# Allylindation of 6-Substituted 2-Hydroxy-1-tetralones in Aqueous and Organic Media. Stereochemistry and Competition Studies

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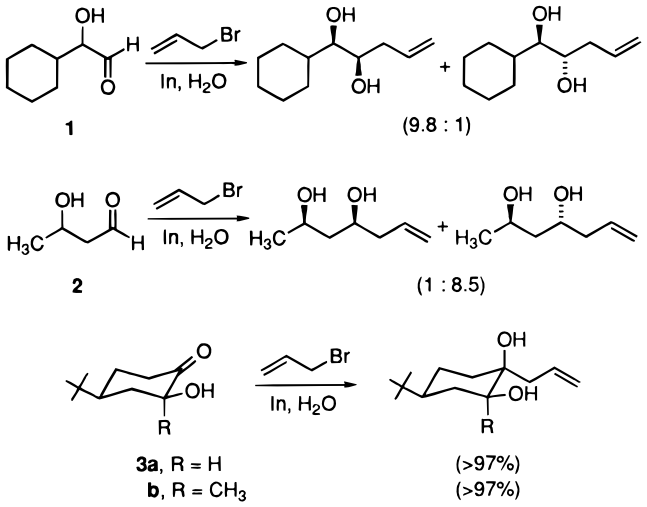
A systematic investigation of the stereoselectivity associated with coupling reactions involving the allylindium reagent and 6-substituted 2-hydroxy-1-tetralones is presented. In each instance, the allylations were carried out in water, 50% aqueous THF, and dry THF. The extent of 1,2-induction was found to be highest in THF−$H_2O$ (1:1) and to favor the trans diol isomer. Somewhat lower levels of stereochemical bias in the same direction were observed in pure water. However, further erosion of this trend was noted for those reactions performed in THF, such that a modest crossover in product distribution became apparent in certain examples. On the basis of competition experiments, both reaction trajectories give evidence of proceeding via chelated intermediates. The extent of stereoinduction was found to be in line with the normal predilection of 2-cyclohexenones for axial attack, which is the process believed to be beset with minimal torsional effects. The substituents situated *para* to the ketone carbonyl do not exert a very large influence on product distribution, although electronic effects are evident in the context of the competition studies. A mechanistic model which integrates these findings is offered.

During the past several years, we have been concerned with the development of new stereoselective reactions relevant to indium-mediated allylations performed in water.[1] One aspect of these studies has focused on the ability of unprotected hydroxyl groups to direct carbon−carbon bond formation as a consequence of chelation to the organometallic reagent in an aqueous environment. Where aldehydes are involved, α- or *β*-oxy substitution such as in **1** and **2** promotes very good diastereofacial control to deliver *syn*-1,2-diols and *anti*-1,3-diols, respectively, as illustrated in Scheme 1.[2] In 2-hydroxycyclohexanones such as **3**, the neighboring hydroxyl substituent very effectively controls the stereochemical outcome of those coupling processes performed in water, irrespective of whether it resides in an axial or equatorial disposition.[3] In all three series, the allylations are accelerated, as anticipated if chelated intermediates intervene.[4] In fact, the reactivity of **3b** suggests that the effects of steric screening in the vicinity of the OH group on the reactivity of the allylindium reagent is virtually inconsequential.

As a natural extension of these studies, we have pursued a complementary investigation aimed at subjecting 6-substituted 2-hydroxy-1-tetralones to comparable scrutiny. The fusion of a benzene ring to an α-hydroxycyclohexanone in this manner brings into existence a number of relevant structural issues that have previously been accorded little attention. These include (a) ground-state conformational preferences, (b) steric effects on chelation capability, (c) $A^{1,3}$ strain considerations involving the *ortho* aromatic position in the two competing

**Scheme 1**




transition states, and (d) *para* substituent contributions to chelation control and the nucleophilic addition process.

It is widely recognized that for 4-substituted cyclohexenes the equatorial conformer is more stable than the axial one.[5] By analogy, **4e** should be favored over **4a**. Furthermore, if the conformational dynamics of 2-methoxycyclohexanone serve as a reliable parallel, the enthalpy difference between these structures should also be at a modest level.[6] Since intramolecular hydrogen bonding is likely to be operative in both geometries, this phenomenon is not expected to introduce any significant bias.

The steric requirements imposed on intramolecular chelation to an allylindium species as depicted in **5** and

(1) Paquette, L. A. In *Green Chemistry: Frontiers in Benign Chemical Synthesis and Processing*; Anastas, P.. Williamson, T., Eds.; Oxford University Press: Oxford, 1998; pp 250−264.
(2) Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931.
(3) Paquette, L. A.; Lobben, P. C. *J. Org. Chem.* **1998**, *63*, 5604.
(4) (a) Chen, X.; Hortelano, E. R.; Eliel, E. L.; Frye, S. V. *J. Am. Chem. Soc.* **1990**, *112*, 6130. (b) Frye, S. V.; Eliel, E. L.; Cloux, R. *J. Am. Chem. Soc.* **1987**, *109*, 1862.
(5) Lambert, J. B. In *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; Rabideau, P., Ed.; VCH: New York, 1989; pp 47−63.
(6) Fraser, R. R.; Faibish, N. C. *Can. J. Chem.* **1995**, *73*, 88 and relevant references therein.

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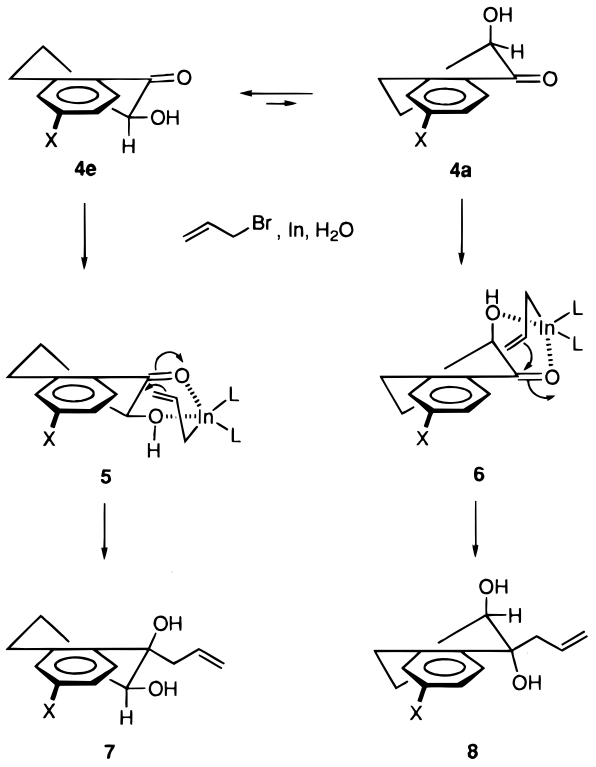
**Scheme 2**



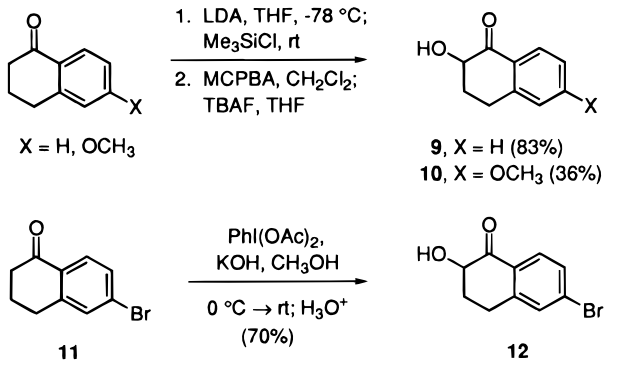

**6** are distinguishable on an a priori basis (Scheme 2). When the OH group is oriented in the equatorial plane, congestion in the vicinity of the binding hydroxyl and ketonic centers is recognized to be well tolerated.[3] Alternative projection of the OH group into the somewhat more crowded axial region present *in cyclohexane frameworks* does not curtail chelation. However, for coordination to be most effective, a twist−boat conformation must be adopted at an added energetic cost. These considerations suggest that **5** might be more accessible than **6**. Superimposition of electronic effects from X could serve to complicate matters. As the 6-substituent is made increasingly electron-withdrawing, intramolecular hydrogen bonding in **4** becomes less influential and has a corresponding consequence on the **4e** ⇄ **4a** equilibrium.

