Intramolecular base-backbone association in 8-bromo-2',3'-O-isopropylidene-adenosine : detection of an O(5')-H...N(3) hydrogen bond via a long range H(5")-N(3) spin-spin coupling

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Intramolecular Base–Backbone Association in 8-Bromo-2′,3′-*O*-isopropylidene-adenosine. Detection of an O(5′)–H · · · N(3) Hydrogen Bond *via* a Long Range H(5″)–N(3) Spin–Spin Coupling

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A completely rigid conformation is found for the *syn*-nucleoside 8-bromo-2′,3′-*O*-isopropylidene-adenosine in apolar solvents, which is due to an effective O(5′)–H · · · N(3) hydrogen bond, as is demonstrated by a substantial N(3) quadrupolar broadening of the H(5″) resonances in the ^{1}H n.m.r. spectra.

In this communication we report the results of a 200 and 300 MHz ^{1}H n.m.r.† conformational study on the modified *syn*-nucleoside 8-bromo-2′,3′-*O*-isopropylidene-adenosine[1] (**1**) in various solvents. It is found that (**1**) displays a conformational rigidity in apolar solvents such as $CDCl_3$ and C_6D_6, owing to an effective hydrogen bond between O(5′) and N(3). Uniquely, this hydrogen bond could be clearly established by a substantial broadening of the H(5″) resonances which is absent in the ^{14}N decoupled spectrum (Figure 1). Apparently, in apolar media the O(5′)–H · · · N(3) hydrogen bond accommodates a planar arrangement of H(5″)–C(5′)–O(5′)–H · · · N(3) which is a prerequisite for the long-range

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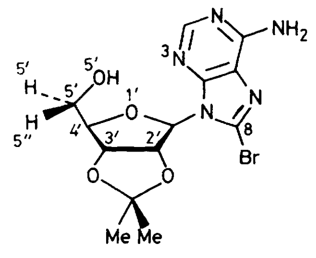
† ^{1}H N.m.r. spectra were run at 200 MHz on a Bruker WM-200 spectrometer (SON high-field n.m.r. facility, Nijmegen), or at 300 MHz on a Bruker CXP-300 spectrometer (n.m.r. facility, Eindhoven University of Technology). ^{14}N Decoupled spectra were run at 200 MHz.



(1)

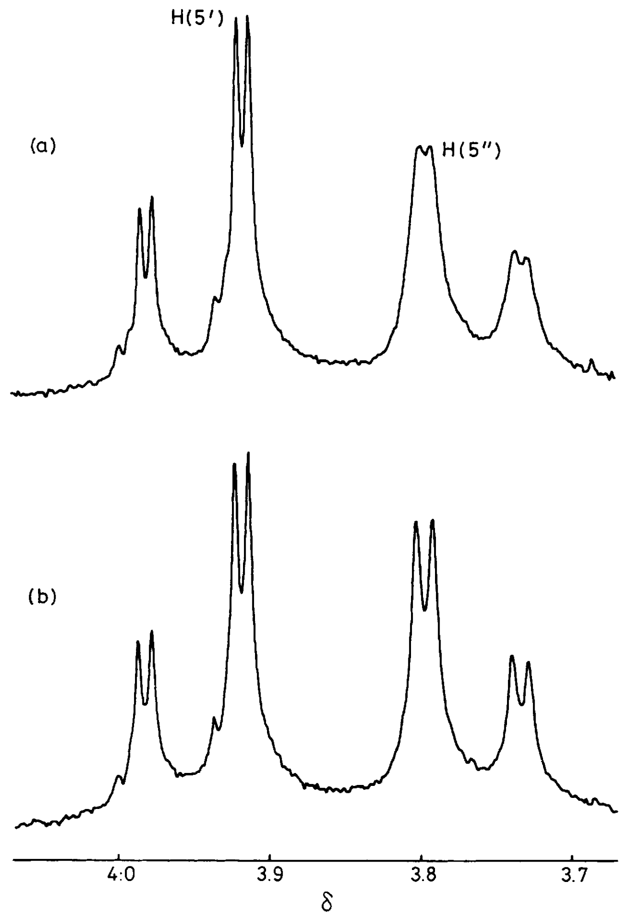


Figure 1. (a) Expansion of the H(5'), H(5'') region of the 200 MHz ^{1}H n.m.r. spectrum of (**1**) in $CDCl_3$. The broadening of the H(5'') resonances is clearly visible. (b) Corresponding ^{14}N decoupled spectrum.

