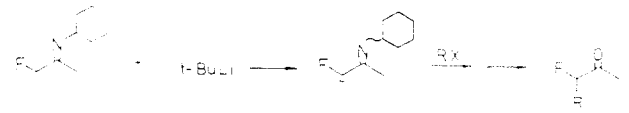
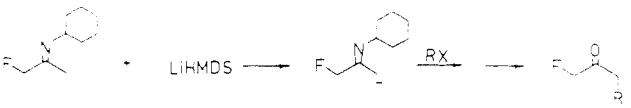
yielded material sufficiently pure for our deprotonation studies.[12] By gas chromatography,[13] the fluoroketimine was found to be >95% a single isomer. NOE studies demonstrated that the principal product was the *E* C–N isomer.[14] Deprotonation was effected by slow addition of the fluoroketimine to a solution of lithium hexamethyldisilazide in tetrahydrofuran (THF) solution containing hexamethylphosphoric triamide[15] or *tert*-butyllithium in THF alone. After being stirred for 2 h at the



desired temperature, a solution of the alkyl halide was added over an additional 2 h at low temperature. The less volatile products were conveniently isolated by hydrolysis of the product imine to the ketone with dilute acetic acid (Table I). Deprotonation of the cyclohexylimine of fluoroacetone was regiospecific and temperature dependent. The tendency of the metalated ketimine to alkylate on the carbon bearing fluorine at low temperatures may be rationalized by suggesting that the increased acidity associated with the protons near fluorine acts in concert with steric effects of the *E* C–N configuration of the imine; i.e., steric interactions of the base with the *N*-cyclohexyl group[16] hinders syn approach.

At higher temperatures, alkylation was directed away from the fluoromethyl group. In control experiments alkylation away from the carbon bearing fluorine did not result when ketimine deprotonated at low temperature was allowed to warm to −30 °C for 2 h. Since decomposition



of the deprotonated imine at temperatures greater than −30 °C becomes a serious problem, equilibration at higher temperatures (such as 25 °C, as reported for isomerization of butanone imines[2]) has not been attempted. Deprotonation of the fluoroketimine on the nonfluorinated carbon to form the thermodynamically favored less substituted azaallyllithium reagent would be enhanced by the greater relative stability of compounds where the fluorine is not bound to an sp^2-hybridized carbon.[17] In contrast to studies with 2-butanone imine it is not necessary to invoke isomerization of the imine to accommodate the observed temperature dependent results.[18]

It appears that at low-temperature deprotonation regioselectivity is dominated by steric and acidity effects, where at higher temperatures the thermodynamic stability of the products is controlling the regiochemistry. We are currently investigating the reaction of deprotonated stereogenic imines. Further studies of the scope and limitations of the temperature dependence of the deprotonation reactions of fluoroketimines are also under way.

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Supplementary Material Available: Analytical and complete spectral data are available (4 pages). Ordering information is given on any current masthead page.

(12) Anal. ($C_9H_{16}FN$) C, H. ^1H NMR ($CDCl_3$) δ 4.63 (d, $J_{H,F}$ = 47 Hz, 2 H, CH_2F), 3.35 (m, 1 H, CH), 1.78 (d, $J_{H,F}$ = 3 Hz, 3 H, CH_3), 1.70–1.10 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 162.1 ($J_{C,F}$ = 20 Hz, C=N), 86.4 ($J_{C,F}$ = 171 Hz, CH_2F), 58.58 (CH), 32.7, 25.1, 24.2, 12.8 (CH_3); ^{19}F NMR ($CDCl_3$) δ −227.1.

(13) Chromatography conditions. OV-101 wall coated on a 25 m× 0.025 mm open tubular fused silica column operated at 70 to 200 °C increasing at 10° per minute.

(14) Irradiation of the resonance at 3.35 ppm resulted in a 4–6% enhancement of the methyl resonance at 1.78 ppm without a concommitant enhancement of the signal at 4.63 ppm.

