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# Chemo- and stereodirectivity of the reaction of thiocarbohydrazide with 1-acetyl-2-phenylacetylene: synthesis and structure of bis(1-methyl-3-phenyl-2-propynylidene)carbonothioic dihydrazide

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1-Acetyl-2-phenylacetylene reacts with thiocarbohydrazide under mild conditions to afford exclusively $N^2$-(*Z-s-trans*), $N^3$-(*Z-s-cis*)-bis(1-methyl-3-phenyl-2-propynylidene)carbonothioic dihydrazide in high yield (up to 92%); the structure of the compound has been confirmed by IR and NMR spectroscopy and X-ray analysis.

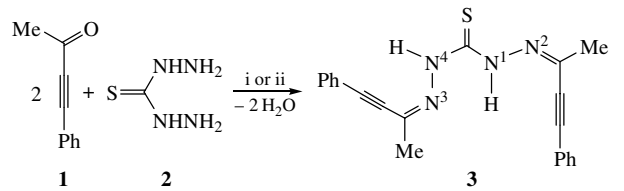
The reactions of thiocarbohydrazide and thiocarbohydrazones with bielectrophilic aryl ethynyl ketones give acyclic adducts due to the addition of nitrogen or sulfur atoms of the nucleophile to the acetylene bond,[1] as well as heterocyclic compounds due to double nucleophilic addition through the acetylene bond[2] or addition–cyclization at the acetylene bond and carbonyl moiety.[3]

We found that 1-acetyl-2-phenylacetylene **1** reacts with thiocarbohydrazide **2** in (i) DMSO or (ii) AcOH at room temperature only through the carbonyl moiety to furnish $N^2$-(*Z-s-trans*), $N^3$-(*Z-s-cis*)-bis(1-methyl-3-phenyl-2-propynylidene)carbonothioic dihydrazide **3** in 76 or 92% yield, respectively (Scheme 1). Compound **3** was also prepared in system aqueous ethanol at 45–50 °C (in 56% yield).

The structure of compound **3** was determined by IR, $^1$H, $^{13}$C, $^{15}$N NMR spectroscopy (in solution)† and X-ray analysis (in crystals).‡ The experimental data are indicative of the same structure of **3** in solid state and in solution.

The IR spectra of diacetylenic dihydrazone **3** showed that the stretching vibrations of NH groups correspond to the double band $\nu_{NH}$ with maxima at 3240, 3310 cm$^{-1}$ (KBr) and 3265, 3320 cm$^{-1}$ ($CHCl_3$, $c \approx 10^{-2}$–$10^{-4}$ mmol dm$^{-3}$), respectively. The $^1$H, $^{13}$C and $^{15}$N NMR spectra ($CDCl_3$) of dihydrazone **3** are characterised by the presence of doubled signals for all structural units of the molecule except for the carbon atom of the thiocarbonyl moiety. The analysis of 2D HSQC, HMBC ($^{13}$C–$^1$H) ($^{15}$N–$^1$H) spectra allowed us to assign signals to different $N^2$ and $N^3$ fragments in diacetylenic dihydrazone **3**.

The IR and NMR spectra reflect the spatial asymmetry of two chemically equivalent moieties in compound **3**, while significant difference in the spin–spin coupling constants $^1J_{N–H}$ [($\delta$ 9.49 ppm, $^1J_{N–H}$ 99.37 Hz) and ($\delta$ 11.13 ppm, $^1J_{N–H}$ 94.19 Hz)] points to various (*s-cis* and *s-trans*) orientations of the NH group protons with respect to the N–C(S) single bond. In amides with different spatial orientations of the N–H bonds with respect to the N–C(O) bond, the value of $^1J_{N–H}$ for *trans*-conformer N–H is by 2–5 Hz higher than that of the *cis*-conformer.[4]




**1** **2** **3**

**Scheme 1** *Reagents and conditions*: i, DMSO, 3 h, room temperature (yield 76%); ii, AcOH, 1 h, room temperature (yield 92%). The product was collected by filtration and recrystallised from MeCN.

