Photochemistry of Heterocycles; Part XII[1]. A Facile and Convenient Synthesis of Aryl Enaminoaldehydes

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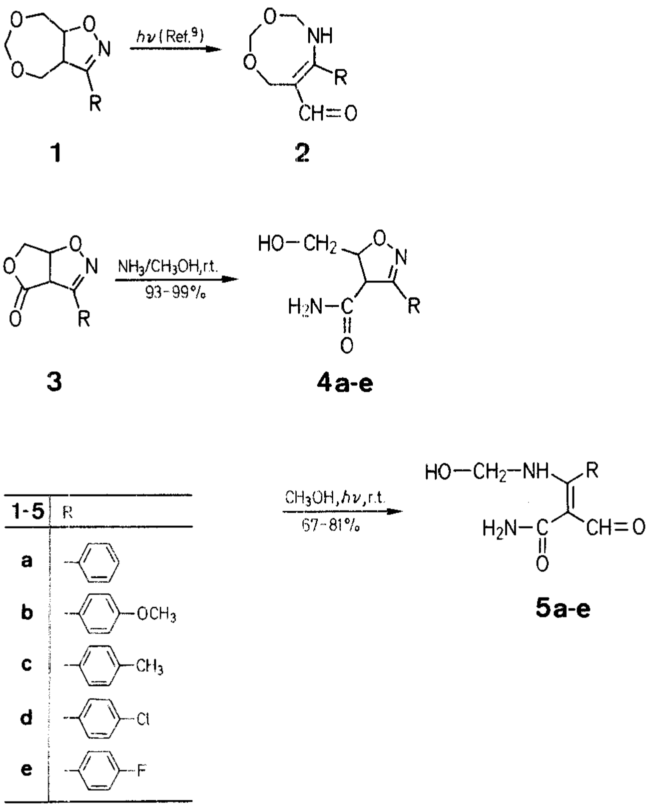
The synthesis of enaminoaldehydes **5** by the reaction of 3-aryl-4-oxo-3a,4,6,6a-tetrahydrofuro[3,4-*d*]-isoxazoles **3** with ammonia to give **4** and subsequent photorearrangement of **4** is described.

Isoxazoline derivatives have been shown to be useful intermediates in organic chemistry, especially for the synthesis of γ-aminoalcohols[2], β-hydroxy-carbonyl compounds and their derivatives[3-5]. Although many attempts have been done to utilize the photochemistry of isoxazolines[6], these photo-rearrangements proceed nonselectively. Recently we have shown that by introducing an oxygen moiety in the β-position to isoxazoline oxygen, the photo-rearrangement can be made selective[7-9]. The photolysis of such products, for example **1** → **2**, leads to heterocyclic enaminoaldehydes exclusively[9]. Based on the results obtained so far and in an attempt to further extend and generalize this synthetic procedure, we now report the synthesis of some new acyclic aryl enaminoaldehydes from isoxazolines **3**.



A parent derivative of the acyclic enaminoaldehydes, useful precursors for the synthesis of heterocycles[10], have been prepared from β-halogenacrolein and ammonia[11]. Enaminoaldehydes possesing secondary amino groups are available from 3-dimethylamino-propin-2-al[12].

The reactions reported here occur under mild conditions affording **5** in good yields without complicated work-up procedures. 3-Aryl-4-oxo-3a,4,6,6a-tetrahydrofuro[3,4-*d*]-isoxazoles **3** are easily prepared by 1,3-dipolar cycloaddition of substituted benzonitrile oxides to 2-(5*H*)-furanone in good yield[13,14]. The formation of the amides **4** from **3** in yields >93% is complete at room temperature within 12–24 h, using a slight excess of a methanolic solution of ammonia (Table 1).

