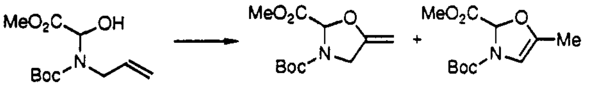
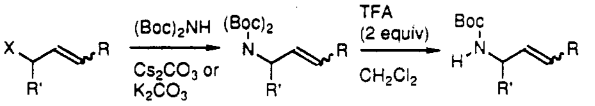
Remarkably, the cyclization to cyclopentene **23** appeared to be the fastest of all substrates tried, while cyclization to cyclooctene **31** was very slow. Clearly, the rate of the Pd(II)-mediated cyclization process is very sensitive to geometrical factors.

The reaction behavior of the parent allylcarbamate **33** was also briefly examined. Although in this case the usual elimination direction was not available (eq 3), cyclization did proceed (same conditions, 3 h) to give the 5-methyleneoxazolidine **34**[7] in 52% yield and a small amount of the double bond isomer **35** (ca. 5%).



33 **34** **35** (3)

The starting allylic carbamates were best prepared by using di-*tert*-butyl imidodicarbonate[12] as the nucleophile in an allylic substitution reaction on the corresponding halides with K_2CO_3 or Cs_2CO_3 as the base, followed by treatment with TFA for clean removal of one Boc-group (eq 4).[13,14]



(4)

To summarize, we have shown that allylic amines can be converted into 1-amino-3-alken-2-ols in a short reaction sequence involving three key steps: (1) *N*,*O*-hemiacetal formation from methyl glyoxylate, (2) Pd(II)-mediated oxidative cyclization, and (3) anodic oxidation (see Scheme I). The regioselectivity of the transformation is high in all cases, while the stereoselectivity is only high when starting from 3-aminocycloalkenes. When compared to the halocyclocarbamation route,[5] the advantage of the present method is the great ease and selectivity of olefin formation.[15] Applications of this methodology to enantiopure systems from α-amino acids and to natural products like the sphingosines[16] will be reported in due course.

Acknowledgment. We thank Professor P. W. N. M. van Leeuwen for useful discussions and the Innovation Oriented Research Program on Catalysis of the Dutch Ministry of Economic Affairs for financial support.

Supplementary Material Available: General experimental procedures for hemiacetal formation, cyclization, and anodic oxidation and spectral and analytical data for new compounds (10 pages). This material is contained in many 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.

---

[12] Ragnarsson, U.; Grehn, L. *Acc. Chem. Res.* **1991**, *24*, 285. For a convenient large-scale synthesis of this nitrogen nucleophile, see: Grehn, L.; Ragnarsson, U. *Synthesis* **1987**, 275.

[13] Connell, R. D.; Rein, T.; Åkermark, B.; Helquist, P. *J. Org. Chem.* **1988**, *53*, 3845.

[14] Details of these synthesis will be provided in a full paper.

[15] The same type of unsaturated β-amino alcohol has been prepared from 1,3-dienes: Garigipati, R. S.; Weinreb, S. M. *J. Am. Chem. Soc.* **1983**, *105*, 4499.

[16] See, e.g.: Dondoni, A.; Fantin, G.; Fogagnolo, M.; Pedrini, P. *J. Org. Chem.* **1990**, *55*, 1439 and references cited therein.

Prismene: A Theoretically Predicted Target for Experimental Studies

Volker Jonas and Gernot Frenking*

Fachbereich Chemie, Universität Marburg, Hans-Meerwein-Strasse, D-3550 Marburg, Germany

Received June 19, 1992

Summary: Two isomers of dehydroprismane with different positions of the double bond are calculated by quantum mechanical ab initio methods as minima on the C_6H_4 potential energy surface, and the most stable one with a double bond between a four-membered and a three-membered ring should be detectable in appropriate experiments.

