Restricted Inversion of Pyramidal Nitrogen through π-Electronic Interaction in an Acyclic System

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An sp^3 noninverting geometry of nitrogen in *N*-(isopropylylideneamino)imide stabilized by the π-electronic system has been demonstrated through ^1H NMR and X-ray crystallography. One of the carbonyls and the —C=N— group of *N*-(isopropylideneamino)-3,4-(9′,10′--dihydroanthracene-9′,-10′-diyl)succinimide (**4**) are reduced to —CHOH and —CHNH— (**8**) with an excess of sodium borohydride in methanol. Shielding parameters of isopropyl methyls and VT NMR studies of **8** have indicated a stable pyramidal geometry of exocyclic nitrogen in solution. X-ray crystallographic studies have demonstrated the sp^3 geometry of nitrogen ($<N_1N_2C = 113.7°$) with the lone electron pair in an *anti* orientation to the cage. The *exo*-OH configuration of **6** has suggested that the *endo*-hydroxy compound formed on reduction isomerized by thermodynamic control through the ring-opened intermediate.

The barrier to pyramidal inversion of nitrogen is not high (20–30 kJ mol^{-1}), and in general the rate of inversion in solution of amines of type R_3N is too fast to be measured by ^1H NMR spectroscopy.[1] Nitrogen atoms invert particularly slowly in a three-membered ring and also when connected to another atom bearing an unshaired pair of electrons.[2-4] A study on the invertomer preferences and inversion barriers in *N*-alkyl-7-azabenzonorbornadienes has shown that the barrier is highest when the nitrogen is flanked by electron-rich π-bonds.[5] Asymmetric cage moieties have been found to be very diagnostic in conformational analysis about N—N[6] and N—C[7] bonds. Two nonplanar conformations *syn* (**1a**) and *anti* (**1b**) (when the substituent at the 2′-position of *N*-phenyl is toward the cage it is named *syn* while in the other case when it is away it is called *anti*) in a 1:1.1 ratio about the N—C (phenyl) bond in *o*-toludide derivative **1** have been demonstrated at the ambient temperature through the duplexity of the methyl resonances, and the high barrier to rotation ($\Delta G^{\ddagger}$ = 86.1 kJ mol^{-1}) has been explained on steric grounds.[7] Conformational analysis about the N—C (pyridyl) bond in **2** has shown that the "effective size"[8] of the sp^2-lone electron pair is sufficient to restrict rotation about the N—C bond, and the pyridyl nitrogen remains in the *anti*-orientation to the cage. This behavior demonstrated a strong repulsion of the sp^2-lone electron pair from a phenyl ring.[9] In order to investigate whether the approach of a π-electronic system from the rear would restrict the pyramidal inversion of nitrogen, a system along the lines of **3** was designed. The geometry of the nitrogen in *N*′-(isopropylideneamino)imide stabilized by a phenyl ring of an asymmetric cage system has been demonstrated through ^1H NMR and X-ray crystallography.

Condensation of *N*-amino-3,4-(9′,10′-dihydroanthracene-9′,10′-diyl)succinimide[10] with acetone yields **4**, and its ^1H NMR spectrum (Figure 1) indicates restricted rotation about the N—N bond with the imine part —N=C(CH_3)$_2$, orthogonal to the succinimidyl plane.[11] The two methyl signals remain sharp and move slowly on raising the temperature ($\Delta\nu$ = 72.7 Hz at 180 °C). The activation energy ($\Delta G^{\ddagger}$ = 116.8 kJ mol^{-1}) is attributed to the rotational energy about the >C=N— bond. This behavior eliminated the possibility of rotation about the N—N bond and inversion at the sp^2-nitrogen atom. Reduction of **4** with sodium borohydride in methanol (equimolar ratio) gave a product **6** in which one of the carbonyls is reduced to —CHOH. Only one isomeric product was obtained, and the *exo*-configuration (in the *exo*-configuration, the —OH group is away from the cage) for the —OH group has been proposed. Further reduction of **6** with an excess of sodium borohydride in methanol yielded **8**, where —N=C(CH_3)$_2$ is transformed into —NHCH(CH_3)$_2$.[12] The ^1H NMR spectrum (Figure 2) of **8** clearly indicates that both of the methyls sit exactly over the cage phenyl ring which would be possible with the noninverting pyramidal geometry of the *exo*-cyclic nitrogen having the lone pair in the *anti* orientation. Multiplicity in the methyls and methine proton resonances is attributed to the chiral center at the carbon atom bearing the —OH group. In the case of a methyl substituent at the 3-position of **5**, the carbonyl adjacent to the 4-hydrogen is reduced to —CHOH[13] and the ^1H NMR of **9** shows a clear multiplet for —C*H*(CH_3)$_2$.

