A Facile Synthesis of 2,5,7-Triaryloxazolo [5,4-*b*]-pyridines

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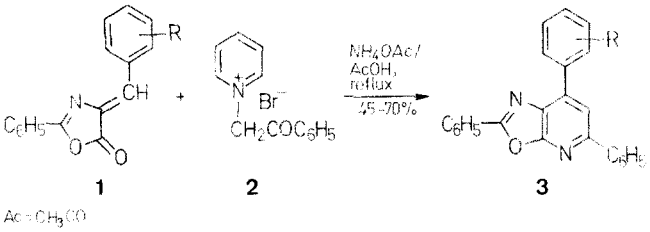
A facile, one-step procedure for the synthesis of 2,5,7-triaryloxazolo[5,4-*b*]pyridines (**3**) from easily obtainable 2-aryl-4-arylmethylene-2-oxazolin-5-ones (**1**) is reported.

Oxazolo [5,4-*b*] pyridines are reported to exhibit interesting biological properties, among them antiinflammatory, analgesic and antipyretic activity. A survey of the literature, however, reveals that only few reports[1-5] are available regarding the synthesis of these compounds. The methods reported so far suffer from the disadvantage of having only limited scope with regard to substitution on the two rings; they also use starting materials that are difficult to synthesize. In this paper, we report a general method for the one-step preparation of 2,5,7-triaryloxazolo[5,4-*b*]pyridines having a wide range of substituents from easily obtainable 2-aryl-4-arylmethylene-2-oxazolin-5-ones[6,7].

Pyridine derivatives can be prepared by the Michael addition of *N*-phenacylpyridinium salts to α,β-unsaturated ketones in the presence of acetic acid and ammonium acetate[8]. This method has been thus far applied[9,10] either to open chain α,β-unsaturated ketones or to carbocyclic rings

incorporating this system. We have now extended this method to 2-aryl-4-arylmethylene-2-oxazolin-5-ones, leading to the formation of 2,5,7-triaryloxazolo[5,4-*b*]pyridines.

2-Aryl-4-arylmethylene-2-oxazolin-5-one **(1)** on refluxing with one equivalent *N*-phenacylpyridinium bromide **(2)** and ammonium acetate in glacial acetic acid afforded the title compounds.



1 **2** **3**

Ac = CH_3CO

Table 1. Preparation of 2,5,7-triaryloxazolo [5,4-*b*]pyridines.

Product	R	Yield [%]	m.b.[b] [°C]	Molecular Formula[a]	
3a	H	50	262	$C_{24}H_{16}N_2O$	(348.4)
3b	2-NO_2	65	230	$C_{24}H_{15}N_3O_3$	(393.4)
3c	4-OCH_3	65	267	$C_{25}H_{18}N_2O_2$	(378.4)
3d	4-Cl	70	158–59	$C_{24}H_{15}N_2OCl$	(382.8)
3e	3-NH_2	45	280d	$C_{24}H_{17}N_3O$	(363.4)
3f	2,5-$(OCH_3)_2$	55	258–60	$C_{26}H_{20}N_2O_3$	(408.5)

[a] New compounds. Satisfactory microanalyses obtained: C ± 0.1, H ± 0.3, N ± 0.5.

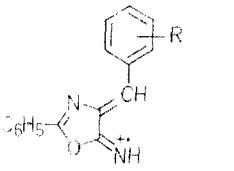
[b] M.p.'s determined on a Toshniwal melting point apparatus (capillary method) and are uncorrected.

All the synthesized 2,5,7-triaryloxazolo[5,4-*b*]pyridines are new, high melting solids (Table 1).

Structures of the newly synthesized compounds have been elucidated on the basis of elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR and mass spectroscopy (Table 2).

In the IR spectra of compounds **3**, two characteristic sharp absorption bands are observed in the range of 1725–1685 and 1680–1620 cm^{-1} attributable to ν(C=N) and ν(C=C) stretching modes.

In ^{1}H-NMR spectra of compounds **3**, a singlet in the range of δ = 6.83–7.25 ppm corresponds to 6-H. The ^{13}C-NMR spectra of **3a, 3f** and of 2-phenyl-4-benzylidene-2-oxazolin-5-one **(1a)** have been recorded. In **1a**, the carbonyl exhibits a weak signal at δ = 207.71 ppm which disappears in **3a**. For the latter, two new signals having comparatively low intensities are observed at δ = 167.84 and 156.63 ppm, which remain singlets even in off-resonance experiments. These signals can therefore be assigned to quaternary carbons 9 and 8 respectively, as these are expected to have long relaxation times (T_1) leading to weak signals in ^{13}C-NMR. Similarly for **3f**, the quaternary carbons 8 and 9 resonate at δ = 154.2 and 161.77 ppm, respectively.



