($^1A^*$) is generated, resulting in detectable fluorescence.

The time-resolved FDMR spectra (Figure 1) of radical ion pairs of cubane$^{\bullet+}$ and $A^{\bullet-}$ at 190 K which recombine to give $^1A^*$ was obtained by measuring the fluorescence intensity as a function of applied magnetic field. The resonant decrease in the intensity of fluorescence was induced by the application of a single 100-ns microwave pulse immediately following the electron beam pulse. An FDMR spectrum provides parameters such as those provided by an EPR spectrum. However, an FDMR spectrum is the fluorescence decrease induced by the pulse of microwave at resonance. The modulation depth, the line width, and thus the spectral resolution are dependent on the lifetime of the radical ion species, the microwave power, and the sampling-time window (microwave pulse width).[11] The criterion that is important is whether a *distinct* hyperfine decrease of fluorescence is present. Its intensity vis-à-vis background intensity should not be compared to that of the conventional EPR spectra.

Figure 1a consists of an intense central line (off scale) due to the unresolved FDMR lines of scintillator radical ions superimposed on the wider, multiplet FDMR spectrum assigned to cubane$^{\bullet+}$. This observed spectrum was not seen when cubane was absent or when other isomeric C_8H_8 hydrocarbons were used in its stead.[13] The multiplet is analyzed as a binomial nine-line pattern with a spacing of 16.1 G resulting from the interaction of the electron with the eight equivalent protons of the cubane molecule (cf. the stick spectrum). The two outermost lines are weak in both the experimental and the simulated stick spectrum. The first derivative (computer generated) in Figure 1b shows the lines more decisively. The eight protons must be equivalent, either by symmetry in a static structure, or by a dynamic Jahn-Teller distortion of cubane$^{\bullet+}$ in which they are averaged. Similar results were obtained in cyclopentane in a temperature range of 190-240 K. The signal-to-noise ratio is better at lower temperatures. The nature of the FDMR experiment tells us that we are observing a *radical cation* and the scintillator (perdeuterated anthracene) *radical anion* which recombine to give the excited state whose emission is being detected. An additional clue is provided by the behavior of cubane solution in hydrocarbons where we find that a given solution can be used very briefly, i.e., one cannot deliver many electron beam pulses to this solution because the intensity of the FDMR signal decreases as the number of pulses increases. This means that the species giving rise to the radical cation is sensitive to the buildup of the radiolysis products that have lower IP, such as olefins, that can compete in charge transfer. This means that the species giving rise to the nine-line spectrum must have an IP lower than that of the alkane being used as a solvent and higher than the IP of the olefin derived from this alkane, which is the main radiolysis product having lower IP. The cyclopentane/cyclopentene (IP = 9.0 eV[14]) and *n*-pentane (IP = 10.2 eV[15])/2-pentene (IP = 9.0 eV[16]) provide the IP bracketing. This is not the case when we study cyclooctatetraene (COT) or semibullvalene solutes, since such solutions are not sensitive to the buildup of the olefin product as COT (IP = 8.4 eV[8]) and semibullvalene (IP = 8.4 eV[8]) have IP values lower than the IP values of these olefins. Such considerations provide additional proof that we are observing a radical cation of cubane.

We have used semiempirical MO calculations such as AM1-UHF[17] to provide qualitative insights into how spin-density distributions, and consequently the coupling constants, depend on the distortions in the structure of cubane$^{\bullet+}$. Heilbronner et al.[1] calculated the ground-state cubane$^{\bullet+}$ by an open-shell MINDO/3 model, suggesting that the cubane radical cation is distorted from O_h to C_{2v}. Twelve equivalent structures of C_{2v} are on the potential surface of the cation. The "transition states" that interconvert these structures were not obtained, however. Indeed, we find static molecular distortions of the cubane radical cation by an AM1-UHF model that can undergo dynamic Jahn-Teller averaging to give an average coupling constant[18] similar to the experimentally observed one. These qualitative calculations suggest that the static distortion (Archimedean antiprism) of cubane, in which all protons are equivalent, is much higher in energy than several other structures of cubane$^{\bullet+}$ in which dynamic Jahn-Teller averaging could occur. A more quantitative analysis awaits development of more sophisticated calculations.

