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Letter

Enantioselective cyclopropanation of styrene with optically active nitrogen ligands based on the pyridine framework

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Abstract

Copper(I) complexes prepared in situ from copper(I)–triflate and 8 optically active pyridine ligands, mainly 2,2′-bipyridines and 2,2′:6′,2′-terpyridines were used as chiral catalysts for the enantioselective cyclopropanation of styrene by ethyl diazoacetate. ee up to 32% was obtained.

Keywords: Copper; Cyclopropanation; Enantioselectivity; Styrene

1. Introduction

In the last few years, chiral pyridine derivatives have attracted increasing interest because of their utility as chiral ligands in metal complexes for enantioselective catalysis [1]. We have contributed in this field by synthesizing a number of pyridine derivatives such as 2,2′-bipyridines [1], 1,10-phenanthrolines [1], pyridyl carbinols [2] and amino pyridines [3], which have been used in asymmetric catalytic hydrosilylation of acetophenone [1] and in the addition of alkylzinc compounds to aldehydes [4]. Moreover, we have recently reported the synthesis of two related 2,2′:6′,2′-terpyridines, the first example of a new class of chiral ligands [5].

Continuing our interest in asymmetric synthesis, we have been evaluating the potential utility of a number of chiral pyridine derivatives as bidentate ligands in the asymmetric cyclopropanation of olefins, taking into account the fact that chiral 2,2′-bipyridines with a C_2-symmetry axis have been found to be very effective ligands for the enantioselective cyclopropanation of various olefins [6].

In this work we report the results of catalytic asymmetric cyclopropanation [7] of styrene with ethyl diazoacetate and the complexes formed in situ from 8 pyridine ligands and Cu(I)–triflate.

The pyridine ligands were prepared according to reported procedures and their configurations are illustrated in Scheme 1. They are two 2,2′:6,6″-terpyridines (**1**, **2**), three 2,2′-bipyridines (**3**, **4**, **5**), one phenanthroline (**6**), one aminopyridine (**7**) and one dipyridine (**8**). Their most remarkable feature is the presence of the 6,6-dimethylnorpynan-2-yl group as common chiral substituent on the heterocyclic ring. Moreover, the bipyridine and phenanthrolines are present both as monosubstituted compounds and as the related C_2-symmetric ones.

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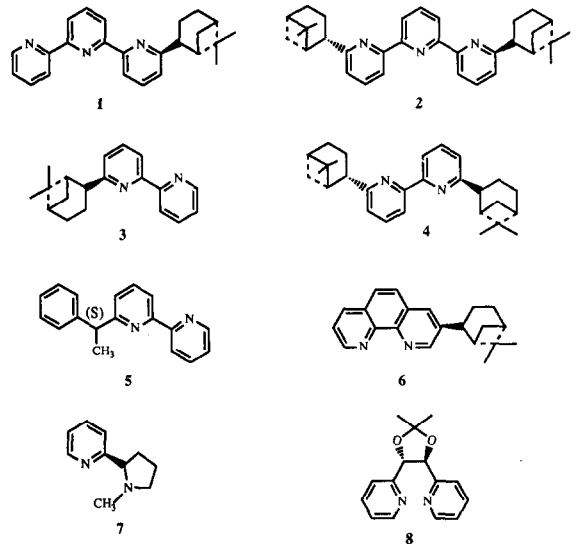


Scheme 1.

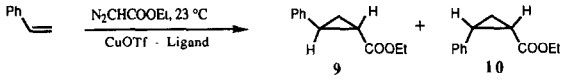
Copper catalysts were prepared in situ from copper(I) trifluoromethanesulphonate benzene complex $[Cu(OTf)(C_6H_6)_{0.5}]$ with ligands according to Evan's procedure and immediately used for the reaction [8].

As shown in Table 1, copper(I) complexes of **1–8** proved to have a moderate level of activity giving cyclopropanes in chemical yields in the 5–70% range as a mixture of *cis*/*trans* isomers, with the *cis* isomer the main component: only in the case of ligand **7** were the results reversed. The enantiomeric excess, determined using a chiral column is 2–32% for the *cis* isomer and 2–20% for the *trans* isomer.

