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Predominance of 2-arylhydrazones of 1,3-diphenyl-propane-1,2,3-trione over its proton-transfer products

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ABSTRACT: 2-Phenylhydrazones of 1,3-diphenyl-1,2,3-trione are the dominant tautomeric form detected in chloroform solution by ^{15}N NMR chemical shifts. The substituent in the phenylhydrazone moiety does not affect this tautomeric preference. The substituent effect is transmitted effectively only to the hydrazone nitrogen and hydrogen atoms. *Ab initio* calculations show that the ketohydrazone tautomer is really very much favoured over its proton-transfer products in chloroform solution. The same tautomer was also detected in the crystal state by X-ray crystallography. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: tautomers; ketohydrazones; hydrogen bonding; X-ray diffraction; NMR; *ab initio* calculations

INTRODUCTION

Ketimines compete with enaminone or enolimine tautomeric forms. Such equilibria were found to take place in solutions prepared by dissolving 2-phenacyl substituted pyridines and quinolines in chloroform.[1,2] Strong electron-donating substituents in the phenacyl moiety of these compounds increase the contribution of the ketimine form (its molecule is not stabilized by the hydrogen bond).[1,2]

Proton transfer in monohydrazones of 1,2-diketones is also possible. There are many different basic centres in their molecules. Thus, the tautomeric forms shown in Scheme 1 have to be considered. Their geometric isomers are not stabilized by intramolecular hydrogen bonds. NMR and IR spectra show that, depending on the solvent used, *s-trans*-**KH** is the major or the only tautomer present in solutions obtained by dissolving benzil monophenylhydrazone, PhCOC(Ph)═NNHPh.[3,4] Some typical chemical shifts are noteworthy: δ(N*H*) = 7.9 ppm,[3] $\delta(^{15}N)$ = 8.2 and 12.1 ppm[4] (solutions in chloroform, two different geometric isomers, no reference compound mentioned). Hydrogen-bonding interactions with the solvent are believed to favour the *s-trans* configuration of benzil monophenylhydrazone.[4] Steric interaction between R and R′ (phenyls) is another explanation of such behaviour.

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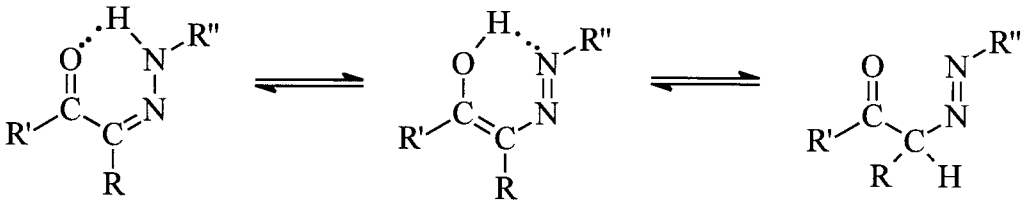
In addition to **KH** (ketohydrazone), **AK** (azoketone) and **AE** (azoenol, see Scheme 1, R = acyl), another azoenol tautomer can also be present in solution obtained by dissolving 2-arylhydrazones of 1,2,3-triones; see Scheme 2.

Studies show that only **KH** is present in solution and in the crystalline state.[5–7] Unlike benzil monophenylhydrazone, 2-arylohydrazones of 1,2,3-triones have the *s-cis* configuration.[5–7] The question arises as to whether the additional carbonyl group in the molecule or substituent in the phenylhydrazone moiety affect the tautomeric and configurational preferences in the mixture containing 2-arylhydrazone of 1,2,3-trione and its products of proton transfer. It is noteworthy that tautomeric equilibrium takes place in solutions of related iminohydrazonopropionitriles and iminohydrazonopropanones.[8,9] Since ketohydrazones contain both the carbonyl group and nitrogen atoms in their molecules, they seemed worthy of study from the point of view of the intramolecular hydrogen bond present. The aim of the present paper is to show the tautomeric preferences in solution of 2-phenylhydrazones of 1,3-diphenylpropane-1,2,3-trione (Scheme 3). Discovering whether the substituent can favour a tautomer different than **KH** seemed very interesting to us.

