Photocycloadditions on 2-Methyloxazolo[5,4-*b*]pyridine

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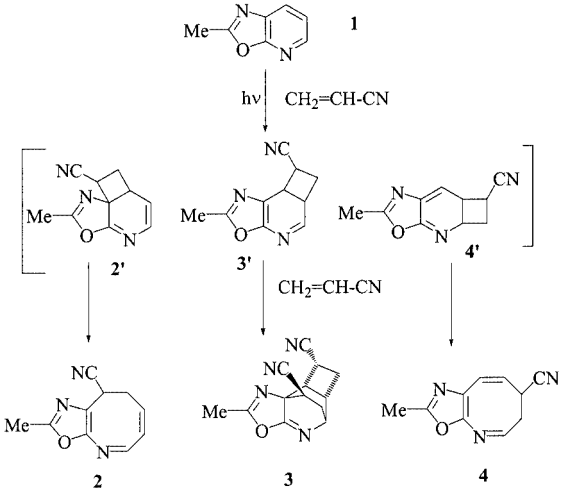
The title compound undergoes photocycloadditions with both electron-poor alkenes (methacrylonitrile) and electron-rich alkenes (ethyl vinyl ether and furan). The initial photoadducts evolve into a variety of compounds. In the photoreaction with methacrylonitrile, oxazoloazocines **5** and **7** and cyclopentenylidenes **6*Z*** and **6*E*** are obtained; the photoadducts with vinyl ether yield oxazoloazocines **9** and **11**, substituted oxazoles **10** and **12**, and pyrrolopyridine **13**; from the reaction with furan the furylpyridine **14** was isolated.

Introduction

During our research on the photochemistry of free or condensed oxazoles with pyridines, we observed various aspects of the rearrangement processes involved[1] and we explored the usefulness of this kind of reaction for synthetic purposes.[2] Unlike other similar heterocyclic rings, the oxazolo[5,4-*b*]pyridine (**1**) was observed to undergo an addition reaction with acrylonitrile leading to oxazolo[5,4-*b*]azocines as the final products. This new heterocyclic system as well as the unusual addition reaction to such a system, prompted us to investigate this reaction, and a preliminary account of the reactivity with acrylo- and crotononitrile has been reported.[3] The main results of this study are summarized graphically in Scheme 1.



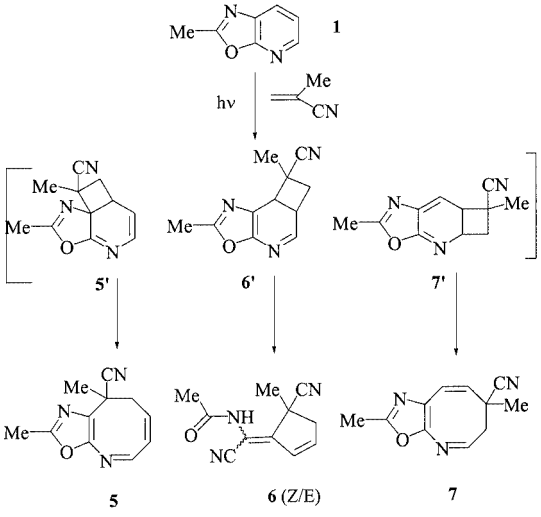
Scheme 1

Eight-membered heterocycles are interesting because of their pharmacological properties.[4] Therefore we recently extended our study to either electron-poor or electron-rich alkenes, hoping to understand the factors affecting the selectivity of this reaction as well as to widen the applicability of the reaction.

Results and Discussion

Irradiation in the Presence of Methacrylonitrile

Irradiation of oxazolopyridine **1** with methacrylonitrile followed by column chromatography on silica gel gave the products **5**, **6*Z***, **6*E***, and **7** (Scheme 2).



Scheme 2

Clearly, the oxazoloazocines **5** and **7** arose from the intermediate cyclobutanes **5′** and **7′** by a thermally allowed ring opening. The structure of **6*Z*** was unambiguously estab-

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lished by X-ray crystallographic analysis and is shown in Figure 1.

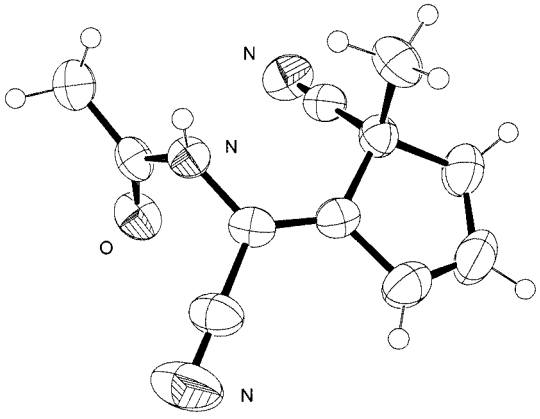
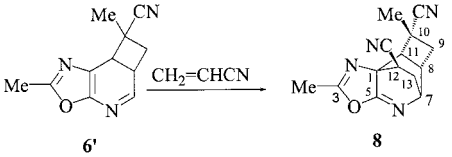


Figure 1. Drawing of the molecular structure of compound **6*Z***; the non-H displacement ellipsoids are drawn at the 50% probability level

