Mass Spectrometry of Halo-pyrazolium Salts

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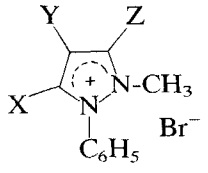
Eleven halogen substituted 1-methyl-2-phenylpyrazolium bromides or chlorides were investigated by field desorption, field ionization, and electron impact mass spectrometry. Dealkylation was found to be the predominant thermal decomposition. An exchange between covalent and ionic halogen prior to dealkylation was observed and is discussed in detail.

INTRODUCTION

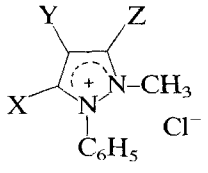
Pyrazolium salts substituted at ring carbon with halogen are key intermediates in the preparation of pyrazolinones, e.g. antipyrin and its derivatives, through nucleophilic displacement of halogen with hydroxyl ions.[1–4] Analogously, halo-pyrazolium salts serve as precursors of pyrazolinimines[1] and pyrazolinthiones, the latter in their turn progenitors of mercaptopyrazoles.[5]

Pyrazolium salts can be characterized by mass spectrometry.[6] Intense cation peaks are observed by field desorption (FD). Through thermolysis of the salts in the ion source, informative mass spectra are obtained by application of field ionization (FI) and electron impact ionization (EI).

This paper discusses the EI/FI/FD mass spectra of halogen substituted 1-methyl-2-phenylpyrazolium bromides and chlorides.



Compound	X	Y	Z	Cation m/z
1	Cl	H	H	193
2	H	Cl	H	193
3	H	H	Cl	193
4	Cl	H	Cl	227
5	Cl	Br	H	271
6	H	Br	Cl	271
7	Cl	Br	Cl	305
8	Cl	H	CH_3	207
9	CH_3	H	Cl	207



Compound	X	Y	Z	Cation m/z
10	H	H	Br	237
11	H	Br	Cl	271

RESULTS AND DISCUSSION

The EI/FI/FD mass spectra of the halogen substituted pyrazolium salts **1–11** are shown in Figs. 1–11.

The FI spectra show that the dominant thermally induced reaction is dealkylation, viz. formation of methyl halide and the free pyrazole base.

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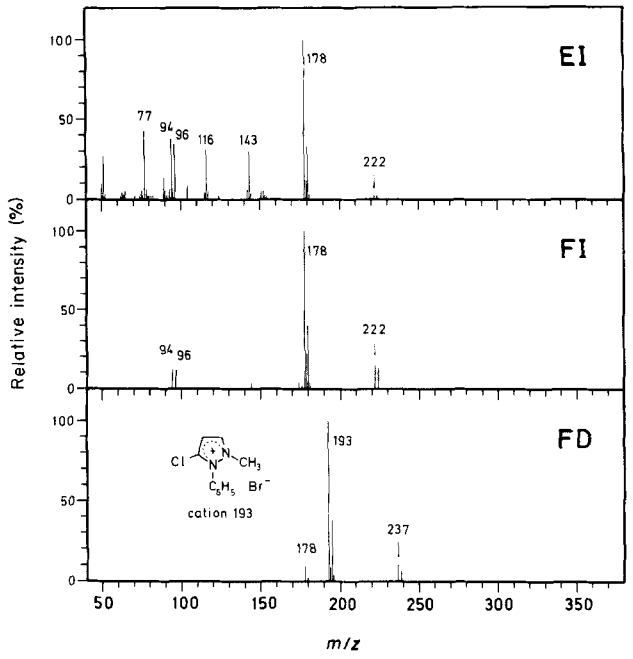

Figure 1. EI/FI/FD mass spectra of 1-methyl-2-phenyl-3-chloropyrazolium bromide (**1**).

The EI fragmentation of the pyrazoles is strongly influenced by the halogen substituent. A primary fragmentation is the elimination of a halogen radical and/or hydrogen halide followed by loss of CH_3CN/HCN or CN depending on the accessibility of hydrogen. The low mass region is characterized by CH_3Cl and by ions from the phenyl group.

