An Environmentally Friendly Synthesis of Functionalized Indanes Using Electrochemical Cyclization of *ortho*-Halo-Substituted Homoallyl Ethers and Esters

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Abstract: The electrochemical cyclization of a series of *ortho*-halo-substituted homoallyl ethers and esters to functionalized indanes catalyzed by Ni(II) catalyst precursors derived from Ni(cyclam)Br_2, (cyclam = 1,4,8,11-tetraazacyclotetradecane) and Ni(tmc)Br_2, (tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane) is reported. The starting homoallyl ethers were synthesized using either a one-pot method for allylation of aldehydes or by direct allylation of the corresponding acetals using bismuth triflate as a catalyst. The remarkably low toxicity, low cost and ease of handling of bismuth salts coupled with the mild nature of the electrochemical procedure makes this approach to indane synthesis especially environmentally friendly and attractive.

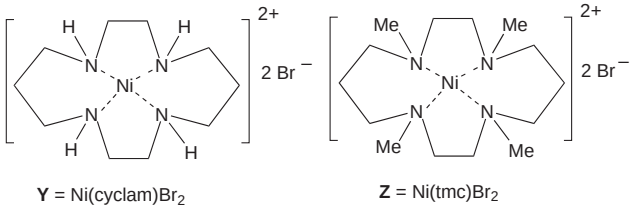
Key words: bismuth, electrochemical cyclization, homoallyl ethers, indanes, Ni(II) cyclam

Intramolecular radical-type cyclizations constitute an efficient method for the construction of carbocycles and heterocycles.[1] Generally, stoichiometric amounts of highly toxic tin hydrides are used for these cyclizations, with AIBN as an initiator.[2] Electrochemistry provides a milder alternative method for radical cyclization using catalytic amounts of metal complexes, in particular of Ni(II) derivatives.[3] The electrochemical synthesis of benzofuran and benzopyran structures have been reported via the cyclization of *ortho*-functionalized aryl halide substrates.[4] Indane-derived skeletons are found in several compounds possessing interesting biological[5] and olfactory activities.[6] We report here the use of a Ni-catalyzed electrochemical synthetic methodology for the construction of functionalized indane skeletons.

The general strategy for the preparation of the starting bromo- and chloroaryl derivatives **1a**–**i** took advantage of methodology previously developed using bismuth(III) catalysts.[7] Bismuth compounds are especially attractive because of their remarkably low toxicity, low cost and ease of handling.[8] The desired substrates were synthesized by one of the following methods (Scheme 1, Methods A–D).

In the first approach, the acetal was reacted with allyltrimethylsilane or methallyltrimethylsilane in the presence of $Bi(OTf)_3 \cdot xH_2O$ ($1 < x < 4$) to yield the homoallyl ether (Method A). In the second approach, the acetal was generated in situ from the corresponding aldehyde and reacted with allyltrimethylsilane in the presence of $Bi(OTf)_3 \cdot xH_2O$ (Method B). The third approach consisted of a one-pot method that involved the $Bi(OTf)_3 \cdot xH_2O$ catalyzed reaction of an aldehyde with an alkoxytrimethylsilane and allyltrimethylsilane (Method C). The *ortho*-halo-substituted homoallyl acetates were generated by a one-pot method in which the corresponding aldehyde was reacted with allyltrimethylsilane in the presence of acetic anhydride (Method D).

Electrochemical cyclization of **1a**–**i** was carried out under catalytic and mild conditions. Two stable and easily available Ni(II) catalyst precursors, Ni(cyclam)Br_2, **Y** (cyclam = 1,4,8,11-tetraazacyclotetradecane) and Ni(tmc)Br_2, **Z** (tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane)[9] were used in 10.0 mol% for cyclization of **1a**–**i** (Figure 1). The electrochemical synthesis was not efficient at less than 10% catalyst loading. These two complexes, which generate Ni(I) intermediates after a one-electron reduction,[10] have been shown to be efficient in reductive processes involving aryl halides.[11]



Y = Ni(cyclam)Br_2 **Z** = Ni(tmc)Br_2

Figure 1

A preliminary screening of the experimental conditions to determine the influence of the solvent, the supporting electrolyte, and the nature of the electrodes on product composition was carried out with substrate **1a**. The key findings are summarized in Table 1 (entries 1–5). The electroreduction of **1a**, conducted in DMF with tetrabutylammonium tetrafluoroborate as the supporting electro-

