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Synthesis and resolution of the planar chirality of ester-functionalised phospharuthenocenes

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Menthyl phospholide ester anions provide an operationally simple and high yielding entry to the first planar chiral enantiopure phospharuthenocene derivatives.

Recent years have seen a renaissance in the chemistry of phosphametallocenes,[1] largely as a result of Ganter,[2] Fu[3–5] and Hayashi's[6] elegant work in preparing and evaluating enantiopure phosphaferrocenes as ligands for asymmetric catalysis. Whilst little explored, this class has already shown its promise through the exceptional *ee*s observed in Cu-catalysed enantioselective [3 + 2] cycloadditions,[3] Rh-based asymmetric Kinugasa[4] and allylic alcohol isomerisations[5] and Pd-catalysed allylic alkylations.[6] Arguably, the principal hurdles to the routine use of such compounds as chiral building blocks are now simple practical problems concerning *a*) the large scale resolution planar chiral Cp*Fe derivatives such as **1a**[3,7] which, to date, have often provided the best excesses and *b*) the well-documented chemical sensitivity[8] of some phosphaferrocenes.

Our studies of phosphametallocenes built around late transition metals (**2** M = Ru,[9] Co,[10] Co$^+$,[11] Rh$^+$,[11] Ir$^+$,[11] Ni,[12] Ni^{+}[12]) suggest that the substitution of ruthenium for iron will generate novel complexes showing improved stability.[13] However, synthesising complexes of type **2** has always involved the use of highly encumbered phospholyl ligands which promote the formation of the desired η^5-complexes by exerting steric pressure upon the otherwise kinetically- favoured dimers (*e.g.* **3**),[13,14] a method which implies extended synthetic pathways[13] and difficulties in the resolution of chirality.[15] An untried but, in principle, generally applicable, higher yielding and less synthetically arduous approach might involve perturbing the *electronics* of the phospholide anion to reduce the charge and/or HOMO localisation at P, thus favouring the formation of the η^5-phosphametallocene. 2-Ester substituted phospholide anions are easily accessible[16] and provide an attractive class for exploring this hypothesis; in addition to any electronic modification, the ester group also provides a convenient basis for the elaboration of the phosphametallocene product.[17]

Initial non-optimised studies using the simplest methoxycarbonyl substituted phospholides were encouraging; reaction of **4**[16] with $[Cp^*RuCl]_4$ in THF gave, after chromatography on alumina, acceptable isolated yields of the pale yellow, air-stable phospharuthenocene **5**, a late intermediate in the synthesis of the racemic phospharuthenocenephosphine **1b**[13] (Scheme 1). Under analogous conditions, the similarly encumbered phospholide **6b** gives > 95% of the unwanted dimer **3**.[13]

This proof of principle experiment spurred the development of a 'second generation' approach involving the additional use of the ester function to resolve the chirality of the phosphametallocene.[18] The cheap commercial availability of both hands of menthylchloroformate, straightforward separation of diastereomeric cyclopentadienyl-[19] and pyrrolyl-[20] derived metallocene menthyl esters, and likely increase in chemical yield when using a more hindered ester functionality,[13] made 2-(menthoxycarbonyl)phospholide anions a clear target. Two readily available phospholides **6a,b** were found to be easily transformed into the new colourless, solid menthoxycarbonylphospholides **8a,b** in excellent yields through a classical[13,16] [1,5] sigmatropic shift protocol linked to a KO*t*Bu induced deprotonation and subsequent precipitation from pentane (Scheme 2).†

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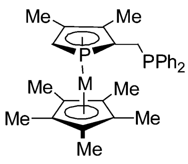
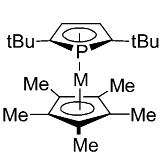
Complexation of $[Cp^*RuCl]_4$ to the menthyl-substituted phospholide anions **8a,b** gave pale yellow air-stable diastereomeric phospharuthenocene pairs in chemical yields of *ca* 90%. The diastereomers show the expected[21] configurational stability (with



1a M= Fe
b M= Ru



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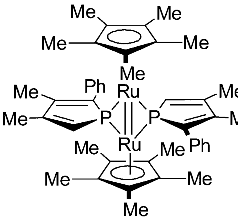

