

Carbon-13 Chemical Shifts and ^{13}C — ^{15}N Coupling Constants of 3,4-Dihydroisoquinoline- ^{15}N , its ^{15}N -Oxide and their Conjugate Acids

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Abstract—On protonation of 3,4-dihydroisoquinoline- ^{15}N $^1J(^{13}\text{C}-1, ^{15}\text{N})$ is increased by a factor of five and $^1J(^{13}\text{C}-3, ^{15}\text{N})$ changes its sign, while on protonation of 3,4-dihydroisoquinoline- ^{15}N -oxide the coupling constants, including the relatively large $^1J(^{13}\text{C}-1, ^{15}\text{N})$, remain practically constant, although significant alterations of the ^{13}C chemical shifts take place.

RECENTLY, the range of known ^{13}C — ^{15}N coupling constants has been extended considerably by $^1J(^{13}\text{C}, ^{15}\text{N})$ in 2,4,6-trimethylbenzotrile oxide, which was found to be 77.5 Hz.¹ In search of further extreme values we have measured the ^{13}C NMR spectra of 3,4-dihydroisoquinoline- ^{15}N (1), its ^{15}N -oxide (3) and their conjugate acids (2) and (4). The results are shown in Table 1.

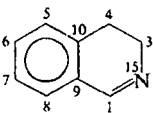
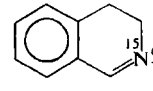
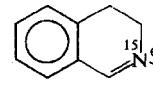
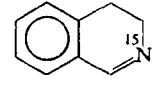
In the aromatic ring of 1 the carbons were characterised on the basis of the similar chemical shifts in isoquinoline,^{2,3} 1.2 ppm being the maximum deviation. Addition of trifluoroacetic acid in an amount insufficient for complete protonation generated a rapid equilibrium between 1 and 2, as indicated by the observation of only one set of slightly broadened carbon signals. Running the spectrum at different acid concentrations allowed the correlation of the assignments in 1 and 2 by following the movement of the signals. As compared to 1, in 2 six carbons absorb at lower field by 2.4 to 8.9 ppm. Only the effects at C-1, C-10, C-6 and C-8 are easily explained, because the positive charge can be localised at these

centres. Highfield shifts of carbon signals on protonation of a nitrogen lone pair, such as the effects at C-3 (−4.4 ppm) and C-9 (−3.7 ppm), have been observed repeatedly.^{4–7} Several approaches to a theoretical understanding have been attempted.^{5,7,8}

In 1 the one bond ^{13}C — ^{15}N coupling constant of C-1 (2.9 Hz) is smaller than those of other aldehyde imines.^{9–11} On stepwise addition of acid this parameter increased steadily to 15.6 Hz, corresponding to the increasing 2 concentration. In contrast, $^1J(^{13}\text{C}-3, ^{15}\text{N})$ decreased to zero at first and on further acidification finally reached a value of 5.9 Hz. Thus, $^1J(^{13}\text{C}-3, ^{15}\text{N})$ changes its sign on formation of 2 from 1.

Compared to protonation, exactly the opposite situation is effected by the addition of an oxygen to the nitrogen in the formal transformation of 1 to 3, as seen from the upfield shifts of most of the signals. One lone pair of the oxygen can enhance the electron density at C-1, C-10, C-6 and C-8. The relatively large effect at C-1 (−27.0 ppm) has to be compared with −81.8 ppm, found as the chemical shift difference between the two *sp*-hybridised carbons of trimethylbenzotrile and its N-oxide.¹ Having rotational symmetry, the nitrile oxide group possesses two π -electron systems perpendicular to each other. Therefore, two resonance formulae localising

TABLE 1. CARBON-13 CHEMICAL SHIFTS^a AND ^{13}C — ^{15}N COUPLING CONSTANTS^b OF 3,4-DIHYDROISOQUINOLINE- ^{15}N (1), 3,4-DIHYDROISOQUINOLINE- ^{15}N -OXIDE (3) AND THEIR CONJUGATE ACIDS (2) AND (4)

