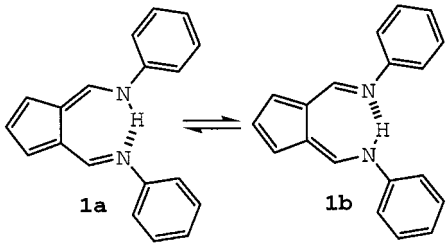
[4] a) M. W. Riggs, M. R. McNeil, L. E. Perryman, A. L. Stone, M. S. Scherman, R. M. O'Connor, *Infect. Immun.* **1999**, *67*, 1317–1322; b) M. Sugita, Y. Sanai, S. Itonori, T. Hori, *Biochim. Biophys. Acta* **1988**, *962*, 159–165.
[5] a) G. Ekborg, B. Lindberg, J. Lonngren, *Acta. Chem. Scand.* **1972**, *26*, 3287; b) H. Paulsen, R. Lebuhn, O. Lockhoff, *Carbohydr. Res.* **1982**, *103*, C7-C11; c) J. Alais, S. David, *Carbohydr. Res.* **1990**, *201*, 69–77; d) W. Gunther, H. Kunz, *Carbohydr. Res.* **1992**, *228*, 217–241; e) F. W. Lichtenthaler, U. Klares, M. Lergenmuller, S. Schwidetzky, *Synthesis* **1992**, 179–184; f) F. Barresi, O. Hindsgaul, *Can. J. Chem.* **1994**, *72*, 1447–1465; g) T. Ziegler, G. Lemanski, *Angew. Chem.* **1998**, *110*, 3367–3369; *Angew. Chem. Int. Ed.* **1998**, *37*, 3129–3132; h) D. Crich, S. Sun, *Tetrahedron* **1998**, *54*, 8321–8348; for reviews, see: i) F. Barresi, O. Hindsgaul in *Modern Methods in Carbohydrate Synthesis* (Eds.: S. H. Khan, R. A. O'Neill), Harwood Academic, Amsterdam, **1996**, pp. 251–276; j) J. J. Gridley, H. M. I. Osborn, *J. Chem. Soc. Perkin Trans. 1* **2000**, 1471–1492.
[6] D. H. G. Crout, G. Vic, *Curr. Opin. Chem. Biol.* **1998**, *2*, 98–111.
[7] a) M. Scigelova, S. Singh, D. H. G. Crout, *J. Chem. Soc. Perkin Trans. 1* **1999**, 777–782; b) N. Taubken, J. Thiem, *Glycoconjugate J.* **1998**, *15*, 757–767; c) H. Prade, L. F. Mackenzie, S. G. Withers, *Carbohydr. Res.* **1998**, *305*, 371–381; d) T. Usui, M. Suzuki, T. Sato, H. Kawagishi, K. Adachi, H. Sano, *Glycoconjugate J.* **1994**, *11*, 105–110; e) S. Kyosaka, S. Murata, Y. Tsuda, M. Tanaka, *Chem. Pharm. Bull.* **1986**, *34*, 5140–5143.
[8] a) G. M. Watt, L. Revers, M. C. Webberley, I. B. H. Wilson, S. L. Flitsch, *Angew. Chem.* **1997**, *109*, 2445–2447; *Angew. Chem. Int. Ed.* **1997**, *36*, 2354–2356; b) G. M. Watt, L. Revers, M. C. Webberley, I. B. H. Wilson, S. L. Flitsch, *Carbohydr. Res.* **1998**, *305*, 533–541; c) L. Revers, R. M. Bill, I. B. H. Wilson, G. M. Watt, S. L. Flitsch, *Biochim. Biophys. Acta* **1999**, *1428*, 88–98; d) Y. Zhao, J. B. Biggins, J. S. Thorson, *J. Am. Chem. Soc.* **1998**, *120*, 12986–12987; e) Y. Zhao, J. S. Thorson, *Carbohydr. Res.* **1999**, *319*, 184–191.
[9] a) S. Fort, V. Boyer, L. Greffe, G. J. Davies, O. Moroz, L. Christiansen, M. Schülein, S. Cottaz, H. Driguez, *J. Am. Chem. Soc.* **2000**, *122*, 5429–5437; b) A. Trincone, G. Perugino, M. Rossi, M. Moracci, *Biorg. Med. Chem. Lett.* **2000**, *10*, 365–368; c) C. Mayer, D. L. Zechel, S. P. Reid, R. A. J. Warren, S. G. Withers, *FEBS Lett.* **2000**, *466*, 40–44; d) C. Malet, A. Planas, *FEBS Lett.* **1998**, *440*, 208–212; e) L. F. Mackenzie, Q. Wang, R. A. J. Warren, S. G. Withers, *J. Am. Chem. Soc.* **1998**, *120*, 5583–5584.
[10] D. L. Zechel, S. G. Withers, *Acc. Chem. Res.* **2000**, *33*, 11–18.
[11] D. Stoll, H. Stalbrand, R. A. J. Warren, *Appl. Environ. Microbiol.* **1999**, *65*, 2598–2605.
[12] S. G. Withers, R. Aebersold, *Protein Sci.* **1995**, *4*, 361–372.
[13] D. Stoll, S. He, S. G. Withers, R. A. J. Warren, *Biochem. J.* **2000**, *351*, 833–838.
[14] More active mannosynthase mutants may prove successful in mannosylating derivatives of GlcNAc. Indeed, it proved possible to synthesize *N*-acetyl lactosamine in good yield from α-galactosyl fluoride and benzyl β-GlcNAc using the more active *Agrobacterium* sp. Glu358Ser glycosynthase.[9c]
[15] The mannoside linkage formed was confirmed to be the β anomer by the 160 Hz J(C,H) coupling constant, which was measured for C-1 of the mannose residue in the disaccharide products **1a** and **3a** (see: K. Bock, C. Pedersen, *J. Chem. Soc. Perkin Trans. 2* **1974**, 293–297).
[16] Branched oligosaccharide products synthesized by glycosynthases have been reported previously.[9a,b]
[17] B. Capon, *Chem. Rev.* **1969**, *69*, 407–498.
[18] H. D. Ly, S. G. Withers, *Annu. Rev. Biochem.* **1999**, *68*, 487–522.
[19] Equivalent concentrations of KCl did not rescue glycosidic bond cleaving activity.
[20] A 10^3-fold enhancement of activity for a mutant glutamate dehydrogenase in the presence of fluoride ions has been reported recently, but is believed to arise from the fluoride ions fulfilling an electrostatic role. See: B. M. Hayden, J. L. E. Dean, S. R. Martin, P. C. Engel, *Biochem. J.* **1999**, *340*, 555–560.
[21] The glycosynthase-catalyzed in situ generation of 1-*O*-formyl α-glycosides from activated β-glycosides and formate has been reported (J.-L. Viladot, E. de Ramon, O. Durany, A. Planas, *Biochemistry* **1998**, *37*, 11332–11342; M. Moracci, A. Trincone, G. Perugino, M. Ciaramella, M. Rossi, *Biochemistry* **1998**, *37*, 17262–17270) and successfully used as a method for oligosaccharide synthesis.[9b]
[22] A. Aiyar, J. Leis, *BioTechniques* **1993**, *11*, 404.
[23] S. C. Gill, P. H. von Hippel, *Anal. Biochem.* **1989**, *182*, 319–326.
[24] 2,4-DNPMan was synthesized in three steps by the method of Garegg et al. (P. J. Garegg, T. Iversen, T. Norberg, *Carbohydr. Res.* **1979**, *73*, 313–314).
[25] Logger Pro Version 1.1, Tufts University and Vernier Software, **1999**.
[26] R. J. Leatherbarrow, GraFit 3.09b, Erithacus Software Ltd., **1996**.