The successful violation of bonding rules is a well-respected discipline in synthetic chemistry, challenging the skills of the inventive chemist. One example concerns the so-called Bredt's rule,[1] which implies the prohibition of bridgehead double bonds. Theoretical studies of strained molecules[2] and experimental efforts to synthesize molecules which violate Bredt's rule have led to the direct or indirect detection of a large number of highly strained compounds.[3] Such efforts are not only valuable for sharpening the skills of the synthetic chemists, they are also important to find out the limits of molecular stabilities. An important milestone to probe the validity of Bredt's rule is 1,2-didehydrocubane (cubene), which was predicted in 1988[4] by quantum mechanical calculations as an observable molecule. This prediction was subsequently confirmed by the synthesis of the highly strained cubene.[5]

In this paper, we report the results of ab initio calculations[6] which predict that the even higher strained and stronger pyramidalized dehydroprismane **1** is an observable species which should be detectable by appropriate experiments. The dehydrogenation of prismane may yield two isomeric alkenes, the tent-shaped prismene[7] (**1a**), in

---

[1] Bredt, J.; Thouet, H.; Schnitz, J. *Liebigs Ann. Chem.* **1924**, *437*, 1.

[2] Borden, W. T. *Chem. Rev.* **1989**, *89*, 1095.

[3] (a) Szeimies, G. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press: New York, 1983; Vol. 3, p 299. (b) Warner, P. M. *Chem. Rev.* **1989**, *89*, 1067. (c) Hassenrück, K.; Martin, H.-D.; Walsh, R. *Chem. Rev.* **1989**, *89*, 1125. (d) Billups, W. E.; Haley, M. M.; Lee, G.-A. *Chem. Rev.* **1989**, *89*, 1147.

[4] Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1988**, *110*, 4710.

[5] Eaton, P. E., Maggini, M. *J. Am. Chem. Soc.* **1988**, *110*, 7230.

[6] The geometries and vibrational frequencies were calculated at HF/6-31G(d) and MP2/6-31G(d) using GAUSSIAN 90: Frisch, M. J., Head-Gordon, M.; Trucks, G. W.; Foreman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M. A.; Binkley, J. S.; Gonzalez, C.; DeFrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. Gaussian Inc., Pittsburgh, PA, 1990. Geometry optimizations have also been carried out with a two-configuration (TCSCF) wave function and a 6-31G(d) basis set using the program GAMESS: Dupuis, M.; Spengler, D.; Wendolowski, J. I. NRCC QG01, Berkeley, 1980. Present version: Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Jensen, J. H.; Koseki, S.; Gordon, M. S.; Nguyen, K. A.; Windus, T. L.; Elbert, S. T. North Dakota State University, 1990.

0022-3263/92/1957-6085$03.00/0 © 1992 American Chemical Society

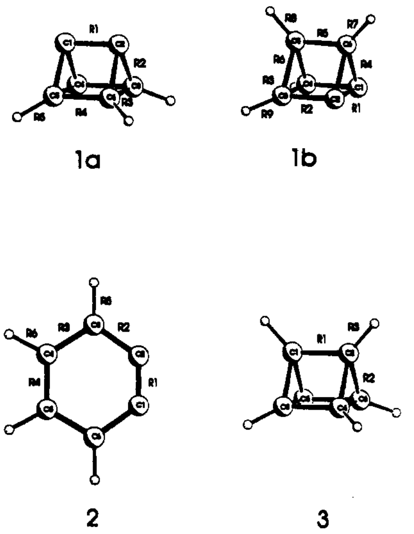


Figure 1. Optimized structures of prismene (**1a**), isoprismene (**1b**), *o*-benzyne (**2**), and prismane (**3**).

Table I. Optimized Geometries of Structures 1a, 1b, 2, and 3 (Bond Lengths in Å, Angles in deg)

