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IR AND RAMAN STUDIES OF 3,7-DIAZABICYCLO(3.3.1)NONANE-9-SPIRO-5'-HYDANTOINS

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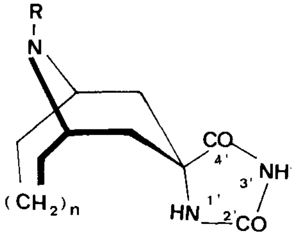
ABSTRACT

The IR and Raman spectra of 3-methyl-7-alkyl-3,7-diazabicyclo(3.3.1)nonane-9-spiro-5' hydantoins have been studied in the solid state and in deuterium oxide solution. The crystalline spirohydantoins are of three types: (1) those containing strong $N_{3'}$—H•••N bonds and N_1—H•••$O\doteq C_2$ bonds between pairs of molecules; (2) those of predominantly zwitterionic structure in the solid state and (3) those of predominantly hydrated zwitterionic structure in the solid state.

All the compounds exists as zwitterions in aqueous solution.

INTRODUCTION

As a continuation of previous studies [1—3] on the relationships between vibrational spectra and strong hydrogen bonding in several monoazabicyclospirohydantoins (1—5) in the solid state we report here the IR and Raman results for a series of diazabicyclospirohydantoins (6).



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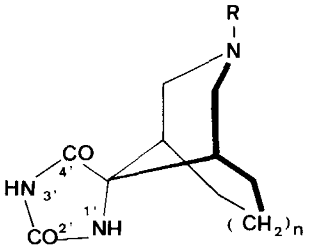

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5 : n=2

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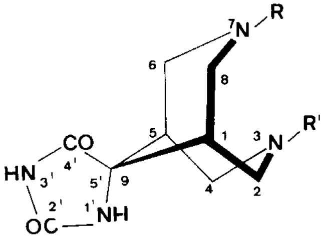

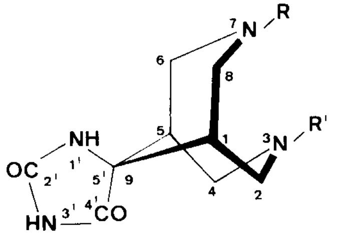

6a : R=R'=CH_3 ; 6b : R=CH_3, R'=C_2H_5 ; 6c : R=CH_3, R'=C_3H_7 ; 6d : R=CH_3, R'=iso-C_3H_7
6e : R=CH_3, R'=n-C_4H_9 ; 6f : R=CH_3, R'=sec-C_4H_9 ; 6g : R=CH_3, R'=CH_2-C_6H_5 ; 6h : R=CH_3
R'=  ; 6i : R=CH_3, R'=CH_2-CH_2-OH ; 6j : R=R'=CH_2-C_6H_5

The ^1H NMR structural analysis of **6a**—**6h** and the X-ray data of **6a**, have already been described [4—6].

EXPERIMENTAL

The synthesis and purification of compounds **6a**—**6i** have been reported previously [7].

Compound **6j** was prepared from the corresponding diazabicyclo(3.3.1)-nonane-9-one by the Bucherer—Bergs reaction and recrystallized from absolute ethanol (m.p. 168°C). Elemental analysis: calculated for $C_{23}H_{26}N_4O_2$: N, 14.34; C, 70.75; H, 6.70(%); found: N, 13.96; C, 70.35; H, 7.06(%).

IR spectra were recorded on a Perkin-Elmer 599B spectrophotometer. Indene and polystyrene were used for instrument calibration. Compounds were compressed into KBr pellets and when the solubility was adequate spectra were also recorded in deuterium oxide and dimethylsulphoxide solutions.

The Raman spectra were measured for powdered samples, mostly using a Ramanor U-1000 (5145 Å) spectrophotometer.

RESULTS AND DISCUSSION

Data for the IR and Raman spectra of compounds **6a** (non-ionic form) and **6b**—**6e** (mainly non-ionic forms) and the band assignments are given in Table 1 and data for compounds **6f**—**6j** (mainly ionic forms) are in Table 2.

