

Solid-State Structure and Tautomerism of 2-Aminotroponimines Studied by X-ray Crystallography and Multinuclear NMR Spectroscopy

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Structural studies in the solid state by X-ray crystallography and by ^{13}C and ^{15}N CPMAS NMR spectroscopy carried out on a series of 2-aminotroponimine derivatives **2–5** has allowed to establish the existence of hydrogen bonding and to determine the most stable tautomer. Almost all the structures reflect the classical double-well potential function for the N–H...N hydrogen bonds. Only in the case of the compound *N*-(pyrrol-1-yl)-2-(pyrrol-1-ylamino)troponimine (**5**) the crystal structure shows two independent molecules, one with a

classical hydrogen bond and another with either a single-well or a low-barrier hydrogen bond. The structure of this compound is discussed with the use of the solid-state NMR spectroscopic data. 2-Aminotropones, as intermediates to the 2-aminotroponimines, show the oxo-tautomer as the stable form. B3LYP/6-31G* calculations are used to rationalise the experimental results.

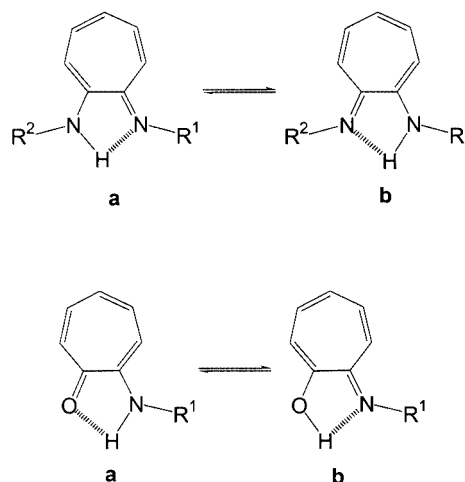
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Introduction

In search of new intramolecular hydrogen-bonded (IMHB) systems, we turned our attention to 2-aminotroponimines **1–5** and 2-aminotropones **6–11** as their intermediates. These compounds, which are diaza and monoaza derivatives of tropolone (**12**), are formally analogues of β -diketones (**13**),^[1] in which the central hydrogen-bonded six-membered ring has been replaced by a five-membered one. In previous papers we already explored the case of 6-amino-fulvene-1-aldimines **14–17**, with a central hydrogen-bonded seven-membered ring.^[2] Our purpose is therefore to provide a complete overview on how these three structural motifs (five-, six- and seven-pseudoring) affect tautomerism, hydrogen bonding and proton transfer, and these changes should be reflected in the NMR parameters.

This paper deals with five 2-aminotroponimines (**1**: $\text{R}^1 = \text{R}^2 = \text{H}$, **2**: $\text{R}^1 = \text{R}^2 = \text{phenyl}$, **3**: $\text{R}^1 = \text{R}^2 = p\text{-bromophenyl}$, **4**: $\text{R}^1 = \text{pyrrol-1-yl}$, **5**: $\text{R}^1 = \text{R}^2 = \text{pyrrol-1-yl}$) and six 2-aminotropones (**6**: $\text{R}^1 = \text{H}$, **7**: $\text{R}^1 = \text{phenyl}$,

8: $\text{R}^1 = p\text{-bromophenyl}$, **9**: $\text{R}^1 = p\text{-chlorophenyl}$, **10**: $\text{R}^1 = \text{pyrrol-1-yl}$, **11**: $\text{R}^1 = 1,2,4\text{-triazol-4-yl}$). Compounds **1** and **6** are model compounds for theoretical studies, as 2-aminotroponimines and 2-aminotropones could exist in two tautomeric forms **a** and **b** (Scheme 1). Tropolone itself (**12**) has been used as a reference compound for structural and proton-transfer studies,^[3] in particular for those concerning the barriers of proton-transfers.

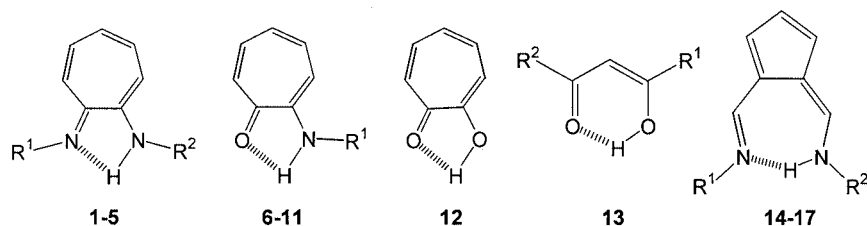


Scheme 1. Tautomeric forms for 2-aminotroponimines and 2-aminotropones

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	R ¹	R ²		R ¹	R ²
1	H	H	9	C ₆ H ₄ -pCl	
2	C ₆ H ₅	C ₆ H ₅	10	Pyrrole	
3	C ₆ H ₄ -pBr	C ₆ H ₄ -pBr	11	1,2,4-Triazole	
4	Pyrrole	C ₆ H ₅	13	H	H
5	Pyrrole	Pyrrole	14	C ₆ H ₅	C ₆ H ₅
6	H		15	Pyrrole	C ₆ H ₅
7	C ₆ H ₅		16	Pyrrole	Pyrrole
8	C ₆ H ₄ -pBr		17	1,2,4-Triazole	C ₆ H ₅

Results and Discussion

Synthesis of 2-Aminotroponimines via 2-Aminotropones

Although *N*-phenyl-2-(phenylamino)troponimine (**2**) had already been prepared from 5,5,6,6- and 6,6,7,7-tetrafluoro-1,3-cycloheptadiene,^[4–6] we have used the more outstanding approach depicted in Scheme 2. The first step was the

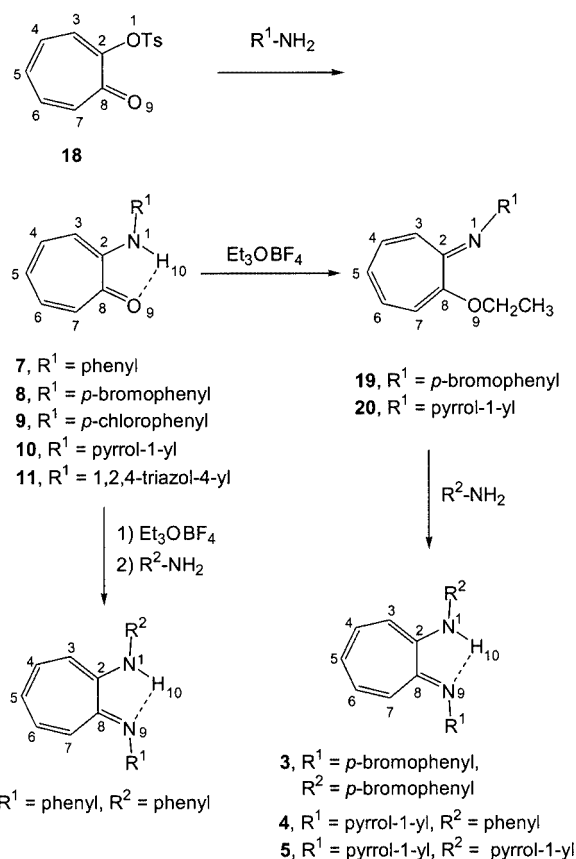
synthesis of 2-(tosyloxy)troponone (**18**, 82% yield)^[7] with a good leaving group to be replaced by anilines and 1-aminoazoles.^[8] For the second step, we modified the method of Rasika et al.^[9] by reducing the excess amine (from 13:1 to 1:1). This second step occurs with moderate yields (**8–11**, 22–40%), but a greater yield is obtained in the case of aniline itself (**7**, 77%).

To transform the 2-aminotropones **7–11** into 2-amino-troponimines **2–5** it was necessary to quaternise them either with triethyloxonium tetrafluoroborate,^[9] methyl trifluoromethanesulfonate,^[10] or dimethyl sulfate.^[11] We selected the triethyloxonium tetrafluoroborate and finally isolated the intermediates **19** and **20**. The reaction with *p*-bromoaniline and 1-aminopyrrole affords the desired compounds **3–5** (44–73% yield). The diphenyl derivative **2** was prepared directly from **7** with 26% yield.

Some labelled derivatives of the four 2-aminotroponimines were analogously prepared: **2**-¹⁵N₂ (N-1, N-9), **2**-²H₁ (10-D), **2**-¹⁵N₂-²H₁ (N-1, N-9, 10-D); **3**-²H₁ (10-D); **4**-¹⁵N (N-1), **4**-²H₁ (10-D), **4**-¹⁵N-²H₁ (N-1, 10-D); **5**-²H₁ (10-D) (Figure 1).

Crystal and Molecular Structures

A search through the Cambridge Crystallographic Data Base (version 5.25, November 2003) resulted in only three X-ray structures of related compounds: *N*-methyl-2-methylamino)troponimine (**21**),^[12] *N*-isopropyl-2-(isopropylamino)troponimine (**22**)^[9] and (*R*)- α -*N*-methylbenzyl-2-[(*R*)- α -(methylbenzylamino)]troponimine (**23**).^[13] In compounds **22** (ZIPKEO, trigonal, *P*3, *Z* = 6) and **23** (VAWTES, orthorhombic, *P*2₁2₁2₁, *Z* = 4), the hydrogen atom is always localised on N1 and the system presents a clear alternation of single and double bonds. From compound **21** (MAMICH, orthorhombic, *I*ba2, *Z* = 8), the authors concluded from the X-ray data that the two nitrogen atoms are chemically equivalent, but they were unable to locate the proton of the hydrogen bond bridge.



Scheme 2. Outline of the synthetic route used to prepare the compounds

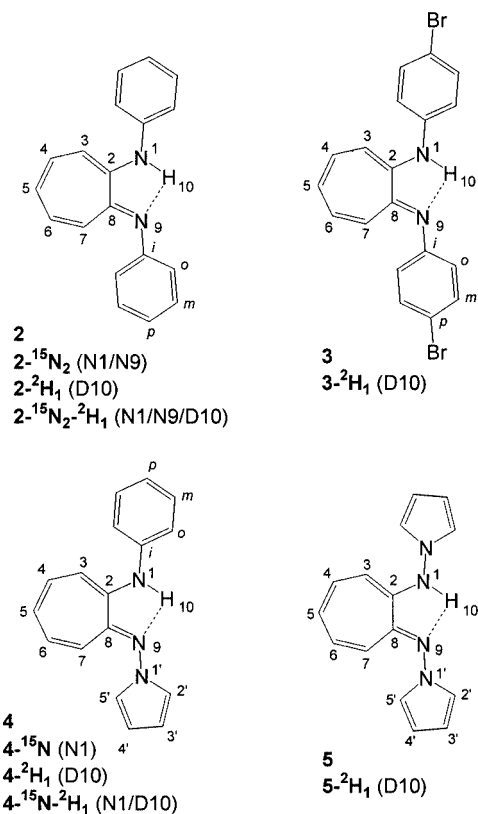
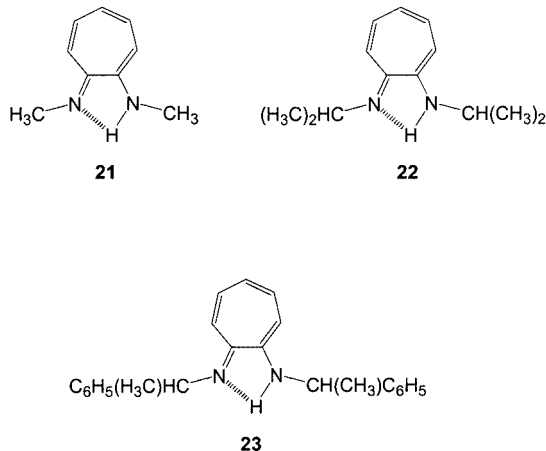


Figure 1. 2-Aminotroponimines 2–5



In the case of the new 2-aminotroponimines 2–5 analysed by X-ray diffraction, we have found two monoclinic crystal systems with space group $P2_1/c$ for compounds 2 and 5 and two triclinic crystal systems with space group $P\bar{1}$ for derivatives 3 and 4 (see Exp. Sect.).

In all cases there are two independent molecules in the asymmetric unit that show slight differences with respect to the hydrogen bond. Selected bond lengths and angles are collected in Table 1. In *N*-phenyl-2-(phenylamino)troponimine (2), both molecules are disposed face-to-face (Figure 2) with the localisation of protons that present intramolecular hydrogen bonds, $\text{N11-H11}\cdots\text{N91}$ and $\text{N12-H12}\cdots\text{N92}$ (Table 2). Additionally, in the *p*-bromophenyl derivative 3, one molecule contains an asymmetrical

bifurcated hydrogen bond which connects both molecules through a weak hydrogen bond $\text{N11-H11}\cdots\text{Br}(12)$. This fact leads to dimer pair units as depicted in Figure 3. In the case of the *N*-(pyrrol-1-yl)-2-(phenylamino)troponimine (4), both molecules have an intramolecular hydrogen bond but their relative disposition can be considered as back-to-back (Figure 4). In compound 5, one molecule has an intramolecular hydrogen bond, $\text{N11-H11}\cdots\text{N91}$, whereas in the second molecule the hydrogen bond involving H12 appears to be centred to both N atoms (Figure 5) and could therefore be considered a symmetric hydrogen bond. This assumption is corroborated by the distances found for $\text{N}(12)\cdots\text{H}(12)$ (1.48 Å) and $\text{N}(92)\cdots\text{H}(12)$ (1.56 Å), as seen in Table 2.