The actual nucleophilic addition to the carbonyl group presents further interesting differences. As the geometric organization develops in **5**, the allyl group needs to access a region proximate to the *ortho* C−H bond of the neighboring benzene ring. $A^{1,3}$ strain[7] is certain to exert a rate-retarding effect. The directionality of attack in **6** avoids this particular interaction but is faced with complementary steric compression arising from the need to move the developing C−O···In functionality out of the pseudoequatorial plane. Of course, inductive and solvent polarity forces will have a role to play in all of this. For example, the inductive effect of the α-hydroxyl substituent is likely to contribute to higher reactivity of the carbonyl group.

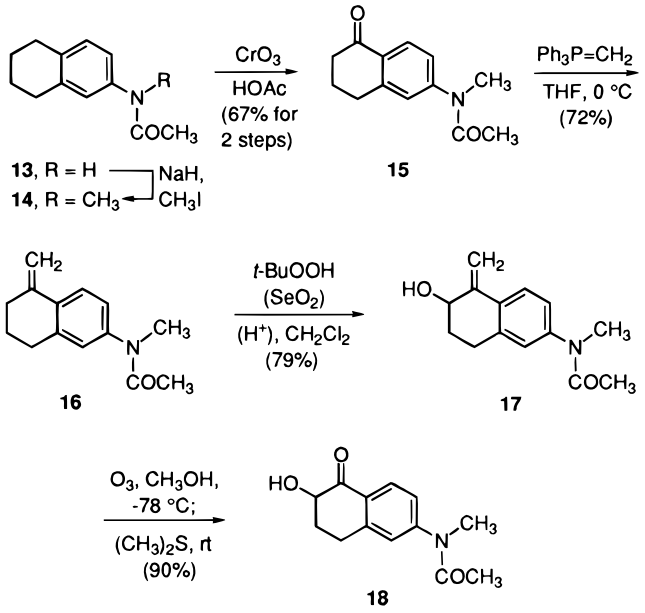
The experiments to be described were undertaken to assess the level at which these stereodifferentiated reactions operate as X is modified from methoxy to cyano and as the solvent system is changed from pure water and 50% aqueous tetrahydrofuran to anhydrous THF.

(7) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

**Scheme 3**




**Scheme 4**




## Results

**Synthetic Considerations.** The 2-hydroxy-1-tetralones **9** and **10** were obtained by Rubottom oxidation[8] of the commercially available ketone precursors (Scheme 3). When attempts to implement the same conversion with **11**[9] were found not to be promising, the Moriarty protocol[10] was used to give **12** in 70% yield.

The *N*-methylacetamido derivative **18** proved more difficult to prepare. Sequential *N*-methylation and chromic acid oxidation[11] of **13**[12] afforded ketone **15** (Scheme 4). In contrast to the other tetralones, **15** proved to be resistant to an array of α-hydroxylation procedures. As a result, recourse was made to Wittig olefination in advance of selenium dioxide oxidation.[13] This last step furnished **17** in 79% yield and set the stage for ozonolytic cleavage of the exocyclic double bond.[3] As expected, the $^1$H and $^{13}$C NMR spectra of **15**−**18** were complicated by

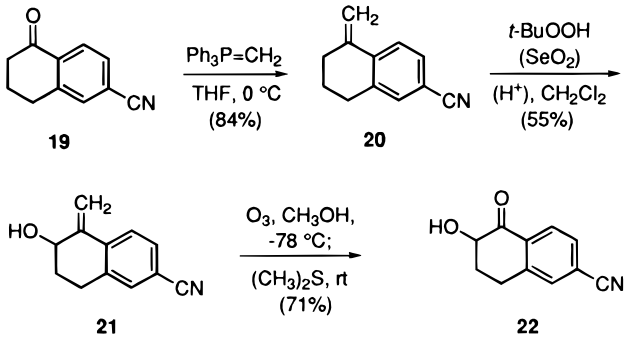
(8) Rubottom, G. M.; Gruber, J. M. *J. Org. Chem.* **1978**, *43*, 1599.
(9) Giardina, G.; Clarke, G. D.; Dondio, G.; Petrone, G.; Sbacchi, M.; Vecchietti, V. *J. Med. Chem.* **1994**, *37*, 3482.
(10) (a) Moriarty, R. M.; Engerer, S. C.; Prakash, O.; Prakash, I.; Gill, U. S.; Freeman, W. A. *J. Org. Chem.* **1987**, *52*, 153 and references therein. (b) Irie, H.; Matsumoto, R.; Nishimura, M.; Zhang, Y. *Chem. Pharm. Bull.* **1990**, *38*, 1852.
(11) Stork, G. *J. Am. Chem. Soc.* **1947**, *69*, 576.
(12) Allinger, N. L.; Jones, E. S. *J. Org. Chem.* **1962**, *27*, 70.
(13) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 7917; **1972**, *94*, 7154.

**Table 1. Indium-Promoted Allylations of 2-Hydroxy-1-tetralones in Various Solvents ($CH_2$=$CHCH_2Br$, 25 °C)[a]**

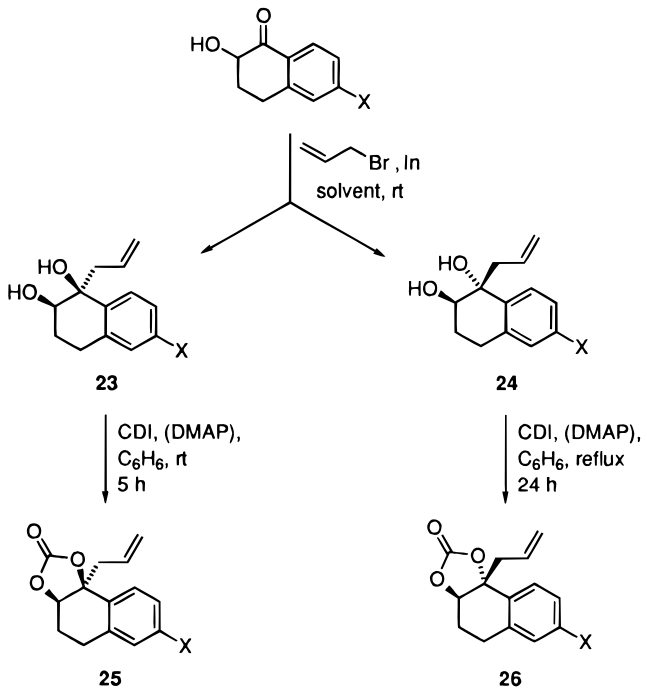
| | | | | product ratio | | |
|---|---|---|---|---|---|---|
| entry | carbonyl reactant | solvent | reactn time, h | *cis* | *trans* | yield, % |
| 1 | **9** (X = H) | $H_2O$ | 1.5 | 1 | 2.5 | 82 |
| 2 | | $H_2O$−THF (1:1) | 1.5 | 1 | 3.8 | 95 |
| 3 | | THF | 144 | 1.7 | 1 | 72 |
| 4 | **10** (X = $OCH_3$) | $H_2O$ | 1.5 | 1 | 3.0 | 76 |
| 5 | | $H_2O$−THF (1:1) | 1.0 | 1 | 4.4 | 91 |
| 6 | | THF | 36 | 2.4 | 1 | 63 |
| 7 | **12** (X = Br) | $H_2O$ | 1.0 | 1 | 4.5 | 89 |
| 8 | | $H_2O$−THF (1:1) | 0.5 | 1 | 5.8 | 93 |
| 9 | | THF | 10 | 1 | 1.5 | 78 |
| 10 | **18** (X = $N(CH_3)COCH_3$) | $H_2O$ | 2.0 | 1 | 1.5 | 69 |
| 11 | | $H_2O$−THF (1:1) | 3.0 | 1 | 4.0 | 94 |
| 12 | | THF | 120 | no reaction | | |
| 13 | | THF[b] | <0.5 | 1 | 2.6 | 81 |
| 14 | **22** (X = CN) | $H_2O$ | 2.0 | 1 | 3.2 | 90 |
| 15 | | $H_2O$−THF (1:1) | 1.5 | 1 | 6.3 | 90 |
| 16 | | THF | 120 | no reaction | | |
| 17 | | THF[b] | 0.5 | 1 | 1.6 | 88 |

[a] All of the reactions were performed at least in duplicate at a concentration of 0.1 M with vigorous stirring for the indicated time span. [b] The THF solution of allyl bromide was heated to reflux with the indium powder for 10 min under $N_2$ and then cooled to rt prior to the introduction of the α-hydroxytetralone.

