Tetrahedron Letters, Vol.32, No.28, pp 3375-3376, 1991 Printed in Great Britain

STEREOSPECIFIC REDUCTION OF DIASTEREOMERICALLY PURE MENTHYL PHOSPHINATES: A NEW ROUTE TO OPTICALLY ACTIVE PHOSPHINE OXIDES

Yasuhiro Koide, Atsushi Sakamoto, and Tsuneo Imamoto^{*} Department of Chemistry, Faculty of Science, Chiba University, Yayoicho, Chiba 260, Japan

Abstract: Diastereomerically pure menthyl phosphinates are stereospecifically reduced by lithium 4,4'-di-*tert*butylbiphenylide. Subsequent treatment with alkyl halides affords phosphine oxides with high optical purity.

Diastereomerically pure or enriched menthyl phosphinates are well known to react with Grignard reagents or organolithium reagents with inversion of configuration at phosphorus to afford optically active phosphine oxides.¹ On the other hand, conversion of these compounds to phosphine oxides with retention of configuration has not yet been reported, despite its anticipated synthetic utility. We envisioned that stereospecific reductive removal of the menthyl group, followed by treatment with alkyl halides, might enable this new transformation.

Our idea behind these experiments is based on the fact that menthyloxyphosphine-boranes are stereospecifically reduced by one-electron reductants.² First, the conversion of (R_P) -menthyl methylphenylphosphinate (1) to (R)-benzylmethylphenylphosphine oxide was examined under various conditions. The results are summarized in Table 1.

	phosphile Oxide		·····		
Entry	Reducing agent	Molar ratio	Reduction conditions ^a	Yield ^b	Optical yield ^c
		Reagent:Substrate		%	%
1	Li	3	rt, 1 day	48	72
2	Li ⁺ [C ₁₀ H ₁₀] ⁺	4	-78 °C, 2h	trace	-
3	>>	4	0 °C, 5 min	36	75
4	LB^{d}	4	-78 °C, 40 min	trace	-
5	39	4	0 °C, 5 min	55	75
6	LDBBe	4	-78°C, 20 min	67	95
_ 7	Li-NH ₃	10	-78 °C, 5 h	trace	-

Table 1. Conversion of (R_p) -Menthyl Methylphenylphosphinate (1) to (R)-Benzylmethylphenyl-

^a After completion of the reduction, a large excess of benzyl bromide was added. ^b Isolated yield. ^c Optical yields were determined from the following literature value: (*R*)-PhMeP(O)CH₂Ph, $[\alpha]^{25}_D$ +51° (*c* 1.0, MeOH) (O. Korpiun, R. A. Lewis, J. Chickos, and K. Mislow, *J. Am. Chem. Soc.*, **90**, 4842 (1968)). ^d LB = lithium biphenylide. ^e LDBB = lithium 4.4'-di-*tert*-butylbiphenylide.

Lithium 4,4-di-*tert*-butylbiphenylide (LDBB),³ which exhibits the highest reducing power among the reductants examined, gave the desired product in good yield with excellent optical purity (Entry 6).^{4,5} In the other cases, the reductions were very sluggish at -78 °C, and at elevated temperatures they resulted in significantly lower optical purity.

On the basis of these results, we next tried to synthesize optically active (S,S)- and (R,R)-1,2ethanediylbis(methylphenylphosphine oxide). Compound 1 and its diastereomer 2 were deprotonated with secbutyllithium and were oxidatively dimerized by CuCl₂ to afford the corresponding C₂-symmetric bisphosphinates (3⁶ and 4⁷). These compounds were allowed to react with LDBB at 0 °C for 40 min and then treated with a large excess of iodomethane to give 5 and 6 in 54% and 29% yield with 98% and 95% optical purity, respectively.⁸



