The relative yields of products by ^1H NMR integration were 14% for **4b** and 86% for **5b**.

4′-(Difluoromethylene)-4′,5′-dihydrospiro[9*H*-fluorene-9,3′-[3*H*]pyrazole] (4c), 5′-(Difluoromethylene)-4′,5′-dihydrospiro[9*H*-fluorene-9,3′-[3*H*]pyrazole] (5c), and 2-(Difluoromethylene)spiro[cyclopropane-1,9′-[9*H*]fluorene] (7). Into a 20-mL glass tube containing 0.485 g (2.52 mmol) of diazofluorene[23] and 7 mL of ether was condensed 0.574 g (7.56 mmol) of difluoroallene. The tube was sealed under vacuum. After 3 h at room temperature, the deep red color had faded to pale amber. The tube was opened and the solvent was removed by rotary evaporation at reduced pressure to give 0.655 g (98%) of thick amber oil. Analysis by ^1H NMR indicated relative yields of 72% for **5c** and 28% for **7**. Flash chromatography (silica gel), eluting with 95% hexane/5% EtOAc, gave 132 mg (20%) of yellow solid **7**: R_f 0.54; mp 78–82 °C (from hexane); IR (CCl_4) 3075, 3050, 3020, 2985, 1844 (s), 1453, 1320, 1240 (s), 1175, 680 cm^{-1}; ^1H NMR (100 MHz) δ 7.85 (m, 2 H), 7.6–7.0 (m, 6 H), 2.42 (t, 2 H, J_{HF} = 5.2 Hz); ^{19}F NMR (300 MHz) ϕ 82.3 (d of t, 1 F, J_{FF} = 56.5, J_{HF} = 5.2 Hz), 86.2 (d of t, 1 F, J_{FF} = 56.5, J_{HF} = 4.8 Hz); ^{13}C NMR (100 MHz) δ 149.9 (dd, J_{CF} = 281.4, 283.4 Hz, $=CF_2$), 144.6, 140.4 (substituted aromatic), 127.4, 127.3, 120.2 (aromatic), 78.2 (t, J_{CF} = 36.0 Hz, C_2), 34.4 (d, J_{CF} = 6.1 Hz, C_1), 20.0 (d, J_{CF} = 4.9 Hz, CH_2); mass spectrum M^+, 240.07408 ± 0.00245 (10 ppm); calcd for $C_{16}H_{10}F_2$, 240.07506; deviation, −0.00098 (4 ppm). Anal. Calcd: C, 79.99; H, 4.20. Found: C, 79.89; H, 4.23.

Compound **7** reacted slowly with oxygen in solution, but was indefinitely stable in the absence of oxygen and the purified solid was stored under nitrogen. The major product **5c** was very unstable in $CHCl_3$ solution and did not elute from the silica gel column. Spectroscopic analysis of the product mixture containing **5c** and **7** gave for pyrazoline **5c**: IR (CCl_4) 1756 (s) cm^{-1}; ^1H NMR (60 MHz) δ 2.97 (t, J_{HF} = 3.8 Hz, CH_2); ^{19}F NMR (100 MHz) ϕ 79.2 (d of t, 1 F, J_{FF} = 15.2, J_{HF} = 3.6 Hz), 89.4 (d of t, 1 F, J_{FF} = 15.2, J_{HF} = 3.8 Hz).

When the reaction was monitored by ^1H NMR (100 MHz), the CH_2 protons of the unstable intermediate **4c** were observed: ^1H NMR (100 MHz) δ 5.65 (t, J_{HF} = 3.7 Hz). By the time the reaction was complete, **4c** was no longer present.

4,5-Dihydro-4-(fluoromethylene)-3*H*-pyrazole (2). An ether solution of diazomethane (70 mL) was prepared from 7.00 g (32.7 mmol) of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide. The solution was vacuum transferred to a 150-mL glass tube and 1.9 g (32.7 mmol) of fluoroallene were condensed into the tube, which was sealed under vacuum. After 10 min at room temperature, the clear, colorless solution was concentrated by rotary evaporation at 200 mm pressure. The residue was distilled at reduced pressure. The pale yellow distillate was collected in an ice-chilled flask. A total of 2.1 g (64%) of **2** was obtained: bp 59–60 °C (23 mm); IR (CCl_4) 2920, 2822, 1710 (s), 1545, 1420, 1340, 1263, 1183, 1092 (s), 926 cm^{-1}; ^1H NMR (300 MHz) δ 6.67 (d of pentet, 1 H, J_{HF} = 83.9, J_{HH} = 2.7 Hz), 5.16 (t, 2 H, J = 2.8 Hz), 5.06 (t, 2 H, J = 2.8 Hz); ^{19}F NMR (100 MHz) ϕ 121.7 (d of pentet, J_{HF} = 84.0, 3 Hz); mass spectrum M^+, 100.04442 ± 0.00195 (20 ppm); calcd for $C_4H_5N_2F$, 100.04368; deviation, −0.00075 (8 ppm). The unstable product **2** could be stored on dry ice under nitrogen.

Acknowledgment. Support of this research in part by the National Science Foundation is gratefully acknowledged.

Registry No. 1, 88766-66-9; 2, 86770-87-8; **3a**, 2684-60-8; **3b**, 883-40-9; **3c**, 832-80-4; **4a**, 89210-55-9; **4b**, 89210-57-1; **4c**, 89210-59-3; **5a**, 89210-56-0; **5b**, 89210-58-2; **5c**, 89210-60-6; **6**, 83849-37-0; **7**, 89210-61-7; DFA, 430-64-8; fluoroallene, 51584-22-6; diazomethane, 334-88-3.

