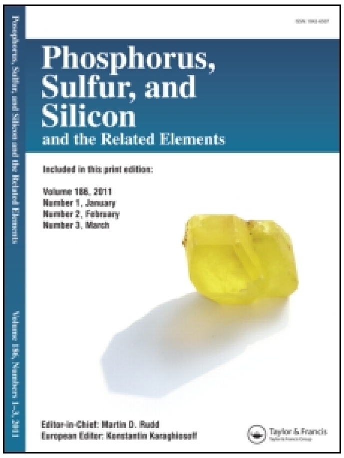

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NOVEL 9,9-DIOL SYSTEMS STARTING FROM A 3,7-DIAZABICYCLO[3.3.1]NONAN-9-ONE NUCLEUS-SINGLE CRYSTAL X-RAY DIFFRACTION ANALYSIS OF 3-(2-PROPYL)-7-BENZYL-3,7-DIAZABICY CL0[3.3.1]NONAN-9,9-DIOL HYDROBROMIDE, 3-(2-PROPY L)-7-[3,4-DIMETHOXYBENZYL)-3,7-DIAZABICY CLO[3.3.1]NONAN-9,9-DIOL HYDROBROMIDE, AND 3,7-DIISOPROPYL-3,7-DIAZABICY CLO[3.3.1]NONAN-9,9-DIOL DIHYDROCHLORIDE

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Attempts to make inorganic metal complexes of 3,7-diazabicyclo[3.3.1]nonan-9-ones and metal bromides in fresh, reagent-grade, undried THF generated rare 9,9-diols. Treatment of the ketones with anhydrous $HBr_{(g)}$ in anhydrous ether gave hydrobromides with the proton on nitrogen and with the carbonyl group intact. The hydrobromides were extremely hygroscopic and exhibited a strong propensity to form the corresponding 9,9-diol system. The mechanism of formation of the diols is discussed as well as a rationale for the stability of such diols via H-bonding in the solid state. The X-ray diffraction analyses of 3-(2-propyl)-7-benzyl-3,7-diazabicyclo[3.3.1]nonan-9,9-diol hydrobromide, 3-(2-propyl)-7-(3,4-dimethoxybenzyl)-3,7-diazabicyclo[3.3.1]nonan-9,9-diol hydrobromide, and 3,7-diisopropyl-3,7-diazabicyclo[3.3.1]nonan-9,9-diol dihydrochloride revealed a proton on N(3) and all bicyclic systems as chair-chair conformations in the solid state. The dihydrochloride was, of course, also protonated on N(7). This is the first systematic study of this type of 9,9-diol of the 3,7-

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* Dedicated to Professor R. Wolf on the occasion of his 75th birthday.

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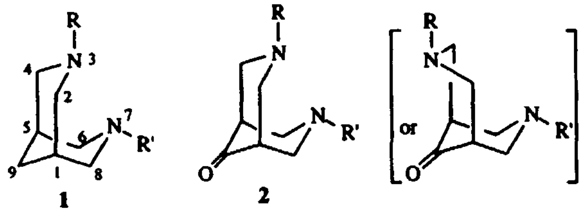
diazabicyclo[3.3.1]nonane system and the corresponding carbonyl-containing hydrobromides with the proton on a nitrogen atom [N(3)].

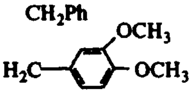
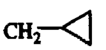
Keywords: 3,7-Diazabicyclo[3.3.1]nonan-9,9-diols; hydrobromides; dihydrochloride; NMR analysis; X-ray diffraction data

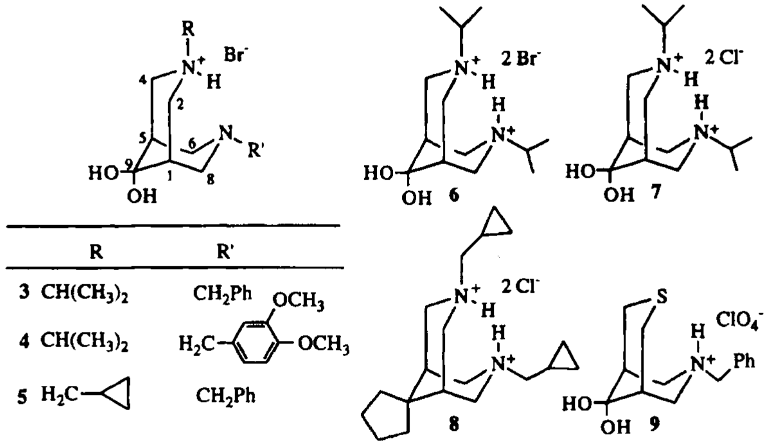
INTRODUCTION

The 3,7-diheterabicyclo[3.3.1]nonanes (DHBCNs) are well known for possessing useful antiarrhythmic properties.[1-6] One objective of the current research in our laboratory was to determine if certain metal complexes could be prepared from DHBCNs **1** and from 3,7-diheterabicyclo[3.3.1]nonan-9-ones (DHBCNONs)[5,7] **2**, since such agents may complex certain metal ions in the process of abolishing arrhythmias in ischemic tissues.[5,6,8] Our investigation has resulted in the development of new methodology to obtain novel 9,9-diols **3-7** of DHBCNONs **2**. It was discovered that DHBCNONs **2a** and **2b**, when mixed with metal bromides $CoBr_2$ or $MgBr_2$ in undried THF, led to the formation of the relatively stable 9,9-diols **3** and **4**, respectively, which were also hydrobromides via protonation on nitrogen [N(3)]. Direct treatment of **2a** and **2b** with 48% $HBr_{(aq)}$ also gave **3** and **4**, respectively, thus confirming the individual structures. Stable diols **3** and **4** are very rare and not well investigated in terms of chemical and physical properties.[9] Treatment of ketone **2c** with $HBr_{(aq)}$ and $HCl_{(aq)}$, surprisingly, produced the dihydrohalides **6** and **7**, respectively, rather than the expected monohydrohalides. Attempts to isolate monohydrohalides proved unsuccessful. It is obvious that the dihydrohalides **6** and **7**are structurally related to the antiarrhyth-



1 **2**

	R	R'
a	$CH(CH_3)_2$	CH_2Ph
b	$CH(CH_3)_2$	
c	$CH(CH_3)_2$	$CH(CH_3)_2$
d		CH_2Ph

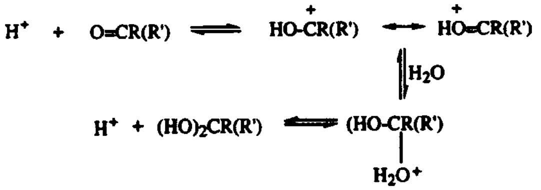


mic agent tedisamil dihydrochloride (**8**).[10] Such diols may possess useful antiarrhythmic activity, although related diol **9** did not exhibit the specifically desired cardiovascular properties in dog models.[11,12]

It is worthy of mention that DHBCNONs, like **2**, can exist in the chair-chair form or the boat-chair form or in an equilibrium involving both.[7] No systematic study of the reactivity of such ketones with aqueous acid has been published to date. However, the ketone precursor of **9** is known[7] to be a boat-chair form in the solid state[12] which is supported in solution via ^{17}O NMR studies.[13]

