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New phosphine-imine and phosphine-amine ligands derived from D-gluco-, D-galacto- and D-allosamine in Pd-catalysed asymmetric allylic alkylation

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New phosphine-imine and phosphine-amine chiral ligands which were easily prepared from D-gluco-, D-galacto- and D-allosamine furnished a high level of enantiomeric excess (up to 99%) in the Pd(0)-catalysed asymmetric allylic alkylation of racemic 1,3-diphenyl-2-propenyl acetate with malonates.

1. Introduction

Catalytic asymmetric synthesis has been one of the most active research areas in modern organic chemistry. To achieve the highest levels of reactivity and selectivity in enantioselective reactions the design of efficient synthetic chiral catalysts is at the center of contemporary studies.

In recent years impressive results have been obtained using carbohydrate-based ligands.[1] These chiral natural derivatives have many advantages: they are readily available, can be easily functionalized, have several stereogenic centers and successfully used in a large number of asymmetric catalytic reactions, such as: hydrogenation,[2] 1,2-addition of nucleophiles to C=O and C=NR,[3] 1,4-addition of nucleophiles to Michael acceptors,[4] hydroformylation,[5] Heck reaction,[6] cyclopropanation[7] and hydrovinylation.[8] Derivatives of the most accessible NH_2-containing sugar, D-glucosamine, have been mainly evaluated as chiral ligands in Pd-catalysed asymmetric allylic substitution reaction which is a fundamental transformation in organic synthesis and one of the most powerful tools for the formation of carbon-carbon and carbon-heteroatom bonds. The best results in Pd-catalysed asymmetric allylic alkylation of 1,3-symmetrically disubstituted acetates (ee up to 98%) provided phosphine-oxazoline,[9] phosphinite-oxazoline,[10] phosphite-oxazoline,[11] phosphite-phosphoramidite[12] and phosphine-amide[13] derivatives of D-glucosamine. Just a few phosphine-imine ligands with a pyranoside backbone have been developed for Pd-catalysed allylic substitution.[13c,13d,14] The studies indicated that the presence of the imine-phosphine residue at C2 provides better enantioselectivities than when the residue is at C1 of the pyranoside backbone. Additionally the C2 imine group in ligands has been replaced by an amine group and also provided good results.[13d]

Herein, we report a simple and efficient synthesis of novel phosphine-imine and phosphine-amine chiral ligands derived from D-gluco-, D-galacto- and D-allosamine hydrochloride (Fig. 1) and their application in the Pd-catalysed allylic alkylation reaction with various nucleophiles.

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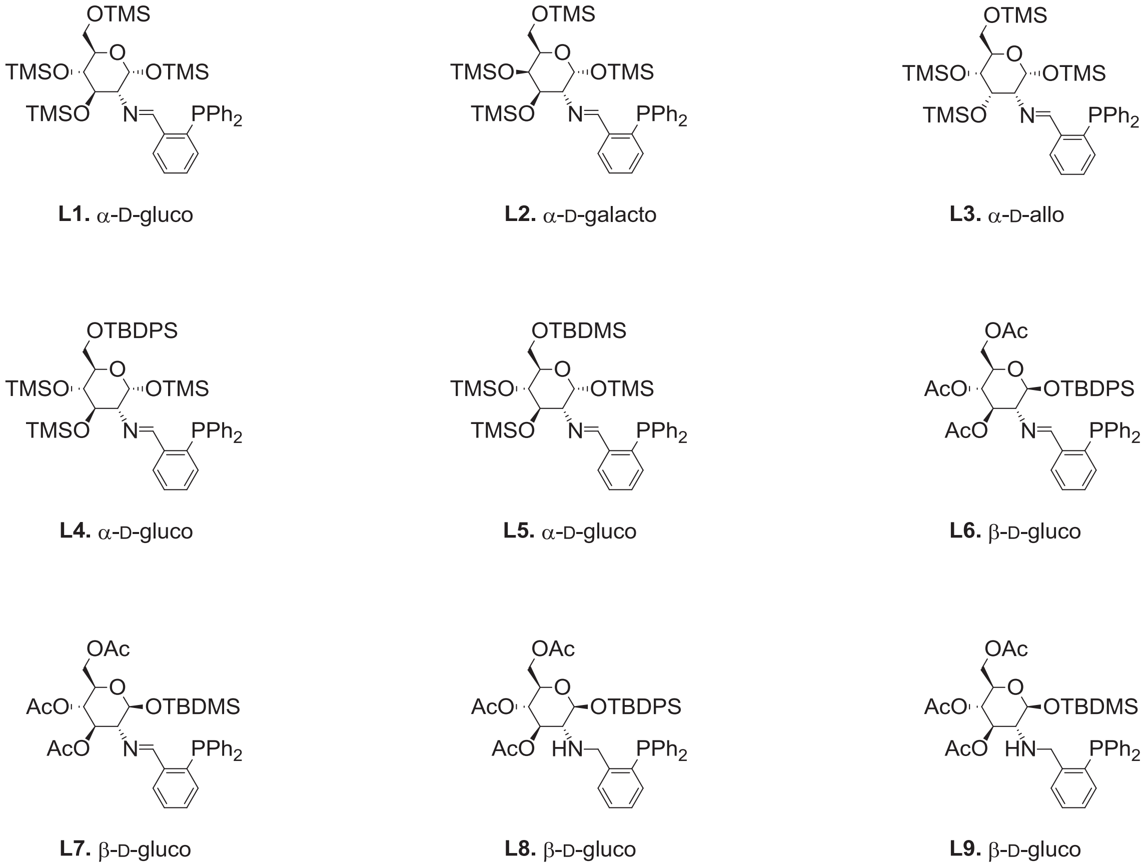