3,7-Dimethyl-3,7-diazabicyclo(3.1.3)nonane-9-spiro-5'-hydantoin (6a)

X-ray diffraction data for **6a** [5, 6] have revealed the existence of an intermolecular N_3, $-H\cdots N$ bond (d = 2.831 Å) and two other intermolecular N_1, $-H\cdots O{=}C_2$ bonds (d = 2.877 Å) formed between pairs of molecules related by a centre of symmetry. This structure is similar to those found in some previously studied monoazabicyclospirohydantoins (1—3 and 5). The two methyl groups are equatorial with respect to the piperidine rings, and

TABLE 1

Infrared and Raman frequencies (cm^{-1}) of non-ionic forms of diazabicyclospirohydantoins in the N—H and C=O stretching regions

Compound	$\nu(N_1'—H)$ (IR; solid)	$\nu(N_3'—H)$ (IR; solid)	$\nu(C=O)$		
			IR		Raman
			Solid	DMSO[a]	Solid
6a	3210 m[b]	~2700[c]	1745 w		1743 m
			1709 vs		
					~1700 vw
6b	3250 w	~2800[c]	1753 w		1746 m
			1712 vs		
					1703 vw
6c	3245 m	~2780[c]	1746 w		
			1711 vs		
6d	3255 w	~2800[c]	1755 m		1747 m
			1717 vs		
					1704 vw
6f			1755[d]		1757[d]
			1715[d]		
6h			1760 m		
			1720 vs		
6i				1761 m	
				1722 vs	
6j				1759 m	
			1755[d]		1743 m
				1721 vs	
			1714[d]		
					1703vw

[a] Intramolecular coupling. [b] Abbreviations: s, strong; m, medium; w, weak; b, broad; v, very; sh, shoulder. [c] Broad and complex absorption with overlapped Bohlmann's bands. [d] Weak bands accompanying the ionic form bands.

the $N_3'—H$ proton is situated between the piperidine nitrogen atoms but only forms a hydrogen bond with the nitrogen atom which is nearer to the $C_4'=O$ group. Although the distance $N_3 \cdots N_7$ is short (3.053 Å) no hydrogen bond is properly formed since the value of the $N_3'—H \cdots N_3$ angle is 114.7°. The two piperidine rings have distorted chair conformations.

The IR spectrum of this compound (Fig. 1) showed, apart from the characteristic $\nu(N_1'—H)$ band at 3210 cm^{-1}, a broad absorption centered at about 2700 cm^{-1} which is produced by a strong $N_3'—H \cdots N$ bond between the weakly acidic $N_3'—H$ hydantoin group and the piperidine nitrogen N_3. In the 1800—1600 cm^{-1} region, the strong carbonyl band at 1709 cm^{-1} and the weaker band at 1745 cm^{-1} are assigned respectively, to the symmetrical and asymmetrical modes of the centrosymmetric ring formed between two molecules ($N_1'—H \cdots O=C_2'$), just as in related monoaza compounds.

The Raman spectrum of the carbonyl stretching region showed a predominant band at 1743 cm^{-1} related to the symmetrical mode of the coupled

TABLE 2

Infrared and Raman frequencies (cm^{-1}) of ionic forms of diazabicyclospirohydantoins in the N—H and C=O stretching regions

Compound	$\nu(N_1\text{—}H)$ (IR; solid)	$\nu(\overset{+}{N}\text{—}H)$ (IR; solid)	$(O\overset{\cdots}{-}C_4\overset{\cdots}{-}N_3\overset{\cdots}{-}C_2\overset{\cdots}{-}O)^-$		
			IR		Raman
			Solid	D_2O	Solid
6a				1679 w[a] 1585 vs	
6f	3190 m		1690 s 1600 vs		1678 m ~1600 vw
6h	3205 m	3000—2000[b]	1696 m 1588 vs		1675 m 1580 vw
6i	3180 m[c]	3000—2000[d]	1699 s 1601 vs	1679 w 1586 vs	
6j	3245 m	3000—2000[d]	1689 m 1599 vs 1580 sh		

[a] Abbreviations as in Table 1. [b] Very broad absorption with many sub-maxima. [c] Probable asignation. [d] Complex absorption.