Compound **6*E***, although not isolated as a pure compound, was characterized in the mixture with **6*Z*** by NMR spectroscopy. Integration of the signals in the ^{1}H NMR spectrum showed the (*Z*) and (*E*) isomers to be present in roughly equal amounts. It should be noted that signals of **6*Z*** and **6*E*** are not present in the ^{1}H NMR spectrum of the crude reaction mixture. The products were obtained by eluting the mixture through a silica gel chromatography column. A possible rationale is to suppose the presence of the intermediate **6′** which, instead of giving further Diels−Alder addition as in the case of acrylonitrile (intermediate **3′** in Scheme 1), rearranges on the silica gel to give **6*Z*** and **6*E***. A careful examination of the crude reaction mixture in the 600-MHz ^{1}H NMR spectrum did not support this idea directly, due to the lack of free signals clearly attributable to **6′**. However, indirect confirmation of this mechanism was obtained by trapping the intermediate **6′** with acrylonitrile; in fact, on irradiating **1** in a 1:1 mixture of acrylo- and methacrylonitrile the Diels−Alder adduct **8** was isolated instead of the cyclopentenylidenes **6*Z*/6*E*** (Scheme 3).



Scheme 3

The structure of **8** was established by comparison of its ^{1}H and ^{13}C NMR spectroscopic data with those of the corresponding compound obtained by irradiation of **1** with acrylonitrile only.[3] The configuration at C(10) was determined by recording a positive NOE effect on H(11) by irradiating the methyl group on C(10), and so confirming also the stereoselectivity of the addition of methacrylonitrile.

The reaction with methacrylonitrile confirms the features already noticed for acrylonitrile; the new products identified are due to the lack of a hetero Diels−Alder reaction on the intermediate **6′**, probably caused by overcrowding in the transition state. The trapping of **6′** with acrylonitrile justifies this assumption. The thermal rearrangement of **6′** to cyclopentenylidenes **6*Z*** and **6*E*** appears to be rather slow and further investigation is required to clarify this point.

Irradiation in the Presence of Ethyl Vinyl Ether

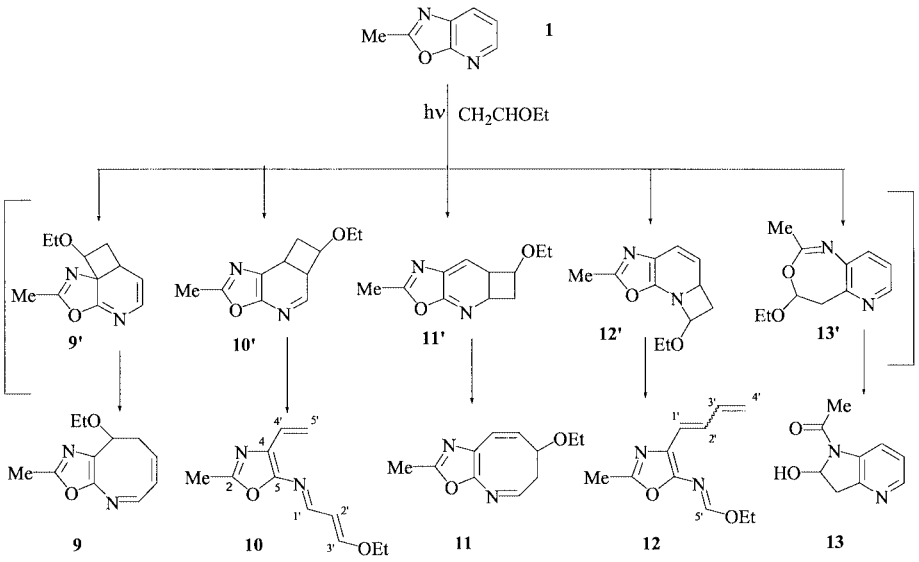
The trend of the reaction using this electron-rich alkene is significantly different. The identified products in a very complex reaction mixture and their relative yields are reported in Scheme 4.

Together with the two azocines **9** and **11**, analogous to those obtained by irradiation of **1** with electron-poor alkenes, the substituted oxazoles **10**, **12*Z***, **12*E*** were found, supposedly derived from the corresponding cyclobutane adducts **10′** and **12′**, as shown in Scheme 4. In addition, the NMR spectrum of the crude reaction mixture shows a set of peaks of another product, which disappeared after elution on silica gel. Further elution on silica gel with methanol gave another product identified as pyrrolopyridine **13** on the basis of its spectroscopic data.

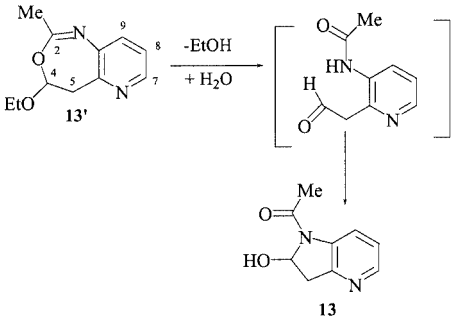
A comparison of the ^{1}H and ^{13}C NMR spectroscopic data recorded before and after elution on silica gel is consistent with the pyridooxazepine **13′**; an aromatic pyridine system is clearly assigned, and the signals at δ = 105.04 ppm in the ^{13}C NMR spectrum and δ = 5.45 ppm in the ^{1}H NMR spectrum are consistent with an acetalic proton. Such a structure, because of the acetalic moiety, justifies the rapid hydrolysis on silica gel to give the more stable **13**.

