Reactions of Diethoxytriphenylphosphorane with Diastereoisomeric 3-Methylcyclohexane-1,2-diols. Control of Regioselectivity by Methyl Substitution during Cyclodehydration and Rearrangement of 1,2-Diols

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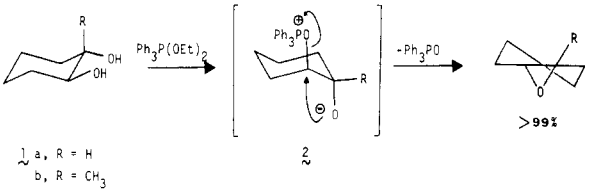
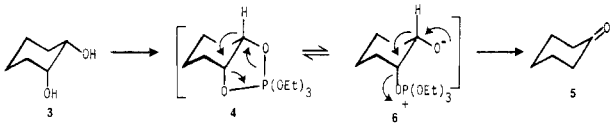
The diastereoisomeric 3-methylcyclohexane-*trans*-1,2-diols undergo cyclodehydration with diethoxytriphenylphosphorane (DTPP) to afford the *cis*- and *trans*-3-methylcyclohexene oxides. The ratio of cis and trans epoxides is best explained by assuming preferential phosphoranylation of the C_1 hydroxyl group followed by "3-exo-tet" alkoxide displacement of triphenylphosphine oxide. The diastereoisomers of 3-methylcyclohexane-*cis*-1,2-diol afford stable σ-dioxyphosphoranes when allowed to react with DTPP. These 1,3,2-dioxaphosphoranes were subjected to flash thermolysis (<300 °C) conditions and afforded the isomeric 2- and 3-methylcyclohexanones via a 1,2-hydride shift.

Quite recently, we reported that *trans*-1,2-cyclohexanediol (**1a**) and 1-methyl-*trans*-1,2-cyclohexanediol (**1b**) react smoothly with diethoxytriphenylphosphorane (DTPP) to afford essentially quantitative yields (>99%) of the corresponding epoxides.[1] These results are consistent with an interpretation involving formation of a transient betaine intermediate (**2**) which undergoes loss of triphenylphosphine oxide (TPPO) via alkoxide displacement to form the epoxides. In an earlier report,



Chang et al.[2a] had shown that the diastereomer of **1a**, *cis*-1,2-cyclohexanediol (**3**), reacts with pentaethoxyphosphorane [$P(OEt)_5$] to afford a stable oxyphosphorane [**4**; ^{31}P NMR δ −53] which is easily thermolyzed at elevated temperature to give cyclohexanone (**5**) and triethyl phosphate. A synchronous 1,2-hydride shift in oxyphosphorane **4** or oxyphosphonium betaine **6** satisfactorily accounts for formation of ketone **5**.[2b]



It seems a reasonable expectation that a proximal ring substituent in the cyclohexane-1,2-diols might control reagent approach as well as create repulsive nonbonding interactions within the intermediates (i.e., **2**, **4**, **6**) and encourage conditions for regioselective cyclodehydration and rearrangement.

In this report, we describe the results of our studies detailing the effect of methyl substitution on the regioselective phosphoranylation and subsequent cyclodehydration and rearrangement of the cis/trans diastereomers of 3-methylcyclohexane-*trans*-1,2-diol and 3-methylcyclohexane-*cis*-1,2-diol with DTPP.

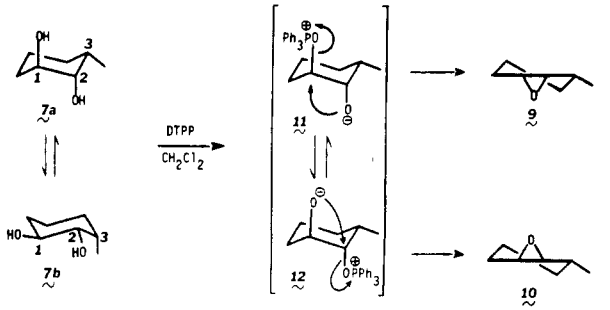
Table I. DTPP-Promoted Cyclodehydration and Rearrangement of Diastereomeric Methyl Cyclohexane-1,2-diols[a]

	yield, %			yield, %	
diol	9	10	diol	20	21
7	78.8	21.2	17	70.4	29.6
8	27.1	72.9	18	42.5	57.5

[a] The percentage of each diastereomeric epoxide/ketone was determined by GLC/^{13}C NMR analysis of reaction mixtures. The identity of each component of the reaction mixture was determined by comparison of GLC retention times and/or ^{13}C NMR spectral properties of authentic materials.

