ELSEVIER

Journal of Molecular Structure 476 (1999) 45–55

Journal of
MOLECULAR
STRUCTURE

IR–Raman, NMR and density functional methods in the examination of tautomerism and features of *N*-methyl substituted 9-acridinamine derivatives

Janusz Rak, Karol Krzymiński, Piotr Skurski, Ludwika Jóźwiak, Jerzy Blażejowski*

Department of Chemistry, University of Gdańsk, J. Sobieskiego 18, 80-952 Gdańsk, Poland

Received 1 April 1998; accepted 9 June 1998

Abstract

Four *N*-methyl substituted derivatives of amino or imino forms of 9-acridinamine were synthesized and subjected to detailed IR–Raman and NMR (^{1}H and ^{13}C) investigations. Harmonic frequencies predicted at the density functional (DFT) level enabled certain modes to be assigned to bands in IR or Raman spectra and those characteristic of either the amino or imino tautomeric forms of 9-acridinamine. Theoretical ^{1}H and ^{13}C chemical shifts, particularly the latter, fit the relevant NMR spectra only qualitatively; both demonstrate a unique pattern for each of the compounds studied. The derivatives examined seem to exhibit their own identity and features, reflected in unique vibrational and NMR spectra, rather than retain those of the parent tautomeric forms of 9-acridinamine. Both experimental and theoretical investigations reveal that two tautomeric forms of *N*-methyl-9-acridinamine, in similar to 9-acridinamine, should co-exist at room temperature. The polarity of the compounds, expressed by dipole moments, as well as distribution of relative atomic partial charges and electrostatic potential around the molecules, are unique for each of the compounds but generally similar in the groups of derivatives originating from the amino or imino tautomers of 9-acridinamine.

Keywords: *N*-Methyl-9-acridinamines; Tautomerism; IR–Raman spectroscopy; NMR spectroscopy; Experimental and theoretical investigations

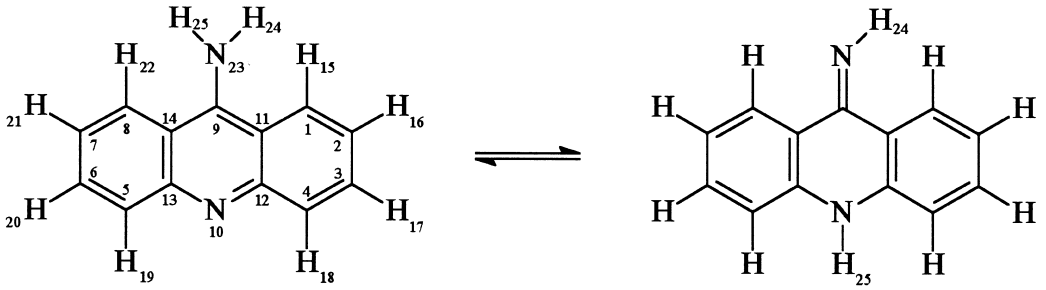
1. Introduction

Our recent semiempirical [1–3] and ab initio [4] quantum mechanical calculations, as well as examinations of electronic absorption [2], fluorescence [5], vibrational [4] and NMR [4] spectra, have revealed that 9-acridinamine can potentially exist in two tautomeric forms—amino or imino—in equilibrium with each other.

In the past, some authors followed up this idea [6–10], while others did not recognize it [11–16]. To shed more light on the tautomerism of 9-acridinamine we have attempted, among other things, to synthesize some simple derivatives with 'blocked' the amino or imino structure. In this publication we present syntheses as well as the results of IR–Raman and NMR investigations of four such compounds: *N*-methyl-9-acridinamine (**1**), 10-methyl-9-acridinimine (**3**), *N*,*N*-dimethyl-9-acridinamine (**4**), and *N*-methyl-10-methyl-9-acridinimine (**5**) (Fig. 1). Parallel, structural optimizations and determinations of harmonic

* Corresponding author. Tel.: +48-58-345-0331; Fax: +48-58-341-0357; E-mail: bla@ewa.chem.univ.gda.pl

0022-2860/99/$ - see front matter
PII: S0022-2860(98)00530-4



frequencies, chemical shifts and some physicochemical features of five molecules originating from amino or imino forms, i.e. the four above-mentioned and *N*-methyl-(10-*H*)-acridinimine (**2**), were carried out at the DFT level. The aim of these studies was to reveal the spectral peculiarities of two types (amino and imino) of 9-acridinamine methyl derivatives, as well as factors determining their ability to intermolecular interactions.

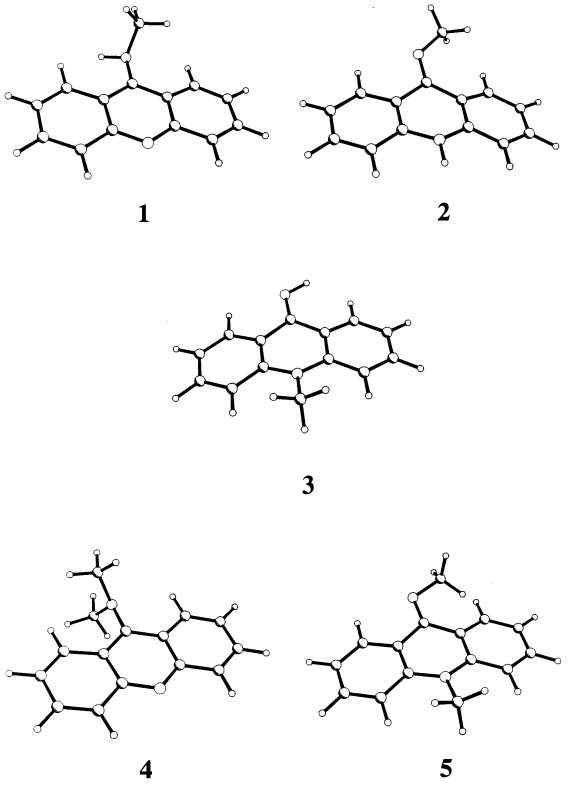


Fig. 1. DFT (B 3LYP)/6-31G** optimized geometries of *N*-methyl-9-acridinamine (**1**), *N*-methyl-9(10-*H*)-acridinimine (**2**), 10-methyl-9-acridinimine (**3**), *N*,*N*-dimethyl-9-acridinamine (**4**) and *N*-methyl-10-methyl-9-acridinimine (**5**).

