Structural and vibrational analysis of indole by density functional and hybrid Hartree–Fock/density functional methods

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Accurately assigned vibrational frequencies for indole and its derivatives, particularly tryptophan, are critical for analyses of vibronic coupling, excited state fluorescence spectra and resonance Raman spectra. Examination of published, assigned, experimental vibrational frequencies for indole reveals that while most observed bands assigned to fundamentals are in agreement among the different reports, there are notable exceptions in six different spectral regions. We have calculated the structure and assigned the harmonic vibrational spectrum of indole by application of local and gradient-corrected density functional theory methods (DFT) and a hybrid Hartree–Fock/density functional (HF/DFT) method. The hybrid method B3LYP predicts the structure of indole within 0.005 Å and 1.1° of a recently published CASSCF structure. Unscaled harmonic frequencies calculated with the gradient-corrected method BLYP with the 6-31G(d) basis set exhibit the best overall agreement with experiment with an RMSD of 31 cm^{-1} for all modes including hydrogen stretching and bending. The hybrid B3LYP method gives frequencies in closest agreement for the out-of-plane modes, except for the NH wagging mode. Our calculations, which include electron correlation effects for approximately the same computational resources as a Hartree–Fock calculation, predict two fundamentals in the 1330–1360 cm^{-1} region, where a Fermi resonance pair has previously been hypothesized. This report demonstrates the utility of DFT and HF/DFT methods for heteroaromatic molecules such as indole. We provide the first complete assignment of vibrational modes for indole based on unscaled calculated frequencies which have not been empirically fit to experiment.

Introduction

The biological, pharmacological and materials applications for indole require detailed knowledge of structural, electronic and spectral properties. Indole, **1a**, and indole related compounds

Indole (Ind)
1a

Tryptophan (Trp)
1b
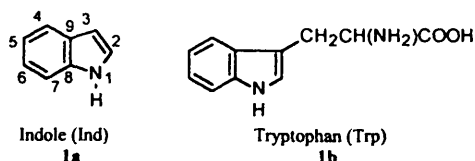
have long been known to form charge-transfer complexes with electron acceptors.[1,2] Only recently, however, has this knowledge been applied to the promising field of heteroaromatic conducting polymers.[3–5] It is postulated that charge-transfer interactions involving indole derivatives such as tryptophan, melatonin and the neurotransmitters serotonin and tryptamine may also be important *in vivo* for molecular recognition and alignment and for electron transfer processes.[1,2,6–8] An accurately assigned vibrational spectrum for indole provides a reference for vibrational frequency shifts in charge-transfer complexes and thus, clues to the molecular orientations.

By virtue of its UV absorption, the aromatic amino acid tryptophan, **1b**, is significant for the characterization of proteins through electronic excitation spectroscopy. With the introduction of UV–resonance Raman spectroscopy, the vibrational spectrum of tryptophan assumed a significant role in the analysis of proteins.[9,10] Selective UV excitation of the tryptophan (trp) residues within a protein allows examination of conformations, hydrogen bonding and the environment of the trp

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residue through time-resolved resonance Raman spectroscopy.[11] The growing field of difference Fourier transform IR (FTIR) spectroscopy of biological systems, including proteins and amino acid radicals, requires detailed, accurate assignments for the vibrational spectra for the reference amino acids and their side chains.[12] Analyses of vibronic coupling and fluorescence spectra, and detailed interpretation of resonance Raman spectra of indole and its derivatives depend on accurately assigned vibrational frequencies for indole.

Because many properties of indole derivatives used in protein and materials characterization result from attributes of the indole side chain, knowledge of the photophysical properties of indole from experimental and computational analyses form the basis for interpreting the protein experiments. This is complicated, however, because reliable data regarding many properties of indole are not available.

