1. Introduction

Glycine, GLY, is the simplest protein structure unit and the smallest achiral amino acid that can act as a neuroinhibitor in the mammalian center nervous system.¹ Sarcoine, SAR, is the N-methyl derivative of glycine and belongs to a group of biologically important compounds containing a carbon atom participating in transmethylation reactions. In nature, it occurs in starfish, sea urchins and in the antibiotic actinomycin.² N,N-Dimethylglycine, DMG, is a sweet-tasting substance classified as a nutrient. It has been presumed to be a key ingredient of vitamin B15 or pangaemic acid. In the living cell, DMG is present as a product of the metabolism pathway of choline and methionine. DMG has been used in the treatment of mental disturbance conditions, like autism and epileptic seizures. DMG is a popular ingredient of supplementary diet tablets and energetic drinks for sportsmen.²³ Betaine, BET, trimethylglycine, is a zwitterion containing an anionic carboxylate group and a positively charged quaternary ammonium group. Betaine is a biological oxidation product of choline and it is widely distributed in plants, algae and animal tissues, where it serves as a methyl transfer agent important in amino acid syntheses.⁴ GLY,¹ SAR,⁵ DMG⁷ and BET⁸ form crystalline adducts mainly with inorganic acids as well as with some organic acids.⁷⁹ Some of them display interesting physical properties exhibiting phase transitions leading to ferroelectric, antiferroelectric and ferroelastic phases as well as phases with commensurate and incommensurate superstructures.¹⁰ The N-alkylation of amino acids is known to increase the population of neutral tautomers in solution.¹¹

Since amino acids and their complexes are of considerable chemical and biological interest we have undertaken a systematic investigation of several squaric acid complexes with the simplest amino acid glycine and its N-methyl derivatives, sarcosine, dimethylglycine and betaine (Fig. 1). Squaric acid, H₂SQ, is a reagent for chemical synthesis, used for instance to make photosensitive squarate dyes,¹² inhibitors of protein tyrosine phosphatases and squaraine-modified DNA.¹³ The structure of squaric acid is not a perfect square.¹⁴ The high acidity of H₂SQ with K₁ = 1.5 for the first proton and pK₂ = 3.4 for the second one¹⁵ is attributable to resonance stabilization of the anion.¹⁶ The conjugate base of squaric acid is the hydrogen squarate anion, HSQ⁻, whereas the conjugate base of the hydrogen squarate anion is the divalent squarate anion, SQ²⁻ (Fig. 1).¹⁷

The proton transfer belongs to the most frequent transformations in Nature, however this process is still not well understood. Squaric acid and amino acids are ideal for investigating the proton transfer. Some earlier papers of the groups of Kolev et al. concern complexes of amino acids and their derivatives with H₂SO.¹⁸ In the present work we report on the synthesis of four new complexes of H₂SO with glycine, GLY, and its methyl derivatives, sarcosine (N-methylglycine, SAR), dimethylglycine (DMG), and betaine (trimethylglycinium, BET). The main aim of this work is investigation of the interaction between the zwitterionic compounds and the proton-donor. These complexes differ in their X-ray data, FTIR and NMR spectra. The differences
are caused by the presence of different number of acidic protons and methyl groups attached to the nitrogen atoms. From the point of view of materials science, the information on the formation of crystal structures of the complexes of glycine and its methyl derivatives with squaric acid is essential for understanding the role of hydrogen bonds and other intermolecular forces in the association of ions in the crystalline state. Quantum chemical calculations have been performed for one unit of all complexes to study their structures in the isolated molecules and their IR frequencies.

2. Results and discussion

GLY, SAR, DMG and BET form stable, crystalline complexes with H$_2$SQ. Their structures are studied by the single-crystal diffraction method, while the molecular structures of the isolated unit of complexes, without any interactions with the neighboring molecules, have been optimized by the B3LYP/6-311G(d,p) approach. The experimental and calculated bond lengths, bond and torsion angles are given in Tables S1 and S2, respectively (ESI†), while the selected ones are listed in Table 1. The hydrogen bond geometries, calculated energies (HF) and dipole moments are listed in Table 2.

2.1. Crystal (1) and optimized (1a) structures of the 2 : 1 complex of glycine with squaric acid

Glycine, GLY, is a non-essential, neutral amino acid without a center of chirality.$^{2,19}$ In an aqueous solution of pH ~ 7 GLY exists as a zwitterion with the positively charged amino group and the negative carboxylate group. Binding of proton to glycine is shown in Scheme 1.$^{20}$ The $K_1$ and $K_2$ constants reflect the intrinsic properties of the amino and carboxyl groups and their interactions on protonation ($pK_1$(COOH) = 2.35 and $pK_1$(NH$_3^+$) = 9.78).

GLY with H$_2$SQ forms a crystalline adduct, 1, at a ratio 2 : 1. Both OH groups of H$_2$SQ are engaged in the short, asymmetric and non-equivalent hydrogen bonds, O(5)–H(3) · · · O(3) and O(5)–H(4) · · · O(4) of 2.444(2) and 2.571(2) Å, respectively. Both O–H protons from H$_2$SQ are transferred to GLY, generating a squarate dianion, SQ$^{2−}$, and two glycinium cations (Fig. 2a, Table 2). Unlike in the crystal of GLY,$^{21}$ the glycine units in the complex exist in the cationic forms. A similar arrangement of the base and SQ$^{2−}$ is observed in the known complexes of H$_2$SQ with bases.$^{17,22}$ However, the optimized structure of the 2 : 1 complex, 1a, is more symmetric than the crystal one, and H$_2$SQ interacts with two uncharged (neutral) forms of GLY units, with the O(3)–H(3) · · · O(5) and O(4)–H(4) · · · O(5) lengths of 2.644 and 2.648 Å, respectively (Fig. 2b, Table 2). The COOH groups in GLY units in 1a have trans conformations. In 1a there are the O(6)–H(N1) · · · N(1) and O(6')–H(N1') · · · N(1') intramolecular contacts between the carboxylic protons and the nitrogen atoms of GLY moieties, of 2.588 and 2.574 Å, respectively (Table 2), while in the crystal of 1 the N–H atoms form several short N–H · · · O contacts with the squarate dianions of the neighboring molecules. Aggregates of bonded molecules are shown in Fig. 3. The structure of the squarate dianion in 1 is almost square and planar. The C–C–C–C bond angles vary from 89.3(1)$^\circ$ to 91.2(1)$^\circ$, whereas the C–C–C–C torsion angles are equal ±0.4(1)$^\circ$ (Table 1).

