DETERMINATION OF THE CONFORMATIONS OF 6-AROYLBENZIMIDAZO[2.1-*b*]QUINAZOLIN-12(6H)-ONES USING PROTON MAGNETIC RESONANCE SPECTROSCOPY

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Abstract—Proton H-7 in 6-aroylbenzimidazo[2.1-*b*]quinazolin-12(6H)-ones gives rise to signals of very different chemical shift in chloroform and in trifluoroacetic acid, and this permits the assignment of conformation. In the acid medium H-7 is shielded by up to about 2 ppm by the aroyl benzene ring. These factors and a loose relationship between the chemical shift of H-7 and the intensity of UV absorption by the aroyl function are discussed.

THE literature abounds with examples and discussions of the effects of shielding of protons by aromatic rings.[1] However, there appears to be no instance in which a *single* proton has been studied with respect to shielding by an aroyl benzene ring and deshielding by the CO group of the *same* aroyl function within *the same* molecule. We have analyzed the spectra of a series of 6-aroylbenzimidazo[2.1-*b*]quinazolin-12(6H)-ones in chloroform and in trifluoroacetic acid and wish to report our findings concerning such a situation.

The NMR spectrum of benzimidazo[2.1-*b*]quinazolin-12(6H)-one (**1**) in trifluoroacetic acid exhibits two partially overlapping single-proton, broad doublets centered about 8·65 and 8·50 ppm. The two protons at C(1) and C(10) in the plane of the neighboring CO group would be expected to give rise to these, the lower field, signals.[2]

The validity of these assignments is quite clearly revealed by the absence of these two peaks in the NMR spectrum of the desoxy compound **2**.


1

2
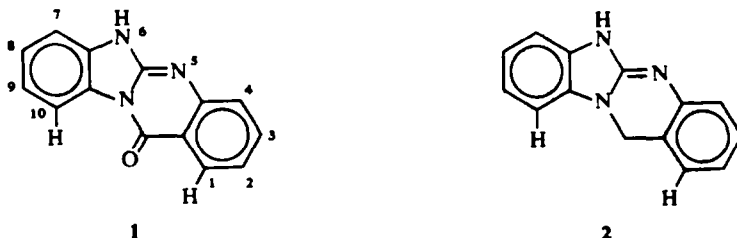
Many derivatives of **1** have been prepared,[3] and only the N(6)-aroyl and N(6)-alkanoyl compounds depart from this pattern at low field. In chloroform these derivatives, for example, exhibit low field signals integrating for three, not two, protons in the region 8·7–7·9 ppm (Table 1). Inspection of Dreiding models suggests

that there is less crowding of the aroyl-benzene ring when it lies *away from* the hydrogen at C(7), in which case the acyl CO function would be directed towards H-7 (though not necessarily in exactly the same plane as the tetracyclic nucleus) as shown in 3. This proton would then lie in the deshielding zone of the CO group, accounting for the extra low field signal.

It is significant that in the spectra of the aroyl derivatives, in chloroform, H-4 gives rise to a signal at higher field than the others arising from the tetracyclic nucleus. This is in accord with H-4 being shielded by the aroyl benzene ring. Clear evidence for this is the shift of the H-4 signal in compounds VII and VIII (Table 1) by about + 0·5 ppm, upfield from the value of 7·53 for the acetyl compound IX. Calculations of the shielding of H-4 by the aromatic ring[4] perpendicular to the plane of the tetracyclic lead to a theoretical value of about 0·7 ppm.

In trifluoroacetic acid both N(6)-aroyl and N(6)-alkanoyl compounds show signals for only two of these low field protons; namely H-1 and H-10. However, with the aroyl, but not the alkanoyl derivatives a new single-proton signal occurs upfield at 6·2–7·0 ppm. We suggest that in this strong acid medium the N(6)-aroyl-1 series exists as the protonated species 4 in which H-7 is shielded by the aroyl benzene ring. In the case of 2,4,6-trimethylbenzoyl derivatives VI and VIII, the steric factors result in both species 3 and 4 being present in trifluoroacetic acid.
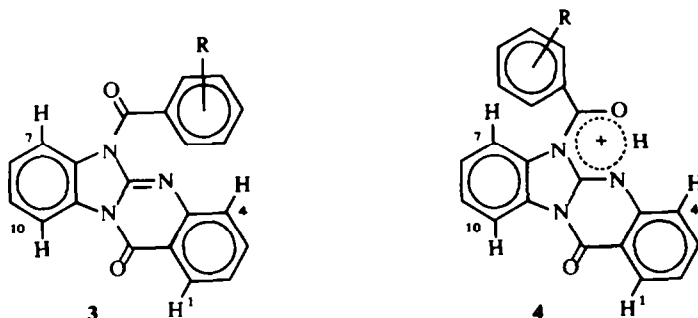
Cursory examination of the figures for aroyl compounds I to VI in Table 1, reveals that the shielding of H-7 is markedly related to the nature of the ortho substitution on the aroyl benzene ring, indicating that steric factors are controlling. The shielding region of the benzene ring has been qualitatively described[5] in Fig 1, while the stereochemistry of the protonated species 4 is detailed in Fig 2*.

