While the solution-phase synthesis of Leu-Arg-Arg-Ala-*P*Tyr-Leu-Gly using synthon **3** was not possible, the above study has demonstrated (a) that the dibenzyl *N,N*-diethylphosphoramidite phosphite-triester phosphorylation procedure is ideal for the phosphorylation of protected tyrosine derivatives, (b) that benzyl phosphate groups undergo rapid acidolytic debenzylation in 40–50% TFA/$CH_2Cl_2$, and (c) that liquid hydrogen fluoride effects quantitative dephosphorylation of *P*Tyr residues. Despite these two latter complications, we can nevertheless suggest the use of Boc-Tyr($PO_3Bzl_2$)-OH as a suitable synthon in the synthesis of N-terminal *P*Tyr peptides providing that the final hydrogenolytic cleavage is not precluded by catalyst-poisoning amino acid residues (e.g., methionine or cystine). Alternatively, we can also recommend the dimethyl phosphate derivative, Boc-Tyr($PO_3Me_3$)-OH, for use in Boc/solution- and Boc/solid-phase *P*Tyr peptide synthesis and that we have successfully used this derivative for the synthesis of large, complex *P*Tyr-containing peptides.[12,17,18]

## Experimental Section

**General Methods.** The $^{13}C$ NMR spectra of Boc-amino acids **2** and **3** and tripeptide **8** were obtained as $CDCl_3$ solutions on a JEOL-FX 100 Fourier transform instrument operating at 25.00 MHz and referenced to internal tetramethylsilane. The $^{13}C$ NMR spectrum of tripeptide **9** was obtained as a $D_2O$ solution and referenced to internal dioxane set to 66.5 ppm. The $^{31}P$ NMR spectra were obtained on a JEOL-FX 100 Fourier transform instrument operating at 40.26 MHz and referenced to external 85% $H_3PO_4$. The FAB mass spectra were obtained on a JEOL-DX 300 mass spectrometer equipped with a FAB source and used acetic acid/glycerol as matrix support. The optical rotation of tripeptides **8** and **9** were obtained as $CHCl_3$ or $D_2O$ solutions, respectively, and were measured on a Perkin-Elmer 241 MC polarimeter with a 1-dm path length cell kept at constant temperature. Acetic acid and trifluoroacetic acid were of analytical reagent grade and used without purification.

**Boc-Tyr($PO_3Bzl_2$)-ONBzl (2).** 1*H*-Tetrazole (1.16 g, 16.5 mmol) was added in one portion to a solution of Boc-Tyr-ONBzl (**1**) (2.08 g, 5.00 mmol) and dibenzyl *N,N*-diethylphosphoramidite (1.74 g, 5.50 mmol) in dry tetrahydrofuran (5 mL), and the resulting solution was then stirred for 15 min at 20 °C. The mixture was then cooled to −40 °C and a solution of 85% *m*-chloroperoxybenzoic acid (1.22 g, 6.00 mmol) in dichloromethane (12 mL) was added such that the temperature of the solution was maintained below 0 °C. After stirring for 10 min at 20 °C, 10% $Na_2S_2O_5$ (25 mL) and diethyl ether (100 mL) were added, the aqueous phase was discarded, and the ethereal phase was washed with 10% $Na_2S_2O_5$ (1 × 50 mL), 5% $NaHCO_3$ (1 × 50 mL), and 1 M HCl (1 × 50 mL), dried ($Na_2SO_4$), and filtered. The solvent was then removed by evaporation under reduced pressure and the light yellow oil then triturated with hexane (3 × 50 mL). On prolonged standing, the light yellow oil (3.24 g, 96%) became an off-white solid, mp 81–82 °C (lit.[13] mp 81–82 °C).

**Boc-Tyr($PO_3Bzl_2$)-OH (3).** Sodium dithionite reduction[16] of **2** (3.04 g, 4.50 mmol) was performed according to previously described procedures[13,20] and gave **3** as a light yellow oil (1.87 g, 77%), which became a white solid on standing, mp 91–92.5 °C (lit.[13] mp 91.5–92.5 °C).

