Chemistry of Heterocyclic Compounds, Vol. 46, No. 12, March, 2011 (Russian Original Vol. 46, No. 12, December, 2010)

LETTERS TO THE EDITOR

SYNTHESIS OF 2-AMINOPYRROLES FROM α-(AMINOCARBONYL)ACETAMIDOXIMES AND BENZOYLPHENYLACETYLENE

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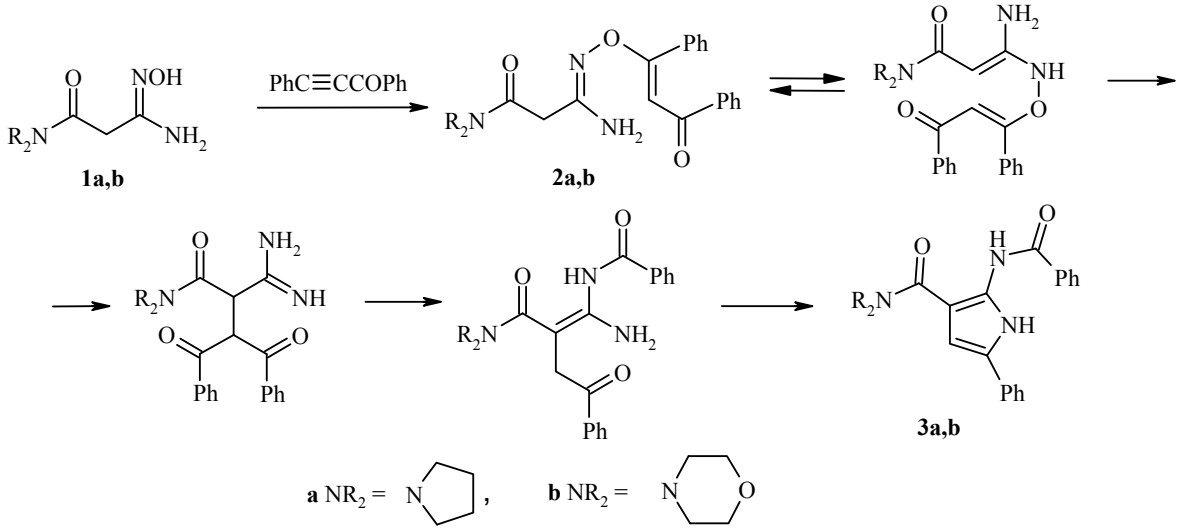
Keywords: 2-aminopyrrole, O-vinyl-α-(aminocarbonyl)acetamidoxime, [3,3]-sigmatropic rearrangement.

We have previously reported the thermal reaction of O-vinylacetamidoximes as adducts of aminocarbonylacetamidoximes with methyl propiolate and dimethylacetylene dicarboxylate to give α-amino-pyrroles and pyrrolinones [1, 2].

The O-vinylacetamidoximes **2**, prepared from the aminocarbonylacetamidoximes **1** and benzoyl-phenylacetylene, undergo a [3,3]-sigmatropic rearrangement similar to a Trofimov reaction [3, 4] under unexpectedly mild conditions – even at room temperature. The rearrangement is accompanied by a previously unobserved cleavage of a C–C bond in the intermediate β-diketones formed and gives the 2-benzoyl-aminopyrrole **3** as the sole product. Formation of imidazoles [5, 6] or the isomeric pyrroles [1, 2] is not observed.



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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1893-1895, December, 2010. Original article submitted November 24, 2010.

Due to the ease of the rearrangement small amounts of the aminopyrroles **3** are formed even during the synthesis of the O-vinylamidoximes **2**. Optimal yields of the aminopyrroles **3** are achieved when carrying out the reaction of amidoximes **1** with the benzoylphenylacetylene at 40ºC without the isolation of the O-vinylamidoximes **2**.

The structure of the pyrroles **3** was identified using ^{1}H and ^{13}C NMR spectroscopy and location of the phenyl at the 5 position was based on the value of the direct spin-spin coupling constant for ^{13}C(4)–^{1}H(4), similarly to that used by us before [1]. The spin-spin coupling was determined from the satellites in the ^{1}H NMR spectra.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 instrument (300 and 75 MHz respectively) using $CDCl_3$. The residual ^{1}H signal for the $CHCl_3$ at 7.26 ppm and $CDCl_3$ itself at 77.2 ppm in the ^{13}C NMR spectra were used as internal standards. Elemental analysis was carried out on a EuroVector EURO EA 3000 automatic CHN analyzer. High resolution mass spectra were recorded on a Bruker Micro TOF instrument with electrospray ionization.

