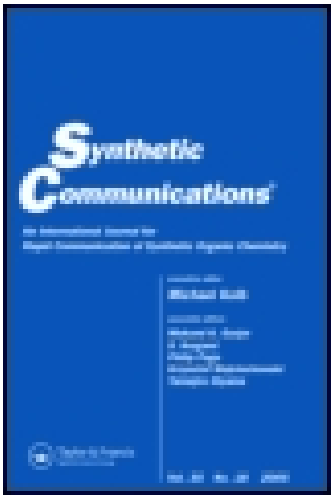

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Expedient Strategy for the Synthesis of 5-Acylethynylpyrrole-2-carbaldehydes

Denis N. Tomilin[a], Lyubov N. Sobenina[a], Marina V. Markova[a], Maxim D. Gotsko[a], Igor A. Ushakov[a], Vladimir I. Smirnov[a], Alexander V. Vaschenko[a], Albina I. Mikhaleva[a] & Boris A. Trofimov[a]

[a] A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences, Irkutsk, Russian Federation

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EXPEDIENT STRATEGY FOR THE SYNTHESIS OF 5-ACYLETHYNYLPYRROLE-2-CARBALDEHYDES

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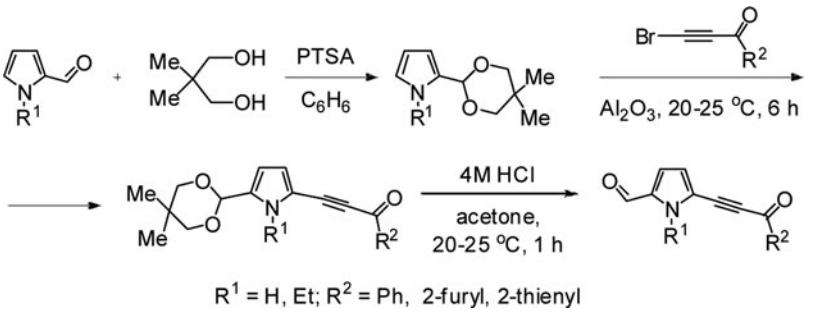
A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences, Irkutsk, Russian Federation

GRAPHICAL ABSTRACT



Abstract *5-Acylethynylpyrrole-2-carbaldehydes have been synthesized from the protected pyrrole-2-carbaldehydes by their transition-metal-free topochemical mechanoactivated ethynylation with acylbromoacetylenes in a solid Al_2O_3 medium (room temperature, 6 h, 41–54% yields).*

Keywords Acylbromoacetylenes; Al_2O_3; ethynylation; 5-ethynylpyrrole-2-carbaldehydes; pyrrole-2-carbaldehydes

INTRODUCTION

The pyrrole ring is a key structural motif of many biologically important natural compounds such as chlorophyll, hemoglobin, vitamin B_{12}, alkaloids, and antibiotics involved in the bioconversion of solar energy, oxygen transfer processes,

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Address correspondence to Boris A. Trofimov, A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences, 1 Favorsky Str., 664033 Irkutsk, Russian Federation. E-mail: boris_trofimov@irioch.irk.ru

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and other life-supporting reactions.[1] Among representatives of the pyrrole series, ethynyl derivatives occupy an important place. Because of the presence of such highly reactive counterparts as the pyrrole ring and the carbon-carbon triple bond in one molecule, these compounds can be divergently used for the synthesis of various functionalized heterocyclic systems as well as conjugated and fused pyrrolic ensembles.[2] Ethynylpyrroles additionally functionalized with the aldehyde group are of even greater biological and synthetic interest. The ethynylpyrrolecarbaldehydes have been employed as precursors for the synthesis of polyfunctional derivatives of pyrrole and indole.[3] They are also used in a design of macrocycles, closely related to natural ones, which possess important biological properties.[4]

In this regard, the search for efficient and facile approaches to preparation of ethynylpyrrolecarbaldehydes represents a timely synthetic task.

Currently, ethynylpyrrolecarbaldehydes are obtained by cross-coupling of hardly available and unstable halopyrrolecarbaldehydes with terminal acetylenes[3d–f,4] (Sonogashira reaction) or their organometallic derivatives[5] in the presence of palladium catalysts. However, the ethynylpyrrolecarbaldehydes containing electron-acceptor functions in the acetylene substituent remain almost unknown. This approach for electron-deficient functionalized acetylenes was stated to be of poor efficiency.[6] Meanwhile, ethynylpyrrolecarbaldehydes with electron-withdrawing functions in acetylene substitutents are desirable building blocks for the preparation of polyfunctional stable organic radicals and polyradicals, which attract intense interest as paramagnetic organic components for the design of molecule-based magnets.[7]

The goal of this article is to elaborate an expedient strategy for the synthesis of 5-acylethynylpyrrole-2-carbaldehydes. For this, we have further developed the transition-metal-free topochemical mechanoactivated ethynylation of the pyrrole ring in a solid Al_2O_3 medium[8] and applied this reaction to pyrrole-2-carbaldehydes.

