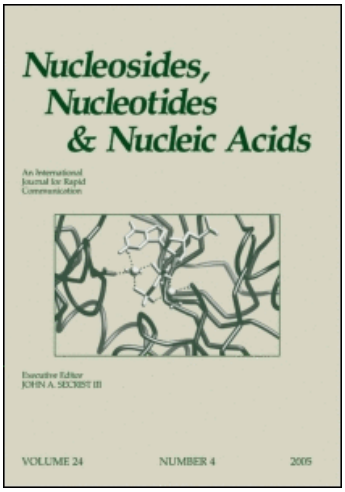


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis and ^{15}N NMR Study of N-7/N-9 Substituted Glyoxal-Guanine Adducts

J. Plavec[a]; J. Kobe[a]
[a] Boris Kidrie Institute of Chemistry, Hajdrihova 19, Ljubljana and Krka, Chemical and Pharmaceutical Works, Novo mesto, Yugoslavia

To cite this Article Plavec, J. and Kobe, J.(1991) 'Synthesis and ^{15}N NMR Study of N-7/N-9 Substituted Glyoxal-Guanine Adducts', Nucleosides, Nucleotides and Nucleic Acids, 10: 1, 249 — 252
To link to this Article: DOI: 10.1080/07328319108046453
URL: http://dx.doi.org/10.1080/07328319108046453

NUCLEOSIDES & NUCLEOTIDES, 10(1-3), 249-252 (1991)

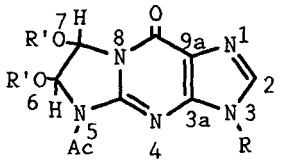
SYNTHESIS AND ^{15}N NMR STUDY OF N-7/N-9 SUBSTITUTED GLYOXAL-GUANINE ADDUCTS

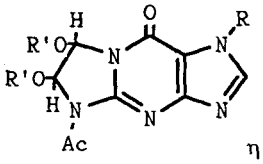
J. Plavec and J. Kobe*

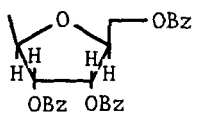
Boris Kidrič Institute of Chemistry, Hajdrihova 19,Ljubljana and Krka, Chemical and Pharmaceutical Works, Novo mesto, Yugoslavia

Abstract : The application of INEPT pulse sequence for the structure considerations about regioisomeric pairs of glyoxal-guanine adducts **I-VI** revealed coupling constants $J_{N,H}$ through up to four bonds at natural isotopic abundance.

The use of glyoxal-guanine adducts (*I*,*R'*=acyl,*R*=*H*) with O-6/N-1 amide and N^2-amino functions of guanine residue protected [1-3] in the condensation reactions with glycosyl acetates and chlorides and their acyclic analogues gives N^3 and N^1 substituted imidazo/1,2-a/purines like **I-VI** with the regio- and stereoselectivity strongly dependent on the reaction conditions.





					η_{tot}	N-3/1	β/α
I	R'= Ac	R = $-CH_2OCH_2CH_2OAc$	II	55%[4a]	1.50		
III	R'= Ac	R = $-CH_2OCH(CH_2OCH_2Ph)_2$	IV	65%[4b]	1.17		
V	R'= iPrCO	R = 	VI	68%[4c]	1.70	19.0	

