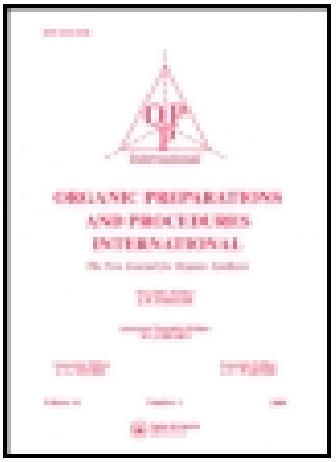

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SYNTHESIS OF ISOMERIC PYRIDOOXAZINONES, PYRIDOPYRIDAZINES AND TRIAZOLOPYRIDOPYRIDAZINES FROM o-AROYLPYRIDINECARBOXYLIC ACIDS

Mohamed Salah K. Youssef [a] , Amin F. Fahmy [b] , Mohamed S. Abdel Halim [b] , Mamdouh A. Hassan [c] & Jürgen Sauer [d]

[a] Department of Chemistry, Faculty of Science , Assiut University , Assiut, EGYPT

[b] Department of Chemistry, Faculty of Science , Ain Shams University , Abbassia, Cairo, EGYPT

[c] Department of Chemistry, Qena Faculty of Science , South Valley University , Qena, EGYPT

[d] Institute of Organic Chemistry, University of Regensburg , 8400, Regensburg, GERMANY E-mail:

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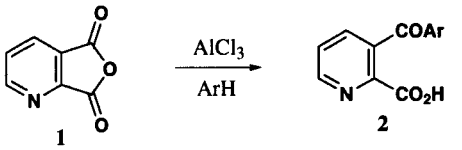
SYNTHESIS OF ISOMERIC PYRIDOOXAZINONES, PYRIDOPYRIDAZINES AND TRIAZOLOPYRIDOPYRIDAZINES FROM *o*-AROYLPYRIDINECARBOXYLIC ACIDS

Mohamed Salah K. Youssef*[†], Amin F. Fahmy[††],
Mohamed S. Abdel Halim[††] and Mamdouh A. Hassan[†††]

[†]*Department of Chemistry, Faculty of Science, Assiut University, Assiut, EGYPT*
[††]*Department of Chemistry, Faculty of Science, Ain Shams University, Abbassia, Cairo, EGYPT*
[†††]*Department of Chemistry, Qena Faculty of Science, South Valley University, Qena, EGYPT*
and
Jürgen Sauer

Institute of Organic Chemistry, University of Regensburg, 8400 Regensburg, GERMANY
e-mail: salah_kamel2000@yahoo.com

In our previous work,[1-3] we examined the chemistry of *N*-hydroxyquinolinimides as starting materials for the synthesis of condensed heterocyclic systems containing the pyridine moiety. It is also known from the literature[4-6] that quinolinic anhydride (**1**) reacts with anhydrous $AlCl_3$ in benzene, toluene and chlorobenzene to give the corresponding 3-aroyl-2-pyridinecarboxylic acids **2**; none of the isomeric 2-aroyl-3-pyridinecarboxylic acids **3** could be isolated. The present investigation deals with the synthesis of isomeric pyridooxazine derivatives and some related compounds *via* an alternative new route using the acids **2** and **3**. Thus, the reaction of quinolinic anhydride (**1**) with anhydrous $AlCl_3$ in benzene, toluene and chlorobenzene was repeated, and also carried out in anisole, to yield **2a-d** in 61-71% yields. As reported previously, none of the corresponding 2-aroyl-3-pyridinecarboxylic acids **3** was obtained. The structure of **2a-d** was confirmed spectroscopically (IR, ^{1}H-NMR and MS; *Table 2*). The mass spectra[7,8] showed (M^+-CO_2H) and absence of (M^+-OH) which suggests that these compounds exist in the open structure. The structure of **2d** was also established by thermal decarboxylation to 3-(*p*-anisoyl)pyridine, identical to an authentic sample prepared by a Friedel-Crafts reaction of nicotinyl chloride with anisole. The mechanism of the decarboxylation occurs similarly to that previously reported for the decarboxylation of picolinic acids.[9-13]