6-Aminofulvene-1-aldimine: A Model Molecule for the Study of Intramolecular Hydrogen Bonds**

Rosa María Claramunt,* Dionísia Sanz, Sergio Hugo Alarcón, Marta Pérez Torralba, José Elguero, Concepción Foces-Foces, Mariusz Pietrzak, Uwe Langer, and Hans-Heinrich Limbach

The search for new systems that sustain phenomena such as intramolecular hydrogen bonds (IMHB),[1, 2] proton transfer along hydrogen bonds,[3, 4] and coupling constants through hydrogen bonds,[5, 6] led us to select 6-aminofulvene-1-aldimines. These compounds were reported in the 1970s by Müller-Westerhoff and Ammon, who determined the X-ray structure of **1** and its NMR spectroscopic properties in solution.[8, 9]



[*] Prof. Dr R. M. Claramunt, Dr. D. Sanz, Dr. S. H. Alarcón, M. Pérez Torralba
Departamento de Química Orgánica y Biología
Facultad de Ciencias, UNED
Senda del Rey 9, 28040 Madrid (Spain)
Fax: (+34) 91-398-6697
E-mail: rclaramunt@ccia.uned.es

Prof. Dr. J. Elguero
Centro de Química Orgánica Manuel Lora-Tamayo, CSIC
Juan de la Cierva 3, 28006 Madrid (Spain)

Prof. Dr. C. Foces-Foces
Departamento de Cristalografía
Instituto de Química Física "Rocasolano", CSIC
Serrano 119, 28006 Madrid (Spain)

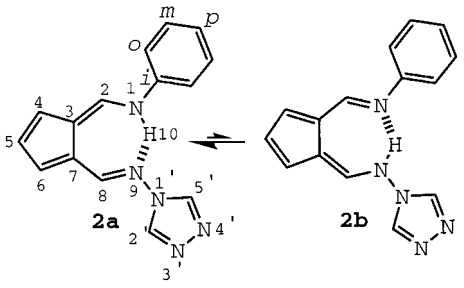
M. Pietrzak, U. Langer, Prof. Dr. H.-H. Limbach
Fachbereich Biologie, Chemie, und Pharmazie
Freie Universität Berlin
Takustrasse 3, 14195 Berlin (Germany)

[**] We are indebted to DGES/MEC (PB96-0001-C03) and Comunidad de Madrid (grant no. 07N/0001/1999) of Spain for financial support and to Dr. Ibon Alkorta for carrying out the B3LYP/6-31G calculations.