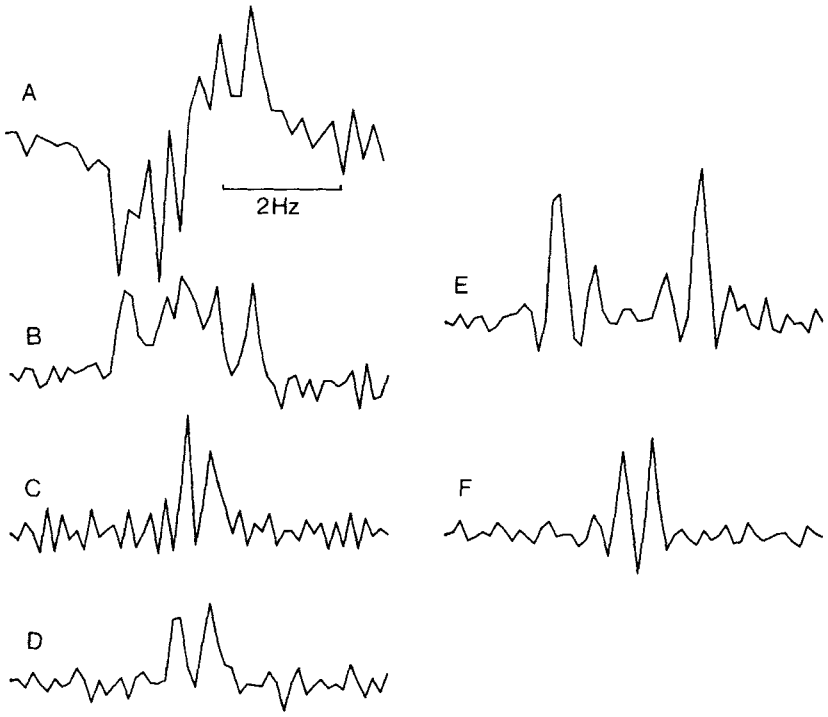


FIG.1 : ^{15}N INEPT spectra of compound **I** : A-unrefocused for atom N-4; B-(N-4) refocused; C-(N-4) selective irradiation of H-2 during acquisition ; D-(N-4) selective irradiation of H-6,7; E-refocused for atom N-5; F-(N-5) H-6,7 selectively irradiated

All ^{15}N NMR resonances were unequivocaly assigned by the application of INEPT[5] pulse sequence and by the observation of a characteristic negative NOE.

In a typical experiment, the assumed J value introduced into the INEPT multipulse sequence was used by standard Varian software to calculate excitation transfer delay (D_3=1/2J) and refocusing delay (D_2=1/3J) enabling the observation of proton coupling through up to four bonds for all nitrogen atoms. There was no peak missing in INEPT spectra in comparison to decoupled ^{15}N NMR spectra as reported for 8,9-dihydro-imidazo/1,2-a/purines[6]. The signal of N-4 in **I** consists of 7 resolved lines (FIG.1A) which suggests coupling with protons H-2, 6 and 7. The complicated

TABLE 1 : ^{15}N NMR chemical shifts and coupling constants $J_{N,H}$ of compounds **I, II, III, IV, V** and **VI**

compound	N-1 (^2J)	N-4 (^4J)	N-3 (^2J)	N-8 ($^2J, ^3J$)	N-5 ($^2J, ^3J$)
I	-130.5 (11.7)	-202.2 (0.3;0.6;1.3)	-207.1 (8.7)	-216.3 (0.3;1.9)	-229.5 (0.5;2.3)
II	-208.4 (7.6)	-183.2 (0.2;0.5;1.0)	-127.6 (11.5)	-216.0 (0.2;2.0)	-229.4 (0.6;1.7)
III	-131.5 (11.6)	-201.1 (0.5;1.0;2.0)	-204.7 (8.6)	-216.3 (0.4;2.0)	-229.4 (0.5;1.3)
IV	-207.9 (0.2;7.9)	-184.4 (0.2;0.5;1.0)	-130.4 (11.7)	-217.9 (0.2;2.0)	-230.8 (2.2)
V	-131.6 -130.6 (11.1) (12.4)	-204.5 (0.5;0.8;1.4)	-210.4 -210.7 (1.5;8.9) (1.4;8.5)	-217.71 -217.76 (0.5;0.8) (0.3;0.5)	-231.0 -231.2 (0.3;0.7;1.6) (0.2;0.5;1.2)
VI	-212.1 -212.5 (8.1) (8.2)	-187.25 (0.3;0.7;1.2)	-130.99 -131.3 (11.5) (11.6)	-219.5 (0.9;1.7)	-232.5 -232.6 (0.6;2.2) (0.6;2.0)

