
Some Syntheses of Optically Active Phosphorus Compounds¹

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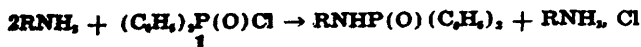
The synthesis of optically active phosphorus compounds for the most part has been limited to those chemicals which contain an asymmetric phosphorus atom. Those compounds which do not contain an asymmetric phosphorus atom include (—)-menthyl- and (—)-bornyl *P*, *P*-diethyl 2-phosphonopropionate (Tomoskozi, 1966) and (—)-menthyl diphenylphosphinate (Lewis, Korpiun and Mislow, 1967). The latter was not well characterized in the report of Lewis, Korpiun and Mislow (1967). Several optically active organophosphorus compounds were synthesized which do not contain an asymmetric phosphorus atom. Condensations of diphenylphosphinyl chloride (1) with either an amine, an alcohol, or a sodium alkoxide were investigated. The reactions involve formation of a P-N or P-O bond *via* nucleophilic displacement on phosphorus by an oxygen or nitrogen atom.

Two equivalents of optically active primary amine per one equivalent of 1 were utilized in the synthesis of three amides of diphenylphosphinic

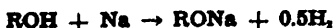
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acid. The sodium alkoxides of (—)-menthol and (—)-borneol were prepared since



esterification of the alcohol with 1 was difficult. Triethylamine was used



as an acid scavenger in the ester synthesis from (—)-2-methyl-1-butanol and 1.



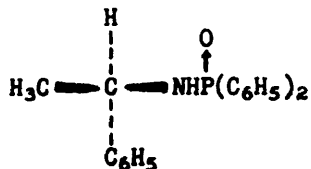
During addition of 1 to an optically active amine in ether, the amide and hydrochloride of the amine began to precipitate. In the workup of the reaction mixture, the solid precipitate was washed with water to dissolve the ionic salt. The residue was then recrystallized to give pure amide.

After reaction of 1 with an alkoxide, the slight excess of 1 was removed by extraction with aqueous sodium bicarbonate. Steam distillation proved useful as a means for removing the unreacted (—)-menthol or (—)-borneol.

The hydrochloride of triethylamine was separated from the reaction mixture by filtration. Then the excess (—)-2-methyl-1-butanol and triethylamine were removed from the ester by evaporation using high vacuum.

The optically active products were as follows: (+)-*N*-(α -methylbenzyl)diphenylphosphinic amide (2), (+)-*N*-(α -methylphenethyl)diphenylphosphinic amide (3), (—)-*N*-[α -(1-naphthyl)ethyl]diphenylphosphinic amide (4), (—)-menthyl diphenylphosphinate (5), (—)-bornyl diphenylphosphinate (6), and (+)-2-methyl-1-butyl diphenylphosphinate (7); see Table I.

I.R. and N.M.R. spectra, specific rotations, and elemental analyses of the products were used for identification purposes. These analyses support the expected ester or amide structures. N.M.R. peaks for the NH proton in the amides are centered at δ 8.38-3.80 (broad multiplet). Likewise, a multiplet at ca. δ 3.39-5.14 is observed for the single methine proton in the amides. Each of the amides also gives doublets in the range of δ 1.23-1.64 with coupling constants of ca. 5.2-6.5 cps for the methyl group.



(+)-*N*-(α -methylbenzyl)diphenylphosphinic amide (2)

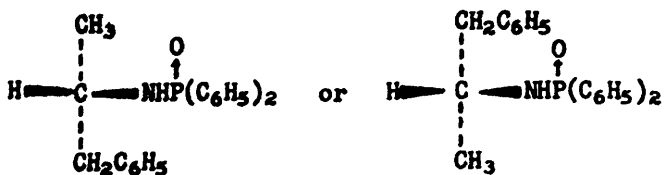
$$[\alpha]_D^{23.5} = +33.5^\circ$$

TABLE I. SYNTHESIS AND PROPERTIES OF COMPOUNDS 2 - 7

Cpd.	Yield, %	Mp, C	[α] _D ²⁰ (c, g/100 ml) (in CHCl ₃)	Analysis, %							
				C		H		N		P	
				Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
2	71.7	192-198	+33.5** (6.160)			4.36	4.31	9.64	9.57		
3	61.3	121.5-122.5	+19.6** (5.467)			4.18	4.05	9.24	9.29		
4	60.8	163-164	-44.8** (3.261)				3.77	3.70	8.34	8.11	
5	51.2	72-73	-73.0** (8.280)	74.13	74.17	8.20	8.15			8.69	8.69
6	53.8	74-75	-14.3** (5.892)	74.55	74.61	7.68	7.66			8.74	9.01
7	48.1**	42-43	+4.18** (4.658)	70.81	71.04	7.34	7.41			10.74	10.89