(23) Staudinger, H.; Kupfer, O. *Chem. Ber.* **1911**, *44*, 2197.

Optically Active Phosphine Oxides. 2.[1] Novel Approach to Enantiomeric Dialkylphenylphosphine Oxides[2]

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New routes to optically active tertiary phosphine oxides of known configuration and of virtually 100% enantiomeric purity have been developed. Alkylation of (−)-(S_P)-ethyl((menthoxycarbonyl)methyl)phenylphosphine oxide (**2**) by treatment with equimolar amounts of sodium hydride and alkyl halide in tetrahydrofuran followed by decarbalkoxylation with LiCl in wet Me_2SO affords (−)-(R_P)-alkylethylphenylphosphine oxides (alkyl: Et-d_3, Pr, *i*-Pr, 4-butenyl, 2-phenylethyl) in satisfactory yields. A considerable degree of asymmetric induction has been observed during the alkylation of **2**. It has also been demonstrated that the enantiomeric phosphine oxide **4b** in which the ligands are isotopically differentiated at the β carbon shows measurable optical activity at 400 nm wavelength. Decarbalkoxylation of **1** gives (−)-(S_P)-methylphenylvinylphosphine oxide (**5**) in 60% yield. The Michael-type reaction of **5** with R_2CuLi provides (−)-(S_P)-(RCH_2CH_2)P(O)MePh (R = Me, Bu) in ca. 65% yield. Sequential treatment of **5** with Bu_2CuLi and allyl bromide gives the addition–alkylation product, i.e., methyl(4-nonen-1-yl)phenylphosphine oxide in 53% yield. In addition reaction of **5** with butadiene is shown to produce cyclohexenylmethylphenylphosphine oxide in 78% yield. Stereochemistry of the latter two conversions is briefly discussed.

Synthesis of chiral phosphines of defined stereochemistry is one of the important objectives of organic chemists during recent years due to the widespread utility of these compounds as ligands in asymmetric catalysis.[3] The possibility of easy, stereoselective interconversion between chiral phosphines and chiral phosphine oxides[4] accords similar importance also to this latter pool of chirality.

A few approaches to optically active phosphine oxides have been developed in the past.[5] However, since the detailed work of Mislow and co-workers in the late sixties

(1) Part 1. Bodalski, R.; Rutkowska-Olma, E.; Pietrusiewicz, K. M. *Tetrahedron* **1980**, *36*, 2353.

(2) Presented in part at the International Conference of Phosphorus Chemistry, Durham, NC, June 1–5, 1981.

(3) Marko, L.; Heil, B. *Catal. Rev.* **1973**, *8*, 269. Morrison, J. D.; Masler, W. F.; Neuberg, M. K. *Adv. Catal.* **1976**, *25*, 81. Scott, J. W.; Valentine, D., Jr. *Science* **1974**, *184*, 943. Valentine, D., Jr.; Scott, J. W. *Synthesis* **1978**, 329. Merrill, R. E. *CHEMTECH* **1981**, 118.

(4) For a recent example and pertinent citations see: Valentine, D., Jr.; Blount, J. F.; Toth, K. *J. Org. Chem.* **1980**, *45*, 3691.

(5) Korpiun, O.; Lewis, R. A.; Chickos, J.; Mislow, K. *J. Am. Chem. Soc.* **1968**, *90*, 4842. In this paper all previously developed routes to optically active phosphine oxides are correspondingly discussed.

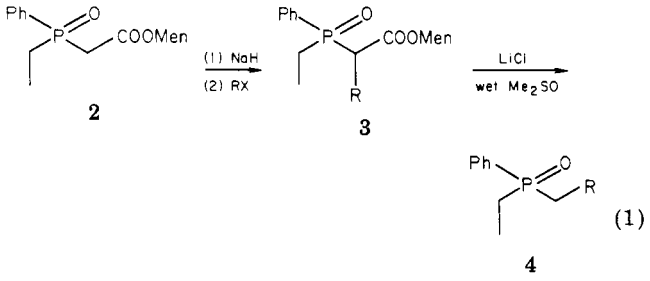
0022-3263/84/1949-1522$01.50/0

Table I. Enantiomeric Alkylethylphenylphosphine Oxides Prepared from 2[a]

entry	RX	yield[b] of 3, %	yield[c] of 4, %	mp, °C	$[\alpha]_{589}$,[d] deg	chirality at P
a			54	49	-20.8[e]	S
b	CD_3I	72	62	66	f	R
c	EtI	65	50	42	-9.1	R
d	CH_2=$CHCH_2Br$	68	70	58	-17.4	R
e	$PhCH_2Br$	79	67	71	-52.1	R
f	CH_3I (2 equiv)	100[g]	9[h]	33	-7.6[i]	R

[a] Cf. eq 1. [b] Calculated from the corresponding ^{31}P NMR spectra. [c] Numbers in this column refer to isolated material pure by TLC, GC, and NMR spectroscopy. [d] Rotations were measured in chloroform at concentrations of 0.03–0.05 g/mL, except as noted. [e] In methanol: $[\alpha]_{589}$ -24.4[13] (lit.[5] $[\alpha]_{589}$ +23). [f] Too small to measure at 589 nm wavelength; $[\alpha]_{400}$ -1.7 (c 1.4, $CHCl_3$). [g] Yield of dialkylated product; 2 equiv of NaH were used in this preparation. [h] Ethylisopropylphenylphosphine oxide. [i] The accuracy of this measurement is not high due to a minute amount of **4f** available (c 0.6).

