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# Mass Spectrometry of Onium Compounds. Part XXXI.* Methiodides of Cyclopentenyl- and Cyclopentadienylpyridines

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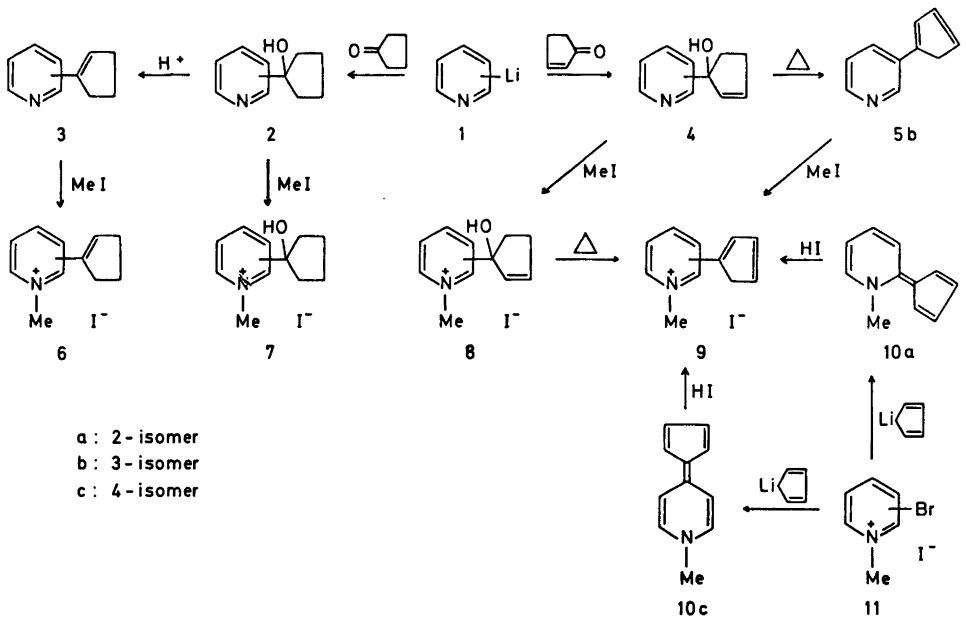
The 2-, 3-, and 4-isomers of 1′-cyclopentenyl-, 1′-hydroxy-2′-cyclopentenyl- and 1′,3′(4′)-cyclopentadienylpyridine methiodides have been synthesised and investigated by mass spectrometry. Pyrolytic demethylation before evaporation varied with the degree of unsaturation in the five-membered ring and with its position in the pyridine ring. Deprotonation of the 2- and 4-isomers yielded the volatile anhydro-bases which in the 1′-hydroxycyclopentenyl series also involves dehydration. The 3-isomers were partially reduced to dihydropyridines before evaporation. The structure analyses of the gaseous species are based on comparative fragmentation studies and on comparisons of ionisation and appearance potentials.