variables	HF/6-31G(d)	MP2/6-31G(d)	CASSCF(2,2)/ 6-31G(d)
	Structure 1a		
R1	1.443	1.483	1.454
R2	1.471	1.484	1.478
R3	1.649	1.641	1.590
R4	1.483	1.494	1.517
R5	1.077	1.092	1.075
$A(C^6–C^3–H)$	123.3	122.5	125.5
$T(C^5–C^6–C^3–H)$	146.6	146.3	148.7
	Structure 1b		
R1	1.359	1.407	1.385
R2	1.543	1.544	1.542
R3	1.454	1.464	1.473
R4	1.521	1.529	1.508
R5	1.485	1.492	1.516
R6	1.570	1.579	1.547
R7	1.071	1.085	1.071
R8	1.079	1.092	1.077
R9	1.076	1.089	1.075
$A(C^5–C^6–H)$	134.3	133.8	133.9
$A(C^6–C^5–H)$	132.6	133.6	132.5
$A(C^1–C^4–H)$	135.2	135.0	134.5
$T(C^2–C^1–C^4–H)$	160.1	161.9	157.8
	Structure 2		
R1	1.223	1.268	1.260
R2	1.383	1.389	1.383
R3	1.392	1.406	1.389
R4	1.410	1.410	1.404
R5	1.073	1.086	1.073
R6	1.076	1.088	1.076
$A(C^1–C^2–C^3)$	127.5	126.6	125.7
$A(C^2–C^3–C^4)$	110.0	110.8	112.4
$A(C^2–C^3–H)$	127.1	126.8	125.3
$A(C^3–C^4–H)$	119.0	118.6	119.3
	Structure 3		
R1	1.549	1.549	
R2	1.507	1.518	
R3	1.074	1.085	
$A(C^1–C^2–H)$	132.5	132.7	

which the double bond is common to two four-membered rings, and isoprismene[7] (**1b**), in which the double bond is common to a four-membered and a three-membered ring (Figure 1). We optimized the geometries and calculated the energies and vibrational frequencies of **1a** and **1b**. For comparison, we also calculated the geometries and energies of *o*-benzyne (**2**) and prismane (**3**). The optimized geometries are shown in Table I. The calculated energies are listed in Table II.

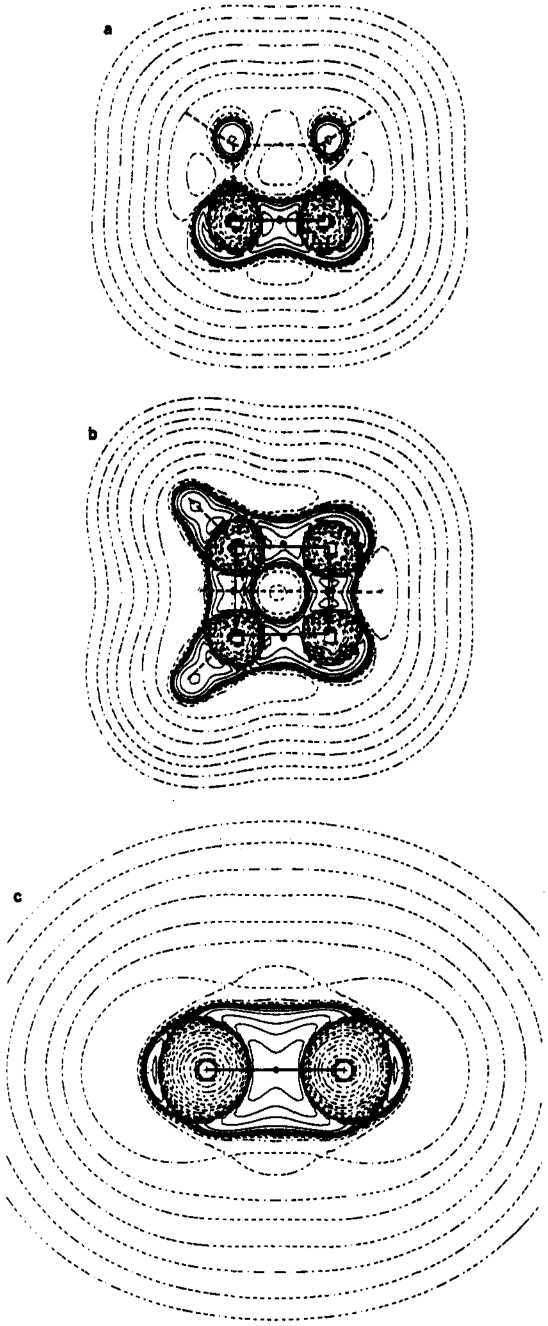


Figure 2. Contour line diagrams of the Laplacian of the electronic charge distribution $\nabla^2\rho(\mathbf{r})$ at MP2/6-31G(d) of (a) **1a** shown in the σ_v plane containing C^1 and C^2, (b) **1b** in the plane containing C^1, C^2, C^3, and C^4, and (c) ethylene in the vertical plane perpendicular to the molecule plane. Solid straight lines connect the atoms in the figure plane, and dashed straight lines connect the atoms which are above and below the figure plane. Dashed contour lines are in regions of charge depletion ($\nabla^2\rho(\mathbf{r}) > 0$) and solid lines in regions of charge concentration ($\nabla^2\rho(\mathbf{r}) < 0$).