  0044-8249/01/11302-0434 $ 17.50+.50/0

It is clear from these studies and from others by Jackman et al.,[10] that **1** is very suitable for advancing the knowledge of the problems that we have summarized above. It is an analogue of the enol of a double imine (the β-enaminoimines),[11] but with a pseudo seven-membered instead of pseudo six-membered ring. The X-ray structure shows that **1** has an asymmetric hydrogen bond in the solid state while in solution it behaves like a symmetric compound, that is, as if **1a** and **1b** were in very rapid equilibrium. These observations can be rationalized with the hypothesis that **1** is a case of low barrier hydrogen bonding (LBHB) with a double-well potential.

The "symmetric" character of **1** makes it difficult to study its NMR properties in solution. Therefore, we decided to synthesize a highly asymmetric 6-aminofulvene-1-aldimine. We chose to replace one of the phenyl groups in **1** with a triazole, which results in compound **2**. For the NMR studies, labeling of the nitrogen atoms of the hydrogen bond, N1 and N9, was required. Since the four nitrogen atoms of aminotriazole (N9, N1′, N3′, and N4′) come from hydrazine, it is easy to prepare the fully labeled compound [$^{15}N_5$]-**2**. Compounds **2** and [$^{15}N_5$]-**2** were prepared, in two steps, from 6-*N*,*N*-dimethylaminofulvene-1-*N*,*N*-dimethylaldimmonium perchlorate (**3**; not shown).[12] First, reaction of **3** with one mole of 4-amino-1,2,4-triazole afforded the intermediate *N*-[{5-[(dimethylamino)methylene]-1,3-cyclopentadien-1-yl}methylene]-4-amino-1,2,4-triazole (**4**; not shown), which after isolation was treated with one mole of aniline. The corresponding $^{15}N_5$-labeled derivative was prepared in the same way but with [^{15}N]-aniline (commercial) and [$^{15}N_4$]-4-amino-1,2,4-triazole (see Experimental Section).



The crystal structure analysis of **2** (Figure 1a) shows[13] that pattern of the bond lengths and angles does not display the C_{2v} symmetry previously observed in compound **1**.[9] This fact is consistent with the presence of a maximum close to the N1 atom and with the lack of electron density near N9 in a difference synthesis computed at the end of the refinement. The C8–N9 and C2–N1 distances are close to the values of 1.279(8) and 1.339(16) Å reported for caryl–C=N–C and C=C–NH–C fragments.[17] In addition, the value of the angle at N1, to which the H atom is bonded, is significantly greater

