Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 62 (2006) 7824–7837
Tetrahedron

Radical dearomatization of arenes and heteroarenes

David Crich* and Mitesh Patel

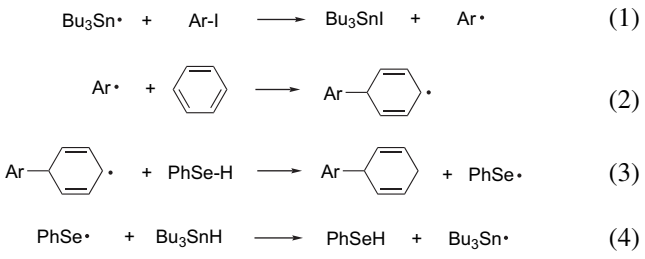
Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, IL 60607-7061, USA

Received 24 March 2006; revised 18 May 2006; accepted 22 May 2006
Available online 15 June 2006

Abstract—The stannane-mediated benzeneselenol-catalyzed addition of aryl iodides to a range of arenes and aromatic hetereocycles has been studied. With furan, thiophene, and several carbocyclic arenes, the addition takes place with quenching of the adduct radical by the catalytic selenol leading to moderate yields of aryl-dihydroarenes. With nitrogen heterocycles, on the other hand, it was not possible to suppress aromatization of the adduct radical and fully aromatized products were isolated. Aryl iodides bearing hydrogen bond donating groups in the *ortho*-position add to nitrogen heterocycles with high selectivity *ortho*- to the nitrogen, affording a simple one-step synthesis of potential chelating ligands. While 2-iodophenol is an excellent aryl radical source in these reactions, the homologous 1-iodo-2-naphthol fails owing to its reaction with diphenyl diselenide, which gives 1-phenylseleno-2-naphthol in high yield.

1. Introduction

A recurring theme in our laboratory in recent years has been the reductive radical arylation of benzene leading to the formation of 3-arylcyclohexa-1,4-dienes, and the application of this reaction in total synthesis. In this chemistry, aryl radicals add rapidly to arenes to give cyclohexadienyl radicals substituted with aryl groups at the 6-position, which undergo hydrogen atom transfer from catalytic benzeneselenol, yielding the reaction product and a benzeneselenyl radical.[1] The benzeneselenyl radical then abstracts hydrogen from tributyltin hydride,[2,3] the stoichiometric reductant, thereby regenerating the catalytic selenol and the stannyl radical necessary for formation of the aryl radical from the aryl iodide. Overall, a four propagation step radical chain sequence is involved (Scheme 1).[1] The catalytic benzeneselenol is necessary because, under typical preparative radical chain conditions, the intermediate cyclohexadienyl radical is insufficiently reactive to propagate the radical chain by hydrogen atom abstraction from stannane or silane hydrogen atom donors. Although the Sn–H and Se–H bond dissociation energies are very similar,[4–6] the selenol traps alkyl radicals some 500 times faster than the stannane,[7–9] because of the operation of a polarity effect.[10] The interrupted propagation in the absence of selenol results in the formation of rearomatized biaryls and the need for large quantities of radical initiator.[11] Similarly, the intramolecular version of simple stannane-mediated, cyclizations of aryl radical onto arenes, is marked by the formation of fully re-oxidized products and the application of copious amounts of initiator.[12] Indeed, the azo-type initiators are now seen to serve the important function of oxidant for the cyclohexadienyl radical in addition to their more obvious planned function.[13–16]



Scheme 1. Mechanism of dearomatizing aryl radical addition to arenes.

The benzeneselenol-catalyzed chemistry is rendered practical by the rapid in situ reduction of diphenyl diselenide to benzeneselenol by the stannane, which enables the direct handling of the air-sensitive selenol to be avoided (Scheme 2).[3]

Scheme 2. In situ selenol generation.

In the reductive radical arylation of benzene (Scheme 1) regiochemistry is not an issue in the addition step, and only becomes a concern in the hydrogen atom transfer step to the cyclohexadienyl radical when formation of the skipped diene is preferred over that of the conjugated diene because of the higher spin density on the central carbon. However, in

Keywords: Radical; Arylation; Cyclohexadienyl; Dearomatization.
* Corresponding author. Tel.: +1 312 996 5189; fax: +1 312 996 0431; e-mail: dcrich@uic.edu

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.05.051

additions to aromatic heterocycles and other simple arenes the question of regioselectivity also arises in the initial addition reaction, resulting in potentially complex reaction mixtures.[17] In spite of this concern, we were motivated to investigate the use of a broader range of arenes and of aromatic heterocycles as substrates in this chemistry, and report here in full on our explorations.[18]

2. Results and discussion

2.1. Nitrogen heterocycles

Our attention was first directed at pyridine as substrate in view of its ready availability, convenient boiling point, and its well-established free addition radical chemistry, especially that of pyridinium salts.[12,19] The addition of aryl radicals to pyridine and substituted pyridines was studied some 40 years ago using diazonium salts as radical precursors in the Gomberg–Hey reaction, and it was determined that the relative rate of addition of the 4-bromophenyl radical to pyridine with respect to benzene was 0.87.[20,21] Relative rates of addition of phenyl radicals, generated by decomposition of benzoyl peroxide, to alkylpyridines and benzene were also known and of a comparable magnitude.[22–24] The photolysis of triphenylbismuth had also been employed as a means of generating phenyl radicals for addition to pyridine.[25] All of the early work on aryl radical addition to pyridine indicated a small preference for attack at the *ortho*-position, the extent of which was found to depend on the nature of the *ortho*-substituent on the attacking aryl radical, with attack at the pyridine *para*-position being the least favored.[20,21,25–27] Much more recently, and while this work was in progress, Alvarez-Builla and co-workers reported on the tris(trimethylsilyl)silane-mediated addition of aryl bromides to pyridine and obtained mixtures of the fully aromatic biaryl products, in which the isomer arising from attack at the pyridine 2-position predominated (2-aryl:3-aryl:4-aryl∼4:1:1).[28]

On the basis of this literature precedent, the success of the selenol-mediated reductive arylations of benzene, and the common occurrence of dihydropyridines in both nature and the laboratory,[29,30] we were surprised to find that the reaction of various aryl iodides with tributyltin hydride and AIBN, catalyzed by diphenyl diselenide yielded, not the anticipated aryl dihydropyridines, but rather the fully aromatic aryl pyridines (Table 1). Dihydropyridines were not formed in these reactions, as determined by inspection of the crude reaction mixtures by NMR spectroscopy; presumably, the azacyclohexadienyl radical intermediates are too stable to propagate the chain by hydrogen atom abstraction from the selenol. Nevertheless, the diphenyl diselenide/benzeneselenol had a beneficial effect on these reactions as significantly lower conversions were obtained in its absence. For example, heating of **2** with tributyltin hydride and AIBN in pyridine in the absence of diphenyl diselenide, but under otherwise standard conditions, gave **13**, **14**, and **15** in 9, 4, and 1% yield, respectively, along with 47% of recovered substrate. The beneficial effect of the selenide is also apparent from comparison with the Alvarez-Builla tris(trimethylsilyl)silane-mediated additions to pyridine,[28] which were conducted with greater than stoichiometric AIBN as opposed to the 20 mol % used in our study. It is not clear at the present time how the selenol/diselenide is achieving catalysis: one possibility is the quenching of the azacyclohexadienyl radical by diphenyl diselenide to give an aryl phenylselenyl azacyclohexadiene, which spontaneously eliminates benzeneselenol to give the final product. Another possibility is the oxidation of the electron-rich azacyclohexadienyl radical to the corresponding cation by an organoselenium species, such as diphenyl diselenide, or tributylstannyl phenyl selenide.

With *N*-methoxycarbonyl-*o*-iodoaniline **1** as substrate 38% of the *ortho*-substitution product **11** was obtained, along with 3% of the *meta*-isomer **12** (Table 1, entry 1). Likewise, *o*-iodophenol **2**, *o*-iodoaniline **7**, and *o*-iodo-*N*-methylaniline **8** all afforded predominantly the *ortho*-products (Table 1, entries 2, 7, and 8). In contrast, with methyl *o*-iodobenzoate **3**, *p*-bromoiodobenzene **4**, 2-iodothiophene **5**, and *o*-iodoanisole **9** the *ortho*:*para* ratio of products was much lower (Table 1, entries 3, 4, 5, and 9). In most cases, minor amounts of the *para*-isomers were also isolated (Table 1). The improved ratios in favor of the *ortho*-substituted product seen with **1**, **2**, **7**, and **8** are attributed to hydrogen bonding of the substrate to pyridine resulting in both an activating and a directing effect. The exception, *o*-iodovanillin **6**, is explained by preferential intramolecular hydrogen bonding to the methoxy group.

In the nitrogen heterocycles, we also briefly investigated additions to quinoline, isoquinoline, benzothiazole, and pyrrole with varying degrees of success (Table 2). In accordance with the literature for the addition of benzoyl peroxide-generated phenyl radicals to quinoline, when phenylation at all positions was found,[31,32] a complex reaction mixture was obtained when *o*-iodophenol was heated to reflux in benzene in the presence of 30 equiv of quinoline, catalytic diphenyl diselenide, and tributyltin hydride. Only one product was isolated pure from this reaction mixture and that in very low yield (Table 2, entry 1). With isoquinoline on the other hand, a much cleaner reaction was observed and one very predominant product **39**, resulting from attack at the 1-position, was obtained in 44% yield. The only other product **40** isolated in low yield was that of substitution at the 3-position (Table 2, entry 2). The formation of the 1-arylisoquinoline as the major product is in accord with earlier work on the addition of phenyl radicals, generated either by photolysis of phenylthallium bis(trifluoroacetate) or by decomposition of the benzenediazonium cation, to isoquinoline.[33] However, the selectivity is greater than would have been anticipated on the basis of those earlier studies. Furthermore, the formation of the 3-arylisoquinoline as the second most abundant product does not agree with the earlier phenylation studies, when the 3-position was found to be one of the least reactive. As with the additions to pyridine, we invoke hydrogen bonding of the heterocycle with the *o*-iodophenol substrate as the factor increasing the selectivity for attack at both the 1- and the 3-positions.

A brief investigation of aryl radical addition to pyrrole under our standard conditions was unsatisfactory, resulting in the isolation of only one major product, the *ortho*-substituted product **41**, in low yield (Table 2, entry 3). With 20 equiv of benzothiazole in benzene the major product **42** was that

Table 1. Aryl radical additions to pyridine

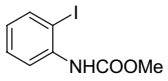
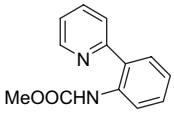
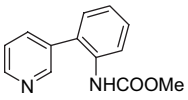
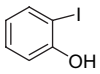
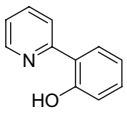
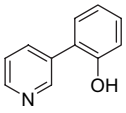
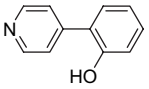
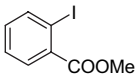
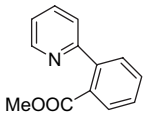
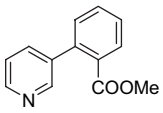
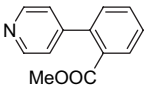
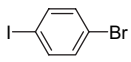
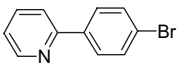
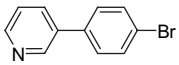
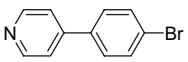
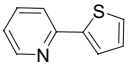
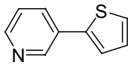
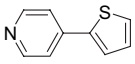
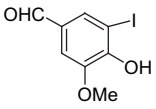
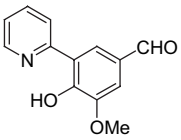
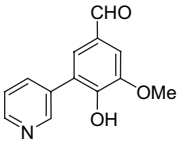
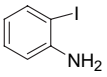
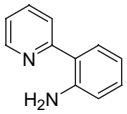
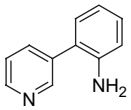
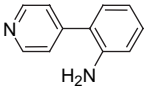
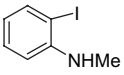
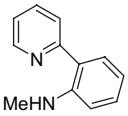
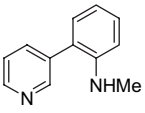
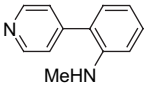
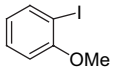
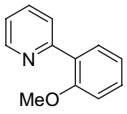
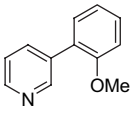
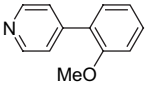
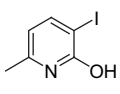
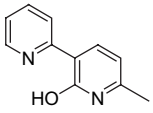
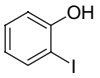
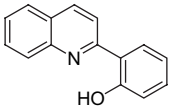
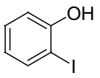
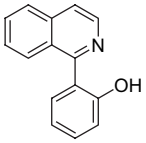
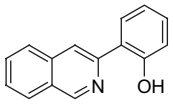
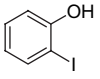
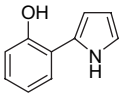
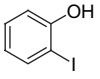
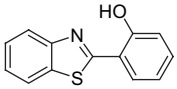
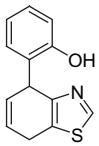
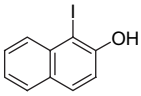
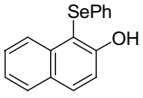
Entry	Substrate	Products (yield)		
1	 **1**	 **11** (38%)	 **12** (3%)	
2	 **2**	 **13** (36%)	 **14** (16%)	 **15** (10%)
3	 **3**	 **16** (20%)	 **17** (22%)	 **18** (9%)
4	 **4**	 **19** (18%)	 **20** (12%)	 **21** (5%)
5	 **5**	 **22** (19%)	 **23** (24%)	 **24** (7%)
6	 **6**	 **25** (17%)	 **26** (17%)	
7	 **7**	 **27** (18%)	 **28** (4%)	 **29** (4%)
8	 **8**	 **30** (25%)	 **31** (7%)	 **32** (5%)
9	 **9**	 **33** (20%)	 **34** (23%)	 **35** (10%)
10	 **10**		 **36** (13%)	