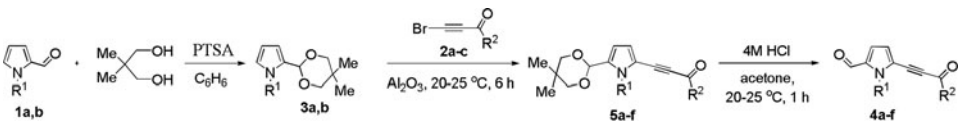
However, under usual conditions of such ethynylation (room temperature, 1 h), pyrrole-2-carbaldehydes **1a,b** prove to be incapable of reacting with acylbromoacetylenes **2a–c**, likely due to the strong electron-withdrawing effect of the aldehyde group, which decreases the pyrrole ring nucleophilicity. After a few unsuccessful attempts, we have managed to circumvent this fundamental hurdle by the acetal protection of the aldehyde function, thus decreasing its electron-withdrawing power. Our preliminary single-example testing[9] of whether protected (as 2-(5,5-dimethyl-1,3-dioxan-2-yl)-1*H*-pyrroles **3a,b**) pyrroles can be ethynylated by acylbromoacetylenes in a solid Al_2O_3 medium under topochemical mechanoactivation appeared to be positive and hence this strategy could be further developed to a general one.

Here we report a newly developed expedient strategy for the synthesis of 5-acylethynylpyrrole-2-carbaldehydes **4a–f** using the acetal protection.

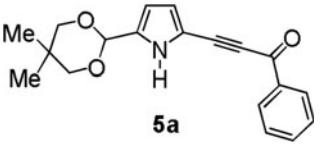
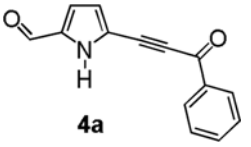
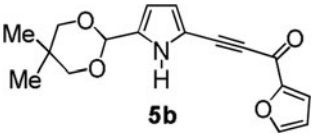
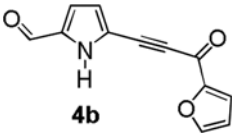
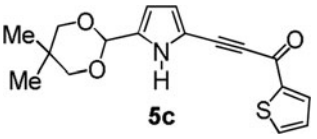
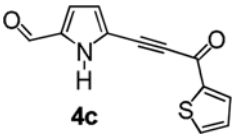
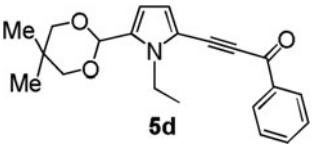
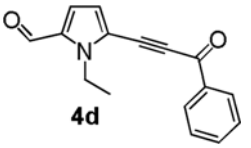
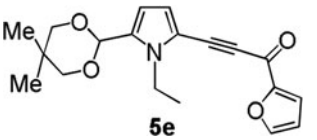
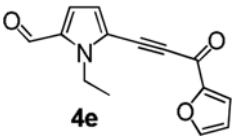
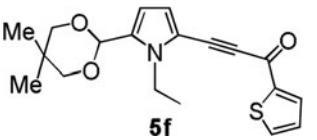
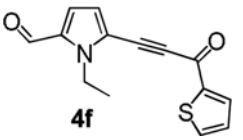
RESULTS AND DISCUSSION

Realization of the strategy starts from the reaction of pyrrole-2-carbaldehydes **1a,b** with 2,2-dimethylpropanediol in the presence of *para*-toluene sulfonic acid (PTSA) to give the corresponding cyclic acetals **3a,b**. The latter are subjected to topochemical mechanoactivated reaction with acylbromoacetylenes **2a–c** in the alumina medium without solvent, which leads to the expected ethynylated pyrroles **5a–f** with protected aldehyde function (Table 1). The deprotection has been implemented upon

Table 1. Cross-coupling of pyrroles **1a,b** with acylbromoacetylenes **2a–c** with subsequent deprotection of acetal **5a–f**



R^1 = H (**1a, 3a**), Et (**1b, 3b**); R^2 = Ph (**2a**), 2-furyl (**2b**), 2-thienyl (**2c**).