Compound	No. Parameter	C-1	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
	(1) $\delta(^{13}\text{C})^c$ $J(^{13}\text{C}, ^{15}\text{N})^c$	159.8 2.9	47.3 3.4	25.0 †	126.9 ^d †	130.8 ^e †	127.3 ^d †	126.9 ^e †	128.4 ~2	136.2 †
	(2) $\delta(^{13}\text{C})^{g,h}$ $J(^{13}\text{C}, ^{15}\text{N})^†$	167.7 15.6	42.9 5.9	25.0 †	129.6 ^d †	139.7 ^e †	130.0 ^d †	135.5 ^e ~1.5	124.7 †	138.6 ~2
	(3) $\delta(^{13}\text{C})^c$ $J(^{13}\text{C}, ^{15}\text{N})^c$	132.8 21.5	57.6 7.8	27.2 †	126.7 ^d †	128.6 ^e †	127.0 ^d †	124.8 ^e 3.4	128.2 †	129.7 2.4
	(4) $\delta(^{13}\text{C})^{g,j}$ $J(^{13}\text{C}, ^{15}\text{N})^{†,j}$	154.3 20.5	54.1 6.8	27.1 †	129.5 †	138.0 ^e †	129.5 †	133.6 ^e 3.9	123.8 †	134.9 2.4

^a In ppm downfield from internal TMS. ^b Absolute values in Hz, accurate to ± 0.5 Hz. ^c CDCl_3 solution. ^{d,e} Assignments may be exchanged. ^f < 1 Hz. ^g In $\text{D}_2\text{O}/\text{DCl}$ solution taken from the unlabelled compounds relative to internal tetramethylammonium chloride and corrected to TMS as external reference by the relation $\delta_{\text{TMS}} = \delta_{\text{N}(\text{CH}_3)_4} + 56.7$ ppm. ^h In $\text{DCCl}_3/\text{CF}_3\text{COOH}$ solution the chemical shifts are further upfield by 0.2 to 1.3 ppm. ⁱ $\text{CDCl}_3/\text{CF}_3\text{COOH}$ solution. ^j In $\text{CDCl}_3/\text{CF}_3\text{COOH}$ solution probably too small an amount of CF_3COOH has been added for complete protonation, as indicated by $\delta(\text{C}-1) = 147.5$ ppm. However, this should have only little impact upon the ^{13}C — ^{15}N coupling constants.

negative charge at the *sp*-hybridised carbon contribute to the ground state, thus justifying the much larger upfield shift. If it is protonated as in **4**, the oxygen of the nitron system has lost its electron donor ability. The protonation shifts of **3** are very similar to those of **1**; only the downfield shift of C-1 (21.5 ppm) being surprisingly high.

As expected on the basis of the situation in trimethylbenzonitrile oxide, $^1J(^{13}\text{C}-1, ^{15}\text{N})$ in **3** proved to be considerably larger than in **1**.¹ On stepwise addition of trifluoroacetic acid the $^{13}\text{C}-^{15}\text{N}$ coupling constants of **3** underwent only very small changes of magnitude; consequently they have the same sign as in **4**.

It should be noted that, although somewhat smaller, the coupling constants in **2** are comparable to those in **3** and **4**, while those of **1** deviate considerably. This is shown by the small values of C-1, C-8 and C-10 especially, and by the measurable size of $^2J(^{13}\text{C}-9, ^{15}\text{N})$ which could not be resolved in **2** to **4**. This fact, together with the results obtained from pyridine,^{11,12} quinoline^{6,11} and nitriles,^{1,11} shows that nitrogen atoms with a lone pair have much smaller reduced one bond coupling constants to neighbouring carbons than comparable carbons. Blocking of the lone pair either by a proton or by an oxygen leads to a dramatic increase of this parameter. Glycine and alanine¹² as well as quinuclidine and 1-propylamine¹³ reveal only relatively small alterations of $^1J(^{13}\text{C}, ^{15}\text{N})$ on protonation. Possibly a sign change takes place, as in the case of $^1J(^{13}\text{C}-3, ^{15}\text{N})$ in the conversion of **1** to **2**.

EXPERIMENTAL

Starting with ammonium- ^{15}N chloride (95% isotopic purity), 3,4-dihydroisoquinoline- ^{15}N (**1**)¹⁴ and therefrom 3,4-dihydroisoquinoline- ^{15}N -oxide (**3**)¹⁵ were prepared according to literature

procedures. The pulse Fourier transform spectra were obtained on a Bruker HX-90 spectrometer.

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