Theoretical Investigation of Electronic Structure and Nuclear Quadrupole Interactions in Cocaine Free Base

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The nuclear quadrupole interaction (NQI) parameters for the ^{14}N nucleus, namely, the quadrupole coupling constant (e^2qQ) and asymmetry parameter (η) have been obtained through first-principles Hartree−Fock investigations on cocaine free base ($C_{17}H_{21}NO_4$). The calculated value −5.038 MHz of e^2qQ is in very good agreement with the experimentally observed magnitude of 5.0229 for e^2qQ, and the small value 0.067 for η is in keeping with the value of 0.0395 from nuclear quadrupole resonance measurements. These results provide strong support for the nature of the electron distribution in the cocaine molecule, including its anisotropy around the ^{14}N nucleus, obtained by the first-principles Hartree−Fock method, in common with the conclusion from recent investigations on the energetic molecules RDX (1,3,5-trinitro-*S*-triazine, $C_3H_6N_6O_6$) and β-HMX (octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine, $C_4H_8N_8O_8$). Additional support for this conclusion is provided by the fact that the positions of three hydrogen atoms in cocaine obtained from structural measurements were reported erroneously in the literature and were redetermined in the present work through total energy minimization by the Hartree−Fock procedure, the calculated results for e^2qQ and η for ^{14}N being based on these corrected H positions. Possible sources that could resolve the small but significant difference for η between theory and experiment are discussed. The calculated NQI parameters for ^{17}O and ^{2}H (deuteron) are presented for cocaine with the hope that they will be measured in the future to allow comparison with theory and thus provide a more complete picture of the electron distribution in this molecule.

I. Introduction

Recently there is considerable interest[1,2] in the study of the spectroscopic properties of molecules of physiological interest. A property of special interest is the nuclear quadrupole interaction of the ^{14}N nucleus in cocaine free base ($C_{17}H_{21}NO_4$), which is well known for its narcotic effects. A major reason for the present study is that recently there is substantial effort being made[2,3] to use ^{14}N as a sensor, for the detection of compounds with physiological or energetics interest, using nuclear quadrupole resonance (NQR) spectroscopy. Since the frequency of the NQR signal depends upon the NQI parameters[4] e^2qQ and η for the nucleus in question,[5] which in turn depend sensitively[6] on the nature of the electron distribution in the neighborhood of the nucleus of interest, the quantitative understanding of the latter from a first-principles quantum mechanical study is of primary interest in this context. Additionally, this information is also important to obtain insights about the changes in the nuclear quadrupole interaction parameters when one introduces molecular groups[2] that can interact with the basic molecule and change the geometry and the electron distribution. In the present paper, we have investigated the electronic structure of cocaine free base, for which experimental information on the ^{14}N nuclear quadrupole interaction[2] has recently become available.

In cocaine there is one ^{14}N nucleus, and hence only one set of nuclear quadrupole interaction parameters e^2qQ and η is observed experimentally.[2] At room temperature, 295 K, the observed values of the nuclear quadrupole coupling constant (e^2qQ) and asymmetry parameter (η) are 5.0229 MHz and 0.0395, respectively. Our aim in this paper is to examine how well one can explain these observed parameters from electronic structure investigations using a first-principles procedure. We have used the variational Hartree−Fock−Roothaan procedure[7] for the present investigation with the variational functions used being based on Gaussian basis functions,[8] in common use currently because of the economy involved in the computation of matrix elements of the Hamiltonian in the Hartree−Fock formalism. The nuclear quadrupole interaction parameters for deuterons replacing the protons in this molecule and for ^{17}O nuclei at the oxygen positions have also been determined in our work with the expectation that they will be measured in the future. Comparison with our predicted results will then provide additional tests of the correctness of the calculated electron distributions in the present work.

In section II we have discussed briefly the procedure employed for the present study. Our results and discussion are presented in section III. Section IV summarizes the conclusions from our analysis with possible suggestions for future work that would be useful to broaden our knowledge of the electron distribution in this system.

II. Procedure

As pointed out in the preceding section, we have used the Gaussian-based variational Hartree−Fock−Roothaan[7,8] proce-

