JOC The Journal of Organic Chemistry

NOTE

pubs.acs.org/joc

Photochemical Approach to Naphthoxazoles and Fused Heterobenzoxazoles from 5-(Phenyl/heteroarylethenyl)oxazoles

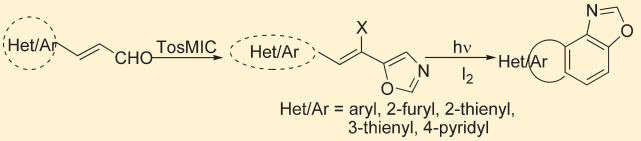
Ivana Šagud,[†] Fabio Faraguna,[†] Željko Marinić,[‡] and Marija Šindler-Kulyk*[,†]

[†]Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, University of Zagreb, Marulićev trg 19, 10000 Zagreb, Croatia

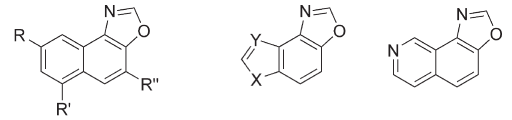
[‡]NMR Center, Rudjer Bošković Institute, Bijenička cesta 54, 10000 Zagreb, Croatia

Supporting Information

ABSTRACT: A new synthetic approach is presented for the synthesis of naphthoxazoles and fused heterobenzoxazoles. The starting 5-(aryl/furyl/thienyl/pyridyl ethenyl)oxazoles are prepared from the corresponding α,β-unsaturated aldehydes using Van Leusen reagent in very good yields and are transformed into naphthoxazoles and fused heterobenzoxazoles on irradiation under aerobic conditions and in the presence of iodine.



It was our goal to synthesize fused aromatic (**1a**−**d**) and heteroaromatic (**2**−**4**) oxazole derivatives by photochemical ring closure of properly substituted oxazoles (**5**−**8**).



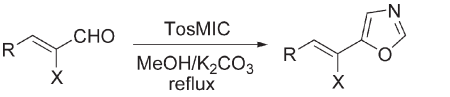
1a: R=H, R'=H, R''=H
b: R=OMe, R'=H, R''=H
c: R=H, R'=OMe, R'=H
d: R=H, R'=H, R''=Me

2: X=O, Y=CH
3a: X=S, Y=CH
b: X=CH, Y=S

4

Naphthoxazoles as a group of compounds have been known and studied for a long period of time, ever since Fisher synthesized 2-methylnaphtho[1,2-*d*]oxazole and 2-methylnaphtho-[2,1-*d*]oxazole in 1906.[1] In the subsequent years many different synthetic approaches have been developed.[2] The benzoxazole system has been found in a number of optical brighteners,[3] and the oxazole subunit is an important building block for the synthesis of many biologically active molecules.[4] A new efficient methodology for the preparation of oxazole derivatives provides a valuable tool to organic chemists. We present here a synthesis of naphthoxazoles and fused heterobenzoxazoles by utilizing light as a very clean reagent[5] in one step of the reaction path. Photochemical electrocyclization reactions are well-known and have been studied with the stilbene and heterostilbene derivatives for their usefulness as a convenient access to polynuclear aromatic compounds.[6] Reactions of photochemical electrocyclization as well as photocycloadition of heterostilbenes and *o*-vinylheterostilbene systems have been studied also in our group extensively.[7] However, to the best of our knowledge the photochemical electrocyclization reactions have never been applied to styryloxazoles. On a literature search, to our surprise, the synthesis of simple 5-phenylethenyl-/5-heteroarylethenyloxazole derivatives (**5**−**8**), the key step for our planned photochemical reactions, was also not reported.[8]

Scheme 1. Preparation of Arylethenyl-/ Heteroarylethenyloxazoles



9a-d
10, 11a-b,12

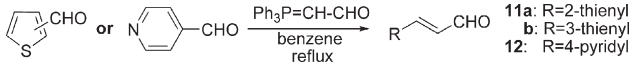
5a: R=Ph, X=H, 94%
b: R=*p*-PhOCH$_3$, X=H, 90%
c: R=*o*-PhOCH$_3$, X=H, 65%
d: R=Ph, X=Me, 97%
6: R=2-furyl, X=H, 98%
7a: R=2-thienyl, X=H, 90%
b: R=3-thienyl, X=H, 93%
8: R=4-pyridyl, X=H, 60%

In this paper we describe the synthesis of new 5-arylethenyl-/ 5-heteroarylethenyloxazoles, **5b**−**d** and **6**−**8**, and their photochemical ring closure to fused aromatic/heteroaromatic oxazole derivatives, **1**−**4**.