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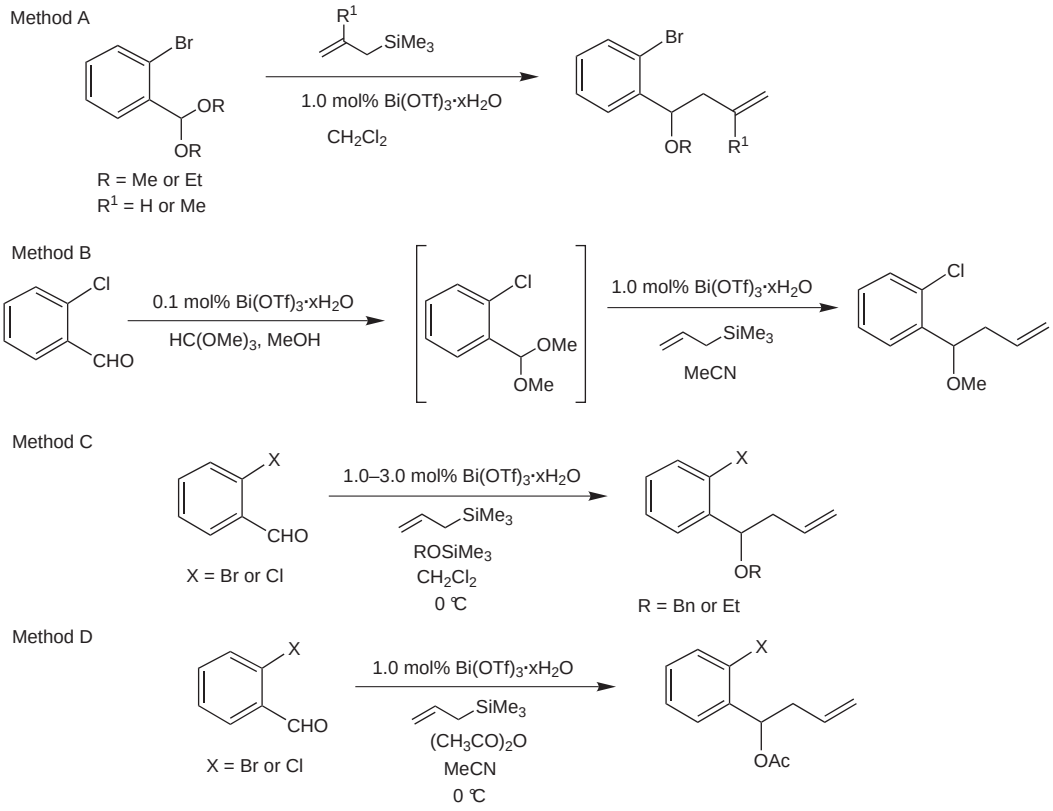
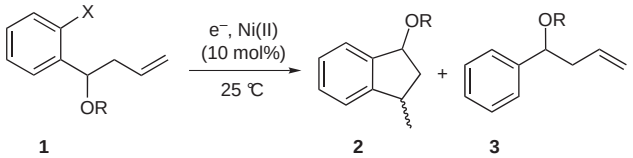


Scheme 1 Synthesis of the *ortho*-halo-substituted homoallyl ethers and esters

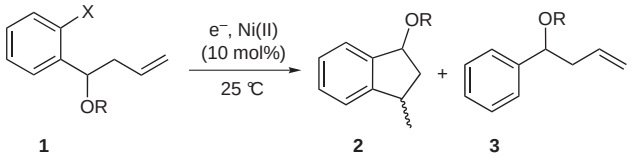
lyte, with a Mg anode and a carbon fiber cathode and catalyst **Y**, led to cyclized indane **2a** in 58% yield (entry 1), together with the dehalogenated compound **3a** (26%). No cyclization to the six-membered ring was observed. GC and NMR-COSY and NOESY experiments indicated that the indane **2a** was obtained as a 40:60 mixture of *syn*/*anti* isomers. Although the *syn*/*anti* mixtures were not fully separable by flash column chromatography, some enrichment of one isomer was seen in the isolated product after chromatography. When the electrolysis of **1a** was run in acetonitrile, the yield of **2a** was 48%, and in absolute ethanol, the cyclized **2a** was obtained in 55% yield (entries 2, 3). The use of potassium bromide instead of tetrabutylammonium tetrafluoroborate as the supporting electrolyte afforded the cyclized product in 76% yield (entry 4). The catalytic activity of **Y** and **Z** was found to be similar for the cyclization of bromo derivative **1a** (entries 4, 5). The cyclization of **1b**–**h** with **Y** or **Z** as the catalyst under the best conditions (DMF, KBr, r.t.) led to the indane derivatives **2** as a mixture of *syn*/*anti* diastereomers, as shown in Table 1.