Table 2. Aryl radical addition to other nitrogen heterocycles

Entry	Heterocycle	Substrate	Products (yield)
1	Quinoline	 **2**	 **38** (5%)
2	Isoquinoline	 **2**	 **39** (44%)  **40** (4%)
3	Pyrrole	 **2**	 **41** (17%)
4	Benzothiazole	 **2**	 **42** (19%)  **43** (7%)
5	Isoquinoline	 **37**	 **44** (88%)[a]

[a] Based on diphenyl diselenide.

of attack in the heterocyclic ring, with rearomatization. However, a minor product **43** was also obtained, which resulted from attack on the benzenoid ring at the 4-position, whose structure was established crystallographically.[†] The predominant attack at the benzothiazole 2-position, with that at the 4-position being the second most important, is in agreement with the earlier literature on the radical phenylation of this heterocycle with benzoyl peroxide.[34]

The clean and successful addition of *o*-iodophenol to isoquinoline prompted an investigation of 1-iodo-2-naphthol **37** in this reaction, with a view to a short synthesis of 1-(2-hydroxy-1-naphthyl)isoquinoline.[35] Contrary to our expectations, a complex reaction mixture was obtained from which we were unable to isolate the desired product, but from which we obtained 1-phenylselenyl-2-naphthol[36] **44** in 88% yield based on diphenyl diselenide (Table 2, entry 5). Blank reactions in which **44** was formed in high yield from the reaction of diphenyl diselenide with **37** in benzene at reflux, in the absence of isoquinoline, stannane and AIBN, indicate that the failure of the radical reaction in this case is the result of consumption of the catalyst in an unanticipated reaction with the β-naphthol.

2.2. Oxygen and sulfur heterocycles

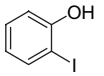
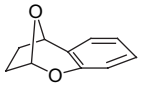
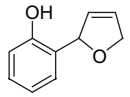
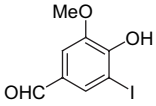
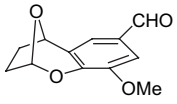
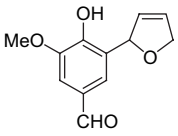
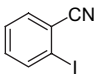
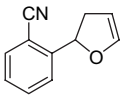
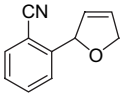
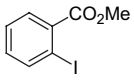
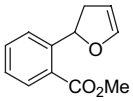
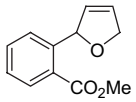
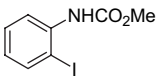
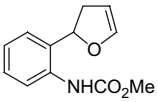
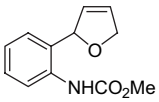
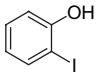
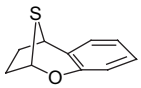
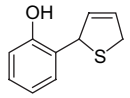
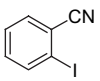
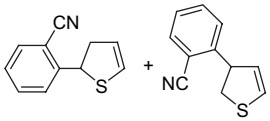
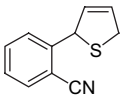
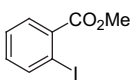
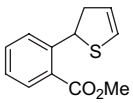
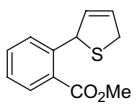
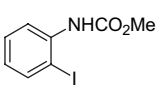
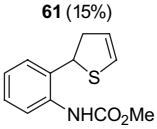
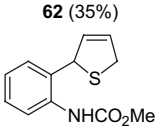
With furan and thiophene as aryl radical trap, the chemistry reverted to the pattern established with benzene, with efficient trapping of the adduct radical, and good chain propagation in the presence of catalytic benzeneselenol. Aryl radical addition to furan and thiophene had been previously studied, with aryl radicals derived from the thermolysis of phenylazotriphenylmethane, and from the metal catalyzed decomposium of the benzenediazonium ion.[37,38] With phenylazotriphenylmethane dearomatized products were obtained, owing to the combination of the initial adduct radical with the triphenylmethyl radical,[37] but the presence of the triphenylmethyl group obviously detracts from the synthetic utility of this method.[38] As expected, rearomatized products were obtained with diazonium salt-derived phenyl radicals. A series of competition reactions revealed the relative rates of addition of the phenyl radical to furan, thiophene, and benzene to be 11.5:2.6:1.[37]

A practical problem faced in the additions to furan was that of initiation. Use of our standard initiator, AIBN, with its half life of 2 h at 80 °C, suitable for reactions in benzene,[39]

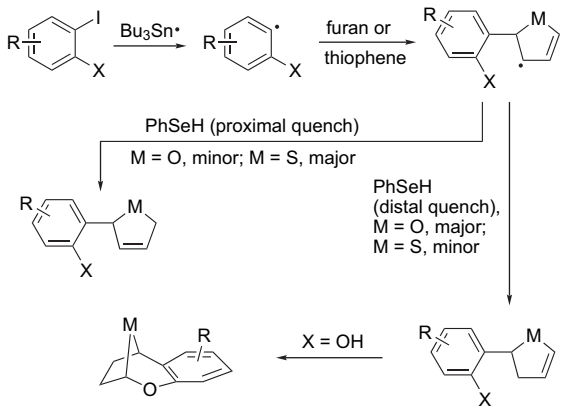
[†] CCDC 607627 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

resulted in no observable reaction at the boiling point (32 °C) of furan. A solution to this problem was found with 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70), which is reported to have a half life of 10 h at 30 °C in toluene,[40,41] for the commercial ±/*meso*-isomer. With this initiator, the benzeneselenol-catalyzed, stannane-mediated addition of aryl iodides to furan took place smoothly, giving yields of isolated products (Table 3, entries 1–5) comparable to those for addition to benzene. Likewise, additions to thiophene (bp 84 °C) proceeded smoothly with V-70 as initiator when the reactions were carried out at an oil bath temperature of 50 °C (Table 3, entries 6–9). In the additions to furan attack of the aryl radical at the 2-position was very strongly favored, in keeping with the previous literature observations.[37] Similarly, the additions to thiophene yielded very predominantly the product of reaction at the 2-position, with only a minor amount of a product from attack at the 3-position isolated in one example (Table 3, entry 7). In the case of furan, the intermediate oxyallyl radical was quenched preferentially at the distal terminus

Table 3. Aryl radical addition to furan and thiophene

Entry	Heterocycle	Substrate	2,3-Dihydro products (yield)	2,5-Dihydro products (yield)
1	Furan	 **2**	 **46** (45%)	 **47** (14%)
2	Furan	 **6**	 **48** (51%)	 **49** (14%)
3	Furan	 **45**	 **50** (45%)	 **51** (22%)
4	Furan	 **3**	 **52** (32%)	 **53** (10%)
5	Furan	 **1**	 **54** (43%)	 **55** (19%)
6	Thiophene	 **2**	 **56** (4%)	 **57** (32%)
7	Thiophene	 **45**	 **58** + **59** (13%) 1.4:1	 **60** (25%)
8	Thiophene	 **3**	 **61** (15%)	 **62** (35%)
9	Thiophene	 **1**	 **63** (11%)	 **64** (31%)

to the oxygen atom, giving the 2,3-dihydro-2-arylfurans, with a preference over the 2,5-dihydro-2-aryl isomers varying between 2:1 and 3.6:1. With thiophene, this preference was reversed with proximal quenching of the 1-thioallyl radical being preferred and the 2,5-dihydro-2-arylthiophenes the major product (Scheme 3). We attribute the differences in regioselectivity of hydrogen atom abstraction between the furan and thiophene series to a change in spin delocalization in the intermediate heteroatom-substituted allyl radicals as the heteroatom is changed from oxygen to sulfur. Indeed, electron spin resonance hyperfine splitting constants indicate that, in the 1-*tert*-butylthioallyl and 1-*tert*-butoxyallyl radicals, the alkylthio group is more effective at localizing spin than the alkoxy group.[42–45] As the recommended C–H bond strengths in methanol, methylamine, and methanethiol are very close,[46] the likelihood that the change in regioselectivity results from any differences in exothermicity of the quenching step is considered small.



Scheme 3. Aryl addition to furan and thiophene.

The use of *o*-iodophenols as substrates in the additions to furan resulted in the immediate cyclization of the 2,3-dihydro-2-aryl adducts to give 2,3,4,5-tetrahydro-2,5-epoxy-1-benzoxepins as the isolated products (Table 3, entries 1 and 2). Presumably, either the phenol itself, or the benzeneselenol catalyst, promotes cyclization directly in the reaction mixture as the initial adducts could not be detected by NMR spectroscopy of the crude reaction mixtures. The analogous cyclization also occurred in the thiophene series (Table 3, entry 6), but much more slowly enabling detection of the intermediate 2,3-dihydro-2-arylthiophene in the crude reaction mixture.

2.3. Carbocyclic arenes

In classical work on the oxidative addition of aryl radicals to arenes it was established that phenyl radicals, obtained on decomposition of *N*-nitrosoacetanilides, add to anisole with a slight preference for the *ortho*-position, over the *para*- and *meta*-positions (3.5:1.5:0.9), and that addition to the *ortho*-position was some three and a half times more rapid than the corresponding addition to benzene.[17,47,48] Under our conditions, with the radical derived from *o*-iodophenol, the main isolated product (Table 4, entry 1) was the methoxytetrahydrodibenzofuran **66**, arising from initial attack at the *ortho*-position. The biphenyl **67** from *ortho*-attack was also obtained, as was a minor amount of the biphenyl **68** from reaction at the *para*-position. Similar results were obtained with *o*-iodobenzoic acid (Table 4, entry 2), and with *o*-iodoaniline (Table 4, entry 3) as the source of aryl radical, except that in the last case only the fully aromatized products were obtained. The *cis*-fused nature of the ring junction in **66** is assigned based on a NOESY cross peak between the bridgehead hydrogen and the pseudoaxial, homoallylic hydrogen adjacent to the methoxy group. The assignment of the *trans*-fused ring junction in **69** follows from the NOESY cross peaks involving the two homoallylic hydrogens, one of which correlates with the bridgehead hydrogen, and the other with the methoxy hydrogens.