Earlier studies[6] on pyrazolium salts have shown that FD spectra of this compound class exhibit an intense cation peak. In the case of halo-pyrazolium salts a pronounced dealkylation is observed. Compound **6** shows a vanishing small cation peak, and in the case of **11** the cation remains undetected. The apparent ease of dealkylation is in accordance with the lower basicity of these pyrazoles due to the electron withdrawing effects of the halogen substituents. The halo-pyrazolium salts show no cluster ions apart from compound **9** where traces are observed at *m/z* 493 and 537. This effect contrasts with *N,N*-dialkyl pyrazolium salts.[6] The low intensity ion patterns at *m/z* 237 and at

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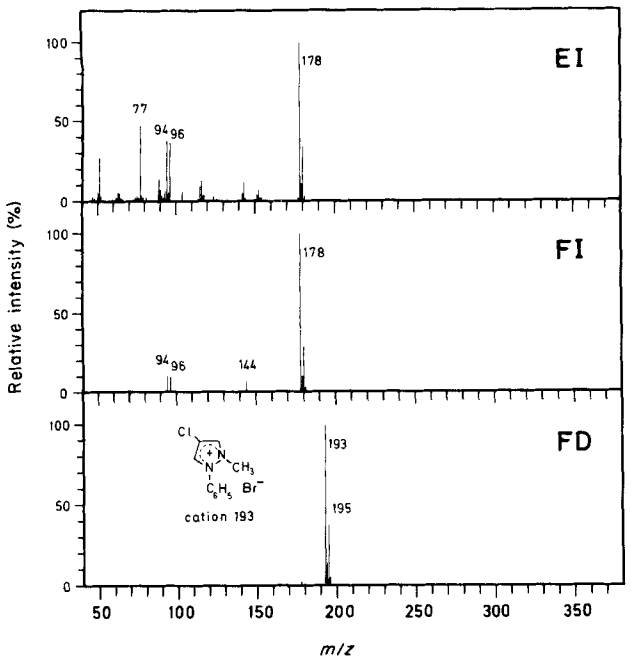


Figure 2. EI/FI/FD mass spectra of 1-methyl-2-phenyl-4-chloropyrazolium bromide (**2**).

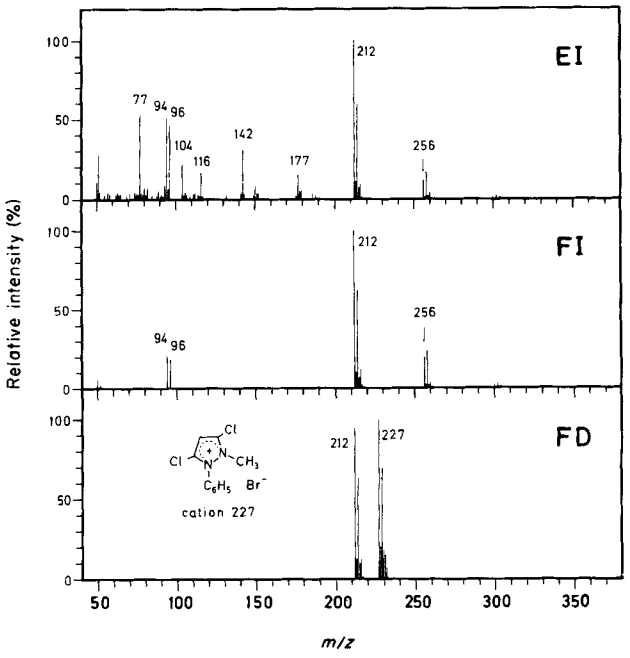


Figure 4. EI/FI/FD mass spectra of 1-methyl-2-phenyl-3,5-dichloropyrazolium bromide (**4**).

m/z 222 (Fig. 1) in the mass spectra of compound **1** are assigned to its bromo analogue formed in the mass spectrometer prior to desorption and dealkylation, respectively, by exchange of the chlorine of **1** with its bromide counter-ion. A similar exchange is observed in all of the pyrazolium salts substituted with halogen at C-3 or C-5. Exchanges of chlorine with bromide ions (**1, 3–9**) and bromine with chloride ions (**10**) are both seen. To a minor extent, the 3,5-dichloro compound **4** is subject to double exchange, as is apparent from the small ion pattern at *m/z* 302 in the EI and FI spectra (Fig. 4). The exchange reaction is most probably a nucleophilic substitution at positions C-3 and C-5. In Scheme 1 the exchange reaction for the two compounds **3**⇆**10** is shown.