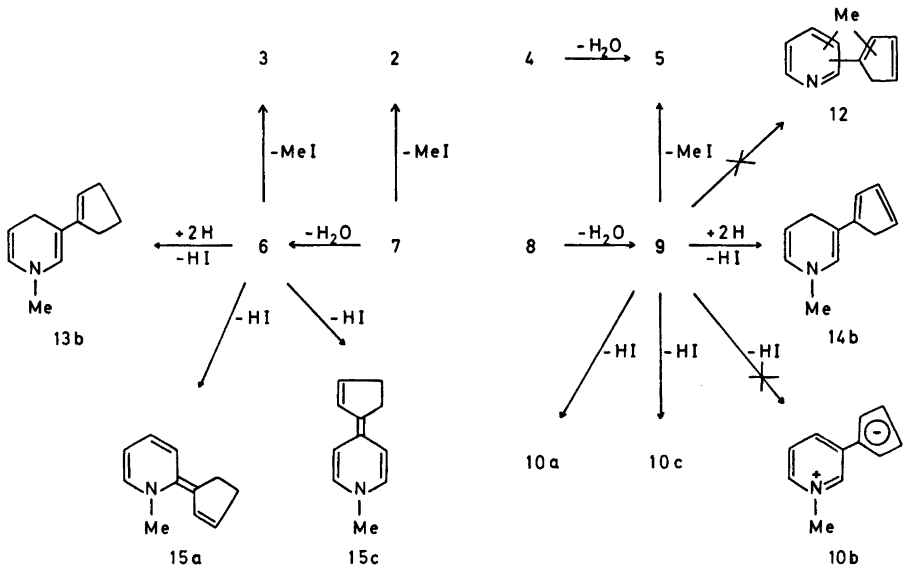
Elimination and dealkylation reactions are common pyrolytic reactions of quaternary ammonium salts in the mass spectrometer.[2] In recent investigations one and two electron reductions of aromatic and heteroaromatic onium systems have been demonstrated.[3] Valence isomerisation and skeletal rearrangements have been demonstrated in labile systems.[1] Stable betaines such as simple pyridinium-3-olates, however, are evaporated in the mass spectrometer without isomerisations to non-charged molecules.[4–6] Their conjugated acids, the 3-hydroxypyridinium salts, are largely dissociated into the pyridine betaine and the acid before evaporation.[6] By analogy to well-established behaviour in solution chemistry, anhydro-base formation may be an important pyrolytic process in heteroaromatic onium systems when the activated side-chain carries a hydrogen atom on the α-carbon atom.[3,7] Thus, the methiodides of the methyl 2- and 4-pyridylacetates furnished the respective volatile anhydro-bases in the mass spectrometer while the 3-isomer suffered a redox process to volatile dihydropyridines.[7] In the work reported herein we have investigated pyrolytic reactions in the mass spectrometer of pyridine methiodides with cyclopentenyl and cyclopentadienyl side-chains.

*Syntheses.* The desired methiodides or trideuteriomethiodides were prepared from the pyridines *2* – *4* and *5b* by reaction with methyl iodide or its trideuterio analogue. The cyclopentadienyl anhydro-bases *10a* and *10c* were prepared from the methiodide of the respective bromopyridine *11* and cyclopentadienyllithium;[8] protonation of *10a* and *10c* by HI yielded the corresponding conjugated acids *9*. Treatment of the unstable 3-cyclopentadienylpyridine *5b* with methyl iodide gave *9b*. The cyclopentenylpyridines *3* were prepared by acid dehydration of *2* [9,10] which were available from cyclopentanone and the respective pyridyllithium isomers. Similarly, the pyridyllithium isomers were reacted with 2-cyclopentenone to yield *4b* and *4c* as reported [8] for *4a*. The dehydration of *4b* was difficult to effect preparatively because the product (*5b*) was sensitive to polymerisation in the presence of acid or base, and *5b* was best obtained by pyrolysis of *4b* in purified sea sand at reduced pressure. The $^1$H NMR spectrum ($CDCl_3$) showed that *5b* consisted mainly of the two cyclopentadienyl tautomers conjugated with the pyridine ring since the spectrum contained two methylene proton signals at $\delta$ 3.2 and 3.4 in the ratio 3:1 and no methine proton signal from the unconjugated isomer was seen. Similar tautomeric mixtures exist in the conjugated acids *9a* and

* Part XXX, see Ref. 1.




*Scheme 1.* Syntheses of pyridine methiodides.




*Scheme 2.* Thermal reactions in the mass spectrometer. Only one of the conjugated tautomers is shown for *12*, *13b*, *14b* and *15a*.

*9c*.[8] Thus, in the 2-isomer formed on protonation of the anhydro-base *10a* in trifluoroacetic acid (TFA) this is also apparent by the two different methyl proton signals at $\delta$ 4.3 and 4.4. Similarly the $^1$H NMR spectrum in methanol-$d_4$ of the methiodide *9b*, which was prepared by methylation of *5b*, contained two methyl proton signals at $\delta$ 4.4 and 4.5.