9-Acridinamine is one of the simplest representatives of the family of heterocyclic nitrogenous bases and a molecule with a well-recognized biological relevance [17,18]. It exhibits distinctive mutagenic activity [19–21] and the ability to interact with DNA [22–28] and other biologically important molecules [24,29,30]. It also appears to be a convenient probe for investigating various physical features of biological systems [31,32] and it is, therefore, important to know whether simple derivatives of 9-acridinamine with fixed structures of both tautomeric forms can be synthesized and investigated experimentally, and what impact the structure may have on their features, including biological activity. This work has extended our knowledge in the first of these topics.

2. Experimental

2.1. Syntheses

N-methyl-9-acridinamine (**1**) and *N*,*N*-dimethyl-9-acridinamine (**4**) hydrochlorides were synthesized by heating 9-phenoxyacridine (obtained from 9-chloroacridine [17,33,34]) with methanamine and *N*-methylmethanamine hydrochloride, respectively, dissolved in phenol [17]. *N*-methyl-9-acridinamine free base was released from the aqueous solution of its hydrochloride by alkalization with sodium hydroxide, extraction with toluene and purification by column chromatography (phase: silica gel 60 from Merck; eluent: toluene/*N*-methylmethanamine = 10/1) (m.p. = 446–447 K, lit. = 446–447 K [17]). *N*,*N*-dimethyl-9-acridinamine free base was also released from the

aqueous solution of its hydrochloride by alkalization with *N*-methylmethanamine, extraction with light petroleum, separation and repeated crystallization [17] from cyclohexane in an inert atmosphere (m.p. = 332–333 K, lit. = 334 [17]). The purity of the products was checked by TLC, their chemical composition proved by elemental analysis using a Carlo–Erba (model EAGER 200) instrument (% found/theoretical: C = 80.71/80.78, H = 5.85/5.78 and N = 13.51/13.44 for **1**; C = 81.12/81.08, H = 6.41/6.31 and N = 12.63/12.61 for **4**), and identity of **4** confirmed by X-ray investigations [35].

10-Methyl-9-acridinimine (**3**) hydriodide was synthesized by heating 9-acridinamine with iodomethane, both dissolved in methanol, in a sealed tube at 373 K [36,37]. The salt was subsequently separated, dissolved in water and treated with cool dilute NaOH. The 10-methyl-9-acridiniminium hydroxide so obtained was purified chromatographically (phase: silica gel 60; eluent: toluene/*N*-ethylethanamine = 10/1) and heated in a vacuum pistol over P_2O_5 at 403 K. The final product was recrystallized from dry cyclohexane in an inert atmosphere, always in the form of thin orange–yellow needles (m.p. = 407–408 K, lit. = 407–409 K [36]). Its purity was checked by TLC and its composition confirmed by elemental analysis (% found/theoretical: C = 80.80/80.78, H = 5.72/5.78, N = 13.56/13.44).

N-Methyl-10-methyl-9-acridinimine (**5**) was synthesized by treating *N*-methyl-9-acridinamine (for 12 h at room temperature) with a stoichiometric quantity of methyl ester of trifluoromethane sulphonic acid, both dissolved in dry dichloromethane, in the presence of an excess of anhydrous caesium carbonate. The salt so obtained was treated with a 33% solution of methanamine in absolute ethanol, then dissolved in toluene, and the solution of crude base was filtered off. Purification was carried out chromatographically (phase: silica gel 60; eluent: toluene/*N*-methylmethanamine = 30/1). The purity of the final product (m.p. = 396–397 K) was checked by TLC, its composition proved by elemental analysis (% found/theoretical: C = 81.00/81.05, H = 6.47/6.35, N = 12.43/12,60), and identity confirmed by X-ray investigations [35].

2.2. NMR and vibrational spectroscopic investigations

^{1}H and ^{13}C NMR spectra for saturated solutions of **1** (or **2**), **3**, **4** and **5** in CD_3CN were recorded on a Varian Unity 500 Plus spectrometer. 1D spectra were collected under standard conditions and chemical shifts were referred to the relevant ^{1}H or ^{13}C nuclei signals in tetramethylsilane (TMS; reference). HSQC and HMBC spectra were acquired by employing the pulsed field gradient technique [38].

Infrared spectra **1** (or **2**), **3**, **4** and **5** dispersed in KBr (4000–400 cm^{-1} region) or polyethylene (400–100 cm^{-1} region) were recorded on a Bruker IFS 66 FTIR instrument at a resolution varying between 1 and 4 cm^{-1}. Raman scattering measurements (resolution 2 cm^{-1}) were carried out on samples of the pure compound (powdered) using a Bruker FRA 106 FT-module connected with an FTIR system (an Nd^{3+}/YAG laser (1064 nm) served as the excitation source).

2.3. Calculations

Unconstrained geometry optimizations of isolated molecules were conducted at the density functional (DFT) [39] level of theory using gradient techniques [40,41], 6-31G** [42,43] basis sets and the Becke 3LYP (B3LYP) nonlocal spin density functional approximation, which uses Becke's nonlocal exchange functional [44,45] and the Lee–Yang–Parr nonlocal correlation functional [46]. DFT geometry optimizations were extended in the case of **3** and **4** utilizing the self-consistent reaction field (SCRF) model [47,48] which simulates the presence of the solvent. In the latter calculations the relative electric constant of acetonitrile (CH_3CN) was assumed to be 38.8, and the spherical cavity radii were evaluated at 4.90 Å for **3** and 5.15 Å for **4** [49]. After each optimization was completed, the Hessian energy (second derivatives of the energy as a function of nuclear coordinates) was calculated and checked for positive definiteness, in order to assess whether the structures were true minima [39,50]. The harmonic vibrational frequencies were subsequently derived on the basis of the numerical values of these second derivatives [39,50]. ^{1}H and ^{13}C magnetic shielding tensors (χ) for **1**, **2, 3**, **4** and **5**, as well as TMS were obtained following the gauge—including atomic orbital (GIAO) approach [51–53]. The differences between isotropic magnetic shielding tensors of nuclei in TMS and the compounds studied ($\chi_{TMS} - \chi_{1,2,3,4,5}$) were considered to be relevant chemical shifts [51].