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(13) Preliminary results show that under similar conditions the FDMR spectra observed when cyclooctatetraene was solute consist of at least 19 lines with a spacing of 1.6 G; while those observed when semibullvalene was solute consist of a triplet (a_{2H} = 36.5 G) superimposed on the background signals. Qin, X.-Z.; Trifunac, A. D., unpublished results.

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(20) FDMR spectra of pure cyclopentane solvent always show a quintet (a_{4H} = 24 G) below 220 K: Qin, X.-Z.; Trifunac, A. D., unpublished result.

Activation in Transition-Metal Catalysis by Catalyst Relay. A Synthetic Approach to (-)-Dendrobine

Barry M. Trost,* Andrew S. Tasker, Gerd Rüther, and Arndt Brandes

Department of Chemistry, Stanford University
Stanford, California 94305-5080

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Probing fundamental factors that control selectivity in transition-metal-catalyzed reactions is a major task in order to improve their applicability in complex synthesis. Defining the role that functionality *remote* from the reaction site in a substrate may play becomes significant in designing appropriate substrates and thereby synthetic strategy. We record a most unusual effect of a distant unsaturation on a transition-metal-catalyzed allylic alkylation[1] discovered in the course of a synthesis of (-)-dendrobine (**1**), an alkaloid constituent of the Chinese ornamental orchid *Dendrobine nobile*, the extracts of which form the basis of the Chinese herbal medicine Chin-Shih-Hu[2] and for which no asymmetric synthesis has been recorded.[3]

Our retrosynthetic analysis of (-)-dendrobine envisioned creation of the perhydroindane nucleus **2** via a palladium-catalyzed cycloisomerization[4] of **3**, which in turn would be available by a palladium-catalyzed allylic alkylation via **4** or **5**. Of these two, the former a priori appears to be the preferred substrate because of its sterically more accessible olefin for initial coordination to Pd(0).

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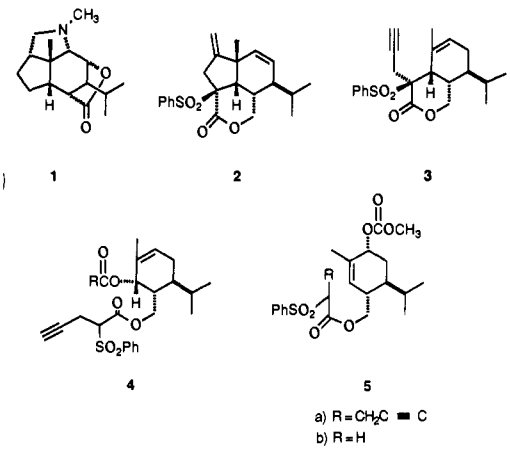
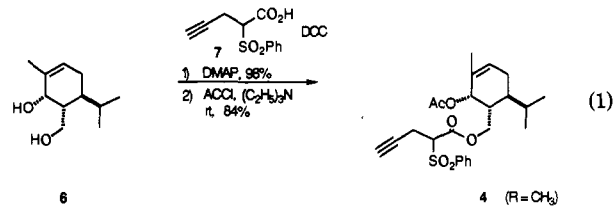


a) R = $CH_2C \equiv C$
b) R = H

Sequential derivatization of diol **6**,[5] itself available in a straightforward manner from (−)-dihydrocarvone,[6] provided the initial substrate **4** (R = CH_3).[5] Subjecting **4** to various Pd(0)