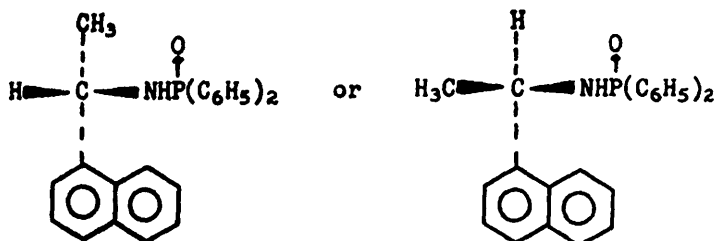
* Yields are based on optically active amine or alcohol as starting material.

** This yield is a minimum since traces of the optically active alcohol were difficult to remove from the product, and thus many recrystallizations were required from ether-petroleum ether to obtain an analytical sample of 7.



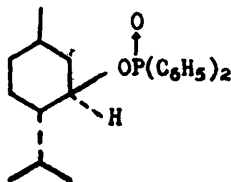
(+)-*N*-(*o*-methylphenethyl)diphenylphosphinic amide (3)

$$[\alpha]_D^{24.0} = +19.6^\circ$$



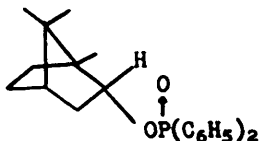
(-)-*N*-[*o*-(1-naphthyl)ethyl]diphenylphosphinic amide (4)

$$[\alpha]_D^{24.5} = -44.8^\circ$$



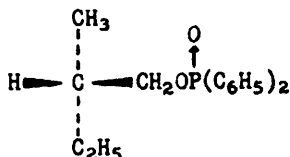
(-)-menthyl diphenylphosphinate (5)

$$[\alpha]_D^{25.5} = -73.0^\circ$$



(-)-bornyl diphenylphosphinate (6)

$$[\alpha]_D^{25.5} = -14.3^\circ$$



(+) -2-methyl-1-butyl diphenylphosphinate (7)

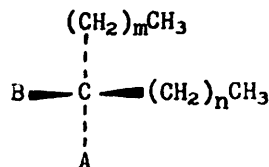
$$[\alpha]_D^{24.0} = +4.18^\circ$$

The OCH proton in 5 and 6 gives a multiplet at δ 4.23 and δ 4.61, respectively. The OCH₂ protons in 7 produce a triplet at δ 3.84 ($J=5.9$ cps). The three methyl groups in 5 give rise to doublets at δ 0.55 ($J=6.8$ cps), 0.88 ($J=7.0$ cps), and 0.83 ($J=5.0$ cps) while the three methyl groups in 6 yield singlets at δ 0.73, 0.82 and 0.87. The two methyl groups in 7 overlap in the spectrum and appear at ca. δ 1.00 and 0.90 ($J=3.0$ cps), respectively.

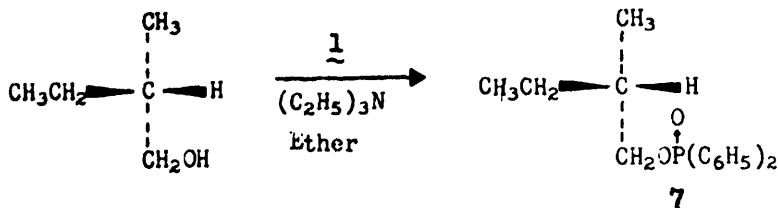
Specific rotations of chloroform solutions containing the *starting materials* leading to 2-7 were $+35.6^\circ$, $+36.2^\circ$, $+41.3^\circ$, -44.7° , -20.8° , and -5.33° , respectively. Those for 2-7 in chloroform were $+33.5^\circ$, $+19.6^\circ$, -44.8° , -73.0° , -14.3° , and $+4.18^\circ$, respectively. It should be noted that the signs of specific rotation for the organophosphorus products, 4 and 7, are opposite to those for the corresponding amine and alcohol. The reversals of sign suggest that (in these compounds) some molecular conformations may be preferred over the corresponding enantiomeric conformations. Brewster (1959) predicted, on the basis of a steric requirement increase, that a change in the sign of optical rotation would be observed for the following model.

