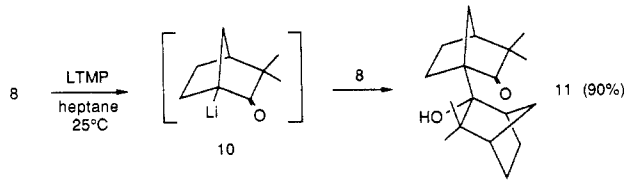
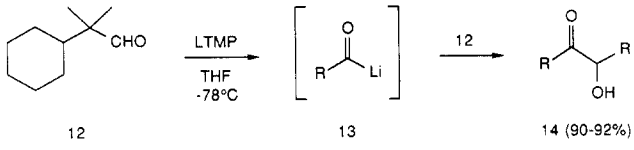
deuteriums, via exchange at C(6), the C(1) bridgehead position, and the two methyl groups. This substance thus afforded an exemplary opportunity to compare the regioselectivity of lithium amide deprotonation with related earlier results. (-)-Camphenilone underwent rapid lithiation by LTMP in heptane at 25 °C (1.1 equiv, 1.5 h), exclusively at the bridgehead position. Exo addition of the α-keto organolithium intermediate **10** to a second molecule of **8** then furnished the formal aldol dimer **11**[10] in 90% yield.[16] Camphenilone did not racemize under these conditions.[17]



Despite long-standing interest, the generation of an acyllithium via deprotonation of the corresponding aldehyde has not previously been achieved. Nonenolizable aldehydes have apparently not been studied under classical homoenolization conditions, but suitable substrates (e.g., trimethylacetaldehyde) do undergo competitive alkyl and formyl deprotonation in the gas phase.[6,18] In solution, acyllithiums have been generated by addition of alkyllithiums to carbon monoxide,[19] and related species are accessible via deprotonation of other formyl derivatives.[20] We now report that the nonenolizable aldehyde **12**[10,21] can be lithiated with remarkable



ease upon exposure to LTMP (1.1 equiv) in THF at -78 °C for 30 min. The acyloin **14**[10] was formed in 90-92% yield, presumably via the intermediacy of acyllithium **13**. A similar reaction of trimethylacetaldehyde at -25 °C for 10 h furnished the expected acyloin **15** in 89% yield.

Dipole and inductive effects[22] should stabilize the metalloketones **2** and **10**, reinforced in the former case by internal complexation.[23] Ab initio studies of formyllithium[24] suggest a preference for ionic η^2-bonding of lithium to the carbonyl moiety in species such as **13**. Complexation of the lithium bases and carbonyl oxygens presumably accelerates the deprotonation reactions[4a] and also accounts for the regioselectivity of camphenilone metalation. Alternative mechanisms for the conversion of **1** to **3** and the formation of **14** and **15**, involving initial electron transfer from LABN or LTMP to the carbonyl compounds,[25] cannot presently be excluded.

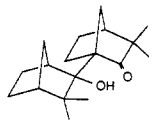
Further studies will address questions of scope and mechanism and will explore the reactivity of acyl and α-keto organolithiums with diverse electrophiles. These efforts, as well as full details of the experiments described herein, will be reported in due course.

Acknowledgment. We are grateful for financial support provided by the National Institutes of Health. We also thank R. Curtis Haltiwanger for determination of the crystal structure of **11**.

Supplementary Material Available: Spectroscopic and analytical data for **3-6**, **11**, **i**, **12**, **14**, and **15** (2 pages). Ordering information is given on any current masthead page.

(16) The structure of **11** has been confirmed by X-ray analysis. The details of the structure determination will be published separately.

(17) Racemization prior to dimerization would afford mixtures of **11** and the diastereomeric dimer **i** (ref 10). Dimerization of **8** of low enantiomeric purity afforded greater than statistical quantities of **i**.



i

(18) Ab initio studies of acyl anions: Chandrasekhar, J.; Andrade, J. G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5612-5614. See, also: ref 24.

(19) For leading references, see: Seyferth, D.; Hui, R. C. *J. Am. Chem. Soc.* **1985**, *107*, 4551-4553. Narayana, C.; Periasamy, M. *Synthesis* **1985**, 253-268.

(20) Metalation of dimethylformamide with LDA in THF at -78 °C furnishes (dimethylcarbamoyl)lithium: Bănhidai, B.; Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 836-837. See, also: Seebach, D.; Lubosch, W.; Enders, D. *Chem. Ber.* **1976**, *109*, 1309-1323.