The regioselectivity of the reaction with electron-rich alkenes may be formally rationalized as a nucleophilic attack on the β-carbon atom of the vinyl ether in the *ortho*/*para* positions of the pyridine ring and a subsequent attack on the α-carbon atom in the adjacent positions. The charge distribution in the excited state or the greater stability of the anions derived by *ortho*/*para* attack, estimated by semiempirical calculations,[5] justifies this assumption. Considering such a regioselectivity as well as the electronic characteristics of the molecules involved, it appears to be more convincing to propose a stepwise mechanism, in which an initial exciplex evolves by the attack of the β-carbon atom of the vinyl ether. The attack on the 4- or 6-position leads to the cyclobutane intermediates **9′**−**10′** or **11′**−**12′**, respectively. It is worth noting that the ring-opening of the cyclobutane ring follows pathways which preserve or reconstitute the aromaticity of the oxazole ring.

The attack on position 7a in compound **1** causes the opening of the oxazole ring and the formation of the pyridooxazepine **13′**, a new heterocyclic system (Scheme 5). The acetalic moiety in this structure justifies the rearrangement on silica gel. A similar mechanism has been proposed for the rearrangement of benzooxazepines to 2-hydroxyindole on silica gel.[6]



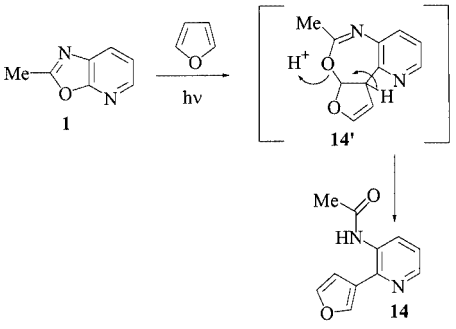
Scheme 4



Scheme 5

Irradiation in the Presence of Furan

The ^{1}H NMR spectrum of the reaction mixture shows that after prolonged irradiation the main product is unchanged **1**. The broad bands in the region $\delta = 3-7$ ppm indicate a very complex mixture, probably due to further photoreactivity of the primary products. However, workup of the reaction at 50−60% completion allowed us to isolate **14** (Scheme 6). The complete structure, obtained by X-ray diffractometric analysis is shown in Figure 2.



Scheme 6

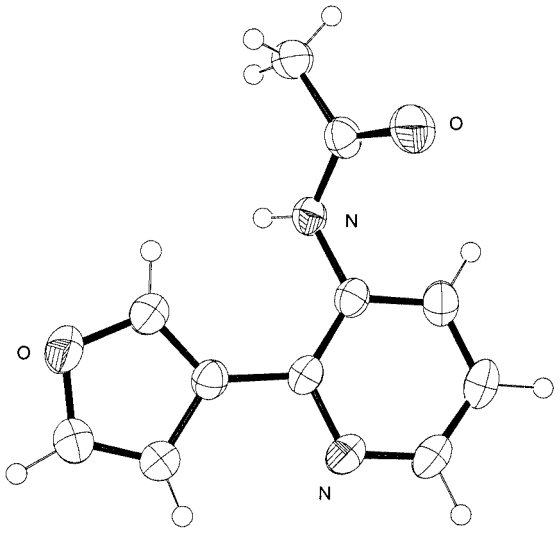


Figure 2. Drawing of the molecular structure of compound **14**; the non-H displacement ellipsoids are drawn at the 50% probability level

Compound **14**, isolated in the photoreaction of **1** with furan, may be explained as a consequence of the attack of the β-carbon atom of furan on the 7a-position of **1**, similar to the attack yielding **13** in the reaction with vinyl ether. However, in this case, the release of the proton from the β-position of furan, owing to the rearomatization of the ring, is a preferred route leading to **14** (Scheme 6). This finding suggests that the underlying mechanism is maintained also for this electron-rich system.

Conclusion

The good yields, the stereoselectivity and the absence of by-products confirm that the photoaddition with electron-

poor alkenes is a suitable procedure for the preparation of substituted oxazolo[5,4-*b*]azocines. However, the photoaddition with electron-rich alkenes in the cases examined shows a low selectivity and therefore decreases the interest from the preparative point of view. Nevertheless, further investigations on the details of the mechanism of electron transfer will be undertaken with the aim of ascertaining the possibility of regiocontrol and therefore improving the synthetic usefulness of this photoaddition.

Experimental Section

General: Melting points were measured with a Kofler apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AC200 instrument operating at 200.13 MHz for ^{1}H and at 50.33 MHz for ^{13}C. Assignment of the ^{13}C NMR spectra was made with the aid of DEPT and HETCOR experiments. Electron impact mass spectra (70 eV) were recorded with a VG 70 250s instrument. Merck Kieselgel (200−400 mesh ASTM) was employed for analytical TLC and column chromatography.