Prismene (**1a**) is predicted to have a rather long CC double bond (1.443–1.483 Å), which is only slightly shorter than the formal single bonds between C2 and C3 (1.471–1.484 Å) and between C3 and C4 (1.483–1.517 Å). The CC single bond between C4 and C5 is calculated as rather long (1.590–1.649 Å), clearly longer than the corresponding CC bond in prismane (1.507–1.518 Å). The lenghtening of the double bond is caused by the substantial pyramidalization at C1 and C2. This is demonstrated by

---

(7) Prismene **1a**: tetracyclo[2.2.0.0^{2,6}.0^{3,5}]hex-1(4)-ene. Isoprismene **1b**: tetracyclo[2.2.0.0^{2,6}.0^{3,5}]hex-1(2)-ene.

Table II. Energies of the Three C_6H_4 Isomers (E_{tot} Are Given in hartree, E_{rel}, $E_{rel'}$, and ZPE Are Given in kcal mol^{-1})

		2		1a				1b			
method	basis	E_{tot}	ZPE[b]	E_{tot}	ZPE[b]	E_{rel}	$E_{rel'}$[c]	E_{tot}	ZPE[b]	E_{rel}	$E_{rel'}$[c]
HF	6-31G(d)	−229.386 85		−229.183 15		+127.7		−229.200 62		+116.8	
MP2	6-31G(d)	−230.191 29	44.0	−230.012 61	42.9	+112.0	+110.9	−230.019 61	43.1	+107.7	+106.8
MP2[a]	6-31G(2d)	−230.212 51		−230.031 98		+113.2	+112.1	−230.037 19		+109.9	+109.0
MP3[a]	6-31G(2d)	−230.218 11		−230.031 17		+117.2	+116.1	−230.041 65		+110.7	+109.8
MP4[a]	6-31G(2d)	−230.281 97		−230.095 18		+117.1	+116.0	−230.103 00		+112.2	+111.3
CAS(2,2)	6-31G(d)	−229.436 08		−229.222 24		+134.1	+133.0	−229.238 80		+123.7	+122.8

[a] Energies calculated at the MP2/6-31G(d) geometries (frozen core). [b] Scaled by 0.92. [c] $E_{rel'}$ = E_{rel} with inclusion of ZPE correction.

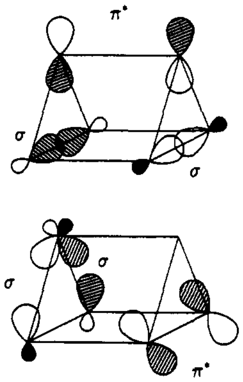


Figure 3. Schematic representation of the most important orbital interactions in **1a** and **1b** calculated by the NBO analysis.

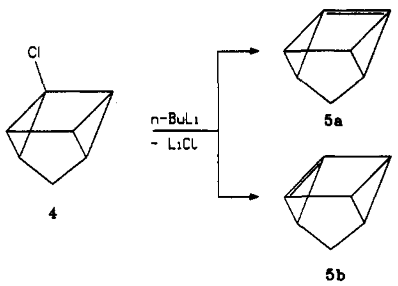
comparing the calculated Laplacian of the electronic charge distribution[8] of **1a** in the molecular plane containing C1 and C2 shown in Figure 2a with the Laplacian distribution for ethylene shown in Figure 2c. There is a region of charge concentration at each olefinic carbon atom of **1a** indicating the accumulation of charge in a nonbonded region which is absent in ethylene. This is at the expense of the charge concentration between the two carbon atoms. The Laplacian distribution calculated for the olefinic bond of **1b** exhibits similar features (Figure 2b).

