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Mass Spectrometry of Pyrazolo[3,4-b]pyrido[2',3'-b]-1,6-naphthyridines and Dipyrazolo[3,4-b];3',4'-h]-1,6-naphthyridines

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The mass spectra of several pyrazolo[3,4-b]pyrido[2',3'-b]-1,6-naphthyridines and dipyrazolo[3,4-b];3',4'-h]-1,6-naphthyridines are presented. The fragmentation is initiated by the elimination of CO molecule [*m/z* 28] followed by other fragments, such as halogen (Cl, Br) or halogen acid (HCl, HBr) and some proton loss is also observed in some cases. Successive loss of HCN (*m/z* 27) molecules also completes the scheme with the stable C_6H_5 fragment.

Keywords: Fragmentations, Pyrazolo[3,4-b]pyrido[2',3'-b]-1,6-naphthyridines, Dipyrazolo[3,4-b];3',4'-h]-1,6-naphthyridines.

INTRODUCTION

Naphthyridine have received considerable attention over the past years because of their wide range of biological activities including antitumor [1-3], anti-inflammatory [4-6] and antifungal [6] activities. Pyridopyrimidine is one of the most important "privileged medicinal scaffolds", which are molecular frameworks used for the development of pharmaceutical agents for diverse applications. A large variety of pyridopyrimidine derivatives have been used as antitumor [7], antibaceterial [8], anti-inflammatory [9], antifungal [10] and antileishmaniasis [11] agents. Therefore, the synthesis of these molecules has attracted considerable attention. Gangjee and co-workers have described the construction of pyrimidonaphthyridine skeleton *via* multistep reaction [3]. However, the continued development of diversity synthesis of compounds library, including pyrimidonaphthyridine, benzonaphthyridine, pyrazolonaphthyridine and azabenzo[*b*]fluorene frameworks, is still strongly desired, because of their profound chemical and biological significance. In this paper, we would like to report highly efficient synthesis of compounds library containing benzo[b]pyrazolo[3,4-b]-1,6-naphthyridines, pyrazolo[3,4-b]pyrido[2',3'-b]-1,6-naphthyridines and dipyrazolo[3,4-b];3',4'-h]-1,6-naphthyridines (**1-6**).

