

5-Imino-3-phenyl-4-thioxo-2-imidazolidinones and Related Compounds

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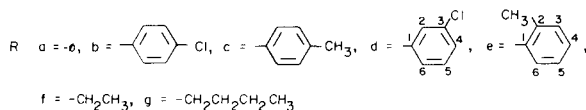
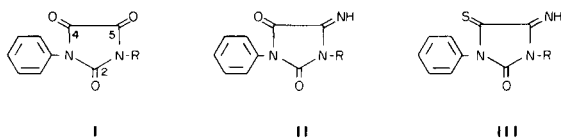
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The cmr spectra of the title compounds have been obtained and the resonances assigned by classical means. Coupling of the imino proton to C-5 is observed to be smaller than that to C-4. A very large downfield shift due to substitution of a carbonyl sulfur at C-4 is observed. The nmr assignments are shown to be self-consistent throughout the series.

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Introduction.

The 1-substituted 5-imino-3-phenyl-4-thioxo-2-imidazolidinones, III, have been shown to be important intermediates in the reactions of the isocyanates of 1-cyanothioformanilide to form 1,3-disubstituted 1*H*-imidazo[4,5-*b*]quinoxalin-2(3*H*)-ones. In addition, 1-aryl-5-imino-3-phenyl-2,4-imidazolidinediones, (II), and the corresponding imidazolidinetriones, (I), can be prepared from 1-cyanofornanilide (1). The present paper reports the cmr chemical shift data for these intermediates.



Results and Discussion.

The chemical shift data are presented in Table I for all compounds involved in the present study.

The assignments are based on similarities and differences in the cmr spectra produced by changes in the R group on N(1). The simplest spectra to begin with are those of I, where R is phenyl and then move to the series containing R = -CH₂CH₃ and *n*-butyl. In the case of Ia, the symmetry of the molecule allows a very clear assignment to be made based on the position and size of the peaks in the aromatic region of the spectrum. The peaks at 126.5 and 129.0 ppm are assigned to the *beta* and *gamma* carbons, respectively, in the phenyl rings. The *gamma* assignment is the result of the known insensitivity of the *meta* carbon to substituent effects in the spectra of substituted benzene compounds (2). The peaks at 130.4 and 128.6 ppm are assigned to the *alpha* and *delta* carbons, respectively, of the phenyl rings. The peak at 130.4

ppm is small, compared to the *beta* and *gamma* peaks indicating a longer T₁ and suggesting a bridgehead carbon. This peak also remains a broadened singlet in coupled spectra. The remaining two peaks at 156.0 and 152.2 ppm are assigned to the heterocyclic ring C-4,5 and C-2 positions, respectively. Because of symmetry, the C-4,5 peak is expected to be twice as large as C-2, which is observed. Having made these assignments, assigning the peaks in IIa and IIIa is reasonably straightforward.

Based on the assumption that the N(3) phenyl group will be least affected by changes at C-5 in IIa, the peaks at 130.9, 126.6, 128.8, and 128.5 ppm are assigned to the *alpha*, *beta*, *gamma*, and *delta* carbons, respectively. These peaks also reflect the intensities expected from symmetry. In addition, comparison (later) with the f and g series which have only one phenyl ring show that these assignments are self-consistent. Then the remaining four peaks in the aromatic region are assigned as given in Table I based on intensity, the appearance of the coupled spectrum and the general insensitivity of *meta* carbons to substituent effects. In the heterocyclic ring, C-2 is expected to remain relatively unchanged and so the peak at 152.7 ppm is assigned to that carbon. In addition, C-4 should also be only minimally affected by replacement of the carbonyl oxygen by an imino nitrogen at C-5 and so the peak at 155.2 ppm is assigned to C-4. The remaining peak at 151.8 ppm is much taller than the other two in the decoupled spectrum, indicating a shorter relaxation time, which is consistent with the presence of the proton on the imino nitrogen at that carbon. In addition, the coupled spectrum shows a doublet at that position in which J = 5.5 Hz. It should be mentioned that the resonance peak for the C-4 position also shows a doublet in coupled spectra and the coupling constant is 11.3 Hz. That the more

remote carbon should have a larger coupling constant is not unique, in fact, quite common, since in the case of thiete sulfone, for example, the couplings of the hydrogen on carbon two to carbons three and four are 2.0 and 9.3 Hz, respectively (3). In the present work, where coupling is

Table I
Carbon-13 NMR Chemical Shift Data (a)