(15) Typical procedure: for reactions at −30 °C. To a magnetically stirred three-necked round-bottom flask under an inert atomosphere, containing 0.0048 mol of lithium hexamethyldisilazide (prepared by deprotonation of 0.77 g (0.0048 mol) of hexamethyldisilazane in 10 mL of THF with 3 mL (0.0048 mol) of 1.6 M solution of methyl lithium in diethyl ether at −20 °C) dissolved in 10 mL of dry THF and 0.6 g (0.0033 mol) hexamethylphosphoric triamide was slowly added over 1 h 0.5 g (0.0031 mol) of the cyclohexylimine of fluoroacetone dissolved in 10 mL of THF. After the mixture was stirred for an additional hour, 0.0026 mol of the alkyl halide in 10 mL of THF was added over 2 h. After quenching with 20 mL of saturated ammonium chloride, the product imine was extracted with two 20-mL portions of diethyl ether. The extracts were washed with brine, dried over anhydrous potassium carbonate, and concentrated in vacuo. The imine products were dissolved in trichlorofluoromethane and were hydrolyzed with 10 mL of 5% acetic acid over 2 h. The product ketones were isolated by separation of the organic phase, washing with 10 mL of saturated sodium bicarbonate solution, drying over anhydrous magnesium sulfate, and fractional distillation.

(16) Houk, K. N.; Stozier, R. W.; Rondan, N. G.; Fraser, R. R.; Chauqui-Offermanns, N. *J. Am. Chem. Soc.* **1980**, *102*, 1426–1429.

(17) Dolbier, W. R., Jr.; Medinger, K. S.; Greenberg, A.; Liebman, J. F. *Tetrahedron* **1982**, *38*, 2415–2420.

(18) Smith, J. K.; Bergbreiter, D. E.; Newcomb, M. *J. Am. Chem. Soc.* **1983**, *105*, 4396–4400.

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Asymmetric Additions to Chiral Naphthalenes. 3. The Synthesis of (+)-*trans*-1,2-Disubstituted-1,2-dihydronaphthalenes

Summary: Organolithium addition to chiral (1-naphthalyl)oxazolines followed by proton quench gives 84–97% diastereofacial selectivity and furnishes the title compounds in high enantiomeric excess after reductive removal of the chiral auxiliary.

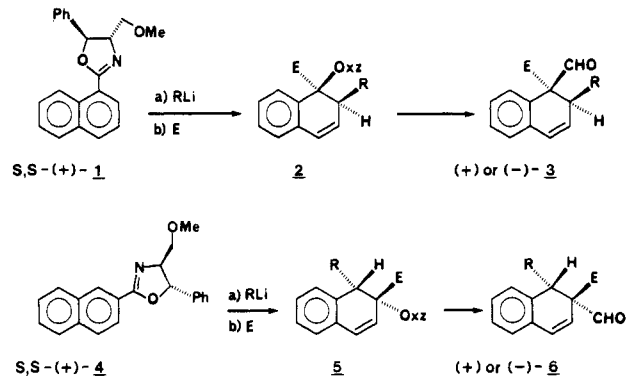
Sir: We recently reported the tandem addition of organolithium reagents and various carbon and sulfur electrophiles to (1-naphthyl)oxazoline **1**[1] and its 2-isomer **4**.[2] The nucleophilic addition[3] occurred with a high degree of diastereofacial selectivity followed by alkylation with the electrophile to give very high ratios of trans addition products **2** and **5**. The trans addition was verified in each system by single-crystal X-ray determination. Thus, in either case, the electrophile entered the naphthalene nucleus from the side opposite to that of the organolithium, and the initial facial entry of the organolithium was determined solely by the chirality of the oxazoline moiety (vide infra). It was of considerable interest to assess the stereochemical protonation in this process by introduction of a proton source after the organolithium addition such that 1,2-disubstituted-1,2-dihydronaphthalenes could be obtained. We now report that this is indeed a highly

(1) Barner, B. A.; Meyers, A. I. *J. Am. Chem. Soc.* **1984**, *106*, 1865.

(2) Meyers, A. I.; Hoyer, D. *Tetrahedron Lett.* **1984**, *25*, 3667.

