The Geometrical Isomers of 4-Benzylidene-2-phenyl-2-oxazolin-5-one: Determination of Absolute Configurations by Nuclear Magnetic Resonance Spectroscopy

By K. BROCKLEHURST

(*Department of Biochemistry and Chemistry, St. Bartholomew's Hospital Medical College, Charterhouse Square, London, E.C.*1)

H. S. PRICE and K. WILLIAMSON*

(*Department of Chemistry and Biology, John Dalton College of Technology, Chester Street, Manchester,* 1)

CURRENT work on oxazolinones as acylating agents[1] and their related esters as substrates[2] for α-chymotrypsin requires that the absolute configurations of these compounds be known. Previous attempts to assign absolute configurations to the geometrical isomers of 4-benzylidene-2-phenyl-2-oxazolin-5-one (Ia) and (Ib) have led to conflicting results.[3,4] We now report that the absolute configurations of these compounds have been deduced from n.m.r. spectroscopy of the oxazolinones themselves, and of their derived methyl α-benzamidocinnamates (IIa) and (IIb).

The stable oxazolinone[3] (m.p. 165—166°) and its labile isomer[5] (m.p. 149·5—151·5°) were converted into the corresponding α-benzamidocinnamates (m.p. 142—143° and 134—135° respectively) by basic methanolysis. It has been established previously,[5] that configurational integrity is retained in such esterification reactions.

It was predicted that the β-olefinic hydrogen in the *trans*-isomer of both the oxazolinone and the ester would be deshielded relative to the β-hydrogen in the corresponding *cis*-isomer, since the in former cases, the β-hydrogen occurs *cis* to the carbonyl moiety.[6,7] The *cis* and *trans* nomenclature used to describe these compounds is that used to describe the corresponding *cis*- and *trans*-methyl cinnamates (IIIa) and (IIIb) which have been used as reference compounds as their configurations are well established.

The n.m.r. spectra of (IIIa) and (IIIb) (see Table) confirm the prediction that the signal of the

TABLE[a]

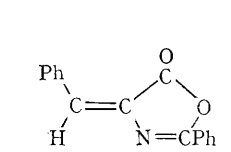
Compound	β-(H) τ	Remarks
Methyl *cis*-cinnamate (IIIa)[b]	3·09 d[c]	J_{AB} 13 c./sec.
Methyl *trans*-cinnamate (IIIb)	2·29 d	J_{AB} 16 c./sec.
Methyl α-benzamidocinnamate, stable isomer (IIa) m.p. 142—143°	2·35—2·72	
Methyl α-benzamidocinnamate, labile isomer (IIb)[d] m.p. 134—135°	2·00—2·29	
4-Benzylidine-2-phenyl-2-oxazolin-5-one, stable isomer (Ia) m.p. 165—166°	2·73 s	Solvent acetic anhydride, temperature[e] 80°.
4-Benzylidene-2-phenyl-2-oxazolin-5-one, labile isomer (Ib) m.p. 149·5—151·5°	2·32—2·61	Solvent acetic anhydride temperature 80°.

[a] N.m.r. spectra were run at room temperature at 60 Mc./sec. in $CDCl_3$ with Me_4Si as internal standard unless otherwise stated; [b] we are indebted to Dr. J. C. Allen for preparative g.l.c. of this compound; [c] previously unreported value, spectrum at 100 Mc./sec.; [d] m.p. not reported previously; [e] this compound is not sufficiently soluble at room temperature either in this solvent or in dioxan.

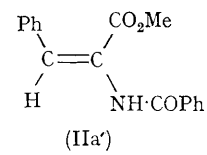
β-hydrogen of (IIIb) would appear downfield from the previously unreported value for the β-hydrogen of the *cis*-ester (IIIa). Interpretation of the spectra of the oxazolinones and their derived esters is complicated by the presence of complex splittings of the aromatic protons, and it is possible to quote only the region of the β-hydrogen signal in all but one case. In spite of the complexity of the spectra, integration ratios enable this to be done with reasonable certainty.

That the β-hydrogen signal for the stable methyl α-benzamidocinnamate appears upfield to that of its labile isomer suggests that the stable isomer has the configuration (IIa′) which is related to that of methyl *cis*-cinnamate (IIIa). Similarly the fact that the β-hydrogen signal of the stable oxazolinone appears upfield to that of its labile isomer suggests that the stable isomer has the configuration (Ia′). This is the configuration which was suggested for this compound by Buckles *et al.*,[3] and is that which would have been predicted for the stable isomer on *a priori* grounds because it is the one which possesses the most extended system of *trans*-conjugation.

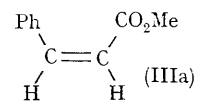
The above discussion of the assignments for the esters has neglected the effect of the α-benzamido-substituent on the β-hydrogen signal. If the assignments suggested above are correct, the introduction of the α-benzamido-substituent into the methyl cinnamates has resulted in a downfield shift of the β-hydrogen signal for both *cis*- and *trans*-isomers. This is the effect expected from the introduction of an electron-attracting substituent. If the correct assignments were the reverse of those suggested above, the effect of introducing the α-benzamido substituent would have been to shift the β-hydrogen signal of methyl *cis*-cinnamate markedly downfield and to shift the β-hydrogen signal of methyl *trans*-cinnamate upfield; such an effect is unlikely.



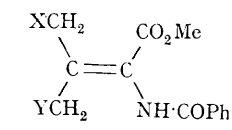
(Ia′)



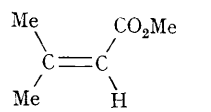
(IIa′)



(IIIa)



(IV)
X = H or AcO
Y = AcO or H



(V)

The α-benzamido-substituent induces a downfield shift of between τ 0·37 to 0·74 in the β-hydrogen signal when it is situated *cis* to this hydrogen (*i.e.* in the *cis*-ester) and between τ 0·00 to 0·29 when it is situated *trans* to it. Although the difference between the two values may be as small as τ 0·08, this does suggest that this substituent, like the ester group, exerts its influence on the β-hydrogen mainly by long-range deshielding.

When a hydrogen atom is separated from the α-benzamido-group by an extra carbon atom, the α-benzamido-group exerts no effect upon it.[7] Thus the positions of the signals of the C-methyl hydrogens in (IV) correspond almost exactly with those of methyl β,β-dimethylacrylate (V). Presumably in this case the α-benzamido-group lies too far from the *C*-methyl hydrogen to be effective in deshielding.

These assignments of configuration to the α-benzamido cinnamates and the corresponding oxazolinones confirm that both the stable and labile

oxazolinones retain their configurations on methanolysis to the esters.

Work is in progress on oxazolinones related to crotonic esters for which no evidence of absolute configuration has been reported.

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