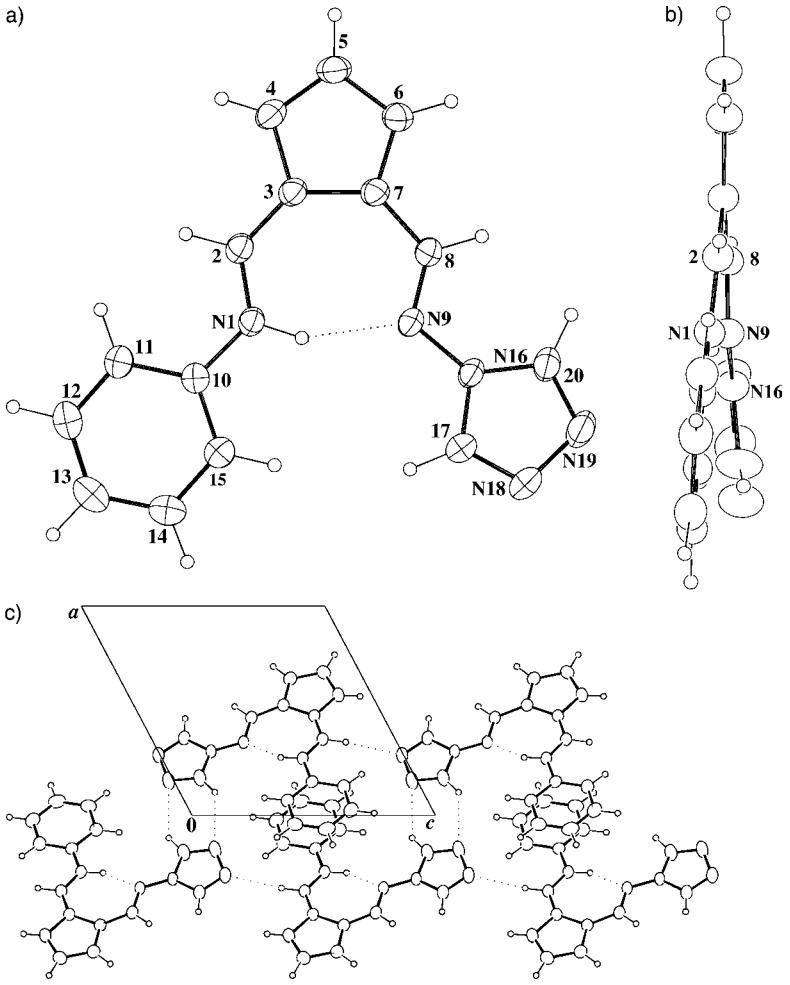


Figure 1. Compound **2** in the solid state. a) Molecular structure which shows the numbering system. Selected bond lengths [Å] and angles [°]: N1-C2 1.321(2), C2-C3 1.377(2), C7-C8 1.423(2), C8-C9 1.285(2); C2-N1-C10 126.1(1), C8-N9-N16 116.0(1). b) A perpendicular view to that of a) which shows the conformation of the molecule. Selected angles [°]: C2-C3-C7-C8 −8.3(3), C3-C7-C8-N9 3.4(3), C7-C8-N9-N16 −179.1(2), C8-N9-N16-C20 −7.0(3), C7-C3-C2-N1 −1.6(3), C3-C2-N1-C10 −178.6(2), C2-N1-C10-C11 1.6(3). c) Partial packing diagram along the *b* axis to illustrate the one strand formed by two centrosymmetric hydrogen-bonding chains. Hydrogen-bonding interactions (given as D–H···A (symmetry operation), D···A and H···A distances [Å], D–H···A angle [°]): N1–H1···N9 (x,y,z), 2.837(2) and 1.97(2), 153(1); C17–H17···N18 ($-x,1-y,-z$), 3.349(3) and 2.55(3), 138(2); C2–H2···N19 ($x,y,1+z$), 3.470(3) and 2.64(3), 141(2).

than the corresponding one at N9. The phenyl and the triazole rings are almost coplanar in **2** (Figure 1b), the greatest torsion angle is the C2–C3–C7–C8 angle, and the C2 and C8 atoms are located on opposite sides of the five-membered plane—0.094(2) and 0.076(2) Å, respectively. The presence of the N1–H1···N9 intramolecular hydrogen bond may be responsible for the planarity of this system, together with some degree of charge delocalization, which is mainly observed in the C7–C3–C2–N1 fragment. Figure 1c illustrates the arrangement of molecules in centrosymmetric dimers through C17–H17···N18 contacts between triazoles. Besides this, weaker C2–H2···N19 contacts form a chain of dimers giving rise to a ribbon-like network and allowing a partial overlap of the phenyl rings. These strands, related by 2_1-screw axis/glide plane, pack in a herringbone fashion. In summary, the structure of **2** determined by X-ray crystal analysis is that of tautomer **2a**, a result that is in agreement with the higher

acidity of the N-triazole group relative to the N-phenyl moiety.

Table 1 summarizes the most relevant data related to the IMHB of compound **2** in solution. Of importance are: 1) the negative primary isotope shift, $^{P}\Delta = -0.13$, which corresponds to an asymmetric double well potential, according to Hibbert and Emsley, between medium and weak hydrogen bonds;[18]

Table 1. Summary of the most relevant NMR spectroscopy data[a] of compound [$^{15}N_5$]-**2** and its derivative [$^{15}N_5$,$^{2}H_1$]-**2** (monodeuterated at position 10).

	[^{15}N,^{1}H]-**2**		[^{15}N,^{2}H]-**2**
δ^{1}H	12.77		–
δ^{2}H	–		12.65
$^{P}\Delta$[b]		−0.13	
δ^{15}N1	−238.1		−239.3
δ^{15}N9	−121.0		−120.9
^{1}J(N1,H)[c]	88.6		–
^{1}J(N1,D)[c]	–		13.2
^{1}J(N1,H)/^{1}J(N1,D)[d]		6.7	
^{1h}J(N9,H)[c]	4.4		–
^{1d}J(N9,D)[c]	–		not observed
^{1}J(N9,H)/^{1}J(N9,D)[d]		<1	
^{2h}J(N1···H···N9)[c]	8.6		–
^{2d}J(N1···D···N9)[c]	–		8.5

[a] Solvent = $CDCl_3$. [b] $\delta^{2}H - \delta^{1}H$. [c] Values in Hz. [d] Theoretical value = 6.5.