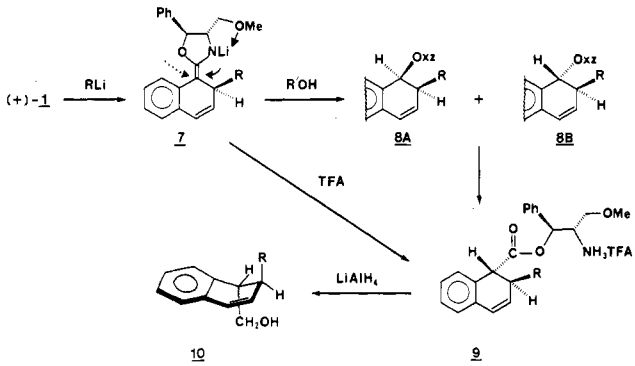
(3) For another study involving nucleophilic addition to naphthalenes, as their chromium carbonyl complexes, see: Kundig, E. P.; Simmons, D. P. *J. Chem. Soc., Chem. Commun.* **1983**, 1320.

0022-3263/86/1951-0120$01.50/0



stereoselective route to these substances but gives rise to a net cis addition rather than the net trans addition observed for **3** and **6**.

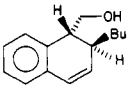
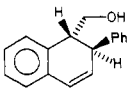
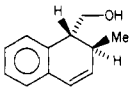
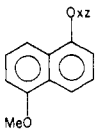
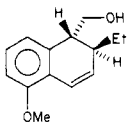
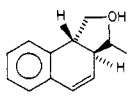
Addition of organolithiums to (+)-**1** in THF followed by quenching in methanol, isopropyl alcohol, or *tert*-butyl alcohol gave the adducts **8A** and **8B** in varying amounts, presumably via the aza enolate **7**. The topside facial



addition leading to **7** has been shown earlier via X-ray diffraction, which confirmed its absolute stereochemistry. When alcohols were used to quench **7**, the epimeric mixtures of **8** were found to be unstable to silica gel chromatography and proved to be of little utility. However, when trifluoroacetic acid was introduced to quench **7**, generally good yields of **9** were obtained.[4] Without attempting further purification of **9**, it was directly reduced (2 equiv of $LiAlH_4$, Et_2O, 25 °C) to the *single* diastereomer **10** in yields given in Table I. No epimers at C-1 were found (NMR). In order to determine the relative configuration at C-1 (the protonation step), a single-crystal X-ray study[5] was undertaken on the crystalline adduct from the methoxy-substituted product derived from **11** (Table I) and confirmed that the TFA quench gave only the *trans*-1,2-disubstituted-1,2-dihydronaphthalene. Thus, the protonation step may have resulted in net trans addition, as with nonprotic electrophiles, followed by rapid epimerization to the more stable trans-1,2-diaxial products **10**.

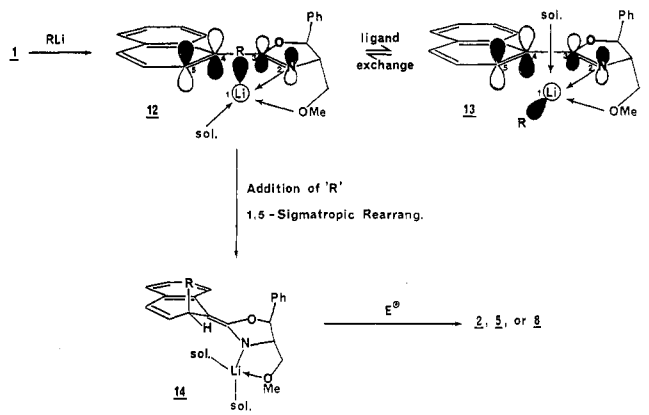
The enantiomeric excess of the dihydronaphthalenes was assessed with either the Mosher ester[6] or Johnson's thiophosphonate esters[7] and examination of the ^{19}F or ^{31}P NMR spectra, respectively. The thiophosphonate esters were found to give superior peak resolution and the ratio

Table I. Optically Active *trans*-1,2-Disbustituted-1,2-dihydronaphthalenes

naphthalene	RLi (T, °C) equiv [t, h]	product **10** (%)	enantiomeric ratios for **10** $[\alpha]_D$, deg (c, $CHCl_3$)
(+)-**1**	*n*-BuLi (−78) 1.2 [2.5]	 a (73)	94:6[a] +366 (1.2)[c]
(+)-**1**	PhLi (−45) 2.2 (3)	 b (62)	85:15[b] +392 (1.1)[c]
(+)-**1**	MeLi (−45) HMPA, 3.0 (3)	 c (42)	84:16[b] +307 (0.7)[c]
 **11**	EtLi (−78) 1.5 (2.5)	 d (85)	97:3[a] +250 (0.7)[c]
(+)-**1**	*i*-PrLi (−78) 1.2 (2.5)	 e (73)	96:4[a] +372 (1.0)[c]

[a] Ratio determined by method of Johnson (ref 7). [b] Ratio determined by Mosher ester (ref 6). [c] The specific rotations are those for the enantiomeric mixtures given.

