SELECTIVE NITRATIONS OF PYRAZOLES-NITRATIONS OF 2-(1′-PHENYLPYRAZOL-4′-YL) BENZIMIDAZOLES

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Abstract

Nitrations of the title ring system were found to be temperature dependent. Room temperature nitration occurred at the phenyl ring of pyrazole while at 100°C a dinitrated product is obtained when the second nitro group is introduced at the 5-position of the benzimidazole ring.

Key Words

Pyrazoles, Benzimidazoles, Nitration, Mass Spectra.

Introduction

In continuation of our work on the synthesis of hetarylpyrazoles (Rashid, Khan and Moazzam, 1999), we have recently prepared some pyrazolylbenzimidazoles (Rashid, Khan and Moazzam). Now we would like to report the nitration of these pyrazolylbenzimidazoles viz-a-viz the relative reactivity of the two heterocyclic rings joined through a C-C bond. The findings together with the mass spectra of the Products are presented here.

Materials and Methods

The proton magnetic resonance (PMR) spectra were obtained on a Brucker AM-500 Spectrometer with tetramethylsilane as an internal standard. The infrared absorption spectra (IR) were taken by the Hitachi-270-30 spectrometer and were measured as potassium bromide disks. Mass spectra were obtained on a Finnigan MAT-112 Spectrometer.

Melting points were taken on Gallenkamp apparatus and are uncorrected. 2-(3′,5′-Dimenthyl-1′-phenylpyrazol-4′-yl) benzimidazole (I) used in the nitrations was prepared earlier from the reaction of 3,5-dimethyl-1-phenylpyrazol-4-carboxaldehyde (Rashid, Khan and Moazzam).

Nitration of 2-(3′,5′-dimethyl-1′-phenylpyrazol-4′-yl)Benzimidazole

At Room Temperature

1g of (**I**) was added to a nitrating mixture of 3 mL concentrated nitric acid and 3 mL of concentrated sulphuric acid at room temperature and allowed to stand for 4hrs at room temperature. Afterwards the reaction mixture was poured over crushed ice, filtered and washed with water. The precipitates were dried and crystallized from aqueous ethanol to give the product (**II**), m.p. 218-220º, yield 80%.

(**II**) Was identical (mixed m.p., IR, PMR spectra) with the product obtained from the reaction of 3,5-dimethyl-1-p-nitrophenylpyrazol-4-carboxaldehyde and o-phenylenediamine (Rashid, Khan and Moazzam 2003). Mass Spectra z/e (%): 333(100);

332(90); 302(04); 287(14); 286(35); 285(07); 245(07); 244(17); 243(05); 219(04); 218(03); 217(02); 190(02); 179(02); 138(10).

At 100ºC

Nitration of (**I**) was carried out as above, the reaction mixture was heated on a water bath for 3 hrs, allowed to cool and poured over crushed ice. After filtration the precipitates were washed, dried and crystallized from ethanol to get (**III**). m.p. 196-198ºC, yield 75%.

(**III**) Was identical with the product of reaction of 3,5-dimethyl-1-p-nitrophenylyrazole-4-carboxaldehyde and 5-nitro-o-phenylenediamine as well as the product obtained from further nitration of (**II**) at 100ºC. Mass spectra z/e (%): 378(100); 377(73); 347(05); 346(03); 332(09); 331(26); 302(02); 301(02); 286(07); 285(08); 273(02); 244(02); 232(01); 217(01); 216(01); 190(01); 170(01); 129(03); 88(02).

Results and Discussion

Nitration of (**I**) with mixed acids at room temperature gives a mononitro-product, which was identified as (**II**) where the nitro group has entered the *Para* position of the phenyl ring of the phenylpyrazole moiety. The nitration reaction at 100°C leads to a dinitro product (**III**) where one nitro group enters the phenyl ring of the phenylpyrazole while the Second nitro group is found at the 5-position of the benzimidazole part of the molecules (Chart-I). No evidence for a trinitro product was found under the reaction conditions. The identity of these compounds (**II**) and (**III**) was established through their m.p. IR and PMR spectra which were compared with these compounds obtained by unambiguous synthesis reported elsewhere (Rashid, Khan and Moazzam 2003).