**Scheme 5**




**Scheme 6**




**a**, X = H; **b**, X = $OCH_3$; **c**, X = Br; **d**, X = $N(CH_3)COCH_3$; **e**, X = CN

the presence of different amide rotamers in an approximately 2:1 ratio.

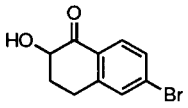
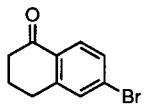
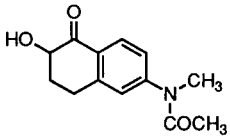
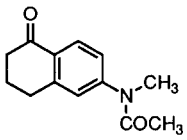
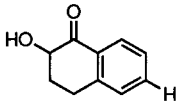
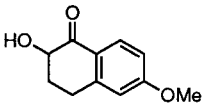
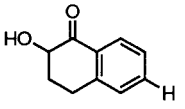
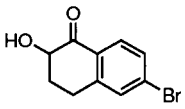
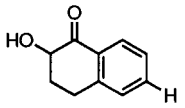
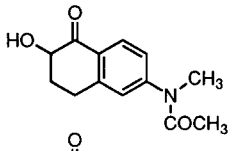
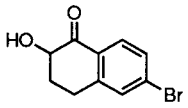
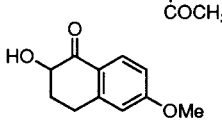
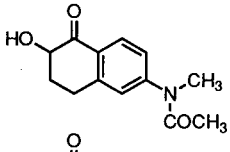
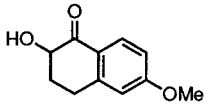
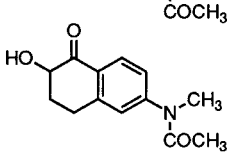
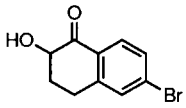
The straightforward nature and overall ease of operation of the preceding synthetic sequence proved to be sufficiently attractive to encourage its adaptation to the cyano derivative. In this instance, the known ketone **19**[12] was transformed satisfactorily via **20** and **21** into **22** (Scheme 5).

**Allylation Stereoselectivity.** The results obtained with the five available α-ketols are summarized in Table 1. The product diols **23** and **24** (see Scheme 6) were separated chromatographically, and their stereochemistries were revealed by conversion to their carbonates **25** and **26** with 1,1′-carbonyldiimidazole (CDI) followed by NOE difference experiments on these cyclic derivatives (consult Experimental Section). The yields in entries 1−17 range from good to excellent.

The data recorded for parent system **9** (entries 1−3) provide important calibration points suitable for comparison with the substituted derivatives. The trans diol **24a** is seen to predominate in water and aqueous THF, reaching a maximum of 3.8:1 in the mixed-solvent system. However, the diastereoselectivity realized in THF is reversed in favor of **23a**, which now dominates by a factor of 1.7:1 as determined by $^1$H NMR integration of unpurified reaction mixtures. This technique was utilized in all of the cases examined here in light of the diagnostic differences in the chemical shifts of the downfield aromatic proton H-8 in the two isomers (see Experimental Section). Particularly striking is the very long elapsed time needed to consume all of **9** when water is absent from the reaction medium. This substantive rate difference was found to persist throughout the entire study.

A very similar crossover in diastereoselectivity was observed for the methoxy-substituted example **10** (entries 4−6). Once again, the use of 50% aqueous THF led to the formation of the highest proportion (4.4:1) of trans diol, i.e., **24b**. While our expectation was that the electron-donating ability of *p*-$OCH_3$ would retard the indium-promoted coupling to allyl bromide, this effect was not observed. In fact, coupling to **10** proceeded four times faster (as judged by the amount of time required

**Table 2. Competitive Indium-Promoted Allylations in Water at 25 °C (see Scheme 6)[a]**

| entry | first ketone | second ketone | reaction time, h | relative rate ratio[b] |
|---|---|---|---|---|
| 18 |  |  | 8 | 4.7 : 1[c] |
| 19 |  |  | 8 | 5.8 : 1[c] |
| 20 |  |  | 3 | 2.8 : 1 |
| 21 |  |  | 9 | 1.2 : 1 |
| 22 |  |  | 8 | 1.1 : 1 |
| 23 |  |  | 9 | 2.8 : 1 |
| 24 |  |  | 8 | 2.5 : 1 |
| 25 |  |  | 8 | 1 : 1.4 |

[a] All experiments were conducted minimally in duplicate except where noted, and the reported data represent the average of these experiments. [b] Relative rate ratios were determined by quantitative analysis via $^1$H NMR spectroscopy of the unreactive tetralones present in the unpurified reaction mixtures. [c] Single-trial experiments.

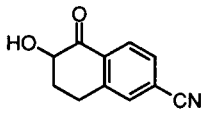
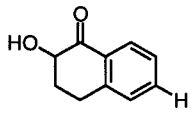
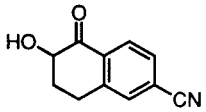
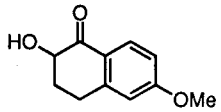
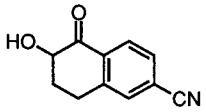
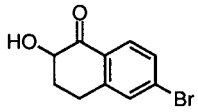
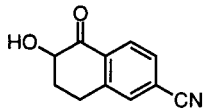
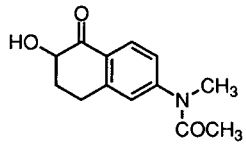
to consume the starting material completely) than the parallel reaction involving **9** in dry THF (entry 6). This *apparent* anomaly foreshadowed related observations to be described below.

The bromo-substituted derivative **12** responded well to the allylindium reagent under the trio of reaction conditions (entries 7−9). Although trans diol **24c** predominated in all three solvent environments, its proportion in the anhydrous THF runs was a factor of 4 less than the maximum of 5.8:1 encountered in aqueous THF, and this magnitude of change was entirely consistent with that encountered in the other cases. In other words, the behavior of **12** does not deviate from the typical trend in which the aqueous THF procedure delivers 20−30% more of **24** relative to the experiment involving pure water as solvent and a 4- to 6-fold increase in the proportion of this isomer relative to the THF protocol.

*N*-Methylacetamido substitution as in **18** resulted in somewhat slower allylation in aqueous media (entries 10 and 11) and no detectable coupling in dry THF after 5 days (entry 12). The latter result is to be contrasted with the data contained in entries 3, 6, and 9. When recourse was made instead to preformation of the allylindium reagent by heating allyl bromide with indium powder under $N_2$ for 10 min prior to the introduction of **18** at room temperature, rapid C−C bond formation ensued to deliver trans diol **26d** with modest diastereoselectivity (entry 13). This was the first time that the amount of trans diol produced in THF alone exceeded (by approximately a factor of 2) that generated in water.

Although the cyano example **22** afforded homoallylic alcohols **23e** and **24e** smoothly (entries 14 and 15), again no reaction was noted in dry THF after 5 days (entry 16). Thus, the pattern of reactivity exhibited when an electron-withdrawing group is oriented *para* to the carbonyl is seemingly to curtail coupling under these conditions. In contrast, preformation of the organometallic reagent leads to the rapid consumption of **22** (entry 17). The diastereomeric ratios exhibited by the cyano derivative are quite normal.

**Table 3. Competitive Indium-Promoted Allylations in THF−$H_2O$ (1:1) at 25 °C**[a]

| entry | first ketone | second ketone | reaction time, h | relative rate ratio[b] |
|---|---|---|---|---|
| 26 |  |  | 8 | 2.5 : 1 |
| 27 |  |  | 8 | >97 : 3 |
| 28 |  |  | 12 | 1.8 : 1 |
| 29 |  |  | 8 | 3.2 : 1 |

[a,b] See footnotes to Table 2.