The size and low symmetry of indole combine to make post Hartree–Fock, configuration interaction frequency calculations with a large basis set extremely expensive. We have used density functional (DFT) and hybrid Hartree–Fock/density functional (HF/DFT) methods[13,14] which allow the inclusion of energy terms for electron correlation for approximately the same amount of computer time as Hartree–Fock calculations. Several groups have demonstrated that density functional methods provide reliable geometries[15,18] and very accurate, unscaled, harmonic vibrational frequencies,[15,18–22] but tests of DFT methods for heterocycles or bicyclic molecules such as indole are rare.[21,22] Details of the methods and explanations of the acronyms used to represent them (SVWN, BLYP, B3LYP) are included in the Appendix.

Prior experimental and theoretical results for indole

A unique, refined experimental structure for indole is not known although it has been examined by X-ray crystallography

and microwave (MW) spectroscopy. The X-ray data[23] contained a considerable degree of disorder, $R = 0.23$, because of alternative orientations of stacked molecules in the unit cell. Two gas-phase structures, related to microwave spectra, ensue from assumptions regarding the similarity of bond distances in indole to those in benzene and pyrrole.[24,25] Another gas-phase structure, related to the rotationally resolved, electronic spectrum from UV fluorescence, results from iteratively adjusting the bond lengths from an X-ray structure of tryptophan.[26] Geometrical adjustments were made in two of these gas-phase structures so that measured rotational constants were reasonably reproduced. Philips and Levy note that these derived geometries are 'by no means unique, but are merely examples of geometries which are consistent with the measured rotational constants'.[26]

While these estimated structures may be sufficient for describing rotational spectra and rotationally resolved electronic spectra, they are not sufficient for predicting the fundamental vibrational spectrum,[27] for analysing a vibronically coupled spectrum,[24-26,28,29] or for calculating the partition function.[30]

A variety of computational methods have been used to predict a structure for indole ranging from semi-empirical[31-33] to molecular orbital methods,[27,34-36] including our preliminary results using local and gradient-corrected DFT.[37] We will compare our calculated structures to the most sophisticated of these, a very recent complete active space self-consistent field (CASSCF) calculated geometry which utilized a contracted, atomic natural orbital type basis set.[36]

Although more experimental work has been carried out to characterize indole's vibrations than its structure, the vibrational assignments for indole are complex. The observed Raman bands of trp have been attributed to corresponding, assigned modes in the indole side chain,[9,38,39] however, much debate remains concerning the entire set of fundamental frequencies and their assignments for indole. Indole is planar and, having C_s symmetry, all 42 fundamental vibrations are active in both IR and Raman spectroscopies. These reduce to 29 modes of a' (in-plane) symmetry and 13 modes of a'' (out-of-plane) symmetry. Experimental data for the fundamental vibrations of indole (Table 1), including some degree of assignment, encompass IR and Raman spectra for liquid indole and many deuteriated derivatives from Lautié and co-workers,[40] as well as several other IR and Raman studies for gas,[27,29,30,41] liquid,[30,42] solution[30] and solid states.[27,42] The level of theory used for the computational approach to predicting the fundamental frequencies of indole[27,28,30,39,43] ranges from an empirical force field normal coordinate analysis[39] (with assignments) to MP2 calculations[43] (with partial assignments) appearing while this manuscript was in preparation.

In Lautié and co-workers' landmark paper regarding indole vibrational spectroscopy,[40] mode assignments resulted from analysing an extensive set of deuteriated derivatives. Takeuchi and Harada[39] subsequently changed several mode assignments in order to optimize the least-squares fit of their empirical force field calculation to the experimental data. Most assignments since that time appear to be based on either the empirically fitted frequencies as assigned by Takeuchi and Harada or on scaled frequencies from molecular orbital calculations which have been iteratively fit to experiment.

Examination of published, assigned, experimental vibrational frequencies for indole (Table 1) reveals that while most observed bands assigned to fundamentals are in agreement among the different reports, there are notable exceptions in six different spectral regions bearing on three main issues.