2) the coupling constants involving the N−H···N system and in particular the scalar one, ^{2h}J(N1−H···N9), of 8.6 Hz. Note that the ratio of ^{1}J(^{15}N,^{1}H) to ^{1}J(^{15}N,^{2}H) is close to the theoretical value of 6.5, while there was no significant effect on the coupling constant ^{2d}J(N−H(D)···N) when deuterium replaced protium. Moreover, we have prepared the N-methyl derivative of [$^{15}N_5$]-**2** (replacement of H10 by a methyl group) and in this case the ^{2h}J($^{15}N_1$,$^{15}N_9$) disappears.

We have carried out HF/6-31G** and HF/6-311G** ab initio calculations on tautomers **2a** and **2b**, and on a model compound **5** (where the phenyl rings of **1** have been replaced by hydrogen atoms). In the case of compound **2**, the HF/6-31G** calculations yield the following values: **2a**: energy = −847.75472 hartrees, $\mu = 7.25$ D, ($r_{NN} = 2.893$ Å); **2b**: energy = −847.74843 hartrees, $\mu = 5.59$ D, ($r_{NN} = 2.833$ Å). Therefore, an extra stabilization of 16.5 kJ mol^{-1} is found for tautomer **2a**; this result corresponds to the experimental findings both in the solid state and in solution.

Three series of calculations were carried out on model compound **5**, HF/6-31G**, HF/6-311G**, and B3LYP/6-31G*. The calculated barriers to proton transfer are 47.8, 49.4, and 18.8 kJ mol^{-1}, respectively. As expected, the inclusion of electronic correlation, through the density functional approach, considerably improves the results.[19] When the zero-point energy correction is included, the last barrier lowers to 7.3 kJ mol^{-1}. Therefore, **5**, and probably **1** and **2** as well, are LBHB although the hydrogen bonds are not necessarily very strong.

Since we have established without doubt that a ^{2h}J(^{15}N,^{15}N) is evident for compound **2** (see Table 1), then the coupling constant of 4.4 Hz could have been assigned to either a ^{1h}J(^{15}N9,^{1}H10) for **2a** or a classical ^{1}J(^{15}N9,^{1}H10) for a small amount of tautomer **2b**. We do not think that the latter explanation is true because both ^{1}J(^{15}N1,^{1}H10) of 88.6 Hz and the ^{1h}J(^{15}N9,^{1}H10) of 4.4 Hz are independent of temperature and solvent (the same values were obtained in THF and DMF). Even if ΔS could be zero, it is highly improbable that the equilibrium **2a**/**2b** would be solvent independent when the difference in dipole moments is taken into account (see above). Therefore, we assume that the large value of ^{1h}J(^{15}N9,^{1}H10) is associated with the special properties of the hydrogen bond in **2**.

A novel, asymmetric ^{15}N-labeled seven-membered hydrogen chelate exhibiting a strong intramolecular asymmetric hydrogen bond has been synthesized, and its structure studied by X-ray crystallography, NMR spectroscopy, and ab initio calculations. The compound does not only exhibit a substantial ^{15}N···^{15}N coupling constant but also an unusually large H···^{15}N coupling across the hydrogen bond. Evidence is provided that this coupling is not the result of a tautomerism. These results open up a new field of hydrogen-bond research by NMR spectroscopy. This work has increased the understanding of the behavior of 6-aminofulvene-1-aldimines, but ^{13}C and ^{15}N NMR studies in the solid state are necessary and ^{15}N-labeled **1** should be prepared in order to determine the values of ^{2h}J(^{15}N,^{15}N) and ^{1h}J(^{15}N,^{1}H) in the case of a "symmetrical" compound by indirect NMR methods in solution.

Experimental Section

General: Melting points were determined by differential scanning calorimetry on a SEIKO DSC 220C connected to a Model SSC5200H Disk Station. Thermograms (sample size 3–10 mg) were recorded at the scanning rate of 2.0 °C min^{-1}. Column chromatography was performed on silica gel (Merck 60; 70–230 mesh) and the R_f values were measured by thin layer chromatography on aluminum sheets of silicagel (60 F254; thickness 0.2 mm) using the appropriate eluent. FAB mass spectrometry of **2** has already been described.[20] Hartree–Fock ab initio calculations were carried out with the Spartan 5.0 package running on a Silicon Graphics O2 workstation. NMR spectra were recorded on a Bruker DRX 400 spectrometer (9.4 Tesla, 400.13 MHz for ^{1}H, 61.42 MHz for ^{2}H, 100.62 MHz for ^{13}C, and 40.56 MHz for ^{15}N). Chemical shifts (δ) are given based on internal $CDCl_3$ (7.26 (^{1}H), 7.25 (^{2}H), and 77.0 ppm (^{13}C)) and external nitromethane for ^{15}N. Coupling constants (J) are accurate to ±0.2 Hz for ^{1}H and ±0.6 Hz for ^{13}C and ^{15}N.