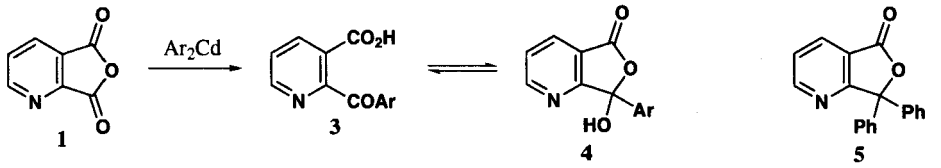


(1)

a) Ar = C_6H_5; b) Ar = *p*-$CH_3C_6H_4$; c) Ar = *p*-ClC_6H_4; d) Ar = *p*-$CH_3OC_6H_4$

The preparation of ketones by the reaction of acyl halides with alkylcadmium compounds has been described.[14] The results were so satisfactory that the reaction was extended to include the preparation of a γ-keto acids from succinic anhydride and to the synthesis of ketones.[15] The reaction of several cadmium alkyls and aryls with phthalic anhydride gave the corresponding *o*-acylbenzoic acids.[16] Wang *et al.*[17] have shown that 3-nitrophthalic acid anhydride could be converted to 2-acetyl-3-nitrobenzoic acid by the reaction with dimethylcadmium; 3,3-dimethyl-4-nitrophthalide was isolated as a minor product (1%).

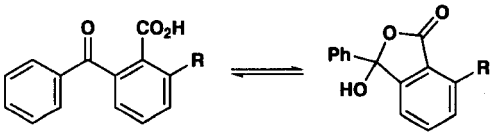
In the present work, an alternative new route for the synthesis of the required 2-aroyl-3-pyridinecarboxylic acids was investigated. Thus, quinolinic anhydride (**1**) was successfully converted to **3** in 18-23% yields by reaction with diarylcadmium reagents; 7,7-diphenyl-furano[3,4-*b*]pyridin-5-one (**5**) was also formed as a by-product (1.5%) from the reaction of **1** with diphenylcadmium. The structures of the compounds **3** and **5** were established on the basis of elemental analysis, IR, ^{1}H-NMR and MS (*Tables 1 and 2*). The relatively low δ values (6.32, 8.27, 6.33) for the OH proton of **3a-c** suggests that **3a-c** exist in a tautomeric equilibrium with the cyclic lactol structure **4**. The mass spectra showed (M^+-OH) and (M^+-CO_2H) confirming both **3** and **4**. The ^{13}C-NMR of **5** showed eleven types of carbon atoms, which indicated the structure to be as shown. The data of ^{1}H-NMR, ^{13}C-NMR and MS are given in *Table 2*.



(2)

a) Ar = C_6H_5; b) Ar = *p*-$CH_3C_6H_4$; c) Ar = *p*-$CH_3OC_6H_4$

The data in the literature point to the fact that the ring-chain tautomeric equilibrium in the case of *o*-benzoylbenzoic acids shifts towards the lactol form in the 6-substituted derivatives.[18] *o*-Benzoylbenzoic acid is reported to be completely open in methanol solution whereas the 6-methyl derivative (R = Me) exists to the extent of 65% in the lactol form at room temperature. Typically, a 6-nitro substituent (R = NO_2) enhances the rate of formation of the lactol due to its electronic effects alone.[19,20]



(3)

