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> LETTERS TO THE EDITOR

Convenient Method for Determination of Optical Purity of Chiral Alcohols and Amines

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Chemical transformation of chiral compounds serves as an important method of determination of their optical purity, and it has been widely explored over the past years [1-5].

We found that di-(1R,2S,5R)-menthyl phosphorochloridite (**I**) is a convenient reagent for the determination of optical purity of chiral alcohols and amines by ³¹P NMR spectroscopy. Phosphorochloridite **I** is prepared by the reaction of phosphorus trichloride with (1R,2S,5R)-menthol and triethylamine in toluene at -20° C and purified by vacuum distillation. Phosphorochloridite **I** should not be distilled and isolated pure to be used in analysis of alcohols and amines. The analysis can be accomplished in one step by successively treating phosphorus trichloride with menthol, triethylamine, and the corresponding alcohol or amine.



X = O (II), NH (III).

Diastereomers of compounds **II** and **III** feature quite different ³¹P NMR shifts, which allows rather accurate integration of the corresponding signals and thus accurate determination of diastereomeric ratios. Evidence for the high accuracy of the determination was obtained by analysis of model enantiomeric mixtures.

The starting materials, particularly menthol and the solvent, should be thoroughly purified, and the reaction should be performed in moisture-proof conditions, since compound **I** is readily hydrolyzed to di-(1R,2S,-SR)-menthyl phosphite [6]. The latter can be removed by vacuum distillation, while its presence in the reaction mixture does not interfere with subsequent determination of alcohols and amines, since the signals of di-(1R,2S,5R)-menthyl phosphite is far from those of transformed compounds **II** and **III** (δ_P 140–145 ppm).

Di-(1*R*,2*S*,5*R*)-menthyl phosphorochloridite (I). A solution of 6.2 g of thoroughly dried (1*R*,2*S*,5*R*)menthol and 8 ml of triethylamine in 15 ml of absolute toluene at -20° C to 2.7 g of freshly prepared phosphorus trichloride in 25 ml of absolute toluene. The mixture was stirred for 2 h at 20°C, triethylamine hydrochloride was filtered off, the solvent was removed, and the residue was vacuum-distilled. Yield 50%, bp 135°C (0.01 mm Hg), $[\alpha]_D^{20}$ –83° (*c* 3, toluene). ³¹P NMR spectrum (CHCl₃): δ_P 165 ppm. Found, %: Cl 9.41; P 8.22. C₂₀H₃₈ClO₂P. Calculated, %: Cl 9.62; P 8.01

Determination of optical purity of chiral alcohols and amines. *a*. A solution of 0.38 g of dimenthyl phosphorochloridite I in 2.5 ml of toluene was added with cooling to -70° C to a solution of 0.001 mol of triethylamine and the corresponding alcohol (or amine) in 2.5 ml of toluene. The reaction mixture was heated to room temperature. After 1 h, the precipitate was separated, and the solution was placed into an NMR ampule, a few drops of deuterobenzene were added, and the ³¹P NMR spectrum was taken.

b. A solution of 0.5 g of menthol and 0.45 ml of triethylamine in 5 ml of toluene was added to a solution of 0.14 ml of phosphorus trichloride in 6 ml of toluene at -20° C. The reaction mixture was heated to room temperature and, after 1-h standing, cooled again to ca. -20° C, and a solution of 0.0015 mol of the corresponding alcohol (or amine) and 0.002 mol of triethylamine in 2 ml of toluene was added. The mixture was stirred, heated to 20° C, and let to stand at 30–60 min, after which its ³¹P NMR spectrum was taken.

Below we give the chemical shifs (δ_P , ppm) of certain alcohols and amines whose optical purity was determined by the proposed method: (*S/R*)-Ph(Me)CHOH 143.0, 143.75; (*S/R*)-Et(Me)CHOH 142.23, 142.50; (*S/R*)-Et₂NCH(Me)CH₂OH 140.54, 140.88; (*S/R*)-Et₂NCH(Et)CH₂OH 142.4, 141.9; (*S/R*)-(EtO)₂P(O)CH(Ph)OH 142.83, 143.37; (1*R*,2*S*,5*R*)/(1*S*,2*R*,5*S*)-menthol 143.17, 143.44; (*S/R*)-Ph(Me)-CHNH₂ 142.3, 143.1; (*S/R*)-Pr(Me)CHNH₂ 143.8, 144.0.

The chemically transformed P(III) derivatives **II** and **III** were isolated individual and subjected to certain chemical transformations for structural assessment. These compounds, as well as a detailed procedure will be described in the following publication.

The NMR spectra were measured on a Varian-300 instrument, internal references TMS (¹H and ¹³C) and 85% H_3PO_4 in D_2O (³¹P). The optical rotations were measured on a Polax-2L polarimeter.

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