Results and Discussion

Reaction of DTPP with Trans 1,2-Diols. *trans*-2-Hydroxy-*trans*-3-methylcyclohexanol (**7**) is prepared by oxidation of 3-methylcyclohexene with hydrogen peroxide–formic acid (40–45 °C), followed by basic hydrolysis with sodium hydroxide.[3,4] *trans*-2-Hydroxy-*cis*-3-methylcyclohexanol (**8**) is prepared by hydroboration–oxidation of 3-methylcyclohex-2-en-1-one.[4] Diol **8** is expectedly conformationally homogeneous, having all the ring substituents in the equatorial conformation, but diastereomer **7** exists presumably as a 1:1 mixture of conformational isomers (**7a**, **7b**) in deuteriochloroform solvent.[4]



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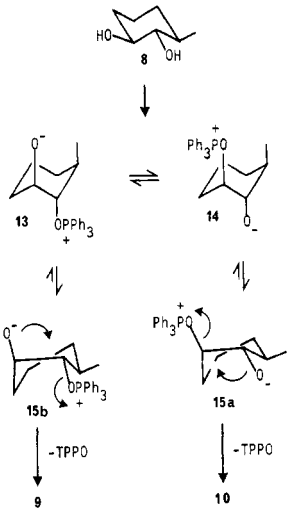
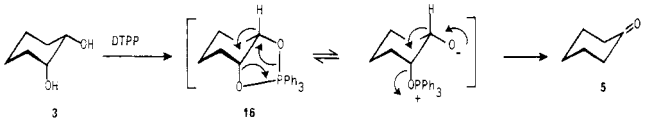
DTPP-promoted diaxial of diol **7** affords 79% of *cis*-3-methylcyclohexene oxide (**9**) and 21% of *trans*-3-methylcyclohexene oxide (**10**) (Table I). Regioselective phosphoranylation of the least sterically hindered axial C_1 hydroxy group in conformer **7a** or the equatorial C_1 hydroxy group in **7b** is apparently favored. The diaxial antiperiplanar array necessary for epoxide formation can be realized in betaines **11** and **12**.

The percentage of epoxide **10** (73%) resulting from cyclodehydration of diol **8** clearly implies preferential phosphoranylation of C_1-OH, but it does not necessarily mean that either of the regioisomeric betaines, **13** or **14**, decomposes via the energetically unfavorable chair transition states having three axial substituents. From an examination of molecular models, we speculate that the stereoelectronic requirement for the "3-exo-tet"[5] alkoxide displacement of TPPO can also be realized if the six-membered rings adopt twist-boat conformations (**15a,b**).



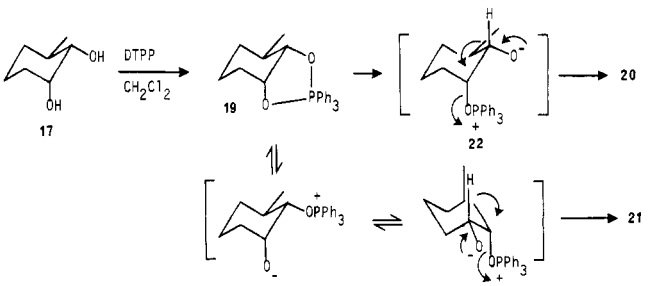
In conformers **15a** and **15b** the methyl group can occupy the most stable pseudoequatorial conformation, and the alkoxide and Ph_3PO groups can assume the prerequisite antiperiplanar orientation necessary for effective cyclodehydration.

Reaction of DTPP with Cis 1,2-Diols. Diol **3** reacts with DTPP in refluxing CH_2Cl_2 (72 h) to afford dioxyphosphorane **16** (^{31}P NMR δ −37.7; >90%) which readily distills at 150 °C (0.05 torr) with only minor decomposition. Flash thermolysis of **16** (300 °C, 14–23 torr) gives cyclohexanone (>80%). It is quite reasonable that formation of ketone **5** occurs by a pathway analogous to that suggested for the decomposition of phosphorane **4** or betaine **6** (vide supra).