The nitration behaviour is reminiscent of the mixed acids nitration pattern earlier observed in the 1-phenylpyrazole series. The *Para*-position of the 1-phenylpyrazole part seems to be relatively more reactive then the 5-position of the benzimidazole. However, there is an indication of the deactivating effect of benzimidazoles on the reactivity of the phenyl ring of the pyrazoles, which is reported to undergo dinitration of the phenyl ring at 100°C (Finar and Hurlock, 1957).

IR and PMR spectra (Rashid, Khan and Moazzam 2003) fully support the structures of the nitration products (**II**) and (**III**). The mass spectra displayed molecular ion peaks at m/z 333 and 378 for the (**II**) and (**III**), respectively, thus confirming mono and dinitration at room temperature and at 100°C, respectively.

A tentative fragmentation pattern of (**II**) and (**III**) observed in their mass spectra are presented in Charts 2a & 2b. The fragmentation takes place in the manner as has already been reported for the benzimidazoles and pyrazoles, separately i.e., loss of successive two HCN from the bezimidazole moiety (Nishiwaki 1968; Lawsson et al. 1968 and Khmel'nitskii et al. 1969) and the loss of CH_3CN from the pyrazole part of the molecule characteristics of a methyl substituent adjacent to the nitrogen atom (Nishiwaki 1967 and Khmel'nitskii et al. 1967). The intense M+ ion for both the compounds (**II**)

and (**III**) was also observed as the base peak. One of the fragmentation routes observed was a prior fission of a C-C bond linking the two rings (route ‘a’). Where the benzimidazole and pyrazole portions fragment as expected (for benzimidazoles it is presented while the pyrazloes behavior would be identical with that of “a” in the mode fragmentation while in “route” “b”, a “pyrazolenitrile” ion is produced which further fragments with successive elimination of a nitrile (C_5H_7, N_2)and NO_2 to give the m/z 76 fragments (Chart-2a).

Loss of a hydrogen atom followed by the loss of a nitro group (for **II**) and successive loss of two nitro group (for **III**) followed by other expected fragmentations was also observed and is presented in the scheme (Chart-2b).