**Boc-Tyr($PO_3Bzl_2$)-Leu-Gly-OBzl (8).** *N*-Methylmorpholine (0.28 g, 2.80 mmol) in THF (1 mL) and isobutyl chloroformate (0.355 g, 2.60 mmol) in THF (1 mL) were successively added to a solution of Boc-Tyr($PO_3Bzl_2$)-OH (1.52 g, 2.80 mmol) in THF (10 mL) at −20 °C. After an activation period of 3 min, a solution of dipeptide **7** (0.63 g, 2.00 mmol) and *N*-methylmorpholine (0.20 g, 2.00 mmol) in THF (4 mL) was added, and the resulting solution was stirred for 2 h at −20 °C prior to the addition of 5% $NaHCO_3$ (5 mL). After 30 min at 20 °C, dichloromethane (100 mL) was added and the organic phase washed with 5% $NaHCO_3$ (2 × 30 mL) and 1 M HCl (2 × 30 mL), dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure gave tripeptide **8** as a light brown oil (1.52 g, 95%): $[\alpha]^{23}_D$ −18.0° (*c* 1, $CHCl_3$); $^1H$ NMR ($CHCl_3$) δ 0.75–1.02 (m, 6 H, Leu $CH_3$), 1.42 (s, 9 H, Boc $CH_3$), 1.50–1.72 (b m, 3 H, Leu γ-CH and Leu β-$CH_2$), 2.00–2.40 (b m), 2.9–3.2 (b m), 3.9–4.1 (b m), 5.10 and 5.13 (each d, 2 H, $J_{PO-CH}$ = 8.35 Hz, $PO_3Bzl_2$), 5.18 (s, 2 H, Bzl $CH_2$), 6.4 and 6.7 (each b d, 1 H, Tyr($PO_3Bzl_2$) and Leu NH), 6.9–7.2 (b dd, Tyr ArH), 7.2–7.4 (m, 15 H, Bzl ArH); $^{13}C$ NMR ($CHCl_3$) δ 21.77, 22.65, 24.35, 28.03, 37.16, 40.79, 41.02, 51.43, 55.53, 66.88, 69.83 (d, *J* = 4.39 Hz), 80.04, 119.80 (d, *J* = 4.40 Hz), 127.84, 128.13, 128.42, 130.53, 135.10 (d, *J* = 5.86 Hz), 149.44 (d, *J* = 7.33 Hz), 155.57, 169.38, 171.60, 171.89, 172.36; $^{31}P$ NMR ($CHCl_3$) δ −6.4.

**H-Tyr($PO_3H_2$)-Leu-Gly-OH TFA (9).** A solution of tripeptide **8** (0.80 g, 1.00 mmol) in 50% TFA/AcOH (4 mL) containing 10% palladium on charcoal (0.30 g) was charged with hydrogen at atmospheric pressure. On cessation of hydrogen uptake 30 min), the catalyst was removed by gravity filtration and the solvent removed under reduced pressure. Repeated trituration of the residue with diethyl ether (3 × 30 mL) followed by high vacuum drying gave tripeptide **9** as a white solid (0.542 g, 99.5%), mp 172–175 dec: $[\alpha]^{23}_D$ −8.30° (*c* 1, $H_2O$); $^{13}C$ NMR ($D_2O$) δ 21.01, 21.84, 24.08, 35.98, 39.93, 41.00, 52.26, 54.02, 120.84 (d, *J* = 4.40 Hz), 129.06, 130.62, 151.56 (d, *J* = 7.69 Hz), 168.65, 172.74, 173.86; $^{31}P$ NMR ($D_2O$) δ −3.8; FAB mass spectrum (Ar, positive mode), *m/z* (rel intensity) 454 ($[M - H + Na]^+$, 1), 432 ($[M]^+$, 16), 416 (1), 352 ($[M - PO_3H]^+$, 9), 336 ($[M - 96]^+$, 1), 329 (3), 245 (4.5), 227 (2.5), 216 (9), 207 (5), 189 (9), 136 (23), 115 (23), 86 (100); FAB mass spectrum (Ar, negative mode), *m/z* (rel intensity) 430 ($[M - 2H]^-$, 57), 415 (7), 372 (4), 350 ($[M - 2H - PO_3H]^-$, 9), 335 (4), 297 (4), 259 (6), 243 (4), 214 (6), 165 (8), 151 (16), 127 (8), 97 (23), 80 (100).

