by distillation of the residue in 50% yield (1.26 g, >98% isomeric purity). ^{1}H NMR δ 3.72 (s, 3 H). Exact mass for $C_6H_3D_7O_2$, calculated 121.1120, found 121.1092.

General Procedure for Intermolecular Isotope Effect Determination with PTAD. To 5-mL equimolar chloroform solutions of deuterated and hydrogenated *E* esters (ca. 10^{-2} M) was added solid PTAD at room temperature at the following three molar ratios: hydrogenated ester: deuterated ester:PTAD, 1:1:0.1, 1:1:0.2, and 1:1:0.4.

After completion of the reaction (decolorization of the red solutions) and removal of the solvent in high vacuum, the oily residues were recrystallized from *n*-hexane/$CHCl_3$. The isotope effects reported were taken as the average of three independent ^{1}H NMR integrations of the appropriate hydrogen peaks and were the same either before or after the recrystallization. Errors are standard deviations.

General Procedure for Intermolecular Isotope Effect Measurements with Singlet Oxygen. The photooxygenations were carried out in an NMR tube at −15 °C. An equimolar solution of the deuterated and hydrogenated esters (10^{-2} M) was dissolved in 1 mL of deuterated solvent. When the solvent was acetone-d_6, a 10^{-4} M solution of rose bengal was used, and in benzene-d_6 a 10^{-4} M solution of mesoporphyrin IX dimethyl ester was used as sensitizer. A tungsten–halogen lamp was used as the light source, with a filter solution to cut off wavelengths <400 nm (0.1 M $K_2Cr_2O_7$). The reaction was monitored three times during the reaction period (until 40–50% overall conversion of the reactant mixture), with ^{1}H NMR integration of the appropriate hydrogen peaks of the product allylic hydroperoxides. The isotope effects are an average of the three runs. Errors are standard deviations.

Acknowledgment. This work was supported by NSF Grant No. CHE89-11916 and NATO Grant No. 01230/88.

The Samarium Grignard Reaction. In Situ Formation and Reactions of Primary and Secondary Alkylsamarium(III) Reagents

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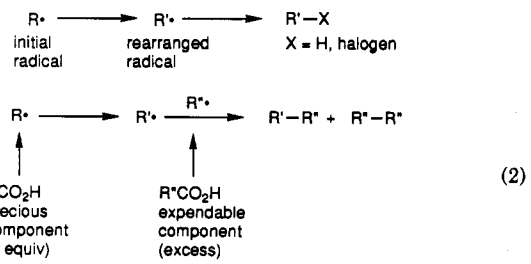
Contribution from the Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260. *Received November 27, 1991*

Abstract: This work shows that primary and secondary radicals are rapidly reduced in THF/HMPA to form primary- and secondary-alkylsamarium reagents. The primary- and secondary-radicals can be formed either by direct SmI_2 reduction of primary- and secondary-halides or by a previous rapid radical cyclization. The samarium reagents have moderate stability in solution, and they react with a variety of typical electrophiles, including aldehydes and ketones. The work further shows that organosamarium intermediates can be involved in the traditional samarium Barbier reaction of aldehydes and ketones conducted in THF/HMPA. A new procedure called the "samarium Grignard" method is introduced, and it is suggested that this new procedure will have considerably more scope and generality than the samarium Barbier reaction.

Introduction

One of the most attractive features of radical reactions in synthesis is the ability to conduct them in sequence.[2] Perhaps the most important step in any radical sequence is the final one, which must convert a radical to a nonradical.[2c] Radical reactions are usually terminated by functional group transformations like atom transfer (hydrogen, halogen, see eq 1), fragmentation (to an alkene), or oxidation (to an alkene or lactone). To increase the power of radical reactions, it would be desirable to terminate a single or tandem radical reaction with another carbon–carbon bond forming step. Becking and Schäfer have accomplished this by conducting mixed Kolbe oxidations of a "precious" carboxylic acid with an "expendable" one (eq 2).[3] An excess of the expendable component is used to maximize the yield of the cross-coupled product; however, large amounts of the dimer of the expendable component are also formed.



(2)

The statistical formation of coupled products is the normal result in radical/radical coupling reactions. However, selective, stoichiometric cross-couplings can be effected if one of the radicals is persistent.[4] Thus, we envisioned that a sequence of radical reactions might be terminated by selective cross-coupling with a ketyl (eq 3). To execute such a sequence, we were immediately attracted to the samarium Barbier reaction (eq 4).[5] This reaction was discovered by Kagan in 1980, and during the ensuing decade it has been developed into a powerful synthetic method.[6] Especially useful are Molander's intramolecular reactions, which

(1) Dreyfus Teacher-Scholar, 1986–1991. NIH Research Career Development Awardee, 1987–1992. ICI Pharmaceuticals Awardee, 1990.

(2) (a) Curran, D. P. *Synthesis* **1988**, 417 and 489. (b) Giese, B. Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds; Pergamon Press: Oxford, 1986. (c) Curran, D. P. *Comprehensive Organic Synthesis*; Trost, D. M., Fleming, I., Eds.; Pergamon: Vol. 4, in press.

(3) Becking, L.; Schäfer, H. J. *Tetrahedron Lett.* **1988**, *29*, 2797, and 2801.

(4) Fischer, H. *J. Am. Chem. Soc.* **1986**, *108*, 3925.

(5) (a) Kagan, H. B. *New J. Chem.* **1990**, *14*, 453. (b) Recent review: Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573. (c) For a detailed discussion of possible mechanisms and available evidence, see: Kagan, H. B.; Namy, J. L.; Girard, P. *Tetrahedron* **1981**, *37*, Suppl. 1, 175. (d) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. (e) Sasaki, M.; Collin, J.; Kagan, H. B. *Tetrahedron Lett.* **1988**, *29*, 6105. (f) Sasaki, M.; Collin, J.; Kagan, H. B. *Tetrahedron Lett.* **1988**, *29*, 4847. (g) Collin, J.; Dallemer, F.; Namy, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1989**, *30*, 7407. (h) Kagan, H. B.; Sasaki, M.; Collin, J. *Pure Appl. Chem.* **1988**, *60*, 1725. (i) Souppe, J.; Danon, L.; Namy, J. L.; Kagan, H. B. *J. Organomet. Chem.* **1983**, *250*, 227.

(6) (a) Review: Molander, G. A. *Chem. Rev.* **1992**, *92*, 29. (b) Review: Soderquist, J. A. *Aldrich. Acta* **1991**, *24*, 15. (c) Molander, G. A.; Etter, J. B. *Synth. Commun.* **1987**, *17*, 901. (d) Molander, G. A.; Etter, J. B.; Zinke, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 453. (e) Molander, G. A.; Etter, J. B. *J. Am. Chem. Soc.* **1987**, *109*, 6556. (f) Imamoto, T.; Takeyama, T.; Yokoyama, M. *Tetrahedron Lett.* **1984**, *25*, 3225. (g) Imamoto, T.; Takeyama, T.; Koto, H. *Tetrahedron Lett.* **1986**, *27*, 3243. (h) Gupta, A. K.; Cook, J. M.; Weiss, U. *Tetrahedron Lett.* **1988**, *29*, 2535. (i) Lannoye, G.; Cook, J. M. *Tetrahedron Lett.* **1988**, *29*, 171. (j) Zoretic, P.; Yu, B. C.; Caspar, M. L. *Synth. Commun.* **1989**, *19*, 1859. (k) Zhang, Y.; Liu, T.; Lin, R. *Synth. Commun.* **1988**, *18*, 2003. (l) Otsubo, K.; Kawamura, K.; Inanaga, J.; Yamaguchi, M. *Chem. Lett.* **1987**, 1487. (m) Moriya, T.; Handa, Y.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1988**, *29*, 6947. (n) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 1195. (o) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3891.

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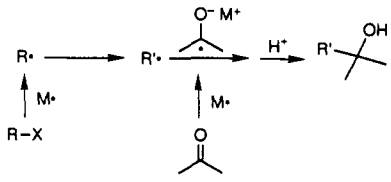
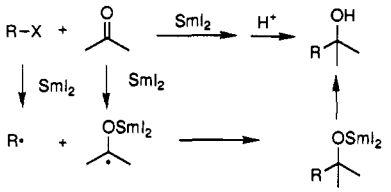
often proceed with exceptional stereocontrol.[6c-e] Although the mechanism of the samarium Barbier reaction is not well understood, it is certain that radicals are involved at some stage,[5c] and results have often been interpreted within the framework of a ketyl/radical coupling mechanism. In this mechanism (eq 4), halides are reduced to radicals, ketones are reduced to ketyls, and the ketyls and radicals couple.

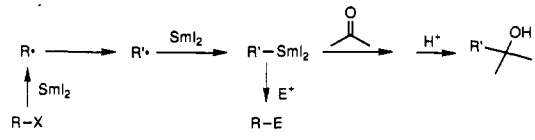


(3)



(4)

We were then attracted to the samarium Barbier reaction because we felt that a sequence of radical reactions might be terminated by coupling with a persistent samarium ketyl (eq 3, M = SmI_2).[7] Indeed, in his early mechanistic work, Kagan reported an example of precisely this transformation: reductive coupling of hexenyl bromide and 2-octanone gave both directly coupled and cyclized/coupled products in pure THF.[5c] However, in implementing this idea, we rapidly discovered that reductions of alkyl iodides by samarium(II) iodide in THF/HMPA produced alkyl samarium reagents (eq 5).[8] These samarium reagents then underwent standard 1,2-additions to aldehydes and ketones, effecting by a different mechanism the same transformation[9] that we had desired.

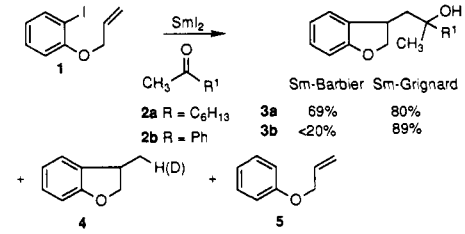


(5)

In their classic 1981 mechanism paper, Kagan, Namy, and Girard made a clear mechanistic distinction between "transient anions" and "alkylsamarium reagents".[5c] They cited evidence for the possible intermediacy of transient anions and against the intermediacy of alkylsamarium reagents in the reductions of alkyl radicals with SmI_2 in pure THF. Recently, both suggestions of and evidence for alkylsamarium intermediates have begun to accumulate.[8,10,11] When we initiated this work,[8a] there were no reports of reductive generation of alkylsamarium species with SmI_2,[12,13] so we decided to investigate in some detail the scope and limitations of this transformation. This paper describes the results of our preparative studies on the formation and reactions of alkylsamarium reagents in THF containing HMPA. These results also have mechanistic significance that potentially impacts much of the known chemistry of samarium(II) iodide. A separate paper will soon provide an expanded mechanistic discussion.[14] Finally, we now know that sequences of radical reactions conducted with samarium iodide cannot easily be terminated by ketyl/radical coupling. But they can be terminated by reduction to an organosamarium reagent, and this is considerably more versatile because a much wider variety of electrophiles can be introduced in the final trapping step.

Results and Discussion

Equation 6 summarizes the results of two preliminary experiments conducted under the standard conditions for the samarium Barbier reaction; one of these succeeded and the other failed. Addition of a THF solution of *O*-allyl-2-iodophenol (**1**) and 2-octanone (**2a**) to an 0.1 M THF solution of SmI_2 containing 5% HMPA[15] produced the cyclized/coupled product **3a** in 69% yield. Also formed were small amounts of the cyclized reduced product **4** (~10%) and the directly reduced product **5** (~3%). Similar addition of **1** and acetophenone (**2b**) to SmI_2 produced **3b** in very low yield (<20%) alongside **4**, **5**, and a number of other products (including 1-phenylethanol). The first reaction was very clean, but the second was not. Rationalizing these observations within the mechanistic framework of ketyl/radical coupling is not easy. The problem is that acetophenone is more easily reduced to a ketyl than 2-octanone,[16] so it should be a better partner in the samarium Barbier reaction. On the basis of the results of experiments like these, we began to question the occurrence of ketyl/radical coupling.