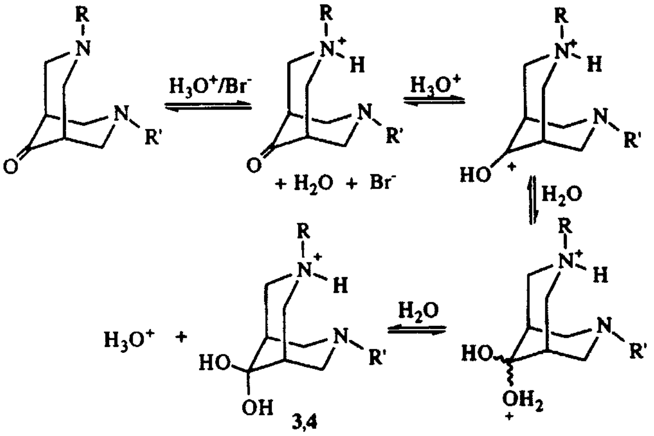
RESULTS AND DISCUSSION

Diols **3** and **4** were produced when solutions of **2a-b** in undried THF were mixed with a metal bromide and allowed to stand in the dark at room temperature for approximately 72 h. The formation of such diols may occur via a possible reaction between the metal bromide and moisture present in THF to produce hydrobromic acid. The acid could protonate the carbonyl oxygen atom (Scheme 1) in **2a-b**, followed by a nucleophilic addition of a water molecule to the activated

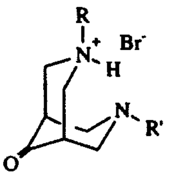


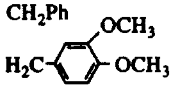
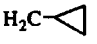
SCHEME 1

carbonyl carbon atom to produce the diols **3** and **4**, respectively. Another conceivable mechanism (Scheme 2) could involve initial protonation for N(3), which in turn could increase the electronic deficit at the carbon of the C=O group (via an induction effect). After initial protonation of the oxygen atom of the C=O group, a fast nucleophilic addition of water to the cation could occur to generate **3** and **4** (Scheme 2). It is thus feasible that quite small amounts of water and acid can lead to the formation of 9,9-diols in these systems. As stated previously, direct treatment of **2a** and **2b** with 48% $HBr_{(aq)}$ led to **3** and **4** in comparable yields. This same situation occurred when **2c** and **2d** were treated individually with aqueous HBr and yielded **6** (di-HBr) and **5**, respectively. In order to gain support for the working hypothesis that water was critical for generating the diols such as **3-6**, ketones **2a-d** were dissolved in anhydrous ether and subjected to a stream of dry $HBr_{(g)}$. Hydrobromides **10-12** were formed from **2a-c**, respec-



SCHEME 2



	R	R'
10	$CH(CH_3)_2$	CH_2Ph
11	$CH(CH_3)_2$	
12	$CH(CH_3)_2$	$CH(CH_3)_2$
13		CH_2Ph

tively, and displayed expected carbonyl frequencies in the IR spectra. Ketone **13** was very probably protonated initially at N(3), but, upon any exposure to the atmosphere, was spontaneously converted to **5**. In contrast, but with considerable care, salts **10-12** could be characterized spectroscopically and are the first reported in this family. These results support our theory and proposed generation of these diols, probably via the second mechanism cited above, namely via the initial protonation at N(3) prior to diol development at C(9). Creation of a positive charge on N(3) may induce sufficient electron deficit on C(9), coupled with protonation of the oxygen atom of the C=O group, to markedly facilitate attack by water. It was observed that hydrobromides **10-13** were extremely hygroscopic, however, and showed a marked tendency to absorb moisture from the atmosphere to produce the corresponding diols.

1,1-Diols of aldehydes and ketones have long been known, but the specific cases found in a search of the literature revealed that all such hydrates have powerful electronegative groups (usually halogens) very close to the carbonyl function except for initial studies with certain DHBCNs.[9] Chloral,[14] hexachloroacetone,[14] and hexafluoroacetone[15] are classic examples. Hydrogen bonding is one theory to account for stabilization of these hydrates, even in the crystalline state such as for chloral.[14,16] Indeed, intermolecular hydrogen bonding occurs between one oxygen atom of a diol group in one molecule with a hydrogen atom of a hydroxyl group of a diol unit in a second molecule in the solid state of **3**. Such hydrogen bonding stabilizes the 9,9-diol systems in **3, 4** and **7** as will be noted in discussions to follow.

A comparison of the ^{1}H and ^{13}C NMR chemical shifts in **3, 4,** and **6** and in **10-12** was made with the corresponding ketones **2a,b,d,** and the results can be found in the Experimental Section. As an example, such a comparison between the spectra of diols **3** and **4** versus ketones **2a** and **2b,** revealed significant *downfield* shift in the diols for the methine proton as well as for the corresponding carbon of the isopropyl group, indicating that protonation occurred at N(3). To illustrate, the methine hydrogen of the isopropyl group attached to N(3) in ketone **2a** had a multiplet at δ 2.87 while in the corresponding diol **3** the same proton appeared at δ 3.28. In the ketone-hydrobromide **10** this proton exhibited a signal at ~δ 3.30, a value very close to that in the diol **3**. In contrast, the corresponding benzyl methylene protons were visible at δ 3.53, 3.57, and 3.58 in **2a, 3,** and **10,** respectively. Since **3** was subjected to X-ray diffraction analysis and clearly revealed that N(3) carried the added proton, it was strongly inferred that N(3) held the proton in ketone-hydrobromide **10** in view of the similar ^{1}H chemical shifts for this proton in both **3** and **10**. It is noteworthy that the chemical shifts of the benzylic protons in **3** and **10** were of very similar magnitude (δ 3.57 versus 3.58), indicative of the presence of a free tertiary amino nitrogen [N(7)].

Similarly, the chemical shift for the exocyclic methylene protons of the cyclopropylmethyl group in **5** was downfield [δ 3.13(d)] compared to that in ketone precursor **2d**[δ 2.32 (d)], suggesting that protonation had occurred at N(3) in **5**. The H(2,4)$_{ax}$ and H(2,4)$_{eq}$ proton signals in diols **3-6** appeared *downfield* relative to the ketones **2a-d.** An interesting observation was that the ^{13}C signals for the bridge carbon [C(9)] in **3-6** appeared in a range of 87-102 ppm. It would suggest that not only the heteroatom present but the substituents on the ring, and possibly the shape of the ring, were also responsible for the chemical shift for the gem-diol carbon C(9). In the salts **10-12,** the C(9) signal for the carbonyl carbon appeared from 205-210 ppm, which was approximately 10-15 ppm *upfield* from the counterpart in ketones **2a-d.** Possibly, there is an increase in sp^2 character in the carbonyl group in **10-12,** thereby increasing the shielding of the carbon atom. This could result from increased flattening of the heterocyclic ring which was noted in the solid state for **7,** for example (see below), and previously in **9.**[9]

Although no crystallographic data are available on **5** , a chair-chair conformation is strongly suspected for this case. A precise knowledge of the preferred conformation in solution remains unclear. As stated earlier, the methine proton of the isopropyl group and the corresponding carbon in **3, 4,** and **6** were *deshielded* compared to the same proton and carbon in the ketone precursors. Interestingly, such deshielding of the ^{13}C did *not* occur at C(2,4) in the diols. In fact, the ^{13}C shifts for C(2,4) in the ketone precursors were deshielded more than those in the corresponding diols as stated earlier. Such an effect may be explained by a possible γ-shielding effect in the diols on the C(2,4) by the C(6)-N(7) and C(8)-N(7) bonds, thereby offsetting to some extent the deshielding of C(2,4) resulting from protonation of N(3).[17,18] Systems **2a** and **2b** may exist in solution to some extent in a boat-chair form in view of the absence of a γ-shielding effect. For instance, the ^{13}C shifts for C(2,4) in **2a** and **2b** are 53.71 ppm and 53.86 ppm, respectively, versus 50.30 ppm and 50.47 ppm in the diols **3** and **4,** respectively. Shieldings for C(2,4) were also observed in **5** (53.9 ppm)and **6** (48.8 ppm) compared to **2d** (58.1 ppm) and **2c** (53.2 ppm), respectively. Based on these observations, a chair-chair conformation in solution may be tentatively assigned for **3-6**. Similarly, the hydrobromides **10-12** exhibit deshielding of the methine proton and attached carbon of the isopropyl group, indicating protonation of N(3). The possibility of a hydrogen bonding between N(7) and the proton H(3), resulting in a chair-chair conformation both in solution as well as in the solid state, cannot be ruled out.

