A Novel Palladium-Mediated Cascade Reaction Triggered by Strain Release of the Cyclobutane System. A New General Route to Benzo- and Naphthohydrindans

Hideo Nemoto,* Junji Miyata, Masahiro Yoshida, Naomi Raku, and Keiichiro Fukumoto

Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980-77, Japan

Received July 25, 1997[⊗]

A novel palladium-mediated cascade reaction was reported. By this procedure, the olefinic cyclobutanols **17**, **24**, and **31**; **41**; **37**; and **45** afforded the benzo- and naphthohydrindans (**46**−**49**, **50**−**53**, **54**−**57**, and **58**−**61**) respectively in one operation in the ratios depending on the mediators and solvents employed. This provides a novel and efficient synthesis of biologically important A-nor and C_{11}-alkylated steroids.

Introduction

In recent years, palladium-mediated cyclization[1−3] of substrates containing various unsaturated systems has provided general and versatile methods for the synthesis of both simple and complex compounds. Of these, cyclic cascade carbopalladations[4,5] have gained wide acceptance and have now become a rapidly growing area in synthetic organic chemistry, because of their increasing synthetic efficiency. In this context, we have developed a novel palladium-mediated cascade reaction providing a new general route to benzo- and naphthohydrindans (A-nor steroid **9** and equilenin type steroid **10**, respectively). The compounds **9** and **10** thus obtained could also be potential intermediates[6] for the synthesis of A-nor steroids **1**−**3**[7] and C_{11} β-substituted estradiols **4**−**6**[8] which have attracted growing attention owing to their neurosteroid analogues (**1**−**3**) and high-affinity ligands for the estrogen receptor (**4**−**6**), respectively (Figure 1). Here, we report the results.

A goal of this cascade reaction was initiated by complexation (**7a** and **8a**) of palladium followed by ring

[⊗] Abstract published in *Advance ACS Abstracts,* October 1, 1997.

(1) For reviews, see: (a) Heck, R. F. *Org. React.* **1982**, *27*, 345−390. (b) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985. (c) Trost, B. M *Acc. Chem. Res.* **1990**, *23*, 34−42. (d) Trost, B. M. *Janssen Chimica Acta* **1991**, *9*, 3−9. (e) Oppolzer, W. *In Comprehensive Organic Synthesis;* Trost, B. M., Fleming, I., Eds., Pergamon Press: Oxford, 1991, Vol. 5, p 29−84. (f) de Meijere, A.; Meyer, F. E. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379−2411. (g) Tsuji, J. *Palladium Reagents and Catalysts Innovations in Organic Synthesis*; John Wiley & Sons: London, 1995. (h) Negishi, E.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365−393. (i) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115−136. (j) Malacria, M. *Chem. Rev.* **1996**, *96*, 289−306.

(2) For recent works in this area, see: (a) Luo, F. T.; Chou, F. L.; Wang, R. T. *J. Org. Chem.* **1990**, *55*, 4846−4849. (b) Negishi, E.; Noda, Y.; Lamaty, F.; Vawter, E. J. *Tetrahedron Lett.* **1990**, *31*, 4393−4396. (c) Nuss, J. M.; Levine, B. H.; Rennels, R. A.; Heravi, M. M. *Tetrahedron Lett.* **1991**, *32*, 5243−5246. (d) Trost, B. M.; Pfrengle, W.; Urabe, H.; Dumas, J. *J. Am. Chem. Soc.* **1992**, *114*, 1923−1924. (e) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1992**, *114*, 791−792. (f) Negishi, E.; Harring, L. S.; Owczarczyk, Z.; Mohamud, M. M.; Ay, M. *Tetrahedron Lett.* **1992**, *33*, 3253−3256. (g) Takacs, J. M.; Zhu, J.; Chandramouli, S. *J. Am. Chem. Soc.* **1992**, *114*, 773−774. (h) Nuss, J. M.; Murphy, M. M.; Rennels, R. A.; Heravi, M. H.; Mohr, B. J. *Tetrahedron Lett.* **1993**, *34*, 3079−3082. (i) Kucera, D. J.; O'Connor, S. J.; Overman, L. E. *J. Org. Chem.* **1993**, *58*, 5304−5306. (j) Brown, S.; Clarkson, S.; Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1993**, *34*, 157−160. (k) Trost, B. M.; Gelling, O. T. *Tetrahedron Lett.* **1993**, *34*, 8233−8236. (l) Trost, B. M.; Czeskis, B. A. *Tetrahedron Lett.* **1994**, *35*, 211−214. (m) Trost, B. M.; Parquette, J. R.; Marquart, A. L. *J. Am. Chem. Soc.* **1995**, *117*, 3284−3285. (n) Trost, B. M.; Gerusz, V. J. *J. Am. Chem. Soc.* **1995**, *117*, 5156−5157. (o) Trost, B. M.; McIntosh, M. C. *J. Am. Chem. Soc.* **1995**, *117*, 7255−7256. (p) Ma, S.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 6345−6357.

(3) For applications to natural product synthesis, see: (a) Abelman, M. M.; Overman, L. E.; Tran, V. D. *J. Am. Chem. Soc.* **1990**, *112*, 6959−6964. (b) Grimins, D. L.; Baevsky, M. F.; Hong, H. *J. Am. Chem. Soc.* **1992**, *114*, 10971−10972. (c) Hudlicky, T.; Olivo, H. F. *J. Am. Chem. Soc.* **1992**, *114*, 9694−9696. (d) Hong, C. Y.; Kado, N.; Overman, L. E. *J. Am. Chem. Soc.* **1993**, *115*, 11028−11029. (e) Rawal, V. H.; Michoud, C.; Monestel, R. F. *J. Am. Chem. Soc.* **1993**, *115*, 3030−3031. (f) Masters, J. J.; Jung, D. K.; Bornmann, W. G.; Danishefsky, S. J. *Tetrahedron Lett.* **1993**, *34*, 7253−7256.

(4) For reviews dealing with the cascade chemistry, see: (a) Posner, G. H. *Chem. Rev.* **1986**, *86*, 831−844. (b) Ho, T.-L. *Tandem Organic Reactions*; Wiley: New York; 1992. (c) Waldmann, H. *Nachr. Chem. Tech. Lab.* **1992**, *40*, 1133−1140. (d) Hoffmann, H. M. R. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1332−1334. (e) Tieze, L. F.; Beifuss, U. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131−163. (f) Davies, H. M. L. *Tetrahedron* **1993**, *49*, 5203−5223. (g) Bunce, R. A. *Tetrahedron* **1995**, *51*, 13103−13159. (h) Denmark, S. E.; Thorarensen, A. *Chem. Rev.* **1996**, *96*, 137−165. (i) Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167−176. (j) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177−194. (k) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195−206. (l) Wang, K. K. *Chem. Rev.* **1996**, *96*, 207−222. (m) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223−269. (n) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307−338. (o) Snider, B. B. *Chem. Rev.* **1996**, *96*, 339−363.

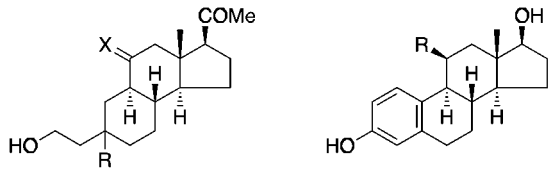
(5) For cyclic cascade carbopalladations, see: (a) Abelman, M. M.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 2328−2329. (b) Carpenter, N. E.; Kucera, D. J.; Overman, L. E. *J. Org. Chem.* **1989**, *54*, 5846−5848. (c) Zhang, Y.; Wu, G.; Agnel, G.; Negishi, E. *J. Am. Chem. Soc.* **1990**, *112*, 8590−8592. (d) Grigg, R.; Dorrity, M. J.; Malone, J. F.; Sridharan, V.; Sukirthalingam, S. *Tetrahedron Lett.* **1990**, *31*, 1343−1346. (e) Meyer, F. E.; de Meijere, A. *Synlett* **1991**, 777−778. (f) Meyer, F. E.; Parsons, P. J.; de Meijere, A. *J. Org. Chem.* **1991**, *56*, 6487−6488. (g) Negishi, E.; Harring, L. S.; Owczarczyk, Z.; Mohamud, M. M.; Ay, M. *Tetrahedron Lett.* **1992**, *33*, 3253−3256. (h) Negishi, E.; Ay, M.; Sugihara, T. *Tetrahedron* **1993**, *49*, 5471−5482. (i) Sugihara, T.; Copéret, C.; Owczarczyk, Z.; Harring, L. S.; Negishi, E. *J. Am. Chem. Soc.* **1994**, *116*, 7923−7924.

(6) For recent studies on the synthesis of benzohydrindans and their transformation into various types of biologically important steroids, see: (a) Nemoto, H.; Ando, M.; Fukumoto, K. *Tetrahedron Lett.* **1990**, *31*, 6205−6208. (b) Nemoto, H.; Matsuhashi, N.; Imaizumi, M.; Nagai, M.; Fukumoto, K. *J. Org. Chem.* **1990**, *55*, 5625−5631. (c) Nemoto, H.; Satoh, A.; Ando, M.; Fukumoto, K. *J. Chem. Soc., Chem. Commun.* **1990**, 1001−1002; *J. Chem. Soc., Perkin Trans. 1* **1991**, 1309−1314. (d) Nemoto, H.; Matsuhashi, N.; Satoh, A.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1992**, 495−498. (e) Nemoto, H.; Satoh, A.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2237−2238. (f) Nemoto, H.; Satoh, A.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 943−946. (g) Nemoto, H.; Satoh, A.; Fukui, H.; Fujimori, S.; Fukumoto, K. *Chem. Pharm. Bull.* **1994**, *42*, 1963−1965. (h) Nemoto, H.; Satoh, A.; Fukumoto, K.; Kabuto, C. *J. Org. Chem.* **1995**, *60*, 594−600. (i) Nemoto, H.; Satoh, A.; Fukumoto, K. *Tetrahedron* **1995**, *51*, 10159−10174. (j) Nemoto, H.; Satoh, A.; Fukumoto, K. *Synlett* **1995**, 199−200.

(7) (a) Rodgers-Neame, N. T.; Covey, D. F.; Hu, Y.; Isenberg, K. E.; Zorumski, C. F. *Mol. Pharmacol.* **1992**, *42*, 952−957. (b) Hu, Y.; Zorumski, C. F.; Covey, D. F. *J. Org. Chem.* **1995**, *60*, 3619−3625.