All the calculations were conducted on HP/735 Apollo and IBM/RS 6000 3CT workstations using GAUSSIAN 92/DFT [54] or GAUSSIAN 94 [55] program packages. The dipole moments were extracted directly from data files following geometry optimizations. The molecular electrostatic potential around the molecules was explored using the SPARTAN 4.0 program package [56]. Relative atomic partial charges were determined either on the basis of Mulliken population analysis (Mul) [57] or from the fit to the molecular electrostatic potential (MEP fit) at points selected according to the Besler–Merz–Kollman scheme [58].

3. Results and discussion

3.1. Structural and physicochemical features

As our recent X-ray investigations revealed, the acridine moiety in **4** is almost planar and the dimethylamine group is twisted relative to it through an angle of 58.6° [35]. On the other hand, the central ring in **5** is folded along the $C_{(9)}\cdots N_{(10)}$ axis through an angle of 26.3° and the exocyclic nitrogen atom with the attached methyl group is directed away from the concave side of the acridine nucleus.

Structures of **1**, **2**, **3**, **4** and **5** obtained at the DFT level of theory are shown in Fig. 1. According to theoretical predictions, the acridine skeleton is almost planar in **1** and **4**, i.e. in molecules retaining the constitution of the amino tautomeric form of 9-acridinamine. The methylamine and dimethylamine groups in **1** and **4**, respectively, are twisted against the acridine moiety; the dimethylamine group in **4** lies perpendicular to the acridine moiety, so that the molecule exhibits c_s symmetry. In **2**, **3** and **5**, which originate from the imino form, the central ring is more or less folded along the $C_{(9)}\cdots N_{(10)}$ axis and the exocyclic nitrogen atom together with the hydrogen atom (**3**) or the methyl group (**2** and **5**) attached to it is bent away from the concave side of the acridine nucleus.

Inclusion of the environment in the calculations at the DFT SCRF level of theory exerts a barely significant influence on the geometries of the molecules.

The DFT method, which seems quite reliable in predicting thermochemical quantities [59], reveals that the thermodynamically more stable of the tautomeric forms **1** and **2** is **1**, whereas **2** and **3**, being isomers, exhibit comparable thermodynamic stability [35]. Of **4** and **5**, which retain the respective constitutions of the amino and imino forms of 9-acridinamine, the former is thermodynamically more stable.

As **1** and **2** represent tautomeric forms one can predict the equilibrium constant ($_{298}K^{\circ}_{\mathbf{1}\rightleftarrows\mathbf{2}}$) which, according to the data relevant to the DFT level of theory, is equal to 0.104 [35]. An almost identical value of this quantity was obtained for the amino $\rightleftarrows$ imino equilibrium in 9-acridinamine [4].

The dipole moment (Table 1) reflects the nonuniform distribution of a charge within the molecule and to some extent the electrostatic potential around the molecules. Examination of the latter reveals that two

Table 1
Dipole moments[a] and atomic partial charges calculated at the DFT level

Compound no. (Fig. 1)	Dipole moment		Atomic partial charge				
		Method	$C_{(9)}$	$N_{(10)}$	$N_{(23)}$	$C_{(24)}$;$H_{(24)}$	$C_{(25)}$;$H_{(25)}$
1	3.09	Mul	0.188	–0.610	–0.573	–0.187	0.253
		MEP fit	0.269	–0.676	–0.595	0.172	0.330
2	3.01	Mul	0.253	–0.475	–0.495	–0.185	0.252
		MEP fit	0.508	–0.658	–0.453	0.045	0.358
3	3.89	Mul	0.242	–0.651	–0.602	0.214	–0.186
		MEP fit	0.492	–0.078	–0.727	0.319	–0.225
4	2.40	Mul	0.149	–0.599	–0.499	–0.160	–0.160
		MEP fit	0.583	–0.736	–0.203	–0.186	–0.186
5	3.01	Mul	0.237	–0.636	–0.484	–0.187	–0.184
		MEP fit	0.481	–0.186	–0.463	0.060	–0.210

[a]Dipole moment in D (1D = 3.336×10^{-30} cm).

zones of potential centred at nitrogen atoms appear in the molecules. The negative potential region is in the neighbourhood of the endocyclic nitrogen atom of **1** and **4** (i.e. derivatives from the amino form of 9-acridinamine) and the exocyclic nitrogen atom of **2, 3** and **5** (i.e. derivatives from the imino form of 9-acridinamine), while the zone of positive potential occurs at the exocyclic nitrogen atom of **1** and **4** and the endocyclic nitrogen atom of **2**, **3** and **5**. This feature is reflected in the atomic partial charges, derived either on the basis of Mulliken population analysis (Mul) or so as to reproduce the molecular electrostatic potential (MEP fit), shown for selected atoms in Table 1. An excess negative charge is predicted at both the endocyclic and exocyclic nitrogen atoms. The negative charge is usually higher at the endocyclic than the exocyclic N atom in **1** and **4** and at the exocyclic than endocyclic N atom in **2**, **3** and **5**. A negative charge deficiency is always predicted at the $C_{(9)}$ atom (higher in **2**, **3** and **5**), whereas at other C atoms an excess of negative charge is usually expected. Finally, a negative charge deficiency is always present at the hydrogen atoms. Nitrogen atoms may primarily be considered sites of specific interactions, including the solute solvent or those leading to the formation of complexes with other molecules [1,4,60]. It is thus possible that methyl derivatives originating from the amino tautomeric form of 9-acridinamine (**1** and **4**) behave differently from those arising from the imino form (**2**, **3** and **5**) in the presence of macromolecules in living matter.

