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Mass Spectrometry of Substituted Ethyl-4-anilinopyrazolo[3,4-b]pyridine-5-carboxylates

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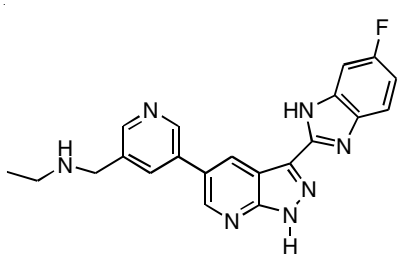
The mass spectra of a number of ethyl 4-anilinopyrazolo [3,4-b]pyridine-5-carboxylates are presented. The fragmentation is initiated by the elimination of ethanol molecule followed by the elimination of CO (*m/z* 28) and HCN molecules. In another alternative route an HCl may be removed followed by the CO loss (*m/z* 28). Further loss of one or more molecules of HCN (*m/z* 27) brings to shorter fragments till a fragment corresponding to a phenyl C_6H_5 (*m/z* 77) radical cation is reached.

Keywords: Fragmentations, Pyrazolopyrimidines, Pyrazolopyridines, Cyclizations.

INTRODUCTION

Pyrazolopyridines [1], pyrazolopyrimidines [2] and related fused heterocyclic compound are of interest as potential bioactive molecules. Pyrazolo[3,4-b]pyridines (**1-4**) are important compounds due to their biological activity and structural relationship with azaindoles [3-8]. A number of pyrazolo[3,4-b]pyridines are potentially biological active compounds as new inhibitors of xantine oxidase [9-13].



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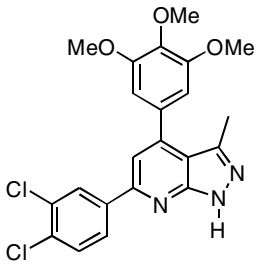

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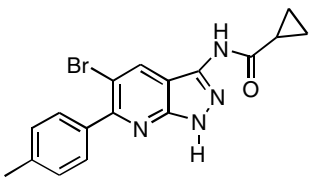

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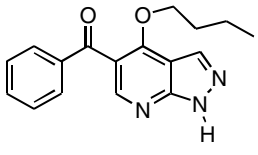

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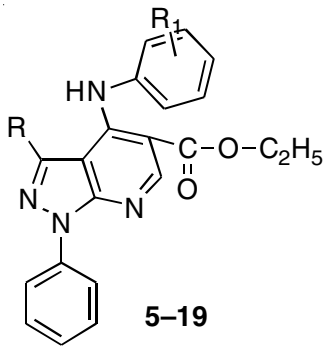
Pyrazolopyridines' chemistry is the subject of continuous interest in our laboratories [14-17] and here we would like to communicate mass spectroscopic fragmentation behaviour of some anilinoesters (**5-19**) which were obtained as intermediates during the synthesis of a new tetracyclic system [18].



5–19

5. R=H, R_1=3-Cl; **6.** R=H, R_1=3-Br; **7.** R=CH_3, R_1=3-Br; **8.** R=H, R_1=3-OCH_3 **9.** R=H, R_1=H; **10.** R= CH_3, R_1=2-OCH_3; **11.** R=H, R_1=2-OCH_3; **12.** R=H, R_1=H; **13**.R=H,R_1=3-CH3; **14.** R=H, R_1= 4-OCH_3; **15.** R=H R_1= 2, 4-Cl_2; **16.** R-H, R_1 = 3,4-Cl_2; **17.** R=H R_1= 2,6 $(CH_3)_2$; **18.** R=H, R1= 2,4-$(OCH_3)_2$; **19** R=H, R1= 2-CH_3

EXPERIMENTAL

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

Synthesis of ethyl 4-anilino-1-phenyl-1*H*-pyrazolo[3,4-b]pyridine-5-carboxylates (5-19): These were prepared from the reaction of ethyl 4-chloro-3-H (or methyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-5carboxylates with anilines in DMF or xylene as reported earlier [18].