Table 1 Electroreductive Cyclization of Derivatives **1** in the Presence of Ni(II) Catalysts[a]



Entry	Starting compound[b]	Catalyst[c]	Conditions	Products[d]	
				2 (*syn*:*anti*)[e]	**3**
1	**1a** R = Et X = Br	**Y**	DMF *n*-Bu_4NBF_4	**2a** 58% (40:60)	**3a** 26%
2	**1a**	**Y**	CH_3CN *n*-Bu_4NBF_4	**2a** 48% (44:56)	**3a** 50%

Table 1 Electroreductive Cyclization of Derivatives **1** in the Presence of Ni(II) Catalysts[a] (continued)



1 **2** **3**

Entry	Starting compound[b]	Catalyst[c]	Conditions	Products[d]	
				2 (*syn*:*anti*)[e]	**3**
3	**1a**	**Y**	EtOH *n*-Bu_4NBF_4	**2a** 55% (47:53)	**3a** 15%
4	**1a**	**Y**	DMF KBr	**2a** 76% (41:59)	**3a** 9%
5	**1a**	**Z**	DMF KBr	**2a** 83% (45:55)	**3a** 17%
6	**1b** R = Me X = Br	**Z**	DMF KBr	**2b** 73% (48:52)	**3b** 22%
7	**1c** R = Ac X = Br	**Z**	DMF KBr	**2c** 70% (43:57)	**3c** 2%
8	**1d** R = Bn X = Br	**Z**	DMF KBr	**2d** 64% (44:56)	**3d** 22%
9	**1e** R = Et X = Cl	**Z**	DMF KBr	**2a** 65% (44:56)	**3a** 20%
10	**1e** R = Et X = Cl	**Y**	DMF KBr	**2a** 68% (37:63)	**3a** 14%
11	**1f** R = Me X = Cl	Y	DMF KBr	**2b** 58% (46:54)	**3b** 22%
12	**1g** R = Ac X = Cl	**Y**[f]	DMF KBr	**2c** 14% (47:53)	**3c** 12%
13	**1h** R = Bn X = Cl	**Y**[g]	DMF KBr	**2d** 47% (47:53)	**3d** 18%

[a] General electrolysis conditions: under an inert gas at r.t., in a single-compartment cell fitted with a consumable sacrificial anode (Mg) and a carbon fiber cathode, 2.0 mmol of **1** was added to 30 mL of solvent containing the supporting electrolyte (0.03 M; KBr or *n*-Bu_4NBF_4) and 0.2 mmol of Ni(II) catalyst (**Y** or **Z**). The electrolysis was carried out at a constant current of 30 mA (J = 0.15 A/dm^2). The reaction was stopped after complete consumption of **1** (1–3 F/mol), unless stated otherwise. After acidic hydrolysis and Et_2O extraction, the crude compounds were purified by column chromatography on silica gel, and characterized by NMR spectroscopy and mass spectrometry.

[b] The synthetic method used for preparation of the starting material along with the isolated yield and spectral data are given in ref.[19] Synthetic procedures for their preparation have been previously described (see ref. 7).

[c] **Y** = Ni(cyclam)Br_2 and **Z** = Ni(tmc)Br_2.

[d] All products **2a**–**i** were characterized by ^1H NMR and ^{13}C NMR spectroscopy. Stereoisomers were identified by NOESY. Satisfactory HRMS was obtained for all new compounds. Compounds **3a**–**c** have been previously reported.[16–18]

[e] Ratios of *syn*/*anti* isomers were obtained by GC analysis of the crude reaction mixture. Refers to isolated yield after flash chromatographic purification of the crude reaction product.

[f] The expected **2c** was partially deacetylated to 1-methylindane, formed in 29% yield.

[g] The starting material **1h** was recovered in 30% yield after 3.4 F/mol electrolysis.

The electroreduction of aryl-bromo derivatives **1b**–**d** carried out with catalyst **Z** in DMF led to 64–73% yields of the corresponding indanes **2b**–**d** with *syn*:*anti* ratios of ca. 45:55 (entries 6–8). When the electroreduction using catalyst **Z** was carried out in ethanol, double bond reduction and debromination were observed. Interestingly, the acetate group of **1c** and the benzyloxy substituent in **1d** were compatible with the reductive reaction conditions. Compound **1g** gave a lower yield presumably due to the difficulty of reducing a C–Cl bond compared to a C–Br bond. The increased activation required to reduce the C–Cl bond can lead to cleavage and/or reduction of the acetate group, accounting for the low observed yield. The best yield of **2a** from the cyclization of **1e** was 68% with a *syn*:*anti* ratio of 37:63. It is interesting to note that by using the electrochemical methodology the Ar–Cl bonds could be efficiently functionalized, which is not the case using the more classical tin hydride methodology. The latter typically works only with more activated C–Br and C–I bonds.[2] Other chloro-aryl derivatives **1f**–**h** underwent intramolecular cyclization with catalyst **Y** (entries 11–13) to afford the corresponding indanes **2** in 14–58% yields. Compound **1i**, prepared according to method A, was reductively electrolyzed to the indane structure **2i**, with both catalysts, **Y** and **Z**, as shown in Scheme 2. The yields were only moderate (35–36%); presumably the steric hindrance of the methallyl group makes the molecule less prone to cyclization. The major product **3i** arose from a protodehalogenation of the starting material.

