Journal of Molecular Structure 997 (2011) 46–52

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Structural studies of PCU-hydrazones: NMR spectroscopy, X-ray diffractions, and DFT calculations

Jelena Veljković [a], Marina Šekutor [a], Krešimir Molčanov [b], Rabindranath Lo [c], Bishwajit Ganguly [c,*], Kata Mlinarić-Majerski [a,*]

[a] Department of Organic Chemistry and Biochemistry, Ruđer Bošković Institute, Bijenička cesta 54, P.O. Box 180, 10 002 Zagreb, Croatia
[b] Department of Physical Chemistry, Ruđer Bošković Institute, Bijenička cesta 54, P.O. Box 180, 10 002 Zagreb, Croatia
[c] Analytical Science Division, Central Salt and Marine Chemicals Research Institute (Council of Scientific and Industrial Research), Bhavnagar, Gujarat 364 002, India

ARTICLE INFO

Article history:
Received 7 February 2011
Received in revised form 18 April 2011
Accepted 18 April 2011
Available online 27 April 2011

Keywords:
PCU-hydrazones
NMR spectroscopy
X-ray structural characterization
Density functional calculations

ABSTRACT

In this article we present a detailed structural investigation for the configurational isomers of PCU-hydrazones. The structural characterization of these hydrazones was performed using NMR spectroscopy, X-ray diffraction analysis and theoretical calculations. The single crystal X-ray structures of PCU-hydrazones **6B** and **6C** have been solved and used to conclusively confirm the characterization obtained via NMR spectra of a particular isomer. Nuclear magnetic shielding values calculated for **6A–C** using DFT calculations were correlated with the experimentally determined chemical shifts. The computed results were found to be in good agreement with the observed ^{13}C NMR values. The computed NMR results helped to ascertain the isomers of PCU-hydrazones **4A–C**.

1. Introduction

Polycarbocyclic cage compounds have attracted attention of organic chemists for years, mostly because of their unique properties, e.g. high density, moderate strain energy and great stability, which are the result of their fascinating structural carbocyclic frameworks [1]. In particular, pentacycloundecane derivatives have presented a fairly attractive goal and various synthetic strategies have been developed for their acquirement [2]. In addition, some PCU derivatives have shown a number of interesting pharmacological properties, including antiviral and anti-Parkinsonian activities [3].

Since the preparation of the superbase, 1,8-bis(dimethylamino)naphthalene, known as "proton sponge" [4], many families of proton sponges have been prepared and a growing number of their application found [5–8]. Recently, new organic superbases with the pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (PCU) framework anchored with amines and imines have been reported [9,10]. Our current interest in different PCU proton sponges led us to the preparation of PCU-hydrazones.

Herein, we report the synthesis and structural characterization of new PCU-hydrazones. The structural elucidations of cage compounds have been reported to be difficult and this difficulty arises due to the pronounced similarity of their physical and chemical properties. In the present work, the structural characterization of new PCU-hydrazones was performed with NMR spectroscopy, X-ray diffraction analysis and theoretical calculations. These combined techniques helped us determine the various configurational isomers of the synthesized PCU-hydrazones. The NMR chemical shift calculations performed with DFT method have been found to correlate well with experimentally observed chemical shifts. In some of the cases, X-ray structure analysis determined the conformational geometries of these synthesized PCU-hydrazones.

2. Experimental

2.1. Synthesis and NMR spectroscopy

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-300 or 600 spectrometer at 300 or 600 MHz, respectively. All NMR spectra were measured in $CDCl_3$ using tetramethylsilane as a reference. The assignment of the signals is based on two-dimensional homonuclear correlated spectroscopy (COSY) and heteronuclear multiple quantum coherence (HMQC). IR spectra were recorded on a FT-IR ABB Bomem MB 102 spectrophotometer. MALDI-TOF MS spectra in reflectron mode were obtained on an Applied Biosystems Voyager DE STR instrument (Foster City, CA). Melting points were obtained using an Original Kofler Mikroheitztisch apparatus (Reichert, Wien) and are uncorrected. Silica gel (Merck 0.05–0.2 mm) was used for

* Corresponding authors. Fax: +385 1 4680 195 (K. Mlinarić-Majerski), fax: +91 278 2567562 (B. Ganguly).
E-mail addresses: ganguly@csmcri.org (B. Ganguly), majerski@irb.hr (K. Mlinarić-Majerski).

0022-2860/$ - see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.molstruc.2011.04.030

chromatographic purifications. Solvents were purified by distillation. Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione **1** was prepared according to the procedure described in literature [11].

*2.1.1. Synthesis of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione bis(diphenylhydrazone) (**6**)*

Diketone **1** (380 mg, 2.18 mmol) was dissolved in 15 ml of absolute ethanol or methanol and then *N,N*-diphenylhydrazine (802 mg, 4.36 mmol) was added to the stirred solution. The reaction mixture was refluxed for 5 h and after that time the solvent was evaporated yielding the crude product as dark brown oil quantitatively. The obtained oil was purified by means of column chromatography (silica, eluent ethyl-acetate:chloroform = 5:95) and three isomers of compound **6** were isolated.