RESULTS AND DISCUSSION

^{15}N NMR chemical shifts for benzaldehyde phenylhydrazone, Ph—CH═N—NH—Ph, are equal to −237.0 [$^1J(^{15}N,^1H)$ = 92.7 Hz] and −54.0 ppm (solution in



KH **AE** **AK**

Scheme 1

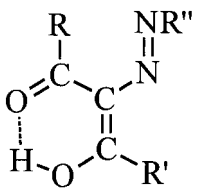
DMSO-d_6).[10,11] Two different ^{15}N signals were always detected in the NMR spectra of compounds **1–14**. Their assignments are based on the cross-peaks in the ^{1}H, ^{15}N heteronuclear multiple-bond connectivities (HMBC) spectra. The chemical shifts (reference: nitromethane) of N1 and N2 in the NMR spectra of compounds **1–14** are very much different from each other and vary in the range $\delta = -210.0$ to -228.0 [$^{1}J(^{15}\mathrm{N},^{1}\mathrm{H}) = 96 \pm 1$ Hz] and -7.0 to -21.8 respectively (Table 1). These numbers show that **KH** is the dominant tautomeric form in chloroform solution. Since the less acidic tautomer always prevails in a tautomeric mixture,[12–16] one can expect this tautomer to be a weaker acid than azoenol, **AE**.

Intramolecular hydrogen bonding in compounds **1–14** results in two benzoyl groups that are not equivalent. This makes their NMR spectra more complex. In order to assign the ^{13}C NMR signals properly, their chemical shifts were calculated using the GIAO-HF/DFT method. Parameterization used in the calculations for the carbon atoms attached to chlorine and bromine is insufficient to obtain reliable ^{13}C NMR chemical shifts (heavy atom effect). The quality of the δ_{calcd} versus δ_{exp} correlation (Table 2) is much better when these chemical shifts are excluded. Thus, the *ab initio* calculations at the HF/B3LYP level of theory (geometry optimization) with the 3-21G and 6-311G (GIAO) basis sets reproduce the experimental ^{13}C chemical shifts with very good accuracy. Similar results were obtained for 2-phenacylpyridines and (*Z*)-2-(2-hydroxy-2-phenylvinyl)pyridines using the same basis set.[17]

It is seen in Table 1 that the chemical shift of H7 is 8.05–8.12 ppm (it was *ca* 7.9 ppm for the *ortho* protons in acetophenone[18]). On the other hand, the position of the H13 signal is *ca* 7.6 ppm. The hydrogen bond is responsible for this downfield shift.

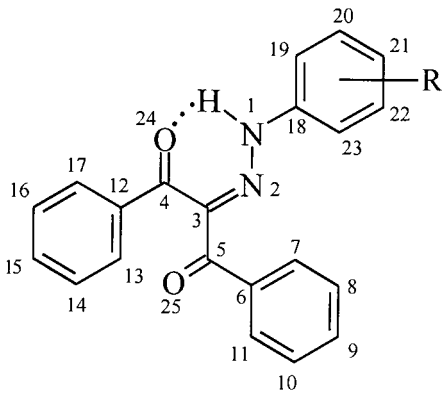
Since only one carbonyl group is involved in the hydrogen bonding, the chemical shifts of C4 and C5 are different from each other (Table 2). The differences δ(C4) $-\delta$(C5) range from 0.75 to 1.71.

The chemical shifts of some atoms were found to be linearly dependent on substituent constants. This is the case for the dependence of H1 (correlation coefficient: 0.972), N1 (0.988), and N2 (0.974) versus σ and H1 (0.990), N1 (0.961), and N2 (0.941) versus σ^{+}. On the other hand, there were no correlations found between the C3, C4, and C5 chemical shifts and both σ and σ^{+}. Thus, the substituent effect in compounds **1–14** is transmitted effectively only to the hydrazone nitrogen and hydrogen atoms. Electron-withdrawing substituents are expected to



AE'

Scheme 2



	R		R
1	4-OMe	**8**	3-OMe
2	4-Me	**9**	2,4-Cl_2
3	H	**10**	2,5-Cl_2
4	4-F	**11**	2,6-Cl_2
5	4-Br	**12**	3,4-Cl_2
6	4-I	**13**	3,5-Cl_2
7	4-NO_2	**14**	2,3,4-Cl_3

