Chiral organophosphorus ligands derived from the levopimaric acid–maleic anhydride adduct

Aleksander G. Tolstikov,*[a] Olga V. Tolstikova,[a] Tatiana B. Khlebnikova,[a] Kirill I. Zamaraev,†[a] Vakhtang G. Kasradze,[b] Olga S. Kukovinets[b] and Leonid V. Spirikhin[b]

[a] *Federal Scientific Centre, G. K. Boreskov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation. Fax: +7 3832 35 5756*
[b] *Institute of Organic Chemistry, Ufa Research Centre of the Russian Academy of Sciences, 450054 Ufa, Russian Federation.*

The levopimaric acid–maleic anhydride adduct 1 has been used as a starting compound to synthesize chiral organophosphorus ligands 11–13 and 15–17 for transition metal complexes.

Asymmetric transformations catalysed by transition metal complexes with chiral organoelement (P-, N-, S-donor) ligands are of common knowledge.[1,2] A great number of optically active compounds capable of catalysing the processes of hydrogenation[3] and isomerization[4] of prochiral substrates to provide high chemical and optical yields of products have been obtained to date. For this purpose a number of organophosphorus ligands based on esters of L-, D-tartaric acids,[5] carbohydrates,[6,7] amino acids,[8] monoterpenes,[9] binaphthyl derivatives,[10] *etc.* have been synthesized. Even with impressive progress in this field, the synthesis of chiral ligands, which combine availability with high selectivity of catalysts based thereon, is still a pressing problem.

While making studies in the field, we paid attention to the adduct of levopimaric acid with maleic anhydride **1**.[11,12] Owing to its enantiomeric purity, specific molecular structure and ease of preparation, it is an attractive substrate to be transformed to chiral compounds. A retrosynthetic analysis allowed us to define three principal routes for transformation of maleopimaric acid **1** to phosphorus-containing ligands (see Scheme 1).

Trimethyl ester **2**[13] was produced *via* route A (Scheme 2); the ester was reduced by $LiAlH_4$ to 5a,8-dimethyl-12-isopropyl-1,2,8-trihydroxymethyl-4,4a,5,5a,6,7,8,8a,9,10-decahydro-3,10a-ethenophenanthrene **3** (80%) which reacted with benzaldehyde dimethoxyacetal to produce a benzylidenedioxy derivative **4** (95%). The latter was transformed to monobenzyl ether **5** (56%) under the action of benzyl chloride in the presence of KOH. Reaction of **4** with 2-methoxyethoxymethylchloride (MEMCl) in a solution of di(isopropyl)ethylamine was used as an alternative to selectively protect the CH_2OH group at the C-8 atom. The yield of the MEM ether **6** was 90%.

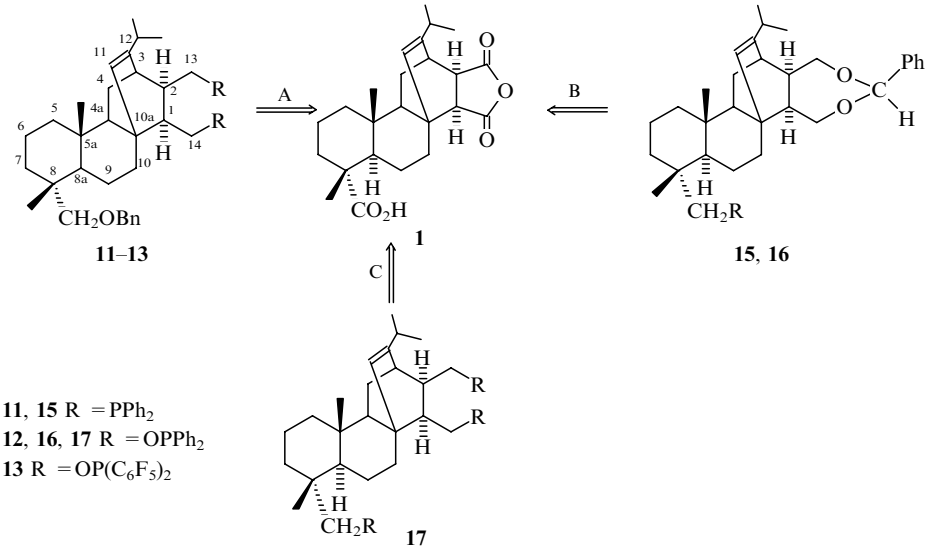
However, it seemed reasonable to use a sample of monobenzyl ether **5** since, apart from the desired deprotection of the 1,2-oxymethyl groups, treatment of compound **6** with *p*-toluenesulfonic acid in methanol resulted in partial hydrolysis of the MEM-protecting function to form the starting triol **3** (40%). Hydrolysis of ether **5** allowed a quantitative yield of diol **7** to be obtained. Along with expected ditosylate **8** (75%), a product **10** from dehydration (25%) was formed upon interaction of **7** with TsCl in a pyridine solution at $-5\,^{\circ}C$. Compound **10** predominated in the reaction mixture (65%) when the reaction was conducted at room temperature.

