shift with increasing interionic ion pair distance,[10] the complexes of **2** have the characteristic feature of loose ion pair. The complex with KSCN caused the specific rotation to change,[11] thereby indicating the conformational change in the polymer structure. These observations, therefore, suggest the formation of helical conformer capable of varying in cavity dimensions according to size of such cations as metal ions and dyes.

In conclusion, the cyclopolymerization of diepoxide, namely, 1,2:5,6-dianhydro-3,4-di-*O*-ethyl-D-mannitol, gave poly[(1→6)-2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol], which would effectively bind various sizes of cations in the helical cavity. Further work in this area is in progress.

Experimental Section

General Procedures. NMR spectra were recorded on a Hitachi R90H, a Bruker MSL-400, or a Bruker AMX-600 spectrometer. DEPT, COSY, HMQC, HMBC, DQF-COSY, and NOESY techniques were utilized for assignment of NMR spectra of model compounds and polymers. IR spectra were measured on a JASCO A-102 spectrometer. Specific rotations were measured with JASCO DIP-140 digital polarimeter. UV spectra were recorded on a JASCO UVIDEC-660 spectrometer. Gel permeation chromatography (GPC) in tetrahydrofuran was performed on a WATERS M45 high-performance liquid chromatograph equipped with three columns (Shodex KF-804F).

Solvents for monomer synthesis and polymerizations were dried by general methods: dichloromethane, 1,2-dichloroethane, and nitroethane were dried over CaH_2, and toluene was distilled from sodium–benzophenone. Dibenzo-18-crown-6 was prepared by the method of Pedersen.[12] Methylene blue, rhodamine 6G, and potassium thiocyanate used commercial reagents. 1,2:5,6-Dianhydro-3,4-di-*O*-ethyl-D-mannitol (**1**) was prepared from D-mannitol by the known method.[4] The specific rotation of **1** in $CHCl_3$ (*c* 1.30) at 22 °C: $[\alpha]_D$ −5.2°, $[\alpha]_{577}$ −4.7°, $[\alpha]_{546}$ −5.2°, $[\alpha]_{435}$ −7.2°, and $[\alpha]_{405}$ −7.8° (ref.[4] $[\alpha]_D$ −6.2° (*c* 1.00 in $CHCl_3$)).

Poly[(1→6)-2,5-anhydro-3,4-di-*O*-ethyl-D-glucitol] (2). A typical polymerization procedure is presented here. Monomer **1** (0.50 g, 2.5 mmol) was dissolved in dry CH_2Cl_2 (5 mL), and $BF_3{\cdot}OEt_2$ (3.1 μL, 0.02 mmol) was added by use of a microsyringe. After 24 h at −30 °C, the solution was poured into a large amount of methanol containing a drop of aqueous ammonia, and the resulting solution was replaced by *n*-hexane. The precipitate was isolated and dried under vacuum to yield **2** (190.9 mg, 38%). The specific rotation of **2** in $CHCl_3$ (*c* 1.14) at 22 °C: $[\alpha]_D$ +32.7°, $[\alpha]_{577}$ +33.3°, $[\alpha]_{546}$ +37.3°, $[\alpha]_{435}$ +60.4°, and $[\alpha]_{405}$ +71.4°; IR (film) 2960, 2920, 2890, 2860 (ν, CH), and 1100 cm^{-1} (ν_{as}, COC); ^1H NMR (400 MHz, $CDCl_3$) δ 4.10, 3.93, 3.80–3.33, and 1.19; ^{13}C NMR ($CDCl_3$) δ 84.34 (C-3), 83.15 (C-4), 82.56 and 82.43 (C-2), 79.84 (C-5), 72.06 and 71.87 (C-1), 69.40 (C-6), 65.20 (CH_3CH_2–), and 15.34 (CH_3CH_2–).

