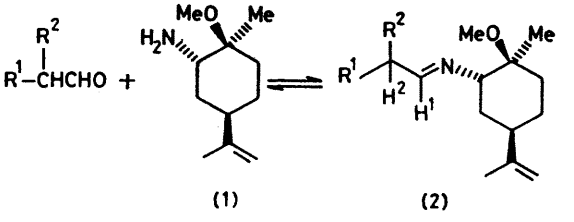
^{1}H N.M.R. Determination of Enantiomeric Purities of 2-Substituted Aldehydes *via* the Aldimine of 2-Amino-1-methoxymenth-8-ene

By A. I. MEYERS* and ZDENEK BRICH
(*Department of Chemistry, Colorado State University, Fort Collins, Colorado* 80523)

Summary The aldimine proton (R–C*H*=NR) from aldehydes and the titled compound exhibits diastereomeric non-equivalence in the ^{1}H n.m.r. spectrum allowing determination of the enantiomeric excess for 2-substituted aldehydes.

WITH the advent in recent years of new and efficient asymmetric syntheses, there has been a concomitant effort to evaluate enantiomeric purities. Unfortunately, the latter effort has lagged behind the synthetic methods and has deterred the preparation of many novel chiral compounds. Indeed, the use of chiral shift reagents, chiral solvent–solute interactions, and diastereomeric derivatives (*e.g.*, Mosher amides) have made ^{1}H and ^{13}C n.m.r. techniques more valuable and, in many instances, more reliable than optical rotations.[1–4]

We here describe a simple, reliable method for determining the enantiomeric excess of 2-substituted aldehydes which, so far, holds considerable promise for this class of compounds.



(1) (2)

When 2-substituted aldehydes, ranging from racemic (entry 1, Table) to various known degrees of enantiomeric purities (entries 2—4) were treated with excess of (+)-2-amino-1-methoxymenth-8-ene (**1**)[5] to avoid possible kinetic resolution, the aldimines (**2**) were formed in quantitative yields.† The 60 MHz n.m.r. spectrum (CCl_4) showed a pair

† A typical procedure for the formation of the aldimines (**2**) is as follows. A solution of the aldehyde (0·7 mmol) and (**1**) (1·4 mmol) in dry ether (10 ml) at 0 °C was left to warm to ambient temperature. Anhydrous Na_2SO_4 (2 g) was added to the solution which was stirred for 30 min and then filtered and concentrated *in vacuo* (0·05 Torr) to furnish the colourless aldimine (95—100%); i.r. data (film) 1660—1690 cm^{-1}. The excess of amine (**1**) did not interfere with the n.m.r. analyses.

TABLE

	Aldehyde				Aldimine	
Entry	R^1	R^2	$[\alpha]_{589}^{25}$/°	Enantiomeric ratio	-C*H*=N- δ(CCl_4) [$J(H^1H^2)$/Hz]	Enantiomeric[e] ratio
1	Me	n-Hexyl	0	50:50	7·53, 7·70 [5·5]	50:50
2	n-Hexyl	Me	+22·2	87·6:12·4[a]	7·53, 7·70 [5·5]	86:13
3	Me	n-Hexyl	−15·9	76·5:23·5	7·53, 7·70 [5·5]	75:25
4	Me	Bu^n	− 7·0	68·5:31·5[b]	7·40, 7·48 [5·5]	69:31
5	n-Hexyl	$MeOCH_2CH_2$–	− 9·1	70·0:30·0[c]	7·53, 7·55 [5·0]	69:31
6	Me	1-Hydroxycyclohexyl	d	—	7·70, 7·80 [5·0]	77:23
7	Me	$Me_2C(OH)$–	d	—	7·68, 7·72 [5·0]	68:32

[a] Based on $[\alpha]_{589}$ 29·9° ($CHCl_3$), G. Consiglio, C. Botteghi, C. Salomon, and P. Pino, *Angew. Chem. Internat. Edn.*, 1968, **7**, 620. [b] Based on corresponding acid after oxidation, P. A. Levene and R. E. Marker, *J. Biol. Chem.*, 1932, **98**, 1. [c] Determined by using the chiral shift reagent, tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]europium(III). The β-hydroxyaldehyde could not be obtained owing to dehydration during the imine hydrolysis. [e] Values represent average of four determinations by peak triangulation and varied by $< \pm 2\%$.

