

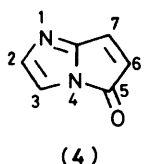
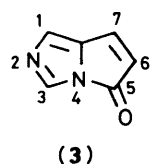
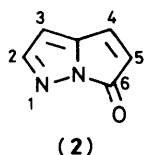
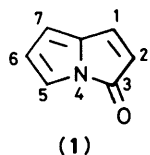
An Analysis of the N.M.R. Spectra (^1H , ^{13}C , and, in part ^{15}N and ^{17}O) of Pyrrolizin-3-one, and of its Aza-derivatives Pyrrolo[1,2-*c*]imidazol-5-one, Pyrrolo[1,2-*a*]imidazol-5-one and Pyrrolo[1,2-*b*]pyrazol-6-one

Hamish McNab

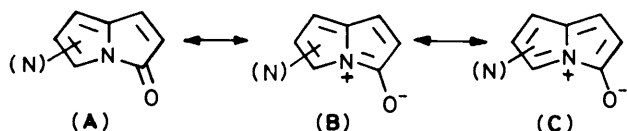
Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh, EH9 3JJ

The ^1H and ^{13}C n.m.r. parameters (chemical shifts and coupling constants) of the title compounds (1)–(4) are assigned unambiguously, and are compared with those of monocyclic model compounds. The picture of the conjugation which emerges—and which is in general supported by ^{15}N and ^{17}O n.m.r. studies of (1)—is indicative of some amide-like interaction between the ring-junction nitrogen atom and the carbonyl group, but there is no evidence for cyclic delocalisation of the resulting 8π -electron system.

Much of the interest in the pyrrolizin-3-one system^{1,2} (1) and its aza-analogues³ pyrrolo[1,2-*b*]pyrazol-6-one (2), pyrrolo[1,2-*c*]imidazol-5-one (3) and pyrrolo[1,2-*a*]imidazol-5-one (4) stems from the possible involvement of the bridgehead nitrogen lone pair in amide-type resonance, which gives rise to formally counter-Hückel canonical forms (Scheme 1). As a probe of the conjugation in these materials we now report a detailed analysis of their ^1H and ^{13}C n.m.r. spectra, which includes the unambiguous assignment of each resonance, and of the magnitude of their proton–proton and carbon–proton coupling constants. In addition, we have obtained ^{15}N and ^{17}O n.m.r. spectra of pyrrolizin-3-one (1), and correlate the observed chemical shifts with those of some simple model compounds.

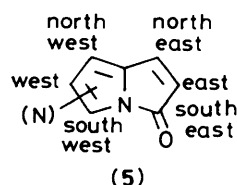


A major problem in describing the molecules (1)–(4) is that the systematic numbering system produces different labels for structurally related sites. A trivial approach, in which the various sites are labelling with the points of the compass, as in (5), is therefore adopted in this paper.



Scheme 1.

^1H N.m.r. Assignments.—The ^1H n.m.r. spectrum of pyrrolizin-3-one (1) in carbon disulphide² or ^2H chloroform is confused by the accidental equivalence of the 'west' and 'north-west' protons, even at 360 MHz, with the associated virtual coupling⁴ of the 'north-west' and 'south-west' protons.



However, in $^2\text{H}_6$ benzene solution, association of the solvent molecules causes shielding effects, particularly over the 'north-west,' 'north-east,' and 'east' portion of the molecule (Figure 1) and allows resolution of the 'west' and 'north-west' protons. Under these conditions, and with resolution enhancement, the spectrum appears as three doublets of doublets (δ 5.23, 5.56, and 6.35), one doublet with apparent triplet fine structure (δ 6.64) and one triplet with doublet fine structure (δ 5.65). The latter is clearly due to the 'west' proton coupled to the 'north-west' and 'south-west' protons which therefore give rise to the resonances at δ_{H} 5.56 and 6.64 ($^3J_{\text{HH}}$ 3.0 Hz): these could be assigned unambiguously (Figure 1) by ^1H – ^{13}C correlation, utilising the known large $^1J_{\text{CH}}$ values for α -positions in pyrroles (see below). The remaining peaks (δ 6.35 and 5.23), with a much larger vicinal coupling ($^3J_{\text{HH}}$ 5.8 Hz) are characteristic of the protons in the enone system ('north-east' and 'east' respectively) (*cf.* Figure 1). Other couplings were assigned by conventional decoupling experiments (Figure 2).