**Competition Experiments.** To gauge the relative reactivities of the 6-substituted 2-hydroxy-1-tetralones more accurately, two series of competition experiments were performed in which a pair of ketones was allowed to vie for a limited amount of the allylindium reagent to the point of its total consumption. In the first, water alone was utilized as the reaction solvent (Table 2). Because solubility factors constitute an added kinetic criterion under these circumstances, a different slate of competitive allylations was performed in 50% aqueous THF, where substrate solubility was not a concern (Table 3). If chelation holds importance, more rapid conversion to product is expected because of a lowering of transition-state energy requirements stemming from preformation of the complex.[4] In addition, the neighboring coordinated hydroxyl group should prove conducive to stereocontrolled delivery of the allyl residue as depicted earlier in **5** and **6**.

Entries 18 and 19 hold interest in that the α-hydroxytetralones are seen to exhibit reactivity 5-fold greater than that of the less functionalized α-tetralones. This trend has been substantiated by means of independent experiments involving the individual pure ketones and therefore cannot be attributed to any great degree to differential solubility in water. Beyond this, entries 20−25 establish the hierarchy for relative reactivity to be of the order H ∼ Br ∼ $N(CH_3)COCH_3$ > $OCH_3$. Thus, although inductive effects are observed, they are of a low order of magnitude. Similarly, the equally competitive natures of the protio, bromo, and *N*-methylacetamido derivatives relative to the methoxy tetralone are very telling in their variance from any reasonable quantitative effect of structure on reactivity.

The lack of correlation could be due to the complex manner in which most indium-promoted allylations occur in water. As the reaction proceeds, globular micelles make their appearance and are gradually replaced by a milky white, inorganic suspension as the extent of coupling becomes increasingly advanced. Accompanying these changes is a significant decrease in the pH of the medium from 7 to about 4.[2] This feature of indium catalysis leads to an acceleration of product formation as time elapses.

When an organic cosolvent was used as in entries 26−29 and **22** was allowed to compete directly with the other four hydroxytetralones (Table 3), a trend not dissimilar from that found in Table 2 was noted. Although the cyano derivative proved to be significantly more reactive than the methoxy example, a nearly identical 2:1 rate ratio was manifested in the remaining three cases. Since micelle formation is not encountered in this medium, further consideration of this issue may not be warranted. Instead, the damping of those factors that might give rise to a greater spread in reactivity can conceivably arise because of the operation of a single electron-transfer mechanism.

## Discussion

The 1,2-addition of a variety of sterically undemanding nucleophiles to 2-cyclohexenones is widely recognized to proceed with substantially enhanced axial stereoselectivity relative to cyanohexanones.[14,15] On the basis of theoretical studies, Houk and co-workers have accounted

(14) Toromanoff, E. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Eds.; Interscience: New York, 1967; Vol. 2, p 157.

(15) (a) Hennion, G. F.; O'Shea, F. X. *J. Am. Chem. Soc.* **1958**, *80*, 614. (b) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 738. (c) Kienzle, F.; Mayer, M. *Helv. Chim. Acta* **1978**, *61*, 2609. (d) Caine, D.; Smith, T. L., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7568. (e) Findlay, J. A.; Desai, D. N.; Lonergan, G. C.; White, P. S. *Can. J. Chem.* **1980**, *58*, 2827. (f) Kuwajima, I.; Nakamura, E.; Hashimoto, K. *Tetrahedron* **1983**, *39*, 975. (g) Stork, G.; Stryker, J. M. *Tetrahedron Lett.* **1983**, *24*, 4887. (h) Fleming, I.; Terreth, N. K. *J. Organomet. Chem.* **1984**, *264*, 99. (i) Trost, B. M.; Florez, J.; Jebaratnam, D. J. *J. Am. Chem. Soc.* **1987**, *109*, 613. (j) Idrissi, M. E.; Santelli, M. *J. Org. Chem.* **1988**, *53*, 1010. (k) Trost, B. M.; Florez, J.; Haller, K. J. *J. Org. Chem.* **1988**, *53*, 2394.

for this kinetic preference in terms of torsional effects operational in the transition-state structures.[16] As a consequence of the fact that the enone subunit of the structure remains more nearly coplanar during axial addition, the associated near-perfect staggering contrasts with the costly eclipsing that necessarily develops during equatorial approach. Typical axial selectivities are on the order of 20:1.[15]

Comparable stereocontrolling effects can be expected to operate during carbanion additions to simple α-tetralones, although we are unaware of any diagnostic studies that would confirm this assumption. The introduction of an α-hydroxy substituent as in **4** has the effect of directing attention to two quite different conformations rather than one. Of these, **4e** can be regarded as more stable than **4a** for the usual reasons.[5] In structure **4a**, the axial positioning of the sterically bulky OH group should serve to deter a syn attack at the neighboring carbonyl unless chelation operates. All indications point to a similar state of affairs in **4e**.

Since the hydroxyl substituent in 2-hydroxycyclohexanones is shown to be eminently capable of engaging effectively in chelation irrespective of an axial or equatorial status,[3] precoordination in the present examples is considered to be highly likely. Entries 18 and 19 support this conclusion. This mechanistic model allows direct correlation with the product ratios compiled in Table 1. In water and 50% aqueous THF, enhanced selectivity is observed for passage via **6** to the trans diol. The selectivity for this reaction channel varies from 1.5:1 to 6.3:1 depending on the nature of X and the percent of water in the reaction medium. The involvement of **6** is less dominant in anhydrous THF. In actuality, formation of the cis diol via **5** is modestly favored when X = H or $OCH_3$. Significant solvent polarity alterations such as those at play here can be expected to have an influence on stereoselectivity. To understand these results in more detail, theoretical studies which incorporate solvation parameters would need to be undertaken.

Further explanation of the findings recorded herein may prove to be unwarranted at this time. Vedejs has indicated that although ground-state torsional interactions have complicated origins, all estimates of the torsional energies of developing bonds are quite unreliable.[17] In the present setting, attempts to separate steric and electronic factors are problematic. Suffice it to indicate therefore that a synthetically useful allylindation process favoring production of the trans diol has been delineated which is consistent with prior chelation and preferred C−C bond formation from the axial direction.

## Experimental Section[18]

**3,4-Dihydro-2-hydroxy-1(2*H*)-naphthalenone (9).** *n*-Butyllithium (15.2 mL of a 1.6 M solution in hexanes, 24.3 mmol) was added at −78 °C to a solution of *N*,*N*-diisopropylamine (2.84 mL, 20.3 mmol) in THF (78 mL) under $N_2$. The reaction mixture was slowly warmed to 0 °C over 3 h and was recooled to −78 °C prior to the addition of 1-tetralone (2.28 g, 15.6 mmol) and chlorotrimethylsilane (2.57 mL, 20.3 mmol) as a solution in THF (80 mL). The reaction mixture was subsequently warmed to room temperature during 12 h, diluted with triethylamine (75 mL), and concentrated *in vacuo*. The residual solid was slurried in pentane and filtered through Celite. Concentration of the filtrate under reduced pressure and subsequent distillation of the resulting crude oil afforded 3.13 g (92%) of the silyl enol ether intermediate as a slightly yellow oil: bp 83 °C, 0.4 mmHg.

*m*-Chloroperbenzoic acid (2.96 g, 17.2 mmol) was cautiously added to a solution of the silyl enol ether (3.13 g, 14.3 mmol) in $CH_2Cl_2$ (72 mL) under $N_2$. The reaction mixture was stirred at room temperature for 14 h, washed with saturated $NaHCO_3$ solution, dried, and concentrated. Tetra-*n*-butylammonium fluoride (14.3 mL of a 1.0 M solution in THF, 14.4 mmol) was added to a solution of the resulting crude oil in THF (55 mL). The mixture was stirred at room temperature for 12 h, diluted with a saturated $NaHCO_3$ solution, and shaken with ether. The separated organic layer was washed with 2 N HCl and brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 33% ethyl acetate in hexanes) to afford 2.09 g (83%) of **9** as a light tan solid: mp 39−40 °C; IR (neat, $cm^{-1}$) 3474 (br), 1682; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.01 (d, $J$ = 7.8 Hz, 1H), 7.50 (ddd, $J$ = 7.5, 7.5, 1.2 Hz, 1H), 7.34−7.23 (m, 2H), 4.37 (dd, $J$ = 13.5, 5.4 Hz, 1H), 3.55 (br s, 1H), 3.13 (ddd, $J$ = 17.1, 12.7, 4.4 Hz, 1H), 3.01 (ddd, $J$ = 17.1, 4.8, 2.6 Hz, 1H), 2.55−2.47 (m, 1H), 2.02 (dddd, $J$ = 12.8, 12.8, 12.8, 4.9 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 199.6, 144.3, 134.1, 130.4, 128.9, 127.5, 126.9, 73.8, 31.8, 27.7; HRMS (EI) $m/z$ ($M^+$) calcd 162.0681, obsd 162.0680.