Scheme I



of enantiomers are presented in Table I.

It is appropriate at this point to provide a rationale for the diastereofacial selectivity by the organolithium reagents to the chiral naphthalenes **1** and **11**. Addition of the organolithium reagent results in the two possible complexes **12** and **13**.[8] The chiral oxazoline moiety, acting as a bidentate ligand occupies two of the four coordination sites of the tetrahedral lithium ion, leaving two sites available

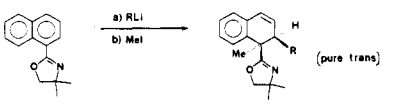
(4) The crude oxazolines **8A,B** were found to open cleanly to the ester ammonium salt **9** during the workup, extraction, and drying (Na_2SO_4, H_2O), procedure. The specificity of Na_2SO_4, H_2O in this process was noted when molecular sieves and/or $MgSO_4$ failed to produce **9** as efficiently.

(5) Details, atomic parameters, and ORTEP structure are given as supplementary material.

(6) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(7) Johnson, C. R.; Elliot, R. C.; Penning, T. D. *J. Am. Chem. Soc.* **1984**, *106*, 5019.

(8) A third mode of addition can occur with achiral oxazolines not containing a methoxymethyl group which involves random facial addition and trans electrophilic trapping; i.e., This yields only the trans addition



product (>98% yield) which, of course, is a racemic mixture (Lutomski, K. Ph.D Thesis, Colorado State University, 1982).

for the R portion of the organolithium and a solvent molecule. The two possible complexes should be capable of ligand exchange, placing R or the solvent (THF) in either of two positions. If the R–Li bond is situated as shown in **12**, then the σ-orbital is aligned parallel to the π-system, whereas in **13**, the R–Li σ-orbital is orthogonal to the π-system (Scheme I). In a formal sense reaction from **12** may be viewed as a concerted suprafacial 1,5-sigmatropic rearrangement from the HOMO (ψ_3) of the six-electron system, according to Woodward–Hoffman rules,[9] to furnish **14**. Electrophilic quench of the latter results in alkylation (or protonation) from the least hindered α-face to provide the absolute stereochemistry observed. For E^+ = H, epimerization to the thermodynamically trans product results. This mechanism is in complete agreement with other "vinyl-substituted" chiral oxazolines (pyridines,[10] quinolines,[11] olefinic,[12] and 2-naphthyl[2]) which have been observed by us, to give absolute stereochemistry in an identical sense. The 3–16% antipode observed in this process may be assumed to arise from a loosely held alkyl carbanion in **12** and **13**, which then adds in a random fashion.[8,13]

We continue to study this interesting and useful route to dihydronaphthalenes and their application to complex natural materials.

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Supplementary Material Available: Experimental details for this process, physical data for products, tables of atomic parameters, and ORTEP structure for **11** adduct (9 pages). Ordering information is given on any current masthead page.

(9) Woodward, R. B.; Hoffman, R. "The Conservation of Orbital Symmetry"; Academic Press: New York, 1970.
(10) Meyers, A. I.; Natale, N. R.; Wettlaufer, D. G. *Tetrahedron Lett.* **1981**, *22*, 5123.
(11) Meyers, A. I.; Wettlaufer, D. G. *J. Am. Chem. Soc.* **1984**, *106*, 1135.
(12) Meyers, A. I.; Smith, R. K.; Whitten, C. E. *J. Org. Chem.* **1979**, *44*, 2250.
(13) Support for facile ligand exchange and thus a more loosely held complex was noted when ether is used in place of THF in this reaction. The diastereofacial selectivity of the organolithium addition was greatly reduced, indicating considerable random additions, due to the poorer binding in the ether complex.

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