The data in the table show that terpyridines and bipyridines are of comparable reactivity (entry 1, 2 vs. 3, 5, 7), but higher asymmetric inductions are achieved with bipyridines. It is important to note that only a slight increase in enantioselection is obtained on passing from monosubstituted compounds to the related C_2-symmetric ones (entry 1, 3 vs. 2, 4). Finally, it should be observed that the enantioselectivity becomes higher as the ligand to metal ratio increases, but a much lower reactivity and yield is obtained (entry 4, 6).

It is indicated in the literature that effective chiral controllers are those ligands in which the substituents at asymmetric centres are forced to

Table 1
Enantioselective cyclopropanation of styrene



Entry	Ligand	Ligand/Cu [a]	Time (h)	Yield [b] (%)	*trans*/*cis* ratio [c]	% ee [d]		Configuration [e]	
				9+10	**9:10**	**9**	**10**	**9**	**10**
1	1	1	2	62	64:36	2	2	1*S*,2*S*	1*R*,2*S*
2	2	1	2	60	78:22	4	5	1*S*,2*S*	1*S*,2*R*
3	3	1	2	54	58:42	20	8	1*R*,2*R*	1*S*,2*R*
4	4	3	24	5	61:39	10	32	1*R*,2*R*	1*S*,2*R*
5	5	1	10	13	69:31	8	15	1*R*,2*R*	1*S*,2*R*
6	6	3	24	6	59:41	1	21	1*R*,2*R*	1*R*,2*S*
7	7	1	2	61	70:30	9	9	1*R*,2*R*	1*R*,2*S*
8	8	1	2	50	68:32	4	1	1*R*,2*R*	1*S*,2*R*
9	9	1	2	64	40:60	9	6	1*R*,2*R*	1*S*,2*R*
10	10	1	2	72	68:32	5	9	1*R*,2*R*	1*R*,2*S*

[a] 2.6 mol% catalyst.
[b] After column chromatography, based on ethyl diazoacetate.
[c] Determined by GC (see Experimental).
[d] Determined by GC on a chiral column (see Experimental).
[e] Assignment according to [16].

be directed toward metal ion on its complex formation [9]. Our findings show that at least in asymmetric cyclopropanation of olefins catalyzed by the copper complexes of ligands **1–4**, **6**, the chiral 6,6-dimethylnorpynan-2-yl group is not able to meet such requirements. This result contrasts with that obtained by ligand **3** in the catalytic hydrosilylation of acetophenone with $[Rh(COD)Cl]_2$ and diphenylsilane where a fairly good level of enantioselectivity (72%) was obtained [10].

Further studies on the chemistry of pyridine ligands are under way in our laboratory.

2. Experimental

2.1. General

Gas chromatographic analyses were performed by a Perkin–Elmer 8600 chromatograph using He_2 as a carrier gas. A 15 m DBWAX wide-bore capillary column (J and W) was used for the determination of *cis*/*trans* ratio: 100°C (2 min), 20°C/min, 280°C. A 30 m BETA DEX-120 column (Supelco) was used for the determination of enantiomeric excesses of ethyl *trans*- and *cis*-2-phenylcyclopropane-1-carboxylates **9** and **10**: 70°C, 1°C/min, 9 ml/min.

2.2. Materials

Copper(I) trifluorometanesulfonate benzene complex $[Cu(OTf)(C_6H_6)_{0.5}]$ and ethyl diazoacetate were purchased from Aldrich. The pyridine ligands **1–8** were prepared according to reported procedures: 6-[6,6-dimethylnorpynan-2-yl]-2,2′:6,6″-terpyridine **1** [5], 6,6′-bis-[6,6-dimethylnorpynan-2-yl]-2,2′:6,6″-terpyridine **2** [5], 6-[6,6-dimethylnorpynan-2-yl]-2,2′-bipyridine **3** [10], 6,6′-bis-[6,6-dimethylnorpynan-2-yl]-2,2′-bipyridine **4** [11], 6-(1-methylbenzyl)-2,2′-bipyridine **5** [12], 3-[6,6-dimethylnorpynan- 2-yl]-1,10-phenanthroline **6** [13], 2-[1-methyl-2-pyrrolidinyl]pyridine **7** [14], 2,2-dimethyl-4,5-bis(2-pyridyl)-1,3-dioxolane **8** [15].

