Heterocyclic Mesomeric Betaines. Part 3.[1] Synthesis and Base-catalysed Exchange Reactions of N-Methyl-5H-pyrrolo[1,2-c]imidazolium Iodide

**W. David Ollis** * and **Stephen P. Stanforth**
Department of Chemistry, The University, Sheffield, S3 7HF, England
Christopher A. Ramsden
The Research Laboratories, May and Baker Ltd., Dagenham, Essex, England

Methylation of 5H-pyrrolo[1,2-c]imidazole (10) with methyl iodide gave N-methyl-5H-pyrrolo[1,2-c]imidazolium iodide (11). This salt underwent an unusual base-catalysed exchange of deuterium for hydrogen *via* a transient dipolar intermediate (9a; Scheme 2). This dipolar intermediate (9a) was trapped with dimethyl acetylenedicarboxylate giving a 2:1 adduct (21).

Conjugated heterocyclic mesomeric betaines which are isoconjugate with the pentalenyl dianion have been described as heteropentalenes.[2-6] Four types of heteropentalene mesomeric betaines have been recognised and designated as types A, B, C, and D[2,3] (Scheme 1). The allocation of heteropentalene
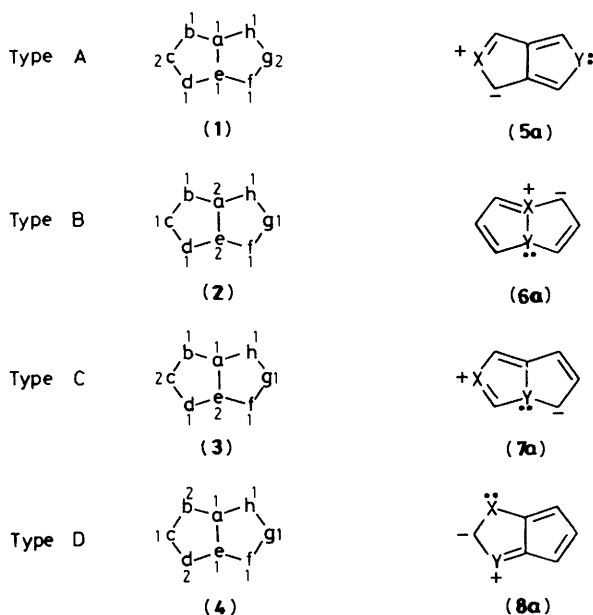
mesomeric betaines to one of these types is dependent upon the relative location of the two heteroatoms which each formally contribute two electrons to the π-molecular orbitals. Types A, B, C, and D have the general formulae (1)—(4), where a—h represent suitably substituted carbon or heteroatoms. The superscripts indicate the number of p-electrons contributed to the π-orbitals by each atom. The structures (5)—(8) depict generalised examples of these heteropentalene mesomeric betaines where X and Y represent heteroatoms.[2,3] The investigation now reported is associated with the examination of a new type C system.

The first example of a type C heteropentalene was described in 1976 by Potts and Marshall.[7] Subsequently other systems have been described.[8-21] We now describe our work directed towards the synthesis of the novel type C heteropentalene (9).

5H-Pyrrolo[1,2-c]imidazole (10) was prepared from imidazole-4-carbaldehyde by the method described by Antonini, Franchetti, Grifantini, and Martelli.[22] The [1]H n.m.r. spectrum

