Structure, Properties, Thermodynamics, and Isomerization Ability of 9-Acridinones

Anna Boużyk, Ludwika Jóźwiak, Agnieszka Wróblewska, Janusz Rak, and Jerzy Błażejowski*

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

Received: December 17, 2001; In Final Form: February 1, 2002

9(10*H*)-Acridinone and its 13 derivatives were examined at the semiempirical (MNDO, AM1, PM3, MNDO/d), ab initio (HF, MP2), and density functional (DFT) levels of theory with the 6-31G**, 6-31++G**, and 6-311G** basis sets to predict structure, enthalpies and free enthalpies of formation, entropies, HOMO and LUMO energies, and dipole moments. The possibilities of some of the compounds occurring in more than one tautomeric (isomeric) form were further considered. The behavior of 9-acridinones and their features, which may be useful if the compounds are to be used as analytical spectral indicators or fragments of fluorescent or chemiluminescent labels, are also briefly discussed.

Introduction

Acridinones are a group of heterocyclic aromatic compounds that contain secondary or tertiary amino and keto fragments within the ring system.[1,2] The presence of these two fragments lends these compounds the ability to interact specifically with solvent or other molecules present in the system. For these reasons acridinones can serve as models suitable for investigating features of entities that are simultaneously aromatic amines and ketones. An important feature of acridinones is their relatively strong absorption[1,3−8] and emission[1,3,4,5−11] in the UV−vis region; hence, the compounds have potentially useful applications as spectral sensors[11,12] or fragments of fluorescent labels.[13−16] Electronically excited acridinones are also formed when strong oxidants, e.g. hydrogen peroxide, react with 9-substituted-10-methylacridinium cations.[17−22] This process forms the basis for the use of these entities as chemiluminescent indicators or fragments of chemiluminescent labels that have found application in the assay of macromolecules present in living matter.[18,22−24] In the design of sensors or labels with potentially interesting applications, it is important to know the properties of fragments absorbing and/or emitting radiation, and this was the reason for undertaking studies of acridinones.

This publication focuses on the theoretical studies of selected 9-acridinones that we think are interesting for the above-mentioned reasons. The aim of these studies was to predict the structure of the compounds and to determine their basic thermodynamic and physicochemical properties, to compare the characteristics thus obtained with those available in the literature, and to indicate how far these data can be helpful in the selection and design of analytically interesting sensors or labels based on 9-acridinones.

Calculations

Unconstrained geometry optimizations of isolated molecules (shown in Chart 1) were carried out at the level of semiempirical MNDO,[25] AM1,[26] PM3,[27] and MNDO/d[28] methods, the ab initio Hartee−Fock (HF)[29] method, and the Møller−Plesset second-order perturbation theory,[30] as well as the density functional theory (DFT)[31] using gradient techniques[32] and the 6-31G**, 6-31++G**, or 6-311G** basis sets.[29,33−35] The density functional calculations were carried out with the B3LYP functional, in which Becke's nonlocal exchange[36,37] and the Lee−Yang−Parr correlation functionals[38] were applied, as well as with the MPW1PW91 functional, in which the Perdew−Wang exchange and correlation functionals—modified by Barone and Adamo[39]—were used.[40] After completion of each optimization, the Hessian (second derivatives of the energy as a function of nuclear coordinates) was calculated and checked for positive definiteness, to assess whether the structures were true minima.[29,31,41] The harmonic vibrational frequencies were subsequently derived from the numerical values of these second derivatives[29,31,41] and used to determine zero-point energies and entropies, as well as enthalpy and free enthalpy contributions at 298.15 K and standard pressure, with the aid of a built-in computational program with statistical thermodynamics routines. The calculations were carried out using the MOPAC 2000 molecular orbital package[42] (semiempirical methods) and the GAUSSIAN 98 program package[43] (on computers of the Tri-City Academic Network Computer Center in Gdańsk, Poland (TASK)).

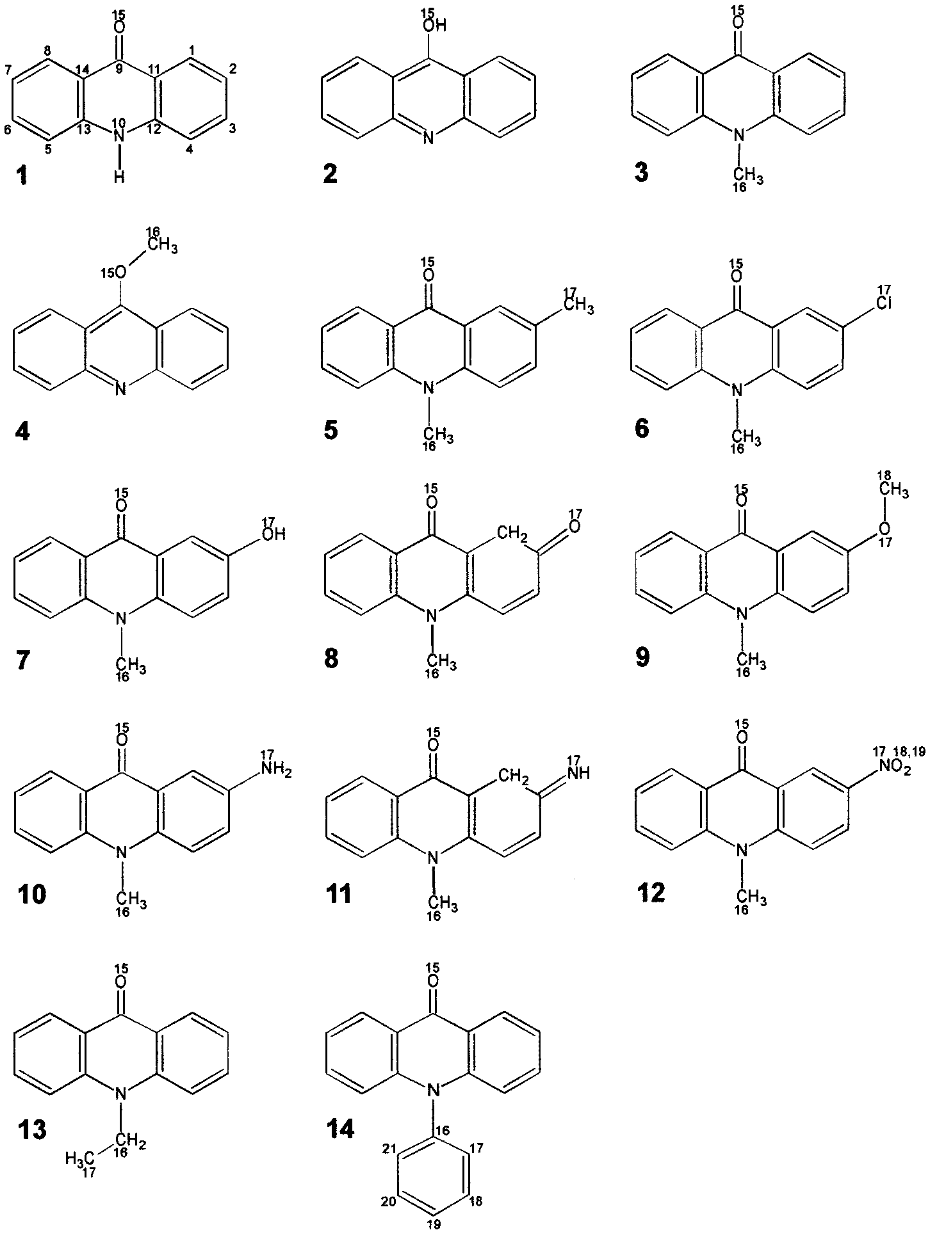
Structural data, dipole moments, HOMO and LUMO energies, enthalpies of formation (in the case of the semiempirical methods), and electronic energies (in the case of ab initio and DFT methods) were extracted directly from data files following the geometry optimizations. Enthalpies (HF, MP2, and DFT) and free enthalpies (DFT) of formation were calculated by following the basic rules of thermodynamics;[44] i.e., the enthalpies (free enthalpies) of gaseous H_2, N_2, O_2, and Cl_2 and solid C (values of the last quantity were obtained by subtracting the enthalpy or free enthalpy of atomization equal to 716.67 and 671.3 (298.15 K, standard pressure) kJ/mol,[45] respectively, from the data of the gaseous entity), multiplied by the relevant stoichiometric coefficients, were subtracted from the enthalpies (free enthalpies) of gaseous 9-acridinones. In the case of HF data, isodesmic correction was additionally introduced—the details are given below in Table 2.