on the preparation of optically active phosphine oxides by reaction of Grignard reagents with menthyl phosphinates,[5,6] methodology toward their synthesis has been very little explored. Recently our attention has been directed toward (-)-(S_P)-((menthoxycarbonyl)methyl)phenylvinylphosphine oxide (**1**) which has been viewed as the potential precursor to other optically active phosphine oxides and has been shown to be readily available in large quantities (ca. 25 g per run) by spontaneous crystallization from the crude reaction mixture.[1] In the course of the pertinent configurational correlation,[1] (-)-(R_P)-ethyl-((menthoxycarbonyl)methyl)phenylphosphine oxide (**2**) the hydrogenated counterpart of **1**, has been shown to undergo smooth decarbalkoxylation[7] upon treatment with LiCl in wet Me_2SO at 180 °C. From this observation we have evolved a procedure which provides convenient access to a variety of alkylethylphenylphosphine oxides of known configuration and of ca. 100% optical purity. Equation 1 outlines the proposed synthetic pathway.

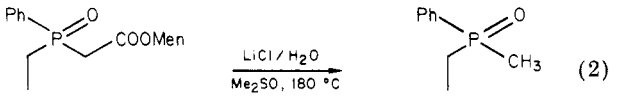


2 3 4 (1)

In addition, we have found that a similar decarbalkoxylation procedure can also be used to effect conversion of **1** into enantiomeric methylphenylvinylphosphine oxide (**5**), a valuable synthetic intermediate per se. Much attention has recently been paid to converting vinyl-substituted P^{III} and P^{IV} compounds into a variety of organic[8] and organophosphorus[9] compounds including bis(tertiary phosphines)[10] and poly(tertiary phosphines).[11] The possibility of analogous elaboration of the vinyl substituent bound to *enantiomeric* phosphorus function has apparently been stymied by the lack of convenient methods for preparing vinyl phosphorus compounds in the optically active form. In this context, the convenient synthesis of **5** has many apparent implications. Utility of **5** for the preparation of other enantiomeric phosphine oxides will be demonstrated here.

Results and Discussion

The alkylation–decarbalkoxylation route commences with the (-)-(R_P)-ethyl((menthoxycarbonyl)methyl)-phenylphosphine oxide (**2**) obtained easily in high yield by low-pressure hydrogenation of **1**.[1,12] Its absolute configuration was established through chemical correlation with (-)-(S_P)-ethylmethylphenylphosphine oxide (**4a**) (eq 2).[1] It should be emphasized that the observed specific



(2)

(-)-(R_P)-2 $[\alpha]_{589}$ -20.1 (CH_3OH)[13]

(-)-(S_P)-4a $[\alpha]_{589}$ -24.4 (CH_3OH)[13]

rotation of -24.4° (in MeOH) represents the highest rotation reported heretofore for **4a**[14] and we believe it can be regarded definitive (vide infra).

Alkylation of **2** in THF at 0 °C in the presence of 1 equiv of NaH gave monoalkylated products **3** in satisfactory yields. In every case **3** was identified (by ^{31}P NMR) as a mixture of epimers with the ratio ranging from ~1:1 in the case of **3b** to ~2:1 in the case of **3e**. This observation raises the possibility, which seems worthy of further pursuing, that a considerable degree of enantioselectivity can be achieved in such alkylations. In view of the fact, that these new asymmetric centers in **3b–e** were of no importance for the sequence as they disappeared in the next step (eq 1), the enantioselectivity of these alkylations was neither optimized nor studied in more details.

Monoalkylated products **3b–e** were usually isolated by means of short column chromatography on silica gel using EtOAc/*i*-PrOH (20:1) as the eluent. Due to the diastereomeric nature of these products they were not rigorously analyzed and after routine checking of their chemical purity (TLC, ^{31}P NMR, MS) they were used for the subsequent transformation.

(6) See also: Lewis, R. A.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7009.

(7) Krapcho, P. A.; Weimaster, J. F.; Eldridge, J. M.; Jahngen, E. G. E., Jr.; Lovey, A. J.; Stephens, W. P. *J. Org. Chem.* **1978**, *43*, 138.

(8) Schweizer, E. E.; O'Neil, B. J. *J. Org. Chem.* **1965**, *30*, 2082. Dauben, W. G.; Robbins, J. R. *Tetrahedron Lett.* **1975**, 151. Bonjouklian, R.; Ruden, R. A. *J. Org. Chem.* **1977**, *42*, 4095. Cory, R. M.; Chan, D. M. T.; Naguib, M. A.; Rastall, M. H.; Renneboog, R. M. *J. Org. Chem.* **1980**, *45*, 1852.

(9) Pudovik, A. N.; Konovalova, I. V. *Synthesis* **1979**, 81. Kabachnik, M. I.; Medved, T. Ya.; Polikarpov, Yu. M.; Yudina, K. C. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1962**, *9*, 1584. Märkl, G.; Merkl, B. *Tetrahedron Lett.* **1981**, *22*, 4459, 4463.