(6)

We next conducted a series of control experiments under what we now call the "samarium Grignard" conditions. Under these conditions, the iodide **1** in THF was first added to the 0.1 M solution of SmI_2 in THF/HMPA (just as one would first add an iodide to the magnesium in a Grignard reaction). After 5 min, neat 2-octanone or acetophenone was added. Starting with 2-octanone, we isolated **3a** in 80% yield, and starting with acetophenone, we isolated **3b** in 89% yield. Small amounts (<5%) of **4** and **5** again formed in both experiments. When a stoichiometric amount of SmI_2 (2 equiv) was used, the characteristic purple color faded to a cloudy yellow toward the end of the addition of the iodide **1**. Workup by quenching this reaction mixture with water instead of a ketone produced **4** and **5** in a ratio of 97/3. Quenching with D_2O prior to workup again provide **4** and **5** (97/3), but this time **4** was about 80% monodeuterated in the methyl position. Reduced product **5** contained <10% D label.

(7) A detailed kinetic analysis shows that such a coupling can occur in essentially quantitative yield if all the appropriate rate constants are in order. See: Walling, C. *J. Am. Chem. Soc.* **1988**, *110*, 6846.

(8) (a) Preliminary communication: Curran, D. P.; Fevig, T. L.; Totleben, M. J. *Synlett* **1990**, 773. (b) Concurrent with our preliminary communication, Molander and Harring reported some similar reactions that were conducted by the traditional samarium Barbier procedure. See: Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1990**, *55*, 6171.

(9) Earlier examples of sequences (1) radical cyclization, (2) reduction to an organometallic, and (3) electrophilic trapping, see: (a) Nugent, W. A.; RajanBabu, T. V. *J. Am. Chem. Soc.* **1988**, *110*, 8561. (b) Takai, K.; Nitta, K.; Fujimura, O.; Utimoto, K. *J. Org. Chem.* **1989**, *54*, 4732.

(10) (a) Molander, G. A.; Kenny, C. A. *J. Org. Chem.* **1991**, *56*, 1439. (b) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1991**, *56*, 4112. (c) Walborsky, H.; Topolski, M. *J. Org. Chem.* **1992**, *57*, 370. (d) Murakami, M.; Hayashi, M.; Ito, Y. *J. Org. Chem.* **1992**, *57*, 793.

(11) Two examples of deuterations were reported with a deuterium source *present in the medium during the reduction*, though the intermediacy of alkylsamarium reagents was not suggested in either report. (a) Inanaga, J.; Ishikawa, M.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485. (b) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236.

(12) Organosamarium intermediates have been formed with $SmCp_2^*$: (a) Collin, J.; Namy, J. L.; Bied, C.; Kagan, H. B. *Inorg. Chem. Acta* **1987**, *140*, 29. (b) Evans, W. J. *Polyhedron* **1987**, *5*, 803.

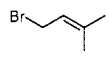
(13) There are isolated reports of generating "alkylsamarium dihalides" by metal–metal exchanges. Structures are now known. (a) BuLi/SmI_3: Kauffman, T.; Pahde, C.; Tannert, A.; Wingbermühle, D. *Tetrahedron Lett.* **1985**, *26*, 4063. (b) BuLi/$SmCl_3$: Ukaji, Y.; Yoshida, A.; Fujusawa, T. *Chem. Lett.* **1990**, 157.

(14) Curran, D. P.; Fevig, T.; Jasperse, C. M.; Totleben, M., submitted for publication.

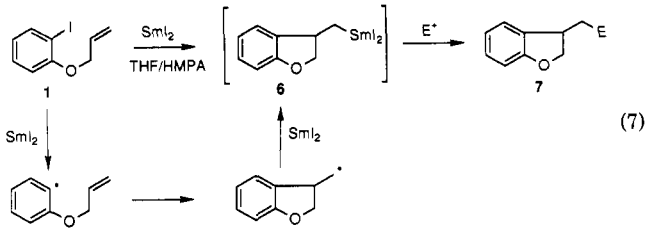
(15) HMPA dramatically accelerates rates of SmI_2 reductions: see ref 11a. For a discussion on the role of HMPA, see: Molander, G. A.; McKie, J. A., submitted for publication. We thank Professor Molander for a preprint of this paper.

(16) Meites, L. Polarographic Techniques, 2nd ed.; Wiley: New York, 1965; pp 671–711.

Table I. Successful Electrophilic Trapping of Samarium Reagent **6**

Entry	Electrophile	Product	Yield
a)	I_2	**7a** E = I	69%
b)	PhSSPh	**7b** E = SPh	65%
c)	PhSeSePh	**7c** E = SePh	72%
d)	Bu_3SnI	**7d** E = $SnBu_3$	82%
e)	PhNCO	**7e** R = NHPh	65%
f)	$(iPrCO)_2O$	**7f** R = i-Pr	55%
g)		**7g** R^1 = Me, R^2 = H **7g'** R^1 = H, R^2 = Me	39% (2/1)

These experiments were the first to show that electrophiles could be added after prereduction of a substrate by SmI_2,[11] and they were also among the first[8a,b,17] to show that SmI_2 could mediate aryl radical cyclizations. *Our observations demand the formation of an intermediate alkylsamarium species* **6** *in the samarium Grignard reaction of* **1** *in THF/HMPA (eq 7).* The formula **6** is written only for convenience; we have no structural information at this time. Alkylsamarium **6** must result from aryl radical cyclization followed by reduction of the ensuing alkyl radical. We can discard an alternative mechanism based on cyclization of an arylsamarium because we know that aryl radicals formed by reduction with SmI_2 abstract hydrogen from solvent faster than they are reduced to arylsamarium (see below).



(7)

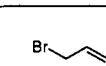
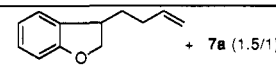
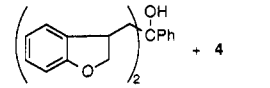
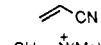
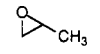
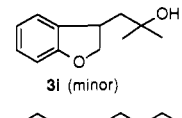
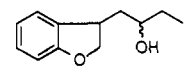
We surveyed the reactivity of the intermediate alkylsamarium species **6** by reacting it with a range of typical electrophiles, and the results of this series of experiments are summarized in Tables I and II. In each experiment, the samarium reagent **6** was generated by addition of iodide **1** to 2 equiv of SmI_2 in THF/HMPA at 25 °C (eq 7). After 5 min, the electrophile (neat or in THF) was added, and the reactions were quenched with 0.5 N HCl or saturated NH_4Cl, followed by standard extraction and chromatography to determine the yield of the trapped product **7**. Table I summarizes the results with electrophiles that gave normal trapping products **7** in moderate to good yields. As with the ketones, formation of small amounts of **4** was common, and we presume that **5** was also formed in trace amounts (although we did not attempt to isolate it). Table II summarizes the results with electrophiles that either gave coupled products in poor yields or did not give the expected products at all. Yields in these unsuccessful reactions were not usually determined, but Table II indicates the products that could be readily identified by comparison of the crude ^1H NMR spectra of these reactions with authentic samples.

The successful trappings in Table I require little comment. Useful electrophiles include the following: molecular iodine, diphenyl disulfide and diphenyl diselenide, tributyltin iodide, phenyl isocyanate, isobutyric anhydride, and prenyl bromide. Trapping with prenyl bromide (entry g) gave of 2/1 mixture of S_N2' to S_N2 regioisomers.

Toward the end of this survey, Ito and co-workers reported the formation and trapping of iminoylsamarium reagents by reduction

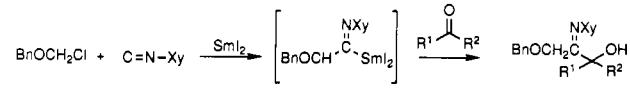
(17) A very recent paper shows that Sm-mediated cyclizations of aryl radicals have considerable potential. Inanaga, J.; Ujikawa, O.; Yamaguchi, M. *Tetrahedron Lett.* **1991**, *32*, 1737.

Table II. Unsuccessful Electrophilic Trapping of Samarium Reagent **6**

Entry	Electrophile	Product(s)
a)		 + **7a** (1.5/1) **7i**
b)	$PhCH_2Br$	$PhCH_2CH_2Ph$ + **7a**
c)	$BrCH_2CO_2Et$	**7a**
d)	$C_6H_{13}OTS$	**4** + unreacted $C_6H_{13}OTs$
e)	PhCOCl	 + **4**
f)	TMSCl	**4**
g)	TsCl	**4**
h)	Br_2 or NBS	**7a**
i)		**4**
j)	$CH_2{=}\overset{+}{N}(Me)_2I^-$	**4**
k)		 **3i** (minor)  **3j** (major)

of benzyl chloromethyl ether in the presence of xylyl isocyanide.[18] These intermediates were trapped by aldehydes and ketones, as indicated in eq 8. We repeated their procedure starting with iodide **1**, xylyl isocyanide, and acetophenone, and we obtained **8** in 67% yield. Three new C–C bonds form in this sequence of reactions.

We also conducted an experiment by first prereducing the iodide **1** with SmI_2, then adding xylyl isocyanide, and finally adding acetophenone. From this experiment, we isolated very pure **8** in 62% yield. Adduct **8** from either experiment was a 55/45 mixture of two isomers. We tentatively assign the imine geometry as *E*. The mechanism must involve addition of alkylsamarium reagent **6** to xylyl isocyanide to give the type of iminoylsamarium reagent proposed by Ito. Thus, we can add insertions into isocyanides to the list of potentially useful reactions of alkylsamarium reagents.



(8)

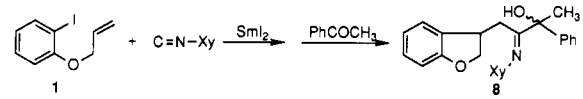


Table II shows unsuccessful electrophiles. These failures could have mechanistic significance. Reaction with allyl bromide produced some of the allylated product **7i** alongside the iodide **7a** (entry a). Indeed, iodide **7a** was the major product in the reactions of **6** with benzyl bromide, ethyl bromoacetate, molecular bromine, or NBS (entries b, c, and h). We speculated that **7a** arose by initial formation of bromide **7j**, followed by halogen exchange (eq 9). Control experiments indicated that alkyl bromides were converted to alkyl iodides under the reaction conditions.[19] However, SmI_3 alone did not convert primary-alkyl bromides to iodides at a rate fast enough to account for the

(18) (a) Murakami, M.; Kawano, T.; Ito, Y. *J. Am. Chem. Soc.* **1990**, *112*, 2437. (b) Kagan proposed related acylsamarium intermediates in reductions of acyl halides. Collin, J.; Namy, J. L.; Dallemer, F.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 3118.

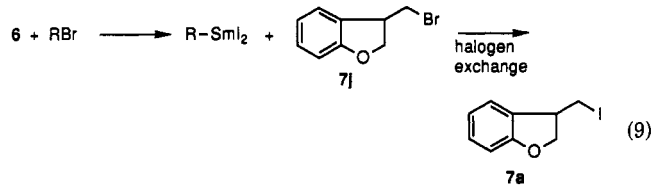
(19) (a) Control experiment: dodecyl bromide was added to 2 equiv SmI_2 as usual. After 5 min (SmI_2 consumed), octyl bromide was added and then benzyl bromide. After quenching, the two major products were dodecyl iodide and octyl iodide. Minor products included bibenzyl, recovered octyl bromide, and dodecane. (b) Kagan has observed the conversion of tosylates to iodides under similar conditions, see ref 5c,d.