Supporting the above observations were the X-ray diffraction analyses of diol-hydrobromides **3** and **4** and that of the diol-dihydrochloride **7**. The data revealed chair-chair conformations with N(3) protonated in **3** and **4** and also N(7) in **7** (Figures 1-3) . The preference for a chair-chair arrangement may arise from favo-

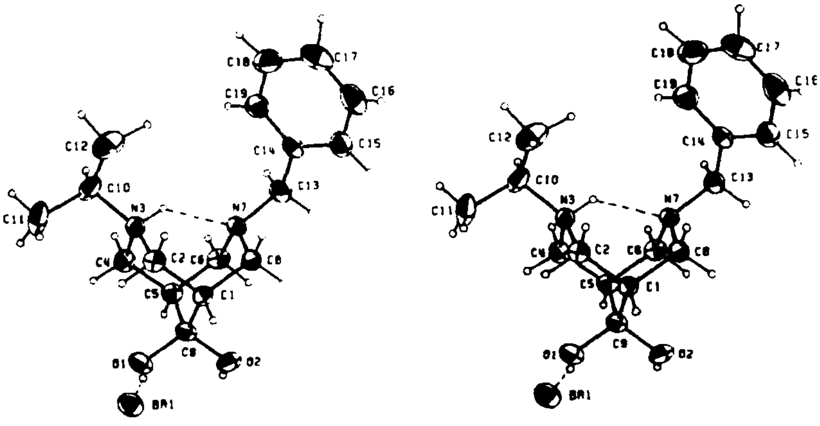


FIGURE 1 A stereo ORTEP plot of compound 3. Thermal ellipsoids are plotted at the 50% probability level. Dashed lines indicate hydrogen bonds

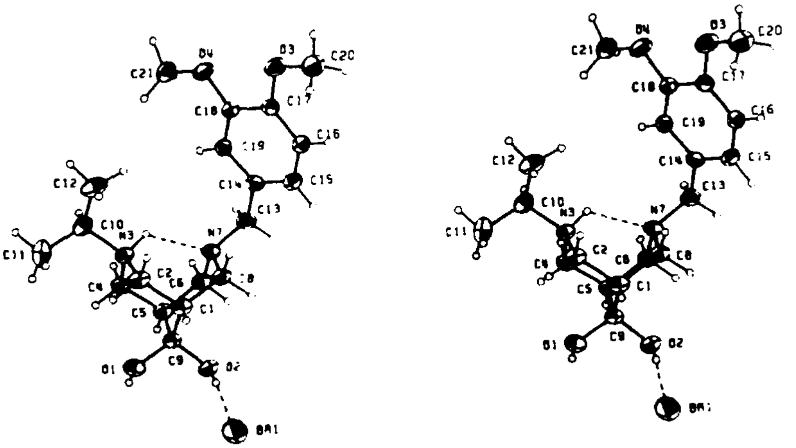


FIGURE 2 A stereo ORTEP plot of compound 4. Thermal ellipsoids plotted at the 35% probability level. Dashed lines indicate hydrogen bonds

rable hydrogen bonding between the N(7) and the proton H(3) in **3** and **4**. In addition to the intermolecular hydrogen bonding between H(01)...H(02), there was found an intermolecular hydrogen bond between H(01)...Br in **3** and **4** while an H(01)...Cl hydrogen bond occurred in **7**. Thus, the crystalline state has several stabilizing intermolecular H-bonds, and, moreover, one intramolecular [H(3)...N(7)] bond each in **3** and **4**. This is reminiscent of that found earlier for chloral in the solid state.[14,16] Detailed discussion of the X-ray work follows.

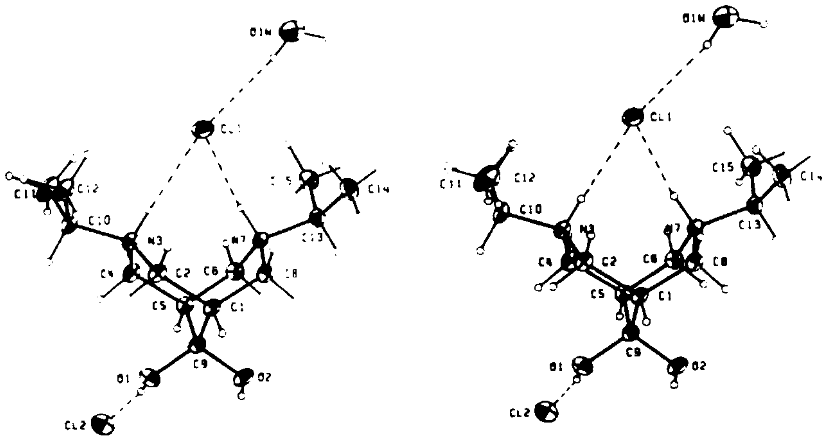


FIGURE 3 A stereo ORTEP plot of compound **7**. Thermal ellipsoids plotted at the 35% probability level. Dashed lines indicate hydrogen bonds

Crystal and Molecular Structures of Compounds 3, 4, and 7

Crystal data for **3**, **4**, and **7** are in Table I. The final atomic parameters of non-hydrogen atoms for the three structures are given in Table II. Bond distances, bond angles and endocyclic torsion angles of the bicyclic system in the three molecules are listed in Table III. Possible hydrogen bonding distances in the three structures are listed in Table IV. Stereo ORTEP plots of the structure of compounds **3**, **4**, and **7** are shown in Figures 1, 2 and 3, respectively. In all three molecules, the diazabicyclo[3.3.1]nonane unit adopts a chair-chair (CC) conformation. In compounds **3** and **4** where only one of the nitrogen atoms [N(3)] is protonated, the CC conformation is stabilized by an intramolecular N...H hydrogen bond. The N...N distances in **3** and **4** are almost identical (2.675 Å in **3** and 2.677 Å in **4**), and the values are comparable to those observed in other related compounds.[19] In compound **3**, the Br^- forms hydrogen bonds with O(1)H of one molecule and with O(2)H of a neighboring molecule, while in compound **4**, the Br^- forms a single hydrogen bond with one of the hydroxyl groups [O(2)H]. The overall geometries of the molecules **3** and **4** are quite similar, indicating that the methoxy substitution on the phenyl ring in **4** has little effect on the molecular structure as a whole. In both **3** and **4**, the C-N distances involving the non-protonated nitrogen [N(7)] are, on the average, 0.037 Å shorter than those involving protonated nitrogen [N(3)]. The piperidine rings in both **3** and **4** are slightly deviated from perfect chair conformations, with the ring torsion angles being between 54.3° and 64.2° in **3** and between 52.6° and 65.6° in **4**.