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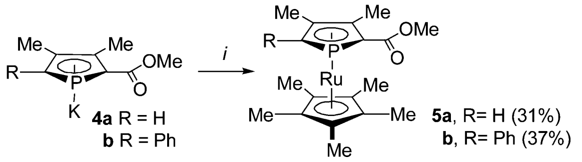
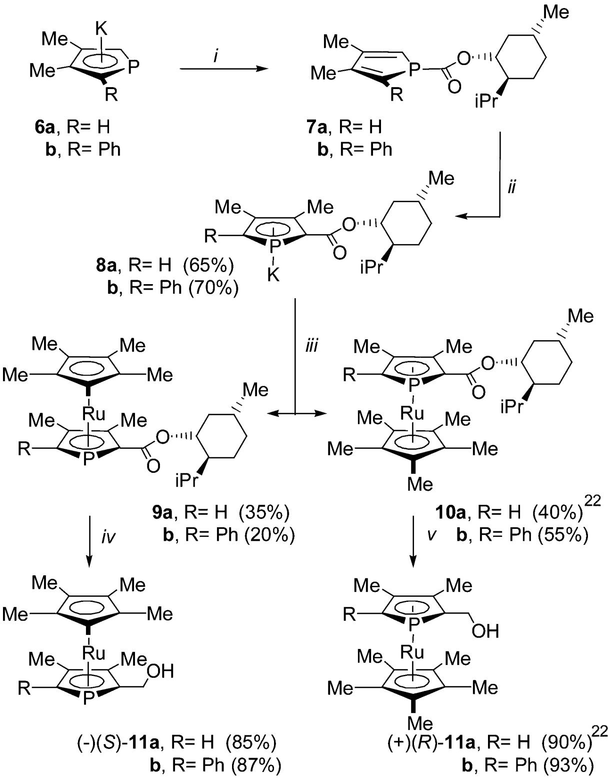


Scheme 1 *Reagents and conditions*: *i*; $[Cp^*RuCl]_4$ (0.25 eq.), THF, rt, 30 min.



Scheme 2 *Reagents and conditions*: *i*: (−)-MenOCOCl (1 eq.), THF, 0 °C, 5 min. *ii*: 65 °C, 3 h, then KO*t*-Bu (1 eq.) THF, 0 °C, 5 min. *iii*:$[Cp^*RuCl]_4$ (0.25 eq.), THF, 30 min. *iv*: $LiAlH_4$, (2eq) THF, rt, 4 h, *v*: $LiAlH_4$, (2eq) THF, 66 °C, 5 h. Isolated yields after crystallisation in parentheses.

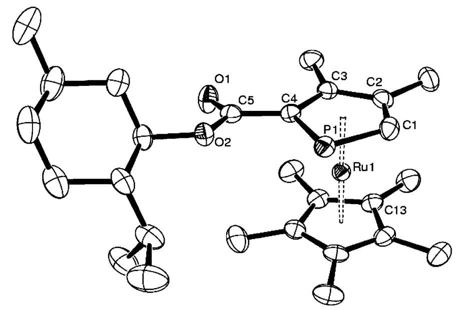


Fig. 1 Molecular structure of **9a**. Selected bond lengths (Å) Ru(1)–P(1), 2.4142(7); Ru(1)–C(1), 2.212(2); Ru(1)–C(2), 2.199(3); Ru(1)–C(3), 2.192(3); Ru(1)–C(4), 2.188(3); P(1)–C(1), 1.773(3); P(1)–C(4), 1.798(3); C(1)–C(2), 1.407(4); C(2)–C(3), 1.436(4); C(3)–C(4), 1.438(4); C(4)–C(5), 1.475(4).

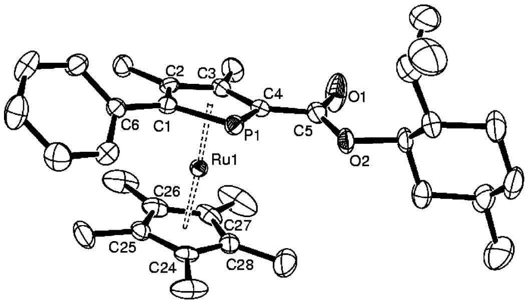


Fig. 2 Molecular structure of **10b**. Selected bond lengths (Å). Ru(1)–P(1), 2.399(1); Ru(1)–C(1), 2.218(3); Ru(1)–C(2), 2.207(3); Ru(1)–C(3), 2.187(3); Ru(1)–C(4), 2.181(3); P(1)–C(1), 1.787(3); P(1)–C(4), 1.784(3); C(1)–C(2), 1.439(4); C(1)–C(6), 1.484(3); C(2)–C(3), 1.434(3); C(3)–C(4), 1.434(4); C(4)–C(5), 1.478(4).