Table 1. Selected bond lengths (Å) and angles (°) for 2-aminotroponimines 2, 3, 4 and 5

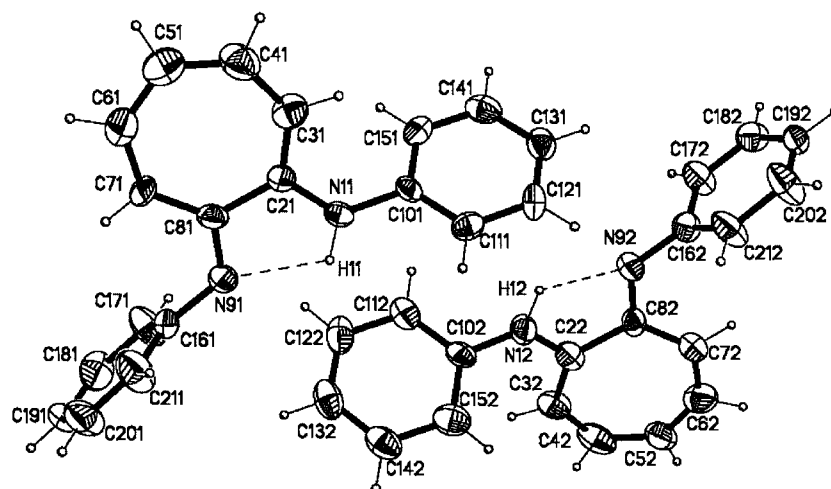
Molecule	2 M1	3 M1	4 M1	5 M1
N11–C21	1.36(1)	1.358(6)	1.367(3)	1.370(4)
N11–El ^[a] 101	1.43(1)	1.426(6)	1.407(3)	1.380(3)
C21–C81	1.48(2)	1.494(6)	1.470(3)	1.465(4)
C81–N91	1.31(1)	1.310(6)	1.312(2)	1.314(4)
N91–El ^[b] 161	1.43(1)	1.429(6)	1.407(2)	1.414(4)
C131–Br11		1.885(5)		
C191–Br21		1.895(5)		
C21–N11–El ^[a] 101	128(1)	129.1(4)	130.4(2)	120.7(3)
C21–N11–H11	117(5)	115.9	106.6	120.5
El ^[a] 101–N11–H11	115(5)	114.9	122.4	118.8
N11–C21–C81	114(1)	112.9(5)	111.7(2)	111.3(4)
C21–C81–N91	112(1)	112.4(5)	112.6(2)	112.2(3)
C81–N91–El ^[b] 161	123(1)	121.7(4)	116.9(2)	114.8(3)
Molecule	M2	M2	M2	M2
N12–C22	1.35(1)	1.345(6)	1.360(3)	1.341(4)
N12–El ^[a] 102	1.37(1)	1.397(6)	1.410(3)	1.394(4)
C22–C82	1.49(2)	1.471(7)	1.484(3)	1.472(5)
C82–N92	1.32(1)	1.316(6)	1.316(3)	1.336(4)
N92–El ^[b] 162	1.38(1)	1.407(6)	1.410(2)	1.384(4)
C132–Br12		1.917(5)		
C192–Br22		1.892(6)		
C22–N12–El ^[a] 102	126(1)	128.0(5)	129.5(2)	118.0(3)
C22–N12–H12	115(5)	116.0	111.9	104.4
El ^[a] 102–N12–H12	117(5)	116.0	118.5	136.8
N12–C22–C82	111(1)	111.0(5)	111.8(2)	111.4(4)
C22–C82–N92	114(1)	114.1(5)	111.6(2)	111.7(4)
C82–N92–El ^[b] 162	120(1)	125.7(5)	116.2(2)	117.2(3)

[a] El $\equiv$ C for 2, 3 and 4 and N for 5. [b] El $\equiv$ C for 2 and 3, and N for 4 and 5.

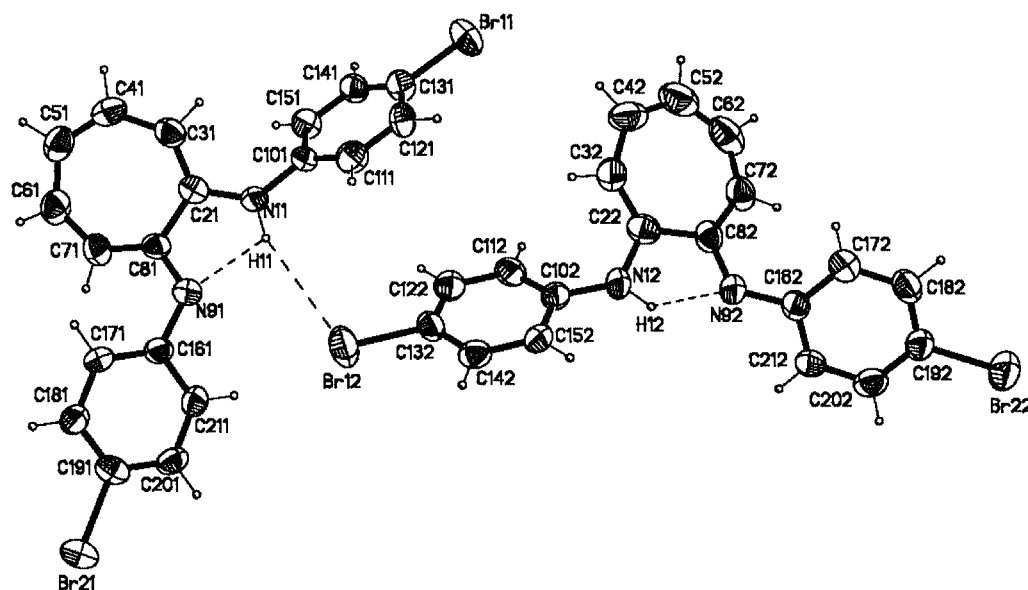
Multinuclear NMR Studies

Solid State

The ^{13}C and ^{15}N CPMAS NMR chemical shifts of 2-aminotroponimines 2–5 are presented in Table 3 and are consistent with the results obtained from the X-ray diffraction analysis. The assignments have been made on the basis of the solution NMR spectroscopic data (see below and Exp. Sect.).

Figure 2. X-ray asymmetric unit of *N*-phenyl-2-(phenylamino)troponimine (**2**)Table 2. Hydrogen bonds for **2**, **3**, **4** and **5** (*d*, Å)

Compound molecule	D–H...A	<i>d</i> (D–H)	<i>d</i> (H...A)	<i>d</i> (D...A)	<(DHA)
2 M1	N(12)–H(12)···N(92)	1.05(9)	1.98(8)	2.51(1)	109(6)
2 M2	N(11)–H(11)···N(91)	0.98(10)	2.05(10)	2.52(2)	107(7)
3 M1	N(11)–H(11)···Br(12)	0.97	3.10	4.031(4)	161.7
3 M1	N(12)–H(12)···N(92)	0.87	2.04	2.505(6)	112.8
3 M2	N(11)–H(11)···N(91)	0.97	2.06	2.532(6)	108.2
4 M1	N(11)–H(11)···N(91)	1.05	1.81	2.482(3)	118.4
4 M2	N(12)–H(12)···N(92)	1.05	1.90	2.480(3)	110.7
5 M1	N(11)–H(11)···N(91)	1.17	2.00	2.464(4)	98.5
5 M2	N(12)···H(12)···N(92)	1.48	1.56	2.455(4)	108.1

Figure 3. X-ray asymmetric unit of *N*-(*p*-bromophenyl)-2-(*p*-bromophenylamino)troponimine (**3**)

In all cases, we observed signals due to the presence of two independent molecules in the asymmetric unit cell. In compounds **2–4**, in which the two molecules contain a

localised proton, N-1/10-H, intramolecularly bonded to N-9, the ^{15}N NMR chemical shift for N-1 appears at about -252 ppm (between -223.2 and -268.2 ppm), whereas for

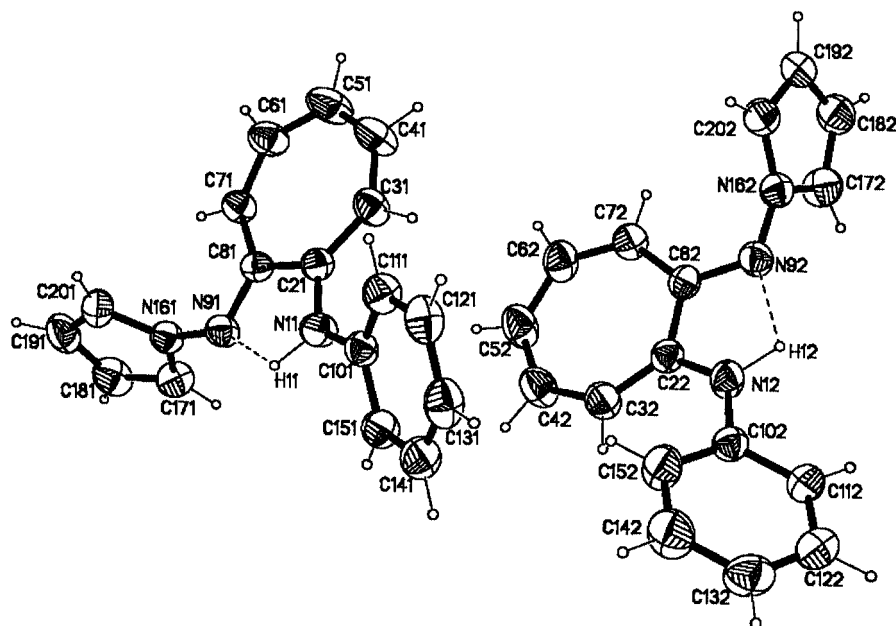


Figure 4. X-ray asymmetric unit of *N*-(pyrrol-1-yl)-2-(phenylamino)troponimine (**4**)

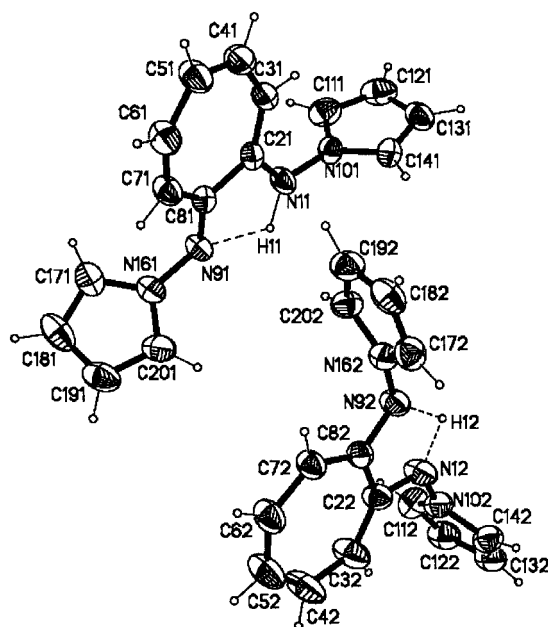


Figure 5. X-ray asymmetric unit of *N*-(pyrrol-1-yl)-2-(pyrrol-1-yl-amino)troponimine (**5**)

N-9 the average value is -122 ppm (between $\delta = -103.8$ and -161.1 ppm). The difference between the N-1/N-9 values of both independent molecules is due to the effect of the substituent on the chemical shift. The observed ^{15}N NMR chemical shift values for the NH_2 group in aniline ($\delta = -322.0$ ppm), *p*-bromophenylaniline ($\delta = -319.7$ ppm) and 1-aminopyrrole ($\delta = -309.5$ ppm) support this statement.

The most interesting case, *N*-(pyrrol-1-yl)-2-(pyrrol-1-yl-amino)troponimine (**5**), also presents two molecules in the unit cell. ^{15}N NMR chemical shifts for one of the molecules

are close to the above-mentioned values for N-1 ($\delta = -253.9$ ppm) and for N-9 ($\delta = -111.5$ ppm). In contrast, only very broad signals in the range of -190 – -170 ppm corresponding to the two types of nitrogen atoms (note that the average of -252 and -122 is -187 ppm) are detected in the second molecule. Sharp signals assigned to the pyrrole nitrogen atoms are observed at $\delta = -194.0$ ppm and -200.6 ppm (Table 3, $\Delta\delta = 6.6$ ppm). For the other independent molecule **5**, these signals appear with a greater separation ($\Delta\delta = 28.3$ ppm).^[14]

In order to better understand this observation, we had a closer look at selected solid-state chemical shifts (Table 3) and tried to align them to geometrical parameters (Table 2). The selected chemical shifts were those corresponding to N-1/N-9 and to C-2/C-8, which are expected to be more sensitive to *a/b* tautomerism in 2-aminotroponimines. Note that the crystallographic data shows two independent molecules (M1 and M2), but it is practically impossible to differentiate between them by use of CPMAS NMR for compounds **2**–**5**. Thus, we decided to simply assume a “normal” molecule in the case of **5** M1 and a “proton-shared molecule” in the case of **5** M2. The most significant NMR spectroscopic results show the differences in chemical shifts ($\Delta\delta$ ppm), whereas the most useful crystallographic data show the differences between distances, i.e. $d(\text{H}\cdots\text{A})$ and $d(\text{D}–\text{H})$, which is a frequent and useful way (usually also described as $r_1 - r_2$) to discuss hydrogen bonds in crystallography^[15] and NMR spectroscopy.^[16] As summarised in Table 4, all parameters could be correlated with sometimes moderate correlation coefficients. Note that all slopes are positive, as expected.