Table III. Trapping with Aldehydes and Ketones

entry	2	3 Samarium Grignard[a] with **1**	3 Samarium Grignard[a] with **7a**	3 Samarium Barbier[b] with **1**
a	$R^1 = CH_3$, $R^2 = C_6H_{13}$	80% (54/46)[c]	nc[g]	68% (57/43)[c]
b	$R^1 = CH_3$, $R^2 = C_6H_5$	89% (56/44)[c]	95% (53/47)[c]	17% (55/45)[c]
c	$R^1 = H$, $R^2 = t\text{-}C_4H_9$	80% (53/47)[c]	nc[g]	69% (55/45)[c]
d	$R^1 = H$, $R^2 = C_5H_{11}$	65% (53/47)[c]	nc[g]	nd[f]
e	$R^1 = R^2 = CH_2CH_3$	83%[d]	nc[g]	nd[f]
f	$R^1 = H$, $R^2 = 4\text{-}MeOC_6H_4$	96% (50/50)[c]	94% (53/47)[c]	nd[f]
g	$R^1 = CH_3$, $R^2 = CH{=}CH_2$	74% (52/48)[c]	nc[g]	nd[f]
h	R^1,$R^2 = (CH_2CH_2)_2CH(t\text{-}Bu)$ (*tert*-butylcyclohexanone)	84% (88/12)[e]	80% (90/10)[e]	76% (84/16)[e]
i	$R^1 = R^2 = CH_3$	80%[d]	nc[g]	nc[g]
j	$R^1 = H$, $R^2 = C_2H_5$	70% (55/45)[c]	nc[g]	nc[g]

[a] Samarium Grignard: iodide added to SmI_2, and carbonyl added after 5 min. [b] Samarium Barbier: iodide and carbonyl are added together to SmI_2. Both methods use 0.1 M SmI_2 in 5% HMPA/THF at 25 °C. [c] Stereostructures not determined. [d] Diastereomers not possible. [e] Axial alcohol predominates. [f] nd = not determined, but <20%. [g] nc = not conducted.

observed exchange. The formation of bibenzyl in entry b is especially significant. The reductive coupling of benzyl halides by SmI_2 is well-known, and it is normally thought to occur by coupling of benzyl radicals.[20] However, the coupling of benzyl bromide to form bibenzyl (yield not determined) in our experiment must have been induced by alkylsamarium reagent **6**. No samarium(II) iodide remained when the benzyl bromide was added. This raises the possibility that reductive couplings of benzyl halides do not proceed through recombination reactions of benzyl radicals.

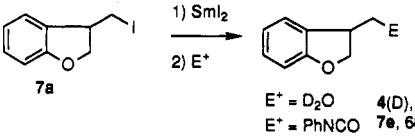


(9)

Reaction of **6** with propylene oxide (entry k) did not produce the products of direct epoxide opening but instead gave two rearranged adducts **3i** and **3j** in moderate isolated yield (43%). These adducts were identical to the adducts prepared by the samarium Grignard procedure with acetone and propanal (see Table III, entries i and j). Apparently, a Lewis acid in the medium (SmI_3?) catalyzes the rearrangement of propylene oxide to acetone and propanal.[21] Reaction of **6** with styrene oxide gave a very complex mixture that we did not analyze.

Reactions with alkyl toslyates failed (entry d), giving recovered tosylate and reduced product **4**. Similar failures were observed with Eschenmoser's salt (entry j) and Me_3SiCl (entry f). We also tried to prereduce Me_3SiCl with SmI_2, followed by addition of iodide **7a**. However, Me_3SiCl did not decolorize SmI_2, and none of the expected silylated derivative of **7** formed. Treatment of Bu_3SnI (or Bu_3SnCl) with SmI_2 did not decolorize the SmI_2 either, but addition of iodide **1** or **7a** then resulted in the formation of stannylated derivative **7d** (reduction of iodide **7a** should give the same samarium reagent as **1**). We believe that neither Me_3SiCl nor Bu_3SnI reacts with SmI_2 under these reactions conditions, and thus it does not matter in what order the reagents are added. In every case, alkylsamarium reagent **6** was formed. Apparently, **6** reacts with Bu_3SnI and Bu_3SnCl but does not react with Me_3SiCl.

That reductions of iodides **7a** and **1** give the same samarium reagent was also demonstrated by reducing **7a** with SmI_2, followed by treatment with D_2O or phenyl isocyanate. The expected trapping products formed, as eq 10 indicates. Reagent **6**, generated from **1** or **7a**, also behaved comparably in the reactions with ketones (see Table III below). The only difference was that no traces of **5** formed when we started with **7a**.



(10)

We also conducted a large number of addition reactions to aldehydes and ketones, and Table III summarizes the results of some of the most important experiments. We routinely conducted two types of experiments: (1) traditional "samarium Barbier" reactions and (2) "samarium Grignard" reactions. In the Barbier procedure,[22a] a THF solution of **1** and the aldehyde or ketone **2** was added to SmI_2 in THF/HMPA, while in the Grignard procedure,[22b] the samarium reagent **6** was preformed by addition of **1** or **7a** to SmI_2 in THF/HMPA, followed by addition of the aldehyde or ketone **2**. In all cases, the samarium Grignard procedure equalled or outperformed the traditional samarium Barbier procedure. With dialkyl ketones (entries a, e, and h), the samarium Grignard procedure was only marginally better than the samarium Barbier procedure; however, with more easily reducible carbonyls like alkyl or aryl aldehydes (entries d and f), or vinyl or aryl ketones (entries b and g), the samarium Grignard procedure was vastly superior. As expected, the samarium reagent adds exclusively 1,2 to methyl vinyl ketone (entry g). Samarium Barbier reactions with the easily reducible substrates were not clean, and common products included reduced carbonyls and pinacols. We usually did not determine yields of coupled products in these reactions, but we doubt that they ever exceeded 20% (see entry b).

In all cases, we obtained very similar results (yield, stereochemistry) in the samarium Grignard procedure whether we started with **1** or **7a**. This provides further evidence that **1** and **7a** generate the same alkylsamarium reagent. Not surprisingly, additions to acyclic aldehydes and ketones proceed with very low levels of stereoselectivity. Addition to *tert*-butylcyclohexanone gives a modest selectivity for equatorial attack (to generate the axial alcohol).[23] Most importantly, the level of stereoselectivity does not depend on the order of addition. Both samarium Grignard and samarium Barbier procedures give the same ratios of stereoisomers within experimental error (see additional examples in Table IV). This strongly suggests that the same intermediates are involved in both reactions. Since we know that organosamarium intermediates are involved in the samarium Grignard

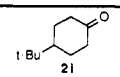
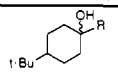
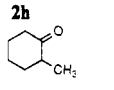
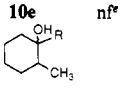
(20) Namy, J. L.; Girard, P.; Kagan, H. B. *Nouv. J. Chem.* **1977**, *1*, 5. See also ref 5c.

(21) Prandi, J.; Namy, J. L.; Menoret, G.; Kagan, H. B. *J. Organomet. Chem.* **1985**, *285*, 449.

(22) (a) Barbier, P. L. C. *C. R. Hebd. Secances Acad. Sci.* **1898**, *128*, 110. (b) Grignard, V. *Hebd. Seances Acad. Sci.* **1900**, *130*, 1322.

(23) Organoytterbium reagents "RM/Yb(OTf)$_3$" show exceptionally high levels of equatorial addition to cyclohexanones. Molander, G. A.; Burkhardt, E. R.; Weinig, P. *J. Org. Chem.* **1990**, *55*, 4990.

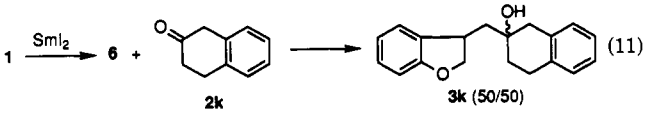
Table IV. Reactions of Iodides **9a–c** by Samarium Grignard and Samarium Barbier Procedures

entry	iodide	ketone	procedure	product	yield (ratio)[a]
	R–I Va	 2l			
1	**9a** R = CH_3	**2h**	Grignard	**10a**	nr (nr)[c]
2	**9a**	**2h**	Barbier	**10a**	64% (70/30)
3	**9b** R = Et	**2h**	Grignard	**10b**	nd[d] (63/37)
4	**9b**	**2h**	Barbier	**10b**	84% (54/46)
5	**9c** R = *i*-Pr	**2h**	Grignard	**10c**	nd[d]
6	**9c**	**2h**	Barbier	**10c**	62% (89/11)[b]
7	**9d** R = $(CH_2)_2Ph$	**2h**	Grignard	**10d**	81% (62/38)
8	**9d**	**2h**	Barbier	**10d**	84% (66/34)
9	**9e** R = *t*-Bu	**2h**	Grignard	**10e**	nf[e]
10	**9e**	**2h**	Barbier	**10e**	nf[e]
	R–I Vb				
11	**9d**	**2l**	Grignard	**11d**	88% (91/9)[b]
12	**9d**	**2l**	Barbier	**11d**	86% (93/7)[b]

[a] Ratio of equatorial to axial attack (axial alcohol to equatorial alcohol) by GC or ^{1}H NMR analysis of the crude reaction. [b] Weight ratio of isolated diastereomers. [c] nr = not reproducable. [d] nd = not determined. [e] nf = not formed.

reactions of **1** and **7**, we conclude that the same organosamarium intermediates are involved in the parallel samarium Barbier reactions. This conclusion squares nicely with the observations on yields as a function of order of addition. Best yields are obtained when the samarium reagent is pregenerated in the absence of the carbonyl component. With dialkyl ketones (which do not react rapidly with SmI_2), only slight yield enhancements are observed when the ketone is added last. But more readily reducible substrates (aldehydes, aryl ketones) compete with the iodide for SmI_2 in the samarium Barbier procedures. This both decreases the yield of samarium reagent that is formed and consumes the electrophile that reacts with it. Our results cannot be interpreted within the framework of the ketyl/radical coupling mechanisms for samarium Barbier reactions.

Organocerium reagents can be generated by cerium–lithium exchange, and they are often the reagents of choice for additions to enolizable carbonyl compounds.[24] By analogy to the cerium reagents, we investigated the addition of in situ generated samarium reagent **6** to β-tetralone (**2k**). We observed formation of the expected 1,2-adduct **3k**; however, the maximum isolated yield was only 28% (eq 11). The use of longer reaction times or lower temperatures did not increase the yield, and large amounts of unreacted β-tetralone were recovered from these experiments. To assay for enolization, we quenched one reaction with AcOD; however, the recovered β-tetralone contained no appreciable quantity of deuterium according to GC-MS analysis. Thus we conclude that the low yields cannot be attributed to proton transfer reactions between β-tetralone and **6**.



