Assignment of the Stereochemistry of α-Benzamido- and α-Phthalimido-crotonates using Nuclear Magnetic Resonance Spectroscopy

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Summary Spectroscopic evidence is presented to show that pencolide and the stable isomer of methyl α-benzamidocrotonate both have the *cis*-configuration.

A recent paper on the stereochemistry of ethyl α-benzamido-3,4-dimethoxycinnamate has assigned the *trans*-configuration to the stable isomer.[1] We have prepared the stable form of methyl α-benzamidocrotonate [(Ib) (m.p. 78—79°)] and present n.m.r. evidence to indicate that this compound has the *cis*-configuration. Since (Ib) was prepared by hydrolysis of the stable oxazolone (m.p. 85—91°)[2] it follows that the structure of this oxazolone is (II).

The chemical shifts for the vinylic proton and methyl group of (Ib) have been compared with the chemical shifts observed for the corresponding acrylate (Ia) and ββ-dimethylacrylate (Ic) (Table). Morgenstern *et al.*[1] have proved that the signals due to the vinyl protons in (Ia) can be assigned as shown. The τ 4·02 proton is a doublet with coupling constant 1·3 Hz but, after shaking the spectroscopic sample with D_2O–DCl, the signal collapsed to a singlet. This treatment resulted in isotopic exchange of the amide NH group and shows that there is allylic coupling between the NH group and the vinyl proton that is *trans* to it. Similar *trans*-coupling has been observed between the 1 and 3 protons of indole.[3]

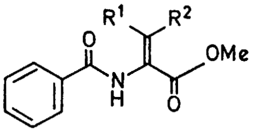
TABLE†

Compound	R¹		R²	
(Ia)	H	3·21(s)	H	4·02(d)
(Ib)	H	3·12(q)	Me	8·16(d)
(Ic)	Me	7·79(s)	Me	8·10(s)
(IIIa)	H	3·31(s)	H	4·01(s)
(IIIb)	H	2·60(q)	Me	8·17(d)
(IIIc)	Me	7·68(d)	H	3·49(q)
(IIId)	Me	7·57(s)	Me	8·14(s)

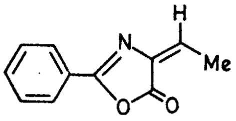
† The spectra were obtained with a Varian A60-A, using deuteriochloroform as solvent. The chemical shifts are expressed as τ values relative to Me_4Si.

The high-field olefinic-proton signal is not present in the n.m.r. spectrum of the crotonate (Ib) and the low-field signal is only 0·09 p.p.m. downfield compared with (Ia); hence the stereochemistry is *cis*, as shown.

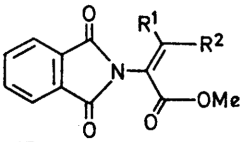
The chemical shifts of the methylene group in methyl α-phthalimidoacrylate (IIIa) are not significantly different from those of (Ia) and it can be concluded that the τ 4·01 signal is due to the hydrogen nucleus *cis* to the ester. A 4 : 1 mixture of (IIIb) and (IIIc) was obtained by condensing phthalic anhydride with (±)-threonine methyl ester followed by dehydration. It has been shown for this system that a proton *cis* to the ester is at higher field than the *trans* proton. Therefore the *cis*-configuration can be given to the crotonate (IIIb) which predominates in the reaction mixture. In view of the similar positions of resonance for the vinylic protons in (Ia) and (IIIa) it is surprising that the olefinic proton of (IIIb) is at such low field compared with (Ib).



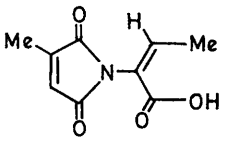
(I)



(II)



(III)



(IV)

The stereochemistry about the crotonate double bond of the mould metabolite pencolide[4] has not been determined. The chemical shifts of the crotonate methyl group and proton are τ 8·18 and 2·54 respectively. Since the shielding differences between a carboxylic acid and an ester are small, it follows that pencolide has structure (IV).

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