TABLE I Crystal date, intensity measurement parameters and refinement parameters for compounds **3**, **4** and **7**

Compound	**3**	**4**	**7**
Formula	$C_{17}H_{27}N_2O_2Br$	$C_{19}H_{31}N_2O_4Br$	$C_{13}H_{28}N_2O_2Cl_2$ + $2H_2O$
FW	371.3	431.4	351.2
Crystal Size(mm)	.32 x .10 x .04	.48 x .13 x .05	.68 x .48 x .33
Color	colorless	colorless	yellow
Space group	$P2_1/n$	$P2_1/c$	$P\bar{1}$
a(Å)	9.237(2)	8.3456(9)	9.772(2)
b	22.167(4)	9.452(1)	11.790(3)
c	8.771(1)	25.909(3)	9.063(2)
α(°)			106.97(2)
β	96.16(1)	93.75(1)	116.41(2)
γ			88.56(2)
no of reflections	25 (10-15°)	25 (10-14°)	25 (10-21°)
V(Å3)	1785.5(5)	2039.4(4)	887.8(5)
Z	4	4	2
$\mu(cm^{-1})$	22.3	27.6	33.0
$Dx(gm/cm^3)$	1.381	1.405	1.313
F(000)	776	904	380
Transmission factor	0.9135/0.8254	0.8727/0.6170	0.4631/0.1895
Temp	203K	203K	203K
Radiation	$MoK\bar{\alpha}$	$CuK\bar{\alpha}$	$Cuk\bar{\alpha}$
$^{2\theta}max$	53°	150°	150°
scan width(°)	(0.8 + .20tanθ)	(1.0 + .20tanθ)	(.90 +.20tanθ)
Apt.(mm)	(3.0 + .86tanθ)	(4.5 + .86tanθ)	(3.0 + .86tanθ)
Tmax(s)	60	60	60
h	0 to 12	-10 to 10	-12 to 12
k	0 to 20	0 to 11	0 to 14
l	-11 to 11	0 to 30	-10 to 10
monitor	3, 2 hrs	3, 2 hrs	3, 2 hrs
Max variation	3.5%	1.5%	2.1%
Total No.measured	3548	4179	3652
No. Observed	2416(I>2σ(I))	3119(I>2σ(I))	3521(I>2σ(I))
Structure Determination	SHELXS	SHELXS	SHELXS
R	0.045	0.046	0.044
Rw	0.044	0.051	0.062
No. parameters	307	311	318
S	1.5	1.6	2.7
(Δρ/σ)max	0.01	0.01	0.05
Δρ	±0.16	±0.20	±0.30

TABLE II Positional and equivalent isotropic thermal parameters for non-hydrogen atoms of **3**, **4**, and **7** Ueq = (1/3) $\Sigma_i\Sigma_jU_{ij}a^*_ia^*_ja_i.a_j$

3

Atom	x	y	z	Ueq
Br1	0.10778(5)	0.16660(2)	0.02224(5)	0.0496(2)
O1	0.2215(3)	0.2373(1)	0.3384(4)	0.049(1)
O2	0.4535(3)	0.2031(1)	0.4111(4)	0.047(1)
N3	0.0713(4)	0.1527(1)	0.5990(4)	0.037(1)
N7	0.3423(3)	0.1181(1)	0.6995(3)	0.034(1)
C1	0.2634(4)	0.1339(2)	0.4274(4)	0.034(1)
C2	0.1027(4)	0.1281(2)	0.4474(5)	0.039(1)
C4	0.1250(4)	0.2166(2)	0.6202(5)	0.041(1)
C5	0.2853(4)	0.2200(2)	0.5999(4)	0.037(1)
C6	0.3798(4)	0.1828(2)	0.7172(5)	0.039(1)
C8	0.3591(4)	0.0973(2)	0.5449(4)	0.037(1)
C9	0.3084(4)	0.2003(2)	0.4391(4)	0.036(1)
C10	-0.0843(4)	0.1450(2)	0.6348(5)	0.052(2)
C11	-0.1885(5)	0.1785(3)	0.5221(7)	0.070(2)
C12	-0.1184(7)	0.0794(4)	0.647(1)	0.086(3)
C13	0.4273(5)	0.0819(2)	0.8176(5)	0.047(2)
C14	0.3686(4)	0.0195(2)	0.8300(4)	0.042(1)
C15	0.4434(5)	-0.0301(2)	0.7876(5)	0.054(2)
C16	0.3868(8)	-0.0876(3)	0.8040(7)	0.072(2)
C17	0.2574(7)	-0.0950(2)	0.8624(6)	0.071(2)
C18	0.1826(6)	-0.0459(2)	0.9037(6)	0.069(2)
C19	0.2389(5)	0.0111(2)	0.8882(5)	0.055(2)

4

Atom	x	y	z	Ueq
Br1	0.12121(6)	0.84388(4)	0.09504(2)	0.0513(2)
O1	0.2203(3)	0.4855(3)	0.0221(1)	0.0322(8)
O2	-0.0089(3)	0.5247(2)	0.06664(9)	0.0301(7)
O3	0.3944(3)	0.0516(3)	0.36514(9)	0.0396(8)
O4	0.4072(3)	-0.1129(3)	0.28543(9)	0.0421(8)
C1	0.2317(4)	0.4276(3)	0.1111(1)	0.026(1)
C2	0.3759(4)	0.3339(4)	0.1019(1)	0.028(1)
N3	0.3251(3)	0.1872(3)	0.0850(1)	0.0241(8)
C4	0.2032(4)	0.1902(3)	0.0391(1)	0.0254(9)
C5	0.0623(4)	0.2847(3)	0.0504(1)	0.0262(9)
C6	-0.0289(4)	0.2318(4)	0.0958(1)	0.028(1)
N7	0.0768(3)	0.2289(3)	0.1436(1)	0.0249(8)

TABLE II Positional and equivalent isotropic thermal parameters for non-hydrogen atoms of **3**, **4**, and **7** Ueq = (1/3) $\Sigma_i \Sigma_j U_{ij} a^*_i a^*_j \mathbf{a}_i . \mathbf{a}_j$

C8	0.1373(4)	0.3730(3)	0.1555(1)	0.028(1)
C9	0.1251(4)	0.4353(3)	0.0613(1)	0.0254(9)
C10	0.4644(4)	0.0888(4)	0.0776(1)	0.032(1)
C11	0.5719(5)	0.1434(5)	0.0372(2)	0.044(1)
C12	0.5543(5)	0.0638(5)	0.1295(2)	0.045(1)
C13	-0.0095(4)	0.1668(4)	0.1857(1)	0.031(1)
C14	0.0983(4)	0.1400(3)	0.2340(1)	0.0273(9)
C15	0.0898(4)	0.2244(4)	0.2771(1)	0.033(1)
C16	0.1874(4)	0.1975(4)	0.3217(1)	0.031(1)
C17	0.2931(4)	0.0859(3)	0.3233(1)	0.0277(9)
C18	0.3009(4)	-0.0021(3)	0.2797(1)	0.0271(9)
C19	0.2053(4)	0.0261(3)	0.2354(1)	0.0263(9)
C20	0.4029(6)	0.1474(5)	0.4075(1)	0.045(1)
C21	0.4182(7)	-0.2064(5)	0.2431(2)	0.049(2)

