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Kinetic resolution of P-chiral tertiary phosphines and chlorophosphines: a new approach to optically active phosphoryl and thiophosphoryl compounds[†]

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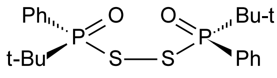
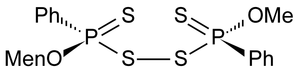
Abstract—Treatment of racemic P-stereogenic tertiary phosphines with enantiomerically pure bis-phosphoryl and bis-thiophosphoryl disulfides under kinetic resolution conditions (2:1 ratio) afforded enantiomerically enriched tertiary phosphine oxides or phosphine sulfides with ee values up to 39%. In a similar way from racemic *tert*-butylphenylchlorophosphine, optically active *tert*-butylphenylphosphinoyl chloride with 50% ee was obtained. The same reaction performed under dynamic kinetic resolution conditions (1:1 ratio of reagents) in the presence of chloride ions gave phosphinoyl chloride with 70% ee. © 2001 Elsevier Science Ltd. All rights reserved.

Asymmetric synthesis mediated by transition metal complexes bearing optically active phosphine ligands is the field which has grown enormously in the last three decades.[1] The first important landmark was the preparation of the soluble Wilkinson phosphine–rhodium complexes containing enantiomerically pure, P-stereogenic tertiary phosphines.[2] Although it was later discovered that chiral phosphine ligands with carbon-based central or axial chirality are more easily prepared and their transition metal complexes are more effective in asymmetric catalysis,[3] the search for efficient and general methods for the synthesis of chiral, non-racemic phosphines and related compounds such as phosphine oxides and phosphine sulfides continues to be of prime importance.[4] As part of our continuing interest in chiral phosphine ligands with applications in catalysis,[5] we decided to explore a new procedure for preparing optically active tertiary phosphines. Our attention was focused on kinetic resolution of P-chiral phosphines. In this context, it is interesting to point out that the first and only example of the kinetic resolution of a phosphine is due to Wittig and co-workers who were able to partially resolve *p*-biphenylyl-1-naphthylphenyl-phosphine by means of its quaternization with half-molar amounts of paraformaldehyde and (+)-camphor-10-sulfonic acid.[6] Here we describe the results of our preliminary study on kinetic resolution of the title racemic compounds which takes place when they are treated with enantiomerically pure bis(phosphinoyl) or bis(phosphinothioyl) disulfides. The choice to study this reaction under kinetic resolution conditions was mainly dictated by the fact that mechanistic features (intermediates, steps, rearrangements) of the desulfurization and/or deoxygenation of achiral bis(phosphinoyl) disulfides by achiral three-coordinate phosphorus compounds are well-known as a result of recent careful investigations by Krawczyk et al.[7]

In the first place, the reactivity of two enantiomerically pure disulfides **2** and **3** was investigated. The enantiomerically pure (+)-(*R*,*R*)-bis(*tert*-butylphenyl-phosphinoyl) disulfide **2** we prepared by oxidation of the (−)-α-phenylethylammonium salt of (+)-(*R*)-*tert*-butylphenylphosphinothioic acid by iodine under two-phase conditions ($CHCl_3/H_2O$). Its stereostructure was confirmed by a single-crystal X-ray analysis (see Fig. 1).[8] Disulfide **3** was prepared according to a previously described procedure.[9] Racemic phosphines **1a**–**c** were obtained via known general methods starting from phenyldichlorophosphine.[4]



(+)-(*R*,*R*)-**2**



(+)-(S_P,S_P)-**3**

Keywords: kinetic resolution; tertiary phosphines; chlorophosphines; optically active phosphoryl (thiophosphoryl) compounds.

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[†] Dedicated to Professor Leopold Horner, a pioneer of phosphorus stereochemistry, on the occasion of his 90th birthday.

