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^{13}C NMR Chemical Shifts, in some *N*-Chloro-2,6-diarylpiperidin-4-ones

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The ^{13}C shifts in several *N*-chloro-2,6-diarylpiperidin-4-ones have been measured and compared with previously reported sifts in the corresponding 2,6-diarylpiperidones. The shifts of the α-carbons in these compounds move downfield by 12–13 ppm, which can be attributed to the increased electronegativity of the nitrogen atoms. The changes in the chemical shifts of the β-carbons are minimal. Surprisingly, the absorptions of the carbonyl carbons move upfield by as much as 4.0 ppm. The magnitude of the shift in the resonance of the carbonyl carbon indicates the possibility of a transannular interaction between the nitrogen and the carbonyl group, which has not previously been observed in these systems. A preferred conformation for the aryl group in these compounds is also proposed.

KEY WORDS ^{13}C NMR N-chloro-2,6-diarylpiperidin-4-ones

INTRODUCTION

Although ^{13}C NMR chemical shifts in several 1-heterocyclohexan-4-one system[1-4] have been found to depend on the nature of the heteroatom, their explanation based on the electronegativity of the heteroatom has been neither straightforward nor adequate. In general, it is observed that the chemical shifts of the carbons α to the heteroatom are moved significantly downfield in comparison with the corresponding cyclohexan-4-one compounds. The downfield shift has been successfully related to the electronegativity of the hetero atom. The chemical shifts of the carbonyl carbon are, however, observed to move significantly upfield, instead of the expected downfield. Although several explanations have been given to justify these upfield shifts, none of them is entirely satisfactory or applicable in all cases. The possibilities of through-space electrostatic effects,[2,3,5] hyperconjugative interactions[6] and transannular interactions[7] between the heteroatom and the carbonyl carbon have been suggested. In order to understand the exact nature of these interactions we have measured the ^{13}C shifts in several *N*-chloro-2,6-diarylpiperidin-4-ones and compared them with those in the corresponding 2,6-diarylpiperidin-4-ones. These differences illustrate the effect of changing an NH to an NCl group on the chemical shift of the heterocyclic ring carbons. Attaching a chlorine atom is expected to increase the electronegativity of nitrogen in these compounds, and the chemical shift of the α-carbon is therefore expected to move significantly downfield.

The conformations of the aryl rings and of the heterocyclic ring can also be established on the basis of their ^{13}C chemical shifts.

Previously we have examined the conformations and ^{13}C NMR spectra of several 2,6-diarylpiperidin-4-ones.[1] In this paper, the ^{13}C chemical shifts of several *N*-chloro-2,6-diarylpiperidin-4-ones are presented and their electronic and steric intractions are discussed. The preferred conformations of the aryl groups (aryl = phenyl, *o*-chlorophenyl) are also proposed.

EXPERIMENTAL

Compounds **1**-**5** were prepared by the known procedure[8] of passing chlorine through the corresponding 2,6-diarylpiperidin-4-ones. In each case the reaction product was recrystallized from ethanol. The melting points of the products were identical with those reported in the literature[8] (**1** = 137-38 °C); **2** = 144-145 °C; **3** = 138-139 °C; **4** = 143-144 °C; **5** = 131-132 °C). Compounds **6**-**9** were prepared by a similar procedure. Recrystallization of the crude products from ethanol provided pure **6**, **7**, **8** and **9** melting at 163-164, 154-155, 185-186 and 133-134 °C, respectively. The elemental analyses of these compounds were consistent with their empirical formulae. Proton decoupled ^{13}C NMR spectra were recorded on a Varian XL-200 NMR spectrometer operating at 50.3 MHz and using 10 mm sample tubes. Solutions for the measurement of the spectra were prepared by dissolving 0.5 g of the sample in 12.5 ml of chloroform-*d* containing a few drops of tetramethylsilane (TMS) as an internal reference. The chloroform-*d* solvent also provided the internal field-frequency lock signal. The experimental parameters were spectral width 11 000 Hz, 32 000 data points, pulse width 6 μs (18 μs = 90°) and 5000 transients.

