

**Asymmetric alkylation of aromatic aldehydes by diethyl zinc in the presence of (S)-
N,N,N',N'-tetramethyl-2,2'-diamino-1,1'-binaphthyl.**

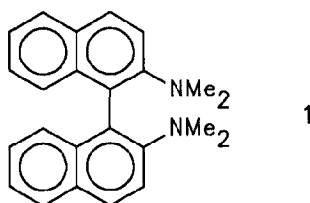
Carlo Rosini, Livia Franzini, Anna Iuliano, Dario Pini and Piero Salvadori*

C.N.R. Centro Studi Macromolecole Stereordinate ed Otticamente Attive, Dipartimento di Chimica e
Chimica Industriale, via Risorgimento 35, 56126 PISA, ITALY.

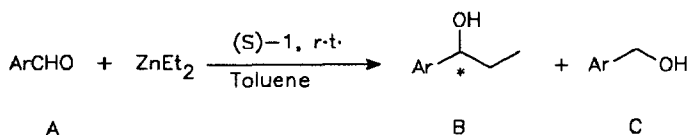
(Received 11 April 1991)

Abstract: The new chiral aprotic ligand **1**, N,N,N',N'-tetramethyl-2,2'-diamino-1,1'-binaphthyl, having C_2 -symmetry structure, affords enantiomeric excesses up to 64% in the asymmetric alkylation of aromatic aldehydes by diethylzinc.

As pointed out by Noyori¹ alkylation of a carbonyl compound by dialkylzincs can only occur after that a zinc-electronegative atom (such as O, N) bond has been created by interaction between the dialkylzinc compound and an external auxiliary. Such ligand-induced perturbation generally accelerates the rate of alkylation (ligand-accelerated reactions²) and, if the external ligand is chiral, optically active alcohols can be obtained. Excellent chemical yields and enantiomeric excesses have been obtained by means of chiral protic ligands (β -aminoalcohols³, diols⁴, piperazines^{5,6} etc.). In principle, even aprotic ligands, such as tertiary diamines, could act as promoter of such reaction (it is known that adducts are formed by diethylzinc and diamines⁷), but there are no reports⁸ describing the reactivity of such species. We decided then to start a study of chiral diamines as catalyst of this reaction. Our attention has been attracted by N,N,N',N'-tetramethyl-2,2'-diamino-1,1'-binaphthyl, **1**:



The choice has been done taking into account the C_2 -symmetry of this binaphthyl system, a property that generally has shown⁹ high efficiency in chiral recognition and the fact that, to the best of our knowledge, **1** has not been used before as chiral director in stereoselective reactions¹⁰. On these bases, we studied¹¹ the reaction between diethylzinc and aromatic aldehydes in toluene at room temperature employing 6% in mol of (S)-**1** (Scheme).



Scheme

In the Table are summarized the results obtained. In absence of the ligand the reaction between diethylzinc and 2-naphthaldehyde (molar ratio 2:1) provides (run 1), after 96 hrs, a yield in addition product (B) of about 40% with 16% of (2-naphthyl)methanol, (C), as side product. By contrast, in the presence of (S)-1, (B) is obtained with 75% yield in 88 hrs and 64% e.e. of the (S) enantiomer. However the rate is quite low (in particular when compared with those provided by the protic ligands^{1,3}). The outcome of the reaction seems to be very sensitive to the nature of the substrate. Para-substituted benzaldehydes with EWGs give almost quantitative yield in relatively short reaction times (entry 8) whilst EDGs provide lower yields (runs 5, 7 and 9). The results obtained in run 4 can be interpreted in terms of hindrance of the reactive zone of the aldehyde: in fact the presence of the peri hydrogen lowers the yields (compare run 4 with run 2). The behaviour of o-methoxybenzaldehyde can look surprising, in particular when compared to that of the para isomer (compare run 5 and 6). In both the cases, the -OCH₃ can coordinate ZnEt₂ giving rise to a species which can competitively alkylate the carbonyl group³. The very different yield of alkylation product in the two cases can be explained assuming that for the ortho isomer the ethyl transfer can be carried out intramolecularly whilst for the para isomer such reaction has to be intermolecular. This different behaviour can explain the different reaction rates. As a matter of fact, when the reaction between o-methoxybenzaldehyde and ZnEt₂ is carried out in absence of 1, the same results reported in run 6 are obtained, indicating that 1 does not take part to the reaction. This obviously explains also why a racemic product is obtained in run 6. The enantiomeric excess obtained in the presence of 1 ranges between 10 and 64%, (S) absolute configuration of the carbinol being preferentially formed when (S)-1 is employed as chiral director. The low e.e. of the alcohol obtained in run 5 may derive once again from the presence of achiral alkylating³ species formed by coordination of the methoxy group of the aldehyde to the organometallic compound, which can give rise to competitive alkylation reactions. p-Chlorobenzaldehyde affords a satisfactory optical yield, although long reaction times are required (owing to the presence of the para chloro atom which deactivates the carbonyl function towards the nucleophilic attack), however no competitive achiral alkylating reagents are formed here and the asymmetric induction remains at satisfactory levels. All these observations indicate that the ethyl-transferring species should have only a weak alkylating power: short reaction times, good chemical and optical yields are obtained for the substrate in run 8, which is strongly activated toward the nucleophilic alkyl transfer by the para CF₃ group. The weak alkylating power may result from a weak interaction between organometallic com-

pound and **1**, due to a limited availability of the nitrogen lone pairs for coordinating the zinc atom. Actually, X-ray analysis shows¹² that, in the solid state, **1** assumes a conformation where each NMe₂ plane is twisted with respect to the plane of the corresponding naphthalene ring of about 30°: this indicates that the nitrogen lone pair is still conjugated with the naphthalene π system and then only partially available for complexing metal centers. As a matter of fact, when an aliphatic tertiary diamine such as sparteine¹³, is employed in the ethylation of 2-naphthaldehyde, excellent conversions (>90%) of secondary alcohol are obtained in only three hours .