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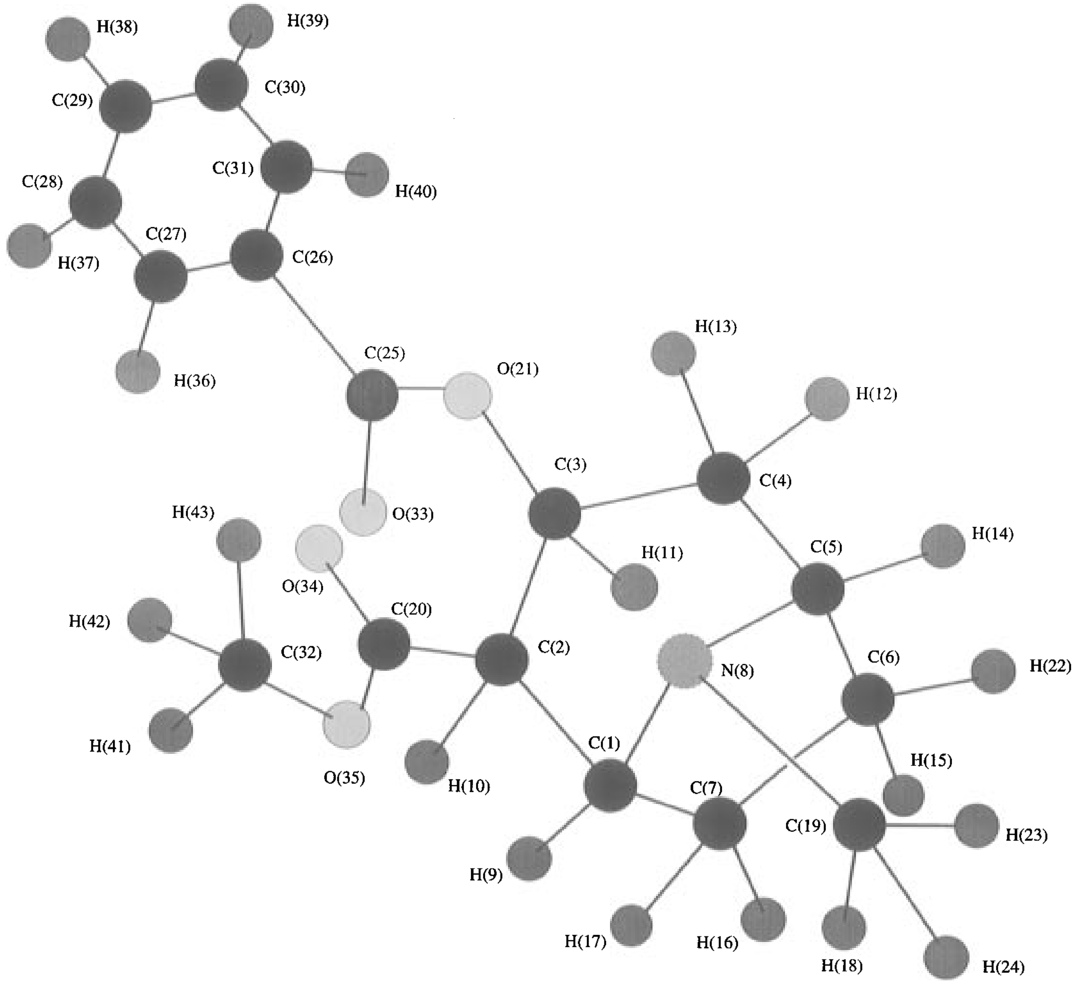

Figure 1. Atomic arrangement in cocaine free base ($C_{17}H_{21}NO_4$). This arrangement is based on the atomic coordinates given in ref 10 except for hydrogens 22−24, which have been determined by the energy optimization procedure discussed in the text, the coordinates for the latter three atoms being presented in Table 1. A gap has been introduced in the line joining C(6) and C(7) to indicate that the N(8)−C(19) bond is above the C(6)−C(7) bond, the atoms C(1) and C(5) through C(7) lying below the N(8) atom and C(19) above the latter.

dure to determine the energy levels and wave functions for the electrons. This procedure is documented extensively in the literature and hence will not be presented here in detail. Only a few points related to the present investigation will be discussed. Since the current system involves an even number of electrons, it is sufficient to use the restricted Hartree−Fock approximation[9] in which both the spin up and spin down electrons in a particular orbital state have the same molecular orbital wave function. We have used linear combinations of Gaussian basis functions[8] for our variational Hartree−Fock−Roothaan investigations, as is the current practice, since, as mentioned in section I, this allows fast evaluation of multicenter integrals in molecular problems.