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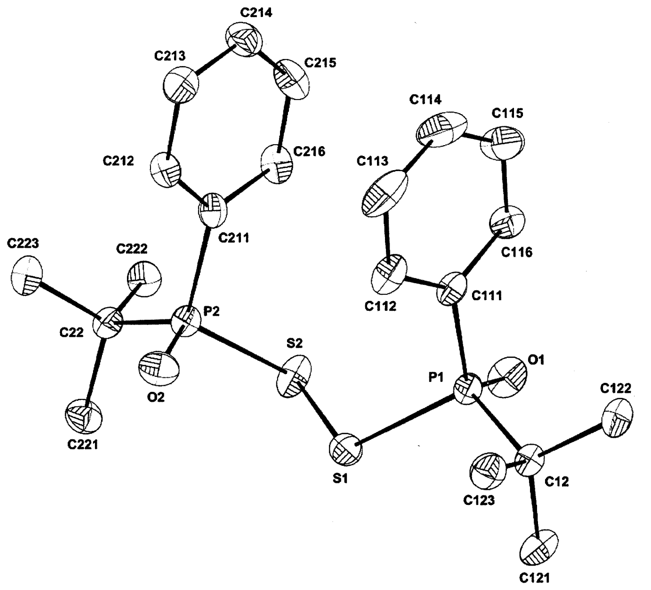


Figure 1. The molecular view of the disulfide (+)-(*R*,*R*)-**2** with atom numbering scheme.

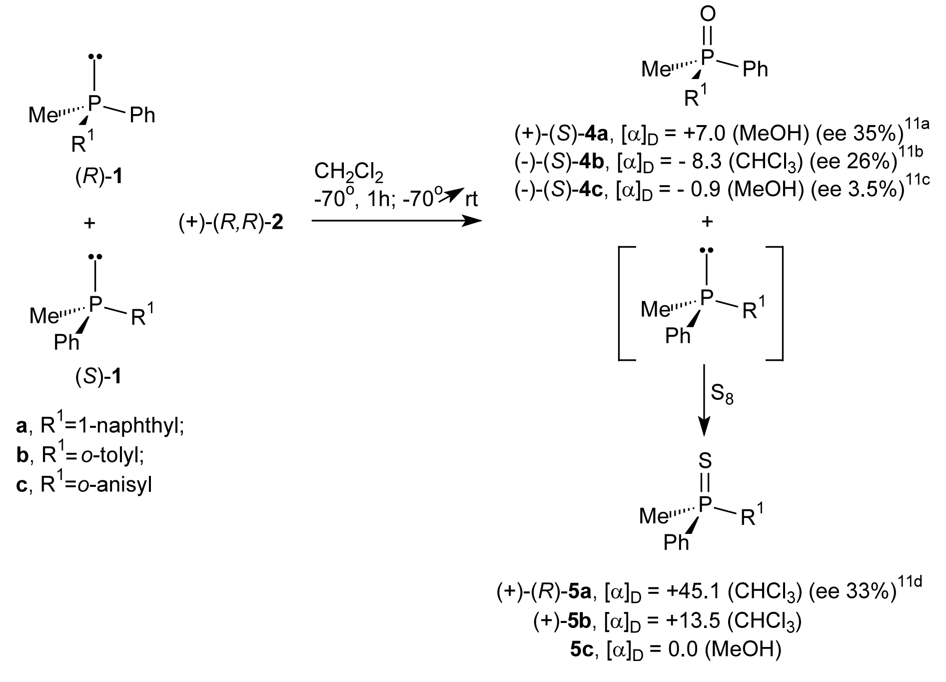
As expected, treatment of the racemic phosphines **1a**–**c** with half-molar amounts of the disulfide (+)-(*R*,*R*)-**2** at low temperature afforded an equimolar mixture of optically active phosphine oxides **4a**–**c** and unreacted starting phosphines.[10] Addition of elemental sulfur to this mixture resulted in the conversion of the latter into the corresponding optically active phosphine sulfides **5a**–**c**. Both reaction products, after typical work-up (washing with 5% aq. solution of $NaHCO_3$ and H_2O) were easily isolated by column chromatography. The results of this set of experiments are summarized in Scheme 1.

