CROATICA CHEMICA ACTA CCACAA 53 (3) 445-447 (1980)

CCA-1223

YU ISSN 0011-1643 UDC 547.5 Preliminary Communication

A Chiral Phosphine (CRC-PHOS) Derived from (+)-Champhanic Acid. A New Ligand for Homogeneous Asymmetric Hydrogenation

G. Comisso, A. Sega, and V. Šunjić

CRC, Chemical Research Company, 33048 San Giovanni al Natisone (UD) Italy

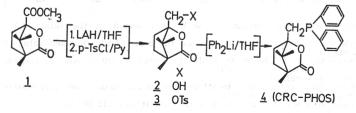
Received April 7, 1980

The lactone of 1S,3S-1-hydroxy-1-diphenylphosphinomethyl--2,2,3-tri-methyl-cyclopentan-3-carboxylic acid (4, CRC-PHOS) was prepared from (+)-camphanic acid methylester *1*, and its complex salt [Rh(CRC-PHOS)₂NBD] \cdot ClO₄ \cdot THF (5) was isolated. The latter exhibited rather a high rate, but low enantioselectivity in the first attempt at asymmetric hydrogenation.

Recently, Bosnich rationalized¹ the existing knowledge in the field of »tailoring« of chiral phosphine ligands in transition metal complexes as homogeneous catalysts for asymmetric hydrogenation. Among specific features required of chiral monophosphines to achieve high enantioselectivity, the presence of an additional coordination site, usually an oxygen atom, is the most important^{2,3}. The »lock and key« relation between catalytic complex and substrate still deserves general full attention in this field, however. Thus we have directed our attention to the preparation of a new chiral phosphine coded CRC-PHOS, and its catalytic activity and conformation in solution⁴.

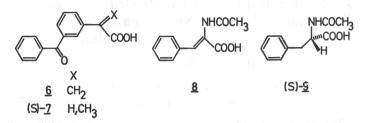
Camphanic acid methyl ester⁵ was reduced with complete site-selectivity to the alcohol 2 (88,9%, m.p. 179—180 °C, $[\alpha]_{\rm D}$ + 1.85 ° (c = 1.90 in CHCl₃) the lactonic group remaining unaffected. Tosylation in pyridine afforded 3 (93%, m.p. 116—117 °C, $[a]_{\rm D}$ + 16,3 (c = 2.12 in CHCl₃)), which was reacted with diphenylphosphine lithium in THF at —10 °C to afford 4 (53,4%, colourless oil after chromatography on silica with *n*-hexane/acetone (7:3) as eluant, $[\alpha]_{\rm D}$ —11.2° (c = 1.93 in CHCl₃).⁷

A cationic complex [Rh(CRC-PHOS)₂NBD] \cdot ClO₄ (5, NBD-norbornadiene) was prepared by the reaction of 4 with [(NBD)₂Rh] \cdot ClO₄ in THF for 1 h at room temperature. It precipitated from THF on slow addition of *n*-hexane as a fine orange-red powder which contained one mole of THF and exhibited amorphous structure, as ascertained by X-ray diffraction⁸.



The two lactone groups in the complex 5 are presumed to coordinate via the tetrahedral oxygen, since low coordination ability was found for the carbonyl oxygen in esters⁹, thus assuring a certain degree of conformational rigidity to the catalytic species.

Hydrogenations of the two model substrates 6 and 8 were routinely carried out in the presence of 5 and triethylamine¹⁰. The reactions proceeded to completion at ambient temperature. The rate of hydrogenation of 6 corresponded



approx. to that obtained with (-)-DIOP, (2,3-isopropylidene-2,3-dihydroxy-1,4 bis(diphenylphosphino)butane) while 8 was reduced at somewhat lower rate than described¹¹. Both products of hydrogenation, 7 and 9, possess S-configuration¹². Low enantiomeric excess was achieved in the first series of experiments, the data of Table I listing the first results obtained on variation of some reaction parameters.

Although these preliminary results may indicate low conformational rigidity of the phosphine ligand in 5, a search for the reaction conditions which could afford higher enantioselectivity in hydrogenation of some other substrates is in progress.