Isomer **6A**, white solid, yield 67 mg (6%). m.p. 170–171 °C. IR (KBr, cm^{-1}): 2926 (w), 1586 (m), 1490 (m), 749 (w), 693 (w). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.32 (d, 1H, J = 11.15 Hz), 1.37 (d, 1H, J = 11.15 Hz), 2.19–2.23 (m, 2H), 2.55–2.58 (m, 2H), 2.81–2.85 (m, 2H), 3.37–3.41 (m, 2H), 6.98–7.01 (m, 4H), 7.00–7.03 (m, 8H), 7.19–7.23 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 38.1, 40.4, 43.9, 45.2, 46.8, 121.4, 123.1, 129.2, 148.5, 169.4. HRMS (MALDI) calculated for $[C_{35}H_{30}N_4 + H]^+$ 507.2543, found 507.2529.

Isomer **6B**, white solid, yield 546 mg (49%). m.p. 169–172 °C. IR (KBr, cm^{-1}): 2971 (w), 1588 (s), 1490 (s), 751 (m), 694 (m). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 1.42 (d, 1H, J = 10.84 Hz), 1.64 (d, 1H, J = 10.84 Hz), 2.33–2.36 (m, 1H), 2.49–2.53 (m, 1H), 2.55–2.62 (m, 1H), 2.68–2.73 (m, 1H), 2.75–2.78 (m, 1H), 2.78–2.81 (m, 1H), 2.86–2.90 (m, 1H), 2.90–2.94 (m, 1H), 6.98–7.02 (m, 2H), 7.02–7.05 (m, 2H), 7.05–7.07 (m, 4H), 7.07–7.08 (m, 4H), 7.20–7.23 (m, 4H), 7.24–7.28(m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 38.1, 38.4, 39.9, 41.1, 44.0, 44.6, 46.0, 47.3, 52.4, 121.8, 121.9, 123.1, 123.3, 129.1, 129.2, 147,7, 148.2, 162.6, 169.5. HRMS (MALDI) calculated for $[C_{35}H_{30}N_4 + H]^+$ 507.2543, found 507.2529.

Isomer **6C**, white solid, yield 139 mg (13%). m.p. 172–174 °C. IR (KBr, cm^{-1}): 2975 (w), 1587 (m), 1489 (s), 751 (m), 701 (m), 693 (m). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 1.47 (d, 1H, J = 10.89 Hz), 1.90 (d, 1H, J = 10.89 Hz), 2.40–2.46 (m, 2H), 2.55–2.59 (m, 2H), 2.60–2.64 (m, 2H), 3.18–3.24 (m, 2H), 6.95–6.98 (m, 4H), 6.98–7.02 (m, 8H), 7.16–7.23 (m, 8H). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 38.0, 38.1, 40.4, 45.2, 52.3, 121.2, 123.0, 129.2, 148.3, 167.5. HRMS (MALDI) calculated for $[C_{35}H_{30}N_4 + H]^+$ 507.2543, found 507.2529.

*2.1.2. 3,5-[bis(N,N-diphenylhydrazine)]-4-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane **5***

Compound **5** can be isolated if the reaction time in preparation of hydrazone **6** is shorter. Purification of compound **5** was done by washing the crude product with methanol in which the oxa-derivative is poorly soluble. m.p. 130–132 °C. IR (KBr, cm^{-1}): 3354 (w), 2969 (m), 1588 (s), 1494 (s), 1336 (m), 1330 (m), 1267 (m), 750 (s), 695 (s). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.46 (d, 1H, J = 10.31 Hz), 1.79 (d, 1H, J = 10.31 Hz), 2.53 (br s, 2H), 2.66–2.73 (m, 4H), 2.75 (br s, 2H), 6.96–7.00 (m, 4H), 7.14–7.24 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 42.1, 42.9, 44.3, 45.4, 55.0, 106.9, 120.6, 122.2, 128.9, 149.5.

*2.1.3. Synthesis of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione bis(dimethylhydrazone) (**4**)*

Compound **4** was synthesized in the same manner as compound **6** using diketone **1** and *N,N*-dimethylhydrazine, the only difference being that the isomers of compound **4** could not be successfully isolated from the mixture despite of the use of various separation techniques. No intermediate formation was noticed in this reaction and the obtained mixture was isolated quantitatively as dark brown oil. IR (KBr, cm^{-1}): 3434 (w), 2954 (s), 2863 (m), 1748 (s), 1665 (s), 1466 (s), 963 (m). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.51–1.64 (m), 1.83–1.91 (m), 2.37 (s), 2.41 (s), 2.47 (s), 2.56–2.66 (m), 2.82–2.89 (m), 3.03–3.11 (m), 3.52–3.69 (m). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 36.9, 37.4, 38.2, 38.3, 38.6, 39.5, 40.2, 40.6, 41.1, 42.0, 42.6, 44.3, 45.2, 45.7, 46.0, 46.1, 46.6, 48.1, 48.2, 48.6, 48.8, 50.4, 51.1, 171.1, 172.2, 172.5. HRMS (MALDI) calculated for $[C_{15}H_{22}N_4 + H]^+$ 259.1917, found 259.1929.

2.2. X-ray diffraction data

Monocrystals of compounds **6B** and **6C** for X-ray analysis were obtained from a CH_3OH/CH_2Cl_2 solvent mixture. Single crystal measurements were performed on an Oxford Diffraction Xcalibur Nova R diffractometer (CCD detector, microfocus Cu tube). Program package CrysAlis PRO [12] was used for data reduction. The structures were solved using SHELXS97 and refined with SHELXL97 [13]. The models were refined using the full-matrix least squares refinement; all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located from the difference Fourier map and refined as free entities. Molecular geometry calculations were performed by PLATON [14], and molecular graphics were prepared using ORTEP-3 [15] and CCDC-Mercury [16]. Crystallographic data collection and refinement data for the structures reported in this paper are shown in Table 1.

