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Engineering Neutral Organic Bases and Superbases by Computational DFT Methods – Carbonyl Polyenes

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The gas-phase proton affinities and basicities of a large number of open-chain zig-zag polyenes involving a carbonyl functional group were examined by using the B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d) computational scheme. Absolute proton affinities (APAs) increased with the number of polyene subunits. The most basic site in all cases was the carbonyl oxygen. It was conclusively shown that basicity of polyenes was dramatically amplified by substitution of NMe_2 and Me groups at the strategic positions on the molecular backbone. Triadic analysis revealed that the dominating effect was relaxation energy released upon formation of the molecular radical cations. Relation between the relaxation and cationic resonance effect was briefly discussed. Moreover, it was shown that the carbonyl oxygen was more basic than the amino nitrogen of the NMe_2 groups because of the larger bond association energy of the hydrogen atom attached to O compared to N atoms, in the conjugate acid in question.

Introduction

The proton is a small particle that plays a crucial role in many chemical phenomena, being of paramount importance in acid–base chemistry and biochemistry.[1–3] Neutral organic (super)bases are useful auxiliaries in chemical synthesis,[4] since they have some distinct advantages over their inorganic ionic counterparts. The latter exhibit some unfavourable features like low solubility in most organic solvents, pronounced sensitivity to moisture and CO_2, etc. On the other hand, neutral organic (super)bases permit mild conditions.[5] They show very good stability at low temperatures[6] and exhibit enhanced reactivity with the naked anions forming the poorly associated ion pairs created upon deprotonation.[7] Finally, it should be pointed out that they are efficient catalysts, particularly if immobilized on appropriate surfaces,[8–11] and are recyclable and consequently desirable and acceptable in green chemistry.Neutral organic (super)bases have also found useful applications in both catalytic and stoichiometric asymmetric syntheses.[12]

It comes as a no surprise that a lot of efforts have been devoted to designing new neutral organic bases with highly pronounced basicities. They include cyclic and acyclic guanidines,[13–17] phosphazenes,[18–20] quinoimines and related systems,[21] quinolylboranes,[22] extended 2,5-dihydropyrrolimines[23] and C_2 diamines.[24] The extensive investigations by Koppel, Leito and co-workers[19,25–29] should be emphasized, since they include both experimental and theoretical results in designing, preparing and measuring basicity constants of neutral organic bases and superbases. The intramolecular hydrogen bonding (IHB) motif has been employed for this purpose too, being particularly useful if utilized in a cooperative way by including multiple hydrogen bonds.[30–32] Special interest has been focused on neutral organic bases known as "proton sponges" possessing chelating proton acceptor functionalities. The archetypal compound is Alder's DMAN [1,8-bis(dimethylamino)naphthalene] synthesized some 35 years ago.[33] The design of proton sponges more basic than DMAN has received unabated attention ever since.[34–44] A useful extension of Alder's seminal idea materialized in DMAN was provided by the recently prepared TMGN [1,8-bis(tetramethylguanidino)-naphthalene][45,46] and HMPN [1,8-bis(hexamethyltriamino-phosphazenyl)naphthalene],[47] where the NMe_2 groups were replaced by the guanidino and phosphazeno functionalities, respectively.

Although all these compounds offer a wide variety of superbases, there is a need for new alternative systems exhibiting different properties and occupying different positions on the basicity scale. It is of utmost importance to construct a dense ladder of strong organic superbases possessing as many rungs as possible for several reasons: (1) their use in various preparative laboratory investigations, (2) their employment in the experimental determination of the basicity of new bases with the bracketing technique, (3) their application in the chemical industry as convenient catalysts and (4) their interactions with strong mineral acids and superacids should lead either to low barrier hydrogen bonds or barrierless spontaneous proton transfer reactions.[48–51] With

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these ideas in mind, we started an extensive study of a large number of carbonyl compounds, which should provide counterparts to the imine systems studied earlier.[17,21,52] This is of considerable importance because there is not a systematic study of absolute proton affinities (APAs) of the carbonyl systems except computations performed on some pyrone-like molecules by Suárez et al.[53] In this paper, we report results on some zig-zag polyenes containing carbonyl groups.

Computational Details

This paper reports on the absolute proton affinities (APAs) of polyenes possessing carbonyl group. The theoretical framework for calculating the absolute proton affinity (APAs) as a negative value of the enthalpy change for the protonation reaction in the gas phase is given by Equations (1), (2) and (3).

$$\mathrm{APA}(\mathbf{B}_\alpha) = (\Delta E_{\mathrm{el}})_\alpha + (\Delta E_{\mathrm{vib}})_\alpha + (5/2)RT \quad (1)$$

$$(\Delta E_{\mathrm{el}})_\alpha = E(\mathbf{B}) - E(\mathbf{B}_\alpha\mathbf{H})^+ \quad (2)$$

$$(\Delta E_{\mathrm{vib}})_\alpha = E_{\mathrm{vib}}(\mathbf{B}) - E_{\mathrm{vib}}(\mathbf{B}_\alpha\mathbf{H})^+ \quad (3)$$

The base in question and its conjugate acid are denoted by **B** and $\mathbf{B}_\alpha\mathbf{H}^+$, respectively, while α denotes the site of proton attack. $(\Delta E_{\mathrm{el}})_\alpha$ is the electronic contribution to proton affinity, E_{vib} includes the zero point vibrational energy and corrections to the room-temperature enthalpy, whereas $(5/2)RT$ accounts for the translational energy of the proton as well as the $\Delta(pV)$ term. As a convenient computational model, we shall employ density functional theory (DFT) in its B3LYP representation.[54,55] The molecular structures were calculated by the efficient, but flexible enough 6-31+G(d) basis set, whereas the final molecular energies were obtained by a more intricate 6-311+G(d,p) basis set in the single point calculations, giving rise to the B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d) scheme. It should be pointed out that extensive calculations have shown that performance of the 6-31+G(d) basis set in reproducing molecular geometries is satisfactory. The true minima on the Born–Oppenheimer potential energy hypersurface (BO) were verified by the vibrational frequencies at the B3LYP/6-31+G(d) level, which were subsequently used in the zero point vibrational energies (ZPVEs) and thermal correction calculations.