Scheme 1.
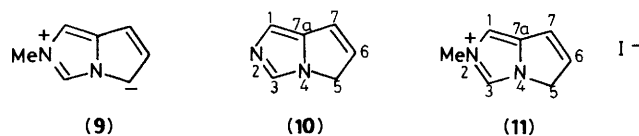
of this molecule (10) exhibits two singlets (δ 6.78 and 7.65) for 1-H and 3-H and an ABX$_2$ system for protons 5-H$_2$, 6-H, and 7-H. Protons 6-H and 7-H were observed as the AB component of the ABX$_2$ system (δ$_A$ 6.52 and δ$_B$ 6.18, J_{AB} 6 Hz, J_{AX} 2 Hz, and J_{BX} 2 Hz): the two protons, 5-H$_2$ (δ$_X$ 4.39) were observed as the X$_2$ component. When compound (10) was treated with methyl iodide, N-methyl-5H-pyrrolo[1,2-c]imidazolium iodide (11) (91% yield) was formed. The empirical formula (C$_7$H$_9$IN$_2$) of compound (11) was established. The [1]H n.m.r. spectrum (CD$_3$OD) of compound (11) showed two singlets, 1-H (δ 7.47) and 3-H (δ 9.11), one singlet for the N-methyl group (δ 4.01) and one singlet for the two protons, 5-H$_2$ (δ 5.06). Surprisingly, the protons 6-H and 7-H were observed as a 2 H singlet (δ 6.82). The coincidental chemical shifts of the protons 6-H and 7-H, and the zero coupling constants between these protons and the two protons, 5-H$_2$, was unexpected. When the [1]H n.m.r. spectrum was redetermined in CD$_3$OD–[2H$_5$]nitrobenzene (*ca.* 1:1) solution, a narrow multiplet (δ 6.75—6.90) was observed for the protons 6-H and 7-H and a multiplet for the two protons, 5-H$_2$ (δ 5.13). The [13]C n.m.r. spectrum (CD$_3$OD) of compound (11) was also unusual in that only six of the seven expected signals were observed. This was attributed to the coincidental chemical shift of atoms C-6 and C-7 (δ 137.2). A low intensity signal (δ 134.3) was assigned to carbon atom C-7a and signals at δ 55.7 and 37.3 were attributed to the atom C-5 and the methyl carbon, respectively. The two remaining signals were assigned to atoms C-1 (δ 113.0) and C-3 (δ 119.7). These assignments were confirmed by off-centre double resonance techniques.

When a solution of the quaternary iodide (11) in CD$_3$OD was treated with sodium [2H$_3$]methoxide (*ca.* 0.18 equiv.) in a [1]H n.m.r. tube, no signals that could be associated with the conjugated heterocyclic mesomeric betaine (9) were observed. However, partial exchange of deuterium for hydrogen at positions 3, 5, and 7 in compound (11) was noted (Table 1). Exchange at positions 3, 5, and 7 was incomplete after 24 h. When an additional amount of sodium [2H$_3$]methoxide solution (*ca.* 0.72 equiv.) was then added and the spectrum redetermined, the following degrees of exchange were apparent: 1-H, 0%; 3-H, >90%; 5-H$_2$, >90%; 6-H, 0%; and 7-H, >90%. Only one of the protons 6-H or 7-H is exchanged for deuterium because the intensity of the singlet signal associated with these two protons decreased by 50%. When a similar experiment was monitored by [13]C n.m.r. spectroscopy using off-centre double resonance, the results were complementary to those described

above. It was firmly established that deuterium for hydrogen exchange did not occur at positions 1 and 6 (Table 2).

If the conjugated heterocyclic mesomeric betaine (9), with its implied delocalisation, was an intermediate in the base-catalysed deuterium for hydrogen exchange, then exchange of the four hydrogen atoms at positions 1, 3, 5, and 7 would have been expected. This is not observed. Exchange occurs only at positions 3, 5, and 7. The absence of exchange at position 1 could, in principle, be associated with low electron density in position 1 in the conjugated heterocyclic mesomeric betaine (9). This rationalisation (pathway A; Scheme 2) cannot be firmly excluded. However, we much prefer an alternative rationalisation involving pathway B (Scheme 2).