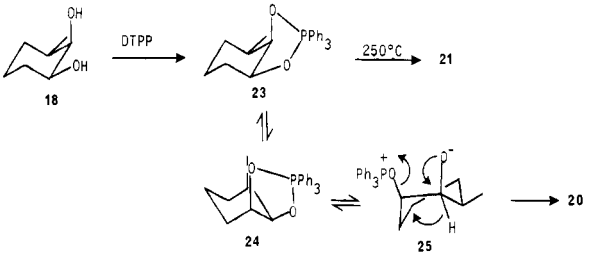


cis-2-Hydroxy-*trans*-3-methylcyclohexanol (**17**) is easily prepared by oxidation of 3-methylcyclohexene by the Woodward–Brutcher procedure[4,6] while *cis*-2-hydroxy-*cis*-3-methylcyclohexanol (**18**) is obtained by hydrogenation (H_2/PtO_2) of 2-hydroxy-3-methyl-2-cyclohexen-1-one.[7]

Diol **17** reacts quantitatively with DTPP in refluxing CH_2Cl_2 to afford the relatively stable dioxyphosphorane **19** (^{31}P NMR δ −39.3). Quantitative thermolysis (220 °C, 5 torr) of phosphorane **19** gives 70.4% of 2-methylcyclohexanone (**20**) and 29.6% of 3-methylcyclohexanone (**21**) (Table I). The major diastereomer **20** is derivable from decomposition of the chair conformer of phosphorane **19** and/or betaine **22** with the attendant 1,2-hydride shift. Formation of the minor isomer, ketone **21**, through a chair-like transition state having an axial methyl group should be energetically less favored (vide supra).



Diol **18** forms dioxyphosphorane **23** (^{31}P NMR δ −41.0) when allowed to reflux with DTPP in CH_2Cl_2. Although flash thermolysis of phosphorane **23** (250 °C, 15–25 torr) affords a nearly quantitative yield of diastereoisomeric ketones, **20** and **21**, the regioselective 1,2-hydride shift only slightly favors formation of ketone **21**. Assuming that stereoelectronic considerations for hydride shifts control these decompositions, it is convenient to rationalize formation of cyclohexanone **21** in terms of dioxyphosphorane **23** in a chair conformation. However, the appropriate chair conformation **24** which might adequately rationalize formation of **20** also encourages unfavorable 1,3-synaxial interactions. These unfavorable steric interactions may be diminished and the antiperiplanar orientation achievable in the twist-boat conformation (e.g., **25**).



Experimental Section

Melting points were obtained with a Mel-Temp melting point apparatus with an open capillary tube, and they are uncorrected.

Proton magnetic resonance (^1H) spectra were recorded on Varian Model XL-100, Perkin-Elmer Model R24B, and Bruker WM-250 NMR spectrometers. All Fourier transformations were based on 8K data points (XL-100) with noise-decoupling and all determinations were performed at ambient temperature (ca. 30 °C). ^{13}C NMR data were collected on the Varian XL-100 and the Bruker WM-250 spectrometers while all of the ^{31}P NMR data was obtained on the Bruker WM-250 NMR spectrometer. All ^1H and ^{13}C NMR shift parameters are presented in parts per million (δ) downfield from internal tetramethylsilane (Me_4Si) while the ^{31}P shifts are referenced to external 85% H_3PO_4.

Gas chromatographic analyses were obtained on the Hewlett-Packard Model 5754B research gas chromatograph, using a stainless steel column [0.125 in. (i.d.) × 10 ft packed with 20% Carbowax 20M on Chromosorb W-HP-AW-DMCS, 100–200 mesh].

Thin-layer chromatography (TLC) analyses using plastic sheets coated with silica gel (Baker-Flex) were used for confirmation of sample homogeneity. Iodine vapor was used for visualization.

Dichloromethane was distilled from P_2O_5 before use.