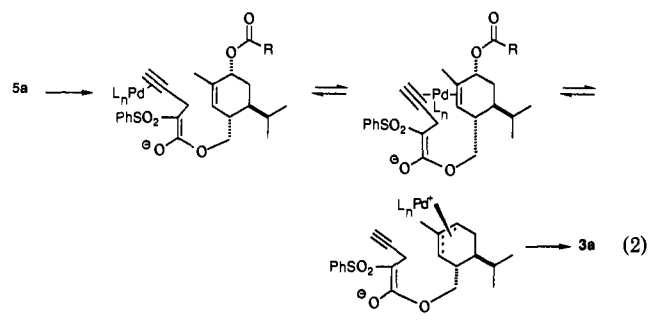
(1)

catalysts in ethereal or aromatic hydrocarbon solvents led to either no reaction or simple decomposition. Enhancing the leaving-group potential by using an allylic carbonate (**4**, R = $CO_2C_4H_9$-*i*) led to similar failures.

The inexplicability of this unreactivity of **4** induced us to examine the alternative allylic isomer **5a**[5] even though we believed this substrate should have shown even poorer reactivity. Scheme I outlines the preparation of the substrate from (−)-dihydrocarvone.[7]

In sharp constrast to substrate **4**, various Pd(0) complexes effect cyclization of **5b** to form a *single* lactone whose stereochemistry is assigned as depicted in **3** on the basis of subsequent conversions. Optimal conditions involved slow addition of **5a** to a solution of 5 mol % palladium acetate and 30 mol % triisopropyl phosphite in THF at reflux to produce crystalline **3**,[5] mp 192–3 °C, in 65% yield.

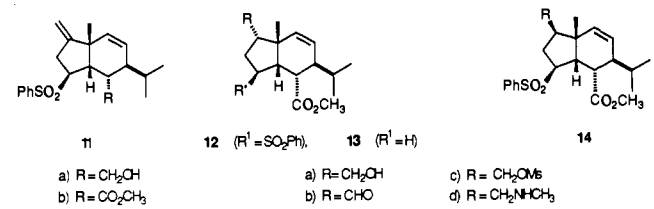
Since palladium-induced ionization involves initial coordination with the olefin, the higher reactivity of the more hindered olefin substrate **5** appears contradictory. The differential juxtaposition of the acetylene with respect to the olefins in the two substrates suggested that it may play a role. To probe this point, the analogue of **5** lacking the propargylic group, **5b**, was subjected to our cyclization conditions. Again, no detectable cyclization products were observed even though removal of the propargyl group should reduce steric interactions. Clearly, the acetylene is playing a role in promoting ionization in **5a** that it cannot play in **4**. A reasonable explanation is depicted in eq 2. Initial coordination of palladium with the readily accessible acetylene provides a kinetic pathway for olefin coordination and subsequent ionization. The tether is long enough to permit the required coordination trans to the leaving group.[8] After ionization, the acetylene ligand is released to permit the final C–C bond formation anti to the palladium. The inability of initial acetylene coordination to lead to olefin coordination in the case of the allylic isomer **4** accounts for the



(2)

differential reactivity. The concept of introducing binding groups to relay the transition metal to a sterically inaccessible reaction center may have general applicability.

The availability of enyne **3** sets the stage for a formal synthesis of (−)-dendrobine since the amine **13d** has previously been converted to (±)-dendrobine.[3c] Palladium-catalyzed cycloisomerization of **3** to **2** was best achieved with 2.5 mol % of $(dba)_3Pd_2{\cdot}CHCl_3$, 5 mol % of triphenylphosphine, and 10 mol % of acetic acid in benzene at 50–55 °C (63% yield). Hydrolysis (KOH, C_2H_5OH, reflux, then HCl, H_2O, 85%) was accompanied by decarboxylation to the alcohol **11a**,[5] which was directly oxidized (Jones reagent) and esterified (CH_2N_2, ether, 90% overall) to the bicycle **11b**.[5]