It is well known that the ^{15}N NMR spectroscopy is more sensitive to tautomerism and steric effects and perturbations than ^{13}C NMR spectroscopy due to the closeness of the relevant atoms to the tautomeric site and the larger

Table 3. ^{13}C and ^{15}N CPMAS NMR chemical shifts (δ , ppm) of **2**, **3**, **4** and **5**

Compound	2		3		4		5	
	M1	M2	M1	M2	M1	M2	M1	M2
C-2	140.2	141.8	139.3	141.1	139.2	137.2	149.6	153.8 (br.)
C-3	108.9	110.5	112.2	110.1	110.8	110.0	113.1	117.5 (br.)
C-4	133.5	133.9	133.8	133.8	135.3	135.3	135.7	134.5 (br.)
C-5	125.4	125.4	125.6	125.6	122.5	122.5	125.5	124.9
C-6	132.3	132.9	132.8	132.8	135.3	135.3	134.5	134.5
C-7	118.9	120.5	120.6	118.9	120.2	119.5	115.6	117.5 (br.)
C-8	151.0	154.5	153.9	151.5	160.8	161.4	160.6	156.3 (br.)
<i>i</i> -C _{arom.} ^[a]	150.7 (2 C)/150.3/149.3		148.6/147.1 (2 C)/144.8		144.4	144.4	—	—
C-2'/C-5'	—	—	—	—	118.0	118.3	121.9/120.9	120.1 (br.)
C-3'/C-4'	—	—	—	—	105.7	105.7	108.8/108.1	107.0 (br.)
N-1	−239.9	−261.5	−251.8	223.2	−268.2	−268.2	−253.9 (br.)	ca. −190 (v br.)
N-9	−134.5	−114.2	−129.4	−161.1	−107.1	−103.8	−111.5 (br.)	ca. −170 (v br.)
−102.4	—	—	—	—	—	—	—	—
N-1'	—	—	—	—	−185.5	−183.9	−183.6/−211.9	−194.0/−200.6

^[a] For compound **1**: *o*-C_{arom.} 124.1/123.5/121.9 (4 C)/121.5/120.5, *m*-C_{arom.} 132.9/130.1(br., 7 C), *p*-C_{arom.} 127.8 (br)/126.5 (br); for compound **2**: *o*-C_{arom.} 125.6 (2 C)/124.2 (2 C)/121.9(2 C)/120.6(2 C), *m*-C_{arom.} 133.8 (br)/132.8 (br)/128.6, *p*-C_{arom.} 115.9 (br); for compound **3**: *o*-C_{arom.} 123.9, *m*-C_{arom.} 131.0 (br), *p*-C_{arom.} 125.4.

Table 4. Most relevant CPMAS NMR spectroscopic data (Table 3, ppm) and crystallographic data [Table 2 (Å)]

Comp.	2 (M1)	2 (M2)	3 (M1)	3 (M2)	4 (M1)	4 (M2)	5 (M1)	5 (M2)
$\Delta\delta$ (N-9/N-1)	105.4	147.3	122.4	62.1	161.1	165.1	142.4	≈ 20
$\Delta\delta$ (C-8/C-2)	10.8	12.7	14.6	10.4	21.6	24.4	11.0	2.5
$r_1 - r_2$	0.93	1.07	1.17	1.09	0.76	0.85	0.83	0.08
ratio ^[a]	1.038	1.023	1.037	1.022	1.042	1.033	1.043	1.004
ratio −1	0.0382	0.0227	0.0366	0.0220	0.0419	0.0334	0.0426	0.0037
Correlations (no intercept) ^[b]								
$\Delta\delta$ (N-9/N-1) = $(8.2 \pm 0.7) \Delta\delta$ (C-8/C-2), $r^2 = 0.95$								
$\Delta\delta$ (N-9/N-1) = $(129 \pm 18) (r_1 - r_2)$, $r^2 = 0.88$								
ratio −1 = $(0.25 \pm 0.02) 10^3 \Delta\delta$ (N-9/N-1), $r^2 = 0.94$								

^[a] The ratio is defined as $d(\text{N1} - \text{C2})/d(\text{C8} - \text{N9})$ (Table 1). ^[b] All these properties became 0 when the proton is in the middle or when the exchange between tautomers is fast in the NMR time scale.

chemical shift anisotropy. By Considering compound **4a** as the model compound without tautomerism or proton disorder and with ^{15}N NMR chemical shift values of $\delta = -268$ ppm [$-\text{N1}(\text{H}) - \text{Ph}$] and -105 ppm ($=\text{N9} - \text{Pyr}$), we have estimated the effect of the replacement of substituents (phenyl ring by a *p*-bromophenyl ring or a 1-pyrrolyl ring^[17–20]) on the ^{15}N chemical shifts. The results are shown in Figure 6 as chemical shifts differences $\Delta\delta$ (N-9/N-1).

A comparison of the estimated values with those of Table 3 shows on one hand that the average values for **2**, **3** and **5** are similar to the values presented in Table 3, which are also very similar to the chemical shifts measured in solution. On the other hand, the differences always lie in the 145–150 ppm range; only **2** M1 and **5** M1 show differences (147 and 142 ppm, respectively). This is in agreement with the presence of only one tautomer with a localised proton in the solid state. In the case of **5** M2, the chemical shift difference of about 20 ppm corresponds to a situation in which two tautomers are present with a very fast proton exchange rate. By X-ray crystallography the foregoing situation cannot be distinguished from another with a localised proton in the centre of both nitrogens (N-1/N-9). The re-

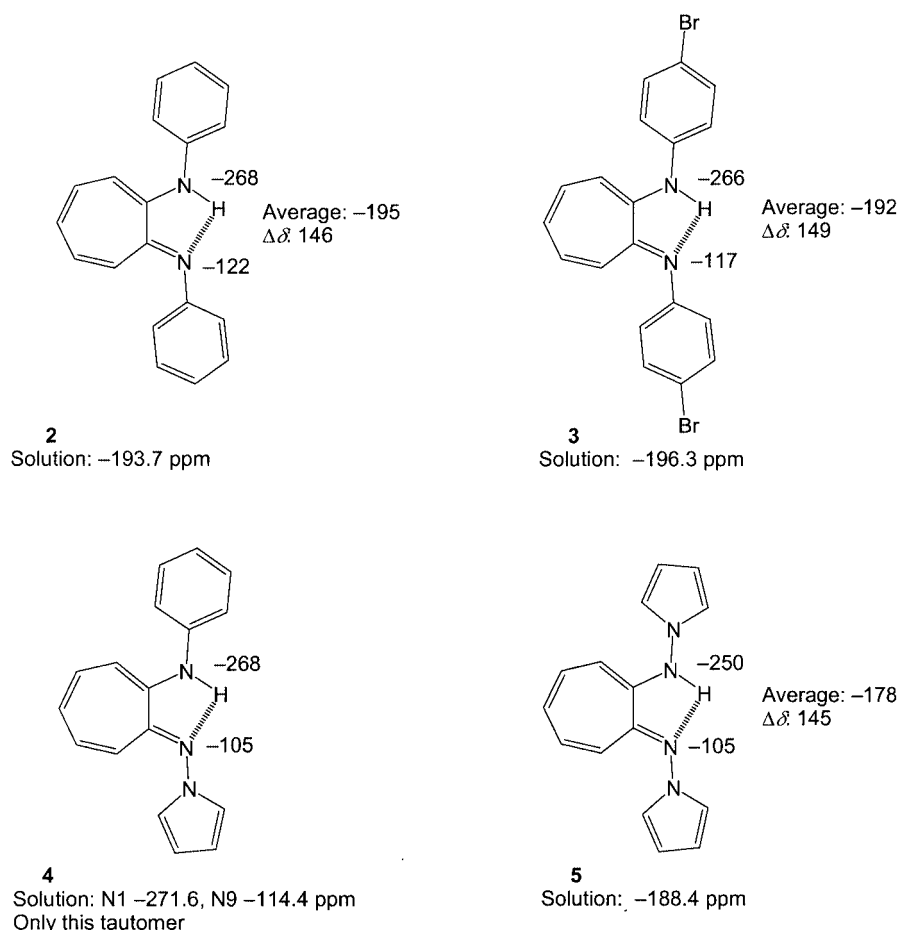
maining three cases (**2** M2 with $\delta = 105$ ppm, **3** M1 with $\delta = 122$ ppm and **2** M2 with 62 ppm) are indicative of some dynamic asymmetric disorder with different **a/b** populations of both tautomers.

Solution NMR Studies Related to Tautomerism

The ^1H NMR, ^2H NMR, ^{13}C NMR, ^{15}N NMR and ^{17}O NMR chemical shifts and coupling constants for 2-aminotroponimines **2–5** and 2-aminotropones **7–11** are reported in the Exp. Sect. (see Scheme 2 for numbering of the NMR positions).

Assignments have been made with the help of ^1H - ^1H gs-COSY, ^1H - ^1H gs-NOESY, ^1H - ^{13}C gs-HMQC and ^1H - ^{13}C gs-HMBC experiments. ^{15}N NMR chemical shifts and coupling constants $^1J(\text{N-1}, 10\text{-H})$ were obtained by 2D inverse proton detection heteronuclear shift correlation spectra gs-HMBC, as depicted for compounds **7** and **10** in Figure 7.

With regard to tautomerism, from the data gathered in Table 5, we can conclude that in the 2-aminotropones only tautomer **a** is present with $\delta^{15}\text{N-1}$ ranges from -266.8 ppm to -288.7 ppm and $\delta^{17}\text{O-9}$ from 381.5 ppm to 395.4 ppm.

Figure 6. ^{15}N CPMAS NMR spectroscopic data for 2-aminotroponimines **2–5**Table 5. Summary of the most relevant NMR spectroscopic data in CDCl_3 at room temperature for aminotroponimines and aminotropones (for the remaining data see the Exp. Sect.)

Compound	δ 10- ^1H	δ 10- $^2\text{H}^{[a]}$	$\delta^{15}\text{N-1}$	$\delta^{15}\text{N-9}$	$\delta^{17}\text{O-9}$	$^1J(\text{N-1},10\text{-H})$	$^{2h}J(\text{N-1},\text{N-9})$
2	9.20	9.09	-193.7	-193.7	—	44.6 ^[b]	5.3 ^[c]
3	9.04	8.99	-196.3	-196.3	—	—	—
4	8.75	8.72	-271.6	-114.4	—	89.9 ^[d]	—
5	8.96	8.93	-188.4	-188.4	—	—	—
7	8.76	8.74 ^[e]	-271.7	—	384.8	92.4 ^[f]	—
8	8.67	8.65	-274.4	—	381.5	92.2 ^[f]	—
9	8.68	8.66	-274.0	—	386.6	92.6 ^[f]	—
10	8.88	8.87	-266.8	—	395.4	103.5 ^[f]	—
11	8.98	8.94	-288.7	—	n.o. ^[g]	n.o. ^[g]	—

[a] $\text{CDCl}_3 + \text{D}_2\text{O}$. [b] $[\text{D}_6]\text{DMSO}$, $2\text{-}^{15}\text{N}_2$. [c] Obtained by iterative analysis using Win-Daisy 3.0.^[23] [d] $[\text{D}_8]\text{THF}$, $4\text{-}^{15}\text{N}(\text{N-1})$. [e] $7\text{-}^{15}\text{N}$. [f] Determined by gs-HMBC. [g] n.o.: not observed.

The ^{13}C and ^{15}N NMR spectra of *N*-phenyl-2-(phenylamino)troponimine (**2**) had previously been recorded by Jackman et al.^[21] in deuteriobromochloroform at 26 °C, and values close to those described in this paper were observed. These authors report a chemical shift for $\delta^{15}\text{N-1/N-9}$ of 164.8 ppm referenced to external 1.0 M aqueous $^{15}\text{NH}_4\text{Cl}$, compared with our experimental value of 144.4 ppm using solid $^{15}\text{NH}_4\text{Cl}$ [in Table 5 our value was referenced to external NO_2CH_3 using the relationship $\delta(\text{external } \text{NO}_2\text{CH}_3) = \delta(\text{solid } ^{15}\text{NH}_4\text{Cl}) - 338.1 \text{ ppm}$]. The 20 ppm difference is

due to the difference between solid and aqueous ammonium chloride.^[22]

For the symmetric derivatives **3** ($\text{R}^1 = \text{R}^2 = p\text{-bromophenyl}$) and **5** ($\text{R}^1 = \text{R}^2 = \text{pyrrol-1-yl}$), only one signal in the ^{15}N NMR spectra is also observed. In the case of *N*-(pyrrol-1-yl)-2-(phenylamino)troponimine (**4**), tautomer **a** is observed, as demonstrated by $\delta^{15}\text{N-1}$ at -271.6 ppm and $\delta^{15}\text{N-9}$ at -114.4 ppm.