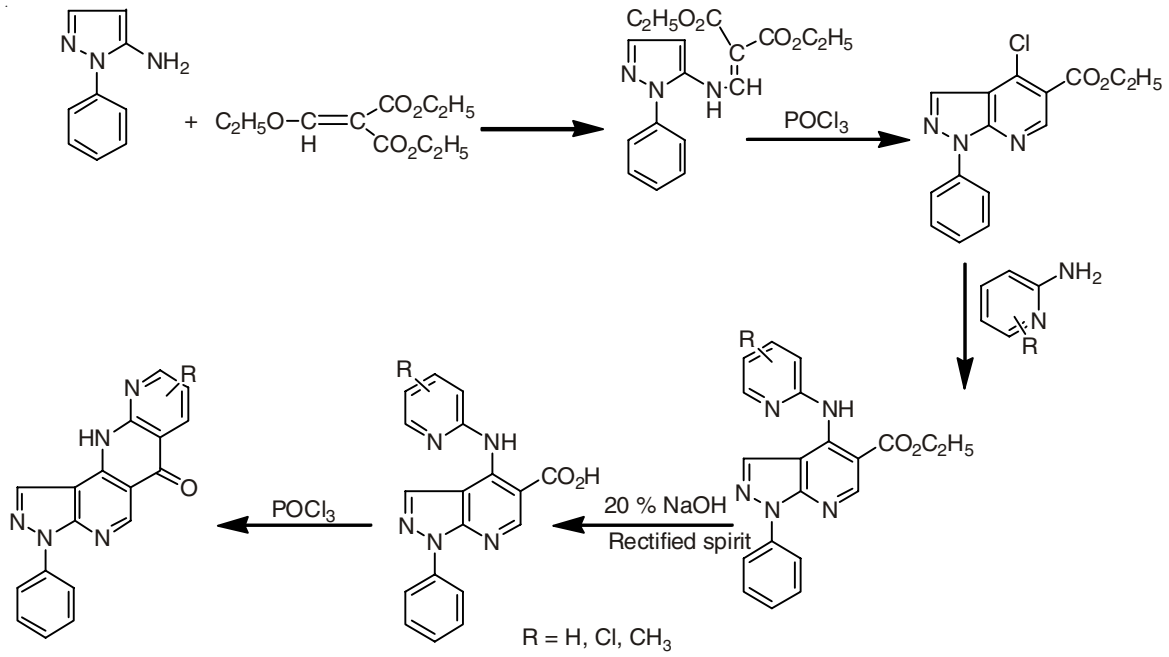
EXPERIMENTAL

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

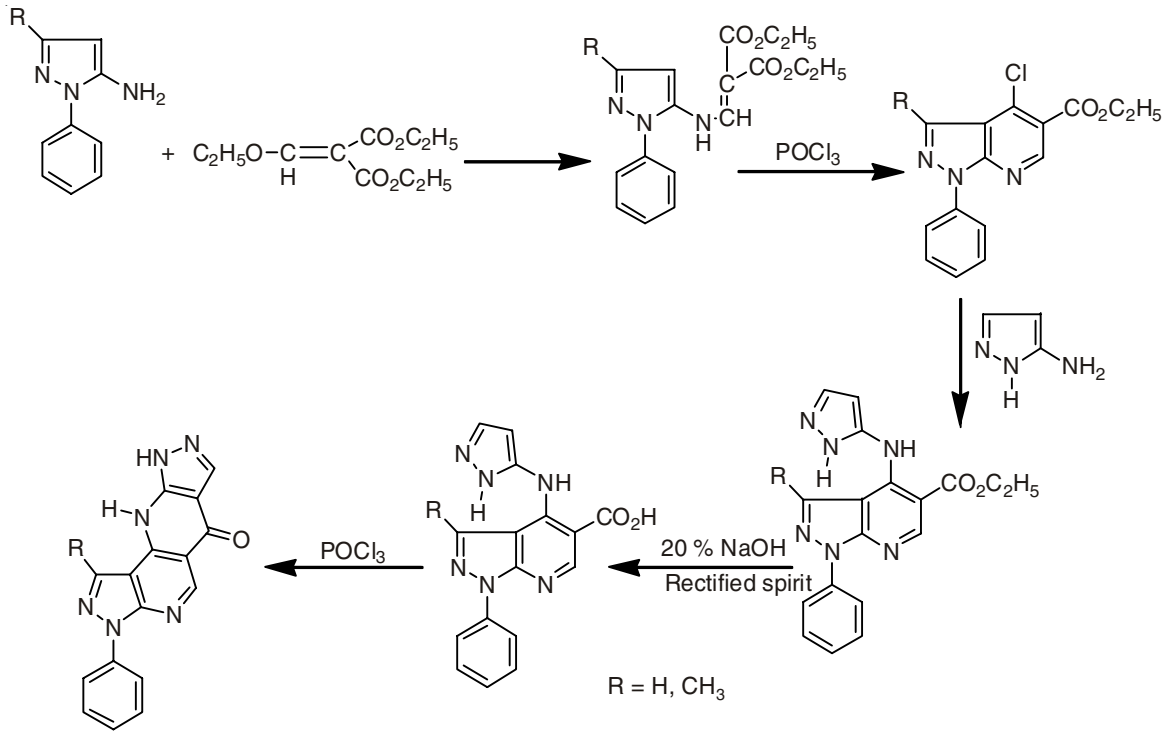
Synthesis of pyrazolo[3,4-b]pyrido[2',3'-b]-1,6-naphthyridines and dipyrazolo[3,4-b];3',4'-h]-1,6-naphthyridines (1-6): These were prepared according to the method already reported in our earlier communication [12]. 5-Amino-1-phenylpyrazole by successive condensation with diethyl ethoxymalonate in ethanol followed by the thermal cyclization (Gould-Jacobs reaction) provided ethyl 4-oxo-1-phenylpyrazolo[3,4-b]pyridine-5-carboxylate. A chlorodes-oxygenation with $POCl_3$ gives the corresponding 4-chloro derivative which in turn reacts with various amino pyridines and amino pyrazoles to give 4-anilino intermediate. This intermediate on tandem hydrolysis and cyclization provides the desired compounds **1-3** (**Scheme-I**), compounds **4** and **5** (**Scheme-II**) and compound **6** (**Scheme-III**).

RESULTS AND DISCUSSION

Mass spectrometric literature, including their fragmentation for various heterocyclic ring systems, was earlier collected in the book by Porter and Baldas [13]. The present series of compounds under study combine a two basis simple systems-



