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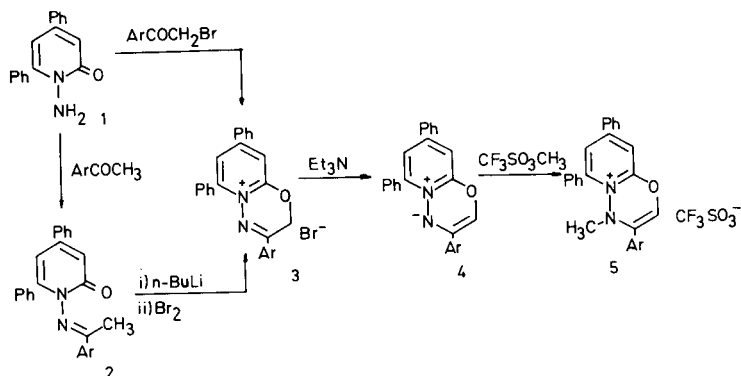
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A convenient synthesis of derivatives of the 4*H*-pyrido[2,1-*b*]-1,3,4-oxadiazine ring system from readily available 1-amino-4,6-diphenyl-2-pyridone and phenacyl bromides or arylmethyl ketones is described.

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We have previously shown that aldehydes and arylglyoxals react with 1-amino-4,6-diphenyl-2-pyridone (**1**) to give the corresponding aldimines which can be converted by heating into nitriles (**3**) and aroyl cyanides (**4**) respectively. Also, compound **1** reacts with phenacyl bromides in dimethyl sulphoxide to give aroyl cyanides and 4,6-diphenyl-2-pyridone (**4**); arylmethylketones react with the reagent selenium dioxide-1-amino-4,6-diphenyl-2-pyridone to give aroyl cyanides (**5**).

We report here attempts to synthesize derivatives of the 4*H*-pyrido[2,1-*b*]-1,3,4-oxadiazine ring system from 1-amino-4,6-diphenyl-2-pyridone (**1**) and phenacyl bromides or arylmethylketones. Compound **1** reacts with phenacyl bromides at reflux temperature in ethanol to give the bicyclic products **2** as crystalline solids in high yields (62-98%) (Method A). An alternative route to **2** involves condensation of **1** with arylmethyl ketones to yield the corresponding ketimines **3** which by metallation with *n*-butyl lithium at -78° followed by addition of bromide lead to **2** in excellent yields (80-95%) (Method B), Table I.



Structures **2** are based on microanalytical data and spectral evidence. In particular each compound displayed in the ¹H-nmr spectra a singlet near 6.3 ppm indicating a methylene group, two doublets centered at δ 8.4 and 8.02 ppm respectively for the pyridinium ring protons and do not show signals of pyridone ring protons. The ir spectra of **3** show a strong absorption at 1630-1635 cm⁻¹ which can

Table I
2*H*-Pyrido[2,1-*b*]-1,3,4-Oxadiazinium Bromides **2**

Compound No.	Ar	Yield (%)		Mp (°C)	Molecular Formula	Analyses (%)					
		A	B			C	Calcd. H	N	C	Found H	N
2a	C ₆ H ₅	96	93	210-212	C ₂₅ H ₁₉ BrN ₂ O (443.4)	67.72	4.28	6.32	67.65	4.27	6.51
2b	4-CH ₃ O-C ₆ H ₄	89	83	151-155	C ₂₆ H ₂₁ BrN ₂ O ₂ (473.4)	65.96	4.43	5.91	66.20	4.60	5.68
2c	4-Br-C ₆ H ₄	96	95	193-195	C ₂₅ H ₁₈ BrN ₂ O (522.2)	56.98	3.44	5.36	57.17	3.48	5.19
2d	4-Cl-C ₆ H ₄	82	84	194-197	C ₂₅ H ₁₈ BrClN ₂ O (477.8)	67.87	4.07	6.33	67.66	3.88	6.13
2e	4-O ₂ N-C ₆ H ₄	62	80	193-195	C ₂₅ H ₁₈ BrN ₃ O ₃ (488.3)	61.47	3.68	8.60	61.22	3.56	8.85
2f	4-C ₆ H ₅ -C ₆ H ₄	98	89	208-209	C ₃₁ H ₂₃ BrN ₂ O (519.5)	71.67	4.43	5.39	71.60	4.44	5.20