**3,4-Dihydro-2-hydroxy-6-methoxy-1(2*H*)-naphthalenone (10).** Comparable treatment of 6-methoxy-1-tetralone (3.52 g, 20.0 mmol) afforded 1.27 g (32%) of **10** as a light tan solid, mp 85.0−86.5 °C (from hexanes/ethyl acetate): IR (KBr, $cm^{-1}$) 3477 (br), 1664; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 8.7 Hz, 1H), 6.85 (dd, $J$ = 8.7, 2.5 Hz, 1H), 6.70 (d, $J$ = 2.4 Hz, 1H), 4.31 (dd, $J$ = 13.3, 5.4 Hz, 1H), 3.85 (s, 3H), 3.10 (dd, $J$ = 12.8, 4.4 Hz, 1H), 2.97 (ddd, $J$ = 17.0, 4.7, 2.6 Hz, 1H), 2.49 (dddd, $J$ = 10.4, 5.3, 4.5, 2.6 Hz, 1H), 2.00 (dddd, $J$ = 12.9, 12.9, 12.9, 4.8 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 198.1, 164.2, 146.9, 130.0, 123.8, 113.6, 112.7, 73.4, 55.5, 31.8, 28.0; HRMS (EI) $m/z$ ($M^+$) calcd 192.0787, obsd 192.0785. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.66; H, 6.32.

**6-Bromo-3,4-dihydro-2-hydroxy-1(2*H*)-naphthalenone (12).** To a $N_2$-blanketed solution of **11**[9] (0.638 g, 2.84 mmol) in methanol (10.0 mL) at 0 °C was added a methanolic solution of KOH (2.387 g, 42.5 mmol, 18 mL), followed by iodobenzene diacetate (1.096 g, 3.40 mmol). As the color changed from green to orange, the reaction mixture was warmed to room temperature over 4 h, diluted with brine, and extracted with ether. The combined organic layers were washed with 10% HCl and brine, dried, and concentrated. The residue was purified chromatographically on silica gel (elution with 10% ethyl acetate in hexanes) to afford 0.476 g (70%) of **12**: mp 89−90 °C; IR (KBr, $cm^{-1}$) 3490, 1679; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.89 (d, $J$ = 8.3 Hz, 1H), 7.50−7.46 (m, 2H), 4.36 (ddd, $J$ = 13.5, 5.4, 2.0 Hz, 1H), 3.83 (d, $J$ = 2.0 Hz, 1H), 3.14 (ddd, $J$ = 17.3, 12.8, 4.5 Hz, 1H), 3.00 (ddd, $J$ = 17.3, 4.7, 2.6 Hz, 1H), 2.57−2.48 (m, 1H), 2.03 (ddd, $J$ = 26.2, 12.9, 4.8 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 198.7, 145.9, 131.8, 130.4, 129.5, 129.1, 73.7, 31.5, 27.4 (one quaternary C not observed); HRMS (EI) $m/z$ ($M^+$) calcd 241.9766, obsd 241.9771.

***N*-Methyl-*N*-(5,6,7,8-tetrahydro-2-naphthyl)acetamide (14).** Sodium hydride (0.72 g, 30 mmol) was added portionwise to a solution of **13**[12] (4.73 g, 25.0 mmol) in dry benzene (50 mol) under $N_2$. After 10 min, methyl iodide (3.1 mL, 50 mmol) was introduced to the reaction mixture, which was stirred at 60 °C under $N_2$ for 12 h before being slowly quenched with brine and concentrated. The residue was partitioned between ether and brine, and the separated aqueous layer was extracted further with ether before the combined organic layers were dried and concentrated. The residue was purified by chromatography on silica gel (elution with 50% ethyl acetate in hexanes) to afford 4.87 g (96%) of

(16) (a) Wu, Y.-D.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1987**, *109*, 5560. (b) Wu, Y.-D.; Houk, K. N.; Florez, J.; Trost, B. M. *J. Org. Chem.* **1991**, *56*, 3656.

(17) Vedejs, E.; Dent, W. H., III; Kendall, J. T.; Oliver, P. A. *J. Am. Chem. Soc.* **1996**, *118*, 3556.

(18) For generic experimental details, see: Paquette, L. A.; Lobben, P. C. *J. Am. Chem. Soc.* **1996**, *118*, 1917.

**14** as an off-white fluffy solid: mp 58−59 °C; IR (KBr, $cm^{-1}$) 2934, 1662; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.04 (d, $J$ = 18.7 Hz, 1H), 6.85−6.83 (m, 2H), 3.19 (s, 3H), 2.73 (br s, 4H), 1.83 (s, 3H), 1.79−1.75 (m, 4H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 170.5, 141.8, 138.5, 136.6, 130.1, 127.1, 123.8, 37.0, 29.2, 28.8, 22.8, 22.7, 22.2; HRMS (EI) $m/z$ ($M^+$) calcd 203.1310, obsd 203.1312.

***N*-Methyl-*N*-(5,6,7,8-tetrahydro-5-oxo-2-naphthyl)acetamide (15).** A solution of chromium trioxide (9.99 g, 0.100 mmol) in acetic acid (25 mL) and water (5 mL) was added dropwise to a chilled (∼10 °C) solution of **14** (5.08 g, 25.0 mmol) in acetic acid (20 mL). The reaction mixture was warmed to room temperature over 8 h, cautiously quenched with 50% $NaHCO_3$ solution, and extracted with ether. The combined organic layers were dried and concentrated to leave a residue, which was purified by column chromatography on silica gel (elution with 50% ethyl acetate in hexanes) to afford 3.71 g (70%) of **15** as a white solid: mp 104−105 °C; IR (KBr, $cm^{-1}$) 3490, 1735, 1664, 1602; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.03 (d, $J$ = 8.2 Hz, 2/3H), 7.80 (s, 1/3H), 7.27−7.25 (m, 2/3H), 7.10 (d, $J$ = 2.1 Hz, 1/3H), 7.07 (d, $J$ = 2.2 Hz, 1H), 3.24 (s, 2/3 of 3H), 3.20 (s, 1/3 of 3H), 2.97−2.93 (m, 2H), 2.65−2.61 (m, 2H) 2.17−2.09 (m, 2H), 1.91 (s, 2/3 of 3H), 1.82 (s, 1/3 of 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm (major rotamer signals) 197.0, 170.0, 148.5, 146.0, 131.8, 131.4, 128.8, 126.7, 38.8, 37.0, 29.6, 23.0, 22.4 (minor rotamer signals) 197.4, 170.4, 130.3, 125.4, 125.0, 38.7, 29.1, 22.9; HRMS (EI) $m/z$ ($M^+$) calcd 217.1103, obsd 217.1104. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96. Found: C, 72.04; H, 7.07.