(*i*) The assignment of observed bands to fundamentals or combinations/overtones,
(*ii*) The symmetry of certain fundamentals, and
(*iii*) The frequency for the NH wagging mode.
Before discussing the relationship of our calculations to these

Table 1 Experimental vibrational frequencies (cm^{-1}) for indole[a]

Lautié[b]	Suwaiyan[c]	Collier[d]	Bickel[e]	Majoube[f]
a'	a'	a'	a'	a'
3523 gas		3520 vap.		3523.2
3123		3140 vap.		3117.8
3106		3080		n/o
3080		3080		3071.7
↑		3060		3050.7
↓		3060		n/o
3050		3060		n/o
1616	1614	1620 vap.	1616	n/o
1576	1575	1576	1576	1576.1
1509	1506	1509	1509	1519.9
1487	1487	1488	1479	1478.6
1455	1458	1458 vap.	1459	1457.7
1412	1415	1410 vap.	1410	1414.2
1352	1355	1348 vap.	1350	1346.8
1334	1336			1330.1[g]
		1300		
1276	1275	1275 vap.	1278	1277.5
1245	1247	1245 vap.	1248	1244.0
				1227.0
1203	1202[g]	1205 vap.	1208	1204.0
1191			h	1196 (IR-solid)[g]
1147	1143	1148	1143	1149.5
1119	1118	1122 vap.	1123	1122.3
1092	1092	1082 vap.	1085	1082.7
1064	1058	1068 vap.	1068	1066.7
1010	1022	1015 vap.	1015	1013.9
895	899 R	900 vap.	902	899.2
	875	870	876	878.9
767				
758	768	761 R	759	744.9
607	611 R	608	609	611.9
542	546 R	543	542	538.2
	505			
		400 R	396	387.4
a''	a''	a''	a''	a''
970		968 R	h	979.3
930	945	930	925	924.6
				904.0
873	898			
		860		
848			849	850.1
		800 vap.		790.8
		762 vap.	765	763.9[g]
743	752	738 vap.	738	737.7
725	730	715 vap.	715	714.5
		625 vap.		
608	612		602	601.3
575		575	570	570.4
487	498		480	516.0
423	425	422	420	419.9[i]
397	395 R	405 vap.	h	
254	254 R	240 R vap.	241	240.0[i]
224	235 R	208 vap.	208	207.0[i]

[a] IR frequencies except where noted by R—referring to Raman bands. [b] Ref. 40 Liquid IR frequencies except for 3523 cm^{-1} from gas-phase measurements. [c] Ref. 42. [d] Ref. 30, Liquid IR except as noted by vap—vapour phase. [e] Ref. 29. [f] Ref. 27. [g] Absorbance observed but not assigned as fundamental. [h] Fundamental assigned though not observed. [i] Taken by Majoube and Vergoten from Smithson (ref. 41).

issues, we describe the DFT and HF/DFT calculated geometries of indole.

Results and discussion

Indole geometry
In our prior report on the distinguishing features of indolyl radical and radical cation,[37] we reported DFT optimized geometries (SVWN and BLYP) for indole and compared them with a 3-alkylindole X-ray diffraction structure averaged from 34

Table 2 Bond lengths (in Å) calculated by various density functional and the unrestricted Hartree–Fock methods for indole compared with the CASSCF[a] calculated bond lengths. Except where otherwise noted, all calculations used the 6-31G(d) basis set.