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**Registry No.** 1, 92264-95-4; 2, 92264-98-7; 3, 92265-01-5; 4, 54244-69-8; 5, 2462-31-9; 6, 37783-45-2; 7, 60079-62-1; 8, 118920-14-2; 9, 118892-04-9; 10, 118892-05-0; 11, 118892-06-1; $(BzlO)_2PNEt_2$, 67746-43-4; BOC-Ala-OH, 15761-38-3; BOC-Leu-OH, 13139-15-6.

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# Generation and Rearrangement of Unsaturated Hydrocarbons from Flash Vacuum Pyrolysis of Dichlorocyclopropanes at 850 °C

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Although the gas-phase, thermal rearrangements of dihalocyclopropanes to halodienes and to trienes have been observed to occur at temperatures <700 °C,[1-6] only in the

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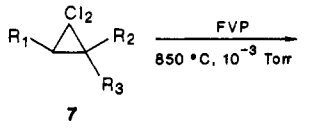
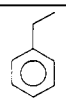
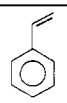
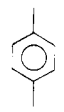
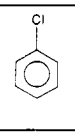
0022-3263/89/1954-1752$01.50/0 

**Table I. Product Distribution for FVP of Some $C_5$-Substituted 1,1-Dichlorocyclopropanes at 850 °C[a,b]**

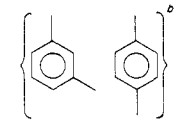



7

| structure 7 | | |  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|
| $R_1$ | $R_2$ | $R_3$ | | | | | | | | |
| H | H | *n*-Am | 59 ± 6 | 30 ± 5 | 0.6 ± 0.1 | 5.5 ± 0.2 | 1.8 ± 0.1 | 1.4 ± 0.2 | 1.3 ± 0.2 | 0.4 ± 0.1 |
| Et | H | *n*-Pr | 73 ± 3 | 21 ± 2 | 1.2 ± 0.6 | 2.5 ± 0.6 | 0.6 ± 0.2 | 0.8 ± 0.3 | 0.5 ± 0.1 | 0.9 ± 0.2 |
| H | Me | *t*-Bu | 32 ± 11 | 55 ± 1 | 3.5 ± 3.0 | 3.4 ± 0.6 | 1.0 ± 0.3 | 2.8 ± 1.4 | 0.6 ± 0.4 | 0.5 ± 0.5 |

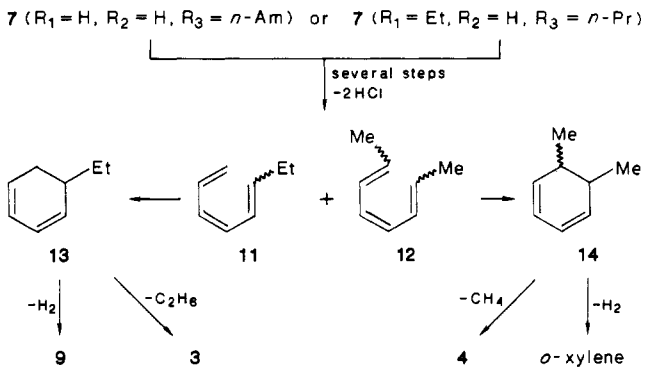
[a] Values in percent total 100 and do not include 2–3% of as many as 10 volatile products of higher molecular weight, among which naphthalene was the only compound positively identified; larger values rounded to nearest percent; errors expressed as ±range/2 for two, five, and three runs, respectively. [b] Qualitatively similar results were obtained for pyrolysis of 1,1-dichloro-2-butyl-2-methylcyclopropane (7, $R_1$ = H, $R_2$ = *n*-Bu, $R_3$ = Me).