(21) Prepared by dimethylation of methyl cyclohexylacetate (LDA, CH_3I, THF, -78 °C; LDA, $(CH_3)_2SO_4$, THF, -45 °C), LAH reduction, and PCC oxidation.

(22) Ab initio studies: Rondan, N. G.; Houk, K. N.; Beak, P.; Zajdel, W. J.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Org. Chem.* **1981**, *46*, 4108-4110.

(23) Cf., Geurink, P. J. A.; Klumpp, G. W. *J. Am. Chem. Soc.* **1986**, *108*, 538-539. See, also: ref 5.

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(25) For discussion of SET from lithium dialkylamides to ketones, see: Newcomb, M.; Burchill, M. T. *J. Am. Chem. Soc.* **1984**, *106*, 8276-8282.

An Asymmetric Intramolecular Michael Reaction. Construction of Chiral Building Blocks for the Synthesis of Several Alkaloids

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An intramolecular Michael reaction is one of the most useful methods for the stereocontrolled assembly of the carbon skeleton in organic synthesis.[1] Although a number of highly enantioselective intermolecular Michael reactions have been reported,[2] few examples are documented of an asymmetric intramolecular Michael reaction that is practically applicable.[3] Here we describe a successful example of the above Michael reaction and its application to the syntheses of several alkaloids. Our study began with the envisaging of asymmetric cyclization **1** → **2** (Scheme I).

The acyclic compound **1** was readily obtained from **3** (Scheme II). Treatment of **3** with 2-(2-bromoethyl)-1,3-dioxolane using sodium hydride as a base followed by partial hydrolysis of the resulting amide afforded the aldehyde **4** in 61% yield. Wittig-type reaction of **4**, followed by the hydrolysis of the resulting product, gave the amine **5**, which was treated with methyl vinyl ketone to furnish **1** in 78% yield.

The key compound **1** was then treated with 1 equiv of (*R*)-(+)-1-phenylethylamine[4] as a chiral base in THF at 5-10 °C to give the optically active cycloadduct **2a** in 80% ee[5] (80% yield) (Scheme III). It should be noted that the use of the 5 Å molecular

(1) Alexakis, A.; Chapdelaine, M. J.; Posner, G. H. *Tetrahedron Lett.* **1978**, 4209. Stork, G.; Shiner, C. S.; Winkler, J. D. *J. Am. Chem. Soc.* **1982**, *104*, 310. Hirai, Y.; Hagiwara, A.; Yamazaki, T. *Heterocycles* **1986**, *24*, 571.

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(3) Stork, G.; Saccomano, N. A. *Tetrahedron Lett.* **1987**, *28*, 2087.

(4) Commercial amine, $[\alpha]^{20}D$ +39° (neat) (ee > 99%), was used.

(5) The optical purity of the obtained cycloadducts was determined by obtaining the ^1H NMR of the corresponding (+)-MTPA ester[6] of the alcohols **6** and **7**.

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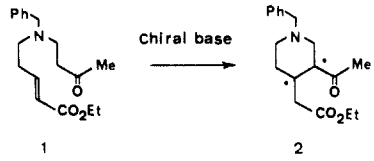
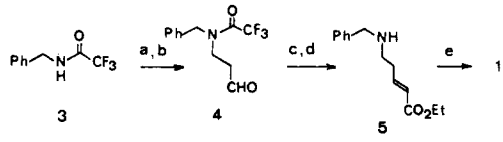
Scheme I

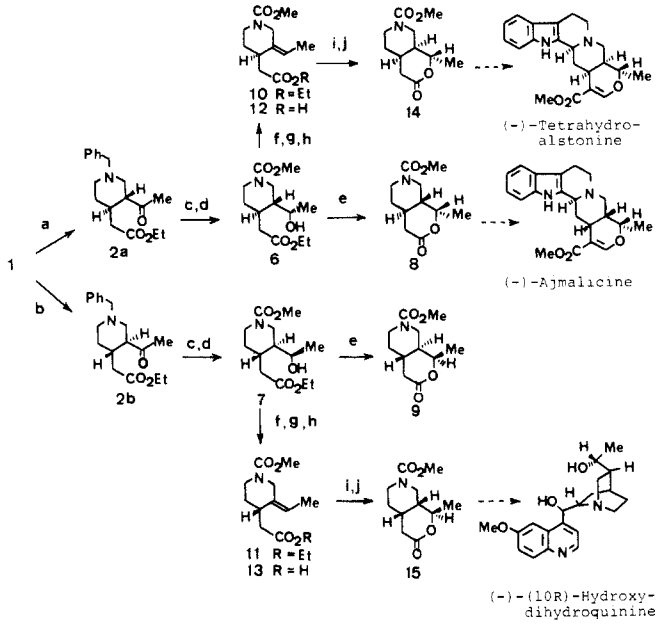


Scheme II[a]