BOND	CASSCF[a] ANO basis	INDOLE SVWN	DF-CAS DIFF	INDOLE BLYP	DF-CAS DIFF	INDOLE B3LYP	HF/DF-CAS DIFF	INDOLE B3LYP 6-311Gdp	HF/DF-CAS DIFF	INDOLE UHF	UHF-CAS DIFF
N1–C2	1.379	1.371	−0.008	1.396	0.017	1.383	0.004	1.382	0.003	1.378	−0.001
C2–C3	1.369	1.369	0.000	1.381	0.012	1.370	0.001	1.367	−0.002	1.348	−0.021
C3–C9	1.445	1.424	−0.021	1.444	−0.001	1.438	−0.007	1.436	−0.009	1.442	−0.003
C4–C9	1.410	1.399	−0.011	1.416	0.006	1.406	−0.004	1.404	−0.006	1.399	−0.011
C4–C5	1.388	1.384	−0.004	1.400	0.012	1.388	0.000	1.386	−0.002	1.375	−0.013
C5–C6	1.417	1.403	−0.014	1.419	0.002	1.410	−0.007	1.408	−0.009	1.404	−0.013
C6–C7	1.389	1.385	−0.004	1.401	0.012	1.390	0.001	1.387	−0.002	1.375	−0.014
C7–C8	1.405	1.391	−0.014	1.407	0.002	1.399	−0.006	1.397	−0.008	1.395	−0.011
C8–C9	1.408	1.421	0.013	1.438	0.030	1.424	0.016	1.422	0.014	1.401	−0.007
C8–N1	1.373	1.369	−0.004	1.392	0.019	1.380	0.007	1.379	0.006	1.371	−0.002
N1–H10	1.000	1.017		1.016		1.008		1.005		0.992	
C2–H11	1.077	1.090		1.088		1.081		1.079		1.071	
C3–H12	1.077	1.090		1.088		1.081		1.079		1.071	
C4–H13	1.081	1.096		1.095		1.087		1.084		1.076	
C5–H14	1.081	1.096		1.094		1.087		1.085		1.075	
C6–H15	1.081	1.096		1.094		1.087		1.084		1.076	
C7–H16	1.081	1.096		1.095		1.087		1.085		1.076	
Average Error[b]			−0.0067		0.0111		0.0005		−0.0015		−0.0100
Avg abs Error			0.0093		0.0113		0.0053		0.0061		0.0096

[a] Ref. 36. [b] The average error and average absolute value error were calculated for non-hydrogen bonds only.

derivatives.[44] A recently published CASSCF structure[36] (using ten π electrons in nine valence orbitals as the active space) is perhaps more suitable and is used for comparison in this paper with both DFT and HF/DFT optimized structures. The bond lengths calculated by the different methods employed are listed in Table 2 for comparison with the CASSCF bond lengths. As shown in the average absolute error, the B3LYP geometry most closely agrees with the CASSCF geometry. The SVWN, UHF and BLYP geometries all differ from the CASSCF structure by approximately 0.01 Å, with BLYP slightly worse than the other two methods. The BLYP method has the single greatest difference of 0.30 Å for the C8–C9 bond length. The even distribution of errors for B3LYP is evident in the computed average errors. The average errors for the other methods show their tendencies to either calculate bond lengths too long (BLYP) or too short (SVWN and UHF) as compared to the CASSCF structure. With one exception the calculated bond distances in Table 2 result from optimization with the 6-31G(d) basis set. Utilizing B3LYP and increasing the basis set size to 6-311G(d,p) changes the bond lengths by not more than 0.003 Å and does not improve the average absolute error.

Examination of the B3LYP and SVWN optimized geometries reveals that fusing the two moieties, benzene and pyrrole, and extending the conjugated system changes the bond lengths from those in either the isolated benzene or pyrrole components. The N–C bonds of the pyrrolic ring of indole are longer than in pyrrole,[45] as is the C3–C9 bond of indole corresponding to the C3–C4 bond of pyrrole. The C2–C3 bond in indole is, however, shorter than the corresponding C2–C3 bond of pyrrole. The ring fusion C8–C9 bond is substantially longer in indole (1.424 Å, column 6, Table 2) than the similar bond in either pyrrole (1.382 Å) or benzene[46] (1.396 Å). Apart from the C8–C9 bond, within the six-membered ring of indole, bond distances range from 1.384 to 1.403 Å by SVWN and from 1.388 to 1.410 Å by B3LYP [6-31G(d) basis], indicating that the equal length bonds of benzene are perturbed considerably in the bicyclic aromatic indole. Thus, the assumption that employing the bond lengths of benzene and pyrrole is sufficient for modelling physical properties of indole appears unsubstantiated.

The bond angles within the optimized structures for indole for the various methods are given in Table 3 with the bond angles from the CASSCF structure.[36] For all density functional methods, the maximum difference between the DFT calculated angles and the CASSCF angles is ≤ 1.1°. There is one angle from UHF differing by this much, but the remaining angles for all DFT methods differ by ≤ 0.06°. The DFT methods exhibit a very high level of agreement with a maximum variation among them of 1.1° and an average variance of 0.5°.

