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Rapid Communication

Synthesis of Chiral Nonionic Superbases Based on Iminophosphoranes

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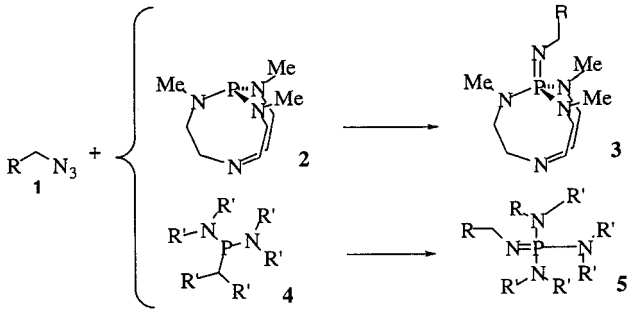
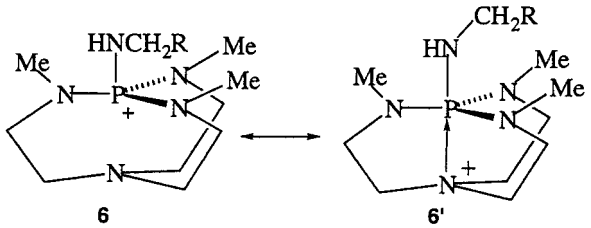
ABSTRACT: *Optically active azides derived from penta-O-acetylglycose tartaric acid and quinine when reacted with the proazaphosphatrane P(MeNCH$_2$-CH$_2$)$_3$N gave highly basic iminophosphoranes that are potential asymmetric catalysts and ligands for a variety of reactions. Preliminary results show that the enantiomers are formed in unequal proportions.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:251–253, 2000

INTRODUCTION

Iminophosphoranes are very strong nonionic superbases with pK_a values for their conjugate acids up to 28 in CH_3CN [1]. They are useful as catalysts in dehydrohalogenations [1], aminoacid synthesis [2], acylation, and Michael addition reactions [3]. They are also nucleophilic catalysts and can catalyze the trimerization of isocyanates [4]. Chiral nonionic superbases and nucleophilic catalysts are useful in many asymmetric transformations. Chiral dimethyl aminopyridine derivatives are known to catalyze the kinetic resolution of secondary alcohols [5] and dynamic kinetic resolution of aminoacids [6]. Chiral guanidines catalyze asymmetric nitro aldol reactions [7] and asymmetric alkylative esterifications [8]. To the best of our knowledge, no chiral derivatives of iminophosphoranes bases of type **3** or **5** (R = chiral moiety) have been reported so far. In this communication we report the first synthesis of such chiral nonionic bases derived from tartaric acid and quinine. We reported earlier that *tris*-dialkyl aminophosphines react with organic azides **1** to give the corresponding iminophosphoranes in very high yields [9]. When the aminophosphine is of type **2**, the iminophosphorane obtained **(3)** is unusually basic compared with its acyclic analogue **5** [5].



The strong basicity of **3** was attributed to the charge delocalization of the corresponding protonated species **6** by three nitrogens directly attached to the phosphorus and the fourth by transannular interaction in **6′**. The latter interaction can also increase the nucleophilicity of the imino nitrogen and perhaps also enhance its complexing ability with metals. Because of these unusual properties arising from transannular interactions, we decided to use **2** (which is commercially available [10]) for the synthesis of the chiral iminophosphoranes **3a** and **3c**.