The atomic arrangement in cocaine free base is depicted in Figure 1, which consists of 43 atoms and 162 electrons. The positions of the various atoms in the molecule, other than hydrogen, are obtained by X-ray diffraction measurements in cocaine hydrochloride molecule.[10] For obtaining the hydrogen positions, a three-dimensional Patterson analysis[11] is used together with the results from X-ray diffraction. However, in the publication[10] presenting the structure, there were some problems with the positions of three of the hydrogens in cocaine, namely, H(22), H(23), and H(24) in Figure 1. When we analyzed the distance matrix, taking the positions from the published structure, we found the corresponding CH bond distances to be 6.6, 7.19, and 6.86 Å, respectively, which are very high compared to 1.09 Å, the usual[12] single-bond CH distance. All the other bond distances were found to be in the range expected both from the covalent radii for the atoms concerned and from the observed bond distances in other molecules. In particular, all the rest of the CH bond distances were in the expected range of 1.06−1.09 Å. To obtain the correct positions for the three hydrogen atoms H(22)−H(24), we followed an optimization procedure that requires one to minimize the total Hartree−Fock energy with respect to simultaneous variations in the positions of these three hydrogens. But such a procedure for a molecule like cocaine involving 162 electrons is quite time-consuming. Hence we followed a procedure involving a few simplifications. First we truncated this large molecule with 43 atoms to two smaller fragments consisting of 17 and 24 atoms, respectively, the two sizes being used to study convergence with respect to cluster sizes. In both these cases, the ends of the two truncated fragments are approximately equidistant from the nitrogen atom, whose nuclear quadrupole interaction parameters are of interest to us. The truncated end is terminated with hydrogen atoms as one does in the Hartree−Fock cluster procedure in solid state systems.[13] The second simplification that we have used is to choose a minimal basis set involving the STO-3G approximation,[14] where three Gaussians are used to represent a single Slater exponential orbital for each state of the atom. Although the STO-3G basis set does not have as much flexibility for variational calculations as other larger basis sets have, it can provide a reasonably accurate description of the geometry of the molecules while

TABLE 1: Results for Selected Hydrogen Positions[a] Obtained through Energy Optimization in Cocaine Free Base System

cluster size[b]	nuclei[a]	X	Y	Z	L(CH)[c]
17	H(22)	5.966	−2.604	8.383	1.112
17	H(23)	7.705	−4.193	5.830	1.093
17	H(24)	7.939	−2.811	4.727	1.084
24	H(22)	5.972	−2.632	8.395	1.101
24	H(23)	7.705	−4.193	5.830	1.093
24	H(24)	7.939	−2.812	4.727	1.084

[a] H(n) in the table refers to the position of the hydrogen labeled by n in Figure 1. These hydrogens are the ones whose positions appeared to be erroneous in ref 10 for the molecular structure and have been redetermined here through energy minimization for the cocaine molecule. X, Y, and Z refer to the same coordinate system used in ref 10. [b] Refers to the number of atoms used in the truncated fragment employed in the energy optimization calculation. [c] Refers to the lengths of the CH bonds between the hydrogen atoms and their nearest carbon neighbors.

reducing the computational effort, as has been seen from an earlier investigation in C_{60} fullerene,[15] where the use of the STO-3G basis set led to C−C bond distances within 1−2% of experimental results. Using these simplifications, we optimized the positions of the three hydrogens, H(22), H(23), and H(24), in both the 17 and 24 atoms clusters. Minimization of the total Hartree−Fock energies for these two clusters with respect to the variation of these three hydrogen positions, for which the published position parameters were apparently incorrect, leads to bond distances for these hydrogens with respect to their nearest neighbor carbon atoms of 1.11, 1.09, and 1.08 Å for the 17-atom cluster, almost identical with the values 1.10, 1.09, and 1.08 Å found for the 24-atom cluster as listed in Table 1. These results suggest that there is a very good convergence in the positions of the three hydrogen atoms with respect to the sizes of the clusters chosen. The good agreement between the two sets of CH bond distances suggests that the hydrogen positions obtained either from the 17-atom cluster or the 24-atom cluster can be considered to be representative of the whole cocaine molecule with little loss of accuracy. Additionally, since these hydrogen atoms are two to three atoms away from the nitrogen atom containing the ^{14}N nucleus, whose nuclear quadrupole interaction is of interest, any small errors in our calculated positions for these atoms is not expected to significantly affect the calculated electric field gradient tensor at the ^{14}N site. From these considerations, we have made use of the positions for the hydrogens H(22), H(23), and H(24) which are obtained from the optimization in the larger 24-atom cluster as representative of the full cocaine molecule for our electronic structure investigations to obtain the electric field gradient tensor (efg) at the ^{14}N nucleus, for study of its NQI parameters.

The efg tensor components at the nucleus are obtained using the following expressions:[16]

$$V_{jk} = \sum_N \zeta_N \frac{(3R_{jN}R_{kN} - {R_N}^2\delta_{jk})}{{R_N}^5} - 2\sum_\mu \left\langle \psi_\mu \left| \frac{3r_jr_k - r^2\delta_{jk}}{r^5} \right| \psi_\mu \right\rangle \qquad (1)$$