Our preference (pathway B; Scheme 2) is best represented as involving the dipolar structure (9a), in which the 6π-imidazolium grouping is positively charged and aromatic. The corresponding negative charge is associated with a delocalised 4π-allylic carbanionoid system. The structure (9a) is, therefore, associated with a high degree of mesomeric stabilisation. We now consider the mechanism of deuteriation. We propose that the base-catalysed exchange of deuterium for hydrogen at positions 5 and 7 in the compound (11) involves the dipolar intermediate (9a) (pathway B; Scheme 2).

A close analogy is provided by the base-catalysed exchange of deuterium for hydrogen of indene (13) in which the base-catalysed exchange is limited to positions 1 and 3.[23-26] This is clearly a consequence of the retention of 6π-aromatic character by the benzene ring and a separate 4π-allylic carbanionoid system (14). This explains why base-catalysed exchange does not involve the benzene ring of indene (13).

It is well known that imidazolium (15), thiazolium (16), and oxazolium (17) cations undergo base-catalysed exchange of deuterium for hydrogen at position 2.[27-31] The corresponding σ-ylides (18)—(20) have been postulated as intermediates in these exchange processes.[32-34] A different exchange process involving an addition–elimination mechanism has been proposed for the thiazolium cation (16),[35] but a subsequent communication argues persuasively against this mechanism.[36] We believe that the exchange process at position 3 in compound (11) involves the σ-ylide (12).

With this pathway (pathway B; Scheme 2) for the exchange of deuterium for hydrogen at positions 3, 5, and 7 in compound (11), it is possible from the [13]C n.m.r. spectrum of compound
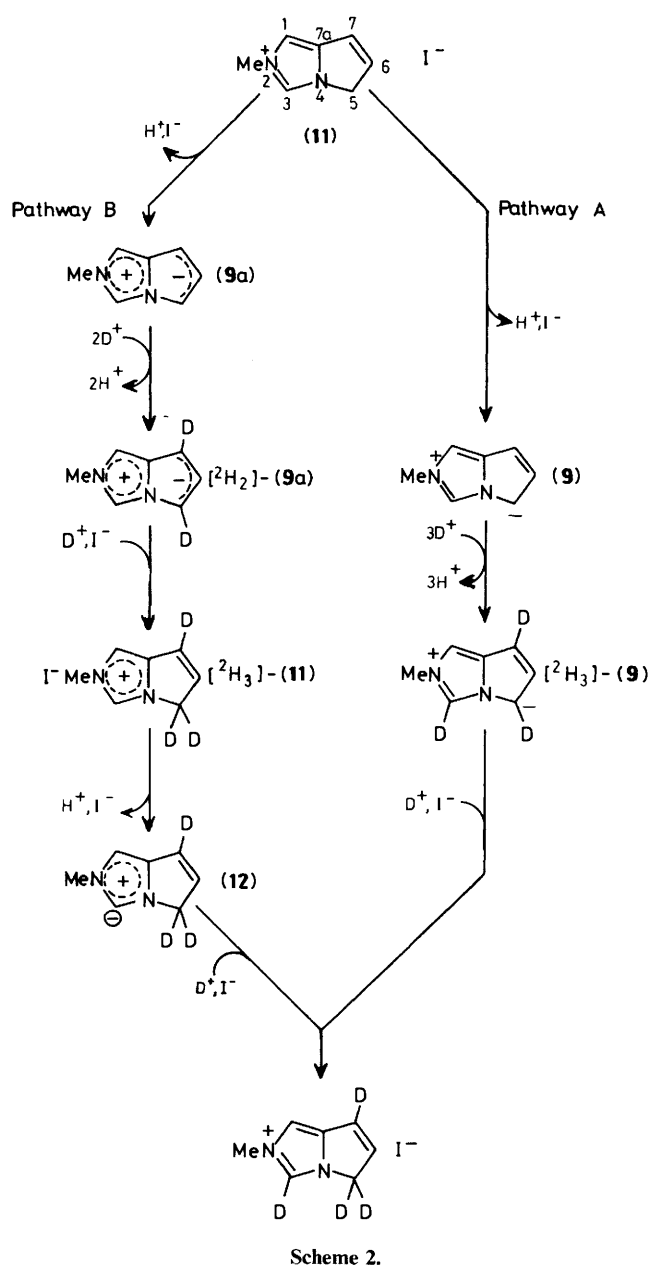

Scheme 2.