Table 1. Yields, mps and Elemental Analyses of Compounds **2,3,5** and **6-15**

Cmpd	Yield (%)	mp (°C)	Elemental Analyses (Found) C	H	N
2a	61	120-122[a]	68.72(68.72)	3.99(4.07)	6.16(5.90)
2b	63	110-112[a]	69.65(69.65)	4.59(4.55)	5.81(5.84)
2c	68	149-150[a†]	59.66(59.67)	3.08(3.18)	5.35(5.21)
2d	71	160-161[b]	65.37(65.39)	4.31(4.32)	5.44(5.38)
3a	18	186-187[c]	68.72(68.75)	3.96(4.01)	6.16(6.23)
3b	22	126-128[c]	69.71(69.73)	4.56(4.60)	5.81(5.75)
3c	23	147-148[c]	65.37(65.41)	4.28(4.31)	5.44(5.45)
5	1.5	160-161[d]	79.44(79.46)	4.53(4.54)	4.87(5.09)
6a	88	198-200[e]	69.64(69.96)	3.59(3.62)	12.49(12.26)
6b	89	215-217[e]	70.53(70.73)	4.20(4.25)	11.76(11.64)
6c	86	257-258[e]	60.35(60.27)	2.72(2.74)	10.83(10.78)
6d	70	190-192[e]	66.14(66.08)	3.93(3.90)	11.02(11.01)
7a	62	242-244[f]	69.95(69.50)	4.06(3.71)	18.83(18.81)
7b	64	243-245[f]	70.86(70.82)	4.67(4.62)	17.71(17.67)
7c	69	246-248[f]	60.59(60.48)	3.13(3.13)	16.31(16.20)
7d	75	268-270[f]	66.38(66.55)	4.38(4.29)	16.59(16.64)
8a	88	136-137[e]	69.64(69.61)	3.59(3.56)	12.49(12.36)
8b	89	133-134[e]	70.59(70.51)	4.23(4.28)	11.76(11.76)
8c	90	159-160[e]	66.14(66.10)	3.93(3.84)	11.02(11.17)
9a	89	238-240[e]	69.95(69.61)	4.06(3.83)	18.83(18.77)
9b	87	250-251[e]	70.86(70.80)	4.67(4.68)	17.71(17.72)
9c	81	241-243[e]	66.38(66.49)	4.38(4.42)	16.59(16.55)
10a	78	218-219[d]	64.54(64.83)	3.31(3.44)	17.38(17.42)
10b	73	140-141[d]	65.70(65.91)	3.91(3.83)	16.43(16.24)
11a	68	220-222[e]	65.74(65.74)	4.64(4.84)	29.51(29.60)
11b	81	195-196[e]	66.85(67.01)	5.17(5.23)	27.87(27.91)
12a	73	155-156[d]	64.54(64.60)	3.31(3.39)	17.38(17.21)
12b	63	134-136[d]	65.70(65.87)	3.91(4.03)	16.43(16.24)
13a	70	225-226[e]	65.74(65.80)	4.64(4.57)	29.51(29.53)
13b	74	230-231[e]	66.85(66.76)	5.17(5.21)	27.87(27.76)
14a	82	257-258[g]	67.93(68.02)	3.64(3.71)	28.32(28.30)
14b	86	229-230[g]	68.97(68.89)	4.21(4.20)	26.80(26.71)
15a	68	206-208[h]	67.93(67.88)	3.64(3.59)	28.32(28.11)
15b	71	222-224[h]	68.97(69.02)	4.21(4.25)	26.80(26.77)

a) From benzene/pet. ether; b) From benzene; c) From ether/per. Ether; d) From ether; e) From ethanol; f) From benzene/ethanol; g) From benzene/methanol (5:1); h) From ethylacetate. †*lit.*[6] mp 147°C

