# THE USE OF BASE LINE TECHNIQUE FOR THE DETERMINATION OF OPTICAL PURITIES USING NMR AND CHIRAL LANTHANIDE SHIFT REAGENTS

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Addition of Chiral Lanthanide Shift Reagent (CLSR) to an optically impure sample renders the isomers diastereoisomeric and hence the corresponding groups have different chemical shifts (Whitesides and Lewis, 1970). Where the chemical shifts of the corresponding groups for the two isomers [(+) and (-)] are large, broadness of the peaks does not have much effect on the accuracy of the analysis since integration of the two peaks can easily be performed. Small chemical shifts coupled with broadening of the peaks presents a problem, since the peaks cannot be integrated accurately due to overlapping and are also not sharp enough to allow peak height measurements to be made. To overcome this problem, a new method called the 'Base Line Technique' has been developed in our Laboratory.

The Base Line Technique concerns the two resonance peaks belonging to the two isomers [(+) and (-)] and from the same functional group which are not completely resolved in the presence of a CLSR due to broadness of peaks. It utilises the fact that the distance between the base line (True base line) and the junction between the two peaks (false base line) is proportional to 1-% Optical purity (O.P.)/100 at a constant reagent to substrate molar ratio. This is illustrated below:
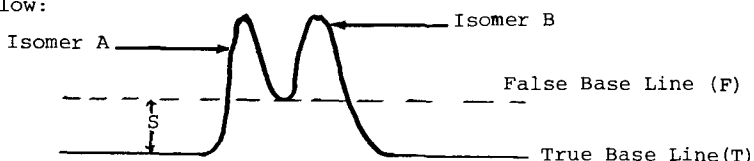
The difference (F-T) is designated as 'Separation' (S).

$$S \propto 1 - \%O.P./100 \quad \text{or} \quad S \propto 1/\%O.P.$$

Thus a plot of S in any units against (1-%O.P./100) gives a straight line.

Table I. Results for the optical purity (O.P.) determination of Ibuprofen using the C-CH$_3$ signal at [Eu(facam)$_3$] / [Ibuprofen] mole ratio of 0.36 – 0.37 in CCl$_4$.

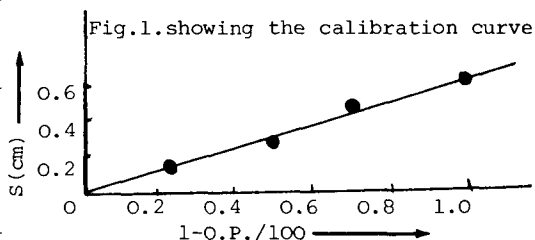| Actual Optical Purity (O.P.)	1-O.P. / 100	Separation (S)
100%	0.000	0.00 cm
75.00%	0.250	0.15 cm
47.56%	0.524	0.29 cm
23.70%	0.763	0.44 cm
Racemic (0%)	1.000	0.59 cm

Fig.1. showing the calibration curve

The success of the experiment depends on the following conditions:
(1) Constant reagent to substrate molar ratio ([CLSR] / [SAMPLE])
(2) Constant instrumental conditions and stable recording, and
(3) The total concentration of the two isomers in the mixture must be the same for all the solutions for the calibration curve.

The technique has proved to be superior to integration, peak height measurement, counting of squares and weighing of the paper under a peak. It is highly accurate and has a standard error of less than 1%. It is very suitable for routine optical purity determination. The optical purities of Propranolol, Naproxen and Salbutamol have also been determined using this technique.

Whitesides, G.M. and Lewis D.W. (1970). J.Am.Chem.Soc., 92, 6978-6981.