Table. Enantioselective alkylation of aromatic aldehydes in the presence of (S)-**1** (Scheme).

Run	Ar	L (mol%)	Time (h)	Products ¹			e.e. ² A.C. ³	
				A	B	C		
1	2-naphthyl	-	96	44	40	16	-	-
2	"	(S)- 1 (6)	88	13	75	12	64	(S)
3	phenyl	"	102	-	94	6	63	(S)
4	1-naphthyl	"	101	46	28	26	33	(S)
5	p-methoxyphenyl	"	96	72	18	10	10	(S)
6	o-methoxyphenyl	"	96	7	78	15	0	-
7	biphenyl	"	93	72	23	5	17	(S)
8	p-trifluoromethyl-phenyl	"	48	-	97	3	50	(S)
9	p-chlorophenyl	"	108	66	28	6	54	(S)

1. Percentages determined by NMR analysis; 2. By HPLC analysis using ionic Pirkle DNBPG column (see ref. 11); 3. Absolute configuration assigned from elution order (see ref. 11).

In conclusion the present investigation indicates that: a) tertiary diamines can act as promoter of the alkylation of aromatic aldehydes by diethylzinc; b) the rate of alkylation is strongly dependent on the zinc-nitrogen bond strength; c) ligand **1** can afford satisfactory e. e. only with non disactivated aldehydes.

REFERENCES AND NOTES.

1. R.Noyori, S.Suga, K.Kawai, S.Okada, M.Kitamura, N.Oguni, M.Hayashi, T.Kaneko, Y.Masuda, *J. Organomet. Chem.*, 1990, 382, 19; R.Noyori, S.Suga, K.Kawai, S.Okada, M.Kitamura, *Pure & Appl. Chem.*, 1988, 60, 1597; M.Kitamura, S.Okada, S.Suga, R.Noyori, *J.Am.Chem.Soc.*, 1989, 111, 4028.
2. Another important example of ligand accelerated reaction: E.N.Jacobsen, I.Marko', W.S. Mungall, G.S. Schroeder, K.B.Sharpless, *J.Am.Chem.Soc.*, 1988, 110, 1968.
3. E.J.Corey, P.Yeun, F.Hannon, D.A.Wierda, *J. Org. Chem.*, 1990, 55, 784.
4. C.Rosini, L.Franzini, D.Pini, P.Salvadori, *Tetrahedron:Asymmetry*, 1990, 1, 587.
5. K.Soai, S.Niwa, Y.Yamada, H.Inoue, *Tetrahedron Lett.*, 1987, 28, 4841.
6. Actually there is not ethane evolution by reacting a secondary amine with diethylzinc: K.Tanaka, H.Oshio, H.Suzuki, *J.C.S. Chem. Commun.*, 1989, 1700.

7. K.H.Thiele and S.Schroeder, *Z. Anorg. Allg. Chem.*, 1965, 337, 14.
8. Only Noyori reports briefly the reaction between diethylzinc and benzaldehyde in the presence of N,N,N',N'-tetramethyl-1,2-diaminoethane and N,N,N',N'-tetramethyl-1,3-diaminopropane, see ref.1
9. R.Noyori and H.Takaya, *Chemica Scripta*, 1985, 25, 83; R.Noyori, *Chem. Soc. Rev.*, 1989, 18, 187.
10. Chiroptical properties of **1** have been already reported: K.Mislow, M.A.W.Glass, R.E. O'Brien, P.Rutkin, D.H.Steinberg, J.Weiss, J.Djerassi, *J.Am.Chem.Soc.*, 1962, 84, 1455. The preparation of optically pure **1** and a NMR method for the evaluation of the e.e. has been recently described while this work was in progress: S.C.Benson, P.Cai, M.Colon, M.A.Haiza, M.Tokles, J.K.Snyder, *J. Org. Chem.*, 1988, 53, 5335.
11. A representative experimental procedure is as follows: to a solution of **1** (0.092 mmol) in toluene (15 ml), diethylzinc (3 mmol, 3 ml of 1 M solution in hexane) was added and the mixture stirred at room temperature for 30 min. After cooling at 0°, 2-naphthaldehyde (0.235 mg, 1.5 mmol) was introduced and the homogeneous solution stirred at room temperature for 88 hrs, monitoring the progress of the reaction by analytical TLC (SiO₂, methylene chloride). The reaction was quenched by adding 10% HCl. After usual work-up, the residue was analyzed by ¹H-NMR spectroscopy (determination of percentages of unreacted aldehyde, reduction alcohol, alkylation product) and chiral HPLC (ionic DNBPG Pirkle column, eluent hexane/2-propanol 99/1) for determining the e.e. and assign the absolute configuration of the alkylation product. (assignment of absolute configuration from elution from a chiral column: W.H.Pirkle and J.M.Finn, *J. Org. Chem.*, 1990, 46, 2935.)
12. L.Franzini, C.Rosini, M.Pasero, *Acta Crystall.*, in the press.
13. Sparteine coordinates the zinc atom of Reformatsky reagents: M.Guette', J.Capillon, J.P.Guette', *Tetrahedron*, 1973, 29, 3659.