9b and **10b** undergoing no detectable decomposition or interconversion in toluene at 110 °C over 1 month) and were obtained in purities exceeding 99% through a single recrystallisation from MeOH after multigram separation by chromatography on alumina (neutral; hexane–dichloromethane 9:1).[22] Their absolute configurations were confirmed by X-ray crystallography‡ for **9a** and **10b** (Figs. 1 and 2). In each case, reduction with $LiAlH_4$ gave the desirable[13] enantiopure phospharuthenocenemethanol building blocks **11a,b** in near-quantitative yields.

The phospholide ester methodology described above provides a simple solution to problems of stability and accessibility of phosphametallocenes for enantioselection, and allows the preparation of only the second series of enantiopure planar chiral phosphametallocene sandwich complexes (after M = Fe). Additional preliminary results show that such carboxymenthyl-substituted phospholides may have a much more profound role to play in the preparation of enantiopure functionalised phosphametallocenes, with reactions of **8b** at $[MnBr(CO)_5]$ or [Cp*FeCl] centres again furnishing ring-functionalised phosphaferrocenes and phosphacymantrenes whose chirality can be resolved through simple crystallisation.[23] Elaboration of these complexes should facilitate access to resolved phosphametallocenes and considerably broaden their availability. A comparison of the behaviour of phosphaferrocene and phospharuthenocene ligands will appear in due course.

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Notes and references

† *Selected spectrocopic data:* **5a**: (THF, 298 K) ^{31}P NMR δ −36 ppm. **5b**: (THF, 298 K) ^{31}P NMR δ −26 ppm. **8a**: (THF, 298 K) ^{31}P NMR δ 102 ppm. **8b**: (THF, 298 K) ^{31}P NMR δ 107 ppm. **9a**: (Et_2O, 298 K) ^{31}P NMR δ −38.6 ppm. $[\alpha]^{25}_D = 45°$ (c = 1.0, DCM). **9b**: ($CDCl_3$, 298 K) ^{31}P NMR δ −28.6 ppm. $[\alpha]^{25}_D = -125°$ (c = 1.0, DCM). **10a**: (Et_2O, 298 K) ^{31}P NMR δ −36.2 ppm. **10b**: ($CDCl_3$, 298 K) ^{31}P NMR δ −25.4 ppm. $[\alpha]^{25}_D = 76.4°$ (c = 1.0, DCM).**11a** $[\alpha]^{25}_D = 6.4°$ (c = 0.5, THF). (+)**11b** ($CDCl_3$, 298 K) ^{31}P NMR δ −37.1 ppm. $[\alpha]^{25}_D = 212°$ (c = 1.0, DCM).

‡ *Crystal data:* **9a**: $C_{27}H_{41}O_2PRu$, M = 529.64, orthorhombic, space group $P2_12_12_1$, a = 9.1310(10), b = 21.5780(10), c = 13.2830(10) Å. U = 2617.1(4) Å^3. Z = 4, D_c = 1.344 g cm^{-3}, $F(000)$ = 1112. Graphite monochromated X-ray Mo–K_α radiation, λ = 0.71069 Å. μ = 0.680 cm^{-1}, T = 150.0(10) K. Of 7586 independent reflections collected on a Kappa CCD diffractometer from a pale yellow plate of dimensions 0.24 × 0.20 × 0.17 mm over $h = -12$ to 12, $k = -30$ to 22°, $l = -18$ to 18, 6650 having $I > 2\sigma(I)$ were refined on F^2 using direct methods in Shelxl. wR_2 = 0.0918, R_1 = 0.0379, GoF = 1.042, Flack's parameter = −0.06(2). **10b**: $C_{33}H_{45}O_2PRu$, M = 605.73, orthorhombic, space group $P2_12_12_1$, a = 10.085(5), b = 11.771(5), c = 26.420(5) Å. U = 3136(2) Å^3. Z = 4, D_c = 1.283 g cm^{-3}, $F(000)$ = 1272. Graphite monochromated Mo–K_α radiation, λ = 0.71069 Å. μ = 0.577 cm^{-1}, T = 150.0(10) K. Of 9007 independent reflections from a pale yellow cube of 0.20 × 0.20 × 0.20 mm collected as above over $h = -14$ to 14; $k = -16$ to 16; $l = -37$ to 37°, 7400 having $I > 2\sigma(I)$ were refined on F^2 using direct methods in Shelxl. wR_2 = 0.0911, R_1 = 0.0399, GoF = 1.039, Flack's parameter = −0.02(2). CCDC 226405 & 226406. See http://www.rsc.org/suppdata/cc/b4/b401088d/ for crystallographic data in .cif or other electronic format.

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23 Details will be provided elsewhere. For a much longer synthesis of enantiopure phosphacymantrenes, see ref. 17.

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