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Three-component condensation of iminoazolidines with aldehydes and 5-aminopyrazole

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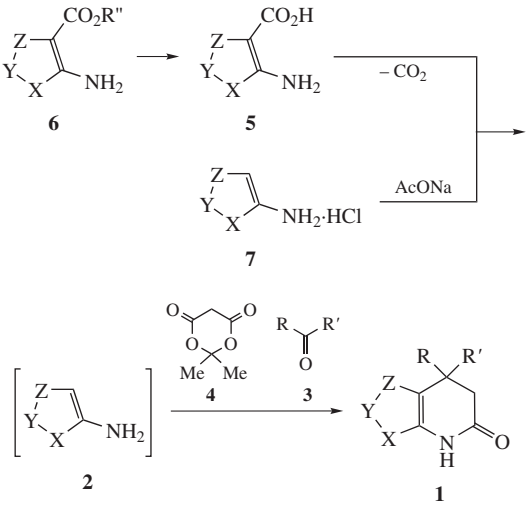
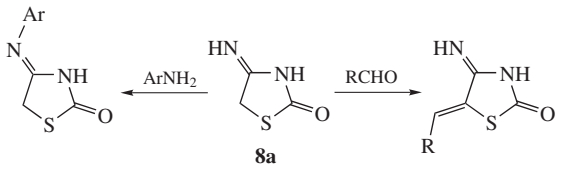
A three-component condensation of 4-iminothiazolidin-2-ones or 4-iminoimidazolidin-2-ones with aldehydes and 5-aminopyrazole affords the corresponding 1,7-dihydro-6*H*-pyrazolo[3,4-*b*][1,3]thiazolo[5,4-*e*]pyridin-6-one or 5,7-dihydroimidazo[4,5-*b*]pyrazolo-[4,3-*e*]pyridin-6(1*H*)-one derivatives.

Previously we have developed a general method for synthesizing fused heterocyclic systems **1** (X, Y, Z are C, N, S or Se-based fragments)[1–9] comprising a dihydropyridin-2-one moiety by condensation of labile heterocyclic amines **2** with carbonyl compounds **3** and Meldrum's acid **4** (Scheme 1). Unstable amino heterocycles **2** were generated *in situ* from vicinal amino acids **5** (available by alkaline hydrolysis of esters **6**) or from the related stable hydrochlorides **7**.



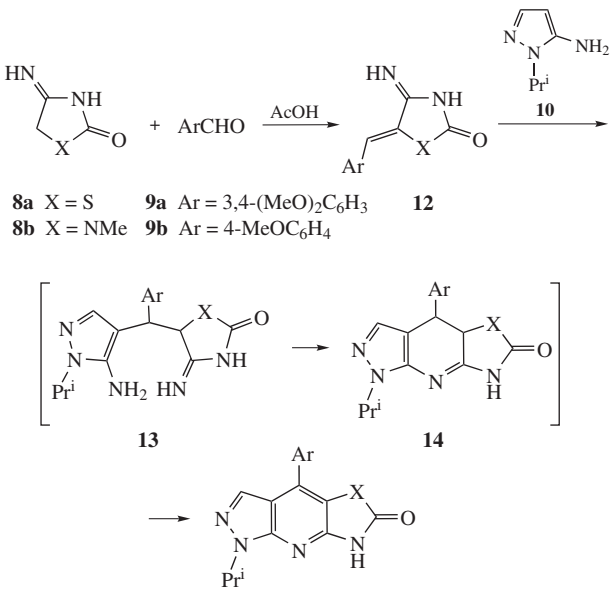
Scheme 1

According to Scheme 1, Meldrum's acid plays the role of a C(2)-synthon incorporating both nucleophilic and electrophilic centres. It seemed reasonable to extend this approach to other compounds of similar reaction centre topology as in Meldrum's acid. Indeed, structures like **8a** (Scheme 2) can be of interest since they incorporate an electrophilic imino carbon atom (known to be reactive towards anilines[10]) as well as a nucleophilic activated methylene unit (known to be reactive towards aldehydes[10]).



Scheme 2

In fact, the reaction of 4-iminoazolidinone derivatives **8** with aldehydes **9** and 5-aminopyrazole **10** in acetic acid afforded previously unknown fused heterocyclic systems **11** containing an azolone moiety (Scheme 3).



Scheme 3

Presumably, the reaction of aldehyde **9** and imine **8** originally gives iminoazolidinone arylmethylidene derivative **12**, which then undergoes a Michael reaction with 5-aminopyrazole **10** to form intermediate product **13**. Intramolecular cyclization of the latter with abstraction of an ammonia molecule results in dihydro derivative **14**. After that, oxidative aromatization of the dihydropyridine ring with atmospheric oxygen occurs to afford the target product **11** (Scheme 3).

Structure of solid crystalline compounds **11a**,**b** was confirmed by elemental analysis, ^{1}H and ^{13}C NMR spectroscopy and mass

Table 1 Absorption and fluorescence characteristics of compounds **11a**,**b** in toluene.[a]

Compound	λ_{max}/ nm	ε/ dm^3 mol^{-1} cm^{-1}	$\lambda^{flu.max}$/ nm	$I^{flu.max}$ (arb. units)	$I^{*flu.max}$ (arb. units)
11a	335	10000	387	715	715
11b	335	5000	398	1245	1245

[a] λ_{max} is the wavelengths of the absorption band maximum, $\lambda^{flu.max}$ is the wavelength of the fluorescence band, $I^{flu.max}$ is the fluorescence intensity at the maximum of the fluorescence band, $I^{*flu.max}$ is the fluorescence intensity at the maximum of the fluorescence band after UV irradiation at the photobalance state.