7

Atom	x	y	z	Ueq
CL1	0.36051(4)	0.50097(3)	0.16484(5)	0.0348(2)
CL2	0.05646(5)	-0.20114(4)	-0.22752(6)	0.0412(2)
O1	0.2991(1)	-0.0248(1)	-0.1915(1)	0.0296(5)
O2	0.1513(1)	0.0378(1)	-0.4286(1)	0.0312(4)
C1	0.3617(1)	0.1704(1)	-0.1813(2)	0.0207(5)
C2	0.4590(1)	0.2009(1)	0.0153(2)	0.0227(5)
N3	0.3682(1)	0.2286(1)	0.1173(1)	0.0217(5)
C4	0.2142(2)	0.1525(1)	0.0305(2)	0.0253(6)
C5	0.1279(1)	0.1248(1)	-0.1665(2)	0.0222(5)
C6	0.0572(1)	0.2290(1)	-0.2289(2)	0.0244(5)
N7	0.1723(1)	0.3246(1)	-0.2036(1)	0.0213(4)
C8	0.2972(2)	0.2740(1)	-0.2492(2)	0.0233(5)
C9	0.2331(1)	0.0709(1)	-0.2464(2)	0.0217(5)
C10	0.4636(2)	0.2193(1)	0.2999(2)	0.0278(6)
C11	0.6187(2)	0.2941(2)	0.3907(2)	0.0338(6)
C12	0.3751(2)	0.2579(2)	0.4047(2)	0.0439(8)
C13	0.0896(2)	0.4092(1)	-0.3066(2)	0.0275(6)
C14	0.2055(2)	0.4984(2)	-0.2961(2)	0.0367(8)
C15	-0.0174(2)	0.4726(2)	-0.2373(2)	0.0336(7)
O1W	0.2573(2)	0.7615(2)	0.1352(2)	0.0614(8)
O2W	0.3433(3)	0.9631(2)	0.4185(3)	0.080(1)

TABLE III Bond distances (Å), bond angles (°) for **3**, **4** and **7**

Bond distances			
	3	**4**	**7**
N3...N7	2.675(4)	2.677(4)	3.203(1)
C1-C2	1.519(5)	1.525(5)	1.531(2)
C1-C8	1.519(5)	1.526(5)	1.525(2)
C1-C9	1.530(5)	1.519(4)	1.520(2)
C2-N3	1.494(5)	1.507(4)	1.512(1)
N3-C4	1.505(5)	1.514(4)	1.514(2)
N3-C10	1.514(5)	1.511(4)	1.532(2)
C4-C5	1.512(5)	1.520(5)	1.529(1)
C5-C6	1.520(5)	1.527(5)	1.523(2)
C5-C9	1.513(5)	1.537(4)	1.532(1)
C6-N7	1.479(5)	1.473(4)	1.507(2)
N7-C8	1.456(4)	1.478(4)	1.511(2)
N7-C13	1.469(5)	1.469(4)	1.533(2)
C9-O1	1.393(5)	1.412(4)	1.393(2)
C9-O2	1.390(5)	1.416(4)	1.409(1)
C10-C11	1.501(7)	1.513(5)	1.511(2)
C10-C12	1.494(8)	1.514(6)	1.522(2)
C13-C14	1.494(6)	1.504(4)	1.518(2)
C13-C15	-	-	1.532(2)
C14-C15	1.370(6)	1.378(4)	-
C14-C19	1.364(6)	1.398(5)	
C15-C16	1.391(8)	1.393(5)	-
C16-C17	1.360(9)	1.374(5)	-
C17-C18	1.358(8)	1.407(4)	-
C18-C19	1.380(7)	1.379(4)	-
C17-O3		1.370(4)	
C20-O3		1.421(5)	
C18-O4		1.375(4)	
C21-O4		1.416(5)	
Bond Angles			
	3	**4**	**7**
C2-C1-C8	112.4(3)	111.9(3)	116.6(1)
C2-C1-C9	109.6(3)	108.6(3)	109.9(1)
C8-C1-C9	109.6(3)	110.7(3)	110.4(1)
C1-C2-N3	110.9(3)	111.7(3)	114.6(1)
C2-N3-C4	111.2(3)	111.9(2)	114.5(1)
C2-N3-C10	115.0(3)	113.5(2)	110.7(1)
C4-N3-C10	112.9(3)	113.3(2)	109.7(1)
N3-C4-C5	110.3(3)	110.4(2)	114.6(1)
C4-C5-C6	113.0(3)	112.8(3)	115.3(1)
C4-C5-C9	109.5(3)	108.7(3)	109.6(1)
C6-C5-C9	110.3(3)	110.0(3)	111.31(6)
C5-C6-N7	110.1(3)	110.7(3)	114.4(1)

TABLE III Bond distances (Å), bond angles (°) for **3**, **4** and **7**

C6-N7-C8	111.0(3)	109.7(2)	112.8(1)
C6-N7-C13	110.7(3)	109.6(2)	110.1(1)
C8-N7-C13	112.4(3)	113.0(2)	111.18(6)
N7-C8-C1	110.4(3)	109.9(2)	114.03(6)
C1-C9-C5	105.9(3)	106.6(2)	105.5(1)
C1-C9-O1	112.9(3)	107.5(3)	108.1(1)
C1-C9-O2	106.9(3)	111.6(2)	109.29(6)
C5-C9-O1	107.0(3)	112.3(2)	112.42(6)
C5-C9-O2	112.8(3)	108.0(3)	109.1(1)
O1-C9-O2	111.3(3)	110.7(2)	111.4(1)
N3-C10-C11	111.3(4)	111.9(3)	111.26(8)
N3-C10-C12	109.7(4)	108.9(3)	109.6(1)
C11-C10-C12	113.8(5)	112.6(3)	110.6(1)
N7-C13-C14	112.7(3)	112.8(3)	110.5(1)
N7-C13-C15	-	-	109.43(6)
C14-C13-C15	-	-	110.0(1)
C13-C14-C15	121.7(4)	120.9(3)	
C13-C14-C19	119.5(4)	119.7(3)	
C15-C14-C19	118.7(4)	119.4(3)	
C14-C15-C16	120.1(5)	120.6(3)	
C15-C16-C17	120.3(5)	120.3(3)	
C16-C17-C18	119.8(5)	119.5(3)	
C17-C18-C19	120.0(5)	119.9(3)	
C18-C19-C14	121.1(4)	120.3(3)	
C16-C17-O3		124.5(3)	
O3-C17-C18		115.9(3)	
C17-C18-O4		115.3(3)	
O4-C18-C19		124.8(3)	
C17-O3-C20		117.3(3)	
C18-O4-C21		117.8(3)	
Torsion angles			
	3	**4**	**7**
C1-C2-N3-C4	54.3(4)	52.6(3)	37.7(1)
C2-N3-C4-C5	-55.3(4)	-53.3(3)	-38.0(1)
N3-C4-C5-C9	61.4(4)	60.0(3)	53.2(1)
C4-C5-C9-C1	-64.2(4)	-65.6(3)	-66.2(1)
C5-C9-C1-C2	62.9(4)	64.2(3)	66.1(1)
C9-C1-C2-N3	-59.0(4)	-58.6(3)	-53.0(1)
C5-C6-N7-C8	57.5(4)	60.1(3)	42.17(8)
C6-N7-C8-C1	-58.3(4)	-59.9(3)	-43.7(1)
N7-C8-C1-C9	60.9(4)	61.0(3)	56.5(1)
C8-C1-C9-C5	-60.9(4)	-59.0(3)	-63.81(7)
C1-C9-C5-C6	60.8(4)	58.2(3)	62.5(1)
C9-C5-C6-N7	-59.9(4)	-60.2(3)	-53.3(1)

TABLE IV Possible hydrogen bonds in **3**, **4**, and **7**

	atom...atom	distance(A)
3		
	N3......N7	2.675(4)
	Br......O1	3.259(3)
	Br......O2[-.5+x,.5-y,-.5-z]	3.321(3)
4		
	N3......N7	2.677(4)
	Br......O2	3.274(2)
	O1......O2[-x,1-y,-z]	2.807(3)
7		
	CL1......N3	3.117(1)
	CL1......N7	3.088(1)
	CL1......O1W	3.257(2)
	CL2......O1	3.036(1)
	CL2......O1W[x,y-1,z]	3.149(1)
	O2......O2[-x,-y,-z-1]	2.696(2)
	O2......O2W[x,y-1,z-1]	2.781(2)
	O1W......O2W	2.751(3)
	O2W......O2W[1-x,2-y,1-x]	2.771(4)