According to the spectra of compounds **2** and **11** neither chlorine nor bromine at position C-4 undergo exchange. This agrees with the inability of those compounds to form the intermediate structure shown in Scheme 1, and the low reactivity towards nucleophilic displacement of C-4 halogen as compared with C-3, and C-5 halogen of pyrazolium salt in solution.[4]

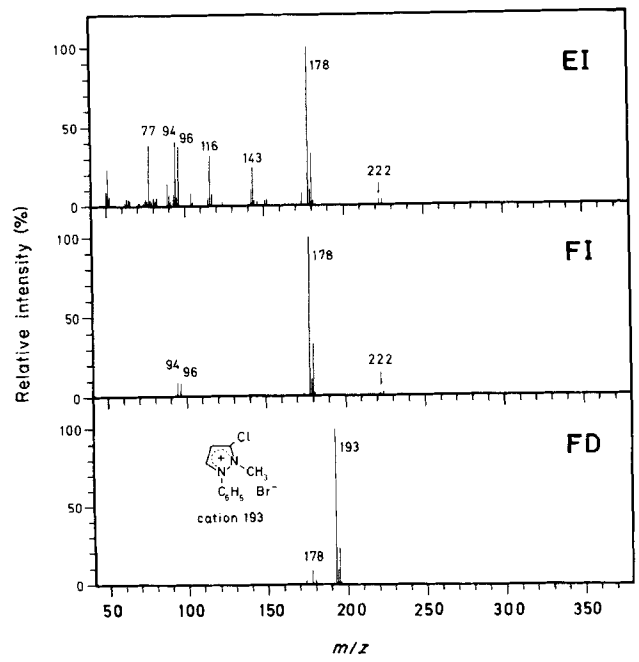


Figure 3. EI/FI/FD mass spectra of 1-methyl-2-phenyl-5-chloropyrazolium bromide (**3**).

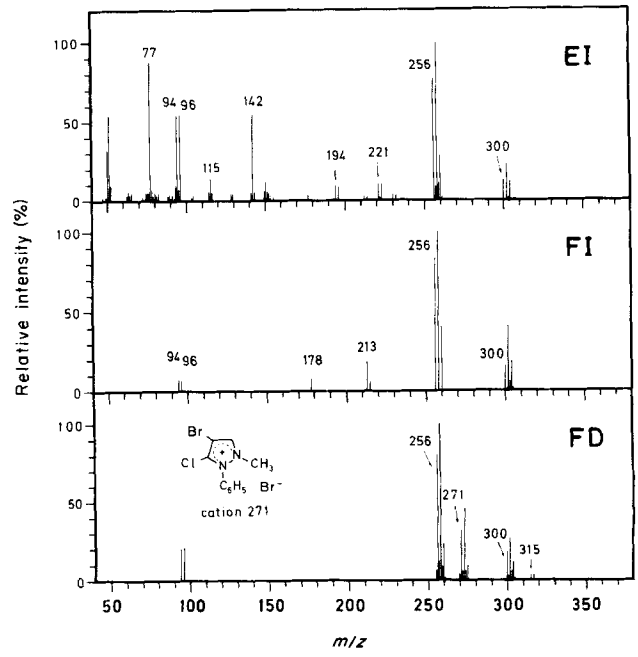


Figure 5. EI/FI/FD mass spectra of 1-methyl-2-phenyl-3-chloro-4-bromopyrazolium bromide (**5**).