Compound	C-5	C-4	C-2	<i>alpha</i>	<i>beta</i>	<i>gamma</i>	<i>delta</i>	R-1 <i>alpha</i>	R-2 <i>beta</i>	R-3 <i>gamma</i>	R-4 <i>delta</i>	R-5 <i>gamma</i>	R-6 <i>beta</i>	CH ₂	CH ₃
Ia	156.0	156.0	152.2	130.4	126.5	129.0	128.6	130.4	126.5	129.0	128.6	129.0	126.5	—	—
IIa	151.8	155.2	152.7	130.9	126.6	128.8	128.5	132.1	127.0	128.7	127.8	128.7	127.0	—	—
IIIa	154.0	182.4	153.4	133.1	127.4	128.9	129.7	132.3	126.9	128.6	127.9	128.6	126.9	—	—
Ib	(155.9)	(155.8)	152.1	130.3	126.5	129.0	128.7	129.2	128.2	129.1	133.2	129.1	128.2	—	—
IIb	151.4	155.0	152.5	130.9	126.6	128.9	128.5	130.8	128.6	128.7	132.2	128.7	128.6	—	—
IIIb	153.7	182.3	153.3	133.1	127.5	129.0	129.3	131.3	128.7	128.8	132.4	128.8	128.7	—	—
Ic	(156.1)	(156.0)	152.3	130.4	126.5	128.9	128.6	127.8	126.3	129.4	138.3	129.4	126.3	—	20.7
IIc	151.8	155.1	152.7	130.9	126.6	128.8	128.3	129.5	126.8	129.1	137.3	129.1	126.8	—	20.7
IIIc	154.2	182.5	153.5	133.2	127.5	129.0	129.1	129.8	126.8	129.1	137.5	129.1	126.8	—	20.7
IId	151.3	154.9	152.4	130.7	126.6	128.9	128.5	133.4	126.6	132.7	127.7	130.2	125.6	—	—
IIId	153.6	182.3	153.2	133.1	127.5	129.1	129.3	133.7	126.7	132.7	127.7	130.4	125.7	—	—
Ie	156.4	156.4	152.4	130.7	126.7	129.1	128.6	129.5	136.6	129.6	128.8	131.0	126.7	—	17.6
IIe	151.6	155.3	152.5	130.9	126.6	128.8	128.4	130.5	136.6	128.8	128.8	130.5	126.4	—	17.6
IIIe	153.6	182.6	153.3	133.1	127.5	(128.9)	129.2	131.2	136.4	(129.0)	(129.0)	130.7	126.6	—	17.5
If	(156.8)	(156.3)	153.1	130.5	126.4	128.9	128.4	—	—	—	—	—	—	33.8	13.0
IIIf	151.1	155.4	153.2	130.9	126.5	128.7	128.2	—	—	—	—	—	—	34.1	12.7
Ig	157.0	156.3	153.3	130.5	126.4	128.8	128.4	—	—	—	—	—	—	NCH ₂ = 38.5	
														CH ₂ = 29.6	
														CH ₂ = 19.4	
														CH ₃ = 13.5	
IIIg	153.6	182.7	154.3	133.1	127.4	128.9	129.1	—	—	—	—	—	—	NCH ₂ = 40.0	
														CH ₂ = 29.1	
														CH ₂ = 19.4	
														CH ₃ = 13.5	

(a) All shifts are reported relative to TMS. Some ambiguity remains in the assignment of peaks within the parentheses.

observed between the proton on the imino nitrogen and heterocyclic ring carbons, the coupling observed at C-5 is invariably smaller than the coupling at C-4, whether a sulfur atom has been substituted for oxygen on C-4 or not. The peak at 151.8 ppm is assigned to C-5. Finally, in IIIa, the aromatic ring assignments were made very much as before with only slight differences in chemical shifts noted for each resonance position. With the replacement of the carbonyl oxygen with a carbonyl sulfur at C-4, however, both C-4 and C-5 show effects. The most dramatic is at C-4 where this replacement produces a 27.2 ppm downfield shift. This is quite dramatic but the large effect in the ring is also seen in the shift of C-5 and *alpha* of the N(3) phenyl ring. Here, a downfield shift of 2.2 ppm is seen. This is similar to a downfield shift of 1.7 ppm for the *alpha* carbon in the neighboring N(1) phenyl ring when an imino nitrogen is substituted for the carbonyl oxygen at C-5 in IIa.

Consider, next, the compounds If and IIIf. Peak assignments in these compounds are entirely similar to the previous assignments. Compounds Ig and IIIg also show the same trends as Ia and IIIa, including the large downfield shift produced by the introduction of the sulfur atom.