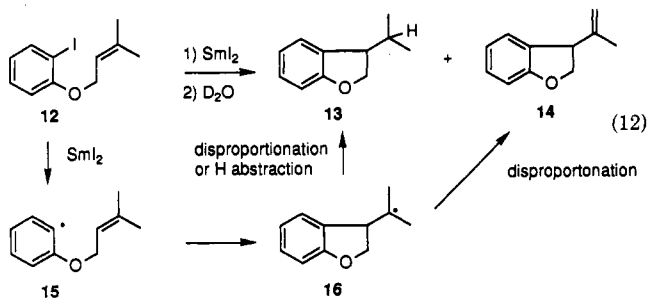
(11)

We progressed next to the study of additions of some simple iodides to substituted cyclohexanones. The initial results were disconcerting. Additions of methyl, ethyl, and isopropyl iodide (**9a–c**) to *tert*-butylcyclohexanone were conducted by both the samarium Grignard and the samarium Barbier procedures. Table IV summarizes some results. Unlike the reactions with **1**, reactions with these simple iodides were significantly better when conducted by the standard samarium Barbier procedure (compare entries 1, 3, and 5 with 2, 4, and 6). The samarium Grignard reaction with methyl iodide was not reproducible, and the reactions with ethyl and isopropyl iodide were reproducible, albeit poor yielding. However, phenethyl iodide (**9d**) was well behaved, giving high yields and similar selectivities when added to *tert*-butylcyclohexanone (to give **10d**) or 2-methylcyclohexanone (to give **11d**) by either the samarium Grignard or samarium Barbier procedure (entries 7, 8, 11, and 12). The same phenethylsamarium intermediate is implicated in both procedures.

We do not currently understand why samarium Grignard procedures with the three simplest iodides are so poor. However, our recent results indicate that these three iodides are the exceptions rather than the rule. We can efficiently generate samarium reagents by the samarium Grignard procedure from phenethyl iodide, dodecyl iodide,[25] octyl bromide,[25] and cyclohexyl iodide (see below). Within our current mechanistic framework, we can only speculate that samarium reagents are formed by the reduction of iodides **9a–c** by SmI_2 and that they add rapidly to ketones that are present in the reaction mixture. However, these reagents are rapidly consumed (by unknown pathways) if not immediately trapped. In the samarium Grignard procedure, they apparently do not survive the delay period between reduction and addition of the ketone.[26]

Reduction of *tert*-butyl iodide (**9e**) in the presence of *tert*-butylcyclohexanone led to no detectable amounts of adduct **11e** under either the samarium Barbier or samarium Grignard conditions (entries 9 and 10). *tert*-Butylcyclohexanone was recovered along with some *tert*-butylcyclohexanol. *tert*-Butylcyclohexanol recovered from such a reaction after quenching with AcOD did not contain a significant amount of deuterium. Further, addition of 1 equiv of *tert*-butyl iodide (**9e**) to 2 equiv of SmI_2 did not dissipate the deep purple color, despite the fact that tertiary iodides must be more readily reduced than aryl or primary iodides.

To decipher what types of products were being formed, we turned to the cyclizable system **12** (eq 12). Addition of **12** to SmI_2, followed by quenching with D_2O, formed a high yield of cyclized products **13** and **14** in a ratio of 60/40.[27] A GC-MS experiment indicated that **13** did not contain significant amounts of deuterium (<5%). Standard samarium Barbier reaction of **12** and 3-pentanone did not give significant amounts of the coupled product. We interpret these observations as a failure of SmI_2 to reduce a tertiary radical. The aryl radical **15** is generated, and it cyclizes normally to **16**. Radical **16** disproportionates to **13** and **14**, but it must also abstract a hydrogen atom[28] from THF or HMPA to account for the observation that **13** and **14** are not present in a 1/1 ratio. To the extent that disproportionation is important, only 1 equiv of SmI_2 is consumed. This nicely accounts for the failure of iodides **9e** and **12** to consume 2 equiv of SmI_2.



(12)

Given that Sm–C bonds are not very strong,[29a] it is perhaps not surprising that SmI_2 is reluctant to reduce a tertiary radical to a tertiary alkylsamarium.[29b] Thus, we were pleased to learn from preliminary experiments that secondary alkylsamarium reagents can be formed in these reductions (eq 13). Addition of

(24) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904.

(25) Totleben, M. J., unpublished observations.

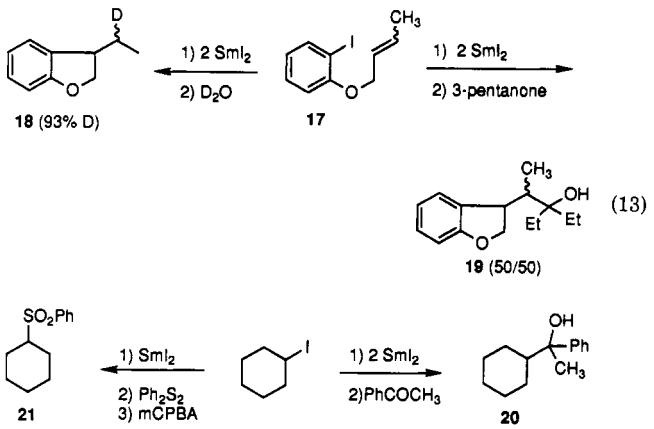
(26) Attempts to conduct reactions with **9a–c** by the samarium Grignard procedure at lower temperatures did not give improved results.

(27) A molecular ion attributed to the recombination product was also observed in the MS of the crude reaction mixture, though we could not isolate this product.

(28) H-abstraction from THF: Matsukawa, M.; Inawana, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 5877.

(29) (a) Nolan, S. P.; Stern, D.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 7844. (b) Electrochemical reduction potentials show increasing ease of reduction of tertiary < secondary < primary radicals; however, the difference in reduction potential between tertiary- and secondary-radicals is small. Andriewa, C. P.; Gallardo, I.; Savéant, J. M. *J. Am. Chem. Soc.* **1989**, *11*, 1620.

iodide **17** to SmI_2 followed by D_2O quench gave a high yield (80%) of **18**, which was 93% deuterium labeled. We did not detect the alkene expected from radical disproportionation; however, the purple color of SmI_2 again persisted at the end of this experiment when the ratio of **17**/SmI_2 was 1/2. Although some of the secondary-alkyl radicals may be lost to radical/radical reactions (thus leaving some unreacted SmI_2), the labeling indicates that most are reduced to secondary alkylsamarium reagents. A standard samarium Grignard reaction of **17** with 3-pentanone provided **19** in 72% yield. The samarium Grignard reaction of cyclohexyl iodide and acetophenone provided **20** in 90% yield. Reaction with diphenyl disulfide, followed by mCPBA oxidation and purification, gave sulfone **21** in 47% yield.



Conclusions

In this paper, we have described a relatively minor modification of existing experimental procedures for the samarium Barbier reaction. This modification, termed the samarium Grignard reaction, arose from simple control experiments in the study of a sequential radical cyclization and coupling to a carbonyl. The early trapping failures experienced by Kagan[5c] have probably discouraged others from attempting this obvious modification. The attribution of observations in the samarium Barbier reaction to ketyl/radical coupling mechanisms (which can only succeed if the carbonyl is added together with or before the halide) has also discouraged this modification. The results that we observed with this trivial experimental change permit important conclusions to be drawn.

(1) Reductions of most primary- and secondary-alkyl iodides by addition to 2 equiv of SmI_2 in THF/HMPA generate solution-stable organosamarium reagents with half-lives on the order of minutes to hours at room temperature.[30]

(2) These reagents react with a wide variety of electrophiles, including some that are certainly not stable to SmI_2 (I_2, PhSSPh, and PhSeSePh). Existing procedures in which all reactants are added together cannot succeed with these reactive electrophiles. Some typical electrophiles react with the alkylsamarium reagents in an unusual way to generate alkyl iodides. The samarium reagents add 1,2 to unsaturated carbonyls, but they currently show only limited potential to add to enolizable carbonyls. Recently, we have discovered that the samarium reagents can be transmetalated with copper, and the resulting reagents (samarium cuprates?) undergo 1,4-additions to enones.[31] This provides a method to effect conjugate additions of iodides and bromides without the intermediacy of lithium or magnesium reagents.

(3) The reduction of an iodide to an alkylsamarium reagent occurs in two stages: (i) reaction of an iodide with SmI_2 probably occurs by dissociative electron transfer[29b] to give a free alkyl radical and SmI_3. (ii) Primary and secondary-radicals are reduced by a second equivalent of SmI_2 to the alkylsamarium reagent. In THF/HMPA, these reductions are generally faster than couplings of radicals with small amounts of ketyls that may be present (in the samarium Barbier procedure). In contrast, tertiary radicals recombine, disproportionate, or abstract hydrogen from solvents faster than reduction to tertiary alkylsamarium reagents.

(4) Since free radicals are cleanly generated in reductions of iodides, SmI_2 is a potentially useful reagent for conducting radical cyclizations and other radical transformations.[8a,b,17,32] Radical reactions of primary- and secondary-alkyl radicals must compete with reduction by samarium(II), which is probably fast. However, this rate can be reduced by decreasing the concentration of samarium. Vinyl, aryl, and tertiary radicals should be excellent candidates for radical reactions since they are not efficiently reduced by samarium(II).[33] Sequences of radical and ionic carbon–carbon bond forming reactions can be conducted provided that the product radicals can be efficiently reduced to organosamarium reagents.

(5) The present work demonstrates that bimolecular samarium Barbier reactions conducted in THF/HMPA can occur by an organometallic addition mechanism involving alkylsamarium intermediates. Caution must still be exercised in generalizing this mechanistic conclusion to either intramolecular reactions or to bimolecular reactions conducted in the absence of HMPA. Molander and McKie have recently provided evidence that certain intramolecular samarium Barbier reactions proceed through organosamarium intermediates.[10a] Additional mechanistic evidence and an in-depth analysis of the bimolecular samarium Barbier reaction (with and without HMPA) will be the subject a forthcoming paper.[14]

(6) With most iodides and bromides, the traditional samarium Barbier procedure should often be replaced by a samarium Grignard procedure. The two procedures may be comparable when dialkyl ketones are used, but the samarium Grignard procedure will be significantly better if the carbonyl component exhibits any tendency to be reduced by SmI_2. Indeed, many classes of carbonyls only give acceptable yields by the samarium Grignard procedure. Exceptions to this generalization include some of the simplest iodides (**9a–c**), which misbehave in the samarium Grignard reaction for reasons that we understand only poorly. These simple iodides can be coupled with dialkyl ketones by the samarium Barbier procedure, but no samarium procedure currently exists to couple them with more easily reducible carbonyls. Because many methyl, ethyl, and isopropyl organometallic reagents are already available, this will not be a serious limitation.

Experimental Section

General Methods. All reactions were conducted under a nitrogen or argon atmosphere. Samarium powder (40 mesh, Aldrich) was used without further purification, and a 0.1 M solution of SmI_2 in THF was prepared as described in the literature.[34] THF was distilled from sodium/benzophenone under Ar. TMSCl and HMPA were distilled from CaH_2, and the HMPA was stored over 4 Å molecular sieves. 2-Nitrophenol, iodine, diphenyl disulfide, diphenyl diselenide, phenyl isocyanate, xylyl isocyanide, propylene oxide, NBS, bromine, and Eschenmoser's salt were used without further purification. All of the other electrophiles and halides were purified by the appropriate methods before use. NMR spectra were recorded at 300 MHz for ^1H and 75 MHz for ^{13}C.