2.3. Computational details

All calculations were performed with the density functional theory using Becke's three-parameter exchange functional with correlation functional of Lee, Yang, and Parr (B3LYP) [17,18]. All species were fully optimized with 6-31+G* basis set [19], and harmonic vibrational frequency calculations were used to confirm that the optimized structures were minima, as characterized by positive vibrational frequencies. The optimized geometries of PCU derivatives and the reference compound tetramethylsilane (TMS) optimized at B3LYP/6-31+G* level were considered for ^{13}C NMR chemical shifts using the gauge-independent atomic orbital (GIAO) methodology [20]. All quantum chemical calculations were performed using Gaussian 03, Revision E.01 program [21].

3. Results and discussion

*3.1. Synthesis and characterization of PCU-derivatives **2**–**6***

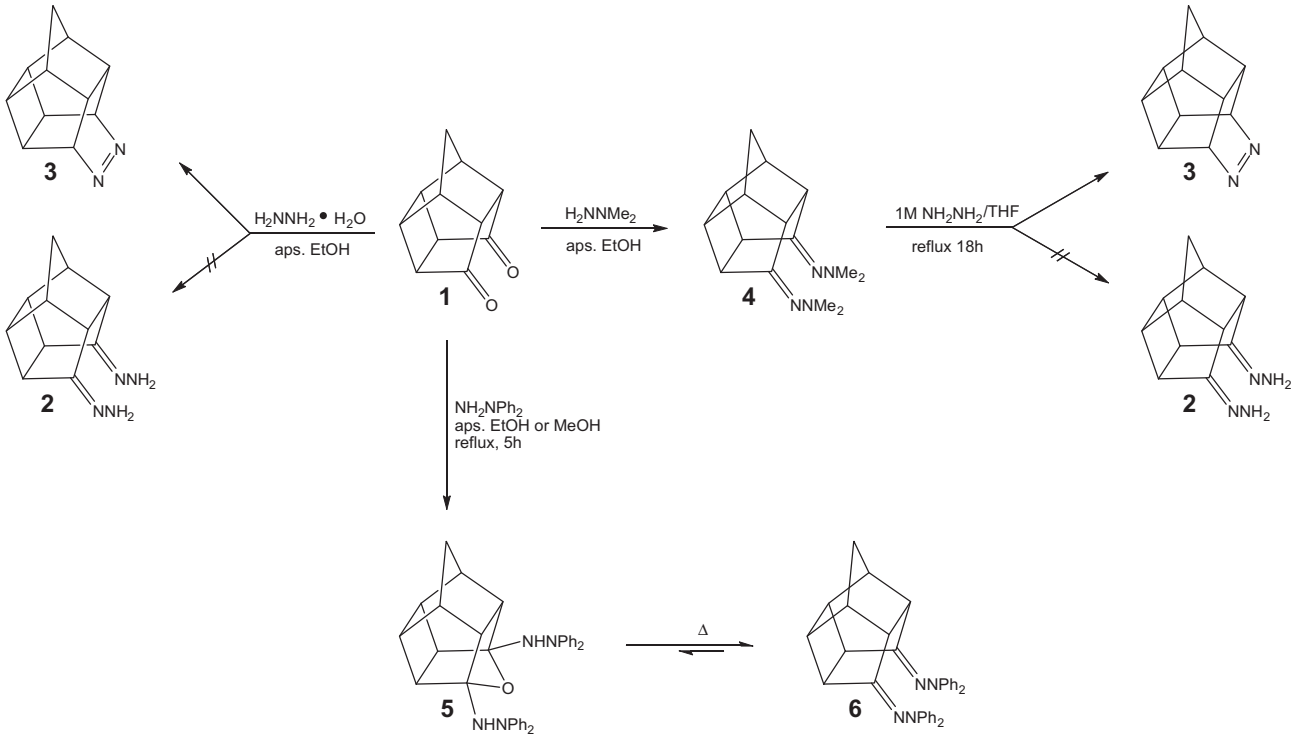
The synthesis of PCU-hydrazones started from Cooksons' dione **1**, as shown in Scheme 1.

The treatment of diketone **1** with hydrazine hydrate, instead of the PCU-hydrazone **2**, afforded diaza-compound **3** as a sole isolated product. However, PCU-hydrazones **4** and **6** have been successfully prepared from diketone **1** and corresponding dimethyl- or diphenylhydrazine, respectively. We used the hydrazone **4** as a starting material for preparation of hydrazone **2** by exchange with H_2NNH_2. Although similar exchange has been reported in the literature [22], again, instead of hydrazone **2** we obtained diaza-PCU-derivative **3**. It is also worth to mention that the formation of hydrazone **6** is a two-step process which proceeds via intermediate **5**. Moreover, we were able to isolate and characterize oxa-PCU derivative **5** (see Section 2). Compound **5** is quite stable as a solid, however, in the solution dehydration to hydrazone **6** takes place.