An important task of theoretical work is the interpretation of experimentally measured or theoretically deduced data pertaining molecular properties. A strong emphasis is given here on the interpretation of the calculated APAs. We found that a triadic (trichotomy) formula is well suited for this purpose;[56] it reads Equation (4),

$$(\mathrm{APA})_\alpha = -(\mathrm{IE})_{\alpha,n}{}^{\mathrm{Koop}} + E(\mathrm{ei})_{\alpha,\mathrm{rex}}{}^{(n)} + (\mathrm{BAE})_\alpha{}^{\cdot+} + 313.6\ \mathrm{kcal\,mol^{-1}} \quad (4)$$

where $(\mathrm{IE})_n{}^{\mathrm{Koop}}$ refers to the n^{th} Hartree–Fock occupied orbital energy ε_n. It corresponds to the n^{th} ionization energy computed in the clamped nuclei and frozen electron density (Koopmans') approximation.[57] It should be noted that the highest occupied molecular orbital (HOMO) will be denoted by a subscript $n = 1$, and that lower MOs will be signified by $n > 1$. The bond association energy $(\mathrm{BAE})_\alpha{}^{\cdot+}$ term yields the exothermic energy release upon formation of a new bond between atom α of the molecular radical cation and the hydrogen atom. It should be kept in mind that Koopmans' ionization corresponds to the sudden electron ejection event. However, true ionization occurs in a

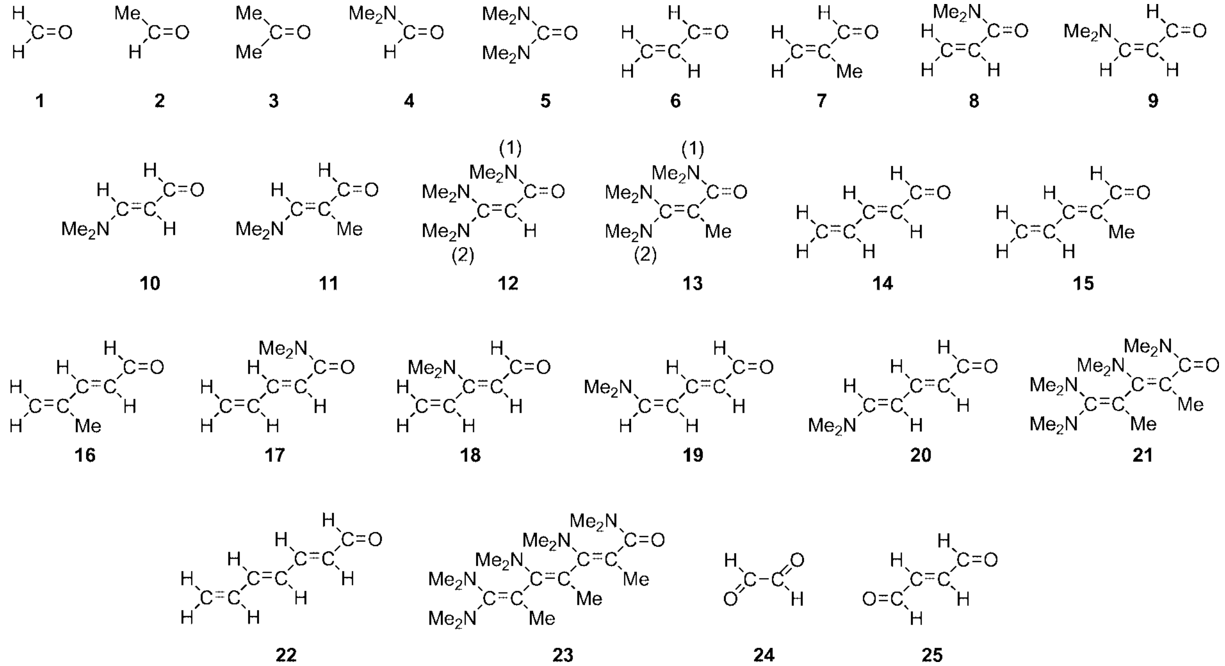


Figure 1. Schematic representation of the studied carbonyl polyenes.

real time and it is generally accepted that the relaxation of the molecular radical cation is completed at the end of the ionization process. Hence, the relaxation energy is given by Equation (5)

$$E(\mathrm{ei})_{\alpha,\mathrm{rex}}{}^{(n)} = (\mathrm{IE})_{\alpha,n}{}^{\mathrm{Koop}} - (\mathrm{IE})_1{}^{\mathrm{ad}} \tag{5}$$

which should be explicitly taken into account in the calculations of APAs. In Equation (5) the first adiabatic ionization energy is signified by $(\mathrm{IE})_1{}^{\mathrm{ad}}$. To summarize, the initial state effect is reflected in the Koopmans' picture of ionization, since it is based on the fixed geometry and frozen electron density of the initial base. The final state effect is given by the bond association $(\mathrm{BAE})_\alpha{}^{\cdot+}$ term. The relaxation yields interplay between the initial and final state effects. Interpretive advantages of the triadic approach was discussed at length by Deakyne.[58] It should also be mentioned that Koopmans' $(\mathrm{IE})_n{}^{\mathrm{Koop}}$ orbital energies were computed by the HF/6-311+G(d,p)//B3LYP/6-31+G(d) model. All calculations were carried out by the GAUSSIAN 03 program.[59]

Results and Discussion

The molecules examined in the present work are depicted in Figure 1. The calculated APAs are compared with the experimental data[60] in Table 1. For the sake of comparison with the experimental measurements, the gas-phase basicity values (GBs) calculated as free energy differences for the protonation reactions are also provided. However, our analysis will focus only on the proton affinities. It should be strongly pointed out that our theoretical estimates of the first adiabatic ionization energies, proton affinities and basicities match very well the available experimental data, thus lending credence to the applied theoretical approach. It appears that linear zig-zag polyenes exhibit APAs within the range 168.5–253.8 kcal mol^{-1}. The upper limit is given by tetraene **23**, which is more basic than the archetypal proton sponge DMAN [1,8-bis(dimethylamino)naphthalene], whose APA is 245.3 kcal mol^{-1}.[47]

It should be indicated that all molecules are protonated at the carbonyl oxygen as the thermodynamically most favourable site. Formaldehyde **1** is a compound of low basicity, which is amplified by the CH_3 substitution in **2** as evidenced by the increase in APA by 15.9 kcal mol^{-1}. The double CH_3 substitution increases the APA value by 26.7 kcal mol^{-1}. On the other hand, single and double NMe_2 substitution of **1** as in **4** and **5**, respectively, leads to a considerable enhancement of basicity, as reflected in APAs increased by 41.7 and 53.6 kcal mol^{-1}, correspondingly.