Scheme-I



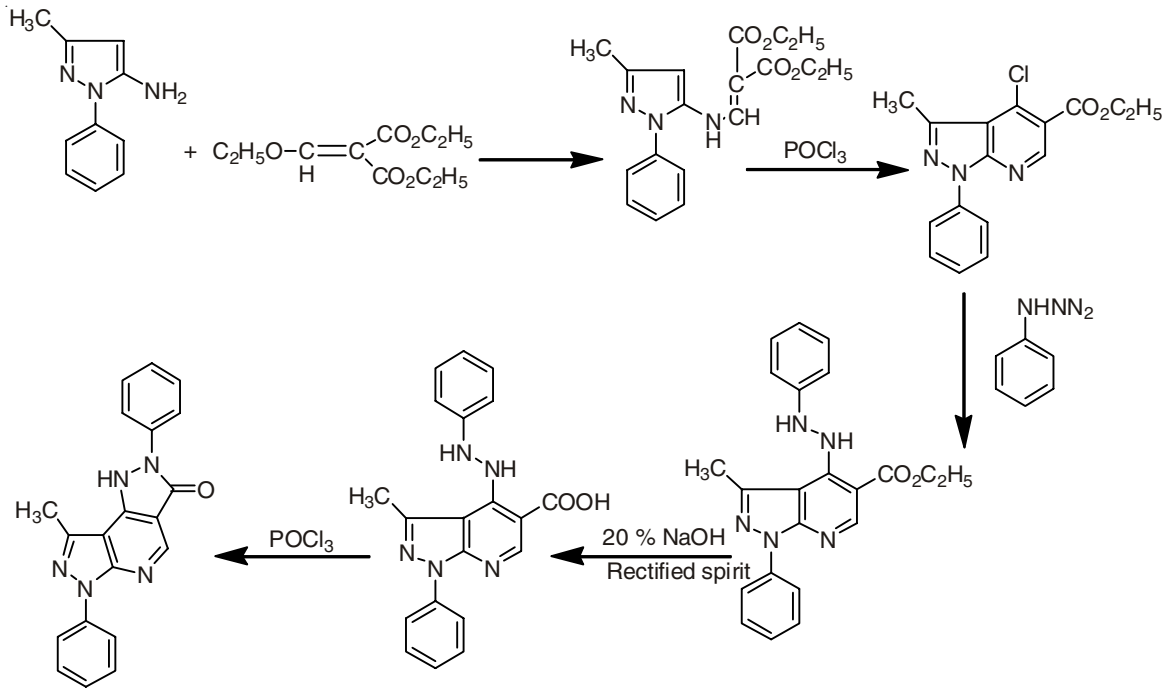
Scheme-II

pyridine and the pyrazole alongwith naphthyridines and should show interesting behaviour in their mass spectrometric behaviour.

Mass spectral data of benzo[b]-pyrazolo[3,4-b]-1,6-naphthyridines (**1-9**) as collected in Table-1 provides main common fragments for the various compounds in the series. All the mass spectra displayed molecular ion peaks as also the base peak, the most intense in the spectrum. The fragmentation as can be seen from various schemes, seems to follow a pattern of the loss of expected fragment CO (*m/z* 28) followed by others, such as halogen (Cl, Br) or halogen acid (HCl, HBr) and some proton loss is also observed in some cases. Successive loss of HCN (*m/z* 27) molecules also completes the scheme with the stable C_6H_5 fragment invariably present as a terminal moiety, which can further break down in the well known pattern [13].

Although, the most common fragments are collected in the Table-2, however a detailed fragmentation scheme is shown in the following **Schemes IV** and **V**.

Fragmentation pattern of compound 3: The fragmentation pattern of compound **3** is presented in **Scheme-IV**. It gives M^+ peak at *m/z* 327, which by the loss of CHO (*m/z* 29)



Scheme-III

TABLE-1
MASS SPECTRAL DATA OF PYRAZOLO[3,4-b]PYRIDO[2',3'-b]-1,6-NAPHTHYRIDINES AND DIPYRAZOLO[3,4-b];3',4'-h]-1,6-NAPHTHYRIDINES (**1-6**)