2.2. Crystal (2) and optimized (2a) structures of the complex of sarcosine with squaric acid and water

Sarcosine, also known as N-methylglycine, is an intermediate and by-product in glycine synthesis and degradation.$^{2}$

SAR forms a hydrated complex with H$_2$SQ at a ratio SAR : H$_2$SQ : 0.5H$_2$O (2). One proton from squaric acid is transferred to sarcosine and the hydrogen squarate anion, HSQ$^-$, interacts with water (Fig. 4a). The protonation at O(5) is reflected in the C(3)–O(5) bond length of 1.314(1) Å, compared with the C(5)–O(6) bond of 1.201(1) Å. These bond lengths in pure sarcosine are 1.271(2) and 1.239(2) Å.$^{23}$ The geometry of the HSQ$^-$ anion shows that the hydroxyl group is located at the C(3)–C(4)–C(1) bond angle of 91.2(1)$^\circ$, which is more open than the other three ones. The HSQ$^-$ anion significantly deviates from planarity, as illustrated by the O–C–O torsion angles varying from −3.1(1)$^\circ$ to 3.1(1)$^\circ$ (Table 1).

The O(1W) oxygen atom of the water molecule is located on a two-fold axis, hence only H(1W) of the water molecule is
Table 1. Selected experimental and calculated bond lengths (\(\text{Å}\)) and bond and torsion angles (\(^\circ\)) for complexes of squaric acid with glycine (1, 1a), sarcosine (2, 2a), dimethylglycine (3, 3a) and betaine (4, 4a) by X-ray diffraction (1, 2, 3, 4) and by the B3LYP/6-311G(d,p) approach (1a, 2a, 3a, 4a).

| Parameters | 1 | 1a | 2 | 2a | 3 | 3a | 4 | 4a |
|------------|---|----|---|----|---|----|---|----|
| Bond lengths | A | B | A | B | A | B | A | B |
| O(1)–C(1) | 1.242(2) | 1.215 | 1.250(1) | 1.208 | 1.236(2) | 1.235(2) | 1.219 | 1.212 |
| O(2)–C(2) | 1.251(2) | 1.201 | 1.215(1) | 1.219 | 1.218(2) | 1.223(2) | 1.201 | 1.220 |
| O(3)–C(3) | 1.265(2) | 1.305 | 1.247(1) | 1.296 | 1.287(2) | 1.258(2) | 1.309 | 1.320 |
| O(4)–C(4) | 1.249(2) | 1.322 | 1.308(1) | 1.323 | 1.300(2) | 1.318(2) | 1.317 | 1.305 |
| O(5)–C(5) | 1.295(2) | 1.312(2) | 1.314(1) | 1.247 | 1.266(2) | 1.305(2) | 1.229 | 1.242 |
| O(6)–C(5) | 1.211(2) | 1.197(2) | 1.201(1) | 1.251 | 1.245(2) | 1.213(2) | 1.267 | 1.255 |

| Bond angles | A | B | A | B | A | B | A | B |
|-------------|---|----|---|----|---|----|---|----|
| C(1)–C(2)–C(3) | 89.9(1) | 91.2(1) | 93.7(1) | 92.4(1) | 90.8(1) | 92.4(1) | 92.7(1) | 92.4(1) |
| C(2)–C(3)–C(4) | 86.7(1) | 89.4(1) | 89.7(1) | 91.4(1) | 89.6(1) | 92.0(1) | 92.9(1) | 92.4(1) |
| C(3)–C(4)–C(1) | 93.0(1) | 94.2(1) | 91.9(1) | 94.2(1) | 92.7(1) | 92.9(1) | 89.9(1) | 89.1(1) |
| C(4)–C(1)–C(2) | 87.4(1) | 89.4(1) | 87.6(1) | 89.0(1) | 88.1(1) | 88.7(1) | 87.9(1) | 88.3(1) |

| Torsion angles | A | B | A | B | A | B | A | B |
|----------------|---|----|---|----|---|----|---|----|
| C(1)–C(2)–C(3)–C(4) | -0.4(1) | 0.16 | -1.3(1) | -0.15 | 1.0(1) | 0.8(1) | 0.42 | -0.31 |
| C(2)–C(3)–C(4)–C(1) | 0.4(1) | -0.17 | 1.3(1) | 0.16 | -1.1(1) | -0.9(1) | -0.43 | 0.32 |
| C(3)–C(4)–C(1)–C(2) | -0.4(1) | 0.16 | -1.3(1) | -0.15 | 1.0(1) | 0.9(1) | 0.42 | -0.30 |
| C(4)–C(1)–C(2)–C(3) | 0.4(1) | -0.15 | 1.3(1) | 0.14 | -1.0(1) | -0.8(1) | -0.39 | 0.28 |
| O(5)–C(5)–C(6)–N(1) | 169.1(1) | 170.4(1) | -176.42 | -160.34 | 178.0(1) | 143.5(1) | 161.8(1) | 166.4(1) |
| O(6)–C(5)–C(6)–N(1) | -11.8(2) | 9.2(2) | 4.05 | 20.24 | -0.5(2) | 34.03 | -21.4(2) | 15.4(2) |

\(a\) Part A - the positions denoted by the unprimed atomic labels. \(b\) Part B - the positions denoted by the primed atomic labels.
Table 2  Experimental and calculated geometry of the hydrogen bonds for complexes of squaric acid with glycine (1, 1a), sarcosine (2, 2a), dimethylglycine (3, 3a) and betaine (4, 4a) by the B3LYP/6-311G(d,p) approach, as well as calculated energies (E, a.u.) and dipole moments (µ, D)

|    | D−H⋅⋅⋅A  | D−H | H⋅⋅⋅D  | D⋅⋅A  | < DHA | Symmetry code |
|----|----------|------|-------|-------|-------|---------------|
| X-Ray |          |      |       |       |       |               |
| 1   | 0.82     | 1.65 | 2.444(2) | 163(2) |       |               |
| 2   | 0.82     | 1.76 | 2.559(4) |       | 164(2) |               |
| 3   | 0.997    | 1.648 | 2.644 |       | 176.57 |               |
| 4   | 0.987    | 1.693 | 2.671 |       | 170.46 |               |
| B3LYP/6-311G(d,p) |          |      |       |       |       |               |
| 1a  | 0.997    | 1.648 | 2.644 |       | 176.57 |               |
| 2a  | 0.995    | 1.658 | 2.537(2) |       | 170(2) |               |
| 3a  | 1.030    | 1.783 | 2.722 | 149.71 |       |               |
| 4a  | 1.052    | 1.427 | 2.473 | 171.71 |       |               |

scheme 1  Binding of protons to glycine.  

