Stereoselective synthesis of a new optically active phosphinoacyloxazolidinone *via* enantioselective hydrogenation

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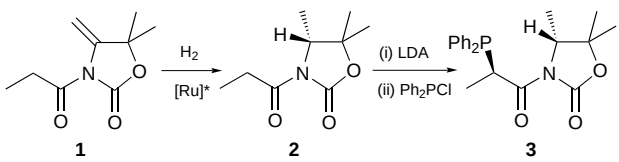
The preparation of a new optically active phosphinoacyloxazolidinone, based on the enantioselective hydrogenation of a 4-methylene-*N*-propionyloxazolidinone in the presence of [(*R*)-BINAP]Ru(O_2CCF_3)$_2$ catalyst followed by stereoselective phosphinylation, is reported.

Chiral diphosphines coordinated to a transition metal centre have demonstrated their power in asymmetric catalysis.[1] More recently, optically active heterobidentate ligands containing only one phosphorus group have proved to be very efficient in a variety of catalytic reactions. Thus, the diphenylphosphino group attached to a functional group such as an amine,[2] an oxazoline,[3] a pyrazole[4] or a quinoline[5] moiety has led to a variety of new P–N ligand–metal catalysts which have contributed to the improvement of enantioselectivity in various catalytic reactions. Other heterobidentate functional phosphine ligands with an additional coordinating oxygen atom have also been used successfully in asymmetric catalysis.[6–9]

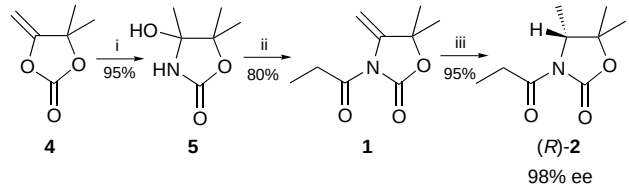
Here we report the preparation of a new P–O heterobidentate ligand of high optical purity based on the synthesis of an optically active acyloxazolidinone followed by its phosphinylation. This synthesis does not involve substrates from the natural chiral pool but is based on two successive selective reactions: (i) the enantioselective hydrogenation of a 4-methylene-*N*-propionyloxazolidin-2-one **1**, and (ii) the stereoselective phosphinylation of the resulting optically active acyloxazolidinone **2**, according to Scheme 1.

Whereas optically active acyloxazolidinones are usually prepared by acylation of oxazolidinones arising from optically active natural amino acids *via* multistep syntheses,[10,11] we have shown that it is possible to obtain both enantiomers of the acyloxazolidinone **2** *via* enantioselective hydrogenation of the 4-methylene-*N*-acyloxazolidinone **1** in the presence of a ruthenium catalyst containing an optically pure diphosphine ligand.

The bubbling of ammonia through an EtOAc solution of the carbonate **4**[12] at room temperature led to 95% yield of the hydroxyoxazolidinone **5**. The treatment of this cyclic carbamate with an excess of propionyl chloride in refluxing CH_2Cl_2 in the presence of $CaCl_2$ led to the isolation of the acyloxazolidinone **1** (80% yield) in a one pot acylation–dehydration reaction. The enantioselective hydrogenation of **1** was performed under 10 MPa of H_2 in MeOH at 50 °C for 18 h in the presence of 1 mol% of [(*R*)-BINAP]Ru(O_2CCF_3)$_2$ as catalyst and led to the (*R*)-*N*-propionyloxazolidinone (*R*)-**2** in 95% yield. Thus, in a four step synthesis involving only small simple molecules (prop-2-ynylic alcohol, CO_2, NH_3, AcCl and H_2), the (*R*)-*N*-propionyloxazolidinone (*R*)-**2** was isolated with an enantiomeric excess



Scheme 1



Scheme 2 *Reagents and conditions*: i, NH_3, room temp.; ii, EtCOCl, CH_2Cl_2 reflux; iii, H_2, [(*R*)-BINAP]Ru(O_2CCF_3)$_2$, MeOH, 50 °C

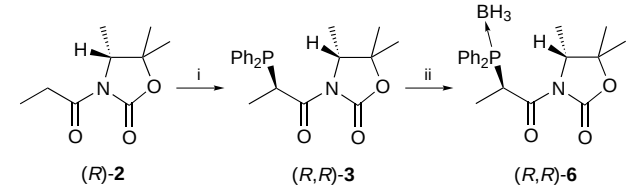
of 98%, according to Scheme 2.‡ Compound (*R*)-**2** appears to be the simplest (*R*)-enantiomer of the family of Superquats, the (*S*)-enantiomer of which has already been prepared from an amino acid.[11]

Advantage was taken of the asymmetric induction offered by chiral acyloxazolidinones to stereoselectively introduce an electrophile on the acyl group.[10,11] We thus attempted to transform (*R*)-**2** into a functional phosphine of type **3** by addition of the electrophilic diphenylphosphino group after deprotonation of the acyl moiety of (*R*)-**2** (Scheme 3).