Results and Discussion

Structural Features. DFT-optimized structures of isolated 9-acridinones are shown in Figure 1, while Table 1 sets out selected bond lengths and dihedral angles obtained on the various levels of theory, together with relevant values extracted from crystallographic data for **1**, **3**, **13**, and **14**. All methods

10.1021/jp014539a CCC: $22.00

CHART 1: Compounds Investigated with the Atom Numbering Indicated



predict the planar or nearly planar ring system in **2** and **4** typical of acridine moieties.[50] The remaining compounds are 9-acridinones, whose central ring only partially participates in conjugation. One can thus expect this ring to be more or less nonplanar, like the side ring in **8** and **11** to which >C═O and >C═NH fragments are attached. These expectations generally confirm the structural data listed in Table 1. 9(10*H*)-Acridinone (**1**) and 10-phenyl-9-acridinone (**14**), whose acridinone moieties are predicted to be planar at the HF, MP2, and DFT (in most cases) levels of theory, are somewhat atypical. As predicted by the results of HF and DFT calculations, the phenyl ring at the heterocyclic nitrogen atom in **14** is perpendicular to the acridine moiety. The central ring in other acridinones is more or less convex at the nitrogen atom site and concave at the keto carbon atom site. The data in Table 1 show that the values arising out of DFT geometry optimizations are generally closest to the crystallographic data available for **1**, **3**, **13**, and **14**. DFT data can thus be regarded as the most reliable. Discrepancies are most pronounced when PM3 data are compared with crystallographic structural data. The PM3 data then seem less reliable. The theoretically predicted $C_{(1)}C_{(2)}$ and $N_{(10)}C_{(12)}$ bond lengths are somewhat longer than those determined by the X-ray method, which is a typical regularity,[51,52] while in the case of the $C_{(9)}O_{(15)}$ bond this tendency is reversed. The general impression is that the theoretically predicted structural data for 9-acridinones (particularly at the DFT level) are roughly comparable with the structural data for these compounds in crystalline phases.

Thermochemistry. The thermochemical data relating to 9-acridinones are given in Table 2. The standard enthalpies of formation predicted at the PM3 level are always the lowest, while those obtained at the HF and DFT levels are higher and are comparable. The experimental value of $\Delta_{f,298}H°$ is available only for gaseous 9(10*H*)-acridinone and is equal to 34.6 kJ/mol.[57] This value is much lower than the ones obtained at the DFT, HF, or even PM3 levels. To discover how the level of theory affects electronic energies and standard enthalpies of formation, we extended the calculations for 9(10*H*)-acridinone to include electron correlation at the MP2 level, for HF or MP2 optimized structure 6-31++G** and 6-311G** basis sets, and