3.2. Vibrational analysis

Infrared and Raman spectra of all the compounds studied, together with the theoretically determined vibrational frequencies (scaled), are demonstrated in Fig. 2. Deformations of the molecules as a whole or their fragments correspond to 78 (in the case of **1**, **2** and **3**) or 87 (for **4** and **5**) normal modes predicted theoretically. To permit comparison of characteristic transitions in which both nitrogen atoms are involved, we have compiled them in Table 2. IR absorption and Raman scattering bands generally appear in the same region in 9-acridinamine, as in its *N*-methyl derivatives with 'blocked' amino or imino structure. Appearing at frequencies higher than those characteristic of any other vibrations in the compounds studied, the absorption corresponding to $N_{(23)}H_{(25)}$, $N_{(10)}H_{(25)}$ and $N_{(23)}H_{(24)}$ stretching vibrations in **1**, **2** and **3**, respectively, is unique. The theoretically predicted frequencies of this mode in 9-acridinamine [4] and **3** match each other very closely. Moreover, they match the band observed in the experimental IR spectrum of 9-acridinamine [4]. This could indicate that at least some 9-acridinamine molecules exist in the imino tautomeric form.

Investigating the vibrational spectra of 9-acridinamine, we noted that the region between 1580–1680 cm^{-1}, in which bending NH vibrations fall, is characteristic of both amino and imino forms [4]. We even ascribed bands to given tautomeric forms. Unfortunately, such an assignment is not feasible in the case of the *N*-methyl substituted derivatives of 9-acridinamine, since bands characteristic of compounds retaining an amino or imino constitution occur in the same region; hence, these molecules are indistinguishable (Fig. 2, Table 2). Examination of the spectra over the whole range of frequencies leaves the impression that they are specific to a particular molecule and reflect their features and identity. Owing to the complex nature of these spectra, it is rather seldom that bands assigned to the same modes of a given type (amino or imino) of molecules appear at the same frequencies. It is thus difficult to obtain information as to the existence of tautomeric phenomena in 9-acridinamine from only vibrational spectroscopic investigations.

3.3. NMR investigations

The ^{1}H NMR spectra of the compounds studied consist of a system of signals arising from the eight aromatic hydrogen atoms: one or two sharp signals originating from the hydrogen atoms of the methyl group(s) attached to the nitrogen atom(s) and one broad signal relevant to the hydrogen atom attached to the exocyclic or endocyclic nitrogen atom (Fig. 3). The ^{13}C NMR spectra of the compounds display clear signals arising from the aromatic and aliphatic carbon atoms (Fig. 4). As we were unable on the basis of these spectra to assign signals to particular atoms, we used HSQC and HMBC (2D spectra are not presented here) for this purpose. The assignments are shown in Fig. 3 and Fig. 4, where at all signals the atoms from which they originate are indicated. These

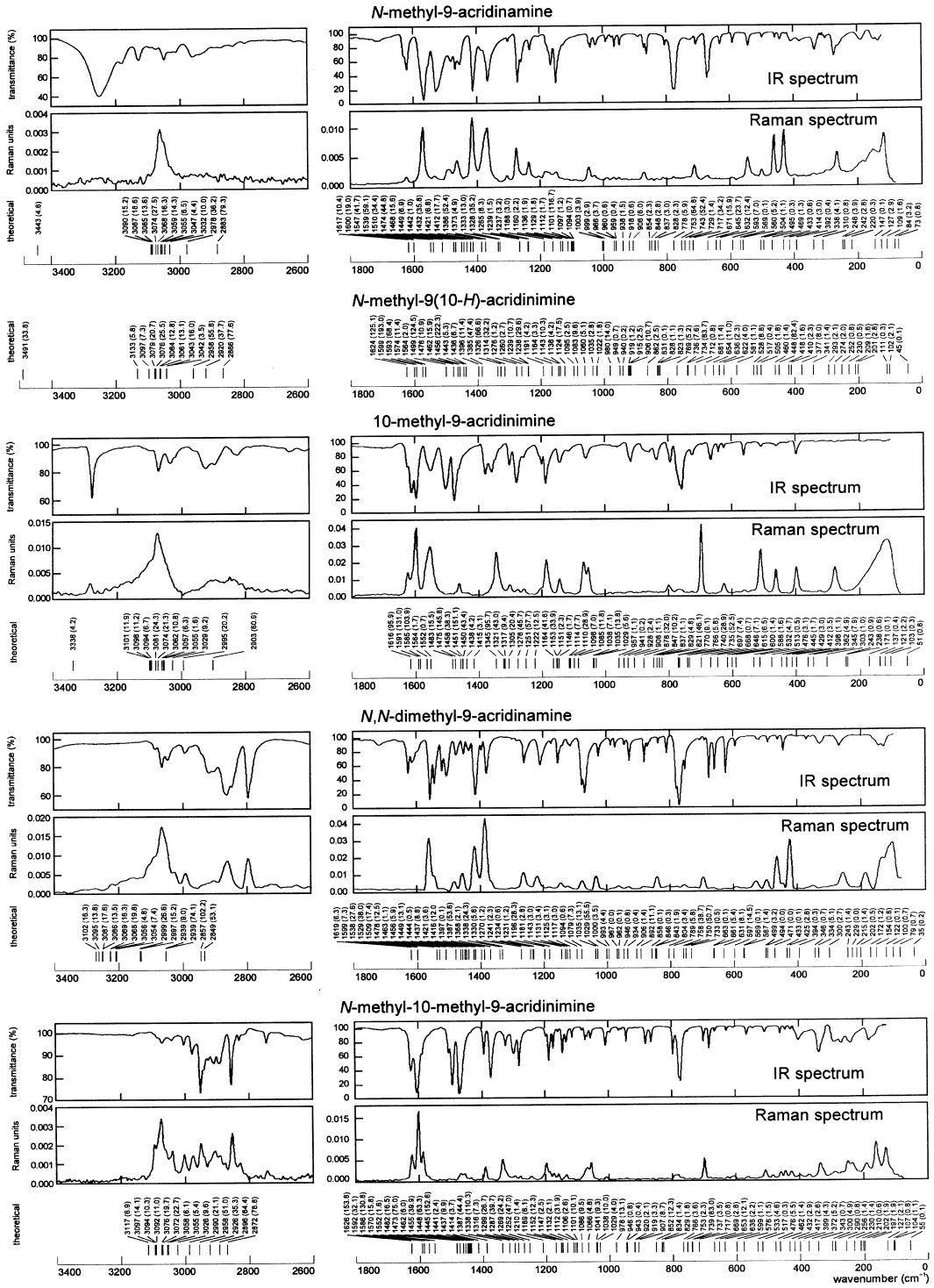


Fig. 2. Infrared (IR) and Raman spectra together with the theoretically predicted frequencies (× 0.96) of vibrational transitions in *N*-methyl substituted 9-acridinamine derivatives (numbers in parentheses indicate IR intensities in KM/mol).