Notes : Measurements were carried out at room temperature using 0.38 M $CDCl_3$ solution of I, 0.6 M of II, 0.65M of III, 0.6 M of IV, 0.6 M of V and 0.51 M of VI. The chemical shifts are reported in ppm with respect to $CH_3{}^{15}NO_2$, coupling constants $J_{N,H}$ are in Hz.

coupling pattern was simplified by selective irradiation of protons[7] H-2 (FIG.1C) and H-6,7 (FIG.1D). The signals of N-1 in **I, III** and **V** are d with $^2J_{N-1,H-2}$= 11.1-12.4 Hz and so are the signals of N-3 in **II, IV** and **VI**. The N-3 atoms in N^3 isomers and N-1 atoms in N^1 isomers exhibit $^2J_{N,H-2}$=7.6-8.9 Hz and $^2J_{N,H-1'}$=0.2 Hz in **IV** and 1.4 and 1.5 Hz in **V**. The observation of two sets of resonance lines for **V** and **VI** is due to the presence of two diastereoisomers (of four possible) with H-6 and H-7 in trans relation. The signals of N-8 in all compounds are dd with small ^2J and ^3J values anticipating H-6,7 in transoid form with respect to the lone

pair of N-8. The coupling patterns of N-5 atoms look like dd at a glance (FIG.1E), but after selective irradiation of both H-6 and H-7 residual coupling of N-5 to protons of AcN group was observed (FIG.1F).

Structural and functional studies of nucleic acids employing glyoxal as modifying reagent[8,9] in connection with the observation of $J_{N,H}$ long range coupling constants and impressive dispersion of ^{15}N NMR chemical shifts offer a versatile method for the structure determination of oligomeric fragments of nucleic acids.

REFERENCES

[1] Sekine, M.; Matsuzaki, J.; Hata, T.; *Tetrahedron Lett.* **1982**, *23*, 5287.

[2] Kobe, J.; Kjellberg, J.; Johansson, N.G. *Acta Chem. Scand., Ser. B* **1987**, *41*, 564.

[3] Kjellberg, J.; Johansson, N.G. *Tetahedron* **1986**, *42*, 6541.

[4] [a]The adduct **I**(R'=Ac,R=H) and 2-oxo-1,4-butandiol diacetate (1.2 eq) were refluxed in toluene in the presence of p-toluenesulfonic acid (PTSA) for 12h. Respective N^3 and N^1 regioisomers were isolated as foams by flash chromatography. [b] Compounds **III** and **IV** were prepared by refluxing the adduct **I**(R'=Ac,R=H) and 2-acetoxymethoxy-1,3-dibenzyloxypropane (1.1 eq) in toluene for 5h in the presence of PTSA. [c] In the preparation of **V** and **VI** we have adopted Dudycz,L.W.; Wright, G.E. procedure *Nucleosides & Nucleotides* **1984**, *3*, 33. The adduct **I**(R'=iPrCO,R=H) was suspended in $CH_2Cl_2$and silylated with bis(trimethylsilyl)-acetamide. 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose (1eq) and timethylsilyltrifluoromethanesulfonate (1.3eq) were added and refluxed in CH_2Cl_2 overnight under N_2 atmosphere.

[5] Morris, G.A.; Freeman, R. *J. Am.Chem. Soc.* **1979**, *101*, 760.

[6] Remaud, G.; Kjellberg, J.; Johansson, N.G.; Chattophadyaya, J. *Tetrahedron* **1987**, *43*, 365.

[7] Sierzputowska-Gracz, H.; Wiewiorowski, M.; Kozerski, L.; Philipsborn, W. *Nucleic Acids Res.* **1984**, *12*, 6247.

[8] Kochetkov, N.K.; Budowsky, E.I.; Broude, N.E.; Klebanova, L.M. *Biochim. Biophys. Acta* **1967**, *134*, 492.

[9] Nakaya, K.; Takenaka, O.; Horinishi, H.; Shibata, K. *Biochim. Biophys. Acta* **1968**, *161*, 23.