3-Methylcyclohexene.[8a-c] Methyllithium (1.154 L, 1.3 M in Et_2O, 1.5 mol) with cuprous chloride (74.31 g, 0.75 mol) was

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allowed to react with 3-bromocyclohexene[9] (50.84 g, 0.3 mol, 95% purity) to give 3-methylcyclohexene (11.0 g, 44%): bp 95–100 °C (lit.[10] bp 100–108 °C); ^{1}H NMR was identical with that reported.[11]

3-Methylcyclohex-2-en-1-one.[12] Ethyl acetoacetate (141 g, 1.08 mol) was allowed to react with formaldehyde (42 g, 0.56 mol, 40% solution) and with piperidine (2.5 mL) catalyst to afford 3-methylcyclohex-2-en-1-one (38 g, 61%): bp 195–210 °C (lit.[12] bp 200–202 °C); ^{1}H NMR ($CDCl_3$) δ 1.97 (d, 3 H, J = 1 Hz, CH_3), 2.00 (p, 2 H, J = 6 Hz, C_5-CH_2) 2.30 (t, 2 H, J = 6 Hz, C_4-CH_2), 2.35 (t, 2 H, J = 6 Hz, C_6-CH_2), and 5.88 (q, 1 H, J = 1 Hz, vinylic CH).

2-Hydroxy-3-methyl-2-cyclohexen-1-one.[13] 2,3-Epoxy-3-methylcyclohexanone[14] (20.0 g, 0.158 mol) was hydrolyzed with 125 mL of concentrated HCl (10 °C) to afford 2-hydroxy-3-methyl-2-cyclohexen-1-one (9.8 g, 49%): mp 58–59 °C (lit.[15] mp 62–63 °C); ^{1}H NMR ($CDCl_3$) δ 1.91 (t, 3 H, J = 1 Hz, CH_3), 1.80–2.12 (m, 2 H, C_5-CH_2), 2.37 (t, 2 H, J = 5 Hz, C_4-CH_2), 2.50 (t, 2 H, J = 6 Hz, C_6-CH_2), and 6.08 (s, 1 H, OH).

***cis*-2-Hydroxy-*trans*-3-methylcyclohexanol (17).**[4,6] Silver acetate (31.2 g, 0.187 mol, 2.25 equiv) was added to a solution of 3-methylcyclohexene (8.0 g, 0.83 mol) in glacial acetic acid (150 mL). Finely ground iodine (22.1 g, 0.087 mol, 1.05 equiv) was added over a 30-min period. After stirring vigorously for 0.75 h, aqueous acetic acid (90 mL, 96%) was added, and the resulting mixture was heated (90–95 °C) for 3 h. After cooling to ambient temperature, sodium chloride (32 g) was added, and the mixture was stirred for an additional 0.75 h, then washed with warm benzene (150 mL), and concentrated (rotary evaporator). Removal of acetic acid by distillation (34–36 °C at 30 torr) gave a viscous dark-orange oil which was dissolved in methanol (100 mL) and subsequently treated with methanolic KOH (10.2 g of KOH in 75 mL of CH_3OH) under an N_2 atmosphere. After being stirred for 24 h, the solution was neutralized (5% HCl, 0 °C) and the methanol was removed (rotary evaporator) to give a black oil. HPLC separation (ethyl acetate–hexanes, 1:1) of the crude oil gave a crude product (4.25 g, 40%): 80% cis,trans isomer and 20% cis,cis isomer. Three recrystallizations from ethyl acetate–hexanes afforded pure *cis*-2-hydroxy-*trans*-3-methylcyclohexanol: mp 80–82 °C; (lit.[4] mp 81–82 °C); ^{1}H NMR ($CDCl_3$) δ 0.87–1.08 (*m*, 1 H, ring CH), 1.01 (d, 3 H, J = 6.5 Hz, CH_3), 1.35–1.97 (m, 6 H, ring CH), 2.42 (br s, 2 H, OH), 3.17 (dd, 1 H, J_{12} = 3 Hz, J_{23} = 9.5 Hz, C_2-C*H*-OH), and 3.95 (q, 1 H, J_{12} = J_{16} = 3 Hz, C_1-C*H*OH);[7b] ^{13}C NMR ($CDCl_3$) δ 18.2 (CH_3), 19.2 (C_5), 31.2 (C_6), 32.4 (C_4), 33.2 (C_3), 69.9 (C_1), and 77.4 (C_2).[7b]