In conclusion, the Ni-catalyzed reductive cyclization of *o*-but-3-enyl-functionalized aryl halides to the corresponding indane structures was carried out in moderate to good yields. The yields of cyclization of bromo derivatives were higher than those of chloro analogues, for which catalyst **Y** showed a better efficiency. The compatibility of the reaction with acetate and benzyloxy functional groups allows the further introduction of different functionalities in the molecules. The combination of non-toxic bismuth-based catalysts for the synthesis of the substrates and a subsequent mild electrochemical cyclization method makes this approach to the synthesis of indane skeletons particularly environmentally friendly and attractive.

Spectral Data

All spectra were recorded in $CDCl_3$. The diastereomeric ratios reported below refer to ratio obtained by NMR analysis after purification of the crude reaction product. The *syn*/*anti* isomers were not fully separable by flash chromatography. The ratio of *syn*/*anti* isomers in the crude product (determined by GC) is given in Table 1.

1-Ethoxy-3-methyl indane (2a)

Mixture of two diastereomers (ratio 70:30). The *syn*/*anti* assignments were determined by NOESY.

***syn* Isomer**: ^{1}H NMR (200 MHz): δ = 7.40–7.00 (m, 4 H), 4.85–4.70 (dd, *J* = 6.35, 2.25 Hz, 1 H), 3.60–3.40 (q, *J* = 7 Hz, 2 H), 3.50–3.25 (m, 1 H), 2.40–2.20 (ddd, *J* = 13.5, 7.2, 2.3 Hz, 1 H), 1.85–1.60 (ddd, *J* = 13.7, 7.6, 6.3 Hz, 1 H), 1.25–1.15 (d, *J* = 7.0 Hz, 3 H), 1.20–1.05 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (12 peaks): δ = 149.8, 142.8, 129.0, 126.7, 125.7, 124.1, 82.4, 64.2, 42.3, 37.4, 20.4. 16.0. MS (70 eV): *m/z* (%) = 176 (17) [M^+], 175 (22), 147 (38), 132 (44), 131 (100), 130 (60), 129 (41), 115 (40), 91 (62), 77 (26).

***anti* Isomer**: ^{1}H NMR (200 MHz): δ = 7.40–7.00 (m, 4 H), 4.90–4.75 (t, *J* = 7 Hz, 1 H), 3.70–3.50 (m, 2 H), 3.10–2.85 (m, 1 H), 2.70–2.50 (dt, *J* = 12.5, 7.1 Hz, 1 H), 1.60–1.40 (ddd, *J* = 12.5, 8.2, 7.1 Hz, 1 H), 1.35–1.20 (d, *J* = 6.9 Hz, 3 H), 1.25–1.15 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (12 peaks): δ = 148.0, 143.7, 128.4, 127.0, 124.7, 123.7, 82.3, 64.8, 42.4, 37.0, 20.9, 16.1. MS (70 eV): *m/z* (%) = 176 (8) [M^+], 175 (15), 147 (24), 132 (34), 131 (100), 130 (71), 129 (40), 115 (35), 91 (64), 77 (20).

COSY (500 MHz) of **2a** (70:30): expected correlations were obtained for both *syn* and *anti* isomers. NOESY (500 MHz) of **2a** (70:30): H_4 and H_2 strong NOESY effect for the *syn* isomer, no correlation H_4 and H_2 for the *anti* isomer.

HRCIMS of **2a**: *m/z* calcd for $C_{12}H_{17}O$: 177.1274; found: 177.1274 [M + H]$^+$.

1-Methoxy-3-methylindane (2b)

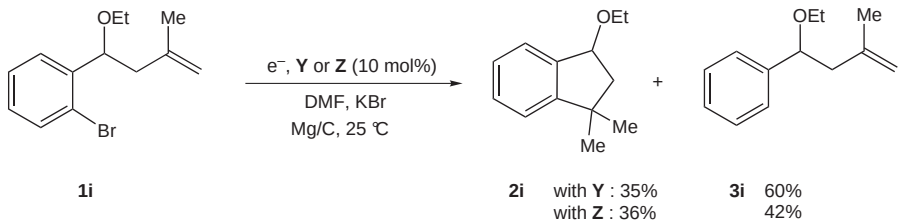
Mixture of two diastereomers (ratio: 64:36). The *syn*/*anti* assignments were made by comparison with literature spectra.[12]

***syn* Isomer**: ^{1}H NMR (200 MHz): δ = 7.40–7.00 (m, 4 H), 4.75–4.6 (dd, *J* = 6.2, 1.9 Hz, 1 H), 3.45–3.20 (m, 1 H), 3.35–3.20 (s, 3 H), 2.40–2.25 (ddd, *J* = 13.5, 7.1, 2 Hz, 1 H), 1.85–1.65 (ddd, *J* = 13.8, 7.8, 6.2 Hz, 1 H), 1.25–1.15 (d, *J* = 7.0 Hz, 3 H). ^{13}C NMR (11 peaks): δ = 149.9, 142.2, 129.2, 126.7, 125.7, 124.1, 83.8, 56.4, 41.9, 37.4, 20.3. MS (70 eV): *m/z* (%) = 162 (25) [M^+], 161 (51), 131 (100), 130 (91), 129 (65), 115 (67), 91 (77), 77 (30).