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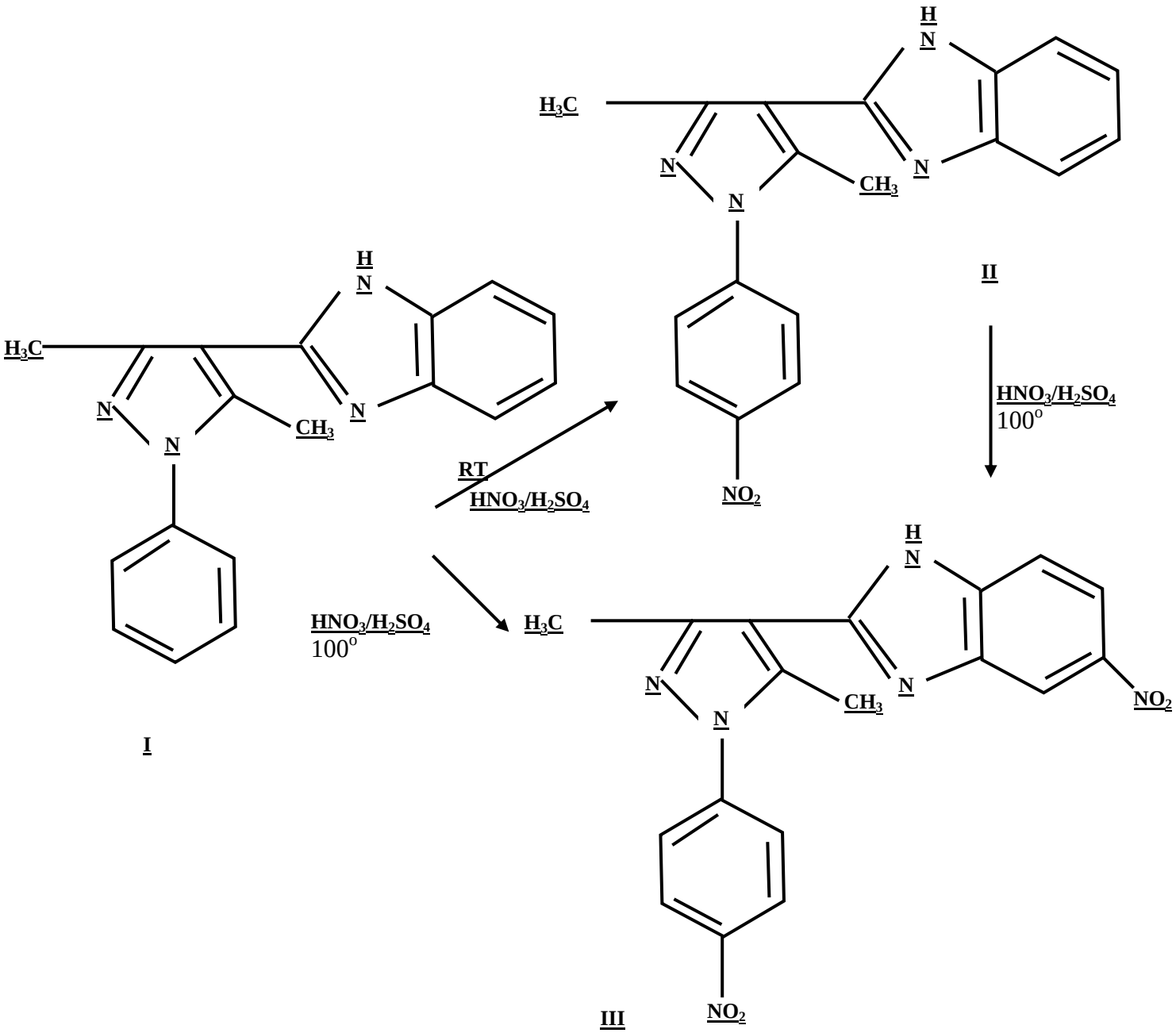
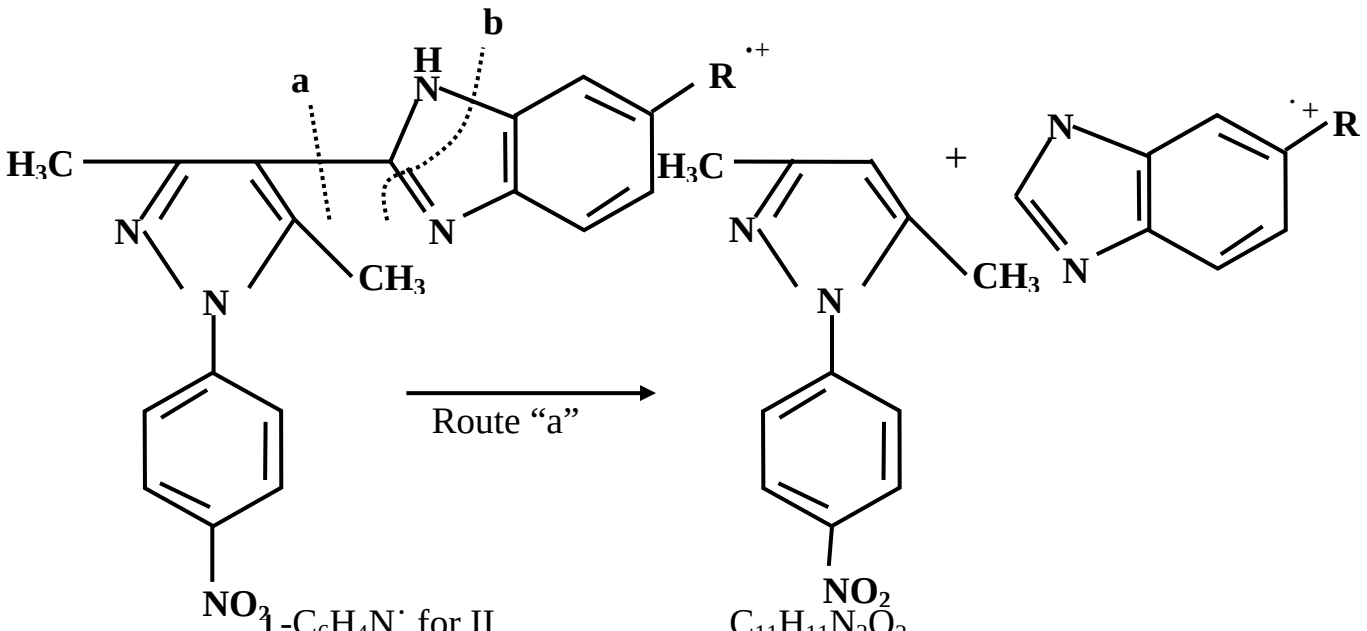