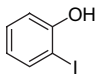
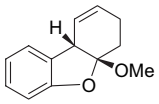
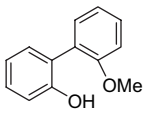
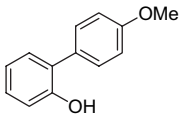
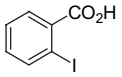
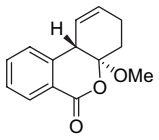
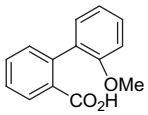
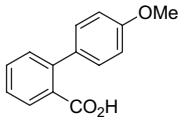
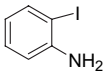
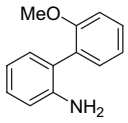
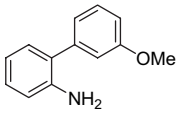
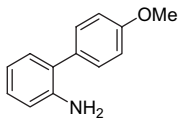
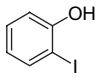
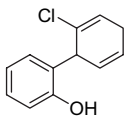
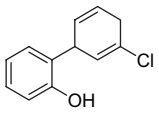
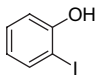
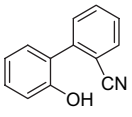
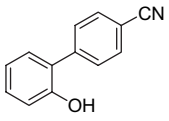
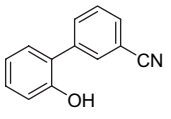
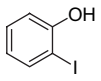
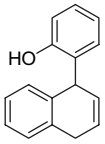
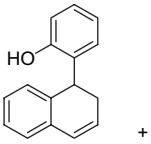
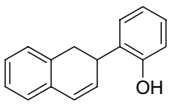
The absolute rate constant for the addition of phenyl radicals to chlorobenzene at 25 °C has been determined to be $1.18\times10^{6}\ M^{-1}\ s^{-1}$, by a laser flash photolytic technique, and so approximately 2.5 times than the comparable addition to benzene.[49,50] Earlier studies found an approximately 1.5:1 preference for the addition of phenyl radicals to the *ortho*-position of chlorobenzene, over addition to the *para*-position (*o*-:*m*-:*p*-=3.1:1:1.5).[47,51] Under the benzeneselenol-catalyzed conditions, two major products were formed in the approximate ratio of 3:1, which was altered in favor of the major isomer on silica gel chromatography owing to the more rapid decomposition of the minor isomer (Table 4, entry 4). Presumably, the more stabilized 3-chloro-6-aryl-1,4-cyclohexadienyl radical arising from attack *para*- to the chlorine did not propagate the radical chain with the selenol, and led to decomposition products. The regiochemistry of **75** and **76** is based on the coupling, in the ^{1}H NMR spectra, of the benzylic hydrogen with a single olefinic hydrogen in **75**, and with two olefinic hydrogens in **76**.

With benzonitrile, previously reported to undergo radical phenylation some 3.9 times faster than benzene,[50] and with a 6:1:3 selectivity for the *ortho*-position over the *meta*- and *para*-positions,[52] we obtained a mixture of three adducts containing approximately equal proportions of the *ortho*- and *para*-adducts, with less of the *meta*-adduct (Table 4, entry 5). Unfortunately, we were unable to suppress rearomatization in these reactions and the products were obtained as the fully aromatic biphenyl derivatives.

Finally, we investigated addition to naphthalene, employed as a solution in benzene. Literature reports on the radical phenylation of naphthalene suggested a strong preference, varying between 3:1 and >8:1, for attack at the 1-position over the 2-position.[53,54] Working with *o*-iodophenol, we found a ratio of 2.8:1 in favor of the adduct at the 1-position (Table 4, entry 6). While quenching of the benzocyclohexadienyl radical derived from addition of the aryl at the 1-position was efficient, enabling isolation of the 1-phenyl dihydronaphthalenes, it was not regioselective and gave an approximately 1:1 mixture of the two regioisomers.

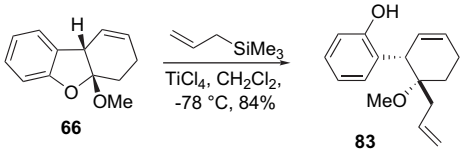
Interestingly, when the methoxytetrahydrodibenzofuran **66** was allowed to react with allyltrimethylsilane in the presence of titanium tetrachloride at −78 °C in dichloromethane the tertiary ether **83** was formed in high yield (Scheme 4). This product, whose stereochemical assignment is based on the NOESY cross peaks of the two homoallylic hydrogens with the benzylic hydrogen and the methoxy hydrogens, arises from Lewis acid-induced cleavage of the

Table 4. Aryl radical additions to carbocyclic arenes

Entry	Arene	Substrate	Products (yield)		
1	Anisole	 **2**	 **66** (20%)	 **67** (12%)	 **68** (5%)
2	Anisole	 **65**	 **69** (19%)	 **70** (7%)	 **71** (2%)
3	Anisole	 **7**	 **72** (21%)	 **73** (4%)	 **74** (5%)
4	Chlorobenzene	 **2**	 **75** (17%)[a]	 **76** (3%)[a]	
5	Benzonitrile	 **2**	 **77** (10%)	 **78** (9%)	 **79** (5%)
6	Naphthalene	 **2**	 **80**	 **81** +  **82**	(40%) **80**:**81**:**82** = 1.4:1.4:1

[a] In the crude reaction mixture, the ratio of **75**:**76** was 3:1. The higher ratio of isolated products is a function of the more rapid decomposition of **76** in the course of the isolation.

endocyclic acetal bond followed by nucleophilic attack on the more open face of the subsequent oxacarbenium ion.



66 **83**

Scheme 4. Reaction of **66** with allyltrimethylsilane and $TiCl_4$.

3. Conclusion

Benzeneselenol catalyzes the addition of aryl radicals, derived from aryl iodides by the action of tributyltin hydride, to a wide range of arenes and hetereoarenes. The ability to isolate arylated dihydroarenes and heteroarenes is strongly system dependent, with nitrogen heterocycles giving only fully aromatic products, but furan and thiophene giving predominantly 2-aryl dihydro systems. Aryl iodides bearing hydrogen bond donating groups in the *ortho*-position add to nitrogen heterocycles with good selectivity *ortho*- to nitrogen, thereby providing a facile synthesis of potential chelating ligands.

4. Experimental

4.1. General

All solvents were dried and distilled by standard procedures. ^1H NMR and ^{13}C NMR spectra were recorded at 500 MHz and 125 MHz, respectively, in $CDCl_3$ with chemical shifts (δ) downfield from tetramethylsilane.

4.2. General protocol for aryl radical addition to nitrogen heterocycles

A solution of aryl iodide (1 mmol), diphenyl diselenide (62 mg, 0.2 mmol), and solvent (20 mL) was sparged with argon for 45 min, followed by heating at 95 °C with stirring. A solution of AIBN (33 mg, 0.2 mmol) and Bu_3SnH (0.47 mL, 1.75 mmol) in degassed solvent (10 mL) was added via syringe pump over 16 h, after which heating was continued for 1 h, before the reaction mixture was cooled to room temperature and concentrated. The residue was taken up in 20% EtOAc in hexane (50 mL) and extracted with 2 N HCl (50 mL), (except Table 2, entries 4 and 5, which were purified without acidic workup). The aqueous phase was neutralized with 3 M NaOH and extracted (EtOAc). The extracts were washed with brine, dried (Na_2SO_4), concentrated, and purified by silica gel chromatography (eluent: EtOAc/hexane).

4.2.1. 2-(2-Pyridyl)methoxycarbamoylbenzene (11). Reaction solvent: pyridine; white solid; mp 32–34 °C; ^{1}H NMR δ: 3.76 (s, 3H), 7.12 (dt, J=7.0, 1.0 Hz, 1H), 7.26 (ddd, J=7.5, 4.5, 1.0 Hz, 1H), 7.40 (dt, J=8.0, 1.5 Hz, 1H), 7.63 (dd, J=7.5, 1.5 Hz, 1H), 7.71 (d, J=8.0 Hz, 1H), 7.81 (dt, J=8.0, 2.0 Hz, 1H), 8.33 (br d, J=8.5 Hz, 1H), 8.65 (br d, J=6.0 Hz, 1H), 11.52 (br s, 1H); ^{13}C NMR δ: 52.0, 120.4, 121.8, 122.6, 122.9, 125.3, 128.9, 130.1, 137.6, 137.8, 147.6, 154.5, 158.2; Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30. Found: C, 68.37; H, 5.19.

4.2.2. 2-(3-Pyridyl)methoxycarbamoylbenzene (12). Reaction solvent: pyridine; white solid; mp 108–110 °C; ^{1}H NMR δ: 3.71 (s, 3H), 6.52 (br s, 1H), 7.20 (m, 2H), 7.41 (m, 2H), 7.70 (d, J=7.5 Hz, 1H), 8.05 (br s, 1H), 8.63 (m, 2H); ^{13}C NMR δ: 52.4, 120.9, 123.8, 124.1, 129.4, 130.3, 134.1, 135.0, 136.9, 149.0, 150.0, 154.0; Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30. Found: C, 68.24; H, 5.20.

4.2.3. 2-(2-Hydroxyphenyl)pyridine (13). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[55] ^{1}H NMR δ: 6.92 (dt, J=8.0, 1.0 Hz, 1H), 7.06 (dd, J=8.0, 1.0 Hz, 1H), 7.19–7.22 (m, 1H), 7.32 (dt, J=7.0, 1.5 Hz, 1H), 7.77–7.80 (m, 2H), 7.88 (d, J=8.5 Hz, 1H), 8.48 (d, J=4.5 Hz, 1H).

4.2.4. 3-(2-Hydroxyphenyl)pyridine (14). Reaction solvent: pyridine; white solid; mp 162–163 °C, lit.[56] 171–172 °C; ^{1}H NMR δ: 4.93 (br s, 1H), 6.91–6.94 (m, 2H), 7.21 (dt, J=9.0, 1.5 Hz, 1H), 7.28 (dd, J=7.5, 1.5 Hz, 1H), 7.43–7.45 (m, 1H), 8.03 (td, J=7.5, 2.5 Hz, 1H), 8.41 (dd, J=4.5, 1.5 Hz, 1H), 8.73 (dd, J=2.0, 0.5 Hz, 1H).

4.2.5. 4-(2-Hydroxyphenyl)pyridine (15). Reaction solvent: pyridine; white solid; mp 208–210 °C, lit.[57] 213–215 °C; spectroscopic data identical to literature values;[57] ^{1}H NMR δ: 4.91 (br s, 1H), 6.92 (m, 2H), 7.24 (dt, J=7.5, 1.0 Hz, 1H), 7.37 (dd, J=7.5, 1.5 Hz, 1H), 7.69 (dd, J=5.5, 1.5 Hz, 2H), 8.50 (dd, J=5.0, 1.5 Hz, 2H).

4.2.6. Methyl 2-(2-pyridyl)benzoate (16). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[58] ^{1}H NMR δ: 3.67 (s, 3H), 7.24 (m, 1H), 7.44–7.48 (m, 2H), 7.55 (dd, J=5.0, 1.0 Hz, 2H), 7.74 (dt, J=8.0, 2.0 Hz, 1H), 7.81 (d, J=7.5 Hz, 1H), 8.63 (qd, J=4.0, 1.0 Hz, 1H).

4.2.7. Methyl 2-(3-pyridyl)benzoate (17). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[59] ^{1}H NMR δ: 3.66 (s, 3H), 7.32 (dd, J=7.5, 0.5 Hz, 1H), 7.37 (br m, 1H), 7.46 (dt, J=7.5, 0.5 Hz, 1H), 7.56 (dt, J=7.5, 1.0 Hz, 1H), 7.63 (d, J=8.0 Hz, 1H), 7.93 (dd, J=8.0, 1.5 Hz, 1H), 8.71 (br s, 2H).

4.2.8. Methyl 2-(4-pyridyl)benzoate (18). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[57] ^{1}H NMR δ: 3.67 (s, 3H), 7.23 (dd, J=4.5, 1.5 Hz, 2H), 7.32 (td, J=8.0, 0.5 Hz, 1H), 7.49 (dt, J=7.5, 1.5 Hz, 1H), 7.58 (dt, J=8.0, 1.5 Hz, 1H), 7.93 (dd, J=7.5, 1.5 Hz, 1H), 8.63 (dd, J=6.0 Hz, 2H).

4.2.9. 2-(4-Bromophenyl)pyridine (19). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[60] ^{1}H NMR δ: 7.24 (m, 1H), 7.60 (d, J=8.5 Hz, 2H), 7.69 (d, J=7.5 Hz, 1H), 7.74 (dt, J=7.5, 1.0 Hz, 1H), 7.86 (d, J=6.5 Hz, 2H), 8.68 (td, J=4.5, 1.0 Hz, 1H).

4.2.10. 3-(4-Bromophenyl)pyridine (20). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[21] ^{1}H NMR δ: 7.36 (m, 1H), 7.44 (d, J=8.5 Hz, 2H), 7.60 (d, J=8.5 Hz, 2H), 7.83 (td, J=8.0, 1.5 Hz, 1H), 8.60 (d, J=3.5 Hz, 1H), 8.80 (s, 1H).

4.2.11. 4-(4-Bromophenyl)pyridine (21). Reaction solvent: pyridine; white solid; mp 129.5 °C, lit.[61] 130 °C; spectroscopic data identical to literature values;[61] ^{1}H NMR δ: 7.47 (dd, J=4.5, 1.5 Hz, 2H), 7.51 (d, J=7.0 Hz, 2H), 7.61 (d, J=7.0 Hz, 2H), 8.67 (dd, J=4.5, 1.5 Hz, 2H).