the indices j and k ranging from 1 to 3 representing the X, Y, and Z coordinates. The first term on the right-hand side of eq 1 represents the contribution from the nuclear charges in the molecule, and the second term represents the contributions from the electrons. In the first term, ζ_N is the nuclear charge for the Nth nucleus, R_{jN} and R_{kN} representing the components of the position vector $\mathbf{R_N}$ for the Nth nucleus with respect to the nucleus at which the efg tensor is being studied, with R_N representing the magnitude of $\mathbf{R_N}$, the distance between the latter nucleus and nucleus N. In the second term on the right in eq 1, the summation over μ is carried out over all the occupied orbitals, ψ_μ representing the wave functions for the μth occupied orbital. The factor 2 arises from the summation over the spin up and spin down states since both states have the same wave functions because of the zero total spin for the molecule. In this second term, r refers to the magnitude of $\mathbf{r}$, the position vector of the electron with respect to the nucleus at the site of which the efg is under study, r_j and r_k representing the components of this position vector. The field gradient tensor with components V_{jk} obtained from eq 1 is diagonalized to give the principal components $V_{j'k'}$. The parameter q in the quadrupole coupling constant e^2qQ, where Q is the nuclear quadrupole moment, is given by principal component $V_{z'z'}$ with the largest magnitude. The convention for choosing the principal axes (X', Y', Z') is such[4] that $|V_{x'x'}| < |V_{y'y'}| < |V_{z'z'}|$, and the asymmetry parameter $\eta = (V_{x'x'} - V_{y'y'})/V_{z'z'}$. It should be noted that since we are dealing with all the electrons in our calculation including the core electrons as well, Sternheimer shielding (or antishielding)[17] effects are directly included,[16,18] and hence there is no need to introduce them through Sternheimer shielding (or antishielding) parameters.[17]

TABLE 2: ^{14}N Nuclear Quadrupole Coupling Constant and Asymmetry Parameter for Cocaine Free Base System

		e^2qQ (MHz)		η	
cluster size[a]	basis set	theory	expt[c]	theory	expt[c]
17	STO-3G[b]	−5.736	5.0229	0.024	0.0395
24	STO-3G	−5.682	5.0229	0.033	0.0395
43	STO-3G	−5.673	5.0229	0.030	0.0395
24	D95v[b]	−4.983	5.0229	0.046	0.0395
43	D95v	−5.030	5.0229	0.068	0.0395
24	D95[b]	−4.990	5.0229	0.045	0.0395
43	D95	−5.038	5.0229	0.067	0.0395

[a] Refers to the different cluster sizes used with nitrogen as origin, with 43 atoms referring to the complete cocaine molecule. [b] STO-3G basis sets are taken from ref 14; D95v and D95 basis sets are taken from ref 19. [c] Experimental results are taken from ref 2, only the magnitude of e^2qQ having been determined but not its sign.

The choice of the basis functions determines the accuracy of the molecular orbital wave functions ψ_μ and is expected to influence the efg tensor more sensitively than the total energy and interatomic distances, because these properties involve averages over the entire region of the molecule, while the efg tensor involves the region near the vicinity of the nucleus under study. Because of this reason, we have studied the efg tensor with three basis sets, the STO-3G basis set[14] as well as two more extensive basis sets referred to as D95v and D95[19] in the literature, which were utilized in our earlier investigations[6,20] on the energetic molecules RDX and β-HMX. The D95v basis set allows for much more flexibility than STO-3G in the variational calculation of the valence molecular orbitals, the D95 basis function in addition allowing for increased flexibility in the core orbital wave functions, a property that is very important for the incorporation of Sternheimer shielding or antishielding effects in the components of the efg tensor. The latter choice of D95 basis set was found in earlier investigations on RDX and β-HMX and other systems to lead to results that changed very little on uncontracting[6,18,20] some of the contracted Gaussian basis functions used in the D95 basis set suggesting that good convergence has been reached for the efg tensor with respect to choice of basis functions. We have calculated the nuclear quadrupole coupling constants (e^2qQ) and asymmetry parameters (η) for both the truncated fragments as well as for the full cocaine molecule, with the results presented in Table 2. The theoretical evaluation of e^2qQ requires a knowledge of the nuclear quadrupole moment Q of the ^{14}N nucleus for which we have used the value 0.015 barns[21] as in earlier work. This choice of Q is obtained[21] from an accurate many-body calculation of the efg in the ground state of the nitrogen atom for which the experimental value for e^2qQ is available. To have an idea about the sizes of basis sets used for the molecular orbital calculation for the full cocaine molecule containing 162 electrons, the STO-3G choice involves 131 basis functions and 393 primitive Gaussians, D95v involves 240 basis functions and 634 primitives, and D95 involves 262 basis functions and 612 primitives.

III. Results and Discussion

We turn next to the results of our calculation for the nuclear quadrupole interaction parameters e^2qQ and η for the ^{14}N, ^{17}O, and ^{2}H nuclei following the procedure for obtaining the electronic wave functions and the evaluation of the efg tensor components described in the preceding section.