RESULTS AND DISCUSSION

The ^{13}C chemical shifts of the *N*-chloro-2,6-diarylpiperidin-4-ones are given in Table 1. The chlorine substituent parameters obtained by comparing the shifts in

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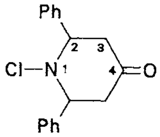
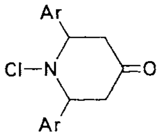
Table ^{13}C **chemical shifts of the heterocyclic ring carbons and of the alkyl substituents in some *N*-chloro-2,6-diarylpiperidin-4-ones (ppm) and their differences from the corresponding 2,6-diarylpiperidin-4-ones**[a]

			C-2	C-3	C-4	C-5	C-6	Alkyl
1			74.1	50.6	204.0			
		Δ	+13.1	+0.4	−3.8			
2	3-Methyl		80.8	51.6	205.5	50.7	74.5	11.5
		Δ	+12.4	0.0	−4.0	−0.2	+13.0	+1.4
3	3,5-Dimethyl		81.2	51.5	207.0			11.7
		Δ	+12.4	−0.5	−4.1			+1.2
4	3,3-Dimethyl		82.0	51.3	209.0	47.5	74.8	22.1, 20.9
		Δ	+12.5	+1.5	−3.8	+0.3	+13.2	+1.7, +0.9
5	3-Ethyl		79.0	57.9	205.2	51.2	74.6	19.1 (CH_2), 11.7(CH_3)
		Δ	+12.3	−0.5	−3.9	−0.3	+12.9	+1.3, −0.9
6			70.3	49.5	203.7			
		Δ	+13.9	+1.7	−3.3			
7	3-Methyl		74.2	52.2	204.5	48.5	69.7	10.4
		Δ	+12.1	+0.6	−4.0	+0.2	+12.8	+0.8
8	3,5-Dimethyl		74.7	52.1	206.5			10.6
		Δ	+12.3	+0.2	−3.7			+0.6
9	3,3-Dimethyl		75.4	52.3	208.0	45.1	70.2	21.3, 21.0
		Δ	+12.4	+1.5	−3.7	+0.5	+13.2	+0.9, +1.0

[a] Δ=*N*-Chloropiperidinone−corresponding piperidinone. Ar=*o*-chlorophenyl.

these compounds with those in the corresponding 2,6-diarylpiperidin-4-ones are also included.

α-Carbons

The chemical shifts of the *α*-carbons (C-2,6) in these compounds are in the range 70–82 ppm. These shifts are 12–13 ppm downfield in comparison with those of the corresponding 2,6-diarylpiperidin-4-ones. This is to be expected as changing the NH to an NCl group is expected to increase the electronegativity of the nitrogen atom. The deshielding of the *α*-carbons has previously been shown to depend on the electronegativity of the heteroatom. Thus, for example, the ^{13}C shifts in a series of 1-heterocyclohexan-4-ones, with various heteroatoms such as NH, O, NCH_3, $NCOCH_3$, $NCOOC_2H_5$, $NCOC_6H_5$, SO and SO_2, were examined by Hirsch and Havinga.[4] Among the O, N and S heterocyclics, the chemical shift of the *α*-carbon moved downfield in the order O > N > S, which seems rational on the basis of the electronegativity of these heteroatoms.

β-Carbons

The chemical shifts of the *β*-carbons (C-3, C-5) are not significantly affected by the change in electronegativity of the heteroatom. In these compounds even the direction of the shift is not the same. Thus, replacement of a hydrogen by chlorine on the nitrogen causes an upfield shift of 0.2–0.5 ppm in some compounds but a downfield shift of 0.2–1.7 ppm in others. We have observed that when only one of the *β*-carbons (C-3) is substituted by an alkyl group, such as in **2**, **4**, **5**, **7** and **9**, the substituted carbon (C-3) is affected to a greater extent than the unsubstituted carbon (C-5), except in the case of **2**.