system. Another very weak band at about 1700 cm^{-1} is probably due to the C_4'=O stretching vibration. As already observed for some monoazaspirohydantoins, the IR and Raman spectra of **6a** showed several sharp bands at 2830—2650 cm^{-1} (Bohlmann's bands) which are assigned to coupled vibrations of the two axial C_α—H bands in a *trans* coplanar position with respect to the lone electron pair of the piperidine nitrogen atom which is not involved in hydrogen bonding [2]. The IR spectrum of **6a** in deuterium oxide showed a strong band at 1585 cm^{-1} and a weak band at 1679 cm^{-1} which are assigned to complex vibrations of the anionic resonance system, $(O\overset{\cdots}{-}C_4'\overset{\cdots}{-}N_3'\overset{\cdots}{-}C_2'\overset{\cdots}{-}O)^-$, formed by proton transfer from the N_3'—H group to both basic piperidine nitrogen atoms in a rapid exchange equilibrium, as was revealed by ^{1}H NMR studies [4].

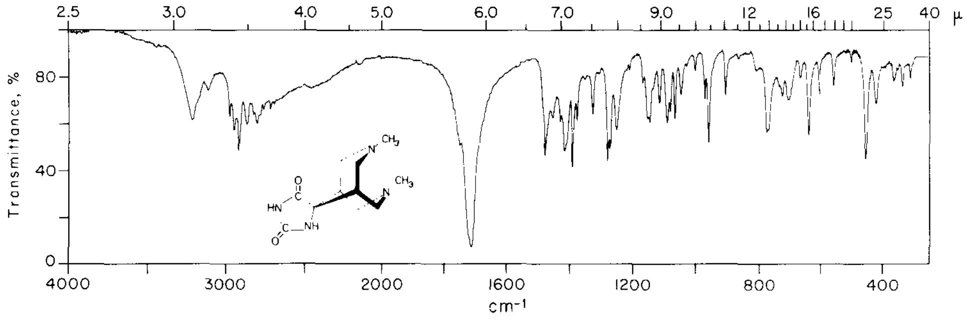

Fig. 1. IR spectrum of 3,7-dimethyl-3,7-diazabicyclo(3.3.1)nonane-9-spiro-5'-hydantoin.

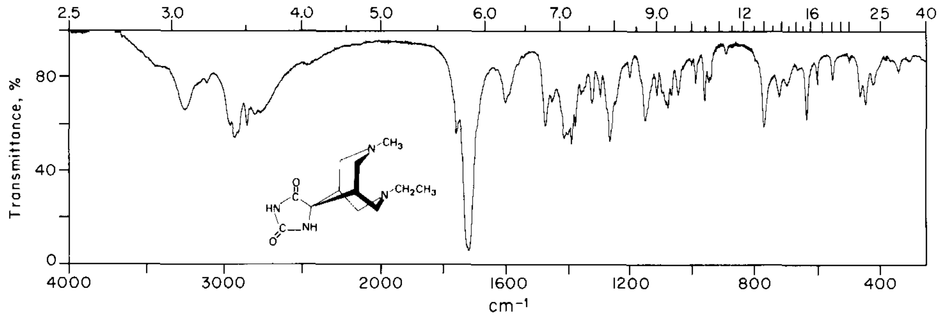

Fig. 2. IR spectrum of 3-methyl-7-ethyl-3,7-diazabicyclo(3.3.1)nonane-9-spiro-5′-hydantoin.

3-Methyl-7-alkyl-3,7-diazabicyclo(3.3.1)nonane-9-spiro-5′-hydantoins (6b—6e)

As an example, Fig. 2 shows the spectrum of compound **6b**. Just like **6a**, **6b** showed a $\nu(N_1—H)$ band at 3250 and a broad absorption at about 2800 cm^{-1}, indicating the existence of an $N_3'—H\cdots N$ intermolecular bond. In the same way the two carbonyl bands at 1753 and 1712 cm^{-1} are assigned to the symmetrical and asymmetrical modes of the coupled system formed by pairs of molecules. Another broad band at 1605 cm^{-1}, the relative intensity of which depended on crystallization conditions, is attributed to an ionic form as will be discussed below. Raman results in the carbonyl region were also similar to those obtained for **6a** (Table 1). Moreover, characteristic Bohlmann's bands were observed below 2825 cm^{-1} in the IR and Raman spectra, as expected.