H
N
H3C
N
CH3
N
N
II
H
N
H3C
N
CH3
N
N
RT
HNO3/H2SO4
NO2
HNO3/H2SO4
100o
HNO3/H2SO4
100o
H3C
H
N
N
CH3
N
NO2
N
I
III
NO2

Chart 1



$-C_6H_4N^{\cdot}$ for II

$C_{11}H_{11}N_3O_2$

(m/z 217)

Route “b” $-C_6H_3N_2O_2$ for III

$C_{12}H_{11}N_4O_2^{+}$

(m/z 243)

$-CN^{\cdot}$

$C_{11}H_{11}N_3O_2^{\cdot+}$

(m/z 217)

$-C_5N^{\cdot}{}_7$

$C_6H_4N_3O_2^{+}$

(m/z 150)

$-N_2$

$C_6H_4NO_2^{+}$

(m/z 122)

$-NO_2$

$C_6H_4^{+}$

(m/z 76)

R=H, $C_7H_4N_2$

(m/z 116)

R=NO_2, $C_7H_3N_3O_2$

(m/z 161)

R=H

-HCN

$C_6H_3N^{\cdot+}$

(m/z 89)

-HCN

$C_5H_2^{\cdot+}$

(m/z 62)

R=NO_2

$-NO_2$

$C_7H_3N_2^{\cdot+}$

(m/z 115)