2,5-Anhydro-3,4-di-*O*-ethyl-D-glucitol (3). A mixture of 0.52 g (2.6 mmol) of **1** and 10 mL of water was heated under reflux for 7 h, and the solution was then evaporated under reduced pressure. A residual syrup from which the water was removed by azeotropic distillation with benzene and chloroform was purified by column chromatography with chloroform/isopropyl alcohol (8/2, R_f 0.76), give pure **3** (0.35 g, 67%). The specific rotation of **3** in $CHCl_3$ (*c* 1.09) at 20 °C: $[\alpha]_D$ +61.0°, $[\alpha]_{577}$ +64.2°, $[\alpha]_{546}$ +71.9°, $[\alpha]_{435}$ +117.8°, and $[\alpha]_{405}$ +139.4°; IR (film) 3390 (OH), 2960, 2930, 2870 (ν, CH), 1100, 1065, and 1040 cm^{-1} (ν, COC); ^1H NMR (600 MHz, $CDCl_3$) δ 4.10 (H-5), 3.95 (H-4, $^3J_{H\text{-}4,H\text{-}5}$ = 5.2 Hz, $^3J_{H\text{-}3,H\text{-}4}$ = 2.1 Hz), 3.92 (H-2, $^3J_{H\text{-}2,H\text{-}3} \cong$ 6 Hz), 3.89 (H-3), 3.88 (A) and 3.83 (B) (H-6, $^3J_{H\text{-}6A,H\text{-}5}$ = 4.7 Hz, $^3J_{H\text{-}6B,H\text{-}5}$ = 3.9 Hz), 3.84 (A) and 3.69 (B) (H-1, $^3J_{H\text{-}2,H\text{-}1A}$ = 2.6 Hz, $^3J_{H\text{-}2,H\text{-}1B}$ = 3.9 Hz), 3.68 (A) and 3.49 (B) (CH_3CH_2–, $^3J_{gem}$ = 9.0 Hz), 3.60 and 3.55 (CH_3CH_2–), 1.22 (CH_3CH_2–, $^3J_{vic}$ = 6.9 Hz), and 1.21 (CH3CH2–, $^3J_{vic}$ = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 84.86 (C-4), 83.67 (C-2), 83.24 (C-3), 80.26 (C-5), 65.64 (CH_3CH_2–), 62.87 (C-1), 61.81 (C-6), 15.45, and 15.31 (CH_3CH_2–). Anal. Calcd for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 53.93; H, 9.40.