Irradiation of 1 in the Presence of Methacrylonitrile: 2-Methylisoxazolo[5,4-*b*]pyridine (**1**; 500 mg) in acetonitrile (100 mL) was mixed with methacrylonitrile (10 mL) and the mixture irradiated for about 6 h with a low-pressure mercury lamp. N_2 was bubbled through the solution during the irradiation. The solvent was then evaporated from the brownish solution and the remaining solid purified by chromatography on silica gel, initially eluting with petroleum ether/diethyl ether (1:1) and thereafter with diethyl ether. Elution order: **1** (110 mg), **5** (160 mg), **7** (80 mg), and **6*Z*** + **6*E*** (130 mg).

8,9-Dihydro-2,9-dimethyloxazolo[5,4-*b*]azocine-9-carbonitrile (5): White solid (160 mg, 41%); m.p. 146−148 °C. ^{1}H NMR (CD_3CN): δ = 1.66 (s, 9-Me), 2.36 (s, 2-Me), 2.43 (dd, $J_{8a\text{-}8b}$ = 12.1, $J_{8a\text{-}7}$ 7.3 Hz, 8a-H), 2.67 (dd, $J_{8a\text{-}8b}$ = 12.1, $J_{8b\text{-}7}$ = 7.0 Hz, 8b-H), 6.33 (dd, $J_{7\text{-}6}$ = 10.6, $J_{6\text{-}5}$ = 1.8 Hz, 6-H), 6.38 (ddd, $J_{7\text{-}6}$ = 10.6, $J_{7\text{-}8a}$ = 7.3, $J_{7\text{-}8b}$ = 7.0 Hz, 7-H), 7.95 (d, $J_{5\text{-}6}$ = 1.8 Hz, 5-H) ppm. ^{13}C NMR (CD_3CN): δ =13.6 (2-Me), 28.0 (9-Me), 35.6 (C-8), 38.4 (C-9), 117.8 (CN), 122.7 (C-9a), 130.6 (C-6), 137.9 (C-7), 149.0 (C-3a), 158.8 (C-2), 161.2 (C-5) ppm. HRMS: calcd. for $C_{11}H_{11}N_3O$ 201.09021; found 201.09016 [M^+].

(*Z*)-*N*-[Cyano(5-cyano-5-methylcyclopent-2-enylidene)methyl]-acetamide (6*Z*): The fraction containing **6*Z*** and **6*E*** (130 mg, 33%) was further purified by chromatography on silica gel (LOBAR Si-60 Merck) obtaining 30 mg of pure (TLC) **6*Z***, which, after crystallization from ethanol, gave a white crystalline solid. M.p. 153−155 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3200 (NH), 2220 (CN), 2200 (CN), 1650 (CO) cm^{-1}. ^{1}H NMR(CD_3OD): δ = 1.6 (s, 5-Me), 2.12 (s, Me-CO), 2.84−3.28 (ddd and dd, $J_{4a\text{-}4b}$ = 18.78, $J_{4a\text{-}3}$ = 2.8, $J_{4b\text{-}3}$ = 1.7, $J_{4a\text{-}2}$ = 1.69 Hz, 4a-H and 4b-H), 6.48−6.64 (dd and ddd, $J_{2\text{-}3}$ = 5.9, $J_{3\text{-}4a}$ = 2.8, $J_{3\text{-}4b}$ = 1.7, $J_{2\text{-}4a}$ = 1.69 Hz, 2-H and 3-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.8 (Me-CO), 25.4 (5-Me), 37.6 (C5), 48.7 (C-4), 100.8 (CNH), 114.1 (CN), 120.5 (CN), 128.2 (C-3), 142.1 (C-2), 155.9 (C-1), 169.4 (CO) ppm. HRMS: calcd. for $C_{11}H_{11}N_3O$ 201.0902; found 201.0916 [M^+].

(*E*)-*N*-[Cyano(5-cyano-5-methylcyclopent-2-enylidene)methyl]-acetamide (6*E*): Obtained as an impure fraction of **6*Z***. ^{1}H NMR ($CDCl_3$): δ =1.9 (s, 5-Me), 2.2 (s, MeCO), 2.8−3.4 (d, $J_{4a\text{-}4b}$ = 19.5 Hz, 4a-H and 4b-H), 6.40 (m, 2 H, 2-H and 3-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.1 (MeCO), 24.9 (5-Me), 37.5 (C-5), 48.0 (C-4), 100.8 (CNH), 114.1 (CN), 120.5 (CN), 128.6 (C-3), 143.1 (C-2), 155.9 (C-1), 169.4 (CO) ppm.