(10) DelGaudio, J.; Grim, S. O. *Inorg. Synth.* **1976**, *16*, 192. Grim, S. O.; DelGaudio, J.; Molenda, R. P.; Tolman, C. A.; Jesson, J. P. *J. Am. Chem. Soc.* **1974**, *96*, 3416. Grim, S. O.; Molenda, R. P.; Keiter, R. L. *Chem. Ind. (London)* **1970**, 13787.

(11) King. R. B.; Bakos, J.; Hoff, C. D.; Marko, L. *J. Org. Chem.* **1979**, *44*, 3095. King, R. B.; Cloyd, J. C., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 53. King, R. B. *Acc. Chem. Res.* **1972**, *5*, 177.

(12) Isolation of the R_P diastereomer of **1**, mp 74.5 °C, $[\alpha]_{589}$ +5.3 (c 3.8, $CHCl_3$), and consequently its reduction to S_P-**2**, mp 78–79 °C, $[\alpha]_{589}$ -61.1 (c 2.35, MeOH), have also been accomplished and will be reported in due course.

(13) These numbers differ somewhat from those of ref 1 due to correction of an error in the earlier results.

(14) Cf. reference 5.

Table II. Optically Active Phosphine Oxides Prepared from 5

entry	phosphine oxide	mp, °C	bp,[a] °C (torr)	yield,[b] %	$[\alpha]_{589}$,[c] deg	chirality at P
1	**6**	60[d]	130 (0.1)	64	-16.4[e]	*S*
2	**7**	63	140 (0.1)	65	-13.7	*S*
3	**8**[f]	*g*	185 (0.4)	53	-2.8	*S*
4	**10**[f]	74	155 (0.05)	78	-6.7	*S*
5	**11**	100[h]	165 (0.05)	92	-12.2[i]	*S*

[a] Kugelrohr distillation, oven temperature given. [b] Yields are of isolated material pure by GC and ^1H and ^{31}P NMR. [c] All measurements were carried out in chloroform at concentrations of 0.03-0.06 g/mL. [d] Lit.[5] 57-58 °C. [e] In methanol $[\alpha]_{589}$ -21.2 (*c* 5.6); lit.[18] $[\alpha]_{589}$ -20 (CH_3OH). [f] A mixture of two diastereomers. [g] An oil. [h] Lit.[5] 99-102 °C. [i] In methanol $[\alpha]_{589}$ -19.9 (*c* 3.2); lit.[5] $[\alpha]_{589}$ +19 (CH_3OH).

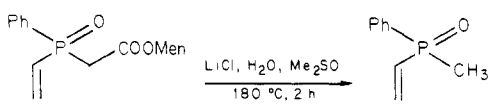
Decarbalkoxylation of **3b–f** was achieved by means of the Krapcho method[7] using LiCl in wet Me_2SO and furnished enantiomeric alkylethylphenylphosphine oxides **4b–f** in satisfactory yields. The pertinent data are collected in Table I.

The collected examples demonstrate clearly that the proposed route to enantiomeric alkylethylphenylphosphine oxides allows easy construction of the alkyl P substituent from the variety of alkyl and functional groups, including isotope labels. The preparation of **4b**, for example, enabled us to make an interesting observation: the enantiomeric phosphine oxide in which the ligands are isotopically differentiated at the β carbon shows measurable optical activity at 400 nm wavelength.[15]

An attempted extention of this approach to the α-branched alkyl substituents (entry f) was only partially successful.. The decarbalkoxylation of **3f** was found feasible but only very low yield of **4f** could be obtained. The failure of **3f** to furnish a fully serviceable yield of ethylisopropylphenylphosphine oxide (**4f**) might be of steric origin which would not be surprising in view of the literature data.[7] However, this synthetic possibility albeit poorly efficient should not be neglected as it may prove useful in situations when optically active phosphine oxides are required in only small quantities but of very high optical purity.

Stereochemistry at phosphorus in **4a–f** may be considered unequivocal. According to eq 1 the phosphorus atom remains intact during the entire process. Also, additional experimental observations[16] suggested strongly that neither alkylation nor decarbalkoxylation was accompanied by a detectable epimerization at phosphorus. Although improvement of the overall yields in the above reaction sequence might seem desirable in some cases, the reactants are readily available and the method guarantees virtually complete optical purity of the phosphine oxide produced.

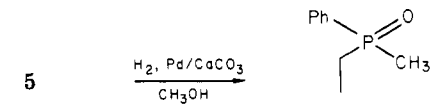
Application of the decarbalkoxylative procedure to **1** offered also a convenient access to optically active methylphenylvinylphosphine oxide (**5**) (eq 3). Exposure of



(3)

(−)-(S_P)-**1** (−)-(S_P)-**5**

1 to LiCl in refluxing wet Me_2SO gave **5** (60%, isolated, unoptimized) in which the expected S_P configuration and high optical purity was confirmed via chemical correlation with **4a** (eq 4).



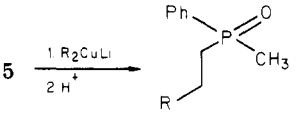
(4)

(S_P)-**5** $[\alpha]_{589}$ -80 ($CHCl_3$) (S_P)-**4a** $[\alpha]_{589}$ -24.4 (CH_3OH)

Additional support for the validity of these assessments was provided also by two other preparations of the optically active phosphine oxides of known configurations (entry 1 and 5 in Table II) and those are discussed later in the text.

From a vast array of the possible synthetic applications of enantiomeric oxide **5** we choose to demonstrate here the utility of **5** for preparation of optically pure alkyl- and cycloalkylmethylphenylphosphine oxides of known configuration.