2,5-Anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol (4). To a stirred solution of 0.72 g (3.3 mmol) of **3** in 4.2 mL of dimethyl sulfoxide were simultaneously added a soluton of 0.7 g of sodium hydroxide in 0.7 mL of water and 1.05 g (8.3 mmol) of dimethyl sulfate at the temperature which did not exceed 60 °C. After standing overnight at room temperature, the mixture was poured into water and extracted with chloroform. The extract was dried and evaporated, and the residue was separated by column chromatography with ether. The fractions with R_f 0.69 gave 2,5-anhydro-3,4-di-*O*-ethyl-1,6-di-*O*-methyl-D-glucitol (**4**) (0.66 g, 81%). The specific rotation of **4** in $CHCl_3$ (*c* 1.07) at 22 °C: $[\alpha]_D$ +54.1°, $[\alpha]_{577}$ +56.9°, $[\alpha]_{546}$ +64.2°, $[\alpha]_{435}$ +105.2°, and $[\alpha]_{405}$ +125.3°; IR (film) 2970, 2910, 2875, 2801 (ν, CH), and 1101 cm^{-1} (ν_{as}, COC); ^1H NMR (600 MHz, $CDCl_3$) δ 4.04 (H-5, $^3J_{H\text{-}6A,H\text{-}5}$ = 6.0 Hz, $^3J_{H\text{-}6B,H\text{-}5}$ = 4.7 Hz, $^3J_{H\text{-}5,H\text{-}4}$ = 3.9 Hz), 3.85 (H-2, $^3J_{H\text{-}2,H\text{-}1A}$ = 6.0 Hz, $^3J_{H\text{-}2,H\text{-}1B}$ = 6.0 Hz, $^3J_{H\text{-}3,H\text{-}2}$ = 3.4 Hz), 3.70 (H-4, $^3J_{H\text{-}5,H\text{-}4}$ = 3.9 Hz, $^3J_{H\text{-}4,H\text{-}3}$ < 0.5 Hz), 3.64 (H-3, $^3J_{H\text{-}3,H\text{-}2}$ = 3.0 Hz, $^3J_{H\text{-}4,H\text{-}3}$ < 0.5 Hz), 3.51 (A) and 3.55 (B) (H-6, $^3J_{H\text{-}6A,H\text{-}5}$ = 6.9 Hz, $^3J_{H\text{-}6B,H\text{-}5}$ = 4.7 Hz, $^3J_{gem}$ = 9.8 Hz), 3.41 (A) and 3.46 (B) (H-1, $^3J_{H\text{-}2,H\text{-}1A}$ = 5.6 Hz, $^3J_{gem}$ = 9.9 Hz), 3.38 (A) and 3.55 (B) (CH_3CH_2–, $^3J_{vic}$ = 6.9 Hz, $^3J_{gem}$ = 9.0 Hz), 3.45 (A) and 3.50 (B) (CH_3CH_2–), 3.31 (CH_3O–), 1.13 (CH_3CH_2–, $^3J_{vic}$ = 6.9 Hz), and 1.12 (CH_3CH_2–, $^3J_{vic}$ = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 84.3 (C-3), 83.1 (C-4), 82.2 (C-2), 79.7 (C-5), 73.1 (C-1), 70.7 (C-6), 65.0, 64.9 (CH_3CH_2–), 59.0 (CH_3O–), and 15.1 (CH_3CH_2–). Anal. Calcd for $C_{12}H_{24}O_5$: C, 58.04; H, 9.74. Found: C, 58.02; H, 9.76.

Cation Binding Ability. Metal picrate extractions were carried out using a similar procedure as the one developed by Pedersen.[9] Dye extractions were performed by using equal volumes of the dye (0.1 mg in 10 mL of H_2O) and **2** (10 mg in 10 mL of CH_2Cl_2).

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Registry No. **1**, 71223-72-8; **2**, 135822-30-9; **3**, 135822-31-0; **4**, 135822-32-1; methylene blue, 61-73-4; rhodamine 6G, 989-38-8; dibenzo-18-crown-6, 14187-32-7; lithium picrate, 18390-55-1; sodium picrate, 3324-58-1; potassium picrate, 573-83-1; rubidium picrate, 23296-29-9; cerium picrate, 3638-61-7.

Supplementary Material Available: Spectral characterization for **1**–**4** (4 pages). Ordering information is given on any current masthead page.

(11) The complex of **2** with KSCN changed the specific rotation in comparison with that of the original polymer was shown in the Experimental Section: $[\alpha]_D$ +42.7°, $[\alpha]_{577}$ +47.0°, $[\alpha]_{546}$ +52.1°, $[\alpha]_{435}$ +81.9°, and $[\alpha]_{405}$ +93.8° (*c* 1.63 in $CHCl_3$ at 22 °C).

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An MC-SCF Study of the Transition Structures for the Aldol Reaction of Formaldehyde with Acetaldehyde Boron Enolate

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The aldol reaction is one of the most important methods of forming C–C bonds and has become an exceptional tool

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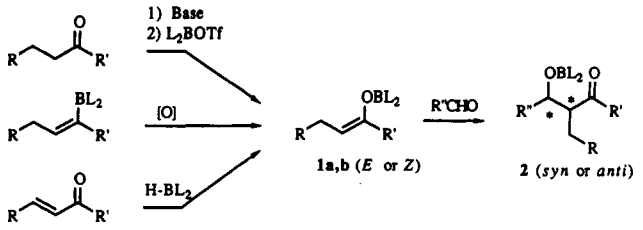
Scheme I[a]



