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Mendeleev Commun., 2005, 15(6), 229–232
Mendeleev Communications

2-(2-Benzoylethynyl)-5-phenylpyrrole: fixation of *cis*- and *trans*-rotamers in a crystal state

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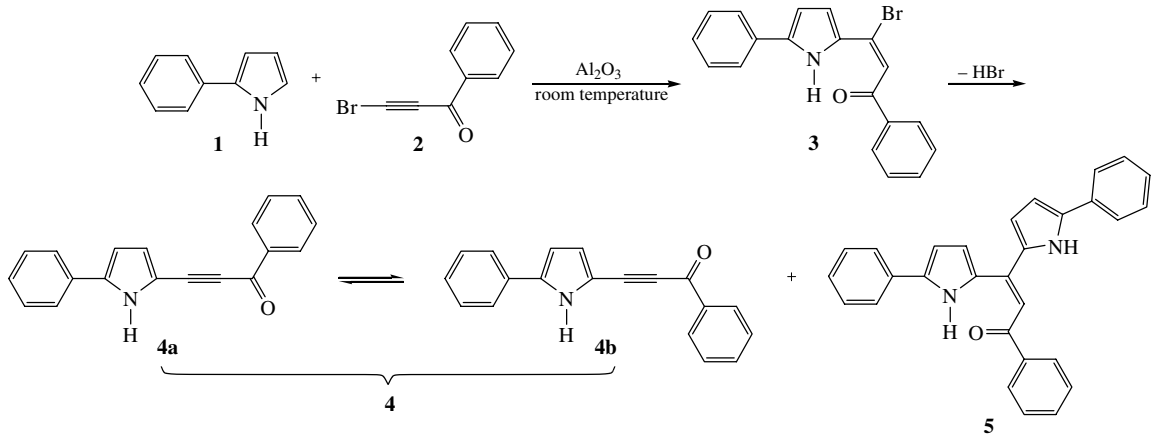
DOI: 10.1070/MC2005v015n06ABEH002190

2-(2-Benzoylethynyl)-5-phenylpyrrole forms two crystal modifications with the carbonyl group oriented in *cis*- and *trans*-positions relative to the nitrogen atom thus representing the first example of the solid state stable rotamers around the C≡C bond system.

The C-ethynylation of pyrroles remains a challenging synthetic problem because the common Pd(Cu)-catalysed cross-coupling of acetylenes with haloheteroarenes[1] has been mainly limited by pyrroles with electron-withdrawing substituents,[1,2] and N-substituted representatives.[2,3] Instability of simpler halogenated pyrroles,[4] their decreased reactivity in the cross-coupling[2(b)] and a significant interference of the side reductive dehalogenation[2(c)] also contribute to the problem.

Recently,[5] we reported a basically novel 'reverse' cross-coupling employing non-halogenated pyrroles and available haloacetylenes. The reaction proceeds on the Al_2O_3 surface at room temperature requiring no palladium, copper, base and



Scheme 1

solvent, as here exemplified by the ethynylation of 2-phenylpyrrole **1** with 1-benzoyl-2-bromoacetylene **2** (Scheme 1). The yield of 2-(2-benzoylethynyl)-5-phenylpyrrole **4** in this particular experiment was 69%† (50% in preliminary report[5]). Intermediate **3**, side adduct **5** and their homologues with other substituents were identified previously.[5]

Unexpectedly, ethynylpyrrole **4** was found to crystallise in two visually distinctive forms: prisms **4a** and needles **4b** with different melting points (173–174 and 192–194 °C, respectively).†

The prisms of **4a** are less stable and, upon repeated recrystallization, transform to the needles of **4b**, which do not give prisms when further recrystallised. The latter can only be isolated by the instant extraction of the alumina used in the reaction.

The X-ray analysis‡ (Figures 1 and 2) revealed that the crystals represent the *cis*- (**4a**) and *trans*- (**4b**) rotamers with respect to mutual disposition of the nitrogen atom and the carbonyl group (Scheme 1). The bond lengths and angles in the vicinity of the triple bond do not remarkably differ from the common values, with the triple bond length corresponding to the normal (1.202±0.005 Å):[6] 1.203 and 1.201 Å for **4a** and **4b**, respectively. The C=O bonds are slightly longer than usual: 1.228 Å for **4a** and 1.230 Å for **4b** against 1.215 Å,[6] while both C_{sp^2}–C_{sp} bonds are considerably shorter: 1.431, 1.411 Å for **4a** and 1.441 and 1.401 Å for **4b** against 1.459 Å.[6] The C≡C bonds are bent toward the C=O bonds: 176.33°, 173.73° for **4a** and 179.8(3)°, 173.2(2)° for **4b**, whereas the angles at the C=O group are distorted toward the C≡C bond: 122.01° for **4a** and 122.1° for **4b**, with some angle decrease from the benzene ring side: 116.65° for **4a** and 116.1° for **4b**.