**Table II. FVP of Selected $C_8H_{10}$ Hydrocarbons at 850 °C[a]**

| compound |  |  |  |  |  |  |
|---|---|---|---|---|---|---|
| *o*-xylene[c] | 2.5 ± 2 | 4.5 ± 3 | 0 | 90 | | 3.0 ± 0.7 |
| *m*-xylene[c] | 0 | 2.0 ± 0.2 | 0 | 2.0 ± 0.1 | | 96 |
| *p*-xylene[c] | 0 | 5.0 ± 3 | 0 | 2.5 ± 1 | | 92 |
| ethylbenzene[d] | 14 ± 6 | 39 ± 3 | 12 ± 3 | | 33 ± 5 | 2.0 ± 0.4 |

[a] Percent of volatile products analyzed on a DB-1 GC capillary column; larger values rounded to nearest percent; errors expressed as ±range/2; some nonvolatile polymeric products were observed in the pyrolysis of each of the xylenes. [b] GC analysis on a DB-1 capillary column did not clearly distinguish these isomers. [c] Average of two runs. [d] Average of four runs.

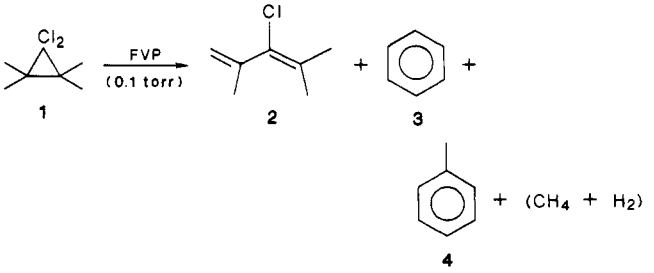
**Scheme I**



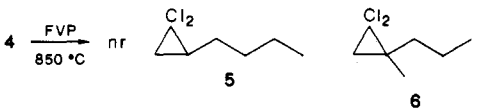

case of 7,7-dihalobicyclo[4.1.0]heptanes have aromatic products been reported.[7-9] As an adjunct to our previous studies of the use of trimethyl(trichloromethyl)silane as a convenient precursor of dichlorocarbene in the gas phase,[10] we now report some fascinating transformations of $C_5$-substituted 1,1-dichlorocyclopropanes to benzene, toluene, and various isomeric $C_8H_{10}$ aromatic hydrocarbons at 850 °C under flash vacuum pyrolysis (FVP) conditions. That these transformations are occurring only slightly above the threshold temperature is evidenced by the lack of any appreciable amount of aromatic products at temperatures ≤800 °C.

## Results and Discussion

In a project unrelated to the current study, we had noted that FVP of 1,1-dichloro-2,2,3,3-tetramethylcyclopropane (1) at 600 °C (0.1 Torr) gave an excellent yield of 3-chloro-2,4-dimethyl-1,3-pentadiene (2)[5-6] but was accompanied by traces of benzene (3) and toluene (4). Although




these aromatic hydrocarbons still represented only 6% and 2%, respectively, of the liquid product mixture from FVP at 800 °C, pyrolysis at 850 °C resulted in a mixture of 2–4 in relative amounts of 33%, 28%, and 39%. FVP of chloro diene 2 gave similar results, and toluene (4) was shown to be stable to these reaction conditions. Benzene and toluene were the only liquid products when the isomeric dichlorocyclopropanes 5 and 6 were pyrolyzed under similar conditions.[11]

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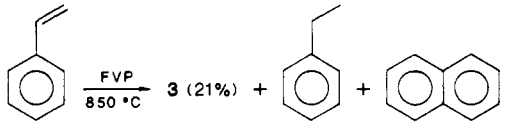
(11) Methane and hydrogen were not trapped and observed directly but are simply inferred from the nature of the other products.