Table 2
Selected bands in the experimental IR and Raman spectra together with harmonic frequencies (cm^{-1}) predicted at the DFT level

Assignment	Mode Description	Theoretical[a]	Frequency IR	Observed Raman
	1			
ν_1(a)	$N_{(23)}H_{(25)}$ stretching	3443	3244	
ν_{13}(a)	whole molecule deformation	1617	1613	1611
ν_{14}(a)	whole molecule deformation	1600		
ν_{15}(a)	$N_{(23)}H_{(25)}$ bending	1547	1559	1559
ν_{16}(a)	whole molecule deformation	1539	1520	
ν_{24}(a);ν_{25}(a)	$N_{(23)}C_{(24)}H_{(25)}$ deformation	1412; 1386	1411	1400
ν_{26}(a);ν_{27}(a)	whole molecule deformation	1373; 1333	1354	1352
ν_{52}(a)	whole molecule deformation	778	762	
	2			
ν_1(a)	$N_{(10)}H_{(25)}$ stretching	3491		
ν_{13}(a)	$C_{(9)}N_{(23)}$ stretching	1624		
ν_{14}(a)	$N_{(10)}H_{(25)}$ bending	1599		
ν_{15}(a)	$C_{(9)}N_{(23)}C_{(24)}$ deformation	1593		
ν_{16}(a)	whole molecule deformation	1574		
ν_{24}(a);ν_{25}(a)	whole molecule deformation	1396; 1385		
ν_{26}(a);ν_{27}(a)	whole molecule deformation	1326; 1314		
ν_{52}(a)	whole molecule deformation	769		
	3			
ν_1(a)	$N_{(23)}H_{(24)}$ stretching	3338	3274	3284
ν_{13}(a)	$C_{(9)}N_{(23)}$ stretching	1616	1607	1618
ν_{14}(a)	whole molecule deformation	1591	1591	1592
ν_{17}(a)	whole molecule deformation	1552	1544	1547
ν_{18}(a);ν_{19}(a)	whole molecule deformation	1483; 1475	1497	
ν_{20}(a);ν_{21}(a)	$C_{(25)}H_{(26,27,28)}$ bending	1458; 1451	1469	1452
ν_{26}(a)	$N_{(23)}H_{(24)}$ bending	1321		1334
ν_{54}(a);ν_{55}(a)	whole molecule deformation	740; 735	743	
	4			
ν_{15}(a′)	s-whole molecule deformation	1619	1624	
ν_{16}(a′)	s-whole molecule deformation	1599	1612	
ν_{17}(a′)	s-whole molecule deformation	1538	1554	1555
ν_{27}(a′)	s-whole molecule deformation	1416	1409	1409
ν_{29}(a′	s-$C_{(9)}N_{(23)}$ stretching; whole molecule deformation	1387	1374	1375
ν_{60}(a″);ν_{61}(a″)	as-whole molecule deformation	758; 750	758	
	5			
ν_{15}(a)	$C_{(9)}N_{(23)}$ stretching	1626	1618	1616
ν_{16}(a)	whole molecule deformation	1592	1597	1596
ν_{17}(a)	whole molecule deformation	1586		1581
ν_{21}(a)	$C_{(25)}H_{(29,30,31)}$ deformation	1473	1484	
ν_{25}(a)	whole molecule deformation	1445	1462	1460
ν_{29}(a)	$C_{(24)}H_{(26,27,28)}$ deformation	1387	1384	1381
ν_{30}(a)	whole molecule deformation	1338	1362	
ν_{60}(a)	whole molecule deformation	739	756	

[a]Values multiplied by 0.96 [4].