Ethynylpyrroles **5a–f**	Yield (%)	Ethynylpyrroles **4a–f**	Yield (%)
 **5a**	54	 **4a**	77
 **5b**	41	 **4b**	87
 **5c**	43	 **4c**	75
 **5d**	54	 **4d**	84
 **5e**	50	 **4e**	81
 **5f**	41	 **4f**	89

stirring of acetals **5a–f** in aqueous acetone at room temperature in the presence of HCl, thus releasing the targeted ethynylated pyrrolecarbaldehydes **4a–f** in 75–89% total yields. Their general structure was proved by X-ray crystallographic analysis of exemplar compound **4b** (Fig. 1).

The key step of this strategy, the cross coupling of acetals **3a,b** with acylbromoacetylenes **2a–c**, proceeds smoothly at room temperature for about 6 h on grinding the reactants with Al_2O_3 powder. The synthesis is carried out in air and does not require

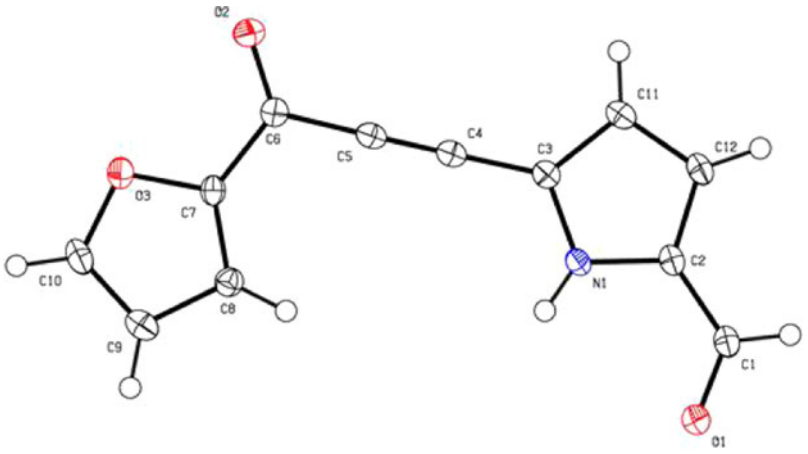
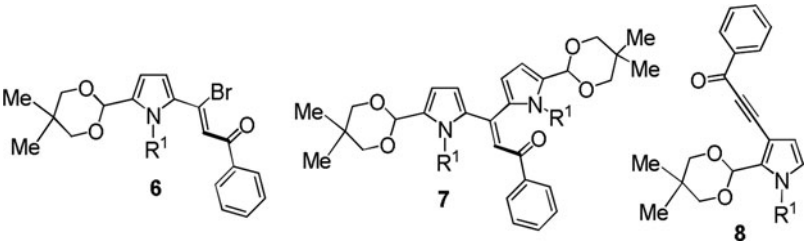


Figure 1. X-ray structure of 5-(3-(furan-2-yl)-3-oxoprop-1-ynyl)-1*H*-pyrrole-2-carbaldehyde (**4b**). Thermal ellipsoids set at 50% probability.



Scheme 1. Possible side products **6–8**.

argon protection. Conversion of reactants **2** and **3** and the extent of ethynylation product **5** formation were monitored by ^{1}H NMR spectroscopic analysis of the $CDCl_3$ extracts from the reaction mixture. Products **4a–f** were isolated and purified chromatographically. The solid reaction mixture was placed on the top of an Al_2O_3-packed column and successively eluted with *n*-hexane and diethyl ether.

The reaction is chemo- and regioselective. The anticipated intermediates,[8b] 2-(1-bromo-2-acylethenyl)pyrroles **6**, and side products **7** as well as 3-ethynylated pyrroles **8** are not detected in the reaction mixtures (Scheme 1).

In some case, insignificant deprotection (5–6%) of both pyrroleacetals **3a,b** and ethynylated products **5a–f** occurs. This can be spotted during the ethynylation and upon chromatographical isolation. In the example of acetal **3a**, it was shown that instead of Al_2O_3, solid K_2CO_3 can also be applied as an active surface, though the yield of the target product was 20% less than that obtained with alumina.

CONCLUSION

In conclusion, an expedient transition-metal-free strategy for the synthesis of inaccessible functionalized pyrroles with reactive substituents, 5-acylethynylpyrrole-2-carbaldehydes, has been elaborated. The key step of the strategy is topochemical

mechanoactivated ethynylation of acetal-protected pyrrole-2-carbaldehydes with acylbromoacetylenes in a solid Al_2O_3 medium. The synthesized compounds represent novel building blocks for the preparation of stable organic radicals and polyradicals, paramagnetic organic components for the design of molecule-based magnets, and a variety of pyrrolic systems.