*Mass spectrometry*. The methiodides were introduced directly into the ionisation chamber of the mass spectrometer. The spectra are sensitive to experimental conditions in accordance with pyrolytic transformations and consist of superimposed electron-impact induced fragmentation patterns of the pyrolytic gaseous species. The analyses are based on comparisons with the fragmentation patterns of the parent pyridines (Table 1) and on comparisons of appearance (AP) and ionisation (IP) potentials.

The spectrum of the cyclopentadienyl derivative *5b* has the molecular ion (*m/e* 143) as base peak. The hydroxy isomers *4* also have the base peak at *m/e* 143 [M − $H_2O$]. Pyrolytic dehydration of *4* to form *5* before ionisation was demonstrated by changes in the operating temperatures at 14 and 70 eV and was most pronounced when the indirect insertion system was used.

By analogy the involatile methiodides *8a* and *8c* were partially dehydrated and deprotonated before evaporation as the anhydro-bases *10a* and *10c* (*m/e* 157); in the trideuteriomethiodide analogues the molecular ion was at *m/e* 160. Pyrolysis is also supported by the fragmentation patterns which were compared with those of *10a* and *10c* (Table 1), and by the AP values (*m/e* 157) 6.6 and 6.7 eV which are in good agreement with the IP values 6.45 and 6.53 eV for the anhydro-bases *10a* and *10c*. The AP values further exclude transfer of the methyl group into the cyclopentadienyl system or into another pyridine position, since the resultant isomer (*12*, Scheme 2) would be expected to have AP value similar to the IP value (8.40 eV) of *5b*. The methiodides *9a* and *9c* were similarly converted to the anhydro-bases *10a* and *10c*, respectively, before evaporation.

The relative intensities of the *m/e* 143 species in the spectra from *8a* and *8c* were 100 and 15 %, respectively; the latter isomer has *m/e* 157 as base peak. The *m/e* 143 species corresponds to dehydration and demethylation to the cyclopentadienyl pyridines *5a* and *5c*; the spectra also contain the appropriate *m/e* 142 peak (high resolution) for methyl iodide. The value (8.30 eV) for the *m/e* 143 species from the 2-isomer (*8a*) is close to the IP value (8.40 eV) of the 3-cyclopentadienylpyridine *5b* which supports pyrolytic formation of *5a* since previous work has shown only small variations in the IP values between positional pyridine isomers.[7] The high AP value (9.9 eV) for the *m/e* 143 species from the 4-isomer, however, strongly indicates electron-impact fragmentations as the principal pathway.

The spectra of the hydroxycyclopentyl methiodides *7* were essentially those of the parent pyridines *2* together with methyl iodide in contrast to the above discussed hydroxycyclopentenyl derivatives *8*. Demethylation was also the major pyrolytic pathway in the cyclopentenyl series *6* which gave spectra very similar to those of the parent cyclopentenyl isomers *3* (Table 1) with high intensity of the molecular ion (*m/e* 145) and the base peak at [M − H]. The spectra from the 2- and 4-isomers of *6* also contain a peak at *m/e* 159 (relative intensity 3 and 20 %, respectively) corresponding to the anhydro-bases *15a* and *15c* (Scheme 2); the corresponding signal from the trideuteriomethiodide analogues of *6* were at *m/e* 162. A change of the anion from iodide to chloride in the 2-isomer increased the relative intensity to 10 %. The AP values for the *m/e* 159 species (*ca*. 6.4 and 6.35 eV, respectively) also show the expected close relationship to the IP values of the anhydro-bases *10a* and *10c*.[7] The cyclopentenyl anhydro-bases *15* have been drawn as the conjugated isomers although no evidence for this is provided; two conjugated isomers are possible for the 2-cyclopentenylidene derivative *15a*. The lower tendency for anhydro-base formation from *6* rather than from the cyclopentadienyl analogues *9* is probably due to greater stabilisation of the more conjugated anhydro-bases *10*.