TABLE 1: Structural Features of the Compounds in the Gaseous Phase

		bond lengths^{a} (Å)					dihedral angles (deg)		
compd no.	method	$C_{(1)}C_{(2)}$/ $C_{(7)}C_{(8)}$	$C_{(2)}A_{(17)}$	$C_{(9)}O_{(15)}$	$N_{(10)}C_{(16)}$	$N_{(10)}C_{(12)}$/ $N_{(10)}C_{(13)}$	$C_{(3)}C_{(2)}C_{(1)}C_{(11)}$/ $C_{(6)}C_{(7)}C_{(8)}C_{(14)}$	$C_{(11)}C_{(12)}N_{(10)}C_{(13)}$/ $C_{(12)}N_{(10)}C_{(13)}C_{(14)}$	$C_{(12)}C_{(11)}C_{(9)}C_{(14)}$/ $C_{(11)}C_{(9)}C_{(14)}C_{(13)}$
1	PM3	1.386		1.221		1.422	−0.03/0.03	−19.11/19.11	9.84/−9.84
	HF^{b}	1.372		1.204		1.374	0.00	−0.06/0.07	0.01/−0.01
	MP2^{b}	1.385		1.240		1.379	0.00	−0.01/0.01	0.00
	MP2^{c}	1.387		1.244		1.381	0.00	−0.01/0.01	0.00
	DFT^{d}	1.381		1.227		1.374	0.00	−0.02/0.02	0.00
	DFT^{e}	1.378		1.221		1.373	0.00	0.01/−0.01	0.00
	DFT^{f}	1.385		1.232		1.381	0.00	0.01/−0.01	0.01/−0.01
	DFT^{g}	1.386		1.235		1.382	0.00	−0.01/0.01	0.00
	DFT^{h}	1.387		1.244		1.382/1.381	3.05/2.17	3.89/0.68	5.59/−1.12
	X-ray^{i}	1.366/1.350		1.250		1.355/1.363	−1.5/−0.3	−0.6/−0.2	0.3/−0.1
2	PM3	1.360/1.362		1.360		1.359/1.363	0.00	0.00	0.00
	HF^{b}	1.347/1.349		1.339		1.327/1.321	0.00	0.00	0.00
	DFT^{f}	1.370/1.371		1.356		1.342/1.345	0.00	0.00	0.00
3	PM3	1.385		1.223	1.482	1.432	−0.17/0.17	−8.87/8.87	1.71/−1.70
	HF^{b}	1.372		1.204	1.453	1.389	−0.61/−0.61	−12.00/12.00	6.73/−6.73
	DFT^{f}	1.384		1.233	1.460	1.397	−0.68/−0.68	−9.57/9.57	4.77/−4.77
	X-ray^{i}	1.342/1.402		1.251	1.491	1.355/1.393	−1.4/−1.9	5.9/5.8	−4.5/−4.5
4	PM3	1.360		1.391		1.359	0.06/−0.10	−0.19/0.23	0.26/−0.22
	HF^{b}	1.348		1.355		1.324	0.04/−0.04	−0.95/0.95	−2.01/−2.01
	DFT^{f}	1.370		1.375		1.344	−0.05/0.05	−0.97/0.97	1.96/−1.96
5	PM3	1.389/1.385	1.485	1.223	1.482	1.432	0.33/−0.17	−8.96/9.01	1.81/−1.77
	HF^{b}	1.373/1.372	1.510	1.205	1.453	1.390/1.387	−0.64/−0.60	−11.67/11.61	6.57/−6.60
	DFT^{f}	1.387/1.384	1.510	1.233	1.460	1.397/1.396	−0.70/−0.64	−9.56/9.58	4.84/−4.80
6	PM3	1.386/1.385	1.686	1.222	1.482	1.430/1.432	0.19/−0.18	8.70/8.63	1.56/−1.63
	HF^{b}	1.368/1.372	1.743	1.203	1.454	1.386/1.390	0.66/−0.62	11.82/−11.91	−6.73/−6.64
	DFT^{f}	1.381/1.384	1.758	1.232	1.461	1.394/1.397	0.69/−0.66	9.58/−9.69	−4.93/−4.81
7	PM3	1.393/1.384	1.370	1.223	1.482	1.435/1.431	0.20/−0.11	−8.03/8.18	0.60/−0.46
	HF^{b}	1.368/1.371	1.354	1.205	1.453	1.393/1.384	−0.77/0.59	−11.53/11.35	6.35/−6.51
	DFT^{f}	1.385/1.383	1.367	1.234	1.460	1.400/1.393	−0.78/0.65	−9.34/9.31	4.56/−4.58
8	PM3	1.508/1.384	1.219	1.223	1.482	1.429/1.431	−5.88/0.06	4.18/−4.34	2.28/−2.46
	HF^{b}	1.509/1.371	1.195	1.207	1.457	1.383/1.389	−9.96/0.47	−9.30/−8.75	5.31/−5.59
	DFT^{f}	1.517/1.384	1.223	1.237	1.465	1.393/1.398	−5.11/0.49	−7.91/7.49	4.07/−4.30
9	PM3	1.391/1.384	1.383	1.223	1.482	1.435/1.431	0.19/−0.15	−8.27/8.42	0.90/−0.75
	HF^{b}	1.369/1.371	1.351	1.205	1.453	1.393/1.384	−0.77/−0.59	−11.39/11.22	6.33/−6.46
	DFT^{f}	1.386/1.383	1.365	1.235	1.460	1.399/1.393	−0.82/−0.65	−9.14/8.95	4.38/−4.55
10	PM3	1.396/1.384	1.432	1.223	1.482	1.435/1.431	0.01/0.06	6.62/−6.58	1.82/−1.79
	HF^{b}	1.375/1.371	1.402	1.204	1.452	1.385/1.383	0.77/−0.57	11.77/−11.67	−6.87/−6.95
	DFT^{f}	1.392/1.383	1.399	1.234	1.459	1.401/1.392	0.67/−0.64	9.42/−9.52	−5.02/−4.92
11	PM3	1.500/1.384	1.293	1.225	1.482	1.427/1.430	−8.52/0.11	5.26/−5.49	0.66/−0.94
	HF^{b}	1.511/1.371	1.257	1.209	1.459	1.381/1.389	21.67/0.50	−9.06/8.31	−4.39/−4.88
	DFT^{f}	1.517/1.384	1.284	1.239	1.464	1.392/1.398	−13.19/0.52	−7.65/7.21	3.57/−3.84
12	PM3	1.395/1.385	1.493	1.221	1.481	1.416/1.434	0.16/−0.24	−7.64/7.11	1.42/−1.92
	HF^{b}	1.371/1.372	1.449	1.202	1.457	1.376/1.396	0.64/−0.64	11.79/−12.19	−6.96/−6.57
	DFT^{f}	1.383/1.385	1.464	1.230	1.463	1.387/1.403	0.67/−0.65	9.67/−9.94	−5.21/−4.94
13	PM3	1.385		1.223	1.489	1.429	−0.04/0.04	3.35/−3.36	4.42/−4.42
	HF^{b}	1.371		1.205	1.462	1.391	−0.39/−0.39	7.04/−7.04	−4.01/−4.01
	DFT^{f}	1.383		1.233	1.470	1.398	−0.44/−0.44	−6.24/6.24	3.09/−3.09
	X-ray^{i}	1.365/1.366		1.238	1.478	1.393/1.390	0.6/0.1	4.8/4.2	−2.7/−3.3
14	PM3	1.385		1.223	1.465	1.429	0.10/−0.10	−13.60/13.62	6.42/−6.42
	HF^{b}	1.371		1.205	1.433	1.393	0.00	0.00	−0.01/−0.01
	DFT^{f}	1.383		1.233	1.441	1.400	0.00	0.00	−0.01/0.00
	X-ray^{i}	1.357/1.359		1.236	1.450	1.391/1.393	0.7/−1.3	4.4/2.3	−1.0/−3.1

[a] A denotes the atom in position (17). [b] 6-31G** basis set. [c] 6-31++G** basis set. [d] MPW1PW91 functional and 6-31G** basis set. [e] MPW1PW91 functional and 6-311G** basis set. [f] B 3LYP functional and 6-31G** basis set. [g] B 3LYP functional and 6-31++G** basis set. [h] B 3LYP functional and 6-311G** basis set. [i] Values taken from crystallographic data in the literature: **1**, ref 46; **3**, ref 47; **13**, ref 48; **14**, ref 49.

