NUCLEAR MAGNETIC RESONANCE AND INFRARED STUDIES OF ACYLATED IMIDAZOLIDINONES AND IMIDAZOLIDINETHIONES[1,2]

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ABSTRACT

The infrared and nuclear magnetic resonance spectra of 1-acyl and 1,3-diacyl derivatives of 2-imidazolidinones and 2-imidazolidinethiones were determined, where the acyl groups were acetyl, benzoyl, or trifluoroacetyl. The frequency of the ring carbonyl stretching vibration increases with the degree of acylation and the electron-withdrawing power of the acyl group. The methylene protons of the diacylated derivatives show a single peak, the paramagnetic shift of which is similarly dependent on these parameters when the ring current effects are allowed for. This correlation between the $\nu_{C=O}$ and τ_{CH_2} favors the conclusion that the anisotropy of the acyl carbonyl group does not affect the relative methylene proton shift in these compounds and hence they all have the same preferred configuration. This was deduced to be the planar *trans,trans* structure with respect to the carbonyls. In the unsymmetrical 1,3-diacyl compounds the methylene protons are also nearly equivalent, the τ-value being the average of those for the symmetrical diacyl derivatives. This, together with the changes in the $\nu_{C=O}$ (acyl), is explained by mesomeric equalization of the electronic environment of nitrogen atoms 1 and 3. The C=S bond is found to have a strong deshielding influence on all protons.

INTRODUCTION

The potentialities of nuclear magnetic resonance (n.m.r.) spectroscopy for assigning structures and conformations in acylated 2-oxo-, 2-thio-, and 2-imino-imidazolidines have not in the past been fully exploited. We have used it to differentiate between the several structures suggested for triacetyl-2-imino-imidazolidine on the basis of its infrared spectrum (1). More recently Roberts (2) has also used n.m.r. to assign a symmetrical structure to diacetyl-2-imidazolidinone. Further aspects of the n.m.r. and infrared spectra of acylated 2-oxo- and 2-thio-imidazolidines will now be discussed.

Mecke *et al.* (3) have examined the infrared spectra of 1,3-dihetero-2-oxo-(or 2-thio-)-cyclopentanes and, in particular, investigated the ring carbonyl stretching vibration. They found that the carbonyl frequency is dependent on the nature of the adjacent atoms by virtue of their mass and their inductive and mesomeric effects, as well as on the ring angle at the carbonyl group. The mesomeric effect leads to an increase in the contribution of the canonical dipolar form $\overset{+}{C}—O^-$ and an increase in the angle, which favor a decrease in the carbonyl frequency. In the present work with compounds where the adjacent atoms are nitrogen, their nature is changed by acylation, thus complementing the work with compounds in which the atoms themselves were varied.

EXPERIMENTAL

The n.m.r. spectra were recorded with a Varian 4300–C spectrometer operating at 60 mc/s. Calibrations were made by the standard side band procedure. Chemical shifts with respect to tetramethylsilane are accurate to better than ±.01 p.p.m. The concentration of the compounds was normally 10% w/v.

A Perkin–Elmer Model 221 spectrophotometer was used to determine the infrared spectra. Solutions were 2% w/v in both chloroform and acetonitrile.

The compounds were prepared as specified below. All commercial samples were purified before use. Melting points are corrected.

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2-Imidazolidinone

A commercial sample obtained from du Pont de Nemour, U.S.A., was recrystallized from alcohol, m.p. 129–131°.

1-Acetyl-2-imidazolidinone

This compound was prepared by warming 2-imidazolidinone with acetic anhydride, m.p. 173–175° (lit. (4) 171.5–173°). The n.m.r. spectrum (D_2O) was analyzed as an A_2B_2 system and gave approximate τ-values of 6.6 and 6.2 for the 4- and 5-methylene protons respectively.

1,3-Diacetyl-2-imidazolidinone

1-Acetyl-2-imidazolidinone was refluxed for 1 h with acetic anhydride to give the diacetyl derivative, m.p. 126–127° (lit.(5) 126.7–127.5°).

1-Trifluoroacetyl-2-imidazolidinone

2-Imidazolidinone (400 mg) was heated under reflux with trifluoroacetic anhydride (2 ml) for 1 h, taken to dryness, and recrystallized from acetone in the form of white prisms, m.p. 166–168°, in 74% yield.