The methiodides of the 3-isomers were largely demethylated before evaporation. Thus the base peak in the spectrum of the cyclopentadienyl derivative *9b* was at *m/e* 143 corresponding to *5b*, and its pyrolytic generation was confirmed by its AP value which was the same

as the IP value (8.40 eV) for the 3-cyclopentadienylpyridine *5b*.

The spectra of *9b* and *6b* also contain a signal corresponding to the reduced cation [M+H] at *m/e* 159 and *m/e* 161, respectively, together with a metastable peak for hydrogen expulsion to the cation or an isobaric ion. No evidence for deprotonation and evaporation of the resultant betaine *10b* was found. The relative intensity of [M+H] varied with the temperature and the length of time the sample was kept in the instrument and was increased from *ca.* 10 to 20 % on change of the iodide anion to chloride. The effect of the nature of the anion was most pronounced in the case of the hydroxycyclopentenyl methiodide *8b* whose very weak signal at *m/e* 159 was increased to *ca.* 20 % in the most favourable cases for the chloride; the genesis of the *m/e* 159 species involves dehydration and reduction. The AP values for this species from both *8b* and *9b* were *ca.* 7 eV which is similar to the IP values for the anhydro-bases *10a* and *10c* and are significantly different from the IP value (8.40 eV) of the 3-cyclopentadienylpyridine *5b*. A close relationship also exists between the AP value (6.30 eV) for the *m/e* 161 species from *6b* and the AP values (6.40 eV) for the suggested anhydro-bases *15a* and *15c*. In previous work we have shown that anhydro-bases and dihydropyridines derived from methiodides of pyridylacetates have similar IP values.[7] By analogy a thermally induced redox process with formation of a dihydropyridine before evaporation is postulated to explain the presence of the [M+H] species in the spectra.

The dihydropyridines *13b* and *14b* have been drawn as the generally more stable 1,4-dihydro-isomer, although no experimental evidence is available to differentiate between the 1,2- and 1,4-isomers; additional isomeric possibilities exist by different double bond locations in the five-membered ring. Differentiation between the possible isomers of *13b* and *14b* may not be possible from the spectra alone since the characteristic fragmentation is expected to be loss of a hydrogen atom or substituent from the pyridine $sp^3$-carbon with formation of the stable pyridinium ion;[11,12] by means of the trideuteriomethiodide analogues the initial hydrogen expulsion ([M+H]→[M]) was shown not to originate from the methyl group.

## EXPERIMENTAL

$^1$H NMR spectra were recorded with a Varian A60-A instrument (60 MHz).

Mass spectra were recorded on an AEI MS-902 spectrometer attached to an AEI DS-30 data system. The compounds were introduced directly into the ion source kept at 220 °C. Low resolution (RP = 1000) spectra were recorded with 70 eV electron energy and 100 μA trap current. High resolution (RP = 10 000) spectra were recorded at 70 eV and 500 μA.

*IP and AP values* were obtained by semilog-plot interpretation of the ionisation efficiency curves as previously described.[13] The values are the average from three determinations, and the deviation was ±0.1 or ¹0.05 eV when the values are given with one or two decimal figures, respectively.

IP/AP values: *5a* as pyrolytic species from *8a*, 8.30 eV (*m/e* 143); *5b*, 8.40 eV (*m/e* 143); *10a* 6.45 eV (*m/e* 157); *10c*, 6.53 eV (*m/e* 157); *14b* or isomer(s) from *8b* and *9b*, *ca.* 7 eV (*m/e* 159); *15a* or isomer from *6a*, 6.4 eV (*m/e* 159); *15c* from *6c*, 6.35 eV (*m/e* 159); *13b* or isomer(s) from *6b*, 6.3 eV (*m/e* 161).