the MPW1PW91 functional. We also performed calculations using MNDO, AM1, and MNDO/d methods. The results are compiled in Table 3. As can be seen, the use of larger basis sets causes a lowering of the electronic energy at the HF, MP2, and DFT levels of theory (DFT values are always lower than the respective HF or MP2 ones), which is an expected regularity. As far as enthalpies of formation are concerned, values determined at the DFT (MPW1PW91) level are substantially lower, while those obtained at the MP2 and DFT (B 3LYP) (using 6-31++G** and 6-311G** basis sets) levels are markedly higher than the experimental value of this quantity—much more than the value obtained at the DFT (B 3LYP)/6-31G** level (listed in Table 2). The values corresponding to the HF level are unrealistic,[50,52] which necessitates the introduction of an isodesmic correction (Table 2). On the other hand, values of $\Delta_{f,298}H°$ emerging from the use of semiempirical methods are lower than the value obtained at the DFT (B 3LYP)/6-31G** level; they are thus closer to the experimental value of this quantity. It is difficult to assess the reasons for the discrepancies between the theoretical and experimental values of $\Delta_{f,298}H°$. Sabbah and El Watik determined the heat of combustion of 9(10*H*)-acridinone, and the standard enthalpy of formation was obtained using basic thermodynamic relations on the assumption that the products of combustion are CO_2 (gaseous), H_2O (liquid),

TABLE 2: Physicochemical Characteristics of the Compounds in the Gaseous Phase[a]

compd no.	method[b]	$\Delta_{f,\,298}H^\circ$ [c,d]	$\Delta_{f,\,298}G^\circ$	${}_{298}S^\circ$	energy		μ
					HOMO	LUMO	
1	PM3	57.2		427.5	−8.533	−0.597	3.78
	HF	93.6		407.9	−7.754	2.183	5.02
	DFT	123.7 (125.9)	220.1	418.2			4.93
2	PM3	104.1		421.8	−8.378	−1.153	2.19
	HF	180.6		410.8	−7.430	1.752	2.70
	DFT	179.1 (177.6)	274.6	421.3			2.56
3	PM3	64.8		458.7	−8.433	−0.579	4.04
	HF	134.2		433.2	−7.711	2.165	5.13
	DFT	148.1 (166.7)	273.7	447.2			5.11
4	PM3	146.6		455.1	−8.547	−1.267	2.03
	HF	215.7		437.8	−7.516	1.637	2.69
	DFT	211.3 (204.0)	335.2	452.9			2.42
5	PM3	25.7		505.1	−8.351	−0.555	3.93
	HF	112.2		472.0	−7.575	2.196	5.04
	DFT	123.4 (131.7)	274.7	488.1			5.00
6	PM3	38.3		492.1	−8.455	−0.709	4.59
	HF	120.0		462.0	−7.883	1.882	6.55
	DFT	117.5 (123.3)	248.2	476.6			6.37
7	PM3	−121.4		486.8	−8.300	−0.651	3.24
	HF	−25.8		459.4	−7.482	2.055	4.20
	DFT	−3.6 (−2.1)	146.0	469.4			4.06
8	PM3	−73.7		496.4	−8.722	−1.181	6.25
	HF	31.9		466.7	−8.173	1.402	7.93
	DFT	56.8 (29.9)	202.6	482.3			7.64
9	PM3	−92.2		526.7	−8.271	−0.612	3.04
	HF	−4.7		485.8	−7.429	2.125	3.97
	DFT	13.2 (24.3)	191.7	499.5			3.90
10	PM3	58.1		489.2	−8.097	−0.561	4.09
	HF	152.4		462.2	−7.201	2.174	4.90
	DFT	151.1 (156.9)	316.6	474.4			4.90
11	PM3	144.0		498.6	−8.552	−0.961	4.33
	HF	274.6		462.1	−8.003	1.758	5.79
	DFT	247.8 (240.6)	410.5	483.8			5.68
12	PM3	26.5		527.3	−8.994	−1.267	8.89
	HF	113.8		489.1	−8.385	1.615	9.45
	DFT	129.6 (137.2)	308.3	505.1			9.12
13	PM3	39.8		459.6	−8.425	−0.562	4.08
	HF	115.9		456.3	−7.675	2.179	5.28
	DFT	130.2 (131.7)	286.9	470.1			5.26
14	PM3	199.8		536.1	−8.384	−0.524	4.66
	HF	273.7		502.8	−7.674	2.256	5.85
	DFT	307.0 (288.8)	444.7	520.4			5.92

[a] $\Delta_{f,298}H^\circ$and $\Delta_{f,298}G^\circ$, in kJ/mol, denote enthalpy and free enthalpy of formation, respectively; ${}_{298}S^\circ$, in J/(mol K), is the entropy; HOMO and LUMO, in eV, indicate the energies of the highest occupied and lowest unoccupied molecular orbitals; μ, in D, is the dipole moment. [b] HF, geometries and Hessian obtained using the 6-31G** basis set; DFT, the same values obtained using the B 3LYP functional and the 6-31G** basis set. [c] $\Delta_{f,298}H^\circ$ values obtained at the HF level were supplemented with the corrections arising out of the consideration of isodesmic reactions[53,54] 9-acridinone + $\nu_1(CH_4) + \nu_2(NH_3) \rightarrow \nu_3(H_3CCOCH_3) + \nu_4(H_3CNH_2) + \nu_5(H_3CCH_3) + \nu_6(H_2CCH_2) + \nu_7(H_2CNH) + \nu_8(H_3COH) + \nu_9(H_3COCH_3) + \nu_{10}(H_3CCl) + \nu_{11}(H_3CNO_2)$ (where $\nu_1, ..., \nu_{11}$ denote the relevant stoichiometric coefficients), which preserve the number and nature of the chemical bonds;[55] these corrections were equal to the sum of the differences between the experimental ($\Delta_{f,298}H^\circ$ equal to (in kJ/mol) −74.4, −45.9, −217.3, −22.5, −83.8, 52.9, 110, −201.5, −184.1, −81.9, and −74.7 for CH_4,[45] NH_3,[45] H_3CCOCH_3,[45] H_3CNH_2,[45] H_3CCH_3,[45] H_2CCH_2,[45] H_2CNH,[56] H_3COH,[45] H_3COCH_3,[45] H_3CCl,[45] and H_3CNO_2,[45] respectively) and theoretical value of the enthalpy of formation of all reactants (with the exception of the molecule studied), multiplied by the relevant stoichiometric coefficients (negative in the case of CH_4 and NH_3 and positive for others), and were added to the theoretically determined $\Delta_{f,298}H^\circ$ values for 9-acridinones. [d] At the DFT (B 3LYP)/6-31G** values of $\Delta_{f,298}H^\circ$, the standard enthalpies of formation reproduced by following eqs 1 and 2 and the procedure described in the text are given in parentheses.