4.2.12. 2-(2-Thienyl)pyridine (22). Reaction solvent: pyridine; white solid; mp 61.5 °C, lit.[62] 61–62 °C; spectroscopic data identical to literature values;[62] ^{1}H NMR δ: 7.13 (m, 2H), 7.39 (dd, J=5.0, 1.0 Hz, 1H), 7.58 (dd, J=4.0, 1.0 Hz, 1H), 7.66 (m, 2H), 8.56 (d, J=4.5 Hz, 1H).

4.2.13. 3-(2-Thienyl)pyridine (23). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[63] ^{1}H NMR δ: 7.12 (dd, J=5.0, 4.0 Hz, 1H), 7.30 (m, 1H), 7.35 (d, J=4.0 Hz, 2H), 7.86 (td, J=8.0, 1.5 Hz, 1H), 8.52 (br s, 1H), 8.89 (br s, 1H).

4.2.14. 4-(2-Thienyl)pyridine (24). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[64] ^{1}H NMR δ: 7.14 (dd, J=5.0, 4.0 Hz, 1H), 7.42 (d, J=5.0 Hz, 1H), 7.51 (m, 3H), 8.61 (br s, 2H).

4.2.15. 5-(2-Pyridyl)vanillin (25). Reaction solvent: pyridine; yellowish solid; mp 160–161 °C; ^{1}H NMR δ: 3.96 (s, 3H), 7.32 (ddd, J=7.5, 5.0, 1.0 Hz, 1H), 7.39 (d, J=1.5 Hz, 1H), 7.90 (dt, J=7.5, 1.5 Hz, 1H), 7.94 (d, J=2.0 Hz, 1H), 8.0 (d, J=8.5 Hz, 1H), 8.52 (ddd, J=5.3, 2.0, 0.5 Hz, 1H), 9.85 (s, 1H); ^{13}C NMR δ: 56.2, 110.2, 117.9, 119.4, 122.4, 123.7, 127.4, 138.4, 145.4, 150.3, 156.6, 156.8, 190.6; Anal. Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84. Found: C, 67.83; H, 4.70.

4.2.16. 5-(3-Pyridyl)vanillin (26). Reaction solvent: pyridine; yellowish solid; mp 162–163 °C; ^{1}H NMR δ: 3.99 (s, 3H), 7.39 (dd, J=8.3, 5.0 Hz, 1H), 7.44 (d, J=2.0 Hz, 1H), 7.50 (d, J=2.0 Hz, 1H), 7.98 (td, J=8.0, 2.0 Hz, 1H), 8.58 (dd, J=5.0, 1.5 Hz, 1H), 8.87 (d, J=2.5 Hz, 1H), 9.87 (s, 1H); ^{13}C NMR δ: 56.5, 108.3, 123.3, 124.1, 128.0, 129.4, 132.5, 136.7, 147.7, 148.4, 149.2, 149.6, 190.7; ESIHRMS, calcd for $C_{13}H_{11}NO_3$: 230.0817 (M+H$^+$), found: 230.0815.

4.2.17. 2-(2-Aminophenyl)pyridine (27). Reaction solvent: pyridine; yellowish oil; spectroscopic data identical to literature values;[65] ^{1}H NMR δ: 5.48 (br s, 2H), 6.78 (m, 2H), 7.18 (m, 2H), 7.51 (dd, J=7.5, 1.0 Hz, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.76 (dt, J=8.0, 2.0 Hz, 1H), 8.61 (td, J=5.0, 0.5 Hz, 1H).

4.2.18. 3-(2-Aminophenyl)pyridine (28). Reaction solvent: pyridine; yellowish oil; spectroscopic data identical to literature values;[66] ^{1}H NMR δ: 3.51 (br s, 2H), 6.78 (d, J=8.0 Hz, 1H), 6.86 (dt, J=7.5, 0.5 Hz, 1H), 7.10 (dd, J=7.5, 2.0 Hz, 1H), 7.21 (dt, J=7.0, 1.0 Hz, 1H), 7.38 (m, 1H), 7.82 (td, J=8.0, 1.5 Hz, 1H), 8.60 (dd, J=4.5, 1.0 Hz, 1H), 8.71 (d, J=2.5 Hz, 1H).

4.2.19. 4-(2-Aminophenyl)pyridine (29). Reaction solvent: pyridine; yellowish oil; spectroscopic data identical to literature values;[57] ^{1}H NMR δ: 3.73 (br s, 2H), 6.77 (d, J=8.0 Hz, 1H), 6.85 (dt, J=8.5, 1.0 Hz, 1H), 7.13 (dd, J=7.5, 1.5 Hz, 1H), 7.21 (tt, J=8.0, 1.0 Hz, 1H), 7.43 (dd, J=5.5, 2.0 Hz, 2H), 8.67 (dd, J=5.5, 1.5 Hz, 2H).

4.2.20. 2-[2-(*N*-Methylamino)phenyl]pyridine (30). Reaction solvent: pyridine; yellowish oil; ^{1}H NMR δ: 2.93 (s, 3H), 6.75 (m, 2H), 7.17 (m, 1H), 7.32 (m, 1H), 7.56 (d, J=7.5 Hz, 1H), 7.67 (dd, J=8.0, 1.0 Hz, 1H), 7.75 (m, 1H), 8.02 (br s, 1H), 8.60 (dd, J=5.0, 1.0 Hz, 1H); ^{13}C NMR δ: 30.0, 110.8, 115.6, 120.8, 121.4, 122.4, 129.4, 130.4, 136.9, 147.5, 148.6, 159.8; ESIHRMS, calcd for $C_{12}H_{12}N_2$: 185.1079 (M+H$^+$), found: 185.1075.

4.2.21. 3-[2-(*N*-Methylamino)phenyl]pyridine (31). Reaction solvent: pyridine; white solid; mp 71–73 °C; ^{1}H NMR δ: 2.80 (s, 3H), 3.80 (br s, 1H), 6.72 (d, J=8.5 Hz, 1H), 6.80 (dt, J=7.5, 1.0 Hz, 1H), 7.07 (dd, J=7.5, 2.0 Hz, 1H), 7.31 (dt, J=8.5, 2.0 Hz, 1H), 7.37 (dd, J=4.5, 1.0 Hz, 1H), 7.76 (td, J=7.5, 2.0 Hz, 1H), 8.59 (dd, J=5.0, 2.0 Hz, 1H), 8.67 (d, J=2.0 Hz, 1H); ^{13}C NMR δ: 30.7, 110.1, 117.1, 123.6, 129.6, 130.3, 135.2, 137.0, 146.3, 148.5, 150.4; ESIHRMS, calcd for $C_{12}H_{12}N_2$: 185.1079 (M+H$^+$), found: 185.1084.

4.2.22. 4-[2-(*N*-Methylamino)phenyl]pyridine (32). Reaction solvent: pyridine; white solid; mp 133–135 °C; ^{1}H NMR δ: 2.82 (s, 3H), 3.93 (br s, 1H), 6.71 (d, J=8.0 Hz, 1H), 6.80 (dt, J=7.5, 1.0 Hz, 1H), 7.09 (dd, J=7.5, 2.0 Hz, 1H), 7.32 (dt, J=7.5, 1.5 Hz, 1H), 7.39 (dd, J=6.0, 2.0 Hz, 2H), 8.66 (dd, J=6.0, 2.0 Hz, 2H); ^{13}C NMR δ: 30.7, 110.3, 117.1, 124.2, 124.4, 129.8, 130.0, 145.8, 147.7, 150.3; ESIHRMS, calcd for $C_{12}H_{12}N_2$: 185.1079 (M+H$^+$), found: 185.1075.

4.2.23. 2-(2-Methoxyphenyl)pyridine (33). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[67] ^{1}H NMR δ: 3.84 (s, 3H), 7.00 (d, J=8.5 Hz, 1H), 7.08 (t, J=7.0 Hz, 1H), 7.20 (m, 1H), 7.37 (dt, J=8.5, 2.0 Hz, 1H), 7.69 (dt, J=7.5, 2.0 Hz, 1H), 7.75 (dd, J=7.5, 2.0 Hz, 1H), 7.81 (d, J=8.0 Hz, 1H), 8.70 (d, J=4.5 Hz, 1H).

4.2.24. 3-(2-Methoxyphenyl)pyridine (34). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[66] ^{1}H NMR δ: 3.82 (s, 3H), 6.99 (d, J=8.5 Hz, 1H), 7.06 (dt, J=7.5, 1.0 Hz, 1H), 7.30–7.39 (m, 3H), 7.86 (tt, J=8.5, 2.5 Hz, 1H), 8.55 (dd, J=5.0, 2.0 Hz, 1H), 8.77 (dd, J=2.5, 1.0 Hz, 1H).

4.2.25. 4-(2-Methoxyphenyl)pyridine (35). Reaction solvent: pyridine; colorless oil; spectroscopic data identical to literature values;[57] ^{1}H NMR δ: 3.83 (s, 3H), 7.00 (dd, J=8.5, 1.0 Hz, 1H), 7.06 (dt, J=7.0, 0.5 Hz, 1H), 7.34 (dd, J=7.5, 1.5 Hz, 1H), 7.40 (dt, J=8.0, 1.5 Hz, 1H), 7.47 (dd, J=4.5, 2.0 Hz, 2H), 8.62 (dd, J=4.5, 1.5 Hz, 2H).

4.2.26. 6-(2-Pyridyl)-2-picolin-5-ol (36). Reaction solvent: pyridine; yellowish solid; mp 47–48 °C; ^{1}H NMR δ: 2.53 (s, 3H), 7.08 (d, J=9.0 Hz, 1H), 7.23 (d, J=9.0 Hz, 1H), 7.31 (ddd, J=11.5, 5.0, 1.5 Hz, 1H), 7.89 (dt, J=7.5, 2.0 Hz, 1H), 8.50 (dd, J=5.0, 1.0 Hz, 1H), 8.63 (d, J=8.0 Hz, 1H), 14.01 (br s, 1H); ^{13}C NMR δ: 23.7, 120.8, 122.8, 125.6, 126.2, 135.3, 137.8, 145.4, 148.1, 154.4, 158.3; Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41. Found: C, 70.89; H, 5.39.

4.2.27. 2-(2-Hydroxyphenyl)quinoline (38). Reaction solvent: benzene (30 equiv of quinoline in benzene); white solid; mp 110–112 °C, lit.[68] 109.8–110.7 °C; spectroscopic data identical to literature values;[68] ^{1}H NMR δ: 6.96 (tt, J=8.0, 1.5 Hz, 1H), 7.11 (d, J=7.5 Hz, 1H), 7.26 (d, J=1.5 Hz, 1H), 7.37 (dt, J=8.5, 1.0 Hz, 1H), 7.54 (dt, J=7.0, 1.5 Hz, 1H), 7.74 (dt, J=8.0, 1.0 Hz, 1H), 7.80 (d, J=8.0 Hz, 1H), 7.94 (d, J=7.5 Hz, 1H), 8.02 (dd, J=8.0, 2.0 Hz, 1H), 8.24 (d, J=8.5 Hz, 1H), 15.27 (br s, 1H).

4.2.28. 1-(2-Hydroxyphenyl)isoquinoline (39). Reaction solvent: benzene (30 equiv of isoquinoline in benzene); white solid; mp 160–162 °C, lit.[69] 166–168 °C; spectroscopic data identical to literature values;[69] ^{1}H NMR δ: 7.02 (dt, J=7.5, 1.0 Hz, 1H), 7.20 (dd, J=8.5, 1.0 Hz, 1H), 7.39 (dt, J=8.5, 1.5 Hz, 1H), 7.59–7.63 (m, 2H), 7.71–7.75 (m, 2H), 7.88 (d, J=8.0 Hz, 1H), 8.45 (m, 2H), 11.82 (br s, 1H).