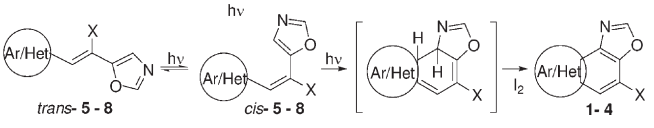
The starting oxazole derivatives **5**−**8** (Scheme 1) were synthesized in one step from aryl-/heteroaryl-substituted α,β-unsaturated aldehydes (**9**−**12**) using Van Leusen reagent, tosylmethyl isocyanide (TosMIC),[9] in refluxing methanol and in the presence of potassium carbonate. After the solvent was evaporated and the crude reaction mixture was passed through a silica gel chromatographic column, the 5-substituted oxazoles **5**−**8** were isolated in good yields (60−98%). In the case of the synthesis of 2- and 3-thienylethenyl- and 4-pyridylethenyloxazoles (**7a**,**b** and **8**) the necessary unsaturated aldehydes **11a**,**b**[10] and **12**[11] have been prepared by a Wittig reaction from the corresponding thiophene-2(3)-carbaldehydes and pyridine-4-carbaldehyde,

Received: December 30, 2010
Published: March 10, 2011

Scheme 2. Preparation of β-Hetarylacroleins



Scheme 3. Preparation of Naphthoxazoles and Furo-, Thieno-, and Pyridinobenzoxazoles



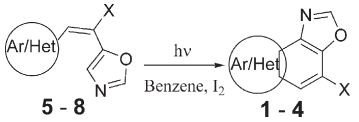
respectively, and formylmethylenetriphenylphosphorane (Scheme 2).[12]

All new compounds have been characterized by spectroscopic methods. As the starting compounds **9**−**12** for the reactions with TosMIC were all in a trans configuration, the obtained 5-arylethenyl-/5-heteroarylethenyloxazoles retained the trans configuration, which is clearly seen from the coupling constants of the ethylene protons (J = 16 Hz) in ^{1}H NMR. It is interesting that H-2 and H-4 oxazole protons of all Ar/Het-ethenyloxazole derivatives **5**−**8** appear at the same δ values: around 7.8 and 7.1 ppm, respectively. The two ethylene protons were also found in all examples in a similarly narrow region as two doublets at 6.7−7.0 and 6.9−7.1 ppm, respectively.

The irradiation experiments (Scheme 3) were performed in benzene solution with the addition of iodine and in a Rayonet reactor equipped with 300 nm lamps. When the irradiation process was carried out and the spectral changes in a UV cuvette were recorded, it was obvious that trans−cis isomerization takes place, followed by formation of the product. The formation of the product had to proceed via a dihydro intermediate, indicated in Scheme 3. The irradiation of all arylethenyl-/heteroarylethenyloxazoles was performed until full conversion (11−20 h). The photoproducts were isolated in good yields (Table 1) by column chromatography and the structures confirmed definitively by spectroscopic methods. In addition to a tarry material which remained on the column, only one photoproduct has been isolated. As we can see from the table, the yields are mostly between 60 and 70%. The lower yield for naphthoxazole **1a** (49%) is still very good, in comparison to other synthetic routes described in the literature (2%,[2e] 25%[2h]). With the electron donor substituent in ortho and para positions of the styryl group, the yield of naphthoxazoles **1b,c** increases to 62% and 70%, respectively. When the benzene ring in the styryl group is replaced with pyridine, as in compound **8**, the yield of cyclization product **4** is lowered to 29%. The yields of furo- and thienobenzoxazoles **2** and **3a** are comparable to the yields of styryl derivatives with electron donor substituents. In case of the 3-thiophene derivative **3b** the yield is lower compared to those for other 2-thiophene and 2-furan derivatives. It appears that the photocyclization reaction is very sensitive to electronic effects in the aryl or heteroaryl ring.

In summary, new 5-arylethenyl-/5-heteroarylethenyloxazoles have been synthesized and photochemically transformed into new naphthoxazoles and furo-, thieno-, and pyridinobenzoxazoles. The advantage of this method is the simplicity of the synthesis of oxazole derivatives with various fused aromatic and heteroaromatic rings which might be further functionalized to a variety of useful compounds.

Table 1. Photochemical Synthesis of Fused Oxazoles[a]



Substrate	Product	Isolated Yield %
5a	**1a**	49
5b	**1b**	62
5c	**1c**	70
5d	**1d**	66
6	**2**	63
7a	**3a**	59
7b	**3b**	41
8	**4**	29

[a] The numbering refers to NMR assignments of protons and carbons.

EXPERIMENTAL SECTION

Irradiation Experiments. A quartz vessel was charged with 5-styryl-/5-heteroaryloxazole (**5**−**8**; 0.9 mmol) and 300 mL of benzene with addition of a small amount of iodine and was irradiated at 300 nm in a Rayonet reactor for 11 h (**7a**), 16 h (**6**, **7b**, **8**), 18 h (**5a**), and 20 h (**5b**−**d**). After irradiation the solvent was removed in vacuo and the residue chromatographed on a silica gel column using petroleum ether/ether (variable ratio) as eluent.