(8) (a) Bindal, R. D.; Carlson, K. E.; Reiner, G. C. A.; Katzenellenbogen, J. A. *J. Steroid Biochem.* **1987**, *28*, 361−370. (b) Sasson, S.; Katzenellenbogen, J. A. *J. Steroid Biochem.* **1989**, *33*, 859−865. (c) Pomper, M. G.; Van Brocklin, H.; Thieme, A. M.; Thomas, R. D.; Kiesewetter, D. O.; Carlson, K. E.; Mathias, C. J.; Welch, M. J.; Katzenellenbogen, J. A. *J. Med. Chem.* **1990**, *33*, 3143−3155. (d) Hanson, R. N.; Napolitano, E.; Fiaschi, R. *J. Med. Chem.* **1990**, *33*, 3155−3160. (e) Tedesco, R.; Fiashi, R.; Napolitano, E. *J. Org. Chem.* **1995**, *60*, 5316−5318.

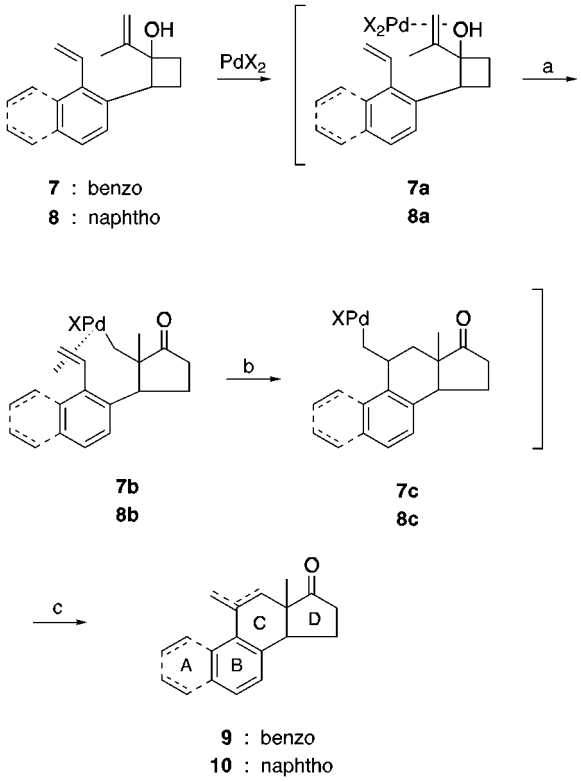
S0022-3263(97)01377-7 CCC: $14.00



1 : X = H_2; R = ····H
2 : X = O; R = ····H
3 : X = O; R = —H
4 : R = Et
5 : R = CH_2Cl
6 : R = CH = CH_2

Figure 1.

Chart 1



7 : benzo
8 : naphtho
7a
8a
7b
8b
7c
8c
9 : benzo
10 : naphtho

expansion (a) of the cyclobutanol ring to a cyclopentanone palladium complex (→**7b** and **8b**), insertion (b) of olefins (→**7c** and **8c**), and elimination (c) of palladium to give **9** and **10** as shown in Chart 1.[9]

Results and Discussion

Synthesis of the Substrates for the Cascade Reaction. The synthesis of the olefinic cyclobutanols **17**, **24**, **31**, and **37** substrates for the cascade reaction was straightforward (Schemes 1 and 2). The triflate **12**, prepared (96%) from 4-methoxysalicylaldehyde (**11**), was subjected to the Stille reaction[10] with tri-*n*-butylvinylstannane to give the styrene **13** (90%), which upon the Wittig reaction with cyclopropylidenetriphenylphosphorane under modified McMurry conditions[11] afforded the cyclopropylidene derivative **14** (97%). Successive treatment of **14** with *m*-chloroperbenzoic acid (*m*CPBA) and then fluoroboric acid gave, *via* the epoxide **15**, the cyclobutanone **16** (83%) which was then converted to **17** (95%) stereoselectively by the Grignard reaction with isopropenylmagnesium bromide in the presence of cerium trichloride. By following the same procedure, **24**, **31**, and **37** were prepared in 36%, 30%, and 20% overall yields starting from **18**, **25**, and **32**[12] *via* **19**−**23**, **26**−**30**, and **33**−**36** respectively.[13]

The diastereoisomer **41** was also prepared in 39% overall yield by successive chlorination of **31**, substitution of the chloride **38** with thiophenoxide, oxidation of the sulfide **39**, and stereoselective [2,3]sigmatropic rearrangement of the resulting sulfoxide **40**. By following the same procedure, the diastereoisomer **45** was prepared in 42% overall yield starting from **37** *via* **42**−**44** (Scheme 3).[14]

Cascade Ring Expansion and Insertion Reaction. As a preliminary experiment, the cascade reaction of **17** was examined using various types of mediators and solvents (Table 1). The reaction proceeded in moderate yield (up to 55%, entry 2) to give the four possible isomers **46**−**49** depending upon the reaction conditions. Although no stereoselectivity was observed in entries 1, 2, 3, 8, 11, and 17 (**48**:**49**/50:50), a moderate (**48**:**49**/40:60 in entry 10, 25:75 in entry 12, and 20:80 in entry 7, and **46**:**47**/17:83 in entries 9 and 13) to high *cis* stereoselectivity (**48**:**49**/9:91 in entry 16 and **46**:**47**/4:96 in entry 14) was recognized. In contrast to these, a moderate *trans* stereoselectivity (**48**:**49**/75:25) was found in entries 4−6.

These characteristic features were found in the same reaction of the substrates **24**, **31**, and **41** examined under the conditions corresponding to entries 2, 6, and 15 in Table 1, although somewhat greater tendencies toward *cis* preference were observed in the case of **31** and **41** (entries 2, 3, 5, 6, and 8 in Table 2). In contrast to the greater *cis* preference for **41** (entries 3 and 6) than that for **31** (entries 2 and 5), the remarkable reverse tendency of **41** favoring *trans* (entry 9) comparing with the complete *cis* selectivity (entry 8) of **31** was noteworthy. Thus, the general features of this reaction were confirmed.

On the basis of the findings described above, our attention was turned to the development of the cascade method to C_{11} alkylated equilenin-type steroid **10**.

The cascade reaction of **37** and **45** was examined under the same conditions as outlined in Table 2 (Table 3). In entry 3, *trans* selectivity which was observed in entries 5 and 6 in Table 1 and entries 4 and 5 in Table 2 was reduced to almost a 50:50 mixture of *cis* and *trans*. A high degree of *cis* selectivity was found in entry 8,

(9) For some previous works on the palladium catalysed ring expansion of cyclobutanes, see: (a) Boontanonda, P.; Grigg, R. *J. Chem. Soc., Chem. Commun.* **1977**, 583−584. (b) Clark, G. R.; Thiensathit, S. *Tetrahedron Lett.* **1985**, *26*, 2503−2506. (c) Liebeskind, L. S.; Mitchell, D.; Foster, B. S. *J. Am. Chem. Soc.* **1987**, *109*, 7908−7910. (d) Demuth, M.; Pandey, B.; Wietfeld, B.; Said, H.; Viader, J. *Helv. Chim. Acta* **1988**, *71*, 1392−1398. (e) de Almeida Barbosa, L.-C.; Mann, J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 177−178. (f) Mitchell, D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 291−296. (g) Nemoto, H.; Nagamochi, M.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2329−2332. (h) Nemoto, H.; Nagamochi, M.; Ishibashi, H.; Fukumoto, K. *J. Org. Chem.* **1994**, *59*, 74−79. (i) Nemoto, H.; Shiraki, M.; Fukumoto, K. *Synlett* **1994**, 599−600. (j) Nemoto, H.; Miyata, J.; Fukumoto, K. *Tetrahedron* **1996**, *52*, 10363−10374. For review, see: (k) Liebeskind, L. S.; Chidambaram, R.; Mitchell, D.; Foster, B. S. *Pure Appl. Chem.* **1988**, *60*, 27−34.

(10) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033−3040.

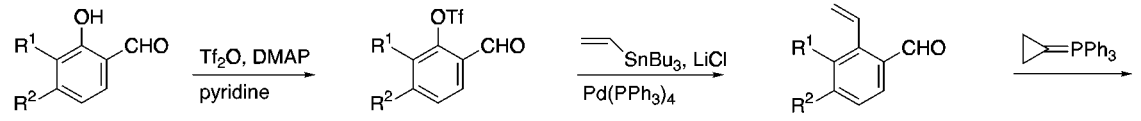
(11) Stafford, J. A.; McMurry, J. E. *Tetrahedron Lett.* **1988**, *29*, 2531−2534.

(12) Narasimhan, N. S.; Mali, R. S.; Barve, M. V. *Synthesis* **1979**, 906−909.

(13) The stereochemistry of **17**, **24**, **31**, and **37** was confirmed by the observation of the definite NOE between methyl protons of isopropenyl group and adjacent methine proton in these NMR spectra, which were observed at 1.83 and 3.95 ppm for **17**, 1.85 and 4.17 ppm for **24**, 1.84 and 4.12−4.19 ppm for **31**, and 1.84 and 4.30 ppm for **37**, respectively.

(14) Brown, W. L.; Fallis, A. G. *Tetrahedron Lett.* **1985**, *26*, 607−610. The direct formation of the sulfoxides **40** and **44** by treatment of **31** and **37** with phenylsulfenyl chloride under basic condition was failed.