H(5'')–N(3) spin–spin coupling.‡ This geometrical situation is also present in the crystalline state, as could be deduced from the published crystallographic data (Figure 2).[2] Correspondingly, the ^{1}H n.m.r. spectra in $CDCl_3$ and C_6D_6 show that the C(4')–C(5') conformation is 100% *gauche* (+) (g^+) (Table 1).§ The complete conformational rigidity is also reflected in the conformation of the ribose ring which is fully locked in a puckered form I (Figure 3) with $P_I = 200°$ and $\nu_{max,\,I} = 26°$,¶[4] differing only slightly from the ring pucker in the crystal structure ($P = 160°$, $\nu_{max} = 26°$).[2] Increasing the medium polarity by using the solvents CD_3CN, $(CD_3)_2CO$, and CD_3OD leads to a sharpening of the H(5'') resonances, indicating that the O(5')–H · · · N(3) bond is weakened, which results in an overall increased conformational flexibility. This is consistent with the observations that (i) the ribose ring is involved in a two-state conformational equilibrium between the pucker forms I and II ($P_{II} = 300°$, $\nu_{max,\,II} = 26°$;

Table 1. Spectral data and the populations of the g^+ rotamer around C(4')–C(5') in various solvents.

Solvent	$J_{4',5'}$/Hz	$J_{4',5''}$/Hz	$x(g^+)$[a]
$CDCl_3$	1.5	1.8	1.00
C_6D_6	1.6	1.9	1.00
CD_3CN	2.7	2.8	0.82
$(CD_3)_2CO$	3.5	3.5	0.68
CD_3OD	4.1	4.7	0.48
$(CD_3)_2SO$	5.8	5.8	0.22
$(Me_2N)_3PO$	5.3	7.5	0.08

[a] Fraction of the g^+ rotamer around C(4')–C(5').

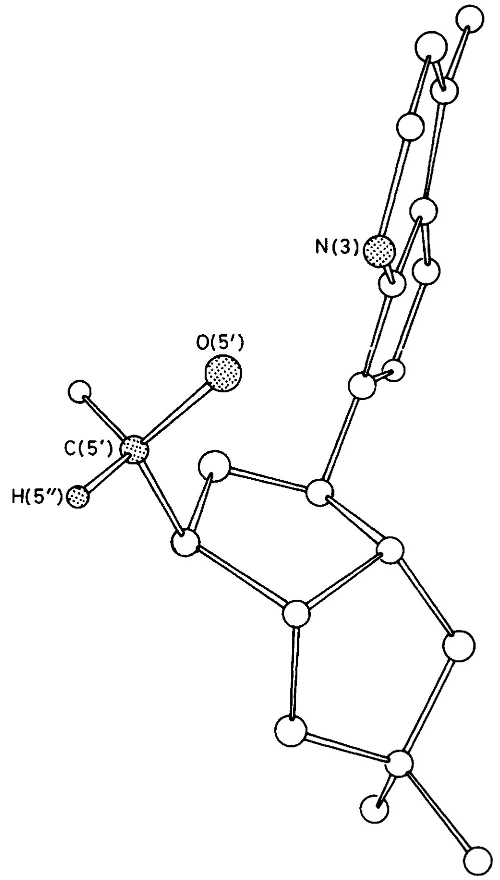


Figure 2. Crystal structure of (**1**), published in ref. 2, viewed along the plane through H(5''), C(5'), O(5'), and N(3).