Naphtho[1,2-d]oxazole[2e,h] (***1a***). Pale yellow crystals (0.08 g, 49%). Mp: 62 °C (lit.[3] mp 65 °C, lit.[2g] mp 60−61 °C). UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 223 (46 071), 276 (6818), 321 (4356). IR (cm^{-1}): 3101, 2920, 1501, 1240, 1001, 746, 631. ^{1}H NMR (600 MHz, $CDCl_3$):

dx.doi.org/10.1021/jo1025942 |J. Org. Chem. 2011, 76, 2904–2908

δ 8.52 (dd, $J_{10,11}$ = 8.22 Hz, $J_{10,12}$ = 0.8 Hz, 1H, H-10), 8.24 (s, 1H, H-2), 7.99 (dd, $J_{11,13}$ = 0.8 Hz, $J_{12,13}$ = 8.22 Hz, 1H, H-13), 7.85 (d, $J_{6,7}$ = 8.93 Hz, 1H, H-6/7), 7.73 (d, $J_{6,7}$ = 8.93 Hz, 1H, H-6/7), 7.68 (ddd, $J_{10,11}$ = 8.22 Hz, $J_{11,12}$ = 7.24 Hz, $J_{11,13}$ = 0.8 Hz, 1H, H-11), 7.57 (ddd, $J_{12,13}$ = 8.22 Hz, $J_{11,12}$ = 7.24 Hz, $J_{10,12}$ = 0.8 Hz, 1H, H-12). ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.5 (d, C-2), 147.5 (s), 135.5 (s), 131.2 (s), 128.5 (d, C-13), 127.2 (d, C-11), 126.7 (s), 126.6 (d, C-6/7), 125.5 (d, C-12), 120.0 (d, C-10), 111.0 (d, C-6/7).

*8-Methoxynaphtho[1,2-d]oxazole (**1b**).* Pale yellow crystals (0.11 g, 62%). Mp: 71.2−71.5 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 231 (55 150), 290 (8350). IR (cm^{-1}): 3094, 1639, 1472, 1242, 821, 694. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21 (s, 1H, H-2), 7.87 (d, $J_{12,13}$ = 8.94 Hz, 1H, H-13), 7.81 (d, $J_{10,12}$ = 2.52 Hz, 1H, H-10), 7.76 (d, $J_{6,7}$ = 8.82 Hz, 1H, H-6/7), 7.57 (d, $J_{6,7}$ = 8.82 Hz, 1H, H-6/7),7.19 (dd, $J_{12,13}$ = 8.94 Hz, $J_{10,12}$ = 2.52 Hz, 1H, H-12), 4.01 (s, 3H, H-OCH_3). ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.0 (s), 151.2 (d, C-2), 148.1 (s), 134.8 (s), 130.2 (d, C-13), 128.0 (s), 126.4 (d, C-6/7), 126.3 (s), 118.1 (d, C-12), 108.3 (d, C-6/7), 100.6 (d, C-10), 55.7 (q, C-OCH_3). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for $C_{12}H_9NO_2$ 200.0706, found 200.0710. Anal. Calcd for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.22; H, 4.35; N, 6.80.

*6-Methoxynaphtho[1,2-d]oxazole (**1c**).* White crystals (0.13 g, 70%). Mp: 107.5−108 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 297 (2003), 316 (1848), 329 (2308). IR (cm^{-1}): 3107, 2965, 1638, 1582, 1458, 1380, 1258. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.34 (d, $J_{6,7}$ = 9.20 Hz, 1H, H-6/7), 8.21 (s, 1H, H-2), 8.09 (d, $J_{11,12}$ = 8.01 Hz, 1H, H-10), 7.69 (d, $J_{6,7}$ = 9.20 Hz, 1, H-6/7), 7.60 (t, $J_{11,12}$ = $J_{10,11}$ = 8.01 Hz, 1H, H-11), 6.92 (d, $J_{10,11}$ = 7.74 Hz, 1H, H-12), 4.05 (s, 3H, H-OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.0 (s), 151.4 (d, C-2), 148.0 (s), 135.3 (s), 127.9 (s), 127.8 (d, C-11), 122.9 (s), 120.8 (d, C-6/7), 114.3 (d, C-10), 109.9 (d, C-6/7), 104.1 (d, C-12), 55.6 (q). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for $C_{12}H_9NO_2$ 200.0706, found 200.0706.