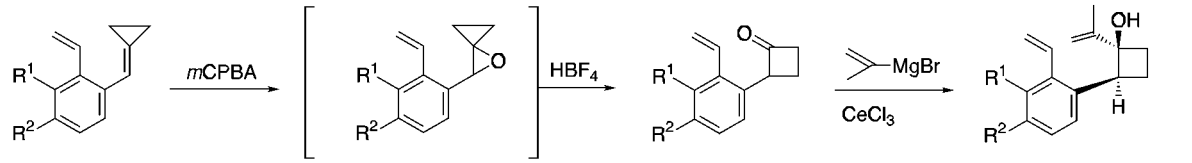
Scheme 1



11 : R^1 = H ; R^2 = OMe
18 : R^1 = OMe ; R^2 = H
25 : R^1 = OTBS; R^2 = H

12 : R^1 = H ; R^2 = OMe
19 : R^1 = OMe ; R^2 = H
26 : R^1 = OTBS; R^2 = H

13 : R^1 = H ; R^2 = OMe
20 : R^1 = OMe ; R^2 = H
27 : R^1 = OTBS; R^2 = H



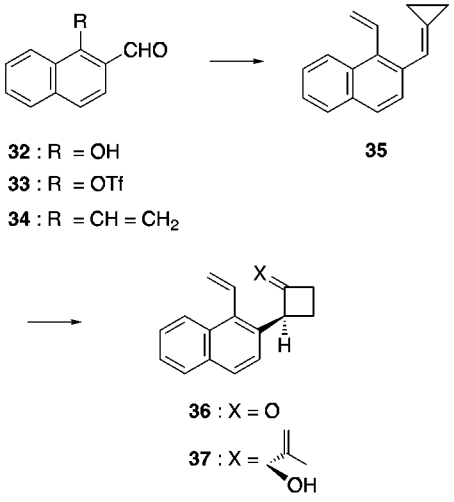
14 : R^1 = H ; R^2 = OMe
21 : R^1 = OMe ; R^2 = H
28 : R^1 = OTBS; R^2 = H

15 : R^1 = H ; R^2 = OMe
22 : R^1 = OMe ; R^2 = H
29 : R^1 = OTBS; R^2 = H

16 : R^1 = H ; R^2 = OMe
23 : R^1 = OMe ; R^2 = H
30 : R^1 = OTBS; R^2 = H

17 : R^1 = H ; R^2 = OMe
24 : R^1 = OMe ; R^2 = H
31 : R^1 = OTBS; R^2 = H

Scheme 2



32 : R = OH
33 : R = OTf
34 : R = CH = CH_2

35

36 : X = O
37 : X = OH

although the high *cis* selectivity was observed in the case of benzohydrindans (entries 14 and 15 in Table 1 and entries 7 and 8 in Table 2). In the case of the isomeric substrate **45**, the moderate *cis* (entry 4) and *trans* (entry 8) selectivities were observed.

From these results, it could be emphasized that the stereoselectivity in these cascade reactions markedly changes from the substrates **17** (Table 1), **24**, and **31** (Table 2) to **37** (Table 3), favoring *cis* stereochemistry under the same conditions, and the reverse stereoselectivities were observed in the isomeric substrates **41** and **45** compared with **31** and **37**, respectively.[15]

Finally, we have examined the catalytic process for this cascade reaction of **31** as a typical example using a catalytic amount of palladium(II) catalyst with some reoxidants (Table 4).

From these results, it became clear that this cascade reaction could be done catalytically with palladium(II) in rather higher yield compared to that with an equimolar amount of palladium(II) under comparable conditions, beside the additives (entry 8 in Table 2), making this process efficient, although the catalytic reaction proceeded slowly. Thus, we could disclose a novel palladium-mediated cascade reaction providing a general route to the stereoselective synthesis of benzo- and naphthohydrindans.

Experimental Section

General Procedure. All nonaqueous reactions were carried out under a positive atmosphere of argon in rigorously dried glassware unless indicated otherwise. Materials were obtained from commercial suppliers and used without further purification except when otherwise noted. Solvents were distilled prior to use: THF, Et_2O, hexane, and DME were freshly distilled from sodium benzophenone; CH_2Cl_2, $ClCH_2$-CH_2Cl, DMF, and triethylamine were distilled from CaH_2 and stored over 4 Å molecular sieves. The phrase "residue upon workup" refers to the residue obtained when the organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. Chromatography was carried out by using Merck 60 (230−400 mesh) or Cica 60 (spherical/40−100 μm) silica gel. Reactions and chromatography fractions were analyzed by employing precoated silica gel 60F254 plates (Merck).

General Experimental Procedures for Schemes 1 and 2. Experimental Details for the Synthesis of 17 *via* 12, 13, 14, and 16. 2-[[(Trifluoromethyl)sulfonyl]oxy]-4-methoxybenzaldehyde (12). To a stirred solution of 4-methoxysalicylaldehyde (**11**) (10.0 g, 65.7 mmol) and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) in pyridine (130 mL) was added trifluoromethanesulfonic anhydride (Tf_2O) (12.2 mL, 72.3 mmol) at 0 °C and stirring was continued for 1 h at room temperature. The resulting solution was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed sequentially with 10% HCl, saturated aqueous $NaHCO_3$, and NaCl. The residue upon workup was chromatographed on silica gel with hexane−AcOEt (9:1 v/v) as eluant to give the triflate **12** (17.8 g, 96%) as a colorless oil.

4-Methoxy-2-vinylbenzaldehyde (13). To a slurry of LiCl (1.44 g, 33.9 mmol) and $Pd(PPh_3)_4$ (159 mg, 0.226 mmol) in THF (110 mL) was added a solution of the triflate **12** (3.22 g, 11.3 mmol) and vinyltributyltin (4.0 mL, 13.6 mmol). The mixture was refluxed for 1 h with stirring, cooled to room temperature, and diluted with Et_2O (100 mL). The resulting

(15) The stereochemistry of these product in Tables 1−3 was confirmed by the observation of the definite NOE between methyl and methine protons at angular positions in these NMR spectra, which were observed at 1.07 and 3.05 ppm for **47**, 1.04 and 3.01 ppm for **49**, 1.01 and 3.12 ppm for **51**, 1.01 and 2.96 ppm for **53**, 1.14 and 3.13−3.22 ppm for **55i**, 1.03 and 2.92−3.01 ppm for **57i**, 1.19 and 3.32 ppm for **59**, and 1.15 and 3.07 ppm for **61**, respectively. In addition to these data, the general tendencies that the angular methyl group of this type of *trans*-benzohydrindan resonates at higher field than that of corresponding *cis* isomer in its NMR spectrum because of the shielding effect of aromatic ring have been recognized (see ref 6).

(16) Larock, R. C.; Hightower, T. R.; Kraus, G. A.; Hahn, P.; Zheng, D. *Tetrahedron Lett.* **1995**, *36*, 2423−2426. Under this condition, the enone **62** was produced in 22% yield beside the cascade products **54**−**57**. The structure of **62** was characterized as its deprotected derivative **62I**.

Scheme 3

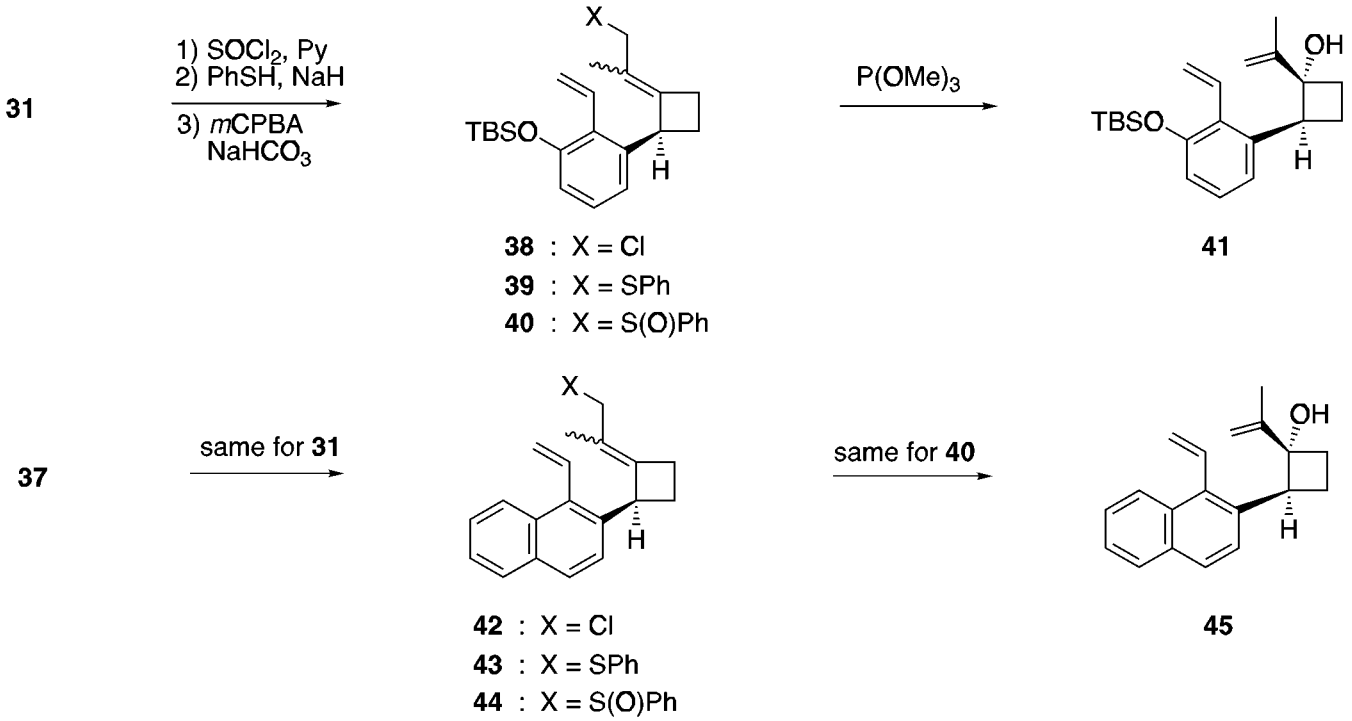
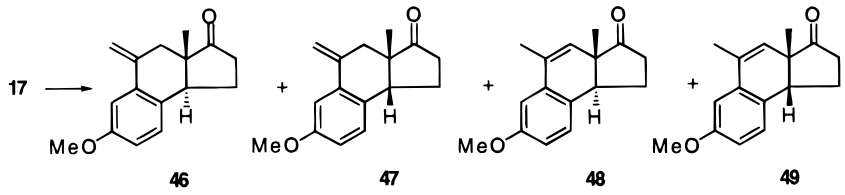


