

OXAZOLONES¹

Part II. Synthesis and Reactions of 4-Arylidene-2-[2'-Furyl]-5 (4)-Oxazolones

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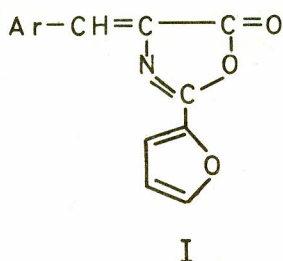
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Abstract. 4-Arylidene -2- [2' -furyl] -5 (4)-oxazolones (I a - d) were prepared. *Ortho*, *meta* and *para*-aminobenzoic acids react with (I a - d) to give α -[2'-furamido-cinnamic acid carboxyanilides (II a - f), (I a - d) react with aromatic amines to give α -[2'-furamido]-N-substituted cinnamamides (III a - h). Also (I a - d) react with hydrazine and hydroxylamine hydrochloride to give (IV a - d) and (V a - d) respectively. Azidolysis of (I d) give α -[tetrazoly -(1)] -5-[2'furyl] acrylic acid (VI).

In the present investigation the effect of substitution at position -2 with (2-furyl group); on the mode of reaction of 4-arylidene -5 (4) -oxazolone was investigated.

4-Arylidene -2- [2'-furyl] -5 (4) -oxazolones (I a-d) were obtained from the reaction of 2-furoylglycine with aromatic aldehydes in the presence of acetic anhydride and sodium acetate.²



a, Ar = C₆H₅; b, Ar = C₆H₄. OCH₃ (p-); c, Ar = C₆H₄. NO₂ (o-); d, Ar = 2 - furyl.

The IR spectra of (I a-b) showed $\nu_{C=O}$ in the region (1810-1785 cm⁻¹).

4-Arylidene -2- [2'-furyl] -5 (4) -oxazolones (I a-d) react with *o*-, *m*-, and *p*-aminobenzoic acids to give the corresponding α - [2'-furamido]- cinnamic acid carboxyanilides (II a-f)^{1,3}

The IR spectra of II a-f show two bands for two amide carbonyls in the range 1630-1610 cm⁻¹ and 1680-1660 cm⁻¹, normal acid carbonyl in the region 1730-1710 cm⁻¹ and bands due to NH in the region 3400-3140 cm⁻¹.

Similarly, 4-arylidene -2- [2'-furyl] -5 (4) -oxazolones (I a-d) react with aromatic amines to give the corresponding α - [2'-furamido] - N-substituted cinnamides (III a-h)¹.

The IR spectra of (III a-h) showed two amide carbonyl bands in the region 1650-1610 cm⁻¹, and 1680-1660 cm⁻¹ respectively, and bands at 3410-3120 cm⁻¹ due to NH

Compounds (I a-d) react with hydrazines to give the corresponding α - [2'-furamido] - cinnamic acid hydrazides (IV a-h).^{1,4}

The IR spectra of (IV a-d) showed $\nu_{C=O}$ of the hydrazide in the region 1690-1660 cm⁻¹.

The hitherto unknown reaction of (I a-d) with hydroxylamine hydrochloride in pyridine gave 4-arylidene -1-hydroxy -2- [2' furyl] -5- imidazolones (V a-d).

