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# Mass Spectrometry of Substituted Ethyl-4-anilinopyrazolo[3,4-*b*]pyridine-5-carboxylic Acids

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The mass spectral fragmentation of ethyl 4-anilinopyrazolo [3,4-*b*]pyridine-5-carboxylic acids are presented. The fragmentation is initiated by the elimination of $CO_2$ molecule followed by other fragments or elimination of water (*m/z* 18) which is then followed by successive loss of CO (*m/z* 28) and HCN (*m/z* 27).

**Keywords: Fragmentations, Aminopyrazoles, Pyrazolopyridines, Cyclizations.**

## INTRODUCTION

Fused pyridines continue to attract considerable attention of a number of researchers because of their great practical usefulness, primarily, due to wide spectrum of their biological activities [1-4]. Along with some other pyridine systems containing an annelated five membered heteroaromatic ring, pyrazolopyridines are isosters of bioactive indoles or indazoles. Pyrazolopyridines are also allosteric modulators of benzodiazepine receptors. They are a class of non-sedating anxiolytics, agreeably more potent than benzodiazepines. The pyrazolo[3,4-*b*]pyridine moieties represent important building blocks in both natural and synthetic bioactive compounds [1]. They show anxiolytic activity along with xanthine oxidase inhibitors, cholesterol formation-inhibitor and anti-alzheimer [4]. Bare *et al*. and others reported the synthesis of pyrazolopyridine esters and amides which gave compounds with potent anxiolytic action. Pyrazolo[3,4-*b*]pyridines have been prepared generally by cyclization reactions starting from different heterocyclic reagents [5-7]. Jachak *et al.* [8] abd Kendre *et al.* [9] reported the synthesis of novel pyrazolo[3,4-*b*]pyridines successfully by sequence of Gould-Jacobs reaction between 5-aminopyrazole and diethyl-ethoxymethylenemalonate in good yield Pyrazolopyridines' chemistry is the subject of continuous interest in our laboratories [10-13] and here we would like to communicate mass spectroscopic fragmentation behaviour of some anilinoacids (**5-8**) which were obtained as intermediates during the synthesis of a new tetracyclic system [14].

## EXPERIMENTAL

Mass spectra (low resolution) were recorded on a Finnegan MAT-112 instrument at HEJ Institute of Chemistry, Karachi, Pakistan.

**Ethyl 4-anilino-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid (1-4):** These were prepared from the reaction of ethyl 4-chloro-3-H (or methyl)-1-phenylpyrazolo-[3,4-*b*]pyridine-5-carboxylates with anilines in DMF or xylene as reported earlier [14].

## RESULTS AND DISCUSSION

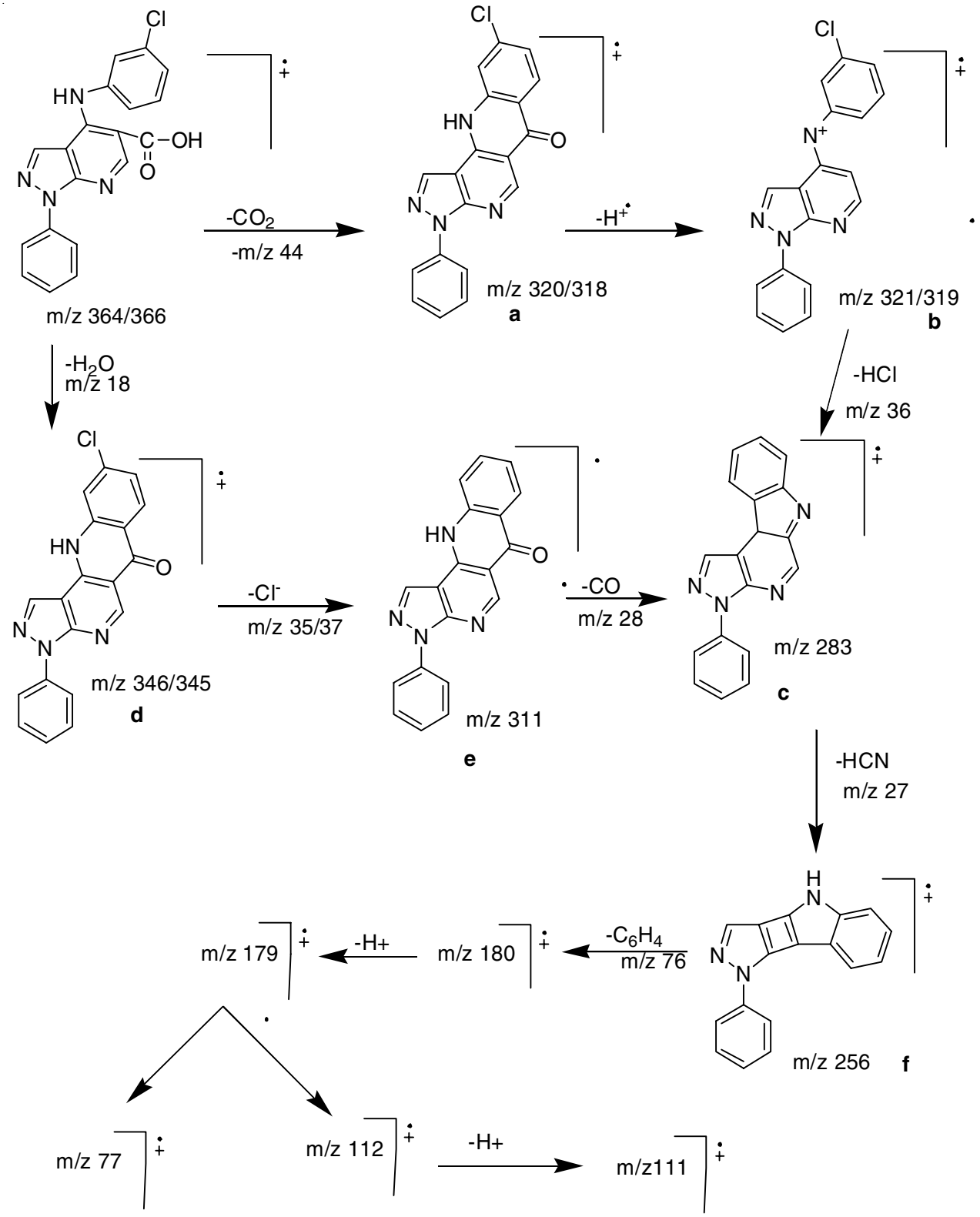
Mass spectrometric literature, including their fragmentation for various heterocyclic ring systems, was earlier collected in the book by Porter and Baldas [15]. The present series of compounds under study combine a two basis simple systems-pyridine and the pyrazole and should show interesting behaviour in their mass spectrometric behaviour.

