Further Studies on the Structural Determination of Esters of 4-Oxo-4*H*-1-benzopyran-2-carboxylic Acids Using the Paramagnetic Shift Reagent Eu(FOD)$_3$

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The effect of Eu(fod)$_3$ on the signals of benzylic methylene protons in the pmr spectra of 4-oxo-4*H*-1-benzopyran derivatives is described. Assignments were confirmed by decoupling experiments. The technique provides a method for distinguishing between structural isomers.

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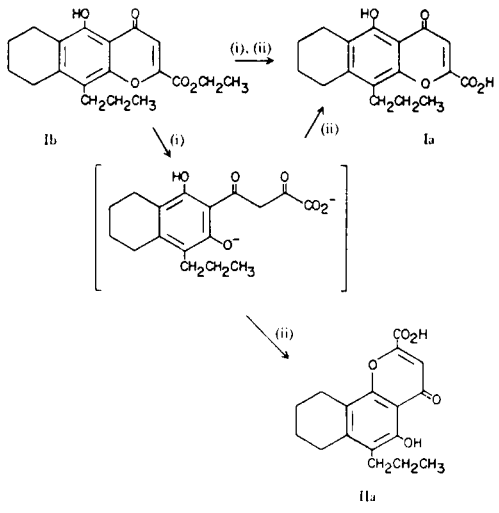
It has previously been reported that the paramagnetic shifts induced by tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium, Eu(fod)$_3$, in the pmr signals of ethyl 4-oxo-4*H*-1-benzopyran-2-carboxylates were useful for distinguishing structural isomers in this series of oxygen heterocycles (1). Similar applications of Eu(fod)$_3$ in the structural elucidation of an analogous series of flavones and isoflavones have also been reported (2-4). However, in all these studies, structural assignments were based essentially on the shifts induced in the signals of the aromatic protons of the benzopyrone molecules. We now show that even when the aromatic ring of these heterocyclic compounds is fully substituted, the shift reagent technique can still be of value in structural elucidation.

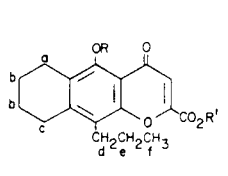
This extension of the previously reported studies arose from the analysis of the structures of the two isomeric 5-hydroxy-4-oxo-4*H*-1-benzopyran-2-carboxylic acids Ia and IIa. Both of these acids were isolated from a single reaction involving the base catalysed hydrolysis of an ester which, as a result of the studies described in this paper, has been assigned the linear structure Ib. The generation of the isomeric acid IIa under these hydrolytic conditions represents an example of the Wesseley-Moser rearrangement of 5-hydroxychromone derivatives (5), in this particular case arising *via* the α,γ-diketo carboxylate anion intermediate shown (Scheme). Thus, because this rearrangement was taking place during the ester hydrolysis, leading to the two isomeric acids, a means of unambiguously assigning the structures Ia and IIa was required.

Each acid contains three sets of benzylic methylene groups and three sets of methylene groups β to an aromatic ring. The small differences in the chemical shifts of the signals due to these protons in the normal pmr spectra of the acids, did not provide conclusive structural identification. The use of paramagnetic shift reagents, on the acids directly, was precluded due to the known lack of

Scheme

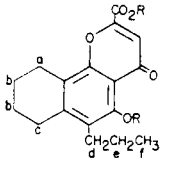


(i) NaHCO$_3$/CH$_3$CH$_2$OH/H$_2$O; (ii) HCl



I

a: R = R' = H
b: R = H; R' = CH$_2$CH$_3$
c: R = R' = CH$_3$



II

a: R = H
b: R = CH$_3$

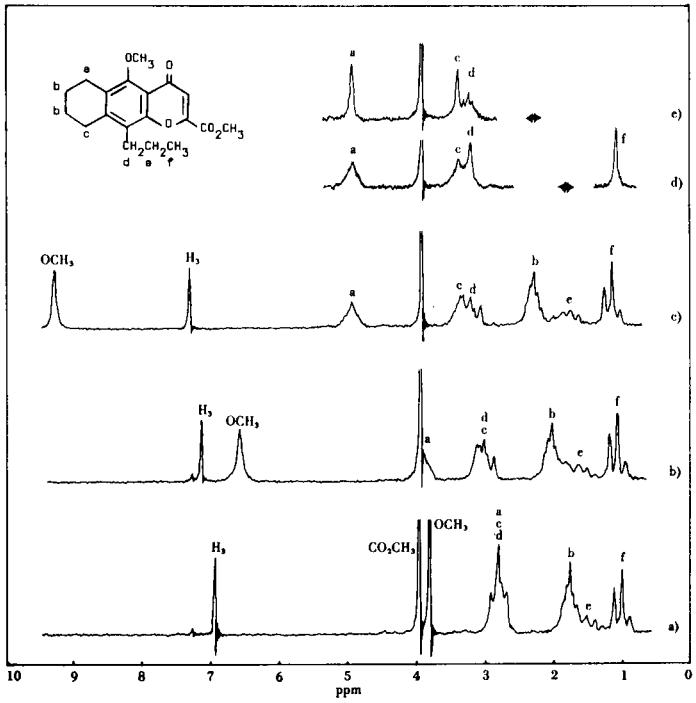


Figure 1. ^{1}H Nmr spectra of isomer Ic. (a) Normal spectrum, 35 mg. in 0.5 ml. of deuteriochloroform; (b) after 20 mg. of Eu(fod)$_3$ added; (c) after 40 mg. of Eu(fod)$_3$ added; (d) decoupling with irradiation at *e*; (e) decoupling with irradiation at *b*.