L1. α-D-gluco **L2.** α-D-galacto **L3.** α-D-allo

L4. α-D-gluco **L5.** α-D-gluco **L6.** β-D-gluco

L7. β-D-gluco **L8.** β-D-gluco **L9.** β-D-gluco

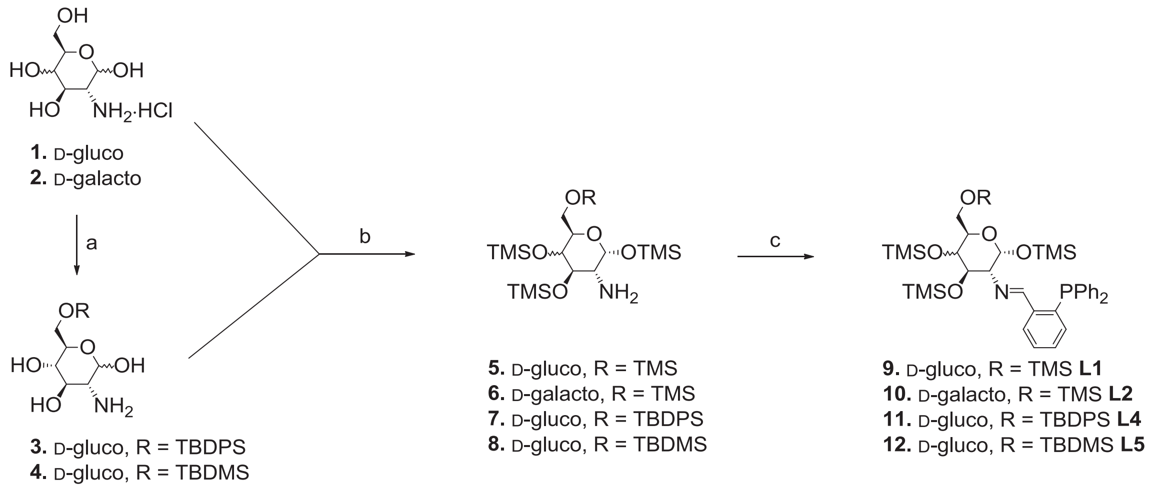
Fig. 1. New *P,N*-ligands used in this work.

2. Results and discussion

2.1. Synthesis of the starting materials

The new phosphine-imine ligands **9**–**12**, derivatives of D-gluco- and D-galactosamine were easily prepared according to Scheme 1.

Glucosamine hydrochloride **1** was first treated with TBDPSCl or TBDMSCl in pyridine to give 6-*O*-silyl protected derivatives **3** and **4** as yellow oil in 63% and 72% yields, respectively. Per-*O*-silyl protected α-derivatives **5**,[15] **6**,[16] **7** and **8** were obtained in 82%, 82%, 55% and 60% yields, respectively, by the reaction of **1**–**4** with trimethylsilyl chloride (TMSCl) and hexamethyl disilazane (HMDS) in pyridine[15,17]. Under these conditions the amino functional group remains unprotected.[15] Condensation of 2-(diphenylphosphino)-benzaldehyde onto D-glucopyranose **5**, **7**–**8** and D-galactopyranose **6** derivatives in toluene furnished the corresponding phosphine-imine derivatives **9**,[18] **10**,[16] **11** and **12** in 77%, 67%, 43% and 45% yields, respectively.



1. D-gluco
2. D-galacto

3. D-gluco, R = TBDPS
4. D-gluco, R = TBDMS

5. D-gluco, R = TMS
6. D-galacto, R = TMS
7. D-gluco, R = TBDPS
8. D-gluco, R = TBDMS

9. D-gluco, R = TMS **L1**
10. D-galacto, R = TMS **L2**
11. D-gluco, R = TBDPS **L4**
12. D-gluco, R = TBDMS **L5**

Scheme 1. Synthesis of ligands **L1, L2, L4 and L5**; reagents and conditions: (a) TBDPSCl or TBDMSCl, Py, rt; (b) TMSCl, HMDS, Py, rt; (c) 1,2-Ph_2P-C_6H_4-CHO, toluene, 60 °C.