Table 1. Cascade Ring Expansion and Insertion Reaction of 17[a]



				product	
entry	mediator	solvent	time (h)	ratio (**46**:**47**:**48**:**49**)[b]	yield (%)[c]
1	$PdCl_2(CH_3CN)_2$	DME	14	0:0:50:50	53
2	$PdCl_2(CH_3CN)_2$	DME	10	0:0:50:50	55 (65)
3	$PdCl_2(CH_3CN)_2$	CH_3CN	10	0:0:50:50	22
4	$PdCl_2(CH_3CN)_2$	THF	14	0:0:75:25	50 (55)
5	$PdCl_2(CH_3CN)_2$	DMF	12	0:0:75:25	53
6	$PdCl_2(CH_3CN)_2$	DMF	10	0:0:75:25	46 (51)
7	$PdCl_2(CH_3CN)_2$	$ClCH_2CH_2Cl$	14	0:0:20:80	33 (42)
8	$Pd(OAc)_2(PPh_3)_2$	DME	144	0:0:50:50	21 (22)
9	$Pd(OAc)_2(PPh_3)_2$	CH_3CN	16	17:83:0:0	40 (44)
10	$Pd(OAc)_2(PPh_3)_2$	THF	144	0:0:40:60	16 (36)
11	$Pd(OAc)_2(PPh_3)_2$	DMF	144	0:0:50:50	30 (36)
12	$Pd(OAc)_2(PPh_3)_2$	$ClCH_2CH_2Cl$	32	0:0:25:75	35 (65)
13	$Pd(OAc)_2(AsPh_3)_2$	DME	24	17:83:0:0	30 (40)
14	$Pd(OAc)_2(AsPh_3)_2$	$ClCH_2CH_2Cl$	12	4:96:0:0	45
15	$Pd(OAc)_2(AsPh_3)_2$	$ClCH_2CH_2Cl$	10	5:95:0:0	53
16	$Pd(OAc)_2$	CH_3CN	21	0:0:9:91	15
17	$PdCl_2(PPh_3)_2$	CH_3CN	20	0:0:50:50	17 (69)

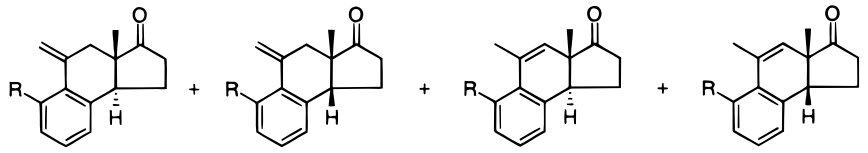
[a] The reaction was carried out under argon at room temperature by using an equimolar amount of mediator. [b] The isomer (**46**, **47**, **48**, and **49**) ratio was determined by ^1H NMR integration of angular methyl signals (δ 0.68 for **46**, δ 1.07 for **47**, δ 0.70 for **48**, and δ 1.04 for **49**). [c] All yields were isolated one. The yields in parentheses were based on recovered **17**.

solution was washed sequentially with water, 10% NH_4OH, water, and saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane−AcOEt (9:1 v/v) as eluant to give the vinylbenzaldehyde **13** (1.89 g, 90%) as a colorless oil.

4-(Cyclopropylidenemethyl)-3-vinylanisole (14). To a stirred suspension of NaH (98.4 mg, of 60% oil suspension, 2.46 mmol) in THF (7 mL) was added cyclopropyltriphenylphosphonium bromide (0.945 g, 2.46 mmol) at room temperature. After the mixture had been stirred for 10 h at 62 °C, a solution of the aldehyde **13** (200 mg, 1.23 mmol) in THF (3 mL) was added in 30 min, and stirring was continued for 1.5 h at the same temperature. The reaction mixture was diluted with water and extracted with Et_2O. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane−AcOEt (9:1 v/v) as eluant to give the cyclopropylidene derivative **14** (222 mg, 97%) as a colorless oil.

2-(4-Methoxy-2-vinylphenyl)cyclobutanone (16). To a stirred solution of the cyclopropylidene derivative **14** (49.3 mg, 0.265 mmol) in CH_2Cl_2 (2 mL) was added *m*-chloroperbenzoic acid (*m*CPBA) (51.9 mg, of 80% purity, 0.265 mmol) at 0 °C, and stirring was continued for 2 h at 0 °C. The reaction mixture was washed with saturated aqueous $NaHCO_2$ and NaCl. To a stirred solution of the residue upon workup in CH_2Cl_2 (2 mL) was added 10% HBF_4 (0.5 mL). The mixture

Table 2. Cascade Ring Expansion and Insertion Reaction of 24, 31, and 41[a]



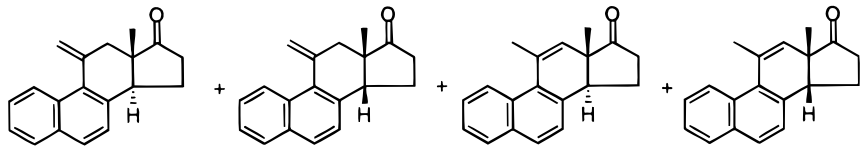
24 ⟶ **50** : R = OMe **51** : R = OMe **52** : R = OMe **53** : R = OMe

31, **41** ⟶ **54** : R = OTBS **55** : R = OTBS **56** : R = OTBS **57** : R = OTBS

					product	
entry	substrate	mediator	solvent	time (h)	ratio[b]	yield (%)[c]
1	**24**	$PdCl_2(CH_3CN)_2$	DME	10	0:0:62:38	71
2	**31**	$PdCl_2(CH_3CN)_2$	DME	10	0:0:60:40	81
3	**41**	$PdCl_2(CH_3CN)_2$	DME	10	0:0:35:65	90
4	**24**	$PdCl_2(CH_3CN)_2$	DMF	10	0:0:78:22	68
5	**31**	$PdCl_2(CH_3CN)_2$	DMF	10	0:0:61:39	62
6	**41**	$PdCl_2(CH_3CN)_2$	DMF	10	2:9:16:73	84
7	**24**	$Pd(OAc)_2(AsPh_3)_2$	$ClCH_2CH_2Cl$	10	0:100:0:0	34
8	**31**	$Pd(OAc)_2(AsPh_3)_2$	$ClCH_2CH_2Cl$	10	0:100:0:0	21 (68)
9	**41**	$Pd(OAc)_2(AsPh_3)_2$	$ClCH_2CH_2Cl$	10	93:4:3:0	35 (95)

[a] The reaction was carried out under argon at room temperature by using an equimolar amount of mediator. [b] The product ratios for entries 1, 4, and 7 corresponded to **50**:**51**:**52**:**53** and were determined by ^{1}H-NMR integration of angular methyl signals (δ 0.61 for **50**, δ 1.01 for **51**, δ 0.67 for **52**, and δ 1.01 for **53**). For entries 2, 3, 5, 6, 8, and 9, the initial products were subjected to deprotection and analyzed. So, these product ratios corresponded to **54i** (R = OH), **55i** (R = OH), **56i** (R = OH), and **57i** (R = OH) and were determined by ^{1}H-NMR integration of angular methyl signals (δ 0.61 for **54i**, δ 1.14 for **55i**, δ 0.69 for **56i**, and δ 1.03 for **57i**). [c] All yields were isolated one. The yields in parentheses were based on recovered **31** and **41**.

Table 3. Cascade Ring Expansion and Insertion Reaction of 37 and 45[a]



37, **45** ⟶ **58** **59** **60** **61**

					product	
entry	substrate	mediator	solvent	time (h)	ratio[b]	yield (%)[c]
1	**37**	$PdCl_2(CH_3CN)_2$	DME	10	23:23:14:40	81
2	**45**	$PdCl_2(CH_3CN)_2$	DME	10	22:26:20:32	63
3	**37**	$PdCl_2(CH_3CN)_2$	DMF	10	4:15:48:33	56
4	**45**	$PdCl_2(CH_3CN)_2$	DMF	10	2:9:16:73	79
5[d]	**37**	$Pd(OAc)_2(AsPh_3)_2$	$ClCH_2CH_2Cl$			
6[d]	**45**	$Pd(OAc)_2(AsPh_3)_2$	$ClCH_2CH_2Cl$			
7	**37**	$Pd(OAc)_2$	$ClCH_2CH_2Cl$	10	0:83:0:17	69
8	**45**	$Pd(OAc)_2$	$ClCH_2CH_2Cl$	10	50:20:26:4	46

[a] The reaction was carried out under argon at room temperature by using an equimolar amount of mediator. [b] The isomer ratio was determined by ^{1}H-NMR integration of angular methyl signals (δ 0.55 for **58**, δ 1.19 for **59**, δ 0.67 for **60**, δ 1.15 for **61**, respectively). [c] All yields were isolated one. [d] Unidentified complex mixture was formed.

was stirred for 0.5 h at room temperature and washed with saturated aqueous $NaHCO_3$ and NaCl. The residue upon workup was chromatographed on silica gel with hexane−AcOEt (95:5 v/v) as eluant to give the cyclobutanone **16** (44.7 mg, 83%) as a colorless oil.

(1*S,2*S**)-1-Isopropenyl-2-(4-methoxy-2-vinylphenyl-)cyclobutanol (17).** To a stirred suspension of $CeCl_3$ (3.80 g, 15.4 mmol) in THF (45 mL) was added a 1.0 M solution of isopropenylmagnesium bromide in THF (15.4 mL, 15.4 mmol) at −78 °C. After stirring had been continued for 1 h, a solution of the cyclobutanone **16** (1.04 g, 5.14 mmol) in THF (15 mL) was added dropwise to this reaction mixture at the same temperature and the temperature was then increased to room temperature in 2 h. The reaction mixture was treated with saturated aqueous NH_4Cl and extracted with Et_2O. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane−AcOEt (98:2 v/v) as eluant to give the cyclobutanol **17** (1.20 mg, 95%) as a colorless oil.

Characterization Data for Schemes 1 and 2. 12: IR (neat) 1700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.93 (3H, s), 6.87 (1H, d, J = 2.2 Hz), 7.03 (1H, dd, J = 2.2 and 8.8 Hz), 7.95 (1H, d, J = 8.8 Hz), 10.13 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 56.2, 108.3, 114.2, 116.5, 121.8, 132.5, 151.3, 165.5, 185.6; MS *m*/*z* 283 (M^+); HRMS calcd for $C_9H_7F_3O_5S$ 283.9966 (M^+), found 283.9966.