EXPERIMENTAL

IR spectra were obtained with a Bruker Vertex 70 spectrometer (400–4000 cm^{-1}, KBr pellets). ^1H (400.1 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded with a Bruker DPX-400 instrument. Elemental analyses were recorded with an EA FLASH 1112 series (CHNS Analyzer) instrument. The determination of the unit cell and the data collection for 5-(3-(furan-2-yl)-3-oxoprop-1-ynyl)-1*H*-pyrrole-2-carbaldehyde (**4b**) was performed on a Bruker D8 Venture Photon 100 CMOS diffractometer with MoK_α radiation ($\lambda = 0.71073$) at 100(2) K using the ω–2θ scan technique. A specimen of $C_{12}H_7N_1O_3$, approximate dimensions $0.118 \times 0.145 \times 0.282$ mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The integration of the data using a monoclinic unit cell with $P2_1/n$ space group yielded a total of 38567 reflections to a maximum θ angle of 30.09° (0.71 Å resolution), of which 2894 were independent (average redundancy 13.327, completeness = 99.9%, $R_{int} = 7.06\%$, $R_{sig} = 3.47\%$) and 2162 (74.71%) were greater than $2\sigma(F^2)$. The final cell constants of $\underline{a} = 6.4543(3)$ Å, $\underline{b} = 13.5519(7)$ Å, $\underline{c} = 11.5474(5)$ Å, $\beta = 101.922(2)°$, and volume = 988.24(8) $Å^3$ are based upon the refinement of the XYZ-centroids of 9923 reflections above 20 σ(I) with $4.693° < 2\theta < 59.68°$. Data were corrected for absorption effects using the multiscan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.905. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9710 and 0.9880. The structure was solved and refined using the Bruker SHELXTL software package.[10]

Pyrrole-2-carbaldehydes **1a,b** are commercial products (Aldrich).

2-(5,5-Dimethyl-1,3-dioxan-2-yl)-1*H*-pyrroles **3a,b** were obtained according to the procedure reported earlier.[11] Acylbromoacetylenes **2a–c** were obtained by bromination[12] of acylacetylenes synthesized by the method.[13]

Synthesis of Ethynylpyrroles 5a–f: General Procedure

Acetal **3a,b** (1.821 mmol) and acylbromoacetylene **2a–c** (1.821 mmol) were carefully ground together with alumina (10-fold amount by weight) for 5 min and allowed to stay at rt for 6 h. Then the solid reaction mixture was placed on the top of an Al_2O_3-packed column and successively eluted with *n*-hexane and systems of *n*-hexane with diethyl ether (hexane/diethyl ether with gradient from 3:1, 1:1, 1:3) to afford ethynylpyrroles **5a–f**.

3-[5-(5,5-Dimethyl-1,3-dioxan-2-yl)-1*H*-pyrrol-2-yl]-1-phenylprop-2-yn-1-one (5a)

Yield: 304 mg (54%); grey needles; mp 141–143 °C. Anal. calcd. for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53%. Found: C, 73.48; H, 6.16; N, 4.51. IR (KBr): 3314 (NH),

2174 (C≡C), 1625 (CO) cm^{-1}. ^1H NMR (400.1 MHz, $CDCl_3$): δ = 9.09 (1H, br. s, NH), 8.18–8.16 (2H, m, H*o* Ph), 7.63–7.59 (1H, m, H*p* Ph), 7.52–7.48 (2H, m, H*m* Ph), 6.82 (1H, dd, *J* = 2.7, 3.4 Hz, H-3), 6.29 (1H, dd, *J* = 2.9, 3.4 Hz, H-4), 5.50 (1H, s, O-CH-O), 3.76 (2H, d, *J* = 11.2 Hz, CH_2), 3.64 (2H, d, *J* = 11.2 Hz, CH_2), 1.26 (3H, s, Me), 0.81 (3H, s, Me). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 177.7 (C=O), 137.0 (C*i*), 134.6 (C-5), 134.0 (C*p*), 129.5 (C*o*), 128.7 (C*m*), 121.1 (C-3), 109.8 (C-2), 108.5 (C-4), 96.1 (O-CH-O), 91.9 (≡C), 88.1 (C≡), 77.5 (CH_2-O), 30.5 ($Me_2\underline{C}$), 23.1 (Me), 22.0 (Me).