The ^1H NMR spectra of $2\text{-}^{15}\text{N}_2$ were recorded in different solvents in order to measure the $^1J(\text{N-1},10\text{-H})$ coupling.

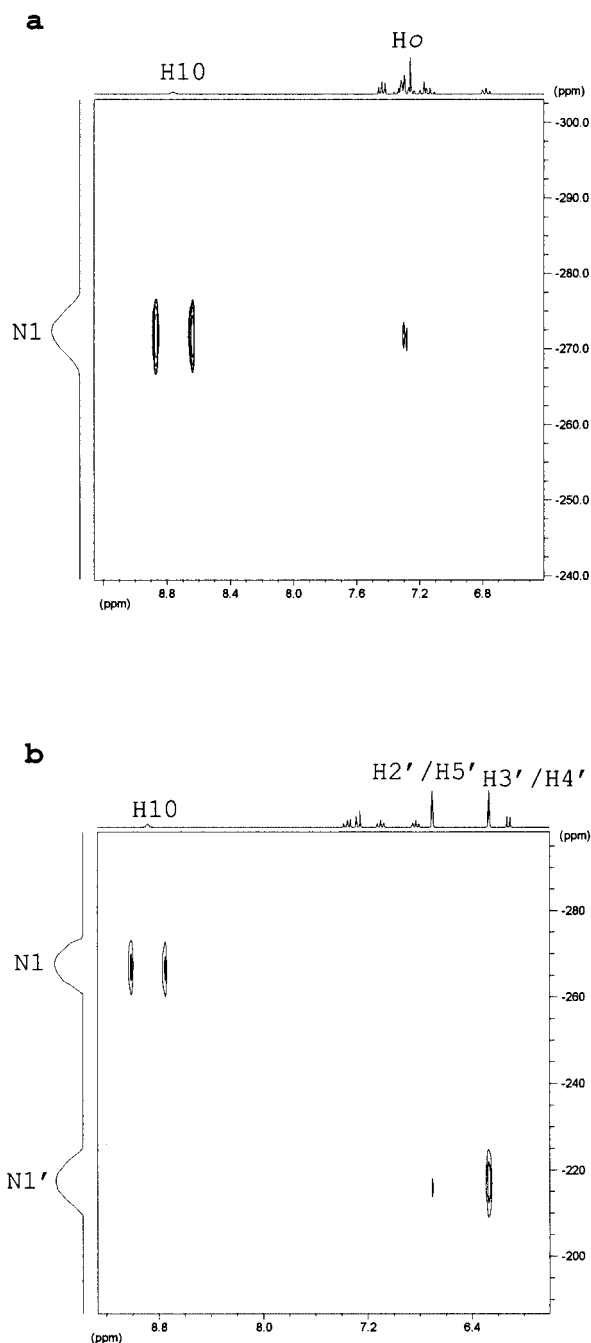


Figure 7. gs-HMBC correlation spectra: a) compound **7** in CDCl_3 ; b) compound **10** in CDCl_3

In CDCl_3 (δ 10- ^1H , 9.20), CD_3CN (δ 10- ^1H , 9.20) and $[\text{D}_8]\text{THF}$ (δ 10- ^1H , 9.32 ppm), only a single signal is observed. However in $[\text{D}_6]\text{DMSO}$ and $[\text{D}_{18}]\text{HMPA}$ a triplet centred at δ = 9.25 ppm and 9.31 ppm, respectively, with a coupling constant value of 44.6 Hz is observed. The $^2J(\text{N-1}, \text{N-9})$ value was indirectly estimated as 5.3 Hz from the ^{13}C NMR spectra of $2\text{-}^{15}\text{N}_2$ in CDCl_3 , by iterative analysis using the Win-Daisy 3.0 program.^[23] All these results prove that, apparently, at 300 K, the proton is symmetrically located but actually corresponds to a pair of rapidly equilibrating degenerate tautomers **2a/2b**.

In an attempt to block the proton transfer, we cooled down the solution of $2\text{-}^{15}\text{N}_2$ in $[\text{D}_8]\text{THF}$ and $[\text{D}_{18}]\text{HMPA}$, but without success (Figure 8). The signals sharpened in $[\text{D}_{18}]\text{HMPA}$, and it was also possible to observe the doublet corresponding to the 10-H proton in the equilibrium $^{15}\text{N}\text{--H10}\cdots^{14}\text{N} \rightleftharpoons ^{15}\text{N}\cdots\text{H10}\text{--}^{14}\text{N}$ (marked with * in Figure 8) due to the small amount of ^{14}N aniline present in ^{15}N aniline.

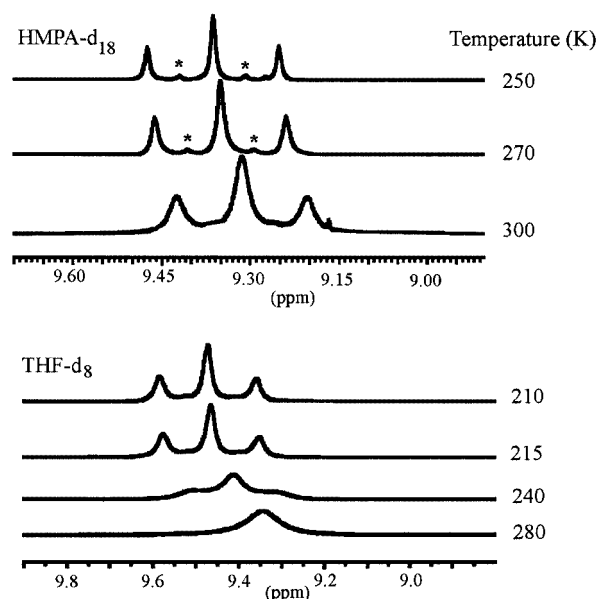


Figure 8. Variable temperature ^1H NMR of $2\text{-}^{15}\text{N}_2$ (10-H region) in $[\text{D}_{18}]\text{HMPA}$ and $[\text{D}_8]\text{THF}$

It was expected that ^1H and ^2H chemical shift values should be the same, and this was indeed the case for aminotropones **7–11**. In the case of aminotroponimines **2–5** these values are only proportional [$\delta^2\text{H} = (1.5 \pm 0.7) + (0.83 \pm 0.08)\delta^1\text{H}$]. We assign this effect to a modification of the geometry of the hydrogen bond produced by the replacement of H by D. In the case of aminotropones, if compound **11** is not considered, there is a proportionality between the ^{15}N and ^1H chemical shift values [$\delta^{15}\text{N} = -(585 \pm 18) + (36 \pm 2)\delta^1\text{H}$; the value predicted for **11** is -253.4 ppm]. A last observation involves the $^2J(\text{N-1}, \text{N-9})$ value for compound **2** (5.3 Hz); this coupling constant was determined at 325 K and increases to 10.5 Hz when the temperature is lowered to 237 K (which is similar to the value of 10.6 Hz measured for **14**). As reported earlier in the literature, this is due to a contraction of the $\text{N}\cdots\text{N}$ distance on cooling [i.e. the value of $^2J(\text{N-1}, \text{N-9})$ increases when $r_1 - r_2$ decreases].^[2c]

DFT Calculations

The calculations were carried out at the hybrid B3LYP/6-31G* level (see Exp. Sect.). Tautomer **a** ($\text{R} = \text{H}$) of the 2-aminotroponone **6** is much more stable than tautomer **b** by $47.3 \text{ kJ}\cdot\text{mol}^{-1}$ ($48.1 \text{ kJ}\cdot\text{mol}^{-1}$ with ZPE). This is consistent with our findings and it is a general finding for all tautomers involving conjugated $\text{C}=\text{O}$ and $\text{C}=\text{NH}$ bonds (for in-

stance, enamino ketones, the monoaza derivatives of **12**), except when they are part of an aromatic ring (e.g. pyridone/hydroxypyridine).

Before discussing the kinetic aspects of the proton transfer in 2-aminotroponimines **1–5**, let us briefly summarise the results for tropolone (**12**). Experimentally, two barriers have been measured for this compound, one corresponding to the monomer either in the gas phase, $57.3 \text{ kJ}\cdot\text{mol}^{-1}$,^[3b,3c] or included in a cyclodextrin, between 39 and $51 \text{ kJ}\cdot\text{mol}^{-1}$.^[3f] In the solid state, the barrier is much higher, $109 \pm 21 \text{ kJ}\cdot\text{mol}^{-1}$ [3a] or 99 ± 8 .^[3h] This interpretation has been contested by Detken, Zimmermann, Haeberle and Luz who proposed a different mechanism with barriers of 29 and $23 \text{ kJ}\cdot\text{mol}^{-1}$.^[3j] These dramatic differences in the barrier (KSSE, kinetic solid-state effect)^[24] are due to the structure of tropolone in the solid state, in which it forms two near planar dimers (**12₂**, Figure 9)^[25] The equilibrium between tropolone tautomers in the solid state involves not only a proton transfer (usually lower in the solid state due to tunneling effects) but a complete reorganisation of the molecule **12₂** in the crystal.

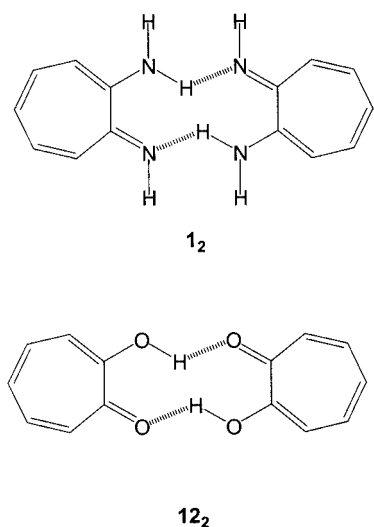


Figure 9. 2-Aminotroponimine and tropolone dimers

Several authors have calculated the barrier for tropolone monomer **12**,^[3e,3g,3k] the most exhaustive work being that of Redington and Bock.^[3d] These authors obtain a reasonable, although low, value at the MP4(DQ) level ($41.6 \text{ kJ}\cdot\text{mol}^{-1}$) that decreases to $15.2 \text{ kJ}\cdot\text{mol}^{-1}$ at the MP2/6-311G** level. These difficulties could be related to the transfer of the proton through the out-of-plane pathway instead of through the in-plane pathway.^[3s,3t]

At the B3LYP/6-31G* level, a value of $22.3 \text{ kJ}\cdot\text{mol}^{-1}$ for the monomer (intramolecular) and $39.3 \text{ kJ}\cdot\text{mol}^{-1}$ for the dimer (intermolecular) was obtained, allowing for a twisted TS (C_2) in the second case. If planarity of **12₂** in the TS is imposed, the barrier increases to $73.8 \text{ kJ}\cdot\text{mol}^{-1}$. ZPE corrections lowers these figures to 12.2, 16.9 and $48.6 \text{ kJ}\cdot\text{mol}^{-1}$, respectively.

For the experimentally studied 2-aminotroponimines no hydrogen-bonded dimers **12** have been observed in the solid state. Nevertheless, for model compound **1**, we have calculated the intramolecular barrier for the monomer ($51.2 \text{ kJ}\cdot\text{mol}^{-1}$) and the dimer **12** (TS C_2 , $62.8 \text{ kJ}\cdot\text{mol}^{-1}$). The ZPE correction results in barriers of 39.9 and $39.2 \text{ kJ}\cdot\text{mol}^{-1}$, respectively.