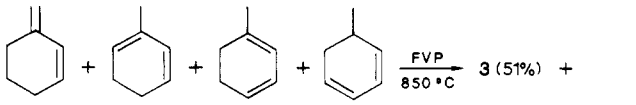
In an effort to test the generality of these observations to gain insight into possible pathways to rationalize product formation, our observations on some pyrolyses of $C_5$-substituted 1,1-dichlorocyclopropanes **7** at 850 °C are summarized in Table I. A system pressure of $10^{-3}$ Torr was used to minimize bimolecular processes. As with the $C_4$-substituted cases mentioned previously, the major products were benzene and toluene together with very small amounts of ethylbenzene, styrene, xylenes, and chlorobenzene. Although toluene was shown to be unreactive under the conditions employed, control reactions listed in Table II indicated that some of the minor products reported in Table I could be the result of secondary reactions of ethylbenzene. While labeled benzene and naphthalene have been shown to interconvert under FVP conditions at 1110 °C,[12] we noted only a very small amount of xylene interconversion at 850 °C accompanied by the apparent formation of polyquinodimethanes, which were not characterized.[13] FVP of styrene (**8**) at 850 °C gave the results shown.




**8** **9** (9%) **10** (2%)

(+ several unidentified hydrocarbons in <1% amounts)

Scheme I outlines some reasonable but speculative paths to account for the major products from 1,1-dichloro-2-pentylcyclopropane (**7**, $R_1 = R_2 = H$, $R_3 = n$-Am) and 1,1-dichloro-2-ethyl-3-propylcyclopropane (**7**, $R_1 = Et$, $R_2 = H$, $R_3 = n$-Pr). The thermal opening of 1,1-dichlorocyclopropanes to chlorodienes,[14,15] followed by double-bond migration via 1,5-sigmatropic rearrangements of hydrogen[16] and thermal loss of HCl[17] to give trienes such as **11** and **12** are well-known types of reactions under FVP conditions. Electrocyclic closure of the trienes[18-23] provides a reasonable known route to cyclohexadienes **13** and **14** from which the major aromatic products **3** and **4** arise by the preferred thermal elimination of ethane and methane, respectively,[17,24] compared with the less favored elimination of hydrogen to form small amounts of ethylbenzene (**9**) and *o*-xylene. The latter suggestion is consistent with our own observations that when the mixture of dienes **15**–**18** was pyrolyzed at 850 °C, the ratio of benzene to toluene was ca. 2:1.[25] It is of some interest that the pyrolysis of 1,1-




**15** (50%) **16** (36%) **12** (10%) **18** (4%)

**4** (24%) + **9** (7%) + **15** (6%) + unidentified hydrocarbons (12%)

dichloro-2-methyl-2-*tert*-butylcyclopropane (**7**, $R_1 = H$, $R_2 = Me$, $R_3 = t$-Bu) also gave benzene and toluene as major products, but with the latter in excess, and requires mechanistic features uniquely different from those outlined in Scheme I.

## Experimental Section

Routine $^1H$ NMR spectra were determined on a Varian EM-360 spectrometer, while both $^1H$ and $^{13}C$ NMR spectra at higher field were obtained on a Varian XL-300 spectrometer. MS data were obtained on a Ribermag R10-10 GC–mass spectrometer equipped with a 25-m OV-101 capillary column or a VG Analytical ZAB-HS high-resolution mass spectrometer. A Perkin-Elmer Sigma 3B chromatograph equipped with a 30-m DB-1 capillary column (Anspec) at 50–90 °C (programmed, 5°/min) and attached to a Hewlett-Packard 3390A recording integrator was used for GC analyses. The separation of *m*-xylene from *p*-xylene was accomplished with a 25-m CP-WAX-52 capillary column (Chrompack) operating at 40 °C.

**Flash Vacuum Pyrolyses.** All of the FVP experiments that are described were done with the simple apparatus previously reported[10] but with a pyrolysis tube containing Vycor chips treated with chlorotrimethylsilane. Normally ca. 400 mg (2.2 mmol) of a $C_8H_{14}Cl_2$ isomer was placed into the pyrolysis flask and allowed to vaporize through the hot zone (840–850 °C) over a period of 5 min with the sample at room temperature or warmed slightly. System pressure was maintained at $10^{-2}$–$10^{-3}$ Torr. Products were trapped on a cold finger at 77 K, rinsed from the slightly warmed surface with methylene chloride (ca. 2 mL), and analyzed by GC and GC–MS procedures.