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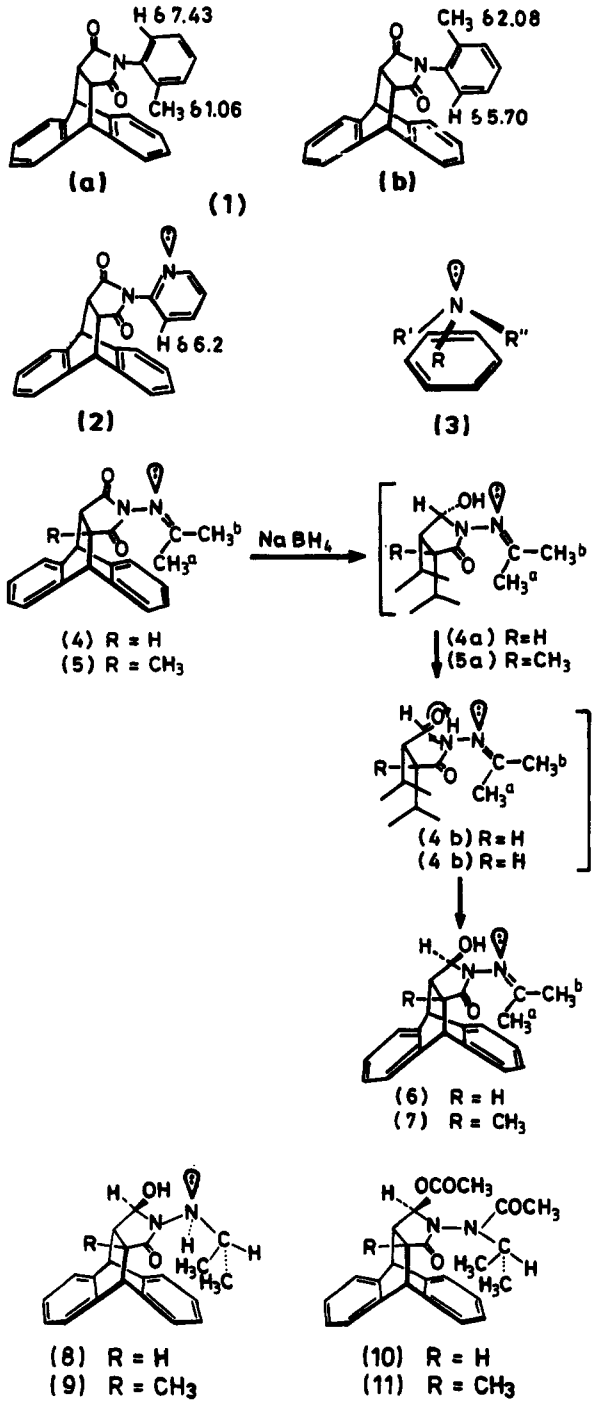

The methyl resonances of **8** remained sharp and moved closer on raising the temperature and practically coalesced at 160 °C in DMSO-d_6. This behavior eliminated the possibility of pyramidal inversion and rotation about the N—N bond as a very different magnetic environment would be attained in these processes. An energy barrier, $\Delta G^{\ddagger} = 92.3$ kJ mol^{-1}, has been evaluated with the Gutowsky–Holm equation[14] and attributed to the barrier about the N_{sp^3}–C_{sp^3} bond. The spectral pattern clearly demonstrates a restricted pyramidal geometry of exocyclic nitrogen resulting from a strong electronic repulsive interaction of the lone electron pair from the cage-phenyl ring.