H_2N-CH_2-COO^-  glycine zwitterion
H_2N-CH_2-COO^-  uncharged form of glycine
H_3N^+CH_2-COO^-  glycine nitium (cation)

symmetry independent. The water molecule links complexes of SAR-HSQ into two cyclamers, R_3^+ (16), through four hydrogen bonds: O(5)−H(3)⋅⋅⋅O(3), O(1W)−H(1W)⋅⋅⋅O(3), O(4)−H(4)⋅⋅⋅O(1) and N(1)−H(2N)⋅O(1) of 2.612(1), 2.849(1), 2.528(1) and 2.924(1) Å, respectively, whereas two squaric units of the neighboring molecules form cyclamer R_3^+ (10) through two O(4)−H(4)⋅⋅⋅O(1) hydrogen bonds of 2.528(2) Å (Fig. 5, Table 2).
structure of 2a differs from the crystal of 2, by the lack of interactions between the neighboring molecules. \( \text{H}_2\text{SQ} \) interacts with SAR by the O(3)–H(3)⋯O(5) hydrogen bond of 2.537 Å. The zwitterionic character of sarcosine is confirmed by the C(5)⋯O(5) and C(5)⋯O(6) bond lengths of 1.247 and 1.251 Å, respectively (Table 1). The water molecule is engaged in the O(W)–H(1W)⋯O(6) hydrogen bonds of 2.815 Å with the carboxylate group of the SAR unit. Additionally, the N(1)–H(2N) group forms an intramolecular hydrogen bond with the O(2) atom of 2.722 Å (Table 2).

2.3. Linear dimer of the 2 : 2 complex of dimethylglycine with squaric acid (3 and 3a)

The DMG molecule has an amphoteric character and can exist in an anionic or a cationic form, as well as in two uncharged tautomeric forms, one of which is with neutral amino and
carboxylic groups, which is more stable in the gas phase and
the dipolar zwitterionic form, which is more stable in aqueous
solution.\textsuperscript{11,25} According to a survey of the Cambridge Structural
Database there are only two reports of crystal structures of the
hydrogen-bonded complexes of DMG with acids,\textsuperscript{7} where DMG
exists in the cationic form.

The investigated complex of DMG with H\textsubscript{2}SQ, 3, consists of
two independent 1 : 1 complexes linked together into a linear
dimer by the O(4')–H(4')...O(1) hydrogen bond of 2.624(2) Å
(Fig. 6a, Table 2). In one of these complexes DMG is bonded
to H\textsubscript{2}SQ through the O(3)–H(3)...O(5) and O(4)–H(4)...O(6)
hydrogen bonds of 2.444(2) and 2.527(2) Å, respectively, with
both of its oxygen atoms of the carboxylate group engaged. In
the second 1 : 1 complex, the proton transfer occurs from H\textsubscript{2}SQ
to DMG, and the DMG cation is joined to the hydrogen squarate
anion through the O(5')–H(3')...O(3) hydrogen bond of 2.514(2) Å.
The O(6') atom is not involved in any hydrogen bonds. The
optimized structure of dimer 3a (Fig. 6b) differs slightly from
the crystal structure of 3. In 3a both DMG units exist in the
zwitterionic forms and interact with two H\textsubscript{2}SQ molecules by
the O–H...O hydrogen bonds longer than in the crystal of
3 (Table 2). The complex 3 has the extended conformation,
whereas the optimized complex 3a is bent. The angles between
the plane of the squarate ring in 3 and 3a are 21.37° and 63.18°,
respectively.

In the crystal of 3 the dimers are linked to form two cyclamers
described by the graph set R\textsubscript{6}(30),\textsuperscript{24} where the N–H atoms
engaged in the N(1)–H(1)...O(1') and N(1')–H(1')...O(2) hydrogen
bonds of 2.870(2) and 2.803(2) Å, respectively (Fig. 7, Table 2),
play the main role.

2.4. Cyclic dimer of betainium hydrogen squarate (4, 4a)
The name betaine (BET) is used, when the bonding proton is
not transferred, and betainium (BETH)\textsuperscript{+} when the proton is
transferred from the acid to betaine.\textsuperscript{8c} BET and H\textsubscript{2}SQ form a crystalline complex 4 at the 2 : 2 ratio
(Fig. 8a). In crystal 4 one proton from each squaric acid
molecule is transferred to two BET molecules, generating
hydrogen squarate anions, HSQ\textsuperscript{−} and protonated betaine
cations, BETH\textsuperscript{+}. The HSQ\textsuperscript{−} anions and the BETH\textsuperscript{+} cations are
linked through the asymmetric O(5')–H(4')...O(4) and O(5')–
H(4')...O(4') hydrogen bonds of 2.559(4) and 2.546(4) Å, respec-
tively. Two 1 : 1 complexes are joined into a cyclic dimer by two
non-equivalent O(3)–H(3)...O(2') and O(3')–H(3')...O(2) hydro-
gen bonds of 2.503(4) and 2.501(4), respectively Å (Table 2). The
formation of the \textalpha-dimer is one of the most common ways
of aggregation of HSQ\textsuperscript{−} anions, which are linked by two short
O–H···O hydrogen bonds of 2.47–2.54 Å. All structures containing α-dimers of HSQ⁻ ions have the interesting property of being completely anhydrous, in spite of the fact that most of them crystallized from water. The crystal packing of dimers 4 in the unit cell along the [010] axis is shown in Fig. 9.

The optimized structure of the dimer, 4a, determined by the B3LYP/6-311G(d,p) approach is much more symmetric than that of crystal 4 (Fig. 8b). No protons are transferred from squaric acid to betaine and complexes form a centrosymmetric dimer. The calculated dipole moment is 0.003 D. In the optimized complex 4a, the O(4)–H(4)···O(5) hydrogen bonds of 2.473 Å, which linked H₂SQ and BET molecules, are shorter than those in complex 4, whereas the O(3)–H(3)···O(2) bonds of 2.591 Å, which joined 1:1 complexes into a centrosymmetric dimer are longer than in 4 (Table 2). The presence of H₂SQ molecules in dimer 4a is confirmed by the C(2)–C(3)–C(4) and C(3)–C(4)–C(1) bond angles of 92.74° and 91.39°, respectively, whereas in 4 the C(2)–C(3)–C(4) bond angles in both HSQ⁻ are ca. 93°, while those of C(3)–C(4)–C(1) are 89.0(3)° and 89.1(3)°. A similar centrosymmetric dimer has been found in the crystal and optimized structures of the complex of quinuclidine betaine with squaric acid.