Conclusions

In the solid state, the most relevant conclusions on the tautomerism of 2-aminotroponimines **2–5** comparatively with that of 6-aminofulvene-1-aldehydes (**14**: $R^1 = R^2 = \text{phenyl}$, **15**: $R^1 = \text{pyrrol-1-yl}$, $R^2 = \text{phenyl}$, **16**: $R^1 = R^2 = \text{pyrrol-1-yl}$, **17**: $R^1 = 1,2,4\text{-triazol-4-yl}$, $R^2 = \text{phenyl}$) [see Figure 10] are that the unsymmetrical compounds ($R^1 \neq R^2$) behave similarly in both series; the N–H amino proton is located on N-1. In the symmetrical derivatives, the *N*-phenyl-2-(phenylamino)troponimine (**2**) presents the proton located on the N-1 but in the *N,N'*-diphenyl-6-aminofulvene-1-aldehyde (**14**) there is a rapid proton transfer at 300 K that could only be frozen at low temperature ($\delta^{15}\text{N-1} = -196.7 \text{ ppm}$ and $\delta^{15}\text{N-9} = -131.0 \text{ ppm}$ at 126 K, 7.1 T).^[14]

1) X-ray crystal structure determination of the *N*-phenyl-2-(phenylamino)troponimine (**2**) affords a N–H bond length of $1.02 \pm 0.10 \text{ \AA}$ and a Ci-N-H bond angle of $108 \pm 7^\circ$ (average of two independent molecules, Table 2). Taking into account crystal packing effects, the agreement between the geometry of the hydrogen bond, determined

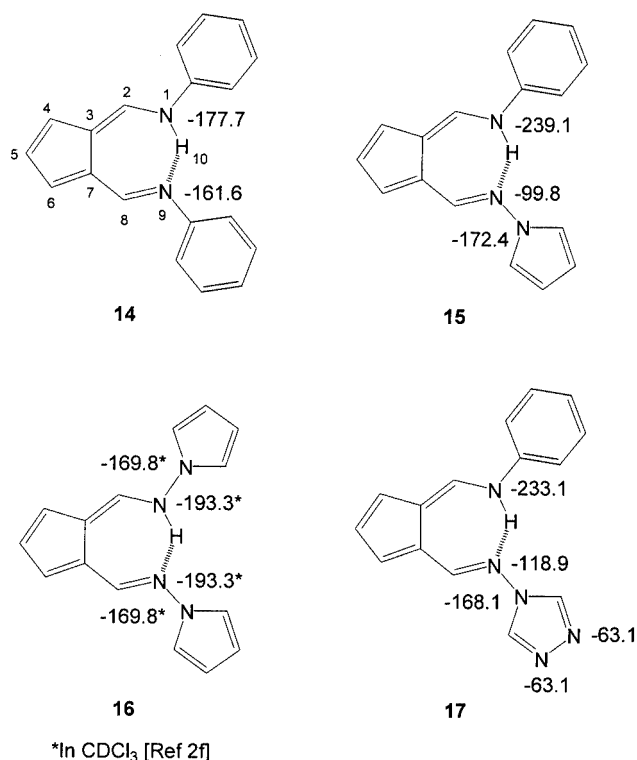


Figure 10. ^{15}N CPMAS NMR spectroscopic data^[2d,2e,14] for 6-aminofulvene-1-aldehydes **14–17**

for **2** in CDBr_3 solution, the N–H bond length of $1.072 \pm 0.004 \text{ \AA}$ and the $\text{C}i\text{--N--H}$ bond angle of $116 \pm 3^\circ$, using spin-lattice relaxation times, is excellent. The position of the mobile proton clearly establishes the symmetric double-well nature of the hydrogen bond.^[21a]

2) The molecule **M2** of compound **5** presents a very interesting structure. The position of the H-12 hydrogen bond centred to both N atoms (Figure 5) can be explained as arising as a result of a single-well situation or, a double-well symmetric situation where a short $\text{N}\cdots\text{N}$ distance is present and where the proton is disordered between two close positions. Because it is always difficult to localise the proton in crystallography, we focussed our discussion on the ratio of the N1--C2 to C8--N9 distances (Table 4). In a symmetric situation the ratio is 1; for a more asymmetric structure, the value will deviate from 1. A closer look at Table 4 shows that the average ratio is 1.034; however, for **5 M2**, the ratio is 1.004 (Figure 11).

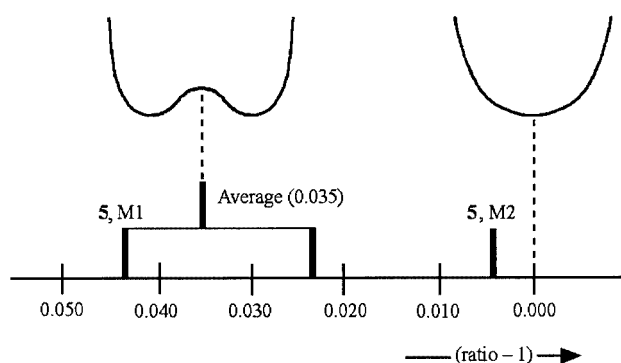


Figure 11. View of the situation present in 2-aminotroponimines regarding the exocyclic C–N bonds

Note finally, that the two independent molecules of **5** correspond to the extreme situations, proof that the packing effects alter the geometry of the molecule to the extent of transforming a classical hydrogen bond into a low barrier hydrogen bond.

3) Assuming that $\delta = 145 \text{ ppm}$ is the maximum value for $\Delta\delta (\text{N-9/N-1})$ and that the exchange rate is fast in the NMR time scale, the differences observed in Table 4 correspond to the following percentages of the presence of the proton on N1: **2 M1** 100%, **2 M2** 86%, **3 M1** 92%, **3 M2** 71%, **5 M1** 100% and **5 M2** 57%. Since no proton disorder was found by crystallography, these values should be taken with caution. It is possible that close contacts with bromine in **3 M2** modify the ^{15}N chemical shifts (Table 3 and Table 4).

4) The relative properties of 6-aminofulvene-1-aldimines (**AFI**), β -enaminoimines (**EAI**) and 2-aminotroponimines (**ATI**) should be related to the geometry of the hydrogen-bonded pseudocycle, a five, six or seven-membered ring. A hydrogen bond is stronger the more linear the $\text{N--H}\cdots\text{N}$ bond and the shorter the $\text{N}\cdots\text{N}$ distance; this, in turn, determines the proton transfer abilities and the $^{2h}J(\text{N-1, N-9})$ coupling constants. Experimentally, for the two systems we have studied (**AFI** and **ATI**), X-ray geometries of these com-

pounds afford the following averaged data: aminotroponimines **2–5** (Table 2, excluding **5 M2** for distances and angles): $2.50 \text{ \AA}$ and 109° ; aminofulvenealdehydes **14–17**:^[2b,2c,2f] $2.82 \text{ \AA}$ and 154° . Information on β -enaminoimines is scarce, only the X-ray structure of **24** (**EAI**, $\text{R} = \text{Ph}$, $\text{R}' = \text{Me}$) has been described before ($\text{N}\cdots\text{N} = 2.67 \text{ \AA}$, $\text{N--H}\cdots\text{N} = 138.9^\circ$).^[26] In the gas phase (theoretical calculations), the barrier to NHN proton transfer is lower in **AFI** than in **ATI**, therefore only the first are low barrier hydrogen bonds. In solution the $^{2h}J(\text{N-1, N-9})$ coupling constant is larger for **AFI** than for **ATI** and in the solid state there are cases of proton disorder in both series. In summary, the linearity of the $\text{N--H}\cdots\text{N}$ angle is more important than the shortness of the $\text{N}\cdots\text{N}$ distance for strong hydrogen bonds (Figure 12).

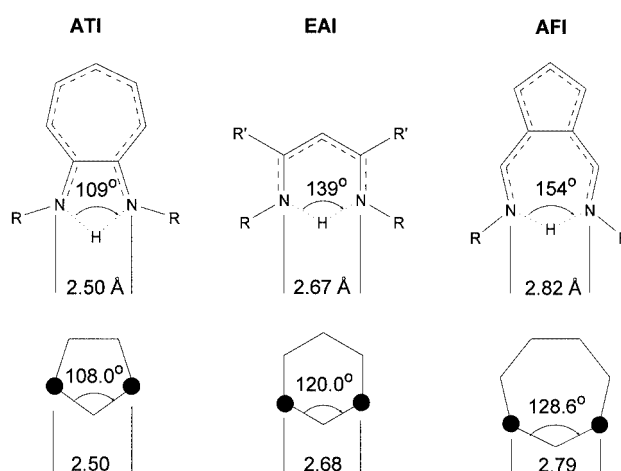


Figure 12. Experimental distances and angles involved in hydrogen bonding for 2-aminotroponimines (**ATI**), β -enaminoimines (**EAI**) and 6-aminofulvene-1-aldehydes (**AFI**)

Comparison of the experimental geometries with those of the corresponding regular polygons (the distance for the pentagon has been fixed at $2.50 \text{ \AA}$) shows that the experimental distances are very similar to the regular polygon distances. This is not the case for the angles, the angles are the same for the five-membered rings, but much higher for the six- and seven-membered rings, which suggests that the proton moves inside the pseudoring.

Finally, are our results concerning NN compounds similar to the corresponding OO compounds? Gilli and Bertolasi^[1b] consider that tropolones are α -diketones in which the $\text{O--H}\cdots\text{O}$ closes a five-membered ring or ζ -diketones considering the seven-membered ring periphery. In tropolones the hydrogen bond is weak due to the unfavourable geometry of the five-membered ring with an $\text{O--H}\cdots\text{O}$ angle of about 110° (the $\text{O}\cdots\text{O}$ distances are about $2.59 \text{ \AA}$), which is quite far from the usual, almost linear $\text{O--H}\cdots\text{O}$ angle of β -diketones (in the case of acetylacetone, $\text{O--H}\cdots\text{O} = 151^\circ$, $\text{O}\cdots\text{O} = 2.54 \text{ \AA}$).^[27] On the other hand, although 6-hydroxy-1-fulvenecarboxaldehydes could be classified as γ -diketones, they are better described as ζ -diketones with much stronger hydrogen bonds than the tropolones

(O–H...O = 173°, O...O = 2.47 Å). There is a perfect correlation between N–H...N and O–H...O angles (NHN angle = 30 + 0.72OHO angle, $r^2 = 1.000$) for the three compounds; this is not the case for the N...N/O...O lengths. This may be because tropolone is a dimer with intermolecular hydrogen bonds.^[1b]

Experimental Section

General: Melting points were determined by DSC with a SEIKO DSC 220C connected to a Model SSC5200H Disk Station. Thermograms (sample size 0.003–0.010 g) were recorded with a scan rate of 2.0 °C·min^{−1}. Unless otherwise stated, column chromatography was performed on silica gel (Merck 60, 70–230 mesh). The R_f values were measured on aluminium-backed TLC plates of silica gel 60 F254 (Merck, 0.2 mm) with the indicated eluent. Compounds **2–5** and **7–11** have been fully characterised by electrospray mass spectrometry.^[28] In addition, mass spectra (HRMS) at 70 eV using electron impact mode was performed with a VG AUTOSPEC spectrometer by Laboratorio de Espectrometría de Masas-UAM, Madrid. Elemental analyses were performed using Perkin–Elmer 240 by Centro de Microanálisis Elemental-UCM, Madrid.

DFT Calculations: The optimisation of the structures of all compounds discussed in this paper was carried out at the hybrid B3LYP/6-31G* level.^[29,30]

NMR Parameters: ¹H (400.13 MHz), ¹³C (100.61 MHz), ²H (61.42 MHz), ¹⁵N (40.56 MHz) and ¹⁷O NMR (54.26 MHz) spectra in solution were obtained with a Bruker DRX-400 instrument at 300 K. Chemical shifts (δ) are given from internal CHCl₃ (7.26) for ¹H NMR, CDCl₃ (7.25) for ²H NMR, ¹³CDCl₃ (77.0) for ¹³C NMR, external nitromethane (0.00) for ¹⁵N NMR and external D₂O (0.00) for ¹⁷O NMR spectroscopy. Coupling constants (J in Hz) are accurate to ± 0.2 Hz for ¹H, and ± 0.6 Hz for ¹³C and ¹⁵N. 2D-Inverse proton detected homonuclear shift correlation spectra gs-COSY, and heteronuclear shift correlation spectra gs-HMQC and gs-HMBC were obtained with the standard pulse sequences.^[31] Solid-state ¹³C (100.73 MHz) and ¹⁵N (40.59 MHz) CPMAS NMR spectra have been obtained with a Bruker WB-400 spectrometer at 300 K with a wide-bore 4-mm DVT probehead at rotational frequencies of approximately 5–10 kHz. Samples were carefully packed in ZrO₂ rotors, and the standard CPMAS pulse sequence and NQS technique (Non Quaternary Suppression to observe only the quaternary C atoms) were employed.^[31]

2-(Tosyloxy)tropolone (18): Compound **18** was synthesised according to a published procedure.^[9] M.p. 156.9 °C (EtOH), (ref. m.p. 159.0–159.5 °C)^[7]. ¹H NMR (CDCl₃): δ = 7.92 (m, 2 H, *o*-H_{arom.}), 7.45 [dd, ³ J (7-H,6-H) = 9.3, ⁴ J (7-H,5-H) = 0.9 Hz, 1 H, 7-H], 7.34 (m, 2 H, *m*-H_{arom.}), 7.20 [ddd, ³ J (4-H,5-H) = 7.8, ⁴ J (4-H,6-H) = 1.2 Hz, 1 H, 4-], 7.13 [d, ³ J (3-H,4-H) = 12.2 Hz, 1 H, 3-H], 7.08 [ddd, ³ J (5-H,6-H) = 10.9 Hz, 1 H, 5-H], 6.97 [ddd, 1 H, 6-H], 2.45 (s, 3 H, CH₃) ppm. ¹³C NMR (CDCl₃): δ = 179.4 (C-8), 155.1 (C-2), 145.5 (*p*-C_{arom.}), 141.2 (¹ J = 162.6, ³ J = 8.8 Hz, C-4), 136.3 (¹ J = 158.5, ³ J = 11.0 Hz, C-3), 134.6 (¹ J = 161.9, ³ J = ³ J = 9.7 Hz, C-5), 133.4 (*i*-C_{arom.}), 130.8 (¹ J = 163.7, ³ J = 9.2 Hz, C-6), 129.9 (¹ J = 158.1, ³ J = 11.2 Hz, C-7), 129.6 (¹ J = 161.7, ³ J = ³ J = 5.2 Hz, *m*-C_{arom.}), 128.6 (¹ J = 166.7, ³ J = 5.4 Hz, *o*-C_{arom.}), 21.7 (¹ J = 127.3, ³ J = 4.4 Hz, CH₃) ppm. ¹⁷O NMR (CDCl₃): δ = 477.9 (O-9), 168.4 (SO₂) ppm. C₁₄H₁₂O₄S (276.31): calcd. C 60.86, H 4.38, S 11.61; found C 60.79, H 4.487, S 11.64.