*4-Methylnaphtho[1,2-d]oxazole (**1d**).* White crystals (0.11 g, 66%). Mp: 48 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 229 (36 250), 280 (7135), 319 (2544). IR (cm^{-1}): 3121, 2920, 1500, 1232, 1085, 959. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.46 (d, $J_{10,11}$ = 8.10 Hz, 1H, H-10), 8.22 (s, 1H, H-2), 7.89 (d, $J_{12,13}$ = 8.10 Hz, 1H, H-13), 7.60 (s, 1H, H-7), 7.61 (t, $J_{10,11}$ = $J_{11,12}$ = 8.10 Hz, 2H, H-7,H-11), 7.52 (t, $J_{11,12}$ = $J_{12,13}$ = 8.10 Hz, 1H, H-12), 2.68 (s, 3H, H-CH_3). ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.8 (d, C-2), 147.7 (s), 134.9 (s), 131.1 (s), 127.3 (d, C-13), 125.7 (d, C-7), 125.3 (d, C-11), 125.0 (d, C-12), 124.9 (s), 121.4 (d, C-10), 121.1 (s), 15.2 (q). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for $C_{12}H_9NO$ 184.0757, found 184.0757.

*Furo[3,2-e]benzoxazole (**2**).* White crystals (0.09 g, 63%). Mp: 39−40 °C. IR (cm^{-1}): 3105, 2918, 2848, 1506, 1095, 795. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (s, 1H, H-2), 7.78 (d, $J_{10,11}$ = 2.13 Hz, 1H, H-11), 7.57 (dd, $J_{6,7}$ = 8.85 Hz, $J_{7,10}$ = 0.8 Hz, 1H, H-7), 7.52 (d, $J_{6,7}$= 8.85 Hz, 1H, H-6), 7.20 (dd, $J_{10,11}$ = 2.1 Hz, $J_{7,10}$ = 0.8 Hz, 1H, H-10). ^{13}C NMR (151 MHz, $CDCl_3$): δ 153.0 (s), 152.6 (d), 146.7 (s), 146.2 (d), 133.0 (s), 119.6 (s), 109.2 (d), 106.5 (d), 104.6 (d). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for $C_9H_5NO_2$ 160.0393, found 160.0395.

*Thieno[3,2-e]benzoxazole (**3a**).* Yellow crystals (0.09 g, 59%). Mp: 40−43 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 247 (1619), 267 (2977), 276 (2907), 296 (2837), 308 (3604). IR (cm^{-1}): 3117, 1740, 1398, 1238, 1022. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (s, 1H, H-2), 7.86 (d, $J_{6,7}$ = 8.75 Hz, 1H, H-6/7), 7.85 (d, $J_{10,11}$ = 5.40 Hz, 1H, H-10/11), 7.66 (d, $J_{10,11}$ = 5.40 Hz, 1, H-10/11), 7.61 (d, $J_{6,7}$ = 8,79 Hz, 1H, H-6/7). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.9 (d, C-2), 147.8 (s), 136.9 (s), 134.7 (s), 132.0 (s), 128.8 (d), 120.6 (d), 119.6 (d), 108.0 (d). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for C_9H_5NOS 176.0164, found 176.0163.

*Thieno[2,3-e]benzoxazole (**3b**).* Yellow oil (0.07 g, 41%). UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 236 (25 022), 242 (22 150), 264 (6570), 293 (1871), 306 (1523). IR (cm^{-1}): 3101, 1498, 1243, 960. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21 (s, 1H, H-2), 7.82 (d, $J_{6,7}$ = 8.67 Hz, 1H, H-6/7), 7.62 (d, $J_{6,7}$ = 8.67 Hz, 1H, H-6/7), 7.49 (d, $J_{11,12}$ = 5.34 Hz, 1H, H-11/12), 7.47 (d, $J_{11,12}$ = 5.34 Hz, 1H, H-11/12). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.2 (d, C-2), 147.5 (s), 137.9 (s), 125.6 (d, C-11/12), 124.4 (d, C-11/12), 121.1 (d, C-6/7), 108.3 (d, C-6/7), 106.4 (s), 82.0 (s). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for C_9H_5NOS 176.0164, found 176.0168.

*Oxazolo[5,4-h]isoquinoline (**4**).* White crystals (0.04 g, 29%). Mp: 166−167 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 319 (3818), 332 (4294). IR (cm^{-1}): 3094, 1639, 1472, 1242, 821, 694. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.95 (s, 1H, H-10), 8.68 (d, $J_{12,13}$ = 5.73 Hz, 1H, H-12), 8.32 (s, 1H, H-2), 7.97 (d, $J_{6,7}$ = 9.06 Hz, 1, H-6/7), 7.85 (dd, $J_{12,13}$ = 5.76 Hz, 1H, H-13), 7.83 (d, $J_{6,7}$ = 9.06 Hz, 1H, H-6/7). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.2 (d, C-2), 147.6 (s, C-5), 146.6 (d, C-10), 142.9 (d, C-12), 134.8 (s), 133.4 (s), 124.5 (d, C-6/7), 120.9 (s, C-4), 120.4 (d, C-13), 115.3 (d, 6/7). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for $C_{10}H_6N_2O$ 171.0553, found 171.0552.