Table II
Anhydro Pyrido[2,1-*f*]-1,3,4-Oxadiazinium Hydroxides 4

Compound No.	Ar	Yield (%) A B	Mp (°C)	Molecular Formula	Analyses (%)					
					C	Calcd. H	N	C	Found H	N
4a	C ₆ H ₅	86	187	C ₂₅ H ₁₈ N ₂ O (362.4)	82.87	4.97	7.73	82.78	5.20	7.60
4b	4-CH ₃ O-C ₆ H ₄	78	185	C ₂₆ H ₂₀ N ₂ O ₂ (392.5)	79.59	5.10	7.14	79.42	4.90	6.93
4c	4-Br-C ₆ H ₄	73	205	C ₂₅ H ₁₇ BrN ₂ O (441.3)	68.02	3.85	6.34	68.17	3.87	6.55
4d	4-Cl-C ₆ H ₄	76	200	C ₂₅ H ₁₇ ClN ₂ O (396.9)	75.66	4.28	7.06	75.80	4.35	6.89
4e	4-O ₂ N-C ₆ H ₄	72	219	C ₂₅ H ₁₇ N ₃ O ₃ (407.4)	73.70	4.17	10.32	73.38	4.06	10.49
4f	4-C ₆ H ₅ -C ₆ H ₄	85	204	C ₃₁ H ₂₂ N ₂ O (438.5)	84.91	5.05	6.39	84.89	4.81	6.29

Table III
4*H*-Pyrido[2,1-*b*]-1,3,4-Oxadiazinium Trifluoromethane Sulphonates 5

Compound No.	Ar	Yield (%)	Mp (°C)	Molecular Formula	Analyses (%)					
					C	Calcd. H	N	C	Found H	N
5a	C ₆ H ₅	87	185-188	C ₂₇ H ₂₁ F ₃ N ₂ O ₄ S (526.5)	61.59	4.02	5.32	61.33	3.83	5.38
5b	4-CH ₃ O-C ₆ H ₄	88	134	C ₂₈ H ₂₃ F ₃ N ₂ O ₅ S (556.5)	60.42	4.16	5.03	60.26	3.99	4.87
5c	4-Br-C ₆ H ₄	60	205	C ₂₇ H ₂₀ BrF ₃ N ₂ O ₄ S (605.4)	53.56	3.33	4.63	53.64	3.45	4.79
5d	4-Cl-C ₆ H ₄	87	217-218	C ₂₇ H ₂₀ ClF ₃ N ₂ O ₄ S (561)	57.81	3.59	4.99	57.91	3.37	4.83
5e	4-O ₂ N-C ₆ H ₄	88	180-182	C ₂₇ H ₂₀ F ₃ N ₃ O ₆ S (571.5)	56.74	3.53	7.39	56.45	3.56	7.12
5f	4-C ₆ H ₅ -C ₆ H ₄	82	189	C ₃₃ H ₂₅ F ₃ N ₂ O ₄ S (602.6)	65.77	4.18	4.65	65.71	4.12	4.79

be attributed to the C=N stretching vibration. The M⁺-HBr peak is the base in the mass spectra.

On the other hand, compound 2, when treated with tetrafluoroboric acid in ethanolic solution for a short period of time was converted into the corresponding tetrafluoroborates in high yields. When ethanolic solutions of the salts 2 were treated at room temperature with base *e.g.* triethylamine, pyridine and sodium acetate, the

colour of the reaction mixture turned deep green indicating the formation of the peripheral ylids, anhydro 3-aryl-5,7-diphenylpyrido[2,1-*f*]-1,3,4-oxadiazinium hydroxides 4, which were isolated as crystalline solids in high yields (72-86%) (Table II). They are non-hygroscopic compounds which are stable at ambient temperature and can be stored without any signs of decomposition; however, they slowly decompose in ethanolic solution.