We turned our attention to the reaction of vinyl phosphine oxide **5** with lithium dialkylcuprates.[18] Treatment of lithium dimethylcuprate with 0.9 equiv of **5** in ether at low temperature afforded, after protonation, methylphenylpropylphosphine oxide (**6**) in 64% yield (eq 5).



(5)

6, R = Me
7, R = *n*-Bu

Analogous reaction of **5** with lithium dibutylcuprate produced *n*-hexylmethylphenylphosphine oxide (**7**) in 65% yield (eq 5). The pertinent data for oxides **6** and **7** are presented in Table II. The optical purity of these oxides can be again reasonably considered as ~100% because the applied procedure leaves the phosphorus atom apparently unaffected. In fact, optical rotation of **6** (Table II) exceeds somewhat the corresponding crosschecked literature values[5,19] and represents the highest figure for optically active methylphenylprophylphosphine oxide reported up to this date.[20]

When aqueous NH_4Cl, used for quenching the reaction in the preparation of **7**, was replaced with allyl bromide, formation of the corresponding addition–alkylation product **8** in 53% yield was observed (eq 6). The oxide **8** was found to be a mixture of diastereomers with the ratio ca.

(15) Contamination of **4b** by traces of menthol or other optically active impurities can possibly be excluded on the basis of careful GC and TLC analysis of the sample.

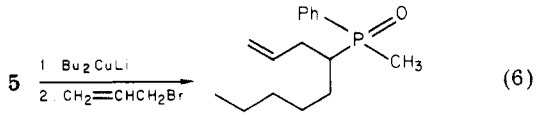
(16) Quenching of representative alkylation and decarbalkoxylation reactions before completion led to the isolation of the unreacted starting materials having unchanged specific rotations. Additionally, prolonged reaction times were found to have apparently no effect on the rotations of final products in both reactions. In these experiments reaction conditions were exactly the same as described in Experimental Section except for the reaction time.

(17) This rotation represents the most often observed value though occasionally somewhat lower as well as somewhat higher numbers were obtained on samples of virtually the same purity; i.e., pure by GC and/or ^1H and ^{31}P NMR spectroscopy.

(18) This type of reaction has recently been discussed in some details: Bodalski, R.; Michalski, T.; Monkiewicz, J.; Pietrusiewicz, K. M. *ACS Symp. Ser.* **1981**, *No. 171*, 243.

(19) Casey, J. P.; Lewis, R. A.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 2789.

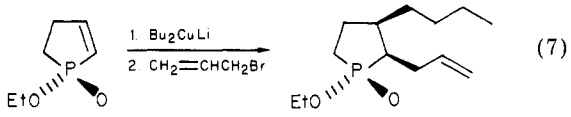
(20) Cf. Denney, D. B.; Hanifin, J. W., Jr. *Tetrahedron Lett.* **1963**, 2177.



(6)

8

7:5 (by ^{13}C NMR), inferring only little stereochemical control during the alkylation step. By contrast, an analogous tandem addition–alkylation reaction in the phospholene system[18] utilizing lithium dibutylcuprate and allyl bromide occurs with complete stereoselectivity affording exclusively cis-substituted phospholane **9** (eq 7). This was

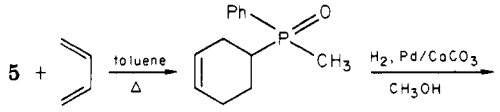


(7)

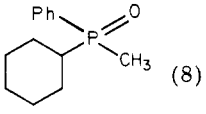
9

interpreted in terms of a syn 3,4-addition mechanism involving precomplexation of the cuprate by the phosphoryl oxygen.[18] Apparently, a similarly high degree of the stereochemical control by the phosphoryl oxygen in systems with much rotational freedom, as in **5**, might prove difficult to achieve.

Another reaction of **5** which we have examined was its Diels–Alder reaction with a diene. Heating of **5** with an excess of butadiene in toluene, in a sealed tube, produced two diastereomeric cycloadducts **10** in good yield but with very little stereochemical preference.[21] Hydrogenation of **10** (eq 8) afforded known cyclohexylmethylphenyl-



10



(8)

11

phosphine oxide (**11**) in which optical rotation and absolute configuration (Table II) compared favorably with the literature data.[5]

To conclude, the presented syntheses of optically active phosphine oxides are short and preparatively very simple and are also, for the first time, fully dependable with regard to enantiomeric purity of the phosphorus center. They should be considered as methods of choice for the preparation of virtually optically pure phosphine oxides to be used as reference compounds as well as for further synthetic transformations.

Further studies of the chemistry of oxides **1**, **2**, and **5** are currently in progress.

Experimental Section

Melting points and boiling points are uncorrected. All solvents and reagents were purified by standard methods before use. ^1H NMR spectra were recorded on a Tesla BS 487 spectrometer (80 MHz) and are reported in δ units using tetramethylsilane as standard. ^{13}C and ^{31}P NMR spectra were obtained on a Jeol-JNM-FX 60 Fourier transform spectrometer at 15 and 24.3 MHz, respectively. Tetramethylsilane and 85% H_3PO_4 were correspondingly used as internal and external standard. Positive ^{31}P NMR signals were assigned to low field from H_3PO_4. Optical rotations were measured on a Perkin-Elmer Model 241 C using a 1-dm path length. Mass spectra were recorded on a LKB-2091 mass spectrometer under standard 70 eV electron-ionization conditions. Gas chromatographic analyses were carried out with a Varian Aerograph 2700 (nitrogen carrier gas, 30 mL/min) instrument with a flame-ionization detector, using a 2-m glass column packed with 10% OV-101 on Chromosorb WAW.