Table 2. Spectral Data of Compounds **2,3,5** and **6-15**

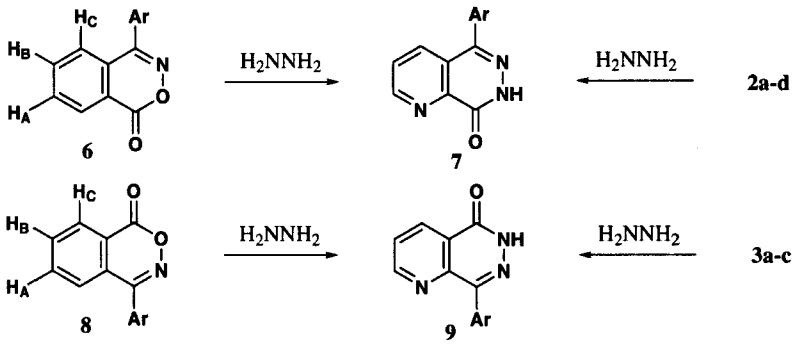
Cmpd	IR (cm^{-1})	^{1}H-NMR (δ)	MS m/z(%)
2a	1690(CO), 3100-2450 (br.OH)	7.16-7.90 (m, 7H, Ar-H + H_B + H_C), 8.75 (d of d, 1H, H_A), 9.80 (s, br, 1H, COOH)	----
2b	1685(CO), 3100-2450 (br.OH)	7.10-7.88 (m, 6H, Ar-H + H_B + H_C), 8.80 (d of d, 1H, H_A), 12.23 (s, br, 1H, COOH), 2.38 (s, 3H, CH_3)	241(24)
2c	----	7.39-7.44, 7.65-7.69 (AA'BB', 4H, Ar-H), 7.7 (d of d, 1H, H_B), 7.86 (d of d, 1H, H_C), 8.88 (d of d, 1H, H_A), 10.30 (s, br, 1H, COOH)	263(15), 261(45)
2d	----	6.90-6.94, 7.67-7.72 (m, 5H, Ar-H + H_B), 7.84 (d of d, 1H, H_C), 8.76, d of d, 1H, H_A, 11.4 (s, br, 1H, COOH), 3.86 (s, 3H, OCH_3)	257(43)
3a	1690(CO), 2480(br.OH)	7.42-7.85 (m, 6H, Ar-H + H_B), 8.44 (d of d, 1H, H_C), 8.80 (d of d, 1H, H_A), 6.32 (s, br, 1H, COOH)	227(19)
3b	1690(CO), 2480(br.OH)	7.27-7.80 (m, 5H, Ar-H + H_B), 8.53 (d of d, 1H, H_C), 8.87 (d of d, 1H, H_A), 2.37 (s, 3H, CH_3), 8.27 (br. s, 1H, OH)	----
3c	1680(CO), 2480(br.OH)	6.86-7.16, 7.46-7.76 (m, 5H, Ar-H + H_B), 8.73 (d of d, 1H, H_C), 8.72 (d of d, 1H, H_A), 3.83 (s, 3H, OCH_3), 6.33 (s, br, 1H, OH)	----
5	1760(CO)	7.28-7.61 (m and d of d, 11H, Ar-H + H_B; J_{BA} = 4.9, J_{BC} = 7.8 Hz), 8.19-8.23 (d of d, 1H, H_C; J_{CA} = 1.6, J_{CB} =7.8 Hz), 8.93-8.96 (d of d, 1H, H_A; J_{AC} = 1.6, J_{AB} = 4.9 Hz) **^{13}C-NMR** (δ) 90.58 (s, C-5), 119.44 (s, C-10), 124.04 (d, C-8), 126.79 (d, C-3), 128.38 (d, C-1) 128.46 (d, C-2), 134.24 (d, C-9), 139.60 (s, C-4) 155.16 (d, C-7), 167.53 (s, C-6), 170.02 (s, C-11)	287 (93)
6a	1765(CO)	7.46-7.66 (m, 5H, Ar-H), 7.76-8.05 (m, 2H, H_B + H_C), 9.16 (d of d, 1H, H_A)	224(100)
6b	1740(CO)	7.37-7.49 (AA'BB', 4H, Ar-H), 7.79 (d of d, 1H, H_C), 9.18 (d of d, 1H,H_A), 2.48 (s,3H,CH_3)	238(100)
6c	----	7.68 (m, 4H, Ar-H), 7.98 (d of d, 1H, H_B), 7.91 (d of d, 1H, H_C), 9.17 (d of d, 1H, H_A; J_{AB} = 4.4 Hz, J_{AC} = 1.8 Hz, J_{BC} = 8.2 Hz)	260(34), 258(100)
6d	----	----	254(100)
7a	1700(CO), 3180(NH)	7.53 (m, 5H, Ar-H), 7.85 (d of d, 1H, H_B), 8.08 (d of d, 1H, H_C), 9.08 (d of d, 1H, H_A), 13.01 (s, 1H, NH)	223(100)
7b	1650(CO), 3200(NH)	7.35-7.50 (AA'BB', 4H, Ar-H), 7.87 (d of d, 1H, H_B), 8.09 (d of d, 1H, H_C), 9.10 (d of d, 1H, H_A), 13.05 (s, 1H, NH), 2.41 (s, 3H, CH_3)	----
7c	1640(CO), 3280(NH)	7.63 (m, 4H, Ar-H), 7.86 (d of d, 1H, H_B), 8.11 (d of d, 1H, H_C), 9.10 (d of d, 1H, H_A), 13.10 (s, 1H, NH)	259(33), 257(100)
7d	----	7.09-7.14, 7.51-7.57 (AA'BB', 4H-Ar-H), 8.11 (d of d, 1H, H_C), 9.11 (d of d, 1H, H_A), 13.03 (s, 1H, NH), 3.48 (s, 3H, OCH_3)	----
8a	1755(CO)	7.26 (m, 6H, Ar-H + H_B), 8.70 (d of d, 1H, H_C), 9.13 (d of d, 1H, H_A)	224(100)

Table 2. Continued...