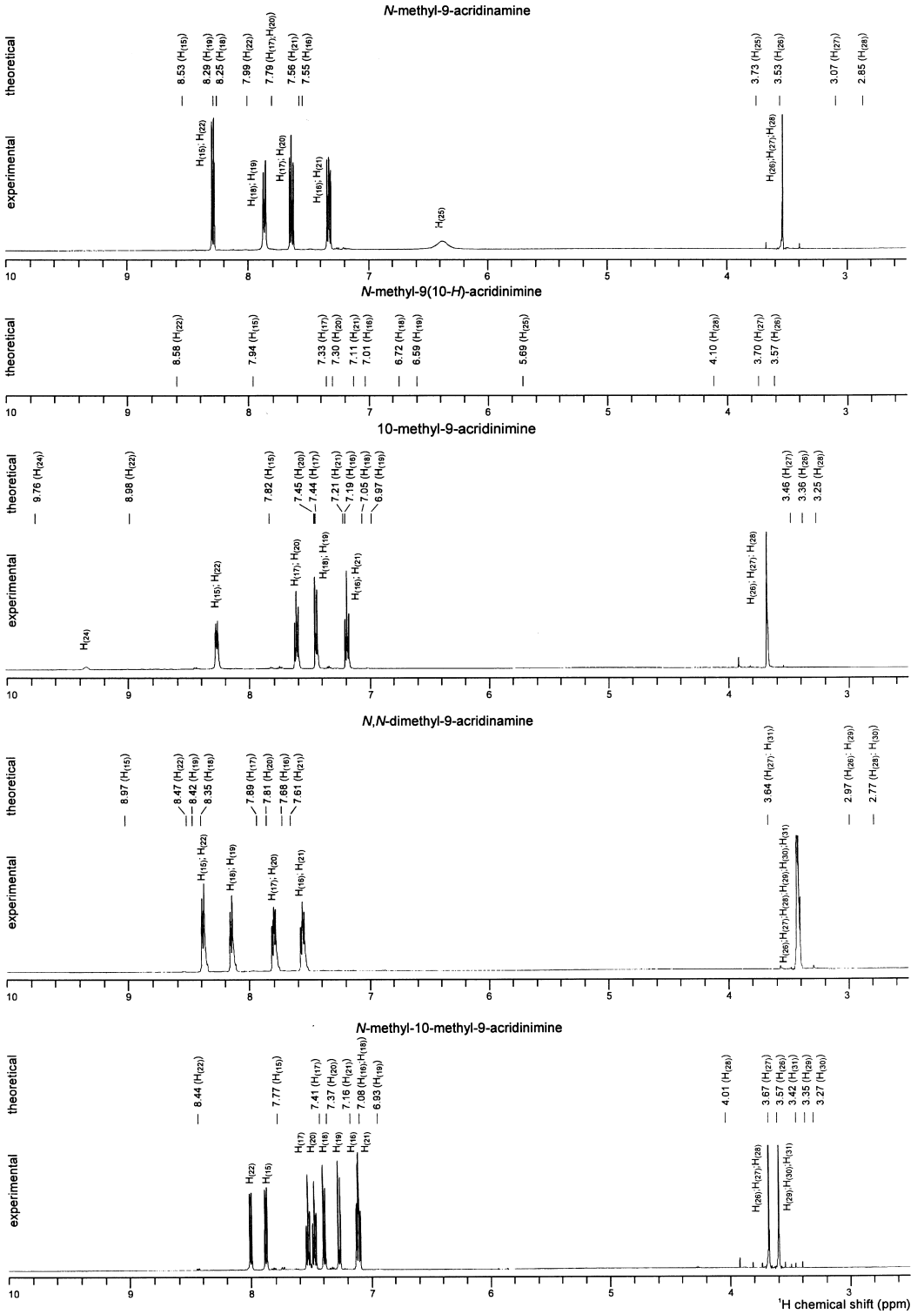


Fig. 3. ^{1}H NMR spectra of *N*-methyl substituted 9-acridinamine derivatives together with chemical shifts predicted by the GIAO method.

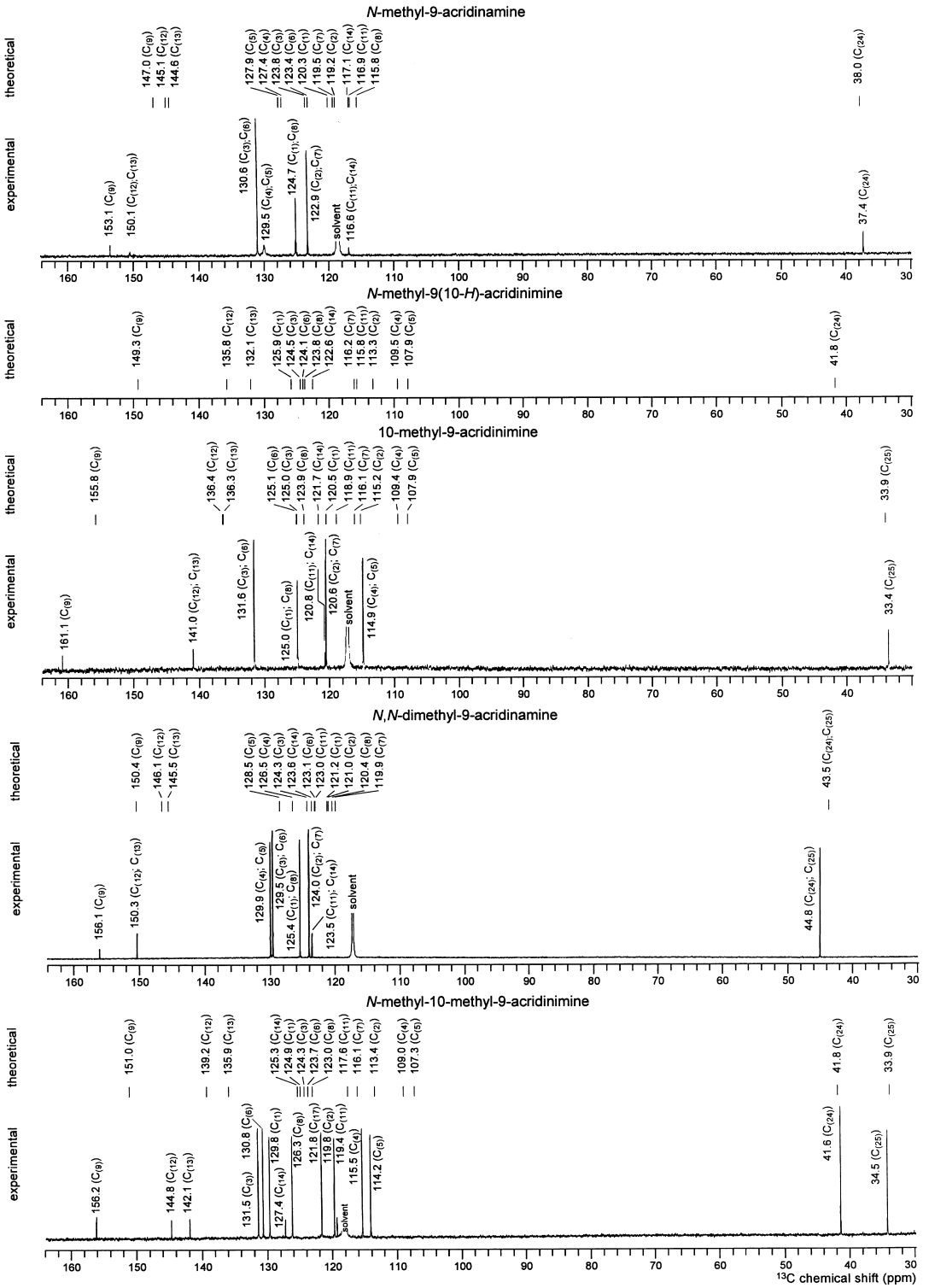


Fig. 4. ^{13}C NMR spectra of *N*-methyl substituted 9-acridinamine derivatives together with chemical shifts predicted by the GIAO method.