2-(Phenylamino)tropolone (7): A solution of **18** (1.00 g, 3.6 mmol) in EtOH (30 mL) was refluxed with aniline (0.37 mL, 4.04 mmol) for 26 h 30 min. The solvent was evaporated, and the crude was purified by column chromatography (EtOAc/hexane, 1:20) to afford **7** as a brown oil (550 mg, 77%). ¹H NMR (CDCl₃): δ = 8.76 (br. s, 1 H, 10-H), 7.43 (m, 2 H, *m*-H_{arom.}), 7.33 [ddd, ³ J (6-H,7-H) = 11.7, ³ J (6-H,5-H) = 8.2, ⁴ J (6-H,4-H) = 1.1 Hz, 1 H, 6-H], 7.30 (m, 3 H, *o*-H_{arom.} and 7-H), 7.25 (m, 1 H, *p*-H_{arom.}), 7.18 [dd, ³ J (3-H,4-H) = 10.4, ⁴ J (3-H,5-H) = 1.3 Hz, 1 H, 3-H], 7.12 [ddd, ³ J (4-H,5-H) = 9.7 Hz, 1 H, 4-H], 6.77 [tdd, ⁴ J (5-H,7-H) = 1.3 Hz, 1 H, 5-H] ppm. ¹³C NMR (CDCl₃): δ = 177.0 (C-8), 153.7 (C-2), 138.3 (*i*-C_{arom.}), 137.5 (¹ J = 154.0 Hz, C-6), 135.9 (¹ J = 155.6, ³ J = 9.2 Hz, C-4), 130.6 (¹ J = 158.2, ³ J = 10.0 Hz, C-7), 129.7 (¹ J = 163.0 Hz, *m*-C_{arom.}), 125.9 (¹ J = 162.9 Hz, *p*-C_{arom.}), 124.5 (¹ J = 159.9, ³ J = ³ J = 9.7 Hz, C-5), 124.1 (¹ J = 161.1 Hz, *o*-C_{arom.}), 110.4 (¹ J = 153.7, ³ J = 10.7, ³ J = 6.0 Hz, C-3) ppm. ¹⁵N NMR (CDCl₃): δ = −271.7 [¹ J (N-1,10-H) = 92.4 Hz, N-1] ppm. ¹⁷O NMR (CDCl₃): δ = 384.8 (O-9) ppm. C₁₃H₁₁NO (197.08): calcd. C 79.16, H 5.62, N 7.10; found C 78.93, H 5.797, N 7.029.

[¹⁵N]-2-(Phenylamino)tropolone: A solution of **18** (1.00 g, 3.6 mmol) in EtOH (30 mL) was refluxed with labelled aniline (400 mg, 3.98 mmol) for 26 h 30 min. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:20) to afford **7-¹⁵N** as a brown oil (380 mg, 52%). ¹H NMR (CDCl₃): δ = 8.75 [d, ¹ J (10-H,N-1) = 92.3 Hz, 1 H, 10-H], 7.43 (m, 2 H, *m*-H_{arom.}), 7.33 [ddd, ³ J (6-H,7-H) = 11.7, ³ J (6-H,5-H) = 8.2, ⁴ J (6-H,4-H) = 1.1 Hz, 1 H, 6-H], 7.30 (m, 3 H, *o*-H_{arom.} and 7-H), 7.25 (m, 1 H, *p*-H_{arom.}), 7.18 [dd, ³ J (3-H,4-H) = 10.4, ⁴ J (3-H,5-H) = 1.3 Hz, 1 H, 3-H], 7.12 [ddd, ³ J (4-H,5-H) = 9.7 Hz, 1 H, 4-H], 6.77 [tdd, ⁴ J (5-H,7-H) = 1.3 Hz, 1 H, 5-H] ppm. ¹³C NMR (CDCl₃): δ = 177.0 (C-8), 153.7 [¹ J (C,N) = 17.5 Hz, C-2], 138.3 [¹ J (C,N) = 16.1 Hz, *i*-C_{arom.}], 137.5 (C-6), 135.9 (C-4), 130.6 (C-7), 129.7 [³ J (C–N) = 1.9 Hz, *m*-C_{arom.}], 126.0 (*p*-C_{arom.}), 124.6 (C-5), 124.1 [² J (C,N) = 2.0 Hz, *o*-C_{arom.}], 110.5 (C-3) ppm. Compound **7-¹⁵N-2-H₁** was prepared directly in the NMR sample tube by agitating the CDCl₃ solution with D₂O: Only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ²H NMR (CDCl₃ + D₂O): δ = 8.74 [¹ J (N,D) = 14.1 Hz, 10-D] ppm. ¹³C NMR (CDCl₃ + D₂O): δ = 176.9 [² J (C–N) = 0.9 Hz, C-8], 153.5 [¹ J (C,N) = 18.2 Hz, C-2], 138.2 [¹ J (C,N) = 16.5 Hz, *i*-C_{arom.}], 137.5 (C-6), 136.0 [³ J (C,N) = 1.9 Hz, C-4], 130.7 (C-7), 129.7 [³ J (C,N) = 1.9 Hz, *m*-C_{arom.}], 126.0 (*p*-C_{arom.}), 124.6 (C-5), 124.1 [² J (C,N) = 1.8 Hz, *o*-C_{arom.}], 110.5 [² J (C,N) = 1.8 Hz, C-3] ppm. ¹⁵N NMR (CDCl₃ + D₂O): δ = −272.4 [¹ J (N-1,10–D) = 14.1 Hz, N-1] ppm.

2-(*p*-Bromophenylamino)tropolone (8): A solution of **18** (1.75 g, 6.3 mmol) in EtOH (60 mL) was refluxed with *p*-bromoaniline (1.25 mL, 7.3 mmol) for 54 h. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:20) to afford **8** (690 mg, 39%). M.p. 158.2 °C (CHCl₃/hexane). ¹H NMR (CDCl₃): δ = 8.67 (br. s, 1 H, 10-H), 7.55 (m, 2 H, *m*-H_{arom.}), 7.34 [dd, ³ J (6-H,7-H) = 11.8, ³ J (6-H,5-H) = 8.5 Hz, 1 H, 6-H], 7.27 (br. d, 1 H, 7-H), 7.18 (m, 2 H, *o*-H_{arom.}), 7.14–7.10 (m, 2 H, 3-H and 4-H), 6.80 (m, 1 H, 5-H) ppm. ¹³C NMR (CDCl₃): δ = 177.1 (C-8), 153.1 (C-2), 137.6 [¹ J = 155.3 Hz, C-6], 137.5 (*i*-C_{arom.}), 135.8 (¹ J = 154.2, ³ J = 9.1 Hz, C-4), 131.8 (¹ J = 167.1 Hz, *m*-C_{arom.}), 131.1 (¹ J = 158.6, ³ J = 9.9 Hz, C-7), 125.5 (¹ J = 163.4 Hz, *o*-C_{arom.}), 125.1 (¹ J = 160.0, ³ J = ³ J = 9.6 Hz, C-5), 118.8 (*p*-C_{arom.}), 110.5 (¹ J = 153.4, ³ J = 11.1, ³ J = 5.4 Hz, C-3) ppm. ¹⁵N NMR (CDCl₃): δ = −274.4 [¹ J (N-1,10-H) = 92.2 Hz, N-1] ppm. ¹⁷O NMR (CDCl₃): δ = 381.5 (O-9) ppm. Compound **8-2-H₁** was prepared directly in the NMR sample

tube by agitating the CDCl_3 solution with D_2O , only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ^2H NMR ($\text{CDCl}_3 + \text{D}_2\text{O}$): $\delta = 8.65$ (10-D) ppm. $\text{C}_{13}\text{H}_{10}\text{BrNO}$ (274.99): calcd. C 56.55, H 3.65, N 5.07; found C 55.85, H 3.70, N 5.16.

2-(*p*-Chlorophenylamino)troponone (9): A solution of **18** (1.75 g, 6.3 mmol) in EtOH (60 mL) was refluxed with *p*-chloroaniline (0.91 mL, 7.12 mmol) for 54 h. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:20) to afford **9** (320 mg, 22%). M.p. 141.0 °C (CHCl_3 /hexane). ^1H NMR (CDCl_3): $\delta = 8.68$ (br. s, 1 H, 10-H), 7.39 (m, 2 H, *m*- $H_{\text{arom.}}$), 7.34 [dd, $^3J(6\text{-H}, 7\text{-H}) = 11.7$, $^3J(6\text{-H}, 5\text{-H}) = 8.4$ Hz, 1 H, 6-H], 7.28 (br. d, 1 H, 7-H), 7.24 (m, 2 H, *o*- $H_{\text{arom.}}$), 7.16–7.09 (m, 2 H, 3-H and 4-H), 6.79 (m, 1 H, 5-H) ppm. ^{13}C NMR (CDCl_3): $\delta = 177.0$ (C-8), 153.3 (C-2), 137.6 ($^1J = 154.7$ Hz, C-6), 137.0 (*i*- $C_{\text{arom.}}$), 135.8 ($^1J = 154.5$, $^3J = 9.0$ Hz, C-4), 131.1 (*p*- $C_{\text{arom.}}$), 131.0 ($^1J = 158.4$, $^3J = 10.0$ Hz, C-7), 129.8 ($^1J = 167.2$ Hz, *m*- $C_{\text{arom.}}$), 125.3 ($^1J = 162.5$ Hz, *o*- $C_{\text{arom.}}$), 125.0 ($^1J = 159.9$, $^3J = ^3J = 9.7$ Hz, C-5), 110.5 ($^1J = 153.4$, $^3J = 11.1$, $^3J = 5.3$ Hz, C-3) ppm. ^{15}N NMR (CDCl_3): $\delta = -274.0$ [$^1J(\text{N-1}, 10\text{-H}) = 92.6$ Hz, N-1] ppm. ^{17}O NMR (CDCl_3): $\delta = 386.6$ (O-9) ppm. Compound **9-2H₁** was prepared directly in the NMR sample tube by agitating the CDCl_3 solution with D_2O , only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ^2H NMR ($\text{CDCl}_3 + \text{D}_2\text{O}$): $\delta = 8.66$ (10-D) ppm. $\text{C}_{13}\text{H}_{10}\text{ClNO}$ (231.05): calcd. C 67.40, H 4.35, N 6.05; found C 66.72, H 4.41, N 6.13.

2-(Pyrrol-1-ylamino)troponone (10): A solution of **18** (1.00 g, 3.6 mmol) in EtOH (30 mL) was refluxed with *N*-aminopyrrole (0.33 mL, 3.99 mmol) for 6 h. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:20) to afford **10** (270 mg, 40%). M.p. 108.4 °C (CHCl_3 /hexane). ^1H NMR (CDCl_3): $\delta = 8.88$ (br. s, 1 H, 10-H), 7.36 [ddd, $^3J(6\text{-H}, 7\text{-H}) = 11.7$, $^3J(6\text{-H}, 5\text{-H}) = 8.6$, $^4J(6\text{-H}, 4\text{-H}) = 1.2$ Hz, 1 H, 6-H], 7.27 (ddd, 1 H, 7-H), 7.10 [dddd, $^3J(3\text{-H}, 4\text{-H}) = 10.1$, $^3J(4\text{-H}, 5\text{-H}) = 8.6$, $^5J(4\text{-H}, 7\text{-H}) = 0.7$ Hz, 1 H, 4-H], 6.83 [ddt, $^4J(5\text{-H}, 7\text{-H}) = 1.1$, $^4J(5\text{-H}, 3\text{-H}) = 0.7$ Hz, 1 H, 5-H], 6.71 (m, 2 H, 2'-H and 5'-H), 6.27 (m, 2 H, 3'-H and 4'-H), 6.12 (dd, 1 H, 3-H) ppm. ^{13}C NMR (CDCl_3): $\delta = 176.7$ (C-8), 155.1 (C-2), 137.7 ($^1J = 155.0$, $^3J = 10.8$ Hz, C-6), 135.9 ($^1J = 156.5$, $^3J = 9.9$ Hz, C-4), 133.5 ($^1J = 159.1$, $^3J = 9.5$ Hz, C-7), 126.2 ($^1J = 159.7$, $^3J = ^3J = 10.2$ Hz, C-5), 120.9 ($^1J = 188.8$ Hz, C-2' and C-5'), 110.5 ($^1J = 154.0$, $^3J = 11.5$ Hz, C-3), 108.6 ($^1J = 172.6$ Hz, C-3' and C-4') ppm. ^{15}N NMR (CDCl_3): $\delta = -266.8$ [$^1J(\text{N-1}, 10\text{-H}) = 103.5$ Hz, N-1], -217.0 (N-1') ppm. ^{17}O NMR (CDCl_3): $\delta = 395.4$ (O-9) ppm. Compound **10-2H₁** was prepared directly in the NMR sample tube by agitating the CDCl_3 solution with D_2O , only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ^2H NMR ($\text{CDCl}_3 + \text{D}_2\text{O}$): $\delta = 8.87$ (10-D) ppm. $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}$ (186.08): calcd. C 70.95, H 5.41, N 15.04; found C 71.05, H 5.435, N 15.04.

