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New Facile Synthesis of 2-Aryloxy-5-(2-furfurylidene)-4H-imidazolin-4-ones

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Abstract: Novel 2-aryloxy-5-(2-furfurylidene)-4H-imidazolin-4-ones **6** were synthesized by aza-Wittig reaction of vinyliminophosphorane **4** with phenyl isocyanate and subsequent condensation with various substituted phenols in the presence of catalytic amount of potassium carbonate. The products are confirmed by ^{1}H NMR, MS, IR and elementary analysis.

Keywords: 4H-Imidazolin-4-one, aza-Wittig reaction, iminophosphorane, synthesis.

Many N-heterocycles including 4H-imidazolin-4-ones exhibit biological activities[1-3]. Some derivatives of 5-(2-furfurylidene)-4H-imidazolin-4-one were found to show good antiinflammatory activity[4]. They can be synthesized by condensation of furfural with 5-unsubsituted 4H-imidazolin-4-ones or from corresponding oxazolones[5,6]. However, no synthesis of 2-aryloxy substituted 5-(2-furfurylidene)-4H-imidazolin-4-one was reported.

Recently, aza-Wittig reaction has received increased attention for its utility in heterocyclic synthesis[7]. We are interested in the synthesis of biologically active imidazolinones *via* aza-Wittig reaction[8-10]. This method has the advantages of mild condition, easily accessible starting material and easiness of introducing substituents to the position 2, 3 and 5 of imidazolinone ring. Here we wish to report a facile synthesis of 2-aryloxy-5-(2-furfurylidene)-4H-imidazolin-4-ones **6** from vinyliminophosphorane **4**.

Vinyliminophosphorane **4** reacted with phenyl isocyanates to give carbodiimide **5**, which then reacted with substituted phenols in the presence of catalytic amount of solid potassium carbonate to give 2-aryloxy-5-(2-furfurylidene)-4H-imidazolin-4-ones **6**. If K_2CO_3 was absent, no **6** could be obtained. The position of substituents on phenol ring did not affect this reaction and all of the reactions were carried out smoothly at room temperature.

The structure of 6 has been characterized spectroscopically. For example, the ^{1}H NMR spectral data of 6c showed the signals of methyl group and the protons at 3, 4 position of furfuryl at 2.23 ppm (s) and 6.91~6.41 ppm (m) respectively. The signals of alkenyl hydrogen were overlapped with the signals of phenyl and furfuryl (7.02~7.52).

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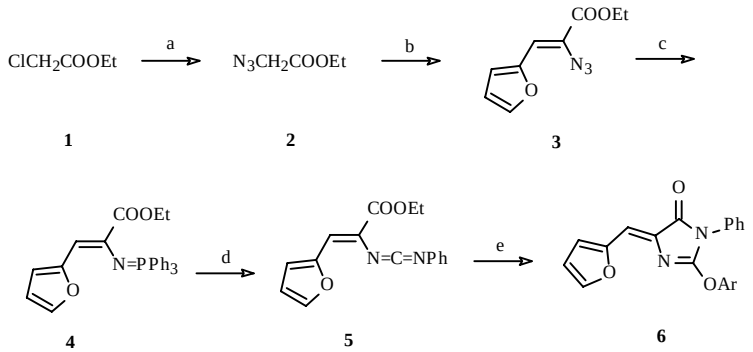
Scheme 1



(a) NaN_3, CH_3CN, 75°C, 20 h, 90%; (b) furfural, NaOEt, EtOH, -10°C, 4h, 61%; (c) Ph_3P, CH_2Cl_2, r.t., 4h, 84%; (d) PhNCO, CH_2Cl_2, r.t., 6 h; (e) ArOH, K_2CO_3(s), CH_3CN, r.t. 6-8 h, 70%-82%.

Table 1 Preparation of **6** from vinyliminophosphorane **4**

	Ar	Condition	Yield (%)	m.p. (°C)	Elementary analysis (%, Calcd.) C	H	N
6a	2-Naphthyl	r.t./7h	72	203-204	75.89(75.78)	4.13(4.24)	7.57(7.36)
6b	2,4-2Cl-Ph	r.t./8h	70	185-187	60.22(60.17)	3.24(3.03)	6.89(7.02)
6c	3,4-2Me-Ph	r.t./6h	78	183-185	73.65(73.73)	5.06(5.23)	7.88(7.82)
6d	Ph	r.t./7h	81	150-152	72.53(72.72)	4.39(4.27)	8.53(8.48)
6e	4-Br-Ph	r.t./8h	74	189-191	58.84(58.70)	3.04(3.20)	6.94(6.85)
6f	4-MeO-Ph	r.t./6h	82	164-165	69.86(69.99)	4.56(4.47)	7.63(7.77)