$m > n$; size A \neq B, - rotation

$m > n$; size A $>$ B, + rotation



The above configuration is comparable with those for (-)-2-methyl-1-butanol and 7 and a similar steric situation and change in sign is observed.



$$[\alpha]_D^{23.0} = -5.33^\circ$$

$$[\alpha]_D^{24.0} = +4.18^\circ$$

EXPERIMENTAL

Analytical methods—The I.R. spectra were determined using a Beckman IR-5A spectrometer and potassium bromide pellets. The N.M.R. spectra were recorded on a Varian A-60 high-resolution spectrometer with tetramethylsilane as the internal standard in CDCl_3 solutions. The optical rotations were obtained with a Model 80 universal high-precision polarimeter manufactured by O. C. Rudolph and Sons, Caldwell, New Jersey. The solvent was Certified A.C.S. chloroform sold by Fisher Scientific Company.

Preparation of (+)-N-(α -Methylbenzyl)diphenylphosphinic amide (2)—A 200-ml 3-necked flask equipped with a magnetic stirring bar, addition funnel, condenser, and thermometer was charged with a solution of 3.50 g (0.0289 mole) of (+)- α -methylbenzylamine in 160 ml of anhydrous (dried over Linde A molecular sieve) ether. Diphenylphosphinyl chloride (1) (3.41 g, 0.0144 mole) in 15 ml of anhydrous ether was added dropwise at such a rate as to cause gentle boiling of the solvent. The addition required 10 min. The reaction mixture was then boiled (34 C) for 6 hr after which the amide and hydrochloride of the amine were removed from the ether by filtration. This solid residue was washed with four 125-ml portions of water. Recrystallization of the remaining solid from ethanol-water (2:1) gave 3.3 g (71.7%) of 2, mp 192-193 C.

Preparation of (-)-Menthyl Diphenylphosphinate (5)—A 500-ml flask was equipped with an immersion thermometer, nitrogen inlet tube, mechanical stirrer, addition funnel, condenser, and drying tube (CaCl_2). An oil bath was placed around the reaction flask. Sodium (2.76 g; 0.12 mole), 15.63 g (0.10 mole) of (-)-menthol, and 50 ml of toluene were stirred vigorously for 7 hr while the oil bath temperature was held at 100-105 C. After the mixture cooled to room temperature, the unreacted chunk of sodium was removed mechanically. Next 26.0 g (0.11 mole) of diphenyl-

phosphinyl chloride in 50 ml toluene was added dropwise to the sodium alkoxide with external cooling. After the 15-min addition, the mixture was boiled at 85 C for 4 hr, cooled, extracted with 200 ml of 5% sodium bicarbonate, and washed with water. Steam distillation of the organic layer was performed until about 1.5 liters of distillate had been collected in order to remove the unreacted menthol. The nonvolatile organic residue was extracted with ethyl ether. The ether solution was dried ($MgSO_4$) and then evaporated. After a small amount of *n*-hexane was added to the residual oil, cooling in a dry ice-acetone bath caused solidification. Recrystallization from *n*-hexane gave 18.25 g (51.2%) of **5**, mp 72-73 C.

Preparation of (+)-2-Methyl-1-butyl Diphenylphosphinate (7)—The apparatus used was the same as that for **5**. Compound **1** (66.7 g; 0.283 mole) in 100 ml of anhydrous (Linde 3A molecular sieve) ether was added dropwise to 43.0 g (0.425 mole) of triethylamine and 30.0 g (0.340 mole) of (-)-2-methyl-1-butanol in 300 ml of anhydrous ether. The temperature rose from 25 to 30 C during the 30-min addition. After the mixture was boiled at 39 C for 3 hr, the triethylamine hydrochloride was filtered from the ether solution. The solid salt was washed 4 times with 100 ml of boiling ether. After combining all the ether portions, the solution was concentrated. The oil was then heated gradually up to 90 C under high vacuum in order to remove the excess triethylamine and alcohol. Cooling of the oil caused solidification. Crystallization from ether-petroleum ether (1:5) yielded **7**; 35.1 g (43.1%).

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