X-ray crystallographic analysis of **8** demonstrated the sp^3 (pyramidal) character of the *exo*-cyclic nitrogen, while the other nitrogen is sp^2 (planar).[17] The lone pair orbital of sp^3 nitrogen is on the same side as the >C=O bond and the —OH group remains in the *exo*-configuration. The perspective view of the molecule to show the bond geometry is given in Figure 3 (Table 1). Nitrogen inversion in the solid state has been reported in crystalline 1,3,5-tribenzyl-1,3,5-triazacyclohexane by X-ray analysis.[15]

Table 1. Bond Distances and Bond Angles (esd's in Parentheses)

C1—C2	1.534(3)	C7—C19	1.510(4)
C1—N1	1.470(3)	C8—C9	1.378(4)
C1—O1	1.404(3)	C8—C13	1.402(4)
C2—C3	1.547(3)	C9—C10	1.389(4)
C2—C7	1.561(3)	C10—C11	1.386(5)
C3—C4	1.495(3)	C11—C12	1.385(4)
C3—C6	1.557(4)	C12—C13	1.383(3)
C4—N1	1.335(3)	C14—C15	1.381(4)
C4—O2	1.243(3)	C14—C19	1.399(4)
C5—N2	1.478(3)	C15—C16	1.399(3)
C5—C20	1.481(6)	C16—C17	1.373(5)
C5—C21	1.513(4)	C17—C18	1.388(5)
C6—C13	1.512(3)	C18—C19	1.398(3)
C6—C14	1.523(3)	N1—N2	1.409(3)
C7—C8	1.516(3)		
O1—C1—C2	110.7(2)	C9—C8—C13	119.8(2)
N1—C1—O1	111.3(2)	C8—C9—C10	120.0(3)
N1—C1—C2	103.7(2)	C9—C10—C11	120.2(3)
C1—C2—O3	106.2(2)	C10—C11—C12	120.0(2)
C1—C2—C7	113.8(2)	C11—C12—C13	119.9(3)
C3—C2—C7	109.0(2)	C6—C13—C8	113.4(2)
C2—C3—C4	105.2(2)	C6—C13—C12	126.6(2)
C2—C3—C6	110.4(2)	C8—C13—C12	120.0(2)
C4—C3—C6	112.5(2)	C6—C14—C15	126.4(2)
N1—C4—C3	109.7(2)	C6—C14—C19	112.9(2)
N1—C4—O2	126.0(2)	C15—C14—C19	120.8(2)
C3—C4—O2	124.3(3)	C14—C15—C16	118.7(3)
N2—C5—C20	110.5(3)	C15—C16—C17	120.9(3)
N2—C5—C21	106.7(2)	C16—C17—C18	120.6(2)
C20—C5—C21	111.6(3)	C17—C18—C19	119.1(3)
C3—C6—C13	105.4(2)	C7—C19—C14	113.7(2)
C3—C6—C14	106.4(2)	C7—C19—C18	126.5(2)
C13—C6—C14	107.9(2)	C14—C19—C18	119.8(3)
C2—C7—C8	106.1(2)	C1—N1—N2	123.5(2)
C2—C7—C19	106.5(2)	C1—N1—C4	115.1(2)
C8—C7—C19	107.8(2)	N2—N1—C4	121.3(2)
C7—C8—C9	127.0(2)	N1—N2—C5	113.7(2)
C7—C8—C13	113.2(2)		

The *exo*-orientation of the —OH group in **6** may suggest the hydride attack to the carbonyl of **4** from the *endo* side which seems to be very hard due to steric repulsion of the phenyl group. It appears that the reduction occurred from the *exo* side and then the *endo*-hydroxy compound **4a** was isomerized to the *exo*-hydroxy compound by thermodynamic control through the ring-opened intermediate **4b**. The proposed pyramidal geometry of nitrogen has been further supported by transformation of the *exo*-cyclic nitrogen (sp^3) into the sp^2 state by acetylation. The acetylated product **10** shows the usual restricted rotation and nonplanar conformation about the N—N bond[16] in its ^{1}H NMR spectrum. A preferred conformation with the *N'*-isopropyl in the *syn*-orientation having a magnetic environment similar to that of **8** is exhibited. Restricted rotation and nonplanar conformations about the N—N bond in *N'*-diacyl[10] and *N'*-alkyl-*N'*-acyl derivatives[6] of *N*-aminosuccinimides have been reported. Normal *O*-acetyl resonances indicate that it is not influenced by the