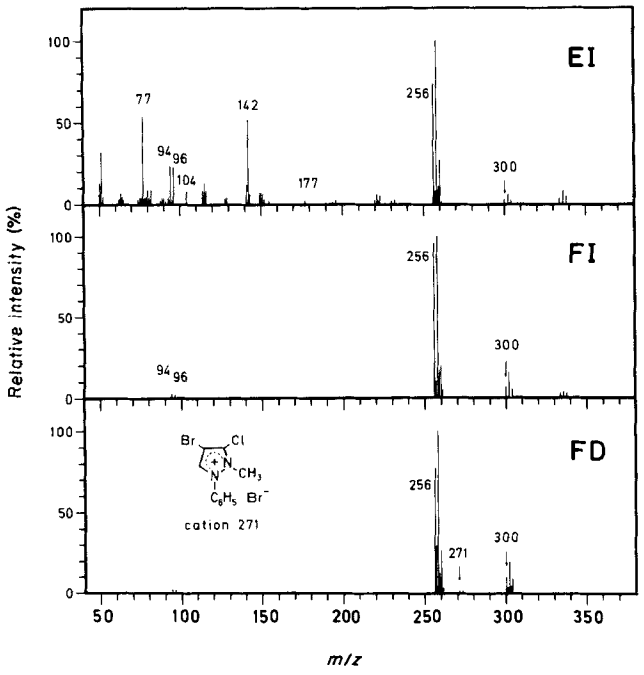
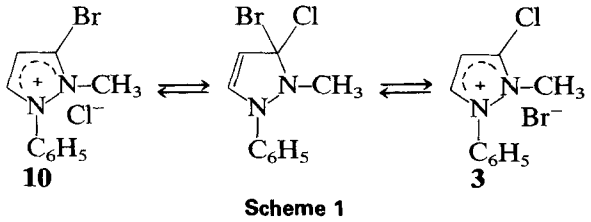


Figure 6. EI/FI/FD mass spectra of 1-methyl-2-phenyl-4-bromo-5-chloropyrazolium bromide (**6**).



Scheme 1

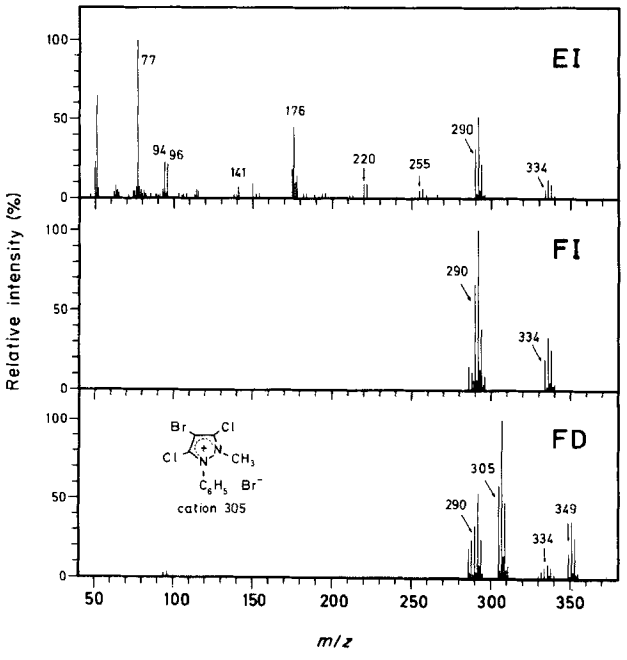


Figure 7. EI/FI/FD mass spectra of 1-methyl-2-phenyl-3,5-dichloro-4-bromopyrazolium bromide (**7**).