Table 1. The calculated absolute proton affinities (APAs), gas-phase basicities (GBs), the first adiabatic ionization energies, the available experimental values and component analysis of the proton affinities offered by the triadic formula (in kcal mol^{-1}).[a]

Molecule	$(\mathrm{IE})_n{}^{\mathrm{Koop}}$	$(\mathrm{IE})_1{}^{\mathrm{ad}}$	$E(\mathrm{ei})^{(n)}{}_{\mathrm{rex}}$	$(\mathrm{BAE})^{\cdot+}$	APA	GB
1	$(276.3)_1$	249.8 [250.9 ± 0.2]	26.5	104.7	168.5 [170.4]	161.5 [163.3]
2	$(268.8)_1$	233.3 [235.9 ± 0.1]	35.5	104.1	184.4 [183.7]	177.0 [176.0]
3	$(260.9)_1$	220.3 [223.8 ± 0.1]	40.6	101.9	195.2 [194.0]	187.5 [186.9]
4	$(269.3)_2$	209.1 [210.5]	60.2	105.7	210.2 [212.1]	202.9 [204.7]
5	$(273.3)_3$	184.4	88.9	92.9	222.1 [222.4]	214.2 [215.0]
6	$(272.6)_2$	228.7 [233.1 ± 0.2]	43.9	107.6	192.5 [190.5]	185.0 [182.9]
7	$(269.8)_2$	223.5 [222.5 ± 0.5]	46.3	105.2	195.3 [199.5]	187.6 [191.9]
8	$(269.0)_3$	198.1	70.9	102.7	218.2 [216.1]	210.3 [208.7]
9	$(254.3)_2$	182.9	71.4	96.1	226.8	219.3
10	$(252.9)_2$	183.5	69.4	97.3	227.4	219.9
11	$(251.9)_2$	175.4	76.5	90.6	228.8	221.1
12	$(254.6)_4$	155.4	99.2	81.2	239.4	231.1
$\mathbf{12}_{\mathrm{N(1)}}$	$(223.5)_2$	155.4	68.1	65.7	223.9	216.6
$\mathbf{12}_{\mathrm{N(2)}}$	$(228.6)_3$	155.4	73.2	71.1	229.3	222.4
13	$(252.5)_4$	149.2	103.3	75.0	239.4	230.9
$\mathbf{13}_{\mathrm{N(1)}}$	$(223.0)_2$	149.2	73.8	61.2	225.6	217.3
$\mathbf{13}_{\mathrm{N(2)}}$	$(226.0)_3$	149.2	76.8	62.2	226.6	219.4
14	$(269.6)_2$	215.2	54.4	107.9	206.3	198.7
15	$(267.3)_2$	202.2	65.1	96.6	208.0	200.2
16	$(268.4)_2$	206.4	62.0	101.0	208.2	200.7
17	$(266.8)_2$	191.4	75.4	100.9	223.1	215.0
18	$(258.0)_3$	178.2	79.8	94.3	229.7	221.9
19	$(255.2)_2$	167.8	87.4	87.0	232.8	225.3
20	$(253.4)_2$	167.1	86.3	87.9	234.4	227.0
21	$(249.3)_5$	140.4	108.9	73.9	247.1	236.6
22	$(267.5)_3$	191.6	75.9	93.5	215.5	207.9
23	$(253.2)_8$	126.8	126.4	67.0	253.8	243.3
24	$(278.7)_1$	231.3 [235.2]	47.4	81.1	163.4	156.7
25	$(282.9)_2$	228.8	54.1	100.2	185.0	177.7

[a] The experimental data are given within square brackets.

It would be of some interest to provide a simple interpretation of this behaviour. For this purpose we shall choose formaldehyde **1** as a standard molecule, and gauge other APAs against the APA(**1**) reference value of 168.5 kcal mol^{-1} obtained by protonation at oxygen. The difference Δ(APA) can be resolved in three contributions according to triadic formula employing Equations (6), (7), (8) and (9)

$$\Delta[\mathrm{APA}(\mathbf{B}_\alpha)] = \mathrm{APA}(\mathbf{B}_\alpha) - \mathrm{APA}(\mathbf{st}) = [-\Delta(\mathrm{IE})_{\alpha,n}{}^{\mathrm{Koop}};\ \Delta E(\mathrm{ei})_{\alpha,\mathrm{rex}}{}^{(n)};\ \Delta(\mathrm{BAE})_\alpha{}^{\cdot+}] \tag{6}$$

where

$$\Delta(\mathrm{IE})_{\alpha,n}{}^{\mathrm{Koop}} = (\mathrm{IE})_{\alpha,n}{}^{\mathrm{Koop}}(\mathbf{B}_\alpha) - (\mathrm{IE})_{\beta,m}{}^{\mathrm{Koop}}(\mathbf{st}) \tag{7}$$

$$\Delta E(\mathrm{ei})_{\alpha,\mathrm{rex}}{}^{(n)} = E(\mathrm{ei})_{\alpha,\mathrm{rex}}{}^{(n)}(\mathbf{B}_\alpha) - E(\mathrm{ei})_{\beta,\mathrm{rex}}{}^{(m)}(\mathbf{st}) \tag{8}$$

$$\Delta(\mathrm{BAE})_\alpha{}^{\cdot+} = (\mathrm{BAE})_\alpha{}^{\cdot+}(\mathbf{B}_\alpha) - (\mathrm{BAE})_\beta{}^{\cdot+}(\mathbf{st}) \tag{9}$$

and where **st** stands in general for the reference molecule selected as a standard. Notice that indices β and m could be different from α and n, respectively, or in other words, that the sites of protonation in **B** and **st** could differ in principle. The square parentheses in Equation (6) imply summation of three terms. By using Equation (6) and APA(**1**) as a standard value, one obtains $\Delta[\mathrm{APA}(\mathbf{2})]_1 = [7.5; 9.0; -0.6] = 15.9$ kcal mol^{-1}. It appears that the enhanced basicity upon methyl substitution is a result of two contributions; the first is the increased HOMO orbital energy and concomitant decrease in instantaneous (Koopmans') ionization energy. Thus, the price to be paid in activating a particular electron in the bond formation process is lower leading to the enhanced basicity. The MO providing an electron in the protonation of bases is termed the principal MO or PRIMO, since it is the molecular orbital most directly involved in the protonation process. In formaldehyde **1**, acetaldehyde **2** and acetone **3** the principal MO corresponds to the in-plane orbital of the oxygen lone pairs (HOMO), since the heavy atoms remain coplanar in the protonated forms (Figure 2). The second important contribution to the basicity of **2** comes from the increased relaxation energy (9.0 kcal mol^{-1}), relative to **1**, while the bond association energy is smaller by the almost negligible amount of 0.6 kcal mol^{-1}. Double substitution by CH_3 groups, providing system **3**, yields [15.4; 14.1; –2.8] = 26.7 kcal mol^{-1}, meaning that the pattern of behaviour is preserved provided particular terms increase their absolute values. Introduction of the NMe_2 group in **1** shifts the principal MO to the lower HOMO–1 orbital (Figure 2). The triadic analysis yields $\Delta[APA(\mathbf{4})]_1$ = [7.0; 33.7; –1.0] = 41.7 kcal mol^{-1}. It appears that the $(IE)^{Koop}$ term is approximately decreased by the same amount as in **2**, whereas the relaxation energy is considerably enlarged. Similarly, the double substitution of the NMe_2 groups in **5** drifts the principal MO to an even lower HOMO–2, which leads to a dramatic increase in the relaxation energy: $\Delta[APA(\mathbf{5})]_1$ =