Scheme 3

Table 1. Selected experimental ^{1}H and ^{15}N NMR chemical shifts δ of compounds **1–14** for 0.1–0.2 M solutions in $CDCl_3$[a]

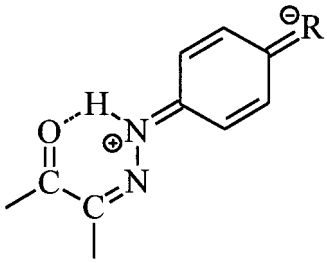
Atom	1	2	3	4	5	6	7	8	9	10	11	12	13	14
H1	13.94	13.72	13.57	13.64	13.44	13.41	13.08	13.46	13.63	13.48	12.99	13.24	13.05	13.57
H7	8.07	8.11	8.12	8.06	8.08	8.07	8.11	8.10	8.09	8.11	8.18	8.08	8.09	8.10
H13	7.66	7.71	7.70	7.68	7.67	7.60	7.68	7.68	7.71	7.69	7.77	7.66	7.66	7.69
N1	−210.7	−211.9	−213.8	−215.6	−217.0	−216.7	−222.2	−214.0	−222.2	−223.5	−228.0	−220.7	−222.1	−222.7
N2	−9.9	−10.9	−12.2	−12.3	−15.0	−15.0	−21.3	−12.1	−20.2	−21.8	−7.0	−17.4	−18.8	−21.8

[a] $^{1}J(^{15}N1, ^{1}H1) = 96 \pm 1$ Hz.

Table 2. Selected experimental[a] and calculated[b] (in parentheses) ^{13}C NMR chemical shifts δ of compounds **1–14**

Atom	1	2	3	4	5	6	7	8	9	10	11	12	13	14
C3	132.99	137.17	136.97	133.80	134.27	134.38	136.69	133.76	135.74	136.19	135.60	134.94	135.42	132.37
	(133.82)	(136.84)	(137.35)	(137.71)	(138.20)	–	(137.48)	(134.63)	(140.62)	(141.00)	(141.66)	(139.55)	(140.09)	(141.24)
C4	192.71	192.68	192.72	192.78	192.75	192.84	192.59	192.78	192.40	192.40	192.51	192.64	192.58	192.32
	(196.15)	(190.93)	(191.20)	(191.37)	(191.49)	–	(196.71)	(196.24)	(191.59)	(191.86)	(191.74)	(196.97)	(192.16)	(191.69)
C5	191.42	191.31	191.32	191.33	191.18	191.21	191.84	191.33	191.09	191.00	191.38	190.98	190.87	190.94
	(192.24)	(197.12)	(197.19)	(197.00)	(196.99)	–	(192.55)	(192.36)	(197.06)	(197.00)	(197.37)	(192.10)	(196.98)	(196.95)
R[c]	0.999	0.999	0.996	0.997	0.976	–	0.997	0.997	0.977	0.979	0.947	0.981	0.978	0.991
					(0.997)				(0.996)	(0.995)	(0.995)	(0.998)	(0.996)	(0.994)

[a] For 0.1–0.2 M solutions in $CDCl_3$ at 303 K.
[b] GIAO-HF/DFT[19] B3LYP/6-311G method.[20]
[c] R is the correlation coefficient of the linear dependence δ_{calcd} versus δ_{exp} for all carbon atoms. Values obtained after rejecting the carbon atoms attached to the heavy atoms (see text) are given in parentheses.



Scheme 4

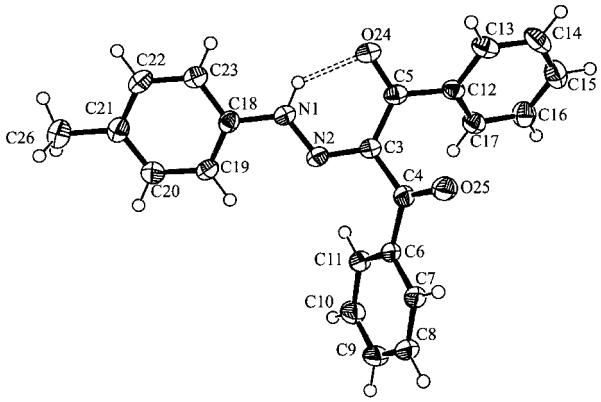
increase the acidity of the hydrogen atom bound to the nitrogen atom (they cause an upfield shift of the N1, N2, and H1 signals). This should result in strengthening of the intramolecular hydrogen bond (Scheme 4).