RESULTS AND DISCUSSION

Mass spectrometric literature, including their fragmentation for various heterocyclic ring systems, was earlier collected in the book by Porter and Co-authors [19]. 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-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylates **(5-19)** is collected in Table-1. Table-2 provides main common fragments for the various compounds.

The mass spectrum of first compound in this series *i.e.*, ethyl 4-(3-chlorophenylamino)-1*H*-pyrazolo[3,4-b]pyridine-5-carboxylate (**5**) was analyzed. Its fragmentation pattern is presented in **Scheme-I**. The molecular ion peak corresponded to the molecular weight of the compound while the base peak (100 %) was the molecular ion corresponding to the ring cyclized one which is formed by the elimination of a molecule of ethanol (*m/z* 46). It is interesting to note that this ester (as well as others in the series) does not undergo an expected McLaffertty rearrangment [20] probably due to the possibility of formation of a more stable radical ion of the cyclized ring. This cyclization of the ester is somewhat reminiscent of the thermal cycization in the Gould-Jacobs reaction of anilino esters [21,22] (**Scheme-II**). Incidentally this cyclized ring is the subject of our publication where it was obtained by the successive hydrolysis and cyclization with phosphoryl chloride [18].

The fragment (*m/z* 346,348) in its turn looses CO (*m/z* 28) 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 HCl may be removed followed by the CO loss (*m/z* 28). Further loss of one or more molecules of HCN (*m/z* 27) brings to shorter fragments till a fragment corresponding to a phenyl C_6H_5 (*m/z* 77) is given off.

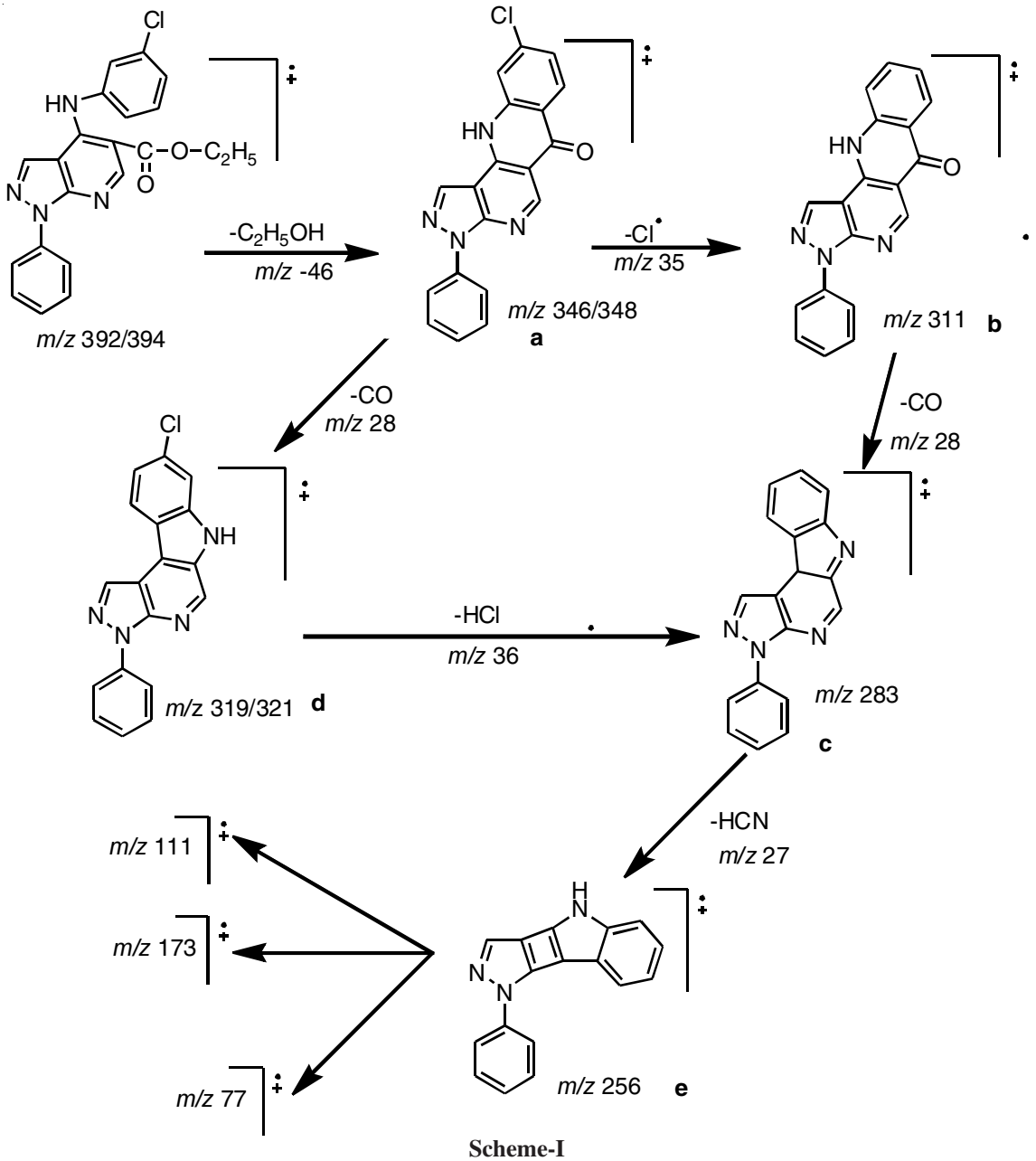
Generally, in present series of anilino esters, the base peaks follow the above general pattern. However in the case, when