Compound [$^{15}N_4$]-**4**: A solution of 6-*N*,*N*-dimethylaminofulvene-1-*N*,*N*-dimethylaldimmonium perchlorate (**3**)[12] (1 g, 3.21 mmol) in EtOH (20 mL) was refluxed with [$^{15}N_4$]-4-amino-1,2,4-triazole[21] (0.57 g, 6.48 mmol) for 21 h. The solvent was removed by evaporation and the crude product was purified by column chromatography with EtOH/chloroform (1/3) to afford [$^{15}N_4$]-**4** (0.42 g, 60%). mp 201.6 °C (decomp up to 207.4 °C); ^{1}H NMR ($CDCl_3$): $\delta = 8.81$ (br. s, H2), 8.47 (ddd, $^{2}J_{H8,N9} = 2.2$, $^{3}J_{H8,N1'} = 8.1$, $^{5}J_{H8,H4} = 0.6$ Hz; H8), 8.42 (m; H2′ and H5′), 6.97 (dd; H4), 6.86 (dd, $^{4}J_{H6,H4} = 1.6$ Hz; H6), 6.52 (ddd, $^{3}J_{H5,H6} = 3.2$, $^{3}J_{H5,H4} = 4.6$, $^{5}J_{H5,H2} = 0.9$ Hz; H5), 3.46 (s, CH_3), 3.36 (s, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 157.5$ ($^{1}J = 156.5$, $^{3}J_{C,H} = 3.4$ Hz; C8), 152.9 ($^{1}J = 170.1$, $^{4}J_{C,N} = 3.8$ Hz; C2), 138.3 ($^{1}J = 211.7$, $^{3}J_{C,H} = 4.0$, $^{1}J_{C,N} = 13.5$ Hz; C2′ and C5′), 134.2 ($^{1}J = 165.2$, $^{3}J_{C,N} = 3.9$ Hz; C6), 125.0 ($^{1}J = 166.2$ Hz; C4), 124.7 ($^{2}J_{C,N} = 5.2$, $^{3}J_{C,N} = 6.9$ Hz; C7), 123.0 ($^{1}J = 167.0$, $^{2}J_{C,H} = {}^{2}J_{C,H} = 3.6$ Hz; C5), 113.1 (C3), 48.2 ($^{1}J = 140.3$ Hz; CH_3), 41.0 ($^{1}J = 140.5$ Hz; CH_3); ^{15}N NMR ($CDCl_3$): $\delta = -268.2$ (N1), −162.6 ($^{1}J_{N9,N1'} = 13.8$ Hz; N1′), −103.6 ($^{1}J_{N9,N1'} = 13.8$ Hz; N9), −66.5 (N3′ and N4′); elemental analysis calcd for unlabeled $C_{11}H_{13}N_5$: C 61.38, H 6.09, N 32.54; found: C 61.59, H 6.18, N 32.42.

Compound [$^{15}N_5$]-**2**: A solution of [$^{15}N_4$]-**4** (0.35 g, 1.60 mmol) in EtOH (18 mL) was refluxed with ^{15}N-labeled aniline (0.19 g, 2.00 mmol) for 7 h. The solvent was removed by evaporation and the crude product was purified by column chromatography with the following eluents: with