and N_2 (gaseous).[57] This last product may be uncertain, and the above assumption may be the reason for the observed discrepancies. It is much more difficult to explain the discrepancies between the predicted values of $\Delta_{f,298}H^\circ$ at various levels of theory. It could be helpful in such a situation to know how theoretical and experimental values of this quality compare for other compounds similar to 9(10*H*)-acridinone. To make such a comparison we carried out additional calculations for acridine, and the results are given in Table 3. It can be noted that when these data, as well as data reported by us earlier,[50,52] are analyzed, the standard enthalpies of formation determined at the DFT (B 3LYP)/6-31G** level correlate also in this case much better with the experimental value than those obtained at other levels of theory. We therefore think that the enthalpies of formation obtained at the DFT (B 3LYP)/6-31G** level may be regarded as the most suitable, especially as they are close to the HF values (after introducing the isodesmic correction), and this was the reason we listed these values in Table 2. It is also worth mentioning that the DFT (B 3LYP) method is considered generally quite reliable for predicting the thermochemical and physicochemical characteristics of gaseous molecules in the ground electronic state.[59]

Standard free enthalpies of formation were determined only at the DFT (B 3LYP/6-31G**) level, since the data necessary for calculating these enthalpies were available directly from theoretical computations. On the other hand, entropies of gaseous compounds were determined by all three methods

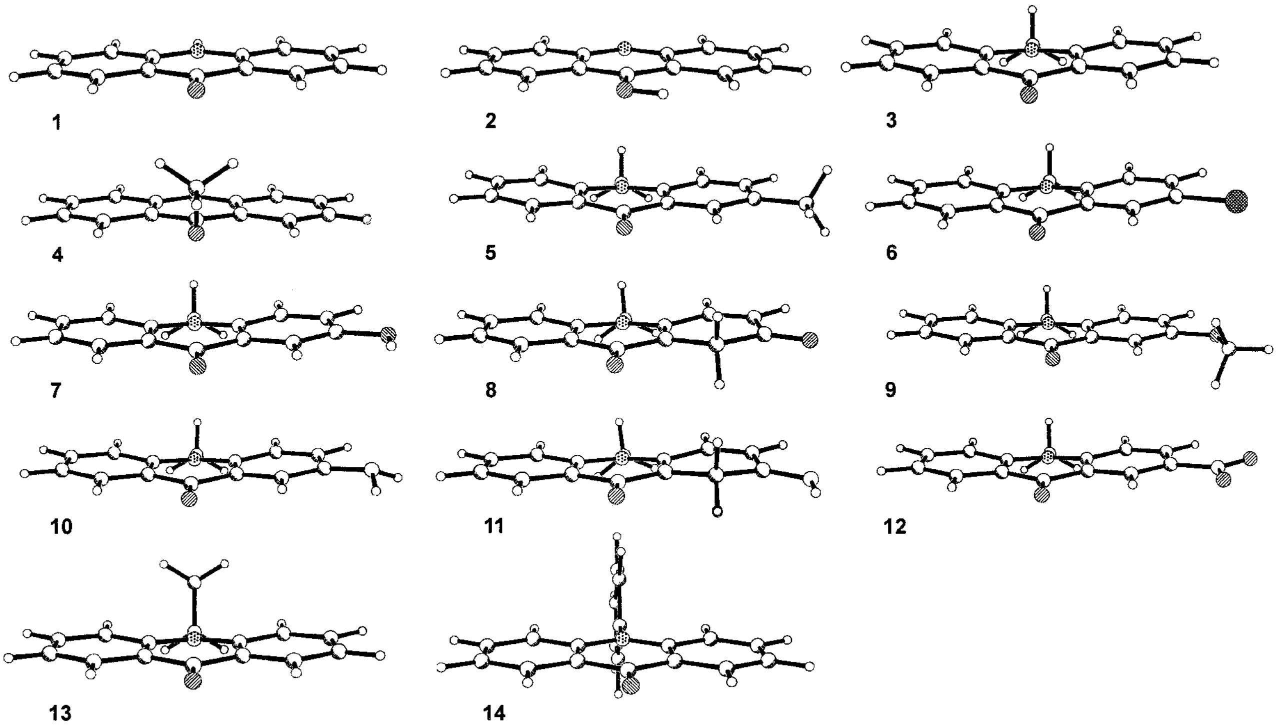


Figure 1. DFT structures of the compounds investigated.

TABLE 3: Energies and Standard Enthalpies of Formation of 9(10*H*)-Acridinone at Various Levels of Theory[a]

	compd		
	9(10*H*)-acridinone		acridine
method or basis set ǁ geometry	energy	$\Delta_{f,298}H°$	$\Delta_{f,298}H°$
Exptl[b]		34.6	292.5
MNDO		73.5	
AM1		92.8	
PM3		57.2	
MNDO/d		74.3	
HF/6-31G** ǁ HF/6-31G**	−626.898553		
MP2/6-31G** ǁ HF/6-31G** [c]	−628.916519	169.0	388.6
MP2/6-31G** ǁ MP2/6-31G** [c]	−628.920500	178.9	384.7
MP2/6-31++G** ǁ MP2/6-31++G** [c]	−628.958310	223.9	
MP2/6-311G** ǁ MP2/6-31++G** [c]	−629.128841	225.0	
MP2/6-311G** ǁ MP2/6-31G** [c]	−629.129068	224.3	433.9
DFT (MPW1PW91)/6-31G** ǁ DFT (MPW1PW91)/6-31G**	−630.680340	−145.5	77.1
DFT (MPW1PW91)/6-311G** ǁ DFT (MPW1PW91)/6-311G**	−630.806378	−75.8	149.9
DFT (B 3LYP)/6-31G** ǁ DFT (B 3LYP)/6-31G**	−630.828284	123.7	336.0
DFT (B 3LYP)/6-31++G** ǁ DFT (B 3LYP)/6-31++G**	−630.851279	257.5	
DFT (B 3LYP)/ 6-311G** ǁ DFT (B 3LYP)/ 6-311G**	−630.965843	205.8	421.2

[a] Energy, in hartrees (1 hartree = 2625.5 kJ/mol), corresponds to the total electronic energy, and $\Delta_{f,298}H°$, in kJ/mol, is the standard enthalpy of formation. [b] Reference 57 (9(10*H*)-acridinone) or ref 58 (acridine). [c] Zero point energy and thermal enthalpy contributions were assumed to be the same as those obtained at the DFT (B 3LYP)/6-311G** ǁ DFT (B 3LYP)/6-311G** level of calculations.

indicated in Table 2. To recapitulate, Table 2 provides unique and hitherto unavailable thermochemical data for 9-acridinones.