Assignment of the four-spin systems (2) and (3) was straightforward. The characteristic enone system was little changed from pyrrolizin-3-one (1) itself and the more deshielded of the remaining peaks, which was generally broad, was placed adjacent to the additional heteroatom ['west' in (2) and 'south-west' in (3)]. This was subsequently confirmed by proton–carbon correlation (see below). Unfortunately, these techniques could not be used to distinguish the corresponding protons in (4) ('west' and 'south-west' δ_{H} 6.96 and 7.03), both of which lie adjacent to a heteroatom. These were eventually differentiated by correlation of long-range ^1H – ^{13}C couplings. Thus, low-power irradiation at δ_{H} 6.96 caused collapse of the *minor* coupling at the 'south-west' carbon atom resonance in the ^{13}C n.m.r. spectrum, which could be identified unambiguously (see below). Hence the peak at δ 6.96 in the proton spectrum must be due to the 'west' proton. Similarly, the 'west' carbon atom was shown to couple (2J 10.4 Hz) to the proton at δ 7.03, which is accordingly assigned as the 'south-west' proton.

^{13}C N.m.r. Assignments.—Recognition of the signals due to the carbonyl and the bridgehead quaternary carbon atoms was possible by inspection, the former always occurring at >160 p.p.m. The remaining peaks of compounds (2) and (3) were all

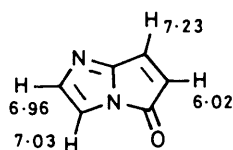
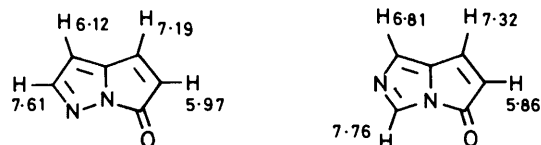
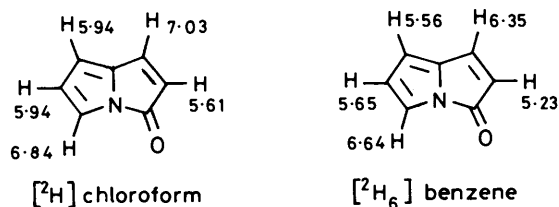
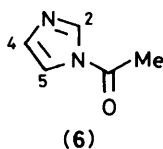
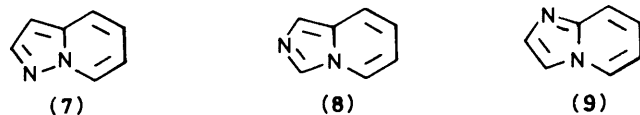


Figure 1. ¹H N.m.r. chemical shifts of compounds (1)–(4)

assigned by specific decoupling of each previously assigned proton resonance, using a moderately high decoupling power level in the DEPT pulse sequence. Similar experiments with (1) and (4) served to distinguish all peaks except the 'west' and 'north-west' carbon atoms of (1) and the 'west' and 'south-west'



carbon atoms of (4) whose corresponding protons were too close together for differentiation at the power levels required for specific ¹J_{CH} decoupling. In (4), the two positions involved have



dramatically different chemical shifts (δ_C 134.93 and 114.12), reminiscent of the shifts of the 4- and 5-positions of 1-acetyl-imidazole (6)⁵ and the 'west' and 'south-west' positions of 1,4-diazaindene (9)⁶ (δ_C 130.5, 115.9 and δ_C 134.04, 113.41 respectively), and so assignment can be made by analogy. By way of confirmation, the relative magnitudes of the one-bond and long-range carbon-proton couplings in (4) match with those of corresponding positions in (6).⁵

Differentiation of the resonances due to the 'west' and 'north-west' carbon atoms of (1) (δ_C 115.43 and 111.14) was possible by correlation of long-range carbon-proton couplings. Low power irradiation at δ_H 5.56 ('north-west' proton) caused collapse of one of the *minor* couplings at δ_C 115.43, and so these cannot be directly attached. Similar irradiation at δ_H 5.65 ('west' proton) affects the carbon resonance at δ_C 111.14 which is accordingly due to the 'north-west' carbon atom.