For **4a**, the torsion angle between the pyrrole and 5-phenyl planes is ~10° and that between the benzoyl is ~17°, whereas in the molecule of **4b** these structural units are essentially planar (~7° and 0°, respectively), that is likely meant a stronger conjugation in the latter. The crystal packing of the two forms are entirely different: the prisms of **4a** consist of H-bonded macrocyclic dimers (Figure 3), while the needles of **4b** are H-bonded chains (Figure 4).

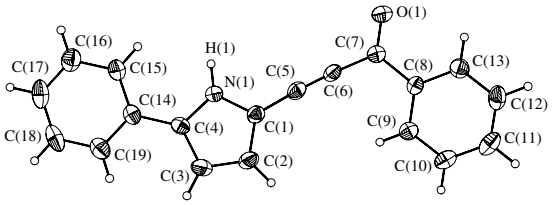


Figure 1 The general view of **4a**. Selected bond lengths (Å): C(7)–O(1) 1.2284(16), C(5)–C(6) 1.2026(19), C(7)–C(6) 1.431(2), C(1)–C(5) 1.411(2), N(1)–H(1) 0.904(15); selected bond angles (°): C(6)–C(5)–C(1) 176.33(16), C(5)–C(6)–C(7) 173.73(15), C(6)–C(7)–C(8) 116.65(12), C(6)–C(7)–O(1) 122.01(13).

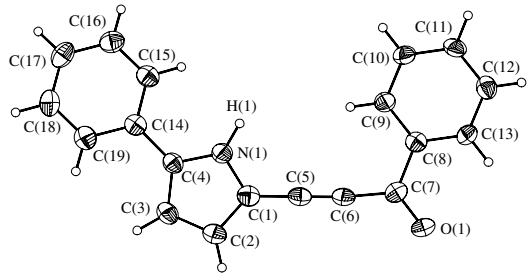


Figure 2 The general view of **4b**. Selected bond lengths (Å): C(7)–O(1) 1.230(3), C(5)–C(6) 1.201(3), C(7)–C(6) 1.441(3), C(1)–C(5) 1.401(3), N(1)–H(1) 0.976; selected bond angles (°): C(6)–C(5)–C(1) 179.8(3), C(5)–C(6)–C(7) 173.2(2), C(6)–C(7)–C(8) 116.1(2), C(6)–C(7)–O(1) 122.1(2).

† 2-Phenylpyrrole **1** (72 mg, 0.5 mmol) and 1-benzoyl-2-bromoacetylene **2** (105 mg, 0.5 mmol) were triturated in a mortar with 3.6 g of Al_2O_3 (Chemapol L 40/250 μ, pH 9.8) at room temperature. In 1 min, the reaction powder turned bright yellow to change in 10 min to yellow orange with the temperature rising by 5 °C. After 45 min, the mixture was washed on a glass filter with *n*-hexane (3×40 ml) to get rid of the starting compounds and intermediates. The reaction products were extracted by an *n*-hexane–Et_2O (2:1) mixture (3×50 ml), and three fractions were collected. After partial evaporation of the solvents in air, from the first fraction, a mixture of small orange crystals (mp 176–179 °C) and single needles (mp 184–186 °C) of 2-(2-benzoylethynyl)-5-phenylpyrrole **4** (65 mg) was isolated. From the mother solution, the dark red needles (mp 202–203 °C) of 1,1-di(5-phenylpyrrol-2-yl)-2-benzoylethene **5** (3 mg) were precipitated. Upon standing overnight, the dark orange prisms from the second fraction and the needles of the same colour from the third fraction were precipitated. The crystals were washed with *n*-hexane to obtain 14 mg (10%) of dark orange prisms (mp 173–181 °C) and 15 mg (11%) of dark orange red shining slim needles (mp 183–184 °C). The total yield of **4** was 94 mg (69%).

From microscopic examination, it is seen that upon melting the prisms or small crude crystals, part of the material is transformed into small needles at 162–172 °C, which further melt at 182–185 °C.

Pure samples of the crystals melt as follows: the prisms (designated as **4a**): 173–174 °C; the needles (designated as **4b**): 192–194 °C (recrystallization twice from benzene), 191–193 °C (ethanol–water, 2:1), 184–186 °C (*n*-hexane–Et_2O, 2:1).