As regards the geometry, as briefly mentioned in section II, we have utilized the position parameters of the various atoms, based on the structural data[10] obtained from X-ray analysis of cocaine hydrochloride. For determining the hydrogen positions in cocaine hydrochloride, a three-dimensional Patterson analysis[11] was carried out with the aid of the (0*kl*) Patterson function[11] for cocaine hydrobromide based on the (0*kl*) electron density map of cocaine hydrochloride. It would have been preferable to use the position coordinates in pure cocaine itself, but unfortunately such information is not available currently, and therefore the atomic positions for pure cocaine were taken from tha analysis of cocaine hydrochloride.[10] However, as mentioned in section II, the published positions of H(22), H(23), and H(24) appeared to be erroneous because they led to very large CH bond distances corresponding to their nearest carbon neighbors, and we have redetermined these positions through energy minimization. The corresponding coordinates of these protons and associated bond distances are listed in Table 1. A determination of all the atomic coordinates in cocaine based on energy optimization for the pure cocaine molecule starting with the coordinates from cocaine hydrochloride would have been too time-consuming.

In Table 2 we have presented the results for both e^2qQ and η in cocaine, the first two rows representing the results for the truncated fragments with 17 and 24 atoms described in section II, the third row referring to the full (43 atoms) cocaine molecule. In all these three cases we have used the minimal basis set STO-3G.[14] In the fourth and fifth rows we have presented the results for the 24-atom fragment and the full molecule with the more flexible basis set D95v.[19] In the sixth and seventh rows the results for the D95 basis set[19] are listed. From the results from the first three rows of Table 2, corresponding to the STO-3G basis set, one can see that there is good convergence in e^2qQ with respect to the sizes of the clusters chosen. Similar convergence is also observed from the fourth and fifth rows with the extended basis set D95v and also from the sixth and seventh rows for D95. These results suggest that in the future one could truncate a large molecule to a smaller cluster for economy of computational time in attempting to determine the efg tensors at the nuclei of interest and obtain reliable results without significant loss of accuracy, provided reasonable cluster sizes are chosen.

Next, examining Table 2 for the results obtained for different basis sets, namely, STO-3G, D95v, and D95, there is a significant difference between the results for both e^2qQ and η for the STO-3G basis set and the two other basis sets. This difference is not unexpected since the efg tensor is very sensitive to the anisotropy of the electron distribution near the ^{14}N nucleus. It can also be seen from the comparison of the results for the D95v basis set in rows four and five of Table 2 and six and seven for the more flexible D95 basis set that both these basis sets lead to results very close to each other when applied to similar size clusters. Since the D95 basis set allows for more flexibility for the core-like molecular orbitals than D95v, the close agreement between the results with both basis sets indicates that Sternheimer shielding effects are weak. This result is not unexpected for nitrogen, from earlier shielding investigations in light atomic systems[17] and from many-body investigations in nitrogen atom.[21] From here on, for the rest of this section, we shall only refer to the results from the D95 basis sets, since both D95v and D95 lead to nearly identical results. It is worthwhile to remark here that the difference between results with the STO-3G and D95 basis sets is more pronounced for η than for e^2qQ. This trend can be understood from the fact[4] that the ^{14}N quadrupole coupling constant depends on a single component $V_{z'z'}$ of the efg, whereas η involves the difference between the principal components $V_{x'x'}$ and $V_{y'y'}$. One therefore expects η to depend more sensitively on the wave functions for the occupied molecular orbitals and hence on the choice of the basis set. In making quantitative comparisons with experiment, it is important to remember that the STO-3G approximation represents the use of a rather limited basis set for the variational calculation of molecular orbital wave functions. Since, in principle, the more flexible basis sets are expected to provide wave functions that are more accurate from a theoretical point of view, it is justifiable to consider the results with the D95 basis set to be more representative than STO-3G of what one expects within the framework of the Hartree−Fock approximation. Therefore it is appropriate to compare only the theoretical results for the D95 case with experiment. In light of this argument, one cannot attach too much significance to the fact that the results for the STO-3G case are in somewhat lesser agreement with experiment for e^2qQ and better for η. The only important feature is the fact that both STO-3G and D95 basis sets lead to small values of η, in qualitative agreement with experiment, suggesting that the electronic environment around the ^{14}N nucleus has symmetry close to axial.

Comparing our results from the seventh row involving the D95 basis set and the whole molecule used as a cluster with experimental results, the experimental value for e^2qQ is seen to be in excellent agreement with theory, while η is significantly different from experiment. There could be a number of possible reasons for the quantitative difference between the experimental and theoretical values of η. One of the reasons could be that the atomic positions employed in the present investigation are based on the structure of cocaine hydrochloride obtained from X-ray studies.[10] It is possible that if one removed the HCl subunit from the cocaine hydrochloride structure, there may be some rearrangement in the positions of the various atoms within the cocaine molecule. In order to take this into account, a full-fledged optimization is required for the positions of all the atoms in cocaine, which would be very time-consuming because of the large size of the cocaine molecule. The second possibility is the process by which the cocaine hydrochloride structure has been determined. The X-ray analysis, combined with Patterson analysis to determine[10] the hydrogen positions in cocaine hydrochloride, is likely to be not as accurate as one would expect from the application of the neutron diffraction procedure.[22] The third possibility is that the experimental values[2] of e^2qQ and η, which we are comparing with our theoretical results, are obtained in the crystal, whereas our theoretical investigation was carried out for a single molecule. Intermolecular interac-