References and Notes

- For representative reviews, see: (a) D. Valentine, Jr., In Asymmetric Synthesis, J. D. Morrison and J. W. Scott, Eds, Academic Press, New York, Vol. 4, Chapter 3, pp 263-312 (1984). (b) G. Zon and K. Mislow, Fortsch. Chem. Forsch., 19, 61 (1971).
- 2. T. Oshiki, T. Hikosaka, and T. Imamoto, Tetrahedron Lett., preceding paper.
- 3. P. K. Freeman and L. L. Hutchinson, J. Org. Chem., 45, 1924 (1980).
- 4. The following optically active phosphine oxides were also synthesized in 60-70% yield by treatment of the reduction mixture with hexyl bromide, *p*-methoxybenzyl bromide, and benzyl chloromethyl ether, respectively: (*R*)-Hexylmethylphenylphosphine oxide, mp 53-55 °C, [α]²⁷_D +16.3° (*c* 1.0, MeOH); (*R*)-(4-methoxybenzyl)methylphenylphosphine oxide, mp 152-153 °C, [α]²⁸_D +38.4° (*c* 1.0, MeOH); (*S*)-(benzyloxymethyl)methylphenylphosphine oxide, mp 56-58 °C, [α]²⁹_D -9.4° (*c* 1.0, MeOH).
- In a similar manner, another diastereomer, (Sp)-menthyl methylphenylphosphinate (2) was converted to (Sbenzylmethylphenylphosphine oxide with 85% optical purity in 73% yield.
- 6. Compound 3: Mp 192-193 °C; $[\alpha]^{26}_{D}$ -26.7 ° (*c* 1.0, MeOH); IR (KBr) 2900, 1440, 1230, 980, 740 cm⁻¹; ¹H NMR (CDCl₃) δ 0.7-1.0 (m, 6 H), 0.71 (d, *J* = 6.6 Hz, 6 H), 0.84 (d, *J* = 6.9 Hz, 6 H), 0.94 (d, *J* = 7.2 Hz, 6 H), 1.3 (m, 2 H), 1.39 (t, *J* = 3.0 Hz, 2 H), 1.6-1.9 (m, 6 H), 1.58 (d, *J* = 2.2 Hz, 2 H), 1.8 (m, 2 H), 2.2 (m, 4 H), 4.2 (m, 2 H), 7.40 (t, *J* = 7.4 Hz, 4 H), 7.49 (t, *J* = 7.4 Hz, 2 H), 7.7 (m, 4 H). Anal. Calcd for C₃₄H₅₂O₄P₂: C, 69.60; H, 8.93. Found: C, 69.49; H, 8.69.
- 7. Compound 4: Mp 132-133 °C; $[\alpha]^{30}_{D}$ -88.4 (*c* 1.0, MeOH); IR (KBr) 2930, 1430, 1220, 980 cm⁻¹; ¹H NMR (CDCl₃) δ 0.27 (d, *J* = 6.9 Hz, 6 H), 0.8-0.9 (m, 4 H), 0.80 (d, *J* = 7.2 Hz, 6 H), 0.90 (d, *J* = 6.3 Hz, 6 H), 1.20 (q, *J* = 6.1 Hz, 2 H), 1.3 (m, 2 H), 1.4 (bs, 2 H), 2.34 (d, *J* = 7.2 Hz, 2 H), 3.9 (m, 2 H), 7.41 (t, *J* = 7.3 Hz, 4 H), 7.49 (t, *J* = 7.7 Hz, 2 H), 7.7 (m, 4 H). Anal. Calcd for C₃₄H₅₂O₄P₂: C, 69.60; H, 8.93. Found: C, 69.65; H, 8.65.
- Optical yields were determined from the following literature value: (S,S)-1,2-ethanediylbis-(methylphenylphosphine oxide), [α]²⁵_D-59.6 ° (CHCl₃) (K. M. Pietrusiewicz, and M. Zablocka, *Tetrahedron Lett.*, 29, 1987 (1988).

(Received in Japan 11 January 1991)