*Table 1.* Relative intensities of major ions in the mass spectra of pyridines *3* – *5* and *10*.

| *m/e* | *3a* | *3b* | *3c* | *m/e* | *4a* | *4b* | *4c* | *m/e* | *5b* | *m/e* | *10a* | *10c* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 145 | 67 | 80 | 78 | 161 | 10 | 37 | 80 | 143 | *100* | *157* | *100* | *100* |
| 144 | *100* | *100* | *100* | 160 | 2 | 16 | 20 | 142 | 50 | 156 | 92 | 10 |
| 143 | 10 | 10 | 15 | 146 | 2 | 84 | 14 | 141 | 8 | 155 | 8 | 2 |
| 130 | 32 | 30 | 30 | 144 | 14 | 50 | 17 | 117 | 20 | 154 | 22 | 3 |
| 117 | 20 | 20 | 22 | 143 | *100* | *100* | *100* | 116 | 14 | 142 | 16 | 5 |
| 115 | 8 | 8 | 10 | 142 | 24 | 32 | 30 | 115 | 27 | 130 | 48 | 5 |
| 106 | 23 | 2 | 2 | 132 | 2 | 49 | 60 | 89 | 10 | 115 | 5 | 15 |
| 79 | 28 | 7 | 6 | 117 | 73 | 77 | 18 | | | | | |
| 28 | 35 | 45 | 67 | 106 | 23 | 50 | 46 | | | | | |

*(1-Hydroxycyclopentyl)pyridines (2)* [9,10] were prepared from cyclopentanone and the respective pyridyllithium as described for the cyclopentenyl analogues (*4*) below. The yields were *ca.* 30 %.

*(1-Cyclopentenyl)pyridines (3)* were formed in 75 – 80 % yield by dehydration of the respective (1-hydroxycyclopentyl)pyridine in 3 parts of conc. $H_2SO_4$ at 60 °C.[9]

*2-(1-Hydroxy-2-cyclopentenyl)pyridine (4)* [8] was prepared as described for *4b* below.

*3-(1-Hydroxy-2-cyclopentenyl)pyridine (*4b*)*. A solution of 3-bromopyridine (15.8 g, 0.10 mol) in anhydrous ether (100 ml) was added dropwise with stirring at – 20 °C to a solution of butyllithium (0.11 mol) in ether (250 ml) in a nitrogen atmosphere. A reddish brown suspension of 3-pyridyllithium was formed.[14] The reaction mixture was stirred for 10 min before the temperature was lowered to – 50 °C and 2-cyclopentenone [15,16] (3.3 g, 0.04 mol) in anhydrous ether (50 ml) was added dropwise. The temperature of the stirred reaction mixture was allowed to reach 0 °C over 4 h and the mixture stirred for another hour at this temperature. The yellowish suspension was then poured into ice/water, the ether layer collected and the aqueous layer extracted with ether. The combined ethereal solutions were concentrated to *ca.* 20 ml and extracted with water (HCl) at pH 5.

Unreacted cyclopentenone remains in the ether solution. The aqueous solution was separated, brought to pH 8 – 9 and extracted with ether. Evaporation of the washed and dried ether solution left an oily product which slowly crystallised at 0 °C and was recrystallised from carbon tetrachloride; yield 2.0 g (37 %). The analytical specimen was sublimed at 40 °C/2.0 Pa; white solid with m.p. 110 – 112 °C. Anal. $C_{10}H_{11}NO$: C, H.

*4-(1-Hydroxy-2-cyclopentenyl)pyridine (*4c*)* was prepared as above from 4-pyridyllithium [14] except that the reaction was run at – 70 °C. The product was recrystallised from carbon tetrachloride: light petroleum (1:1); yield 1.8 g (33 %). The analytical specimen was sublimed at 30 °C/2.0 Pa, m.p. 124 – 125 °C. Anal. $C_{10}H_{11}NO$: C, H.