In general, the calculated lengths of the intramolecular hydrogen bonds in compounds **1–14** (Table 3) follow the substituent effect.

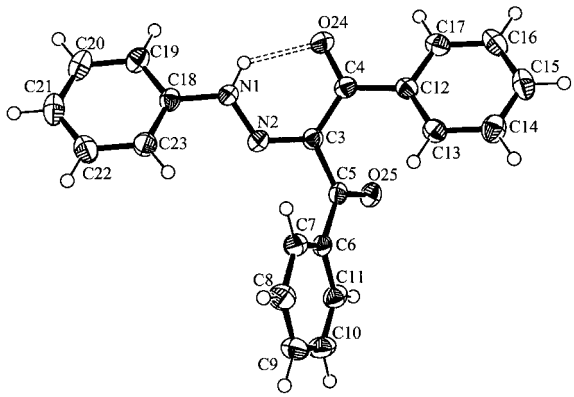
The molecular geometry for **2** and **3** is shown in Fig. 1, and selected geometric data are given in Table 4. In general, the bond lengths and bond angles are comparable for **2** and **3**. Neither molecule is planar. The most significant twist was observed around the C3—C5, C4—C12, C5—C6, and N1—C18 bonds. Surprisingly, the values calculated for **2** and **3** are close to 60°, whereas those found in their crystal structures are close to (−)140°.

One should bear in mind that not only the N—H···O=C in **KH** but also the OH···N and OH···O=C hydrogen bonds in the **AE** and **AE′** tautomers respectively are of resonance-assisted hydrogen bond (RAHB) type.[7] The question arises why only **KH**, including the N—H···O=C hydrogen bond, is present in chloroform solution. Intramolecular hydrogen bonds in the **KH** and **AE** tautomers are both expected to be strong. Another acyl group in the molecule additionally strengthens this bond in **KH**[7] but not in **AE** (Scheme 5).

Theoretical calculations (Table 5) show that **KH** is the most stable tautomer. Energetical differences between



2



3

Figure 1. The ORTEP-3[21] plots of the crystal structures of compounds **2** and **3**. The thermal ellipsoids are drawn at the 50% probability level and the hydrogen bonds are shown as broken bars

the **KH** and **AE** tautomeric forms (strong RAHB are expected to be formed in all these molecules) are large enough to preclude them from being present in the

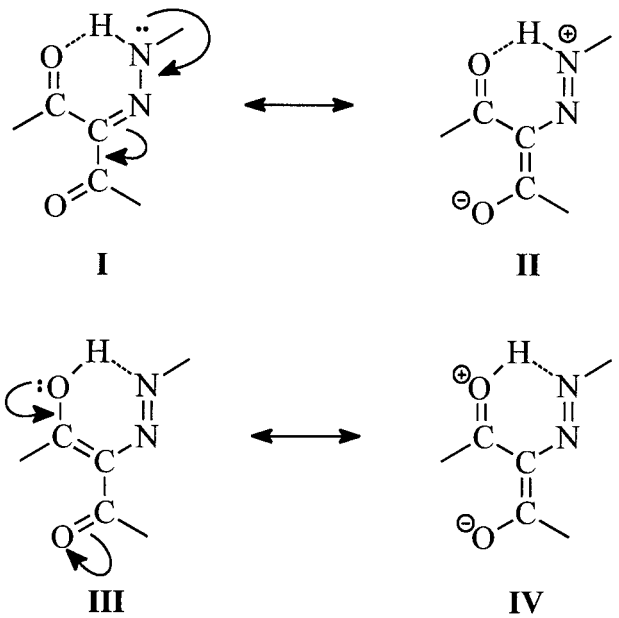
Table 3. *Ab initio* (HF/3-21G) calculated interatomic distances and dihedral angles for the **KH** tautomers **1–14**