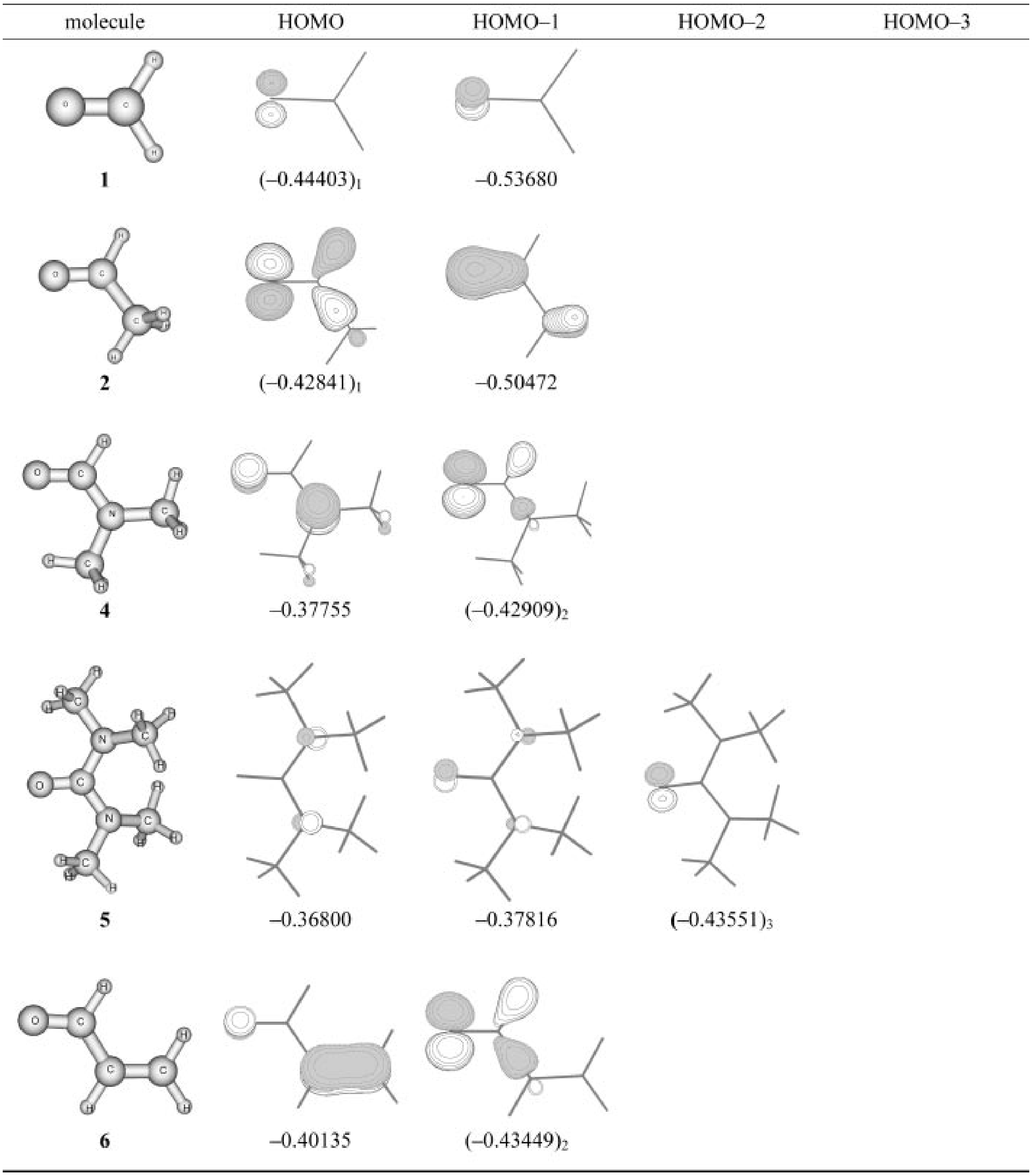


Figure 2. Principal molecular orbitals PRIMOs (given within parentheses) in some characteristic molecules.