6,7-Dihydro-2,7-dimethyloxazolo[5,4-*b*]azocine-7-carbonitrile (7): Colourless oil (80 mg, 20%). ^{1}H NMR ($CDCl_3$): δ = 1.61 (s, 7-Me), 2.45 (s, 2-Me), 2.89 (d, $J_{6a,b\text{-}5}$ =6.4 Hz, 6a-H and 6b-H), 5.83 (d, $J_{9\text{-}8}$ = 13.0 Hz, 9-H), 6.42 (d, $J_{8\text{-}9}$ = 13.0 Hz, 8-H), 7.97 (t, $J_{5\text{-}6a}$ = $J_{5\text{-}6b}$ = 6.4 Hz, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ =13.9 (2-Me), 30.4 (7-Me), 38.7 (C-7), 39.0 (C-6), 120.4 (CN), 121.5 (C-9 or C-8),121.7 (C-9a),131.1 (C-8 or C-9), 150.0 (C-3a), 160.1 (C-2), 163.7 (C-5) ppm. HRMS: calcd. for $C_{11}H_{11}N_3O$ 201.09021; found 201.09003 [M^+].

3,10-Dimethyl-4-oxa-2,6-diazatetracyclo[5.4.2.0.^{1,5}0^{8,11}]trideca-2,5-diene-10,12-dicarbonitrile (8): Compound **1** (500 mg) in acetonitrile (100 mL) was mixed with methacrylonitrile (5 mL) and acrylonitrile (5 mL) and then irradiated for about 6 h with a low-pressure mercury lamp. N_2 was bubbled through the solution during irradiation. The brownish solution was then concentrated and the solid purified by chromatography on LOBAR Merck Si-60 with $CHCl_3$/MeOH (9:1) as eluent, using a refractive index detector. Fractions containing both **8** and the homolog derived from double addition of acrylonitrile[3] were obtained (230 mg, 25%). NMR spectroscopic data were obtained from a fraction enriched in **8**. ^{1}H NMR ($CDCl_3$): δ = 1.53 (s, 10-Me), 1.80 (ddd, $J_{13a\text{-}13b}$ = 12.5, $J_{13a\text{-}12}$ = 5.01, $J_{13\text{-}7}$ = 3.48 Hz, 13a-H), 2.00 (ddd, $J_{13b\text{-}13a}$ = 12.5, $J_{13b\text{-}12}$ = 9.96, $J_{13b\text{-}7}$ = 1.37 Hz, 13b-H), 2.01 (dd, $J_{9a\text{-}9b}$ = 13.26, $J_{9a\text{-}8}$ = 2.9 Hz, 9a-H), 2.36 (dd, $J_{9b\text{-}9a}$ = 13.26, $J_{9b\text{-}8}$ = 6.71 Hz, 9b-H), 2.61 (d, $J_{11\text{-}8}$ = 8.78 Hz, 11-H), 2.44 (s, 3-Me), 2.76 (dddd, $J_{11\text{-}8}$ = 8.78, $J_{8\text{-}9b}$ = 6.71, $J_{7\text{-}8}$ = 3.36, $J_{8\text{-}9a}$ = 2.9 Hz, 8-H), 3.07 (dd, $J_{12\text{-}13b}$ =9.96, $J_{12\text{-}13a}$ =5.01 Hz, 12-H), 4.45 (ddd, $J_{7\text{-}8}$ = 3.36, $J_{7\text{-}13a}$ = 3.48, $J_{7\text{-}13b}$ = 1.37 Hz, 7-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.9 (3-Me), 27.4 (10-Me), 28.6 (C-13), 30.0 (C-9), 31.4 (C-12), 33.2 (C-8), 45.9 C-11), 54.33 (C-7), 63.57 (C-10), 67.7 (C-1), 117.4 (CN), 120.0 (CN), 169.8 (C-3 or C-5), 174.1 (C-5 or C-3) ppm. HRMS: calcd. for $C_{14}H_{14}N_4O$ 254.1167; found 254.1162 [M^+].

Irradiation of 1 in the Presence of Vinyl Ether: 2-Methylisoxazolo[5,4-*b*]pyridine (**1**; 500 mg) in acetonitrile (100 mL) was mixed with vinyl ether (10 mL) and irradiated for about 6 h with a low-pressure mercury lamp. N_2 was bubbled through the solution during the irradiation. The solvent was then evaporated from the brownish solution and the solid purified by chromatography on silica gel, initially eluting with petroleum ether/diethyl ether (1:1) and then with diethyl ether and finally with methanol. Elution order: **12*E***, **12*Z***, **10**, **1** (150 mg), **9**, **11**, **13**.

9-Ethoxy-8,9-dihydro-2-methyloxazolo[5,4-*b*]azocine (9): Colourless oil (75 mg, 21%). ^{1}H NMR ($CDCl_3$): δ = 1.25 (t, J = 7.0 Hz, CH_2CH_3), 2.41 (dd, $J_{8a,b\text{-}7}$ =8.0, $J_{8a,b\text{-}9}$ = 6.0 Hz, 8a,b-H), 3.79 (m, OCH_2), 2.42 (s, 2-Me), 4.63 (t, $J_{9\text{-}8a,b}$ = 6.0 Hz, 9-H), 6.14 (dd, $J_{6\text{-}7}$ = 10.9, $J_{5\text{-}6}$ = 2.8 Hz, 6-H), 6.26 (dt, $J_{6\text{-}7}$ = 10.9, $J_{7\text{-}8a,b}$ = 8.0 Hz, 7-H), 7.99 (d, $J_{5\text{-}6}$ = 2.8 Hz, 5-H) ppm. MS (EI): *m*/*z* (%) = 206 (47) [M^+], 191 (61.7), 177 (74.5), 163 (43.6), 160 (100), 148 (94), 135 (81.9), 134 (86.7), 117 (76.5), 110 (88), 94 (55.7), 80 (63), 72 (75.2), 68 (49), 65 (53), 53 (71.8), 52 (43). HRMS: calcd. for $C_{11}H_{14}N_2O_2$ 206.1055; found 206.1061 [M^+].