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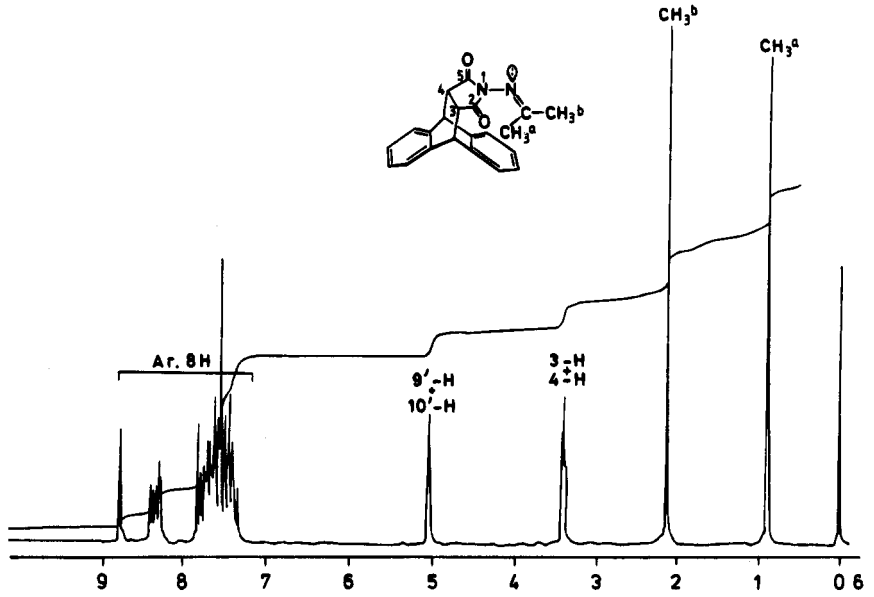

Figure 1. ^{1}H NMR (90 MHz) spectrum of compound **4** in $CDCl_3$.

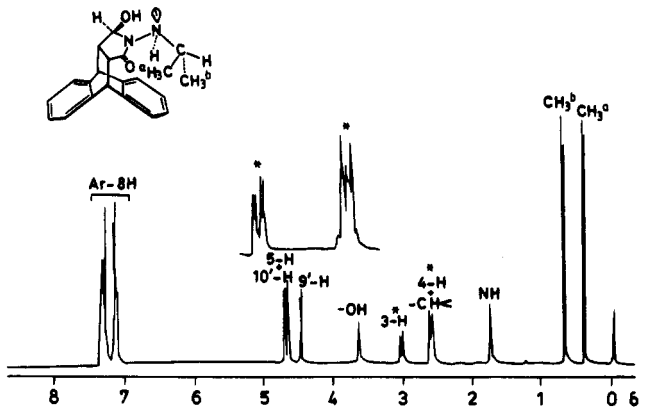

Figure 2. ^{1}H NMR (270 MHz) spectrum of compound **8** in $CDCl_3$.

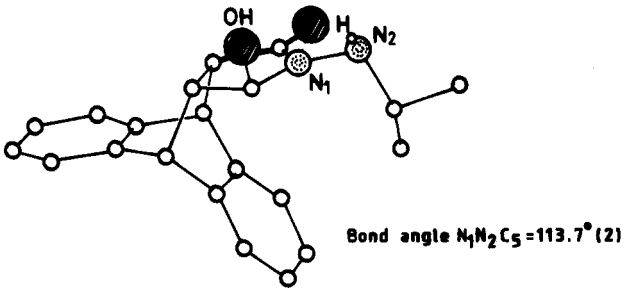

Figure 3. X-ray crystallographic computer-generated perspective drawing of **8**.

anisotropy of the cage and support the *exo*-configuration of the —OH group.

Experimental Section

All the melting points reported are uncorrected. ^{1}H NMR spectra were recorded on a JEOL 90Q multinuclear spectrometer at 25 °C in $CDCl_3$ with TMS as the internal standard (chemical shift in δ ppm). ^{1}H NMR (270 MHz) of **8** was obtained from CDRI, Lucknow. IR spectra were recorded as Nujol mulls on a Perkin-Elmer 720 spectrometer (ν_{max} in cm^{-1}).

***N*-(Isopropylideneamino)-3,4-(9′,10′-dihydroanthracene-9′,10′-diyl)succinimide (4)** was prepared by refluxing the *N*-aminoimide[10] of the anthracene—maleic anhydride adduct with an equimolar amount of acetone in EtOH for 2 h. On cooling, the product separated and then was recrystallized from EtOH: mp 218 °C; IR 1775 m, 1700 s, 1630 m cm^{-1}; ^{1}H NMR δ 0.87 (3H, s, $=CCH_3^a$), 2.17 (3H, s, $CH_3^bC=$), 3.4 (2H, bs, 3- and 4-H), 4.8 (2H, bs, 9′- and 10′-H), 7.17—8.48 (8H, bm, ArH).