Cmpd	IR (cm^{-1})	^{1}H-NMR (δ)	MS m/z(%)
8b	1730(CO)	7.33-7.37, 7.79-7.85 (AA'BB', 4H, Ar-H), 7.79 (d of d, 1H, H_B), 8.71 (d of d, 1H, H_C), 9.16 (d of d, 1H, H_A), 2.45 (s, 3H, CH_3)	238(100)
8c	----	6.90-7.15, 7.63-7.96 (AA'BB',5H, Ar-H + H_B), 8.68 (d of d, 1H, H_C), 9.13 (d of d, 1H, H_A), 3.87 (s, 3H, OCH_3)	----
9a	1660(CO), 3160(NH)	7.45-8.08 (m, 6H, Ar-H + H_B), 8.77 (d of d, 1H,H_C), 9.23 (d of d,1H,H_A), 13.20 (s,1H, NH)	----
9b	----	7.22-8.00 (m, 5H, Ar-H + H_B), 8.70 (d of d, 1H, H_C), 9.20 (d of d, 1H, H_A), 13.13 (s, 1H, NH), 2.43 (s, 3H, CH_3)	----
9c	1690(CO), 3170(NH)	6.93-8.07 (m, 5H, Ar-H + H_B), 8.70 (d of d, 1H, H_C), 9.16 (d of d, 1H, H_A), 13.05 (s, 1H, NH), 3.82 (s, 3H, OCH_3)	253(100)
10a	absence of (CO) and (NH)	7.62 (m, 5H, Ar-H), 7.84 (d of d, 1H, H_B), 8.43 (d of d, 1H, H_C), 9.34 (d of d, 1H, H_A)	243 (23), 241(69)
10b	absence of (CO) and (NH)	7.39-7.42, 7.61-7.64 (AA'BB', 4H, Ar-H), 7.87 (d of d, 1H, H_B), 8.47 (d of d, 1H, H_C), 9.35 (d of d, 1H, H_A), 2.49 (s, 3H, CH_3)	257(23), 255(67)
11a	3320, 3240(NH)	----	----
11b	3320, 3240(NH)	----	----
12a	absence of (CO) and (NH)	7.40-7.68, 8.03-8.23 (m, 5H, Ar-H), 7.87 (d of d, 1H, H_B), 8.63 (d of d, 1H, H_C), 9.30 (d of d, 1H, H_A)	243(5), 241(19)
12b	absence of (CO) and (NH)	7.36-7.40, 8.03-8.00 (AA'BB', 4H, Ar-H), 7.81 (d of d, 1H, H_B), 8.65 (d of d, 1H, H_C), 9.33 (d of d, 1H, H_A), 2.47 (s, 3H, CH_3)	257(23), 255(14)
13a	3320, 3080(NH)	----	----
13b	3320, 3080(NH)	----	----
14a	----	7.67 (m, 6H, Ar-H + H_B), 8.30 (d of d, 1H, H_C), 9.15 (s, 1H, H_D), 9.25 (d of d, 1H, H_A)	----
14b	----	7.41-7.45, 7.54-7.58 (4H, Ar-H), 7.71 (d of d, 1H, H_B), 8.29 (d of d, 1H, H_C), 9.14 (s, 1H, H_D), 9.23 (d of d, 1H, H_A), 2.51 (s, 3H, CH_3)	261(100)
15a	----	7.35-8.05 (m, 6H, Ar-H + H_B), 8.88 (d of d, 1H, H_C), 9.02 (d of d, 1H, H_A), 9.41 (s,1H, H_D)	----
15b	----	7.36-7.40, 7.81-7.85 (AA'BB', 4H, Ar-H), 7.04 (d of d, 1H, H_B), 8.97 (d of d, 1H, H_C), 9.15 (d of d, 1H, H_A), 9.70 (s, 1H, H_D), 2.43 (s, 3H, CH_3)	261(100)