**1,1-Dichloro-2-pentylcyclopropane: General Procedure.** Various dichlorocyclopropanes were synthesized by dichlorocarbene addition to the commercially available alkenes by a combination of phase transfer[26] and ultrasonication as suggested without detail by Bremmer.[27]

1-Heptene (4.0 mL, 2.8 g, 28.5 mmol), 50% (w/w) aqueous NaOH (9.2 g, 115 mmol), and benzyltriethylammonium chloride (66 mg, 0.29 mmol) were placed into a 50-mL three-necked flask equipped with a small overhead stirrer, a reflux condenser, and a rubber stopple. The contents of the flask were stirred and ultrasonicated (cleaning bath) while chloroform (9.2 mL, 13.7 g, 115 mmol) was added slowly (55 min) from a 5-mL hypodermic syringe. The mixture was stirred and ultrasonicated for an additional 2.5 h.

The reaction mixture was rinsed into a separatory funnel with water (20–25 mL) and extracted with diethyl ether (3 × 10 mL), and the ether extracts were washed with saturated NaCl, dried ($CaCl_2$), evaporated, and distilled to give product (2.20 g, 12.2 mmol, 42.8%): bp 70–80 °C (10–15 Torr) (lit.[28,29] bp 67–69 °C (10 Torr) and 76 °C (15 Torr)); $^1H$ NMR ($CCl_4$) $\delta$ 0.5–1.0 (4 H, m), 1.0–1.72 (10 H, m); MS (CI, isobutane) *m/e* (relative intensity) 184, 182, 180 (2,5,8; isotopic cluster for $Cl_2$), 109 (100, $C_7H_{13}$). Anal. Calcd for $C_8H_{14}Cl_2$: C, 53.06; H, 7.79. Found: C, 52.88; H, 7.50.

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**1,1-Dichloro-2-ethyl-3-propylcyclopropane** was prepared from (*E*)-3-heptene (62% yield): bp 70–80 °C (10–15 Torr) (lit.[30] bp 76–77 °C (20 Torr)); $^1$H NMR δ 0.7–1.24 (8 H, m), 1.24–1.76 (6 H, m); MS (CI, $NH_3$) *m/e* (relative intensity) 184, 182, 180 (2, 5, 8; isotopic cluster for $Cl_2$), 109 (100, $C_7H_{13}$). Anal. Calcd for $C_8H_{14}Cl_2$: C, 53.06; H, 7.79. Found: C, 52.78; H, 7.60.

**1,1-Dichloro-2-methyl-2-*tert*-butylcyclopropane** was prepared from 2,3,3-trimethyl-1-butene (62.2% yield): bp 70–75 °C (15 Torr); $^1$H NMR δ 1.08 (1 H, d, *J* = 7), 1.10 (9 H, s), 1.32 (3 H, s), 1.60 (1 H, d, *J* = 7). The compound has been reported, but without characterization data.[31] Anal. Calcd for $C_8H_{14}Cl_2$: C,53.06; H, 7.79. Found: C, 53.14; H, 7.92.

**Methylcyclohexadienes.** A mixture of methylenecyclohexane (50%), 2-methyl-1,3-cyclohexadiene (36%), 1-methylcyclohexadiene, and 5-methylcyclohexadiene (14% for the latter two isomers) was prepared in 85% yield (distilled) by heating 1-methyl-2-cyclohexen-1-ol in DMSO at 160–170 °C for 2.75 h according to the general method of Traynelis, Hergenrother, Hanson, and Valicenti.[32] The mixture was analyzed by GC and NMR procedures.

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**Registry No.** **7** ($R_1$ = $R_2$ = H; $R_3$ = *n*-Am), 3722-09-6; **7** ($R_1$ = Et; $R_2$ = H; $R_3$ = *n*-Pr), 40347-50-0; **7** ($R_1$ = H; $R_2$ = Me; $R_3$ = *t*-Bu), 85653-76-5.

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## An Improved Synthesis of (−)-(2*R*,5*R*)-2,5-Dimethylpyrrolidine

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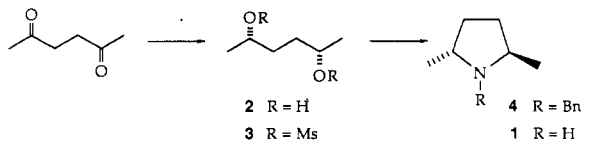
Reagents of $C_2$ symmetry have demonstrated utility in asymmetric synthesis.[1] With the notable exception of those derived from tartaric acid,[2] most $C_2$ symmetrical reagents are of synthetic origin, and thus, the preparation of these substances in optically pure form is subject to continual refinement.