3-Methyl-7-sec-butyl, 3-methyl-7-benzyl- and 3,7-dibenzyl-3,7-diazabicyclo-(3.3.1)nonane-9-spiro-5′-hydantoins (6f, 6g and 6j)

In this type of compound the IR data revealed ionic structures in the solid state and in aqueous solution. Figure 3 shows the IR spectrum of compound

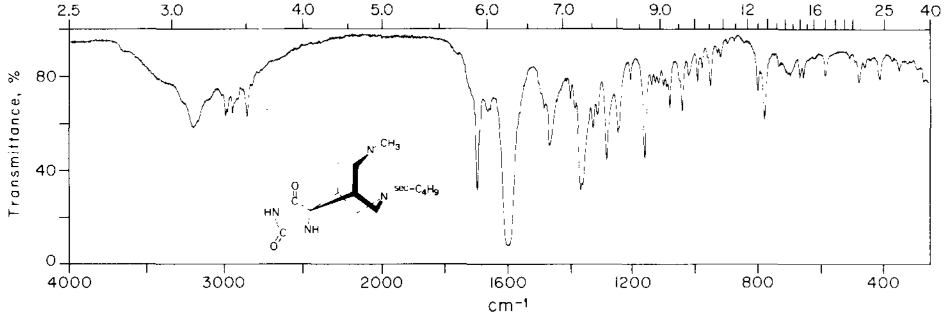

Fig. 3. IR spectrum of 3-methyl-7-sec-butyl-3,7-diazabicyclo(3.3.1)nonane-9-spiro-5′-hydantoin.

6f in the solid state. The band at 3190 cm^{-1} is assigned to the $\nu(\mathrm{N_{1'}}\text{—H})$ vibration but unlike the results for **6a—6e** no absorption was observed in the 2700 cm^{-1} region. In the carbonyl region a sharp band at 1690 cm^{-1} and a broad and complex band at 1600 cm^{-1} are assigned to complex vibrations of the resonance system $(\mathrm{O}\overset{\cdots}{-}\mathrm{C_{4'}}\overset{\cdots}{-}\mathrm{N_{3'}}\overset{\cdots}{-}\mathrm{C_{2'}}\overset{\cdots}{-}\mathrm{O})^-$ present in a zwitterionic structure and formed by proton transfer from the acidic $\mathrm{N_{3'}}$—H group to the basic piperidine nitrogen atoms, giving rise to a monoprotonated species (Fig. 4). In other words, the proton is shared by both nitrogen atoms in the same way as was deduced for aqueous solutions by ^{1}H NMR spectroscopy. In this context it is worth noting that no clear $\overset{+}{\mathrm{N}}$—H absorptions are observed in the IR spectrum in the expected regions, contrary to the results obtained for some related monoazaspirohydantoins [8].

The Raman spectrum of **6f** showed a strong band at 1678 and a very weak band at 1600 cm^{-1}. The intensity ratio was the reverse of that in the IR spectrum. These results suggest that the high frequency band must be attributed to a symmetrical mode and the low frequency band to an asymmetrical mode of the coupled system.

In the case of **6j** the IR spectrum also revealed the existence of an ionic form, and a small proportion of the non-ionic form in the solid state. By dissolving in dimethylsulphoxide a complete transformation into the non-ionic form took place. On the other hand, the Raman spectrum showed the coexistence of both forms, the non-ionic form being predominant. These results indicate that a tautomerization to the non-ionic form has occurred under laser radiation.

It seems that in these compounds, which crystallize in anhydrous form, the stability of the ionic form is less than in the related hydrated ionic compounds (see below).

3-Methyl-7-cyclohexyl- and 3-methyl-7-β-hydroxyethyl-3,7-diazabicyclo-(3.3.1)nonane-9-spiro-5'-hydantoins (6h and 6i)

Figure 5 shows the IR spectrum of compound **6h**. The spectrum of **6i** (Fig. 6) is similar in the 1750—1550 cm^{-1} region and both spectra indicate

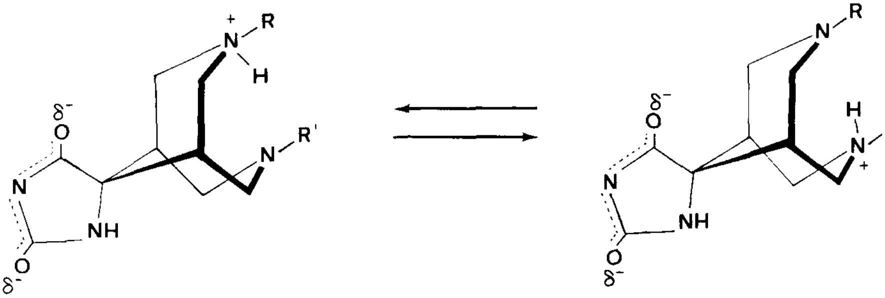

Fig. 4. Zwitterionic structure of compounds 6.