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‡ Variable temperature ^{1}H n.m.r. measurements have shown that the observed H(5'') broadening is not due to coupling with the OH proton, since no sharpening is observed upon increasing the temperature of the $CDCl_3$ sample to *ca.* 50 °C.

§ In the g^+ rotamer, O(5') is in a gauche orientation with respect to O(1') and C(3'). The g^+ populations were calculated from $J_{4',5'}$ and $J_{4',5''}$ using the generalised Karplus relation developed by Altona *et al.* See ref. 3.

¶ The conformation of the ribose ring was analysed according to Olson and Sussman (see ref. 5), using Figure 3, which was calculated for $\nu_{max.} = 26°$.

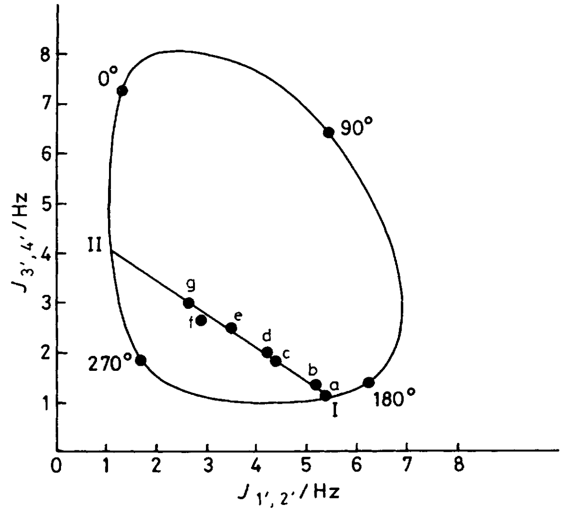

Figure 3. Dependence of the transoidal proton–proton coupling constants $J_{1',2'}$ and $J_{3',4'}$ upon P in ribose systems.[5] The experimental data refer to $CDCl_3$ (a), C_6D_6 (b), CD_3CN (c), $(CD_3)_2CO$ (d), CD_3OD (e), $(Me_2N)_3PO$ (f), and $(CD_3)_2SO$ (g).

see Figure 3), and (ii) the fraction of the g^+ conformation around C(4′)–C(5′), decreases markedly from 1.00 for $CDCl_3$ and C_6D_6 to 0.48 for CD_3OD (Table 1). Very small g^+ populations are found for the hydrogen-bond disrupting solvents $(CD_3)_2SO$ and $(Me_2N)_3PO$[6] (respectively 0.22 and 0.08; see Table 1). Consequently, the broadening of the H(5″) resonances in these media is completely absent.

The present results reveal that the O(5′)–H · · · N(3) hydrogen bond favours the g^+ conformation around the C(4′)–C(5′) linkage and *syn* base-conformation in apolar solvents. Obviously, this hydrogen bond is so tuned that H(5″)–N(3) spin–spin coupling is observable on account of the unique planar arrangement H(5″)–C(5′)–O(5′)–H · · · N(3). To the best of our knowledge this is the first experiment which provides information about an intramolecular long range spin–spin coupling *via* a distinct hydrogen bridge.

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References

1 M. Ikehara, S. Uesugi, and M. Kaneko, *Nucl. Acid Chem.*, 1978, **2**, 837.
2 S. Fujii, T. Fujiwara, and K. Tomita, *Nucl. Acids Res.*, 1976, **3**, 1985.
3 C. A. G. Haasnoot, F. A. A. M. de Leeuw, and C. Altona, *Tetrahedron*, 1980, **36**, 2783.
4 C. Altona and M. Sundaralingam, *J. Am. Chem. Soc.*, 1972, **94**, 8205.
5 W. K. Olson and J. L. Sussman, *J. Am. Chem. Soc.*, 1982, **104**, 270.
6 H. Normant, *Angew. Chem.*, 1967, **23**, 1029.