The rotational constants shown in Table 4 (in MHz) from each of the calculations [with 6-31G(d) basis set] show that the structure from B3LYP yields rotational constants in excellent agreement with the measured values[24] (differences of A < 1, B < 5, C < 1.5 MHz). The rotational constants from SVWN are larger than, but still within 3% of, the measured values. The errors in rotational constants for BLYP and UHF are considerably larger than those for either of the other methods.

The structure reported here calculated by B3LYP is an improvement over our previously reported structures calculated by SVWN and BLYP whether the comparison is made to averaged X-ray data as in the previous paper or is made to CASSCF calculations as shown here. The predicted rotational constants are also in much better agreement with experiment from the B3LYP calculations than from the two density functional method calculations. Additionally, for the B3LYP method the 6-311G(d,p) basis set provides no improvement of the structure over that from the 6-31G(d) basis set. We note that the structure of indole bears little resemblance to the bond lengths and angles of benzene and pyrrole which are apparently not accurate approximations for the structure of indole.

Indole harmonic vibrational frequencies and mode assignments

For the discussion of the vibrational modes certain conventions have been followed. (i) The benzene ring of indole is sometimes referred to as Φ, while the pyrrole ring and its vibrations are sometimes designated with Π; (ii) the abbreviations ν, δ and γ represent stretching, in-plane bending and out-of-plane bending or wagging, respectively; (iii) reference is frequently made to the Wilson modes of benzene in the manner Φ 9b, for example, indicating similarity to the 9b mode of an ortho-disubstituted benzene ring;[47,48] and (iv) reference is made to vibrational modes of tryptophan using the W# convention of physical biochemists. The calculated, unscaled frequencies and intensities from SVWN, B3LYP and BLYP are given in Table 5 along with,

Table 3 Bond angles (in degrees) calculated by various density functional and the unrestricted Hartree–Fock methods for indole compared with calculated bond angles from CASSCF." Except where noted all calculations used the 6-31G(d) basis set.

ANGLE	CASSCF" ANO basis	SVWN	BLYP	B3LYP	B3LYP 6-311G(d,p)	UHF
C8–N1–C2	N.a.[b]	109.6	109.3	109.3	109.3	109.0
N1–C2–C3	109.6	109.4	109.4	109.6	109.5	110.0
C2–C3–C9	106.7	107.1	107.3	107.1	107.2	106.7
C3–C9–C8	N.a.	106.9	106.9	106.9	106.8	106.7
C9–C8–N1	N.a.	107.1	107.0	107.1	107.2	107.5
C8–C9–C4	N.a.	118.5	118.5	118.6	118.7	119.1
C9–C4–C5	118.9	119.1	119.2	119.2	119.1	119.1
C4–C5–C6	120.9	121.2	121.2	121.2	121.1	120.9
C5–C6–C7	121.2	121.2	121.2	121.2	121.2	122.3
C6–C7–C8	117.5	117.4	117.5	117.5	117.6	117.5
C7–C8–C9	N.a.	122.6	122.5	122.4	122.3	122.1
H1–N1–C2	N.a.	125.4	125.3	125.3	125.2	125.3
H2–C2–N1	120.5	120.6	120.2	120.3	120.5	120.3
H3–C3–C9	N.a.	126.9	126.8	126.9	127.0	127.1
H4–C4–C5	120.6	120.7	120.6	120.5	120.5	120.5
H5–C5–C4	119.9	119.6	119.6	119.6	119.7	119.9
H6–C6–C7	119.3	119.4	119.3	119.3	119.4	119.4
H7–C7–C6	121.1	121.3	121.1	121.2	121.0	121.1

" Ref. 36. [b] Not given in ref. 36.