13: IR (neat) 1690 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.91 (3H, s), 5.50 (1H, dd, J = 1.5 and 11.0 Hz), 5.70 (1H, dd, J = 1.5 and 17.0 Hz), 6.93 (1H, dd, J = 2.6 and 8.4 Hz), 7.02 (1H, d, J = 2.6 Hz), 7.56 (1H, dd, J = 11.0 and 17.0 Hz), 7.79 (1H, d, J = 8.4 Hz), 10.15 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 54.9, 111.7, 112.9, 118.5, 126.1, 133.0, 133.6, 142.2, 190.3; MS *m*/*z* 162 (M^+); HRMS calcd for $C_{10}H_{10}O_2$ 162.0680 (M^+), found 162.0681.

14: IR (neat) 1620 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.14−1.19 (2H, m), 1.34−1.39 (2H, m), 3.83 (3H, s), 5.33 (1H, dd, J = 1.5 and 11.0 Hz), 5.63 (1H, dd, J = 1.5 and 21.0 Hz), 6.83 (1H, dd, J = 2.6 and 8.4 Hz), 6.97 (1H, d, J = 2.6 Hz), 6.98 (1H, br s), 7.10 (1H, dd, J = 11.0 and 21.0 Hz), 7.67 (1H, d, J = 8.4 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 1.0, 4.0, 55.2, 110.8, 114.1, 114.8, 116.2, 123.9, 127.9, 129.0, 135.0, 136.9, 158.7;

Table 4. Catalytic Process for Cascade Ring Expansion and Insertion Reaction of 31[a]

31 → 54 + 55 + 56 + 57

				product	
entry	additive	solvent	time (day)	ratio (**54**:**55**:**56**:**57**)[b]	yield (%)[c]
1	$Cu(OAc)_2$	$ClCH_2CH_2Cl$	37	8:92:0:0	77
2[9a]	$Cu(OAc)_2$	$ClCH_2CH_2Cl$	33	12:86:1:1	66
3[9b,d]	benzoquinone	$ClCH_2CH_2Cl$	36	2:98:0:0	77
4[16]		DMSO	25	34:64:0:2	44

[a] The reaction was carried out under an argon (entries 1 and 3) or oxygen (entries 2 and 4) atmosphere at room temperature by using 0.1 equimolar amount of $Pd(OAc)_2(AsPh_3)_2$ as catalyst and 2 equimolar amounts of additives (entries 1−3). [b] The product ratios corresponded to **54i**:**55i**:**56i**:**57i**. [c] The yields were isolated one.

MS *m*/*z* 186 (M^+); HRMS calcd for $C_{13}H_{14}O$ 186.1044 (M^+), found 186.1045.

16: IR (neat) 1780 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.05−2.19 (1H, m), 2.45−2.58 (1H, m), 2.95−3.09 (1H, m), 3.13−3.27 (1H, m), 3.81 (3H, s), 4.66−4.73 (1H, m), 5.33 (1H, dd, *J* = 1.1 and 11.0 Hz), 5.63 (1H, dd, *J* = 1.1 and 17.0 Hz), 6.80 (1H, dd, *J* = 2.8 and 8.5 Hz), 6.88 (1H, dd, *J* = 11.0 and 17.0 Hz), 7.03 (1H, d, *J* = 2.8 Hz), 7.22 (1H, d, *J* = 8.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 18.7, 44.4, 55.2, 61.6, 111.7, 113.4, 116.7, 126.8, 127.8, 134.6, 137.9, 158.8, 208.8; MS *m*/*z* 186 (M^+); HRMS calcd for $C_{13}H_{14}O$ 186.1044 (M^+), found 186.1044.

17: IR (neat) 3500, 1620 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.51 (1H, s), 1.83 (3H, s), 1.83−1.91 (1H, m), 2.04−2.41 (1H, m), 2.37−2.47 (2H, m), 3.83 (3H, s), 3.95 (1H, t, *J* = 8.5 Hz), 4.84 (1H, br s), 5.00 (1H, br s), 5.25 (1H, dd, *J* = 1.0 and 7.3 Hz), 5.55 (1H, dd, *J* = 1.0 and 16.0 Hz), 6.89 (1H, dd, *J* = 2.9 and 9.0 Hz), 6.91 (1H, dd, *J* = 7.3 and 16.0 Hz), 7.00 (1H, d, *J* = 2.9 Hz), 7.42 (1H, d, *J* = 9.0 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 18.7, 20.8, 31.0, 43.9, 55.1, 80.6, 110.1, 111.9, 113.2, 116.4, 128.0, 129.5, 135.4, 139.4, 148.6, 158.5; MS *m*/*z* 244 (M^+); HRMS calcd for $C_{16}H_{20}O_2$ 244.1462 (M^+), found 244.1463.

19: yield 100%; mp 50 °C (from Et_2O); IR ($CHCl_3$) 1700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.97 (3H, s), 7.31 (1H, dd, *J* = 1.0 and 7.8 Hz), 7.47 (1H, t, *J* = 7.8 Hz), 7.54 (1H, dd, *J* = 1.0 and 7.8 Hz), 10.26 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 56.54, 116.7, 118.7, 120.9, 121.3, 129.7, 151.9, 186.8; MS *m*/*z* 151 (M^+ −133). Anal. Calcd for $C_9H_7F_3O_5S$: C, 38.04; H, 2.48; S, 11.28. Found: C, 38.27; H, 2.52; S, 11.40.

20: yield 91%; mp 59 °C (from Et_2O); IR ($CHCl_3$) 1690 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.90 (3H, s), 5.35 (1H, dd, *J* = 1.6 and 18.0 Hz), 5.77 (1H, dd, *J* = 1.6 and 11.0 Hz), 7.05 (1H, dd, *J* = 11.0 and 18.0 Hz), 7.09 (1H, dd, *J* = 1.0 and 8.6 Hz), 7.37 (1H, t, *J* = 8.6 Hz), 7.54 (1H, dd, *J* = 1.0 and 8.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 55.37, 114.6, 119.8, 123.6, 128.4, 131.3, 135.2, 157.3, 192.0; MS *m*/*z* 162 (M^+). Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.06; H, 6.21. Found: C, 74.01; H, 6.29.

21: yield 86%; oil; IR (neat) 1580 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.13−1.18 (2H, m), 1.36−1.42 (2H, m), 3.82 (3H, s), 5.51 (1H, dd, *J* = 2.0 and 17.0 Hz), 5.59 (1H, dd, *J* = 2.0 and 11.0 Hz), 6.75 (1H, br s), 6.85 (1H, dd, *J* = 11.0 and 17.0 Hz), 7.09 (1H, dd, *J* = 1.1 and 7.0 Hz), 7.18 (1H, t, *J* = 7.0 Hz), 7.42 (1H, dd, *J* = 1.1 and 7.0 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 0.9, 4.0, 55.6, 108.6, 116.8, 119.4, 120.8, 125.2, 127.7, 131.1, 133.1, 137.4, 157.6; MS *m*/*z* 186 (M^+); HRMS calcd for $C_{13}H_{14}O$ 186.1044 (M^+), found 186.1050.

23: yield 55%; oil; IR (neat) 1780, 1580 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.12−2.19 (1H, m), 2.47−2.49 (1H, m), 3.04−3.20 (2H, m), 3.82 (3H, s), 4.86 (1H, t, *J* = 9.4 Hz), 5.53 (1H, dd, *J* = 1.5 and 18.0 Hz), 5.54 (1H, dd, *J* = 1.5 and 11.0 Hz), 6.73 (1H, dd, *J* = 11.0 and 18.0 Hz), 6.80 (1H, d, *J* = 7.5 Hz), 6.92 (1H, d, *J* = 7.5 Hz), 7.22 (1H, t, *J* = 7.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 19.6, 44.5, 55.4, 62.5, 109.2, 119.3, 120.1, 126.7, 128.2, 131.2, 135.9, 157.6, 208.7; MS *m*/*z* 202 (M^+). Anal. Calcd for $C_{13}H_{14}O$: C, 77.13; H, 6.99. Found: C, 77.11; H, 7.08.

24: yield 83%; oil; IR (neat) 3400 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.85 (3H, br s), 1.88−2.19 (2H, m), 2.31−2.48 (2H, m), 3.82 (3H, s), 4.17 (1H, dd, *J* = 4.8 and 16.0 Hz), 4.83 (1H, br s), 5.01 (1H, br s), 5.44 (1H, dd, *J* = 2.2 and 17.0 Hz), 5.50 (1H, dd, *J* = 2.2 and 11.0 Hz), 6.65 (1H, dd, *J* = 11.0 and 17.0 Hz), 6.83 (1H, dd, *J* = 1.0 and 7.5 Hz), 7.22 (1H, dd, *J* = 1.0 and 7.5 Hz), 7.30 (1H, t, *J* = 7.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 18.9, 21.7, 31.8, 44.5, 55.7, 80.6, 109.4, 110.1, 120.6, 120.8, 128.0, 128.2, 131.6, 138.1, 148.6, 157.7; MS *m*/*z* 244 (M^+). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.72; H, 8.26. Found: C, 78.72; H, 8.06.

26: yield 98%; oil; IR (neat) 1705 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.31 (6H, s), 1.01 (9H, s), 7.26 (1H, dd, *J* = 1.5 and 7.8 Hz), 7.37 (1H, t, *J* = 7.8 Hz), 7.53 (1H, dd, *J* = 1.5 and 7.8 Hz), 10.21 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ −4.7, 18.4, 25.5, 116.5, 120.5, 122.1, 126.5, 128.8, 129.8, 148.8, 186.8; MS *m*/*z* 327 (M^+ −57). Anal. Calcd for $C_{14}H_{18}F_3O_5SSi$: C, 46.04; H, 5.31; S, 9.45. Found: C, 46.24; H, 5.41; S, 9.36.

27: yield 50%; oil; IR (neat) 1700 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.20 (6H, s), 1.00 (9H, s), 5.28 (1H, dd, *J* = 1.1 and 16.0 Hz), 5.72 (1H, dd, *J* = 1.1 and 11.0 Hz), 6.99 (1H, dd, *J* = 11.0 and 16.0 Hz), 7.02 (1H, dd, *J* = 1.2 and 7.8 Hz), 7.26 (1H, t, *J* = 7.8 Hz), 7.53 (1H, dd, *J* = 1.2 and 7.8 Hz), 10.19 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ −4.2, 18.2, 26.0, 121.3, 123.9, 124.1, 128.2, 129.7, 134.2, 136.0, 154.0, 192.8; MS *m*/*z* 262 (M^+). Anal. Calcd for $C_{15}H_{22}O_2Si$: C, 74.04; H, 6.23. Found: C, 74.38; H, 6.04.

