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DETERMINATION OF CONFORMATIONS IN 2-ACETYLFURANS BY NUCLEAR OVERHAUSER EFFECTS.

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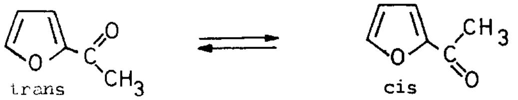
Studies of the conformations of 2-furanaldehyde and 2-acetylfuran have attracted great interest in recent years, but the results obtained to date have been mutually contradictory [1-9].

At low temperatures the interconversion of the two conformers, cis and trans, is slowed down, and has been recently studied by PMR technique [1].



The assignment of the 3-proton absorptions of the cis and trans forms may be based on what is known about the effects of the anisotropy of the carbonyl group, for which there are at least two models. The model suggested by Jackman [10], and based on Pople's calculation [11], predicts that the diamagnetic anisotropy effect of the carbonyl group will cause shielding of nuclei inside a conical surface over and under a trigonal C=O plane, and nuclei outside this surface will be deshielded. The shape of the surface dividing the regions of diamagnetic and paramagnetic shielding effects of the C=O group has been critically discussed by Karabatsos et al. [12], who propose another model, based on calculations by ApSimon et al. [13] and results from studies of conformations of aliphatic aldehydes [14]. The conformer with its 3-proton absorption at lowest field is favoured in the equilibrium, and using the Jackman model this should be the trans form, while the other model indicates the cis form to be dominant.

The intricacy of the problem of determining conformations is further illustrated by investigations of 2-furanaldehyde. Its low temperature PMR spectrum also shows two conformers in the proportions 1:7, where the dominant isomer has its 3-proton absorption at lower field [2], as in the case of 2-acetylfuran. Gas phase microwave [3,4] and IR-spectroscopy [5] studies also show that the molecule exists in two planar conformations and indicate that the trans conformer is lower in energy than the cis conformer. Dipole moment data [6], on the other hand, suggest that the cis conformer dominates in the equilibrium. Karabatsos and Vane [7] have come to the same conclusion by applying the rule of spin-spin coupling through the "straightest zigzag path", proposed by Banwell and Sheppard [15], to the long-range spin-spin coupling between the aldehyde and ring protons in the room temperature PMR spectrum of 2-furanaldehyde.

As there is disagreement about the stereospecificity of the spin-spin coupling through the "straightest zigzag path", Roques et al. [8] have studied 4-bromo-2-furanaldehyde in solution at low temperature by PMR and have carried out X-ray investigations of the solid state. A comparison of these results led to the conclusion that the long-range coupling followed the "zigzag path" and consequently was stereospecific.

In all these earlier investigations the determination of the conformation has been dependent on information obtained by other methods, and in some cases carried out in different phases. By studying the nuclear Overhauser effect of 2-acetylfuran at low temperature it is, however, possible to make an unambiguous assignment of the 3-proton absorptions.

Independently, a similar study has been carried out by Combrisson et al. [9] who investigated nuclear Overhauser effects in 4-bromo-2-thiophene aldehyde, 4,5-dibromo-2-acetylthiophene, and 4-bromo-2-furanaldehyde at -90°, a temperature at which they assume that at least the 4-bromo-2-furanaldehyde system is exchanging. In our case, on the other hand, the temperature was as low as -120°and the rotation should be effectively inhibited, which is also obvious from the well-resolved spectrum obtained (cf.Fig.1), and thus the usual treatment of nuclear Overhauser effect can be used.

The nuclear Overhauser effect (NOE) occurs during nuclear magnetic double resonance experiments, and allows the detection of nuclear-nuclear mutual relaxation processes. An enhancement of the absorption intensity of certain protons is observed on irradiation of other protons in close proximity within the same molecule [17,18]. Obviously NOE studies would make it possible to solve the conformational problem in the 2-acetylfurans, since the distance between the methyl and the 3-proton is 2.8 Å in the cis form and 4.9 Å in the trans form. Irradiation of the methyl band would thus result in enhancement of the 3-proton absorption only in the cis form.

The acetylfurans studied in this work are the unsubstituted compound and the 4,5-dibromo, 4-bromo-5-deuterio, and 4,5-dideuterio derivatives. The spectrum of 2-acetylfuran at -120° is shown in Fig.1. Of the aromatic protons the resonances due to the 4- as well as the 5-proton of the two conformers overlap, while the 3-proton absorptions are separated by 0.222 ppm. The other compounds show only the 3-proton absorptions in the aromatic region, and the separation between them is reduced as the number of bromine atoms in the molecule increases. Introduction of the bromine also favours the more stable conformer. In all four cases it is the absorption at lower field (A) that is due to the conformer favoured in the equilibrium. With regard to the methyl absorptions it is just the opposite, and the two bands are separated by only a few Hz. The chemical shifts and the equilibrium ratios (A/B) between the two conformers are given in Table 1.