3-[5-(5,5-Dimethyl-1,3-dioxan-2-yl)-1*H*-pyrrol-2-yl]-1-(furan-2-yl) prop-2-yn-1-one (5b)

Yield: 223 mg (41%); yellow crystals; mp 142–146 °C. Anal. calcd. for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68%. Found: C, 68.48; H, 5.56; N, 4.61. IR (KBr): 3206 (NH), 2174 (C≡C), 1612 (CO) cm^{-1}. ^1H NMR (400.1 MHz, C_6D_6): δ = 8.72 (1H, br. s, NH), 7.05 (1H, dd, *J* = 0.7, 3.5 Hz, H-5 furan), 6.90 (1H, dd, *J* = 0.7, 1.7 Hz, H-3 furan), 6.66 (1H, dd, *J* = 1.6, 3.6 Hz, H-3), 6.29 (1H, dd, *J* = 1.7, 3.5 Hz, 1H, H-4 furan), 5.83 (1H, dd, *J* = 1.6, 3.6 Hz, H-4), 5.09 (1H, s, O-CH-O), 3.39 (2H, d, *J* = 10.8 Hz, CH_2), 3.15 (2H, d, *J* = 10.8 Hz, CH_2), 1.05 (3H, s, Me), 0.33 (3H, s, Me). ^{13}C NMR (100.6 MHz, C_6D_6): δ = 164.5 (C=O), 153.9 (C-2 furan), 147.0 (C-5 furan), 135.1 (C-5), 120.8 (C-3 furan), 118.9 (C-3), 112.4 (C-4 furan), 110.0 (C-2), 108.5 (C-4), 96.3 (O-CH-O), 91.7 (≡C), 86.8 (C≡), 77.0 (CH_2-O), 30.1 ($Me_2\underline{C}$), 23.0 (Me), 21.6 (Me).

3-[5-(5,5-Dimethyl-1,3-dioxan-2-yl)-1*H*-pyrrol-2-yl]-1-(thiophen-2-yl) prop-2-yn-1-one (5c)

Yield: 247 mg (43%); yellow crystals; mp 141–143 °C. Anal. calcd. for $C_{17}H_{17}NO_3S$: C, 64.74; H, 5.43; N, 4.44; S, 10.17%. Found: C, 64.58; H, 5.66; N, 4.21; S, 10.01. IR (KBr): 3314 (NH), 2175 (C≡C), 1605 (CO) cm^{-1}. ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.97 (1H, br. s, NH), 7.94 (1H, dd, *J* = 1.2, 3.8 Hz, H-3 thiophene), 7.70 (1H, dd, *J* = 1.2, 4.9 Hz, H-5 thiophene), 7.18 (1H, dd, *J* = 3.8, 4.9 Hz, 1H, H-4 thiophene), 6.79 (1H, dd, *J* = 2.4, 3.8 Hz, H-4), 6.28 (1H, dd, *J* = 2.4, 3.8 Hz, H-3), 5.49 (1H, s, O-CH-O), 3.75 (2H, d, *J* = 10.8 Hz, CH_2), 3.63 (2H, d, *J* = 10.8 Hz, CH_2), 1.26 (3H, s, Me), 0.81 (3H, s, Me). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.6 (C=O), 144.0 (C-2 thiophene), 133.8 (C-5 thiophene), 133.7 (C-3 thiophene), 133.6 (C-5), 127.4 (C-4 thiophene), 120.0 (C-3), 108.7 (C-2), 107.4 (C-4), 95.0 (O-CH-O), 90.2 (≡C), 86.0 (C≡), 76.5 (CH_2-O), 29.5 ($Me_2\underline{C}$), 22.1 (Me), 21.0 (Me).

3-[5-(5,5-Dimethyl-1,3-dioxan-2-yl)-1-ethyl-1*H*-pyrrol-2-yl]-1-phenylprop-2-yn-1-one (5d)

Yield: 331 mg (54%); yellow crystals; mp 70–72 °C. Anal. calcd. for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15%. Found: C, 74.62; H, 6.98; N, 4.18. IR (KBr): 2171 (C≡C), 1624 (CO) cm^{-1}. ^1H NMR (400.1 MHz, $CDCl_3$): δ = 8.17 (2H, m, H*o* Ph), 7.63–7.59 (1H, m, H*p* Ph), 7.52–7.49 (2H, m, H*m* Ph), 6.78 (1H, d, *J* = 4.0 Hz, H-3), 6.30 (1H, d, *J* = 4.0 Hz, H-4), 5.47 (1H, s, O-CH-O), 4.39 (2H,

q, $J = 7.2$ Hz, NCH_2), 3.78 (2H, d, $J = 10.8$ Hz, CH_2), 3.62 (2H, d, $J = 10.8$ Hz, CH_2), 1.48 (3H, t, $J = 7.2$ Hz, $\underline{Me}CH_2$), 1.30 (3H, s, Me), 0.81 (3H, s, Me). ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 177.4$ (C=O), 137.3 (C*i*), 134.4 (C-5), 133.8 (C*p*), 129.3 (C*o*), 128.7 (C*m*), 120.4 (C-3), 113.5 (C-2), 109.8 (C-4), 97.1 (O-CH-O), 94.8 (≡C), 87.5 (C≡), 78.0 (CH_2-O), 41.7 (NCH_2), 30.3 ($Me_2\underline{C}$), 23.3 (Me), 22.0 (Me), 16.7 ($\underline{Me}CH_2$).