Treatment of acids **2a-d** and acids **3a-c** with hydroxylamine hydrochloride in pyridine afforded the isomeric, 5-arylpyrido[3,2-*d*][1,2]oxazin-8-ones (**6a-d**) and 8-arylpyrido[2,3-*d*]-[1,2]oxazin-5-ones (**8a-c**) respectively, in better yields (70-90%) than those reported (6-45%) in the previous publication.[3] The structures of **6a-d** and **8a-c** were confirmed by microanalytical

data and spectroscopically (*Tables 1 and 2*). In addition, their structures were confirmed from the the fact that they were identical with the products obtained from the action of anhydrous $AlCl_3$ on *N*-hydroxyquinolinimide in aromatic substrates.[3]

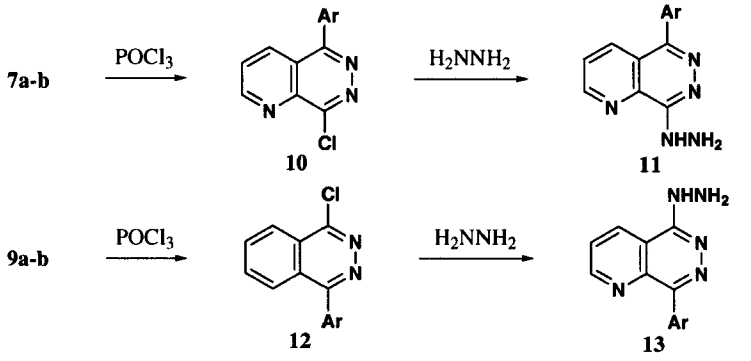


(4)

6: a) Ar = C_6H_5; b) Ar = *p*-$CH_3C_6H_4$; c) Ar = *p*-ClC_6H_4; d) Ar = *p*-$CH_3OC_6H_4$
8: a) Ar = C_6H_5; b) Ar = *p*-$CH_3C_6H_4$; c) Ar = *p*-$CH_3OC_6H_4$

Hydrazinolysis of **2a-d** and **3a-c** with hydrazine hydrate in acetic acid led to the formation of 5-arylpyrido[2,3-*d*]pyridazin-8(7*H*)-ones (**7a-d**) and 8-arylpyrido[2,3-*d*]pyridazin-5(6*H*)-ones (**9a-c**) respectively, in 62-89% yields. The IR, ^{1}H-NMR and MS for **7a-d** and **9a-c** are given in *Table 2*. When **6** or **8** was heated with hydrazine hydrate at reflux in acetic acid, the same products **7** or **9** were formed. The products obtained by this method[3] (80-89% yields) were identical in all aspects (elemental analysis, mp, mixed mp and spectral data) with those prepared above.

The reaction of **7a,b** or **9a,b** with phosphorus oxychloride[21,22] gave 5-aryl-8-chloropyrido-[2,3-*d*]pyridazine (**10a,b**) or 8-aryl-5-chloropyrido[2,3-*d*]pyridazine (**12a,b**) respectively.

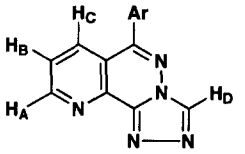


(5)

a) Ar = C_6H_5; b) Ar = *p*-$CH_3C_6H_4$

Treatment of **10a,b** or **12a,b** with hydrazine hydrate[23] afforded the corresponding 5-aryl-8-hydrazinopyrido[2,3-*d*]-pyridazines (**11a,b**) or 9-aryl-5-hydrazinopyrido[2,3-*d*]pyridazines (**13a,b**). The structures of **10-13** were confirmed on the basis of elemental analyses as well as spectral data (IR, ^{1}H-NMR and MS; *Tables 1 and 2*).

Hydrazino derivatives **11a,b** or **13a,b** upon heating with formic acid,[3,24-27] underwent cyclization to afford the corresponding 6-aryl-1,2,4-triazolo[4,3-*b*]pyrido[2,3-*d*]pyridazines (**14a,b**) or 6-aryl-1,2,4-triazolo[4,3-*b*]pyrido[3,2-*d*]pyridazines (**15a,b**) respectively, based on elemental and spectroscopic data (*Tables 1 and 2*).