[a] (a) NaH, benzene–DMF (5:1), 2-(2-bromoethyl)-1,3-dioxolane, reflux; (b) oxalic acid, aqueous THF, reflux; (c) $Ph_3P{=}CHCO_2Et$, CH_2Cl_2; (d) K_2CO_3, aqueous EtOH; (e) methyl vinyl ketone, CH_2Cl_2.

Scheme III[a]

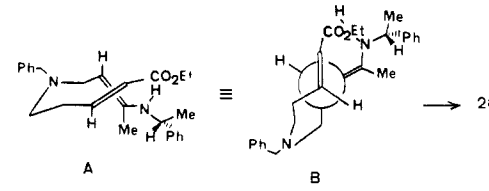


[a] (a) (*R*)-(+)-1-phenylethylamine (1 equiv), THF, molecular sieve 5Å, 5–10 °C; (b) (*S*)-(−)-1-phenylethylamine (1 equiv), THF, molecular sieve 5Å, 5–10 °C; (c) $ClCO_2Me$, benzene, 60 °C; (d) $NaBH_4$, MeOH, −10 °C; (e) TsOH, benzene, reflux; (f) MsCl, pyridine, room temperature; (g) NaI, acetone and then DBU, benzene, reflux; (h) 5% NaOH, room temperature; (i) 9-BBN, THF, room temperature; (j) H_2O_2 and then workup with 1 N HCl.

sieve in this reaction increased the ee of **2a**, $[\alpha]^{24}D$ −21.6° ($CHCl_3$), to 90% ee (78% yield). On the other hand, **2b**, $[\alpha]^{24}D$ +22.0° ($CHCl_3$), was obtained in 90.6% ee (83% yield), (*S*)-(−)-1-phenylethylamine[7] being used as a chiral base in this case. These chiral auxiliary bases were recovered in quantitative yield without any loss of optical purity.

The optically active cycloadducts **2a** and **2b** provide versatile chiral building blocks for the synthesis of biologically active natural products. Treatment of **2a** with methyl chloroformate, followed by reduction with $NaBH_4$, afforded alcohol **6** stereoselectively in 67% yield. Heating of **6** in benzene in the presence of TsOH gave the lactone **8**, $[\alpha]^{26}D$ − 43.3° (MeOH), in 80% yield. Its enantiomer **9**,[8] $[\alpha]^{26}D$ + 44.4° (MeOH), was obtained from **2b** via **7** in 50% yield. The lactone **8** is an important synthetic intermediate for (−)-ajmalicine.[9] Furthermore, **6** and **7** were converted to the lactones **14** and **15**, respectively. Treatment of **6** with mesyl chloride in pyridine followed by treatment with sodium iodide and then with DBU afforded the olefin compound **10**[11] in 70% yield, which was readily hydrolyzed to furnish the acid **12**, $[\alpha]^{26}D$ +14.2° ($CHCl_3$), in 80% yield. Similarly, the acid **13**, $[\alpha]^{26}D$ −14.4° ($CHCl_3$), was obtained from **7** via **11** in 58% yield. The acids **12** and **13** were converted to the lactones **14** and **15**, respectively, according to the method of Dr. Uskoković.[12,13] Each of the lactones, **14** and **15**, is an important synthetic intermediate for (−)-tetrahydroalstonine[12] and (−)-(10*R*)-hydroxydihydroquinine, respectively.

Scheme IV



The observed high enantioselectivity may be explained by assuming the thermodynamically more stable conformation **A** (having quasi chair form[14] and *E* configuration of enamine) shown in Scheme IV, in which the unsaturated ester should approach preferentially the reaction site from the less hindered metine side. D. Seebach et al. have presented the kinetically controlled intermolecular Michael reactions, which follow a topological rule.[15] We assume also that the kinetically controlled cycloaddition of enamine to unsaturated ester occurs with the (Re–Re) approach of the two components as depicted in the Newmann projection **B**.