***N*-Methyl-*N*-(5,6,7,8-tetrahydro-5-methylene-2-naphthyl)acetamide (16).** To a suspension of methyltriphenylphosphonium iodide (2.53 g, 6.27 mmol) in THF (3.1 mL) at 0 °C under $N_2$ was added potassium hexamethyldisilazide (12.5 mL of a 0.5 M solution in toluene, 6.27 mmol), followed after 10 min by solid **15** (1.24 g, 5.69 mmol), at which time the reaction mixture changed from a deep yellow color to a ruby red. The reaction mixture was warmed to room temperature over 4 h, diluted with a saturated $NH_4Cl$ solution, and extracted with ether. The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (gradient elution with 50−66% ethyl acetate in hexanes) to afford 0.235 g (19%) of unreacted **15** and 0.880 g (72%) of **16** as a white solid: mp 49−51 °C; IR (KBr, $cm^{-1}$) 1655; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.64 (d, $J$ = 8.3 Hz, 2/3H), 7.41 (d, $J$ = 2.1 Hz, 1/3H), 7.13 (d, $J$ = 8.0 Hz, 1/3H), 6.96−6.90 (m, 5/3H), 5.46 (s, 2/3H), 5.43 (s, 1/3H), 4.98 (s, 1H), 3.22 (s, 1/3 of 3H), 3.22 (s, 2/3 of 3H), 2.84−2.80 (m, 2H), 2.55−2.51 (m, 2H), 1.91−1.82 (m, 2H), 1.87 (s, 1/3 of 3H), 1.86 (s, 2/3 of 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm (complicated by rotamers) 170.6, 170.5, 143.6, 142.5, 142.4, 142.3, 138.7, 136.8, 136.1, 134.1, 130.5, 127.2, 125.9, 125.5, 124.4, 122.5, 108.9, 108.8, 37.1, 37.0, 32.9, 32.8, 32.7, 30.3, 30.0, 23.4, 22.3; HRMS (EI) $m/z$ ($M^+$) calcd 215.1310, obsd 215.1313. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 77.94; H, 7.94.

***N*-Methyl-*N*-(5,6,7,8-tetrahydro-6-hydroxy-5-methylene-2-naphthyl)acetamide (17).** *tert*-Butyl hydroperoxide (0.411 mL of a 4.0 M solution in $CH_2Cl_2$, 1.64 mmol) was added to a mixture of selenium dioxide (3.0 mg, 23 $\mu$mol) and salicylic acid (6.0 mg, 46 $\mu$mol), followed by **16** (96 mg, 0.46 mmol) as a solution in $CH_2Cl_2$ (0.46 mL). The reaction mixture was stirred at room temperature for 4 h, diluted with 10% KOH solution, and extracted with $CH_2Cl_2$. The combined organic layers were washed with a 50% $K_2CO_3$ solution, dried, and concentrated. The residue was chromatographically purified on silica gel (elution with 65% ethyl acetate in hexanes) to afford 82 mg (79%) of **17** as a white solid: mp 146−147 °C; IR (neat, $cm^{-1}$) 3417 (br), 1652; $^1H$ NMR (300 MHz, $d_6$-DMSO, $T$ = 363 K) $\delta$ 7.66 (d, $J$ = 8.2 Hz, 2/3H), 7.53 (d, $J$ = 2.1 Hz, 1/3H), 7.16 (d, $J$ = 8.4 Hz, 1/3H), 7.09−7.04 (m, 5/3H), 5.58 (d, $J$ = 14.3 Hz, 1H), 5.32−5.30 (m, 1H), 4.32 (ddd, $J$ = 8.7, 1.7, 1.7 Hz, 1H), 3.73 (br s, 1H), 3.16 (s, 1/3 of 3H), 3.15 (s, 2/3 of 3H), 2.96 (ddd, $J$ = 17.0, 6.0, 6.0 Hz, 1H), 2.81 (ddd, $J$ = 16.8, 5.8, 5.8 Hz, 1H), 2.01−1.91 (m, 1H), 1.83 (s, 2/3 of 3H), 1.82 (s, 1/3 of 3H), 1.83−1.74 (m, 1H); $^{13}C$ NMR (75 MHz, $d_6$-DMSO, $T$ = 363 K) ppm (complicated by rotamers) 168.7, 167.8, 145.9, 143.4, 142.4, 137.2, 132.3, 129.5, 126.3, 125.6, 124.5, 124.2, 122.7, 108.4, 107.8, 68.6, 68.5, 36.5, 36.4, 31.3, 31.3, 26.2, 25.9, 21.8, 21.7; HRMS (EI) $m/z$ ($M^+$) calcd 231.1259, obsd 231.1253. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.54; H, 7.39.

***N*-Methyl-*N*-(5,6,7,8-tetrahydro-6-hydroxy-5-oxo-2-naphthyl)acetamide (18).** A −78 °C solution of **17** (0.502 g, 2.17 mmol) in a 1:1 mixture of $CH_2Cl_2$ and methanol (22 mL) containing 1% pyridine was ozonolyzed until a faint blue color persisted (∼20 min) and was quenched with dimethyl sulfide (0.32 mL). The reaction mixture was warmed to room temperature over 4 h, diluted with $CH_2Cl_2$, partitioned with brine, and extracted with ethyl acetate. The combined organic layers were dried and concentrated to leave a residue, which was purified by column chromatography on Florisil (elution with 75% ethyl acetate in hexanes) to afford 0.376 g (74%) of **18** as a colorless oil: IR (neat, $cm^{-1}$) 3422 (br), 1688; $^1H$ NMR (300 MHz, $d_6$-DMSO, $T$ = 363 K) $\delta$ 7.91 (d, $J$ = 8.9 Hz, 2/3H), 7.73 (d, $J$ = 2.3 Hz, 1/3H), 7.48 (dd, $J$ = 8.2, 2.3 Hz, 1/3H), 7.39 (d, $J$ = 8.2 Hz, 1/3H), 7.29−7.27 (m, 4/3H), 4.31 (ddd, $J$ = 12.0, 4.8, 4.8 Hz, 1H), 4.24 (br s, 1H), 3.21 (s, 2/3 of 3H), 3.18 (s, 1/3 of 3H), 3.09−3.03 (m, 2H), 2.33−2.24 (m, 1H), 2.05−1.93 (m, 1H), 1.91 (s, 2/3 of 3H), 1.84 (s, 1/3 of 3H); $^{13}C$ NMR (75 MHz, $d_6$-DMSO, $T$ = 363 K) ppm (complicated by rotamers) 197.4, 168.8, 148.4, 145.2, 142.8, 142.6, 132.1, 131.6, 129.8, 129.4, 127.7, 126.1, 124.5, 124.1, 72.5, 36.6, 36.4, 31.6, 26.7, 26.4, 22.0, 21.7; HRMS (EI) $m/z$ ($M^+$) calcd 233.1052, obsd 233.1055.

**5,6,7,8-Tetrahydro-5-methylene-2-naphthonitrile (20).** Potassium hexamethyldisilazide (6.14 mL of a 0.5 M solution in toluene, 3.07 mmol) was added via syringe to a suspension of methyltriphenylphosphonium bromide (1.19 g, 3.33 mmol) in THF (2.5 mL) at 0 °C under $N_2$. The reaction mixture was allowed to warm to room temperature over 1 h and was recooled to 0 °C prior to the addition of solid **19**[12] (0.438 g, 2.56 mmol). The reaction mixture, which turned from intense yellow to very deep purple, was warmed to room temperature over 4 h, quenched with a saturated $NH_4Cl$ solution, and extracted with ether. The combined organic layers were dried and concentrated to leave a residue, which was purified by silica gel chromatography (elution with 17% ethyl acetate in hexanes) to afford 0.365 g (84%) of **20** as carmine crystals: mp 52−53 °C; IR (KBr, $cm^{-1}$) 1624, 1489, 1406; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.68 (d, $J$ = 8.7 Hz, 1H), 7.39 (d, $J$ = 8.7 Hz, 1H), 7.38 (s, 1H), 5.58 (s, 1H), 5.12 (s, 1H), 2.84 (t, $J$ = 6.3 Hz, 2H), 2.55 (t, $J$ = 5.9 Hz, 2H), 1.88 (q, $J$ = 6.2 Hz, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 141.9, 139.3, 138.1, 132.9, 129.2, 124.9, 119.0, 111.6, 32.5, 30.1, 23.0; HRMS (EI) $m/z$ ($M^+$) calcd 169.0891, obsd 169.0898.