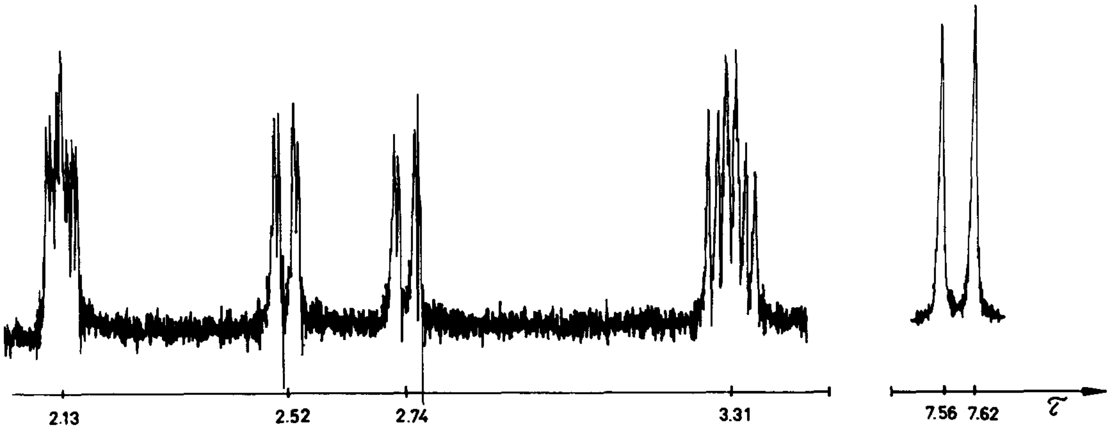


Fig. 1. PMR spectrum of 2-acetylfuran in hexadeuteriodimethylether at -120°.

The NOE experiments were performed in hexadeuteriodimethylether in order to reduce interproton relaxation, and care was taken in the preparation of the sample to remove the paramagnetic impurities, especially oxygen. Upon irradiation of the methyl bands all four compounds show an enhancement of their low-field 3-proton absorption. The NOE values are given in Table 1.

Table 1. Chemical shifts (τ values), equilibrium ratios and observed NOE:s for some 2-acetylfurans in hexadeuteriodimethylether at -120°.

Compound	A-H_3 ppm	B-H_3 ppm	A-CH_3 ppm	B-CH_3 ppm	A/B	NOE o/o
2-acetylfuran	2.52	2.74	7.62	7.56	1.10	30,33
4,5-dibromo-2-acetylfuran	2.29	2.44	7.64	7.58	1.56	27,25
4-bromo-5-deuterio-2-acetylfuran	2.30	2.48	7.61	7.56	1.37	31
4,5-dideuterio-2-acetylfuran	2.47	2.71	7.61	7.55	1.10	26

From the PMR experiments presented above it is obvious that the 2-acetylfurans studied in this work at low temperature exist in an equilibrium in which the cis conformer (A) dominates, and that the cis form shows its 3-proton absorption at lower field than the trans form (B). Consequently an unambiguous assignment of the conformation of 2-acetylfuran has been obtained. It would thus appear from our results and those obtained for 4-bromo-2-furanaldehyde by Combrisson et al. that the Karabatsos-ApSimon model for carbonyl anisotropy is to be preferred. However, it is of interest to note that when the acetyl group is placed on a nitrogen instead of a carbon, the situation is apparently quite different. Preliminary low-temperature experiments with N-acetylpyrrole indicate that it is the α-proton absorption at highest field that shows NOE enhancement, which would be predicted on the basis of the Jackman-Pople model for carbonyl anisotropy. It is thus evident that anisotropy effects can not be the only factor determining the chemical shifts of the ortho hydrogens in different conformers, and that possibly electronic effects also are involved. Chemical shift considerations should therefore be used with some care for identification of conformers.

Experimental. All experiments were carried out on solutions (1-2 o/o) of the compounds in hexadeuteriodimethylether in sealed tubes. Before sealing, most of the oxygen was removed by repeated freeze-pump-thaw cycles under high vacuum. The spectra were recorded on a Varian HA-100 spectrometer at -120° using a variable temperature accessory. The sample temperature was obtained from the precalibrated scale controller. Spectra were calibrated with the HA-100 equipment and the precision of the measurements is judged to be $\pm$ 0.1 Hz for the shifts. The nuclear Overhauser enhancements were calculated from measurements of the quotient of the integrated intensities of the 3-proton absorptions with and without irradiation of the methyl protons signal. The irradiating power used was 10-20 mV. The enhancements are calculated from the averages of at least twenty integrations and have a precision of $\pm$ 2 o/o.

The 2-acetylfurans were prepared via the following sequence of reactions. 2-Acetylfuran (Aldrich quality) was brominated in the presence of anhydrous aluminium chloride in analogy with the procedure described by Gol'dfarb [19], and the thus obtained 4,5-dibromo-2-acetylfuran was treated with acetic acid anhydride, deuterium oxide and zink [20], whereupon 5-deuterio-4-bromo-2-acetylfuran was obtained. The melting point for this compound was 66-67° after recrystallisation from ethanol-petroleum ether. Most of the yield was converted to the ethylene acetal in the conventional way [21], and then treated with ethyllithium followed by deuterium oxide, yielding pure 4,5-dideuterio-2-acetylfuran after recrystallisation from petroleum ether; m.p. 31-32°. Hexadeuteriodimethylether was prepared from CD_3OD (Ciba quality) and deuteriosulfuric acid [22].

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