(3-Ethoxyallylidene)(2-methyl-4-vinyloxazol-5-yl)amine (10): Pale yellow oil (7 mg, 2%). ^{1}H NMR ($CDCl_3$): δ = 1.36 (t, J = 7.0 Hz, $MeCH_2$), 2.40 (s, Me), 3.97 (q, J = 7.0 Hz, OCH_2), 5.24 (dd, $J_{5'a\text{-}5'b}$ = 1.9, $J_{5'a\text{-}4'}$ = 1.0 Hz, 5′a-H), 5.87 (dd, $J_{2'\text{-}3'}$ = 12.0, $J_{1'\text{-}2'}$ = 9.5 Hz, 2′-H), 5.90 (dd, $J_{5'a\text{-}5'b}$ = 1.9, $J_{5'b\text{-}4'}$ = 16.5 Hz, 5′b-H), 6.74 (dd, $J_{4'\text{-}5'a}$ = 1.0, $J_{4'\text{-}5'b}$ = 16.5 Hz, 4′-H), 8.07 (d, $J_{1'\text{-}2'}$ = 9.5 Hz, 1′-H), 7.10 (d, $J_{2'\text{-}3'}$ = 12.0 Hz, 3′-H) ppm.

7-Ethoxy-6,7-dihydro-2-methyloxazolo[5,4-*b*]azocine (11): Colourless oil (33 mg, 9%). ^{1}H NMR ($CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, *Me*CH_2) 2.68 (ddd, $J_{6a\text{-}6b}$ = 12.0, $J_{7\text{-}6a}$ = 8.6, $J_{6a\text{-}5}$ = 6.4 Hz, 6a-H), 2.45 (s, Me), 2.93 (ddd, $J_{6a\text{-}6b}$ = 12.0, $J_{6b\text{-}5}$ = 6.4, $J_{7\text{-}6b}$ = 2.0 Hz, 6b-H), 3.65 (m, *J* = 7.1 Hz, OCH_2), 4.26 (m, $J_{7\text{-}6a}$ = 8.6, $J_{7\text{-}8}$ = 3.5, $J_{7\text{-}6b}$ = 2.0, $J_{7\text{-}9}$ = 0.8 Hz, 7-H), 6.15 (dd, $J_{9\text{-}8}$ = 13.0, $J_{8\text{-}7}$ = 3.5 Hz, 8-H), 6.48 (dd, $J_{9\text{-}8}$ = 13.0, $J_{9\text{-}7}$ = 0.8 Hz, 9-H), 7.7 (t, $J_{5\text{-}6a,6b}$ = 6.4 Hz, 5-H) ppm. HRMS: calcd. for $C_{11}H_{14}N_2O_2$ 206.1055; found 206.1064 [M^+].

Ethyl *N*-[(1*Z*)-4-Buta-1,3-dienyl-2-methyloxazol-5-yl]formimidate (12*Z*): Pale yellow oil (9 mg, 3.5%). ^{1}H NMR ($CDCl_3$): δ = 1.34 (t, *J* = 7.1 Hz, *Me*CH_2), 2.38 (s, Me), 4.30 (q, *J* = 7.1 Hz, OCH_2), 5.25 (2 dd, $J_{4'a\text{-}4'b}$ = 1.5, $J_{3'\text{-}4'a}$ = 17.1, $J_{3'\text{-}4'b}$ = 9.5 Hz, 4′a-H and 4′b-H), 6.05 (dd, $J_{1'\text{-}2'}$ = 11.0, $J_{2'\text{-}3'}$ = 10.1 Hz, 2′-H), 6.10 (d, $J_{1'\text{-}2'}$ = 11.0 Hz, 1′-H), 7.75 (dt, $J_{3'\text{-}2'}$ = 10.1, $J_{3'\text{-}4'a}$ =17.1, $J_{3'\text{-}4'b}$ =9.5 Hz, 3′-H), 8.05 (s, 5′-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.06 (Me), 14.21 (Me), 62.93 (OCH_2), 116.79 (C-4′), 118.33 (C-3′), 128.88 (C-2′), 129.21 (C-5), 134.00 (C-1′), 147.43 (C-4), 154.47 (C-5′), 155.66 (C-2) ppm. MS (EI): *m*/*z* (%) = 206 (22.5) [M^+], 149 (100), 134 (24), 106 (13.6), 99 (16.4), 91 (13), 77 (12.2), 71 (11.9), 65 (10.6), 57 (37.9), 55 (12.3). HRMS: calcd. for $C_{11}H_{14}N_2O_2$ 206.1055; found 206.1060 [M^+].