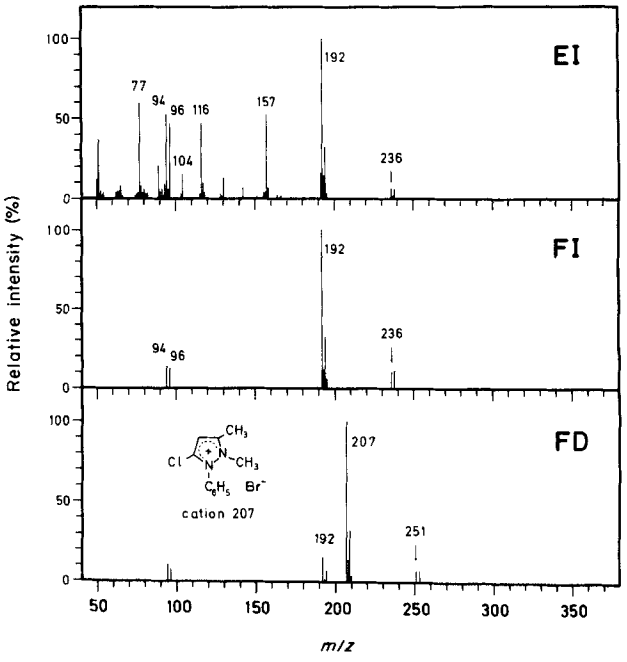


Figure 8. EI/FI/FD mass spectra of 1-methyl-2-phenyl-3-chloro-5-methylpyrazolium bromide (**8**).

To support further the observed exchange as a thermally induced reaction, the compounds **4** and **6** (the same specimens as those analysed) were converted to the corresponding chloride salts. The EI/FI/FD mass spectra of the crude chlorides showed no ions corresponding to bromine compounds. Consequently, the peaks at m/z 256 and 300 (exchange of one and two chlorine with bromine respectively) in Fig. 4 and the peaks at m/z 300 in Fig. 6 are due to exchange reactions alone.

At present, knowledge about the mechanism of the thermochemical reaction is small. However, it may be appropriate to sketch the free energy profiles of the

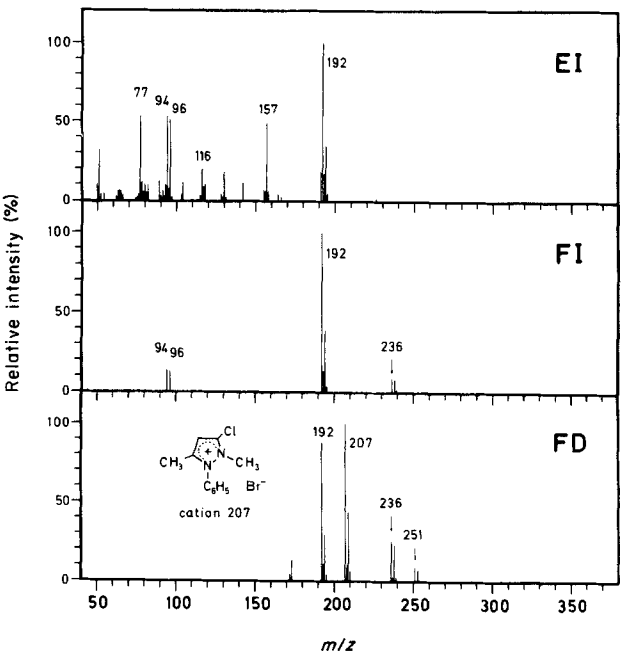


Figure 9. EI/FI/FD mass spectra of 1-methyl-2-phenyl-3-methyl-5-chloropyrazolium bromide (**9**).

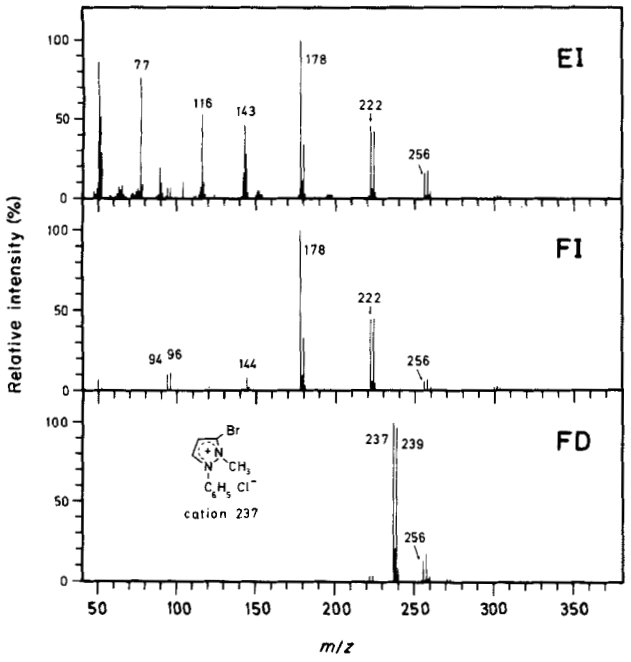


Figure 10. EI/FI/FD mass spectra of 1-methyl-2-phenyl-5-bromopyrazolium chloride (**10**).