The squares of the two coefficients in the TCSCF calculation indicate that **1a** has about 12% diradical character and thus should still be considered as an olefin.

The CC double bond in isoprismene (**1b**) is calculated as significantly shorter (1.359–1.407 Å) than in **1a**. The interatomic distances for the CC single bonds in **1b** differ less from the calculated values for prismane **3** than those of **1a** (Table I). The NBO analysis[9] of the wave functions of **1a** and **1b** gives an explanation for the differences in the optimized geometries. There is significant orbital interaction in **1a** between the occupied C3–C6 and C4–C5 σ orbitals and the empty C1–C2 π* orbital as shown in Figure 3. This yields rather short interatomic distances for the C1–C4, C1–C5, C2–C3, and C2–C6 bonds, while the C1–C2, C3–C6, and C4–C5 bonds become longer. The corresponding orbital interactions in **1b** between the occupied C3–C5 and C4–C5 σ orbitals and the vacant C1–C2 π* orbital is much weaker because the overlap is smaller (Figure 3).

The squares of the two coefficients in the TCSCF wave function of **1b** indicate 9% diradical character, less than in **1a**. Figure 2b shows the Laplacian of the electronic charge distribution of **1b** in the plane containing C1, C2, C3, C4. The regions of electronic charge concentration around C1 and C2 indicate the outward bending of the pyramidalized π-bond, which has its maximum below the plane shown in Figure 2b.

Scheme I



Both C_6H_4 isomers **1a** and **1b** are calculated at HF/6-31G(d) and MP2/6-31G(d) as minima on the potential energy hypersurface (only positive eigenvalues of the Hessian matrix). The lowest lying vibrational mode for **1a** and **1b** has a theoretical value of 552 cm^{-1} (MP2/6-31G(d)), which indicates that the potential well may be deep enough for a sufficient lifetime[10] to allow for specific reactions, although **1a** and **1b** are predicted to be much higher in energy than o-benzyne (**2**) (Table I). At the highest level of theory employed in this study (MP4/6-31G(2d)//MP2/6-31G(d) + zero point correction), **1a** is 116.0 kcal mol^{-1} less stable than **2**, and **1b** is 111.3 kcal mol^{-1} less stable than **2**. At all levels of theory, isoprismene (**1b**) is predicted to be lower in energy than prismene (**1a**).[11] Unlike **2**, which has been isolated and studied in low-temperature matrices[12] as well as in the gas phase,[13] the prismene isomers **1a** and **1b** may be difficult to observe directly. However, dehydrohalogenation of haloprismane should lead to formation of dehydroprismane (prismene) as an intermediate that could be trapped in a Diels–Alder reaction. In fact, such an approach has successfully been employed to study the related dehydroquadricyclane (**5**) (Scheme I).

Dehydrohalogenation of chloroquadricyclane (**4**) in the presence of dienes such as anthracene and 2,5-dimethylfuran yields Diels–Alder products of **5b**, but not of **5a**.[14] Further experiments have shown that the preference for

---

[8] Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*; Oxford University Press: Oxford, 1990.

[9] NBO 3.0: Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinfold, F. Department of Chemistry, University of Wisconsin, Madison. For a description of the method see: Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

[10] The corresponding mode is a twisting mode of the carbon skeleton. The lowest frequencies which can be identified as CC stretching modes have even higher wave numbers.

[11] After this study was completed, a work was published which gives in a footnote a calculated energy difference between **1a** and **1b** of 6.3 kcal/mol without further details: Branan, B. M.; Paquette, L. A.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* **1992**, *114*, 774.

[12] (a) Chapman, O. L.; Mattes, K.; McIntosh, C. L.; Pacansky, J.; Calder, G. V.; Orr, G. *J. Am. Chem. Soc.* **1973**, *95*, 6134. (b) Wentrup, C.; Blanch, R.; Briehl, H.; Gross, G. *J. Am. Chem. Soc.* **1988**, *110*, 1874.