Anal. Calcd. for $C_5H_5O_2N_2F_3$: C, 32.96; H, 2.75; N, 15.38. Found: C, 33.13; H, 2.65; N, 15.46.

1,3-Ditrifluoroacetyl-2-imidazolidinone

2-Imidazolidinone (500 mg) was heated under reflux with trifluoroacetic anhydride (3 ml) for 24 h. Evaporation to dryness and recrystallization from chloroform/acetone gave white prisms, m.p. 123–124°, in 67% yield.

Anal. Calcd. for $C_7H_6O_3N_2F_6$: C, 29.10; H, 1.30; N, 9.72. Found: C, 29.29; H, 1.25; N, 10.03.

1-Acetyl-3-trifluoroacetyl-2-imidazolidinone

1-Acetyl-2-imidazolidinone (350 mg) was heated under reflux for 24 h with trifluoroacetic anhydride (1 ml). After the solution was concentrated, recrystallization of the product twice from ether gave white plates, m.p. 88–89°, in 81% yield.

Anal. Calcd. for $C_7H_7O_3N_2F_3$: C, 37.50; H, 3.12; N, 12.50. Found: C, 37.79; H, 3.15; N, 12.62 (Kjeldahl).

1,3-Dibenzoyl-2-imidazolidinone

2-Imidazolidinone (500 mg) and benzoyl chloride (2.5 ml) were dissolved in pyridine (5 ml) and heated on a steam bath for 30 min. The solid residue from evaporation was extracted with benzene, and removal of the benzene gave a crystalline residue. The product was finally recrystallized from chloroform to give white needles, m.p. 238–239°, in 42% yield.

Anal. Calcd. for $C_{17}H_{14}O_3N_2$: C, 69.40; H, 4.76; N, 9.52. Found: C, 69.80; H, 4.84; N, 9.57.

1-Acetyl-3-benzoyl-2-imidazolidinone

1-Acetyl-2-imidazolidinone (750 mg) and benzoyl chloride (2 ml) were dissolved in pyridine (5 ml) and heated for 45 min on a steam bath. The material that was left after evaporation to dryness was extracted with hot benzene, which was then removed, and the product was recrystallized from ethanol as white needles (61% yield) m.p. 182–184°.

Anal. Calcd. for $C_{12}H_{12}O_3N_2$: C, 62.00; H, 5.17; N, 12.05. Found: C, 62.20; H, 5.16; N, 11.97.

2-Imidazolidinethione

This material was obtained from the Matheson, Coleman, and Bell Co. U.S.A., and was recrystallized from alcohol, m.p. 202–203°.

1-Acetyl-2-imidazolidinethione

This substance was prepared by treating 2-imidazolidinethione with acetyl chloride in glacial acetic acid, m.p. 165–167° (lit. (6) 161–163°). The n.m.r. spectrum ($CHCl_3$) was analyzed as an A_2B_2 system and gave approximate τ values of 6.4 and 5.8 for the 4- and 5-methylene protons respectively.

1,3-Diacetyl-2-imidazolidinethione

2-Imidazolidinethione was refluxed with acetic anhydride, m.p. 87–89° (lit. (6) 85–87°).

1,3-Ditrifluoroacetyl-2-imidazolidinethione

2-Imidazolidinethione (500 mg) was heated under reflux for 5 h with trifluoroacetic anhydride (10 ml). When the solution was cooled crystals appeared, which were recrystallized from benzene to give red prisms, m.p. 142–144°, in 53% yield.

Anal. Calcd. for $C_7H_4O_2N_2SF_6$: C, 28.55; H, 1.36; N, 9.54; S, 10.88. Found: C, 28.68; H, 1.43; N, 9.58; S, 10.63.

RESULTS AND DISCUSSION

A list of the compounds studied in this investigation together with the main absorption bands in the 1 850–1 600 cm^{-1} region of the infrared is given in Table I.