(−)-(R_P)-Ethyl((menthoxycarbonyl)methyl)phenylphosphine Oxide (2). **2** was obtained from **1** (mp 152 °C, $[\alpha]_{589}$ −93[13,17] (*c*, 4.88, $CHCl_3$)) by hydrogenation over $Pd/CaCO_3$ as described earlier.[1] Crystallization from hexane afforded an analytically pure sample: mp 93 °C; $[\alpha]_{589}$ −20.1[13] (*c* 4.9, CH_3OH); $[\alpha]_{589}$ −50.7[13] (*c* 3.9, $CHCl_3$).

(−)-(S_P)-Ethylmethylphenylphosphine Oxide (4a). A mixture of **2** (4.38 g, 0.0125 mmol), Me_2SO (40 mL), H_2O (0.225 g, 0.0125 mol), and LiCl (1.05 g, 0.025 mol) was kept at reflux for 15 h. Me_2SO was then distilled off under reduced pressure and a dry brown residue was extracted several times with chlorofrom. The extracts were combined and dried over anhydrous magnesium sulfate. After evaporation of chloroform crude **4a** was Kugelrohr distilled at 145 °C (0.01 torr) (oven temperature) and provided 1.13 g (54%) of **4a**: mp 54.5 °C (lit.[5] 52 °C); $[\alpha]_{589}$ −24.4[13] (*c* 2.0, CH_3OH) [lit.[5] $[\alpha]_{589}$ +23 (CH_3OH)]; $[\alpha]_{589}$ −20.8[13] (*c* 3.7, $CHCl_3$); ^{31}P NMR ($CHCl_3$) δ 39.1 [lit.[22] 37.5 ppm (CD_3OD)].

Monoalkylation of 2. General Procedure. To a suspension of 0.144 g (0.005 mol) of sodium hydride in dry tetrahydrofuran (40 mL) was added an equimolar amount of **2** in one portion. After evolution of hydrogen had ceased the solution was cooled to 0 °C and 0.005 mol of the corresponding alkylating agent was slowly added (in a period of ca. 0.5 h). The resulting mixture was stirred at that temperature for 2 h and then at room temperature for an additional 2 to 3 h. Progress of alkylation was usually monitored by TLC and/or ^{31}P NMR spectroscopy and, when the concentration of **2** had been minimized the reaction was quenched with a few milliliters of 5% HCl and then partitioned between ether and brine. The aqueous phase was further extracted with ether and the combined ethereal extracts were dried over anhydrous magnesium sulfate. Evaporation of ether under reduced pressure afforded crude alkylation products **3b–e**. These were purified by means of a short column chromatography on silica gel (EtOAc, *i*-PrOH, 20:1) and were in each case identified by their ^{31}P NMR spectra as a mixture of two diastereomers. The corresponding ^{31}P NMR ($CHCl_3$) signals (and relative intensities) were as follows: **3b**, 38.8 and 39.5 ppm (1:1); **3c**, 39.1 and 39.3 ppm (2:3); **3d**, 39.1 and 39.5 ppm (3:5), and **3e**, 38.9 and 39.6 ppm (2:1). All samples were screened for purity and identity by TLC and mass spectrometry and all gave correct molecular ions. Yields of these preparations are indicated in Table I.

(−)-(R_P)-Ethyl((menthoxycarbonyl)dimethylmethyl)phenylphosphine Oxide (3f). To a suspension of 0.316 g (0.012 mol) of sodium hydride in dry tetrahydrofuran (30 mL) was added 2.1 g (0.006 mol) of **2**. After 10 min, an excess (0.018 mol) of methyl iodide was added in three portions. The reaction mixture was refluxed for ca. 2 h and, after cooling and addition of a few milliliters of 5% aqueous HCl, extracted with ether. Ethereal extracts were dried over anhydrous magnesium sulfate and then evaporated in vacuo. The resulting white solid was chromatographed over silica gel (EtOAc, *i*-PrOH, 20:1) to afford pure **3f** in almost quantitative yield: mp 111–112 °C; $[\alpha]_{589}$ −90.2 (*c* 3.3, $CHCl_3$); MS, *m/e* 379 (M^+), 241, 240, 171 (base), 154, 153, 125; ^1H NMR ($CDCl_3$) δ 0.65 (d, J = 7 Hz, 3 H), 0.83 (d, J = 7 Hz, 3 H), 0.92 (d, J = 6 Hz, 3 H), 1.12 (dt, J = 18, 8 Hz, 3 H), 1.31 (d, J = 14 Hz, 3 H), ~1.0–1.9 (m, 9 H), 1.9–2.6 (m, 2 H), 4.73 (m, 1 H), 7.45–7.95 (m, 5 H); ^{31}P NMR ($CHCl_3$) δ 47.0.

Decarbalkoxylation of 3b–f. General Procedure. In a 50-mL round-bottom flask equipped with a magnetic spin bar and a reflux condenser were placed Me_2SO (30 mL), water (0.0033 mL), LiCl (0.28 g, 0.0066 mol), and the corresponding phosphine oxide **3** (0.0033 mol). The solution was refluxed with stirring for 6–18 h. Me_2SO was then distilled off under reduced pressure and a dry brownish residue was extracted several times with chloroform. The extracts were combined and dried over anhydrous magnesium sulfate. After evaporation of chloroform crude

(21) Use of oxide **1** instead of **5** in this reaction offered seemingly no advantage in terms of asymmetric induction.