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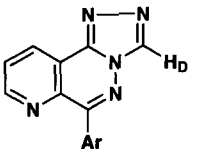

15

(6)

a) Ar = C_6H_5; b) Ar = *p*-$CH_3C_6H_4$

EXPERIMENTAL SECTION

Mps are uncorrected. The IR spectra were carried out on an Acculab 1, Beckman using the KBr wafer technique. The ^{1}H-NMR spectra (60 MHz and 250 MHz) were measured on T 60, Varian and PTF-NMR spectrophotometer WM 250 (measuring temperature T = 35±1°C and 23±1°C) respectively. The ^{13}C-NMR spectra were measured on PTF spectrophotometer WM 90, Bruker (measuring temperature T = 31±2°C). Mass spectra (low resolution) were recorded on a monofocusing varian MAT CH-5 mass spectrophotometer at ionization energy 70 eV and using direct insertion probe. High resolution and metastable MS were recorded on a Varian 311 A, double focusing instrument with reversed goemetry at 70 eV.

3-Aroyl-2-pyridinecarboxylic Acids (2a-d). General Procedure.- Anhydrous aluminum chloride (16.0 g, 120 mmol) was added to a stirred mixture of quinolinic anhydride (3.0 g, 20.12 mmol) in the dry aromatic substrate (20 mL). The reaction mixture was heated under reflux at 80°C for 6 h and the complex formed was decomposed with ice-cold conc. hydrochloric acid. The solvent was steam distilled and upon cooling, solid crystals formed. They were collected and recrystallized from the appropriate solvent to give 3-aroyl-2-pyridinecarboxylic acids (**2a-d**). Fusion of **2d** (500 mg, 1.94 mmol) at 210-220°C for 30 min under reduced pressure (5 mmHg) gave, after cooling, a solid product which after purification over silica gel using ether as an eluent gave 3-(*p*-anisoyl)pyridine, mp 93-95°C, identical with an authentic sample (*see below*).

Authentic Synthesis of 3-(*p*-Anisoyl)pyridine.- To a suspension of nicotinyl chloride (3 g, 20 mmol) in dry anisole (20 mL), anhydrous aluminium chloride (16 g, 120 mmol) was added with stirring. The reaction mixture was heated at 80°C under reflux for 6 h. The complex formed was decomposed with cold dilute hydrochloric acid (70 mL), then steam distilled to remove excess anisole. The residue obtained was neutralized with sodium carbonate solution (50 mL) and extracted with chloroform. The chloroform layer was separated, washed throughly with water, dried over sodium sulfate and evaporated under reduced pressure whereby a colorless solid was formed. The product obtained was purified over silica gel using chloroform as eluent to give 3-(*p*-anisoyl)pyridine, mp 93-94°C; ^{1}H-NMR ($CDCl_3$,250 MHz) δ 3.90 (s, 3H, OCH_3), 6.97-7.01

and 7.82-7.85 (AA'BB', 4H, Ar-H), 7.41-7.47 (d of d of d, 1H, H_B; J_{BC} = 7.9, J_{BA} = 4.9, $J_{BA'}$ = 0.8 Hz), 8.05-8.10 (d of d of d, 1H, H_C; J_{CB} = 7.9, J_{CA} = 1.8, $J_{CA'}$ = 2.1 Hz), 8.78-8.80 (d of d, 1H, H_A; J_{AB} = 4.9, J_{AC} = 1.7 Hz) and 8.95-8.96 (d of d, 1H, $H_{A'}$[28,29]; $J_{A'C}$ = 2.1, $J_{A'B}$ = 0.8 Hz).

Anal. Calcd. for $C_{13}H_{11}NO_2$: C, 73.24; H, 5.16; N, 6.57.Found: C, 73.37; H, 5.28; N, 6.61

2-Aroyl-3-pyridinecarboxylic Acids (3a-c) and 7,7-Diphenylfurano[3,4-*b*]pyridin-5-one (5). General Procedure.- Diarylcadmium was prepared according to the method of Gilman and Nelson[14] by the addition of anhydrous cadmium chloride (10.38 g, 56 mmol) to the Grignard reagent (prepared from 2.43 g, 100 mmol of magnesium and 130 mmol aryl bromide). The mixture containing the arylcadmium was surrounded by an ice bath and the solid quinolinic anhydride (7.45 g, 50 mmol) slowly added with good stirring over a period of 15-30 min. The ice bath was removed and the mixture was heated under reflux with stirring on a water bath for 1 h. The mixture was cooled in an ice bath and hydrolyzed by careful addition of a slight excess (120 mL) of 10% sulfuric acid. When the hydrolysis was completed, the mixture was extracted with ether and the ethereal layer was shaken with 10% potassium carbonate (70 mL) and treated with an excess of dilute sulfuric acid. The precipitated keto acid **3a-c** was collected, dried and recrystallized from ether/pet.ether. The ethereal layer was evaporated, the oily residue obtained was purified over silica gel using ether as an eluent to give **5**.