[13] (a) Leopold, D. G.; Miller, A. E. S.; Lineberger, W. C. *J. Am. Chem. Soc.* **1986**, *108*, 1379. (b) Brown, R. D.; Godfrey, P. D.; Rodler, M. *J. Am. Chem. Soc.* **1986**, *108*, 1296. (c) Riveros, J. M.; Ingemann, S. Nibbering, N. M. M. *J. Am. Chem. Soc.* **1991**, *113*, 1053. (d) Wenthold, P. G.; Paulino, J. A.; Squires, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 7414.

[14] (a) Harnisch, J.; Baumgärtel, O.; Szeimies, G.; Van Meerssche, M.; Germain, G.; Declercq, J.-P. *J. Am. Chem. Soc.* **1979**, *10*, 3370. (b) Baumgärtel, O.; Harnisch, J.; Szeimies, G.; Van Meerssche, M. Germain, G.; Declercq, J.-P. *Chem. Ber.* **1983**, *116*, 2205. (c) Kenndorf, J.; Polborn, K.; Szeimies, G. *J. Am. Chem. Soc.* **1990**, *112*, 6117.

the formation of **5b** rather than **5a** is not caused by kinetic reasons but rather by the higher stability of the former isomer.[15] This agrees with our calculated result that **1b** is lower in energy than **1a**. Since the olefinic strain energy in **1** should not be significantly higher than in **5**, analogous experiments to prove the existence of **1b** as intermediate might also be successful.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the computer companies Silicon Graphics and Convex. Additional computer time was given by the HLRZ Jülich and the HHLR Darmstadt.

---

[15] Szeimies, G. Personal communication to G.F.

A Polymer-Supported Chiral Auxiliary Applied to the Iodolactonization Reaction: Preparation of γ-Butyrolactones

Hong-sik Moon, Neil E. Schore,* and Mark J. Kurth*,[1]

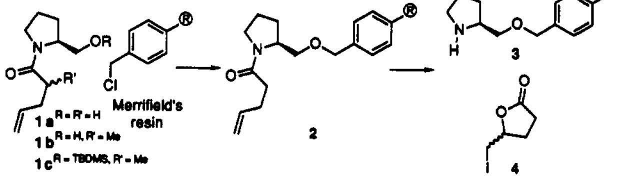
Department of Chemistry, University of California, Davis, California 95616

Received August 4, 1992

Summary: A reactive polymer strategy for the preparation of nonracemic 3,5-disubstituted γ-butyrolactones from a novel (*S*)-2-pyrrolidine-functionalized polystyrene resin is presented.

Resident stereochemistry can profoundly influence the course of electrophilic cyclization reactions as demonstrated by the iodo cyclizations of hepta-1,6-diene-4-carboxylic acids (olefin and face selectivity),[2] 3-hydroxy-2-(2′-methylenecyclohex-1′-yl)butyric acids (nucleophile [i.e., –OH vs –CO$_2$R] and face selectivity),[3] and of α-branched γ,δ-unsaturated N,N-dialkylamides (enantioselective olefin and face selectivity).[4] This, coupled with the fact that polymer-supported synthesis is emerging as an important tool in the development of new synthetic strategies in organic chemistry,[5,6] led us to explore the exciting potential of polymer-bound chiral auxiliaries[7] in enantioselective electrophilic cyclization protocols. Presumably, the advantages of polymer-supported synthetic strategy would include ease of workup, ease of product isolation, ready recovery of the polymer-supported chiral auxiliary by a simple filtration technique, and minimization of side-product formation.[8]

Scheme I



Intrigued by these potential advantages, we set out to explore the application of polymer-supported chiral auxiliary reactions in enantioselective synthesis and describe herein a polymer-supported strategy for a three-step process consisting of N-acylation of a chiral amine, amide Cα-alkylation,[9] and iodo cyclization,[10] which leads to the enantioselective preparation of α-substituted γ-butyrolactones. Having already reported the solution-phase version of this process,[4] we decided to extend this chemistry to a polymer-supported version by preparing a polymer-bound secondary amine. Our plan was to N-acylate the secondary amine, Cα-alkylate the resulting amide, and finally iodolactonize to a 3,5-substituted γ-butyrolactone. It is noteworthy that the final step of this process would not only produce the targeted iodo lactone but would also simultaneously regenerate the reactive polymer replete with its secondary amine chiral auxiliary.