In summary the differences between the crystal forms and optimized structures arise from the lack of N–H···O interactions in all isolated glycine–squaric acid complexes.

2.5. Correlation between the number of N⁺H donors and the number of the methyl groups in glycine derivatives with the ionization of squaric acid

The increasing presence of N⁺H-donors in the glycine derivatives (in the sequence BET → DMG → SAR → GLY) leads to systematic changes in the H-bonding patterns, the molecular arrangement, hydration and, most importantly, in the dissociation of protons transferring from squaric acid to glycine derivatives (Fig. 10). We found that the presence of three N⁺H donors in 1 results in the full dissociation of squaric acid. The dissociation reduces through two N⁺H donors, when even a neutral squaric acid...
molecule was obtained. When $N^+$ donors are absent (in 4), half-dissociated squaric acid anions ($HSO^-$) are observed and they aggregate into doubly $O-H\cdot\cdot\cdot O$ bonded dimers. This process cannot be reproduced by calculations involving one isolated structural unit only, as it does not include $N^+H=O$ bonds to the squaric acid oxygen atoms. Fig. 10 shows the correlation between the frequency of $N^+H=O$ hydrogen bonds as a function of the number of methyl groups in the glycine derivatives (no methyl in GLY, one methyl in SAR, two methyls in DMG and three methyl groups in 2GLY + 3a). This systematic happens for DMG structure 3 attributed to $O_0(O(3,4))=H\cdot\cdot\cdot N$ vibrations, while those at 3212 and 3188 cm$^{-1}$ to the $\nu(O(3),4)=H\cdot\cdot\cdot O(5)$ modes (Fig. 11b).

In the FTIR spectrum of 1 (Fig. 11a) the $\nu NH$ band appears at 3160 cm$^{-1}$, while the $\nu OH$ vibration is assigned to the broad band in the 3000–2000 cm$^{-1}$ region. The calculated asym. and sym. stretching, in-plane bending and out-of-plane bending NH vibrations for GLY units in 1a are observed at 3614 and 3603, 3538 and 3507, 1663 and 1643, 984 and 935 cm$^{-1}$, respectively. The bands at 3367 and 3344 cm$^{-1}$ are attributed to the $\nu(\nu(O(6))=H\cdot\cdot\cdot N$ vibrations, while those at 3212 and 3188 cm$^{-1}$ to the $\nu(O(3),4)=H\cdot\cdot\cdot O(5)$ modes (Fig. 11b).

2.7. Infrared spectra

Amino acids exhibit a great deal of hydrogen bonding as evidenced by the presence of many broad bands in their infrared spectra especially in the region 3000–2000 cm$^{-1}$. The solid-state FTIR spectra of complexes 1, 2, 3 and 4 are shown in Fig. 11a, c, e, g, while the frequencies computed by the B3LYP/6-31G(d,p) approach for optimized structures 1a, 2a, 3a and 4a are shown as vertical lines in Fig. 11b, d, f, h, respectively. The proposed assignments of bands were made using the Gauss View molecular visualization program.

In the FTIR spectrum of 1 (Fig. 11a) the $\nu NH$ band appears at 3160 cm$^{-1}$, while the $\nu OH$ vibration is assigned to the broad band in the 3000–2000 cm$^{-1}$ region. The calculated asym. and sym. stretching, in-plane bending and out-of-plane bending NH vibrations for GLY units in 1a are observed at 3614 and 3603, 3538 and 3507, 1663 and 1643, 984 and 935 cm$^{-1}$, respectively. The bands at 3367 and 3344 cm$^{-1}$ are attributed to the $\nu(O(6))=H\cdot\cdot\cdot N$ vibrations, while those at 3212 and 3188 cm$^{-1}$ to the $\nu(O(3),4)=H\cdot\cdot\cdot O(5)$ modes (Fig. 11b).

In the FTIR spectrum of 2 (Fig. 11c) the bands at 3350, 2830 and 2470 cm$^{-1}$ are assigned to the $\nu O-H$ mode in water, $\nu N-H\cdot\cdot\cdot O$ and $\nu O-H\cdot\cdot\cdot O$ vibrations, respectively. The calculated $\nu O-H$ in water, $\nu N-H\cdot\cdot\cdot O$ and $\nu O-H\cdot\cdot\cdot O$ vibrations for 2a appear at 3640, 2335 and 2715 cm$^{-1}$, respectively (Fig. 11d).

The experimental infrared spectrum of 3 (Fig. 11e) shows broad bands at 2720 and 2480 cm$^{-1}$ attributed to $\nu NH$ and $\nu OH$ modes, respectively. However, in the calculated spectrum of 3a (Fig. 11f) there are several intensive bands at 3365 and 3243 cm$^{-1}$ assigned to the $\nu O(3)=H\cdot\cdot\cdot O(5)$ and $\nu O(4)=H\cdot\cdot\cdot O(6)$ modes, at 3133 cm$^{-1}$ to the $\nu O(4)=H\cdot\cdot\cdot O(1)$ mode, at 2878 cm$^{-1}$ to the $\nu O(3)=H\cdot\cdot\cdot O(5)$ vibration and at 2471 cm$^{-1}$ to the $\nu N-H$ mode of atoms engaged in the strong intramolecular hydrogen bonds (Table 2).