As part of the strategy of reagent-controlled asymmetric synthesis,[3] we were interested in developing new reagents of $C_2$ symmetry and noted with particular interest the isostructural relationship between the titled compound (**1**)[4] and *trans*-2,5-dimethylborolane.[5a] The latter reagent,

**Scheme I**




developed in our laboratories, effects near-complete asymmetric induction in the hydroboration[5b] and aldol reactions[5c] and also in the reduction of aryl and aliphatic ketones.[5d,e]

Continuing interest in *trans*-2,5-dimethylpyrrolidine has been evidenced by recent reports on the application[6] and synthesis[7] of this versatile base, and we therefore wish to report a reaction sequence (Scheme I) which, by emphasizing brevity and minimal purification of intermediates, provides for the rapid synthesis of multigram quantities of **1** in optically pure form.

### Experimental Section

Boiling points and melting points are uncorrected. Reactions were run in oven-dried glassware under Ar. Methanesulfonyl chloride was distilled before use. Triethylamine, benzylamine, and dichloromethane were distilled from $CaH_2$ in an atmosphere of dry $N_2$. Enzymatic reductions employed Fleishmann's "active dry yeast", distributed through local retail grocers. $^1$H NMR spectra were recorded at 250 MHz on a Bruker WM 250 spectrometer, and $^{13}$C NMR spectra were recorded on a Bruker WM 270 (67.9 MHz) or Varian XL-400 (100.6 MHz) spectrometer as indicated. Optical rotations were recorded on an Autopol III polarimeter. HPLC analysis was performed on a Waters 6000A instrument equipped with a Chemcosorb 3 Si column (4.6 × 250 mm) and UV detection (254 nm). Analytical gas chromatography was performed on a Hewlett-Packard 5880A instrument using a 12-m cross-linked methyl silicone column. Mass spectra were obtained with a Finnigan MAT 8200 spectrometer. Commercial (*S*)-(−)-MTPA (Aldrich) was upgraded to >99.5% ee by recrystallization of the (−)-phenylethylamine salt, and MTPA derivatives were prepared by the method of Mosher.[8]

**(+)-(2*S*,5*S*)-2,5-Hexanediol (2).** Reduction of 2,5-hexanedione with baker's yeast was carried out as described by Lieser[9] (0.125-mol scale) to give diol **2** (7–8 g, 50% yield) after chromatography over silica gel (EtOAc) and distillation, bp 122–125 °C (20 mm). The product solidified on standing, mp 48–53 °C, $[\alpha]^{24}_D$ +33.1° (*c* 9.87, $CHCl_3$) [lit.[10] mp 53.0–53.3 °C, $[\alpha]^{25}_D$ +35.1° (*c* 9.49, $CHCl_3$)]. HPLC analysis of the corresponding bis-MTPA esters (7% ether/hexane, 2 mL/min) indicated the presence of *S,S*, *R,S*, and *R,R* diols in the ratio 49.8:1.04:1.00 (96% ee, 2% meso). This could be upgraded to >98% ee, <1% meso by recrystallization from $Et_2O$ [80% recovery, mp 52–53 °C, $[\alpha]^{24}_D$ +34.9° (*c* 9.48, $CHCl_3$)]. The combined product from six runs was used in the following reaction.

**(−)-*N*-Benzyl-(2*R*,5*R*)-2,5-dimethylpyrrolidine (4).** To a solution of (+)-(2*S*,5*S*)-2,5-hexanediol (**2**) (46.5 g, 0.39 mol) in 800 mL of $CH_2Cl_2$ was added triethylamine (137 mL, 0.98 mol). The solution was cooled to −15 °C, and methanesulfonyl chloride (67 mL, 0.87 mol) was added dropwise with vigorous stirring over 90 min while the temperature was maintained between −20 and −15

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