a) R = CH_2OH
b) R = CO_2CH_3

a) R = CH_2OH
b) R = CHO

c) R = CH_2OMs
d) R = CH_2NHCH_3

Hydroboration [(thexyl)$BH_2{\cdot}S(CH_3)_2$, CH_2Cl_2–ether (1:4), 10 °C, then NaOH, H_2O_2, 84%] was anticipated to occur from the convex face to give **12a**. However, subsequent failure to achieve the formation of the pyrrolidine ring led us to question this stereochemical assignment. To examine this question, the primary alcohol was oxidized [$(COCl)_2$, DMSO, CH_2Cl_2, $(C_2H_5)_3N$, 95%] and the resultant aldehyde equilibrated [DBU, PhH, quant] to an epimeric aldehyde. Benzene-induced shifts in the NMR spectra suggested that the kinetic aldehyde and the alcohol from the hydroboration were **14b** and **14a**, respectively.[9] Confirmation of these conclusions derived from reduction ($NaBH_4$, CH_3OH, THF, 99%) and desulfonylation [6% Na(Hg), Na_2HPO_4, CH_3OH, THF, 88%] of the thermodynamically more stable aldehyde to an alcohol whose properties are identical with those of the known **13a**.[3c] The fact that aldehyde **12b** is thermodynamically more stable than its epimer **14b** is in agreement with the equilibrium (~2:1) for the corresponding nitriles **13** (R = CN) and its epimer although quantitatively the equilibrium favoring **12b** is much larger since we see only one epimer. Completion of our synthetic goal was achieved by mesylation of **12a** to **13c** [CH_3SO_2Cl, $(C_2H_5)_3N$, CH_2Cl_2, 0 °C, 95%] and alkylation of methylamine [DMSO, 85 °C, 86%] to give a product **13d** whose spectral properties are in full accord with those reported.[3c] Since our route starts with (−)-carvone, it is the first report of an asymmetric approach to this compound.

The ability to turn on transition-metal catalyzed reactions by incorporation of appropriate remote binding sites should prove to be a more generally useful concept. Such a binding site must not coordinate too strongly but provide a rapid kinetic intramolecular exchange from the initial binding site to the reaction center. Exploration of this effect will be the topic of further work in these laboratories. The high diastereoselectivity of this cyclization is noteworthy and also may be a more general feature of such metal-catalyzed allylations. This approach also illustrates the utility of the palladium-catalyzed enyne cycloisomerization to

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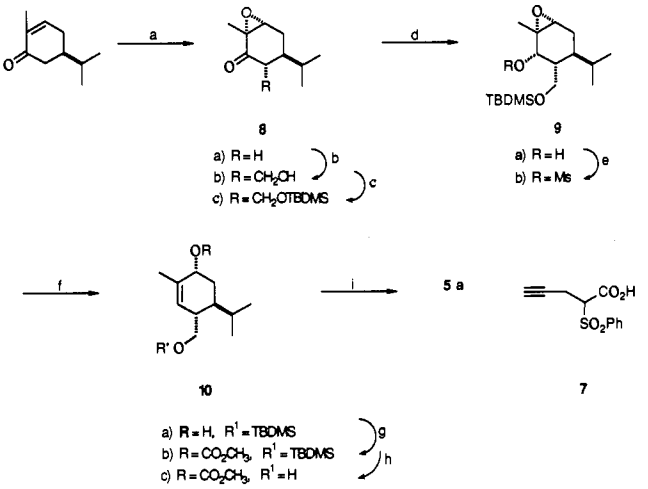
(9) **12b**: δ 1.05 for angular methyl, δ 2.96 for H(9), and δ 9.37 for CHO. **14b**: δ 0.94 for angular methyl, δ 2.13 for H(9), and δ 10.09 for CHO.