Because the only structural changes in the b and c series involve *para* substitution of -Cl and -CH₃ in the N(1) phenyl ring, comparison of the data for the a series to these two should point out typical substituent effects in the N(1) phenyl ring. Thus, based on data for chlorobenzene and toluene (4), peak assignments can be made. From Table I, one can find that direct substitution of -Cl produces an average downfield shift of about 4.5 ppm at C-4 in the N(1) ring compared to 6.2 ppm at C-1 in chlorobenzene (4). The effect on the carbon *para* to the -Cl, *alpha* in the N(1) ring, is an average upfield shift of 1.2 ppm and at the carbon *meta* to the substitution, *beta* in the N(1) ring, the effect is an average downfield shift of 1.7 ppm. Including the very small *ortho* effect, these average shifts are consistent with the listed data for chlorobenzene. Similarly, substitution of -CH₃ at the C-4 position in the N(1) ring causes a downfield shift of 9.6 ppm (average) at that carbon. The *alpha* carbon in that ring shifts upfield by an average of 2.6 ppm. These values compare well with the expected substituent effects.

It should also be noted that the same trends in the heterocyclic ring carbon shifts exist in the b and c series as exist in the other three series presented above. Especially noteworthy are the dramatic effects which result from

substitution of a carbonyl sulfur for the carbonyl oxygen at C-4 and the long-range shift noted at the *alpha* carbon in the N(3) ring in each case. An inspection of Table I will show matching trends in each set of compounds which tend to support the assignments already made.

The assignment of the heterocyclic ring carbons is aided by the shorter relaxation time which is observed (by smaller peaks) for C-5 whenever an imino nitrogen is present as opposed to a carbonyl oxygen. Thus, the peak at 153.7 ppm can definitely be assigned to C-5 in IIIb even though C-2 (153.3 ppm) is very close by. This same spectral effect is used in assigning C-5 in the spectrum of IIIc.

The remaining two sets of compounds (d and e) are a bit more complex because of the lack of symmetry in the N(1) ring and the additional resonances produced thereby. The carbons in the N(1) ring are labeled R-1 through R-6 as shown in the structural diagram above for the d and e series. Assignments in the N(3) phenyl ring and the heterocyclic ring are straightforward throughout, as before. In the Cl-substituted ring, in IIId and IIIId, the directly substituted carbon, R-3, is at 132.7 ppm, about 4.0 ppm downfield from the parent (IIa). This assignment is made, not only from expected substituent effects but from the fact that this peak has smaller intensity indicating a bridgehead carbon and that it remains a broadened singlet without decoupling. Positions *ortho* to the -Cl substitution, R-2 and R-4, are seen to move upfield slightly and those *meta*, R-1 and R-5, are seen to move downfield appropriately (between 1.3 and 1.8 ppm). The position *para* to the -Cl substitution moves upfield by an average of 1.3 ppm, very similar to the shifts observed in b. In fact, although other assignments could be made, those given in Table I are all consistent, not only with literature values but with b.

Not all assignments in the e series are unambiguous but there are some interesting results and observations to be made. In the spectrum of Ie, however, aside from the heterocyclic ring peaks whose assignments are obvious, the peaks at 136.6, 130.7, and 129.5 ppm are all small indicating that they are to be assigned to ipso carbons. The assignment of the peak at 130.7 ppm to *alpha* in the N(3) ring is done, primarily by comparison to the other I compounds in the present study. Thus, comparing the *alpha* positions in the N(3) ring of Ie, IIe, and IIIe with all other series, the similarities are obvious. It is also fairly clear that the peak at 136.6 ppm should be assigned to R-2 because of the assignments for R-4 in Ic, IIc, and IIIc (also methyl substituted) and comparing with R-2 in Ia, in which the typical 9 ppm downfield effect of direct substitution by methyl is observed. This leaves the peak at 129.5 ppm to be assigned to R-1 by elimination. The position of this peak implies (upon comparing Ia) that methyl substitution at R-2 produces an upfield shift of 0.9 ppm. *Ortho*

substituent effects in toluene are downfield by 0.6 ppm and we are lead to the inescapable conclusion that other effects must be at work here. Nor is this the only assignment which requires disregarding substituent effects in toluene.