  0044-8249/01/11302-0436 $ 17.50+.50/0

AcOEt/hexane (5/1) [$^{15}N_2$]-**1** (R_f 0.88 in $CHCl_3$/EtOH (10/1)) was eluted first, followed by unreacted aniline (R_f 0.67 in $CHCl_3$/EtOH (10:1)); with AcOEt [$^{15}N_5$]-**2** was eluted (R_f 0.46 in $CHCl_3$/EtOH (10:1)); finally, with $CHCl_3$/EtOH (10/1), the starting material [$^{15}N_4$]-**4** was recovered (R_f 0.24 in $CHCl_3$/EtOH (10:1)). Product: [$^{15}N_5$]-**2** (0.21 g, 49%); mp 213.9°C (decomp); ^{1}HNMR ($CDCl_3$): $\delta = 12.77$ (ddd, $^1J_{N1,H10} = 88.6$, $^3J_{H10,H2} = 13.9$, $^{1h}J_{N9\cdots H10} = 4.4$ Hz; H10), 8.54 (ddd, $^2J_{H8,N9} = 2.4$, $^3J_{H8,N1'} = 7.3$ Hz; H8), 8.51 (m; H2′ and H5′), 8.06 (td, $^4J_{H2,N9} = {}^5J_{H2,H6} = 0.9$ Hz; H2), 7.44 (t; ArH(*m*)), 7.26 (ddd; H6), 7.24 (m; ArH(*o*)), 7.20 (m; ArH(*p*)), 7.08 (ddd, $^4J_{H6,H4} = 1.9$, $^5J_{H4,H8} = 0.7$ Hz; H4), 6.53 (dd, $^3J_{H5,H6} = 3.2$, $^3J_{H5,H4} = 4.3$ Hz; H5); ^{13}CNMR ($CDCl_3$): $\delta = 157.9$ ($^1J = 159.4$, $^3J_{C,H} = 4.0$, $^1J_{C,N} = 4.8$ Hz; C8), 143.9 ($^1J = 166.7$, $^1J_{C,N} = 15.9$ Hz; C2), 141.4 ($^1J = 159.4$, $^3J_{C,N} = 4.8$ Hz; C6), 139.0 ($^1J_{C,N} = 14.8$ Hz; ArC(*i*)), 138.4 ($^1J = 211.1$, $^1J_{C,N} = 12.3$ Hz; C2′ and C5′), 135.9 ($^1J = 166.4$, $^3J_{C,N} = 3.5$ Hz; C4), 130.2 ($^1J = 162.1$, $^3J_{C,N} = 1.9$ Hz; ArC(*m*)), 125.8 ($^1J = 163.8$ Hz; ArC(*p*)), 122.3 ($^1J = 168.7$ Hz; C5), 120.0 ($^2J_{C,N} = 5.2$, $^3J_{C,N} = 8.5$ Hz; C7), 117.4 ($^1J = 155.3$ Hz; ArC(*o*)), 116.9 (C3); ^{15}N NMR ($CDCl_3$): $\delta = -238.1$ ($^{2h}J_{N1-H10\cdots N9} = 8.6$ Hz; N1), −167.7 ($^1J_{N9,N1'} = 11.8$ Hz; N1′), −121.0 ($^{2h}J_{N1-H10\cdots N9} = 8.6$, $^1J_{N9,N1'} = 11.8$ Hz; N9), −64.4 (N3′ and N4′); ^{15}N NMR ($CDCl_3$+D_2O): $\delta = -239.3$ ($^1J_{N1,D} = 13.2$, $^{2h}J_{N1-D\cdots N9} = 8.5$ Hz; N1), −167.3 ($^1J_{N9,N1'} = 12.0$ Hz; N1′), −120.9 ($^1J_{N9,N1'} = 11.9$, $^{2h}J_{N1-D\cdots N9} = 8.5$ Hz; N9), −66.8 (N3′ and N4′); elemental analysis calcd for unlabeled $C_{15}H_{13}N_5$: C 68.42, H 4.98, N 26.60; found: C 68.60, H 4.96, N 26.52.

The N-methyl derivative of [$^{15}N_5$]-**2** in [D_8]THF presents the following ^{15}N NMR signals: $\delta = -254.2$ (N1), −163.6 (N1′), −100.2 (N9) and −63.5 (N3′ and N4′).

Received: September 4, 2000 [Z15758]

[1] C. L. Perrin, J. L. Nielson, *Annu. Rev. Phys. Chem.* **1997**, *48*, 511–544.

[2] J. M. Ugalde, I. Alkorta, J. Elguero, *Angew. Chem.* **2000**, *112*, 733–737; *Angew. Chem. Int. Ed.* **2000**, *39*, 717–721.

[3] S. Scheiner, *Molecular Interactions. From van der Waals to Strongly Bound Complexes*, Wiley, New York, **1997**.

[4] M. A. García, C. López, O. Peters, R. M. Claramunt, O. Klein, D. Schagen, H.-H. Limbach, C. Foces-Foces, J. Elguero, *Magn. Reson. Chem.* **2000**, *38*, 604–614.

[5] Scalar couplings transmitted through the hydrogen bond were first observed in proteins and very recently Limbach et al. detected a range of ^{nh}J coupling values (with *n* being the number of bonds, including the hydrogen bond) across hydrogen bonds in small molecules.[6] These coupling values prove to be very accurate measures for the strength of bonds.[7]

[6] S. Borman, *Chem. Eng. News.* **1999**, *77*(19), 36–38, and references therein.

[7] I. Shenderovich, S. Smirnov, G. S. Denisov, V. Gindin, N. S. Golubev, A. Dunger, R. Reibke, S. Kirpekar, O. L. Malkina, H. H. Limbach, *Ber. Bunsenges. Phys. Chem.* **1998**, *102*, 422–428; N. S. Golubev, I. G. Shenderovich, S. N. Smirnov, G. S. Denisov, H.-H. Limbach, *Chem. Eur. J.* **1999**, *5*, 492–497; H. Benedict, I. G. Shenderovich, O. L. Malkina, V. G. Malkin, G. S. Denisov, N. S. Golubev, H. H. Limbach, *J. Am. Chem. Soc.* **2000**, *122*, 1979–1988.

[8] U. Müller-Westerhoff, *J. Am. Chem. Soc.* **1970**, *92*, 4849–4855.