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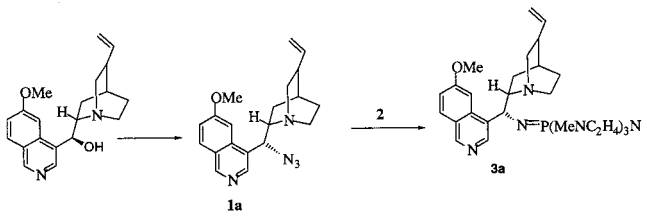
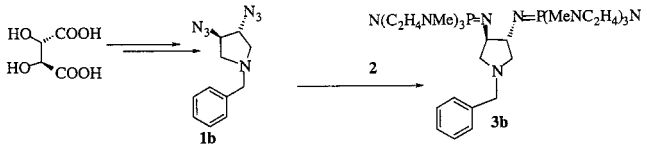
Chinchona alkaloids and their derivatives are useful ligands and catalysts in asymmetric synthesis [11]. Their rigid structures play an important role in asymmetric interactions that lead to optical induction. Recently Brunner et al. synthesized 9-amino 9-deoxy quinine derivatives in a synthesis involving the azide intermediate **1a,** which was not isolated [12]. We have isolated **1a** and found that it is stable. When the azide **1a** was treated with the aminophosphine **2** at room temperature for 17 hours, the corresponding iminophosphorane **3a** was isolated in 80% yield and in ^{1}H NMR spectroscopically pure form.

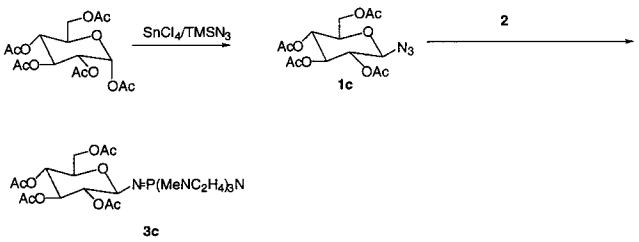


SCHEME 2

C2 symmetric diamine ligands such as bis-oxazolines [13] or diamines [14] have gained attention because of their ability to coordinate with metals that catalyze a variety of asymmetric transformations. When the C2 symmetric diazide **1b** (made according to the reported procedure[16]) was treated with aminophosphine **2,** the corresponding ^{1}H NMR-spectroscopically pure product **3b** was isolated in 80% yield. Similar but less Lewis basic chiral diiminophosphoranes derived from the reaction of triphenyl phosphine dibromide [15], and diamines have



recently been reported [15]. In the chemical synthesis of asymmetric compounds, carbohydrates and their derivatives have often been used as sources of chiral reagents because they are readily available. Conversions of carbohydrates into enantiomerically pure noncarbohydrate compounds have developed rapidly and represent a commonly selected means for the synthesis of natural products [17,18]. The creation of a chiral center from a prochiral carbon atom in the absence of an asymmetric influence such as solvent, catalyst, or reagent gives racemic product, whereas enantiomers are formed in unequal proportions if the environment is asymmetric. Carbohydrates are often employed as chiral auxiliaries by bonding them to a reactant, thereby providing localized asymmetric environments [19,20]. Herein, we report the synthesis of the chiral nonionic glycosyl base **3c.**



Azide intermediate **1c** (synthesized according to a previously reported method [21] with a minor modification) was reacted with **2** in toluene at −78°C at RT under an argon atmosphere to produce glycosyl base **3c** as a white solid in 92% yield. Preliminary screening experiments show that excesses of one enantiomer are formed in some reactions.

