Mendeleev Commun., 1998, 8(4), 140–141

Synthesis of some novel water-soluble chiral phosphines

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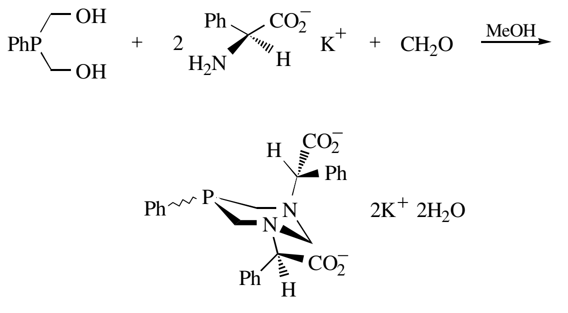
Two individual (*RR*)- and (*SS*)-isomers of dipotassium 1,3-di[phenyl(carboxylato)methyl]-5-phenyl-1,3,5-diazaphosphorinane have been synthesized in the reaction of bis(hydroxymethyl)phenylphosphine, paraformaldehyde and the potassium salt of (*R*)- or (*S*)- -phenylglycine.

In the last decade a rapid development of catalytic reactions in aqueous/organic biphasic systems, especially enantioselective processes,[1–3] has focused the attention of chemists on synthetic routes to the chiral water-soluble phosphine ligands. The functionalisation of well-known optically active phosphines: BINAP, BDPP, DIOP, CHIRAPHOS and cyclobutaneDIOP with highly polar sulfonate,[4–6] carboxylate[7,8] or ammonium[9] groups is a general route to such compounds.

Reactions of hydroxymethylphosphines with primary and secondary amines are a powerful method for constructing numerous classes of air-stable linear and cyclic aminomethylphosphine ligands.[10–12] A number of water soluble[13–14] and some optically active aminomethylphosphines[10] have already been obtained.

We suggest using the reactions of hydroxymethylphosphines with derivatives of amino acids to obtain water-soluble chiral heterocyclic phosphine precursors of catalysts for aqueous/organic biphasic catalytic reactions. Amino acids have been used in the construction of chiral phosphine ligands as a source of asymmetric carbon atoms, but their highly polar carboxylic and amine groups have usually been displaced.[15] Both enantiomers of amino acids are accessible. We now introduce the synthesis of two individual (*RR*)- and (*SS*)-isomers of dipotassium 1,3-di[phenyl(carboxylato)methyl]-5-phenyl-1,3,5-diazaphosphorinane **1**.



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It has been shown in previous investigations that crystalline, air-stable, non bulky 1,3-di-R-5-phenyl-1,3,5-diazaphosphorinane ligands[12] are obtained in high yields from bis(hydroxymethyl)phenylphosphine, paraformaldehyde and primary aryl- or benzylamine in benzene or acetone. We used the potassium salt of (*S*)- or (*R*)-phenylglycine and methanol as a solvent in this reaction, because the reactivity of free amino acids in the nucleophilic substitution reactions are low due to their betaine structure and all reagents are soluble in methanol.†

In both cases white, highly water soluble, crystalline compounds with identical physical characteristics‡ (except specific rotation) were obtained. The values of specific rotation ($[\alpha]^{20}_{546}$) for the isomers show that *S*-(+)- and *R*-(–)-amino acid salts give *SS*-(+)- and *RR*-(–)-isomers of phosphine, respectively. The IR spectra of the compounds exhibit absorption bands due to Ph and CO_2^- groups and H_2O. In the ^{31}P NMR spectra only one signal shifted to higher fields corresponding to initial hydroxymethylphosphine was observed. The ^{31}P NMR data show that one isomer of heterocyclic phosphine[11] was formed. The ^1H NMR data are not informative, because of the overlapping of the signals of methylene and methyne protons. The ^{13}C NMR spectra are consistent with the structure of heterocyclic phosphine.[16] In the ^{13}C NMR spectra signals of two types of methylene groups from $P–CH_2–N$ and $N–CH_2–N$ fragments were recorded. The methylene carbon signal of the $P–CH_2–N$ fragment was located to low field and revealed the direct coupling constant $^1J_{P–C}$. Only one asymmetric carbon atom signal was observed, confirming the formation of an individual enantiomer. The NMR data of the phosphine obtained, dissolved in water and methanol, are similar.