(22) Mikolajczyk, M.; Omelańczuk, J.; Perlikowska, W. *Tetrahedron* **1979**, *35*, 1531.

phosphine oxide **4** was usually twice kugelrohr distilled and in some cases chromatographed over silica gel using EtOAc–*i*-PrOH (20:1) as eluent. All final products **4** were tested for purity by TLC, GC, and spectroscopic techniques.

4b: MS, *m/e* 185 (M^+), 157, 156 (base), 153, 126, 125; ^1H NMR ($CDCl_3$) δ 1.12 (dt, J = 17, 7 Hz, 3 H), 1.6–2.3 (m, 4 H), 7.45–8.0 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 5.58 (d, J = 3.9 Hz), 22.09 (d, J = 70.3 Hz), 22.35 (d, J = 70.2 Hz), 128.65 (d, J = 11.7 Hz), 130.61 (d, J = 7.8 Hz), 131.64 (br s);[23] ^{31}P NMR ($CHCl_3$) δ 43.8.

4c: MS, *m/e* 196 (M^+), 154, 140 (base), 125; ^1H NMR ($CDCl_3$) δ 0.8–1.3 (8 lines, 6 H), 1.3–2.35 (m, 6 H), 7.4–7.9 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 5.59 (d, J = 3.9 Hz), 15.2 (br s), 15.72 (d, J = 15.6 Hz), 22.87 (d, J = 70.3 Hz), 31.64 (d, J = 68.4 Hz), 128.66 (d, J = 11.7 Hz), 130.53 (d, J = 9.8 Hz), 131.51 (br s);[23] ^{31}P NMR ($CHCl_3$) δ 41.85.

4d: MS, *m/e* 208 (M^+), 180, 154, 153, 125 (base); ^1H NMR ($CDCl_3$) δ 1.15 (dt, J = 17, 8 Hz, 3 H), 1.3–1.9 (m, 6 H), 4.9–5.25 (m, 2 H), 5.65–6.15 (m, 1 H), 7.4–7.9 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 5.59 (d, J = 3.9 Hz), 23.19 (d, J = 76.2 Hz), 25.47 (br s), 28.78 (d, J = 68.4 Hz), 115.13 (s), 128.71 (d, J = 9.8 Hz), 130.53 (d, J = 9.8 Hz), 131.64 (br s), 137.98 (d, J = 15.6 Hz);[23] ^{31}P NMR δ 36.7.

4e: MS, *m/e* 258 (M^+), 155, 125, 84 (base); ^1H NMR ($CDCl_3$) δ 1.12 (dt, J = 16, 7 Hz, 3 H), 1.62–3.15 (m, 6 H), 7.0–7.4 (m, 5 H), 7.45–7.9 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 5.59 (d, J = 3.9 Hz), 23.13 (d, J = 70.3 Hz), 27.55 (br s), 31.58 (d, J = 66.4 Hz), 126.31 (s), 128.13–129.17 (4 lines), 130.6 (d, J = 7.8 Hz), 131.78 (br s), 141.31 (d, J = 13.7 Hz);[23] ^{31}P NMR ($CHCl_3$) δ 39.7.

4f: MS, *m/e* 196 (M^+), 154, 153 (base), 125; ^1H NMR ($CDCl_3$) δ 1.1 (dd, J = 16, 7 Hz, 6 H), 1.2 (dt, J = 16, 6 Hz, 3 H), 1.5–2.4 (m, 3 H), 7.4–7.9 (m, 5 H); ^{31}P NMR ($CHCl_3$) δ 47.6.

(–)-(S_P)-Methylphenylvinylphosphine Oxide (5). Decarbalkoxylation of **1** was carried out in exactly the same manner as described for oxides **3b–f** and afforded pure oxide **5** in 60% yield as a white hygroscopic solid: mp 80 °C (lit.[24] 78–79 °C); bp 110 °C (0.1 torr) (Kugelrohr) [lit.[24] 127 °C (1.5 torr)]; $[\alpha]_{589}$ –80[17] (*c* 2.6, $CHCl_3$); MS, *m/e* 166 (M^+), 151, 139; ^1H NMR ($CDCl_3$) δ 1.78 (d, J = 14 Hz, 3 H), 5.8–6.65 (m, 3 H), 7.45–7.95 (m, 5 H); ^{31}P NMR ($CHCl_3$) δ 26.4. Hydrogenation of **5** over $Pd/CaCO_3$ in MeOH gave **4a** (95%) which was identical in every respect with the one obtained by decarbalkoxylation of **2**.

Reaction of 5 with Lithium Dialkylcuprates. To a slurry of 0.575 g (0.003 mol) of CuI in 200 mL of dry diethyl ether cooled to –78 °C was added 2 equiv of *n*-BuLi (0.006 mol) and after ca. 15 min the mixture was warmed up to –30 °C for 45 min. A solution of 0.415 g (0.0025 mol) of **5** in 5 mL of diethyl ether was then added in one portion at –78 °C and the resulting mixture was kept at that temperature for 1 h, then an additional hour at –40 °C, and 15 min at –15 °C. In the preparation of oxides **6** and **7** the reaction was quenched by addition of 10 mL of saturated aqueous NH_4Cl and in case of **8** the addition of NH_4Cl was preceded by a dropwise addition of allyl bromide (3 equiv) at –78 °C and allowing the mixture to warm up to –15 °C for 1 h. The layers were separated and the aqueous layer was extracted twice with diethyl ether. The combined ethereal extracts were dried over magnesium sulfate and filtered and the solvent was removed under reduced pressure. The crude products were finally purified by Kugelrohr distillation under reduced pressure. Yields and some physical data of oxides **6–8** are listed in Table II.