Procedure for the Synthesis of 5-Styryl-/5-Heteroarylox-azoles. Compounds **5**−**8** were prepared from the corresponding acrylaldehydes (**9**−**12**) and 4-toluenesulfonylmethyl isocyanide (TOSMIC) as described in the literature for 5-phenyloxazole.[9a,b] 4-Toluenesulfonylmethyl isocyanide (1 eq, 0,005 mol), acryladehyde (1 equiv, 0,005 mol), and potassium carbonate (1 equiv, 0.005 mol) in 30 mL of methanol were heated under reflux for 3−4 h. After removal of the solvent the residue was worked up with ice−water and ether. Ether extracts were dried over anhydrous $MgSO_4$. Evaporation under reduced pressure afforded the crude product, which was further purified by column chromatography on silica gel using petroleum ether/ether (variable ratio) as eluent.

trans-5-Styryloxazole[8a] *(**5a**).* Yellow crystals (0.80 g, 94%). Mp: 60.8−61.1 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 227 (10 603), 295 (28 745), 306 (29 990), 321 (21 107). IR (cm^{-1}): 3121, 1684, 1495, 1352, 947, 636. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.85 (s, 1H, H-2), 7.48 (d, $J_{9,10}$ = 7.38 Hz, 2H, H-9), 7.37 (t, $J_{9,10}$ = $J_{10,11}$ = 7.38 Hz, 2H, H-10), 7.30 (t, $J_{9,10}$ = $J_{10,11}$= 7.38 Hz, 1H, H-11), 7.11 (d, $J_{6,7}$ = 16.29 Hz, 1H, H-6/7), 7.08 (s, 1H, H-4), 6.92 (d, $J_{6,7}$ = 16.29 Hz, 1H, H-6/7). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.5 (d, C-2), 150.3 (s, C-5), 136.2 (s, C-8), 130.3 (d, C-6/7), 128.9 (d, C-10), 128.5 (d, C-11), 126.6 (d, C-9), 124.1 (d, C-4), 112.9 (d, C-6/7).

*trans-5-(4-Methoxystyryl)oxazole (**5b**).* Pale yellow crystals (0.91 g, 90%). Mp: 103.5−104.0 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 229 (10 573), 307 (31 474), 318 (32 742). IR (cm^{-1}): 3109, 1603, 1508, 1244, 951, 640. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.82 (s, 1H, H-2), 7.42 (d, $J_{9,10}$ = 8.46 Hz, 2H, H-9), 7.05 (d, $J_{6,7}$ = 16.26 Hz, 1H, H-6/7), 6.78 (d, $J_{6,7}$ = 16.26 Hz, 1H, H-6/7), 7.02 (s, 1H, H-4), 6.90 (d, $J_{9,10}$ = 8.46 Hz, 2H, H-10), 3.83 (s, 3H, H-OCH_3). ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.9 (s, C-11), 150.8 (s, C-5), 150.0 (d, C-2), 129.9 (d, C-7), 129.0 (s, C-8), 127.9 (d, C-9), 123.3 (d, C-4), 114.3 (d, C-10), 110.9 (d, C-6), 55.3 (q, C-OCH_3). HRMS (MALDI-TOF/TOF; *m*/*z*): $[M + H]^+$ calcd for $C_{12}H_{11}NO_2$ 202.0863, found 202.0860. Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.36; H, 5.36; N, 6.59.

*trans-5-(2-Methoxystyryl)oxazole (**5c**).* White crystals (0.65 g, 65%). Mp: 71.4−71.6 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 234 (7033), 291 (14 606), 302 (14 350), 318 (13 943), 329 (14 553). IR (cm^{-1}): 3142, 2942, 2837, 1579, 1470, 1238. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (s, 1H, H-2), 7.49 (dd, $J_{9,10}$ = 8.30 Hz, $J_{9,11}$ = 1.29 Hz, 1H, H-9), 7.40 (d, $J_{6,7}$ = 16.6 Hz, 1H, H-6/7), 7.27 (dt, $J_{9,11}$ = 1.29 Hz, $J_{10,11}$ = $J_{11,12}$ = 8.30 Hz, 1H, H-11), 7.05 (s, 1H, H-4), 7.00 (d, $J_{6,7}$ = 16.60 Hz, 1H, H-6/7), 6.97 (t, $J_{9,10}$ = $J_{10,11}$ = 8.30 Hz, 1H, H-10), 6.91 (d, $J_{11,12}$ = 8.30 Hz, 1H, H-12), 3.90 (s, 3H, H-OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.3 (s, C-13), 151.1 (s, C-5), 150.2 (d, C-2), 129.4 (d, C-11), 127.2 (d, C-12), 125.6 (d, C-6/7), 125.1 (s, C-8), 123.7 (d, C-4), 120.8 (d, C-10), 113.6 (d, C-6/7), 111.0 (d, C-9), 55.5

(q, C-OCH_3). HRMS (MALDI-TOF/TOF; m/z): $[M + H]^+$ calcd for $C_{12}H_{11}NO_2$ 202.0862, found 202.0868.