	O24···H1 (pm)	O24C4C12C17 (°)	O25C5C6C11 (°)	N2C3C4O24 (°)	N2C3C5O25 (°)
1	188.65	−23.19	−15.26	−18.59	140.99
2	189.49	−23.47	−9.39	−18.99	−56.38
3	189.64	23.37	9.21	19.18	56.85
4	189.32	23.22	9.14	19.27	56.77
5	189.60	−23.07	−8.88	−19.57	−57.48
7	189.71	−21.08	−13.38	−21.35	137.84
8	190.15	−22.36	−14.21	−20.10	140.34
9	191.48	21.89	8.60	21.39	57.95
10	191.29	22.04	8.03	21.08	59.36
11	190.40	22.30	7.24	21.67	63.68
12	189.40	22.60	8.53	20.18	58.19
13	189.22	22.70	7.93	19.93	59.65
14	191.08	21.66	8.45	21.70	58.24

Table 4. Selected bond lengths (pm) and bond and dihedral angles (°) for compounds **2** and **3** at 173 K

	2	**3**
N1—N2	131.1 (2)	131.9 (1)
N2—C3	132.5 (2)	131.8 (2)
C3—C4	147.7 (2)	147.3 (2)
C3—C5	148.8 (2)	149.4 (2)
C4—C12	148.5 (2)	149.1 (2)
C5—C6	149.4 (2)	148.7 (2)
C4—O24	123.9 (2)	123.5 (2)
C5—O25	122.5 (2)	122.9 (2)
N1···O24	257.9 (2)	261.3 (1)
N1···O25	447.0 (2)	444.5 (1)
O24···O25	396.4 (2)	404.8 (1)
N1—C18	140.8 (2)	141.2 (2)
N1N2C3	119.3 (1)	121.2 (1)
N2C3C4	123.8 (1)	124.5 (1)
N2C3C5	115.8 (1)	113.3 (1)
C3C4C12	120.5 (1)	121.0 (1)
C3C5C6	122.6 (1)	120.4 (1)
O24C4C12	118.6 (1)	119.5 (1)
O25C5C6	119.9 (2)	121.4 (1)
C3C4O24	120.7 (2)	119.5 (1)
C3C5O25	117.5 (1)	118.2 (1)
C18N1N2C3	176.0 (1)	−177.5 (1)
N1N2C3C4	−5.2 (2)	8.2 (2)
N1N2C3C5	165.5 (1)	−164.9 (1)
N2C3C4O24	15.1 (2)	−15.2 (2)
N2C3C5O25	−141.1 (2)	132.2 (1)
C3C4C12C17	−145.8 (2)	157.3 (1)
C3C5C6C11	−162.1 (2)	164.0 (1)
O24C4C12C17	39.4 (2)	−26.1 (2)
O25C5C6C11	16.4 (2)	−15.3 (2)
C19C18N1N2	165.3 (1)	−153.6 (1)

tautomeric mixture. As a consequence, **KH** is the only tautomer detected. The large difference in energy between the most stable and the other tautomers is



Scheme 5

Table 5. Calculated[a] relative energies (kJ mol^{-1}) for **3** and its tautomers and absolute energy (a.u.) of the most stable tautomer

Tautomer	Energy
KH	0.00
AE	46.48
AE′	46.70
AK	53.79
Most stable tautomer	−1066.586 370 5

[a] MP2/6-31G**//HF/6-31G** method, polarized continuum model of solvation (solvent: chloroform).

noteworthy. The N—H···O=C in the ketohydrazone tautomer seems to be much stronger than the other hydrogen bonds (OH···N and OH···O=C) present in the molecules of the other tautomers. The dependence of the chemical shifts on the substituent is due to the variation in hydrogen-bond strength.

EXPERIMENTAL

The compounds were obtained by coupling the benzenediazonium ion to 1,3-diphenyl-1,3-propanedione. In principle, the synthetic procedure was that described earlier.[5] The products were purified by recrystallization from ethanol. The yields were very high (71–95%). The melting points (°C) are as follows: **1**, 139–141 (141[22]); **2**, 127–128 (127–129[23]); **3**, 154–155 (154–155[22]); **4**, 118–121; **5**, 143–145 (152–153[22]); **6**, 146–148 (142–143[23]); **7**, 174–176 (173[24]); **8**, 154–156; **9**, 160–162; **10**, 153–154; **11**, 160–164; **12**, 152–153; **13**, 163–165; **14**, 170–173. Satisfactory analytical data (±0.3% for C, H, and N) were obtained for all compounds prepared.