The dihydrochloride **7** adopts a highly flattened CC conformation for its bicyclic skeleton like that in tedisamil (**8**).[9] This conformation is achieved by flattening the piperidine rings at their nitrogen ends and puckering at the corresponding carbon ends, resulting in a N...N distance of 3.203 Å, *one of the longest observed for such a system.* Fernandez and co-workers[20] observed N...N contact distances of 3.150 Å and 3.125 Å for the two independent molecules in 3,7-dimethyl-9-amino-3,7-diazabicyclo[3.3.1]nonane-9-carboxamide dihydrochloride. The N...N distance in tedisamil (**8**) was found to be 3.15 Å.[10] The CC conformation in **7** is stabilized by a pair of hydrogen bonds formed by a chlorine ion with both of the piperidine nitrogen atoms. The second chlorine ion forms hydrogen bonds with an hydroxyl group and a water molecule. The piperidine rings deviate from the ideal chair conformation significantly as reflected by the ring torsion angles which range between 37.7° and 66.2°. The distortion of the bicyclic skeleton is further indicated by angles C2-C1-C8 (116.6°), C4-C5-C6(115.3°), N3-C4-C5(114.6°), C5-C6-N7(114.4°), and C1-C2-N3(114.6°), all of which are about 4-5° larger than those observed in compounds **3** and **4**. It is apparent that these distortions are the result of an effort to compensate for the severe steric interactions between the H(3) and H(7) attached to the corresponding nitrogen atoms. The C-N distances in **7** for the two nitrogen atoms are almost equivalent and compare with those for the protonated nitrogens in compounds **3** and **4** , confirming that both the nitrogen atoms in **7** are protonated.

Substitution at the 9-position can drastically effect the conformational behavior of the 3,7-diazabicyclic system as demonstrated by the solid state and solution structures of 3-benzyl-7-methyl-3,7-diazabicyclo[3.3.1]nonane-9-one and 3,7-dimethyl-3,7-diazabicyclo[3.3.1]nonan-9-ol and related structures.[18,21] The three structures **3**, **4**, and **7** in the present report have diol substitution at the 9-position, and all adopt a CC conformation. In addition we have also determined the corresponding structure of the bromide analog of **7**, namely **6**, (from the X-ray data of a poorly diffracting crystal-data not reported herein), which is isomorphous with the structure of **7**. It may be concluded from these results that diol substitution at C-9 strongly favors a CC conformation in its 3,7-diazabicyclic system.

The hydrogen bonding pattern and packing of the three compounds are different. In **3**, the bromide ion bridging the neighboring molecule through Br...O(1) and Br...O(2) hydrogen bonds. In **4**, the centrosymmetrically-related molecules form dimeric pair through O(1)...O(2) hydrogen bonds. In **7**, the two chloride ions and two water molecules form an extensive hydrogen bonding network.

In summary, we have discovered a simple method to obtain stable 9,9-diols from the family of 3,7-diazabicyclo[3.3.1]nonan-9-ones by treatment with aqueous hydrobromic acid or hydrochloric acid. Exposure of the same ketones in anhydrous ether to hydrogen bromide gas led to the respective hydrobromides with the proton on nitrogen. However, these hydrobromides were very hygroscopic and were quickly converted to the corresponding 9,9-diol-hydrobromide upon instant exposure to the atmosphere. Spectral data support chair-chair conformations in all systems. The diols are quite rare and very little chemistry has heretofore been reported for such heterocycles. Keto-N-hydrobromides could be obtained under rigorous anhydrous conditions, but such salts were very hygroscopic and scavenged moisture and were readily converted to the corresponding 9,9-diols upon any exposure to the atmosphere.

EXPERIMENTAL

General Information: All ^1H and ^{13}C spectral data were obtained on a Varian XL-400 NMR spectrometer operating at 399.5 and 100.6 MHz, respectively. Chemical shifts for ^1H and ^{13}C NMR spectra were recorded in δ or ppm values, respectively, downfield from the tetramethylsilane (TMS). IR spectra were recorded on a Nicolet impact 400 FTIR spectrometer as KBr pellets or as films. Melting points, which were uncorrected, were recorded on a Thomas-Hoover capillary melting point apparatus. High resoultion mass spectral analyses were performed on a VG analytical instrument, model ZAB-2SE. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. The following compounds were prepared by known methods: 7-benzyl-3-isopropyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2a**),[5b,7] 3-(2–propyl)-7-(3,4-dimethoxybenzyl)-3,7-diazabicyclo[3.3.1]-nonan-9-one (**2b**),[5b,7] 3,7-diisopropyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2c**),[5b,7] and 7-benzyl-3-cyclopropyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2d**).[5b,5m,22] All solvents were reagent grade and were dried and used without further purification, unless otherwise indicated.

3-(2-Propyl)-7-benzyl-3,7-diazabicyclo[3.3.1]nonan-9,9-diol Hydrobromide (**3**). To a system containing dried $MgBr_2$ (0.092 g, 0.50 mmol) dissolved in 10 mL of undried THF was added a solution of 3-(2–propyl)-7-benzyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2a**, 0.204 g, 0.75 mmol) in 10 mL of THF. The resulting solution mixture was protected from the atmosphere by covering the system with paraffin film and was allowed to stand (72 h) at room temperature in the dark. Crystals formed and were filtered under vaccum and then washed with copious amounts of THF. The solid was recrystallized (1:1, isopropyl alcohol:H_2CCl_2) to give 0.140 g (51%) of **3**, mp 159-160 °C. IR (KBr) 3330 (O-H), 3096 (Ar-H), 2943, 2830 (C-H) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.16 [d, 6 H, CH_3], 1.95 [bs, 2 H, H(1, 5)], 2.81 [d, 2 H, H(6,8)$_{ax}$], 2.97 [d, 2 H, H(2, 4)$_{ax}$], 3.28 [m, 3 H, H(6,8)$_{eq}$ and $CH(CH_3)_2$], 3.57 [m, 2 H, H(2,4)$_{eq}$ and 2 H, Ar-CH_2], 6.15, 6.18 [s, 2 H, OH], 6.36-7.61 [m, 5 H, Ar-H]; ^{13}C NMR (DMSO-d_6) ppm 16.29 [CH_3], 38.45 [C(1, 5)], 50.47 [C(2, 4)], 53.65 [C(6, 8)], 55.25 [$CH(CH_3)_2$], 60.26 [Ar-CH_2], 89.37[C(9)], 126.74, 128.53, 129.80, 137.00 [Ar-C]. Anal. Calcd for $C_{17}H_{27}N_2O_2Br$: C, 51.61; H, 6.87; N, 7.08. Found: C, 51.60 ; H, 7.17 ; N, 6.97. When attempts were initiated with rigorously purified and dried THF, only starting materials were recovered unchanged. Treatment of **2a** with 48% HBr under conditions described for the preparation of **5** led to **3** in comparable yields.