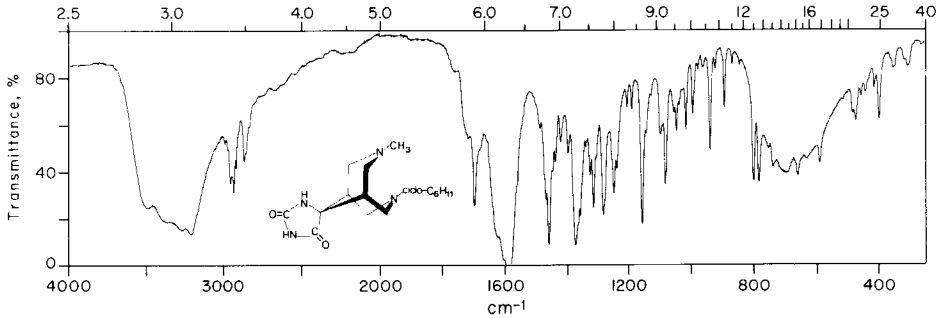

Fig. 5. IR spectrum of 3-methyl-7-cyclohexyl-3,7-diazabicyclo(3.3.1)nonane-9-spiro-5′-hydantoin.

ionic forms (bands in about 1700 and 1600 cm^{-1}). Examination of the 3600—3000 cm^{-1} region reveals the presence of bands due to water of crystallization, a fact also deduced from microanalysis results. (Two H_2O and one H_2O per mol of hydantoin, for **6h** and **6i**, respectively).

When compound **6h** was heated at 80° C, water was lost and a transformation into the non-ionic form took place; this result indicates that the water molecules stabilize the ionic form which is the only one observed in aqueous solution.

In the case of compound **6i** no transformation to a non-ionic form was found by heating at 110° with loss of water. Moreover, when cooled the sample reabsorbed water. On the other hand, by recrystallization from absolute ethanol some change to the non-ionic form was observed. Only in dimethylsulphoxide solution was the non-ionic form preponderant, as already observed for compound **6j**.

CONCLUSIONS

X-ray data for compound **6a** have revealed that the bicyclo(3.3.1)nonane system adopts a chair—chair conformation. If we assume the same chair—

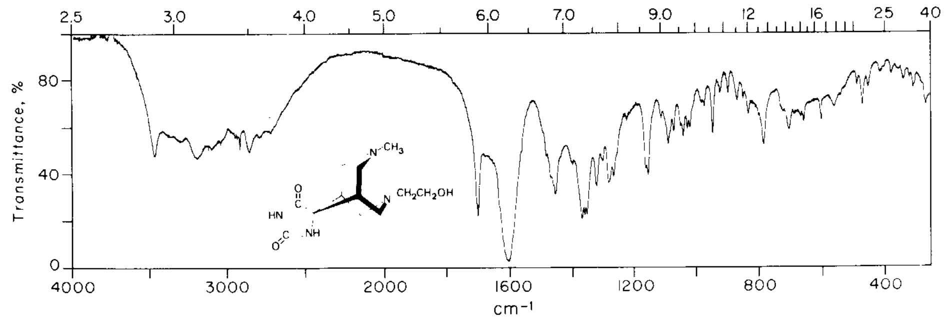

Fig. 6. IR spectrum of 3-methyl-7-β-hydroxyethyl-3,7-diazabicyclo(3.3.1)nonane-9-spiro-5′-hydantoin.

chair conformation for compounds **6b—6j** in the solid state, the steric effects of the piperidine *N*-substituents must be major factors in the formation of a $N_3'—H\cdots N_7$ intermolecular hydrogen bond which stabilizes the non-ionic forms. When these effects increase in importance, the compounds will crystallize in the ionic form. Furthermore the ionic forms will be favoured by an increase in the basicity of the piperidine nitrogen atoms as well as by the presence of water of crystallization or by solvating, protic, polar solvents.

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