The assignments of ¹³C n.m.r. chemical shifts and one bond coupling constants, are given in Figure 3. Long range coupling

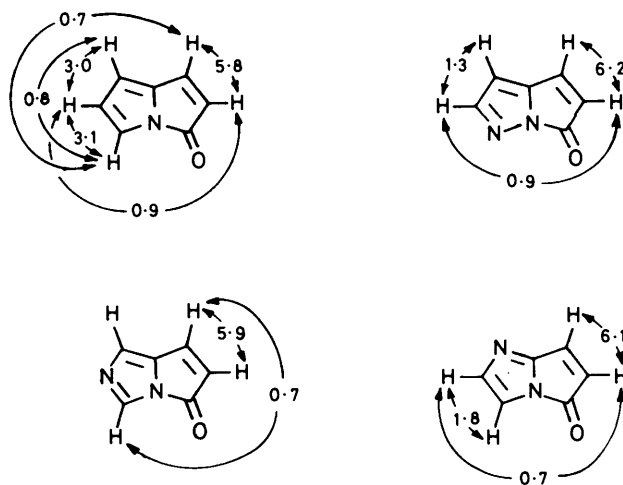


Figure 2. ¹H N.m.r. coupling constants (Hz) of compounds (1)–(4)

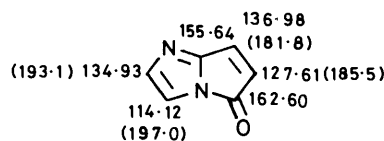
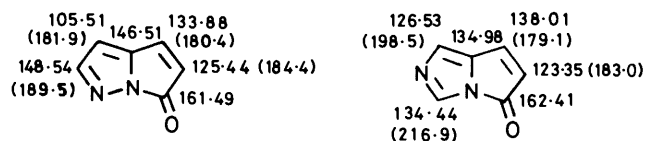
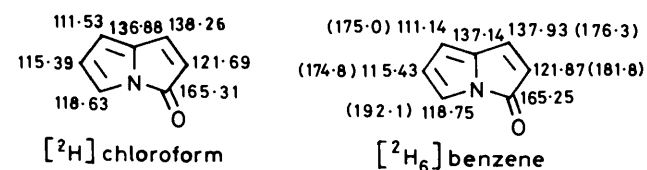


Figure 3. ¹³C N.m.r. chemical shifts and ¹J_{CH} (Hz) (in parentheses) of compounds (1)–(4)

constants were identified by specific lower power ¹H decoupling as described above and are given in Figure 4. Except for the case of compound (1) there was generally insufficient material for specific assignment of the long-range couplings to the carbonyl carbon atom, and so these were made by analogy with (1). The signals due to the ring junction quaternary carbon atoms in the fully coupled ¹³C n.m.r. spectra were broad and complex, and no attempt was made to resolve them.

Discussion.—The ¹H n.m.r. parameters of the entire 'west' ring of compounds (1)–(4) are closely similar to those of monocyclic model compounds. In particular, the 'north-west' and 'south-west' positions show little effect of the adjacent ring. This is well illustrated for pyrrolizin-3-one itself, for which the two pyrrole β -positions ('west' and 'north-west') have identical chemical shifts in [2H]chloroform. However, in all cases, there is a small but consistent *shielding* effect of the resonances [(1) relative to *N*-acetylpyrrole;⁷ (2) relative to *N*-carboxamidopyrrole;⁸ (3) and (4) relative to *N*-acetylimidazole (6)⁹]. These shifts are in the *opposite* direction to those expected from the

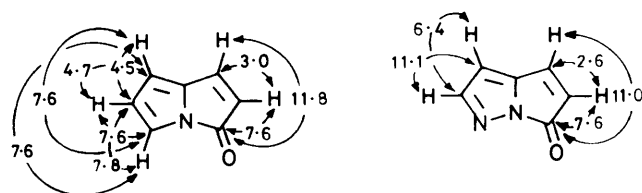


Figure 4. Long range ${}^nJ_{\text{CH}}$ (Hz) of compounds (1)–(4)