Scheme I. Synthesis of Pd(0) Substrate **5**[a]



[a](a) H_2O_2, NaOH, CH_3OH, 93%; (b) LDA, THF, CH_2O, −78 °C, 68%; (c) TBDMS-Cl, $(C_2H_5)_3N$, DMAP, CH_2Cl_2, 95%; (d) L-Selectride, THF, −78 °C, 91%; (e) CH_3SO_2Cl, $(C_2H_5)_3N$, CH_2Cl_2, 0 °C, 85%; (f) $NaC_{10}H_8$, THF, room temperature, 90%; (g) nC_4H_9Li, $ClCO_2CH_3$, 70-30 ether-hexane, 0 °C, 98%; (h) TBAF, THF, room temperature, 90%; (i) **7**, DCC, CH_2Cl_2, 0 °C, room temperature, 98%.

evolve an effective asymmetric synthesis of this alkaloid family.

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Supplementary Material Available: Analytical details including melting points, specific rotations, and IR, ^1H NMR, and ^{13}C NMR spectral data for compounds **2**, **3**, **5**, **8b**, **9a**, **10a**,**c**, **11b**, **12a**,**b**, **13a**,**d**, and **14a**,**b** (5 pages). Ordering information is given on any current masthead page.

New Trialkylsilyl Enol Ether Chemistry. Synthesis of the Benzomorphanone Core Structure Using a Stereoelectronic Conformational Lock

Philip Magnus* and Iain Coldham

Department of Chemistry and Biochemistry
The University of Texas at Austin
Austin, Texas 78712

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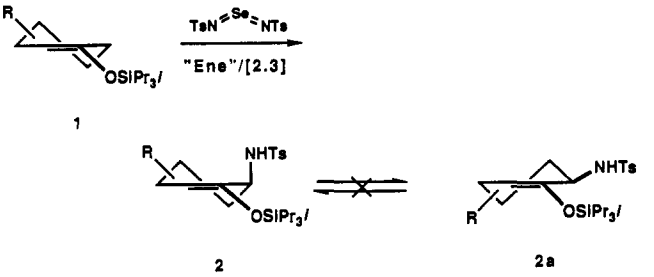
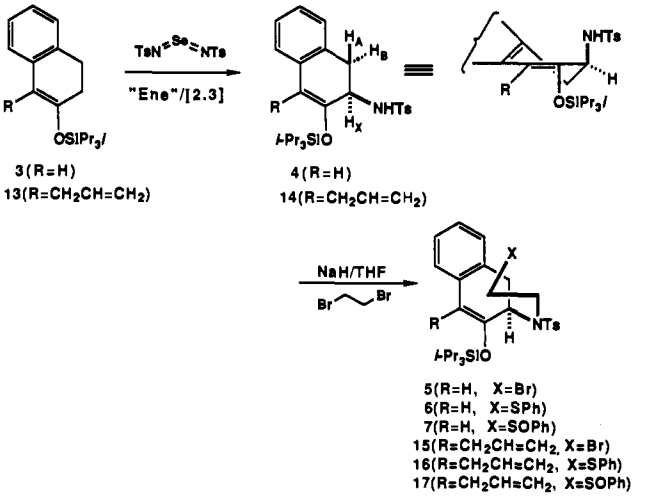
Triisopropylsilyl enol ethers **1** derived from cyclohexanones react with the Sharpless aminating reagent TsN=Se=NTs[1] at 0-20 °C to give the *axially aminated* adducts **2**.[2] We believe that the origin of the thermodynamically preferred axial conformation is the result of π-σ^* stabilization combined with $A^{1,3}$ strain.[3] The

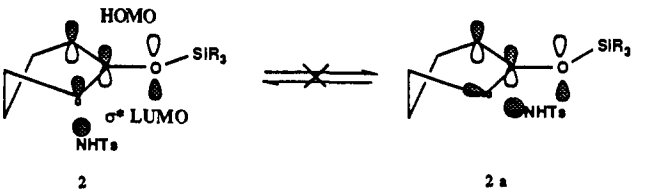
Scheme I



Scheme II



reaction depicted in Scheme I is ideally suited for the construction of the morphine alkaloids, in particular 9-ketobenzomorphans, since the axial nitrogen functionality is correctly oriented to direct intramolecular transformations.[4]



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