*3-(1,3(4)-cyclopentadienyl)pyridine (*5b*)*. 3-(1-Hydroxy-2-cyclopentenyl)pyridine (*4b*, 50 mg) and purified sea sand (*ca.* 2 g, Merck) were well-mixed and the mixture heated in a sublimation apparatus at 220 – 240 °C (oil bath) at 4.0 – 5.4 kPa. The yellowish volatile material was removed from the coldfinger by immersion in an ether solution. The combined products from 3 experiments were chromatographed on a neutral silica gel column wrapped in a dark coloured aluminium foil. Cooled ether was used as eluent and all operations were run under nitrogen as the product is very readily polymerised. The middle fractions (TLC) contained the *title compound* which was best stored in the ether solution under nitrogen in the cold; yield 40 mg (30 %). Elemental analysis was not carried out due to the instability of the compound, but the elemental composition was confirmed by high resolution MS. $^1$H NMR ($CDCl_3$): $\delta$ 3.2 and 3.4 ($CH_2$ from different isomers, ratio 1:3), and 6.6 and 7.0 (3H, olefinic protons).

*Syntheses of methiodides (*6 – 8*)*. The substituted pyridine and excess methyl iodide (3 – 4 times by weight) were dissolved in ether or benzene and the solution left in the dark at room temperature. The methiodides were precipitated in 70 – 90 % yield. The reaction of 3- and 4-substituted pyridines was over in 24 h while 2-substituted pyridines required 1 – 2 weeks for the reaction to go to completion. The product was recrystallised once from ethanol to which was added a little ether.

The Me-protons in the NMR spectra ($D_2O$) of the 2-isomers appeared at $\delta$ 4.5 – 4.6 and of the 3- and 4-isomers at $\delta$ 4.3 – 4.5; in general the spectra were not well resolved.

N-*Methyl-(1-cyclopentenyl)pyridinium iodides (*6*)*.

*6a*: Decomp. 111 – 112 °C.[8]

*6b*: Decomp. 160 – 163 °C. Anal. $C_{11}H_{14}IN$: C, H.

*6c*: Decomp. 196 – 199 °C. Anal.: C, H.

N-*Methyl-(1-hydroxycyclopentyl)pyridinium iodides (*7*)*.

*7a*: Decomp. 115 – 120 °C. Anal.: $C_{11}H_{16}INO$: C, H.

*7b*: Decomp. 125 – 130 °C. Anal.: C, H.

*7c*: Decomp. 130 – 133 °C. Anal.: C, H.

N-*Methyl-(1-hydroxy-2-cyclopentenyl)pyridinium iodides (*8*)*.

*8a*: Decomp. 110 – 115 °C. Anal. $C_{11}H_{14}INO$: C, H.

*8b*: Decomp. 125 – 127 °C. Anal.: C, H.

*8c*: Decomp. 165 – 168 °C. Anal.: C, H.

N-*Methyl-3-(1,3- and 1,4-cyclopentadienyl)-pyridinium iodide (*9b*)* was prepared from the cyclopentadienylpyridine *5b* at 0 °C in ether solution. The product was sensitive to light and contact with air and was readily polymerised. Therefore no elemental analysis was carried out; NMR and MS data confirmed the structure assigned to the product.

*(*N-*Methyl-2- and 4-(1,3(4)-cyclopentadienyl)pyridinium iodides (*9a, 9c*)*. The anhydrobase (*10a* or *10c*) was dissolved in acetic acid and aq. HI added. Evaporation at reduced pressure left the solid title compounds identified by spectroscopy.[8]

*Pyridinium chlorides* for mass spectrometry studies were prepared by passing an aqueous solution of the iodide over a column of Amberlite IRA 400 in the chloride form.

*Trideuteriomethiodides*. The trideuteriomethiodide analogues *6, 8* and *9b* were prepared as above from *3, 4* and *5b* and equimolar amounts of trideuteriomethyl iodide.

N-*Methyl-2-cyclopentadienylidene-1,2-dihydropyridine (*10a*)* was prepared from cyclopentadienyllithium [17] and *N*-methyl-2-bromopyridinium iodide as described for the reaction

between cyclopentadienylsodium and *N*-methyl-2-iodopyridinium iodide;[8] m.p. 73–74 °C (pentane:ether).

*N-Methyl-4-cyclopentadienylidene-1,4-dihydropyridine* (10c) was synthesised in the same way from *N*-methyl-4-bromopyridinium iodide, m.p. 200 °C (slow decomp.).[8]

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