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A NEW METHOD OF PREPARING OPTICALLY ACTIVE ALKYL PHENYL PHOSPHONATES

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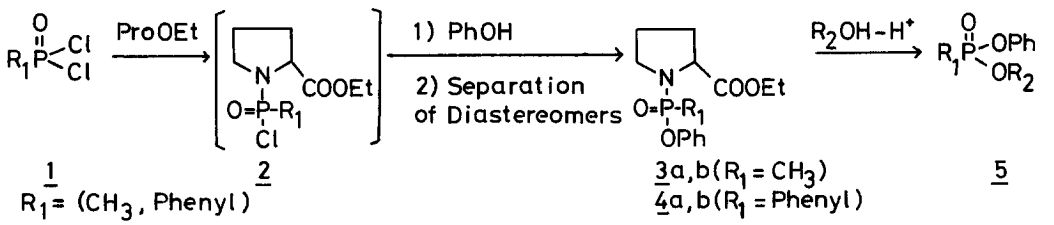
Recently we have reported a novel preparation method[1] of chiral dialkyl phenyl phosphates utilizing the chirality of L-proline ethyl ester and the stereospecificity in solvolytic P-N bond cleavage.

We describe here an extension of the above method to the preparation of optically active alkyl phenyl phosphonates which are potentially useful for the mechanistic investigations of their solvolysis and of the action of various phosphonate insecticides[2]. The reaction sequence of the present method is shown below. Again the separation of diastereoisomeric phosphonic amides and their acid catalyzed alcoholysis are the key steps.



1 R_1 = (CH_3, Phenyl) 2 3a,b(R_1 = CH_3) 4a,b(R_1 = Phenyl) 5

The phosphonic amide monochloride 2, prepared[3] in situ by the reaction of freshly distilled L-proline ethyl ester with methyl or phenylphosphonic dichloride 1 in anhydrous pyridine, was treated [4] with an excess of phenol to afford a diastereomeric mixture of corresponding phosphonic amide phenyl ester(3a,b or 4a,b). The isomers were separated by silica gel column chromatography (benzene-ethyl acetate) and isolated by distillation in fair yields[5]: 3a[6](18 %), bp 142-148°C(0.02 mm), $[\alpha]_D^{23}$ -50°(c 2.1); 3b(38 %). bp 142-150°C(0.02 mm), $[\alpha]_D^{23}$ -82°(c 2.1); 4a (16 %), bp 171-180°(0.06 mm), $[\alpha]_D^{19}$ +3.6(c 1.8); 4b (28 %), bp 169-171°(0.04), $[\alpha]_D^{20}$ -43° (c 1.8)[7].

Acid catalyzed alcoholysis[8] of each diastereomer at ambient temperature gave the corresponding phosphonate 5[9] in a good yield with high degree of optical purity[10]. The yields and physical data of products are shown in Table.

We believe that the present method is superior to the existing preparation methods[11] of chiral phosphonates in its simple experimental procedure employing readily available starting material and therefore will find wider applications. The application of the present method to other phosphonates is now in progress.

Table Yields and Physical Data of Optically Active Alkyl Phenyl Phosphonates

Phosphonic amide	Alkyl phenyl phosphonates				
	R_1	R_2	Yield %	Bp °C(mm)	$[\alpha]_D$ deg(c, °C)
3a	CH_3	CH_3	73	75(0.02)	+21(3.3, 19)
3b	CH_3	CH_3	68	75(0.02)	-20(3.2, 19)
3a	CH_3	C_2H_5	58	80(0.05)	+10(3.0, 18)
3b	CH_3	C_2H_5	54	80(0.05)	-10(2.8, 18)
3a	CH_3	n-C_3H_7	45	70(0.04)	+7.3(2.2, 14)
3b	CH_3	n-C_3H_7	37	70(0.04)	-7.0(1.9, 14)
4a	Phenyl	CH_3	86	115(0.03)	+51(2.3, 16)
4b	Phenyl	CH_3	100	115(0.03)	-49(2.6, 16)
4a	Phenyl	C_2H_5	85	120(0.04)	+47(2.6, 16)
4b	Phenyl	C_2H_5	83	120(0.04)	-46(3.1, 16)
4a	Phenyl	n-C_3H_7	81	120(0.03)	+37(3.0, 14)
4b	Phenyl	n-C_3H_7	96	120(0.03)	-38(3.9, 15)

References and Notes

1) T. Koizumi, Y. Kobayashi, H. Amitani, and E. Yoshii, J. Org. Chem., 42, 3459(1977).
2) For examples with phosphonothioates, see: L. P. A. DeJong, and C. Van Dijk, Biochimica Biophysica Acta., 268, 680(1972); H. Ohkawa, N. Mikami, and J. Miyamoto, Agr. Biol. Chem., 41, 369(1977).
3) The reaction was carried out at ambient temperature for 3-5 hours.
4) The reaction was carried out at ambient temperature for 12-18 hours.
5) Yields are based on phosphonic dichlorides. All distillations were performed with a short path distillation apparatus and bath temperatures are described.
6) All new compounds gave satisfactory elemental analyses and spectral data(IR, NMR, and Mass).
7) All $[\alpha]_D$ were taken in CCl_4 solution.
8) The alcoholysis was performed with 3-4 mM of the phosphonic amide in 5 ml of 1 M H_2SO_4-alcohol for 12-18 hours.
9) After the usual work-up(ref. 1), almost pure oily phosphonate was obtained, which was subjected to microdistillation.
10) The enantiomeric purities of methyl phenyl methylphosphonate and methyl phenyl phenylphosphonate were determined as >97 % observing P-OCH_3 doublet according to the method previously reported (ref. 1). Other phosphonates are considered to possess similar degree of optical purity, because the acid catalyzed alcoholysis of phosphonamides should proceed by similar A-2 mechanism.
11) a) M. Green and R. F. Hudson, J. Chem. Soc., 1958, 3129; b) C. R. Hall, T. D. Inch, G. J. Lewis, and R. A. Chittenden, Chem. Commun., 1975, 720; c) R. B. Cooper, C. R. Hall, and T. D. Inch, Chem. Commun., 1975, 721.

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