***O*-Allyl-2-iodophenol (1).** Allyl bromide (1.6 mL, 18 mmol) was added neat to a solution of 2-iodophenol (3.3 g, 15 mol), anhydrous K_2CO_3 (6.2 g, 45 mmol), and DMF (50 mL). The reaction was stirred for 24 h at 25 °C, poured into water, and extracted with pentane (4×). The pentane extracts were combined and washed with H_2O (3×), 10% KOH (2×), 3% $Na_2S_2O_3$, and brine. The pentane layer was dried over $MgSO_4$, filtered, and concentrated. The product was purified by Kugelrohr distillation (bp = 91 °C, 0.1 mm) to give 3.85 g (99%) of a colorless oil: IR (neat) 3063, 2925, 2865, 1570, 1471, 1438, 1276, 1247, 1097, 1018, 996, 928, 748, 706 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.76 (d, J = 8 Hz, 1 H), 7.27 (t, J = 8 Hz, 1 H), 6.79 (d, J = 8 Hz, 1 H), 6.69 (t, J = 8 Hz, 1 H), 6.04 (m, 1 H), 5.51 (br d, J = 17 Hz, 1 H), 5.30 (br d, J = 10 Hz, 1 H), 4.58 (dd, J = 2, 5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 157.1, 139.5, 132.5, 129.4, 122.6, 117.6, 112.5, 69.6; MS (EI) m/e 260 (M^+, 100%), 220 (17%), 191 (10%), 133 (27%), 119 (13%), 105 (30%),

(30) If the samarium reagents are allowed to stand for 24 h prior to quenching with D_2O, the %D label decreases significantly (<40%).

(31) Totleben, M. J.; Curran, D. P.; Wipf, P. *J. Org. Chem.*, in press.

(32) Bennet, S. M.; Larouche, D. *Synlett* **1992**, 805.

(33) Reductions of aryl (ref 11a) and vinyl radicals by SmI_2 are slower than bimolecular hydrogen abstractions from solvents. Fevig, T. L.; Elliott, R. L.; Curran, D. P. *J. Am. Chem. Soc.* **1988**, *110*, 5064.

(34) Malinovsky, M. S.; Olifirenko, S. P. *Zh. Obsch. Khim.* **1956**, *26*, 118.

92 (32%), 64 (24%); HRMS (EI) m/e calculated for C_9H_9IO 259.9698, found 259.9698.

3-(Iodomethyl)-2,3-dihydrobenzofuran (7a). Compound **7a** was prepared by literature methods[35] from 2-nitrophenol. The product was purified by Kugelrohr distillation (bp = 95 °C, 0.1 mm): ^{1}H NMR ($CDCl_3$) δ 7.22–7.15 (m, 2 H), 6.87 (t, J = 7 Hz, 1 H), 6.79 (d, J = 8 Hz, 1 H), 4.63 (t, J = 9 Hz, 1 H), 4.32 (dd, J = 5, 9 Hz, 1 H), 3.83 (m, 1 H), 3.44 (dd, J = 4, 10 Hz, 1 H), 3.19 (t, J = 10 Hz, 1 H).

General Procedure for the SmI_2 Promoted Couplings of Halides with Electrophiles (Grigard Method). The halide (0.5 mmol) in dry THF (1.5 mL) was added over 1–2 min to a 0.1 M solution of SmI_2 in THF (11 mL) and HMPA (0.62 mL). After 5 min at 25 °C, the electrophile (0.5 mmol, neat or in 1.5 mL dry THF) was added, and the reaction was stirred at 25 °C for 30–40 min. The reaction was quenched with 0.5 N HCl or saturated NH_4Cl and extracted with pentane/ether (1:1). The organic extracts were combined and washed with H_2O (2×), 3% $Na_2S_2O_3$, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The crude products were purified by flash chromatography on silica in the designated solvents.

General Procedure for the SmI_2 Promoted Couplings of Halides with Electrophiles (Barbier Method). The halide (0.5 mmol) and the electrophile (0.5 mmol) in dry THF (1.5 mL) were added to a 0.1 M solution of SmI_2 in THF (11 mL) and HMPA (0.62 mL) over 1–2 min. The mixtures were stirred at room temperature for 30–40 min, then quenched, and worked up as above.

1-[3-(2*H*,3*H*-Benzofurfuryl)]-2-methyl-2-octanol (3a). Compound **3a** was prepared by the Grignard method with **1** and 2-octanone and was purified by flash chromatography in hexanes/EtOAc (4:1) to give 105 mg (80%) as a 54/46 mixture of diastereomers. Compound **3a** was prepared by the Barbier method, and the yield was 68% as a 57/43 mixture of diastereomers: IR (neat) 3473, 2956, 2931, 2870, 2857, 1597, 1481, 1460, 1375, 1162, 1016, 954, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.01 (m, 2 H), 6.84 (t, J = 7 Hz, 1 H), 6.76 (d, J = 8 Hz, 1 H); 4.77 and 4.76 (2t, J = 9 Hz, 1 H), 4.24 and 4.23 (2t, J = 9 Hz, 1 H), 3.65 (m, 1 H), 2.01 (m, 1 H), 1.76 (m, 1 H), 1.60–1.30 (m, 10 H), 1.24 and 1.21 (2s, 3 H), 1.16 and 1.10 (2s, 1 H), 0.81 (br t, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.6 (2 C), 131.4 (2 C), 128.0 (2 C), 123.9 (2 C), 123.9, 123.8, 109.4 (2 C), 78.6 (2 C), 72.6, 72.5, 46.8, 46.5, 43.8, 42.1, 38.1, 37.9, 31.8 (2 C), 29.8 (2 C), 27.9, 26.5, 24.2, 23.9, 22.6 (2 C), 14.1 (2 C); MS (EI) m/e 262 (M$^+$, 16%), 244 (M – H_2O, 15%), 231 (29%), 177 (14%), 159 (99%), 119 (100%), 91 (60%), 69 (16%); HRMS (EI) m/e calculated for $C_{17}H_{26}O_2$ 262.1933, found 262.1933.

1-[3-(2*H*,3*H*-Benzofurfuryl)]-2-phenyl-2-propanol (3b). Compound **3b** was prepared by the Grignard method with **1** and acetophenone and was purified by flash chromatography in hexanes/EtOAc (4:1) and then Kugelrohr distillation (50 °C, 0.2 mm) to remove remaining acetophenone. The yield of product was 113 mg (89%) as a 56/44 mixture of diastereomers. Compound **3b** was prepared by the Grignard method with **7a**, and the yield was 95% as a 53/47 mixture of diastereomers. Compound **3b** was prepared by the Barbier method, and the yield was 17% as a 55/45 mixture of diasteromers: IR (neat) 3481, 3028, 2974, 2931, 2890, 1598, 1493, 1482, 1460, 1229, 1162, 1017, 955, 764, 752, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.45 (m, 2 H), 7.35 (m, 2 H), 7.30–6.65 (m, 5 H), 4.62 and 4.23 (2t, J = 9 Hz, 1 H), 4.15 and 3.72 (2m, 1 H) 3.63 and 3.22 (m, 1 H), 2.37 (br t, J = 14 Hz, 1 H), 2.07 (dd, J = 11, 14 Hz, 1 H), 1.68 and 1.60 (2s, 1 H), 1.66 and 1.64 (2s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.5 (2 C), 147.5, 146.9, 131.1 (2 C), 128.4, 127.9 (2 C), 127.0, 126.8, 124.7 (2 C), 123.9, 126.6, 120.3, 120.2, 109.3 (2 C), 78.3, 77.7, 74.8, 74.0, 49.8, 49.2, 38.3, 37.9, 31.6, 30.5; MS (EI) m/e 254 (M$^+$, 14%), 236 (M – H_2O, 20%), 223 (32%), 118 (33%), 91 (40%); HRMS (EI) m/e calculated for $C_{17}H_{18}O_2$ 254.1307, found 254.1307.

1-[3-(2*H*,3*H*-Benzofurfuryl]-3,3-dimethyl-2-butanol (3c). Compound **3c** was prepared by the Grignard method with **1** and pivaldehyde and was purified by flash chromatography in hexanes/EtOAc (4:1) to give 88 mg (80%) as a 53/47 mixture of diastereomers. Compound **3c** was prepared by the Barbier method with **1**, and the yield was 76 mg (69%) as a 55/45 mixture of diastereomers: IR (neat) 3481, 2954, 2870, 1596, 1481, 1460, 1364, 1230, 1075, 1005, 967, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.22–7.05 (m, 2 H), 6.93–6.75 (m, 2 H), 4.72–4.64 (2t, J = 9 Hz, 1 H), 4.37–4.20 (m, 2 H), 3.68 and 3.57 (m, 1 H), 3.45 and 3.22 (m, 1 H), 2.01–1.52 (2m, 2 H), 1.48 and 1.42 (2d, J = 5 Hz, 1 H), 0.89 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 159.9, 159.8, 131.3, 131.0, 128.2, 128.1, 124.5, 124.2, 120.5, 120.3, 109.6, 109.5, 79.0, 78.4, 77.6, 76.5, 40.4, 39.0, 37.0, 36.6, 35.1, 35.0, 25.6 (2 C), 25.5; MS (EI) m/e 220 (M$^+$, 23%), 163 (15%), 145 (38%), 132 (20%), 119 (100%), 91 (48%), 57 (65%); HRMS (EI) m/e calculated for $C_{14}H_{20}O_2$ 220.1463, found 220.1463.

1-[3-(2*H*,3*H*-Benzofurfuryl)]-2-heptanol (3d). Compound **3d** was prepared by the Grignard method with **1** and hexanal, the product was purified by flash chromatography in hexanes/EtOAc (4:1) to give 76 mg (65%) of an oil as a 53/47 mixture of diastereomers: IR (neat) 3424 (br), 2930, 1653, 1481, 1458, 1250, 1130, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20–7.05 (m, 2 H), 6.92–6.74 (m, 2 H), 4.75–4.60 (2 overlapping t, 1 H), 4.35–4.20 (2 overlapping dd, 1 H), 3.87–3.55 (m, 3 H), 1.90 (m, 1 H, one isomer), 1.68 (m, 1 H overlapping), 1.52–1.20 (m, 8 H), 0.87 (t, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.8 (2 C), 131.1, 130.8, 128.2, 128.1, 124.5, 124.1, 120.5, 120.3, 109.6, 109.5, 78.1 (2 C), 70.9, 69.9, 42.5, 42.4, 39.8, 38.5, 38.3, 31.8, 25.3, 22.7, 14.1; MS (EI) m/e 234 (M$^+$, 30%), 132 (72%), 119 (100%), 107 (15%), 91 (51%); HRMS (EI) m/e calculated for $C_{15}H_{22}O_2$ 234.1620, found 234.1620.

3-[[3-(2*H*,3*H*-Benzofurfuryl)]methyl]-3-pentanol (3e). Compound **3e** was prepared by the Grignard method with **1** and 3-pentanone and was purified by flash chromatography in hexanes/EtOAc (4:1) to give 95 mg (83%): IR (neat) 3649, 2966, 2934, 1653, 1481, 1458, 1220, 1010, 980, 930, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.24 (m, 2 H), 6.93–6.72 (m, 2 H), 4.75 (t, J = 9 Hz, 1 H), 4.25 (t, J = 9 Hz, 1 H), 3.64 (m, 1 H), 2.00 (m, 1 H), 1.74 (m, 1 H), 1.55 (m, 4 H), 0.89 (t, 6 H); ^{13}C NMR ($CDCl_3$) δ 159.7, 131.5, 128.0, 123.8, 120.3, 109.4, 78.6, 74.6, 43.5, 37.7, 31.9, 30.5, 8.2, 7.7; MS (EI) m/e 220 (M$^+$, 17%), 202 (M – H_2O, 13%), 189 (19%), 173 (68%), 119 (100%), 91 (45%), 57 (23%); HRMS (EI) m/e calculated for $C_{14}H_{20}O_2$ 220.1465, found 220.1463.