The FTIR spectrum of 4 (Fig. 11g) is characterized by a broad absorption centered at 2450 cm$^{-1}$, which is attributed to the $\nu O-H\cdot\cdot\cdot O$ vibration. A similar absorption is observed in the spectra of betaine complexes with mineral and organic acids, and its shifts to lower or higher wavenumbers depend on the hydrogen bond strength. The calculated frequencies for 4a at 3160 and 2260 cm$^{-1}$ are assigned to the stretching

2.6. 1H and 13C NMR spectra

Both proton and carbon-13 NMR spectra of complexes of glycine and its methyl derivatives with squaric acid are very simple, however the effect of the number of methyl groups attached to the quaternary nitrogen atom on the proton and carbon-13 chemical shifts is significant. With increasing number of methyl groups in glycines the resonance signals of the CH$_2$ and CH$_3$ protons and methylene and methyl carbon-13 atoms are linearly shifted to a lower magnetic field, whereas the resonance signal of the COOH carbon atom undergoes an upfield shift (Fig. S1, ESf?). The proton and carbon-13 chemical shifts are given in the Experimental section. The single $^{13}$C resonance signal of the hydrogen square carbon atoms appear in the lower magnetic field and it is observed between 198.64 and 198.86 ppm. The C=O and C–OH groups can form similarly strong H-bonds to the surrounding water molecules and carboxylate groups, leading to the $\pi$-conjugation of their C=C and C–O bonds.
The vibrations of the O–H groups engaged in the longer O(3)–H···O(1) and shorter O(4)–H···O(5) hydrogen bonds, respectively (Fig. 11h, Table 2).

The broadening of the IR absorption in the spectra of the complexes investigated is also observed in the region below 1500 cm\(^{-1}\). A similar broad band in this region was observed in the infrared spectrum of \(\text{H}_2\text{SQ}\)\(^{29}\) and in the spectra of squaric acid complexes with various bases.\(^{17j,30}\) This broad absorption overlaps the deformation vibrations of the methyl and methylene groups, hydroxyl groups, and ring and skeletal modes. However, the bands in the 1800–1500 cm\(^{-1}\) region are attributed to the \(\nu\text{C}–\text{O}, \nu\text{C}–\text{C}\) and \(\nu\text{COO}\) vibrations. Two bands at 1759 and 1723 cm\(^{-1}\) are assigned to \(\nu\text{C}–\text{O}\) of glycinium moieties in the spectrum of 1. Similarly, the \(\nu\text{C}–\text{O}\) band at 1740 cm\(^{-1}\) was observed in the spectrum of glycinium monophosphonate.\(^{5a}\) In the spectrum of 2 the \(\nu\text{C}–\text{O}\) band at 1729 cm\(^{-1}\) of the sarcosinum cation is observed and it appears in a similar frequency as in the spectrum of sarcosinium iodide.\(^{6d}\) In the spectrum of the complex of 3, both \(\nu\text{as}\text{COO}\) and \(\nu\text{C}–\text{O}\) bands at 1674 and 1731 cm\(^{-1}\) are observed and they are assigned to dimethylglycine and the dimethylglycinium cation, respectively. The band at 1740 cm\(^{-1}\) in the spectrum of 4 confirms the presence of the betainium cation in complex with squaric acid. In the spectrum of the proton-transfer complex of BET with 2,6-dichloro-4-nitrophenol the \(\nu\text{C}–\text{O}\) band appears at 1720 cm\(^{-1}\), while in the spectrum of the molecular complex formed between BET and pentachloro-l-phenylphosphate the \(\nu\text{as}\text{COO}\) band appears at 1664 cm\(^{-1}\).\(^{9b}\)

The frequencies of the squaric acid moiety are much better recognized in the calculated IR spectra than in the experimental ones, where the \(\nu\text{C}–\text{O}\) vibrations appear as a single band in the 1815–1790 cm\(^{-1}\) region. The calculated frequencies from the 1885–1865 cm\(^{-1}\) range are assigned to the \(\nu\text{as}\text{C}–\text{O}\), while those in the 1790–1745 cm\(^{-1}\) region are attributed to the \(\nu\text{as}\text{C}–\text{O}\) modes in the \(\text{H}_2\text{SQ}\) moiety. The spectral features of the squarate units are similar to those observed earlier.\(^{17f,18e,27a,31}\) The experimental and calculated spectra are slightly different, because the experimental spectrum is recorded for the complex in the solid state, while the computations are made for the vibrations of the isolated molecule in the gas phase, and the calculations are based on harmonic frequencies, while the experimental ones are based on the anharmonic frequencies.

The experimental FTIR spectra confirm the crystal structure of the complex investigated, whereas the calculated frequencies correspond well with the structures of the isolated molecules.

The IR data confirm the key information about the proton positions determined in the crystalline complexes by X-ray diffraction.

3. Conclusions

In the crystals of complexes of squaric acid, \(\text{H}_2\text{SQ}\), with glycine, GLY, 1, sarcosine, SAR, 2, dimethylglycine, DMG, 3 and betaine, BET, 4, the proton from \(\text{H}_2\text{SQ}\) is transferred to amino acid molecules. The exception is the 2:2 complex of 3 in which one molecule of DMG is protonated, while the other remains in the zwitterionic form. In the optimized structures of one unit of complexes investigated (1a, 2a, 3a, 4a) by the B3LYP/6-311G(d,p) approach, the amino acid moieties are in their zwitterionic forms with the exception of 1a, in which GLY exists...
in an uncharged (neutral) form. The HSQ− and amino acid molecules are linked by the O–H···O hydrogen bonds with the O···O distances from 2.444 to 2.624 Å. Depending on methylation of glycine in its co-crystals with squaric acid, its dianion, monoanion, neutral and mixed forms are stabilized. Methylation of glycine gradually reverses the dissociation of squaric acid in crystals. The resonance signals of the proton and carbon-13 of the methylene and methyl groups are shifted to a lower magnetic field with increasing number of methyl groups attached to the amino group, while the resonance signal of the carboxylic group is linearly shifted to a higher magnetic field.

4. Experimental section

4.1. General procedure

Amino acids, GLY, SAR and DMG were purchased from Aldrich Chemical Co., whereas BET from Sigma. FTIR spectra were measured in Nujol and Fluorolube suspensions between KBr plates using a Bruker IFS 66/S instrument, with a resolution of 2 cm−1. Each spectrum was accumulated for 64 scans. The NMR spectra were recorded using a Varian VNMRS-400 spectrometer operating at 402.6435 and 101.2440 MHz for 1H and 13C, respectively. The spectra were measured in D2O relative to an internal standard of 3-(trimethylsilyl)propionic-d4 acid sodium salt. Elemental analysis was made using an Elemental Model Vario EL III.

4.2. Preparations

4.2.1. Synthesis of diglycinium squarate (1). 0.85 g of GLY and 0.64 g of H2SQ were dissolved in 2 mL of water. The solvent was evaporated and the residue was recrystallized from a mixture of methanol–water (2 : 1), m.p. 180 °C. Elemental analysis calculated for C8H10N2O8: %C, 36.65; %H, 3.84; %N, 10.68; found: %C, 36.33; %H, 3.75; %N, 10.43. 1H NMR (D2O, ppm) δ 3.89 (CH3); 13C NMR (D2O, ppm) δ 43.07 (CH3), 51.96 (CH3), 172.28 (COO), 198.86 (C–O, H2SQ).