Ethyl *N*-[(1*E*)-4-Buta-1,3-dienyl-2-methyloxazol-5-yl]formimidate (12*E*): Pale yellow oil (58 mg, 16%). ^{1}H NMR ($CDCl_3$): δ = 1.37 (t, *J* = 7.3 Hz, *Me*CH_2), 2.38 (s, Me), 4.35 (q, *J* = 7.3 Hz, OCH_2), 5.10 (dd, $J_{3'\text{-}4'a}$ = 11.0, $J_{4'a\text{-}4'b}$ = 1.7 Hz, 4′a-H), 5.28 (dd, $J_{4'b\text{-}3'}$ = 16.0, $J_{4'b\text{-}4'a}$ = 1.7 Hz, 4′b-H), 6.45 (d, $J_{1'\text{-}2'}$ = 14.4 Hz, 1′-H), 6.46 (dt, $J_{3'\text{-}4'b}$ = 16.0, $J_{3'\text{-}4'a}$ = 11.0, $J_{3'\text{-}2'}$ = 10.3 Hz, 3′-H), 6.87 (dd, $J_{1'\text{-}2'}$ = 14.4, $J_{2'\text{-}3'}$ = 10.3 Hz, 2′-H), 8.06 (s, 5′-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.06 (Me), 14.13 (Me), 62.94 (OCH_2), 117.02 (C-4′), 120.67 (C-3′), 125.75 (C-4) 129.38 (C-2′), 137.09 (C-1′), 146.27 (C-5), 154.40 (C-5′), 156.24 (C-2) ppm. MS (EI): *m*/*z* (%) = 206 (86.3) [M^+], 149 (73), 132 (10.4), 105 (16.6), 99 (100), 93 (15.5), 92 (17.6), 81 (15.2), 79 (13.4), 72 (12.8), 70 (43.1), 65 (27.8), 53 (51.8), 52 (21.1), 51 (11.7). HRMS: calcd. for $C_{11}H_{14}N_2O_2$ 206.1055; found 206.1059 [M^+].

1-Acetyl-2,3-dihydro-1*H*-pyrrolo[3,2-*b*]pyridin-2-ol (13): White solid (83 mg, 23%); m.p. 139−140 °C. ^{1}H NMR ($CDCl_3$): δ = 2.42 (s, Me), 3.11 (d, $J_{3a\text{-}3b}$ = 17.9 Hz, 3a-H), 3.52 (dd, $J_{3a\text{-}3b}$ = 17.9, $J_{3b\text{-}2}$ = 7.3 Hz, 3-H), 5.82 (d, *J* = 7.3 Hz, 2-H), 7.0 (dd, $J_{5\text{-}6}$ = 8.3, $J_{6\text{-}7}$ = 5.3 Hz, 6-H), 7.93 (d, $J_{6\text{-}7}$ = 5.3 Hz, 7-H), 8.20 (d, $J_{5\text{-}6}$ = 8.3 Hz, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.9 (Me), 40.4 (C-3), 82.3 (C-2), 122.3 (C-6 or C-7), 123.1 (C-7 or C-6), 136.1 (C-7a), 143.7 (C-5), 150.1 (C-3a), 171.0 (CO) ppm. MS (EI): *m*/*z* (%) = 178 (49.7) [M^+], 50 (12.4), 136 (69.1), 119 (37.2), 108 (100.0), 91 (10.1), 85 (24.2), 83 (36.9), 80 (18.8), 65 (10.7). HRMS: calcd. for $C_9H_{10}N_2O_2$ 178.07423; found 178.07427 [M^+].

4-Ethoxy-4,5-dihydro-2-methylpyrido[3,2-*d*][1,3]oxazepine (13′): ^{1}H NMR and ^{13}C NMR spectra were recorded of the crude reaction mixture in $CDCl_3$. This $CDCl_3$ solution was then eluted on a silica gel bed, and new spectra were recorded. The following spectroscopic data for **13′** were obtained by comparison.^{1}H NMR ($CDCl_3$): δ = 1.18 (t, *J* = 7.2 Hz, CH_2*Me*), 2.27 (s, N=C*Me*), 3.31 (m, $J_{5a\text{-}5b}$ = 16.4, $J_{4\text{-}5a}$ = 6.5, $J_{4\text{-}5b}$ = 2.5 Hz, 5a-H and 5b-H), 3.64 (dq, ^2J = 9.7, ^3J = 7.2 Hz, OC*H*H), 3.86 (dq, ^2J = 9.7, ^3J = 7.2 Hz, OC*H*H), 5.43 (dd, $J_{4\text{-}5}$ = 6.5, $J_{4\text{-}5'}$ = 2.5 Hz, 4-H), 7.18 (dd, $J_{8\text{-}9}$ = 8.1, $J_{7\text{-}8}$ = 4.6 Hz, 8-H), 7.44 (dd, $J_{7\text{-}9}$ = 1.4, $J_{8\text{-}9}$ = 8.1 Hz, 9-H), 8.26 (dd, $J_{7\text{-}9}$ = 1.4, $J_{7\text{-}8}$ = 4.6 Hz, 7-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.4 (2-Me), 24.2 (C-5), 42.8 (OCH_2), 104.4 (C-4), 122.2 (C-8 or C-9), 133.1 (C-9 or C-8), 144.7 (C-7), 139.5 (C-5a or C-9a), 148.2 (C-9a or C-5a), 155.9 (C-2) ppm.