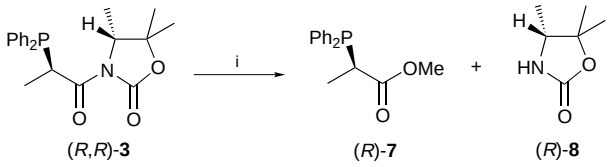
The *N*-propionyloxazolidinone (*R*)-**2** (4.3 mmol) was first deprotonated in THF at −90 °C using LDA (1 equiv.). Then, chlorodiphenylphosphine (4.3 mmol) was added and the reaction mixture was kept at −90 °C for 15 h before warming to room temperature. The resulting phosphinoacyloxazolidinone (*R*,*R*)-**3** was purified by chromatography over alumina and isolated in 87% yield. The ^{31}P NMR spectrum of the crude oil showed two singlets at δ 5.84 and 4.87, indicating the presence of the two diastereoisomers in the ratio 95 : 5. This result shows that the novel transformation of acyloxazolidinones by phosphinylation is stereoselective and that the optically pure *N*-propionyloxazolidinone (*R*)-**2** provides efficient asymmetric induction as already observed for the alkylation with BnBr, of (*S*)-**2** prepared *via* a different route.[11]

This functional phosphine is very air-sensitive and it is preferable to stabilize it as a phosphine–borane adduct. The addition of BH_3·SMe at −80 °C at the end of the reaction leading to **3** made possible the preparation of the corresponding phosphine–borane (*R*,*R*)-**6**.§ Chromatography over silica gel allowed the isolation of only the major diastereoisomer in 47% yield (100% de).

Cleavage of the *N*-acyl bond of (*R*,*R*)-**3** was carried out under mild conditions in MeOH at room temperature in the presence of K_2CO_3 and led to the chiral oxazolidinone auxiliary (*R*)-**8** and



Scheme 3 *Reagents and conditions*: i, LDA, THF, −90 °C, then Ph_2PCl, −90 °C to room temp.; ii, BH_3·SMe_2



Scheme 4 *Reagents and conditions*: i, MeOH, K_2CO_3, room temp.

the optically active phosphine methyl ester (*R*)-**7** in 90% yield after column chromatography under N_2 (Scheme 4).

In conclusion, we report the selective preparation of an optically pure phosphinoacyloxazolidinone. The synthesis involves the preparation of an optically active acyloxazolidinone *via* catalytic enantioselective hydrogenation and its use as chiral inductor for stereoselective phosphinylation. This type of new compound has potential as a new heterobidentate ligand in asymmetric catalysis, and as a building block for access to a variety of optically active phosphorus derivatives *via* cleavage of the oxazolidinone ring.

Notes and References

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‡ *Selected data* for (*R*)-**2**: δ_H (300 MHz, $CDCl_3$) 1.14 (3 H, t, *J* 7.3, *Me*CH_2), 1.26 (3 H, d, *J* 6.6, *Me*CH), 1.39 and 1.41 (2 × 3 H, 2 s, Me_2C), 2.88 and 2.90 (2 H, m, *J* 16.0, 7.35, MeCH_2CO), 4.16 (1 H, q, *J* 6.6, *CH*Me); δ_C(75.5 MHz, $CDCl_3$) 8.35 (q, *J* 128), 14.69 (q, *J* 128), 21.55 (q, *J* 127), 27.83 (q, *J* 128), 29.33 (t, *J* 128), 58.88 (d, *J* 147), 81.41 (s), 152.79 (s), 174.34 (s); Calc. for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.07; H, 8.45; N, 7.60%. $[\alpha]_D$ −51 (*c* 0.9, $CHCl_3$).

§ *Selected data* for (*R*,*R*)-**6**: mp 141 °C; δ_P(121.5 MHz, $CDCl_3$) 26.76 (q, *J* 48.8); δ_H(300 MHz, $CDCl_3$) 1.09 (3 H, d, *J* 6.6, NCHCH_3), 1.17 (3 H, s, CMe_2), 1.35 (3 H, s, CMe_2), 1.42 [3 H, dd, *J* 15.5, 6.9, *Me*CH(PPh_2)], 4.03 (1 H, q, *J* 6.6, N*CH*CH_3), 5.50 [1 H, dq, *J* 12.7, 6.9, *CH*(PPh_2)], 7.39–7.90 (10 H, Ph); δ_C(75.5 MHz, $CDCl_3$) 13.39 (q, *J* 131.2), 13.68 (q, *J* 128.2), 21.59 (q, *J* 127.5), 27.51 (q, *J* 127.5), 34.75 (dd, *J* 137.9, 25.5), 59.37 (d, *J* 141.6), 81.46 (s), 126.65–133.72 (m), 152.87 (s), 171.09 (s); Calc. for $BC_{21}H_{27}NO_3P$: C, 65.81; H, 7.10; N, 3.65; P, 8.08. Found: C, 65.81; H, 7.14; N, 3.65; P, 7.93%. $[\alpha]_D$ + 58 (*c* 1.0, $CHCl_3$).

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