4.2.2. Synthesis of sarcosinium hydrogen squarate hemihydrate (2). To 0.60 g of SAR in 2 mL of a methanol–water mixture (2 : 1), 0.76 g of H2SQ in 1 mL water was added. The solvents were evaporated and the residue was recrystallized from a mixture of methanol–water (2 : 1), m.p. 163–164 °C. Elemental analysis calculated for C14H18N2O12: %C, 39.63; %H, 4.75; %N, 6.60; found: %C, 39.47; %H, 4.74; %N, 6.45. 1H NMR (D2O, ppm) δ 2.80 (CH3), 3.93 (CH2); 13C NMR (D2O, ppm) δ 35.67 (CH3), 51.96 (CH3), 172.28 (COO), 198.86 (C–O, H2SQ).

4.2.3. Synthesis of the 2 : 2 complex of dimethylglycine with squaric acid (3). 0.40 g of DMG and 0.44 g of H2SQ were dissolved in 1 mL of water. The crystals were filtered off and recrystallized from a mixture of methanol–water (3 : 1), m.p. 182–183 °C. Elemental analysis calculated for C9H13NO6: %C, 44.24; %H, 5.10; %N, 6.45; found: %C, 44.15; %H, 5.03; %N, 6.10. 1H NMR (D2O, ppm) δ 2.99 (CH3), 4.06 (CH2); 13C NMR (D2O, ppm) δ 46.70 (CH3), 60.58 (CH2), 171.41 (COO), 198.64 (C–O, H2SQ).

4.2.4. Synthesis of betainium hydrogen squarate (4). 0.67 g of BET and 0.46 g of H2SQ were dissolved in 2 mL of water. The crystals were filtered off and recrystallized from methanol, m.p. 191 °C. Elemental analysis calculated for C12H22N2O12: %C, 46.76; %H, 5.67; %N, 6.06; found: %C, 46.64; %H, 5.61; %N,

| Table 3 Crystal data and structure refinement for complexes of squaric acid with glycine (1), sarcosine (2), dimethylglycine (3) and betaine (4) |
|---------------------------------------------------------------|
| 1 | 2 | 3 | 4 |
| Empirical formula | C8H10N2O8 | C14H18N2O12H2O | C12H22N2O12 | C14H13NO8 |
| Formula weight | 264.20 | 424.32 | 434.36 | 213.20 |
| Temperature (K) | 296(2) | 296(2) | 296(2) | 296(2) |
| Wavelength (Å) | 1.71073 | 1.54184 | 0.71073 | 0.71073 |
| Crystal system | Monoclinic | Monoclinic | Monoclinic | Orthorhombic |
| Space group | C2/c | C2/c | P21/c | Pcc21 |
| Unit cell dimensions | | | | |
| a (Å) | 16.8392(3) | 16.6068(2) | 17.5110(5) | 21.8227(8) |
| b (Å) | 8.3163(2) | 7.21436(8) | 6.5385(2) | 1836.43(4) |
| c (Å) | 15.8267(3) | 15.4410(17) | 17.3475(4) | 1886.32(9) |
| β (°) | 90.063(2) | 97.0249(11) | 90.00 | 90.00 |
| Volume (Å3) | 2182.27(8) | 1836.43(4) | 1886.32(9) | 2191.4(2) |
| Calculated density (g cm−3) | 1.608 | 1.535 | 1.529 | 1.402 |
| 1/w coefficient (mm−1) | 0.146 | 1.213 | 0.133 | 0.119 |
| F(000) | 1104 | 888 | 912 | 976 |
| Crystal size (mm) | 0.18 × 0.22 × 0.36 | 0.16 × 0.26 × 0.33 | 0.22 × 0.28 × 0.38 | 0.19 × 0.23 × 0.38 |
| θ range for data collection (°) | 3.13–27.59 | 5.37–75.31 | 2.47–29.13 | 2.22–29.14 |
| Max/min indices k, l | −20/20, −11/10, −19/19 | −20/20, −8/7, −18/19 | −23/22, −7/8, −23/22 | −29/20, −5/8, −22/18 |
| Reflections collected/unique | 10909/2371 | 6657/1962 | 11666/4520 | 862/1068 |
| | 0.0156 | 0.0098 | 0.0206 | 0.0353 |
| Completeness (%) | 93.5 | 98.0 | 89.3 | 88.7 |
| Refinement method | Full-matrix least-squares on F2 | Full-matrix least-squares on F2 | Full-matrix least-squares on F2 | Full-matrix least-squares on F2 |
| Data/restraints/parameters | 2371/0/199 | 1862/0/147 | 4520/0/341 | 4068/1/297 |
| Goodness-of-fit on F2 | 0.697 | 0.807 | 0.968 | 0.766 |
| Final R/Fo values [I > 2sigma] | 0.0382/0.1098 | 0.0331/0.1013 | 0.0318/0.0970 | 0.0400/0.0891 |
| R1/WR1 values (all data) | 0.0420/0.1159 | 0.0337/0.1020 | 0.0610/0.1042 | 0.0942/0.1069 |
| Largest diff. peak and hole (e Å−3) | 0.296 and −0.278 | 0.234 and −0.141 | 0.297 and −0.328 | 0.156 and −0.185 |
6.02. $^1$H NMR (D$_2$O, ppm) δ 3.32 (CH$_3$), 4.21 (CH$_2$); $^{13}$C NMR (D$_2$O, ppm) δ 56.73 (CH$_3$), 66.88 (CH$_3$), 170.30 (COO), 198.73 (C=O, H$_2$SO).

4.3. Single crystal X-ray diffraction

X-ray diffraction data of complexes were collected on a KUMA KM-4 CCD diffractometer. The structure was solved by direct methods using SHELXS-97 and refined on $F^2$ by the full-matrix least-squares with SHELXL-97. The crystal data, details of data collection and structure refinement are given in Table 3 and the final atomic coordinates in Table S3 of ESI.

4.4. Computation details

The DFT calculations were performed using the GAUSSIAN 03 program package. The calculations employed the B3LYP exchange–correlation functional, which combines the hybrid exchange functional of Becke with the gradient-correlation functional of Lee et al. and the split-valence polarized 6-311G(d,p) basis set. The X-ray geometry was used as a starting point for the calculations. The calculated IR frequencies are positive and confirmed that the optimized structures were in the states of minimum energy.

