Tetrahedron Letters,Vol.29,No.22,pp 2677-2680,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

RESOLUTION AND DETERMINATION OF ENANTIOMERIC EXCESSES OF CHIRAL ALDEHYDES VIA CHIRAL IMIDAZOLIDINES

P. MANGENEY*, A. ALEXAKIS, J.F. NORMANT

Laboratoire de Chimie des Organo-éléments, tour 44
Université P. et M. Curie, 4 place Jussieu F-75252 PARIS Cédex 05

Summary - Enantiomeric purity of chiral aldehydes was determined by NMR analysis of derived imidazolidines. The diastereomeric imidazolidines were easily separated by silica gel column and converted into enantiomerically pure aldehyde by acid hydrolysis.

The use of chiral auxiliaries for converting chiral aldehyde into diastereomeric mixtures is a convenient and practical way of determining the enantiomeric purity and/or effecting a resolution[1].

We have found that the enantiomeric purity of aldehydes can be conveniently determined by NMR or chromatographic methods after converting them into diastereomeric imidazolidines by condensation with N,N' dimethyl-1,2-diphenyl ethylene diamine (DMPEDA).[2]

Indeed, because of the C_2 symmetry there is no need of diastereomeric control. Moreover, very mild conditions are required for this reaction (Et_2O, molecular sieves, room temperature) and, in order to avoid kinetic resolution, an excess of DMPEDA can be used.

R,R or S,S DMPEDA

We summarize in table I the results obtained with a number of chiral aldehydes. For all of them the diastereomeric imidozolidines have chemical shifts (^1H and/or ^{13}C) sufficiently different to allow accurate integration of signals, thus furnishing several data for the determination of diastereomeric ratios.

Moreover the absolute configuration of β-disubstituted aldehydes (entries 3,4,5) can be deduced from ^1H NMR analysis.

For an imidazolidine prepared from S,S(-)DMPEDA, the more shielded signal for C_4-H(or C_5-H) belongs to the configuration 1 of the corresponding aldehyde in which the R^1 substituent is the bulkiest (fig. 1). For such a configuration the signal for C_2-H appears as a pseudo triplet (fig. 2) whereas for configuration 2 it appears as a doublet of doublet (fig. 3).

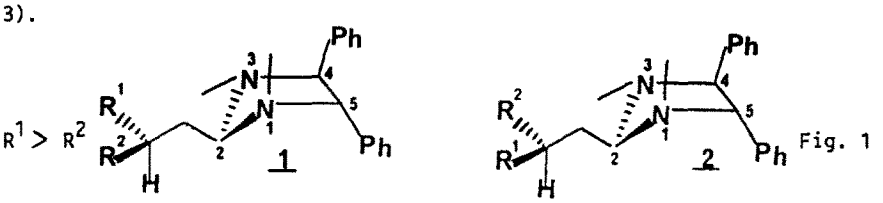
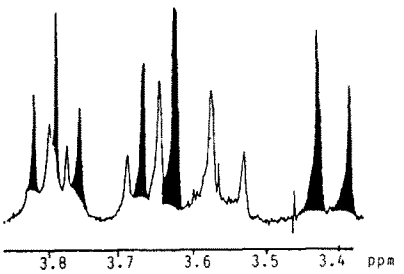


Fig. 1



50% 1 + 50% 2

R^1 = Ph

R^2 = CH_3

Fig. 3

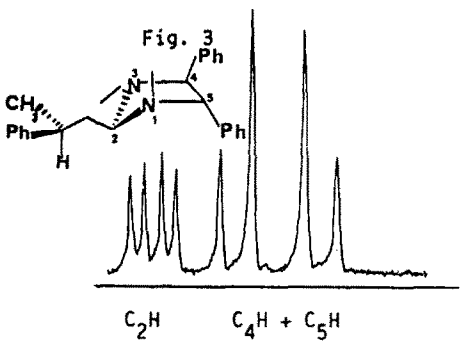
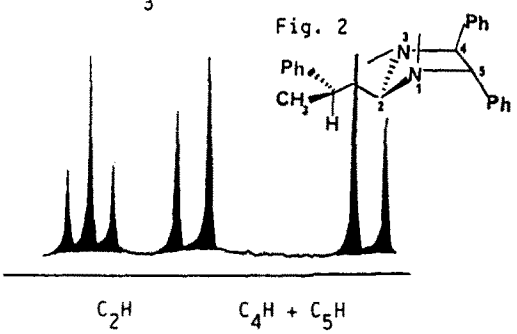


Fig. 2



^{1}H NMR (200 MHz)

For all of the imidazolidines, except for the one derived from cyclohexene carboxaldehyde (entry 1) a chromatographic separation of diastereomeric imidazolidines is possible thus affording an efficient method for the resolution of chiral aldehydes. Resolution was effected on the following aldehydes (table II). The optical purity of the obtained aldehydes was determined by NMR ^{13}C and ^{1}H of the imidazolidine obtained with S,S DMPEDA.