(11) to assign the chemical shifts of the carbon atoms C-1 and C-3 unambiguously. 1-H Is not expected to undergo exchange with deuterium so, after the exchange process has taken place, the carbon atom C-1 is expected to be observed as a doublet in the off-centre double resonance spectrum. This was observed experimentally.

Further evidence that the dipolar structure (9a) is generated as a transient intermediate by treatment of compound (11) with

Table 1. The exchange of hydrogen for deuterium in N-methyl-5H-pyrrolo[1,2-c]imidazolium iodide (11). Monitored by [1]H n.m.r. spectroscopy

| Time | Percentage incorporation of deuterium at position[a] | | | |
	1-H	3-H	5-H	6-H + 7-H
ca. 2 min	0	25	34	12
20 min	0	89	50	19
24 h	0	>90	85	30
24 h[b]	0	>90	>90	50

[a] Determined by integration with an accuracy of ± 15%; [b] After addition of further 0.72 equivalents of sodium [2H3]methoxide.

Table 2. The exchange of hydrogen for deuterium in N-methyl-5H-pyrrolo[1,2,-c]imidazolium iodide (11). Monitored by [13]C n.m.r. spectroscopy

| | Multiplicity of signals associated with chemical shift (δ)[a] | | | | | |
Conditions	113.0 (C-1)	119.7 (C-3)	55.7 (C-5)	137.2 (C-6 and C-7)	134.3 (C-7a)	37.3 (CH3)
Before addition of base	d	d	t	d	s	q
After (22 days) addition of base	d	b	b	b	b	q

[a] s = singlet, d = doublet, t = triplet, q = quartet; [b] This signal had broadened and could not be observed above the noise level.
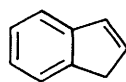
(13)
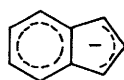
(14)

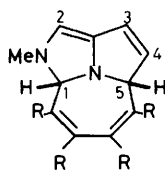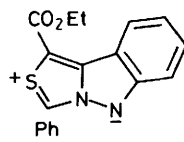(15) X = NR
(16) X = S
(17) X = O

(18) X = NR
(19) X = S
(20) X = O

base has been provided by a trapping experiment. Compound (11) and dimethyl acetylenedicarboxylate with an excess of methanolic sodium methoxide at 0 °C yielded the 2:1 cycloadduct (21) (10% yield).

A similar 2:1 cycloadduct is produced by the reaction of dimethyl acetylenedicarboxylate with the type C hetero-pentalene (22).[7]

(21) R = CO₂Me

(22)

Experimental

General experimental directions are given in Part 1.[37]

N-Methyl-5H-pyrrolo[1,2-c]imidazolium Iodide (11).—To a solution of 5H-pyrrolo[1,2-c]imidazole (10) (1.17 g)[22] [δ 7.65 (1 H, s, 3-H), 6.78 (1 H, s, 1-H), 6.34 (2 H, ABX₂ system, δ_A 6.52 and δ_B 6.18, J_AB 6 Hz, J_AX 2 Hz, and J_BX 2 Hz) and 4.39 (2 H, m, ABX₂ system, J_AX 2 Hz and J_BX 2 Hz)] in methyl acetate (12 ml) was added methyl iodide (1.0 ml). A yellow precipitate immediately formed. The mixture was kept overnight (nitrogen atmosphere) and the yellow solid was then collected giving the title compound (11) (2.52 g, 91%). Recrystallisation from acetonitrile–ether gave tan prisms, m.p. 132—136 °C (Found: C, 34.0; H, 3.6; I, 51.1; N, 11.0. C₇H₉IN₂ requires C, 33.9; H, 3.7; I, 51.2; N, 11.3%); ν_max.(KBr) 1 565, 1 530, 1 320, 1 140, and 770 cm⁻¹; δ(CD₃OD) 9.11 (1 H, s, 3-H), 7.47 (1 H, s, 1-H), 6.82 (2 H, s, 7-H and 6-H), 5.06 (2 H, s, 5-H), and 4.01 (3 H, s, CH₃); δ(CD₃OD-[²H₅]nitrobenzene, ca. 1:1) 9.22 (1 H, s, 3-H), 7.47 (1 H, s, 1-H), 6.75—6.90 (2 H, m, 7-H and 6-H), 5.13 (2 H, m, 5-H), and 4.16 (3 H, s, CH₃); δ_C(CD₃OD) 137.2 (C-6 and C-7), 134.3 (C-7a), 119.7 (C-3), 113.0 (C-1), 55.7 (C-5), and 37.3 (CH₃).