4.2.29. 3-(2-Hydroxyphenyl)isoquinoline (40). Reaction solvent: benzene (30 equiv of isoquinoline in benzene); white solid; mp 112–113 °C; ^{1}H NMR δ: 6.96 (dt, J=7.0, 1.0 Hz, 1H), 7.06 (d, J=7.0 Hz, 1H), 7.32 (tt, J=7.0, 1.5 Hz, 1H), 7.60 (dt, J=8.0, 1.0 Hz, 1H), 7.74 (dt, J=7.0, 1.5 Hz, 1H), 7.89 (d, J=8.0 Hz, 1H), 7.92 (d, J=6.0 Hz, 1H), 8.00 (d, J=8.0 Hz, 1H), 8.22 (s, 1H), 9.19 (s, 1H), 14.05 (br s, 1H); ^{13}C NMR δ: 115.4, 118.7, 119.1, 119.5, 126.2, 126.9, 127.1, 127.4, 127.9, 130.9, 131.4, 137.0, 149.0, 151.2, 159.3; Anal. Calcd for $C_{15}H_{11}NO$: C, 81.43; H, 5.01. Found: C, 81.39; H, 5.00.

4.2.30. 2-(2-Hydroxyphenyl)-1*H*-pyrrole (41). Reaction solvent: pyrrole; yellowish oil; spectroscopic data identical to literature values;[70] ^{1}H NMR δ: 5.52 (s, 1H), 6.33 (d, J=3.0 Hz, 1H), 6.58 (s, 1H), 6.85 (d, J=8.0 Hz, 1H), 6.89 (s, 1H), 6.97 (t, J=7.0 Hz, 1H), 7.09 (t, J=7.5 Hz, 1H),

7.55 (d, J=8.0 Hz, 1H), 9.42 (br s, 1H); ^{13}C NMR δ: 106.2, 109.2, 116.3, 118.6, 119.6, 121.5, 127.0, 127.2, 128.8, 151.0.

4.2.31. 2-(2-Hydroxyphenyl)benzothiazole (42). Reaction solvent: benzene (20 equiv of benzothiazole in benzene); white solid; mp 130–131 °C, lit.[71] 130–132 °C; ^{1}H NMR δ: 6.96 (tt, J=7.5, 1.0 Hz, 1H), 7.12 (dd, J=8.5, 1.0 Hz, 1H), 7.37–7.42 (m, 2H), 7.50 (dt, J=8.5, 1.5 Hz, 1H), 7.69 (dd, J=8.5 Hz, 1.5 Hz, 1H), 7.89 (d, J=8.5 Hz, 1H), 7.99 (dd, J=8.0, 1.0 Hz, 1H), 12.53 (s, 1H).

4.2.32. 4-(2-Hydroxyphenyl)-4,7-dihydrobenzothiazole (43). Reaction solvent: benzene (20 equiv of benzothiazole in benzene); white solid; mp 210–212 °C; ^{1}H NMR δ: 3.57–3.59 (m, 2H), 5.12–5.15 (m, 1H), 6.07–6.11 (m, 1H), 6.22–6.26 (m, 1H), 6.89 (dt, J=7.5, 1.5 Hz, 1H), 7.05 (dd, J=8.0, 1.5 Hz, 1H), 7.15–7.19 (m, 2H), 8.67 (s, 1H), 10.10 (br s, 1H); ^{13}C NMR δ: 25.4, 37.8, 119.3, 120.7, 124.6, 125.5, 126.9, 127.4, 128.4, 130.3, 150.7, 151.2, 155.5; EIHRMS, calcd for $C_{13}H_{11}NOS$: 229.0561 (M^+), found: 229.0557.

4.3. Reaction of diphenyl diselenide with 1-iodo-2-naphthol (44)

A solution of 1-iodo-2-naphthol (1.0 mmol) and diphenyl diselenide (62.0 mg, 0.2 mmol) in degassed benzene was heated to reflux for 4 h. The solvent was evaporated off under reduced pressure. Purification by silica gel column chromatography (EtOAc/hexane) afforded compound **44** in quantitative yield. White solid; mp 79 °C, lit.[36] 77–78 °C; ^{1}H NMR δ: 7.14–7.17 (m, 6H), 7.37–7.40 (m, 2H), 7.51 (dt, J=7.0 Hz, 1.0 Hz, 1H), 7.82 (d, J=8.0 Hz, 1H), 7.90 (d, J=9.0 Hz, 1H), 8.29 (d, J=8.5 Hz, 1H).

4.4. General protocol for aryl radical addition to oxygen and sulfur heterocycles

A solution of aryl iodide (1.0 mmol), diphenyl diselenide (62.0 mg, 0.2 mmol), and freshly distilled furan (thiophene) (20 mL) was sparged with argon for 45 min, followed by heating at 50 °C (bath temperature) with stirring. A solution of 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70) (62.0 mg, 0.2 mmol) and Bu_3SnH (0.47 mL, 1.75 mmol) in degassed furan (thiophene) (10 mL) was added via syringe pump over 16 h, after which heating was continued for 1 h, before the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was taken up in acetonitrile (75 mL) and washed with hexane (4×25 mL). The acetonitrile phase was concentrated and purified by silica gel column chromatography (eluent: EtOAc/hexane).

4.4.1. 2,3,4,5-Tetrahydro-2,5-epoxy-1-benzoxepin (46).[72] Colorless oil; ^{1}H NMR δ: 2.19–2.28 (m, 4H), 5.12 (d, J=4.5 Hz, 1H), 5.94 (m, 1H), 6.75 (d, J=8.5 Hz, 1H), 6.84 (dt, J=7.5, 1.5 Hz, 1H), 6.94 (dd, J=7.0, 2.0 Hz, 1H), 7.15 (dt, J=7.5, 2.0 Hz, 1H); ^{13}C NMR δ: 33.4, 35.7, 77.2, 100.4, 116.1, 120.1, 124.4, 127.2, 128.7, 150.0.

4.4.2. 2-(2,5-Dihydrofuran-2-yl)phenol (47). Colorless oil; ^{1}H NMR δ: 4.79 (m, 1H), 4.86 (m, 1H), 6.07 (m, 3H), 6.86 (m, 2H), 7.02 (ddd, J=7.5, 2.0, 1.0 Hz, 1H), 7.17 (dt, J=7.5, 1.5 Hz, 1H), 7.98 (s, 1H); ^{13}C NMR δ: 75.5, 87.2, 117.1, 119.9, 124.8, 126.5, 126.6, 128.8, 129.0, 155.2; ESIHRMS, calcd for $C_{10}H_{10}O_2$: 185.0579 (M+Na), found: 185.0570.

4.4.3. 9-Methoxy-2,3,4,5-tetrahydro-2,5-epoxy-1-benzoxepin-7-carbaldehyde (48). White solid; mp 100–102 °C (EtOAc/hexane); ^{1}H NMR δ: 2.25–2.35 (m, 4H), 3.90 (s, 3H), 5.20 (d, J=5.5 Hz, 1H), 6.09 (d, J=4.0 Hz, 1H), 7.14 (d, J=1.0 Hz, 1H), 7.30 (d, J=1.5 Hz, 1H), 9.79 (s, 1H); ^{13}C NMR δ: 34.0, 35.3, 56.1, 77.0, 101.5, 109.7, 121.1, 127.8, 129.1, 145.2, 148.5, 190.6; Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.36; H, 5.57.

4.4.4. 3-(2,5-Dihydrofuran-2-yl)-4-hydroxy-5-methoxybenzaldehyde (49). Colorless oil; ^{1}H NMR δ: 3.95 (s, 3H), 4.83 (dd, J=12.0, 3.5 Hz, 1H), 4.92 (dd, J=14.0, 6.5 Hz, 1H), 6.03 (s, 2H), 6.16 (q, J=4.5 Hz, 1H), 6.70 (s, 1H), 7.35 (d, J=2.0 Hz, 1H), 7.47 (d, J=1.5 Hz, 1H), 9.82 (s, 1H); ^{13}C NMR δ: 56.3, 75.8, 82.6, 107.7, 124.7, 126.7, 128.0, 128.4, 129.3, 147.1, 148.4, 191.1; ESIHRMS, calcd for $C_{12}H_{12}O_4$: 243.0634 (M+Na), found: 243.0627.

4.4.5. 2-(2,3-Dihydrofuran-2-yl)benzonitrile (50). Colorless oil; ^{1}H NMR δ: 2.53 (m, 1H), 3.30 (m, 1H), 4.99 (q, J=2.0 Hz, 1H), 5.83 (dd, J=11.0, 7.5 Hz, 1H), 6.48 (q, J=2.5 Hz, 1H), 7.38 (dt, J=7.0, 2.0 Hz, 1H), 7.59 (m, 2H), 7.65 (dd, J=7.5, 1.0 Hz, 1H); ^{13}C NMR δ: 37.8, 79.8, 99.2, 109.6, 117.3, 125.8, 127.9, 132.9, 133.1, 145.2, 147.3; ESIHRMS, calcd for $C_{11}H_9NO$: 194.0582 (M+Na), found: 194.0590.

4.4.6. 2-(2,5-Dihydrofuran-2-yl)benzonitrile (51). Colorless oil; ^{1}H NMR δ: 4.84 (m, 1H), 4.98 (m, 1H), 5.92 (m, 1H), 6.10 (m, 2H), 7.37 (dt, J=7.5, 1.5 Hz, 1H), 7.50 (dd, J=8.0, 1.0 Hz, 1H), 7.58 (dt, J=7.5, 1.5 Hz, 1H), 7.66 (dd, J=7.5, 1.0 Hz, 1H); ^{13}C NMR δ: 76.5, 86.1, 110.1, 117.4, 127.1, 127.8, 128.1, 133.0, 133.3, 146.2; ESIHRMS, calcd for $C_{11}H_9NO$: 194.0582 (M+Na), found: 194.0577.

4.4.7. Methyl 2-(2,3-dihydrofuran-2-yl)benzoate (52). Colorless oil; eluent: 1:1 (hexane/benzene with 0.5% EtOAc); ^{1}H NMR δ: 2.34–2.40 (ddt, J=15.5, 10.5, 2.0 Hz, 1H), 3.31–3.37 (ddt, J=15.5, 10.5, 2.5 Hz, 1H), 3.90 (s, 3H), 4.90 (app. q, J=2.5 Hz, 1H), 6.26 (dd, J=11.5, 7.5 Hz, 1H), 6.51 (q, J=3.0 Hz, 1H), 7.33 (dt, J=8.0, 1.5 Hz, 1H), 7.54 (dt, J=7.5, 1.0 Hz, 1H), 7.63 (dd, J=7.5, 1.0 Hz, 1H), 7.98 (dd, J=7.5, 1.0 Hz, 1H); ^{13}C NMR δ: 38.6, 52.1, 79.7, 99.0, 125.5, 126.8, 126.9, 130.7, 132.7, 145.1, 145.8, 167.2; ESIHRMS, calcd for $C_{12}H_{12}O_3$: 227.0684 (M+Na), found: 227.0691.

4.4.8. Methyl 2-(2,5-dihydrofuran-2-yl)benzoate (53). Colorless oil; eluent: 1:1 (hexane/benzene with 1.5% EtOAc); ^{1}H NMR δ: 3.90 (s, 3H), 4.85 (m, 1H), 4.95 (m, 1H), 5.92 (m, 1H), 6.04 (m, 1H), 6.50 (m, 1H), 7.31 (dt, J=7.5, 1.0 Hz, 1H), 7.53 (dt, J=7.5, 1.5 Hz, 1H), 7.63 (dd, J=7.0, 1.0 Hz, 1H), 7.92 (dd, J=8.0, 1.0 Hz, 1H); ^{13}C NMR δ: 52.1, 76.2, 85.4, 125.5, 126.6, 127.0, 127.3, 130.2, 130.9, 132.8, 145.1, 167.5; ESIHRMS, calcd for $C_{12}H_{12}O_3$: 227.0684 (M+Na), found: 227.0686.

4.4.9. Methyl [2-(2,3-dihydrofuran-2-yl)phenyl]carbamate (54). Colorless oil; eluent: 1.5:1 (hexane/chloroform with 1.5% EtOAc); ^{1}H NMR δ: 2.78 (m, 1H), 2.92 (m,

1H), 3.77 (s, 3H), 5.15 (q, J=2.5 Hz, 1H), 5.53 (t, J=10.5 Hz, 1H), 6.45 (q, J=2.5 Hz, 1H), 7.08 (t, J=7.5 Hz, 1H), 7.23 (d, J=7.0 Hz, 1H), 7.34 (dt, J=7.5, 1.5 Hz, 1H), 7.38 (br s, 1H), 7.95 (br s, 1H); ^{13}C NMR δ: 35.0, 52.4, 82.8, 101.4, 121.9, 123.7, 127.7, 129.1, 129.3, 136.6, 144.6, 154.3; ESIHRMS, calcd for $C_{12}H_{13}NO_3$: 242.0793 (M+Na), found: 242.0794.