Table 4 Calculated [with the 6-31G(d) basis set] and experimental rotational constants (in MHz) for indole

	A	B	C
Exp."	3877.8366(64)	1636.0461(48)	1150.0900(19)
SVWN	3902.9045	1650.1124	1159.7716
BLYP	3819.7999	1608.0059	1131.6287
B3LYP	3878.6645	1631.4119	1148.3869
UHF	3951.1683	1652.7014	1165.2843

" Ref. 24, standard deviation in parentheses as difference in last two digits

for ease of comparison, the liquid IR frequencies and intensities of Lautié et al.[40] and the gas-phase IR frequencies and intensities of Majoube and Vergoten.[27]

Obviously, mode assignments and identification of fundamentals are extremely complicated in a molecule the size of indole, especially with its very low symmetry. There are, for example, 16 normal modes, all having a′ symmetry, within the 600 cm⁻¹ range from 1014 to 1616 cm⁻¹. Thus, considerable mixing of the modes is expected with very few pure C–H bending (δCH) or pure skeletal modes in this region. The modes are also delocalized to some extent with many modes showing vibrations in both rings.

The root mean square deviations (RMSD) for each method compared with the frequencies of Lautié et al.[40] are shown in Table 6. Because calculated CH stretching frequencies generally deviate more than other modes and the Φ CH stretches were given in the paper as a range, we separated the RMSD for those modes from the other a′ symmetric modes. Our overall RMSD is 31 cm⁻¹ for BLYP and 64 cm⁻¹ for B3LYP. As indicated in Table 6, for the more numerous a′ modes the accuracy of BLYP is over four times that of B3LYP. For the a″ symmetric modes, B3LYP frequencies are closer to the experimental values. Although it seems customary to discuss the same method for geometry and frequency calculations, we will discuss and analyse the unscaled, calculated harmonic frequencies from BLYP as we address discrepancies among experimentalists regarding the designations of frequencies as fundamentals and certain mode assignments. At times the questioned frequencies are within 15–20 cm⁻¹ of each other, therefore, the greater accuracy of the BLYP calculated frequencies is necessary to address these issues. The NH wagging mode which is not predicted well by either BLYP or B3LYP is discussed later in detail.

The experimental frequencies reported by Lautié and co-workers[40] (LL) have become a benchmark for subsequent vibra-

tional studies of indole and tryptophan because their thorough assignments are based on spectra of an extensive set of isotopically substituted derivatives. Where important differences exist among the experimentalists or between experiment and our calculations, we will necessarily compare with the results of other experimentalists, primarily those from the gas-phase IR experiments of Majoube and Vergoten (MV).[27] MV assigned the gas-phase frequencies by comparing experiment with calculated frequencies scaled with multiple scaling factors. The practice of using different scaling factors for different type modes can result in reordering of modes having different symmetries. Generally, gas-phase experimental frequencies would be considered a better test of the computational accuracy; however, because of the method by which they were assigned and because of the precedent for comparing with Lautié et al., we will generally focus our comparisons on the experimental data published by Lautié and co-workers. For the readers' convenience, in addition to the brief mode descriptions given in Table 5, sketches for significant modes are included in Fig. 1.

In order to be brief and not attempt to describe and compare every one of the 42 fundamentals, our discussion will focus first on the six areas of disagreement alluded to in the introduction and second on modes of importance in tryptophan vibrational spectroscopy.

Addressing discrepancies in published assigned fundamental vibrations of indole

The frequencies near 1350 cm⁻¹. A particularly interesting feature of our calculations is the identification of two fundamentals in the 1330–1360 cm⁻¹ range where a Fermi-type resonance was proposed. This is evident in the fundamentals determined by all three computational methods. Although all the experimental reports included the observation of two strong vibrational bands in the 1330–1360 cm⁻¹ region, only two, those of Lautié and co-workers and of Suwaiyan and Zwarich,[42] assigned both bands to fundamental vibrational modes. The other spectroscopists assign these two strong bands to a Fermi doublet identified by Takeuchi and Harada through empirical force field calculations for indole and solvent effect studies on skatole (3-methylindole) and tryptophan derivatives.[39,49]