TABLE 3: Nuclear Quadrupole Coupling Constants and Asymmetry Parameters for ^{17}O and ^{2}H in Cocaine Free Base System

nuclei	e^2qQ (MHz)	η
H(9)	0.239	0.063
H(10)	0.245	0.039
H(11)	0.228	0.168
H(12)	0.255	0.041
H(13)	0.230	0.019
H(14)	0.232	0.051
H(15)	0.286	0.027
H(16)	0.236	0.059
H(17)	0.258	0.015
H(18)	0.234	0.070
H(22)	0.213	0.059
H(23)	0.212	0.054
H(24)	0.208	0.100
H(36)	0.253	0.038
H(37)	0.243	0.068
H(38)	0.256	0.052
H(39)	0.240	0.070
H(40)	0.257	0.038
H(41)	0.195	0.083
H(42)	0.258	0.085
H(43)	0.481	0.094
O(21)	−12.526	0.563
O(33)	11.712	0.027
O(34)	12.816	0.236
O(35)	−12.193	0.293

TABLE 4: Effective Charges on Different Atoms in Cocaine Free Base System

nuclei	charge	nuclei	charge
C(1)	−0.076	H(23)	0.191
C(2)	−0.307	H(24)	0.141
C(3)	0.143	C(25)	0.514
C(4)	−0.437	C(26)	0.120
C(5)	−0.143	C(27)	−0.275
C(6)	−0.220	C(28)	−0.236
C(7)	−0.477	C(29)	−0.181
N(8)	−0.349	C(30)	−0.232
H(9)	0.269	C(31)	−0.280
H(10)	0.306	C(32)	−0.391
H(11)	0.223	O(33)	−0.393
H(12)	0.230	O(34)	−0.473
H(13)	0.196	O(35)	−0.468
H(14)	0.229	H(36)	0.263
H(15)	0.136	H(37)	0.218
H(16)	0.199	H(38)	0.220
H(17)	0.222	H(39)	0.217
H(18)	0.199	H(40)	0.255
C(19)	−0.456	H(41)	0.198
C(20)	0.551	H(42)	0.218
O(21)	−0.549	H(43)	0.307
H(22)	0.177		

tions could influence the nature of the electron distribution in the neighborhood of the ^{14}N nucleus and hence the calculated values for e^2qQ and η. This again would be a rather time-consuming investigation, but we hope it can be carried out in the future to examine if the influence of the intermolecular interactions can improve the small but significant difference between theory and experiment for η, without affecting the excellent agreement for e^2qQ.

In Table 3, we have presented our predictions for the nuclear quadrupole coupling constants (e^2qQ) and asymmetry parameters (η) for ^{17}O and ^{2}H nuclei with spins respectively $I = 5/2$ and $I = 1$ in the two cases. These results are obtained using our calculated wave functions with the D95 basis set and the quadrupole moments of −0.025 78[23] and 0.002 86[23] barns for ^{17}O and ^{2}H (deuteron) nuclei. Looking at the results in Table 4, one can see that the e^2qQ for all the ^{2}H nuclei are similar in value, with the exception of H(43), for which the value of e^2qQ is somewhat higher. This suggests that the bonding for all the H atoms to its nearest neighbor carbon atoms are essentially like the bonding in methane or benzene molecules, with the CH bonds essentially isolated from neighboring groups. This is supported by the geometries[10] of the hydrogen around the carbon atoms to which they are bonded, which indicate that the bonds with these atoms are disposed in a nearly tetrahedral or trigonal manner. The geometry for the locations of the neighboring atoms around H(43) suggests a possible explanation for the larger e^2qQ for the deuteron at this position, namely, the relatively strong interaction between the neighboring O(35) and H(43) attached to C(32). This expectation is based on the facts that the C(32)−H(43) bond distance is only 0.93 Å, substantially smaller than the corresponding distances of the other two H atoms H(41) and H(42) which are also bonded to C(32); the bond angle H(43)−C(32)−O(35) is 95.2°, significantly smaller than the ideal tetrahedral bond angle of 109.47°; and the O(35)−H(43) distance is only 1.77 Å as compared to the corresponding distances of 2.18 and 2.06 Å for H(41) and H(42). It would be very helpful to have experimental data for e^2qQ and η for deuterons at all the hydrogen positions in Table 4 and particularly H(43), by selective deuteration if possible, using conventional or special nuclear magnetic resonance techniques for nonabundant nuclei,[24,25] to compare with theory. Additionally, it would be helpful to have, through neutron diffraction studies, a more accurate knowledge of the hydrogen atom positions than currently available from X-ray measurements.