[a] Key: a, L = alkyl; b, L = alkoxy.

in the area of stereocontrolled organic synthesis.[2] Of outstanding interest is the use of boron enolates, in particular vinyl borinates **1a** and borates **1b** (Scheme I), which afford high levels of both relative and absolute stereocontrol.[3] So far, a variety of protocols are available to prepare boron enolates and condense them with aldehydes to give a structurally and stereochemically defined aldol **2**. A widely applied route to boron enolates involves the enolization of the carbonyl compound with a base in the presence of a dialkyl- or dialkoxyboron halide or triflate,[3c-i,3k-q] but other indirect methodologies are available, such as the oxidation of vinyl boronates[3j,4] to **1b** or the conjugate addition of dialkylboranes to α,β-unsaturated ketones leading to (*Z*)-vinylborinates **1a**.[5] As far as the diastereoselectivity of the boron enolate mediated aldol reaction is concerned, the following general trend is observed: the relative stereochemistry syn/anti of aldols **2** depends on the enolate geometry ((*Z*)-**1a** → syn; (*E*)-**1a** → anti) in the case of vinylborinates, while both (*E*)- and (*Z*)-**1b** stereoconverge to the same *syn*-aldol.[3] Moreover, strategies based on chiral auxiliaries (for example, R′ or L attached to the carbonyl carbon or to boron) have allowed the synthesis of enantiomerically pure compounds.[3e,f,h,i,l,n-q,4c,5]

Various empirical models have been invoked to rationalize these results.[4,6] They are generally based on the cyclic, chairlike structures originally proposed by Zimmerman and Traxler[6a] in order to account for the diastereoselectivity exhibited in the condensation of lithium enolates. More recently, the existence of boatlike structures has been proposed by Evans[2b] to explain the behavior of certain boron enolates and by Hoffmann[4b] and Gennari[3g] to rationalize the syn selectivity of (*E*)-vinylborates. The results obtained from the condensation of (*E*)-vinylborates of butanone with aldehydes strongly support this last hypothesis.[4c]

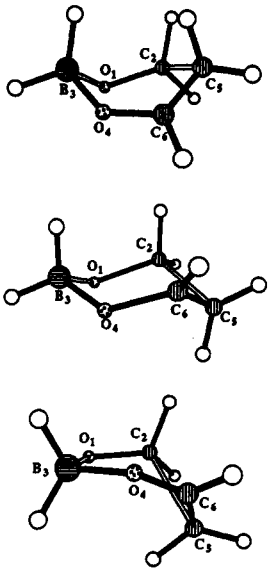


Figure 1. Three six-membered cyclic transition structures found for the reaction of acetaldehyde boron enolate with formaldehyde.

Recently, Houk et al.[7] have reported the results of an ab initio SCF study at the 3-21G[8] level on the transition structures of the aldol reaction in order to obtain information about the aldol mechanism. In particular, they have located the ab initio RHF 3-21G transition structures for the gas-phase aldol reaction of lithium and boron acetaldehyde enolates with formaldehyde. These results show that in both reactions the transition structures correspond to highly asynchronous "pericyclic" transition states, where the metal–oxygen bond is almost completely formed and the C–C bond is still very long. In the model reaction of (ethenyloxy)borane with formaldehyde, a "chair" and a "boat" transition structure has been found. Afterwards, Gennari, Paterson et al.[6e] repeated Houk's calculations and found a new transition structure (they called it "boat B") in addition to the previous two.