The calculated atomic displacements, depicted in Fig. 1, for these modes at 1357 and 1340 cm⁻¹ (BLYP) show that while both modes contain significant motion of the hydrogens, the mode at 1340 cm⁻¹ also involves skeletal stretches. The mode at 1357 cm⁻¹ is analogous to Wilson mode Φ 3, but with involve-

Table 5 Calculated frequencies (cm⁻¹), IR intensities and approximate descriptions calculated with DF and HF/DF methods and the 6-31G(d) basis set compared to experimental frequencies and intensities[a]

Lautié[b]	Int.	M & V[c]	Int.	SVWN	Int.	B3LYP	Int.	BLYP	Int.	Approx. Description
3523 gas	—	3523	s	3582	65.1	3665	55.7	3547	39.0	NH v
3123	—	3118	vw	3215	0.8	3278	6.4	3194	8.5	Π CH v
3106	—	—		3197	0.6	3259	2.0	3174	3.0	Π CH v
3080	—	3072	s	3147	11.7	3209	26.2	3122	31.0	Φ CH v
↑	—	3051	m	3136	20.1	3198	41.7	3112	50.1	Φ CH v
↓	—	—		3127	1.9	3188	4.5	3102	5.3	Φ CH v
3050	—	—		3121	1.4	3180	1.1	3094	1.3	Φ CH v
1616	m	(1616)	m	1679	2.0	1678	2.9	1613	2.6	Φ 8b & sl. Π N1C8 v & C3C9 v
1576	w	1576	w	1628	2.5	1636	1.6	1572	1.5	Φ 8a & sl. Π H δ
1509	s	1520	w	1558	5.4	1571	6.5	1514	4.1	C2C3 v.
1487	s	1479	w	1519	7.4	1542	3.1	1491	1.7	Φ 19a, NH δ, & H5δ
1455	vs	1458	s	1502	12.3	1501	23	1450	17.6	Φ 19b & H2δ
1412	s	1414	s	1457	5.4	1463	16	1414	9.8	Π 14/6, NH δ & H6δ
1352	vs	1347	s	1357	8.1	1398	8.1	1357	9.9	all H bend Π and Φ asynch.
1334	vs	(1330)	(s)	1414	44.3	1381	24	1340	17.9	Φ 14 & N1C2 v
1276	s	1278	m	1309	3.2	1313	12.6	1269	15.4	Π ring bend/str. & sm. H4 δ
1245	s	1244	m	1242	9.9	1280	11.3	1242	11	all H bend synch.
		1227	vw							
1203	m	1204	w	1211	3.5	1231	3.3	1192	2.4	Π 14/6, NH δ, & sm. H5δ
1191	w									
1147	w	1150	vw	1144	0.7	1186	1.5	1157	1.6	Φ CH δ (15)
1119	m	1122	vw	1125	1.1	1152	0.8	1119	0.7	Φ CH δ (9b) & Π CH δ
1092	vs	1083	m	1099	22.1	1117	22.0	1082	15.9	N1H & C2H δ
1064	s	1067	m	1062	5.2	1100	6.6	1065	9.2	C3H δ, sl. N1H δ, & v.sl. Π ring bend
1010	s	1014	m	1035	5.3	1044	4.1	1012	4.0	Φ ≈ 18b
970	sh	979	vw	931	0.1	968	0.02	926	0.02	a" Φ CH γ (5)
930	w	925	m	885	2.8	924	1.9	880	1.7	a" Φ CH γ (10a)
895	s	899	m	892	6.1	910	6.1	882	5.9	Π ring bend
not obs.		879	vw	865	0.4	886	0.3	861	0.2	skeletal bend both rings
873	w	850	w	839	4.2	863	2.6	829	2.1	a" Φ CH γ (10b)
848	w	904	w	816	4.2	850	2.5	803	6.4	a" Π CH γ asynch.
(767)	s	791 (764)	m (m)	768	1.6	785	8.0	757	3.3	a" C8C9 torsion; C2H γ
758	sh	745	m	772	2.1	777	2.4	753	1.8	indole breathing
743	vs	738	vs	730	77.6	756	63	729	47.3	a" Φ CH γ (11)
725	s	714	s	703	34.8	729	34	698	38.5	a" Π CH γ synch.
607	s	612	vw	602	1.2	617	1.1	599	1.0	C8–C9 in-plane rock
608		601	m	612	6.3	617	4.2	596	4.6	a" Π ring butterfly
575	w	570	vw	576	0.7	585	0.8	566	0.95	a" Φ ring twist (16a)
542	sh	538	vw	542	0.1	553	0.06	538	0.05	Φ bend (6a)
423	vs	420	w	415	67	435	1.3	422	1.2	Φ 16b [mixed w/γNH for SVWN (ca.50:50)]
487 437[d]	s	516 (403)[e]	m	432	17.9	360	84	330	71	γNH [mixed w/Φ16b. for SVWN (ca.50:50)]
(397)	s	387	s	394	3.6	405	3.8	394	3.5	in plane ring twist
254	w	240		244	0.2	246	0.1	236	0.2	a" twisting butterfly
224	s	207		214	9.7	214	14	206	15.6	a" butterfly