In all the investigated cases, the phosphines **1a**–**c** with the *R*-configuration at phosphorus were found to react faster with the disulfide (+)-(*R*,*R*)-**2**. Their conversion into the phosphine oxides (−)-(*S*)-**4** may be easily explained by the sequence of events shown in Scheme 2. Nucleophilic attack of (*R*)-**1** at sulfur in (*R*,*R*)-**2** leads to the first phosphonium intermediate **6** that undergoes intramolecular thiolo-thiono isomerization to **7** with retention of configuration at phosphorus. Decomposition of the latter results in the formation of (−)-(*S*)-**4** and dithioanhydride.[10]

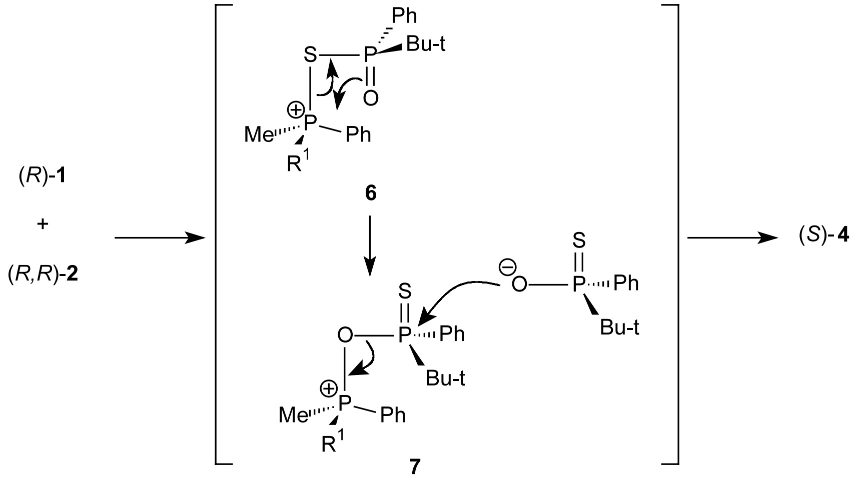
When racemic *tert*-butylmethylphenylphosphine **1d** was treated with half molar amounts of the disulfide (+)-(*R*,*R*)-**2**, the corresponding phosphine oxide (−)-(*S*)-**4d** with 39% of enantiomeric purity was obtained. However, the phosphine sulfide (+)-(*R*)-**5d** exhibited lower enantiomeric purity (Scheme 3).

Similarly, partial resolution was observed in the reaction of racemic phosphines **1** with enantiopure (+)-(S_P,S_P)-bis[menthoxy-phenyl(phosphinothioyl)] disulfide **3**[11] used in a 2:1 ratio. In this case, the reaction took the desulfurization course and gave optically active phosphine sulfides **5**. The remaining phosphines **1** were oxidized to the corresponding phosphine oxides **4**. The absolute configurations, optical rotations and ee values of both separated products are shown in Scheme 4.