† The IR spectra were measured on a Specord IR 75 instrument (in KBr, $CHCl_3$). The NMR spectra were recorded on Bruker DPX 400 and AV-400 spectrometers (400.13 MHz, $^1$H; 100.61 MHz, $^{13}$C) in $CDCl_3$ with HMDS as an internal standard. The $^{15}$N chemical shifts (40.53 MHz) were referenced to $MeNO_2$ used as an external standard. The assignments of $^1$H and $^{13}$C NMR spectra were performed by NOESY, HSQC, and HMBC experiments. The values of $\delta_N$ were measured through 2D $^1$H-$^{15}$N HMBC experiment.

$N^2$-(Z-s-trans), $N^3$-(Z-s-cis)-*Bis(1-methyl-3-phenyl-2-propynylidene)-carbonothioic dihydrazide* **3**: colourless crystals, mp 150–152 °C. IR (KBr, $\nu$/cm$^{-1}$): 2180 (w, C≡C), 3240 (NH), 3310 (NH) (3265 and 3320 cm$^{-1}$, respectively, in $CHCl_3$). $^1$H NMR, $\delta$: 2.17 (s, 3H, Me), 2.37 (s, 3H, Me), 7.42 (m, 4H$_o$, 2Ph), 7.44 (m, 2H$_p$, 2Ph), 7.58 (m, 4H$_m$, 2Ph), 9.49 (s, 1H, NH, $^1J_{N–H}$ 99.37 Hz), 11.13 (s, 1H, NH, $^1J_{N–H}$ 94.19 Hz). $^{13}$C NMR, $\delta$: 22.47 (*Me*–C=N$^2$), 22.66 (*Me*–C=N$^3$), 79.42 (N$^2$=C–*C*≡), 80.25 (N$^3$=C–*C*≡), 103.30 (Ph–*C*≡C–C=N$^2$), 103.75 (Ph–*C*≡C–C=N$^3$), 119.95, 120.42, 128.65, 130.33, 130.48, 132.05, 132.25 (2Ph), 131.08 (C=N$^2$), 137.25 (C=N$^3$), 173.78 (C=S). $^{15}$N NMR, $\delta$: –210.3 (NH, $^1J_{N–H}$ 99.37 Hz), –205.6 (NH, $^1J_{N–H}$ 94.19 Hz), –71.7 (N$^2$=C), –60.7 (N$^3$=C). Found (%): C, 70.01; H, 5.18; N, 15.64; S, 9.21. Calc. for $C_{21}H_{18}N_4S$ (%): C, 70.36; H, 5.06; N, 15.63; S, 8.95.

‡ *Crystallographic data for* **3**: $C_{21}H_{18}N_4S$, $M$ = 358.45, monoclinic, space group $P2_1/n$, $a$ = 7.465(1), $b$ = 24.001(5) and $c$ = 11.465(2) Å, $\beta$ = 107.96(3)°, $V$ = 1954.1(7) Å$^3$, $Z$ = 4, $\lambda$ = 0.7107 Å, $d_{calc}$ = 1.22 g cm$^{-3}$, $\mu$ = 0.191 mm$^{-1}$. X-ray diffraction studies were carried out on a KM-4 KUMA DIFFRACTION diffractometer at room temperature ($\omega/2\theta$-scan mode; MoK$\alpha$ radiation; graphite monochromator). The number of measured reflections, 3957; the number of independent reflections, 2989; the number of refined parameters, 272; $R$-factor 0.054 for 886 reflections with [$F_0 > 4\sigma(F_0)$]. The crystal structure was solved by direct methods and following Fourier synthesis using SHELXS-97.[19] The structure was refined by full-matrix least squares procedures using an anisotropic approximation for all non-hydrogen atoms with the SHELXL-97 program.[20] Hydrogen atoms partly were found experimentally, and partly calculated.

CCDC 645358 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2008.

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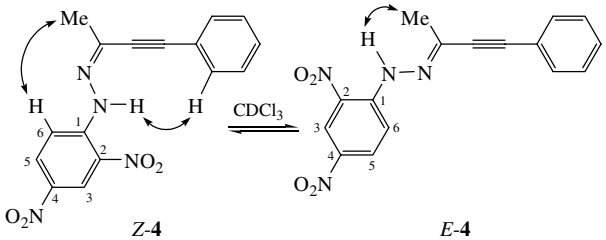
In the $^{13}C$ NMR spectra of hydrazone **3** a very significant difference (~23 ppm) in chemical shifts for α- and β-*sp*-hybridised carbon atoms (internal chemical shift $\Delta\delta_{C_{sp}}$) is observed. This fact can be attributed to the relative positions (*anti*- or *syn*-) of the acetylene moieties and unshared electron pairs of the hydrazone $N^2$ and $N^3$ atoms or, correspondingly, to the possibility of *Z*- and *E*-isomerism of acetylene fragments and NH groups relative to the C=N bonds.

