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A NEW APPROACH TO THE SYNTHESIS OF (-)-2,3-O-ISOPROPYLIDENE-2,3-DIHYDROXY-1,4-BIS(DIPHENYLPHOSPHINO)BUTANE(DIOP)

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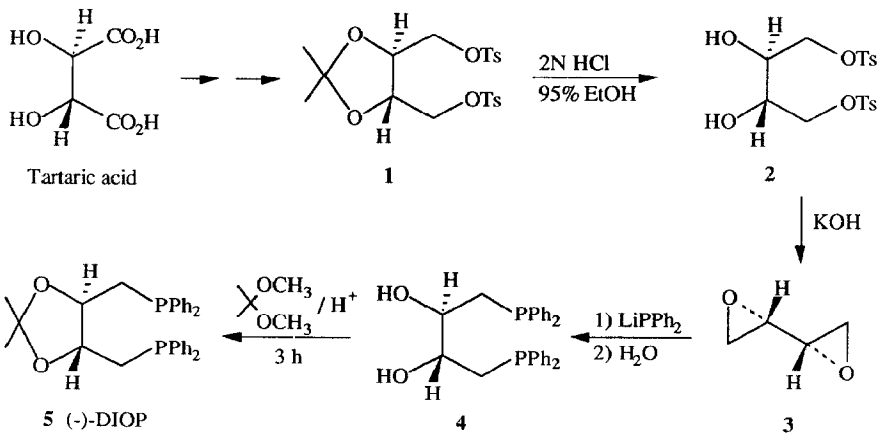
Abstract: (-)-2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (DIOP) has been prepared by reaction of (-)-1,2:3,4-diepoxybutane with lithium diphenylphosphide followed by ketalisation with 2,2-dimethoxypropane.

In the field of asymmetric hydrogenation spectacular progress was achieved by the utilisation of homogeneous catalysts based on transition metal complexes modified by a chiral diphosphine. At the same time, quite high ee's were achieved in asymmetric isomerisation, in hydroformylation, in epoxidation and in Grignard cross-coupling.[1] Chiral diphosphines became important in asymmetric synthesis after DIOP was first prepared by Kagan and Dang in 1971.[2] But, so far, chiral diphosphines have been synthesised by nucleophilic substitution of tosylates or halides or by Diels-Alder reactions, and, sometimes even obtained by tedious resolution. The nucleophilic substitution of halides or tosylates does not always give very high yields because of competitive reactions such as elimination. We now wish to describe the first example of DIOP synthesis by nucleophilic additions to a bisepoxide.[3]

Synthesis of (2S,3S)-1,4-di-O-tosyl-2,3-O-isopropylidenethreitol **1** was accomplished in four steps from (2R,3R)-tartaric acid via (2R,3R)-diethyl 2,3-O-isopropylidene tartrate and (2R,3R)-2,3-O-isopropylidene threitol (total yield 68%, m.p. 88.5-90°C). (2S,3S)-**1** was refluxed in 2N hydrogen chloride and 95% ethanol for 2 hrs. The crude product was recrystallised from chloroform to afford (2S,3S)-1,4-di-O-tosylthreitol **2** (yield 85%, mp 75°-73.5°C), $[\alpha]_D^{22}$ -5.4 (c, 5 in DMF) {(lit[5], mp 73°C $[\alpha]_D$ -5.7 (c, 5 in DMF)}. (2S,3S)-**2** and pulverised potassium hydroxide were refluxed in diethyl ether for 2.5 hrs, to produce (S,S)-1,2:3,4-diepoxybutane **3** (bp 68.0-70.0°C / 6KPa), $[\alpha]_D^{22}$ -24 (c, 4.5 in CCl_4) {lit[5] (bp 64°C / 6.66KPa), $[\alpha]_D^{22}$ +23 (c, 4.5 in CCl_4)}. (S,S)-**3** reacted on $LiPPh_2$ under a stream of nitrogen at 0°C for 5 hrs. and then deoxygenated water was added to give (2R,3R)-(-)-1,4-bis(diphenylphosphino)-2,3-butane-diol **4**. Without further purification, **4** was treated with 2,2-dimethoxypropane in the presence of catalytic amounts of



p-toluenesulfonic acid to yield (2R,3R)-(-)-2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino) butane **5** [(-)-DIOP]. The yield of **5** is 56% from **3**; (mp 87.5-89°C) $[\alpha]_D^{22}$ -12.5 (c, 4.19 in C_6H_6) {lit[2] (mp 88-89°C) $[\alpha]_D^{22}$ -12.3 (c, 4.57 in C_6H_6)}, IR : 3080, 3070, 2997, 2950, 2880, 1592, 1490, 1382, 1374 cm^{-1}. ^1H NMR ($CDCl_3$) : δ : 1.27 (s, 6H, $C(CH_3)_2$), 2.31 (d, 4H, CH_2), 3.83 (m, 2H, CH), 7.31 (m, 20H, ArH) ppm.

Dihydroxydiphosphine **4** has been prepared by Stille[6] by hydrolysis of DIOP **5**. We were also able to isolate **4** as a crystalline product $[\alpha]_D^{22}$ -34.2 (c, 0.76 in $CHCl_3$), mp = 99-100°C {lit[5] : mp = 75°C}. It is a good precursor for the synthesis of various modifications of DIOP by reaction with ketones or aldehydes. We are currently looking at the use of chiral diepoxides derived from sugars or other natural products as starting materials in the synthesis of other chiral diphosphines.

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References

1. J.W. ApSimon and T. Lee Collier, *Tetrahedron*, **42**, 5157 (1986).
2. a-T.P. Dang and H.B. Kagan, *J.C.S., Chem. Commun.*, 481 (1971);
   b-H.B. Kagan and T.P. Dang, *J. Am. Chem. Soc.*, **94**, 6429 (1972).
3. Epoxyalcohols available by Sharpless epoxidation have been recently transformed by $LiPPh_2$ into chiral hydroxyphosphines. H. Brunner and A. Sicheneder, *Angew. Chem. Int. Ed. Engl.*, **27(5)**, 718 (1988).
4. P.W. Feit, *J. Med. Chem.*, **1**, 14 (1964).
5. D. Seebach, H.-O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Dörr, N.P. Dupreez, V. Ehrig, W. Langer, C. Nusler, H.A. Oei and M. Schmidt, *Helv. Chim. Acta*, **60**, 301 (1977).
6. R. Descheneaux and J.K. Stille, *J. Org. Chem.*, **50**, 2299 (1985).