3-(2-Propyl)-7-(3,4-dimethoxybenzyl)-3,7-diazabicyclo[3.3.1]nonan-9,9-diol Hydrobromide (**4**). To a system containing dried $CoBr_2$ (0.109 g, 0.50 mmol) dissolved in 10 mL of undried THF was added a solution of 3-(2-propyl)-7-(3,4-dimethoxybenzyl)-3,7-diazabicyclo[3.3.1]nonan-9-one (**2b**, 0.249 g, 0.75 mmol) in 10 mL of THF. The resulting solution mixture was allowed to stand at room temperature in dark for approximately 72 h. Crystals formed and were filtered under vaccum and then washed with copious amounts of THF. The solid was recrystallized (1:1 isopropyl alcohol:CH_2Cl_2) to give 0.152 g (49%) of **4**, mp 158-159 °C (hygroscopic). IR (KBr) 3347 (O-H), 3213 (N-H), 3043 (Ar-H), 2981, 2842 (C-H) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.16 [d, 6 H, CH_3], 1.95 [bs, 2 H, H(1, 5)], 2.85 [d, 2 H, H(6,8)$_{ax}$], 3.05 [d, 2 H, H(2, 4)$_{ax}$], 3.25-3.55 [m, 5 H, H(2,4,6,8)$_{eq}$ and $CH(CH_3)_2$], ~3.40 [s, 2 H, Ar-CH_2], 3.87 [s, 3 H, OCH_3], 3.88 [s, 3 H, OCH_3], 6.19, 6.21 [s, 2 H, OH], 6.89-7.15 [m, 3 H, Ar-H]; ^{13}C NMR (DMSO-d_6) ppm 16.46 [CH_3], 40.12 [C(1,5)], 50.30 [C(2,4)], 53.82 [C(6,8)], 54.92 [CH(CH$_3$)2], 55.52, 55.42 [OCH$_3$], 59.98 [Ar- CH$_2$], 89.45[C(9)], 111.37, 113.26, 122.15, 128.10, 148.50, 148.73 [Ar-C]. High resolution mass spectral (FAB) data calcd for $C_{19}H_{31}N_2O_4Br$ *m/z* (M$^+$): 351.2283 (-Br). Found: 351.2273. Treatment of **2b** with 48% HBr as described to obtain **5** led to **4** in comparable yields.

3-Cyclopropylmethyl-7-benzyl-3,7-diazabicyclo[3.3.1]nonan-9,9-diol Hydrobromide (**5**). A system was equipped with a magnetic stirrer and an ice bath. A solution of HBr (48%, 1.040 g, 6.16 mmol) in 2-propanol (1 mL) was added dropwise over a period of 15 min to a stirred, cold (0 °C) solution of 7-benzyl-3-cyclopropylmethyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2d**, 0.6 g, 2.20 mmol) in dry ether (20 mL) and produced a white solid. This solid was vaccum filtered, then washed with copious amounts of ether, and recrystallized (1:1, 2-propanol:chloroform) to give **5** (0.540 g, 67%), mp 155-156.5 °C (hygroscopic). IR (KBr) 3240 (O-H), 3094 (Ar-H), 2933, 2833 (C-H) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.47 [m, 2 H, CH$_2$, cyclopropyl ring], 0.57 [m, 2 H, CH$_2$, cyclopropyl ring], 1.04 [m, 1 H, C-H, cyclopropyl ring], 1.93 [bs, 1 H, H(1) or H(5)] 2.13 [bs, 1 H, H(1) or H(5)], 2.70 [dd, 2 H, H(6,8)$_{ax}$], 2.93 d, 2 H, H(2,4)$_{ax}$], 3.13 [d, 2 H, H_2CN], 3.24 [dd, 2 H, H(6,8)$_{eq}$], 3.53 [m, 4 H, H(2,4)$_{eq}$ and $CH_2C_6H_5$], 4.23 [bs, 2 H, OH], 7.30-7.52 [m, 5 H, Ar-H]; ^{13}C NMR (DMSO-d_6) ppm 4.08 [CH$_2$, cyclopropyl ring], 6.61 [CH, cyclopropyl ring], 38.8 [C(1,5)], 53.90 [C(2,4)], 54.98 [C(6,8)], 60.09 [Ar-CH$_2$], 60.80 [CH$_2$, cyclopropyl ring], 89.63[C(9)], 127.74, 128.53, 129.70, 137.00 [Ar-C]. High resolution mass spectral (FAB) data calcd for $C_{18}H_{27}N_2O_2Br$ *m/z* (M$^+$): 303.2071(-Br). Found: 303.2060.

3, 7-Diisopropyl-3, 7-diazabicyclo[3.3.1]nonan-9,9-diol Hydrobromide (**6**). To a system equipped with a magnetic stirrer and an ice bath was added a solution of HBr (48%, 1.04 g, 6.16 mmol) dropwise over a period of 15 min to a stirred, cold (0 °C) solution of 3,7-diisopropyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2c**, 0.6 g, 2.60 mmol) in undried THF (20 mL) to produce a light yellow oil, which crystallized after 48 hours at -10 °C The solid was filtered under vacuum, washed with dry ether, and recrystallized (H_2CCl_2:H_3CCN, 2:1) to give **6** (0.35 g, 47%), mp 98-99 °C. Diol **6** was quite hygroscopic. IR (KBr) 3403 (O-H) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.37 [d, 12 H, CH$_3$], 2.29 [bs, 2 H, H(1,5)], 3.13-3.6 [m, 10 H, H(2,4,6,8) and the 2 HC(CH$_3$)$_3$], 4.40 [bs, 1 H, OH]; 9.45 [bs, 1 H, NH]. ^{13}C NMR (DMSO-d_6) ppm 16.7 [CH$_3$], 36.8 [C(1, 5)], 48.8 [C(2,4,6,8)], 60.9 [CH(CH$_3$)$_2$], 86.6 [C(9)]. High resolution mass spectral (FAB) data calcd for $C_{13}H_{28}N_2O_2Br_2$ *m/z* (M$^+$): 243.2072 (-2 Br). Found: 243.2082.

3,7-Diisopropyl-3,7-diazabicyclo[3.3.1]nonan-9,9-diol Dihydrochloride (**7**). To a cold (0 °C) solution of ketone **2c** (0.930 g, 4.15 mmol) in undried THF (10 mL) was added dropwise with stirring HCl (37%, 1.28 g, 13.07 mmol) over 10 min. The resulting solution was stirred for another 0.25 h and produced a colorless oil. The oil was drawn off and was washed with copious amounts of THF. Chilling of this oil for 72 h produced a white solid **7** (1.11 g, 86%), mp 91-92 °C. IR (KBr) 3403 (O-H) ^{1}H NMR (DMSO-d_6) d 1.30 [d, 12 H, CH_3], 2.36 [bs, 2 H, H(1,5)], 3.38 [m, 10 H, H(2,4,6,8) and 2 *H*C(CH_3)$_3$], 5.36 [bs, 1 H, OH], 10.27 [bs, 1 H, NH]; ^{13}C NMR (DMSO-d_6) ppm 16.8 [CH_3], 36.8 [C(1,5)], 48.9 [C(2,4,6,8)], 60.5 [*C*H(CH_3)$_2$], 86.9 [C(9)]. Anal. Calcd for $C_{13}H_{28}N_2O_2Cl_2$ • 2 H_2O: N, 7.97. Found: N,7.79. Calcd for $C_{13}H_{27}N_2O_2Cl_2$ *m/z* (M^+): 243.2072 (–2 Cl). Found: 243.2089.