***trans*-2-Hydroxy-*trans*-3-methylcyclohexanol (7).**[3,4] 3-Methylcyclohexene (10.0 g, 0.104 mol) was bis-hydroxylated by (a) oxidation with hydrogen peroxide (14.5 mL, 30%) and formic acid (62.4 mL, 88%) at 40–45 °C and (b) hydrolysis of the formate ester with sodium hydroxide (8.1 g in 15.5 mL of H_2O). HPLC separation (30% hexanes/70% ethyl acetate) of the crude material gave 93% yield of the mixture of diastereomers [trans,trans diol (12.6 g, 88%) and trans,cis diol (12%)]. Fractional recrystallization from chloroform afford homogeneous trans,trans diol: mp 97 °C (lit.[4] mp 96 °C); ^{1}H NMR ($CDCl_3$) δ 0.96 (d, 3 H, J = 7 Hz, CH_3), 1.10–1.70 (m, 5 H, ring CH's), 1.76–2.33 (m, 2 H, ring CH's) 3.18 (s, 2 H, OH), 3.36–3.80 (m, 2 H, C*H*OH);[7b] ^{13}C NMR ($CDCl_3$) δ 12.8 (CH_3), 19.3 (C_5), 30.3 (C_4), 32.4 (C_6), 33.6 (C_3), 70.4 (C_1), and 76.9 (C_2).[7b]

***trans*-2-Hydroxy-*cis*-3-methylcyclohexanol (8).**[4] Reduction of 3-methylcyclohex-2-en-1-one (10.0 g, 0.091 mol) with borane (144 mL, 1 M solution in THF, 0.144 mol) followed by oxidation with sodium hydroxide (57 mL, 10% aqueous solution) and hydrogen peroxide (57 mL, 30%) afforded *trans*-2-hydroxy-*cis*-3-methylcyclohexanol (4.6 g, 39%) after distillation: bp 90–95 °C (1 torr) [lit.[4] bp 90–95 °C (1 torr)]; ^{1}H NMR ($CDCl_3$) δ 1.03 (d, 3 H, J = 6 Hz, CH_3), 1.16–2.09 (m, 7 H, C*H*CH_3 and CH_2), 2.93 (t, 1 H, J_{12} = J_{23} = 9 Hz, C_2-CH), 3.38 (dt, 1 H, J_{12} = J_{16} = 9 Hz, $J_{16'}$ = 4 Hz, C_1-CH), and 3.80 (br s, 2 H, OH);[7b] ^{13}C NMR ($CDCl_3$) δ 18.3 (CH_3), 23.5 (C_5), 33.1 (C_6), 33.5 (C_4), 37.7 (C_3), 75.3 (C_1), and 81.3 (C_2).[7b]

***cis*-2-Hydroxy-*cis*-3-methylcyclohexanol (18).**[7a,b] Reduction of 2-hydroxy-3-methyl-2-cyclohexen-1-one (11.63 g, 0.0923 mol) in methanol (82 mL) with H_2 over PtO_2 (300 mg) gave 13.4 g of a crude oil. "Rapid" chromatography (silica with 50:50 ethyl acetate–hexanes as eluants) of this material gave 5.0 g of a mixture of diols: 80% cis,cis diol and 20% cis,trans diol. Three recrystallizations from ethyl acetate–hexanes gave homogeneous cis,cis diol (2.5 g, 62%): mp 63–64 °C (lit.[7b] mp 64–65 °C); ^{1}H NMR ($CDCl_3$) δ 1.03 (d, 3 H, J = 6.5 Hz, CH_3), 1.16–1.36 (m, 3 H, ring CH's), 1.44–1.62 (m, 2 H, ring CH's), 1.45–1.77 (m, 2 H, ring CH's), 1.96 (d, 1 H, J = 2.8 Hz, C_2-OH), 2.05 (d, 1 H, J = 7 Hz, C_1-OH), 3.56 (m, 1 H, C_1-CH), and 3.76 (q, 1 H, J_{12} = J_{23} = 2.8 Hz, C_1-CH);[7b] ^{13}C NMR ($CDCl_3$) δ 18.2 (CH_3), 23.7 (C_5), 26.9 (C_6), 28.1 (C_4), 35.6 (C_3), 72.5 (C_2), and 73.7 (C_1).[7b]