4.4.10. Methyl [2-(2,5-dihydrofuran-2-yl)phenyl]carbamate (55). Colorless oil; ^{1}H NMR δ: 3.77 (s, 3H), 4.79 (m, 2H), 5.89 (m, 1H), 6.04 (m, 1H), 6.13 (m, 1H), 7.04 (t, J=8.0 Hz, 1H), 7.12 (dd, J=7.5, 1.5 Hz, 1H), 7.31 (dt, J=9.0, 1.5 Hz, 1H), 7.82 (br s, 1H), 7.93 (br s, 1H); ^{13}C NMR δ: 52.3, 75.3, 85.9, 121.4, 123.4, 127.0, 127.7, 128.1, 128.9, 129.2, 137.1, 154.3; ESIHRMS, calcd for $C_{12}H_{13}NO_3$: 220.0974 (M+H), found: 220.0967.

4.4.11. 2,3,4,5-Tetrahydro-2,5-epithio-1-benzoxepin (56). Colorless oil; eluent: 1:1:1 (benzene/chloroform/hexane); ^{1}H NMR δ: 2.26–2.53 (m, 4H), 4.36 (d, J=5.0 Hz, 1H), 6.19 (d, J=4.5 Hz, 1H), 6.81 (m, 2H), 6.99 (dd, J=7.5, 2.0 Hz, 1H), 7.13 (dt, J=7.5, 1.5 Hz, 1H); ^{13}C NMR δ: 38.0, 40.4, 49.9, 86.9, 117.6, 120.1, 126.0, 128.6, 129.5, 151.3; ESIHRMS, calcd for $C_{10}H_{10}OS$: 179.0531 (M+H), found: 179.0536.

4.4.12. 2-(2,5-Dihydrothiophen-2-yl)phenol (57). White solid; mp 67–68 °C (EtOAc/hexane); ^{1}H NMR δ: 3.95 (m, 2H), 5.57 (m, 1H), 5.85 (m, 1H), 6.03 (m, 1H), 6.40 (br s, 1H), 6.85 (d, J=8.5 Hz, 1H), 6.88 (dt, J=7.5, 1.0 Hz, 1H), 7.15 (dd, J=7.5, 2.0 Hz, 1H), 7.19 (dt, J=7.0, 1.5 Hz, 1H); ^{13}C NMR δ: 39.6, 56.0, 117.2, 120.7, 126.1, 129.2, 129.2, 129.4, 132.5, 155.0; Anal. Calcd for $C_{10}H_{10}OS$: C, 67.38; H, 5.65. Found: C, 67.16; H, 5.44.

4.4.13. 2-(2,3-Dihydrothiophen-2-yl)benzonitrile (58) and 2-(2,3-dihydrothiophen-3-yl)benzonitrile (59). Compounds **58** and **59** were obtained as a 1.4:1 inseparable mixture with ESIHRMS, calcd for $C_{11}H_9NS$: 210.0354 (M+Na), found: 210.0352. Compound **58** was characterized by ^{1}H NMR δ: 2.89 (m, 1H), 3.35 (m, 1H), 5.27 (dd, J=10.0, 5.5 Hz, 1H), 5.58 (m, 1H), 6.25 (m, 1H), 7.36 (m, 1H), 7.62 (dd, J=7.5, 1.0 Hz, 1H), 7.75 (d, J=8.0 Hz, 1H), 7.26–7.66 (1H). Compound **59** was characterized by ^{1}H NMR δ: 3.13 (ddd, J=11.0, 6.5, 2.0 Hz, 1H), 3.83 (dt, J=11.5, 2.0 Hz, 1H), 4.73 (m, 1H), 5.65 (m, 1H), 6.47 (m, 1H), 7.35 (t, J=7.0 Hz, 1H), 7.53 (d, J=8.0 Hz, 1H), 7.57 (t, J=8.0 Hz, 1H), 7.66 (d, J=7.5 Hz, 1H). Compounds **58** and **59** ^{13}C NMR δ: 39.5, 43.6, 49.3, 51.0, 111.1, 111.7, 117.5, 117.8, 120.1, 123.9, 125.4, 127.6, 127.6, 127.7, 129.3, 132.7, 133.0, 133.32, 133.36, 146.6, 147.5.

4.4.14. 2-(2,5-Dihydrothiophen-2-yl)benzonitrile (60). White solid; mp 80–81 °C (EtOAc/hexane); ^{1}H NMR δ: 3.93 (m, 1H), 4.03 (m, 1H), 5.70 (m, 1H), 5.78 (m, 1H), 6.08 (m, 1H), 7.32 (dt, J=8.0, 1.5 Hz, 1H), 7.48 (dd, J=7.5, 1.0 Hz, 1H), 7.55 (dt, J=7.5, 1.5 Hz, 1H), 7.62 (dd, J=7.5, 1.5 Hz, 1H); ^{13}C NMR δ: 40.3, 56.5, 111.5, 117.4, 127.7, 128.9, 130.6, 130.9, 133.1, 133.1, 147.3; Anal. Calcd for $C_{11}H_9NS$: C, 70.55; H, 4.84. Found: C, 70.47; H, 4.88.

4.4.15. Methyl 2-(2,3-dihydrothiophen-2-yl)benzoate (61). Colorless oil; eluent: 1:1 (hexane/benzene); ^{1}H NMR δ: 2.89 (m, 1H), 3.31 (m, 1H), 3.91 (s, 3H), 5.58 (m, 1H), 5.69 (dd, J=10.0, 4.5 Hz, 1H), 6.23 (m, 1H), 7.29 (dt, J=7.5, 1.5 Hz, 1H), 7.49 (dt, J=7.5, 1.5 Hz, 1H), 7.76 (dd, J=8.0, 1.0 Hz, 1H), 7.85 (dd, J=8.0, 1.5 Hz, 1H); ^{13}C NMR δ: 43.3, 47.9, 52.2, 120.4, 125.5, 126.9, 127.8, 128.2, 130.2, 132.6, 145.3, 167.9; ESIHRMS, calcd for $C_{12}H_{12}O_2S$: 221.0636 (M+H), found: 221.0635.

4.4.16. Methyl 2-(2,5-dihydrothiophen-2-yl)benzoate (62). Colorless oil; eluent: 1:1 (hexane/benzene); ^{1}H NMR δ: 3.81–3.93 (m, 2H), 3.90 (s, 3H), 5.85 (m, 1H), 6.05 (m, 1H), 6.13 (m, 1H), 7.27 (dt, J=6.5, 1.5 Hz, 1H), 7.48 (m, 2H), 7.85 (d, J=9.0 Hz, 1H); ^{13}C NMR δ: 39.1, 52.2, 54.8, 126.9, 128.7, 128.7, 129.5, 130.2, 132.5, 132.5, 144.9, 167.8; ESIHRMS, calcd for $C_{12}H_{12}O_2S$: 221.0636 (M+H), found: 221.0636.

4.4.17. Methyl [2-(2,3-dihydrothiophen-2-yl)phenyl]carbamate (63). Colorless oil; eluent: 1:1 (hexane/benzene with 2% EtOAc); ^{1}H NMR δ: 2.97 (m, 1H), 3.17 (m, 1H), 3.77 (s, 3H), 5.09 (dd, J=10.5, 8.0 Hz, 1H), 5.68 (m, 1H), 6.23 (m,1H), 7.06 (t, J=7.0 Hz, 1H), 7.15 (br s, 1H), 7.29 (m, 2H), 7.81 (br s, 1H); ^{13}C NMR δ: 41.8, 50.2, 52.5, 122.3, 123.3, 124.4, 124.9, 128.5, 129.0, 132.0, 136.0, 154.5; ESIHRMS, calcd for $C_{12}H_{13}NO_2S$: 258.0565 (M+Na), found: 258.0558.

4.4.18. Methyl [2-(2,5-dihydrothiophen-2-yl)phenyl]carbamate (64). Colorless oil; ^{1}H NMR δ: 3.75 (s, 3H), 3.94 (br m, 2H), 5.50 (br s, 1H), 5.81 (m, 1H), 6.03 (m, 1H), 7.08 (t, J=7.0 Hz, 1H), 7.20 (d, J=7.5 Hz, 1H), 7.22 (br s, 1H), 7.27 (dt, J=9.5, 2.0 Hz, 1H), 7.73 (br s, 1H); ^{13}C NMR δ: 39.8, 52.4, 56.7, 123.5, 124.6, 128.6, 129.4, 129.5, 132.2, 136.2, 154.5; ESIHRMS, calcd for $C_{12}H_{13}NO_2S$: 258.0565 (M+Na), found: 258.0568.

4.5. General protocol for aryl radical addition to carbocyclic arenes

A solution of aryl iodide (1.0 mmol), diphenyl diselenide (62.0 mg, 0.2 mmol), and freshly distilled solvent (20 mL) was sparged with argon for 45 min, followed by heating at 90 °C (bath temperature) with stirring. A solution of AIBN (33.0 mg, 0.2 mmol) and Bu_3SnH (0.47 mL, 1.75 mmol) in degassed solvent (10 mL) was added via syringe pump over 16 h, after which heating was continued for 1 h, before the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was taken up in acetonitrile (75 mL) and washed with hexane (4×25 mL) (except Table 4 entries 1 and 4, which were purified without acetonitrile/hexane workup). The acetonitrile phase was concentrated and purified by silica gel chromatography.

4.5.1. (±)-(4a*R,9b*S**)-4a-Methoxy-3,4,4a,9b-tetrahydrodibenzofuran (66).** Reaction solvent: anisole; colorless oil; eluent: 1:4 (hexane/benzene); ^{1}H NMR δ: 1.82–1.88 (m, 1H), 2.14–2.18 (m, 2H), 2.42–2.46 (td, J=13.0, 4.5 Hz, 1H), 3.39 (s, 3H), 3.71 (s, 1H), 5.73–5.79 (m, 2H), 6.86 (d, J=8.0 Hz, 1H), 6.90 (t, J=8.0 Hz, 1H), 7.16 (t, J=8.0 Hz, 1H), 7.20 (d, J=7.5 Hz, 1H); ^{13}C NMR δ: 22.0, 27.8, 47.3, 49.5, 110.1, 111.6, 121.1, 124.3, 126.4, 126.9, 128.1, 130.3, 157.6; EIHRMS, calcd for $C_{13}H_{14}O_2$: 202.0994 (M^+), found: 202.0999.

4.5.2. 2-(2-Methoxyphenyl)phenol (67). Reaction solvent: anisole; white solid; mp 72 °C, lit.[73] 73–74 °C; spectroscopic data identical to literature values;[73] ^{1}H NMR δ: 3.91 (s, 3H), 6.29 (s, 1H), 7.02–7.08 (m, 3H), 7.14 (dt, J=7.5, 1.0 Hz, 1H), 7.29 (dd, J=8.0, 1.5 Hz, 1H), 7.32 (dt, J=8.5, 1.5 Hz, 1H), 7.37 (dd, J=8.0, 1.5 Hz, 1H), 7.42 (dt, J=8.0, 1.5 Hz, 1H).

4.5.3. 2-(4-Methoxyphenyl)phenol (68). Reaction solvent: anisole; white solid; mp 60–62 °C, lit.[74] 65–66 °C; spectroscopic data identical to literature values;[74] ^{1}H NMR δ: 3.87 (s, 3H), 5.23 (s, 1H), 6.97–7.00 (m, 2H), 7.03 (d, J=9.0 Hz, 2H), 7.22–7.26 (m, 2H), 7.40 (d, J=9.0 Hz, 2H).

4.5.4. (±)-(4a*R,10b*S**)-4a-Methoxy-3,4,4a,10b-tetrahydro-4*H*-dibenzo[*b*,*d*]pyran-6-one (69).** Reaction solvent: anisole; colorless oil; eluent: 1:9 (EtoAc/hexane); ^{1}H NMR δ: 1.68–1.74 (ddd, J=17.5, 11.0, 6.0 Hz, 1H), 2.26–2.32 (m, 1H), 2.40–2.47 (m, 1H), 2.54–2.58 (ddd, J=13.5, 6.0, 2.0 Hz, 1H), 3.40 (s, 3H), 3.67 (m, 1H), 5.37–5.40 (qd, J=10.0, 2.0 Hz, 1H), 5.73–5.77 (m, 1H), 7.31 (dd, J=7.5, 1.0 Hz, 1H), 7.38 (dt, J=7.5, 1.0 Hz, 1H), 7.59 (dt, J=7.5, 1.0 Hz, 1H), 8.10 (dd, J=7.5, 1.0 Hz, 1H); ^{13}C NMR δ: 23.5, 28.0, 43.7, 49.3, 103.7, 123.3, 126.7, 126.8, 127.5, 128.0, 130.0, 134.5, 141.3, 164.2; ESIHRMS, calcd for $C_{14}H_{14}O_3$: 231.1016 (M+H), found: 231.1015.