Table IV
Spectral Properties of Compounds 2, 4 and 5

Compound No.	IR ν (cm ⁻¹)	¹ H-NMR δ (ppm)	MS m/e (%)
2a	1630, 1600, 1550, 1480, 1360, 1230, 1150, 1000, 980, 870, 785, 765, 710, 690	7.3-8.1 (17H, m) 6.3 (2H, s)	362 (M ⁺ -HBr) (100), 349 (41), 246 (24), 235 (29), 231 (80), 230 (64), 200 (20), 152 (27)
2b	1630, 1600, 1550, 1460, 1360, 1260, 1180, 1150, 1050, 985, 840, 760, 750, 700	7.2-8.2 (16H, m) 6.3 (2H, s) 3.68 (3H, s)	392 (M ⁺ -HBr) (15), 380 (55), 287 (15), 246 (65), 230 (40), 219 (50), 203 (30), 133 (100), 119 (90), 115 (75)
2c	1635, 1585, 1550, 1480, 1360, 1150, 1070, 1000, 990, 825, 760, 700	7.1-8.1 (16H, m) 6.28 (2H, s)	442 (M ⁺ + 2-HBr) (40), 440 (M ⁺ -HBr), (39) 429 (100), 427 (100), 286 (36), 246 (75), 230 (55), 219 (61), 182 (50), 180 (50), 115 (80), 103 (90)
2d	1635, 1590, 1550, 1475, 1360, 1230, 1150, 1060, 1000, 990, 820, 760, 700	7.0-7.9 (16H, m) 6.3 (2H, s)	398 (M ⁺ + 2-HBr) (5), 396 (M ⁺ -HBr), (15) 384 (100), 382 (30), 246 (75), 230, (45), 203 (70), 103 (80)
2e	1635, 1550, 1520, 1350, 1230, 1150, 1000, 990, 860, 850, 770, 750, 700, 680	7.4-8.2 (16H, m) 6.3 (2H, s)	407 (M ⁺ -HBr) (10), 377 (10), 276 (8), 230 (95), 202 (50), 148 (30), 103 (100)
2f	1635, 1620, 1560, 1480, 1375, 1365, 1230, 1150, 1010, 1000, 990, 860, 850, 780, 770, 703, 690	7.06-8.1 (21H, m) 6.3 (2H, s)	438 (M ⁺ -HBr) (5), 424 (15), 274 (10), 259 (10) 247 (82), 246 (78), 231 (42), 230 (46), 219 (53), 202 (20), 179 (100), 152 (60), 115 (52)
4a	1620, 1605, 1570, 1560, 1535, 1520, 1500, 1400, 1355, 1335, 1310, 1290, 1215, 1200, 1160, 1125, 1090, 1050, 1030, 960, 875, 865, 775, 760, 695	8.2-6.8 (18H, m)	362 (M ⁺) (40), 230 (100), 203 (40), 152 (20), 127 (30), 115 (18)
4b	1635, 1610, 1585, 1570, 1525, 1500, 1435, 1310, 1250, 1210, 1190, 1180, 1040, 845, 835, 765, 700, 695	8.2-6.7 (17H, m) 3.7 (3H, s)	392 (M ⁺) (25), 378 (45), 230 (100), 203 (60), 115 (20),
4c	1630, 1600, 1525, 1495, 1395, 1245, 1210, 1075, 1060, 1015, 855, 830, 770, 760, 755, 720, 700	8.2-6.58 (17H, m)	442 (M ⁺ + 2) (30), 440 (M ⁺), (28), 259 (10), 231 (100), 229 (79), 200 (34), 185 (37), 183 (58), 181 (26), 157 (29), 155 (30), 102 (43)
4d	1635, 1600, 1575, 1525, 1500, 1490, 1470, 1400, 1345, 1365, 1250, 1215, 1160, 1095, 1060, 1020, 960, 860, 835, 775, 765, 730, 700	8.17-6.52 (17H, m)	398 (M ⁺ + 2) (10), 396 (M ⁺), (30), 384 (100), 382 (30), 230 (45), 203 (70), 115 (25), 77 (20)
4e	1620, 1600, 1520, 1495, 1345, 1210, 1155, 1110, 1070, 865, 850, 760, 700, 690	8.2-7.1 (17H, m)	407 (M ⁺) (5), 392 (100), 346 (30), 276 (15), 230 (95), 203 (65), 115 (10), 103 (65)
4f	1630, 1600, 1545, 1525, 1495, 1485, 1405, 1345, 1305, 1240, 1215, 1095, 1080, 1060, 1010, 960, 875, 850, 840, 775, 760, 740, 700	8.18-6.52 (22H, m)	438 (M ⁺) (20), 424 (100), 230 (80), 203 (60), 202 (15), 179 (40), 152 (40), 115 (35), 77 (20)
5a	1625, 1600, 1540, 1460, 1295, 1235, 1220, 1155, 1025, 765, 730, 700, 685	8.36-7.92 (18H, m) 3.31 (3H, s)	377 (M ⁺ -CF ₃ SO ₃ -) (30), 362 (30), 349 (10), 246 (25), 230 (100), 202 (20), 152 (10), 115 (8), 103 (26)
5b	1630, 1615, 1580, 1550, 1520, 1470, 1295, 1260, 1230, 1185, 1170, 1120, 1075, 1035, 900, 850, 775, 765, 755, 700, 640	8.4-7.8 (17H, m) 3.7 (3H, s) 3.31 (3H, s)	407 (M ⁺ -CF ₃ SO ₃ -) (40), 396 (23), 380 (25), 370 (23), 352 (20), 276 (23), 230 (100), 203 (53), 139 (58), 137 (52), 103 (60)
5c	1630, 1600, 1545, 1465, 1425, 1300, 1235, 1210, 1155, 1070, 1025, 1005, 870, 855, 830, 760, 700	8.4-7.71 (17H, m) 3.3 (3H, s)	457 (M ⁺ + 2-CF ₃ SO ₃ -) (10), 455 (M ⁺ -CF ₃ SO ₃ -) (8), 443 (60), 441 (22), 230 (100), 203 (60), 115 (43)
5d	1635, 1600, 1585, 1550, 1505, 1490, 1475, 1405, 1305, 1245, 1225, 1215, 1100, 1035, 880, 845, 770, 710, 695	8.44-7.82 (17H, m) 3.31 (3H, s)	413 (M ⁺ + 2-CF ₃ SO ₃ -) (5), 411 (M ⁺ -CF ₃ SO ₃ -) (18) 399 (23), 397 (60), 230 (100), 203 (28), 202 (15), 115 (39)
5e	1630, 1600, 1545, 1520, 1485, 1450, 1350, 1300, 1285, 1230, 1165, 1110, 1025, 865, 855, 770, 705	8.3-7.5 (17H, m) 3.32 (3H, s)	422 (M ⁺ -CF ₃ SO ₃ -) (10), 418 (22) 406 (13), 379 (10), 352 (10), 275 (11), 230 (100), 203 (45), 150 (33) 103 (34)
5f	1635, 1605, 1565, 1500, 1475, 1270, 1255, 1150, 1025, 870, 845, 760, 755, 735, 690	9.04-7.70 (22H, m) 3.31 (3H, s)	452 (M ⁺ -CF ₃ SO ₃ -) (5), 438 (25), 423 (100), 260 (21), 234 (15), 230 (18), 202 (13), 179 (30), 153 (10), 140 (8)