The values found for 2-imidazolidinone and its acylated derivatives differ from those

TABLE I

The infrared absorption of solutions of acylated 2-imidazolidinones and 2-imidazolidinethiones in the region 1 850–1 600 cm^{-1}

	Frequency (cm^{-1})					
	$CHCl_3$			CH_3CN		
2-Imidazolidinone	1 703			1 712		
1-Acetyl-2-imidazolidinone	1 739 (VS)		1 680 (S)	1 741 (VS)		1 680 (S)
1,3-Diacetyl-2-imidazolidinone	1 759 (S)		1 698 (VS)	1 760 (S)		1 702 (VS)
1-Trifluoroacetyl-2-imidazolidinone	1 774 (VS)		1 710 (S)	1 774 (VS)		1 707 (S)
1,3-Ditrifluoroacetyl-2-imidazolidinone	1 810 (S)		1 739 (VS)	1 813 (S)		1 737 (VS)
1-Acetyl-3-trifluoroacetyl-2-imidazolidinone	1 781 (S)	1 722 (VS)	1 710 (Sh)	1 782 (S)	1 724 (VS)	1 709 (S)
1,3-Dibenzoyl-2-imidazolidinone	1 768 (S)		1 679 (VS)			
1-Acetyl-3-benzoyl-2-imidazolidinone	1 765 (S)	1 695 (Sh)	1 685 (VS)			
2-Imidazolidinethione	—	—	—	—	—	—
1-Acetyl-2-imidazolidinethione			1 677			1 681
1,3-Diacetyl-2-imidazolidinethione			1 695			1 692
1,3-Ditrifluoroacetyl-2-imidazolidinethione	1 780 (W)		1 740 (S)			1 720

quoted by Mecke *et al.* (3) and Roberts (2). This is attributed to the fact that the present values were obtained from solution spectra, whereas the other workers used potassium bromide pellets. A similar effect has been noted in this series by Hall and Zbinden (7).

The assignment of the acyl carbonyl vibration, by comparison of the acylated 2-imidazolidinethiones with the acylated 2-imidazolidinones (2), to the lower frequency band is confirmed by the fact that the relative intensity of this band with respect to the one at higher frequency is greater for diacyl than for monoacyl 2-imidazolidinone. The similarity in the frequency of the acyl carbonyl vibration for the acylated imidazolidinones and imidazolidinethiones also excludes the interpretation that the two carbonyl bands in the series of acylated imidazolidinones are due to coupled vibrations, as was suggested for N,N-diacylamines (8) and anhydrides (9). It may be seen from Table I that the frequency of the ring carbonyl is always higher than that of the acyl carbonyl, which agrees with the results obtained from a study of solid phase spectra.

The infrared spectra of 1-acetyl-3-trifluoroacetyl-2-imidazolidinone and 1-acetyl-3-benzoyl-2-imidazolidinone show three carbonyl peaks, which are attributed to the ring carbonyl and the two different acyl carbonyl bonds. It can be seen that the carbonyl frequency of the acetyl group in 1,3-diacetyl-2-imidazolidinone is 1 698 cm^{-1}, and that of the trifluoroacetyl group in 1,3-ditrifluoroacetyl-2-imidazolidinone is 1 739 cm^{-1}. In the mixed derivative, 1-acetyl-3-trifluoroacetyl-2-imidazolidinone, the two acyl carbonyls appear at 1 710 cm^{-1} and 1 722 cm^{-1}. The decrease in the difference between the acetyl and the trifluoroacetyl carbonyl absorption in going from the symmetrical to the mixed diacyl compounds indicates some form of mutual interaction in which there is an equalization of the electron densities on the nitrogen atoms by mesomerism through the ring.

The frequency assigned to the ring carbonyl is seen to increase with the degree of acylation of the molecule and with the electron-withdrawing power of the acyl group. Acylation reduces the availability of the electrons on the nitrogen atom, thus decreasing the mesomeric effect with the ring carbonyl, which results in a higher carbonyl frequency. This is in accord with the conclusions of Mecke *et al.*, who found that as the hetero-atoms in the series of 1,3-dihetero-2-cyclopentanones are changed from oxygen to nitrogen to sulphur, the frequency decreases with increasing mesomeric effect.

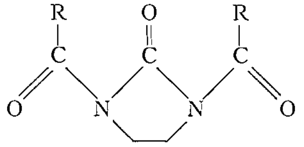
These considerations involving electronic effects may be applied to the interpretation of the n.m.r. results which are shown in Table II.