TABLE-1
MASS SPECTRAL DATA OF ETHYL-4-ANILINO-1-PHENYL-1*H*-PYRAZOLO[3,4-b]PYRIDINE-5-CARBOXYLATES (**5-19**)

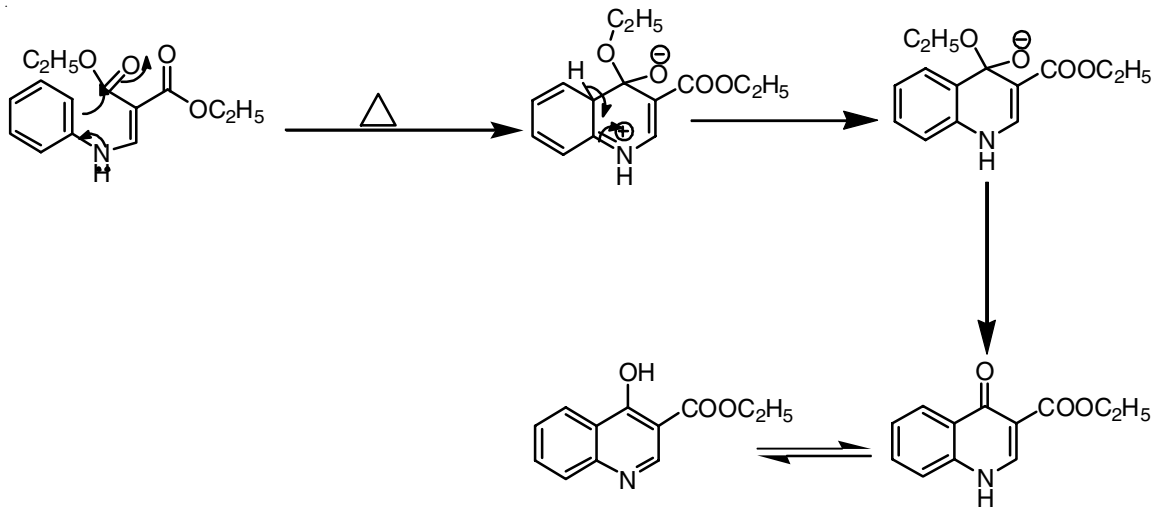
Compd. No.	Substituents R^1 and R	Mass spectra *m/z* (relative intensity)
5	3-Cl	395 (7), 394 (34), 393 (22), 392 (95), 349 (9), 348 (35), 347 (41), 346 (100), 345 (43), 319 (8), 311 (25), 284 (6), 283 (10), 282 (7), 256 (4), 173 (9), 111 (7), 77 (35)
6	3-Br	439 (22), 438 (93), 436 (95), 394 (13), 392 (48), 391 (27), 390 (48), 389 (14), 312 (27), 311 (100), 285 (6), 284 (15), 283 (35), 282 (15), 257 (8), 256 (8), 229 (5), 180 (5), 156 (22), 101 (5), 77 (47), 65 (6), 51 (12).
7	3-Br, CH_3	395 (7), 394 (26), 393 (18), 392 (78), 349 (8), 348 (34), 347 (36), 346 (100), 345 (35), 319 (7), 312 (8), 311 (37), 310 (7), 284 (6), 283 (13), 282 (7), 256 (5), 196 (5), 173 (9), 155 (5), 111 (7), 77 (36), 51 (5)
8	3-OCH_3	439 (13), 438 (47), 436 (48), 392 (13), 391 (7), 390 (13), 312 (24), 311 (100), 310 (6), 284 (8), 283 (20), 282 (8), 256 (5), 155 (12), 77 (7)
9	H	453 (15), 452 (69), 451 (15), 450 (70), 407 (13), 406 (52), 405 (24), 404 (52), 403 (13), 378 (5), 377 (6), 376 (5), 375 (5), 327 (6), 326 (25), 325 (99), 324 (8), 323 (5), 299 (6), 298 (20), 297 (37), 296 (10), 295 (8), 282 (6), 270 (10), 269 (6), 268 (5), 257 (8), 256 (8), 229 (6), 193 (5), 192 (6), 166 (5), 165 (5), 162 (12), 140 (6), 127 (5), 102 (6), 91 (5), 90 (5), 78 (7), 77 (67), 76 (9), 75 (8), 66 (7), 64 (6), 51 (20)
10	CH_3, 2-OCH_3	402 (1), 389 (27), 388 (100), 343 (9), 342 (32), 341 (73), 327 (5), 315 (8), 313 (31), 312 (20), 311 (9), 271 (14), 235 (10), 194 (6), 171 (5), 156 (5), 77 (18), 51 (4)
11	2-OCH_3	388 (31), 387 (97), 342 (24), 341 (58), 340 (100), 326 (5), 313 (15), 312 (49), 311 (26), 297 (95), 284 (6), 271 (7), 270 (19), 234 (15), 193 (7), 171 (80), 156 (9), 92 (5), 78 (9), 77 (43), 65 (9), 64 (6), 52 (6), 51 (19)