We succeeded in obtaining the target bis(phosphine) **11** in 45% yield through interaction of ditosylate **8** with PPh_2Na; the latter was prepared *in situ* according to ref. 14. To enhance the yield of the target product, we tried to involve dimesylate **9** which was synthesized in its turn from monobenzyl ether **7**. Unfortunately, reaction of **9** with a nucleophilic reactant produced a mixture of polar products, among which only diol **7** was isolated and identified.

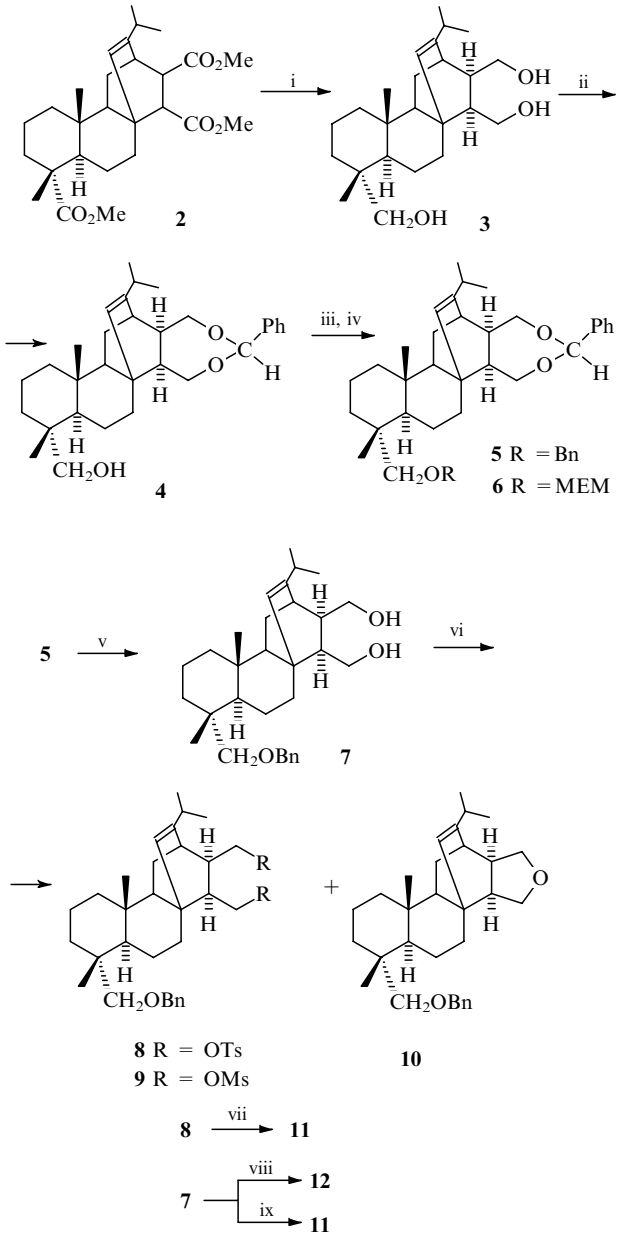
Optically active phosphinites **12** (62%) and **13** (75%) were synthesized *via* interaction of diol **7** with PPh_2Cl and $(C_6F_5)_2PCl$, respectively, in the presence of equimolar amounts of pyridine in a solution of anhydrous THF. The formation of substituted tetrahydrofuran **10** ($\approx$ 12%) along with the target products was observed in both cases.