-HCN

$C_6H_2N^{\cdot+}$

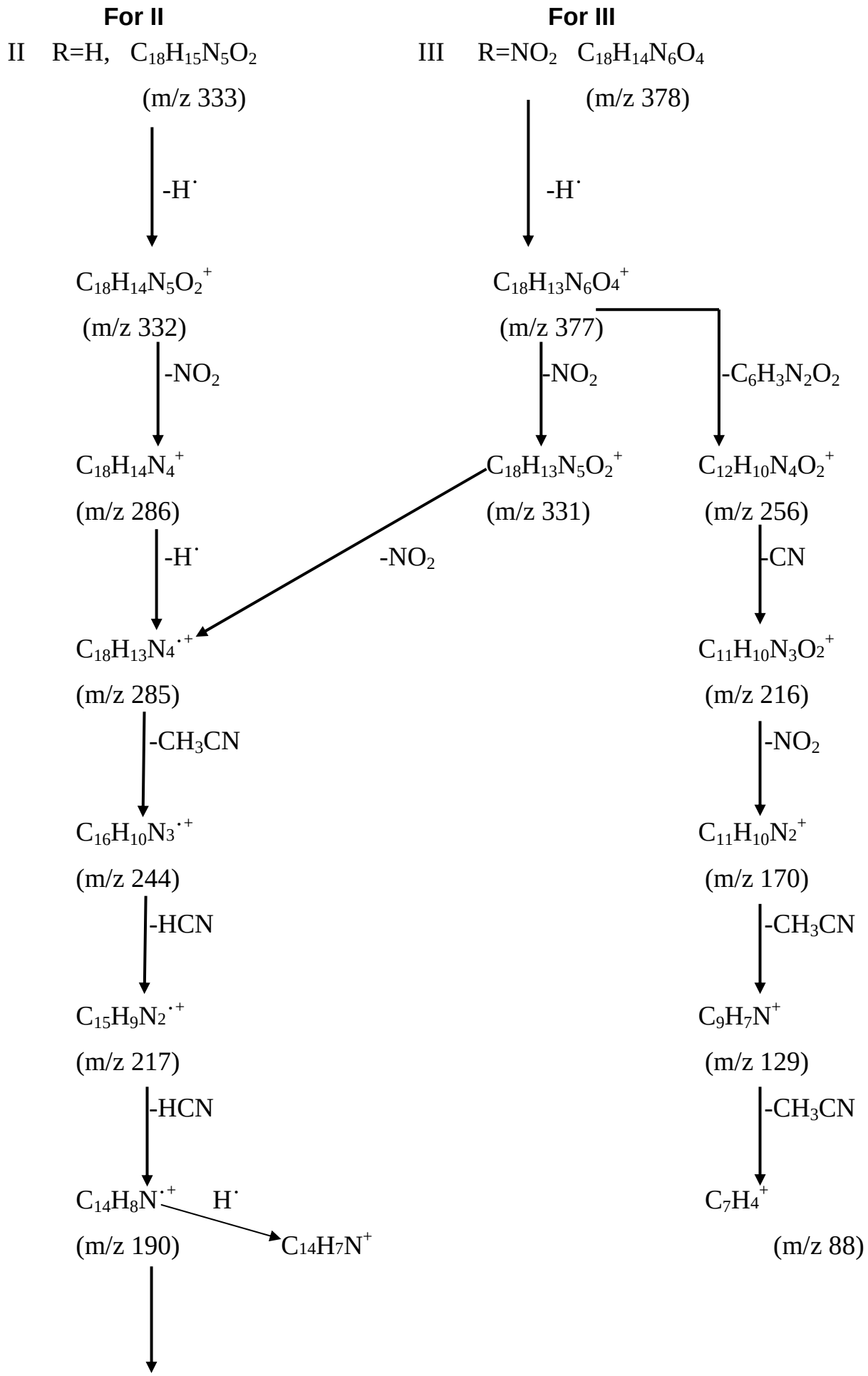
(m/z 88)

-HCN

$C_5H^{\cdot+}$

(m/z 61)

Chart 2a


For II
For III
II R=H, $C_{18}H_{15}N_5O_2$
(m/z 333)
III R=NO_2 $C_{18}H_{14}N_6O_4$
(m/z 378)
-H·
$C_{18}H_{14}N_5O_2^+$
(m/z 332)
$C_{18}H_{13}N_6O_4^+$
(m/z 377)
$-NO_2$
$-C_6H_3N_2O_2$
$C_{18}H_{14}N_4^+$
(m/z 286)
$C_{18}H_{13}N_5O_2^+$
(m/z 331)
$C_{12}H_{10}N_4O_2^+$
(m/z 256)
$-NO_2$
-CN
$C_{18}H_{13}N_4^{\cdot+}$
(m/z 285)
$C_{11}H_{10}N_3O_2^+$
(m/z 216)
$-CH_3CN$
$C_{16}H_{10}N_3^{\cdot+}$
(m/z 244)
$C_{11}H_{10}N_2^+$
(m/z 170)
-HCN
$C_{15}H_9N_2^{\cdot+}$
(m/z 217)
$C_9H_7N^+$
(m/z 129)
$C_{14}H_8N^{\cdot+}$
H·
$C_{14}H_7N^+$
(m/z 190)
$C_7H_4^+$
(m/z 88)

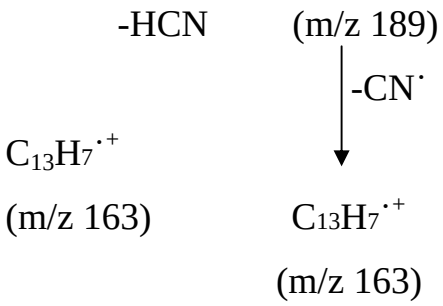


Chart 2b