12	H	359 (15), 358 (63), 313 (26), 312 (100), 311 (75), 286 (6), 285 (13), 284 (8), 283 (9), 257 (7), 256 (6), 209 (5), 180 (8), 156 (13), 155 (6), 154 (7), 153 (7), 129 (5), 128 (8), 127 (14), 103 (7), 102 (6), 89 (7), 78 (9), 77 (92), 76 (5), 65 (8), 53 (5), 52 (30)
13	3-CH_3	373 (19), 372 (72), 327 (27), 326 (100), 325 (50), 299 (7), 298 (5), 297 (6), 270 (4), 194 (3), 163 912), 162 (5), 91 (10), 85 (8), 83 (12), 77 (20), 65 (7), 51 (4)
14	4-OCH_3	389 (30), 388 (100), 343 (13), 342 (38), 341 (82), 327 (7), 314 (10), 313 (39), 312 (27), 311 (13), 299 (5), 297 (5), 285 (5), 271 (21), 270 (5), 235 (13), 194 (7), 171 (5), 156 (5), 77 (12)
15	2,4-Cl_2	428 (1), 426 (1), 381 (1), 379 (1), 345 (1), 311 (18), 310 (97), 281 (23), 266 (18), 265 (100), 264 (7), 263 (39), 250 (5), 249 (23), 237 (9), 236 (8), 235 (10), 222 (7), 221 (13), 209 (5), 208 (12), 195 (5), 194 (8), 193 (8), 168 (5), 167 (6), 140 (8), 104 (6), 91 (5), 78 (5), 77 (38), 51 (9)
16	3,4-Cl_2	430 (1), 429 (1), 428 (3), 427 (1), 426 (6), 383 (1), 382 (4), 381 (3), 380 (6), 345 (3), 311 (17), 310 (85), 281 (23), 266 (18), 265 (100), 264 (16), 263 (40), 250 (6), 249 (22), 237 (8), 236 (7), 235 (10), 222 (7), 221 (11), 209 (5), 208 (12), 200 (5), 199 (7), 198 (7), 168 (5), 167 (5), 140 (8), 133 (5), 103 (7), 91 (5), 78 (5), 77 (35), 66 (5), 51 (9)
17	2,6-$(CH_3)_2$	387 (3), 341 (3), 317 (4), 311 (18), 310 (74), 281 (20), 266 (17), 265 (90), 264 (15), 263 (38), 250 (5), 249 (20), 247 (7), 237 (8), 236 (6), 235 (10), 222 (6), 221 (12), 209 (5), 208 (12), 207 (5), 206 (18), 205 (100), 203 (5), 195 (5), 194 (7), 193 (7), 176 (5), 167 (6), 140 (8), 118 (6), 110 (15), 104 (7), 91 (10), 89 (7), 85 (5), 84 (48), 83 (11), 78 (7), 77 (44), 72 (42), 71 (11), 66 (5), 65 (5), 58 (7), 57 (4), 55 (10), 51 (13)
18	2,4-$(OCH_3)_3$	419 (28), 418 (100), 373 (9), 372 (32), 371 (78), 357 (6), 344 96), 343 (27), 342 (18), 341 (15), 313 (7), 285 (4), 209 (4), 186 (16), 150 (5), 77 (14)
19	H, CH_3	388 (9), 387 (34), 342 (24), 341 (100), 340 (10), 312 (5), 296 (7), 222 (5), 207 (5), 117 (5), 105 (15), 93 (7), 83 (5), 78 (7), 77 (85), 65 (7), 51 (5)