Products **4** and **6** were obtained as mixtures of three possible configurational isomers **A**, **B** and **C** (Fig. 1) in a ratio of 1:9:2 and 1:8:2, respectively. The **A** and **C** are *meso* compounds and that fact simplifies the NMR spectra since all the atoms except the methylene group at C-4 exist as pairs. In the ^{13}C NMR spectrum of the mixture, based on the symmetry elements of the assumed isomers, there should be, besides the 16 aromatic signals and 4 signals corresponding to four different carbons of C=N groups, 5 signals

Table 1
Crystallographic, data collection and structure refinement details for hydrazones **6B** and **6C**.

Compound	**6B**	**6C**
Empirical formula	$C_{35}H_{30}N_4$	$C_{35}H_{30}N_4$
Formula (wt./g mol^{-1})	506.63	506.63
Crystal dimensions (mm)	0.27 × 0.23 × 0.15	0.37 × 0.30 × 0.23
Space group	$P\,\bar{1}$	$P\,2_1/c$
a (Å)	10.1957(5)	10.7051(1)
b (Å)	11.2141(6)	16.5369(1)
c (Å)	12.9827(7)	15.1857(1)
α (°)	110.889(5)	90
β (°)	102.558(4)	97.928(1)
γ (°)	92.416(4)	90
Z	2	4
V (Å^3)	1341.93(12)	2662.62(3)
D_{calc} (g cm^{-3})	1.254	1.264
μ (mm^{-1})	0.575	0.580
Θ range (°)	2.67–76.07	3.97–76.25
T (K)	293 (2)	293 (2)
Diffractometer type	Xcalibur Nova	Xcalibur Nova
Range of h, k, l	$-10 < h < 12$; $-13 < k < 14$; $-16 < l < 16$	$-13 < h < 13$; $-20 < k < 16$; $-18 < l < 19$
Reflections collected	12,091	25,869
Independent reflections	5532	5532
Observed reflections ($I \geq 2\sigma$)	4496	4992
Absorption correction	Multi-scan	Multi-scan
R_{int}	0.0315	0.0198
R (F)	0.0620	0.0386
R_w (F^2)	0.1858	0.1087
Goodness of fit	1.090	1.075
H atom treatment	Free	Free
No. of parameters	472	473
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (eÅ^{-3})	0.391; −0.260	0.189; −0.163



Scheme 1.

corresponding to configurational isomer **A**, 5 signals for configurational isomer **C**, and 9 signals corresponding to configurational isomer **B** in the aliphatic region. Some signals overlap in the actual spectrum. Based on the molecular symmetry of the configurational isomers and the observed ^{13}C NMR signals, it appears that **B** is the major isomer in this case (Table 2).

We could successfully isolate all three isomers of the phenyl PCU-derivative **6A**, **6B** and **6C** by means of column chromatography and we were able to determine their exact structures by elucidation of their corresponding ^{1}H and ^{13}C NMR spectra, Table 2. The isomer **6B** is obtained as a major product, whereas the isomers **6A** and **6C** are yielded in a much smaller quantity, especially isomer

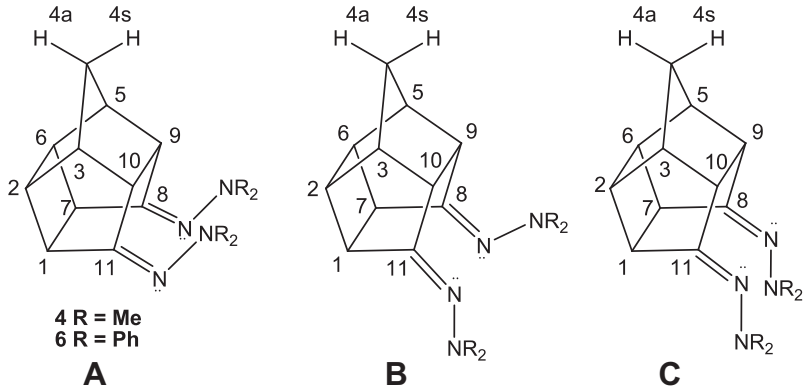
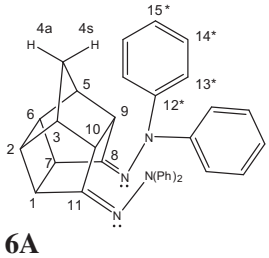
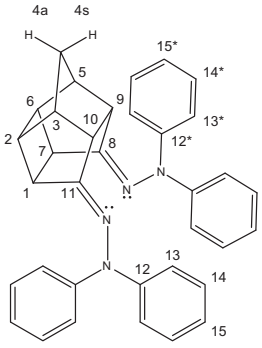


Fig. 1. The possible configurational isomers of PCU-hydrazones **4** and **6**.

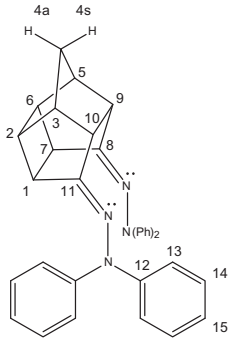
Table 2
^{1}H and ^{13}C NMR chemical shifts for PCU derivatives **6A**, **6B** and **6C** and computed ^{13}C NMR chemical shifts at the B3LYP/6-31+G* level given in parenthesis.