**5,6,7,8-Tetrahydro-6-hydroxy-5-methylene-2-naphthonitrile (21).** *tert*-Butyl hydroperoxide (1.62 mL of a 4.0 M solution in $CH_2Cl_2$, 6.48 mmol) was added to a mixture of salicylic acid (30 mg, 0.22 mmol) and selenium dioxide (12 mg, 0.11 mmol), followed by a solution of **20** (0.365 g, 2.16 mmol) in $CH_2Cl_2$ (2.7 mL). The reaction mixture was stirred at room temperature for 12 h, diluted with $CH_2Cl_2$, and washed successively with 10% KOH and 50% $K_2CO_3$ solutions. The separated aqueous layers were individually extracted with $CH_2Cl_2$, and the combined organic layers were dried and concentrated. The residue was purified by column chromatography on silica gel (elution with 33% ethyl acetate in hexanes) and recrystallized (ethyl acetate/hexanes) to afford 0.218 g (55%) of **21** as an off-white solid: mp 82−84 °C; IR (KBr, $cm^{-1}$) 3323 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.68 (d, $J$ = 8.8 Hz, 1H), 7.43 (d, $J$ = 8.8 Hz, 1H), 7.41 (s, 1H), 5.70 (s, 1H), 5.47 (s, 1H), 4.54 (dd, $J$ = 7.2, 3.7 Hz, 1H), 3.08 (ddd, $J$ = 17.2, 6.8, 6.8 Hz, 1H), 2.85 (ddd, $J$ = 17.2, 6.3, 6.3 Hz, 1H), 2.11−1.94 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 144.8, 137.6, 137.2, 132.7, 129.5, 125.7, 118.9, 112.3, 111.1, 70.1, 30.7, 25.9; HRMS (EI) $m/z$ ($M^+$) calcd 185.0841, obsd 185.0834. Anal. Calcd for $C_{12}H_{11}NO$: C, 77.80; H, 5.99. Found: C, 77.56; H, 5.94.

**5,6,7,8-Tetrahydro-6-hydroxy-5-oxo-2-naphthonitrile (22).** A −78 °C solution of **21** (0.254 g, 1.37 mmol) in a 1:1 mixture of methanol and $CH_2Cl_2$ (13.8 mL) containing 10%

pyridine (1.4 mL) was ozonolyzed (~20 min) until the faint yellow solution gave way to a clear reaction solution. The reaction mixture was quenched with dimethyl sulfide (0.20 mL, 2.7 mmol), warmed to room temperature over 2 h, partitioned with brine, and extracted with $CH_2Cl_2$. The combined organic layers were dried and concentrated. The residue was purified by column chromatography on Florisil (elution with 33% ethyl acetate in hexanes) to afford 0.969 g (71%) of **22** as a light yellow solid: mp 133−135 °C; IR (KBr, $cm^{-1}$) 3482, 1692; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.12 (d, $J$ = 7.9 Hz, 1H), 7.62 (d, $J$ = 7.9 Hz, 1H), 7.60 (s, 1H), 4.43 (dd, $J$ = 13.6, 5.5 Hz, 1H), 3.77 (br s, 1H), 3.19 (ddd, $J$ = 17.4, 5.1, 2.7 Hz, 1H), 3.08 (ddd, $J$ = 17.4, 5.1, 2.7 Hz, 1H), 2.61−2.53 (m, 1H), 2.07 (dddd, $J$ = 12.8, 12.8, 12.8, 5.2 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 198.4, 144.7, 133.4, 132.8, 130.2, 128.2, 117.7, 117.3, 73.9, 31.3, 27.4; HRMS (EI) $m/z$ ($M^+$) calcd 187.0633, obsd 187.0637. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.56; H, 4.85. Found: C, 70.51; H, 4.90.

**Prototypical Indium-Promoted Couplings. A. In Water.** A mixture of **9** (41 mg, 0.25 mmol), allyl bromide (32 $\mu$L, 0.38 mmol), and indium powder (43 mg, 0.38 mmol) in water (2.5 mL) was tightly stoppered and stirred at room temperature for 1.5 h, producing a milky white solution. The reaction mixture was diluted with brine, quenched with 10% HCl, and extracted with ether. In most instances, the 10% HCl quench was deemed detrimental to the products and its use was therefore not implemented. After the combined organic layers were dried and concentrated, the products were separated chromatographically as described below.

**B. In 50% THF.** Indium powder (43 mg, 0.38 mmol) was added to a magnetically stirred solution of allyl bromide (32 $\mu$L, 0.38 mmol) and **9** (41 mg, 0.25 mmol) in a 1:1 mixture of THF and water (2.5 mL). The reaction mixture was stirred at room temperature for 1.5 h, diluted with brine, quenched with 10% HCl, and extracted with ether. In several instances, the 10% HCl was deemed to be detrimental to the products and was therefore avoided without adverse effects. The identical workup followed.

**C. In Anhydrous THF.** A THF (2.5 mL) solution of allyl bromide (32 $\mu$L, 0.38 mmol) and **9** (41 mg, 0.25 mmol) with added indium powder (43 mg, 0.38 mmol) was tightly stoppered and was vigorously stirred at room temperature for 6 d. The reaction mixture was diluted with ether, partitioned with brine, quenched with 10% HCl, and extracted with ether. An equally effective procedure that avoided the 10% HCl quench entailed direct filtration of the reaction mixture through a pipet containing silica gel (elution with ethyl acetate). The combined organic layers were dried and concentrated, and the usual chromatographic purification followed.

**D. Preformation of the Allylindium Reagent in THF.** A suspension of indium powder (17 mg, 0.15 mmol) in a THF solution (1.0 mL) and allyl bromide (13 $\mu$L, 0.15 mmol) was vigorously stirred at the reflux temperature for 15 min under $N_2$, ultimately producing a slightly cloudy homogeneous solution. The reaction mixture was cooled to room temperature prior to the addition of **18**, stirred at room temperature for 30 min, quenched with brine, and extracted with ether. The predescribed workup ensued.

***cis*-1-Allyl-1,2,3,4-tetrahydro-1,2-naphthalenediol (23a):** colorless oil; IR (neat, $cm^{-1}$) 3406 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.58−7.55 (m, 1H), 7.26−7.07 (series of m, 3H), 5.79−5.65 (m, 1H), 5.14−5.07 (m, 2H), 3.94 (dd, $J$ = 6.7, 3.2 Hz, 1H), 2.96 (dd, $J$ = 17.1, 7.2 Hz, 1H), 2.77−2.50 (series of m, 5H), 2.08−1.90 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 139.6, 135.8, 133.4, 128.5, 127.4, 127.4, 126.4, 118.8, 73.6, 70.7, 45.0, 26.2, 25.2; HRMS (EI) $m/z$ ($M^+$) calcd 204.1150, obsd 204.1167. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.29; H, 7.97.

***trans*-1-Allyl-1,2,3,4-tetrahydro-1,2-naphthalenediol (24a):** colorless white solid; mp 91−92 °C; IR (KBr, $cm^{-1}$) 3360 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.44−7.39 (m, 1H), 7.23−7.15 (m, 2H), 7.10−7.07 (m, 1H), 5.94−5.80 (m, 1H), 5.18−5.11 (m, 2H), 3.97 (dd, $J$ = 11.4, 4.4 Hz, 1H), 3.00−2.87 (m, 2H), 2.74 (dd, $J$ = 13.9, 8.2 Hz, 1H), 2.57, (br s, 2H), 2.47 (dd, $J$ = 13.9, 6.7 Hz, 1H), 2.11 (dddd, $J$ = 13.3, 6.6, 4.3, 4.3 Hz, 1H), 2.04−1.90 (m, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 140.4, 134.8, 133.8, 128.5, 127.3, 126.3, 125.7, 119.3, 75.1, 74.4, 40.6, 26.8, 26.1; HRMS (EI) $m/z$ ($M^+$) calcd 204.1150, obsd 204.1148. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.33; H, 7.89.

***cis*-1-Allyl-1,2,3,4-tetrahydro-6-methoxy-1,2-naphthalenediol (23b):** colorless oil; IR (neat, $cm^{-1}$) 3401 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.49 (d, $J$ = 8.7 Hz, 1H), 6.81 (dd, $J$ = 8.7, 2.7 Hz, 1H), 6.60 (d, $J$ = 2.7 Hz, 1H), 5.77−5.63 (m, 1H), 5.15−5.06 (m, 2H), 3.95 (br s, 1H), 3.78 (s, 3H), 2.94 (ddd, $J$ = 17.1, 6.9, 6.9 Hz, 1H), 2.77−2.66 (m, 2H), 2.60−2.53 (m, 2H), 2.33 (br s, 1H), 2.04−1.94 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 158.7, 137.5, 133.6, 131.7, 128.8, 118.7, 112.9, 112.7, 73.4, 70.7, 55.2, 44.7, 26.4, 25.9; HRMS (EI) $m/z$ ($M^+$) calcd 234.1256, obsd 234.1260. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.49; H, 7.74.