Table 2. X-ray Crystal Structure Analysis of 8

molec form	$C_{21}H_{22}N_2O_2 \cdot 2H_2O$
molec wt	370
crystal syst	monoclinic
space grp	$P2_1/c$
Z	4
cell param	
a =	11.553(2) Å
b =	17.045(3) Å
c =	10.975(2) Å
β =	117.30(1)°
data collectn	
diffractometer	Euraf-Nonius CAD-4 graphite monochromator
radiatn used	Cu Kα λ = 1.5418 Å
crystal size	0.15 × 0.20 × 0.25 mm
lattice param determinatn	15 reflns (15° < θ < 20°)
scan mode	$w/2\theta$
maximum θ	60°
intens control	every 2 h (<2% change)
correctn factors	Lorentz, polarizn, absorpn
empirical absorpn correctn factor	min 0.85; max 1.00
no. of unique reflns	3259
no. of data with $I > 3\sigma$	2432, treated as obsd
full-matrix least-squares, anisotropic temperature factors for "heavy-atoms", isotropic thermal parameters for hydrogen atoms	
final reliability factors	$R = 0.045$; $R_w = 0.043$
weighting function based on counting statistics	

***N*-(Isopropylideneamino)-3,4-(9′,10′-dihydroanthracene-9′,10′-diyl)-3-methylsuccinimide (5)** was obtained by the reaction of the *N*-aminoimide of the anthracene—citraconic anhydride adduct with acetone in EtOH as described for **4**: mp 174 °C; IR 1770 m, 1710 s, 1630 m cm^{-1}; ^{1}H NMR δ 0.90 (3H, s, $CH_3^aC=$), 1.27 (3H, s, 3-CH_3), 2.09 (3H, s, $CH_3^bC=$), 2.86 (1H, d, 4-H), 4.54 (1H, s, 9′-H), 4.88 (1H, d, 10′-H), 7.13—8.59 (8H, bm, ArH). Anal. Calcd for $C_{22}H_{20}N_2O_2$: C, 76.74; H, 5.81. Found: C, 76.61; H, 5.66.

***N*-(Isopropylideneamino)-3,4-*endo*-(9′,10′-dihydroanthracene-9′,10′-diyl)-5-*exo*-hydroxy-2-pyrrolidone (6).** Imide **4** (1 mol) was dissolved in excess MeOH, and $NaBH_4$ (1 mol) was added portionwise while the mixture was stirred over a period of 30 min. After 6 h at 25 °C, the borate complex was hydrolyzed with water and extracted with Et_2O. The ether extract was dried (Na_2SO_4) and concentrated to give the

crystalline product: mp 239 °C; IR 3430 m, 1670 m cm^{-1}; ^1H NMR δ 1.18 (3H, s, $CH_3{}^aC=$), 2.0 (3H, s, $CH_3{}^bC=$), 2.81 (1H, m, 4-H), 3.31 (1H, dd, 3-H), 3.5 (1H, bs, —OH), 4.59 (1H, d, 9′-H), 4.88 (1H, d, 10′-H), 4.80 (1H, s, >C*H*OH), 7.27–8.86 (8H, bm, ArH). Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.90; H, 6.02. Found: C, 76.11; H, 5.88.

***N*-(Isopropylideneamino)-3,4-*endo*-(9′,10′-dihydroanthracene-9′,10′-diyl)-5-*exo*-hydroxy-3-methyl-2-pyrrolidone (7)** was obtained by the reduction of **5** with $NaBH_4$ (equimolar) in MeOH as described for **6**: mp 185 °C; IR 3440 m, 1675 m cm^{-1}; ^1H NMR δ 1.20 (3H, s, $CH_3{}^aC=$), 1.27 (3H, s, 3-CH_3), 2.0 (3H, s, $CH_3{}^bC=$), 2.35 (1H, d, 4-H), 3.50 (1H, bs, —OH), 4.27 (1H, s, 9′-H), 4.38 (1H, d, 10′-H), 4.62 (1H, s, >C*H*OH), 7.13–8.59 (8H, bm, ArH). Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.30; H, 6.35. Found: C, 76.21; H, 6.42.