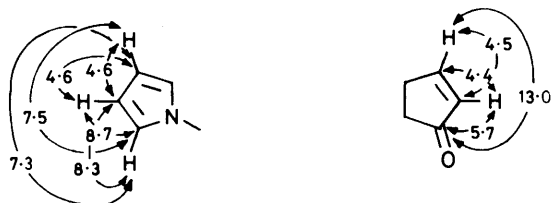
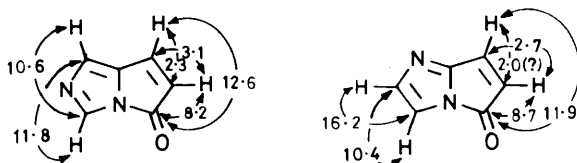


Figure 5. Selected long range ${}^nJ_{\text{CH}}$ (Hz) of pyrrole¹³ and cyclopentenone¹⁵

increase in positive charge due to contribution of the resonance structures of Scheme 1 though they may be indicative of a small paramagnetic ring current. Within experimental error, the ${}^1\text{H}$ – ${}^1\text{H}$ coupling constants are of similar magnitude to those of simple heterocycles, though the absence of a significant ${}^4J_{\text{north-west}, \text{south-west}}$ in (3) is surprising (${}^4J_{2,4}$ in (6) is 0.8 Hz⁸). Some cross-ring couplings are present, noticeably ${}^6J_{\text{north-east}, \text{south-west}}$ (ca. 0.7 Hz), which is not always observable, and ${}^6J_{\text{east}, \text{west}}$ (ca. 0.8 Hz), which is always present, and which is a characteristic of conjugated fused five-membered ring systems with a nitrogen atom at the ring junction.¹⁰ The conjugation in the 'east' ring as a whole is scarcely influenced by the fused heterocycle. Although the chemical shift separation of the enone proton resonances are rather less than in cyclopentenone itself [cyclopentenone, $\Delta\delta$ 1.61 p.p.m.;¹¹ (1)–(4), $\Delta\delta$ 1.2–1.5 p.p.m.] the effect is much more pronounced in the ${}^{13}\text{C}$ n.m.r. spectra (see below). The vicinal coupling constant ${}^3J_{\text{east}, \text{north-east}}$ is ca. 6 Hz, which is a typical value for five-membered ring enones.¹²

These features are also reflected in the ${}^{13}\text{C}$ n.m.r. spectra. The chemical shifts of the entire 'west' ring positions in (2)–(4) follow the same trends as simple mono-heterocycles, and also those of the azaindolizines (7)–(9) respectively,⁶ though in some cases the absolute values of the chemical shifts differ significantly. As has been noted above for *N*-acetylimidazole the pattern of ${}^1\text{H}$ – ${}^{13}\text{C}$ couplings is remarkably constant, and extends even to parent, unsubstituted analogues. For comparison, the data for pyrrole itself are displayed in Figure 5.¹³ The complete absence of cross-ring proton–carbon couplings in (1)–(4) is also noteworthy. The chemical shifts of the enone methine carbon atom signals are less strongly polarised than is normal for cyclic enones [e.g. cyclopentenone $\Delta\delta > 30$ p.p.m.;¹⁴ (1)–(4) $\Delta\delta$ 8–17 p.p.m.], while the carbonyl carbon resonance appears in the amide rather than in the ketone region¹⁴ [e.g. cyclopentenone $\delta_{\text{C}}(\text{CO})$ 208.1; $\delta_{\text{C}}(\text{amide})$ ca. 160–170; $\delta_{\text{C}}[\text{CO};$ (1)–(4)] 161–165 p.p.m.]. These features suggest significant

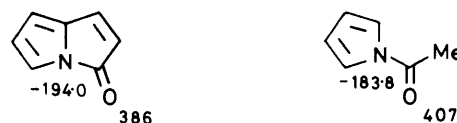
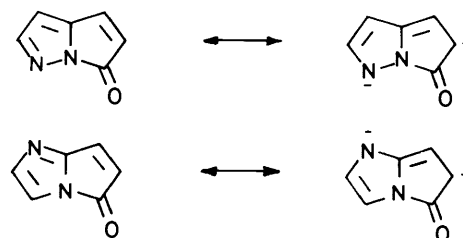


Figure 6. ${}^{15}\text{N}$ and ${}^{17}\text{O}$ n.m.r. chemical shifts of compound (1) and *N*-acetylpyrrole

influence of resonance structure B (Scheme 1), which is not compounded by further delocalisation (as in C). With the exception of ${}^2J_{\text{south-east}, \text{east}}$, which is abnormally large in the present series, coupling constants in the 'east' ring as a whole follow similar trends to other cyclic enones¹⁵ (Figure 5), and are effectively independent of the 'west' ring.