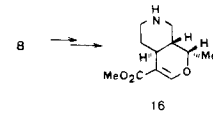
In conclusion, the asymmetric intramolecular Michael reaction of the acyclic compound **1** has been established to give **2a** and **2b**, which are versatile building blocks for various alkaloids.

The use of this reaction in the synthesis of other alkaloids (kainic acid, yohimbine, and strychnine) and the further development of the methodology are currently under way.

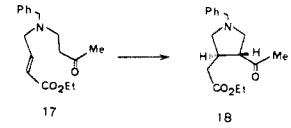
Acknowledgment. We are grateful to Dr. Uskoković, Hoffmann-La Roche Inc., for his kind gift of the spectral data of the

(6) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.
(7) Commercial amine, $[\alpha]^{20}D$ −39° (neat) (ee > 99%), was used.
(8) The absolute configuration of **9** was proven by comparison with an authentic sample, $[\alpha]^{20}D$ +41.7° (*c* 0.59, MeOH), which was elaborated from diethyl L-tartrate via an intramolecular hetero-Diels–Alder reaction. Takano, S.; Satoh, S.; Ogasawara, K. *Abstracts of Papers*, 27th Symposium on the Chemistry of Natural Products, Hiroshima, Japan; Oct 15th, 1985; p 236.

(9) The lactone **8** was converted to the amine **16**,[10] which was an important intermediate for the synthesis of ajmalicine, by the sequence of the following reactions: tritylsodium/methyl formate/dioxane/room temperature; HCl gas/MeOH/reflux; and HBr/AcOH/room temperature. The detail experimental results will be presented in due course.



(10) Gutziller, J.; Pizzolate, G.; Uskoković, M. R. *J. Am. Chem. Soc.* **1971**, *93*, 5907. Martin, S. F.; Benge, B.; Williamson, S. A.; Brown, S. P. *Tetrahedron* **1986**, *42*, 2903.
(11) The *Z* configuration of the double bond of **10** and **11** was determined by the ^{13}C NMR comparison with the corresponding methyl ester compound of **11**.[12]
(12) Uskoković, M. R.; Lewis, R. L.; Partrige, J. J.; Despreaux, C. W.; Pruess, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 6742.
(13) Uskoković, M. R.; Kompis, I. M. *Organic Synthesis Today and Tomorrow*; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: New York, 1981; p 299.
(14) Cyclization reaction of **17** gave **18**, $[\alpha]^{26}D$ +7.1° (*c* 0.93, $CHCl_3$), in 61.9% ee under the same conditions as that in the case of **2** [(*R*)-(+)-1-phenylethylamine (1 equiv)/THF/molecular sieve 5Å/5–10 °C].



(15) Seebach, D.; Golinski, J. *Helv. Chem. Acta* **1981**, *64*, 1413.

lactone **14**. We also thank Professor S. Takano and Dr. K. Ogasawara, Tohoku University, for their kind gift of the spectral data of the lactones **9** and **15**.

Supplementary Material Available: Optical rotations and spectral and analytical data for **1-13** (4 pages). Ordering information is given on any current masthead page.

The Ring Opening Metathesis Polymerization of 7-Oxabicyclo[2.2.1]hept-5-ene Derivatives: A New Acyclic Polymeric Ionophore

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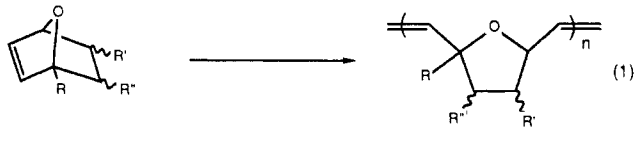
Received September 24, 1987