EXPERIMENTAL

Iminophosphoranes **3a** *and* **3b**

To a stirred solution of azide **1a** and **1b,** respectively, (1 mmol) in benzene (5 mL) at room temperature, a benzene (5 mL) solution of **2** (1.1 mmol) was added. After 15–17 hours, benzene was evaporated under vacuum to give a pasty residue. Hexanes (25 mL) were added, and the mixture was stirred until all the pasty residue became a fine white powder. The powder was filtered off and dried to give the pure product, which was characterized by spectroscopic methods. **3a**: ^{1}H NMR (300 MHz, C_6D_6): δ 2.14 (d, 6H), 2.33 (t, 6H), 2.43 (d, 9H), 2.54–2.56 (m, 1H), 2.70–2.72 (m, 1H), 2.94–2.97 (m, 1H), 3.59 (s, 3H), 3.62–3.71 (m, 1H), 4.10–4.12 (m, 1H), 4.93–5.01 (m, 2H), 5.56 (d, 1H), 5.72–5.77 (m, 1H), 7.35 (d, 1H), 7.65–7.66 (m, 2H), 8.28–8.40 (m, 2H), 8.88–8.90 (m, 1H). ^{13}C NMR (CD_3CN): δ 13.5, 22.4, 26.3, 28.1 (d, J_{PC} = 26 Hz), 31.4, 34.6 (d, J_{PC} = 12 Hz), 40.3 (d, J_{PC} = 23 Hz), 49.3, 51,2, 55.4, 56.1, 58.4, 72.1, 103.5, 113.4, 120.8 (d J_{PC} = 29 Hz), 128.5 (d, J_{PC} = 29 Hz), 131.4, 142.6, 144.8, 145.6, 147.7, 157.2. ^{31}P NMR (C_6D_6): δ 35.7, LRMS (EI mode): 537 (M+), 427, 401, 368, 306, 262, 216. HRMS: Calculated for $C_{29}H_{44}N_7OP$ = 537.33440; Measured = 537.33451 **3b**: ^{1}H NMR (C_6D_6): δ 2.13 (t, 12H), 2.30–2.38 (m, 12H), 2.55 (d, 18H), 3.29 (t, 4H), 2.63 (d, 2H), 5.1 (t, 2H), 6.97–7.40 (m, 5H), ^{13}C NMR (CD_3OD): δ 34.3, 49.2, 51.1, 58.7, 60.3, 73.1, 126.9, 127.9, 128.8. ^{31}P NMR (C_6D_6): 36.2. LRMS (EI mode): 619 (M^+), 537, 486, 452, 388, 361, 297, 271, 244. HRMS: Calculated for $C_{29}H_{55}N_{11}P_2$ = 619.41241; Measured = 619.41173.

2,3,4,6-tetra-O-acetyl-b-D-pyroglucosyl azide **1c**

To a stirred solution of the α-D-glucose pentaacetate (2 g, 5 mmol) dissolved in CH_2Cl_2 (10 mL), Me_3SiN_3 (3 mL, 11 mmol) was added at 0°C under argon. After 5 min, $SnCl_4$ (0.4 mL, 5 mmol) and $BF_3 \cdot Et_2O$ (0.65 mL, 5 mmol) were added. The starting material disappeared overnight (TLC pentane: ethyl acetate 2:1). The reaction mixture was poured into 250 mL of ethyl acetate and washed three times with water. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was separated by silica gel column chromatography to afford 1.806 g of **1c** in 95% yield. The ^{1}H and ^{13}C NMR spectral data corresponded with those in the literature [22].

Iminophosphorane 3c

To a solution of the **1c** (0.410 g, 1.07 mmol) in toluene (15 mL) at 78°C under argon was added **2** (0.223 g, 1 equiv) dissolved in 2 mL of toluene. The reaction mixture was allowed to warm to room temperature. After 3 hours, the starting material disappeared and a white solid was produced. Toluene was removed by centrifugation and decantation to give a white solid, which was washed three times with pentane and dried under vacuum to afford an ^{1}H NMR pure product **3c** in 92% yield.

$[a]_D^{20}$ = 43.3 (c o.55, $CHCl_3$); m.p.: 137–138.5°C (dec); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.36 (t, 1H, J = 9.0 Hz), 5.25 (t, 1H, J = 9.3 Hz), 5.18 (t, 1H, J = 9.5 Hz), 4.80 (d,1H,J = 8.8 Hz), 4.12 (dq, 2H, J = 4.6 Hz, J = 12.0 Hz), 3.77 (m, 1H), 2.95–2.89 (m, 6H), 2.87–2.75 (m, 6H), 2.71 (d, 9H, J = 8.1 Hz), 2.00 (s, 6H), 1.97 (s, 3H), 1.85 (s, 3H), ^{31}P NMR ($CDCl_3$) δ 38.01; ^{13}C NMR ($CDCl_3$) δ 170.94, 170.84, 169.51, 169.10, 95.01, 74.75, 73.21, 71.91, 68.81, 62.65, 51.38, 49.90, 35.43 (d, 3.5 Hz), 20.81 (d, 12.9 Hz), 20.83; EI-MS: 561 (M^+), 502, 443, 258, 232, 176; HRMS Calculated for $C_{23}H_{40}N_5O_9P$ = 561.25636, Measured = 561.25616.

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