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References

1. (a) J. H. Caldwell, N. W. Daw and H. J. Wyatt, J. Physiol., 1978, 276, 277–298; (b) L. Rajendra, J. W. Lynch and P. Schofield, PharmacoL Ther., 1997, 73, 121–146; (c) P. Schofield, Adv. Neurol., 2002, 89, 263–274.

2. (a) H. D. Jakubke and H. Jeschkeit, Aminosäuren, Peptide, Proteine, Akademischer Verlag, Berlin, 1982; (b) H.-L. Lane, C.-L. Huang, P.-L. Wu, Y.-C. Liu, Y.-C. Chang, P.-Y. Lin, P.-W. Chen and G. Tsai, Biol. Psychiatry, 2006, 60, 645–649.

3. (a) R. N. Girandola, R. A. Wiswell and R. Bulbulian, Biochem. Med., 1980, 24, 218–222; (b) W. M. Bolman and J. A. Richmon, J. Autism Dev. Disord., 1999, 29, 191–194; (c) M. E. Tonda and L. L. Hart, Ann. Pharmacother., 1992, 26, 935–937.

4. (a) X. Domingo, in Betaines in Ampholytic Surfactants, ed. E. G. Lomax, Marcel Dekker Inc, New York, 1996, vol. 59, pp. 75–190; (b) N. Van Thoai, in Nitrogenous Bases in Comprehensive Biochemistry, ed. M. Florkin and E. H. Stotz, Elsevier Publ. Comp. Amsterdam, 1965, vol. 6, pp. 208–252; (c) G. Blunden and S. M. Gordon, Prog. Physiol. Res., 1986, 4, 39–80; (d) W. A. Rees, T. D. Yager, J. Korte and P. H. von Hippel, Biochemistry, 1993, 32, 137–144.

5. (a) T. Gliowiak and A. W. Szemik, J. Crystallogr. Spectrosc. Res., 1986, 16, 79–89; (b) S. Natarajan, K. Ravikumar and S. S. Rajan, Z. Kristallogr., 1984, 168, 75–82; (c) A. R. Al-Karaghouli, F. E. Cole, M. S. Lehmann, C. F. Miskell, J. J. Verbit and T. F. Koetzle, J. Chem. Phys., 1975, 63, 1360–1366; (d) J. Baran, K. Łukaszewicz, A. Pietraszko and M. Śledź, J. Mol. Struct., 2002, 611, 155–168; (e) D. Tran Qui, B. Lambert-Andron and J. X. Boucherle, Acta Crystallogr., Sect. C: Cryst. Struct. Commun., 1987, 43, 907–909; (f) D. Tran Qui, J. Vicat and A. Durif, Acta Crystallogr., Sect. C: Cryst. Struct. Commun., 1984, 40, 181–184; S. Natarajan, Z. Kristallogr., 1983, 163, 305–306; (g) T. Gliowiak and I. Wnuk, J. Kristallogr. Spectrosc. Res., 1985, 15, 157–171.

6. (a) S. C. Bhattacharyya and N. N. Saha, J. Mol. Struct., 1978, 8, 105–113, 209–215; (b) R. V. Krishnakumar and S. Natarajan, J. Mol. Struct., 1995, 380, 825–830; (c) M. T. Averbuch-Pouchot, Z. Kristallogr., 1988, 183, 285–291; M. T. Averbuch-Pouchot, Z. Kristallogr., 1993, 207, 149–150; (d) V. V. Ghazaryan, M. Fleck and A. M. Petrosyan, J. Mol. Struct., 2013, 1032, 35–40; (e) R. V. Krishnakumar, M. P. Rameela and S. Natarajan, Cryst. Res. Technol., 1996, 31, 203–207; (f) J. Mostad and S. Natarajan, Cryst. Res. Technol., 1996, 31, 295–300.

7. (a) B. D. Santarsiero and R. E. Marsh, J. Crystallogr. Spectrosc. Res., 1983, 11, 245–251; (b) V. H. Rodrigues, J. A. Piaxão, M. M. R. Costa and A. M. Matos Beja, Acta Crystallogr., Sect. C: Cryst. Struct. Commun., 2001, 57, 417–420.

8. (a) J. Baran, M. Drozd, T. Gliowiak, M. Śledź and H. Ratajczak, J. Mol. Struct., 1995, 372, 131–144; (b) M. Iczyszyn, D. Godisz and M. M. Iczyszyn, J. Mol. Struct., 2003, 611, 103–118; (c) D. Godisz, M. M. Iczyszyn and M. Iczyszyn, J. Mol. Struct., 2002, 606, 123–137; (d) W. H. Yip, R.-J. Wang and T. C. W. Mak, Acta Crystallogr., Sect. C: Cryst. Struct. Commun., 1990, 46, 717–719; (e) J. Baran, M. Drozd, T. Lis, M. Śledź, A. J. Barnes and H. Ratajczak, J. Mol. Struct., 1995, 354, 109–118; (f) D.-D. Wu and T. W. C. Mak, J. Chem. Crystallogr., 1994, 24, 689–694.

9. (a) Z. Dega-Szafran, I. Kowalczyk and M. Szafran, Bull. Pol. Acad. Sci., Chem., 1995, 43, 303–312; (b) Z. Dega-Szafran, A. Komasa, M. Grundwald-Wypianśka, M. Szafran, G. Buczak and A. Katusiak, J. Mol. Struct., 1997, 404, 13–23; (c) M. M. Iczyszyn, T. Lis and H. Ratajczak, J. Mol. Struct., 1995, 372, 9–27; (d) J. Baran, A. J. Barnes, B. Engelen, M. Panthofer, A. Pietraszko and H. Ratajczak, J. Mol. Struct., 1995, 372, 29–40.

10. (a) S. Haussühl, Z. Kristallogr., 1989, 188, 311–320; (b) S. Sato, J. Phys. Soc. Jpn., 1968, 25, 185–201; (c) G. Schaack, Ferroelectrics, 1990, 104, 147–158.

11. A. D. Headley, R. E. Corona and E. T. Cheung, J. Phys. Org. Chem., 1997, 10, 898–900.

12. (a) A. H. Schmidt, Synthesis, 1980, 961–994; (b) M. Panigrahi, S. Dash, S. Patel and B. K. Mishra, Tetrahedron, 2012, 68, 781–805.