***anti* Isomer**: ^{1}H NMR (200 MHz): δ = 7.40–7.00 (m, 4 H), 4.80–4.65 (t, *J* = 6.8 Hz, 1 H), 3.45–3.35 (s, 3 H), 3.10–2.90 (six line multiplet, *J* = 6.8 Hz, 1 H), 2.75–2.50 (ddd, *J* = 13.0, 7.0, 6.8 Hz, 1 H), 1.60–1.40 (ddd, *J* = 13.0, 7.8, 6.7 Hz, 1 H), 1.35–1.25 (d, *J* = 6.9 Hz, 3 H). ^{13}C NMR (11 peaks): 149.9, 142.2, 128.6, 126.9, 124.8, 123.9, 83.9, 56.8, 41.5, 37.0, 21.0. MS (70 eV): *m/z* (%) = 162 (58) [M^+], 161 (87), 131 (100), 130 (85), 129 (65), 115 (66), 91 (81), 77 (30).

3-Methylindyl Acetate (2c)

Mixture of two diastereomers (ratio: 46:54). The *syn*[13]/*anti*[14] assignments were made by comparison with literature data.



1i **2i** with **Y** : 35% with **Z** : 36% **3i** 60% 42%

Scheme 2 Electrochemical cyclization of methallyl derivative **1i**

***syn* Isomer**: ^{1}H NMR (500 MHz): δ = 7.45–7.40 (d, *J* = 7.6 Hz, 1 H), 7.40–7.20 (m, 3 H), 6.20–6.15 (dd, *J* = 6.6, 2.0 Hz, 1 H), 3.50–3.40 (six line multiplet, *J* = ca. 7.1 Hz, 1 H), 2.40–2.30 (ddd, *J* = 14.0, 7.2, 2.1 Hz, 1 H), 2.05–2.00 (s, 3 H), 2.05–1.90 (ddd, *J* = 14.1, 7.3, 6.7 Hz, 1 H), 1.35–1.25 (d, *J* = 7.0 Hz, 3 H). ^{13}C NMR (12 peaks): δ = 171.5, 150.2, 141.1, 129.7, 127.2, 126.3, 123.9, 77.8, 42.0, 37.4, 21.8, 20.2. MS (70 eV): *m/z* (%) = 190 (1) [M$^+$], 148 (25), 131 (50), 130 (100), 129 (50), 115 (60), 91 (46), 77 (41).

***anti* Isomer**: ^{1}H NMR (500 MHz): δ = 7.40–7.20 (m, 4 H), 6.20–6.10 (t, *J* = 6.6 Hz, 1 H), 3.20–3.10 (ca. six line multiplet, *J* = 7.0 Hz, 1 H), 2.85–2.75 (dt, *J* = 13.4, 7.45 Hz, 1 H), 2.15–2.05 (s, 3 H), 1.70–1.60 (ddd, *J* = 13.1, 6.8, 6.1 Hz, 1 H), 1.40–1.30 (d, *J* = 6.9 Hz, 3 H). ^{13}C NMR (12 peaks): δ = 171.6, 148.8, 141.2, 129.2, 127.3, 125.2, 124.0, 77.6, 41.7, 37.4, 21.4, 20.2. MS (70 eV): *m/z* (%) = 190 (0) [M$^+$], 131 (38), 130 (100), 129 (43), 115 (46), 91 (33), 77 (30).

1-Benzyloxy-3-methylindane (2d)

Mixture of two diastereomers (ratio: 55/45). The *syn*/*anti* assignments were made by comparison with spectrum of **2a**.

***syn* Isomer**: ^{1}H NMR (200 MHz): δ = 7.40–6.90 (m, 4 H and 5 H), 4.95–4.80 (m, 1 H), 4.55–4.45 (s, 2 H), 3.50–3.25 (m, 1 H), 2.45–2.25 (ddd, *J* = 13.5, 7.2, 2.2 Hz, 1 H), 1.85–1.60 (ddd, *J* = 13.7, 7.6, 6.3 Hz, 1 H), 1.25–1.15 (d, *J* = 7.0 Hz, 3 H). ^{13}C NMR (15 peaks): δ = 149.9, 142.6, 139.3, 129.2, 128.8, 128.1, 127.9, 126.8, 125.8, 124.2, 81.8, 70.8, 42.2, 37.5, 20.5. MS (70 eV): *m/z* (%) = 238 (0) [M$^+$], 147 (50), 131 (30), 115 (14), 105 (21), 92 (40), 91 (100), 77 (34), 65 (26).