4a: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.07 (br. s, 1H, NH), 8.16 (m, 2H, H_o COPh), 7.58 (m, 1H, H_p COPh), 7.50 (m, 4H, H_m COPh, H_o Ph-5), 7.40 (m, 2H, H_m Ph-5), 7.29 (m, 1H, H_p Ph-5), 6.91 (dd, 1H, H-3, ^3J 3.6 Hz, ^4J 2.5 Hz), 6.56 (dd, 1H, H-4, ^3J 3.6 Hz, ^4J 2.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.67 (C=O), 137.56 (C-5 of pyrrole), 136.90 (C_i COPh), 133.98 (C_p COPh), 130.85 (C_i Ph-5), 129.45 (C_o COPh), 129.26 (C_m Ph-5), 128.60 (C_m COPh), 128.08 (C_p Ph-5), 124.72 (C_o Ph-5), 122.64 (C-3 of pyrrole), 110.87 (C-2 of pyrrole), 108.40 (C-4 of pyrrole), 93.38 (C_α), 88.88 (C_β). Found (%): C, 83.81; H, 5.00; N, 5.24. Calc. for $C_{19}H_{13}NO$ (%): C, 84.11; H, 4.83; N, 5.16.

4b: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.98 (br. s, 1H, NH), 8.16 (m, 2H, H_o COPh), 7.59 (m, 1H, H_p COPh), 7.49 (m, 4H, H_m COPh, H_o Ph-5), 7.40 (m, 2H, H_m Ph-5), 7.29 (m, 1H, H_p Ph-5), 6.92 (dd, 1H, H-3, ^3J 3.6 Hz, ^4J 2.5 Hz), 6.58 (dd, 1H, H-4, ^3J 3.6 Hz, ^4J 2.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.70 (C=O), 137.60 (C-5 of pyrrole), 136.92 (C_i COPh), 133.95 (C_p COPh), 131.00 (C_i Ph-5), 129.46 (C_o COPh), 129.25 (C_m Ph-5), 128.66 (C_m COPh), 128.06 (C_p Ph-5), 124.75 (C_o Ph-5), 122.65 (C-3 of pyrrole), 110.88 (C-2 of pyrrole), 108.40 (C-4 of pyrrole), 93.39 (C_α), 89.00 (C_β). Found (%): C, 83.75; H, 5.09; N, 5.31. Calc. for $C_{19}H_{13}NO$ (%): C, 84.11; H, 4.83; N, 5.16.

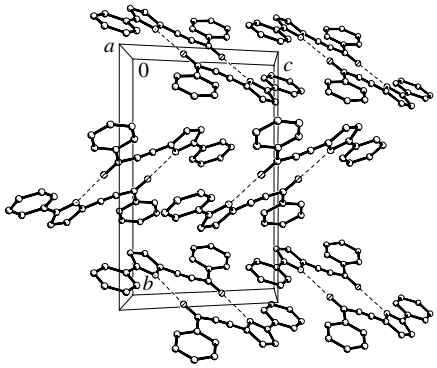


Figure 3 The H-bonded macrocyclic dimers in the crystal structure of **4a**.

The crystals of **4a** and **4b** have different IR spectra§ (in KBr pellets, ν/cm^{-1}); the major differences occur in the following regions: (ν_{NH}) 3311 for **4a** and 3332 for **4b**; (ν_{CO}) 1630 (s), 1617 (sh, m) for **4a**, 1623 (s), 1610 (s) for **4b**; ($\delta_{\equiv C-}$) 650 (s) for **4a**, 651 and 647 (m) for **4b**.

However, in solution (CCl_4, 50–2 mmol dm^{-3}) these differences disappear and only a higher intensity of the C=O absorption [1637 cm^{-1} (s) for both **4a** and **4b**] and a slight lower

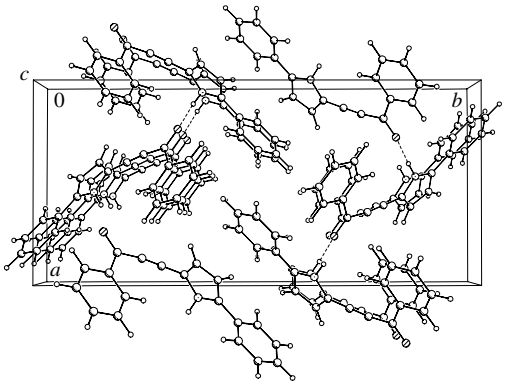
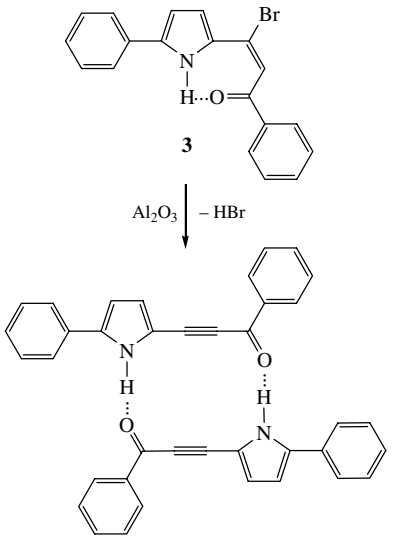


Figure 4 The H-bonded chains in the crystal structure of **4b**.