TABLE II

The τ-values of the methylene and acetyl protons in 2-imidazolidinone, 2-imidazolidinethione, and some of their acyl derivatives

Compound	Solvent	τ	
		—CH_2—	—CH_3
2-Imidazolidinone	D_2O	6.50	
1,3-Diacetyl-2-imidazolidinone	D_2O	6.26	7.62
	$CHCl_3$	6.17	7.47
1-Acetyl-3-trifluoroacetyl-2-imidazolidinone	$CHCl_3$	6.05	7.32
	CCl_4	6.10	7.51
1,3-Ditrifluoroacetyl-2-imidazolidinone	$CHCl_3$	5.93	
1-Acetyl-3-benzoyl-2-imidazolidinone	$CHCl_3$	6.05	7.55
1,3-Dibenzoyl-2-imidazolidinone	$CHCl_3$	5.93	
2-Imidazolidinethione	D_2O	6.32	
1,3-Diacetyl-2-imidazolidinethione	$CHCl_3$	6.00	7.18
1,3-Ditrifluoroacetyl-2-imidazolidinethione	$CHCl_3$	5.74	

The spectra of the methylene protons in the series of diacylated-2-imidazolidinones are singlets, and this is consistent with acylation of the nitrogens. The τ-values decrease in the order, unacylated $>$1,3-diacetyl $>$ 1,3-dibenzoyl = 1,3-ditrifluoroacetyl. The similarity of the last two compounds was unexpected, since the τ-value for the benzoyl derivative would be expected to be nearer that of the acetyl because of the relative strengths of the respective acids. Other factors, however, notably the magnetic anisotropy of the C=O group and the aromatic ring current, affect these τ-values. Following the method of calculation and the suggested values of the anisotropies given by Narasimhan and Rogers (10) for the carbonyl bond, and using interatomic distances from related compounds (11), we calculated that, for the planar configuration I, the side-chain carbonyls decrease the screening of the methylenic protons by about 0.24 p.p.m., and that for configuration II the decrease is 0.10 p.p.m. The ring carbonyl further descreens by 0.04 p.p.m. Because of the partial double bond character of the exocyclic C—N bond, only configurations I and II would be expected to make significant contributions. As the π-electron distribution varies in the series there will, no doubt, be a concomitant variation of the location of the equivalent C$\cdots$O dipole, but the resultant changes in anisotropy are very likely small. If it is assumed that the compounds in the above series have similar configurations, the carbonyl anisotropy is not then a factor in determining the relative shifts of the methylene protons. For the benzoyl derivatives, however, the contribution from the ring current must also be considered. This was calculated from the unsubstituted benzene model by the method of Johnson and Bovey (12) to be -0.29 p.p.m. for configuration I, a value which may produce an overcorrection, but the amended τ-values are now more as expected from electronic effects. Some evidence in support of these assumptions is provided by a correlation which is seen to exist between the τ-value of the methylene protons and the ring carbonyl frequency, which is shown in Table III. This correlation would be expected only if the carbonyl anisotropic contributions are constant and τ and $\nu_{C=O}$ are similarly dependent on electronegativity.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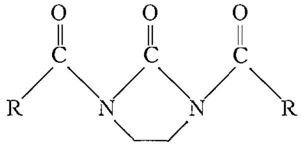
II

TABLE III
Correlation between τ of methylene protons and ring carbonyl frequency in 2-imidazolidinones

	τ	ν (cm^{-1})
2-Imidazolidinone	6.50	1 703
1,3-Diacetyl-2-imidazolidinone	6.17	1 759
1,3-Dibenzoyl-2-imidazolidinone	6.22*	1 768
1-Acetyl-3-trifluoroacetyl-2-imidazolidinone	6.05	1 781
1,3-Ditrifluoroacetyl-2-imidazolidinone	5.93	1 810

*Corrected for ring current effects from aromatic rings.

For 1,3-dibenzoyl-2-imidazolidinone it is possible to utilize the ring current calculations to determine the preferred configuration. In configuration II, the ring current effect (-0.7 p.p.m.), when deducted, would increase the τ of the methylenes to a value higher than that for 2-imidazolidinone. On the other hand, in configuration I the maximum correction (all rings coplanar) is only 0.29 p.p.m., and thus 1,3-dibenzoyl-2-imidazolidinone is mainly in this configuration.

The mixed 1,3-diacyl compounds give methylene proton spectra which are, surprisingly, almost A_4 ($J/\delta \sim 10$) and have τ-values which are the means of those of the respective unmixed diacyl compounds. Assuming certain configurations in the unmixed derivatives, the approximation to A_4 character can be calculated for a number of configurations of the mixed derivatives. The averaging of the τ-values indicates, however, that the overriding effect operating here is the equalization of the electron densities on the nitrogens via the urea moiety of the ring. Evidence for this effect has already been mentioned in connection with the infrared results. This equalization of the electron density allows an independent means of deducing the configuration of the acyl groups. If it is assumed that there is complete equalization of the shift contribution from the electron density, then, because the methylene protons are virtually an A_4 system, it follows that the anisotropy contributions are also equal, and that consequently the acyl groups have the same configuration.