2-(1,2,4-Triazol-1-ylamino)troponone (11): A homogeneous mixture of **18** (1.00 g, 3.6 mmol) and 4-amine-1,2,4-triazole (610 mg, 7.25 mmol) was melted at 120–130 °C for 5 h. The crude product was purified by column chromatography (CHCl_3 /EtOH, 10:1) to afford a mixture of **11** and 4-amine-1,2,4-triazole. The unchanged amine was then removed using acetone, and **11** remained (230 mg, 33%). M.p. 253.0 °C (dec.). ^1H NMR (CDCl_3): $\delta = 8.98$ (br. s, 1 H, 10-H), 8.33 (s, 2 H, 2'-H and 5'-H), 7.44 [ddd, $^3J(6\text{-H}, 7\text{-H}) = 11.9$, $^3J(6\text{-H}, 5\text{-H}) = 8.5$, $^4J(6\text{-H}, 4\text{-H}) = 1.1$ Hz, 1 H, 6-H], 7.33 (d, 1 H, 7-H), 7.12 (br. t, 1 H, 4-H), 6.97 (br. t, 1 H, 5-H), 6.14 [d, $^3J(3\text{-H}, 4\text{-H}) = 9.7$ Hz, 1 H, 3-H] ppm. ^{13}C NMR (CDCl_3): $\delta =$

177.1 (C-8), 152.7 (C-2), 143.3 ($^1J = 215.1$, $^3J = 4.1$ Hz, C-2' and C-5'), 135.1 ($^1J = 160.7$, $^3J = 9.4$ Hz, C-4 and C-7), 138.4 ($^1J = 156.1$, $^3J = 11.5$ Hz, C-6), 128.4 ($^1J = 163.6$, $^3J = ^3J = 10.3$ Hz, C-5), 111.3 ($^1J = 152.3$, $^3J = 11.2$ Hz, C-3) ppm. ^{15}N NMR (CDCl_3): $\delta = -288.7$ (N-1), -203.7 (N-1'), -60.7 (N-3' and N-4') ppm. Compound **11-2H₁** was prepared directly in the NMR sample tube by agitating the CDCl_3 solution with D_2O , only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ^2H NMR ($\text{CDCl}_3 + \text{D}_2\text{O}$): $\delta = 8.94$ (10-D) ppm. $\text{C}_9\text{H}_8\text{N}_4\text{O}$ (188.07): calcd. C 57.44, H 4.28, N 29.77; found C 57.36, H 4.244, N 29.63.

2-(*p*-Bromophenylimino)-*O*-ethyltroponone (19): Prepared using the procedure described in ref.^[11]. Triethyloxonium tetrafluoroborate (2.22 g, 11.7 mmol) in dry dichloromethane (12 mL) was slowly added to a solution of **8** (3.00 g, 10.9 mmol) in dry dichloromethane (40 mL) at room temperature under argon. After the addition was completed, the reaction was stirred for one week. The solvent was evaporated, and the crude product was purified by column chromatography with the following eluents: EtOAc/hexane (1:5), **8**, CHCl_3 /EtOH (5:1), **19**. Yield for **19** (1.99 g, 47%). M.p. 100.0 °C. ^1H NMR (CDCl_3): $\delta = 7.46$ (m, 2 H, *m*- $H_{\text{arom.}}$), 6.89–6.75 (m, 5 H, *o*- $H_{\text{arom.}}$, 4-H, 6-H and 7-H), 6.58 (m, 2 H, 3-H and 5-H), 4.26 [q, $^3J(\text{CH}_2, \text{CH}_3) = 6.9$ Hz, 2 H, CH_2], 1.54 (t, 3 H, CH_3) ppm. ^{13}C NMR (CDCl_3): $\delta = 160.1$ (C-8), 158.4 (C-2), 148.3 (*i*- $C_{\text{arom.}}$), 134.0 ($^1J = 157.2$ Hz, C-6), 132.5 ($^1J = 165.8$, $^3J = 5.5$ Hz, *m*- $C_{\text{arom.}}$), 132.0 ($^1J = 154.1$ Hz, C-4), 126.5 ($^1J = 161.4$, $^3J = ^3J = 9.1$ Hz, C-5), 126.3 ($^1J = 159.3$, $^3J = 9.2$ Hz, C-7), 122.7 ($^1J = 162.3$, $^3J = 5.0$ Hz, *o*- $C_{\text{arom.}}$), 116.6 (C-4'), 111.0 ($^1J = 151.6$, $^3J = 11.9$ Hz, C-3), 65.4 ($^1J = 145.2$, $^2J = 4.0$ Hz, CH_2), 14.2 ($^1J = 127.3$ Hz, CH_3) ppm. ^{15}N NMR (CDCl_3): $\delta = -274.3$ (N-1) ppm. $\text{C}_{15}\text{H}_{14}\text{BrNO}$ (303.03): calcd. C 59.23, H 4.64, N 4.60; found C 58.99, H 4.55, N 4.90.

***O*-Ethyl-2-(pyrrol-1-ylimino)troponone (20):** Prepared using the procedure described in ref.^[11]. Triethyloxonium tetrafluoroborate (1.32 g, 7.0 mmol) in dry dichloromethane (9 mL) was slowly added to a solution of **10** (1.15 g, 6.2 mmol) in dry dichloromethane (13 mL) at room temperature under argon. After the addition was completed, the reaction was stirred for one week. The solvent was evaporated, and the crude product was purified by column chromatography with the following eluents: EtOAc/hexane (1:5), **10**, CHCl_3 /EtOH (5:1), **20**. Yield for **20** (580 mg, 31%). M.p. 83.5 °C. ^1H NMR (CDCl_3): $\delta = 6.73$ (m, 2 H, 2'-H and 5'-H), 6.69–6.57 (m, 4 H, 3-H, 4-H, 6-H and 7-H), 6.39 (m, 1 H, 5-H), 6.29 [br. d, $^3J(3\text{-H}, 4\text{-H}) = 9.2$ Hz, 1 H, 3-H], 6.18 (m, 2 H, 3'-H and 4'-H), 4.18 [q, $^3J(\text{CH}_2, \text{CH}_3) = 7.0$ Hz, 2 H, CH_2], 1.53 (t, 3 H, CH_3) ppm. ^{13}C NMR (CDCl_3): $\delta = 161.5$ ($^3J = ^3J = 9.8$ Hz, C-8), 157.3 (C-2), 133.2 ($^1J = 158.6$, $^3J = 13.0$ Hz, C-6), 130.8 ($^1J = 156.2$, $^3J = 8.7$ Hz, C-4), 125.8 ($^1J = 159.2$, $^3J = ^3J = 9.9$ Hz, C-5), 123.9 ($^1J = 161.0$, $^3J = 9.1$ Hz, C-7), 117.0 ($^1J = 187.4$ Hz, C-2' and C-5'), 110.0 ($^1J = 151.7$, $^3J = 11.6$ Hz, C-3), 106.8 ($^1J = 171.5$, $^3J = ^3J = 7.6$, $^2J = 3.0$ Hz, C-3' and C-4'), 65.1 ($^1J = 144.5$, $^2J = 4.5$ Hz, CH_2), 14.3 ($^1J = 127.3$, $^2J = 2.4$ Hz, CH_3) ppm. $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}$ (214.11): calcd. C 72.87, H 6.59, N 13.07; found C 72.82, H 6.72, N 12.95.

***N*-Phenyl-2-(phenylamino)troponimine (2):** Triethyloxonium tetrafluoroborate (720 mg, 3.78 mmol) in dry dichloromethane (4 mL) was slowly added to a solution of **7** (700 g, 3.55 mmol) in dry dichloromethane (4 mL) at room temperature under argon. After stirring for 3 h, aniline (4.15 mL, 45.54 mmol) was slowly added to the solution. The mixture was then stirred for 32 h. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:30) to afford **2** (250 g, 26%).

M.p. 78.4 °C (ref.^[5] m.p. 86.5–87.0 °C). ¹H NMR (CDCl₃): δ = 9.20 (br. s, 1 H, 10-H), 7.41 (m, 4 H, *m*-H_{arom.}), 7.15 (m, 2 H, *p*-H_{arom.}), 7.14 (m, 4 H, *o*-H_{arom.}), 6.84 [dd, ⁴J(3-H,7-H/5-H) = 0.8 Hz, 2 H, 3-H and 7-H], 6.73 [dd, ³J(4-H/6-H,3-H/7-H) = 12.1, ³J(4-H/6-H,5-H) = 9.2 Hz, 2 H, 4-H and 6-H], 6.34 (tt, 1 H, 5-H) ppm. ¹³C NMR (CDCl₃): δ = 151.9 (³J = ³J = 10.0 Hz, C-2 and C-8), 145.2 (³J = ³J = 8.7 Hz, *i*-C_{arom.}), 133.4 (¹J = 155.0, ³J = 10.7 Hz, C-4 and C-6), 129.5 (¹J = 158.3, ³J = 8.0 Hz, *m*-C_{arom.}), 123.9 (¹J = 159.6, ³J = ³J = 7.7 Hz, *p*-C_{arom.}), 122.6 (¹J = 159.5, ³J = ³J = 6.8 Hz, *o*-C_{arom.}), 122.1 (¹J = 159.2, ³J = ³J = 10.6 Hz, C-5), 114.9 (¹J = 155.1, ³J = ³J = 10.3 Hz, C-3 and C-7) ppm. ¹⁵N NMR (CDCl₃): δ = –193.7 (N-1 and N-9) ppm. Compound **2-²H₁** was prepared directly in the NMR sample tube by agitating the CDCl₃ solution with D₂O, only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ²H NMR (CDCl₃ + D₂O): δ = 9.09 (10-D) ppm. C₁₉H₁₆N₂ (272.13): calcd. C 83.79, H 5.92, N 10.29; found C 83.67, H 5.97, N 10.23.

[¹⁵N₂]-*N*-Phenyl-2-(phenylamino)troponimine (**2-¹⁵N₂**): Triethyl-oxonium tetrafluoroborate (960 mg, 4.80 mmol) in dry dichloromethane (6 mL) was slowly added to a solution of **7-¹⁵N** (940 mg, 4.73 mmol) in dry dichloromethane (6 mL) at room temperature under argon. After stirring for 3 h, labelled aniline (5.95 g, 60.1 mmol) was slowly added to the solution. The mixture was then stirred for 43 h. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:30) to afford **2-¹⁵N₂** (390 mg, 30%). ¹H NMR ([D₆]DMSO): δ = 9.25 [br. t, ¹J(10-H, N-1/N-9) = 44.6 Hz, 1 H, 10-H], 7.41 (m, 4 H, *m*-H_{arom.}), 7.14 (m, 2 H, *p*-H_{arom.}), 7.11 (m, 4 H, *o*-H_{arom.}), 6.82 [dd, ³J(4-H/6-H,5-H) = 9.2 Hz, 2 H, 4-H and 6-H], 6.73 [d, ³J(4-H/6-H,3-H/7-H) = 10.6 Hz, 2 H, 3-H and 7-H], 6.37 (t, 1 H, 5-H) ppm. ¹³C NMR (CDCl₃): δ = 151.9 [¹J(C,N) = 14.0 Hz, C-2 and C-8], 145.2 [¹J(C,N) = 10.4 Hz, *i*-C_{arom.}], 133.4 (C-4 and C-6), 129.5 (*m*-C_{arom.}), 123.9 (*p*-C_{arom.}), 122.6 (*o*-C_{arom.}), 122.1 (C-5), 114.9 (C-3 and C-7) ppm. ¹⁵N NMR (CDCl₃): δ = –193.2 (N-1, N-9) ppm. Compound **2-¹⁵N₂-²H₁** was prepared directly in the NMR sample tube by agitating the CDCl₃ solution with D₂O, only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ²H NMR (CDCl₃ + D₂O): δ = 9.14 (10-D) ppm.