We performed the spectroscopic studies of 4-phenyl-3-butyn-2-one *N*-(2,4-dinitrophenyl)hydrazone specially synthesised using a known procedure.[5] In the $^1H$ and $^{13}C$ NMR spectra of compound **4**,§ two sets of signals indicated the presence of *Z*- and *E*-isomers (ratio of *Z*:*E* ≈ 4:1). Scheme 2 shows (by arrows) doublet–doublet interaction leading to the appearance of cross-peaks in the NOESY spectrum of each isomer: Me ↔ $H^6$, NH ↔ $H_o$ (for *Z*-isomer) and Me ↔ HN (for *E*-isomer).




**Scheme 2**

The value $\Delta\delta_{C_{sp}}$ (23.93 ppm) of the *Z*-isomer of compound **4** observed in the $^{13}C$ NMR spectrum is significantly higher than that of the *E*-isomer ($\Delta\delta_{C_{sp}}$ 4.59 ppm). These data are in good accordance with the results obtained[6] for 4-phenyl-3-butyn-2-one *N*-phenylhydrazone. The signal of carbon atom of the methyl group, which is in an *anti* orientation with respect to the NH group (*Z*-isomer), is shifted low field (δ 22.58 ppm) as compared to the signal of the *E*-isomer (δ 18.11 ppm). Similar difference in chemical shifts of the methyl moiety carbons has been observed for *Z*- and *E*-isomers of ketoximes.[7] Chemical shifts of carbon atoms of the methyl groups in compound **3** are δ 22.47 and 22.66 ppm.

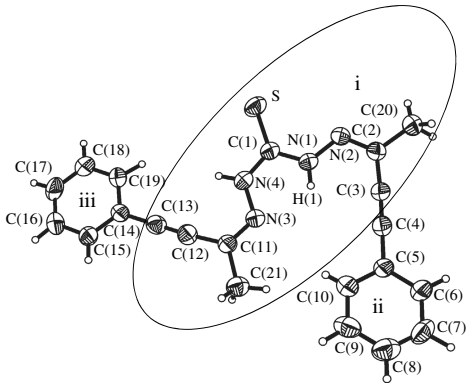



**Figure 1** Conformation and atom labeling in the molecule of **3**. Selected torsion angles (°): N(1)–N(2)–C(2)–C(20) 179.7(6), C(1)–N(1)–N(2)–C(2) 178.0(6), N(2)–N(1)–C(1)–S 5.2(8), N(2)–N(1)–C(1)–N(4) 178.0(5), N(3)–N(4)–C(1)–S 179.8(4), N(3)–N(4)–C(1)–N(1) 2.8(8), C(11)–N(3)–N(4)–C(1) 177.1(5), C(20)–C(2)–C(3)–C(4) 153(11).