X (R see Table 1)

3a: *m/e* = 248 (100%)
3b: *m/e* = 293 (4%)
3c: *m/e* = 278 (67%)
3d: *m/e* = 282 (25%) and *m/e* = 284 (12%)

Table 2. Spectral Data of the Compounds **1a**, **3a–f**

Compound	IR (KBr)[a] ν [cm^{-1}]	^{1}H-NMR ($CDCl_3$)[b] δ [ppm]	^{13}C-NMR (DMSO)[c] δ [ppm]	MS[d] *m/e* (%)
1a	1780, 1625, 1440, 1360, 1290, 1160, 980, 860, 760, 695	6.4 (s, 1H, C–H); 6.6–7.4 (m, 11H_{arom})	126.77, 126.99, 127.37, 127.69, 127.85, 128.45, 128.72, 130.89, 207.7 (CO)	
3a	1685, 1625, 1440, 1250, 910, 870, 760	7.01 (s, 1H, 6-H); 7.42–8.37 (m, 15H_{arom})	120.92, 123.19, 123.68, 124.55, 124.82, 125.85, 127.85, 128.40, 130.13, 130.20, 156.62, 167.83	350 (8), 348 (M^+, 6), 347 (10), 288 (20), 249 (20), 248 (100), 247 (18), 117 (68), 104 (64), 77 (28)
3b	1720, 1630, 1525, 1360, 930, 750, 695	7.31 (s, 1H, 6-H); 7.46–8.97 (m, 14H_{arom})		350 (10), 349 (37), 348 (42), 321 (12), 320 (41), 293 (4), 140 (42), 122 (76), 119 (30), 109 (25), 105 (100), 79 (40), 77 (64)
3c	1700, 1640, 1600, 1515, 1460, 1310, 1180, 1035, 930, 835, 700	3.77 (s, 3H, OCH_3); 6.87 (s, 1H, 6-H); 7.02–8.33 (m, 14H_{arom})		297 (6), 296 (13), 279 (30), 278 (67), 147 (28), 132 (14), 105 (100), 104 (18), 77 (38)
3d	1690, 1630, 1440, 1350, 1250, 1085, 910, 815, 780, 690	7.0 (s, 1H, 6-H); 7.29–8.39 (m, 14H_{arom})		329 (M^+ –73, 70), 284 (12), 283 (25), 282 (25), 151 (15), 105 (100), 104 (28), 77 (48)
3e	3310, 1725, 1680, 1660, 1615, 1415, 1260, 1240, 1180, 940, 790, 710	6.05 (s, 2H, NH_2); 6.25–9.23 (m, 14H_{arom})		
3f	1680, 1620, 1480, 1290, 1220, 1040, 920, 735, 690	3.64 (3H, OCH_3); 3.86 (3H, OCH_3); 6.87 (s, 1H, 6-H); 6.98–8.41 (m, 13H_{arom})	55.5, 56.39, 113.31, 117.31, 118.64, 123.98, 127.98, 128.87, 130.20, 133.76, 149.77, 154.21, 161.77, 173.33	

[a] IR spectra were taken on a Perkin-Elmer 577 grating spectrophotometer.

[b] ^{1}H-NMR were recorded on a Bruker WM 400 (400 MHz).

[c] ^{13}C-NMR were scanned on a Jeol FX 90 Q (22.49 MHz).

[d] Mass spectra were taken on an Hitachi Model RMU6E at 70 eV.

The structures of 2,5,7-triaryloxazolo[5,4-*b*]pyridines are further confirmed by mass spectral studies of the four products **3a–d**. The ion **X** forms the base peak in the mass spectrum of **3a** but in case of **3b–d**, it appears as an intense to weak ion.

2,5,7-Triaryloxazolo[5,4-*b*]pyridines; General Procedure:
2-Aryl-4-arylmethylene-2-oxazolin-5-one[6,7] (**1**; 10 mmol) and *N*-phenacylpyridinium bromide (**2**; 10 mmol) are refluxed for 1–3 h in acetic acid (8 ml) containing ammonium acetate (6 g). The resulting mixture is poured into crushed ice and the solid mass is recrystallised from ethanol.

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