O-Vinylacetamidoxime 2a. A solution of the acetamidoxime **1a** (1.25 g, 7.30 mmol), benzoylphenylacetylene (1.51 g, 7.30 mmol), and triethylamine (0.05 ml) in 2-propanol (100 ml) was held for 10 days at room temperature. Solvent was evaporated *in vacuo* without heating and the residue was chromatographed on silica gel using CH_2Cl_2–MeOH (100:1) as eluent to give the adduct **2a** (2.0 g, 73%) as a viscous, yellow oil. The compound exists as a mixture of stereoisomers. ^{1}H NMR spectra, δ, ppm: main isomer: 1.87-2.08 (4H, m, CH_2–CH_2); 3.30 (2H, s, $COCH_2$); 3.50 (2H, m, NCH_2); 3.61 (2H, m, NCH_2); 5.63 (2H, br. s, NH_2); 7.03 (1H, s, C<u>H</u>=C); 7.34-7.51 (8H, m); 7.90 (2H, m, H Ar); minor isomer: 1.80-1.92 (4H, m, CH_2–CH_2); 2.97 (2H, s, $COCH_2$); 3.30 (2H, m, NCH_2); 3.41 (2H, m, NCH_2); 6.05 (2H, br. s, NH_2); 6.22 (1H, s, C<u>H</u>=C); 7.32-7.50 (6H, m); 7.67 (2H, m); 7.94 (2H, m, H Ar).

N-[3-(Pyrrolidin-1-ylcarbonyl)-5-phenylpyrrol-2-yl]benzamide (3a). Compound **2a** (0.72 g, 1.91 mmol) was dissolved in acetonitrile (12 ml) and refluxed to the disappearance of starting material (TLC, about 2-3 h). Solvent was evaporated and the residue was chromatographed on silica gel eluting with CH_2Cl_2–MeOH (12:1) to give the pyrrole **3a** as yellow crystals. Yield 0.33 g (47%); mp 175-176ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.87-2.13 (4H, m); 3.64-3.95 (4H, m, pyrrolidine); 6.70 (1H, d, J = 2.9, $^1J_{C\text{-}H}$ = 172.2, H-4); 7.22 (1H, t, J = 7.3); 7.38 (2H, t, J = 7.6); 8.02 (2H, d, J = 6.5, COPh); 7.46-7.61 (5H, m, Ph); 11.38 (1H, br. s, CONH); 12.46 (1H, s, H-1). ^{13}C NMR spectrum, δ, ppm: 26.88 (CH_2); 47.27 (NCH_2); 48.55 (NCH_2) (pyrrolidine, signals broadened due to hindered rotation around the amide bond); 101.95, 103.50, 123.60, 125.67, 126.54, 127.50, 128.99, 129.04, 131.79, 132.44, 132.89, 138.13 (Ar); 165.26, 166.00 (CON, CONH). Mass spectrum (ESI, MeOH+HCOOH), found: *m/z* 360.1650. Calculated for $[C_{22}H_{21}N_3O_2^+ + H]^+$ 360.1706. Found, %: C 73.03; H 5.88; N 11.76. $C_{22}H_{21}N_3O_2$. Calculated, %: C 73.52; H 5.89; N 11.69.

Preparation of Pyrroles 3 without Isolation of the O-vinylacetamidoximes 2. Benzoylphenylacetylene (2 mmol) and triethylamine (0.2 mmol) were added to a suspension of the acetamidoxime **1** (2 mmol) in 2-propanol (10 ml) and stirred for 10 days at 40ºC. Solvent was removed *in vacuo* to half volume and the precipitated crystals of pyrrole **3** were filtered off. The filtrate was evaporated and the residue was chromatographed on silica gel eluting with CH_2Cl_2–MeOH (100:1) to allow the separation of an additional, substantial amount of pyrrole **3**.

N-[3-(Pyrrolidin-1-ylcarbonyl)-5-phenylpyrrol-2-yl]benzamide (3a). Overall yield 76%; mp 175-176ºC.

N-[3-(Morpholin-4-ylcarbonyl)-5-phenylpyrrol-2-yl]benzamide (3b). Overall yield 40%; mp 208-209ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.73-3.82 (4H, m), 3.83-3.93 (4H, m, morpholine); 6.50 (1H, d, J = 2.6, $^1J_{C\text{-}H}$ = 171.7, H-4); 7.24 (1H, t, J = 7.5, Ph); 7.39 (2H, t, J = 7.5, Ph); 7.45-7.62 (5H, m, Ph); 7.99 (2H, d, J = 7.5, Ph); 11.32 (1H, br. s, CONH); 11.63 (1H, s, H-1). ^{13}C NMR spectrum, δ, ppm: 45.55 (NCH_2); 67.15 (OCH_2); 100.67, 103.72, 123.73, 125.91, 126.84, 127.40, 129.06, 129.11, 131.49, 132.61, 132.77, 132.29 (Ar); 165.29, 167.11 (CON, CONH). Mass spectrum (ESI MeCN + HCOOH), found: *m/z* 376.1590. Calculated for $[C_{22}H_{21}N_3O_3 + H]^+$ 376.1661. Found, %: C 70.25; H 5.61; N 11.20. $C_{22}H_{21}N_3O_3$. Calculated, %: C 70.38; H 5.64; N 11.19.

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