3-[5-(5,5-Dimethyl-1,3-dioxan-2-yl)-1-ethyl-1*H*-pyrrol-2-yl]-1-(furan-2-yl)prop-2-yn-1-one (5e)

Yield: 298 mg (50%); yellow crystals; mp 68–70 °C. Anal. calcd. for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N 4.28%. Found: C, 69.79; H, 6.67; N, 4.20. IR (KBr): 2177 (C≡C), 1626 (CO) cm^{-1}. ^{1}H NMR (400.1 MHz, $CDCl_3$): $\delta = 7.65$ (1H, dd, $J = 0.7$, 1.7 Hz, H-5 furan), 7.32 (1H, dd, $J = 0.7$, 3.5 Hz, H-3 furan), 6.75 (1H, d, $J = 3.4$ Hz, H-3), 6.59 (1H, dd, $J = 1.7$, 3.5 Hz, H-4 furan), 6.28 (1H, d, $J = 3.4$ Hz, H-4), 5.46 (1H, s, O-CH-O), 4.36 (2H, q, $J = 7.0$ Hz, NCH_2), 3.77 (2H, d, $J = 10.8$ Hz, CH_2), 3.63 (2H, d, $J = 10.8$ Hz, CH_2), 1.46 (3H, t, $J = 7.0$ Hz, $\underline{Me}CH_2$), 1.30 (3H, s, Me), 0.81 (3H, s, Me). ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 164.6$ (C=O), 153.4 (C-2 furan), 147.5 (C-5 furan), 134.5 (C-5), 120.3 (C-3), 119.3 (C-3 furan), 113.3 (C-2), 112.6 (C-4 furan), 109.8 (C-4), 97.1 (O-CH-O), 93.9 (≡C), 86.6 (C≡), 78.0 (CH_2-O), 41.6 (NCH_2), 30.3 ($Me_2\underline{C}$), 23.3 (Me), 22.0 (Me), 16.7 ($CH_2\underline{Me}$).

3-[5-(5,5-Dimethyl-1,3-dioxan-2-yl)-1-ethyl-1*H*-pyrrol-2-yl]-1-(thiophen-2-yl)prop-2-yn-1-one (5f)

Yield: 256 mg (41%); yellow crystals; mp 88–90 °C. Anal. calcd. for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16; N 4.08; S, 9.34%. Found: C, 66.18; H, 6.12; N, 4.20; S, 9.02. IR (KBr): 2175 (C≡C), 1610 (CO) cm^{-1}. ^{1}H NMR (400.1 MHz, $CDCl_3$): $\delta = 7.92$ (1H, dd, $J = 1.2$, 3.8 Hz, H-3 thiophene), 7.69 (1H, dd, $J = 1.2$, 4.9 Hz, H-5 thiophene), 7.17 (1H, dd, $J = 3.8$, 4.9 Hz, H-4 thiophene), 6.77 (1H, d, $J = 3.8$ Hz, H-3), 6.29 (1H, d, $J = 3.8$ Hz, H-4), 5.46 (1H, s, O-CH-O), 4.38 (2H, q, $J = 7.0$ Hz, NCH_2), 3.78 (2H, d, $J = 10.8$ Hz, CH_2), 3.63 (2H, d, $J = 10.8$ Hz, CH_2), 1.48 (3H, t, $J = 7.0$ Hz, $\underline{Me}CH_2$), 1.30 (3H, s, Me), 0.81 (3H, s, Me). ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 169.2$ (C=O), 145.1 (C-2 thiophene), 134.5 (C-3 thiophene), 134.4 (C-5), 133.8 (C-5 thiophene), 128.3 (C-4 thiophene), 120.4 (C-3), 113.2 (C-2), 109.8 (C-4), 97.0 (O-CH-O), 94.0 (≡C), 86.0 (C≡), 77.9 (CH_2-O), 41.6 (NCH_2), 30.3 ($Me_2\underline{C}$), 23.2 (Me), 21.9 (Me), 16.8 ($CH_2\underline{Me}$).