(*RR*)- and (*SS*)-isomers of dipotassium 1,3-di[phenyl(carboxylato)methyl]-5-phenyl-1,3,5-diazaphosphorinane show high water solubility, and a 1 M solution in water can be obtained. This phosphine concentration in water is therefore in the range practical for catalytic applications.

The authors are grateful for financial support of this work by INTAS (grant no. 93-2011-ext.).

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† *General procedure for the synthesis of* (*RR*)- *and* (*SS*)-*dipotassium* 1,3-*di*[*phenyl*(*carboxylato*)*methyl*]-5-*phenyl*-1,3,5-*diazaphosphorinanes*. Paraformaldehyde (0.215 g, 7.2 mmol) was dissolved in bis(hydroxymethyl)phenyl phosphine (1.23 g, 7.2 mmol) with mild heating and the mixture was diluted with 5 ml of dry methanol. A solution of *S*-(+)- or *R*-(–)- -phenylglycine (2.19 g, 14.5 mmol) and KOH (0.81 g, 14.5 mmol) in 10–15 ml methanol $\{[\alpha]^{20}_{546} = \pm 125°$ for potassium salts (H_2O, $c =$ = 2.86)} was prepared separately. The two mixtures were combined at room temperature with good mixing. The mixture became absolutely transparent and was noticeably warm. After no later than 2 h the reaction mixture was filtered through filter paper and the filtrate was concentrated to about 3–4 ml. After 0.5–1 h the white fine solid which formed was filtered on a thick glass filter, washed twice with MeOH–Et_2O (1:1), then Et_2O, and dried *in vacuo*. The resulting white fine crystals are hygroscopic and decompose in air.

‡ (*RR*)- *and* (*SS*)-*potassium* 1,3-*di*[*phenyl*(*carboxylato*)*methyl*}-5-*phenyl*-1,3,5-*diazaphosphorinanes*. Global yields about 75–80%, mp 244–246 °C (decomp.). ^{13}C NMR (100.6 MHz, D_2O) δ: 48.72 (d, 2C, C*H, J_{CH} 142.2 Hz), 72.26 (t, 1C, $N–CH_2–N$, J_{CH} 145.9 Hz), 74.11 (dt, 2C, $P–CH_2–N$, J_{CH} 135.9 Hz, J_{PC} 74.37 Hz), 127.28 (d, 1C, $P–C_6H_5$-*p*, J_{CH} 156.0 Hz), 128.04 (d, 2C, $C^*H–C_6H_5$-*p*, J_{CH} 161.0 Hz), 128.13 (d, 4C, $C^*H–C_6H_5$–*m*, J_{CH} 161.3 Hz), 128.30 (d, 4C, $C^*H–C_6H_5$-*o*, J_{CH} 161.0 Hz), 128.74 (s, 2C, $C^*H–C_6H_5$-*ipso*), 128.76 (dd, 2C, $P–C_6H_5$-*m*, J_{CH} 145.5 Hz, J_{PC} 5.0 Hz), 130.79 (dd, 2C, $P–C_6H_5$-*o*, J_{CH} 162.0 Hz, J_{PC} 14.7 Hz), 137.74 (d, 1C, $P–C_6H_5$-*ipso*, J_{PC}, 46.1 Hz), 177.97 (s, 2C, COOK); ^{31}P NMR (162.5 MHz, MeOH) δ: –59.84; ^{31}P NMR (162.5 MHz, H_2O) δ: –60.35; IR (Nujol, KBr, ν/cm^{-1}) 1580 (CO), 1590 (Ph), 1620, 3300–3360 (H_2O). $[\alpha]^{20}_{546}$: (*RR*) –38.8° (MeOH, $c = 7.13$), (*RR*) –107.8° (H_2O, $c = 7.15$); (*SS*) +38.7° (MeOH, $c = 7.15$); (*SS*) +107.8° (H_2O, $c = 7.14$). Found (%): C, 52.97; H, 4.92; N, 5.06; P, 5.24. Calc. for $C_{25}H_{27}K_2N_2O_6P$ (%): C, 53.57; H, 4.82; N, 5.00; P, 5.54.

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Received: Moscow, 14th May 1998
Cambridge, 18th June 1998; Com. 8/03648I