Ring opening metathesis polymerization (ROMP) methods have been shown to be quite effective for the polymerization of strained cyclic, olefinic hydrocarbons.[1] Recently, the utility of this polymerization technique was considerably expanded by the development of well-characterized alkylidene catalysts[2] which are able to produce living monodispersed polymers.[3] In addition, these living polymers can be specifically end-capped with a variety of carbonyl compounds.[4] The extension of ROMP methods, however, to monomers other than hydrocarbons has been significantly more challenging. Metathesis polymerizations of monomers containing pendant functionalities have met with only limited success,[5] and successful metathesis polymerizations of strained heterocyclic monomers are even more rare.[6] These limitations are primarily the result of side reactions between the heteroatoms in the monomers and the typically oxophilic alkylidene ROMP catalysts.[7] In an effort to further the development of the polymerization of heterocyclic monomers, we report herein the first successful ring opening metathesis polymerization of a series of monomers based on the 7-oxabicyclo[2.2.1]hept-5-ene (7-oxanorbornene) ring structure[8] (eq 1). The poly(ethenylidene-*co*-2,5-tetrahydrofuran) (poly(7-oxanorbornene)) materials resulting from the selective metathesis polymerization of the 7-oxanorbornene monomers are of keen interest due to their potential ionophoric properties. CPK molecular model studies indicate that these poly(7-oxanorbornene) polymers have the ability to form helical structures with all of the tetrahydrofuran oxygens facing into the interior of the helix (Figure 1). This unique helical conformation may allow these polymers, when in solution, to act as useful acyclic ionophores,[9] much like their cyclic analogues, the cyclic crown ethers.[10] In addition, thin films composed of these poly(7-oxanorborne) materials may possess oxygen rich ionophoric channels that would enable them to act as ion permeable membranes.[11]



(1)

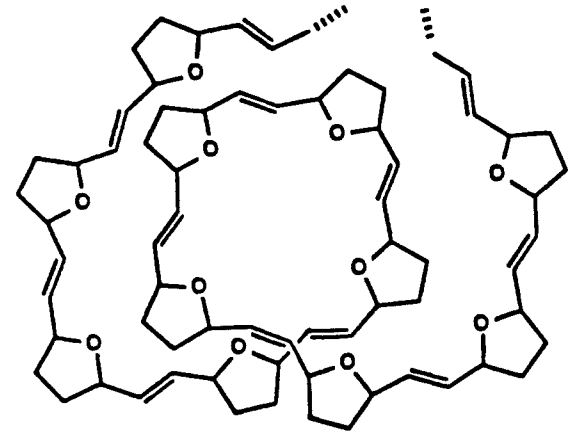


Figure 1. Ion binding cavity formed from a helical turn of poly(7-oxanorbornene).

Table I. Derivations of 7-Oxanorbornene

compd	R	R′	R″	catalyst[c]
I	H	H	CH_3[a]	IX, X, XI, XII, XII
II	H	H	CH_2OCH_3[a]	IX, X, XI, XII, XIII
III	H	H	CH_2OH[a]	XI, XII, XIII
IV	H	CH_2OH	CH_2OH[b]	XI, XII, XIII
V	H	CH_2OTMS	CH_2OTMS[b]	XI, XII, XIII
VI	H	CH_2OCH_3	CH_2OCH_3[b]	IX, X, XI, XII, XIII
VII	CH_3	CH_2OCH_3	CH_2OCH_3[b]	X
VIII	CH_2CH_3	CH_2OCH_3	CH_2OCH_3[b]	X

[a] Endo/exo = 3/1. [b] Greater than 95% exo. [c] Catalysts: IX, $((CH_3)_3CCH_2O)_2W(CH\text{-}t\text{-}Bu)Br_2$; X, $((CF_3)_2(CH_3)CO)_2W(CH\text{-}t\text{-}Bu)(C_6H_3\text{-}2,6(CH(CH_3)_2)N)$; XI, $RuCl_3$; XII, Ru(1,5-cyclooctadiene)Cl_3; XIII, $OsCl_3$.

Table II. Cis Double Bond Content, Ring Diad Tacticity, Molecular Weight, and PDI's of Poly VI Synthesized by Various Catalysts

catalyst	solvent	% cis[a]	syn/iso[b]	M_w ($\times 10^{-3}$)[c]	M_N ($\times 10^{-3}$)[c]	PDI
IX	C_6H_6	42		5.80	3.20	1.81
X	$C_6H_5CH_3$	93	55/45	29.5	19.4	1.52
XI	C_6H_6/EtOH; 5/1	7	28/72	338	172	1.97
XI	EtOH	34		1120	973	1.15
XII	C_6H_6/EtOH	18	50/50	133	77.6	1.71
XII	CH_3OH	30		965	792	1.22

[a] Determined by ^{13}C NMR. [b] Determined by ^{13}C NMR of saturated poly VI. [c] Determined by GPC relative to PS.

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(4) Cannizo, L.; Grubbs, R. H. *Macromolecules* **1987**, *20*, 1488.

(5) Mol, J. C. *J. Mol. Catal.* **1982**, *15*, 35.

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