A solution of **4** in methanol was irradiated with monochromatic light at 253.7 nm in a quartz vessel in a forced circulation reactor with temperature control, using Toshiba GL-15 (15 W) mercury low pressure lamp as an internal light source. The work-up of the reaction mixture yielded the corresponding enaminoaldehydes **5** in good yields (67–81%). In all photoreactions, only one stereoisomer of **5** was obtained as evident from the signal of the aldehyde proton in the ^{1}H-N.M.R. spectra of **5** (Table 2). The mechanistic considerations of these photoreactions seem, in

Table 1. Compounds **4** Prepared

Product No.	R	Yield[a] [%]	m.p. [°C]	Molecular Formula[b]	UV (CH$_3$OH)[c] λ_{max} [nm] (log ε)	^{1}H-N.M.R. (DMSO-d_6)[d] δ [ppm]	^{13}C-N.M.R. (DMSO-d_6)[e] δ [ppm]
4a	C_6H_5	99	164–166°	$C_{11}H_{12}N_2O_3$ (220.2)	264 (3.99)	3.50 (dd, 2H, CH_2); 4.30 (d, 1H, 4-H); 4.61 (m, 1H, 5-H); 4.99 (t, 1H, OH); 7.25–7.67 (m, 5H_{arom})	55.48 (d, 4-C); 62.11 (t, OCH_2); 87.06 (d, 5-C); 126.43, 128.17, 129.16, 129.81 (C_{arom}); 155.02 (s, C=N); 171.0 (s, C=O)
4b	4-H_3CO—C_6H_4	97	188–191°	$C_{12}H_{14}N_2O_4$ (250.2)	276 (4.11)	3.70 (s, 3H, CH_3); 3.47 (dd, 2H, CH_2); 4.26 (d, 1H, 4-H); 4.57 (m, 1H, 6-H); 5.00 (t, 1H, OH); 6.84–7.57 (m, 4H_{arom}); 7.81 (2H, NH_2)	55.29 (q, CH_3); 55.70 (d, 4-C); 62.02 (t, CH_2); 86.65 (d, 5-C); 114.15, 121.46, 127.95, 160.42 (C_{arom}); 154.40 (s, C=N); 171.01 (s, C=O)
4c	4-H_3C—C_6H_4	98	201–204°	$C_{12}H_{14}N_2O_3$ (234.2)	270 (4.06)	2.25 (s, 3H, CH_3); 3.62 (dd, 2H, CH_2); 4.37 (d, 1H, 4-H); 4.62 (m, 1H, 5-H); 4.92 (t, 1H, OH); 7.10–7.50 (m, 4H_{arom}); 7.72 (2H, NH_2)	20.92 (q, CH_3); 54.57 (d, 4-C); 59.90 (t, CH_2); 84.33 (d, 5-C); 126.18, 129.29, 139.69, 168.15 (C_{arom}); 155.93 (s, C=N); 171.19 (s, C=O)
4d	4-Cl—C_6H_4	96	221–222°	$C_{11}H_{11}ClN_2O_3$ (254.7)	269 (4.13)	3.52 (dd, 2H, CH_2); 4.33 (d, 1H, 4-H); 4.67 (m, 1H, 5-H); 5.02 (t, 1H, OH); 7.27–7.67 (m, 4H_{arom}); 7.87 (2H, NH_2)	54.18 (d, 4-C); 59.77 (t, CH_2); 84.59 (d, 5-C); 125.39, 127.86, 128.64, 134.36, 167.76 (C_{arom}); 155.15 (s, C=N); 170.49 (s, C=O)
4e	4-F—C_6H_4	93	163–165°	$C_{11}H_{11}FN_2O_3$ (238.2)	264 (4.08)	3.52 (dd, 2H, CH_2); 4.33 (d, 1H, 4-H); 4.66 (m, 1H, 5-H); 5.03 (t, 1H, OH); 7.10–7.75 (m, 4H_{arom}); 7.87 (2H, NH_2)	54.67 (d, 4-C); 60.12 (t, CH_2); 84.67 (d, 5-C); 115.18, 118.61, 128.30, 128.82, 171.15 (C_{arom}); 155.31 (s, C=N); 168.17 (s, C=O)

[a] Yield of pure isolated product.

[b] Satisfactory microanalyses obtained: C ±0.32, H ±0.18, N ±0.24.

[c] Recorded on a Perkin-Elmer spectrophotometer.

[d] Recorded on a Tesla B 487 C spectrometer.

[e] Recorded on a Jeol FX spectrometer.