***anti* Isomer**: ^{1}H NMR (200 MHz): δ = 7.40–6.90 (m, 4 H and 5 H), 4.95–4.8 (m, 1 H), 4.70–4.50 (2 d, *J* = 11.9 Hz, 2 H), 3.10–2.85 (m, 1 H), 2.70–2.45 (dt, *J* = 12.6, 7.1 Hz, 1 H), 1.65–1.45 (ddd, *J* = 12.6, 8.0, 7.0 Hz, 1 H), 1.35–1.20 (d, *J* = 6.9 Hz, 3 H). ^{13}C NMR (15 peaks): δ = 148.1, 143.5, 139.3, 128.8, 128.6, 128.1, 127.9, 127.0, 124.9, 123.8, 81.9, 71.3, 42.3, 37.1, 21.0. MS (70 eV): *m/z* (%) = 238 (0) [M$^+$], 147 (50), 131 (30), 115 (14), 105 (21), 92 (40), 91 (100), 77 (34), 65 (26). HRMS: *m/z* calcd for $C_{17}H_{18}ONa$: 261.1259; found: 261.1263 [M + Na]$^+$.

1-Ethyloxy-3,3-dimethylindane (2i)

^{1}H NMR (200 MHz): δ = 7.42–7.15 (m, 4 H), 4.92 (dd, *J* = 6.7, 5.3 Hz, 1 H), 3.77–3.59 (m, 2 H), 2.30–2.19 (dd, *J* = 13.0, 6.7 Hz, 1 H), 1.98–1.89 (dd, *J* = 12.9, 5.3 Hz, 1 H), 1.21–1.29 (m, 3 H), 1.23 (s, 6 H). ^{13}C NMR (13 peaks): δ = 152.2, 141.9, 128.5, 125.3, 124.9, 122.3, 81.2, 64.3, 48.3, 42.4, 30.1, 29.8, 15.8. MS (70 eV): *m/z* (%) = 190 (22) [M$^+$], 188 (21), 175 (11), 161 (17), 146 (53), 145 (100), 131 (75), 129 (50), 128 (32), 105 (10), 91 (27), 77 (18). HRMS: *m/z* calcd for $C_{13}H_{18}O$: 190.1353; found: 190.1351 [M$^+$].

(1-Ethoxy-3-methyl)but-3-enylbenzene (3i)

^{1}H NMR (500 MHz): δ = 7.35–7.23 (m, 5 H), 4.76 (br s, 1 H), 4.69 (br s, 1 H), 4.38 (dd, *J* = 8.0, 5.3 Hz, 1 H), 3.37 (dq, *J* = 7.3, 6.8 Hz, 1 H), 3.32 (dq, *J* = 7.3, 6.8 Hz, 1 H), 2.54 (dd, *J* = 14.4, 8.0 Hz, 1 H), 2.29 (dd, *J* = 14.4, 5.3 Hz, 1 H), 1.72 (s, 3 H), 1.16 (dd, *J* = 7.3, 6.8 Hz, 3 H). ^{13}C NMR (11 peaks): δ = 142.8, 142.6, 128.7, 127.4, 126.6, 112.4, 80.9, 64.1, 46.6, 29.9, 15.3. MS: *m/z* (%) = 190 (0) [M$^+$], 134 (8), 107 (59), 106 (33), 91 (8), 70 (100), 77 (61).

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References and Notes

(1) (a) Giese, B. In *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon Press: Oxford, **1986**. (b) Stork, G. In *Radical-Mediated Cyclization Processes – A Goal for Synthetic Efficiency*; Bartmann, W.; Trost, B. M., Eds.; Verlag Chemie: Basel, **1984**.

(2) (a) Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P. *Tetrahedron* **2004**, *60*, 6239. (b) Davies, A. G. *Organotin Chemistry*, 2nd ed.; Wiley and Sons: London, **2004**.

(3) Duñach, E.; Franco, D.; Olivero, S. *Eur. J. Org. Chem.* **2003**, 1605.

(4) Olivero, S.; Rolland, J.-P.; Duñach, E. *Organometallics* **1998**, *17*, 3747.

(5) (a) Hong, B.-C.; Sarshar, S. *Org. Prep. Proced. Int.* **1999**, *1*, 1. (b) Wickens, P.; Cantin, L.-D.; Chuang, C.-Y.; Dai, M.; Hentemann, M. F.; Kumarasinghe, E.; Liang, S. X.; Lowe, D. B.; Shelekhin, T. E.; Wang, Y.; Zhang, C.; Zhang, H.-J.; Zhao, Q. PCT Int. Appl., WO 2004011446, **2004**. (c) Sekiguchi, T.; Nakagawa, S.; Fujikura, Y. JP 03044337, **1991**. (d) Meakins, S. E.; Motion, K. R. Eur. Pat. Appl., EP 393742, **1990**. (e) Frank, W. C. USA, US 93-79008, **1994**. (f) Ohnuma, H.; Fujikura, Y.; Fujita, M.; Toi, N. Eur. Pat. Appl., EP 385497, **1990**. (g) Sprecker, M. A.; Weiss, R. A.; Belko, R. P.; Molner, E. A. USA, US 6342612, **2002**.