[9] H. L. Ammon, U. Müller-Westerhoff, *Tetrahedron* **1974**, *30*, 1437–1443.

[10] L. M. Jackman, J. C. Trewella, R. C. Haddon, *J. Am. Chem. Soc.* **1980**, *102*, 2519–2525.

[11] G. Gilli, P. Gilli, *J. Mol. Struct.* **2000**, *552*, 1–15.

[12] K. Hafner, K. H. Vöpel, G. Ploss, C. König, *Justus Liebigs Ann. Chem.* **1963**, *661*, 52–75.

[13] Crystal data: $C_{15}H_{13}N_5$, dark yellow prism crystal of dimensions 0.43 × 0.23 × 0.23 mm, monoclinic, $P2_1/c$, $a = 9.7535(4)$, $b = 15.0973(8)$, $c = 10.0325(4)$ Å, $\beta = 117.852(3)°$, $V = 1306.2(1)$ Å^3, $\rho_{calcd} = 1.339$ g cm^{-3}, $Z = 4$, $\mu = 6.085$ cm^{-1}, 2328 independent reflections, $R(Rw) = 0.038/0.042$ for 2008 observed reflections with $I > 2\sigma(I)$. Maximum peak in the final difference synthesis 0.17 e Å^{-3}. Philips PW1100 diffractometer, Cu $K\alpha$ radiation, graphite monochromator, $\omega/2\theta$ scans, $\theta_{max} = 67°$. The structure was solved by direct methods[14] and all hydrogen atoms were obtained unambiguously from difference Fourier synthesis. No indication of proton disorder was observed either in terms of the values of bond angles at N1 and N9 or from difference Fourier maps. The weighting scheme was established in an empirical way so as to give no trends in $\langle \omega\Delta^2F \rangle$ versus $\langle F_o \rangle$ or $\langle \sin\theta/\lambda \rangle$ ($\omega = K/(a + bF_o)^2][c + d\sin\theta/\lambda]$; the *a*, *b*, *c*, and *d* parameters were adjusted to flatten the initial trends.[15] Most calculations have been performed with the Xtal system.[16] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-144230. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[14] SIR97: A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, M. C. Burla, G. Polidori, M. Camalli, R. Spagna, University of Bari, Italy, **1997**.

[15] PESOS: M. Martínez-Ripoll, F. H. Cano, Instituto Rocasolano, CSIC, Madrid, Spain, **1975**.

[16] Xtal 3.2: S. R. Hall, H. D. Flack, J. M. Stewart, University of Western Australia, Australia, University of Geneva, Switzerland, and University of Maryland, USA, **1992**.

[17] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc. Perkin. Trans. 2* **1987**, S1.

[18] F. Hibbert, J. Emsley, *Adv. Phys. Org. Chem.* **1990**, *26*, 255–377. (Note that these authors and Perrin and Nielson[1] use different signs for $^P\Delta$.)

[19] L. González, O. Mó, M. Yañez, *J. Phys. Chem.* **1997**, 101, 9710–9719; Y. Kim, S. Lim, Y. Kim, *J. Phys. Chem. A* **1999**, *103*, 6632–6637.

[20] C. Enjalbal, J. L. Aubagnac, M. Pérez Torralba, D. Sanz, R. M. Claramunt, J. Elguero, ARKIVOC **2000**, *Vol. 1*, part 6 pp. 843–853.

[21] M. Pérez Torralba, PhD Thesis, UNED (Spain), in preparation.

Identification and Isolation of a Receptor for *N*-Methyl Alkylammonium Salts: Molecular Amplification in a Pseudo-peptide Dynamic Combinatorial Library**

Graham R. L. Cousins, Ricardo L. E. Furlan, Yiu-Fai Ng, James E. Redman, and Jeremy K. M. Sanders*

Dynamic combinatorial chemistry[1] (DCC) offers a new strategy for the identification of new host and guest compounds with the potential for catalysis and drug activity.[1, 2] It combines the merits of combinatorial chemistry[3] with molecular evolution, whereby a combinatorial library of candidate molecules is generated by the assembly of building blocks through reversible bonds. As a consequence, all the library members are interconverting through exchange processes to give a product distribution which is under thermody-

[*] Prof. J. K. M. Sanders, G. R. L. Cousins, Dr. R. L. E. Furlan, Dr. Y.-F. Ng, Dr. J. E. Redman
Cambridge Centre for Molecular Recognition
University Chemical Laboratory, University of Cambridge
Lensfield Road, Cambridge, CB2 1EW (UK)
Fax: (+44) 1223-336-017
E-mail: jkms@cam.ac.uk

[**] This work was supported by the Biotechnology and Biological Sciences Research Council (UK), Engineering and Physical Sciences Research Council (UK), Ethyl Corporation (UK), and Fundacion Antorchas and Consejo Nacional de Investigaciones Cientficas y Tecnicas (Argentina).