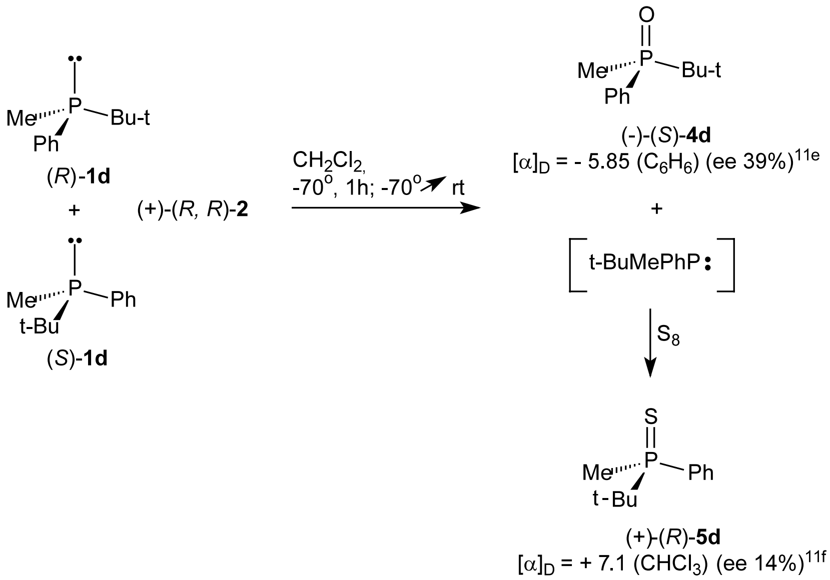
A very important extension of our approach to optically active phosphorus compounds involves kinetic resolution of P-chiral chlorophosphines. Thus, treatment of two moles of *tert*-butylphenylchlorophosphine **8** with one mole of the disulfide (+)-(*R*,*R*)-**2** afforded (+)-(*S*)-*tert*-butylphenylphosphinoyl chloride **9** and (−)-(*R*)-*tert*-butylphenylphosphinothioyl chloride **10**, which



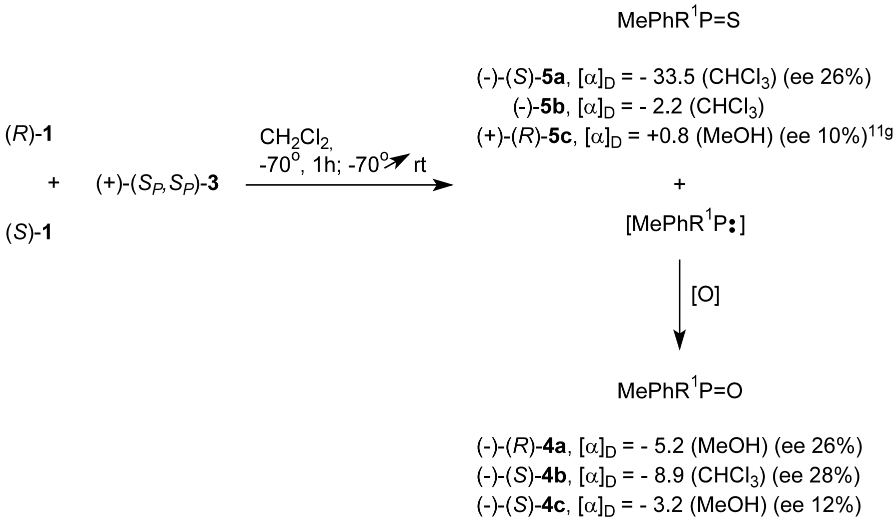
Scheme 1.



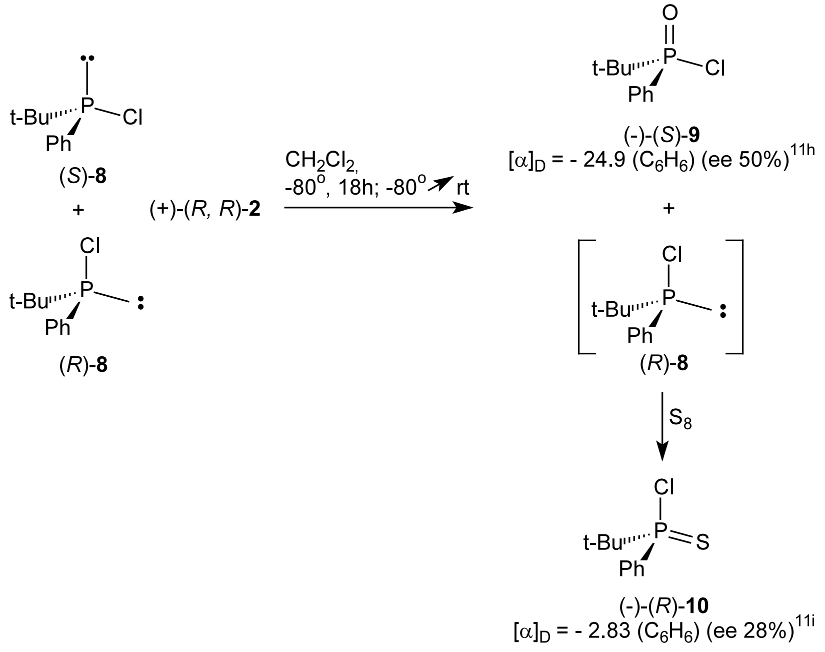
Scheme 2.