A residual inequality of 0.12 p.p.m. (from the ring current effect) in the shift of the methylene protons is calculated for 1-acetyl-3-benzoyl-2-imidazolidinone when the simple model is used. This model treats the carbonyl and the benzene ring as independent systems and assumes a planar molecule. Although this is probably incorrect in the present case, these crude ring current calculations show that the benzoyl group has a preference for the *trans*- rather than the *cis*-configuration with respect to the ring carbonyl, since in the *cis*-structure the calculated methylenic proton non-equivalence is 0.3 p.p.m., which is unlikely to disappear even in an improved model. In addition the planar *trans*-configuration I exhibits some steric interaction between the ring carbonyl oxygen and an ortho aromatic proton.* This will most likely result in a twisting of the benzene ring out of the plane of the imidazolidine ring. Hence the ring current effect and the residual inequality will now be decreased. The preference of the *trans*-configuration might be expected, since in the *cis*-configuration there would be considerable carbonyl dipole–dipole interaction, which is virtually absent in the *trans*-form. This argument, which supports the conclusions from the dibenzoyl derivative, implies that all the other diacyl compounds will assume preferentially the *trans*-configuration since no steric factors are involved.

A striking result, which is apparent from Table II, is that in all the 2-imidazolidinethiones the methylene protons are deshielded by approximately the same amount, 0.18 p.p.m., from their counterparts in the 2-imidazolidinones. The acetyl protons are also quite strongly deshielded. This would not be expected on the basis of electronegativity considerations although similar descreening effects have been observed before when C=S replaces C=O (13). The reason for this behavior probably lies in the utilization of the sulphur d-orbitals in the C=S bond. This would markedly change the pattern and values of the magnetic anisotropy from that of the C=O bond. Since the ring carbonyl anisotropy only descreens the methylene protons by 0.04 p.p.m.,† a quite large effect is necessary to explain 0.18 p.p.m. The even larger effect on the methyl protons may be considered as supporting evidence for the supposition that the acetyl C=O group is located in the *trans*-configuration relative to the ring C=O or C=S, as this would reduce the distance of the methyl group from the anisotropic center.

In conclusion it may be pointed out that unlike the diacylated imidazolidinones, the

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†This value may be different if the magnetic anisotropies given in the recent paper by Hooper and Kaiser (14) are used. However, the argument remains unaffected.

monoacyl-imidazolidinones and imidazolidinethiones give well pronounced but not quite symmetrical A_2B_2-like spectra for the methylene protons. Although this is in agreement with the N-acyl structure, it is not conclusive evidence for it.

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REFERENCES

1. R. Greenhalgh and R. A. B. Bannard. Can. J. Chem. **39**, 1017 (1961).
2. J. G. Roberts. J. Chem. Soc. 176 (1964).
3. R. Mecke, R. Mecke, and A. Lüttringhaus. Chem. Ber. **90**, 975 (1957).
4. H. K. Hall and A. K. Schneider. J. Am. Chem. Soc. **80**, 6409 (1958).
5. M. N. Kirkwood and G. F. Wright. J. Am. Chem. Soc. **76**, 1836 (1954).
6. J. E. Baer and R. G. Lockwood. J. Am. Chem. Soc. **76**, 1162 (1954).
7. H. K. Hall and R. Zbinden. J. Am. Chem. Soc. **80**, 6428 (1958).
8. R. A. Abramovitch. J. Chem. Soc. 1413 (1957).
9. L. J. Bellamy, B. R. Connelly, A. R. Philpotts, and R. L. Williams. Z. Elektrochem. **64**, 563 (1960).
10. P. T. Narasimhan and M. T. Rogers. J. Phys. Chem. **63**, 1388 (1959).
11. Chemical Society. Interatomic distances. Special Publication. No. 11. London. 1958.
12. C. E. Johnson and F. A. Bovey. J. Chem. Phys. **29**, 1012 (1958).
13. I. D. Rae. Private communication.
14. D. L. Hooper and R. Kaiser. Can. J. Chem. **43**, 2363 (1965).