Compounds **4** have a C=N stretching vibration at 1630-1645 cm^{-1} in the ir spectra and no signal for methylene hydrogens were revealed in the ^1H -nmr spectra.

Upon reaction with methyl trifluoromethane sulphonate, compounds **4** gave the *N*-methyl derivatives **5**, which shown in the ^1H -nmr spectra a singlet at δ 3.3 ppm attributable to N-CH₃ group (Table III).

EXPERIMENTAL

The melting points were determined with a Kofler hot stage microscope and were uncorrected. The ir spectra were recorded of mineral oil mulls with a Perkin-Elmer 457 instrument. The ^1H -nmr spectra were obtained on solutions in DMSO-*d*₆ with TMS as internal standard using a Varian FT-80 instrument. Mass spectra were obtained with a Hewlett-Packard 5980A GC/MS system; compounds were introduced through the direct insertion probe. The electron beam energy was 70 eV and the ion source was at ca. 200°C. Microanalysis were performed with a Perkin-Elmer 240 instrument.

3-Substituted-5,7-diphenyl-2*H*-pyrido[2,1-*f*]-1,3,4-oxadiazinium Bromides **2**. General Procedure.

Method A.

1-Amino-4,6-diphenyl-2-pyridone (**1**) (10 mmoles) was dissolved in dry ethanol (75 ml), the appropriate phenacyl bromide (10 mmoles) was added and the reaction mixture was heated at reflux temperature for 12 hours. After cooling, dry ether (25 ml) was added and the resulting solid was removed off by filtration and recrystallised from chloroform-benzene (1:1) to give **2**.

Method B.

A well stirred solution of ketimine **3** (10 mmoles) in dry tetrahydrofuran (THF) (100 ml) was cooled at -78° and 0.9 ml of 1.6 *M* *n*-butyllithium in hexane (10 mmoles) was added under nitrogen. The resultant solution

was stirred for 30 minutes and a solution of bromine (10 mmoles) in dry THF (10 ml) was added. The reaction mixture was stirred for 30 minutes and allowed to warm at room temperature. The solvent was removed off under reduced pressure at room temperature and the residual material was recrystallised from ethanol to give **2** as crystalline solid (Table I).

Anhydro 3-Substituted-5,7-diphenylpyrido[2,1-*b*]-1,3,4-oxadiazinium Hydroxides **4**. General Procedure.

To a solution of **2** (10 mmoles) in dry ethanol (5 ml), triethylamine (20 mmoles) was added. The reaction mixture acquired a deep green colour and was stirred at room temperature for 1 hour. The precipitated solid was separated by filtration and recrystallised from ethanol-chloroform (1:1) to give **4** as yellow-green crystals (Table II).

3-Substituted-5,7-diphenyl-4-methyl-4*H*-pyrido[2,1-*b*]-1,3,4-oxadiazinium Trifluoromethane sulphonates **5**. General Procedure.

To a solution of **4** (2 mmoles) in dry benzene (40 ml), methyl trifluoromethane sulphonate (0.33 g, 2 mmoles) was added. The reaction mixture was stirred under reflux temperature for 2 hours. After cooling to room temperature, the yellow solid precipitated was separated by filtration and recrystallised from ethanol-ether (1:1) to give **5** (Table III).

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