The last four rows of Table 3 list the e^2qQ and η for the ^{17}O nuclei for the four oxygens in cocaine. It is interesting that the quadrupole interaction parameters for the four oxygens divide into two pairs, O(21) and O(35), and O(33) and O(34). For the first pair, e^2qQ are negative and comparable in magnitude and the η are sizable. The second pair have positive signs for e^2qQ and have magnitudes similar to the other pair but smaller values of η. The similarity between the members within the pairs is not unexpected, since both O(21) and O(35) are bonded to two carbons, while the atoms O(33) and O(34) are bonded to single carbons. Hence the electronic charge distributions in the neighborhood of the oxygen nuclei for the two pairs are expected to be substantially different from each other. It would be very helpful to have experimental results for e^2qQ and η for the ^{17}O nuclei to examine how the predicted trends in e^2qQ and η compare with those from experiment and also the nature of the quantitative agreement between theory and experiment.

Lastly, in Table 4, we have presented the results for the charges associated with different atoms in the cocaine molecule that are obtained through the Mulliken approximation[26] using our calculated Hartree−Fock wave functions for the D95 basis set. It is hoped that these will be useful in the understanding of the affinity of different molecular groups for attachment at the various atomic sites of this molecule. It would also be helpful to have X-ray photoemission spectroscopy (ESCA)[27] measurements for the core 1s electrons in the carbon, nitrogen, and oxygen atoms to obtain experimental information about the charges at the various atoms to compare with our results in Table 4. The ionization energies of the core 1s electrons have been found[28] to have a systematic dependence on the charges on these atoms in various molecules.

IV. Conclusion

The results for the nuclear quadrupole interaction parameters for cocaine provide excellent agreement with experiment[2] for the ^{14}N nuclear quadrupole coupling constant and reasonably good agreement for the asymmetry parameter, in the latter case, at least to the extent that both theory and experiment lead to values for η significantly smaller than 0.1. Additionally, the position parameters for the hydrogen atoms that were incorrectly presented in ref 10 dealing with structural data for cocaine hydrochloride and are redetermined in the present work through energy minimization are found to be in good agreement when two different sized fragments involving 17 and 24 atoms are used, showing good convergence with respect to cluster size, suggesting that the same hydrogen positions would apply for the full cocaine molecule. Similar good agreement is found (Table 2) also for the calculated ^{14}N nuclear quadrupole interaction parameters between that for the 24-atom cluster and the entire molecule involving 43 atoms and also with the experimental values.[2] All these results provide support for the Hartree–Fock procedure for the treatment of the energetics of large drug molecules as well as properties that depend on the electronic wave functions and also for truncating the large molecules to reasonable size clusters to make the procedure for quantitative analysis practicable in terms of time. These conclusions should be helpful in the future in dealing with the properties of large molecules.

The very good agreement between theory and experiment for the nuclear quadrupole interaction parameters leads us to look at the causes for the remaining small differences between the two for the asymmetry parameter, to see if one could further improve the quantitative agreement with experiment. Among the possible causes pointed out in section III are the need for the determination of the positions of the hydrogen atoms for free cocaine by the neutron diffraction technique,[22] which is more accurate in contrast to the Patterson analysis[10,11] based on X-ray diffraction, the effect of the intermolecular interactions between neighboring molecules, which one expects to influence the efg tensor, and also many-body effects. The latter effects are expected to be rather time-consuming, but should be attempted in the future, to provide greater insights into the origin of the efg tensors at the nuclei in cocaine. The understanding of the intermolecular interactions in the solid state would be very helpful in the future study of the more complicated phenomenon of the temperature dependences[2] of the nuclear quadrupole interaction parameters. Further, many-body effects, which are rather difficult to study in such a complex molecule, seem to be not too important because of the good agreement found between the theoretical results in the present work and experimental results.[2] Nevertheless, it would be interesting to test this conclusion in the future by a many-body calculation.

Lastly, the other results of our investigation discussed in section III would be helpful to test by future experimental measurements to obtain a more complete understanding of the electron distribution over the cocaine molecule. Among these results are the nuclear quadrupole interaction parameters for ^{17}O and ^{2}H nuclei substituted respectively for the abundant ^{16}O nuclei and the protons in the molecule. The other property refers to the charges on the atoms in the cocaine molecule which can be tested using the ionization energies of the core 1s states of carbon and nitrogen atoms through the ESCA technique.[27,28]

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References and Notes

(1) Farmilo, C. G.; Levi, L. *Bull. Narc. U.N. Dept. Social Affairs* **1953**, *5* (4), 20. Grechishkin, V. S. *Appl. Phys. A* **1992**, *55*, 505. Grechishkin, V. A. *Z. Naturforsch.* **1990**, *45a*, 559.

(2) Yesinowski, J. P.; Buess, M. L.; Garroway, A. N.; Ziegewid, M.; Pines, A. *Anal. Chem.* **1995**, *34*, 2256.