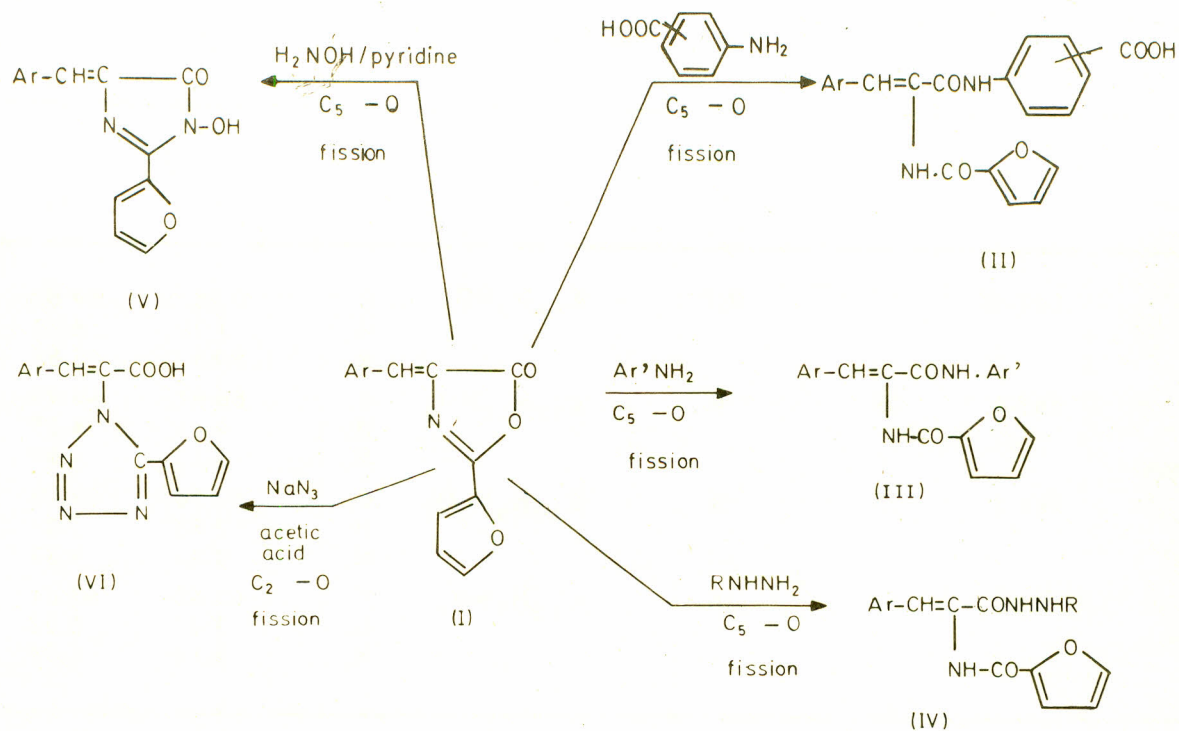
Compounds (V a-d) showed in the infrared $\nu_{C=O}$ in the region 1730-1650 cm⁻¹, $\nu_{C=N}$ at 1600 cm⁻¹ and ν_{OH} in the region 3120-2800 cm⁻¹

The NMR spectrum of compound (V c) shows singlet at δ 7.0 ppm attributed to one olefinic proton, multiplet at δ 7.02 ppm attributed to two protons of β -furyl group, multiplet at δ 7.46 ppm attributed to one proton of α -furyl group, and multiplet at δ 8.12 ppm attributed to four aromatic protons.

The mass spectrum of (V b) shows molecular ion (at M⁺, m/e = 284), M⁺ - O; m/e = 268) and (M⁺ - OH; m/e = 267). (I d) Reacts with sodium azide in acetic acid to give α - [tetrazolyl-(1)] -5- [2' furyl] -2- furyl acrylic acid (VI).⁵

The IR spectrum of VI showed bonded OH stretching frequency in the region 3140-2530 cm⁻¹ and $\nu_{C=O}$ at 1685 cm⁻¹ and ν tetrazolyl ring at 1100-900 cm⁻¹.⁶

All the previous data can be summarized in the following scheme:



Taking all previous data into considerations we can conclude that azidolysis of (Id) involves opening of $\text{C}_2\text{-O}$ bond, contrary to the ring opening of the 5 (4) -oxazolone ring (fission of $\text{C}_5\text{-O}$ bond) with other compounds, viz R-NH_2 , R-NH-NH_2 etc.

Also the substitution in position 2 with 2-furyl group in 5 (4) -oxazolone, does not affect this mode of reaction.

Experimental Procedure

Melting points are not corrected, IR spectra were measured on a Perkin-Elmer IR model 137, Unicam sp 1200, and Beckman IR-20 IR spectrophotometers using KBr pellet.

4-Arylidene-2-[2'-furyl]-5(4)-oxazolones (I a-d).

A mixture of aromatic aldehyde (0.12 mole), 2-furoylglycine (0.1 mole), acetic anhydride, and sodium acetate were heated on a steam bath for 3 hr and then cooled. A solid product was obtained which was recrystallized from the given solvent as listed in Table 1.

Reaction of (I a-d) with Aromatic Aminoacids: Formation of α -[2'-furyl]-5(4)-oxazolone-*N*-substituted cinnamides (II a-f). A solution of (I a-d) (0.1 mole) in ethanol containing few drops of pyridine, was treated with *o*-, *m*-, or *p*-aminobenzoic acids (0.1 mole). The reaction mixture was heated under reflux for 5 hr, cooled in ice, and acidified with 20% hydrochloric acid. The solid product was filtered off, and recrystallized from the given solvent as listed in Table 2.