The impression left by the above-mentioned difficulties in explaining the discrepancies between the predicted and experimental standard enthalpies of formation would not be so bad if it were possible to demonstrate the internal consistency of the theoretically determined thermochemical data. To do so, we followed the general idea which states that enthalpies of formation of gaseous entities from gaseous atoms ($\Delta^{at}{}_{f,298}H°$) are reflected by the negative values of the sum of energies (enthalpies) of all bonds forming molecules (H_{bonds}),[44]

$$\Delta^{at}{}_{f,298}H° = -\sum_i (H_{bonds})_i \qquad (1)$$

where values of $\Delta^{at}{}_{f,298}H°$ can be obtained by subtracting the sum of the products of the dissociation enthalpies of molecular substrates (H_2, O_2, N_2, Cl_2) or sublimation enthalpy of C (equal to 716.67 kJ/mol[45])—denoted in both cases as $\Delta_{d,298}H°$—and the relevant stoichiometric factors (ν) from the standard enthalpies of formation of the compounds ($\Delta_{f,298}H°$):

$$\Delta^{at}{}_{f,298}H° = \Delta_{f,298}H° - \sum_k (\nu \Delta_{d,298}H°)_k \qquad (2)$$

We employed this approach by taking data determined at the DFT (B 3LYP)/6-31G** level of theory. Treating bond enthalpies as adjustable parameters, we fitted $\Delta^{at}{}_{f,298}H°$ values of 14 compounds investigated and 17 similar compounds (for which $\Delta_{f,298}H°$ values were additionally determined) using the least-squares method[60] implemented in the STATISTICA program.[61] This procedure yielded the following values of bond enthalpies

TABLE 4: Thermodynamics of Transformation

	$\Delta_{f,298}H°$			$\Delta_{f,298}G°$		
transformation	PM3	HF	DFT	PM3	HF	DFT
1 → **2**	46.9	87.0	55.4	48.6	86.1	54.4
3 → **4**	81.8	20.8	63.2	82.9	19.4	61.4
7 → **8**	47.8	57.7	60.4	44.9	55.5	56.5
10 → **11**	85.9	122.2	96.7	83.1	122.2	93.9

(bond/energy, in kJ/mol): C−H/382.37; C−C/431.23; C═C/615.72; C═O/579.14; C−N/340.43; N−H/367.28; C−O/398.24; O−H/410.73; C═N/426.16; C−Cl/305.21; N→O/414.83. Using these bond enthalpies we calculated the standard enthalpies of formation on the basis of eqs 1 and 2. The values thus determined are given in Table 2. The procedure presented above reproduces values of $\Delta_{f,298}H°$ quite well, so the thermochemical characteristics that we determined are presumably internally consistent.

Physicochemical Characteristics. According to Koopmans' theorem,[62] which does not apply to the density functional formalism,[63] the negative energies of the lowest unoccupied (LUMO) and highest occupied (HOMO) molecular orbitals (Table 2) approximate the electron affinity and the first ionization potential of a molecule, respectively.[64,65] The ionization potentials (in eV) of 9(10*H*)-acridinone (7.60[66] or 7.69[67]), 10-methyl-9-acridinone (**3**) (7.53[66]), 10-ethyl-9-acridinone (**13**) (7.49[66]), and 10-phenyl-9-acridinone (7.46[66]) compare well with the negative HOMO energies determined at the HF level (discrepancies do not exceed 0.22 eV). PM3 HOMO energies are from 0.549 to 1.031 lower than the corresponding values predicted at the HF level, which means that they are less reliable. HF LUMO energies are always positive, which suggests that an electron attachment would lead to unstable negative ions of 9-acridinones. By contrast, PM3 LUMO energies are negative, which would mean that the compounds form stable negative ions upon electron attachment. As the latter feature did not find experimental confirmation, we do not think that the PM3 method provides reliable values of LUMO energies.

Dipole moments (μ) are a reflection of nonuniform negative charge distribution within molecules. Values of this quantity (in D) for 9(10*H*)-acridinone (6.0[68]), 10-methyl-9-acridinone (5.3[68] or 5.39[69]), and 10-phenyl-9-acridinone (5.4[68]) compare reasonably well with those predicted at the HF and DFT levels. Both DFT and HF methods yield values of μ that differ by less than 0.34 D (in most cases they are higher in the case of HF). On the other hand, dipole moments predicted at the PM3 level are always the lowest among those determined. The compounds which may be regarded as highly polar, like **6**, **8**, and **12**, exhibit relatively high dipole moments, while less polar compounds, such as **2** and **4**, have lower dipole moments. These values may be considered a measure of the ability of 9-acridinones to participate in nonspecific interactions with other molecules, and the data in Table 2 can serve as a convenient source of information enabling the features of such interactions to be predicted.

Possibilities of Tautomerization (Isomerization). 9(10*H*)-Acridinone and 9-hydroxyacridine (**2**) are tautomeric forms which could potentially coexist, as has been postulated in the past.[70−77] The 9(10*H*)-Acridinone ⇄ 9-hydroxyacridine tautomerism also appears in 9-acridinone crown ethers having 2,7-dihydroxy-9-acridinone rings linked by poly(ethylene)glycol chains.[78−80] According to the results of our theoretical calculations, **1** is energetically and thermodynamically more stable than **2** by 50 kJ/mol (Table 4). This is most probably the reason why 9(10*H*)-acridinone is the only form that exists in the solid phase.[46] In solutions, however, **1** and **2** may coexist, since the two molecules differ in polarity, and by changing solvents, one can shift the equilibrium toward **1** in more polar media or toward **2** in less polar ones. It may also be expected that the proton of the hydroxy group in **2** can be removed in alkaline media, which would lead to the formation of a 9-oxoacridine anion.[1,17,71,77]

3 and **4** are the isomers and methyl-substituted derivatives of **1** and **2**, respectively. In this case, too, the acridinone isomer (**3**) is thermodynamically more stable than the acridine isomer (**4**) (Table 4). This explains why, when 9-acridinones are alkylated, it is 10-alkyl-9-acridinones that are predominantly formed.[81]

We also considered the possibilities of the coexistence of **7** and **8** (light emitters which appear upon photooxidation of adamantylideneacridines[82]) and **10** and **11**. In both cases, 9-acridinone forms are predicted to be thermodynamically more stable (**7** and **10**) (Table 4). The free enthalpy gap between **8** and **7** is comparable to that between **2** and **1,** which means that under favorable conditions both forms could coexist. However, alkaline media, which could favor the existence of **2**, would in this case act in the opposite direction; i.e., they would favor the existence of **7**.