assignments are set down with the chemical shifts predicted by the GIAO method. As can be seen, both experimental and theoretical ^{13}C chemical shifts are unique to each molecule investigated and, with respect to both numerical values and mutual relations, do not correlate with those found for 9-acridinamine [4]. The experimental ^{1}H NMR spectrum of **4** is very similar to that of 9-acridinamine [4] as regards mutual relations and the alteration of signals corresponding to the aromatic hydrogen atoms; however, the chemical shifts of these are somewhat higher in the case of the former molecule. On the other hand, the range in which the aromatic ^{1}H NMR signals appear in all the other compounds studied is similar to that in 9-acridinamine, although their mutual relations are different. In all the compounds the signals corresponding to the hydrogen atoms in methyl groups are sharp, not split, and appear in regions typical of such atoms. The theoretically predicted ^{1}H chemical shifts differ from each other and from those in 9-acridinamine [4]. Two other features are worth mentioning. Firstly, the ^{1}H signal originating from the hydrogen atom attached to the exocyclic nitrogen atom in **3** appears at a relatively high chemical shift—as was observed and predicted theoretically. Secondly, the shape of the ^{1}H signals of the hydrogen atoms in the methyl groups (one or two sharp signals) indicates that these groups undergo rapid rotation; in **1** or **4** the whole $NH(CH_3)$ or $N(CH_3)_2$ groups most probably rotate against the acridine moiety.

Examination of NMR spectra reveals that some of them are similar (^{1}H NMR spectrum of **4**) to the corresponding ones for 9-acridinamine (amine tautomer [4]) but others are not. This means that it is not generally possible to ascribe ^{1}H and ^{13}C signals to given tautomeric forms and implies that NMR spectra reflect the unique features of the molecules investigated.

4. Final remarks

One derivative of 9-acridinamine with fixed amino constitution (**4**) and two more with retained imino (**3** and **5**) structures were synthesized and examined by IR, Raman and NMR spectroscopy. A fourth compound obtained can exist in two tautomeric forms (**1** or **2**); this was suggested by theoretical studies, as well as analyses of NMR and to some extent vibrational spectra.

All the compounds investigated both experimentally and theoretically exhibit unique structural properties and spectral features. This means that the replacement of the hydrogen atom(s) attached to the nitrogen atom(s) by the methyl group(s) is of limited importance in studies of tautomeric phenomena in 9-acridinamine. This finding does not conform with our traditional conviction that 'blocked' derivatives retain all the features of the parent molecules.

The charge distribution and electrostatic potential in molecules with a 'blocked' amino or imino structure is very similar to that in the parent 9-acridinamine tautomers. This indicates that zones of positive and negative potential are located at the exocyclic and endocyclic nitrogen atoms and that they change when moving from one tautomer (or its 'blocked' derivative) to another. As distribution of the electrostatic potential affects the mode of interaction with other molecules, the 'blocked' compounds can serve as model derivatives in investigations of interactions of 9-acridinamine with solvent molecules and macromolecules in living matter. Some investigations concerning this problem have already been undertaken by others [61,62].

Acknowledgements

The authors thank Dr P. Sowiński for his help in the NMR studies. The financial support of this work from the Polish State Committee for Scientific Research (KBN) under Grants 2 P303 058 06 (Contract No. PB-0593/P3/94/06) and BW/8000-5-0355-7 is gratefully acknowledged.

References

[1] J. Rak, J. Blazejowski, R.J. Zauhar, J. Org. Chem. 57 (1992) 3720.
[2] J. Rak, J. Blazejowski, J. Photochem. Photobiol. A.: Chem. 67 (1992) 287.
[3] J. Rak, P. Skurski, L. Jozwiak, J. Blazejowski, Aust. J. Chem. 50 (1997) 97.
[4] J. Rak, P. Skurski, M. Gutowski, L. Jozwiak, J. Blazejowski, J. Phys. Chem. A 101 (1997) 283.
[5] L. Jozwiak, P. Skurski, J. Rak, J. Blazejowski, Spectrochim. Acta A 53 (1997) 1723.
[6] A.V. Karyakin, A.M. Grigorovskii, N.G. Yaroslavskii, Dokl. Akad. Nauk SSSR 67 (1949) 679.