^{1}H, ^{13}C and ^{15}N NMR experiments were run with a Bruker Avance DRX 500 spectrometer working at 500.13 MHz, 125.77 MHz and 50.69 MHz respectively, and equipped with a 5 mm diameter inverse detection probehead and *z*-gradient accessory for 0.1–0.2 M solutions in $CDCl_3$ at 303 K. ^{1}H and ^{13}C NMR chemical shift assignments are based on homonuclear two-dimensional (2D) double quantum filtered (DQF) correlated spectroscopy (COSY) and (2D) heteronuclear pulsed field gradient (PFG) selected ^{1}H, ^{13}C heteronuclear multiple-quantum correlation (HMQC) and HMBC experiments as described in our previous papers.[1,2] The ^{1}H and ^{13}C NMR chemical shifts are referenced to the solvent signal 7.26 ppm from tetramethylsilane (TMS) in ^{1}H experiments and 77.00 ppm from TMS in ^{13}C experiments respectively. ^{15}N NMR chemical shifts are measured from PFG ^{1}H, ^{15}N HMBC correlation maps as before.[1,2] A 1 mm diameter capillary of CH_3NO_2 inserted coaxially inside the 5 mm diameter NMR-tube was used as an external reference for ^{15}N chemical shifts. Detailed NMR

Table 6. Experimental data for the X-ray diffraction studies on **2** and **3** at 173 K

	2	**3**
Formula	$C_{22}H_{18}N_2O_2$	$C_{21}H_{16}N_2O_2$
Formula weight/ g mol^{-1}	342.38	328.36
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/n$ (no. 14)	$P2_1/n$ (no. 14)
Crystal size/mm	$0.30 \times 0.40 \times 0.40$	$0.30 \times 0.35 \times 0.40$
D_{calc}/Mg m^{-3}	1.295	1.313
a/Å	12.2247(5)	9.7232(3)
b/Å	10.2064(5)	10.1709(4)
c/Å	14.1663(6)	17.1549(4)
β/°	96.528(3)	101.756(2)
V/Å^3	1756.1(1)	1660.63(9)
Z	4	4
μ(Mo $K\alpha$)/mm^{-1}	0.084	0.086
Reflections collected	10 221	8814
Independent reflections	3087	2920
R_{int}	0.036	0.025
$\Delta\rho_{max}$, $\Delta\rho_{min}$/e$^-$ Å^{-3}	0.198, −0.185	0.154, −0.181
R/%[a]	4.02	3.60
R_w/%[a]	8.77	8.46
GOF	1.058	1.059

[a] $I > 2\sigma I$

acquisition and processing parameters are available from E.K. on request.

The X-ray crystallographic data for both compounds were recorded with a Nonius Kappa CCD area-detector diffractometer using graphite monochromatized *Mo Kα* radiation [$\lambda(Mo\ K\alpha) = 71.073$ pm] and temperature of 173.0 ± 0.1 K. Lattice parameters were determined from ten images recorded with 1° φ scans and subsequently refined on all data. The data collections were performed using φ and ω scans with 3° steps, an exposure time of 30 s per frame for **2** and 20 s for **3**, and the crystal-to-detector distance was fixed at 30 mm. The data were processed with Denzo-SMN v0.93.0[25] and no absorption correction was applied.

The structures were solved by direct methods (SHELXS-97[26]) and refined on F^2 by full-matrix least-squares techniques (SHELXL-97[27]). The hydrogen atoms were located from the difference Fourier maps, but in the final refinement they were calculated to their idealized positions with isotropic temperature factors (1.2 or 1.5 times the carbon temperature factor) and refined as riding atoms. Other experimental X-ray data are given in Table 6.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos CCDC-157090 and CCDC-157091. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

The substituent constants used are these compiled in Ref. 28. Quantum chemical calculations were performed at the HF and B3LYP levels of theory with the Gaussian 94 package.[29] Geometries were optimized to the global minima at the *ab initio* HF level with the 3-21G basis set using C1-symmetry (no symmetry constraints). The GIAO/DFT calculations for ^{13}C chemical shifts were performed at the B3LYP level with the 6-311G basis set. The chemical shifts are referenced to TMS for ^{1}H and ^{13}C NMR (both in experiment and in calculations), and to nitromethane for ^{15}N NMR.

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