(6) (a) Wickens, P.; Cantin, L.-D.; Chuang, C.-Y.; Dai, M.; Hentemann, M. F.; Kumarasinghe, E.; Liang, S. X.; Lowe, D. B.; Shelekhin, T. E.; Wang, Y.; Zhang, C.; Zhang, H.-J.; Zhao, Q. PCT Int. Appl., WO 2004011446, **2004**. (b) Sekiguchi, T.; Nakagawa, S.; Fujikura, Y. JP 03044337, **1991**. (c) Meakins, S. E.; Motion, K. R. Eur. Pat. Appl., EP 393742, **1990**. (d) Frank, W. C. USA, US 93-79008, **1994**.

(7) Anzalone, P. W.; Baru, A. R.; Danielson, E. M.; Hayes, P. D.; Nguyen, M. P.; Panico, A. F.; Smith, R. C.; Mohan, R. S. *J. Org. Chem.* **2005**, *70*, 2091.

(8) (a) Reglinski, J. In *Chemistry of Arsenic, Antimony and Bismuth*; Norman, N. C., Ed.; Blackie Academic and Professional: New York, **1998**, 403–440. (b) *Organobismuth Chemistry*; Suzuki, H.; Matano, Y., Eds.; Elsevier: Amsterdam, **2001**. (c) Leonard, N. M.; Wieland, L. C.; Mohan, R. S. *Tetrahedron* **2002**, *58*, 8373. (d) Antoniotti, S. *Synlett* **2003**, 1566. (e) Gaspard-Iloughmane, H.; Le Roux, C. *Eur. J. Org. Chem.* **2004**, 2517.

(9) Bosnich, B.; Tobe, M. L.; Webb, G. A. *Inorg. Chem.* **1965**, *4*, 1109.

(10) Gosden, C.; Healy, K. P.; Pletcher, D. *J. Chem. Soc., Dalton Trans.* **1978**, *8*, 972.

(11) Duñach, E.; Esteves, A. P.; Medeiros, M. J.; Olivero, S. *New J. Chem.* **2005**, *4*, 633.

(12) Armstrong, D. W.; Gahm, K. H.; Chang, L. W. *Microchem. J.* **1997**, *57*, 149.

(13) Izumi, T.; Murakami, S. *J. Chem. Technol. Biotechnol.* **1994**, *60*, 23.

(14) Miura, M.; Yoshida, M.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Perkin Trans. 1* **1982**, *1*, 79.

(15) Yadav, J. S.; Subba Reddy, V. B.; Srihari, P. *Synlett* **2001**, 673.

(16) Watahiki, T.; Akabane, Y.; Mori, S.; Oriyama, T. *Org. Lett.* **2003**, *5*, 3045.

(17) Hosomi, A.; Masahiko, E.; Sakurai, H. *Chem. Lett.* **1976**, 941.

(18) Aggarwal, V. K.; Vennall, G. P. *Synthesis* **1998**, 1822.

(19) (a) Compound **1a** (Method A, 76%): ^{1}H NMR: δ = 1.79 (t, 3 H, *J* = 7.2 Hz), 2.42–2.46 (m, 2 H), 3.35–3.39 (m, 2 H), 4.72–4.73 (m, 1 H), 5.01–5.10 (m, 2 H), 5.83–5.89 (m, 1 H), 7.25–7.52 (m, 4 H). ^{13}C NMR (12 peaks): δ = 14.8, 40.7, 64.1, 79.4, 116.4, 122.5, 127.1, 127.2, 128.2, 132.1, 134.2,