Reaction of Primary Aromatic Amines with (I a-d) Formation of α -[2'-furyl]-5(4)-oxazolone-*N*-substituted cinnam-

mides (III a-h). A solution of (I a-d) (0.1 mole in benzene and/or pyridine) was heated with primary aromatic amines, viz aniline, *p*-toluidine and *m*-chloroaniline (0.1 mole). The reaction mixture was heated under reflux for 3 hr, and cooled. The solid products were filtered off and recrystallized from suitable solvent as listed in Table 3.

Reaction of Hydrazine with (I a-d): Formation of α -[2'-furyl]-5(4)-oxazolone-*N*-substituted cinnamides (V a-d). A solution of (I a-d) (0.1 mole) in ethanol containing a few drops of pyridine was treated with hydrazine and/or phenylhydrazine (0.1 mole). The reaction mixture was heated under reflux for 6 hr, and then cooled. The solid product was filtered off and recrystallized from suitable solvent as listed in Table 4.

Reaction of Hydroxylamine hydrochloride with (I a-d): Formation of 4-arylidene-1-hydroxy-2-[2'-furyl]-5(4)-imidazolones (VI a-d). A solution of (I a-d) (0.1 mole) in pyridine was treated with hydroxylamine hydrochloride (0.1 mole). The reaction mixture was heated under reflux for 6 hr and then cooled. The solid product filtered off and recrystallized from suitable solvent as listed in Table 5.

Reaction of Aqueous Sodium Azide-acetic Acid with (Id): Formation of α -[tetrazolyl(-1)]-5-[2'-furyl]-2-furyl-acrylic acid (VI). A solution of (I d) (0.1 mole in hot acetic acid) was treated with sodium azide (0.4 mole) dissolved in the least amount of water and the reaction mixture heated under reflux on a steam bath for 3 hr, and poured on crushed ice. The solid product was filtered off, and recrystallized

TABLE 1.

Product	M.p.	Yield %	Solvent of crystallization	Mol. formula	Analysis %		
					Req.	Found	
I a	148-50	51	B/P	$C_{14}H_9NO_3$	C, 7 H, N,	0.28 3.79 5.85	69.62 4.13 5.53
I b	165-6	28	B	$C_{15}H_{11}NO_4$	C, H, N,	66.91 4.11 5.20	66.97 4.15 4.69
I c	184-5	50	B	$C_{14}H_8N_2O_5$	C, H, N,	59.16 2.83 9.85	59.15 3.3 9.53
I d	212	51	A	$C_{12}H_7NO_4$	C, H, N,	62.88 3.07 6.11	62.61 5.22 6.32

A = acetic acid, B = benzene and P = petroleum ether.

TABLE 2.

Compound	Ar	Position of -COOH	M.p.	Yield %	Solvent of crystallization	Mol. formula	Analysis %		
							Req.	Found	
II a	C_6H_5	o-	232	51	B/M	$C_{21}H_{16}N_2O_5$	C, H, N,	67.01 4.28 7.44	66.54 4.20 7.00
II b	$C_6H_4OCH_3$	(p-) o-	225-6	67	E	$C_{22}H_{18}N_2O_6$	C, H, N,	65.01 4.46 6.89	65.23 4.64 6.63
II c	C_6H_5	m-	230-1	64	N/M	$C_{21}H_{16}N_2O_5$	C, H, N,	67.01 4.28 7.44	67.65 4.41 6.77
II d	$C_6H_4OCH_3$	(p-) m-	237	80	M	$C_{22}H_{18}N_2O_6$	C, H, N,	65.01 4.46 6.54	65.12 4.44 6.54
II e	C_6H_5	p-	155-7	51	B/M	$C_{21}H_{16}N_2O_5$	C, H, N,	67.01 4.28 7.44	66.93 4.76 7.15
II f	$C_6H_4OCH_3$	(p-) p-	240	40	M	$C_{22}H_{18}N_2O_6$	C, H, N,	65.01 4.16 6.89	65.45 4.2 6.5

B = benzene, E = ethanol and M = methanol.