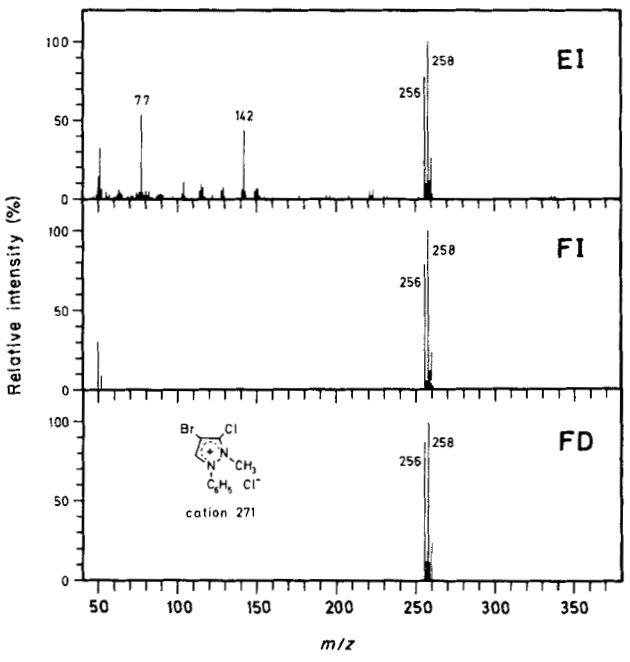


Figure 11. EI/FI/FD mass spectra of 1-methyl-2-phenyl-4-bromo-5-chloropyrazolium chloride (**11**).

possible reaction paths (Fig. 12). The EI/FI mass spectra of the bromo-substituted salt **10** show a relatively high content of chloropyrazole formed through halogen exchange. In contrast, the spectra of the chloro-substituted salt **3** exhibit a minute content of bromopyrazole as the result of halogen exchange. This may indicate a faster conversion of **10** to **3** than in the opposite case, but more likely, it reflects the difference in activation energies towards dealkylation, as shown in Fig. 12.