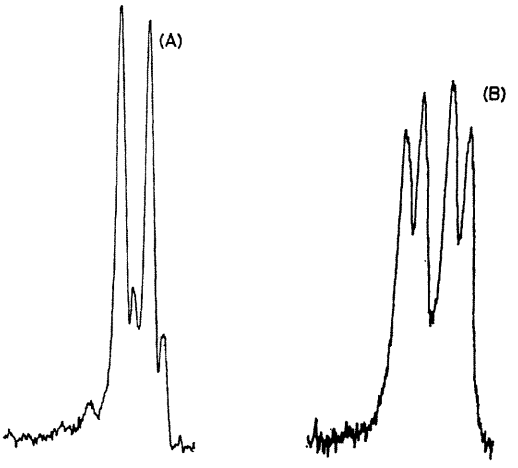
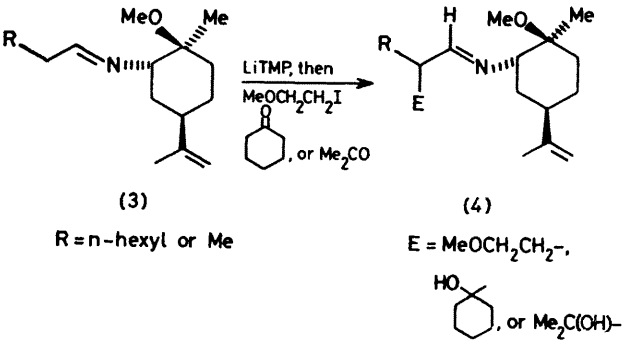


FIGURE. Chemical shifts of C-1 proton (-C*H*=N-). (A) Imine prepared from racemic 2-methyloctanal; (B) imine prepared from 2-methyloctanal of 73% enantiomeric purity (enantiomeric ratio 86:13).

of doublets (Figure) for the enantiomeric aldehydes originating from the C-1 proton of the aldimine. Integration of these signals led to close agreement (±2%) with the reported enantiomeric purities of the aldehydes (Table, entries 1—4). This method was shown to be devoid of any racemization in the aldehyde by hydrolysis of (**2**) in aqueous (±)-tartaric acid and once again measuring the optical rotation (Table, entries 2—4). The methoxyamine (**1**) was also used as a chiral auxiliary agent which allowed asymmetric alkylation of the imines (**3**) leading to the 2-substituted imine (**4**). The extent of the asymmetric synthesis was readily assessed from the C-1 proton n.m.r. signal of (**4**).[5]



Thus, a technique is now available for determining the enantiomeric excess of chiral aldehydes by use of easy formation of a chiral aldimine.

We thank the National Science Foundation for support and the Swiss Science Foundation for a Postdoctoral Fellowship to Z. B.

(*Received*, 16*th February* 1979; *Com.* 158.)

[1] For a review of n.m.r. techniques see A. Gaudener, 'Determination of Configurations by NMR Spectroscopy,' in 'Stereochemistry,' ed. H. B. Kagan, Vol. 1, G. Thieme, Stuttgart, 1977, pp. 117—136.
[2] I. J. Jakovac and J. B. Jones, *J.C.S. Chem. Comm.*, 1978, 1306.
[3] F. Yasuhara, K. Kabuto, and S. Yamaguchi, *Tetrahedron Letters*, 1978, 4289.
[4] W. H. Pirkle and P. L. Rinaldi, *J. Org. Chem.*, 1977, **42**, 385, 3217.
[5] A. I. Meyers, Z. Brich, G. W. Erickson, and S. G. Traynor, *J.C.S. Chem. Comm.*, 1979, preceding paper.