6A



6B



6C

	^{1}H (ppm)	^{13}C (ppm)	^{1}H (ppm)	^{13}C (ppm)	^{1}H (ppm)	^{13}C (ppm)
1	3.37–3.41 (2H, m)	43.9 (49.1)	2.75–2.78 (1H, m)	38.4 (40.6)	2.40–2.46 (2H, m)	40.4 (41.7)
2	2.81–2.85 (2H, m)	40.4	2.55–2.62 (1H, m)	41.1	2.60–2.64 (2H, m)	38.1
3	2.19–2.23 (2H, m)	45.2	2.49–2.53 (1H, m)	44.6	2.55–2.59 (2H, m)	45.2
4a	1.32 (1H, d, *J* = 11.15 Hz)	38.1	1.42 (1H, d, *J* = 10.84 Hz)	38.1	1.47 (1H, d, *J* = 10.89 Hz)	38.0
4s	1.37 (1H, d, *J* = 11.15 Hz)		1.64 (1H, d, *J* = 10.84 Hz)		1.90 (1H, d, *J* = 10.89 Hz)	
5	2.19–2.23 (2H, m)	45.2	2.33–2.36 (1H, m)	46.0	2.55–2.59 (2H, m)	45.2
6	2.81–2.85 (2H, m)	40.4	2.68–2.73 (1H, m)	39.9	2.60–2.64 (2H, m)	38.1
7	3.37–3.41 (2H, m)	43.9 (51.4)	2.86–2.90 (1H, m)	44.0 (49.1)	2.40–2.46 (2H, m)	40.4 (45.4)
8	–	169.4	–	169.5	–	167.5
9	2.55–2.58 (2H, m)	46.8 (49.6)	2.90–2.94 (1H, m)	47.3 (51.3)	3.18–3.24 (2H, m)	52.3 (55.1)
10	2.55–2.58 (2H, m)	46.8 (52.1)	2.78–2.81 (1H, m)	52.4 (59.4)	3.18–3.24 (2H, m)	52.3 (59.9)
11	–	169.4	–	162.6	–	167.5
12	–	–	–	147.7	–	148.3
				148.2		
12*		148.5				–
13	–	–	7.07–7.08 (4H, m)	121.8	6.98–7.02 (8H, m)	121.2
13*	7.00–7.03 (8H, m)	121.4	7.05–7.07 (4H, m)	121.9	–	–
14	–	–	7.20–7.23 (4H, m)	129.1	7.16–7.23 (8H, m)	129.2
14*	7.19–7.23 (8H, m)	129.2	7.24–7.28 (4H, m)	129.2	–	–
15	–	–	6.98–7.02 (2H, m)	123.1	6.95–6.98 (4H, m)	123.0
15*	6.98–7.01 (4H, m)	123.1	7.02–7.05 (2H, m)	123.3	–	–

6A which we isolated in an amount sufficient only for the recording of various spectra. During the isolation we have noticed that isomer **6A** rearranges to isomer **6B** in the solution. Similar rearrangement was observed for the isomer **6C**, but with a slower rate (Fig. S6). Obviously, the **6A**, **6B** and **6C** are configurational isomers stable in the solid state but rearrange to the most stable configurational isomer **6B** in the solution.

The ^{1}H NMR spectrum of isomer **6C** showed geminal bridge methylene protons resonance at δ 1.47 and δ 1.90 ppm (d, *J* = 10.89 Hz), which were assigned to H-4a and H-4s, respectively. The COSY spectrum shows correlations between these methylene protons and resonance at δ 2.55–2.59 ppm which was attributed to H-3/H-5. Protons H-3/H-5 showed COSY correlation to the resonance at δ 3.18–3.24 ppm which is the interaction with H-9/H-10. The remaining methine resonances at δ 2.60–2.64 ppm and δ 2.40–2.46 ppm showed correlation with each other and were assigned as the H-2/H-6 and H-1/H-7, respectively. The assignment of the protons H-2/H-6 at the resonance δ 2.60–2.64 ppm was proved by the correlation with the protons H-9/H-10. Since the proton resonance at δ 6.98–7.02 ppm (*J* = 8.1 Hz) showed correlation with the protons at δ 7.16–7.23 ppm (*J* = 8.1 Hz), they were assigned as the phenyl protons H-13 and H-14, respectively. The remaining resonance

