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DETERMINATION OF ENANTIOMERIC PURITY AND ABSOLUTE CONFIGURATION OF CHIRAL β-PROPIOLACTONES BY NUCLEAR MAGNETIC RESONANCE IN OPTICALLY ACTIVE SOLVENTS.

Alain Leborgne*, Michel Moreau and Nicolas Spassky
Laboratoire de Chimie Macromoléculaire, LA 24
Université Pierre et Marie Curie
4, Place Jussieu 75230 PARIS Cédex 05
(France)

Abstract Enantiomeric purities and absolute configurations of chiral β-propiolactones can be easily determined from the NMR spectra of diastereomeric solvates resulting from the interaction between the lactone and optically active 2,2,2 trifluoro-1 (9-anthryl) ethanol.

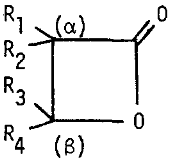
Chiral β-propiolactones substituted in α or β position are used as starting materials for the preparation of optically active polyesters [1,2]. The latter may be also prepared starting from a racemic monomer and using a chiral initiator (so-called "stereoelective polymerization"). In that case the unreacted monomer is enantiomerically enriched [3]. The physical properties of described polyesters are depending on their enantiomeric composition [2] and therefore it is important to know the enantiomeric purity of the corresponding chiral β-propiolactones.

Although methods of determination of enantiomeric purity of γ, δ and ε-lactones were described in the literature, no application of these methods were reported for β-lactones. Jakovac and Jones [4,5] proposed a method involving a reaction of γ, δ and ε-lactones with methyl-lithium followed by NMR examination of the corresponding produced diols in the presence of europium chiral shift reagent. A more direct method has been described by Pirkle et al [6,7] : γ-lactones in the presence of chiral 2,2,2 trifluoro-1 (9-anthryl)ethanol(I) give rise to enantiomeric pairs allowing the determination of enantiomeric purity from NMR spectra.

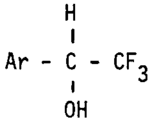
The use of optically active solvents for configurational correlations in heterocyclic compounds by NMR spectroscopy was also described for epoxides [8].

In this paper we wish to report the application of this method to α,α- disubstituted and β-substituted β-propiolactones using chiral carbinol (I).

In the presence of optically active 2,2,2 trifluoro-1 (9-anthryl)-ethanol (I) a doubling of all groups of protons was observed in the NMR spectra for all presented monomers with the exception of (4).



	R_1	R_2	R_3	R_4
(1)	Me	Et	H	H
(2)	Me	n-Pr	H	H
(3)	Me	n-Bu	H	H
(4)	Et	n-Bu	H	H
(5)	H	H	Me	H
(6)	H	H	CCl_3	H



$$Ar-\underset{OH}{\overset{H}{C}}-CF_3$$

(I)

Ar = 9-anthryl

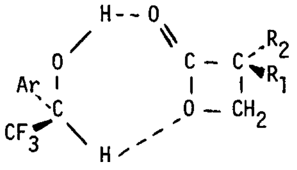
The most useful signals for the determination of enantiomeric excess are usually the methyl protons of R_1 or R_3 group located around 1.10-1.15 ppm. They appear as a doublet in the case of α,α disubstituted lactones (1)-(3). The enantiomeric chemical shift differences observed are reported in the table. They increase with the bulkiness of the substituent group located in α of methyl group.

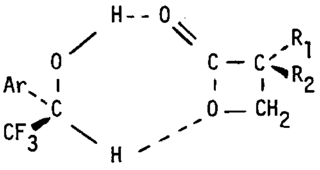
The enantiomeric excess can be easily determined from the areas of well separated peaks. The validity of the method was ascertained on the example of lactone (1) which enantiomeric purity is known.

In the case of β-substituted lactone (5) two pairs of enantiomerically differenciated peaks are observed for methyl protons as expected. Using carbinol (I) of both chiralities, differences in non equivalence were observed : S(+) (I) gives a low field non-equivalence with S(-)(5), while R(-)(I) gives a high field one.

A determination of the absolute configuration on this basis is therefore possible. The enantiomeric excesses observed in both cases are very similar. From these results the rotatory power α_o of the optically pure lactone (5) was taken equal to -27.8 ± 1.6 (neat,dm.)

The comparison of field position of methyl signal in the case of α,α disubstituted and β-substituted lactones, e.g. (1) and (5), seems indicate an opposite sense of non equivalence. However in lactone (1) methyl is the smaller group on asymmetric carbon while it is not so in (5). Therefore considering diastereomeric solvates lactone-carbinol similar to those proposed by Pirkle et al [6,7], one finds that in one case the methyl group is cis with the anthryl while it is in trans situation in the other case. These solvates occur the most likely by hydrogen bonding between the two oxygen atoms of the β-lactone and the hydrogen atoms, one from the hydroxyl group,the other in α of CF_3 group of the carbinol, as shown below :





Table

NMR non-equivalence data for β-lactones in the presence of chiral shift reagent (I) [(a)]

Shift reagent (I) (b)	Lactone	Methyl group [(c)] Δδ (ppm)	Field position [(d)]	e.e. (%)	α_D^{25} (neat,dm)
S (+)	R (1)	0.0215	low	16.7 (17.2)[(e)]	+ 5.88
S (+)	R (1)	0.0215	low	36.4 (36.7)[(e)]	+ 12.59
R (-)	S (2)	0.0310	low	2.5	- 1.43
S (+)	R,S (3)	0.0340	-	0	-
S (+)	S (5)	0.0165	low	23.2	- 6.05
R (-)	S (5)	0.0165	high	21.3	- 6.05
S (+)	S (5)	0.0165	low	44.2	-12.8

(a) Spectra recorded at 250 MHz on CCl_4-C_6D_6 (10 %) solutions. Conc. of lactone ≃ 0.1 mol/l. (I)/|lactone| ≃ 3.

(b) Purchased from Aldrich:(+)(I) $[\alpha]_D^{25}$ + 29 (c 6.3 , $CHCl_3$) ; (-) (I)$[\alpha]_D^{25}$ - 29 (c 6.0,$CHCl_3$)

(c) $R_1 = CH_3$ for (1), (2) and (3) $R_3 = CH_3$ for (5)

(d) for the predominant enantiomer

(e) in brackets values calculated from optical rotation reported in literature (2)

Finally the enantiomeric excess could be simply determined in lactone (6) by looking on the non-equivalence of the proton R_4 = H of the asymmetric carbon. A great simplification in the spectrum leading to only two well separated non-equivalent peaks is obtained by irradiation on the methylenic protons.

The method described for β-lactones is very convenient and does not require any chemical transformation. Only 5-10 mg of lactone are necessary for the determination of enantiomeric purity and configuration.

Further investigations on configurational correlations and enantiomeric purity determinations applied to other β-lactones and other heterocycles are in progress.

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