***trans*-1-Allyl-1,2,3,4-tetrahydro-6-methoxy-1,2-naphthalenediol (24b):** colorless solid; mp 107−108 °C; IR (KBr, $cm^{-1}$) 3356 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.34 (d, $J$ = 8.7 Hz, 1H), 6.76 (dddd, $J$ = 8.6, 2.7, 0.7, 0.7 Hz, 1H), 6.60 (d, $J$ = 2.7 Hz, 1H), 5.96−5.82 (m, 1H), 5.19−5.11 (m, 2H), 3.96 (dd, $J$ = 11.0, 4.2 Hz, 1H), 3.77 (s, 3H), 2.96−2.90 (m, 2H), 2.72 (dddd, $J$ = 13.9, 8.1, 1.1, 1.1 Hz, 1H), 2.48 (dddd, $J$ = 13.9, 6.7, 1.2, 1.2 Hz, 1H), 2.11 (dddd, $J$ = 13.4, 6.6, 4.4, 4.4 Hz, 1H), 1.97 (dddd, $J$ = 13.4, 11.0, 9.0, 7.9 Hz, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 158.7, 136.4, 134.0, 132.8, 127.6, 119.2, 112.9, 112.1, 74.7, 74.6, 55.2, 40.8, 27.0, 26.1; HRMS (EI) $m/z$ ($M^+$) calcd 234.1256, obsd 234.1238. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.72; H, 7.68.

***cis*-1-Allyl-6-bromo-1,2,3,4-tetrahydro-1,2-naphthalenediol (23c):** colorless oil; IR (neat, $cm^{-1}$) 3401 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.44 (d, $J$ = 8.4 Hz, 1H), 7.34 (dd, $J$ = 8.4, 2.0 Hz, 1H), 7.25 (dd, $J$ = 3.8, 3.0 Hz, 1H), 5.81−5.67 (m, 1H), 5.14−5.07 (m, 2H), 3.98 (br s, 1H), 2.97 (ddd, $J$ = 15.4, 7.7, 7.7 Hz, 1H), 2.74 (br s, 1H), 2.71 (ddd, $J$ = 17.3, 5.8, 5.8 Hz, 1H), 2.61 (dd, $J$ = 14.3, 7.4 Hz, 1H), 2.49 (dd $J$ = 14.3, 7.2 Hz, 1H), 2.30 (br s, 1H), 2.06−1.99 (m, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 138.8, 138.0, 133.0, 131.1, 129.5, 129.3, 121.3, 119.2, 73.4, 70.5, 45.2, 25.9, 24.7; HRMS (EI) $m/z$ ($M^+ - H_2O$) calcd 266.0129, obsd 266.0137. Anal. Calcd for $C_{13}H_{15}BrO_2$: C, 55.14; H, 5.34. Found: C, 55.18; H, 5.40.

***trans*-1-Allyl-6-bromo-1,2,3,4-tetrahydro-1,2-naphthalenediol (24c):** colorless solid; mp 120−121 °C; IR (KBr, $cm^{-1}$) 3364 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.32−7.23 (m, 3H), 5.91−5.76 (m, 1H), 5.20−5.10 (m, 2H), 3.93 (dd, $J$ = 11.4, 4.4 Hz, 1H), 3.00−2.83 (m, 2H), 2.71 (dd, $J$ = 13.9, 8.1 Hz, 1H), 2.62 (br s, 1H), 2.58 (br s, 1H), 2.41 (dd, $J$ = 13.9, 6.8 Hz, 1H), 2.15−2.06 (m, 1H), 2.02−1.88 (m, 1H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm 139.5, 137.1, 133.3, 131.2, 128.8, 128.2, 121.3, 119.8, 74.8, 74.0, 40.4, 26.6, 25.9; HRMS (EI) $m/z$ ($M^+ - H_2O$) calcd 266.0129, obsd 266.0096. Anal. Calcd for $C_{13}H_{15}BrO_2$: C, 55.14; H, 5.34. Found: C, 54.90; H, 5.32.

***N*-(*cis*-5-Allyl-5,6,7,8-tetrahydro-5,6,-dihydroxy-2-naphthyl)-*N*-methylacetamide (23d):** pale yellowish oil; IR (neat, $cm^{-1}$) 3420 (br), 1737; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.62 (d, $J$ = 8.3 Hz, 1H), 7.04 (dd, $J$ = 8.4, 2.0 Hz, 1H), 6.91 (s, 1H), 5.85−5.71 (m, 1H), 5.24−5.06 (m, 2H), 4.03 (br d, $J$ = 4.2 Hz, 1H), 3.23 (s, 3H), 3.04−2.94 (m, 1H), 2.81−2.45 (series of m, 3H), 2.10−2.04 (m, 2H), 1.87 (d, $J$ = 3.7 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm (complicated by rotamers); HRMS (EI) $m/z$ ($M^+$) calcd 275.1522, obsd 275.1500.

***N*-(*trans*-5-Allyl-5,6,7,8-tetrahydro-5,6,-dihydroxy-2-naphthyl)-*N*-methylacetamide (24d):** faint yellowish oil; IR (neat, $cm^{-1}$) 3404 (br), 1735; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.48 (d, $J$ = 3.8 Hz, 2/3H), 7.12−6.89 (series of m, 7/3H), 5.95−5.72 (m, 1H), 5.22−5.02 (m, 2H), 4.03−3.98 (m, 1H), 3.21 (s, 3H), 3.03−2.92 (m, 1H), 2.82−2.35 (series of m, 3H), 2.20−1.95 (series of m, 2H), 1.84 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) ppm (complicated by rotamers); HRMS (EI) $m/z$ ($M^+$) calcd 275.1522, obsd 275.1520.

***cis*-5-Allyl-5,6,7,8-tetrahydro-5,6-dihydroxy-2-naphthonitrile (23e):** clear oil; IR (neat, $cm^{-1}$) 3432 (br); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.69 (d, $J$ = 8.1 Hz, 1H), 7.49 (dd, $J$ = 8.2, 0.8 Hz, 1H), 7.39 (s, 1H), 5.85−5.71 (m, 1H), 5.18−5.08 (m, 2H),

4.05 (dd, $J = 4.0, 4.0$ Hz, 1H), 3.04 (ddd, $J = 17.4, 8.6, 8.6$ Hz, 1H), 2.92 (br s, 1H), 2.76 (ddd, $J = 17.4, 5.4, 5.4$ Hz, 1H), 2.56 (dd, $J = 14.4, 7.2$ Hz, 1H), 2.46 (dd, $J = 14.3, 7.5$ Hz, 1H), 2.32 (br s, 1H), 2.12−2.05 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) ppm 145.6, 136.9, 132.4, 132.1, 129.6, 128.5, 119.7, 118.9, 111.0, 73.5, 70.4, 45.4, 25.6, 24.1; HRMS (EI) *m*/*z* ($M^+$) calcd 229.1103, obsd 229.1093.

***trans*-5-Allyl-5,6,7,8-tetrahydro-5,6-dihydroxy-2-naphthonitrile (24e):** off-white solid; mp 97−98 °C; IR (KBr, $cm^{-1}$) 3446 (br); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.54 (d, $J = 8.1$ Hz, 1H), 7.45 (d, $J = 8.2$ Hz, 1H), 7.38 (s, 1H), 5.87−5.73 (m, 1H), 5.22−5.10 (m, 2H), 3.97 (dd, $J = 11.5, 4.5$ Hz, 1H), 3.05−2.89 (m, 2H), 2.79−2.72 (m, 2H), 2.54 (br s, 1H), 2.39 (dd, $J = 13.9, 6.9$ Hz, 1H), 2.21−2.12 (m, 1H), 2.06−1.92 (m, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) ppm 145.8, 136.1, 132.7, 132.2, 129.1, 127.4, 120.3, 118.8, 111.1, 74.8, 73.6, 40.2, 26.4, 25.7; HRMS (EI) *m*/*z* ($M^+$) calcd 229.1103, obsd 229.1093.

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**Supporting Information Available:** Experimental procedures, characterization data, and the results of NOE studies for **25a**−**e** and **26a**−**e** (6 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.

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