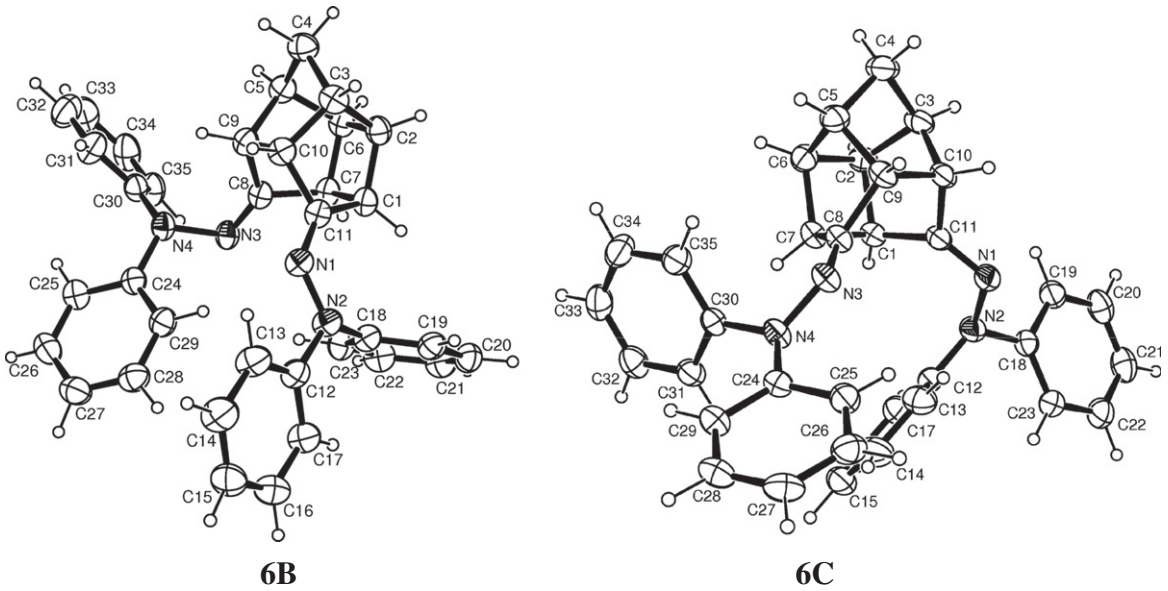


Fig. 2. ORTEP-3 [15] drawing of **6B** and **6C**. Atomic displacement ellipsoids are drawn for the probability of 50% and hydrogen atoms are depicted as spheres of arbitrary radii.

at δ 6.95–6.98 ppm was assigned to H-15. The positions of the corresponding carbon signals were obtained from the HMQC spectrum.

The same methodology was used to solve the NMR spectra of isomer **6A**, and the data of all NMR assignments are given in Table 2.

The major isomer **6B** is an unsymmetrical molecule and its NMR spectra are more complex. The geminal methylene protons H-4a (1.42 ppm, d, J = 10.84 Hz) and H-4s (1.64 ppm, d, J = 10.84 Hz) which exhibit COSY interactions with H-3 (δ 2.49–2.53 ppm) and H-5 (δ 2.33–2.36 ppm) again were the starting point to solve the NMR spectra of isomer **6B**. The H-5 interactions with the resonance at δ 2.68–2.73 ppm and δ 2.90–2.94 ppm were assigned as the interactions with H-6 and H-9 where only H-6 can interact with H-7 (δ 2.89–2.90 ppm). Also, H-3 interactions with the resonance at δ 2.55–2.62 ppm and δ 2.78–2.81 ppm were assigned as the interactions with H-2 and H-10 where only H-2 can interact with H-1 (δ 2.75–2.78 ppm). Regarding the phenyl groups, there are two sets of signals which are assigned according to the coupling constants and the positions in the symmetrical isomers **6A** and **6C** (Table 2). The assignments of the carbon resonances were obtained by APT and HMQC spectra. The structures of isomers **6B** and **6C** were also determined by single X-ray crystallography, Fig. 2.

Significant deviations of N—N bonds can be observed (Table 3), which are result of strain due to sterically bulky $NNPh_2$ substituents. Particularly notable are extremely elongated N1—N2 bond of isomer **6C** and N3—N4 bond of **6B**, which are significantly longer than the sum of covalent radii of nitrogen atoms (1.42 Å).

Elongated N—N bonds are relatively rare, but not uncommon. About 900 such bonds (length 1.42–1.52 Å; a few examples of even longer bonds are outliers and probably results of unresolved errors) are found in the Cambridge Structural Database (CSD), version 5.31, November 2009 and updates 2010 [23]. They are especially common in sterically strained compounds. N—N bonds longer than 1.42 Å are present in 13 out of 23 crystal structures comprising a diphenylhydrazone moiety which have been deposited in the CSD. Due to steric strain, C=N—N angles vary widely between 100 and 130°, as was the case in **6B** and **6C** (data provided in the deposited cif files). Similar steric strain can be observed in analogous diphenylmethylenes: 19% of the fragments (1613 out of 8463 structures) display elongated bonds (more than the sum of covalent radii), with bond angles 100–125°.

Table 3
N—N bond lengths (Å) for PCU derivatives **6B** and **6C**.

Compound	N1—N2	N3—N4
6B	1.385(2)	1.460(2)
6C	1.446(1)	1.407(1)

However, the attempts to separate the PCU-methyl derivatives **4** have failed. The structural determination of **6A**–**6C** using ^{13}C NMR studies can help to establish the conformational geometries of **4A**–**4C**. To ascertain this, we have performed the geometry optimizations using B3LYP/6-31+G* level for **6A**–**6C** and **4A**–**4C**, respectively. Furthermore, we have calculated the ^{13}C NMR chemical shifts for **6A**–**6C** and **4A**–**4C** configurational isomers at the same level of theory. The observed ^{13}C NMR chemical shifts of **6A**–**6C** were compared with the calculated ^{13}C NMR chemical shifts to examine the reliability and its efficacy to establish the conformational geometries of **4A**–**4C**. First, we have performed the DFT B3LYP/6-31+G* calculations for **6A**–**6C** to determine the relative stabilities of these configurational isomers. The calculated geometries were further taken for ^{13}C NMR spectral studies. The phenyl groups of the optimized **6A**–**6C** configurational isomers were modeled with vinyl groups to minimize the computational time. The positions of the atoms in **6A**–**6C** retained the same locations, except for hydrogens which were placed to the deleted carbon centers (Fig. S7).