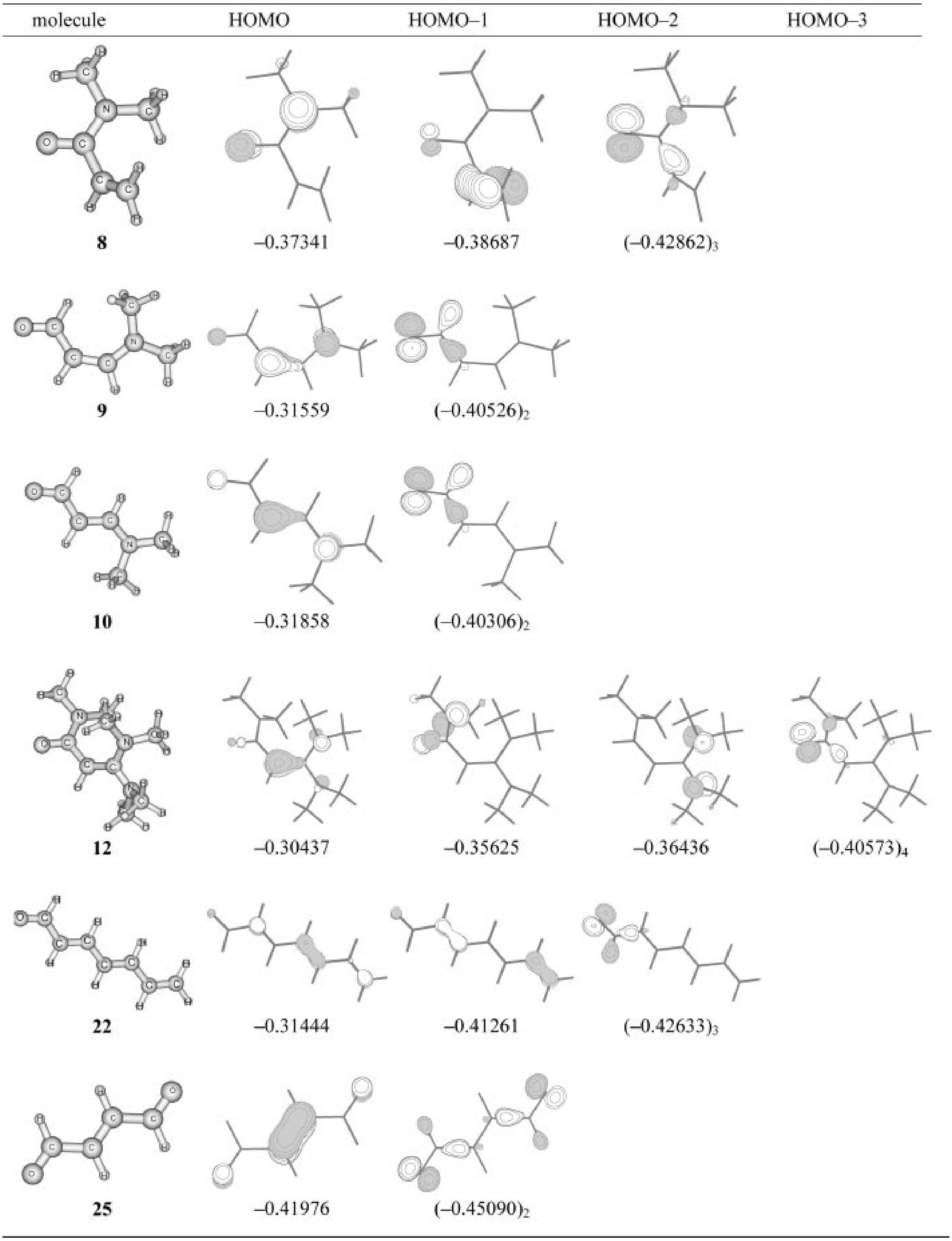
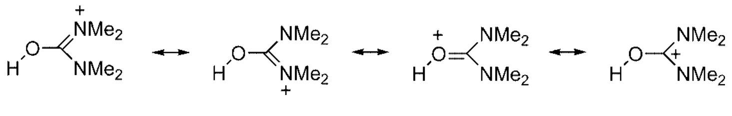


Figure 2. *(continued)*.

[3.0; 62.4; –11.8] = 53.6 kcal mol^{-1}, thus being the main cause of the highly increased basicity. It is noteworthy that the (BAE)$^{\cdot+}$ diminishes basicity by some 12 kcal mol^{-1}. This is in accordance with our previous results, which revealed that the CH_3 group enhances the basicity of the imino group in methanimine $H_2C=NH$ through an initial state effect, while upon NH_2 (or NMe_2) substitution, the same molecule is made more basic due to the increase in the relaxation energy, or in other words, via an intermediate effect.[56] The substantial increase in the relaxation energy in **4** and **5** is at least partly a result of the cationic resonance in the conjugate acids as illustrated by **5** in Scheme 1.

An interesting point is that the relaxation effect is related in a broad sense to the delocalization (conjugation) energy in neutral polyenes and to the cationic resonance effect in their protonated forms efficiently transmitted by the mobile



Scheme 1.

π-electrons. In order to illustrate this intuitively appealing conjecture, we shall employ a conceptual scheme developed in discussing polyguanides earlier[17] based on homodesmotic reactions.[61,62] Let's consider the cationic resonance in **4** and **5** as a simple example. The corresponding homodesmotic reactions are shown in Equations (10) and (11).

$$(NMe_2)HC{=}O + H_2C{=}CH_2 = (NMe_2)HC{=}CH_2 + H_2C{=}O + \varepsilon^1 - E_{conj}^{(1)} \quad (10)$$

$$(NMe_2)_2C{=}O + H_2C{=}CH_2 = (NMe_2)_2C{=}CH_2 + H_2C{=}O + \varepsilon^2 - E_{conj}^{(2)} \quad (11)$$

The conjugation energies in $(NMe_2)HC{=}CH_2$ and $(NMe_2)_2C{=}CH_2$ are denoted by ε^1 and ε^2, respectively. If they were negligible, then $E_{conj}^{(1)}$ and $E_{conj}^{(2)}$ would yield the conjugation energy of $(NMe_2)HC{=}O$ and $(NMe_2)_2$-$C{=}O$, correspondingly. This is, however, not the case. The conjugation energy ε^1 is obtained by the rotation barrier of the NMe_2 group in $(NMe_2)HC{=}CH_2$. It is 6.3 kcal mol^{-1}, which together with reaction in Equation (12)

$$(NMe_2)_2C{=}CH_2 + H_2C{=}CH_2 = 2\ (NMe_2)HC{=}CH_2 + 2\ \varepsilon^1 - \varepsilon^2 \quad (12)$$

gives ε^2 = 13.7 kcal mol^{-1}. It is worth noting that this effect is almost additive. Taking ε^1 and ε^2 into account, one obtains $E_{conj}^{(1)}$ and $E_{conj}^{(2)}$ from Equations (10) and (11), correspondingly. They are 28.2 kcal mol^{-1} and 41.3 kcal mol^{-1}, respectively. The cationic resonance effect is calculated analogously from homodesmotic reactions (13) and (14).

$$(NMe_2)HC{=}OH^+ + H_2C{=}CH_2 = (NMe_2)HC{=}CH_2 + H_2C{=}OH^+ + \varepsilon^1 - E_{res}^{+(1)} \quad (13)$$

$$(NMe_2)_2C{=}OH^+ + H_2C{=}CH_2 = (NMe_2)_2C{=}CH_2 + H_2C{=}OH^+ + \varepsilon^2 - E_{res}^{+(2)} \quad (14)$$

The adopted B3LYP method gives, in the same way, the cationic resonance energies $E_{res}^{+(1)}$ = 69.8 kcal mol^{-1} and $E_{res}^{+(2)}$ = 94.9 kcal mol^{-1}, thus indicating that the increase in the stabilization energy triggered by protonation of derivatives **4** and **5** is 41.6 kcal mol^{-1} and 53.6 kcal mol^{-1}, respectively. These numbers should be compared with the relaxation energies $E(ei)_{\alpha,rex}^{(n)}$ in **4** and **5**, which are 33.7 and 62.4 kcal mol^{-1}, respectively. They are qualitatively comparable, the latter values being lower and higher by 8 and 9 kcal mol^{-1}, respectively. It should be strongly pointed out that the relaxation effect and cationic resonance contribution to APAs are by no means identical. It is easy to show that $\Delta[APA(\mathbf{4})]_1 = E_{res}^{+(1)} - E_{conj}^{(1)}$ and $\Delta[APA(\mathbf{5})]_1 = E_{res}^{+(2)} - E_{conj}^{(2)}$, implying that amplification of the basicity is proportional to cationic resonance. On the other hand, the relaxation is just one component in the triadic analysis given by Equations (6)–(9), which describes enhancement in basicity of **1** upon single and double NMe_2 substitution. Triadic formula takes into account the influence of the initial and final states too, treating all three effects on an equal footing. Bearing this in mind, it is also intuitively clear that systems undergoing large cationic resonance stabilization, triggered by protonation, should have considerable relaxation upon an ionization event, which becomes the dominant effect in the protonation process in many cases, as exemplified here by derivatives **4** and **5**.

