ISSN 1070-4280, Russian Journal of Organic Chemistry, 2013, Vol. 49, No. 8, pp. 1241–1243. © Pleiades Publishing, Ltd., 2013.
Original English Text © L.N. Sobenina, M.V. Markova, D.N. Tomilin, E.V. Tret'yakov, V.I. Ovcharenko, A.I. Mikhaleva, B.A. Trofimov, 2013, published in Zhurnal Organicheskoi Khimii, 2013, Vol. 49, No. 8, pp. 1255–1256.

SHORT COMMUNICATIONS

First Example of the Synthesis of Pyrrolecarbaldehyde with Electron-Deficient Acetylene Substituents

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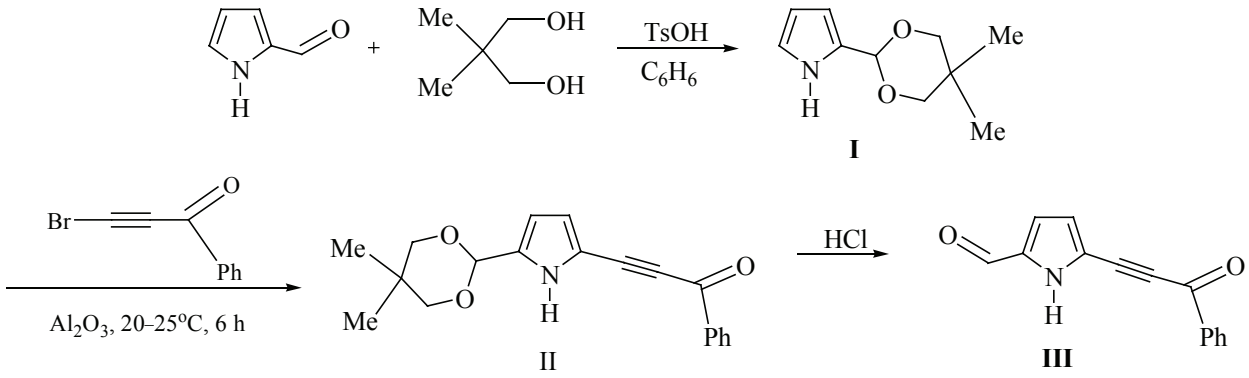
Received February 28, 2013

DOI: 10.1134/S1070428013080265

Pyrrolecarbaldehydes with acetylene substituents are widely applied to organic syntesis although the systematic research in this field has been started only a little earlier than a decade ago. Now the ethynyl pyrrolecarbaldehydes are used for the preparation of polyfunctional derivatives of pyrrole and indole of definite structure and properties [1–6]. They also play a key role in designing macrocycles whose natural analogs possess special kinds of biological action [7–12].

Now the ethynylpyrrolecarbaldehydes are obtained as a rule by criss-coupling of difficultly available and unstable halopyrrolecarbaldehydes with terminal acetylenes [4–12] or their organometallic derivatives [13] in the presence of palladium catalysts (Sonogashira reaction). However the ethynylpyrrolecarbaldehydes containing in the acetylene substituent electron-acceptor functions are not known up till now since the Sonogashira reaction is of low efficiency with activated acetylenes [14]. Yet such ethynylpyrrolecarbaldehydes would provide new opportunities to the targeted organic synthesis, in particular, for the preparation of polyfunctional stable organic radicals and polyradicals [15–17].

In this communication we describe for the first time a simple convenient protocol of the synthesis of such compounds by an example of the preparation of the first specimen of pyrrolecarbaldehydes with the electron-deficient acetylene substituent. It includes the acetal protection of the aldehyde group of the pyrrole-2-carbaldehyde by the reaction with 2,2-dimethylpropanediol in the presence of *p*-toluenesulfonic acid, introducing benzoylethynyl group into the pyrrole ring of acetal **I** by "palladiumless" cross-coupling with 3-bromo-1-phenyl-2-propyn-1-one on alumina, and the removal of the acetal protection in ethynylpyrrole **II** by the mild acid-catalyzed hydrolysis



in aqueous acetone. The key stage, the cross coupling of acetal **I** with 3-bromo-1-phenyl-2-propyn-1-one, proceeds without compounds of transition metals, bases, and solvent at room temperature.

The efficiency of this new reaction of "palladium-less" cross-coupling is already confirmed by numerous syntheses of ethynylpyrroles and indoles [18–21]. Taking this into account further systematic development and optimization of all three stages of the suggested protocol may provide a general approach to the synthesis of pyrrolecarbaldehydes with electron-deficient acetylene substituents.