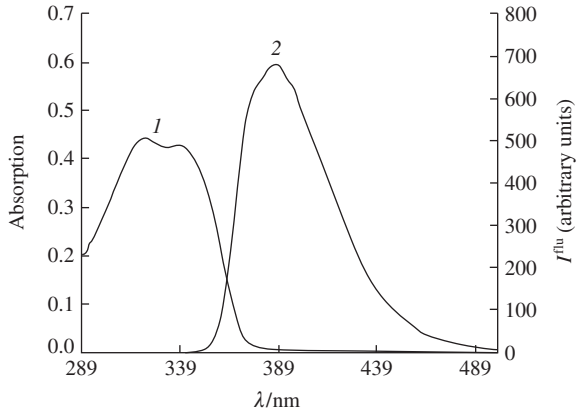


Figure 1 (*1*) Absorption and (*2*) fluorescence spectra for compound **11a** in toluene. Fluorescence is recorded during excitation by light with a wavelength of 335 nm.

spectrometry.† It is important to note that the products obtained have intense fluorescence (for their absorption and fluorescence spectra, see Table 1 and Figure 1).

It follows from Figure 1 that the fluorescence band maximum for fluorophore **11a** settles down at 387 nm and the Stokes shift is about 50 nm. The fluorescence intensity of solution does not change under UV irradiation (Table 1).

Thus, three-component condensation of 4-iminoazolidinones, aldehydes and 5-aminopyrazoles is a convenient method for synthesizing new polycyclic systems containing an azolone moiety and possessing fluorescence.

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† ^{1}H NMR spectra were recorded on a Bruker AM-300 (300 MHz) instrument in [$^2H_6$]DMSO. Melting points were measured on a Boetius hot stage and not corrected. Mass spectra were determined on FINNIGAN MAT INCOS 50 (direct injection, electronic impact, 70 eV).

The starting iminoazolidinones **8**[10,11] and aminopyrazole **10**[12] were synthesized using the procedures described in literature.

*1-Isopropyl-4-(3,4-dimethoxyphenyl)-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]-[1,3]thiazolo[5,4-*e*]pyridin-6-one* **11a**. A mixture of 2-isopropyl-2*H*-pyrazol-3-ylamine **10** (0.41 g, 3.3 mmol), 3,4-dimethoxybenzaldehyde (0.55 g, 3.3 mmol) and 4-iminothiazolidin-2-one **8a** (0.35 g, 3 mmol) in acetic acid (20 ml) was refluxed for 20 h, then the solvent was evaporated *in vacuo* and the residue was recrystallized from a minimum amount of acetic acid (3 ml). Yield 57%, mp 231–233 °C. ^{1}H NMR (DMSO-d_6) δ: 1.51 (d, 6H, 2Me, *J* 6.6 Hz), 3.86 (s, 6H, 2OMe), 5.08 (q, 1H, CH_{Pr^i}, *J* 6.6 Hz), 7.19 (d, 1H, Ar, *J* 7.9 Hz), 7.29 (s, 1H, Ar), 7.32 (d, 1H, Ar, *J* 7.9 Hz), 8.12 (s, 1H, CH_{Pyr}), 12.77 (br. s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ: 21.8, 48.1, 55.1, 55.6, 110.7, 110.9, 11.5, 112.3, 120.8, 123.4, 127.1, 130.9, 137.2, 147.4, 149.2, 150.1, 169.1. EI MS, *m*/*z*: 370 (100) [M]$^+$, 355 (33). Found (%): C, 58.51, H, 4.98, N, 15.24. Calc. for $C_{18}H_{18}N_4O_3S$ (%): C, 58.36; H, 4.90; N, 15.12.

*1-Isopropyl-4-(4-methoxyphenyl)-5-methyl-5,7-dihydroimidazo[4,5-*b*]-pyrazolo[4,3-*e*]pyridin-6(1*H*)-one* **11b**. A mixture of 2-isopropyl-2*H*-pyrazol-3-ylamine **10** (0.41 g, 3.3 mmol), 4-methoxybenzaldehyde (0.45 g, 3.3 mmol) and 4-imino-1-methylimidazolin-2-one **8b** (0.34 g, 3 mmol) in acetic acid (7 ml) was refluxed for 20 h, then the solvent was evaporated *in vacuo* and the residue was recrystallized from ethanol. Yield 51%, mp > 250 °C. ^{1}H NMR (DMSO-d_6) δ: 1.51 (d, 6H, 2Me, *J* 7.1 Hz), 2.91 (s, 3H, NMe), 3.86 (s, 3H, OMe), 5.08 (q, 1H, CH_{Pr^i}, *J* 7.1 Hz), 7.12 (d, 2H, Ar, *J* 8.5 Hz), 7.52 (d, 2H, Ar, *J* 8.5 Hz), 7.63 (s, 1H, CH_{Pyr}), 11.91 (br. s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ: 21.9, 29.3, 47.9, 55.2, 111.8, 121.7, 124.9, 130.2, 131.0, 144.4, 145.3, 154.8, 159.5. EI MS, *m*/*z*: 337 (100) [M]$^+$, 324 (22), 323 (32). Found (%): C, 64.22, H, 5.78, N, 20.61. Calc. for $C_{18}H_{19}N_5O_2$ (%): C, 64.08; H, 5.68; N, 20.76.