An important role of the relaxation energy is best illustrated by the APAs along the series **1**, **6**, **14** and **22**, which assume values of 168.5, 192.5, 206.3 and 215.5 kcal mol^{-1}, respectively. Hence, polyenes become more basic with an increased number of subunits, but exhibit a saturation effect as observed earlier.[17,52] The corresponding triads relative to **1** are $\Delta[APA(\mathbf{6})]_1$ = [3.7; 17.4; 2.9] = 24.0 kcal mol^{-1}, $\Delta[APA(\mathbf{14})]_1$ = [6.7; 27.9; 3.2] = 37.8 kcal mol^{-1} and $\Delta[APA(\mathbf{22})]_1$ = [8.8; 49.4; –11.2] = 47.0 kcal mol^{-1}. Obviously, the relaxation energy dominates and increases in the series. It is also self-evident that the cationic resonance stabilization of the protonated forms increases too, which can be easily checked by counting Pauling's resonance structures.

Substituent effects in acrolein **6** are studied in mono- (**7**, **8**, **9**, **10**), bis- (**11**) and poly-substituted (**12**, **13**) derivatives. The influence of substituents on APA is revealed by triads taking **6** as a reference system. The effect of monosubstition is reflected in the following triads: $\Delta[APA(\mathbf{7})]_6$ = [2.8; 2.4; –2.4] = 2.8 kcal mol^{-1}, $\Delta[APA(\mathbf{8})]_6$ = [3.6; 27.0; –4.9] = 25.7 kcal mol^{-1}, $\Delta[APA(\mathbf{9})]_6$ = [18.3; 27.5; –11.5] = 34.3 kcal mol^{-1} and $\Delta[APA(\mathbf{10})]_6$ = [19.7; 25.5; –10.3] = 34.9 kcal mol^{-1}. It appears that the methyl substitution effect in **7** is effectively given by Koopmans' contribution, which in turn is small, since the relaxation energy and (BAE) terms cancel each other out. The electron releasing NMe_2 group in **8** affects APA essentially through the relaxation effect, as expected. It is interesting to observe that the relaxation effect and Koopmans' term remain practically constant in **9** and **10**. They both substantially contribute to enhanced basicities relative to **6** by overcoming smaller bond association energies. The reason behind the appreciable increase in Koopmans' term is that the NMe_2 group destabilizes the PRIMOs in **9** and **10**, despite the fact that the appropriate in-plane lone pair orbitals belong to lower HOMO–1 molecular orbitals (Figure 2). The fully substituted acrolein **13** has an APA value of 239.4 kcal mol^{-1}, undergoing an increase relative to the parent compound **6** $\Delta[APA(\mathbf{13})]_6$ = [20.1; 59.4; –32.6] = 46.9 kcal mol^{-1}, where the relaxation energy has a predominant effect, in accordance with chemical intuition.

The substituent effect in **14** follows the same pattern. The persubstituted derivative **21** exhibits enhanced basicity relative to the parent molecule **14**, as described by $\Delta[\mathrm{APA}(\mathbf{21})]_{14}$ = [20.3; 54.5; –34.0] = 40.8 kcal mol^{-1}. This increase is lower by 6 kcal mol^{-1} than in the persubstituted acrolein (see above). It is clear that substituted polyenes exhibit a saturation effect too, just like the parent pure hydrocarbon compounds, which occurs for two reasons: (1) the cationic resonance diminishes with the length of a zig-zag chain, and (2) the substituted polyene becomes increasingly nonplanar due to steric interactions of bulky NMe_2 groups (vide infra).

Finally, the substituted tetraene **23** has APA = 253.8 kcal mol^{-1}, which is well above the superbasic threshold of DMAN (245.3 kcal mol^{-1}). It is of interest to compare this value with that of formaldehyde **1**. The triad $\Delta[\mathrm{APA}(\mathbf{23})]_1$ = [23.1; 99.9; –37.7] = 85.3 kcal mol^{-1} illustrates once more the fact that the relaxation effect plays a leading role in determining basicity of polyenes.

Useful byproducts of the present study are proton affinities of diketones **24** and **25**. Their APAs of 163.4 and 185.0 kcal mol^{-1}, respectively, are considerably lower than those of the corresponding monoketones **6** and **14**. The triadic differences $\Delta[\mathrm{APA}(\mathbf{24})]_6$ = [–6.1; 3.5; –26.5] = –29.1 kcal mol^{-1} and $\Delta[\mathrm{APA}(\mathbf{25})]_{14}$ = [–13.3; –0.3; –7.7] = –21.3 kcal mol^{-1} reveal a distinctly different behaviour compared to monoketones. The relaxation effect becomes small or even negligible; whereas both the initial (Koopmans) and final state (bond association energy) contribute to attenuation of basicity. Interestingly enough, the latter two effects dominate in opposite fashion in pairs **24**–**6** and **25**–**14**. Obviously, the carbonyl group at the other end is a poor promoter of the cationic resonance effect.

Triadic analysis gives a simple rationalization of the finding that oxygen is the most basic site in substituted ketones. Let us consider the alternative protonation N(1) and N(2) positions in **12**. It appears that $\mathrm{APA}(\mathbf{12})_{\mathrm{N(1)}}-\mathrm{APA}(\mathbf{12})_{\mathrm{O}}$ = [31.1; –31.1; –15.5] = –15.5 kcal mol^{-1} and $\mathrm{APA}(\mathbf{12})_{\mathrm{N(2)}}-\mathrm{APA}(\mathbf{12})_{\mathrm{O}}$ = [26.0; –26.0; –10.1] = –10.1 kcal mol^{-1}, thus implying that Koopmans' and relaxation effects exactly cancel out, as it should be according to Equation (5). This holds for any molecule, leading to the conclusion that the difference in APA for various α and β basic sites in the same compound is given by the difference in the bond association energies $(\mathrm{BAE})_\alpha^{\cdot+}-(\mathrm{BAE})_\beta^{\cdot+}$. Therefore, amino nitrogens in **12** are less basic than oxygen due to diminished bond association energies $(\mathrm{BAE})_{\mathrm{N}}^{\cdot+} < (\mathrm{BAE})_{\mathrm{O}}^{\cdot+}$ in the corresponding $\mathbf{12}^{\cdot+}$ radical cation.