^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker DPX-400 [400 (^{1}H), 100.6 MHz (^{13}C)]. IR spectra were recorded on a spectrophotometer Bruker IFS25 from pellets with KBr.

2-(5,5-Dimethyl-1,3-dioxan-2-yl)pyrrole (**I**) was obtained by procedure [22].

3-[5-(5,5-Dimethyl-1,3-dioxan-2-yl)pyrrole-2-yl]-1-phenyl-2-propyn-1-one (II). In a porcelain mortar were thoroughly ground for 5 min 0.33 g (1.821 mmol) of 2-(5,5-dimethyl-1,3-dioxan-2-yl)pyrrole (**I**) and 0.38 g of (1.821 mmol) 3-bromo-1-phenyl-2-propyn-1-one with 7 g (10-fold excess with respect to the reagents mass) of alumina, and the mixture was left standing with alumina at room temperature for 6. Then the reaction mixture was applied to a column packed with Al_2O_3 and by elution first with hexane, then with hexane–ethyl ether, 3 : 1, 1 : 1, 1 : 3, we isolated first unreacted 3-bromo-1-phenyl-2-propyn-1-one, then ethynylpyrrole **II**. Yield 0.24 g (43%), lustrous gray-green needle crystals, mp 141–143°C. IR spectrum, ν, cm^{-1}: 3314 (NH), 2174 (C≡C), 1625 (CO). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.84 s (3H, Me), 1.24 s (3H, Me), 3.64, 3.76 d.d (4H, 2CH_2, *J* 11.2 Hz), 5.51 s (1H, OCHO), 6.30 d.d (1H, H^4, *J* 2.9, 3.4 Hz), 6.83 d.d (1H, H^3, *J* 2.7, 3.4 Hz), 7.53 m (2H, H^m), 7.61 m (1H, H^n), 8.18 m (2H, H^o), 9.10 br.s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 21.9 (Me), 23.1 (Me), 30.4 ($Me_2\underline{C}H$), 77.5 (CH_2O), 88.0 (C≡), 91.9 (≡C), 96.0 (OCHO), 108.4 (C^4), 109.8 (C^2), 120.9 (C^3), 128.6 (Cm), 129.4 (C^o), 133.9 (C^n), 134.5 (C^5), 136.8 (C^u), 177.6 (C=O). Found, %: C 73.48; H 6.16; N 4.51. $C_{19}H_{19}NO_3$. Calculated, %: C 73.77; H 6.19; N 4.53.

5-(3-Oxo-3-phenylprop-1-yn-1-yl)pyrrole-2-carbaldehyde (III). A solution of 0.71 g (2.295 mmol) of pyrrole **II** in 30 ml of acetone was added to 4 M HCl solution (9.5 ml) in acetone (20 ml), and the mixture was stirred for 1 h at room temperature. Then 50 ml of ethyl ether was added, the solution obtained was twice washed with brine and 5% solution of $NaHCO_3$, and dried with K_2CO_3. The residue after removing ether (0.59 g) was purified by column chromatography on Al_2O_3 (eluents hexane, then hexane–ethyl ether, 3 : 1, 1 : 1, 1 : 3,. Yield 0.24 g (42%) yellow crystals, mp 195–199°C. IR spectrum, ν, cm^{-1}: 3230 (NH), 2194 (C≡C), 1662 (HCO), 1630 (COPh). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 6.97 d.d (1H, H^3, *J* 2.9, 3.4 Hz), 7.11 d.d (1H, H^4, *J* 2.7, 3.4 Hz), 7.58 m (2H, H^m), 7.72 m (1H, H^n), 8.23 m (2H, H^o), 9.67 s (1H, HCO), 12.07 br.s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 85.1 (C≡), 91.5 (≡C), 120.4 (C^5), 121.9 (C^4), 129.7 (Cm), 130.07 (C^o, C^3), 135.2 (C^n), 136.7 (C^2), 137.6 (C^u), 177.3 (PhC=O), 180.4 (HC=O). Found, %: C 75.36; H 4.09; N 6.29. $C_{14}H_9NO_2$. Calculated, %: C 75.33; H 4.06; N 6.27.

ACKNOWLEDGMENTS

The study was carried out under the financial support of the Russian Foundation for Basic Research (grant no.13-03-91150 GFEN-a) and of the Presidium of the Russian Academy of Sciences (project no. 28).

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