TABLE 3

Compound	Ar	Ar'	M.p.	Yield %	Solvent of crystallization.	Mol. formula	Analysis %		
							Req.	Found	
III a	C ₆ H ₅	C ₆ H ₅	200	73	B	C ₂₀ H ₁₆ N ₂ O ₃	C,	72.27	72.98
							H,	4.85	5.65
							N,	8.42	9.14
III b	C ₆ H ₅	C ₆ H ₄ CH ₃ (p-)	177	98	B	C ₂₁ H ₁₈ N ₂ O ₃	C,	72.81	73.30
							H,	5.23	6.10
							N,	8.08	8.53
III c	C ₆ H ₄ OCH ₃ (p-)	C ₆ H ₅	205-6	75	M	C ₂₁ H ₁₈ N ₂ O ₄	C,	69.60	70.22
							H,	5.00	4.80
							N,	7.73	7.60
III d	C ₆ H ₄ OCH ₃ (p-)	C ₆ H ₄ -Cl(m-)	219-21	68	E	C ₂₁ H ₁₇ N ₂ ClO ₄	C,	63.55	64.06
							H,	4.31	4.42
							N,	7.05	7.47
III e	C ₆ H ₄ NO ₂ (o-)	C ₆ H ₅	190-2	91	B	C ₂₀ H ₁₅ N ₂ O ₅	C,	63.55	63.15
							H,	4.00	4.75
							N,	11.13	11.17
III f	C ₆ H ₄ NO ₂ (o-)	C ₆ H ₄ CH ₃ (p-)	182-90	96	B/M	C ₂₁ H ₁₇ N ₃ O ₅	C,	64.44	64.77
							H,	4.37	4.47
							N,	10.73	10.50
III g	2-furyl	C ₆ H ₅	182	72	B/M	C ₁₈ H ₁₄ N ₂ O ₄	C,	67.07	66.71
							H,	4.37	4.28
							N,	8.69	8.04
III h	2-furyl	C ₆ H ₄ Cl (m-)	199	65	B	C ₁₈ H ₁₃ N ₂ ClO ₄	C,	60.59	60.94
							H,	3.67	3.91
							N,	7.85	7.49

Medium of reaction is pyridine. B = benzene, E = ethanol and M = methanol.

TABLE 4.

Compound	Ar	R	M.p.	Yield %	Solvent of crystallization.	Mol. formula	Analysis %		
							Req.	Found	
IV a	C ₆ H ₅	C ₆ H ₅	204-5	98	B	C ₂₀ H ₁₇ N ₃ O ₃	C,	69.15	69.32
							H,	4.93	5.37
							N,	12.09	12.30
IV b	C ₆ H ₄ OCH ₃ (p-)	C ₆ H ₅	204-5	57	E	C ₂₁ H ₁₉ N ₃ O ₄	C,	66.83	67.20
							H,	5.07	5.20
							N,	11.13	10.67
IV c	C ₆ H ₄ NO ₂ (o-)	H	123-4	100	B/M	C ₁₄ H ₁₂ N ₄ O ₅	C,	53.17	53.70
							H,	3.82	4.50
							N,	17.71	16.98
IV d	2-furyl	H	179	89	M	C ₁₂ H ₁₁ N ₃ O ₄	C,	55.17	55.33
							H,	4.24	4.47
							N,	16.08	15.51

B = benzene, E = ethanol, and M = methanol.

TABLE 5.

Compound	Ar	M.p.	Yield %	Solvent of crystallization.	Mol. formula	Analysis %	
						Req.	Found
V a	C ₆ H ₅	236	57	B/M	C ₁₄ H ₁₀ N ₂ O ₃	C, 66.13 H, 3.96 N, 11.01	65.70 4.03 10.71
V b	C ₆ H ₄ OCH ₃ (p-)	219	59	M	C ₁₅ H ₁₂ N ₂ O ₄	C, 63.37 H, 4.25 N, 9.85	63.06 4.23 9.94
V c	C ₆ H ₄ NO ₂ (o-)	230	58	B/M	C ₁₄ H ₉ N ₃ O ₅	C, 56.19 H, 3.03 N, 14.04	56.03 3.57 13.46
V d	2-furyl	240	57	B/M	C ₁₂ H ₈ N ₂ O ₄	C, 59.01 H, 3.27 N, 11.47	58.92 3.58 10.99

M = methanol, and B/M = Benzene/methanol.

from benzene/methanol to give VI, m.p. 201^o, yield 17%. (Found C, 52.74; H, 3.24; N, 20.47. C₁₂H₈N₄O₄ required C, 52.94; H, 2.96; N, 20.58).

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