Synthesis of 5-Ethynylpyrrole-2-carbaldehydes 4a–f: General Procedure

A solution of pyrrole **5a–f** (2.295 mmol) in acetone (30 ml) was added to a 4 M solution of HCl (9.5 ml) in acetone (20 ml) and the mixture was stirred at room temperature for 1 h. Then diethyl ether was added (50 ml) and resulting solution was washed twice by saturated NaCl and 5% $NaHCO_3$ solutions and then dried over K_2CO_3. Residue after removing solvent was purified by flash chromatography on Al_2O_3 (eluents: *n*-hexane, hexane/diethyl ether with gradient from 3:1, 1:1, 1:3) to give pyrroles **4a–f**.

5-(3-Oxo-3-phenylprop-1-ynyl)-1*H*-pyrrole-2-carbaldehyde (4a)

Yield: 394 mg (77%); grey solid; mp 197–199 °C. Anal. calcd. for $C_{14}H_9NO_2$: C, 75.33; H, 4.06; N, 6.27%. Found: C, 75.56; H, 4.19; N, 6.09. IR (KBr): 3230 (NH), 2194 (C≡C), 1662 (HCO), 1630 (COPh) cm^{-1}. ^1H NMR (400.1 MHz, acetone-d_6): δ = 12.06 (1H, br. s, NH), 9.66 (1H, s, HC=O), 8.22–8.21 (2H, m, H*o* Ph), 7.72–7.69 (1H, m, H*p* Ph), 7.59–7.56 (2H, m, H*m* Ph), 7.09 (1H, dd, *J* = 2.7, 3.4 Hz, H-4), 6.98 (1H, dd, *J* = 2.9, 3.4 Hz, H-3). ^{13}C NMR (100.6 MHz, acetone-d_6): δ = 180.5 (HC=O), 177.5 (C=O), 137.7 (C*i*), 136.8 (C-2), 135.4 (C*p*), 130.3 (C*o*, C-3), 129.9 (C*m*), 121.7 (C-4), 120.6 (C-5), 91.6 (≡C), 85.3 (C≡).

5-[3-(Furan-2-yl)-3-oxoprop-1-ynyl]-1*H*-pyrrole-2-carbaldehyde (4b)

Yield: 425 mg (87%); yellow crystals; mp 168–170 °C. Anal. calcd. for $C_{12}H_7NO_3$: C, 67.61; H, 3.31; N, 6.57%. Found: C, 67.29; H, 3.07; N, 6.34. IR (KBr): 3240 (NH), 2207 (C≡C), 1658 (HCO), 1628 (CO) cm^{-1}. ^1H NMR (400.1 MHz, $CDCl_3$): δ = 9.69 (1H, br. s, NH), 9.61 (1H, s, HC=O), 7.72 (1H, dd, *J* = 0.8, 1.7 Hz, H-5 furan), 7.43 (1H, dd, *J* = 0.8, 3.6 Hz, H-3 furan), 6.98 (1H, dd, *J* = 2.5, 4.0 Hz, H-4), 6.85 (1H, dd, *J* = 2.4, 4.0 Hz, H-3), 6.64 (1H, dd, *J* = 1.7, 3.6 Hz, H-4 furan). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 179.5 (HC=O), 163.0 (C=O), 153.1 (C-2 furan), 148.4 (C-5 furan), 134.9 (C-2), 121.2 (C-3 furan), 120.8 (C-3), 120.4 (C-4), 117.2 (C-5), 113.0 (C-4 furan), 91.0 (≡C), 82.9 (C≡).

5-[3-Oxo-3-(thiophen-2-yl)prop-1-ynyl]-1*H*-pyrrole-2-carbaldehyde (4c)

Yield: 394 mg (75%); yellow solid; mp 185 °C. Anal. calcd. for $C_{12}H_7NO_2S$: C, 62.87; H, 3.08; N, 6.11; S, 13.99%. Found: C, 62.69; H, 3.11; N, 6.24; S, 14.15. IR (KBr): 3251 (NH), 2195 (C≡C), 1658 (HCO), 1617 (CO) cm^{-1}. ^1H NMR (400.1 MHz, acetone-d_6): δ = 12.02 (1H, br. s, NH), 9.65 (1H, s, H-CO), 8.17 (1H, dd, *J* = 1.0, 3.8 Hz, H-3 thiophene), 8.02 (1H, dd, *J* = 1.0, 4.9 Hz, H-5 thiophene), 7.28 (1H, dd, *J* = 3.8, 4.9 Hz, H-4 thiophene), 7.09 (1H, d, *J* = 3.9 Hz, H-4), 6.94 (1H, d, *J* = 3.9 Hz, H-3). ^{13}C NMR (100.6 MHz, acetone-d_6): δ = 180.5 (HC=O), 169.4 (C=O), 145.6 (C-2 thiophene), 137.0 (C-3,5 thiophene), 136.8 (C-2), 129.7 (C-4 thiophene), 121.6 (C-3), 120.5 (C-4), 117.3 (C-5), 90.9 (≡C), 83.7 (C≡).