***N*-(Isopropylamino)-3,4-*endo*-(9′,10′-dihydroanthracene-9′,10′-diyl)-5-*exo*-hydroxy-2-pyrrolidone (8)** was obtained by reduction of **4** with excess of $NaBH_4$ (3 mol) in the same way as described for **6**: mp 207 °C; IR 3430 m, 3160 m, 1670 m cm^{-1}; ^1H NMR δ 0.38 (3H, d, C*H*$_3{}^a$CH—), 0.67 (3H, d, $CH_3{}^b$CH—), 2.5 (1H, bs, —NH), 2.59 (2H, m, 4-H and $(CH_3)_2CH$—), 3.0 (1H, dd, 3-H), 3.7 (1H, bs, —OH), 4.43 (1H, d, 9′-H), 4.62 (1H, s, >C*H*OH), 4.66 (1H, d, 10′-H), 7.15–8.42 (8H, bm, ArH); MS (EI) *m/e* $[M]^+$ 334, base peak 178 $(C_{14}H_{10})^+$. Anal. Calcd for $C_{21}H_{22}N_2O_2$: C, 75.44; H, 6.58. Found: C, 75.22; H, 6.42.

***N*-(Isopropylamino)-3,4-*endo*-(9′,10′-dihydroanthracene-9′,10′-diyl)-5-*exo*-hydroxy-3-methyl-2-pyrrolidone (9)** was obtained from **7** according to the method described for **8**: mp 165 °C; IR 3440 m, 3170 m, 1670 m cm^{-1}; ^1H NMR δ 0.47 (3H, d, C*H*$_3{}^a$CH—), 0.75 (3H, d, C*H*$_3{}^b$CH—), 1.13 (3H, s, 3-CH_3), 2.15 (1H, d, 4-H), 2.53 (1H, m, $(CH_3)_2CH$), 3.75 (2H, bs, —NH and —OH), 4.27 (1H, s, 9′-H), 4.38 (1H, d, 10′-H), 4.62 (1H, s, >C*H*OH), 7.13–8.59 (8H, m, ArH). Anal. Calcd for $C_{22}H_{24}N_2O_2$: C, 75.86; H, 6.89. Found: C, 75.66; H, 6.76.

1-(*N*-Acetyl-*N*-isopropylamino)-3,4-*endo*-(9′,10′-dihydroanthracene-9,10-diyl)-5-*exo*-acetoxy-2-pyrrolidone (10) was obtained by refluxing **8** with an excess of Ac_2O for 2 h. The excess Ac_2O was removed in vacuo to give a solid which was recrystallized (EtOH): mp 185 °C; IR 1735 s, 1670 s cm^{-1}; ^1H NMR δ 0.43 (3H, d, $(CH_3)_2CH$—), 0.70 (3H, d, $(CH_3)_2CH$—), 2.04 (3H, s, —$NCOCH_3$), 2.18 (3H, s, —$OCOCH_3$), 2.67 (1H, m, 4-H), 3.11 (1H, dd, 3H), 3.65 (1H, septet, C*H*$(CH_3)_2$, 4.69 (1H, d, 9′-H), 4.74 (1H, d, 10′-H), 5.78 (1H, s, >C*H*OAc), 7.28–8.41 (8H, bm, ArH). Anal. Calcd for $C_{25}H_{26}N_2O_4$: C, 73.40; H, .6.38. Found: C, 73.52; H, 6.42.

1-(*N*-Acetyl-*N*-isopropylamino)-3,4-*endo*-(9′,10′-dihydroanthracene-9′,10′-diyl)-5-*exo*-acetoxy-3-methyl-2-pyrrolidone (11) was obtained by acetylation of **9** as described for **10**: mp 150 °C; IR: 1735 s, 1670 s cm^{-1}; ^1H NMR δ 0.50 (3H, d, $(CH_3)_2CH$—), 0.77 (3H, d, $(CH_3)_2CH$—), 1.18 (3H, s, 3-CH_3), 2.04 (3H, s, $NCOCH_3$), 2.13 (3H, s, —$OCOCH_3$), 3.0 (1H, d, 4-H), 3.68 (1H, m, $(CH_3)_2CH$—), 4.45 (1H, s, 9′-H), 4.81 (1H, d, 10′-H), 6.0 (1H, s, >CHOAc), 7.13–8.59 (8H, bm, ArH). Anal. Calcd for $C_{26}H_{28}N_2O_4$: C, 73.84; H, 6.66. Found: C, 73.66; H, 6.48.

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