4.5.5. 2-(2-Methoxyphenyl)benzoic acid (70). Reaction solvent: anisole; white solid; mp 150–152 °C, lit.[75] 149–152 °C; spectroscopic data identical to literature values;[75] ^{1}H NMR δ: 3.71 (s, 3H), 6.88 (d, J=8.0 Hz, 1H), 7.05 (dt, J=7.5, 1.0 Hz, 1H), 7.28 (dd, J=7.0, 1.5 Hz, 1H), 7.32–7.36 (m, 2H), 7.42 (dt, J=8.0, 1.5 Hz, 1H), 7.59 (dt, J=7.5, 1.5 Hz, 1H), 7.94 (dd, J=8.0, 1.5 Hz, 1H).

4.5.6. 2-(4-Methoxyphenyl)benzoic acid (71). Reaction solvent: anisole; white solid; mp 140–141 °C, lit.[76] 140–143 °C; spectroscopic data identical to literature values;[76] ^{1}H NMR δ: 3.85 (s, 3H), 6.93 (d, J=9.0 Hz, 2H), 7.28 (d, J=9.0 Hz, 2H), 7.35 (dd, J=8.0, 2.0 Hz, 1H), 7.40 (dt, J=8.0, 1.0 Hz, 1H), 7.54 (dt, J=8.5, 1.0 Hz, 1H), 7.93 (dd, J=8.5, 1.5 Hz, 1H).

4.5.7. 2-(2-Methoxyphenyl)aniline (72). Reaction solvent: anisole; yellowish solid; mp 65–67 °C, lit.[77] 80 °C; spectroscopic data identical to literature values;[77] ^{1}H NMR δ: 3.52 (br s, 2H), 3.82 (s, 3H), 6.80 (dd, J=8.5, 1.5 Hz, 1H), 6.85 (dt, J=7.0, 1.0 Hz, 1H), 7.01 (d, J=9.0 Hz, 1H), 7.05 (dt, J=7.5, 1.0 Hz, 1H), 7.12 (dd, J=7.5, 1.5 Hz, 1H), 7.18 (dt, J=8.0, 2.0 Hz, 1H), 7.27 (dd, J=7.5, 2.0 Hz, 1H), 7.37 (dt, J=8.5, 2.0 Hz, 1H).

4.5.8. 2-(3-Methoxyphenyl)aniline (73). Reaction solvent: anisole; yellowish oil; eluent: 1:19 (EtoAc/hexane); ^{1}H NMR δ: 3.83 (s, 3H), 6.80 (d, J=7.5 Hz, 1H), 6.85 (dt, J=7.0, 1.0 Hz, 1H), 6.90 (ddd, J=8.5, 2.5, 1.0 Hz, 1H), 7.00 (t, J=2.0 Hz, 1H), 7.05 (td, J=7.5, 1.0 Hz, 1H), 7.14–7.19 (m, 2H), 7.36 (t, J=8.0 Hz, 1H); ^{13}C NMR δ: 55.3, 113.0, 114.5, 115.9, 118.9, 121.4, 127.8, 128.6, 129.8, 130.3, 140.8, 142.9, 159.9; ESIHRMS, calcd for $C_{13}H_{13}NO$: 200.1070 (M+H), found: 200.1069.

4.5.9. 2-(4-Methoxyphenyl)aniline (74). Reaction solvent: anisole; colorless oil; spectroscopic data identical to literature values;[78] ^{1}H NMR δ: 3.84 (s, 3H), 6.79 (dd, J=8.0, 0.5 Hz, 1H), 6.84 (dt, J=7.5, 1.0 Hz, 1H), 6.99 (d, J=8.5 Hz, 2H), 7.11–7.16 (m, 2H), 7.38 (d, J=9.0 Hz, 2H).

4.5.10. 1-(2-Hydroxyphenyl)-2-chloro-cyclohexa-2,5-diene (75). Reaction solvent: chlorobenzene; colorless oil; eluent: 2:1:1 (hexane/benzene/chloroform); ^{1}H NMR δ: 2.93–2.98 (m, 2H), 4.42–4.45 (m, 1H), 5.12 (s, 1H), 5.74–5.78 (m, 1H), 5.82–5.85 (m, 1H), 6.05 (m, 1H), 6.82 (d, J=8.5 Hz, 1H), 6.93 (t, J=7.0 Hz, 1H), 7.15–7.18 (m, 2H); ^{13}C NMR δ: 28.2, 43.2, 116.4, 121.2, 122.9, 123.5, 127.1, 127.4, 128.5, 130.2, 131.9, 153.9; EIHRMS, calcd for $C_{12}H_{11}ClO$: 206.0498 (M^+), found: 206.0508.

4.5.11. 1-(2-Hydroxyphenyl)-3-chloro cyclohexa-2,5-diene (76). Reaction solvent: chlorobenzene; colorless oil; eluent: 2:1:1 (hexane/benzene/chloroform); ^{1}H NMR δ: 3.02–3.05 (m, 2H), 4.41–4.45 (m, 1H), 5.03 (br s, 1H), 5.78–5.81 (m, 1H), 5.83–5.86 (m, 1H), 5.90–5.91 (m, 1H), 6.77–6.78 (dd, J=8.0, 1.0 Hz, 1H), 6.90–6.93 (dt, J=7.5, 1.5 Hz, 1H), 7.10–7.15 (m, 2H); ^{13}C NMR δ: 33.1, 39.3, 115.9, 121.2, 123.8, 124.8, 126.7, 128.2, 128.3, 129.5, 129.9, 153.4; ESIHRMS, calcd for $C_{12}H_{11}ClO$: 205.0420 (M−H), found: 205.0411.

4.5.12. 2-(2-Hydroxyphenyl)benzonitrile (77). Reaction solvent: benzonitrile; white solid; mp 92–93 °C, lit.[79] 71–73 °C, eluent: 1:19 (EtOAc/hexane); spectroscopic data identical to literature values; ^{1}H NMR δ: 7.32–7.38 (m, 2H), 7.48 (dt, J=8.5, 1.5 Hz, 1H), 7.58 (dt, J=8.0, 0.5 Hz, 1H), 7.82 (dt, J=8.0, 1.5 Hz, 1H), 8.06 (dd, J=7.5, 1.0 Hz, 1H), 8.12 (d, J=8.0 Hz, 1H), 8.40 (dd, J=7.5, 1.0 Hz, 1H); ^{13}C NMR δ: 117.8, 118.1, 121.3, 121.7, 122.8, 124.6, 128.9, 130.5, 130.6, 134.8, 134.7, 151.3, 161.2; ESIHRMS, calcd for $C_{13}H_9NO$: 196.0757 (M+H), found: 196.0756.

4.5.13. 4-(2-Hydroxyphenyl)benzonitrile (78). Reaction solvent: benzonitrile; white solid; mp 111–113 °C, lit.[80] 111–112 °C; spectroscopic data identical to literature values; ^{1}H NMR δ: 5.13 (s, 1H), 6.95 (dd, J=8.0, 0.5 Hz, 1H), 7.04 (t, J=8.0 Hz, 1H), 7.26–7.32 (m, 2H), 7.67 (d, J=8.5 Hz, 2H), 7.74 (d, J=8.5 Hz, 2H).

4.5.14. 3-(2-Hydroxyphenyl)benzonitrile (79). Reaction solvent: benzonitrile; colorless oil; spectroscopic data identical to literature values;[79] ^{1}H NMR δ: 4.99 (s, 1H), 6.95 (dd, J=8.0, 1.0 Hz, 1H), 7.04 (dt, J=7.5, 1.0 Hz, 1H), 7.25–7.31 (m, 2H), 7.56 (t, J=8.0 Hz, 1H), 7.66 (tt, J=8.0, 1.5 Hz, 1H), 7.78 (tt, J=7.5, 1.5 Hz, 1H), 7.85 (t, J=2.0 Hz, 1H).

4.5.15. 1-(2-Hydroxyphenyl)-1,4-dihydronaphthalene (80). Reaction solvent: benzene (80 equiv of naphthalene in benzene); colorless oil; eluent: 1:1 (hexane/benzene); ^{1}H NMR δ: 3.53–3.58 (m, 2H), 4.86 (m, 1H), 5.00 (s, 1H), 5.98–6.01 (m, 1H), 6.11–6.14 (m, 1H), 6.79 (dd, J=8.0, 1.5 Hz, 1H), 6.90 (dt, J=7.0, 1.0 Hz, 1H), 7.05 (d, J=8.0 Hz, 1H), 7.10–7.19 (m, 5H); ^{13}C NMR δ: 29.7, 41.3, 116.6, 120.9, 125.3, 126.6 (2C), 128.1, 128.3, 128.4, 129.0, 130.6, 130.7, 133.3, 136.0, 153.8; ESIHRMS, calcd for $C_{16}H_{14}O$: 221.0966 (M−H), found: 221.0961.

4.5.16. 1-(2-Hydroxyphenyl)-1,2-dihydronaphthalene (81) and 2-(2-hydroxyphenyl)-1,2-dihydronaphthalene (82). Compounds **81** and **82** were obtained as a 1.4:1 mixture. Reaction solvent: benzene (80 equiv of naphthalene in benzene); eluent: 1:1 (hexane/benzene); Characteristic ^{1}H NMR peaks of compound **81** δ: 2.61–2.71 (m, 2H), 4.47–4.51 (dd, J=10.5, 8.0 Hz, 1H), 4.81 (s, 1H), 6.03–6.07 (m, 1H), 6.57 (d, J=10.0 Hz, 1H); Characteristic ^{1}H NMR peaks of compound **82** δ: 3.03 (dd, J=16.0, 12.0 Hz, 1H), 3.13 (dd, J=15.5, 7.5 Hz, 1H), 4.09–4.13 (m, 1H), 4.96 (s, 1H), 6.09–6.11 (dd, J=9.5, 3.5 Hz, 1H), 6.68–6.70 (dd, J=9.5, 2.5 Hz, 1H); **81** and **82** ^{1}H NMR δ: 6.80–6.81 (dd, J=8.0, 0.5 Hz, 1H), 6.84–6.85 (dd, J=8.0, 1.0 Hz 1H), 6.90–6.93 (m, 3H), 7.06–7.26 (m, 11H); ^{13}C NMR δ: 30.0, 34.6, 35.3, 38.4, 115.8, 116.1, 121.05, 121.08, 126.2, 126.4, 126.7, 127.2, 127.3, 127.5, 127.6, 127.7, 127.81, 127.83, 127.88, 127.89, 129.0, 129.1, 129.8, 130.24, 130.28, 131.2, 133.3, 134.4, 134.6, 136.2, 153.2, 153.3; ESIHRMS, calcd for $C_{16}H_{14}O$: 221.0966 (M−H), found: 221.0961.

4.6. (±)-(3*S**,4*R**)-Allyl-3-(2-hydroxyphenyl)-4-methoxycyclohexene (83)

To a solution of compound **66** (50 mg, 0.25 mmol) and allyltrimethylsilane (0.039 mL, 0.25 mmol) in CH_2Cl_2 (3.0 mL) under argon at −78 °C was added $TiCl_4$ (0.027 mL, 0.25 mmol). The reaction mixture was quenched with saturated $NaHCO_3$ after 15 min of stirring and extracted with diethyl ether (3×20 mL). The combined organic layer was dried (Na_2SO_4), and the solvent was removed under reduced pressure. Purification by silica gel column chromatography (EtOAc/hexane) afforded compound **83** in 84%, yield. Colorless oil; ^{1}H NMR δ: 1.78–1.83 (m, 1H), 1.90–1.95 (m, 1H), 2.11–2.16 (m, 1H), 2.23–2.30 (m, 1H), 2.36–2.48 (dq, J=14.0, 7.5 Hz, 2H), 3.28 (s, 3H), 3.63 (t, J=2.5 Hz, 1H), 5.13–5.19 (m, 2H), 5.50–5.53 (qd, J=7.5, 2.5 Hz, 1H), 5.84–5.89 (m, 2H), 6.83 (dt, J=7.5, 1.5 Hz, 1H), 6.90 (dd, J=8.0, 1.0 Hz, 1H), 7.09 (dd, J=7.5, 2.0 Hz, 1H), 7.17 (dt, J=8.0, 2.5 Hz, 1H), 8.34 (br s, 1H); ^{13}C NMR δ: 22.9, 26.3, 38.8, 48.0, 48.8, 79.7, 118.0, 119.1, 119.6, 126.8, 127.6, 127.8, 128.5, 132.4, 133.2, 156.5; EIHRMS, calcd for $C_{16}H_{20}O_2$: 244.1463 (M^+), found: 244.1460.