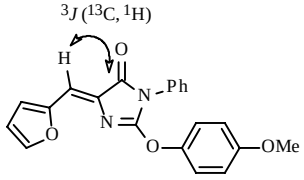
Table 2 IR, MS and ^{1}H NMR of **6**

	IR (KBr, cm^{-1})	MS (*m/z*, %)	^{1}H NMR ($CDCl_3$, 200MHz, δ, *ppm*)
6a	1731, 1651, 1567, 1414, 1299	380 (M^+, 3), 233 (6), 127 (100), 106 (36)	7.82~7.04 (m, 14H, Ar-H and =CH), 6.94~6.43 (m, 2H, Furfuryl-H)
6b	1730, 1657, 1571, 1410, 1295	398 (M^+, 10), 400 (7), 363 (5), 264 (26), 145 (73), 106 (100)	7.70~7.06 (m, 10H, Ar-H and =CH), 6.92~6.46 (m, 2H, Furfuryl-H)
6c	1723, 1652, 1566, 1414, 1300	358 (M^+, 11), 224 (6), 211 (16), 105 (100)	7.52~7.02 (m, 10H, Ar-H and =CH), 6.91~6.41 (m, 2H, Furfuryl-H), 2.23 (s, 6H, $2CH_3$)
6d	1730, 1657, 1571, 1410, 1295	330 (M^+, 6), 196 (11), 183 (4), 106 (21), 77 (100)	7.50~7.00 (m, 12H, Ar-H and =CH), 6.92~6.46 (m, 2H, Furfuryl-H)
6e	1720, 1654, 1562, 1409, 1301	410 (M^+, 8), 408 (8), 276 (15), 274 (14), 195 (33), 157 (79), 155 (80), 106 (100)	7.52~6.49 (m, 11H, Ar-H and =CH), 6.95~6.47 (m, 2H, Furfuryl-H)
6f	1720, 1652, 1571, 1414, 1301	360 (M^+, 13), 226 (11), 213 (25), 107 (100)	7.43~7.00 (m, 11H, Ar-H and =CH), 6.90~6.41 (m, 2H, Furfuryl-H), 3.77 (s, 3H, OCH_3)

The IR of 6c showed the strong stretching resonance peak of imidazolinone C=O at 1723 cm^{-1} and υ of C=C or C=N at about 1652 cm^{-1} or 1566 cm^{-1}. The signal at about 1300 cm^{-1} is probably due to the stretching resonance of C-O-C. The MS of 6c showed M^+ at *m/z* 358 with 11% abundance.

In order to determine the configuration of **6**, **6f** was selected to analyze its ^{13}C NMR spectrum. The ^{13}C NMR spectrum of **6f** provided quaternary carbonyl carbon signals at

δ 167.2 in double absorption. The coupling constant was 5.8 Hz and it was due to ^3J (^{13}C, ^{1}H) between the carbonyl carbon and the olefinic hydrogen (^{1}H-C=C-^{13}C=O). The literature reported the^3J (^{13}C, ^{1}H) of some analogues of 5-furfurylideneimidazolinone (^3J of *Z*-form was in range of 3-6 Hz whereas^3J of *E*-form was in range of 8-11 Hz)[5]. So the configuration of **6f** was determined as in *Z* form.



6f

General procedure for synthesis of 2-aryloxy-5-(2-furfurylidene)-4H-imidazolin-4-ones **6**:

To a solution of vinyliminophosphorane **4** (2.21 g, 5 mmol) in dry methylene dichloride (15 mL) was added phenyl isocyanate (0.55 mL, 5 mmol) under nitrogen at room temperature. After the reaction mixture was stood for 6 hours, the solvent was removed off under reduced pressure and ether / petroleum ether (1:2, 20 mL) was added to precipitate triphenyl phosphine oxide. After filtration, the solvent of the filtrate was removed to give carbodiimide **5**, which was used directly without further purification. To the above prepared solution of **5** in CH_3CN (30 mL) was added substituted phenol (5 mmol) and solid K_2CO_3 (0.05 g). The reaction mixture was stirred for 6-8 hours at room temperature and filtered, the filtrate was concentrated and the residue was recrystallized from methylene dichloride / petroleum ether to give **6**. The yields of **6** based on iminophosphorane **4** are listed in **Table 1**.

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