*(E)-5-(1-Phenylprop-1-en-2-yl)oxazole (**5d**).* White crystals (0.90 g, 97%). Mp: 83−83.4 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 288 (22 359). IR (cm^{-1}): 1445, 947, 829, 631, 504. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.85 (s, 1H, H-2), 7.39 (t, $J_{9,10} = J_{10,11}$ = 7.80 Hz, 2H, H-9/10), 7.37 (d, $J_{9,10}$ = 7.80 Hz, 2H, H-9/10), 7.29−7.26 (m, 1H, H-11), 7.13 (broad singlet, $J_{7,CH3}$ = 1.32 Hz, 1H, H-7), 7,08 (s, 1H, H-4), 2.20 (d, $J_{7,CH3}$ = 1.32 Hz, 3H, H-CH_3). ^{13}C NMR (151 MHz, $CDCl_3$): δ 153.6 (s, C-5), 150.3 (d, C-2), 136.6 (s, C-8), 129.3 (d, C-9/10), 128.3 (d, C-9/10), 127.2 (d, C-12), 126.8 (d, C-7), 123.4 (s, C-6), 122.6 (d, C-4), 14.8 (q, C-CH_3). HRMS (MALDI-TOF/TOF; m/z): $[M + H]^+$ calcd for $C_{12}H_{11}NO$ 186.0913, found 186.0904.

*trans-5-[2-(Furan-2-yl)vinyl]oxazole (**6**).* Yellow crystals (0.79 g, 98%). Mp: 61.9−62.3 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 316 (38 504), 330 (31 148). IR (cm^{-1}): 3099, 1497, 1246, 1026, 943, 634, 592. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.82 (s, 1H, H-2), 7.42 (d, $J_{5,4}$ = 1.50 Hz, H-11), 7.04 (s, 1H, H-4), 6.87 (d, $J_{6,7}$ = 16.05 Hz, 1H, H-6/7), 6.82 (d, $J_{6,7}$ = 16.05 Hz, 1H, H-6/7), 6.43 (dd, $J_{4,3}$ = 3.33 Hz, $J_{4,5}$ = 1.5 Hz, 1H, H-10), 6.40 (d, $J_{3,4}$ = 3.33 Hz, 1H, H-9). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.1 (d, C-2), 150.2 (2s, C-5,8), 142.9 (d, C-11), 124.2 (d, C-4), 117.7 (d, C-6/7), 111.9 (d, C-10), 111.1 (d, C-6/7), 110.2 (d, C-9). HRMS (MALDI-TOF/TOF; m/z): $[M + H]^+$ calcd for $C_9H_7NO_2$ 162.0550, found 162.0554.

*trans-5-[2-(Thiophen-2-yl)vinyl]oxazole (**7a**).* White crystals (0.79 g, 90%). Mp: 64.9−66 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 322 (28 390). IR (cm^{-1}): 3117, 2158, 2006, 1483, 1246, 947. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.82 (s, 1H, H-2), 7.24 (d, $J_{9,10}$ = 4.98 Hz, 1H, H-9), 7.21 (d, $J_{6,7}$ = 16.02 Hz, 1H, H-6/7), 7.10 (d, $J_{10,11}$ = 3.50 Hz, 1H, H-11), 7.04 (s, 1H, H-4), 7.01 (dd, $J_{9,10}$ = 4.98 Hz, $J_{10,11}$ = 3.5 Hz, 1H, H-10), 6.72 (d, $J_{6,7}$ = 16.02 Hz, 1H, H-6/7). ^{13}C NMR (151 MHz, $CDCl_3$): δ 149.8 (d, C-2), 149.5 (s, C-5), 141.1 (s, C-8), 127.4 (d, C-10), 126.9 (d, C-9/11), 125.0 (d, C-9/11), 123.6 (d, C-4), 122.8 (d, C-6/7), 111.7 (d, C-6/7). HRMS (MALDI-TOF/TOF; m/z): $[M + H]^+$ calcd for C_9H_7NOS 178.0321, found 178.0323.