The calculated results suggest that **6B** is energetically more stable than the corresponding isomers **6A** and **6C**, which corroborates the experimental observation (Fig. 3). The orientations of phenyl groups are similar to the X-ray structure obtained for **6B** (Fig. 2 and Fig. 3). The ^{13}C NMR of **6A**, **6B** and **6C** showed an interesting trend in their observed chemical shifts (Table 2). The aliphatic cage carbons show that their chemical shifts depend on the orientation of imine nitrogen lone-pairs. The imine nitrogen lone-pair closer to the carbon centers leads to deshielding of the carbon nuclei compared to the case where such lone-pairs are away from these centers. The imine nitrogen lone-pairs are orientated in the opposite direction in the case of **6B** (Figs. 2 and 3) and it can be seen that

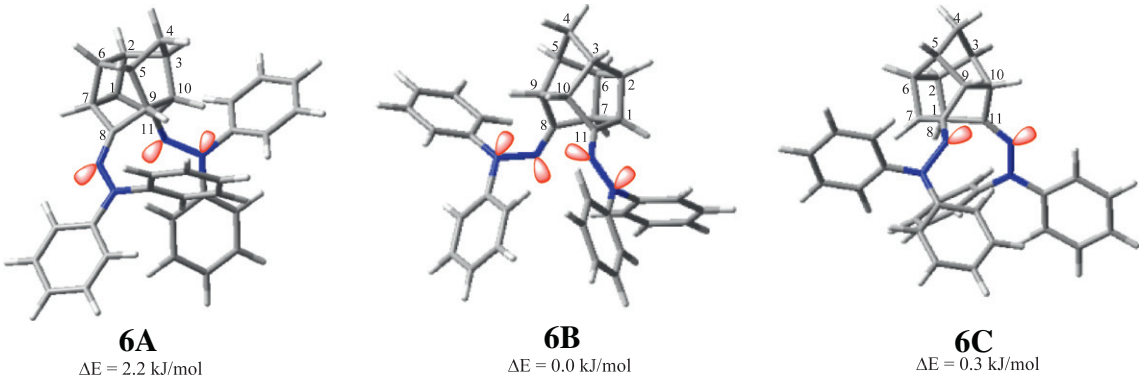


Fig. 3. B3LYP/6-31+G* optimized geometries of three isomers of compound **6** and their relative energies (kJ/mol).

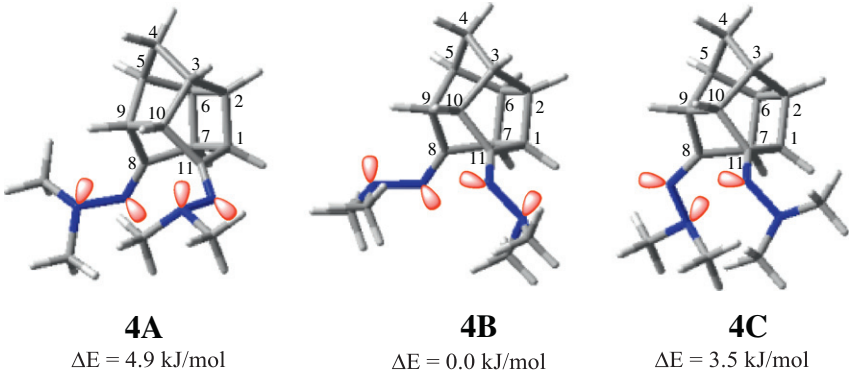


Fig. 4. B3LYP/6-31+G* optimized geometries of three isomers of compound **4** and their relative energies (kJ/mol).

C_7 carbon is more deshielded compared to C_1 (Table 2). A similar situation is observed for the aliphatic carbon centers C_9 and C_{10}, respectively. In the case of **6A** and **6C**, the imine lone-pairs are either oriented towards C_1 and C_7 carbons or C_9 and C_{10} carbons and the lone-pair effect on the chemical shift values of these carbon centers should be observed. The ^{13}C chemical shifts showed the variation in these aliphatic carbon centers for **6A** and **6C** (Table 2). It has been reported that the ^{13}C NMR of α-position to imine center is significantly influenced due to steric compression effect [24]. The ^{13}C NMR chemical shift calculations using GIAO method [20] with B3LYP/6-31+G* level of theory predicted the observed trend for **6A**–**6C**, respectively (Table 2). The variation in the chemical shift values of C_1, C_7 and C_9, C_{10} compared to the experimentally observed values presumably arises due to the modeling of phenyl groups with the vinyl units. Nevertheless, the effect of imine lone-pairs on the ^{13}C chemical shift values for these carbon centers was observed. Interestingly, the isomer **6C** was found to be more stable than **6A** by 1.9 kJ/mol which corroborates the experimental ratios obtained for these isomers. These results indicate that the NMR chemical shift can ascertain the conformation geometries in similar systems.

The DFT B3LYP/6-31+G* calculations were extended with **4A**–**4C**. The calculated results suggest that **4B** is the most stable isomer compared to **4A** and **4C**, respectively (Fig. 4). The calculated product ratios using the energies obtained for the three isomers were 1:7.1:1.7 in reasonable agreement with the observed results.