It is of some interest to examine the additivity of the multiple substitution effect on proton affinity, which works so well in polysubstituted aromatics.[63–68] For this purpose we shall employ again the concept of homodesmotic reactions. The first step is to determine the increment I(X) caused by a single substituent, see Equations (15) and (16).[63]

$$\mathrm{I(X)_1}^+ = \mathrm{APA(XHC{=}O)} - \mathrm{APA}(\mathbf{1}) \tag{15}$$

It is then easy to show that:

$$\mathrm{APA(XYC{=}O)} = \mathrm{APA}(\mathbf{1}) + \mathrm{I(X)_1}^+ + \mathrm{I(Y)_1}^+ + \Delta(\mathrm{X,Y})_1 \tag{16}$$

where $\Delta(\mathrm{X,Y})_1$ is the deviation from the additivity given by $\Delta(\mathrm{X,Y})_1 = \delta(\mathrm{X,Y}) - \delta^+(\mathrm{X,Y})$. Here, $\delta(\mathrm{X,Y})$ and $\delta^+(\mathrm{X,Y})$ are the interference energies in disubstituted formaldehyde and its oxygen protonated form, respectively; see Equations (17) and (18).

$$\mathrm{XYC{=}O} + \mathbf{1} = \mathrm{XHC{=}O} + \mathrm{YHC{=}O} + \delta(\mathrm{X,Y}) \tag{17}$$

$$\mathrm{XYC{=}OH^+} + \mathbf{1}\mathbf{H}^+ = \mathrm{XHC} + \mathrm{OH^+} + \mathrm{YHC{=}OH^+} + \delta^+(\mathrm{X,Y}) \tag{18}$$

Taking substituents X = Me and Y = NMe_2, one obtains the increments $\mathrm{I(Me)_1}^+$ = 18.9 kcal mol^{-1} and $\mathrm{I(NMe_2)_1}^+$ = 44.7 kcal mol^{-1}. Further, the interference energies δ(Me, NMe_2) = 7.3 kcal mol^{-1} and δ^+(Me, NMe_2) = 16.7 kcal mol^{-1} imply that the nonadditivity effect $\Delta(\mathrm{Me, NMe_2})_1$ = 9.4 kcal mol^{-1} is large in sharp contrast with the situation in aromatic systems, where additivity holds to good accuracy. The reason behind the nonadditivity is that both substituents Me and NMe_2 are placed at the same carbon. Hence, their effects are strongly coupled. In aromatics the situation is different, since each carbon atom is linked to a single substituent. Consequently, each substituent behaves as if the others were nonexistent. Moreover, linear polyenes polysubstituted by bulky groups exhibit considerable nonplanarity, which is usually not the case in large aromatic systems.

Full discussion of the structural characteristics and changes induced by protonation are beyond the scope of this paper. Instead, we shall focus on the nonplanarity of some simple systems, which serve an illustrative purpose. The nonplanarity of **5** and **13** is illustrated by Figure 3. Let us consider compound **5** first. The molecular plane is given by the C=O functional group and two nitrogens, since the C(1), O(2), N(3) and N(4) atoms are coplanar. The planes C(8)–N(4)–C(1) and C(7)–N(4)–C(1) close with the molecular plane dihedral angles –7.7° and 138.8°, respectively. In spite of the small and modest nonplanarity, the conjugation effect is strong, being 41.3 kcal mol^{-1}, as discussed earlier. That modest nonplanarity does not hinder the π-electron conjugation is in harmony with our experience gained in studying large π-systems. Somewhat surprisingly, the nonplanarity in $\mathbf{5H^+}$ upon protonation is increased. A part of the enhanced nonplanarity is certainly given by the additional H atom (conditionally denoted H^+). It is shifted out of the molecular plane by 23.9°. Nevertheless, the cationic resonance is even stronger than in neutral molecule **5**, attaining a high value of 94.9 kcal mol^{-1} (vide supra). Both findings are compatible with the highly pronounced delocalized nature of the electron. It should be also mentioned that the molecular backbone N(4)–C(1)–O(2)–N(3) remains planar. The same pattern holds in the more complex system **13** and its protonated form $\mathbf{13H^+}$. A molecular fragment formed by N(3)–C(1)–O(2)–C(4) is planar. The additional C=C double bond is twisted, however, by –135.0° and –158.5° relative to the molecular plane in **13** and $\mathbf{13H^+}$, respectively, due to steric effects. Nevertheless, the calculated relaxation energy effect in $\mathbf{13H^+}$ is large at