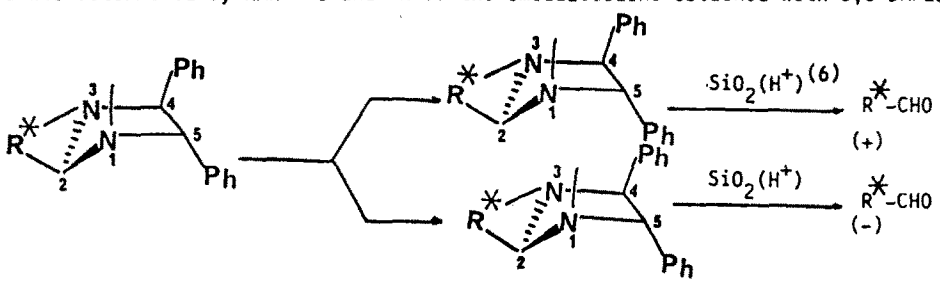
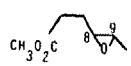
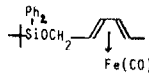


Table I - ^{1}H and ^{13}C NMR spectra of imidazolidines

Imidazolidine	R (ref)	^{1}H Chemical shifts: $N_1-\underline{CH_3}$ + $N_3-\underline{CH_3}$	^{1}H: C_2-H	^{1}H: C_4-H + C_5-H	^{1}H: other	^{13}C Chemical shifts: N_1-CH_3 + N_3-CH_3	^{13}C: C_2	^{13}C: C_4 + C_5	^{13}C: other	Δ R_F (SiO_2+1% NEt_3) (solvent)
1		b 2.21/2.22	3.48/3.35	3.44/3.46 3.6 /3.69		b 39.02/39.20	85.22/85.80	75.28/76.29 72.42/72.78		0
2		2.40/2.52 b	b	b 3.71/3.84	C_8H 2.55/2.72 C_9H 2.84/2.91	b	85.06/86.17	b	C_8 51.53/54.88 C_9 57.32/59.21	0.1 (Et_2O/C_6H_{12} 30-70)
3	 (3)	2.11/2.18 2.19/2.27	b	b 3.45/3.56		b b	83.5 /83.58	80.17/80.70 76.48/76.64	C_8 22.61/24.6	0.2 (Et_2O/C_6H_{12} 30-70)
4		2.12/2.21 2.22/2.31	3.91/3.96	b 3.47/3.56		b b	83.49/83.68	80.17/80.43 76.58/76.95		0.1 (Et_2O/C_6H_{12} 30-70)
5	 (4)	2.12/2.21 2.24/2.30	3.92/3.99	3.50/3.57 b	C_8H_3 1.02/1.09	b 40.07/41.14	83.38/83.54	76.53/76.88 80.22/80.41		0.2 ($AcOEt/C_6H_{12}$ 95-5)
6		2.45/2.57 b	b	b b		34.2 /37.11 39.51/40.00	b	75.55/76.67 79.28/79.80		0.2 ($AcOEt/C_6H_{12}$ 95-5)
7	 (5)	b b	4.0 /4.2	3.60/3.78 4.10/4.14	C_8H 5.7 /5.81	40.60/41.94	85.71/85.90	b 79.33/78.58		0.2 (Et_2O/C_6H_{12} 90-10)

a/ NMR spectra were recorded on a Bruker AC 250 spectrometer as solutions in C_6D_6. Chemical shifts are given in ppm (TMS=0)

b/ No baseline separation

Imidazolidine	$[\alpha]_D^{25}$ aldehyde [a] C, solvent)	e.e. %	Yield %
3	-38 (0.2 Et_2O) 38 (0.2 Et_2O)	95	82
5	-16 (2.5 $CHCl_3$) 17 (2.5 $CHCl_3$)	95	80
6	-95 (0.2 Et_2O) 78 (0.2 Et_2O)	95 74	60 60
7	50 (0.7 Et_2O) -50 (0.7 Et_2O)	95	80

a/ Underlined values are connected to the aldehyde obtained from the less polar imidazolidine

Table II

It should be noted that it is also possible to determine the d.e. by the use of analytical HPLC as it was shown for imidazolidines 2 (C_6H_{12}/CH_3CO_2Et 95-5 + NEt_3 1%) and 3 (C_6H_{12}/CH_3CO_2Et 95-5 + NEt_3 1%).

Acknowledgements - We thank the C.N.R.S. (U.A. 473) for financial support. We kindly thank Prof. Depezay and Dr Grée and Lellouche for generous gift of aldehydes used for imidazolidines 2 and 6.

References -

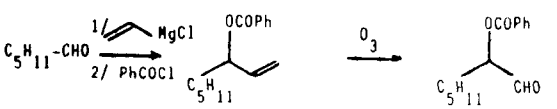
(1) - G. Just, C. Luthe, P. Potvin, Tetrahedron Lett., 23, 2285 (1982)
- C. Agami, F. Meynier, J. Berlan, Y. Besace, L. Brochard, J. Org. Chem. 51, 73 (1986)
- J. Fujiwara, Y. Fukutani, M. Hasegawa, K. Maruoka, H. Yamamoto, J. Am. Chem. Soc., 106, 5004 (1984)

(2) Preceding letter

(3) S.I. Hasmito, N. Kameshima, S.I. Yamada, K. Koga, Chem. Pharm. Bull., 27, 2437 (1979)

(4) S. Takano, H. Chiba, J. Kudo, M. Takahashi, K. Ogasawara, Heterocycles, 26, 2461 (1987)

(5) Prepared as follow :



(6) F. Huet, A. Le Chevallier, M. Pellet, J.M. Conia, Synthesis 63 (1978)

(Received in France 16 March 1988)