(3) Shaw, J. *NQI News Lett.* **1994**, *1*, 26. Buess, M. L.; Garroway, A. N.; Miller, J. B.; Yesinowski, J. P. *Adv. Anal. Detect. Explos. Proc. Int. Symp.* **1992**, *4*, 361.

(4) Das, T. P.; Hahn, E. L. *Nuclear Quadrupole Resonance Spectroscopy*; Academic Press: New York, 1957. Lucken, E. A. C. *Nuclear Quadrupole Coupling Constants*; Academic Press: New York, 1969.

(5) Karpowicz, R. J.; Brill, T. B. *J. Phys. Chem.* **1983**, *87*, 2109.

(6) Pati, R.; Srinivas, S.; Briere, T.; Das, T. P.; Sahoo, N.; Ray, S. N. *J. Phys. Chem.* **1995**, *99*, 9051.

(7) Roothaan, C. C. J. *Rev. Mod. Phys.* **1951**, *23*, 69.

(8) Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *Gaussian 92, Revision C*; Gaussian, Inc.: Pittsburgh, PA, 1992.

(9) Hartree, D. R. *The Calculation of Atomic Structures*; John Wiley and Son: New York, 1955.

(10) Gabe, E. J.; Barnes, W. J. *Acta. Crystallogr.* **1963**, *16*, 796.

(11) Bacon, G. E. *X-ray and Neutron Diffraction Pergamon*: New York, 1966; Chapter 5, pp 55–59.

(12) Gray, H. B. *Electrons and Chemical Bonding*; W. A. Benjamin, Inc.: New York, 1965.

(13) Sahoo, N.; Sulaiman, S.; Mishra, K. C.; Das, T. P. *Phys. Rev. B* **1989**, *39*, 13389. Dev, B. N.; Mohapatra, S. M.; Sahoo, N.; Mishra, K. C.; Gibson, W. M.; Das, T. P. *Phys. Rev. B* **1988**, *38*, 13335. Clotet, A.; Ricart, J. M.; Rubio, J.; Illas, F. *Phys. Rev. B* **1995**, *51*, 1581.

(14) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

(15) Donzelli, O.; Briere, T.; Das, T. P. *Hyperfine Interact.* **1996**, *97/98*, 373.

(16) Mphapatra, S. M.; Dev, B. N.; Luo, L.; Thundat, T.; Gibson, W. M.; Mishra, K. C.; Sahoo, N.; Das, T. P. *Rev. Solid State Sci.* **1990**, *4*, 873.

(17) Sternheimer, R. M. *Z. Naturforsch.* **1986**, *41a*, 24. Schmidt, P. C.; Das, T. P. *Z. Naturforsch.* **1986**, *41a*, 47.

(18) Mitchell, D. W.; Sulaiman, S. B.; Sahoo, N.; Das, T. P.; Potzel, W.; Kalvius, G. M. *Phys. Rev. B* **1991**, *44*, 6728. Steiner, M.; Potzel, W.; Kofferlin, M.; Karzel, H.; Schiessl, W.; Kalvius, G. M.; Mitchell, D. W.; Sahoo, N.; Klauss, H. H.; Das, T. P.; Feigelson, R. S.; Schmidt, G. *Phys. Rev. B* **1994**, *50*, 13335.

(19) Dunning, T. H.; Hay, P. J. *Modern Theoretical Chemistry*; Plenum: New York, 1976; Chapter 1, pp 1–28.

(20) Pati, R.; Das, T. P.; Sahoo, N.; Ray, S. N. Submitted to *J. Phys. Chem.*

(21) Raghunathan, K.; Andriessen, J.; Ray, S. N.; Das, T. P. *Phys. Rev. Lett.* **1980**, *44*, 312.

(22) Choi, C. S.; Prince, E. *Acta Crystallogr. Sect. B* **1972**, *28*, 2857.

(23) Raghavan, P. *At. Nucl. Data Tables* **1989**, *42*, 203.

(24) Leppelmeier, G. W.; Hahn, E. L. *Phys. Rev.* **1966**, *142*, 179. Slusher, R. E.; Hahn, E. L. *Phys. Rev.* **1968**, *166*, 332.

(25) Grechishkin, V. S. *J. Struct. Chem.* **1991**, *32*, 609.

(26) Mulliken, R. S. *J. Chem. Phys.* **1955**, *23*, 1833.

(27) Carlson, T. A. *Photoelectron and Auger Spectroscopy*; Plenum: New York, 1975.

(28) Siegbahn, K.; Nordling, C.; Johansson, G.; Hedman, J.; Heden, P. F.; Hamrin, K.; Gelius, U.; Bergmark, T.; Werme, L. O.; Manne, R.; Baer, Y. *ESCA Applied to Free Molecules*; North-Holland: Amsterdam, 1969.