γ-Carbon

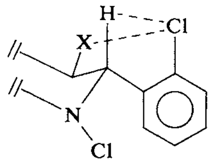
The chemical shift of the *γ*-carbon (C-4) is in the range of 204–209 ppm. When compared with the shifts in the corresponding amino compounds, the chlorine substituent causes an upfield shift of 3.3–4.0 ppm for the carbonyl carbon. A shielding of 1–2 ppm for the carbonyl group has been previously reported for several similar systems.[2] Although several possible explanations have been put forward, the cause of this upfield shift in these systems is still a subject of controversy. The shielding of the carbonyl carbon has been related to the electronegativity of the heteroatom.[2] A through-space electrostatic field effect has been invoked by Dutch[5] for 4-piperidinone systems and by Jones and Hassan[3] for hydrochloride and methiodide salts of *N*-methylpiperidin-4-ones. This electrostatic field model has been rejected by Elliel *et al.*[6] because of the observed dependence of the upfield shift on the position of the heteroatom in the Periodic Table and not on the heteroatom electronegativity. They therefore proposed a hyperconjugative type of interaction of free electron pairs centred on second-row heteroatoms with the C-*α*—C-*β* bond, accompanied by a subsequent alteration of the electron density at the *γ*-antiperiplanar carbon. The absorption of the carbonyl carbon, which is in a *γ*-antiperiplanar conformation, is therefore expected to move upfield as observed. A third explanation based on transannular interactions between the heteroatom and the carbonyl carbon should also be considered. A transannular lone pair electron donation from the heteroatom to the carbonyl carbon has been proposed by Hirsch and Jarmas[7] in 1-thiacyclohexan-3-one and 1-thiacyclohexane-4-one systems. Similarly, Nakashima and Maciel[11] have provided evidence for transannular electron donation from the heteroatom to the carbonyl group in 5-heteroacyclooctanones. The carbonyl shifts in these compounds moved upfield by 1.5–4.0 ppm in comparison with the corresponding cyclooctanones.

On the basis of the observed upfield shifts of approximately 4.0 ppm for the carbonyl carbon, it is possible that transannular interactions are partly responsible for its shielding in these compounds.

Methyl Carbons

The resonances for the methyl carbons in these compounds together with their differences from the corresponding NH compounds are shown in Table 1. The methyl shifts, in general, are downfield by 0.6–1.7 ppm. The exact cause of this deshielding is not clear, but it is possible that the increased electronegativity of the NCl in comparison with the NH group is responsible. The downfield shifts are, in general, greater in the phenyl-substituted compounds **1**–**5**.

The methyl carbon shifts in compounds which bear an *o*-chlorophenyl group at C-2 (C-6) are upfield by approximately 1.3 ppm in comparison with compounds which bear a phenyl group at this position. This can be easily explained on the basis of our previously proposed conformation[1] for the aryl ring in these compounds. In this preferred conformation, the phenyl group lies parallel to the axial hydrogen at C-2 such that the chlorine substituent is now *syn* to the hydrogen at C-2, as shown below. This causes steric interactions between the chlorine and the C-3 methyl group.



The conformation proposed by us is reasonable since, although the aryl group can have fast rotation it has already been shown by theoretical calculations[12] that an equatorial phenyl group in phenylcyclohexane prefers to lie parallel to the axial hydrogen at C-1.

The study of ^{13}C NMR shifts in *N*-chloro-2,6-diarylpiperidin-4-ones has thus provided an insight into the conformation and electronic interactions in these molecules.

REFERENCES

1. M. U. Hasan, M. Arab, K. Pandia Rajan, P. Sekar and D. Marko, *Magn. Reson. Chem.* **23**, 292 (1985)
2. K. Rasmalingam, K. D. Berlin, N. Satyamurthy and R. Sivakumar, *J. Org. Chem.* **44**, 471 (1979).
3. A. J. Jones and M. A. Hassan, *J. Org. Chem.* **37**, 2332 (1972).
4. J. A. Hirsch and E. Havinga, *J. Org. Chem.* **41**, 455 (1976).
5. M. W. Dutch, Dissertation, University of Utah (1970); *Diss. Abstr. Int. B* **31**, 1200 (1970).
6. E. L. Eliel, W. F. Baily, L. D. Kopp, R. L. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, M. W. Duch, E. Wenkert, F. M. Schell and D. W. Cockran, *J. Am. Chem. Soc.* **97**, 322 (1975).
7. J. A. Hirsch and A. A. Jarmas, *J. Org. Chem.* **43**, 4106 (1978).
8. K. Ganepathy and B. Vijayan, *J. Indian Chem. Soc.* **60**, 572 (1983).
9. J. B. Lambert, D. A. Netzel, H. Sun and K. K. Lilianstrom, *J. Am. Chem. Soc.* **98**, 3778 (1976).
10. J. A. Pople and M. Gordon, *J. Am. Chem. Soc.* **89**, 4253 (1967).
11. T. T. Nakashima and G. E. Maciel, *Org. Magn. Reson.* **4**, 321 (1972).
12. N. L. Allinger and M. T. Tribble, *Tetrahedron Lett.* 3259 (1971).