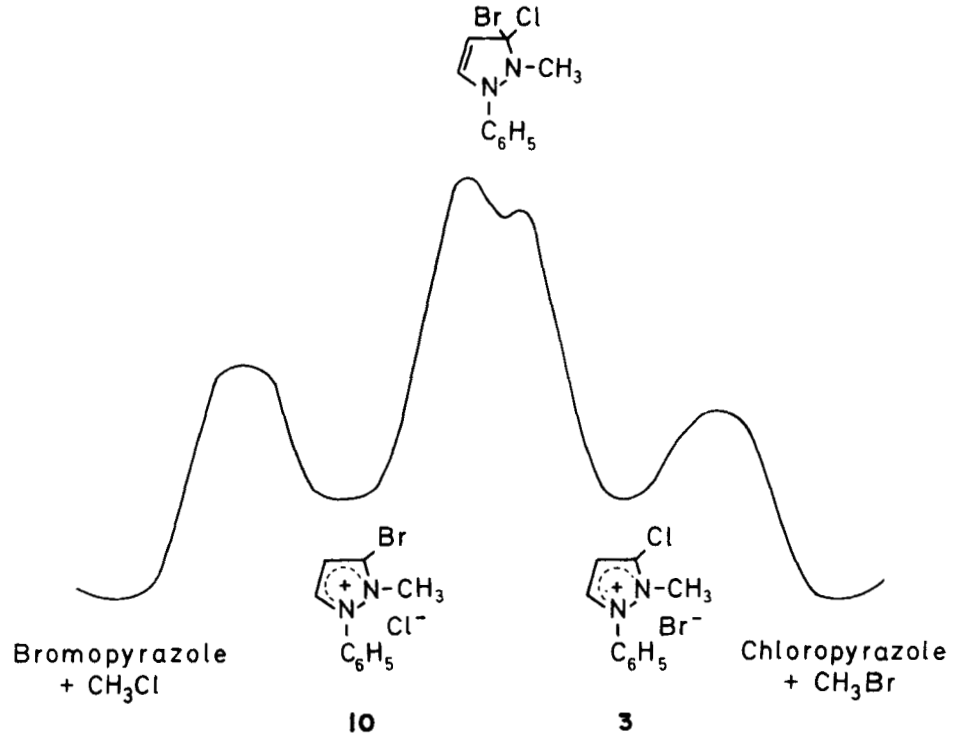


Figure 12. The energy diagram is suggested on the basis of bond energies (C—Cl 351, C—Br 293, NH_4^+ Cl^- 300.4 and NH_4^+ Br^- 254.0 kJ mol^{-1}).[7] The barrier for the alkylation of the chloropyrazole is lower than that for alkylation of the bromo analogue, since bromide ions are better leaving groups than chloride ions. The energy course of the interconversion between **3** and **10** has been constructed according to Ref. 8.

EXPERIMENTAL

Mass spectrometric measurements were performed on a Varian MAT CH 5D instrument equipped with a combined EI/FI/FD ion source. The emitter was a 10 μm tungsten wire activated in benzonitrile vapour. The ion source temperature was about 200 °C. EI spectra were measured at 70 eV (100 μA) with a resolution of approximately 1000. The samples were introduced in aluminium crucibles by the direct inlet system with a probe temperature of 150–225 °C. The emitter dipping technique (methanolic solution) was used for FD. As the salts decompose at higher temperatures the FD spectra were obtained at as low an emitter current as possible optimizing the signal for the cation. The mass spectra were obtained on an oscillographic recorder.

Compounds **1–3** were prepared as described previously.[9] Compound **4** was obtained by heating (120 °C, 4 h) 1-phenyl-3,5-dichloropyrazole[10] with dimethyl sulphate (1.2 equivalents). The product, dissolved in water, was subjected to ion exchange (Amberlite IRA 400, Br^--form)[7] producing **4** (76%, m.p. 105 °C (methanol–ether)). Similarly were prepared: **5** (from 1-phenyl-4-bromo-5-chloropyrazole[11]) (66%, m.p. 201 °C (water)), **6** (from 1-phenyl-4-bromo-3-chloropyrazole (m.p. 45 °C from 50% ethanol) obtained by bromination[11] of 1-phenyl-3-chloropyrazole[12] in 96% yield) (84%, m.p. 129–130 °C (methanol–ether)), **7** (from 1-phenyl-4-bromo-3,5-dichloropyrazole[11]) (76%, m.p. 105 °C (methanol–ether)), **8** (from 1-phenyl-5-chloro-3-methyl-pyrazole[13]) (85%, m.p. 206–207 °C (methanol–ether)), **9** (from 1-phenyl-3-chloro-5-methylpyrazole obtained in 69% yield by heating (sealed tube, 200 °C, 24 h) 1-phenyl-3-hydroxy-5-methylpyrazole[14] with phosphorous oxychloride (2.2 equivalents) and working up as described for 1-phenyl-5-chloro-3-methylpyrazole[13]) (72%, oil), and the Br^--form of **10** (from 1-phenyl-3-bromopyrazole[12]) (96% (methanol–ether)). The chlorides of 1-methyl-2-phenyl-3,5-dichloropyrazolium and 1-methyl-2-phenyl-4-bromo-5-chloropyrazolium were obtained by stirring the bromides **4** and **6** in aqueous solution with freshly precipitated AgCl overnight, followed by filtration and removal of the water. Alternatively, **6** was converted into the corresponding chloride **11** by ion exchange (Amberlite IRA 400, Cl^--form). Similarly, compound **10** was obtained. All compounds gave analytical data for C, H, N and halogen, deviating less than 0.3% from the calculated values. Compounds **6, 10** and **11** contained minor amounts of di- and trihalogenated pyrazoles as is apparent from their mass spectra.

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