1-(4-Methoxyphenyl)-2-[3-(2*H*,3*H*-benzofurfuryl]ethanol (3f). Compound **3f** was prepared by the Grignard method with **1** and *p*-anisaldehyde and was purified by flash chromatography in hexanes/EtOAc (7:3) to give 130 mg (96%) of a viscous oil as a 50:50 mixture of diastereomers. Compound **3f** was prepared by the Grignard method with **7a**, and the yield was 94% as a 53:47 mixture of diastereomers: IR (neat) 3426, 2934, 2837, 1610, 1597, 1512, 1481, 1246, 1034, 958, 833, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.36–7.26 (m, 2 H), 7.21–7.05 (m, 2 H), 6.95–6.72 (m, 4 H), 4.87 (m, 1 H), 4.67 and 4.54 (2t, J = 9 Hz, 1 H), 4.25 and 4.18 (2dd, J = 7, 9 Hz, 1 H), 3.80 (s, 3 H), 3.70–3.50 (m, 1 H), 2.35–1.88 (m, 2 H), 1.77 and 1.82 (2d, J = 3 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 159.7 (2 C), 159.2 (2 C), 136.4, 136.3, 130.8, 130.6, 128.2, 128.1, 127.0 (2 C), 124.4, 124.1, 120.5, 120.5, 120.3, 113.9 (2 C), 109.5 (2 C), 77.6, 76.8, 72.8, 72.3, 55.3 (2 C), 43.9 (2 C), 39.6, 38.7; MS (EI) m/e 270 (M$^+$, 19%), 252 (M – H_2O, 27%), 144 (11%), 137 (100%), 121 (40%), 91 (30%), 77 (22%); HRMS (EI) m/e calculated for $C_{17}H_{18}O_3$ 270.1256, found 270.1256.

1-[3-(2*H*,3*H*-Benzofurfuryl)]-2-methyl-3-buten-2-ol (3g). Compound **3g** prepared by the Grignard method with **1** and methyl vinyl ketone and was purified by flash chromatography in hexanes/EtOAc (4:1) to give 75 mg (74%) as a 52/48 mixture of diastereomers: IR (neat) 3476, 3100, 2972, 2928, 1597, 1481, 1460, 1227, 1017, 955, 926, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.08 (m, 2 H), 6.83 (m, 1 H), 6.75 (d, J = 7 Hz, 1 H), 5.96 and 5.95 (2dd, J = 10, 16 Hz, 1 H), 5.24 (d, J = 16 Hz, 1 H), 5.15 and 5.11 (2d, J = 10 Hz, 1 H), 4.71 and 4.68 (2 overlapping t, J = 9 Hz, 1 H), 4.24 and 4.15 (2t, J = 9 Hz, 1 H), 3.13 and 3.06 (2m, 1 H), 2.10 (2t, 1 H), 1.85 (2dd, 1 H), 1.36 and 1.34 (2s, 3 H), 1.41 and 1.30 (2s, 1 H); ^{13}C NMR ($CDCl_3$) δ 159.6 (2 C), 145.09, 144.3, 131.1 (2 C), 127.9 (2 C), 123.9, 123.8, 120.4, 120.3, 112.6, 112.1, 109.3 (2 C), 73.3, 72.9, 47.5, 46.7, 38.2, 37.8, 29.6, 28.4; MS (EI) m/e 204 (M$^+$, 49%), 186 (M – H_2O, 46%), 173 (30%), 131 (30%), 118 (100%), 91 (94%), 71 (53%); HRMS (EI) m/e calculated for $C_{13}H_{16}O_2$ 204.1125, found 204.1125.

1-[3-(2*H*,3*H*-Benzofurfuryl)methyl]-4-*tert*-butylcyclohexan-1-ol (3h). Compound **3h** was prepared by the Grignard method with **1** and 4-*tert*-butylcyclohexan-1-one and was purified by flash chromatography in hexanes/EtOAc (9:1) to give separable axial and equatorial alcohols. The axial epimer was subjected to a Kugelrohr distillation (80 °C, 0.2 mm) to remove the remaining ketone. The combined yield was 121 mg (84%) in a ratio of 88/12 of axial/equatorial alcohols (based on isolated yields). By the Grignard method with **7a**, the yield was 80% (90/10 axial/equatorial). Compound **3h** was prepared by the Barbier method with **1**, and the yield was 76% (84/16 axial/equatorial). For the axial (major) epimer: mp = 98–99 °C; IR (neat) 3439, 2936, 2862, 1597, 1482, 1458, 1232, 1020, 960, 945, 830, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.10 (m, 2 H), 6.84 (t, J = 7 Hz, 1 H), 6.77 (d, J = 8 Hz, 1 H), 4.76 (t, J = 9 Hz, 1 H), 4.23 (t, J = 9 Hz, 1 H), 3.70 (m, 1 H), 2.00 (dd, J = 2, 15 Hz, 1 H), 1.85 (m, 1 H), 1.73 (m, 1 H), 1.90–0.90 (2m, 9 H), 0.86 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 159.6, 131.5, 127.9, 123.9, 120.3, 109.3, 78.7, 70.5, 49.4, 47.8, 38.6, 37.5, 37.2, 32.4, 27.6 (3 C), 22.4 (2 C); MS (EI) m/e 288 (M$^+$, 9%), 270 (M – H_2O, 16%), 257 (12%), 171 (15%), 132 (100%), 119 (67%), 91 (33%), 57 (40%); HRMS (EI) m/e calculated for $C_{19}H_{28}O_2$ 288.2089, found 288.2089. For the equatorial

(35) Beckwith, A. L. J.; Meijs, G. F. *J. Org. Chem.* **1987**, *52*, 1922.
(36) Labar, D.; Krief, A.; Norberg, B.; Evrard, G.; Durant, F. *Bull. Soc. Chim. Belg.* **1985**, *94*, 1083.
(37) Purification by Kugelrohr distillation as with **1** causes decomposition, which is indicated by impurities in the GC and NMR spectrum of the distilled product.

(minor) epimer: mp = 92–95 °C; IR (neat) 3410, 2942, 2863, 1563, 1493, 1460, 1256, 1000, 960, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.10 (m, 2 H), 6.86 (t, J = 7 Hz, 1 H), 6.77 (d, J = 8 Hz, 1 H), 4.77 (t, J = 9 Hz, 1 H), 4.27 (t, J = 9 Hz, 1 H), 3.64 (m, 1 H), 2.20 (dd, J = 2, 15 Hz, 1 H), 1.95 (m, 1 H), 1.80–1.00 (m, 10 H), 1.85–0.90 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 159.8, 131.6, 128.1, 123.9, 120.4, 109.4, 78.8, 72.3, 47.7, 41.6, 41.1, 38.6, 37.7, 32.4, 27.7, 24.8, 24.5.

1-[3-(2*H*,3*H*-Benzofurfuryl)]-2-methyl-2-propanol (3i). Compound **3i** was prepared by the Grignard method with **1** and acetone, and the product was purified by flash chromatography in hexanes/EtOAc (4:1) to give 77 mg (80%): IR (neat) 3470 (br), 2965, 1595, 1480, 1460, 1223, 1165, 1155, 1015, 947, 747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.10 (t, J = 9 Hz, 2 H), 6.84 (t, J = 7 Hz, 1 H), 6.76 (d, J = 8 Hz, 1 H), 4.77 (t, J = 9 Hz, 1 H), 4.24 (t, J = 9 Hz, 1 H), 3.66 (m, 1 H), 2.04 (dd, J = 3, 15 Hz, 1 H), 1.77 (dd, J = 10, 13 Hz, 1 H), 1.29 (d, J = 5 Hz, 6 H), 1.15 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 159.6, 131.2, 128.0, 123.9, 120.4, 109.4, 78.5, 70.7, 48.5, 38.4, 30.8, 29.3; MS (EI) m/e 192 (M^+, 38%), 174 (M – H_2O, 30%), 159 (80%), 119 (100%), 91 (89%), 59 (61%), 43 (64%); HRMS (EI) m/e calculated for $C_{12}H_{16}O_2$ 192.1150, found 192.1158.

1-[3-(2*H*,3*H*-Benzofurfuryl)]-2-butanol (3j). Compound **3j** was prepared by the Grignard method with **1** and propanal, and the product was purified by flash chromatography in hexanes/EtOAc (4:1) to give 67 mg (70%) as a 55/45 mixture of diastereomers: IR (neat) 3470, 2963, 2928, 1595, 1482, 1458, 1210, 1090, 945, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.22–7.05 (m, 2 H), 6.94–6.75 (m, 2 H), 4.79–4.64 (1 H, 2 overlapping t), 4.26 (1 H, 2 overlapping t), 3.73 and 3.58 (2 m, 1 H), 1.91 (m, 1 H), 1.74 (m, 1 H), 1.51 (m, 2 H), 1.33 and 1.23 (2 s, 1 H), 0.95 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.7 (2 C), 130.9, 130.7, 128.1, 128.0, 124.4, 124.0, 120.4, 120.2, 109.5, 109.4, 77.9, 77.4, 71.9, 71.1, 41.9, 41.8, 39.6, 38.4, 30.9 (2 C), 9.8 (2 C); MS (EI) m/e 192 (M^+, 46%), 174 (M – H_2O, 11%), 145 (67%), 119 (100%), 91 (80%), 43 (28%); HRMS (EI) m/e calculated for $C_{12}H_{16}O_2$ 192.1150, found 192.1158.

6-[3-(2*H*,3*H*-Benzofurfuryl)methyl]-5,6,7,8-tetrahydro-6-naphthol (3k). Compound **3k** was prepared by the Grignard method with **1** and β-tetralone (**2k**), and the product was purified by flash chromatography in hexanes/EtOAc (5:1) to give 39 mg (28%) as a 50:50 mixture of diastereomers: ^1H NMR ($CDCl_3$) δ 7.22–7.05 (m, 6 H), 6.33 (t, J = 8 Hz, 1 H), 6.26 (2d, J = 7 Hz, 1 H), 4.83 and 4.82 (2t, J = 9 Hz, 1 H), 4.32 and 4.28 (2t, J = 9 Hz, 1 H), 3.79 (m, 1 H), 3.10–2.75 (m, 4 H), 2.20–1.80 (m, 4 H), 1.48 and 1.46 (2s, 1 H); ^{13}C NMR ($CDCl_3$) δ 159.7 (2 C), 135.2 (2 C), 133.8, 78.7 (2 C), 70.8 (2 C), 46.7, 46.1, 43.4, 41.6, 37.7 (2 C), 35.3, 33.7, 26.0, 25.8; MS (EI) m/e 280 (M^+, 19%), 262 (M – H_2O, 13%), 225 (16%), 132 (100%), 119 (100%), 91 (74%); HRMS (EI) m/e calculated for $C_{19}H_{20}O_2$ 280.1463, found 280.1463.

Preparations of Adducts 7. Adducts **7** were prepared by the Grignard method with iodide **1**, and the products were purified by flash chromatography on silica in the designated solvents.

3-(Iodomethyl)-2,3-dihydrobenzofuran (7a). Compound **7a** was prepared by using I_2 as the electrophile and was purified by flash chromatography in petroleum ether/ether (17:1) to give 90 mg (0.35 mmol, 69%) of a colorless oil. The spectra are identical with that of a sample prepared above.

3-[(Thiophenyl)methyl]-2,3-dihydrobenzofuran (7b). Compound **7b** was prepared by using PhSSPh as the electrophile and was purified by flash chromatography twice in hexanes/EtOAc (19:1) to give 79 mg (0.32 mmol, 65%): IR (neat) 3055, 2950, 2875, 1610, 1595, 1481, 1460, 1232, 1016, 966, 845, 750, 691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44–7.03 (br m, 7 H), 6.85 (d, J = 8 Hz, 1 H), 6.79 (t, J = 8 Hz, 1 H), 4.62 (t, J = 9 Hz, 1 H), 4.43 (dd, J = 6, 9 Hz, 1 H), 3.61 (m, 1 H), 3.29 (dd, J = 5, 13 Hz, 1 H), 2.99 (dd, J = 10, 13 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 160.0, 135.5, 129.9, 129.1, 128.9, 126.6, 124.6, 120.5, 109.9, 76.1, 41.6, 38.9 (expected 13 resonances, observed 12); MS (EI) m/e 242 (M^+, 14%), 119 (100%), 91 (93%), 77 (32%), 65 (24%), 51 (24%), 45% (26%); HRMS (EI) m/e calculated for $C_{15}H_{14}OS$ 242.0765, found 242.0765.