Since it is important to have reliable information on this important reaction, and since it is not obvious that SCF theory can properly describe highly asynchronous six-membered cyclic transition structures, we have carried out a 3-21G MC-SCF investigation on the transition structures for the reaction of (ethenyloxy)borane with formaldehyde. The MC-SCF codes used here have been previously de-

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scribed.[9] All computations have been carried out using the GAUSSIAN 88[10] series of programs on the IBM 3090 of the CINECA computer center of Bologna and the CRAY X-MP at the University of London computer center. In all cases, a full-valence CI space (CAS SCF) has been used for the expansion of the wave function. The initial orbitals of the valence space have been obtained from the isolated fragments (i.e., boron enolate and formaldehyde). The choice of the valence space has been dictated by the consideration that we are describing the breaking–forming of the C–C bond since the O–B bond is almost completely formed in the boron enolate–formaldehyde complex (see the geometrical parameters in ref 7). To this purpose we have chosen a valence space that consists of the π and π^* orbitals of formaldehyde and of the boron enolate, which involves 20 configurations. Since we expect that the transition structures under study are not planar, the σ and π orbitals of the fragments can mix. Therefore, since the MC-SCF procedure optimizes the orbitals, it will always find the correct subsets of four orbitals most suitable for the description of the bonds from an appropriate mixing of the π orbitals with the oxygen lone pairs, if required.

In our study we have located three six-member cyclic critical points, one corresponding to a twist-boat structure (I), the second to a chair structure (II), and the third to a half-chair structure (III). These structures have also been investigated at the SCF level and found to correspond to critical points. Structures I and II correspond to those found by Houk et al.,[7] while structure III corresponds to the "boat B" found by Gennari and Paterson.[6e]

The geometries of these critical points have been fully optimized with gradient techniques at both SCF and MC-SCF computational levels. For these structures we have computed the SCF analytical Hessians, which have shown that all these three critical points are transition structures with the direction of negative curvature corresponding to the formation of the C–C bond. The diagonalization of the updated MC-SCF Hessian has given similar results.

These structures are shown in Figure 1, while the relevant geometrical parameters and the total energy values, computed both at the MC-SCF and at the SCF level, are listed in Table I.

The analysis of the computational results shows that either at the MC-SCF or at the SCF level the twist-boat structure I is more stable than the chair structure II by 1.7 (1.3) kcal/mol and the additional half-chair structure III is less stable than I by 2.5 (1.7) kcal/mol. In all three structures, the reaction coordinate mainly consists of the forming C–C bond, and in all cases the transition structure is found at almost identical values along the reaction coordinate. The comparison among the other geometrical parameters shows that the bond lengths and the bond angles are very similar in the three structures, while the dihedral angles differ significantly in the three cases. These structures can be considered as conformers that mainly differ for the spatial arrangement of the BH_2 moiety, and consequently they assume a chair, a half-chair, and a twist-boat conformation, which represent three minima in the conformational problem (i.e., three transition states overall). Another point of interest is the fact that in all three structures the formed B–O bond is almost identical with the B–O bond of the boron enolate.

Table I. Relevant Geometrical Parameters[a] and Energy Values[b] of the Three Six-Membered Cyclic Transition Structures Computed at the MC-SCF and at the SCF[c] Levels

	structures		
	I	II	III
$D(B_3–O_1)$	1.576 (1.613)	1.553 (1.569)	1.577 (1.616)
$D(O_1–C_2)$	1.301 (1.267)	1.332 (1.279)	1.306 (1.271)
$D(C_2–C_5)$	2.100 (2.322)	2.004 (2.204)	2.001 (2.235)
$D(C_5–C_6)$	1.382 (1.354)	1.381 (1.358)	1.388 (1.360)
$D(C_6–O_4)$	1.294 (1.312)	1.295 (1.315)	1.246 (1.310)
$D(O_4–B_3)$	1.543 (1.514)	1.566 (1.558)	1.545 (1.516)
$A(O_1B_3O_4)$	96.5 (96.8)	99.5 (98.7)	102.6 (102.5)
$A(B_3O_1C_2)$	120.2 (120.5)	119.3 (120.4)	126.0 (126.1)
$A(O_1C_2C_5)$	106.8 (103.3)	105.6 (102.8)	101.6 (98.3)
$A(C_2C_5C_6)$	95.1 (91.2)	91.6 (86.4)	90.4 (86.7)
$A(C_5C_6O_4)$	123.6 (125.6)	121.5 (122.5)	126.2 (126.8)
$A(C_6O_4B_3)$	123.2 (123.5)	120.1 (117.3)	125.4 (126.1)
$DA(B_3O_1C_2C_5)$	33.8 (37.5)	63.2 (64.3)	44.8 (47.2)
$DA(O_1C_2C_5C_6)$	27.7 (25.0)	58.0 (57.3)	69.4 (72.5)
$DA(C_2C_5C_6O_4)$	55.6 (56.9)	63.7 (68.0)	56.9 (55.0)
$DA(C_5C_6O_4B_3)$	21.3 (24.9)	72.8 (83.3)	12.9 (8.8)
$DA(O_4B_3O_1C_2)$	69.9 (74.8)	54.8 (61.1)	1.0 (2.4)
$DA(C_6O_4B_3O_1)$	46.1 (47.7)	48.4 (52.8)	29.0 (36.5)
E_T	−290.46711 (−290.43047)	−290.46434 (−290.42834)	−290.46321 (−290.42770)
ΔE	0.00 (0.00)	1.7 (1.3)	2.45 (1.74)