Concluding Remarks

The molecules examined in this work were selected with regard to their potential application as fragments of absorption, fluorescent, or chemiluminescent analytical sensors or labels. For these reasons we investigated mainly 10-substituted-9-acridinones, which are most often used in analytical assays. 9(10*H*)-Acridinone and its tautomer, 9-hydroxyacridine, are basic molecules and a convenient reference to which one can relate the properties of this group of compounds.

Geometry optimizations provided structural data which, for the majority of compounds, had not been available earlier. When these data were compared with those obtained from X-ray measurements, it appeared that the DFT method provides structural characteristics that are closest to the experimental ones. This latter finding therefore indicates that the DFT method is suitable for predicting the structure of unknown 9-acridinones.

The thermochemical data for 9-acridinones also seem the most suitable when determined at the DFT (B 3LYP)/6-31G** level, this being borne out by the work of other authors.[59] The only value of the standard enthalpy of formation of 9(10*H*)-acridinone that originates from measurements[58] is much lower than that predicted theoretically, and we have indicated reasons for possible discrepancies. Nevertheless, the thermochemical data in Table 2 constitute a unique set of information which may be helpful in evaluating the relative stabilities of the compounds and their ability to undergo transformations.

The HF method provides reliable values of HOMO and LUMO energies, since negative HOMO energies compare well with the experimentally determined ionization potentials of several molecules. Dipole moments determined at the HF and DFT levels correlate well with each other and those available in the literature, so they can be regarded as more reliable than values calculated at the PM3 level. Physicochemical characteristics can be helpful in predicting the properties of the compounds investigated in liquid phases with various properties.

Forecasting the utility of the results obtained during this work is related to the possibilities of predicting the features and behavior of 9-acridinones (when they are regarded as absorption or fluorescence fragments of sensors) or their precursors (when they are regarded as chemiluminogenic fragments or sensors). To do so, it is important to know whether theoretically derived characteristics correlate with the measured properties of 9-acridinones. We have already correlated IR absorption data with the theoretically predicted structural and physicochemical characteristics of 9-acridinones.[83] We have also undertaken further work in the search for a correlation between ^{1}H and ^{13}C NMR signals,[84] as well as absorption and fluorescence spectra with structural and physicochemical characteristics.[85] This bodes well for the design of 9-acridinones or their precursors with interesting utilitarian properties.

Acknowledgment. The financial support of this work from the Polish State Committee for Scientific Research (KBN) under Grant 3 T09A 083 16 (Contract No. 1177/T09/99/16) is gratefully acknowledged.