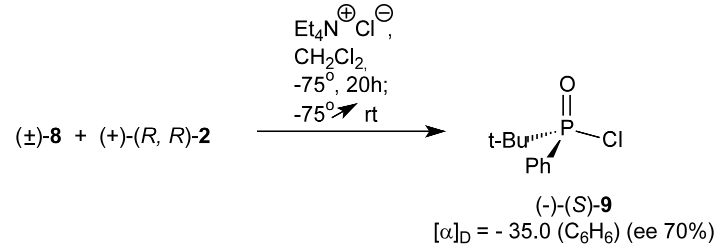
Scheme 3.



Scheme 4.



Scheme 5.



was obtained by sulfurization of the unreacted chlorophosphine **8** (Scheme 5).

In contrast to much higher enantiomeric purity (50%) of the phosphinoyl chloride **9**, the chloride **10** is formed with a lower ee value (28%). This is most probably due to partial racemization of the unreacted chlorophosphine **8** caused by trace amounts of the chloride anion present in the reaction mixture.

This observation and assumption that the chloride–chloride exchange in chlorophosphine **8** is faster than its reaction with disulfide (+)-**2** prompted us to perform this reaction under dynamic kinetic resolution conditions, i.e. in the presence of chloride ions using equimolar amounts of (±)-**8** and (+)-**2**. It was gratifying to find that phosphinoyl chloride **9** was obtained with 70% ee.

In summary, we have developed a novel, facile method for the synthesis of enantiomerically enriched P-stereogenic phosphoryl and thiophosphoryl compounds based on the kinetic resolution of P-chiral three-coordinate phosphorus compounds. The kinetic resolution products obtained may be easily converted into the corresponding P^{III}-compounds by known stereoselective methods.[12]

References

1. (a) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley & Sons: New York, 1994; (b) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, 1999; (c) Ojima, I., Ed. *Catalytic Asymmetric Synthesis*, 2nd ed.; VCH Publishers: Weinheim, 2000.
2. (a) Horner, L.; Siegel, H.; Büthe, H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 942; (b) Knowles, W. S.; Sabacky, M. J. *J. Chem. Soc., Chem. Commun.* **1968**, 1445–1446.
3. Brunner, H. *Top. Stereochem.* **1988**, *18*, 129–247.
4. (a) Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375–1410; (b) Kolodiazhnyi, O. I. *Tetrahedron: Asymmetry* **1998**, *9*, 1279–1332.
5. (a) Tissot, O.; Gouygou, M.; Dallemer, F.; Daran, J.-C.; Balavoine, G. G. A. *Angew. Chem., Int. Ed. Engl.* **2001**, 1076–1078; (b) Tissot, O.; Gouygou, M.; Dallemer, F.; Daran, J.-C.; Balavoine, G. G. A. *E. J. Inorg. Chem.* **2001**, 2385–2389.
6. Wittig, G.; Cristau, H.-J.; Braun, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 700–701.
7. Krawczyk, E.; Skowrońska, A.; Michalski, J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 89–99.
8. Selected physico-chemical and X-ray data for (+)-(*R*,*R*)-**2**: mp 152–154°C; $[\alpha]_D=+183.8$ (0.77, C_6H_6); ^{31}P NMR ($CDCl_3$): 68.4 ppm; ^1H NMR ($CDCl_3$): 1.14 (d, 18H,