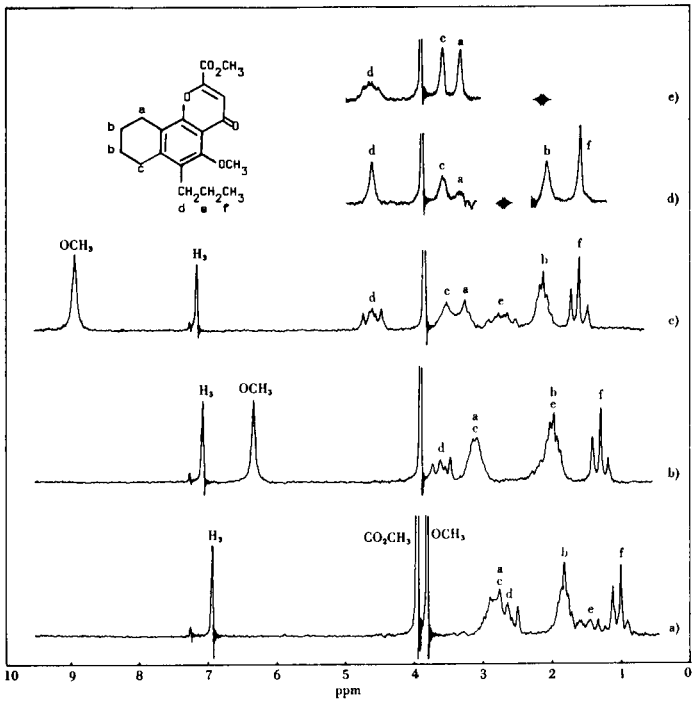


Figure 2. ^{1}H Nmr spectra of isomer IIb. (a) Normal spectrum, 35 mg. in 0.5 ml. of deuteriochloroform; (b) after 20 mg. of Eu(fod)$_3$ added; (c) after 40 mg. of Eu(fod)$_3$ added; (d) decoupling with irradiation at *e*; (e) decoupling with irradiation at *b*.

stability of such complexes in the presence of carboxylic and phenolic groups. Therefore, before shift reagent studies could be carried out, it was necessary to convert the phenolic-acids to the corresponding methyl ether-methyl ester derivatives Ic and IIb (6).

Previous studies established that Eu(fod)$_3$ co-ordinates predominantly at the alkoxy oxygen atom in esters of 5-alkoxy-4-oxo-4*H*-1-benzopyran-2-carboxylic acids (1). Thus it would be expected that the shifts induced in the signals of the three pairs of benzylic methylene protons *a*, *c* and *d* would be different for the two isomers, thereby allowing a distinction between the linear and angular structures.

The effect of successive additions of Eu(fod)$_3$ on the pmr spectra of the esters Ic and IIb are shown in Figures 1a-c and 2a-c respectively. In each case a large displacement of the 5-methoxyl singlet and a rather small displacement of the signal due to the olefinic proton H-3 confirms that the shift reagent co-ordinates mainly at the methoxyl oxygen atom.

In the compound with structure Ic two benzylic methylene groups *c* and *d* are about equidistant and somewhat remote from the co-ordination site whereas the third benzylic methylene group *a* lies much nearer. In the normal spectrum (Figure 1a) all three benzylic methylene groups contribute to a multiplet centred at δ = 2.8 ppm; but addition of Eu(fod)$_3$ (Figures 1b and 1c) separates out the signal due to the methylene group *a* shifting it well downfield. The signals due to methylene groups *c* and *d* are shifted much less and do not quite separate. Assignments for the benzylic proton signals shown in Figure 1c were confirmed by decoupling experiments. Thus irradiation of the signal due to the propyl β-methylene group *e* collapses the multiplet due to the adjacent methylene group *d* but has no effect on the multiplets due to the methylene groups *a* and *c* (Figure 1d). Irradiation of the ring β-methylene multiplet *b* collapses only the multiplets due to *a* and *c* (Figure 1e). Of the benzylic methylene groups in IIb it is the propyl methylene group *d* that lies closest to the co-ordination site; the methylene groups *a* and *c* being more remote. The effect of Eu(fod)$_3$ on the pmr spectrum is as expected. The signals due to the three benzylic methylene groups are eventually separated, that due to *d* (approximately a triplet) shifting furthest (Figure 2c). Furthermore, in the angular isomer IIb the β-methylene *e* and methyl *f* groups of the propyl substituent also lie close to the co-ordination site and as a result their signals are displaced considerably more than the corresponding signals in the spectrum of the linear isomer Ic. Again decoupling experiments provided confirmation of the signal assignments. All three signals of the propyl substituent are established by irradiating the signal due to the β-

methylene group *e* which collapses the triplets due to the methylene group *d* and the methyl group *f* (Figure 2d). Only multiplets due to *a* and *c* collapse to give singlets on irradiation of the ring β-methylene multiplet *b* (Figure 2e).

The results of these pmr studies support the structural assignment of the two isomeric esters Ic and IIb. The technique can clearly be extended to the structural determination of any series of fully substituted 5-alkoxybenzopyran derivatives of synthetic or natural origin.

EXPERIMENTAL

Pmr spectra were determined at 60 MHz on a Perkin-Elmer R12 spectrometer using TMS as an internal lock signal. The spectrum of each substrate (35 mg.) dissolved in 0.5 ml. of deuteriochloroform was recorded and re-run after two successive additions (20 mg.) of Eu(fod-d_9)$_3$. Decoupling experiments were carried out in the frequency sweep mode of operation.

REFERENCES AND NOTES

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