28: yield 84%; oil: IR (neat) 1620 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.22 (6H, s), 1.00 (9H, s), 1.13−1.20 (2H, m), 1.37−1.45 (2H, m), 5.45 (1H, dd, *J* = 2.3 and 17.9 Hz), 5.58 (1H, dd, *J* = 2.3 and 11.6 Hz), 6.71 (1H, d, *J* = 8.1 Hz), 6.84 (1H, dd, *J* = 11.6 and 17.9 Hz), 7.09 (1H, br s), 7.10 (1H, t, *J* = 8.1 Hz), 7.44 (1H, d, *J* = 8.1 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ −4.1, 0.8, 4.0, 18.3, 25.8, 117.2, 117.4, 119.9, 120.8, 124.6, 127.4, 128.9, 132.0, 137.7, 153.7; MS *m*/*z* 286 (M^+). Anal Calcd for $C_{18}H_{26}OSi$: C, 75.46; H, 9.15. Found: C, 75.22; H, 8.89.

30: yield 86%; oil; IR (neat) 1790, 1630 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.19 (6H, s), 0.99 (9H, s), 2.08−2.22 (1H, m), 2.40−2.54 (1H, m), 2.96−3.09 (1H, m), 3.11−3.25 (1H, m), 4.79−4.88 (1H, m), 5.43 (1H, dd, *J* = 2.1 and 18.0 Hz), 5.50 (1H, dd, *J* = 2.1 and 11.4 Hz), 6.70 (1H, dd, *J* = 11.4 and 18.0 Hz), 6.72 (1H, d, *J* = 7.8 Hz), 6.90 (1H, d, *J* = 7.8 Hz), 7.10 (1H, t, *J* = 7.8 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ −4.1, 18.2, 19.9, 25.8, 44.7, 63.0, 118.0, 120.0, 120.3, 128.0, 130.0, 132.4, 136.3, 153.7, 209.3; MS *m*/*z* 302 (M^+); HRMS calcd for $C_{18}H_{26}O_2Si$ 302.1701 (M^+), found 302.1729.

31: yield 74%; oil; IR (neat) 3500, 1640 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.17 (3H, s), 0.18 (3H, s), 0.97 (9H, s), 1.65 (1H, br s), 1.84 (3H, br s), 1.92−2.16 (2H, m), 2.29−2.44 (2H, m), 4.12−4.19 (1H, m), 4.81−4.84 (1H, m), 5.00 (1H, br s), 5.34 (1H, dd, *J* = 2.1 and 17.9 Hz), 5.47 (1H, dd, *J* = 2.1 and 11.4 Hz), 6.60 (1H, dd, *J* = 11.4 and 17.9 Hz), 6.75 (1H, dd, *J* = 2.6 and 6.9 Hz), 7.17 (1H, t, *J* = 6.9 Hz), 7.19 (1H, dd, *J* = 2.6 and 6.9 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ −4.2, −4.1, 18.2, 18.9, 21.7, 25.8, 31.8, 44.7, 80.6, 110.0, 118.0, 120.7, 121.2, 127.6, 131.3, 132.5, 138.2, 148.6, 153.6; MS *m*/*z* 344 (M^+). Anal. Calcd for $C_{21}H_{32}O_2Si$: C, 73.20; H, 9.36. Found: C, 72.82; H, 9.12.

34: yield 58% (from **32**); mp 74 °C (from MeOH); IR ($CHCl_3$) 1680 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.49 (1H, dd, *J* = 2.1 and 18.2 Hz), 6.01 (1H, dd, *J* = 2.1 and 11.8 Hz), 7.37 (1H, dd, *J* = 11.8 and 18.2 Hz), 7.54−7.66 (2H, m), 7.83 (1H, d, *J* = 8.6 Hz), 7.87 (1H, d, *J* = 8.6 Hz), 7.99 (1H, d, *J* = 8.6 Hz), 8.18 (1H, d, *J* = 8.6 Hz), 10.44 (1H, s); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 122.9, 125.9, 126.1, 127.0, 128.1, 128.5, 128.9, 130.6, 131.4, 131.6, 135.8, 143.4, 192.8; MS *m*/*z* 182 (M^+). Anal. Calcd for $C_{13}H_{10}O$: C, 85.69; H, 5.53. Found: C, 85.84; H, 5.81.

35: yield 86%; oil; IR (neat) 1620 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.14−1.23 (2H, m), 1.46−1.55 (2H, m), 5.45 (1H, dd, *J* = 2.1 and 18.0 Hz), 5.82 (1H, dd, *J* = 2.1 and 11.8 Hz), 7.13 (1H, dd, *J* = 11.8 and 18.0 Hz), 7.25 (1H, s), 7.38−7.49 (2H, m), 7.71 (1H, d, *J* = 8.6 Hz), 7.77 (1H, d, *J* = 8.6 Hz), 8.03 (1H, d, *J* = 8.6 Hz), 8.10 (1H, d, *J* = 8.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 0.7, 4.4, 117.2, 122.4, 124.4, 125.4, 125.5, 125.7, 125.8, 126.1, 127.3, 128.2, 132.2, 132.7, 132.9, 133.8; MS *m*/*z* 206 (M^+); HRMS calcd for $C_{16}H_{14}$ 206.1095 (M^+), found 206.1098.

36: yield 80%; oil; IR (neat) 1780 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.17−2.29 (1H, m), 2.46−2.61 (1H, m), 3.02−3.14 (1H,

m), 3.17−3.32 (1H, m), 4.98−5.08 (1H, m), 5.45 (1H, dd, J = 2.1 and 18.2 Hz), 5.78 (1H, dd, J = 2.1 and 11.8 Hz), 7.18 (1H, dd, J = 11.8 and 18.2 Hz), 7.39 (1H, d, J = 8.6 Hz), 7.40−7.51 (2H, m), 7.72−7.82 (2H, m), 8.01−8.09 (1H, m); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 19.6, 45.0, 63.4, 122.3, 124.7, 125.8, 125.9, 126.3, 128.0, 128.2, 131.5, 132.0, 132.6, 134.0, 135.6, 209.2; MS m/z 222 (M^+). Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.17; H, 6.31.

37: yield 82%; oil; IR (neat) 3400 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.52 (1H, s), 1.84 (3H, s), 2.01−2.11 (1H, m), 2.12−2.21 (1H, m), 2.40−2.59 (2H, m), 4.30 (1H, t, J = 8.7 Hz), 4.81 (1H, s), 4.97 (1H, s), 5.32 (1H, dd, J = 2.3 and 17.6 Hz), 5.74 (1H, dd, J = 2.3 and 11.2 Hz), 6.99 (1H, dd, J = 11.2 and 17.6 Hz), 7.12−7.27 (1H, m), 7.40−7.47 (2H, m), 7.76−7.83 (3H, m), 8.05−8.12 (1H, m); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 18.9, 21.7, 37.5, 44.8, 81.4, 110.0, 122.1, 125.5, 126.0, 126.2, 126.3, 127.2, 128.1, 131.9, 132.6, 133.5, 134.5, 136.7, 148.7; MS m/z 264 (M^+). Anal. Calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 85.95; H, 7.74.

General Experimental Procedures for Scheme 3. Experimental Details for the Synthesis of 41 *via* 38−40. 1-[3-(*tert*-Butyldimethylsiloxy)-2-vinylphenyl]-2-(1-methyl-2-thiophenylethylidene)cyclobutane (39). To a stirred solution of the cyclobutanol **31** (1.11 g, 3.22 mmol) and pyridine (0.52 mL, 6.4 mmol) in THF (30 mL) was added thionyl chloride (0.31 mL, 4.2 mmol) at 0 °C and stirring was continued for 1 h at room temperature. The reaction mixture was diluted with water and extracted with Et_2O. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was dissolved in DMF (5 mL). To a stirred suspension of NaH (0.26 g, of 60% oil suspension, 6.5 mmol) was added thiophenol (0.83 mL, 8.1 mmol) at 0 °C and stirring was continued. After 10 min, to the reaction mixture was added a solution of the residue at 0 °C and stirring was continued for 6 h at room temperature. The resulting solution was diluted with water and extracted with Et_2O. The combined extracts were washed with 10% aqueous NaOH and saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane−AcOEt (99:1 v/v) as eluant to give the phenyl sulfide **39** (822 mg, 58%) as a colorless oil.

1-[3-(*tert*-Butyldimethylsiloxy)-2-vinylphenyl]-2-[1-methyl-2-(phenylsulfinyl)ethylidene]cyclobutane (40). To a stirred solution of the sulfide **39** (57.9 mg, 0.133 mmol) in CH_2Cl_2 (3 mL) were added $NaHCO_3$ (22.3 mg, 0.266 mmol) and *m*-chloroperbenzoic acid (*m*-CPBA) (28.6 mg, 80%, 0.133 mmol) at −78 °C and stirring was continued for 1 h at the same temperature. The temperature was increased to 0 °C in 1 h. The reaction mixture was diluted water and extracted with Et_2O. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane−AcOEt (92:8 v/v) to give the sulfoxide (54.6 mg, 91%) as a colorless oil.

(1*R,2*S**)-2-[3-(*tert*-Butyldimethylsiloxy)-2-vinylphenyl]-1-isopropenylcyclobutan-1-ol (41).** A solution of the sulfoxide **40** (775 mg, 1.71 mmol) and trimethyl phosphite (2.2 mL, 19 mmol) in methanol (60 mL) was refluxed for 9 h. The solvent was evaporated and the residue was chromatographed on silica gel with hexane−AcOEt (98.5:1.5 v/v) to give the cyclobutanol **41** (440 mg, 75%) as a colorless oil.