***cis*- and *trans*-3-Methylcyclohexene 1,2-Oxides (9, 10).**[16] 3-Methylcyclohexene (10.0 g, 0.104 mol) was oxidized with *m*-chloroperoxybenzoic acid (25.5 g, 85%, 0.126 mol) in chloroform solvent (300 mL) to afford, after fractional distillation, 5.27 g (45%) of *cis*- and *trans*-3-methylcyclohexene oxides: bp 60 °C (45 → 10 torr) [lit.[17] bp 143–144 °C]; cis epoxide: ^{13}C NMR ($CDCl_3$) δ 18.5 (CH_3), 20.2 (C_5), 23.7 (C_6), 27.1 (C_4), 20.1 (C_3), 53.6 (C_1), and 57.0 (C_2); trans epoxide: ^{13}C NMR ($CDCl_3$) δ 17.1 (C_5), 19.1 (CH_3), 24.8 (C_6), 29.1 (C_3), 29.2 (C_4), 52.6 (C_1), and 57.2 (C_2).[18]

Reaction of *trans*-2-Hydroxy-*trans*-3-methylcyclohexanol (7) with DTPP. Diethyl peroxide (440 mg, 4.9 mmol) in CH_2Cl_2 (5 mL) was added to Ph_3P (1.29 g, 4.9 mmol), and the resulting mixture was allowed to reflux for 0.5 h. *trans*-2-Hydroxy-*trans*-3-methylcyclohexanol (583 mg, 45 mmol) in CH_2Cl_2 (3 mL) was added and the resulting mixture was refluxed (120 h). GLC analyses indicated 67% conversion of diol to epoxides and the mixture of epoxides consisted of 78.8% cis and 21.2% trans. These data were confirmed by ^{13}C NMR analysis.

Reaction of *trans*-2-Hydroxy-*cis*-3-methoxycyclohexanol (8) with DTPP. Diethyl peroxide (700 mg, 7.7 mol) in CH_2Cl_2 (5 mL) was mixed with Ph_3P (2.028 g, 7.7 mmol) and refluxed for 0.5 h. *trans*-2-Hydroxy-*cis*-3-methylcyclohexanol (915 mg, 7.0 mmol) in CH_2Cl_2 (2 mL) was added, and the mixture refluxed for 120 h. GLC analyses indicated 94% conversion of diol to a mixture of 72.9% trans epoxide and 27.1% cis epoxide which was confirmed by ^{13}C NMR analysis.

Reaction of *cis*-2-Hydroxy-*trans*-3-methylcyclohexanol (17) with DTPP. Diethyl peroxide (152 mg, 1.69 mmol) in CH_2Cl_2 (2 mL) was added to Ph_3P (443 mg, 1.69 mmol), and the resulting solution was refluxed for 0.5 h. *cis*-2-Hydroxy-*trans*-3-methylcyclohexanol (200 mg, 1.54 mmol) was added, and the resulting mixture was refluxed for 120 h. ^{13}C NMR analyses of the reaction mixture gave no evidence of the isomeric ketones. Toluene solvent (3 mL) was added, and the mixture was maintained at 80 °C for 48 h. ^{13}C and ^{31}P NMR analyses indicated the presence of only the 1,3,2-dioxaphospholane and the reaction mixture was allowed to stir at 90 °C for 1 week with no apparent decomposition of the 1,3,2-dioxaphospholane **19**. Quantitative flash thermolysis of **19** in a Kugelrohr apparatus (220 °C, 5 torr) gave a mixture containing 29.6% 3-methylcyclohexanone and 70.4% 2-methylcyclohexanone by ^{13}C NMR analysis.

Reaction of *cis*-2-Hydroxy-*cis*-3-methylcyclohexanol (18) with DTPP. Diethyl peroxide (152 mg, 1.69 mmol) in CH_2Cl_2 (2 mL) was added to Ph_3P (443 mg, 1.69 mmol) and refluxed for 0.5 h. *cis*-2-Hydroxy-*cis*-3-methylcyclohexanol (200 mg, 1.54 mmol) was added and the resulting mixture was refluxed for 120 h. ^{13}C NMR analyses indicated the presence of the 1,3,2-dioxa-