13. L. I. Markova, V. L. Malinovskii, L. D. Patsenker and R. Häner, Org. Biomol. Chem., 2012, 10, 8944–8947.

14. (a) Y. Wang, G. D. Stucky and J. M. Williams, J. Chem. Soc., Perkin Trans. 2, 1974, 35–38; (b) D. Semmingsen, F. J. Hollander and T. F. Koetzle, J. Chem. Phys., 1977, 66, 4405–4412; (c) F. J. Hollander, D. Semmingsen and
T. F. Koetzle, J. Chem. Phys., 1977, 67, 4825–4831; (d) D. Semmingsen, Acta Chem. Scand., Ser. A, 1973, 27, 3961–3972; (e) A. Katsusiak and R. J. Nelmès, J. Phys. C: Solid State Phys., 1986, 19, L765–L772.

15 (a) S. Cohen, J. R. Lacher and J. D. Park, J. Am. Chem. Soc., 1959, 81, 3480; (b) D. J. MacDonald, J. Org. Chem., 1968, 33, 4559–4560; (c) D. T. Ireland and H. F. Walton, J. Phys. Chem., 1967, 71, 751–754.

16 R. West and D. L. Powell, J. Am. Chem. Soc., 1963, 85, 2577–2579.

17 (a) G. Gilli, V. Bertolasi, P. Gilli and V. Ferretti, Acta Crystallogr., Sect. B: Struct. Sci., 2001, 57, 859–865; (b) G. Gilli and P. Gilli, The Nature of the Hydrogen Bond, Outline of a Comprehensive Hydrogen Bond Theory, Oxford University Press, 2009, pp. 251–253; (c) V. Bertolasi, P. Gilli, V. Ferretti and G. Gilli, Acta Crystallogr., Sect. B: Struct. Sci., 2001, 57, 591–598; (d) B. B. Koleva, T. Kolev, R. W. Seidel, M. Spiteller, H. Mayer-Figge and W. S. Sheldrick, J. Phys. Chem. A, 2009, 113, 3088–3095; (e) S. Mathew, G. Paul, K. Shivasanankar, A. Choudhury and C. N. R. Rao, J. Mol. Model., 2002, 8, 261–279; (f) B. B. Koleva, T. Kolev, R. W. Seidel, H. Mayer-Figge, M. Spitteler and W. S. Sheldrick, J. Phys. Chem. A, 2008, 112, 2899–2905; (g) T. Kolev, R. Wortmann, M. Spitteler, W. S. Sheldrick and M. Heller, Acta Crystallogr., Sect. E: Struct. Rep. Online, 2004, 60, 0956–0957; (h) A. Bulut, O. Z. Yeşilöl, N. Dege, H. Icbudak, H. Olmez and O. Büyükükgör, Acta Crystallogr., Sect. C: Crystallogr. Commun., 2003, 59, o727–o729; (i) I. Uçar, A. Bulut, O. Z. Yeşilöl and O. Büyükükgör, Acta Crystallogr., Sect. C: Crystallogr. Commun., 2004, 60, o585–o588; (j) B. B. Koleva, T. Kolev, R. W. Seidel, T. Tsanev, H. Mayer-Figge, M. Spitteler and W. S. Sheldrick, Spectrochim. Acta, Part A, 2008, 71, 695–702; (k) I. L. Karle, D. Ranganathan and V. Haridas, J. Am. Chem. Soc., 1996, 118, 7128–7133.

18 (a) T. Kolev, D. Yancheva, M. Spitteler, W. S. Sheldrick and H. Mayer-Figge, Acta Crystallogr., Sect. E: Struct. Rep. Online, 2006, 62, o463–o465; (b) O. Angelova, R. Petrova, V. Radomirska and T. Kolev, Acta Crystallogr., Sect. C: Crystallogr. Comm., 1996, 52, 2218–2220; (c) O. Angelova, V. Velikova, T. Kolev and V. Radomirska, Acta Crystallogr., Sect. C: Crystallogr. Comm., 1996, 52, 3252–3256; (d) T. Kolev, H. Mayer-Figge, R. W. Seidel, W. S. Sheldrick, M. Spitteler and B. B. Koleva, J. Mol. Struct., 2009, 919, 246–254; (e) T. Kolev, R. Stahl, H. Preut, V. Konicek, P. Bleckmann and V. Radomirska, Z. Kristallogr. - New Crystal. Struct., 1998, 213, 167–169; (f) T. Kolev, R. Stahl, H. Preut, P. Bleckmann and V. Radomirska, Z. Kristallogr. - New Crystal. Struct., 1998, 213, 169–170; (g) T. Kolev, Z. Glavcheva, R. Stahl, H. Preut, P. Bleckmann and V. Radomirska, Z. Kristallogr. - New Crystal. Struct., 1999, 214, 193–194; (h) T. Kolev, M. Spitteler, W. S. Sheldrick and H. Mayer-Figge, Acta Crystallogr., Sect. C: Crystallogr. Comm., 2006, 62, o299–o300; (i) T. Kolev, M. Spitteler, W. S. Sheldrick and H. Mayer-Figge, Acta Crystallogr., Sect. C: Crystal. Struct. Comm., 2005, 61, o4292–o4294.
1018, 28–34; (h) P. Barczyński, Z. Dega-Szafran, A. Katrusiak and M. Szafran, J. Mol. Struct., 2012, 1013, 95–101; (i) Z. Dega-Szafran, A. Katrusiak, A. Komasa and M. Szafran, Supramol. Chem., 2013, 25, 432–440.

32 (a) KUMA KM4 CCD Software, version 161, Kuma Diffraction, Wroclaw, Poland, 1999; (b) CrysAlis 162, Kuma Diffraction, Wroclaw, Poland, 1999.

33 G. M. Sheldrick, Acta Crystallogr., Sect. A: Found. Crystallogr., 2008, 64, 112–122.

34 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, GAUSSIAN 03, Revision C.02, Gaussian, Inc., Wallingford CT, 2004.

35 A. D. Becke, J. Chem. Phys., 1993, 98, 5648–5652; A. D. Becke, J. Chem. Phys., 1997, 107, 8554–8580.

36 C. Lee, W. Yang and G. R. Parr, Phys. Rev. B: Condens. Matter Mater. Phys., 1988, 37, 785–789.

37 W. J. Hehre, L. Random, P. V. R. Schleyer and J. A. Pople, Ab Initio Molecular Orbital Theory, Wiley, New York, 1986.