6: MS, *m/e* 182 (M^+), 181, 154, 140, 139 (base), 125; ^1H NMR ($CDCl_3$) δ 0.82 (br t, J = 5.5 Hz, 3 H), 1.15–1.45 (m, 2 H), 1.7 (d, J = 12.5 Hz, 3 H), 1.7–2.05 (m, 2 H), 7.50–7.90 (m, 5 H); ^{31}P NMR ($CHCl_3$) δ 37.0.

7: MS, *m/e* 224 (M^+), 195, 154 (base), 140, 139, 125; ^1H NMR ($CDCl_3$) δ 0.85 (t, J = 5.5 Hz, 3 H), 1.10–1.50 (m, 8 H), 1.7 (d, J = 12 Hz, 3 H), 1.7–2.1 (m, 2 H), 7.4–7.9 (m, 5 H); ^{31}P NMR ($CHCl_3$) δ 36.4.

8: MS, *m/e* 264 (M^+), 221, 207, 194, 167, 140 (base), 139, 125; ^1H NMR ($CDCl_3$) δ 0.85 (t, J = 5.5 Hz, 3 H), 0.8–1.4 (m, 8 H), 1.7 (d, J = 12 Hz, 3 H), 1.8–2.4 (m, 3 H), 4.8–5.15 (m, 2 H), 5.2–5.4 (m, 1 H), 7.5–7.8 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 13.89, 14.49 (d, J = 67 Hz), 14.7 (d, J = 67 Hz), 22.17, 22.33, 27.21, 27.69, 31.59, 31.84, 32.88, 39.6 (d, J = 67 Hz), 39.75 (d, J = 67 Hz), 116.79, 116.95, 128.16, 128.89, 130.12, 130.67, 130.44, 131.41, 131.57, 135.71, 136.36, 136.61; ^{31}P NMR ($CHCl_3$) δ 38.3.

Cyclohexenylmethylphenylphosphine Oxide (10). A mixture of 200 mg (0.0012 mol) of **5** and 0.5 mL (0.06 mole) of butadiene in 2 mL of toluene was heated in a sealed tube at 180 °C for 24 h. Removal of solvent and volatile byproducts under reduced pressure followed by Kugelrohr distillation afforded 206 mg (78%) of oxide **10** as a ~1:1 mixture of two diastereomers: MS, *m/e* 220 (M^+), 141, 140 (base), 125; ^1H NMR ($CDCl_3$) δ 1.68 (d, J = 12.5 Hz, 3 H), 1.7 (d, J = 12.5 Hz, 3 H), 1.3–2.4 (m, 7 H), 5.7 (br s, 2 H), 7.4–7.95 (m, 5 H); ^{31}P NMR ($CHCl_3$) δ 41.0, 41.3.

(–)-(S_P)-Cyclohexylmethylphenylphosphine Oxide (11). Low-pressure hydrogenation of **10** was carried out in methanol at room temperature using $Pd/CaCO_3$ as catalyst. After cesation of hydrogen uptake (ca. 6 h) the reaction mixture was filtered and methanol was evaporated under reduced pressure. Kugelrohr distillation of crude **11** gave pure material in practically quantitative yield: MS, *m/e* 222 (M^+), 221, 167, 140 (base), 125; ^1H NMR ($CDCl_3$) δ 1.05–2.1 (m, 11 H), 1.65 (d, J = 12.5 Hz, 3 H), 7.4–7.9 (m, 5 H); ^{31}P NMR ($CHCl_3$) δ 45.7.

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Registry No. (–)-(S_P)-**1**, 77085-89-3; **2**, 89496-38-8; **3b**, 89438-68-6; **3c**, 89438-69-7; **3d**, 89438-70-0; **3e**, 89438-71-1; **3f**, 89438-72-2; **4a**, 26515-05-9; **4b**, 89438-73-3; **4c**, 89438-74-4; **4d**, 89438-75-5; **4e**, 89438-76-6; **4f**, 89438-77-7; (–)-(S_P)-**5**, 89438-78-8; **6**, 4653-63-8; **7**, 89438-79-9; **8**, 89438-80-2; **9**, 89438-81-3; **10** (isomer 1), 89438-82-4; **10** (isomer 2), 89438-83-5; **11**, 42366-51-8; CD_3I, 865-50-9; EtI, 75-03-6; CH_2=$CHCH_2Br$, 106-95-6; $PhCH_2Br$, 100-39-0; CH_3I, 74-88-4; LiCl, 7447-41-8; Bu_2CuLi, 24406-16-4; CH_2=$CHCH$=CH_2, 106-99-0; 1-ethoxy-2,3-dihydro-1*H*-phosphole 1-oxide, 695-63-6.

(23) A doublet for aromatic ipso carbon was partially obscured and the accurate assignment was not possible.

(24) Kabachnik, M. I.; Chang, C.-Y.; Tsvetkov, E. N. *Dokl. Akad. Nauk SSSR.* **1960**, *135*, 603; *Chem. Abstr.* **1961**, *55*, 12272a.