To obtain monophosphine **15** (route B, Scheme 3), transformation of acetonide **4** to the corresponding monotosylate **14** (70%) followed by interaction of the latter with

† Academician Kirill I. Zamaraev, an outstanding specialist in catalysis and chemical kinetics, died on the 26th June 1996.



Scheme 1

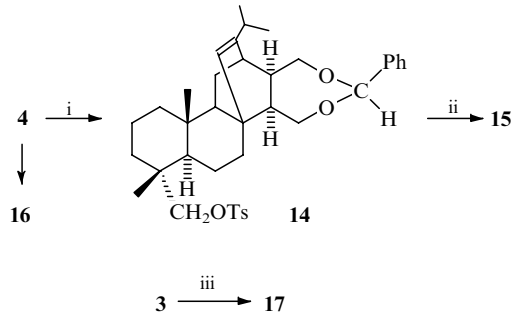


Scheme 2 *Reagents and conditions*: i, $LiAlH_4$, Et_2O, 35 °C, 48 h; ii, $(MeO)_2CHPh$, *p*-TsOH, CH_2Cl_2, 20 °C, 10 h; iii, BnCl, KOH, DMSO, 25 °C, 24 h; iv, MEMCl, Pr^i_2EtN, 25 °C, 12 h; v, *p*-TsOH, MeOH, 25 °C, 2.5 h; vi, TsCl, Py, −5 °C, 48 h or MsCl, Et_3N, −5 °C, 3 h; vii, PPh_2Na, 1,4-dioxane–THF, 25 °C, 3 h; viii, PPh_2Cl, Py, THF, 25 °C, 12 h; ix, $(C_6F_5)_2PCl$, Py, THF, 25 °C, 12 h.

PPh_2Na under the conditions reported in ref. 14 were needed. The yield of phosphine **14** was not higher than 32%. Chiral ligand **16** (65%) was prepared *via* treatment of **4** with PPh_2Cl in a solution of anhydrous pyridine.

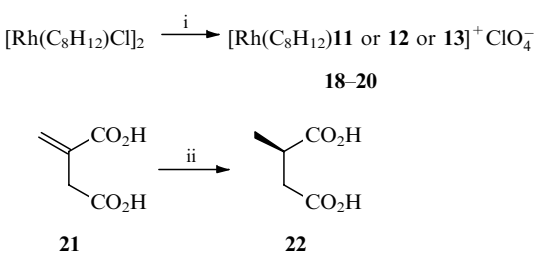
Phosphinite **17** originating from a family of tridentate organophosphorus ligands (route C) was synthesized from triol **3** using a conventional procedure (see Scheme 3). The structures of all the final and intermediate compounds are supported by spectral and elemental analytical data.‡

Chiral complexes **18** to **20** were obtained through the interaction of bidentate ligands **11** to **13** with di-μ-chlorobis(cyclooctadiene)dirhodium and $NaClO_4$ in acetone solution. We studied their catalytic activities and enantioselectivities with hydrogenation and isomerization of some prochiral substrates as examples. Hydrogenation of itaconic acid **21** in the presence of Et_3N in a solution of THF catalysed by $[Rh(C_8H_{12})\,\mathbf{11}]^+ClO_4^-$ **18** (0.1 mmol of catalyst; 0.6 mmol



Scheme 3 *Reagents and conditions*: i, TsCl, Py, 20 °C, −5 °C, 24 h; ii, PPh_2Na, 1,4-dioxane–THF, 25 °C; iii, PPh_2Cl, Py, 20 °C, 3 h.

of Et_3N; 10 mmol of olefinic acid) produced (*R*)-methylsuccinic acid **22**, $[\alpha]_D^{22}$ +1.27° (*c* 0.4, EtOH), e.e. 7.5%, in 85% yield.