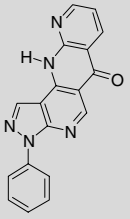
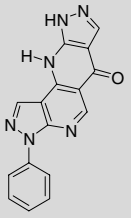
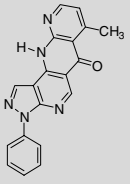
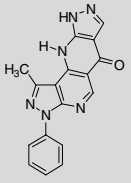
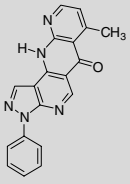
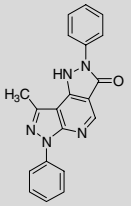
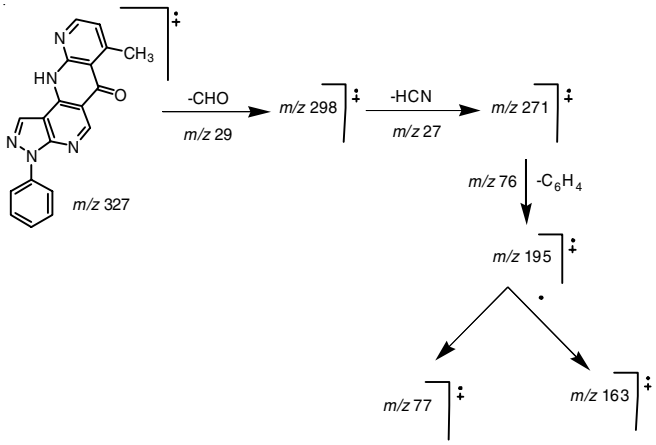
Compd. No.	Structure	Mass spectra *m/z* (relative intensity)	Compd. No.	Structure	Mass spectra *m/z* (relative intensity)
1		314 (23), 313 (100), 312 (31), 286 (6), 284 (10), 258 (5), 257 (5), 180 (3), 156 (11), 79 (9), 78 (36), 77(20), 51 (14)	**4**		303 (19), 302 (100), 301 (11), 274 (6), 273 (26), 247 (6), 245 (7), 218 (5), 193 (6), 77 (31), 51 (9)
2		328 (22), 327 (100), 326 (28), 300 (5), 298 (7), 271 (4), 195 (2), 164 (11), 92 (13), 77 (10), 65 (9)	**5**		317 (22), 316 (100), 315 (8), 287 (9), 259 (7), 158 (5), 90 (5), 77 (29), 51 (5)
3		328 (2), 327 (100), 326 (28), 298 (8), 163 (10), 93 (5), 92 (17), 77 (18), 65 (19), 51 (5)	**6**		342 (35), 341 (100), 340 (12), 312 (7), 207 (7), 77 (9)

TABLE-2
VARIOUS COMMON FRAGMENTS FOR COMPOUNDS **1-6**

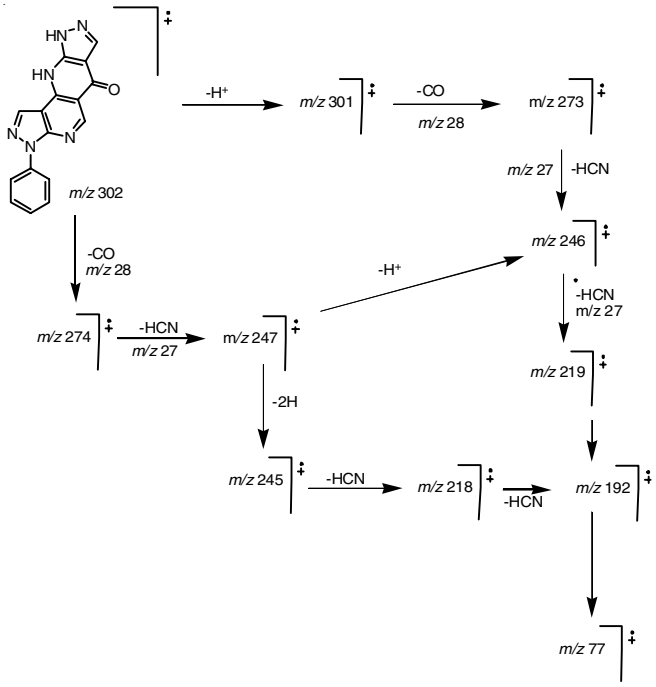
Comp. No.	M	M-H^+	M-CO	M-HCN	M-2HCN
1	313	312	–	286	258
2	327	326	299	300	271
3	327	326	299	–	271
4	302	301	–	273	246
5	316	315	274	287	260
6	341	34	313	–	–

group gives peak at *m/z* 298 which further loses HCN molecule followed by the loss of C6H4 (*m/z* 28) and gives a peak at *m/z* 195 which further loses different fragment till a fragment corresponding to a phenyl C_6H_5 (*m/z* 77) is given off.

Fragmentation pattern of compound 4: The fragmentation pattern of compound **4** is presented in **Scheme-V**. It gives M^+ peak at *m/z* 302, which by the loss of proton and CO (*m/z* 28) group gives peak at *m/z* 273 which further loses two HCN molecules and gives a peak at *m/z* 219. It further loses



Scheme-IV



Scheme-V

shorter fragments till a fragment corresponding to a phenyl C_6H_5 (*m/z* 77) is given off. In an alternative route molecular ion peak (*m/z* 302) loses CO molecule which further loses two HCN molecule and two proton and gives a peak at *m/z* 192 and this peak after the lose of shorter fragment end up at phenyl peak (*m/z* 77).

Conclusion

In this communication, we have presented a possible mass fragmentation pattern of a number of pyrazolo[3,4-b]pyrido-[2',3'-b]-1,6-naphthyridines and dipyrazolo[3,4-b];3',4'-h]-1,6-naphthyridines are presented, The fragmentation involves elimination of CO molecule followed by other fragments, such as halogen (Cl, Br) or halogen acid (HCl, HBr) and HCN, *etc*.

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