References and Notes

(1) Albert, A. *The Acridines*, 2nd ed.; Edward Arnold Ltd.: London, 1966.
(2) Acheson, R. M. *Acridines*, 2nd ed.; Interscience: New York, 1973.
(3) Siegmund, M.; Bendig, J. *Z. Naturforsch. A* **1980**, *35*, 1076.
(4) Abdullah, K. A.; Kemp, T. J. *J. Photochem.* **1986**, *32*, 49.
(5) Kronfeld, K.-P.; Timpe, H.-J. *J. Prakt. Chem.* **1988**, *330*, 571.
(6) Shcherbo, S. N.; Val'kova, G. A.; Savchenko, I. V.; Shigorin, D. N. *Zh. Fiz. Khim.* **1988**, *62*, 2269.
(7) Niizuma, S.; Kawata, H. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1627.
(8) Nikolov, P.; Petkova, I.; Köhler, G.; Stojanov, S. *J. Mol. Struct.* **1998**, *448*, 247.
(9) Fushimi, K.; Kikuchi, K.; Kokubun, H. *J. Photochem.* **1976**, *5*, 457.
(10) Siegmund, M.; Bendig, J.; Wilda, J.; Teuchner, K. *Z. Chem.* **1985**, *25*, 372.
(11) Albrecht, S.; Brandl, H.; Zimmermann, T. *Chemiluminescence*; Hüthing Verlag: Heidelberg, Germany, 1996.
(12) Reymond, J.-L.; Koch, T.; Schroer, J.; Tierney, E. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 4251.
(13) Crisp, G. T.; Gore, J. *Tetrahedron* **1997**, *53*, 1505.
(14) Bahr, N.; Tierney, E.; Reymond, J.-L. *Tetrahedron Lett.* **1997**, *38*, 1489.
(15) Faller, T.; Hutton, K.; Okafo, G.; Gribble, A.; Camilleri, P.; Cames, D. E. *Chem. Commun.* **1997**, 1529.
(16) Rothman, J. H.; Still, W. C. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 509.
(17) White, E. H.; Roswell, D. F.; Dupot, A. C.; Wilson, A. A. *J. Am. Chem. Soc.* **1987**, *109*, 5189.
(18) Zomer, G.; Stavenuiter, J. F. C.; Van Den Berg, R. H.; Jansen, E. H. J. M. *Prakt. Spectrosc.* **1991**, *12*, 505.
(19) Kaltenbach, M. S.; Arnold, M. A. *Microchim. Acta* **1992**, *108*, 205.
(20) Papadopoulos, K.; Hadjianestis, J.; Nikokavouras, J. *J. Photochem. Photobiol., A* **1993**, *75*, 91.
(21) Rak, J.; Skurski, P.; Blazejowski, J. *J. Org. Chem.* **1999**, *64*, 3002.
(22) Dodeigne, C.; Thunus, L.; Lejeune, R. *Talanta* **2000**, *51*, 415.
(23) Weeks, I.; Beheshti, I.; McCapra, F.; Campbell, A. K.; Woodhead, J. S. *Clin. Chem.* **1983**, *29*, 1474.
(24) Zomer, G.; Stavenuiter, J. F. C. *Anal. Chim. Acta* **1989**, *227*, 11.
(25) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 1285.
(26) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.
(27) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209, 221.
(28) Thiel, W.; Voityuk, A. A. *J. Phys. Chem.* **1996**, *100*, 616.
(29) Hehre, W. J.; Radom, L.; Schleyer, P.v. R.; Pople, J. A. *Ab initio Molecular Orbital Theory*; Wiley: New York, 1986.
(30) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.
(31) *Density Functional Methods in Chemistry*; Labanowski, J. K., Andzelm, J. W., Eds.; Springer-Verlag: New York, 1991.
(32) Schlegel, H. B. In *Modern Electronic Structure Theory: Geometry Optimization on Potential Energy Surfaces*; Schlegel, H. B., Ed.; World Scientific Publishing: Singapore, 1994.
(33) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.
(34) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *27*, 5639.
(35) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P.v. R. *J. Comput. Chem.* **1983**, *4*, 294.
(36) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.
(37) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372, 5648.
(38) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
(39) Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664.
(40) Perdew, J. P.; Burke, K.; Wang, Y. *Phys. Rev. B* **1996**, *54*, 16533.
(41) Handy, N. C.; Tozer, D. J.; Laming, G. J.; Murray, C. W.; Amos, R. D. *Isr. J. Chem.* **1993**, *33*, 331.
(42) Stewart, J. J. P. *MOPAC 2000*; Fujitsu Ltd.: Tokyo, 1999.
(43) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *GAUSSIAN 98, Revision A.9*; Gaussian, Inc.: Pittsburgh, PA, 1998.
(44) Atkins, P. W. *Physical Chemistry*, 5th ed.; Oxford University Press: Oxford, U.K., 1994.
(45) *Handbook of Chemistry and Physics*, 76th ed.; Lide, D. R., Ed.; CRS Press: Boca Raton, FL, 1995−1996.
(46) Potts, G. D. *Acta Crystallogr., Sect. C* **1995**, *51*, 267.
(47) Dzyabchenko, A. V.; Zavodnik, V. E.; Bel'skii, V. K. *Kristallografiya* **1980**, *25*, 72.
(48) Zavodnik, V. E.; Chetkina, L. A.; Val'kova, G. A. *Kristallografiya* **1979**, *24*, 592.
(49) Zavodnik, V. E.; Chetkina, L. A.; Val'kova, G. A. *Kristallografiya* **1981**, *26*, 392.
(50) Rak, J.; Krzyminski, K.; Skurski, P.; Jozwiak, L.; Konitz, A.; Dokurno, P.; Blazejowski, J. *Aust. J. Chem.* **1998**, *51*, 643.
(51) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1.
(52) Rak, J.; Skurski, P.; Gutowski, M.; Jozwiak, L.; Blazejowski, J. *J. Phys. Chem. A* **1997**, *101*, 283.
(53) Hehre, W. J.; Ditchfield, R.; Radom, L.; Pople, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 4796.
(54) Shibaev, A. Yu.; Puzanov, Yu. V. *Zh. Fiz. Khim.* **1989**, *63*, 888.
(55) Sana, M.; Leroy, G. *Ann. Soc. Sci. Bruxelles, Ser. 1* **1991**, *105*, 67.
(56) *NIST Chemistry Webbook*; http://webbook.nist.gov/cgi/cbook.cgi.
(57) Sabbah, R.; El Watik, L. *Can. J. Chem.* **1992**, *70*, 24.
(58) Stein, S. E.; Barton, B. D. *Thermochim. Acta* **1981**, *44*, 265.
(59) Jursic, B. S. In *Theoretical and Computational Chemistry*; Seminario, J. M., Ed.; Elsevier: Amsterdam, 1996; Vol. 4.
(60) Marquart, D. W. *J. Soc. Ind. Appl. Math.* **1963**, *11*, 431.
(61) *STATISTICA 5.1 G*; StatSoft, Inc.: Tulsa, OK, 1997.
(62) Koopmans, T. *Physica* **1934**, *1*, 104.
(63) Trickey, S. B. In *Conceptual Trends in Quantum Chemistry*; Kryachko, E. S., Calais, J. L., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1994.
(64) Roothaan, C. C. J. *Rev. Mod. Phys.* **1951**, *23*, 61.
(65) Hush, N. S.; Pople, J. A. *Trans. Faraday Soc.* **1955**, *51*, 600.
(66) Potapov, V. K.; Filyugina, A. D.; Shigorin, D. N.; Ozerova, G. A. *Dokl. Akad. Nauk SSSR* **1968**, *180*, 398.
(67) Ishijima, S.; Higashi, M.; Yamaguchi, H.; Kubota, M.; Kobayashi, T. *J. Electron Spectrosc. Relat. Phenom.* **1996**, *82*, 71.
(68) Siegmund, M.; Bendig, J. *Ber. Bunsen-Ges. Phys. Chem.* **1978**, *82*, 1061.
(69) Koutek, B. *Collect. Czech. Chem. Commun.* **1984**, *49*, 1680.
(70) Hunter, L. *J. Chem. Soc.* **1945**, 806.
(71) Zanker, V.; Wittwer, A. *Z. Phys. Chem. (Munich)* **1960**, *24*, 183.
(72) Zanker, V.; Reichel, A. *Z. Elektrochem.* **1960**, *64*, 431.
(73) Albert, A.; Short, L. N. *J. Chem. Soc.* **1945**, 760.
(74) Acheson, R. M.; Burstall, M. L.; Jefford, C. W.; Sansom, B. F. *J. Chem. Soc.* **1954**, 3742.
(75) Beak, P.; Fry, F. S.; Lee, J.; Steele, F. *J. Am. Chem. Soc.* **1976**, *98*, 171.
(76) Karyakin, A. V.; Shablya, A. V. *Dokl. Akad. Nauk SSSR* **1957**, *116*, 969.
(77) Kokubun, H. *Z. Elektrochem.* **1958**, *62*, 599.
(78) Faure, R.; Galy, J.-P.; Vincent, E. J.; Elguero, J.; Galy, A.-M.; Barbe, J. *Chem. Scr.* **1980**, *15*, 62.
(79) Faure, R.; Mahamoud, A.; Galy, J.-P.; Vincent, E. J.; Galy, A.-M.; Barbe, J. *Spectrosc. Lett.* **1981**, *14*, 223.
(80) Vichet, A.; Patellis, A.-M.; Galy, J.-P.; Galy, A.-M.; Barbe, J.; Elguero, J. *J. Org. Chem.* **1994**, *59*, 5156.
(81) Postescu, I. D.; Suciu, D. *J. Prakt. Chem.* **1976**, *318*, 515.
(82) Adam, W.; Reinhardt, D. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1453.
(83) Bouzyk, A.; Jozwiak, L.; Rak, J.; Blazejowski, J. *Vib. Spectrosc.* **2001**, *27*, 139.
(84) Bouzyk, A.; Jozwiak, L.; Blazejowski, J. *J. Mol. Struct.* In press.
(85) Bouzyk, A.; Jozwiak, L.; Kolendo, A. Yu.; Blazejowski, J. Submitted for publication.