Scheme 4 *Reagents and conditions*: i, $NaClO_4$, **11** or **12** or **13**, Me_2CO, 20 °C, 0.5 h; ii, $[Rh(C_8H_{12})\,\mathbf{11}]^+ClO_4^-$, Et_3N, 1 atm. of H_2, THF, 25 °C, 1.5 h.

A detailed discussion of the results of enantioselective transformations involving the new Rh^I-based catalysts will follow.

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‡ *Spectral data for* **11**: mp 102–104 °C (MeOH), $[\alpha]_D^{20}$ −20.3° (*c* 0.7, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 15.61 (CH_3), 17.28 (C-6), 18.20 (CH_3CH), 19.44 (C-9), 20.30 (CH_3CH), 21.45 (CH_3), 29.87 (C-4), 32.61 (C-10), 33.16 (C-3), 35.80 (C-5), 36.42 (C-7), 36.89 (C-10a), 37.32 (C-4a), 38.34 (C-8), 38.50 (C-5a), 41.12 (C-13), 42.43 (C-14), 46.12 (C-8a), 48.00 [$HC(CH_3)_2$], 48.36 (C-2), 51.19 (C-1), 73.18 (CH_2OBn), 79.82 (OCH_2Ph), 124.63 (C-11), 148.12 (C-12), 127.21, 127.06, 128.21, 128.28, 128.37, 128.42, 128.56, 130.33, 130.50, 130.62, 130.89, 131.13, 131.34, 131.54, 131.66, 131.79, 132.01, 132.14, 133.28, 133.86, 135.07, 136.37 [$CH_2C_6H_5$, $2P(C_6H_5)_2$].

13: $[\alpha]_D^{25}$ −3.8° (*c* 0.35, $CHCl_3$); ^{19}F NMR (CCl_4) δ 2.68 [m, 8F, $2P(C_6F_5)_2$], 17.17 [m, 4F, $2P(C_6F_5)_2$], 32.16 [m, 8F, $2P(C_6F_5)_2$]; ^1H NMR ($CDCl_3$) δ 0.54 (s, 3H, CH_3), 0.72 (c, 3H, CH_3), 0.96 (d, 3H, CH_3CH, *J* 6.8 Hz), 0.99 (d, 3H, CH_3CH, *J* 6.8 Hz); 2.18 [m, 1H, $CH(CH_3)_2$], 2.88 (d, 1H, CH_2OBn, *J* 8.9 Hz), 3.19 (d, 1H, CH_2OBn, *J* 8.9 Hz), 3.42–3.75 (m, 2H, 13-Ha, 14-Ha), 4.36–4.56 (m, 2H, OCH_2Ph, 2H, 13-Hb, 14-Hb), 5.32 (s, 1H, 11-H), 7.48 (m, 5H, Ph).

16: $[\alpha]_D^{19}$ +20.8° (*c* 0.65, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.57 (s, 3H, CH_3), 0.79 (s, 3H, CH_3), 1.03 (d, 3H, CH_3CH, *J* 7 Hz), 1.05 (d, 3H, CH_3CH, *J* 7 Hz), 2.43 [m, 1H, $CH(CH_3)_2$], 3.39 (d, 1H, CH_2OPPh_2, *J* 9.0 Hz), 3.57 (dd, 1H, 13-Ha, J_{hem} 12.0, $J_{13a,2}$ 4.9 Hz), 3.70 (dd, 1H, 14-Ha, J_{hem} 12.5, $J_{14a,1}$ 4.7 Hz), 3.94 (dd, 1H, 13-Hb, J_{hem} 12.0, $J_{13b,2}$ 4.9 Hz), 4.09 (d, 1H, CH_2OBn, *J* 8.9 Hz), 4.22 (dd, 1H, 14-Hb, J_{hem} 12.0 Hz, $J_{14b,1}$ 4.9 Hz), 5.19 (s, 1H, CHPh), 5.38 (s, 1H, 11-H), 7.47 and 7.79 (m, 15H, PPh_2, CHPh).

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