H-7 is quite close to the aroyl benzene ring. In fact the geometry of the system is such that, regardless of angle θ, H-7 is 2·1 Å from the middle of an imaginary line joining aroyl C atoms 2 and 6. In effect then, the amount of shielding will be a function,

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* A possible alternative conformation with the aroyl group approximately perpendicular to the plane of the tetracyclic would also be expected to result in the shielding of H-7. Calculations indicate that the shielding contributions from the aroyl CO group[2] and benzene ring[4] would amount to about 0·1–0·2 and < 0·1 ppm respectively. The sum of these is much smaller than the shielding of 1·5–1·8 ppm actually witnessed (compounds VII and VIII relative to IX). In any case one would expect the acyl oxygen to participate in H-bonding as shown.

not of distance from the ring, but of θ alone; this latter is controlled by the following factors:

1. The tendency for the aroyl benzene ring to assume coplanarity with the CO function ($\phi = 0$, $\theta = 90°$) when the resonance energy of conjugation can assume a maximum value.

2. The extent to which substituents on the aroyl ring interfere with this tendency.

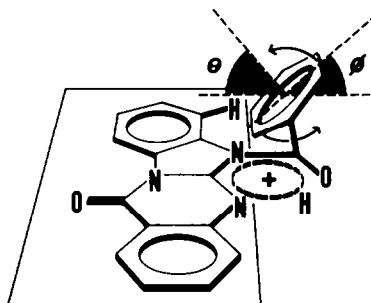3. The steric interaction of H-7 with the aroyl ring and its substituents.

FIG 1

FIG 2

It is immediately apparent that the last mentioned factor is of some importance, since in the cases of the trimethylbenzoyl derivatives VI and VIII, wherein the Me groups should inductively help stabilize species 4, both 3 and 4 coexist.

Some idea of the relative degree to which various *ortho* substituents on the aroyl benzene ring tend to affect angle ϕ (and hence θ) can be obtained from the intensity of the electron transfer band (K band) for the aroyl function in the UV spectrum.[6] This intensity will increase with increasing coplanarity of the benzene ring and the CO group; that is, it will be inversely related to angle ϕ.

Unfortunately, in these N(6)-aroyl tetracyclic compounds, this absorption is hidden by an intense band arising from the benzoquinazolone system itself. Thus, the intensities of the electron transfer bands of the corresponding benzoic acids were measured; the results are recorded in Table 1. It was hoped that these intensities would provide guidelines with respect to θ in the aroyl tetracycles.

Generally the qualitative correlation between the chemical shift of H-7 and the intensity of the aroyl ET band is quite good. The exception to this correlation, namely the 3,5-dimethylbenzoyl derivative, serves to point out the fact that the intensity of the ET band is much more sensitive to electronic effects than is the shielding ability of the benzene ring.

Taking 7·81 ppm, the chemical shift of H-7 in species IX as the standard, then the values of 6·35 and 5·94 ppm for compounds VII and VIII indicate that the shielding arising from just the aroyl benzene ring is 1·46 and 1·87 ppm, respectively. This is in reasonable accord with the value of about 2 ppm calculated for the shielding of H-7 by the aroyl benzene ring[4] in the conformation shown in Fig 2 with θ equal to zero. It may be presumed that the same scale of shielding values is approximately applicable to the derivatives of 1.

W. H. W. LUNN and R. W. HARPER

TABLE 1

No.	R'	R	Chemical shift (ppm) in CDCl₃				Chemical shift (ppm) in CF₃COOD				Approximate molar absorptivity (×10⁻³) of ET band of corresponding benzoic acid
			H-7	H-4	H-10	H-1	H-7	H-4	H-10	H-1	
I		3,5-dimethylphenyl	7·94	>7·25	8·73	8·42	6·98	*	8·87	8·63	9·5
II		phenyl	8·06	7·25	8·75	8·42	6·92	*	8·88	8·66	11·5
III	H	2,4-dimethylphenyl	8·19	7·11	8·73	8·40	6·64	*	8·86	8·67	11·3
IV		2,4-dichlorophenyl	8·51	7·04	8·71	8·37	6·61	*	8·88	8·68	9·2
V		2-chlorophenyl	8·53	6·98	8·72	8·38	6·49	*	8·83	8·63	6·2
VI		3,4,6-trimethylphenyl	8·49	7·08	8·75	8·38	6·23	*	8·86	8·68	2·8
VII		2,4-dimethylphenyl	8·02	7·04	8·48	8·15	6·35	8·03	8·63	8·45	6·2
VIII	CH₃	2,4,6-trimethylphenyl	8·28	6·96	8·51	8·15	5·94	8·05	8·63	8·46	2·8
IX		methyl	8·20	7·53	8·38	8·13	7·81	7·96	8·70	8·42	—

* Signal cannot be identified with certainty.

Inspection of Dreiding models of the 6-(2,4,6-trimethylbenzoyl) compounds shows that when θ is zero, the distance between proton H-7 and the C atoms of the benzoyl *ortho* Me groups is about 3·3 Å. This approximates the sum of the Van der Waals radii of the H atom (1·2 Å) and the Me group (2·0 Å) and explains why both species **3** and **4** co-exist in the cases of these trimethylbenzoyl derivatives. Furthermore, θ must indeed approximate zero in these compounds. With H-7 being 2·1 Å from the plane of the aroyl benzene ring, the value 1·87 ppm probably represents the order of maximum possible shielding which can arise from an aroyl benzene ring not further substituted with markedly polar groups. It must be borne in mind, however, that in this instance the CO function is itself strongly H-bonded.

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