TABLE-2
MASS SPECTRAL FRAGMENTS OF ETHYL 4-ANILINO-1-PHENYL-1*H*-PYRAZOLO[3,4-b]PYRIDINE-5-CARBOXYLATES (**5-19**), *m/z* (RELATIVE INTENSITIES)

Fragments/Compd. No.	M^+	a	b	c	d	e
5	395 (7)	346 (100)	311 (25)	283 (10)	319 (8)	256 (4)
6	438 (22)	390 (48)	311 (100)	283 (35)	–	256 (8)
7	392 (75)	346 (100)	311 (35)	285 (11)	–	256 (6)
8	438 (48)	391 (10)	311 (100)	285 (20)	–	256 (4)
9	453 (15)	404 (52)	325 (100)	297 (37)	–	282 (6)
10	402 (1)	343 (77)	388 (100)	271 (16)	–	235 (10)
11	388 (31)	341 (100)	313 (15)	–	–	285 (6)
12	359 (15)	326 (10)	284 (8)	312 (100)	–	257 (7)
13	373 (19)	326 (100)	298 (5)	–	–	270 (4)
14	388 (100)	343 (74)	–	313 (32)	–	271 (15)
15	428 (1)	380 (1)	310 (97)	282 (23)	265 (100)	238 (9)
16	426 (5)	380 (6)	310 (82)	282 (18)	265 (100)	238 (8)
17	387 (3)	310 (74)	281 (20)	–	205 (100)	221 (12)
18	418 (100)	372 (32)	344 (6)	–	286 (4)	209 (4)
19	388 (9)	341 (100)	313 (5)	296 (7)	–	207 (5)



Scheme-I



Scheme-II

halogens (Cl, Br) are present in the molecule, the molecular ion and subsequent fragments containing halogens 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. In case of compounds having certain methyl and methoxy substituents showed the loss of these groups during fragmentation process.

Table-2 represents the common ion fragments, which demonstrate a similar behaviour adopted for the fragmentation processes for these anilino esters.

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