Characterization Data for Scheme 3. 39 (*E*:*Z*/19:81): IR (neat) 1630 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.17 (3H, s), 0.19 (3H, s), 0.98 (9H, s), 1.38−1.42 (2.43H, m), 1.62−1.83 (1.57H, m), 2.19−2.36 (1H, m), 2.37−2.63 (1.81H, m), 2.63−2.72 (0.19H, m), 3.02 (0.19H, br d, J = 12.6 Hz), 3.31−3.41 (1H, m), 3.63 (0.81H, br d, J = 12.6 Hz), 4.03−4.13 (0.19H, m), 4.26−4.34 (0.81H, m), 5.32 (0.19H, dd, J = 2.1 and 18.3Hz), 5.37 (0.81H, dd, J = 2.1 and 17.3 Hz), 5.43 (0.19H, dd, J = 2.1 and 11.7 Hz), 5.45 (0.81H, dd, J = 2.1 and 11.9 Hz), 6.56−6.71 (2.81H, m), 6.92−6.98 (1H, m), 7.06 (0.19H, t, J = 7.8 Hz), 7.15−7.36 (3.38H, m), 7.41−7.47 (1.62H, m); MS m/z 436 (M^+): HRMS calcd for $C_{27}H_{36}OSSi$ 436.2254 (M^+), found 436.2258.

40 (*E*:*Z*/20:80): IR (neat) 1630 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.25−0.35 (6H, m), 0.95−1.06 (9H, m), 1.34−1.43 (2.4H, m), 1.64−1.79 (1.6H, m), 1.79−2.07 (0.4H, m), 2.08−2.42 (1.6H, m), 2.42−2.73 (1H, m), 3.03 (0.1H, br d, J = 12.0 Hz), 3.14 (0.1H, br d, J = 12.0 Hz), 3.17 (0.1H, br d, J = 12.0 Hz), 3.30 (0.1H, br d, J = 12.0 Hz), 3.39 (0.4H, br d, J = 12.0 Hz), 3.47 (0.4H, br d, J = 12.0 Hz), 3.63 (0.8H, br d, J = 11.1 Hz), 4.27−4.43 (1H, m), 5.19 (0.1H, dd, J = 18.0 and 2.4 Hz), 5.30−5.41 (1H, m), 5.43−5.52 (0.9H, m), 6.48 (0.1H, dd, J = 18.0 and 11.4 Hz), 6.61−6.78 (2.5H, m), 6.82−6.91 (0.4H, m), 6.97−7.13 (1H, m), 7.26−7.75 (5H, m); MS m/z 327 (M^+ − 57); HRMS calcd for $C_{21}H_{31}OSi$ (M^+ − 57) 327.2144, found 327.2136.

41: IR (neat) 1620, 3480 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.15 (6H, s), 0.97 (9H, s), 1.27 (3H, br s), 1.89−2.00 (2H, m), 2.02−2.14 (1H, m), 2.21 (1H, br s), 2.38−2.48 (1H, m), 3.97 (1H, t, J = 9.6 Hz), 4.87 (1H, br s), 4.99 (1H, br s), 5.59 (1H, dd, J = 2.4 and 11.4 Hz), 5.62 (1H, dd, J = 2.4 and 17.9 Hz), 6.71 (1H, br d, J = 7.8 Hz), 6.79 (1H, br d, J = 7.8 Hz), 6.87 (1H, dd, J = 11.4 and 17.9 Hz), 7.05 (1H, t, J = 7.8 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ −4.1, −4.0, 17.7, 18.2, 18.4, 25.9, 31.7, 50.3, 82.8, 111.5, 118.0, 120.4, 121.0, 127.3, 130.0, 133.2, 139.7, 145.1, 153.0; MS m/z 344 (M^+). Anal. Calcd for $C_{21}H_{30}OSi$: C, 73.20; H, 9.36. Found: C, 73.13; H, 9.23.

43 (*E*:*Z*/69:31): yield 60% (from **37**); oil; IR (neat) 1630 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.34 (2.07H, s), 1.73 (0.93H, s), 1.75−1.83 (1H, m), 2.26−2.40 (1H, m), 2.44−2.86 (2H, m), 2.95 (0.31H, d, J = 14.0 Hz), 3.28 (0.31H, d, J = 14.0 Hz), 3.37 (0.69H, d, J = 13.0 Hz), 3.64 (0.69H, d, J = 13.0 Hz), 4.35 (0.31H, m), 4.54 (0.69H, m), 5.25−5.38 (1H, m), 5.67−5.77 (1H, m), 6.91−7.09 (1H, m), 7.10−7.54 (8H, m), 7.61−7.75 (1H, m), 7.76−7.82 (1H, m), 8.03−8.10 (1H, m); MS m/z 356 (M^+); HRMS calcd for $C_{25}H_{24}S$ (M^+) 356.1599, found 356.1587.

44 (*E*:*Z*/69:31): yield 98%; oil; IR (neat) 1630 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.28 (1.38H, s), 1.30 (0.69H, s), 1.61−2.18 (1.93H, m), 2.18−2.46 (1H, m), 2.51−2.91 (2H, m), 2.91−3.24 (0.62H, m), 3.34−3.49 (0.69H, m), 3.56−3.66 (0.69H, m), 3.85−4.25 (0.31H, m), 4.50−4.66 (0.69H, m), 5.17−5.38 (1H, m), 5.63−5.80 (1H, m), 6.79−7.85 (11H, m), 7.86−8.14 (1H, m); MS m/z 355 (M^+ − 17); HRMS calcd for $C_{25}H_{23}S$ (M^+ −17) 355.1521, found 355.1499.

45: yield 71%; oil; IR (neat) 3000 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.19 (3H, s), 2.00−2.24 (4H, m), 2.48−2.57 (1H, m), 4.15 (1H, t, J = 9.0 Hz), 4.90 (1H, s), 5.08 (1H, s), 5.52 (1H, dd, J = 2.6 and 18.1 Hz), 5.87 (1H, dd, J = 2.6 and 11.5 Hz), 7.25 (1H, dd, J = 11.5 and 18.1 Hz), 7.37−7.50 (3H, m), 7.71 (1H, d, J = 9.1 Hz), 7.76−7.85 (1H, m), 8.10−8.18 (1H, m); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.9, 18.5, 32.0, 50.8, 82.9, 111.8, 122.2, 125.1, 125.3, 125.9, 126.1, 127.0, 128.1, 131.6, 132.5, 134.9, 135.4, 145.1; MS m/z 264 (M^+) HRMS calcd for $C_{19}H_{20}O$ 264.1514 (M^+), found 264.1553.

General Procedure for Cascade Ring Expansion and Insertion Reaction. Procedure for the Reaction of 17 (entry 1 in Table 1). A slurry of the cyclobutanol **17** (10.3 mg, 0.042 mmol) and $PdCl_2(CH_3CN)_2$ (10.9 mg, 0.042 mmol) in DME (0.5 mL) was stirred for 14 h at room temperature. After evaporation of the solvent, the residue was passed through a short pad of silica gel with Et_2O as eluant to give a mixture of the benzohydrindans **48** and **49** (5.5 mg, 53%) as a colorless oil.

Characterization Data for Products in Tables 1−3. Samples for analysis were prepared by careful column chromatography of all products in the tables on silica gel using each solvent systems.

46 + **47** (ratio of 6:94, entry 9 in Table 1, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.68 (0.18H, s), 1.07 (2.82H, s), 1.78−1.91 (1.06H, m), 2.08 (0.94H, d, J = 14.0 Hz), 2.28−2.75 (4H, m), 2.93−3.07 (1H, m), 3.83 (3H, s), 5.06 (0.94H, s), 5.12 (0.06H, s), 5.52 (0.94H, s), 5.75 (0.06H, s), 6.82−6.89 (1H, m), 7.04−7.16 (1.94H, m), 7.21−7.24 (0.06H, m); MS m/z 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1306 (M^+), found 242.1297.

47 (entry 15 in Table 1, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.07 (3H, s), 1.79−1.93 (1H, m), 2.08 (1H, d, J = 14.0 Hz), 2.28−2.48 (3H, m), 2.54 (1H, d, J = 14.0 Hz), 3.05 (1H, dd, J = 6.0 and 10.0 Hz), 3.83 (3H, s), 5.06 (1H, s), 5.52 (1H, s), 6.88 (1H, dd, J = 2.2 and 8.0 Hz), 7.10 (1H, d, J = 2.2 Hz), 7.15 (1H, d, J = 8.0 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 20.4, 29.4, 36.3, 37.5, 47.0, 48.3, 55.4, 108.7, 111.9, 115.3, 129.9, 130.2, 134.7, 139.8, 158.2,

221.4; MS m/z 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1306 (M^+), found 242.1321.

48 (entry 1 in Table 1, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.70 (3H, s), 1.95−2.09 (1H, m), 2.06 (3H, s), 2.25−2.39 (1H, m), 2.44 (1H, dd, J = 8.5 and 18.0 Hz), 2.67 (1H, dd, J = 8.5 and 18.0 Hz), 3.09 (1H, dd, J = 5.0 and 12.0 Hz), 3.84 (3H, s), 6.25 (1H, s), 6.81 (1H, dd, J = 2.2 and 8.2 Hz), 6.90 (1H, d, J = 2.2 Hz), 7.09 (1H, d, J = 8.2 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.8, 19.6, 19.8, 37.0, 46.2, 49.3, 55.5, 111.2, 111.3, 125.1, 129.1, 130.0, 133.0, 137.8, 158.6, 216.0; MS *m/z* 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1306 (M^+), found 242.1299.

49 (entry 1 in Table 1, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, s), 1.60−1.77 (1H, m), 2.07 (3H, s), 2.09−2.20 (1H, m), 2.23−2.33 (2H, m), 3.01 (1H, dd, J = 6.5 and 11.0 Hz), 3.84 (3H, s), 5.25 (1H, s), 6.81 (1H, dd, J = 2.2 and 7.9 Hz), 6.92 (1H, d, J = 2.2 Hz), 7.16 (1H, d, J = 7.9 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 19.5, 21.4, 29.0, 36.6, 47.4, 52.5, 55.4, 110.4, 112.3, 125.2, 128.8, 129.0, 132.1, 133.4, 158.8, 221.4; MS *m/z* 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1306 (M^+), found 242.1304.

50 + **51** (ratio of 20:80, entry 7 in Table 2, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.61 (0.6H, s), 1.01 (2.4H, s), 1.75−2.72 (6H, m), 3.08−3.14 (1H, m), 3.86 (3H, s), 5.34 (0.8H, s), 5.41 (0.2H, s), 5.96 (0.8H, s), 6.09 (0.2H, s), 6.77−6.93 (2H, m), 7.10−7.24 (1H, m); MS *m/z* 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1306 (M^+), found 242.1305.