$J_{P-H}=17.3$ Hz, *t*-Bu) 7.14–7.64 (m, 10H, Ph). Orthorhombic non-centrosymmetric, $P2_1,2_1,2_1$; $M=426.51$; $dx=1.316$ g cm^{-3}; $\mu=4.081$ cm^{-1}; $a=7.4824(6)$, $b=10.2879(8)$, $c=27.9659(18)$ Å; $V=2152.8(3)$ Å^3; $Z=4$; $R=0.0203$; $wR=0.0227$, Flack's parameter [Bernardinelli, G.; Flack, H. D. *Acta Crystallogr*., *Sect A* **1985**, *41*, 500–511] = –0.04(5). Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 163287. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Read, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail:deposit@ccdc.cam.ac.uk].

9. Łopusiński, A.; Łuczak, L.; Michalski, J.; Kozioł, A. E.; Gdaniec, M. *J. Chem. Soc*., *Chem. Commun*. **1991**, 889–890.
10. The ^{31}P NMR spectra of the reaction mixture also revealed the presence of the dithiopyro-phosphinate product at $\delta_P=94.0$ ppm which upon work-up was hydrolyzed to the corresponding thiophosphinic acid.
11. The enantiomeric purity was calculated based on the following literature data: (a) for **4a**: $[\alpha]_D=-19.8$ (MeOH). Luckenbach, R. *Phosphorus* **1972**, *1*, 223–228; (b) for **4b**: $[\alpha]_D=+31.8$ (CHCl$_3$), Chodkiewicz, W.; Jore, D.; Pierrat, A.; Wodzki, W. *J. Organomet. Chem*. **1979**, *174*, C21–C23; (c) for **4c**: $[\alpha]_D=+29.5$ (MeOH), Vineyard, B. D.; Knowles, V. S.; Sabacky, M. J.; Bachmann, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc*. **1977**, *99*, 5946–5952; (d) for **5a**: $[\alpha]_D=+129$ (CHCl$_3$), Kawashima, T.; Kojima, S.; Inamoto, N. *Chem. Lett*. **1989**, 849–852; (e) for **4d**: $[\alpha]_D=-10.2$ (C_6H_6) (ee 68%), Michalski, J.; Skrzypczynski, Z. *J. Organomet. Chem*. **1975**, *97*, C31–C32; (f) for **5d**: $[\alpha]_D=+52.1$ (CHCl$_3$), Kawashima, T.; Kojima, S.; Inamoto, N. *Chem. Lett*. **1989**, 849–852; (g) for **5c**: $[\alpha]_D=-7.9$ (MeOH), Corey, E. J.; Chen, Z.; Tanoury, G. J. *J. Am. Chem. Soc*. **1993**, *115*, 11000–11001; (h) for **9**: $[\alpha]_D=+49.8$ (C_6H_6), Luckenbach, R.; Bechtolsheimer, H.-H. *Zeit. Naturforsch. B* **1977**, *32B*, 584–587; (i) for **10**: $[\alpha]_D=+8.0$ (C_6H_6) (ee 76.5%), Omelańczuk, J.; Mikołajczyk, M. *J. Chem. Soc*., *Chem. Commun*. **1994**, 2223–2224.

    In the case of the phosphoryl compounds **4a**–**d** and **9**, the enantiomeric excess values were also determined by ^{1}H NMR method using (–)-(*S*)-*t*-butylphenylphosphinothioic acid as chiral solvating agent. The ee values obtained in this way were in good agreement (±1.5%) with the calculated ones.
12. For stereoselective reduction of phosphine oxides, see: Imamoto, T.; Kihuchi, S.; Miura, T.; Wada, Y. *Org. Lett*. **2001**, *3*, 87–90 and references cited therein; for stereoselective desulfurization of thiophosphoryl compounds, see: Omelańczuk, J.; Mikołajczyk, M. *J. Am. Chem. Soc*. **1979**, *101*, 7292–7295; *Tetrahedron Lett*. **1984**, *25*, 2493–2496.