A prolinol-functionalized reactive polymer was required to launch this project, and a C–O linkage of the chloromethylated polystyrene resin[11] and (*S*)-(+)-2-pyrrolidinemethanol (L-prolinol) was targeted. While Evans' pioneering chiral amide Cα-alkylation work established that solution-phase selectivity is highest when the prolinol hydroxyl is unblocked,[12] we chose to pursue this O-alkylated strategy for two reasons: (i) it would allow us to compare directly our anticipated polymer-supported results to previously reported solution-phase results[4,12] and (ii) O-alkylative coupling of L-prolinol to Merrifield's polymer appeared to offer quickest access to a reactive polymer. As illustrated in Scheme I, we decided to introduce L-prolinol in its amide form since the resulting 5-pentenamide functionalized polymer would be immediately poised for the key iodo cyclization reaction (**2** → **4**).

---

[1] Sloan Foundation Fellow (1987–1991) and NIH RCDA recipient (1989–1994; EC00182).

[2] Kurth, M. J.; Brown, E. G. *J. Am. Chem. Soc.* **1987**, *109*, 6844.

[3] Kurth, M. J.; Beard, R. L.; Macmillan, J. G.; Olmstead, M. *J. Am. Chem. Soc.* **1989**, *111*, 3712.

[4] Najdi, S. D.; Reichlin, D.; Kurth, M. J. *J. Org. Chem.* **1990**, *55*, 6241.

[5] Reviews: (a) Hodge, P. Polymer-supported Reagents. In *Polymer-supported Reactions in Organic Synthesis*; Hodge, P., Sherrington, D. C., Eds.; Wiley-Interscience: Chichester, 1980; Chapter 2. (b) Pittman, C. U., Jr. Catalysis by Polymer-supported Transition Metal Complexes. In *Ibid.*; Chapter 5. (c) Bergbreiter, D. E. Soluble Polymer-Bound Reagents and Catalysts. In *Polymer Reagents and Catalysts*; Ford, W. T., Ed.; ACS Symposium Series; American Chemical Society: Washington, DC, 1986; Vol. 308, 17. (d) Hodge, P. Organic Reactions Using Polymer-supported Catalysts, Reagents or Substrates. In *Synthesis and Separations using Functional Polymers*; Sherrington, D. D., Hodge, P., Eds.; Wiley: Chichester, 1988; Chapter 2. (e) Hodge, P. Polymer-supported Asymmetric Organic Synthesis. In *Innovation and Perspectives in Solid Phase Synthesis, 1990*; Epton, R., Ed. Collected Papers, First International Symposium, 1989; Oxford, Eng. SPCC (UK) Ltd.; Birmingham, 1990.

[6] (a) Schore, N. E.; Najdi, S. D. *J. Am. Chem. Soc.*, **1990**, *112*, 441. (b) Gerlach, M., Jördens, F.; Kuhn, H.; Neumann, W. P.; Peterseim, M. *J. Org. Chem.* **1991**, *56*, 5971. (c) Blanton, J. R.; Salley, J. M. *J. Org. Chem.* **1991**, *56*, 490.

[7] Itsuno, S.; Sakurai, Y.; Ito, K.; Maruyama, T.; Nakahama, S.; Frechet, J. M. J. *J. Org. Chem.* **1990**, *55*, 304.

[8] (a) Hodge, P. *Rapra Rev. Rep.* **1992**, *5*, 1. (b) Guyot, A.; Hodge, P.; Sherrington, D. C.; Widdecke, H. *React. Polym.* **1992**, *16*, 233.

[9] Evans, D. A.; Dow, R. L.; Shih, T. L.; Takacs, J. M.; Zahler, R. *J. Am. Chem. Soc.* **1990**, *112*, 5290.

[10] Bartlett, Paul A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, 1983; Vol. 3, pp 411–54.

[11] Merrifield's peptide resin (i.e., chloromethylated form of 2% cross-linked polystyrene/divinylbenzene copolymer): Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149.

[12] Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.

0022-3263/92/1957-6088$03.00/0 © 1992 American Chemical Society