Scheme 2

frequency shift of the bound NH are observed for **4a** as compared to those of **4b** [3306 cm^{-1} (s) for **4a** and 3312 cm^{-1} (w) for **4b**]. In the UV-VIS spectra (in cyclohexane), the absorption maxima are the same for both crystals, though they are all systematically more intense for **4b** [λ_{max}/nm (lg ε for **4a**, **4b**)]: 218 (sh) (4.04, 4.13), 237 (3.91, 4.02), 269 (4.23, 4.31), 286 (sh) (4.14, 4.22), 385 (4.52, 4.58), reproducibility of the lg ε value being within 2–4% (from three concentrations).

The ^{1}H and ^{13}C NMR spectra are identical for both crystals in accordance with the expected low-rotation barrier between the two rotamers. Indeed, the B3LYP/6-311G(d) calculations (the detailed account of the calculations, including those of vibrational spectra for both rotamers will be published elsewhere) of isolated molecules gave the total energy difference of 0.77 kcal mol^{-1} in favour of **4b** with the **4b** → **4a** barrier equal to 2.6 kcal mol^{-1}. Upon thin layer chromatography (Alufol; eluent: *n*-hexane–Et_2O, 2:1) the crystals of **4a** and **4b** showed the same R_f (0.39).

All the data obtained can be rationalised as follows: *cis*-rotamer **4a** is likely originated from an alumina-induced *cis*-elimination in intermediate **3** with immediate stabilization of the *cis*-oriented N–H and C=O bonds in macrocyclic dimer 2×**4a**, which then further transforms to H-chained **4b**.

Thus, the fixation of *cis*- and *trans*-rotamers **4a** and **4b** is likely due to the strong H-bonding in the crystal state, which keeps retaining for a while in solution.

Recently,[7] a crystalline diacetylene, 1,4-di(α-naphthyl)-1,3-butadiyne, was found to adopt a centrosymmetric conformation of the naphthalene rings around the –C≡C–C≡C– axis. However, the corresponding *cis*-rotamer has not been detected.

This work was supported by the Russian Foundation for Basic Research (grant no. 05-03-32289).

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‡ *XRD data for* **4a** *and* **4b**.

At 190 K, crystals of **4a** ($C_{19}H_{13}NO$) are monoclinic, space group $P2_1/c$, a = 9.367(3), b = 15.704(5) and c = 10.592(2) Å, β = 116.15(3)°, V = 1398.5(7) Å^3, Z = 4, M = 271.30, d_{calc} = 1.289 g cm^{-3}, μ(MoKα) = = 0.80 cm^{-1}, F(000) = 568.

At 120 K, crystals of **4b** ($C_{19}H_{13}NO$) are orthorhombic, space group $Pna2_1$, a = 10.684(4), b = 23.336(11) and c = 5.5288(16) Å, V = 1378.5(9) Å^3, Z = 4, M = 271.30, d_{calc} = 1.307 g cm^{-3}, μ(MoKα) = 0.81 cm^{-1}, F(000) = 568.

Intensities of 3601 (**4a**) or 9690 (**4b**) reflections were measured with a Syntex P2$_1$ [λ(MoKα) = 0.71072 Å, $\theta/2\theta$-scans, $2\theta < 54°$] or Smart 1000 CCD [λ(MoKα) = 0.71072 Å, ω-scans, $2\theta < 52°$] diffractometer and 3404 (**4a**) or 2653 (**4b**) independent reflections [R_{int} = 0.0548 (**4a**), 0.0447(**4b**)] were used in a further refinement. The structures were solved by a direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Hydrogen atoms except H(1) were included in calculated positions and refined as riding atoms, H(1) atoms were located from the Fourier synthesis and refined in the isotropic approximation. The refinement converged to: wR_2 = = 0.0831 and GOF = 0.973 [R_1 = 0.0402 for 1946 observed reflections with $I > 2\sigma(I)$] for **4a**; wR_2 = 0.0895 and GOF = 1.005 [R_1 = 0.0440 for 2160 observed reflections with $I > 2\sigma(I)$] for **4b**. All calculations were performed using SHELXTL PLUS 5.1.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 271208 for **4a** and 271209 for **4b**. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2005.

§ IR spectra were measured on a Bruker IFS25 spectrometer in KBr pellets and in CCl_4. UV-VIS spectra were measured on a Lambda 35 UV/VIS spectrometer (in cyclohexane). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 (400 MHz) spectrometer in $CDCl_3$ with HMDS as an internal standard.

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Received: 24th May 2005; Com. 05/2516