141.1. HRMS: *m/e* calcd for $C_{12}H_{15}BrO$: 254.0306 [M]; found: 253.0231 [M – 1]. (b) Compound **1b** (Method A, 88%): ^{1}H NMR: δ = 2.45 (m, 2 H), 3.24 (s, 3 H), 4.65 (dd, 1 H), 5.07 (m, 2 H), 5.85 (dp, 1 H), 7.42 (m, 4 H). ^{13}C NMR (11 peaks): δ = 41.0, 50.9, 81.7, 117.0, 123.1, 127.5, 127.6, 128.8, 132.6, 134.4, 140.7. HRMS: *m/e* calcd for $C_{11}H_{13}BrO$: 240.0150 [M]; found: 239.0066 [M – 1]. (c) Compound **1c** (Method D, 27%): ^{1}H NMR: δ = 2.09 (s, 3 H), 2.55–2.60 (m, 2 H), 5.04–5.10 (t, 2 H, *J* = 6.43 Hz), 5.72–5.78 (m, 1 H), 6.12–6.15 (dd, 1 H, *J* = 7.67, 2.73 Hz), 7.09–7.54 (m, 4 H). ^{13}C NMR (12 peaks): δ = 21.0, 39.5, 73.8, 118.1, 122.0, 127.2, 127.4, 129.0, 132.7, 132.9, 139.6, 169.7. HRMS: *m/e* calcd for $C_{12}H_{13}BrO_2$: 268.0099 [M]; found: 268.0098 [M – 1]. (d) Compound **1d** (Method C, 27%): ^{1}H NMR: δ = 2.48 (t, 2 H, *J* = 6.9 Hz), 4.28–4.48 (dd, 2 H), 4.86 (t, 1 H, *J* = 6.18 Hz), 5.02–5.10 (m, 2 H), 5.81–5.94 (m, 1 H), 7.12–7.55 (m, 9 H). ^{13}C NMR (15 peaks): δ = 41.2, 70.9, 79.6, 117.1, 123.1, 127.6, 127.7 (2 peaks), 127.9, 128.3, 128.9, 132.7, 134.5, 138.2, 141.0. HRMS: *m/e* calcd for $C_{17}H_{17}BrO$: 316.0463 [M]; found: 315.0381 [M – 1]. (e) Compound **1e** (Method C, 77%): ^{1}H NMR: δ = 1.18 (t, 3 H, *J* = 7.18 Hz), 2.42–2.46 (m, 2 H), 3.36–3.39 (m, 2 H), 4.76–4.80 (m, 1 H), 5.00–5.10 (m, 2 H), 5.79–5.92 (m, 1 H), 7.16–7.50 (m, 4 H). ^{13}C NMR (12 peaks): δ = 14.7, 40.6, 64.1, 77.1, 116.3, 126.5, 126.9, 127.8, 128.8, 132.3, 134.2, 139.6. HRMS: *m/e* calcd for $C_{12}H_{15}ClO$: 210.0811 [M]; found: 209.0740 [M – 1]. (f) Compound **1f** (Method B, 81%): this compound has been reported previously.[15] The spectral data are given here. ^{1}H NMR: δ = 2.46 (m, 2 H), 3.22 (s, 3 H), 4.70 (dd, 1 H, *J* = 7.3, 4.9 Hz), 5.02 (m, 2 H), 5.86 (m, 1 H), 7.32 (m, 4 H). ^{13}C NMR: (11 peaks): δ = 40.9, 56.9, 79.4, 116.9, 126.9, 127.2, 128.3, 129.3, 132.8, 134.3, 139.1. (g) Compound **1g** (Method D, 33%): this compound has been reported previously.[15] The spectral data are given here. ^{1}H NMR: δ = 2.09 (s, 3 H), 2.54–2.62 (m, 2 H), 5.03–5.10 (t, 2 H, *J* = 6.18 Hz), 5.68–5.81 (m, 1 H), 6.18–6.23 (dd, 1 H, *J* = 7.7, 2.5 Hz), 7.19–7.41 (m, 4 H). ^{13}C NMR (12 peaks): δ = 20.9, 39.4, 71.6, 118.1, 126.8, 127.1, 128.7, 129.5, 132.0, 132.9, 137.9, 169.7. (h) Compound **1h** (Method C, 35%): ^{1}H NMR: δ = 2.50 (app t, 2 H), 4.38 (dd, 2 H), 4.91 (t, 1 H, *J* = 6.2 Hz), 5.02 (m, 1 H), 5.90 (dquar, 2 H), 7.30 (m, 9 H). ^{13}C NMR (15 peaks): δ = 41.1, 70.9, 77.2, 117.0, 127.0, 127.5, 127.6, 127.7, 128.3, 128.4, 129.3, 132.9, 134.4, 138.2, 139.4. HRMS: *m/e* calcd for $C_{17}H_{17}ClO$: 272.0968 [M]; found: 271.0894 [M – 1]. (i) Compound **1i** (Method A, 43%): ^{1}H NMR: δ = 1.18 (t, 3 H, *J* = 7.18 Hz), 1.84 (s, 3 H), 2.26–2.42 (m, 2 H), 3.32–3.42 (m, 2 H), 4.78–4.85 (m, 3 H), 7.08–7.52 (m, 4 H). ^{13}C (13 peaks): δ = 15.3, 22.9, 45.2, 64.6, 79.1, 112.4, 123.0, 127.6, 127.7, 128.6, 132.6, 142.1, 142.6. HRMS: *m/e* calcd for $C_{13}H_{17}BrO$: 268.0463 [M]; found: 267.0379 [M – 1].