Table 2. Compounds **5** Prepared

Product No.	Yield [%]	m.p. [°C]	Molecular Formula[a]	UV (CH_3OH) λ_{max} [nm] (log ε)	^{1}H-N.M.R. (DMSO-d_6) δ [ppm]	^{13}C-N.M.R. (DMSO-d_6) δ [ppm]
5a	75	125–127°	$C_{11}H_{12}N_2O_3$ (220.2)	240 (3.97) 284 (4.11)	4.27 (dd, 2H, CH_2); 6.07 (t, 1H, OH); 7.29–7.5 (m, 5H_{arom}); 8.49 (s, 1H, CHO); 8.83 (m, 1H, NH)	67.39 (t, CH_2); 102.46 (s, C=C); 128.56, 130.12 (C_{arom}); 170.24 (s, C=C); 174.53 (s, C=O); 188.16 (d, CHO)
5b	67	171–172°	$C_{12}H_{14}N_2O_4$ (250.2)	244 (3.88) 291 (4.12)	3.77 (s, 3H, OCH_3); 4.35 (dd, 2H, CH_2); 6.96–7.33 (m, 4H_{arom}); 8.56 (s, 1H, CHO); 8.87 (m, 1H, NH)	55.32 (q, CH_3); 67.39 (t, CH_2); 102.59 (s, C=C); 113.88, 122.06, 127.78, 130.25 (C_{arom}); 170.37 (s, C=C); 174.65 (s, C=O); 188.42 (d, CHO)
5c	81	237–240°	$C_{12}H_{14}N_2O_3$ (234.2)	244 (4.01) 284 (4.06)	2.32 (s, 3H, CH_3); 4.31 (dd, 2H, CH_2); 6.07 (t, 1H, OH); 7.25 (s, 4H_{arom}); 8.53 (s, 1H, CHO); 8.83 (m, 1H)	20.79 (q, CH_3); 67.31 (t, CH_2); 102.30 (s, C=C); 127.21, 128.51, 128.90, 139.56 (C_{arom}); 170.23 (s, C=C); 174.77 (s, C=O); 188.29 (d, CHO)
5d	67	168–170°	$C_{11}H_{11}ClN_2O_3$ (254.7)	244 (3.71) 288 (3.58)	4.30 (dd, 2H, CH_2); 6.11 (t, 1H, OH); 7.43–7.61 (m, 4-H_{arom}); 8.51 (s, 1H, CHO); 8.80 (m, 1H, NH)	67.18 (t, CH_2); 102.52 (s, C=C); 127.86, 128.51, 128.77, 130.46, 134.75 (C_{arom}); 170.10 (s, C=C); 173.47 (s, C=O); 188.02 (d, CHO)
5e	69	113–115°	$C_{11}H_{11}FN_2O_3$ (238.2)	244 (3.89) 288 (3.88)	4.47 (dd, 2H, CH_2); 7.25–7.62 (m, 4H_{arom}); 8.66 (s, 1H, CHO)	67.39 (t, CH_2); 102.85 (s, C=C); 115.05, 126.61, 130.90, 131.54, 167.91 (C_{arom}); 170.37 (s, C=C); 173.87 (s, C=O); 188.29 (d, CHO)

[a] Satisfactory microanalyses obtained: C ±0.30, H ±0.25, N ±0.21.

principle, to be the same as discussed in detail in previous papers[8,9]. Thus, the present procedure provides a high yield route for **5** from readily available and cheap 2-(5*H*)-furanone.

3-Aryl-4-aminocarbonyl-5-hydroxymethyl-4,5-dihydro-1,2-oxazoles; General Procedure:

A 13% (by weight) solution of ammonia in methanol (10 ml, 80 mmol) is added to a solution of isoxazolines **3** (25 mmol) in benzene (20 ml). The reaction mixture is allowed to stand at room temperature overnight, then concentrated under vacuum to give the crude isoxazolines **4**, which are purified by recrystallization from acetone to afford pure products (Table 1).

(*Z*)-2-Hydroxymethylamino-2-aryl-1-formylacrylamides *5*; General Procedure:

A methanolic solution of isoxazoline **4** (4 mmol/l) is irradiated (see text for details) until the starting material disappears (T.L.C. control). The reaction mixture, after concentration is triturated with methanol (5 ml) to give the rearrangement products **5** as light-yellow solids which are further purified by recrystallization from methanol (Table 2).

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