Further, the ^{13}C NMR chemical shifts have been calculated for the optimized geometries of **4A**–**4C**. The calculated chemical shifts are given in Table 4. The variation in the observed chemical shifts of the aliphatic carbons C_1, C_7 and C_9, C_{10} (**4A**–**4C**) were found to be similar to the values obtained for **6A**–**6C** (Tables 2 and 4). The assignments of ^{13}C NMR chemical shifts for the configurational isomers **4A**–**4C** were based on the relative comparisons of the computed and observed chemical shift values (Table 4). The relative trend of chemical shifts assigned from the observed ^{13}C NMR spectrum for **4B** was found to be in good agreement with the calculated chemical shifts for C_1, C_7 and C_9, C_{10} carbon atoms (Table 4).

Table 4
Computed ^{13}C NMR chemical shifts (in ppm) for compounds **4A**, **4B** and **4C** at the B3LYP/6-31+G* level. Experimental ^{13}C NMR chemical shifts assigned for **4A**–**4C** are given in parenthesis.

Atoms	^{13}C (ppm)		
	4A	**4B**	**4C**
1	47.4 (42.6)	39.5 (37.4)	39.3 (36.9)
7	47.4 (42.6)	47.0 (42.1)	39.3 (36.9)
9	47.5 (45.6)	47.2 (46.1)	55.3 (51.1)
10	47.5 (45.6)	54.9 (50.5)	55.3 (51.1)

4. Conclusions

In the present work, novel PCU-hydrazones have been synthesized. The structural elucidations of PCU-hydrazones configurational isomers were carried out with NMR, single crystal X-ray analysis and DFT calculations. The complete resonance assignments of the ^1H and ^{13}C NMR signals for the PCU-hydrazones **6A–C** are given by using 1D and 2D NMR techniques. Nuclear shielding obtained by using DFT calculations for the optimized molecular geometries of **6A–C** are applied for the identification of similar configurational isomers of PCU-hydrazones **4A–C**.

Acknowledgements

The authors gratefully acknowledge to the Ministry of Science, Education, and Sports of the Republic of Croatia. (Grant Nos. 098-0982933-2911 and 098-1191344-2943) and the Department of Science and Technology, (DST) New Delhi, India, (Grant No. DST/INT/CROATIA/P8/05). One of the authors RL is thankful to UGC, New Delhi, India for Junior research fellowship.

Appendix A. Supplementary material

CCDC 807889 and 807890 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2011.04.030.

References

[1] (a) G.W. Griffin, A.P. Marchand, Chem. Rev. 89 (1989) 997;
(b) A.P. Marchand, Chem. Rev. 89 (1989) 1011;
(c) A.P. Marchand, Advances in Theoretically Interesting Molecules, vol. 1, JAI Press, USA, 1989.
[2] (a) A.P. Marchand, Aldrichim. Acta 28 (1995) 95;
(b) A.P. Marchand, Synlett 2 (1991) 73.
[3] W.J. Geldenhuys, S.F. Malan, J.R. Bloomquist, A.P. Marchand, C.J. Van der Schyf, Med. Res. Rev. 25 (2005) 21.
[4] R.W. Alder, P.S. Bowman, W.R. Steele, D.R. Winterman, Chem. Commun. 13 (1968) 723.
[5] A.F. Pozharskii, Russ. Chem. Rev. 67 (1998) 1.
[6] H.A. Staab, T. Saupe, Angew. Chem. 100 (1988) 895;
Angew. Chem. Int. Ed. Engl. 27 (1988) 865.
[7] R.W. Alder, Chem. Rev. 89 (1989) 1215.
[8] A.L. Llamas-Saiz, C. Foces-Foces, J. Elguero, J. Mol. Struct. 328 (1994) 297.
[9] A. Singh, B. Ganguly, Eur. J. Org. Chem. 23 (2007) 420.
[10] A. Singh, B. Ganguly, New J. Chem. 33 (2009) 583.
[11] A.P. Marchand, R.W. Allen, J. Org. Chem. 39 (1974) 1596.
[12] CrysAlis PRO, Oxford Diffraction Ltd., UK, 2007.
[13] G.M. Sheldrick, Acta Crystallogr., Sect. A: Found. Crystallogr. A64 (2008) 112.
[14] A.L. Spek, J. Appl. Crystallogr. 36 (2003) 7.
[15] L.J. Farrugia, J. Appl. Crystallogr. 30 (1997) 565.
[16] C.F. Macrae, P.R. Edgington, P. McCabe, E. Pidcock, G.P. Shields, R. Taylor, M. Towler, J. ven de Streek, J. Appl. Crystallogr. 39 (2006) 453.
[17] A.D. Becke, J. Chem. Phys. 98 (1993) 5648.
[18] C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785.
[19] W.J. Hehre, L. Radom, P.v.R. Schleyer, J.A. Pople, Ab Initio Molecular Orbital Theory, Wiley, New York, 1988.
[20] K. Wolinski, J.F. Hinton, P. Pulay, J. Am. Chem. Soc. 112 (1990) 8251.
[21] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery Jr., T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J. J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen. M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian 03, Revision E.01, Gaussian, Inc., Wallingford CT, 2004.
[22] G.R. Newkome, D.L. Fishel, J. Org. Chem. 31 (1966) 677.
[23] F.H. Allen, Acta Crystallogr., Sect. B: Struct. Sci. B58 (2002) 380.
[24] (a) C.A. Bunnell, P.L. Fuchs, J. Org. Chem. 42 (1977) 2614;
(b) N.K. Wilson, J.B. Stothers, Top. Stereochem. 8 (1974) 1.