Tetramethyl 4a,8a-Dihydro-1-methyl-1H-1,8b-diazacyclo-pent[cd]azulene-5,6,7,8-tetracarboxylate (21).—To a cooled (0 °C), stirred solution of N-methyl-5H-pyrrolo[1,2-c]imi-dazolium iodide (11) (0.44 g) and dimethyl acetylenedi-carboxylate (0.80 ml) in dry methanol (7 ml) was added (5 min) sodium methoxide solution (1.1 ml) [prepared from sodium (0.20 g) and dry methanol (5 ml)]. The deep red mixture was then stirred (45 min). After evaporation, the residue was purified by preparative thick layer chromatography (silica gel; ether). The yellow band (R_F 0.4—0.5) was collected giving a yellow oil which on trituration with di-isopropyl ether gave a solid.

Recrystallisation from ethanol–ether gave the title compound (21) (68 mg, 10%) as pale yellow plates, m.p. 136—139 °C (Found: C, 56.5; H, 5.2; N, 6.8%; M⁺˙, 404. C₁₉H₂₀N₂O₈ requires C, 56.4; H, 5.0; N, 6.9%; M, 404); ν_max. 1 720br; δ(C₆D₆) 9.66 (1 H, br s, 5-H), 6.61 (1 H, dd, J 4 and 3 Hz, 3-H or 4-H), 6.57 (1 H, s, 1-H or 2-H), 6.35 (1 H, s, 1-H or 2-H), 5.94 (1 H, dd, J 4 and 3 Hz, 3-H or 4-H), 3.82 (3 H, s, OCH₃), 3.52 (3 H, s, OCH₃), 3.46 (3 H, s, OCH₃), 3.32 (3 H, s, OCH₃), and 2.58 (3 H, s, NCH₃).

Base-catalysed Exchange of Hydrogen for Deuterium in N-Methyl-5H-pyrrolo[1,2-c]imidazolium Iodide (11).—Monitored by ¹H n.m.r. spectroscopy. To a solution of N-methyl-5H-pyrrolo[1,2-c]imidazolium iodide (11) in [²H₄]methanol (0.5 ml) was added sodium [²H₃]methoxide solution (0.18 equiv.) [prepared from sodium (30 mg) and [²H₄]methanol (0.25 ml)]. The ¹H n.m.r. spectrum was determined at various time intervals and the results are summarised in Table 1. After 24 h a further portion (0.72 equiv.) of sodium [²H₃]methoxide was added and the spectrum redetermined. With time, the mixture slowly turned brown and after 4 days the spectrum was dominated by decomposition products.

Monitored by ¹³C n.m.r. spectroscopy. To a solution of N-methyl-5H-pyrrolo[1,2-c]imidazolium iodide (11) in [²H₄]-methanol was added sodium [²H₃]methoxide solution (0.1 equiv.). The ¹³C n.m.r. spectrum of the mixture was monitored until the exchange process was complete (ca. 22 days). The off-centre double resonance spectrum was then determined. The results are summarised in Table 2.

Acknowledgements

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