Although the interpretation of these spectra strongly suggests that the two rings behave independently, save for some *N*-carbonyl interaction, it is clear from the u.v. spectra³ that there must be some more deep-seated inter-ring effects. This is perhaps reflected in the relatively small influence on the ${}^1\text{H}$ and ${}^{13}\text{C}$ n.m.r. chemical shifts of the 'east' atoms which is observed, on variation of the position of the aza-nitrogen atom in (2)–(4). In each case, the chemical shift of the 'east' position is deshielded relative to (1), but the effect is most pronounced for (2) and (4) in which conventional pyridine-type resonance structures can be drawn with charge located on the heteroatom (Scheme 2).



Scheme 2.

${}^{15}\text{N}$ and ${}^{17}\text{O}$ N.m.r. Spectra of Pyrrolizin-3-one (1).—The conclusions of the previous section, that the (aza)pyrrolizinones (1)–(4) behave as *N*-acylazoles, with little participation of the 'north-east'–'east' double bond, are fully corroborated by the ${}^{15}\text{N}$ and ${}^{17}\text{O}$ spectra of pyrrolizin-3-one (1) itself. Its chemical shifts are shown in Figure 6, along with those of *N*-acetylpyrrole, which was chosen as a representative model compound. Lone pair delocalisation tends to deshield the nitrogen nucleus¹⁶ (cf. pyrrole, δ_{N} ca. –234.5; ¹⁷ *N*-acetylpyrrole, δ_{N} –183.8 p.p.m.) and so any increased effect due to conjugation in (1) (Scheme 1) should result in a further shift to high frequency. The observed shift—to low frequency—[δ_{N} (1) –194.0] may indicate some reduced lone pair involvement due to competitive enone-type conjugation, but the effect is small.

Relatively little work on ${}^{17}\text{O}$ n.m.r. spectra has been published, but it is known that there is a ca. 300 p.p.m. chemical shift difference between the signals for simple ketones and simple amides (e.g. acetone, δ_{O} 572;¹⁸ acetamide, δ_{O} 286,¹⁸ 313.5 p.p.m.¹⁹). Ketone shifts are relatively insensitive to conjugation (e.g. methyl vinyl ketone, δ_{O} 561 p.p.m.¹⁹), though substitution in amides may cause substantial effects (e.g. *N,N*-dimethylacetamide, δ_{O} 324 p.p.m.¹⁸). The chemical shifts of pyrrolizin-3-one (1) and *N*-acetylpyrrole (Figure 6) are almost within experimental error of one another (line width ca. 8 p.p.m.) and are significantly deshielded from normal amide resonances, reflecting the competition of the heterocycle with the carbonyl group for the lone pair of the nitrogen atom. This trend towards ketonic character is much more apparent in the i.r. spectra^{2,3} but the ${}^{17}\text{O}$ n.m.r. seems better to reflect the chemical properties of the carbonyl group.²⁰

Experimental

The ^1H (200 MHz) and ^{13}C (50 MHz) spectra were obtained with a Bruker WP 200 SY instrument, while the ^{15}N (36.5 MHz) and ^{17}O (48.8 MHz) were recorded with a Bruker WH 360 instrument; both spectrometers employed Aspect 2000 data systems. For the ^1H n.m.r. spectra, resolution enhancement was carried out where appropriate: the digital resolution was 0.27 Hz. The digital resolution in the ^{13}C n.m.r. spectra was generally 1.4 Hz, and so the error limits for the values given in Figures 3 and 4 are ± 0.7 Hz. Chromium tris(acetylacetonate) was used as the relaxation reagent for ^{15}N n.m.r. spectra, which are reported relative to nitromethane (external). The ^{17}O n.m.r. spectra are reported relative to H_2O (external): the linewidth at half-height was ca. 400 Hz. All spectra were recorded for solutions in $[\text{H}^2]\text{chloroform}$ except for ^1H and ^{13}C spectra of pyrrolizin-3-one (**1**), where $[\text{H}_6^2]\text{benzene}$ was used. In all cases, the spectra could be analysed on a first-order basis.

Acknowledgements

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