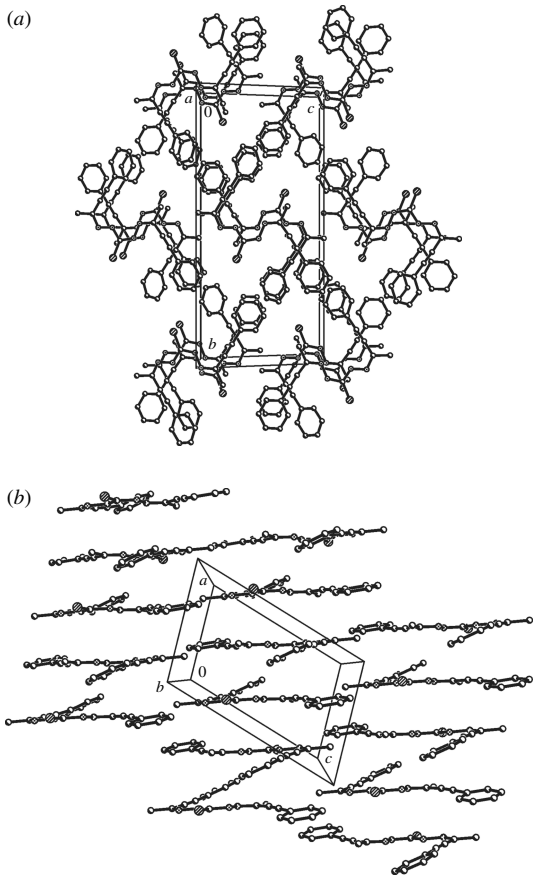



**Figure 2** Crystal structure of **3**.

Thus, the basic spectral characteristics of compound **3** are analogous to those of compound **4** *Z*-isomer that is indicative of close electron structure of (1-methyl-3-phenyl-2-propynylidene)-hydrazine fragments of these compounds. This fact makes it possible to consider these fragments in compound **3** as *Z*-isomers (with respect to the C=N bond).

X-ray analysis data confirm the proposed conformation (*Z-s-trans*), (*Z-s-cis*) of dihydrazone **3**. The crystal structure of the compound is formed by $C_{21}H_{18}N_4S$ molecules (Figure 1), taking general positions in the unit cell. The molecule has a practically planar conformation; a maximum deviation of non-hydrogen atoms from the average plane is 0.61 Å [atom C(9)]. A maximal deviation from the plane (i) for all atoms of the molecule except for the atoms of phenyl group is 0.20 Å [atom C(4)]. The dihedral angle between the planes of phenyl rings (ii) and (iii) equals 161.4°, dihedral angles between planes (i)–(ii) and (i)–(iii) are 156.9° and 169.0°, respectively. In the crystal structure, the molecules are placed one above another, thus forming stacks [Figure 2(*a*),(*b*)] with no short intermolecular contacts.

In summary, we proposed a simple method for the preparation of previously unknown highly functionalised dihydrazone having acetylene bonds – a promising precursor of drugs[8–12] and ligand for the design of multinuclear complexes[10–15] possessing specific properties (redox activity and magnetism).[10,14,16–18]

§ *4-Phenyl-3-butyn-2-one* N-*(2,4-dinitrophenyl)hydrazone* **4**: orange solid, yield 88%, mp 193–194 °C (lit.,[5] mp 193 °C). IR (KBr, ν/cm$^{-1}$): 2175 (w, C≡C), 3266 (NH). $^1H$ NMR, δ: *Z*-isomer: 2.34 (s, 3H, Me), 7.40 (m, $5H_{m,p}$, arom.), 7.69 (d, $2H_o$, arom.), 7.96 (d, $1H^6$, arom.), 8.28 (d, $1H^5$, arom.), 9.12 (s, $1H^3$, arom.), 11.96 (s, 1H, NH); *E*-isomer: 2.32 (s, 3H, Me), 7.40 (m, $5H_{m,p}$, arom.), 7.54 (d, $2H_o$, arom.), 8.05 (d, $1H^6$, arom.), 8.22 (d, $1H^5$, arom.), 9.12 (s, $1H^3$, arom.), 11.28 (s, 1H, NH). $^{13}C$ NMR, δ: *Z*-isomer: 22.58 (Me), 80.33 (≡*C*–CMe), 104.26 (≡*C*Ph), 116.82, 120.20, 123.45, 128.79, 129.31, 129.85, 130.53, 132.59, 138.23, 144.12 (arom.), 136.16 (C=N); *E*-isomer: 18.11 (Me), 87.71 (≡*C*–CMe), 92.30 (≡*C*Ph), 117.04, 121.43, 123.20, 128.52, 129.31, 129.59, 130.09, 132.06, 138.23, 143.96 (arom.), 138.92 (C=N). $^{15}N$ NMR, δ: *Z*-isomer: –224.6 (NH, $^1J_{N–H}$ 98.0 Hz), –65.0 (N=C); *E*-isomer: –225.0 (NH, $^1J_{N–H}$ 97.09 Hz), –64.0 (N=C). Found (%): C, 59.48; H, 3.58; N, 17.15. Calc. for $C_{16}H_{12}N_4O_4$ (%): C, 59.26; H, 3.73; N, 17.28.

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