*trans-5-[2-(Thiophene-3-yl)vinyl]oxazole (**7b**).*)Yellow crystals (0.82 g, 93%). Mp: 101.9−102.1 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 299 (29 987), 313 (22 492). IR (ν_{max}/cm^{-1}): 3126, 3093, 2923, 1640, 1509, 1486, 1298, 1113. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (s, 1H, H-2), 7.24−7.28 (m, 3H, H-9,10,12), 7.10 (d, $J_{6,7}$ = 16.20 Hz, 1H, H-6/7), 7.04 (s, 1H, H-4), 6.75 (d, $J_{6,7}$ = 16.02 Hz, 1H, H-6/7). ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.4 (s, C-5), 150.2 (d, C-2), 139.0 (s, C-8), 126.6 (d), 124.6 (d, C-6/7), 124.4 (d, C-4), 123.8 (d), 123.7 (d), 112.9 (d, C-6/7). HRMS (MALDI-TOF/TOF; m/z): $[M + H]^+$ calcd for C_9H_7NOS 178.0321, found 178.0318.

*trans-4-[2-(Oxazol-5-yl)vinyl]pyridine (**8**).* White crystals (0.52 g, 60%). Mp: 89−91 °C. UV (EtOH; λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})): 293 (20 994), 304 (22 128), 311 (20 186). IR (cm^{-1}): 3068, 2949, 2183, 1593, 1419, 1213, 1107, 947, 800, 636, 521. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (d, 2H, $J_{9,10}$ = 5.55 Hz, H-12, H-10), 7.90 (s, 1H, H-2), 7.33 (d, 2H, $J_{9,10}$ = 5.55 Hz, H-9), 7.19 (s, 1H, H-4), 7.11(d, $J_{6,7}$ = 16.26 Hz, 1H, H-6/7), 7.02(d, $J_{6,7}$ = 16.26 Hz, 1H, H-6/7). ^{13}C NMR (151 MHz, $CDCl_3$): δ 151.1 (d, C-2), 150.4 (d, C-10), 149.5 (s, C-5), 143.4 (s, C-8), 127.4 (d, C-6/7), 126.2 (d, C-4), 120.8 (d, C-9), 117.0 (d, C-6/7). HRMS (MALDI-TOF/TOF; m/z): $[M + H]^+$ calcd for $C_{10}H_8N_2O$ 173.0709, found 173.0705.

■ ASSOCIATED CONTENT

Supporting Information. Text and figures giving ^{1}H and ^{13}C NMR spectra of compounds **1a**−**d**, **2**, **3a**,**b**, **4**, **5a**−**d**, **6**, **7a**,**b**, and **8**, general experimental comments and procedure for the synthesis of β-hetarylacrylaldehydes (**11** and **12**), and UV spectra of the photolysis of **5b**,**d**, **6**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: marija.sindler@fkit.hr.

■ ACKNOWLEDGMENT

This work was supported by grants from the Ministry of Science, Education and Sports of the Republic of Croatia (Grant Nos. 125-0982933-2926 and 098-0982929-2917).

■ REFERENCES

(1) Fisher, N. I.; Hamer, F. M. *J. Chem. Soc.* **1934**, 962–965.

(2) (a) Desai, R. D.; Hunter, R. F.; Khalidi, A. R. K. *J. Chem. Soc.* **1938**, 321–329. (b) Somayajulu, V. V.; Subba Rao, N. V. *Proc. Indian Acad. Sci. Sect. A* **1964**, *61*, 139–145. (c) Moskal, J.; Van Stralen, R.; Postma, D.; Van Leusen, A. M. *Tetrahedron Lett.* **1986**, *27*, 2173–2176. (d) Kauffman, J. M.; Litak, P. T.; Adams, J. K. *J. Heterocycl. Chem.* **1992**, *29*, 1245–1273. (e) Katrizky, A. R; et al. *J. Heterocycl. Chem.* **1993**, *30*, 135–139. (f) Nicolaides, D. N; Wajih Awad, R.; Varella, E. A. *J. Heterocycl. Chem.* **1996**, *33*, 633–637. (g) Nicolaides, D. N.; Wajih Awad, R.; Papageorgiou, G. K. *J. Heterocycl. Chem.* **1997**, *34*, 1651–1656. (h) Novikov, R. A.; Klimenko, I. P.; Shulishov, E. V.; Korolev, V. A.; Tomilov, Yu. V. *Russ. Chem. Bull., Int. Ed.* **2008**, *57*, 1718–1724.

(3) *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1978; Vol. 23, pp 195−197.