1-Ethyl-5-(3-oxo-3-phenylprop-1-ynyl)-1*H*-pyrrole-2-carbaldehyde (4d)

Yield: 484 mg (84%); yellow solid; mp 84–86 °C. Anal. calcd. for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57%. Found: C, 76.19; H, 5.30; N, 5.21. IR (KBr): 2183 (C≡C), 1662 (HCO), 1634 (CO) cm^{-1}. ^1H NMR (400.1 MHz, $CDCl_3$): δ = 9.65 (1H, s, H-CO), 8.18–8.16 (2H, m, H*o* Ph), 7.68–7.64 (1H, m, H*p* Ph), 7.56–7.52 (2H, m, H*m* Ph), 6.95 (1H, d, *J* = 4.0 Hz, H-4), 6.81 (1H, d, *J* = 4.0 Hz, H-3), 4.62 (2H, q, *J* = 7.2 Hz, CH_2), 1.45 (3H, t, *J* = 7.2 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 179.8 (HC=O), 177.2 (C=O), 136.8 (C*i*), 134.5 (C*p*), 133.6 (C-2), 129.5 (C*o*), 128.9 (C*m*), 123.2 (C-3), 120.8 (C-5), 119.7 (C-4), 94.9 (≡C), 83.0 (C≡), 42.7 (CH_2), 16.6 (CH_3).

1-Ethyl-5-[3-(furan-2-yl)-3-oxoprop-1-ynyl]-1*H*-pyrrole-2-carbaldehyde (4e)

Yield: 448 mg (81%); yellow solid; mp 82–84 °C. Anal. calcd. for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81%. Found: C, 69.58; H, 4.88; N, 5.47. IR (KBr): 2178 (C≡C), 1659 (HCO), 1620 (CO) cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): $\delta = 9.63$ (1H, s, H-CO), 7.71 (1H, dd, $J = 0.7$, 1.7 Hz, H-5 furan), 7.38 (1H, dd, $J = 0.7$, 3.5 Hz, H-3 furan), 6.93 (1H, d, $J = 4.2$ Hz, H-4), 6.77 (1H, d, $J = 4.2$ Hz, H-3), 6.63 (1H, dd, $J = 1.7$, 3.5 Hz, H-4 furan), 4.59 (2H, q, $J = 7.2$ Hz, CH_2), 1.42 (3H, t, $J = 7.2$ Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 179.7$ (HC=O), 164.0 (C=O), 153.1 (C-2 furan), 148.2 (C-5 furan), 133.6 (C-2), 123.1 (C-3), 120.6 (C-5), 120.4 (C-4), 119.6 (C-3 furan), 113.0 (C-4 furan), 94.0 (≡C), 82.2 (C≡), 42.6 (CH_2), 16.6 (CH_3).

1-Ethyl-5-[3-oxo-3-(thiophen-2-yl)prop-1-ynyl]-1*H*-pyrrole-2-carbaldehyde (4f)

Yield: 525 mg (89%); yellow solid; mp 90–92 °C. Anal. calcd. for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44; S, 12.46%. Found: C, 65.21; H, 4.28; N, 5.15; S, 12.08. IR (KBr): 2181 (C≡C), 1663 (HCO), 1604 (CO) cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): $\delta = 9.65$ (1H, s, H-CO), 7.96 (1H, dd, $J = 1.0$, 3.8 Hz, H-3 thiophene), 7.77 (1H, dd, $J = 1.0$, 4.9 Hz, H-5 thiophene), 7.22 (1H, dd, $J = 3.8$, 4.9 Hz, H-4 thiophene), 6.94 (1H, d, $J = 4.2$ Hz, H-4), 6.79 (1H, d, $J = 4.2$ Hz, H-3), 4.61 (2H, q, $J = 7.2$ Hz, CH_2), 1.44 (3H, t, $J = 7.2$ Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 179.7$ (HC=O), 168.7 (C=O), 144.5 (C-2 thiophene), 135.6 (C-3 thiophene), 134.6 (C-5 thiophene), 133.5 (C-2), 128.6 (C-4 thiophene), 123.1 (C-3), 120.6 (C-5), 119.7 (C-4), 94.3 (≡C), 81.6 (C≡), 42.6 (CH_2), 16.6 (CH_3).

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SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website.

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