Acknowledgements

We thank the NSF (CHE 9986200) for partial support of this work and Bhushan Surve for the X-ray crystal structure.

References and notes

1. Crich, D.; Hwang, J.-T. *J. Org. Chem.* **1998**, *63*, 2765–2770.
2. Crich, D.; Yao, Q. *J. Org. Chem.* **1995**, *60*, 84–88.
3. Crich, D.; Jiao, X.-Y.; Yao, Q.; Harwood, J. S. *J. Org. Chem.* **1996**, *61*, 2368–2373.
4. The BDE's for Me_3Sn-H and PhSe-H are 78 and 78±4 cal mol^{-1}, respectively.[5,6]
5. Laarhoven, L. J. J.; Mulder, P.; Wayner, D. D. M. *Acc. Chem. Res.* **1999**, *32*, 342–349.
6. Leeck, D. T.; Li, D. T.; Chyall, L. J.; Kenttamaa, H. I. *J. Phys. Chem.* **1996**, *100*, 6608–6611.
7. The rate constants for trapping of primary alkyl radicals by PhSeH and Bu_3SnH at 25 °C are, respectively, 1×10^9 and 2×10^6 M^{-1} s^{-1}.[8,9]
8. Newcomb, M.; Choi, S.-Y.; Horner, J. H. *J. Org. Chem.* **1999**, *64*, 1225–1231.
9. Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739–7742.
10. Roberts, B. P. *Chem. Soc. Rev.* **1999**, *28*, 25–36.
11. Martínez-Barrasa, V.; Garcia de Viedma, A.; Burgos, C.; Alvarez-Builla, J. *Org. Lett.* **2000**, *2*, 3933–3935.
12. Studer, A.; Bossart, M. *Radicals in Organic Synthesis*; Renaud, P., Sibi, M., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 2, pp 62–80.
13. Beckwith, A. L. J.; Bowry, V. W.; Bowman, W. R.; Mann, E.; Parr, J.; Storey, J. M. D. *Angew. Chem., Int. Ed.* **2004**, *43*, 95–98.
14. Curran, D. P.; Yu, H.; Liu, H. *Tetrahedron* **1994**, *50*, 7343–7366.
15. Curran, D. P.; Liu, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1377–1393.
16. Engel, P. S.; Wu, W.-X. *J. Am. Chem. Soc.* **1989**, *111*, 1830–1835.
17. For an excellent overview of the large body of early work on the oxidative radical arylation of arenes, including relative rates and regioselectivities see: Williams, G. H. *Homolytic Aromatic Substitution*; Pergamon: New York, NY, 1960.
18. Preliminary communications: (a) Crich, D.; Patel, M. *Heterocycles* **2004**, *64*, 499–564; (b) Crich, D.; Patel, M. *Org. Lett.* **2005**, *7*, 3625–3628.
19. Harrowven, D. C.; Sutton, B. J. *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Amsterdam, 2005; Vol. 16.
20. Abramovitch, R. A.; Saha, M. *J. Chem. Soc.* **1964**, 2175–2187.
21. Abramovitch, R. A.; Saha, M. *J. Chem. Soc. B* **1966**, 733–739.
22. Vernin, G.; Dou, H.-J. M. *C. R. Acad. Sci.* **1967**, *265C*, 828–830.
23. Further data on the relative rates of addition of substituted phenyl radicals to pyridines may be found in Ref. 17 and in the Landolt-Börnstein series.[24]
24. Lorand, J. P. *Landolt-Börnstein New Series*; Fischer, H., Ed.; Springer: Berlin, 1984; Vol. 13a, pp 202–248.
25. Hey, D. H.; Shingleton, D. A.; Williams, G. H. *J. Chem. Soc.* **1963**, 5612–5619.
26. Abramovitch, R. A.; Saha, M. *Can. J. Chem.* **1966**, *44*, 1765–1771.
27. Except in solvents such as acetonitrile, when a significant preference for the *para*-position was reported. Gurczynski, M.; Tomasik, P. *Org. Prep. Proced. Int.* **1991**, *23*, 438–441.
28. Núñez, A.; Sánchez, A.; Burgos, C.; Alvarez-Builla, J. *Tetrahedron* **2004**, *60*, 6217–6224.
29. Fowler, F. W. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 2, pp 365–394.
30. Lounasmaa, M.; Tolvanen, A. *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 5, pp 135–165.
31. Pausacker, K. H. *Aust. J. Chem.* **1958**, *11*, 200–210.
32. Vernin, G.; Dou, H. J. M.; Metzger, J. *Bull. Soc. Chim. Fr.* **1971**, 2612–2616.
33. Dyall, L. K.; Pullin, C. J. *Aust. J. Chem.* **1979**, *32*, 345–352.
34. Vernin, G.; Dou, H. J. M.; Loridan, G.; Metzger, J. *Bull. Soc. Chim. Fr.* **1970**, 2705–2707.

35. Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743–756.
36. Barton, D. H. R.; Brewster, A. G.; Ley, S. V.; Read, C. M.; Rosenfeld, M. N. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1473–1476.
37. Benati, L.; La Barba, N.; Tiecco, M.; Tundo, A. *J. Chem. Soc. B* **1969**, 1253–1256.
38. Camaggi, C. M.; Leardini, R.; Tiecco, M.; Tundo, A. *J. Chem. Soc. B* **1969**, 1251–1253.
39. Walling, C. *Tetrahedron* **1985**, *41*, 3887–3900.
40. Kita, Y.; Gotanda, K.; Sano, A.; Oka, M.; Murata, K.; Suemua, M.; Matsugi, M. *Tetrahedron Lett.* **1997**, *38*, 8345–8348.
41. Kita, Y.; Matsugi, M. *Radicals in Organic Synthesis*; Sibi, M. P., Renaud, P., Eds.; Wiley-VCH: Weinheim, 2001; Vol. 1, pp 1–10.
42. Griller, D.; Nonhebel, D. C.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1817–1821.
43. Korth, H.-G.; Sustmann, R. *Tetrahedron Lett.* **1985**, *26*, 2551–2554.
44. Korth, H.-G.; Lommes, P.; Sustmann, R. *J. Am. Chem. Soc.* **1984**, *106*, 663–668.
45. Edge, D. J.; Kochi, J. K. *J. Chem. Soc., Perkin Trans. 2* **1973**, 182–190.
46. 96.06±0.15, 93.9±2, and 93.9±2 kcal mol^{-1}, respectively. Luo, Y.-R. *Handbook of Bond Dissociation Energies in Organic Compounds*; CRC: Boca Raton, FL, 2003.
47. Itô, R.; Migita, T.; Morikawa, N.; Simamura, O. *Tetrahedron* **1965**, *21*, 955–961.
48. Pyror, W. A.; Echols, J. T.; Smith, K. *J. Am. Chem. Soc.* **1966**, *88*, 1189–1199.
49. Scaiano, J. C.; Stewart, L. C. *J. Am. Chem. Soc.* **1983**, *105*, 3609–3614.
50. Levy, A.; Meyerstein, D.; Ottolenghi, M. *J. Phys. Chem.* **1973**, *77*, 3044–3047.
51. Kryger, R. G.; Lorand, J. P.; Stevens, N. R.; Herron, N. R. *J. Am. Chem. Soc.* **1977**, *99*, 7589–7600.
52. Dannley, R. l.; Gregg, E. C. *J. Am. Chem. Soc.* **1954**, *76*, 2997–3000.
53. Dickerman, S. C.; Vermont, G. B. *J. Am. Chem. Soc.* **1962**, *84*, 4150–4151.
54. Bonnier, J.-M.; Rinaudo, J.; Bouvier, C. *Bull. Soc. Chim. Fr.* **1967**, 4067–4069.
55. Dix, I.; Doll, C.; Hopf, H.; Jones, P. G. *Eur. J. Org. Chem.* **2002**, 2547–2556.
56. Abramovitch, R. A.; Shinkai, I. *J. Am. Chem. Soc.* **1974**, *96*, 5265–5267.
57. Ishikura, M.; Ohta, T.; Terashima, M. *Chem. Pharm. Bull.* **1985**, *33*, 4755–4763.
58. Malmberg, H.; Nilsson, M. *Tetrahedron* **1986**, *42*, 3981–3986.
59. Edwards, M. L.; Stemerick, D. M.; Sabol, J. S.; Diekema, K. A.; Dinerstein, R. J. *J. Med. Chem.* **1994**, *37*, 4357–4362.
60. Sledeski, Y. M.; McGarry, D. G.; Green, D. M.; Mason, H. J.; Becker, M. R.; Davis, R. S.; Ewing, W. R.; Dankulich, W. P.; Manetta, V. E.; Morris, R. L.; Spada, A. P.; Cheney, D. L.; Brown, K. D.; Colussi, D. J.; Chu, V.; Heran, C. L.; Morgan, S. R.; Bentley, R. G.; Leadley, R. J.; Maignan, S.; Guilloteau, J. P.; Dunwiddie, C. T.; Pauls, H. W. *J. Med. Chem.* **1999**, *42*, 3572–3587.
61. Boy, P.; Combellas, C.; Thiébault, A.; Amatore, C.; Jutland, A. *Tetrahedron Lett.* **1992**, *33*, 491–494.
62. Tingoli, M.; Tiecco, M.; Testaferri, L.; Andrenacci, R.; Balducci, R. *J. Org. Chem.* **1993**, *58*, 6097–6102.
63. Novak, I.; Ng, S.-C.; Mok, C.-Y.; Huang, H.-H.; Fang, J.; Wang, K. K.-T. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1771–1775.
64. Abbotto, A.; Bradamante, S.; Facchetti, A.; Pagani, G. A. *J. Org. Chem.* **1997**, *62*, 5755–5765.
65. Molina, P.; Lorenzo, A.; Aller, E. *Tetrahedron* **1992**, *48*, 4601–4616.
66. Rebstock, A.-S.; Mongin, F.; Trecourt, F.; Quequiner, G. *Org. Biomol. Chem.* **2003**, *1*, 3064–3068.
67. Mongin, F.; Mojovic, L.; Guillamet, B.; Trecourt, F.; Quequiner, G. *J. Org. Chem.* **2002**, *67*, 8991–8994.
68. Barros, A. I. R. N. A.; Silva, A. M. S. *Tetrahedron Lett.* **2003**, *44*, 5893–5896.
69. Nelson, J. T.; Davis, R. S. *Magn. Reson. Chem.* **1991**, *29*, 513–517.
70. Xu, Z.; Lu, X. *J. Org. Chem.* **1998**, *63*, 5031–5041.
71. Tachikawa, R.; Wachi, K.; Terada, A. *Heterocycles* **1981**, *16*, 1165–1168.
72. Holzapfel, C. W.; Williams, D. B. G. *Synth. Commun.* **1994**, *24*, 2139–2146.
73. Baret, P.; Beguin, C.; Gaude, D.; Gellon, G.; Mourral, C. *Tetrahedron* **1994**, *50*, 2077–2094.
74. Abramovitch, R. A.; Alvernhe, G.; Bartnik, R.; Dassanayake, N. L.; Inbasekara, M. N.; Kato, S. *J. Am. Chem. Soc.* **1981**, *103*, 4558–4565.
75. Xia, M.; Chen, Z. *Synth. Commun.* **2000**, *30*, 63–68.
76. Tao, B.; Goel, S. C.; Singh, J.; Boykin, D. W. *Synthesis* **2002**, 1043–1046.
77. Downie, I. M.; Heaney, H.; Kemp, G.; King, D.; Wosley, M. *Tetrahedron* **1992**, *48*, 4005–4016.
78. Takeuchi, H.; Taniguchi, T.; Ueda, T. *J. Chem. Soc., Perkin Trans. 2* **2000**, 295–300.
79. Rossiter, B. E.; Reese, S. L.; Morgan, S. R.; Malik, A.; Bradshaw, J. S.; Lee, M. L. *J. Microcolumn Sep.* **1992**, *4*, 521–527.
80. Haga, N.; Takayanagi, H. *J. Org. Chem.* **1996**, *61*, 735–745.