[a] Bond lengths (D) in Å and angles (A) and dihedral angles (DA) in degrees. [b] Total energy values (E_T) in au and energy differences (ΔE) in kcal/mol. [c] Values in brackets.

The main difference between MC-SCF and SCF geometrical results concerns the length of the forming C–C bond, which, in all the cases, is significantly reduced at the MC-SCF level (from 2.3 to 2.0 Å). The variation of the other bond distances is less significant and in all cases is in agreement with a more advanced nature of the transition states at the MC-SCF level along the reaction coordinate. The variations of the remaining geometrical parameters are quite small. These changes at the MC-SCF level likely introduce larger steric effects between substituents at the C_2 and C_5 carbons. The relevant aspects of this study can be summarized as follows:

1. The reaction of boron enolates with formaldehyde can be considered a highly asynchronous [4 + 2] cycloaddition reaction that proceeds through cyclic six-membered transition structures.

2. The reaction is mainly described by a single configuration (the coefficient of this configuration is larger than 0.98 in all cases), and therefore problems of this type can be correctly described at the SCF level. This finding provides greater reliability to the SCF results obtained by Houk[7] and Gennari[6e] and consequently to their chemical implications.

3. The present reaction involves three different transition structures that are very close in energy. These results are valid for the gas-phase reaction. Solvent effects will certainly be important, and, because of the small energy differences, it can become a crucial factor in determining the preferred reaction path.

4. The unambiguous proof of the existence of cyclic transition states for the model reaction of ethenyloxyborane and formaldehyde in the gas phase supports the mechanistic rationale invoked by several authors[2-6] in order to account for the stereochemical outcome of the condensation reaction.

In conclusion, we can presume that in general the aldol condensation of boron enolates with aldehydes can follow three mechanistic pathways identified by different structures of the pericyclic transition state. The nature and the arrangement of substituents in one or both the reaction

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partners as well as solvent effects will differentially affect the relative energies of the three transition states so favoring as a consequence a well-defined stereochemical outcome.

Synthesis of 3-Pyrrolines by an Intramolecular Wittig Reaction

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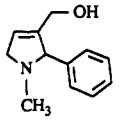
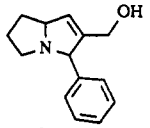
Intramolecular Wittig reactions have been applied successfully to the synthesis of unsaturated carbocycles and certain heterocycles.[1,2] This cyclization strategy has been used to prepare numerous β-lactam antibiotics[3] (i.e. cephalosporins, oxadethiacephams, olivanic acid derivatives, and thienamycin analogues). However, very few examples exist for the preparation of 3-pyrrolines using this methodology.[4] The preparation of unsaturated heterocycles by the intramolecular Wittig reaction typically requires an intermediate that contains the heteroatom and carbonyl moiety (Scheme I).