5-Arylpyrido[3,2-*d*][1,2]oxazin-8-ones (6a-d) and 8-arylpyrido[2,3-*d*][1,2]-oxazin-5-ones (8a-c). General Procedure.- 3-Aroyl-2-pyridinecarboxylic acid (**2a-d**) or 2-aroyl-3-pyridinecarboxylic acid (**3a-c**) (1.0 mmol) was heated under reflux with hydroxylamine hydrochloride (2.0 mmol) in pyridine (5 mL) for 30 min. The reaction mixture was poured on ice-cold hydrochloric acid and the colorless solid which separated was collected and recrystallized from ethanol.

5-Arylpyrido[2,3-*d*]pyridazin-8-ones (7a-d) and 8-Arylpyrido[2,3-*d*]pyridazin-5-ones (9a-c). General Procedure.- A solution of 3-aroyl-2-pyridinecarboxylic acids (**2a-d**) or 2-aroyl-3-pyridinecarboxylic acids (**3a-c**) (1.0 mmol) in acetic acid (10 mL) was treated with hydrazine hydrate (2.0 mmol). The reaction mixture was refluxed for 2 h, then cooled. The solid crystalline product was collected and recrystalized from the appropriate solvent.

5-Aryl-8-chloropyrido[2,3-*d*]pyridazines (10a,b) and 8-aryl-5-chloropyrido[2,3-*d*]pyridazines (12a,b). General Procedure.- 5-Arylpyrido[2,3-*d*]pyridazin-8-ones (**7a,b**) or 8-arylpyrido[2,3-*d*] pyridazin-5-ones (**9a,b**) (1.0 mmol) was treated with pyridine (1.0 mmol) and phosphorus oxychloride (20 mmol). The reaction mixture was heated under reflux for 1h at 110°C in a nitrogen atmosphere. After cooling, the reaction was poured into 50 mL ice-cold water and extracted with 100 mL chloroform. The organic layer was separated and washed with water, then with 1N sodium hydroxide and then with water again. The extracted chloroform was dried over sodium sulfate and evaporated under reduced pressure. The oily residue obtained was purified over silica gel using ether as an eluent to give **10a,b** or **12a,b**.

5-Aryl-8-hydrazinopyrido[2,3-*d*]pyridazines (11a,b) and 8-Aryl-5-hydrazinopyrido[2,3-*d*]-

pyridazines (13a,b). General Procedure.- Hydrazine hydrate (59 mg, 1.18 mmol) and 5-aryl-8-chloropyrido[2,3-*d*]pyridazine (**10a,b**) or 8-aryl-5-chloropyrido[2,3-*d*]pyridazine (**12a,b**) (0.59 mmol) were refluxed in ethanol for 1 h. The reaction mixture was cooled and the solid formed was collected and crystallized from ethanol to give **11a,b** or **13a,b**.

6-Aryl-1,2,4-triazolo[4,3-*b*]pyrido[2,3-*d*]pyridazines (14a,b) and 6-Aryl-1,2,4-triazolo[4,3-*b*]pyrido[3,2-*d*]pyridazines (15a,b). General Procedure.- A solution of 5-aryl-8-hydrazinopyrido[2,3-*d*]pyridazine (**11a,b**) or 8-aryl-5-hydrazinopyrido[2,3-*d*]pyridazine (**13a,b**) (0.1 mmol) in excess formic acid (30 mL) was warmed on an oil bath at 45-50°C for 12 h. The solution was cooled and poured into an ice-water mixture. The precipitate obtained was collected, washed with sodium bicarbonate solution, then with water and dried. The product was purified over silica gel using a suitable eluent to give **14a,b** or **15a,b**.

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