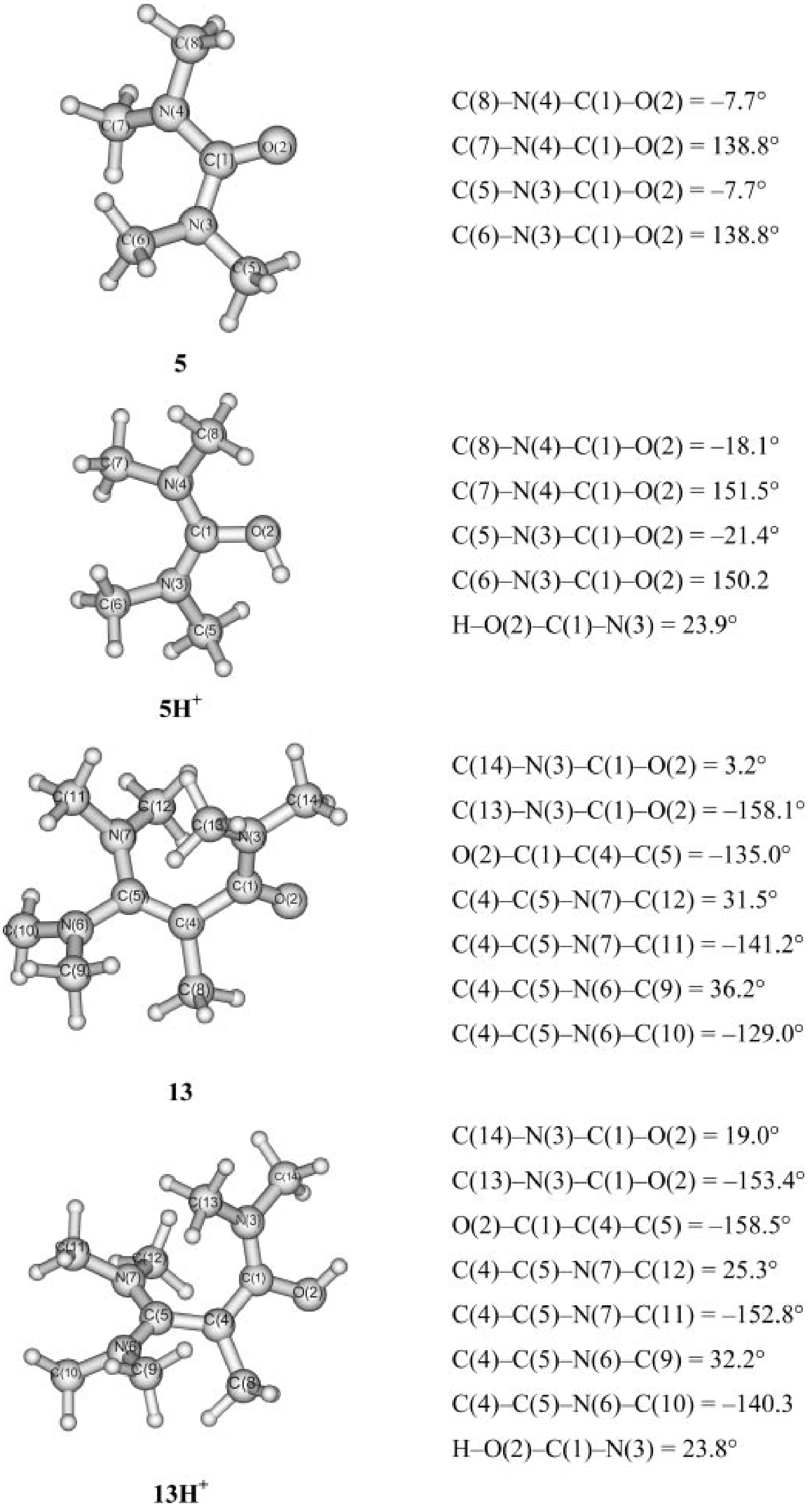


Figure 3. Nonplanarity of systems **5** and **13** and their protonated forms.

103.3 kcal mol^{-1} (Table 1). It is worth noting that H$^+$ is drifted out of the molecular plane by the OH$^+$ angle of 23.8°, in analogy with the **5H$^+$** case.

Another parameter of interest is given by the pyramidalization of nitrogen atoms. The degree of pyramidalization in percents (DP%) is computed by a formula described elsewhere.[69] It appears that pyramidalization in **4** is almost negligible, which is compatible with the large conjugation energy. Both conjugation and cationic resonance are at maximum in perfectly planar systems. A sizeable py-

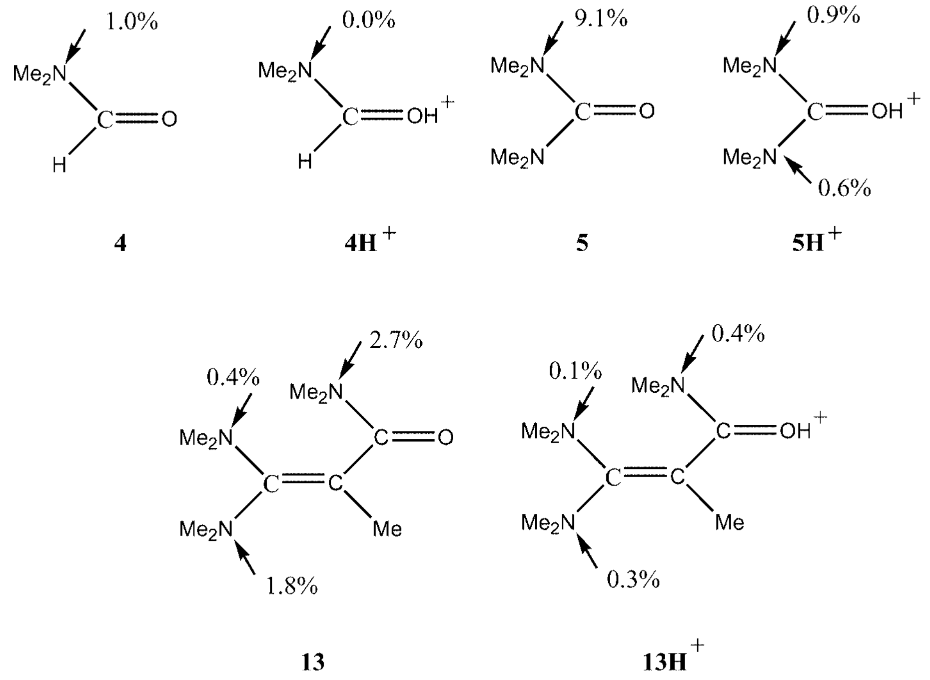


Figure 4. Pyramidalization of nitrogen atoms in **4**, **4H$^+$**, **5**, **5H$^+$**, **13** and **13H$^+$**.

ramidalization is found in **5** presumably due to steric repulsion between the NMe_2 groups. In contrast, considerable planarization takes place in the protonated form **5H$^+$** (Figure 4). A similar pattern occurs in **13** and **13H$^+$**. Undoubtedly, planarization is a consequence of the fact that cationic resonance in the conjugate acids is much stronger than the conjugation effect in neutral systems.

Conclusions

Computational study of proton affinities of open-chain polyenes involving a single carbonyl group has shown that the APA values increased with the length of the polyene. The basic site most susceptible to proton attack is the carbonyl oxygen. Triadic analysis reveals that the dominant effect exerted on APAs is the relaxation energy of the nuclei and electrons upon protonation, or more precisely, after ionization of a base in question, as described in the triadic picture. It was shown that the cationic resonance triggered by protonation is closely related to the relaxation intermediate effect, as intuitively expected, but analysis revealed that it is also distinctly different at the same time. Distribution of the σ electron accepting and π electron releasing NMe_2 groups and electron-donating methyl substituents at the strategic position over the molecular backbone leads to dramatic amplification of basicity. The underlying reason is considerable increase in the relaxation effect. The tetraene derivative **23** exhibits superbasicity, because it is significantly more basic than prototypical DMAN. Triadic analysis conclusively shows that the carbonyl oxygen is more basic than the amino nitrogens in all the studied substituted polyenes due to larger bond association energies of the H atoms attached to O atoms in the corresponding conjugate acid cations, compared to the N–H bond energy. The initial state effect is reflected in Koopmans' sudden ionization of the base in question, and the importance of the principal MO lying lower than the HOMOs is underlined.

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