(4) (a) Sobarzo-Sanchez, E.; Jullian, C.; Cassels, B. K.; Saitz, C. *Synth. Commun.* **2002**, *32*, 3687–3693. (b) Yeh, V. S. C. *Tetrahedron* **2004**, *60*, 11995–12042. (c) Ashton, W. T.; Sisco, R. M.; Dong, T.; Lyons, K. A.; He, H.; Doss, G. A.; Leiting, B.; Patel, R. A.; Wu, J. K.; Marsilio, F.; Thornberry, N. A.; Weber, A. E. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2253–2258. (d) Voets, M.; Antes, I.; Scherer, Ch.; Mueller-Vieira, U.; Biemel, K.; Barassin, C.; Marchais-Oberwinkler, S.; Hartmann, R. W. *J. Med. Chem.* **2005**, *48*, 6632–6642. (e) Ryu, C.-K.; Lee, Ra-Y.; Kim, Na Y.; Song, Ae L. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 5924–5926. (f) Kumar, A.; Ahmad, P.; Maurya, R. A.; Singh, A. B.; Srivastava, A. K. *Eur. J. Med. Chem.* **2009**, *44*, 109–116. (g) Voight, E. A.; Daanen, J. F.; Kort, M. E. *J. Org. Chem.* **2010**, *75*, 8713–8715.

(5) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052–1103.

(6) (a) Gilbert, A. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. H., Ed.; CRC Press: Boca Raton, FL, 1995; pp 291−300. (b) Laarhoven, W. H. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1989; Vol. 10, pp 163−308. (c) Mallory, F. B.; Mallory, C. W. *Org. React.* **1984**, *30*, 1–456. (d) Muszkat, K. A. *Top. Curr. Chem.* **1980**, *88*, 89–138.

(7) (a) Vidaković, D.; Škorić, I.; Horvat, M.; Marinić, Ž.; Šindler-Kulyk, M. *Tetrahedron* **2008**, *64*, 3928–3934. (b) Basarić, N.; Marinić, Ž.; Šindler-Kulyk, M. *J. Org. Chem.* **2006**, *71*, 9382–9392. (c) Škorić, I.; Basarić, N.; Marinić, Ž.; Višnjevac, A.; Kojić-Prodić, B.; Šindler-Kulyk, M. *Chem. Eur. J.* **2005**, *11*, 543–551. (d) Basarić, N.; Marinić, Ž.; Šindler-Kulyk, M. *J. Org. Chem.* **2003**, *68*, 7524–7527. (e) Škorić, I.; Basarić, N.; Marinić, Ž.; Šindler-Kulyk, M. *Heterocycles* **2001**, *55*, 1889–1896. (f) Šindler-Kulyk, M.; Škorić, I.; Tomšić, S.; Marinić, Ž.; Mrvoš-Sermek, D. *Heterocycles* **1999**, *51*, 1355–1369. (g) Šindler-Kulyk, M.; Kragol, G.; Piantanida, I.; Tomšić, S.; Vujković Cvijin, I.; Marinić, Ž.; Metelko, B. *Croat. Chem. Acta* **1996**, *69*, 1593–1602.

(8) During the course of our study the 5-styryloxazole was described: (a) Companayo, X.; Moyano, A.; Rios, R. *Lett. Org. Chem.* **2009**, *6*, 293–296. 5-[2-(2-Nitrophenylethenyl)]oxazole was obtained in a sequence of reactions (including Diels−Alder) from 1-formamido-2-siloxy-4-(2-nitrophenyl)-1,3-butadiene: (b) Alonso, D.; Caballero, E.; Medarde, M.; Tome, F. *Tetrahedron Lett.* **2007**, *48*, 907–910.

(9) (a) Van Leusen, M.; Hoogenboom, B. E.; Siderius, H. *Tetrahedron Lett.* **1972**, *23*, 2369–2372. (b) Saikachi, H.; Kitagawa, T.; Sasaki, H.; Van Leusen, A. M. *Chem. Pharm. Bull.* **1979**, *2*, 793–796. (c) Bheemashankar, A. K.; Ganesan, A. *Tetrahedron Lett.* **1999**, *40*, 5633–5638. (d) Dhar, T. G. M.; Shen, Z.; Fleener, C. A.; Rouleau,

K. A.; Barrish, J. C.; Hollenbaugh, D. L.; Iwanowicz, E. J. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3305–3308. (e) Krishna, P. R.; Reddy, V. V. R.; Sharma, G. V. M. *Synlett* **2003**, *11*, 1619–1622.

(10) (a) Klemm, L. H.; Gopinath, K. W. *J. Heterocycl. Chem.* **1965**, *2(3)*, 225–227. (b) Duhamel, L.; Ple, G.; Contreras, B. *Org. Prep. Proced. Int.* **1986**, *18*, 219–226. (c) Spangler, C. W.; McCoy, R. K. *Synth. Commun.* **1988**, *18*, 51–59. (d) Reid, M.; Rowe, D. J.; Taylor, J. K. *Chem. Commun.* **2003**, *18*, 2284–2285.

(11) Hagedorn, I.; Hohler, W. *Angew. Chem.* **1975**, *87*, 486.

(12) Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266–1271.