Continuing to assign peaks from those in the spectrum, the two peaks at 129.1 and 126.7 ppm are large, indicating that these should be assigned to *gamma* and *beta* in the N(3) ring, respectively. That leaves four small peaks (131.0, 129.6, 128.8, and 128.6 ppm) to be assigned to five unique carbons. However, the large peak at 126.7 ppm is a bit too large to be simply assigned to the *beta* carbons alone. The peak at 126.7 ppm has an area of 7.48 while the peak at 129.1 ppm is only 5.25. The peak at 131.0 ppm assigned to a singlet ring carbon has an area of 2.57 and, added together, the double peak at 129.1 ppm and the single peak at 131.0 ppm combine to give a total area (for 3 carbons) of 7.82. This compares very favorably with the 7.48 area of the peak at 126.7 ppm, lending strong support for placing the fifth single-carbon peak required at that position. Electronic integration was not used here because of the closeness of the peaks and the significant overlap resulting. The peak at 131.0 ppm was chosen as the arch-type single carbon intensity because it is the most isolated peak available and belongs to a carbon having a directly bonded proton.

Thus, it remains to assign *delta* in the N(3) ring, R-3, R-4, R-5, and R-6 to the five unassigned peaks. In these cases, the small differences between peaks leave the assignments ambiguous. The peak at 128.6 ppm is assigned to *delta* of the N(3) ring because it coincides with the unequivocally assigned *delta* peak for the N(3) ring in Ia. The remaining assignments are made as follows: the peaks at 129.6, 128.8, and 126.7 ppm are assigned to R-3, R-4, and R-6, respectively, giving substituent shifts of +0.6, +0.2, and +0.2 ppm, respectively (derived from Ia). These can be compared to the toluene substituent shifts of +0.6, +0.3, and +0.3 ppm, respectively. Finally, the peak at 131.0 ppm is assigned to R-5, *para* to the methyl substituent, even though the substituent shift is +2.0 ppm (derived from Ia) which is exactly opposite to the predicted substituent shift of -0.3 ppm.

In assigning the peaks in the spectra for IIe and IIIe, it is immediately apparent that some peaks must mask others since there are not enough separated resonances to account for all unique carbons. Thus, the very large peak at 128.8 ppm in the spectrum for IIe assumes an importance beyond being the position for the *gamma* carbon in the N(3) ring. By assigning the readily distinguishable peaks based on previously applied rules and by comparison with Ie, all resonances can be assigned as listed in Table I except R-3 and R-4. Measuring the area of the 128.8 ppm peak, it is found to be 21.7. The resonance at

130.5 ppm (comprising a single carbon resonance) has an area of about 5.62. By dividing the area of one by the other the peak at 128.8 ppm is found to represent about 4 carbons. Thus, one is justified in assigning the remaining two single carbon positions to that resonance, those being R-3 and R-4.

Assignments in IIIe can proceed in an entirely equivalent manner as above, including the assignment of R-3 and R-4. However, because the peaks at 128.9 and 129.0 ppm reflect intensities characteristic of two carbons and because they overlap significantly, the assignments given in Table I are ambiguous. Other ambiguous assignments are given in Table I and labeled with parentheses.

Conclusions.

Substitution of a carbonyl oxygen with the electronically equivalent imino nitrogen at C-5 produces an upfield shift, on the average, of 4.7 ppm at that carbon and a downfield shift of 1.5 ppm at the *alpha* carbon of the N(1) ring. Substitution of the carbonyl oxygen with a carbonyl sulfur at C-4 causes a very dramatic downfield shift. The average shift produced by this substitution is 27.3 ppm at

C-4 and 2.24 ppm, 2.26 ppm, and 0.78 ppm at C-5, *alpha* of the N(3) ring, and C-2, respectively.

EXPERIMENTAL

All cmr spectra were obtained from compounds supplied by Professor E. Paul Papadopoulos (Chemistry Department, University of New Mexico) on a Varian XL-100 nmr spectrometer utilizing the gated decoupling capability of the Nicolet TT-100 FT system (5). Samples were dissolved in DMSO and all chemical shifts are reported relative to TMS based on a shift difference of 40.4 ppm between DMSO and TMS. Measurements were made at normal probe temperature (29°) and on saturated samples. Generally, spectral data were gathered under slightly saturating conditions with a pulse angle of about 30° and an interpulse delay of 1.36 s. The sweep width was ± 3000 Hz utilizing the Quadrature Phase Detection method for most spectra.

REFERENCES AND NOTES

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- (3) *Ibid.*, p 68.
- (4) *Ibid.*, p 81.
- (5) An acknowledgment is extended to the NSF (Grant MPS75-06111) for partial support of this work through purchase of the Nicolet TT-100 data acquisition system.