Mass spectral data of various ethyl 4-anilino-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid (**1-4**) is collected in Tables 1 and 2 provides main common fragments for the various compounds.

The mass spectrum of first compound in this series *i.e.* 4-(3-chlorophenylamino)-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid (**1**) was analyzed. Its fragmentation pattern is presented in **Scheme-I**. The molecular ion peak corresponded to the molecular weight of the compound, which was also the base peak (100 %). A common fragmentation feature of these

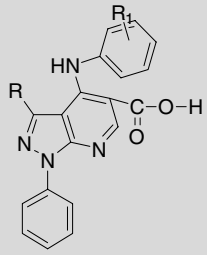
acids is the immediate loss of a molecule of $CO_2$ (*m/z* 44) from the molecular ion. The fragment (*m/z* 320) in its turn looses a proton followed by an HCl (in the case of chloro anilines), which subsequently eliminates an HCN (*m/z* 27). An alternative route suggested is the one in which an $H_2O$ (*m/z* 18) may be removed followed by the Cl loss (*m/z* 35, *m/z* 37). Further loss of one molecule of CO (*m/z* 28) brings to shorter fragments till a fragment corresponding to a phenyl $C_6H_5$ (*m/z* 77) is given off.

Generally, in the present series of "anilino acid", the base peaks follow the above general pattern. However in the case, when halogens (Cl, Br) are present in the molecule, the molecular ion and subsequent fragments containing halogens




**Scheme-I:** Fragmentation pattern of 4-(3-chlorophenylamino)-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid (**1**)

TABLE-1
MASS SPECTRAL DATA OF 4-ANILINO-1-PHENYL-1H-PYRAZOLO[3,4-*b*]PYRIDINE-5-CARBOXYLIC ACID (**1-4**)




| Compound No. | Substituents $R^1$ and R | Mass spectra *m/z* (relative intensity) |
|---|---|---|
| **1** | 3-Cl, H | 367 (8), 366 (35), 365 (23), 364 (100), 349 (8), 348 (35), 347 (39), 346 (99), 345 (52), 321 (5), 320 (8), 319 (10), 318 (5), 312 (12), 311 (52), 310 (12), 284 (10), 283 (26), 282 (13), 281 (5), 257 (6), 256 (8), 255 (5), 237 (7), 229 (5), 237 (7), 229 (5), 182 (6), 180 (7), 173 (6), 160 (5), 155 (8), 143 (8), 142 (11), 128 (9), 127 (6), 114 (6), 113 (7), 111 (17), 103 (6), 102 (8), 78 (7), 77 (69), 76 (8), 75 (14), 65 (7), 64 (5), 63 (6), 53 (5), 51 (16) |
| **2** | 3-Br, H | 409 (57), 407 (56), 391 (31), 389 (31), 365 (8), 363 (8), 311 (25), 310 (100), 283 (14), 282 (29), 281 (16), 256 (7), 229 (7), 191 (60), 189 (6), 180 (50), 179 (7), 164 (6), 156 (10), 155 (27), 142 (15), 127 (6), 126 (13), 125 (7), 114 (7), 113 (5), 103 (50), 102 (10), 101 (5), 88 (5), 77 (75), 76 (75), 74 (13), 64 (12), 63 (99), 62 (12), 52 (9), 51 (35) |
| **3** | 2-Cl, H | 323 (7), 322 (34), 321 (30), 320 (100), 319 (26), 292 (7), 284 (8), 257 (7), 143 (6), 111 (8), 77 (28), 75 (9), 65 (5), 52 (16) |
| **4** | H, $CH_3$ | 345 (22), 344 (92), 327 (24), 326 (100), 325 (73), 300 (7), 299 (12), 298 (60), 297 (7), 270 (5), 194 (4), 163 (8), 162 (6), 140 (5), 91 (180, 89 (5), 78 (5), 77 (38), 70 (17), 51 (16) |

TABLE-2
MASS SPECTRAL FRAGMENTS OF 4-ANILINO-1-PHENYL-1H-PYRAZOLO[3,4-*b*]PYRIDINE-5-CARBOXYLIC ACID (**1-4**), *m/z* (RELATIVE INTENSITIES)

| Fragments/ Compound No. | $M^+$ | a | b | c | d | e | f |
|---|---|---|---|---|---|---|---|
| **1** | 364 | 320 | 319 | 283 | 346 | 311 | 256 |
| **2** | 408 | 363 | – | 282 | 389 | 310 | 256 |
| **3** | 364 | – | 319 | – | 346 | 311 | 256 |
| **4** | 344 | 300 | 299 | 326 | – | 298 | 270 |

displayed expected ratios for their isotopes. In these molecules during fragmentation halogens (Cl, Br) or halo acids (HCl or HBr) has been indicated to be lost.

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