Substrate	Solvent	Substrate/5 ratio	Press. atm	Temp. °C	Timeh	e.e. (%) (config.)
6	EtOH abs.	86	95.5	20	23	13.6 (S)
6	EtOH abs./Bz(1:2)	86	70.0	20	20	14.9 (S)
6	EtOH abs.	86	84.0	20	55	3.1 (S)
6	EtOH abs.	86	14.0	50	3	12.6 (S)
6	EtOH abs.	86	70.0	2	21°	14.1 (S)
6	EtOH abs.	86 ^d	14.0	50	3	13.2 (S)
8	EtOH 99.8%	70	84.0	20	65	3.2 (S)
8	EtOH 99.8%	70	84.0	20	48	3.4 (S)

TABLE I

Asymmetric Hydrogenation of 6 and 8 with $[Rh(CRC-PHOS)_2NBD] \cdot ClO_4^{a}$

^a All hydrogenations were carried out with Et₃N added in the ratio 7.7/1 (mmol/mmole) related to 5. ь

Enantiomeric excess (e. e.) was calculated on the basis of the reported values for the optical pure compounds: S-7; [α]_D - 57.4 (N. Blažević, M. Žinić, T. Kovač, V. Šunjić and F. Kajfež, Acta Pharm. Jugoslav. 25 (1975) 155);

S-9; $[\alpha]_D + 46.0$ (ref. 1) ^o Chemical conversion was ca. 80%. In all other runs conversion was quantitative according to TLC, isolated yields were over 90%. ^d The total conc. of 6 was 1.12 10⁻² M, in other runs it was 1.12 10⁻¹ M.

CHIRAL PHOSPHINE

REFERENCES AND NOTES

- 1. M. D. Fryzuk and B. Bosnich, J. Amer. Chem. Soc. 99 (1977) 6262. 2. W. S. Knowles, M. J. Sabacky, and B. D. Vineyard, Chem. Commun.
- 1972, 10.
- 3. W. S. Knowles, M. J. Sabacky, B. D. Vineyard, and D. J. Weinkauff, J. Amer. Chem. Soc. 97 (1975) 2567.
- 4. LIS-NMR measurements and computer assisted data evaluation were performed for CRC-PHOS and some related model compounds in order to determine conformation of the lanthanide complexes in solution — manuscript in preparation.
- 5. Prepared from (+)-camphanic acid, lit.⁶ mp. 108–109 °C. $[\alpha]_D$ -22.8 °C. (c = 3.25 in CHCl₃). (+)-Camphanic acid (now available commercially from Fluka) is a well established chiral resolving agent, see e.g. H. Gerlach and W. Müller, Helv. Chim. Acta 55 (1972) 2277; V. Šunjić, F. Kajfež, D. Kolbah, and N. Blažević, Croat. Chem. Acta 43 (1971) 205; A. Konoval, Y. Yurczak, and A. Zamojski, Tetrahedron 32 (1976) 2957.
- 6. V. Šunjić, F. Kajfež, M. Oklobđija, and M. Štromar, Croat. Chem. Acta 45 (1973) 569.
- 7. Satisfactory spectral and microanalytical data were obtained for all new compounds.
- 8. B. Prodić-Kojić (»Ruđer Bošković« Institute, Zagreb) private communication.
- 9. P. Braustein, D. Matt, F. Mathey, and D. Thavard, J. Chem. Research 1978, 232; 3041.
- 10. It is interesting to note that complex 5 exhibited high diastereoselectivity in hydrogenation of metacycline-hydrochloride into 6-a-methyl-6-deoxy-tetracycline. At 14 atm and 100 °C the 6-epimer was quantitatively formed after 4 h., diasteromeric purity being over 95%. 11. H. B. Kagan and T. P. Dang, J. Amer. Chem. Soc. 94 (1972) 6429.
- 12. The S-configuration has been recently determined by chemical and spectroscopic correlation, for $(+)-\alpha-(3-benzoyl)$ -phenyl propionic acid, which was obtained in 66% e.e. by asymmetric hydrogenation of 6 with (--)-DIOP.¹³ 13. G. Comisso, M. Mihalić, F. Kajfež, V. Šunjić, and G. Snatzke,
- Gazz. Chim. Ital. 110 (1980) 123.

SAŽETAK

Kiralni fosfin (CRC-PHOS) izveden od (+)-kamfan-kiseline. Novi ligand za homogenu asimetričnu hidrogenaciju

G. Comisso, A. Sega i V. Šunjić

1S,3S-1-hidroksi-1-difenilfosfometil-2,2,3-trimetil-ciklopentan-3-karbo-Lakton ksilne kiseline (4, CRC-PHOS), pripravljen je pošavši od metilnog estera (+)-kamfan-kiseline, i izolirana je njegova kompleksna sol [Rh(CRC-PHOS)2NBD] · ClO4 · • THF (5). Taj je katalitički kompleks pokazao visoku reaktivnost, ali nisku enantioselektivnost u prvim pokušajima asimetričnih hidrogenacija.

CRC, CHEMICAL RESEARCH COMPANY, 33048 SAN GIOVANNI AL NATISONE (UD) ITALIJA

Prispjelo 7. travnja 1980.