Irradiation of 1 in the Presence of Furan: 2-Methylisoxazolo[5,4-*b*]pyridine (**1**; 500 mg) in acetonitrile (100 mL) was mixed with furan (10 mL) and irradiated for about 3 h with a low-pressure mercury lamp. N_2 was bubbled through the solution during the irradiation. The solvent was then evaporated from the brownish solution and the remaining solid purified by chromatography on silica gel, with diethyl ether, obtaining 210 mg of **1**. Subsequent elution with $CHCl_3$/MeOH (95:5) gave **14**.

***N*-(2-Furan-3-ylpyridin-3-yl)acetamide (14):** White solid (110 mg, 28%), m.p. 145−147 °C (from EtOH). ^{1}H NMR ($CDCl_3$): δ = 2.15 (s, Me), 6.78 (br. s, 2′-H), 7.19 (dd, $J_{4\text{-}5}$ = 8.2, $J_{5\text{-}6}$ = 4.8 Hz, 5-H), 7.54 (br. s, 4′-H and NH), 7.81 (br. s, 5′-H), 8.38 (br. m, 4-H and 6-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.4, 110.4, 122.4, 123.4, 130.1, 131.6, 141.4, 142.7, 143.9, 145.5, 168.7 ppm. HRMS: calcd. for $C_{11}H_{10}N_2O_2$ 202.0742; found 202.0737 [M^+].

X-ray Crystal Structure Determinations of 6*Z* and 14: Single crystals of **6*Z*** and **14** were obtained by slow concentration of ethanolic solutions. The cell parameters and intensities were measured with a Siemens P4 four-circle diffractometer with graphite-monochromated Mo-K_α radiation (λ = 0.71069 Å). The intensities were corrected for Lorentz and polarization effects; no absorption correction was applied. The structures were solved by using direct methods (SHELX-97);[7] the hydrogen atoms were localized in the Fourier maps and included in the structure factor calculations. Refinement against all F^2 data was performed with SHELX-97.[7] CCDC-177333 (**6*Z***) and -177334 (**14**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Data for 6*Z*: $C_{11}H_{11}N_2O$, monoclinic, space group *Cc*, *a* = 11.747(2), *b* = 11.409(2), *c* = 9.330(2) Å, β = 120.10(1)°, *V* = 1081.8(4) Å^3, *Z* = 4, $D_{calcd.}$ = 1.236 Mg/m^3, μ(Mo-K_α) = 0.083 mm^{-1}. Total reflections 3424, unique reflections (R_{int} = 0.0305) 1578. Final refinement of 178 parameters gave *R* = 0.0541 for 2022 reflections with $I > 2\sigma(I)$ and *R* = 0.0945, w$R(F^2)$ = 0.1231 for all 3424 data (Friedel pairs not merged).

Data for 14: $C_{11}H_{10}N_2O_2$, monoclinic, space group $P2_1/c$, *a* = 4.836(1), *b* = 14.963(2), *c* = 13.460(1), β = 94.00(1)°, *V* = 971.6(2) Å^3, *Z* = 4, $D_{calcd.}$ = 1.382 Mg/m^3, μ(Mo-K_α) = 0.098 mm^{-1}. Reflections measured 5112, unique reflections (R_{int} = 0.0298) 2212, used in all calculations. Final refinement of 176 parameters gave *R* = 0.0470 for 1548 reflections with $I > 2\sigma(I)$. *R* = 0.0763 and w$R(F^2)$ = 0.1346 for all 2212 data.

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[1] D. Donati, F. Ponticelli, P. Bicchi, M. Meucci, *J. Phys. Chem.* **1990**, *94*, 5271−74.
[2] D. Donati, S. Fusi, F. Ponticelli, P. Tedeschi, *Heterocycles* **1988**, *27*, 1899−905.
[3] D. Donati, S. Fusi, F. Ponticelli, *Tetrahedron Lett.* **1996**, *37*, 5783−86.
[4] A. P. Evans, A. B. Holmes, *Tethrahedron* **1991**, *47*, 9131; *Compr. Heterocycl. Chem. II*, vol. 9 (Ed.: G. R. Newkome), Elsevier, Oxford, **1996**, pp. 403−428, 1039−1146.
[5] Anions derived from an attack of H^- at different positions

of **1** were used as simplified models in AM1 calculations. The following heats of formation [kcal/mol] were obtained: **3a**: 9.75; **5**: 7.56; **6**: 16.52; **7**: 2.75; **7a**: 20.88. The AM1 calculations were performed with the MOPAC package implemented in CS Chem3D Ultra (version 6.0) from CambridgeSoft, 100 Cambridge Park Dr., Cambridge MA 02140-2317, U.S.A.

[6] C. Kaneko, S. Yamada, I. Yokoe, *Tetrahedron Lett.* **1996**, *39*, 4701−705.
[7] G. M. Sheldrick, *SHELXL-97, Program for the refinement of crystal structures*, University of Göttingen, Germany, **1997**.

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