2.3. Asymmetric cyclopropanation of styrene: typical procedure

A solution of the ligand (34 mmol) in CH_2Cl_2 (2.5 ml) was added to a suspension of $[Cu(OTf)(C_6H_6)_{0.5}]$ (8 mg, 32 mmol) in CH_2Cl_2 (2.5 ml). After 30 min, the mixture was filtered through packed adsorbent cotton under argon and, to the filtrate, was added styrene (1.59 ml, 13.87 mmol). Then a solution of ethyl diazoacetate (285 mg, 2.5 μmol) in CH_2Cl_2 (2.5 ml) was added dropwise over a period of 1 h. The mixture was stirred for the proper time and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 15/1) to afford a mixture of ethyl *trans*- and *cis*-2-phenyl-cyclopropane-1-carboxylates as a colourless oil. This mixture was analyzed by GC. The enantiomeric excess was determined by capillary GC with a chiral column: (1*S*,2*S*)/(1*R*,2*R*)-**9**: 64.5/65.0 min; (1*S*,2*R*)/(1*R*,2*S*)-**10**: 61.1/61.9 min.

Acknowledgements

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References

[1] For a review, see: G. Chelucci, Gazz. Chim. Ital., 122 (1992) 89. G. Chelucci, M.A. Cabras, C. Botteghi and M. Marchetti, Tetrahedron : Asymmetry, 5 (1994) 299. R.-Y. Yang and L.-X. Dai, J. Mol. Catal., 87 (1994) L1. J.M. Brown, D.I. Hulmes and T.P. Layzell, J. Chem. Soc., Chem. Comm., (1993) 1673.
[2] G. Chelucci and F. Soccolini, Tetrahedron: Asymmetry, 3 (1992) 1235.
[3] M. Falorni, G. Chelucci, S. Conti and G. Giacomelli, Synthesis, (1992) 972.
[4] M.A. Cabras, G. Chelucci, G. Giacomelli and F. Soccolini, Gazz. Chim. Ital., 124 (1994) 23.
[5] G. Chelucci, Synth. Commun., 23 (1993) 1897.

[6] K. Ito and T. Katsuki, Synlett, (1993) 639; K. Ito and T. Katsuki, Tetrahedron Lett., 34 (1993) 2661.
[7] M.P. Doyle, Recl. Trav. Chim. Pays-Bas, 110 (1991) 305.
[8] D.A. Evans, K.A. Woepel, M.M. Hinman and M.M. Faul, J. Am. Chem. Soc., 113 (1991) 726.
[9] U. Leutenegger, G. Umbricht, C. Fahrni, P. von Matt and A. Phaltz, Tehrahedron, 48 (1992) 2143; R.E. Lowenthal, A. Abiko and S. Mamasume, Tetrahedron Lett., 32 (1991) 7373; H. Nishiyama, M. kondo, T. Nakamura and K. Itoh, Organometallics, 10 (1991) 500.
[10] C. Botteghi, A. Schionato, G. Chelucci, H. Brunner, A. Kurginger and U. Obermann, J Organomet. Chem., 370 (1989) 17.
[11] G. Chelucci, M. Falorni and G. Giacomelli, Tetrahedron, 48 (1992) 3653.
[12] C. Botteghi, G. Chelucci, G. Chessa, G. Delogu, S. Gladiali and F. Soccolini, J Organomet. Chem., 304 (1986) 217.
[13] S. Gladiali, G. Chelucci, F. Soccolini, G. Delogu and G. Chessa, J Organomet. Chem., 327 (1989) 285.
[14] G. Chelucci, M. Falorni and G. Giacomelli, Synthesis, (1990) 1121.
[15] G. Chelucci, M. Falorni and G. Giacomelli, Gazz. Chim. Ital., 190 (1990) 731.
[16] H. Fritschi, U. Leutenegger and A. Pfaltz, Helv. Chim. Acta, 71 (1988) 1553.