3-[(Selenophenyl)methyl]-2,3-dihydrobenzofuran (7c). Compound **7c** was prepared by using PhSeSePh as the electrophile and was purified by flash chromatography twice in hexane/EtOAc (19:1) to give 104 mg (72%): IR (neat) 3055, 2954, 2889, 1610, 1595, 1481, 1460, 1232, 1024, 1016, 966, 845, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.51 (dd, J = 4, 7 Hz, 2 H), 7.40–7.08 (m, 3 H), 7.20 (d, J = 7 Hz, 1 H), 7.12 (t, J = 7 Hz, 1 H), 6.83 (t, J = 7 Hz, 1 H), 6.77 (d, J = 7 Hz, 1 H), 4.60 (t, J = 9 Hz, 1 H), 4.37 (dd, J = 6, 9 Hz, 1 H), 3.65 (m, 1 H), 3.29 (dd, J = 5, 12 Hz, 1 H), 2.98 (dd, J = 10, 13 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 160.0, 133.1, 129.7, 129.4, 129.2, 128.8, 127.3, 124.4, 120.5, 109.9, 76.8, 42.2, 32.4; MS (EI) m/e 290 (M^+, 30%), 172 (12%), 133 (80%), 119 (61%), 112 (100%), 91 (20%); HRMS (EI) m/e calculated for $C_{15}H_{14}OSe$ 290.0210, found 290.0210.

3-[(Tri-*n*-butylstannyl)methyl]-2,3-dihydrobenzofuran (7d). Compound **7d** was prepared by using Bu_3SnI as the electrophile and was purified by flash chromatography in hexanes/EtOAc (19:1) to give 174 mg (0.4 mmol, 82%). Preparation of **7d** by the Barbier method yielded 157 mg (74%): IR (neat) 2957, 2924, 2872, 2853, 1610, 1597, 1481, 1460, 1227, 1017, 970, 839, 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.11 (m, 2 H), 6.84 (t, J = 8 Hz, 1 H), 6.74 (d, J = 8 Hz, 1 H), 4.63 (t, J = 9 Hz, 1 H), 3.95 (t, J = 9 Hz, 1 H), 3.71 (m, 1 H), 1.50–1.38 (m, 13 H), 1.08 (dd, J = 9, 12 Hz, 1 H), 0.97–0.60 (br m, 15 H); ^{13}C NMR ($CDCl_3$) δ 159.5, 133.9, 127.9, 123.8, 120.6, 109.6, 79.5, 40.4, 29.3, 27.5, 14.8, 13.8, 9.4; MS (EI) m/e 367 (M – C_4H_9, 100%), 253 (18%), 235 (20%), 179 (60%), 121 (19%), 91 (8%); HRMS (EI) m/e calculated for $C_{17}H_{27}OSn$ (M – C_4H_9) 367.1084, found 367.1084.

***N*-Phenyl-[2*H*,3*H*-benzofurfuryl]acetamide (7e).** Compound **7e** was prepared by using phenyl isocyanate and was purified by flash chromatography in hexanes/EtOAc (4:1) after dissolving in $CHCl_3$ to give 82 mg (65%) of a solid: mp = 125–126 °C; IR (neat film) 3297, 1653, 1599, 1559, 1497, 1481, 1260, 1170, 950, 746, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46 (d, J = 8 Hz, 2 H), 7.31, (m, 2 H), 7.20–6.98 (m, 4 H), 6.81 (m, 2 H), 4.76 (t, J = 9 Hz, 1 H), 4.31 (dd, J = 6, 9 Hz, 1 H), 4.00 (m, 1 H), 2.75 (dd, J = 6, 15 Hz, 1 H), 2.63 (dd, J = 5, 15 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.1, 159.9, 137.5, 129.4, 128.8, 124.6, 124.4, 120.7, 120.1, 109.9, 76.7, 42.8, 38.7; MS (EI) m/e 253 (M^+, 14%), 135 (100%), 119 (20%), 93 (98%), 77 (31%); HRMS m/e calculated for $C_{16}H_{15}NO_2$ 253.1102, found 253.1103.

1-[2*H*,3*H*-Benzofurfuryl]-3-methyl-2-butanone (7f). Compound **7f** was prepared by using isobutyric anhydride as the electrophile and was purified by flash chromatography in hexanes/EtOAc (7:1) to give 56 mg (0.27 mmol, (55%)): IR (neat) 2970, 2892, 1709, 1596, 1481, 1461, 1234, 1017, 966, 750, 731; ^1H NMR ($CDCl_3$) δ 7.11 (m, 2 H), 6.80 (m, 2 H), 4.76 (t, J = 9 Hz, 1 H), 4.05 (t, J = 9 Hz, 1 H), 3.85 (m, 1 H), 2.95 (dd, J = 5, 8 Hz, 1 H), 2.78 (dd, J = 9, 18 Hz, 1 H), 2.58 (m, 1 H), 1.09 (d, J = 7 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 213.0, 159.8, 129.8, 128.5, 124.2, 120.5, 109.7, 77.3, 45.9, 40.9, 37.1, 18.3 (2 C); MS (EI) m/e 204 (M^+, 38%), 161 (22%), 133 (18%), 118 (100%), 91 (43%), 71 (22%); HRMS (EI) m/e calculated for $C_{13}H_{16}O_2$ 204.1150, found 204.1150.

4-[2*H*,3*H*-Benzofurfuryl]-3,3-dimethyl-1-butene (7g) and 5-[2*H*,3*H*-Benzofurfuryl]-2-methyl-2-pentene (7g′). Compounds **7g** and **7g′** were prepared by using prenyl bromide as the electrophile and were purified by flash chromatography in pentane/ether (19:1) to give 38 mg (37%) as a 2/1 mixture of S_N2' to S_N2 products (**7g**/**7g′**): ^1H NMR ($CDCl_3$) δ 7.07 (m, 4 H, **7g** and **7g′**), 6.83 (t, J = 7 Hz, 2 H, **7g** and **7g′**), 6.75 (t, J = 7.5 Hz, 2 H, **7g** and **7g′**), 5.90 (dd, J = 10, 18 Hz, 1 H, **7g**), 5.11 (br t, 1 H, **7g′**), 5.00 (m, 2 H, **7g**), 4.65 (m, 2 H, **7g** and **7g′**), 4.19 (t, 1 H, **7g′**), 4.07 (t, 1 H, **7g′**), 3.41 (m, 1 H, **7g** and **7g′**), 2.05 (m, 2 H, **7g**), 1.90 (dd, J = 2, 14 Hz, 2 H, **7g′**), 1.68 (s, 3 H, **7g′**), 1.63 (m, 2 H, **7g**), 1.80–1.50 (m, 2 H, **7g′**), 1.59 (s, 3 H, **7g′**), 1.08 (s, 3 H, **7g**), 1.04 (s, 3 H, **7g**); MS (EI) m/e 202 (M^+, 9%), 132 (66%), 119 (67%), 91 (100%), 65 (31%) for both **7g** and **7g′**.

***N*-(2,6-Dimethylphenyl)-[2*H*,3*H*-benzofurfuryl]-α-[α-hydroxyphenethyl]imine (8).** Compound **8** was prepared from **1** by Ito's procedure[16a] and was purified by flash chromatography in hexanes/EtOAc (5:1), then Kugelrohr distillation (85 °C, 0.2 mm) to remove remaining acetophenone. The yield was 129 mg (67%). Compound **8** was prepared from **1** by adding the isocyanide after the reduction of iodide; the yield was 119 mg (62%). By this latter method, the crude mixture and pure product are cleaner: IR (neat) 3330, 3058, 3026, 2976, 2935, 1660, 1596, 1481, 1460, 1230, 1207, 1124, 1066, 964, 912, 751, 700 cm^{-1}, ^1H NMR ($CDCl_3$) 7.22–6.22 (series of m, 12 H), 3.68 and 3.53 (2t, J = 9 Hz, 1 H), 3.34 and 2.57 (2dd, J = 6, 9 Hz, 1 H), 2.96 and 2.85 (2m, 1 H), 2.50 (m, 1 H), 2.38 (dd, J = 10, 16 Hz, 1 H), 2.13, 2.11, 2.10, 2.03, 1.93 and 1.87 (6s, 9 H); ^{13}C NMR ($CDCl_3$) δ 174.9, 174.8, 158.9, 145.4, 143.2, 142.6, 129.8, 129.7, 128.7, 128.6, 128.4, 128.2, 128.0, 126.8, 126.7, 126.4, 125.1, 124.7, 124.1, 124.0, 123.7, 123.6, 120.4, 109.3, 76.8, 76.6, 75.9, 39.1, 38.9, 36.6, 36.3, 25.3, 18.5, 18.4, 17.9, MS (EI) m/e 385 (M^+, <1%), 367 (M – H_2O, 1%), 264 (73%), 146 (35%), 119 (100%), 91 (44%); HRMS (EI) m/e calculated for $C_{26}H_{27}NO_2$ 385.2042, found 385.2042.

Addition of Alkyl Samariums to 4-*tert*-Butylcyclohexan-1-one. These reactions were conducted by the Grignard and Barbier methods described above. Alcohols **10a–c** are known compounds,[36] and their spectra were checked against the literature spectra.

4-*tert*-Butyl-1-Phenethyl-1-cyclohexanol (10d). Compound **10d** was produced by the Grignard method and was purified by flash chromatography in hexanes/EtOAc (9:1) to give 106 mg (81%) as a 75/25 mixture of diastereomers (crude ratio was 62/38 by NMR). Compound **10d** was prepared by the Barbier method, and the yield was 84% as a 77/23 mix of diatereomers (crude ratio was 66/34 by NMR). Major isomer, axial alcohol: mp = 71–73 °C; IR (neat film) 3443, 3028, 2932, 2860, 1456, 1365, 1313, 1210, 1142, 987, 924, 731, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34–7.20 (m, 5 H), 2.70 (m, 2 H), 1.73 (m, 4 H), 1.62 (m, 1 H), 1.33 (m, 4 H), 0.95 (m, 2 H), 0.86 (s, 9 H); ^{13}C NMR ($CDCl_3$)

δ 142.9, 128.4 (4 C), 125.7, 70.7, 48.0, 46.2, 37.6 (2 C), 32.5, 29.7, 27.7 (2 C), 22.5 (3 C); MS (EI) *m/e* 242 (M − H_2O, 38%); 186 (25%), 155 (63%), 104 (42%), 91 (100%), 57 (86%); MS (CI isobutane) *m/e* 243 (M − OH); HRMS (EI) *m/e* calculated for $C_{18}H_{26}$ (M − H_2O) 242.2034, found 242.2034. Minor isomer, equatorial alcohol: mp = 114–116 °C; IR (neat film) 3260, 2938, 2864, 1497, 1450, 1363, 1200, 1105, 1065, 984, 713, 705, 695; ^{1}H NMR ($CDCl_3$) δ 7.37–7.24 (m, 5 H), 2.66 (m, 2), 1.83 (m, 4 H), 1.67 (m, 1 H), 1.32 (m, 2 H), 1.06 (m, 5 H), 0.84 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 149.9, 128.5 (4 C), 125.8, 72.3, 47.6, 38.9 (2C), 38.7, 32.3, 29.4, 27.7 (2 C), 24.5 (3 C), (EI) *m/e* 242 (M − H_2O, 27%), 186 (18%), 155 (53%), 104 (44%), 91 (100%), 57 (90%); HRMS (EI) *m/e* calculated for $C_{18}H_{26}$ (M − H_2O) 242.2035, found 242.2035.