3-(2-Propyl)-7-benzyl-3,7-diazabicyclo[3.3.1]nonan-9-one Hydrobromide (**10**). Gaseous $HBr_{(g)}$ was generated in a standard setup with a 250-mL collection flask containing solid KBr. The H_2SO_4 (~15 mL) was added dropwise (~1 mL/min), and the gas generated was passed through a $CaCl_2$ drying tube. Into a system with an ice bath was bubbled HBr(g) to a chilled solution of 7-benzyl-3-isopropyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2a**, 0.250 g, 0.919 mmol) in anhydrous ether (15 mL) over a 15-min period. The mixture was allowed to stir an additional 15 min at 0-5 °C. A white solid was formed which was filtered under vaccum and then washed with cold ether. The solid was recrystallized (1:1, 2-propanol/chloroform) to give **10** (0.233 g, 72%), mp 152-154 °C. This solid was sensitive to moisture, and the elemental analysis supported a monohydrate. IR (KBr) 3319 (N-H), 3067 (Ar-H), 2982, 2842 (C-H), 1747 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.17 [d, 6 H, CH_3], 1.97 [bs, 2 H, H(1,5)], 2.81 [d, 2 H, H(6,8)$_{ax}$], 3.01 [d, 2 H, H(6, 8)$_{eq}$], 3.12-3.56 [m, 5 H, *H*C(CH_3)$_2$ andH(2,4,6,8)$_{eq}$], 3.58 [s, 2 H, ArC*H*$_2$], 7.37-7.73 [m, 5 H, Ar-H]; ^{13}C NMR (DMSO-d_6) ppm 17.54 [CH_3], 45.16 [C(1, 5)], 50.27 [C(2, 4)], 53.07 [CH(CH_3)$_2$], 57.76 [C(6, 8)], 59.76 [ArCH_2], 128.87, 129.45, 130.55, 133.14 [Ar-C], 192.85 [C=O]. Anal. Calcd for $C_{17}H_{25}N_2OBr$•1 H_2O: C, 54.99; H, 7.32; N, 7.54. Found: C, 54.70; H, 7.35; N, 7.45.

3-(2-Propyl)-7-(3,4-dimethoxybenzyl)-3,7-diazabicyclo[3.3.1]nonan-9-one Hydrobromide (**11**). Gaseous $HBr_{(g)}$was generated in a standard setup as described for **10** above. The $HBr_{(g)}$ generated was bubbled into a chilled solution of 3-(2-propyl)-7-(3,4-dimethoxybenzyl)-3,7-diazabicyclo[3.3.1]nonan-9-one (**2b**, 0.250 g, 0.75 mmol) in anhydrous ether (15 mL) over a 15-min period. The mixture was allowed to stir an additional 15 min at 0-5 °C. A white precipitate formed and was filtered under vacuum and washed with cold ether. The solid was recrystallized (1:1, 2-propanol:chloroform) to give **11** (0.198 g, 64%), mp 179– 180.5 °C. The solid was very hygroscopic, and thus a satisfactory elemental analysis was not possible. IR (KBr) 3326 (N-H), 3039 (Ar-H), 2973, 2865 (C-H), 1735 (C=O), 1620, 1605 (C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.14 [d, 6 H, CH_3], 1.96 [s, 2 H, H(1,5)], 2.86 [d, 2 H, H(6,8)$_{ax}$], 3.05 [d, 2 H, H(2,4)$_{ax}$], 3.24 [m, 3 H, H(6,8)$_{eq}$ and *H*C(CH_3)$_2$], 3.41-3.54 [m, 2 H, H(2,4)$_{eq}$], 3.56 [s, 2 H, ArC*H*$_2$], 3.75 [s, 3 H, OCH_3], 3.76 [s, 3 H, OCH_3], 6.92-7.22 [m, 3 H, Ar-H]; ^{13}C NMR

(DMSO-d_6) ppm 17.17 [CH_3], 45.16 [C(1, 5)], 50.54 [C(2, 4)], 53.55 [C(6,8)], 55.85, 56.46 [OCH_3], 57.76 [$CH(CH_3)_2$], 59.76 [$ArCH_2$], 110.92, 113.90, 122.88, 126.81, 149.12, 149.37 [Ar-C], 206.62 [C=O]. High resolution mass spectral (FAB) data calcd for $C_{19}H_{29}N_2O_3Br$ *m/z*(M^+): 333.2179 (-Br). Found: 333.2196.

3,7-Diisopropyl-3,7-diazabicyclo[3.3.1]nonan-9-one Hydrobromide(**12**). Gaseous $HBr_{(g)}$ was generated in a standard setup as described for **10**. The $HBr_{(g)}$ was bubbled into a chilled solution of 3,7-diisopropyl-3,7-diazabicyclo[3.3.1]nonan-9-one **2c** (0.150 g, 0.660 mmol) in anhydrous ether (10 mL) over a 15-min period. A white solid was formed, and the mixture was allowed to stir an additional 15 min at 0-5 °C. The supernatant ether layer was discarded, and fresh anhydrous ether (25 mL) was added. The reaction mixture was stirred for 15 min. This process was repeated 2 times to remove unreacted **2c**. Residual ether was then removed by evaporation to give **12** as a white solid (0.095 g, 64%). Neither the mp or elemental analysis of **12** could be obtained because of its extreme hygroscopic nature. IR (KBr) 3403 (N-H), 2979 (C-H), 1749 (C=O) cm^{-1}; ^1H NMR ($DCCl_3$) δ 1.14 [d, 12 H, CH_3], 2.48 [m, 2 H, H(1,5)], 3.16-3.23 [m, 4 H, $H(2,4,6,8)_{ax}$], 3.40 [m, 4 H, $H(2,4,6,8)_{eq}$ and 2 C*H*(CH_3)$_2$]; ^{13}C NMR (DMSO-d_6) ppm 16.69, 17.02 [CH_3], 37.57 [C(1, 5)], 53.45 [C(2, 4)], 54.48 [C(6, 8)], 65.40 [$CH(CH_3)_2$]. High resolution mass spectral (FAB) data calcd for $C_{13}H_{25}N_2OBr$ *m/z* (M^+): 225.1966 (-Br). Found: 225.1957.

Attempted Preparation of 3-Cyclopropylmethyl-7-benzyl-3,7-diazabicyclo[3.3.1]nonan-9-one Hydrobromide (**13**); *Formation of* **6**. Gaseous $HBr_{(g)}$ was generated as described for **10**. The $HBr_{(g)}$was bubbled into a chilled solution of 3-cyclopropyl-7-benzyl-3,7-diazabicyclo[3.3.1]nonan-9-one (**2d**, 0.150 g, 0.528 mmol) in anhydrous ether (10 mL) over a 15-min period. A white solid was formed, and was allowed to stir an additional 15 min at 0-5 °C. The supernatant ether layer was discarded, and fresh anhydrous ether (25 mL) was added. The reaction mixture was stirred for 15 min, and the process was repeated twice to remove unreacted **2d**. Residual ether was then removed by evaporation to give **13** as a white solid (0.117 g, 64%). Unfortunately, any exposure of the white solid **13** to the atmosphere caused instantaneous conversion to diol-hydrobromide **6** which had identical properties to that cited above. All additional attempts to isolate and purify **13** were unsuccessful.

Crystallographic Data. Compounds **3, 4** and **7** were obtained as described previously and all three compounds showed some mosaicity. All X-ray measurements were carried out on an Enraf-Nonius CAD- 4 automatic diffractometer equipped with a liquid N_2 low-temperature device. Crystal data, data collection parameters and refinement results for **3, 4** and **7**are given in Table 1. The cell parameters of each crystal were determined by a least-squares fit to the ±2 θ of 25 reflections. The intensities were measured for all unique reflections at low temperature employing θ - 2θ scan technique. Absorption corrections were applied by using the absorption routine in SHELX76 program.[23] All three structures were solved by the direct methods using the program SHELXS-86[24] and refined by a full-matrix least-squares routine[23]where the quantity $\Sigma w(F_0-F_c)^2$ was minimized. The crystal structure of **7** contains two water molecules. All the hydrogen atoms including those belonging to nitrogen atoms were located from difference maps and the hydrogen parameters were refined using isotropic thermal parameters. The non-hydrogen atoms were refined anisotropically.

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