[7] R.M. Acheson, M.L. Burstall, C.W. Jefford, B.F. Sansom, J. Chem. Soc. (1954) 3742.
[8] A.V. Karyakin, A.V. Shablya, Dokl. Akad. Nauk SSSR, Ser. Khim. 116 (1957) 969.
[9] A.C. Capomacchia, J. Casper, S.G. Schulman, J. Pharm. Sci. 63 (1974) 1272.
[10] A.C. Capomacchia, S.G. Schulman, J. Pharm. Sci. 64 (1975) 1256.
[11] L.N. Short, J. Chem. Soc. (1952) 4584.
[12] Z.V. Pushkareva, Z.Yu. Kokoshko, Dokl. Akad. Nauk SSSR 93 (1953) 77.
[13] A.K. Sukhomlinov, Zh. Obshch. Khim. 28 (1958) 1038.
[14] Yu.N. Sheinker, E.M. Pieresleni, Dokl. Akad. Nauk. SSSR, Ser. Khim. 131 (1960) 1366.
[15] J.P. Kokko, J.H. Goldstein, Spectrochim. Acta 19 (1963) 1119.
[16] F.N. Li, O.G. Rodin, V.V. Redchenko, V.F. Traven, Zh. Obshch. Khim. 61 (1991) 186.
[17] A. Albert, The Acridines, 2nd ed., Edward Arnold, London, 1966.
[18] R.M. Acheson, Acridines, 2nd ed., Interscience, New York, 1973.
[19] L.S. Lerman, J. Mol. Biol. 3 (1961) 18.
[20] A. Orgel, S. Brenner, J. Mol. Biol. 3 (1961) 762.
[21] B. Pullman, Compt. Rend. 255 (1962) 3255.
[22] A. Kellmann, J. Phys. Chem. 81 (1977) 1195.
[23] G. Duportail, Y. Maussa, J. Chambron, Biopolymers 16 (1977) 1397.
[24] Y. Kubota, Y. Motoda, J. Phys. Chem. 84 (1980) 2855.
[25] L.A. Diverdi, M.R. Topp, J. Phys. Chem. 88 (1984) 3447.
[26] M. Wirth, O. Buchardt, T. Koch, P.E. Nielsen, B. Norden, J. Am. Chem. Soc. 110 (1988) 932.
[27] Y. Baba, A. Kunihiro, A. Kagemoto, Thermochim. Acta 202 (1992) 241.
[28] G. Albiser, Compt. Rend., Ser. III 315 (1992) 265.
[29] M.E. Nuss, F.J. Marsh, P.A. Kollman, J. Am. Chem. Soc. 101 (1979) 825.
[30] K.J. Miller, Macromolecules 17 (1984) 1709.
[31] S. Grzesiak, H. Otto, N.A. Dencher, Biophys. J. 55 (1989) 1101.
[32] P. Proks, T. Hianik, P. Kvasnicka, Gen. Physiol. Biophys. 11 (1992) 441.
[33] N.S. Drozdov, O.M. Cherntzov, Zh. Obshch. Khim. 5 (1935) 1576, 1736.
[34] D.J. Dupre, F.A. Robinson, J. Chem. Soc. (1945) 549.
[35] J. Rak, K. Krzyminski, P. Skurski, L. Jozwiak, A. Konitz, P. Dokurno, J. Blazejowski, Aust. J. Chem., in press.
[36] A. Albert, B. Ritchie, J. Chem. Soc. (1943) 458.
[37] J. Rulewski, K. Krzyminski, A. Konitz, P. Dokurno, J. Rak, J. Blazejowski, Mol. Cryst. Liq. Cryst. 276 (1996) 91.
[38] R. Croasman, R.M.K. Carlson, Two-Dimensional NMR Spectroscopy: Applications for Chemists and Biochemists, 2nd ed., VCH, New York, 1994.
[39] J.K. Labanowski, J.W. Andzelm (Eds.), Density Functional Methods in Chemistry, Springer Verlag, New York, 1991.
[40] J. Baker, J. Comput. Chem. 7 (1986) 385.
[41] H.B. Schlegel (Ed.), Modern Electronic Structure Theory: Geometry Optimization on Potential Energy Surfaces, World Scientific, Singapore, 1994.
[42] M.M. Francl, W.J. Pietro, W.J. Hehre, J.S. Binkley, M.S. Gordon, D.J. DeFrees, J.A. Pople, J. Chem. Phys. 77 (1972) 3654.
[43] P.C. Hariharan, J.A. Pople, Theor. Chim. Acta 28 (1973) 213.
[44] A.D. Becke, Phys. Rev. A 38 (1988) 3098.
[45] A.D. Becke, J. Chem. Phys. 98 (1993) 1372, 5648.
[46] C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785.
[47] H.S. Rzepa, Y.Y. Man, M.M. Karelson, M.C. Zerner, J. Chem. Soc., Perkin Trans. 2 (1991) 635.
[48] M.W. Wong, K.B. Wiberg, M.J. Frisch, J. Am. Chem. Soc. 114 (1992) 523, 1645.
[49] J.B. Foresman, A. Frisch, Exploring Chemistry with Electronic Structure Methods: A Guide to Using Gaussian, Gaussian, Pittsburgh, PA, 1993.
[50] N.C. Handy, D.J. Tozer, G.J. Laming, C.W. Murray, R.D. Amos, Isr. J. Chem. 33 (1993) 331.
[51] R. Ditchfield, Mol. Phys. 27 (1974) 789.
[52] K. Wolinski, J.F. Hinton, P. Pulay, J. Am. Chem. Soc. 112 (1990) 8251.
[53] J. Gauss, J. Chem. Phys. 99 (1993) 3629.
[54] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.W. Wong, J.B. Foresman, M.A. Robb, M. Head-Gordon, E.S. Replogle, R. Gomperts, J.L. Andres, K. Raghavachari, J.S. Binkley, C. Gonzales, R.L. Martin, D.J. Fox, D.J. DeFrees, J. Baker, J.J.P. Stewart, J.A. Pople, Gaussian 92/DFT, Revision F.2, Gaussian, Pittsburgh, PA, 1993.
[55] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.A. Robb, J.R. Cheeseman, T. Keith, G.A. Petersson, J.A. Montgomery, K. Raghavachari, M.A. Al-Laham, V.G. Zakrzewski, J.V. Ortiz, J.B. Foresman, J. Cioslowski, B.B. Stefanov, A. Nanayakkara, M. Challacombe, C.Y. Peng, P.Y. Ayala, W. Chen, M.W. Wong, J.L. Andres, E.S. Replogle, R. Gomperts, R.L. Martin, D.J. Fox, J.S. Binkley, D.J. DeFrees, J. Baker, J.J.P. Stewart, M. Head-Gordon, C. Gonzales, J.A. Pople, Gaussian 94, Revision B.2, Gaussian, Pittsburgh, PA, 1995.
[56] Available from Wavefunction, 8401 Von Karman, Suite 370, Irvine, CA 92715, USA.
[57] R.S. Mulliken, J. Chem. Phys. 23 (1955) 1833, 1841.
[58] B.H. Besler, K.M. Merz, P.A. Kollman, J. Comput. Chem. 11 (1990) 431.
[59] B.G. Johnson, P.M.W. Gill, J.A. Pople, J. Chem. Phys. 98 (1993) 5612.
[60] D. Hadzi, J. Koller, M. Hodoscek, D. Kocjan, in: Z.B. Maksic (Ed.), Modeling of Structure and Properties of Molecules, Ellis Harwood, London, 1987.
[61] Y. Mandi, K. Regely, I. Ocsovszky, J. Barbe, J.P. Galy, J. Molnar, Anticancer Res. 14 (1994) 2633.
[62] I.B. Petri, I. Berek, A.-M. Galy, J. Barbe, L. Berek, J. Molnar, Acta Microbiol. Immunol. Hung. 42 (1995) 203.