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phospholane **23**. Toluene solvent (3 mL) was added, and the resulting mixture allowed to stir at 80 °C (48 h). ^{13}C and ^{31}P NMR analyses indicated only the dioxyphosphorane, and this sample was allowed to stir at 90 °C for a week. Reexamination of the solution indicated approximately 50% phosphorane and 50% diol. The latter apparently resulting from hydrolysis of phosphorne **23**. Additional Ph_3P (222 mg, 0.85 mmol) and diethyl peroxide (80 mg, 0.9 mmol) were added to the mixture of phosphorane **23** and diol **18** and the mixture was stirred at 80 °C for 48 h. ^{13}C and ^{31}P NMR confirmed that all the diol had been quantitatively converted to 1,3,2-dioxaphospholane **23**. Quantitative flash thermolysis (250 °C; 15–25 torr) of 1,3,2-dioxaphospholane **23** gave 57.5% 3-methylcyclohexanone and 42.5% 2-methylcyclohexanone by ^{13}C NMR analysis.

Reaction of *cis*-Cyclohexane-1,2-diol (3) with DTPP. Diethyl peroxide (495 mg, 5.5 mmol) in CH_2Cl_2 (5 mL) was added to Ph_3P (1.44 g, 5.5 mmol). *cis*-Cyclohexane-1,2-diol (0.58 g, 5.0 mmol) was added, and the reaction mixture was refluxed for 72 h. ^{13}C and ^{31}P NMR analyses indicated the presence of phosphorane **4** as the major product (>90%) which was distilled (bp 150 °C, 0.05 torr) with minor decomposition. Flash thermolysis (330 °C, 15–23 torr) gave cyclohexanone (>80%).

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Enantioselective Synthesis of α-Functionally Substituted Cyclic Ketones via Chiral Organotin Enamines

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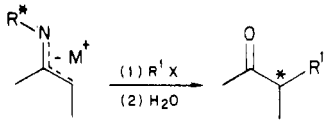
Chiral organotin enamines **1a–f** are easily prepared from cyclic ketones, chiral amino alcohols **5a–c** (derived from amino acids), and an organotin precursor. Nucleophilic addition of these compounds to electrophilic alkenes followed by hydrolysis leads to the title compounds **2a–d** in 10–98% ee. The determination of the enantiomeric excess was carried out by using ^{13}C NMR spectroscopy on the diastereoisomeric ketals. ^{119}Sn spectra of chiral organotin enamines exhibit two high-field singlets. These signals are indicative of associated species.

The alkylation of metallo enamines[3] has been used in the enantioselective synthesis of α-alkylcarbonyl compounds as shown initially by Horeau.[4]

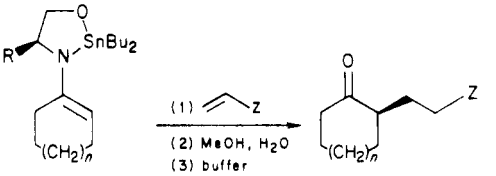


72% ee

Some years later, Meyers[5] and Whitesell[6] proposed an important improvement by using intramolecularly bonded lithium or magnesium salts, resulting in optical yields that were sometimes better than 90%.

In a preliminary paper we have reported the first results concerning enantioselective addition of chiral organotin enamines to electrophilic alkenes leading to optically active α-substituted cyclohexanones.[7] This paper deals with the scope and limitations of this reaction (Scheme I). Chiral organotin enamines were synthesized according to the reactions reported in Scheme II.

Scheme I



90% ee

The key step of the cyclization can be explained by the existence of a ring–chain tautomerism of the 1,3-oxazolidine[8] and by reaction of the open-chain tautomer with the aminotin compound. This leads to the formation of an imino alkoxy organotin compound which is itself in tautomeric equilibrium with a secondary enamine.[9] The secondary enamine is acidic enough to effect an intramolecular transamination. The reaction is monitored by ^1H NMR spectroscopy: the singlet (δ_{N-Me} 2.6) corresponding to the organotin amine decreases sharply leading to two singlets (δ 2.1–2.2), one from each of the two nonequivalent dimethylamino groups of the transient secondary enamine (Scheme II). As the reaction proceeds, these signals decrease while a broad triplet (δ 4.5) due to the olefinic proton of the chiral metallo enamine (**1a–f**) increases. Because of their thermal instability, organotin enamines

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