51 (entry 7 in Table 2, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.01 (3H, s), 1.76−1.94 (1H, m), 2.01 (1H, d, J = 11.0 Hz), 2.26−2.48 (3H, m), 2.52 (1H, d, J = 11.0 Hz), 3.12 (1H, dd, J = 5.4 and 9.5 Hz), 3.86 (3H, s), 5.34 (1H, s), 5.96 (1H, s), 6.80 (1H, d, J = 7.4 Hz), 6.86 (1H, d, J = 7.4 Hz), 7.21 (1H, t, J = 7.4 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 20.8, 29.7, 37.6, 39.5, 47.8, 48.1, 55.5, 108.9, 118.0, 121.5, 123.1, 128.2, 135.4, 140.4, 157.4, 220.0; MS *m/z* 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1306 (M^+), found 242.1320.

52 (entry 1 in Table 2, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.67 (3H, s), 1.91−2.07 (1H, m), 2.22 (3H, s), 2.24−2.38 (1H, m), 2.44 (1H, dd, J = 8.5 and 16.0 Hz), 2.66 (1H, dd, J = 8.5 and 16.0 Hz), 3.01 (1H, dd, J = 5.5 and 12.0 Hz), 3.82 (3H, s), 6.17 (1H, s), 6.80 (1H, d, J = 7.3 Hz), 6.87 (1H, d, J = 7.3 Hz), 7.24 (1H, t, J = 7.3 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.2, 20.2, 23.3, 37.2, 47.5, 48.5, 55.6, 111.0, 117.4, 125.1, 128.3, 130.1, 133.5, 139.2, 157.0, 216.3; MS *m/z* 242 (M^+); HRMS calcd for $C_{16}H_{18}O_2$ 242.1306 (M^+), found 242.1296.

53 (entry 1 in Table 2, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.01 (3H, s), 1.71−1.86 (1H, m), 2.07−2.40 (3H, m), 2.24 (3H, s), 2.96 (1H, dd, J = 6.9 and 12.0 Hz), 3.81 (3H, s), 5.07 (1H, s), 6.84 (1H, d, J = 7.1 Hz), 6.86 (1H, d, J = 7.1 Hz), 7.20 (1H, t, J = 7.1 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 20.2, 24.3, 27.8, 36.7, 48.9, 51.8, 55.6, 111.1, 121.4, 124.5, 128.5, 130.2, 133.3, 139.3, 157.6, 221.7; MS *m/z* 242 (M^+); HRMS calcd for $C_{16}H_{20}O_2$ 242.1306 (M^+), found 242.1298.

54i (entry 9 in Table 2, AcOEt−hexane 0.8:99.2 v/v): mp 158−159 °C (from hexane−AcOEt); IR ($CHCl_3$) 3500, 1730 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.61 (3H, s), 1.98−2.16 (1H, m), 2.31−2.44 (2H, m), 2.52−2.70 (2H, m), 2.72−2.91 (2H, m), 5.43 (1H, br s), 5.68 (1H, br s), 5.84 (1H, s), 6.74 (1H, d, J = 8.1 Hz), 6.88 (1H, d, J = 8.1 Hz), 7.18 (1H, t, J = 8.1 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 16.8, 20.9, 36.5, 39.2, 46.5, 48.6, 115.0, 116.0, 117.0, 122.2, 128.8, 139.5, 139.7, 153.1, 220.1; MS *m/z* 228 (M^+); HRMS calcd for $C_{15}H_{16}O_2$ 228.1149 (M^+), found 228.1147.

55i (entry 8 in Table 2, AcOEt−hexane 0.8:99.2 v/v): mp 133−134 °C (from hexane−AcOEt); IR ($CHCl_3$) 3530, 1730 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.14 (3H, s), 1.75−1.93 (1H, m), 2.08 (1H, d, J = 12.6 Hz), 2.30−2.48 (3H, m), 2.56 (1H, d, J = 12.6 Hz), 3.13−3.22 (1H, m), 5.36 (1H, s), 5.59 (1H, s), 5.79 (1H, s), 6.80 (1H, d, J = 7.5 Hz), 6.82 (1H, d, J = 7.5 Hz), 7.15 (1H, t, J = 7.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 21.8, 29.7, 37.7, 39.9, 47.8, 48.6, 114.1, 114.6, 121.1, 121.5, 129.1, 138.9, 140.7, 153.0, 222.2; MS *m/z* 228 (M^+); HRMS calcd for $C_{15}H_{16}O_2$ 228.1149 (M^+), found 228.1182. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.54; H, 6.84.

56i (entry 2 in Table 2, AcOEt−hexane 0.8:99.2 v/v): mp 94 °C (from hexane−AcOEt); IR ($CHCl_3$) 3600, 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.69 (3H, s), 1.92−2.08 (1H, m), 2.28 (3H, s), 2.28−2.51 (2H, m), 2.61−2.74 (1H, m), 2.99−3.08 (1H, m), 5.10 (1H, s), 6.19 (1H, s), 6.69 (1H, d, J = 7.8 Hz), 6.76 (1H, d, J = 7.8 Hz), 7.13 (1H, t, J = 7.8 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.2, 20.0, 22.9, 37.0, 47.3, 48.6, 116.1, 117.5, 123.1, 128.4, 130.3, 132.9, 139.7, 153.1, 216.9; MS *m/z* 228 (M^+); HRMS calcd for $C_{15}H_{16}O_2$ 228.1149 (M^+), found 228.1152.

57i (entry 2 in Table 2, AcOEt−hexane 0.5:99.5 v/v): mp 164 °C (from hexane−AcOEt); IR ($CHCl_3$) 3640, 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.03 (3H, s), 1.71−1.86 (1H, m), 2.04−2.19 (1H, m), 2.21−2.30 (1H, m), 2.30 (3H, s), 2.30−2.42 (1H, m), 2.92−3.01 (1H, m), 5.01 (1H, s), 5.08 (1H, s), 6.64 (1H, br d, J = 7.8 Hz), 6.82 (1H, br d, J = 7.8 Hz), 7.09 (1H, t, J = 7.8 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 21.5, 25.2, 29.6, 37.6, 50.2, 52.9, 117.5, 120.9, 122.2, 125.5, 130.4, 135.3, 141.6, 157.1, 221.5; MS *m/z* 228 (M^+). Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.83; H, 6.98.

58 + **60** (ratio of 48:52, entry 1 in Table 3, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.55 (1.44H, s), 0.67 (1.56H, s), 2.00−2.39 (2H, m), 2.39−2.54 (1H, m), 2.43 (1.56 H, s), 2.57−2.75 (1H, m), 2.67 (0.48H, d, J = 13.6 Hz), 2.94 (0.48H, d, J = 13.6 Hz), 3.00 (0.48H, dd, J = 6.3 and 12.0 Hz), 3.23 (0.52H, dd, J = 6.3 and 12.0 Hz), 5.48 (0.48H, s), 5.55 (0.48H, s), 6.51 (0.52H, s), 7.30−7.49 (3H, m), 7.74−7.88 (2H, m), 8.26 (0.52H, d, J = 8.4 Hz), 8.41 (0.48H, d, J = 9.3 Hz); HRMS calcd for $C_{19}H_{18}O$ 262.1357 (M^+), found 262.1355.

59 (entry 7 in Table 3, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.19 (3H, s), 1.82−1.95 (1H, m), 2.21 (1H, d, J = 12.9 Hz), 2.33−2.54 (3H, m), 2.71 (1H, d, J = 12.9 Hz), 3.32 (1H, t, J = 7.5 Hz), 5.46−5.56 (2H, m), 7.31 (1H, d, J = 9.4 Hz), 7.43−7.53 (2H, m), 7.74 (1H, d, J = 9.4 Hz), 7.82 (1H, d, J = 8.6 Hz), 8.49 (1H, d, J = 8.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 22.6, 29.6, 38.0, 40.6, 48.8, 49.2, 117.9, 125.5, 125.9, 126.4, 126.9, 128.2, 128.5, 130.1, 132.4, 133.2, 136.6, 138.9, 222.5; MS *m/z* 262 (M^+); HRMS calcd for $C_{19}H_{18}O$ 262.1357 (M^+), found 262.1379.

60 + **61** (ratio of 62:38, entry 4 in Table 3, AcOEt−hexane 1:99 v/v): oil; IR (neat) 1740 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.67 (1.86H, s), 1.15 (1.14H, s), 1.82−1.99 (0.38H, m), 2.00−2.12 (0.62H, m), 2.23−2.39 (1H, m), 2.39−2.56 (1H, m), 2.43 (1.86H, s), 2.48 (1.14H, s), 2.64−2.75 (1H, m), 3.07 (0.38H, dd, J = 6.3 and 12.0 Hz), 3.23 (0.62H, dd, J = 6.3 and 12.0 Hz), 5.36 (0.38H, s), 6.51 (0.62 H, s), 7.33−7.49 (3H, m), 7.74−7.88 (2H, m), 8.26 (0.62H, d, J = 8.4 Hz), 8.38 (0.38H, d, J = 8.7 Hz); MS *m/z* 262 (M^+); HRMS calcd for $C_{19}H_{18}O$ 262.1357 (M^+), found 262.1354.

6-(3-Hydroxy-2-vinylphenyl)-2-methyl-1-hexen-3-one (62i): oil; IR (neat) 3400, 1660 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.82−1.94 (5H, m), 2.60 (2H, t, J = 7.8 Hz), 2.70 (2H, t, J = 7.2 Hz), 5.58 (1H, dd, J = 1.8 and 18.3 Hz), 5.62 (1H, br s), 5.72 (1H, dd, J = 1.8 and 11.4 Hz), 5.75 (1H, br s), 5.90 (1H, br s), 6.74 (1H, d, J = 7.8 Hz), 6.80 (1H, d, J = 7.8 Hz), 7.10 (1H, t, J = 7.8 Hz); MS *m/z* 230 (M^+); HRMS calcd for $C_{15}H_{18}O_2$ 230.1307 (M^+), found 230.1307.

Supporting Information Available: ^{1}H-NMR spectra of compounds **12**−**14**, **16**, **17**, **21**, **30**, **35**, **39**, **40**, **43**−**45**, **46**+**47**, **47**−**49**, **51**−**53**, **54i**, **56i**, **58** + **59**, **59**, **60** + **61**, and **62** (26 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO971377Z