N-(*p*-Bromophenyl)-2-(*p*-bromophenylamino)troponimine (**3**): A solution of **19** (1.75 g, 4.5 mmol) and *p*-bromoaniline (4.66 g, 26.8 mmol) in ethanol (75 mL) was stirred for 24 h at room temperature. Dichloromethane (85 mL) was then added to the reaction mixture, and the mixture was allowed to stir for an additional four days at 40 °C. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:30) to afford **3** (1.92 g, 73%). M.p. 195.6 °C. ¹H NMR (CDCl₃): δ = 9.04 (br. s, 1 H, 10-H), 7.50 (m, 4 H, *m*-H_{arom.}), 7.00 (m, 4 H, *o*-H_{arom.}), 6.81–6.72 (m, 4 H, 3-H, 4-H, 6-H and 7-H), 6.39 [tt, ³J(5-H,4-H/6-H) = 8.3, ⁴J(5-H,3-H/7-H) = 1.7 Hz, 1 H, 5-H) ppm. ¹³C NMR (CDCl₃): δ = 151.8 (³J = ³J = 9.2 Hz, C-2 and C-8), 144.1 (³J = ³J = 8.6 Hz, *i*-C_{arom.}), 133.8 (¹J = 155.0, ³J = 9.3 Hz, C-4 and C-6), 132.6 (¹J = 165.7 Hz, *m*-C_{arom.}), 124.3 (¹J = 162.1 Hz, *o*-C_{arom.}), 122.9 (¹J = 159.3, ³J = ³J = 9.5 Hz, C-5), 116.8 (*p*-C_{arom.}), 115.3 (¹J = 154.8, ³J = 10.6 Hz, C-3 and C-7) ppm. ¹⁵N NMR (CDCl₃): δ = –196.3 (N-1 and N-9) ppm. Compound **3-²H₁** was prepared directly in the NMR sample tube by agitating the CDCl₃ solution with D₂O, only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ²H NMR (CDCl₃ + D₂O): δ = 8.99 (10-D) ppm. C₁₉H₁₄Br₂N₂ 1/2 H₂O (436.96): calcd. C 51.98, H 3.44, N 6.38; found C 52.08, H 3.26, N 6.47.

N-(Pyrrol-1-yl)-2-(phenylamino)troponimine (**4**): A solution of **20** (450 g, 1.49 mmol) and aniline (1.6 mL, 17.9 mmol) in dichloromethane (37 mL) was stirred for 6 days at 40 °C. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:30) to afford the desired product **4**, accompanied by **2**. The mixture was separated by preparative TLC, and the plate was eluted three times (EtOAc/hexane, 1:30) to give pure **4** (255 mg, 66%). M.p. 125.9 °C. ¹H NMR (CDCl₃): δ = 8.75 (br. s, 1 H, 10-H), 7.43 (m, 2 H, *m*-H_{arom.}), 7.32 (m, 2 H, *o*-H_{arom.}), 7.23 (m, 1 H, *p*-H_{arom.}), 6.90 [dd, ³J(3-H,4-H) = 10.2 Hz, 1 H, 3-H], 6.86–6.79 (m, 2 H, 4-H and 6-H), 6.76 [dd, ³J(7-H,6-H) = 12.0 Hz, 1 H, 7-H], 6.71 (m, 2 H, 2'-H and 5'-H), 6.42 [tdd, ³J(5-H,4-H) = 8.0, ³J(5-H,6-H) = 10.0, ⁴J(5-H,3-H) = ⁴J(5-H,7-H) = 1.0 Hz, 1 H, 5-H], 6.26 (m, 2 H, 3'-H and 4'-H) ppm. ¹³C NMR (CDCl₃): δ = 159.4 (³J = ³J = 9.9 Hz, C-8), 146.9 (³J = ³J = 9.8 Hz, *i*-C_{arom.}), 139.1 (³J = ³J = 9.8 Hz, C-2), 134.5 (¹J = 155.3, ³J = 10.9 Hz, C-4), 134.1 (¹J = 156.3, ³J = 9.4 Hz, C-6), 129.6 (¹J = 162.6, ³J = 8.7 Hz, *m*-C_{arom.}), 125.5 (¹J = 163.0, *p*-C_{arom.}), 124.4 (¹J = 160.5, ³J = ³J = 6.7 Hz, *o*-C_{arom.}), 123.5 (¹J = 159.9, ³J = ³J = 9.9 Hz, C-5), 119.4 (¹J = 158.6, ³J = 10.0 Hz, C-7), 117.0 (¹J = 186.7, C-2' and C-5'), 109.9 (¹J = 153.4, ³J = ³J = 11.0 Hz, C-3), 106.8 (¹J = 171.6, C-3' and C-4') ppm. ¹⁵N NMR (CDCl₃): δ = –271.6 (N-1), –187.0 (N-1'), –114.4 (N-9) ppm. Compound **4-²H₁** was prepared directly in the NMR sample tube by agitating the CDCl₃ solution with D₂O, only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ²H NMR (CDCl₃ + D₂O): δ = 8.72 (10-D) ppm. HRMS [M⁺] *m/z*: C₁₇H₁₅N₃ (436.96): calcd. 261.12732; found 261.12660.

[2-¹⁵N]-*N*-(Pyrrol-1-yl)-2-(phenylamino)troponimine (**4-¹⁵N**): Compound **4-¹⁵N** was synthesised according to a procedure described for **4**. ¹H NMR ([D₈]THF): δ = 9.01 [d, ¹J(10-H,N-1) = 89.9 Hz, 1 H, 10-H], 7.41 (m, 2 H, *m*-H_{arom.}), 7.33 (m, 2 H, *o*-H_{arom.}), 7.19 (m, 1 H, *p*-H_{arom.}), 6.86 [dd, ³J(3-H,4-H) = 10.2 Hz, 1 H, 3-H], 6.85–6.78 (m, 2 H, 4-H and 6-H), 6.69 [dd, ³J(7-H,6-H) = 12.0 Hz, 1 H, 7-H], 6.63 (m, 2 H, 2'-H and 5'-H), 6.37 [tdd, ³J(5-H,4-H) = 8.0, ³J(5-H,6-H) = 10.0, ⁴J(5-H,3-H) = ⁴J(5-H,7-H) = 1.0 Hz, 1 H, 5-H], 6.11 (m, 2 H, 3'-H and 4'-H) ppm. ¹³C NMR (CDCl₃): δ = 159.4 (C-8), 146.9 [¹J(C,N) = 16.3 Hz, *i*-C_{arom.}], 139.1 [¹J(C,N) = 15.6 Hz, C-2], 134.6 (C-4), 134.0 (C-6), 129.6 (*m*-C_{arom.}), 125.5 (*p*-C_{arom.}), 124.4 [²J(C,N) = 2.0 Hz, *o*-C_{arom.}], 123.0 (C-5), 119.4 (C-7), 117.0 (C-2' and C-5'), 109.9 (C-3), 106.9 (C-3' and C-4') ppm. ¹⁵N NMR (CDCl₃): δ = –271.8 (N-1) ppm.

N-(Pyrrol-1-yl)-2-(pyrrol-1-ylamino)troponimine (**5**): A solution of **20** (788 mg, 2.25 mmol) and *N*-aminopyrrole (402 mg, 4.90 mmol) in dry methanol (20 mL) was stirred for 4 days at room temperature under argon. The solvent was evaporated, and the crude product was purified by column chromatography (EtOAc/hexane, 1:30) to afford **5** (247 mg, 44%). M.p. 137.6 °C. ¹H NMR (CDCl₃): δ = 8.96 (br. s, 1 H, 10-H), 6.78 (m, 2 H, 4-H and 6-H), 6.75 (m, 4 H, 2'-H and 5'-H), 6.44 [tt, ³J(5-H,4-H/6-H) = 9.4, ⁴J(5-H,3-H/7-H) = 0.7 Hz, 1 H, 5-H], 6.35 [dd, ³J(3-H/7-H,4-H/6-H) = 10.8 Hz, 2 H, 3-H and 7-H], 6.27 (m, 4 H, 3'-H and 4'-H) ppm. ¹³C NMR (CDCl₃): δ = 153.5 (³J = ³J = 10.0 Hz, C-2 and C-8), 134.3 (¹J = 155.7, ³J = 10.7 Hz, C-4 and C-6), 124.5 (¹J = 159.9, ³J = ³J = 10.4 Hz, C-5), 119.0 (¹J = 187.4 Hz, C-2' and C-5'), 115.3 (¹J = 156.4, ³J = ³J = 10.1 Hz, C-3 and C-7), 107.6 (¹J = 172.2 Hz, C-3' and C-4') ppm. ¹⁵N NMR (CDCl₃): δ = –202.4 (N-1'), –188.4 (N-1 and N-9) ppm. Compound **5-²H₁** was prepared directly in the NMR sample tube by agitating the CDCl₃ solution with D₂O, only 10-H exchange. The NMR spectroscopic data for the corresponding 10-D deuterated derivative; ²H NMR (CDCl₃ + D₂O): δ =

Table 6. Crystal and refinement data for **2**, **3**, **4** and **5**

	2	3	4	5
Formula	C ₁₉ H ₁₆ N ₂	C ₁₉ H ₁₄ Br ₂ N ₂	C ₁₇ H ₁₅ N ₃	C ₁₅ H ₁₄ N ₄
<i>M</i> _r	272.34	430.14	261.32	500.60
Temperature K	293(2)	293(2)	293(2)	293(2)
Crystal system	monoclinic	triclinic	triclinic	monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> (Å)	14.569(4)	9.6533(9)	10.492(1)	13.934(5)
<i>b</i> (Å)	20.710(6)	10.2638(9)	11.839(2)	19.770(5)
<i>c</i> (Å)	10.159(3)	19.302(2)	13.082(2)	10.129(5)
α (°)	—	96.335(2)	72.928(2)	—
β (°)	100.166(5)°	99.005(2)	89.832(2)	103.765(5)
γ (°)	—	114.689(2)	65.217(2)	—
<i>V</i> (Å ³)	3017(2)	1683.0(3)	1396.7(3)	2710 (2)
<i>Z</i>	8	4	4	8
<i>F</i> (000)	1152	848	552	1056
Crystal size (mm ³)	0.38 × 0.18 × 0.12	0.24 × 0.14 × 0.10	0.23 × 0.16 × 0.14	0.18 × 0.13 × 0.07
<i>D</i> _{calcd.} (g·cm ^{−3})	1.199	1.698	1.243	1.227
μ (mm ^{−1})	0.071	4.817	0.076	0.077
Scan technique	ω and ϕ	ω and ϕ	ω and ϕ	ω and ϕ
Data collected (<i>h</i> , <i>k</i> , <i>l</i>)	(−16, −19, −12) to (17, 24, 11)	(−11, −11, −20) to (5, 12, 22)	(−12, −9, −15) to (12, 14, 15)	(−16, −23, −11) to (16, 19, 12)
θ (°)	1.42 to 25.0	1.09 to 25.0	1.64 to 25.0	1.50 to 25.0
Reflections, collected	15347	8833	7346	14069
Reflections, independent	5305 (<i>R</i> _{int} = 0.26)	5838 (<i>R</i> _{int} = 0.047)	4846 (<i>R</i> _{int} = 0.045)	4766 (<i>R</i> _{int} = 0.090)
Data/restraints/parameters	5305/0/385	5838/0/415	4846/0/364	4766/0/344
Reflections, obsd.	953	2937	2075	1364
[<i>I</i> > 2 σ (<i>I</i>)]				
<i>R</i> (Reflections, obsd.) ^[a]	0.11	0.043	0.043	0.052
<i>R</i> _w (all reflections) ^[b]	0.41	0.099	0.101	0.140

^[a] $\sum ||F_o| - |F_c|| / \sum |F_o|$. ^[b] $\{\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]\}^{1/2}$.

8.93 (10-D) ppm. C₁₅H₁₄N₄ (250.12): calcd. C 71.98, H 5.64, N 22.38; found C 70.88, H 5.598, N 21.92.

X-ray-Diffraction Studies: Suitable crystals for X-ray experiments were obtained from chloroform/ethanol for **2**, from chloroform for **3**, and from hexane for **4** and **5**.

For compound **2**, the poor quality of the crystals made it necessary to repeat the data collection and refinement procedure several times with different crystals. Finally, a crystal of sufficient quality to properly solve the structure was obtained.

Data collection was carried out at room temperature on a Bruker Smart CCD diffractometer using graphite-monochromated Mo-*K* α radiation (λ = 0.71073 Å) operating at 50 kV and 25 A or 20 A. In all cases, data were collected over a hemisphere of the reciprocal space by combination of three exposure sets. Each exposure of 20 s covered 0.3 in ω . The cell parameters were determined and refined by a least-squares fit of all reflections collected. The first 50 frames were recollected at the end of the data collection to monitor crystal decay, and no appreciable decay was observed. A summary of the fundamental crystal and refinement data is given in Table 6. The structures were solved by direct methods (SHELXS-97)^[32] and Sir,^[33] and refined by full-matrix-block least-squares on *F*² for **2**, and full-matrix least-squares on *F*² for **3**, **4** and **5**.^[32] Anisotropic parameters were used in the last cycles of refinement for all non-hydrogen atoms. All hydrogen atoms were included in calculated positions and refined riding on the respective carbon atoms, except H11 and H12 bonded to nitrogen atoms. For **2**, **4** and **5**, these hydrogen atoms have been located in a Fourier synthesis, included,

and their coordinates refined for **2**, refined riding on the respective nitrogen atoms for **4** and fixed for **5**. In compound **3**, only the H11 atom has been located in a Fourier synthesis, included and fixed, and the other hydrogen atom, H12, was included in calculated position and refined riding on N12 atom. Largest peaks and holes in the final difference map were 0.504 and −0.265, 0.434 and −0.285, 0.122 and −0.123, 0.115 and −0.301 e·Å^{−3} for **2**, **3**, **4**, and **5**, respectively.

CCDC-230113 (for **2**), -230114 (for **3**), -230115 (for **4**) and -230116 (for **5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

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