Cyclization is facilitated when the heteroatom attacks the electrophilic β-carbon of a vinylphosphonium[5] salt or phosphonate[6] to generate the ylide. This procedure works well when the heteroatom is oxygen, sulfur, or a resonance-delocalized nitrogen. However, in the case of aliphatic amines,[7] the preparation and storage of the required amino ketones (or amino aldehydes) can be problematic, thereby discouraging their use as practical intermediates.

This report demonstrates a novel, efficient method for the synthesis of *N*-alkyl-3-pyrrolines through an intramolecular Wittig reaction in which the starting material is a β-aminophosphonium salt. The 3-pyrroline 1 and pyrrolizine 2 were prepared by short convergent syntheses.



1

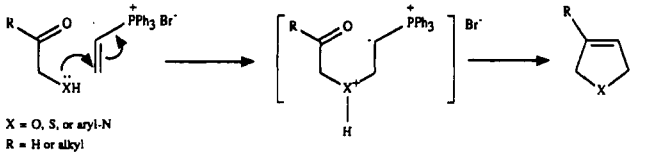


2

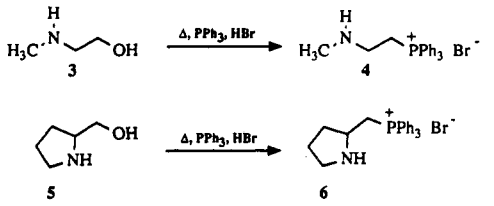
The β-aminophosphonium salts (*N*-methyl-β-aminoethyl)triphenylphosphonium bromide (4) and (2-pyrrolidinylmethyl)triphenylphosphonium bromide (6) were readily prepared from the appropriate β-amino alcohol by treatment with triphenylphosphine and HBr as described by Marxer[8] (Scheme II). The hydroxy ketone 8a was prepared by using a one-pot procedure (Scheme III). Treatment of α-bromophenylacetyl chloride [7b, from α-bromophenylacetic acid (7a) and thionyl chloride] with diazomethane and triethylamine in ether gave the diazo ketone 7c that was hydrolyzed in situ with aqueous trifluoroacetic acid (TFA) to give 8a. The hydroxy ketone 8a was purified by flash chromatography[9] and the hydroxyl moiety was protected by using dihydropyran (DHP) and a catalytic amount of TFA in dichloromethane. The resulting THP ether 8b could be stored for greater than 6 months if kept cold and free from light.

The intermediates 4 and 8b were smoothly coupled at room temperature in dichloromethane and triethylamine to give the crude amino ketone 9 (Scheme IV). Wittig cyclization was accomplished by the portion-wise addition of a THF solution of 9 to an excess of sodium hydride suspended in THF. The reaction products were partitioned between ethyl acetate and 5% aqueous HCl, which simultaneously separated the pyrroline from triphenylphosphine oxide and removed the THP protecting group. The alcohol 1 was an oil so it was converted to the crystalline carbamate 10 by treatment with isopropyl iso-

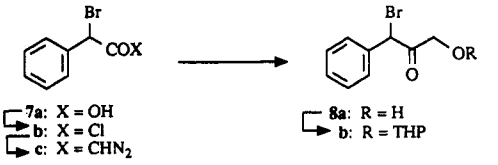
Scheme I



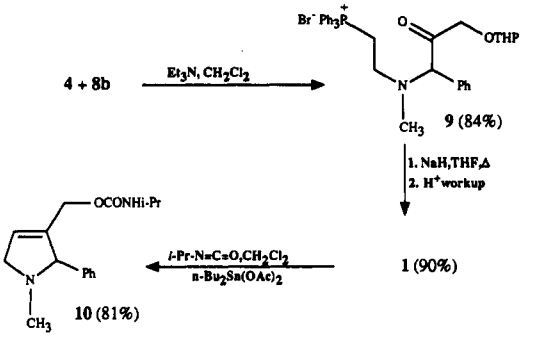
Scheme II



Scheme III



Scheme IV



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