.20 (m, 1H), 2.03−1.84 (m, 3H), 1.78 (dd, J = 7.6, 4.6 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, appears as an unresolved mixture of amide bond rotamers): δ (ppm) 159.6, 154.5, 130.5, 123.8, 122.7, 118.0, 113.3, 79.6, 68.3, 55.8, 46.7, 28.5, 28.4, 23.4. FTIR: 2970, 2937, 1691, 1590, 1476, 1392, 1167, 1034 cm^{-1}. HRMS (ESI) m/z: $[M + Na]^+$ calculated for $C_{16}H_{22}BrNNaO_3^+$ 378.0675; found 378.0688. R_f: 0.6 in 50% diethyl ether/hexane.

4-(2-(5-Ethylpyridin-2-yl)ethoxy)benzaldehyde (3nn). Prepared according to the general procedure above on a 0.51 mmol-scale and obtained in 45% (0.059 g) isolated yield as a colorless oil. Spectroscopic data were consistent with those previously reported.[62] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.41 (d, J = 1.9 Hz, 1H), 7.80 (d, J = 8.0 Hz, 2H), 7.47 (dd, J = 7.9, 2.3 Hz, 1H), 7.27 (s, 1H), 7.19 (d, J = 7.9 Hz, 1H), 7.0 (d, J = 8.2 Hz, 2H), 4.44 (t, J = 6.5 Hz, 2H), 3.27 (t, J = 6.7 Hz, 2H), 2.64 (q, J = 7.6 Hz, 2H), 1.25 (t, J = 9.4, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 190.8, 163.9, 155.0, 149.0, 137.3, 136.0, 131.9, 129.9, 123.4, 114.8, 67.6, 37.2, 25.7, 15.3. R_f: 0.25 in 60% ethyl acetate/hexane.

1-Bromo-3-phenoxybenzene (4aa). Prepared according to the general procedure above on a 0.51 mmol-scale and a 0.51 mmol-scale and obtained in 56% (0.071 g) and 57% (0.072 g) isolated yields, respectively, as a colorless oil (56% average of two runs). Spectroscopic data were consistent with those previously reported.[63] ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.37 (t, J = 8.0 Hz, 2H), 7.24−7.14 (m, 4H), 7.05−7.02 (dd, J = 8.5, 0.9 Hz, 2H), 6.96−6.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.3, 156.2, 130.7, 129.9, 126.0, 123.9, 122.8, 121.6, 119.3, 117.1. R_f: 0.42 in 100% hexane.

1-Fluoro-3-phenoxybenzene (4ma). Prepared according to the general procedure above on a 0.48 mmol-scale and a 0.50 mmol-scale and obtained in 68% (0.062 g) and 71% (0.067 g) isolated yields, respectively, as a colorless oil (69% average of two runs). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33 (t, J = 8.0 Hz, 2H), 7.24−7.20 (m, 1H), 7.12 (t, J = 7.4 Hz, 1H), 7.02−7.00 (dd, J = 8.7, 1.2 Hz, 2H), 6.78−6.73 (m, 2H), 6.69−6.65 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)) 163.4 (d, J_{C-F} = 246.2 Hz), 158.9 (d, J_{C-F} = 10.4 Hz), 156.2, 130.4 (d, J_{C-F} = 9.6 Hz), 129.9, 124.0, 119.5, 113.9 (d, J_{C-F} = 3.9 Hz), 109.9 (d, J_{C-F} = 21.0), 105.9 (d, J_{C-F} = 24.8 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) −110.99. FTIR: 3072, 3040, 1594, 1484, 1271, 1212, 1121, 959 cm^{-1}. HRMS (EI) m/z: $[M]^+$ calculated for $C_{12}H_9FO^+$ 188.0637; found 188.0639. R_f: 0.38 in 100% hexane.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C, and ^{19}F NMR spectra of all new compounds are provided. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00907.

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Notes

The authors declare no competing financial interest.

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