2-Methyl-1-phenethyl-1-cyclohexanol (11d). Compound **11d** was prepared by the Grignard method with phenethyl iodide (**9d**) and 2-methylcyclohexanone (**2l**) and was purified by flash chromatography in hexanes/EtOAc (9:1) to give 96 mg (0.43 mmol, 88%) in a ratio of 91/9 axial/equatorial alcohol (ratio of isolated diastereomers). Preparations by the Barbier method yielded 101 mg (0.46 mmol, 93%): major isomer IR (neat) 3485, 3025, 2930, 2855, 1610, 1495, 1452, 1271, 949, 908, 733, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.35–7.22 (m, 2 H), 7.21–7.09 (m, 3 H), 2.61 (m, 2 H), 1.76–1.18 (br, 12 H), 0.88 (d, *J* = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 142.7, 128.4 (2C), 128.3 (2 C), 72.9, 42.9, 38.3, 35.9, 30.5, 30.1, 25.7, 21.8, 14.9; MS (EI) *m/e* 218 (M^+, 45%), 161 (60%), 113 (97%), 104 (32%), 91 (100%); HRMS (EI) *m/e* calculated for $C_{15}H_{22}O$ 218.1671, found 218.1676.

***O*-Prenyl-2-iodophenol (12).** Prenyl bromide (0.95 mL, 8.21 mmol) was added to a solution of 2-iodophenol (1.5 g, 6.89 mmol), anhydrous K_2CO_3 (2.35 g, 17 mmol), and DMF (50 mL). After 21 h at 25 °C, the reaction was poured into H_2O and extracted with pentane (4×). The pentane extracts were washed H_2O (2×), 10% KOH (2×), 3% $Na_2S_2O_3$, and brine. The pentane was dried over $MgSO_4$, filtered, and concentrated. The product was purified by flash chromatography in hexane/ether (19:1) to give 1.54 g (78%) of a colorless oil.[37] The NMR spectrum showed the presence of a small quantity of what appeared to be the S_N2' product: IR (neat) 2974, 2930, 2860, 1582, 1560, 1470, 1439, 1390, 1275, 1238, 1016, 995 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.74 (d, *J* = 8 Hz, 1 H), 7.25 (m, 1 H), 6.80 (d, *J* = 8 Hz, 1 H), 6.67 (m, 1 H), 5.48 (m, 1 H), 4.57 (d, *J* = 7 Hz, 2 H), 1.77 (s, 3 H), 1.72 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 157.5, 139.5, 137.9, 129.4, 122.5, 119.6, 112.8, 87.0, 66.3, 25.8, 18.4; MS (EI) *m/e* 288 (M^+, 3%), 220 (100%), 92 (11%), 69 (55%); HRMS (EI) *m/e* calculated for $C_{11}H_{13}IO$ 288.0011, found 288.0011.

3-(2-Propyl)-2,3-dihydrobenzofuran (13). Compound **13** was prepared by the Grignard method with **12** and H_2O as the electrophile. The crude mixture contained the reduced product **13** plus the olefin **14** in a ratio of 60/40, tentatively assigned by ^{1}H NMR and GC-MS. These two compounds were inseparable on analytical TLC. The crude mixture was treated with BH_3·THF followed by basic peroxide workup and then purified by flash chromatography in pentane/ether (9:1, then 4:1) to give **13** in a yield of 32 mg (39%): IR (neat) 3034, 2959, 2875, 1611, 1595, 1483, 1458, 1387, 1370, 1232, 1163, 1017, 959, 824, 749, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.21–7.05 (m, 2 H), 6.82 (t, *J* = 7 Hz, 1 H), 6.75 (d, *J* = 8 Hz, 1 H), 4.49 (t, *J* = 9 Hz, 1 H), 4.35 (dd, *J* = 6 Hz, 1 H), 3.29 (m, 1 H), 1.93 (m, 1 H), 0.93 (d, *J* = 7 Hz, 3 H), 0.82 (d, *J* = 7 Hz, 3 H) ^{13}C NMR ($CDCl_3$) δ 160.4, 129.5, 128.2, 125.1, 120.1, 109.4, 73.9, 48.2, 31.7, 19.9, 18.5; MS (EI) *m/e* 161 (M − H), (4%), 119 (100%), 91 (33%), 69 (20%), 55 (27%), 43 (61%).

***O*-Crotyl-2-iodophenol (17).** Crotyl chloride (0.82 mL, 8.2 mmol) was added to a solution of 2-iodophenol (1.50 g, 6.8 mmol), anhydrous K_2CO_3 (2.35 g, 17 mmol), and DMF (50 mL). The reaction was stirred for 21 h at 25 °C. The workup and purification is the same for iodide **12**. The yield was 1.62 g (87%) of a colorless oil that was a mixture of *E* and *Z* isomers (3/1) by NMR:[34] IR (neat) 3023, 2915, 2855, 1580, 1568, 1459, 1438, 1376, 1274, 1121, 1045, 1091, 998, 988, 964, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.75 (m, 2 H, *E* and *Z*), 7.35–7.20 (m, 2 H, *E* and *Z*), 6.81 (m, 2 H, *E* and *Z*), 4.64 (d, *J* = 2 Hz, 2 H, *Z*), 4.51 (d, *J* = 6 Hz, *E* and *Z*), 5.80–5.65 (m, 2 H, *E* and *Z*), 4.64 (d, *J* = 7 Hz, 2 H, *Z*), 4.51 (d, *J* = 6 Hz, 2 H, *E*), 1.76 (d, *J* = 6 Hz, 3 H, *Z*), 1.73 (d, *J* = 6 Hz, 3 H, *E*); ^{13}C NMR ($CDCl_3$) δ 157.3 (2 C, *E* and *Z*), 139.5 (2 C, *E* and *Z*), 130.1 (2 C, *E* and *Z*), 129.4 (E), 128.7 (*Z*), 125.6 (*E*), 125.4 (*Z*), 122.5 (2 C, and *E* and *Z*), 86.8 (2 C, *E* and *Z*), 69.8 (*E*), 65.2 (*Z*), 17.9 (*E*), 13.5 (*Z*); MS (EI) *m/e* 274 (M^+, 10%), 220 (100%), 93 (10%), 55 (46%); HRMS (EI) *m/e* calculated for $C_{10}H_{11}IO$ 273.9855, found 273.9855.

3-Ethyl-2,3-dihydrobenzofuran (18). Compound **18** was prepared by the Grignard method with iodide **17** and H_2O as the electrophile and was purified by flash chromatography in pentanes/ether (39:1) to give 116 mg (78%) of a yellow oil: IR (neat) 3033, 2963, 2876, 1611, 1597, 1558, 1558, 1481, 1460, 1381, 1229, 1165, 1016, 974, 943, 833, 750; ^{1}H NMR ($CDCl_3$) δ 7.20–7.05 (m, 2 H), 6.84 (t, *J* = 8 Hz, 1 H), 6.76 (d, *J* = 8 Hz, 1 H), 4.61 (t, *J* = 9 Hz, 1 H), 4.20 (t, *J* = 7 Hz, 1 H), 3.36 (m, 1 H), 1.79 (m, 1 H), 1.61 (m, 1 H), 0.96 (t, *J* = 8 Hz, 3 H), ^{13}C NMR ($CDCl_3$) δ 160.0, 130.9, 128.1, 124.4, 120.3, 109.5, 76.6, 43.4, 27.7, 11.4; MS (EI) *m/e* 148 (M^+, 17%), 119 (48%), 91 (30%), 74 (60%), 59 (100%); HRMS (EI) *m/e* calculated for $C_{10}H_{12}O$ 148.0888, found 148.0888.

3-[3-2*H*,3*H*-Benzofurfuryl]-3-ethyl-3-pentanol (19). Compound **19** was prepared by the Grignard method with iodide **17** and 3-pentanone as the electrophile and was purified by flash chromatography in hexanes/EtOAc (4:1) to give 85 mg (0.36 mmol, 72%): IR (neat) 3522, 2968, 2882, 1611, 1595, 1481, 1458, 1383, 1227, 1161, 1094, 1019, 951, 835, 750; ^{1}H NMR ($CDCl_3$) δ 7.39 (d, *J* = 8 Hz, 1 H), 7.09 (t, *J* = 8 Hz, 1 H), 6.89–6.71 (m, 2 H), 4.64 and 4.54 (2t, *J* = 9 Hz, 1 H), 4.54 (d, *J* = 9 Hz, 1 H), 4.35 (t, *J* = 7 Hz, 1 H), 3.86 and 3.82 (2m, 1 H) 2.12 and 1.83 (2m, 1 H), 1.75–1.50 (m, 5 H), 1.18 and 1.10 (2s, 1 H), 1.00–0.70 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 161.1, 160.0, 130.9, 128.2, 127.9, 127.8, 127.5, 123.6, 120.2, 119.8, 109.3, 109.1, 78.2, 76.4, 72.6, 42.6, 41.9, 41.6, 41.3, 28.8 (2 C), 28.7, 28.4, 10.9, 8.4, 7.9 (2 C), 7.8 (2 C); MS (EI) *m/e* 234 (M^+, 8%), 216 (M − H_2O, 11%), 187 (34%), 119 (100%), 91 (48%), 45 (24%); HRMS (EI) *m/e* calculated for $C_{15}H_{22}O_2$ 234.1620, found 234.1620.

1-Cyclohexyl-1-phenylethanol (20). Compound **20** was prepared by the Grignard method with cyclohexyl iodide (2 equiv) and acetophenone and was purified by flash chromatography in hexanes/EtOAc (9:1) and then Kugelrohr distillation to remove remaining acetophenone. The yield was 87 mg (86% based on ketone): IR (neat) 3443, 3010, 2928, 2851, 1495, 1447, 1374, 1061, 1028, 940, 890, 750, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.38 (d, *J* = 7 Hz, 2 H), 7.31 (t, *J* = Hz, 2 H), 7.19 (t, *J* = 7 Hz, 1 H), 1.72–1.54 (m, 6 H), 1.51 (s, 3 H), 1.28–0.88 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 147.9, 127.8 (2 C), 126.4, 125.4 (2 C), 76.7, 49.0, 27.4, 27.2, 26.8, 26.7 (2 C), 26.4; MS (CI, isobutane) *m/e* 203 (M − 1, 3%), 187 (M − OH, 100%), 127 (28%), 121 (49%), 105 (49%).

Cyclohexyl Phenyl Sulfone (21). Prepared by the Grignard method with cyclohexyl iodide (2 equiv) and PhSSPh, the crude mixture was oxidized with mCPBA and then purified by flash chromatography in benzene/EtOAc (19:1) to give 53 mg (47%) of the sulfone: IR (neat) 3050, 2934, 2857, 1575, 1447, 1304, 1269, 1219, 1180, 1145, 1120, 1086, 998, 875, 821, 773, 744, 717, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, *J* = 7 Hz, 2 H), 1.82 (m, 2 H), 1.44 (m, 2 H), 1.18 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 137.2, 133.5, 128.9 (4 C), 63.4, 25.4 (2 C), 25.0 (3 C); MS (CI, isobutane) *m/e* 225 (M^+, H, 100%), 143 (22%), 125 (4%), 83 (8%).

Acknowledgment. We thank the donors of the Petroleum Research Fund for supporting this work. We are also indebted to Dr. Thomas Fevig for conducting key preliminary experiments and to both Dr. Fevig and Dr. Craig Jasperse for helpful discussions.