[a] The assignment comparisons are discussed in the text. Abbreviations: sm.-small, sl.-slight, str.-stretch, v.-very, synch.-synchronous, asynch.-asynchronous. [b] Ref. 40 Experimental frequencies from liquid IR, except NH stretch. Numbers in parentheses are the bands that have been reassigned symmetry, see text. [c] Ref. 27 Experimental frequencies from gas-phase IR; 1616 cm⁻¹ was not observed, but assigned based on Lautié *et al.*; 1330, 764 and 403 cm⁻¹ vibrations (in parentheses) were observed, but not assigned to fundamentals; 420, 240, 207 cm⁻¹ were taken by Majoube and Vergoten from Ref. 41. [d] This is the hypothesized, non-self-associated NH wag frequency suggested by Lautié and co-workers. [e] From Ref. 52, non-hydrogen-bonded NH wag.

ment of the Π hydrogens as well. The mode at 1340 cm⁻¹ is best described as a mixture of Φ 14 and N1–C2 stretch.

If the observed experimental bands are assumed to be a doublet, then not only are the RMSD worse (compared to the gas-phase experiment which makes this assumption), but, perhaps more importantly, the relative calculated intensities no longer correlate with the observed intensities. Scaled frequencies from Hartree–Fock molecular orbital calculations [with 3-21G[27,28] or 6-31G(d)[50] basis sets; 0.90 scaling factor], which do not include electron correlation, indicate only one fundamental in this region. Application of the standard MP2 scaling factor[51] (0.95) to published MP2/6-31G(d) frequencies for indole[43] is consistent with two fundamentals in the mid 1300 cm⁻¹ range. Thus, density functional and MP2 calculations, the

only quantum chemical methods applied to indole and including electron correlation, both predict two fundamentals near 1350 cm⁻¹.

We examined several isotopically substituted variations of indole to identify experiments which might clarify the Fermi doublet issue. Calculations with ¹⁵N isotopic substitution show that both the higher frequency band and the lower frequency band shift to lower frequency only by about 3 cm⁻¹. ¹³C isotopic substitution at C8 and C9, while being more synthetically challenging, could be quite enlightening as the 1340 cm⁻¹ band shifts to 1317 cm⁻¹ and the 1357 cm⁻¹ band shifts to 1354 cm⁻¹. Less synthetically challenging but still potentially useful, ¹³C substitution at C8 only is predicted to shift the 1340 cm⁻¹ band to *ca.* 1332 cm⁻¹, but shift the 1357 cm⁻¹ band by less than

Table 6 Root mean square deviations (cm^{-1}) of calculated fundamental frequencies *versus* experimental frequencies from Lautié *et al.*[a]

Mode Type	SVWN	B3LYP	BLYP
4000–3000 cm^{-1}	62	138	50
remaining a' modes	33	39	7
a"	23	23	41
Overall	37	64	31
a" without NH wag	23	9	28
Overall without NH wag	37	63	27

[a] Ref. 40
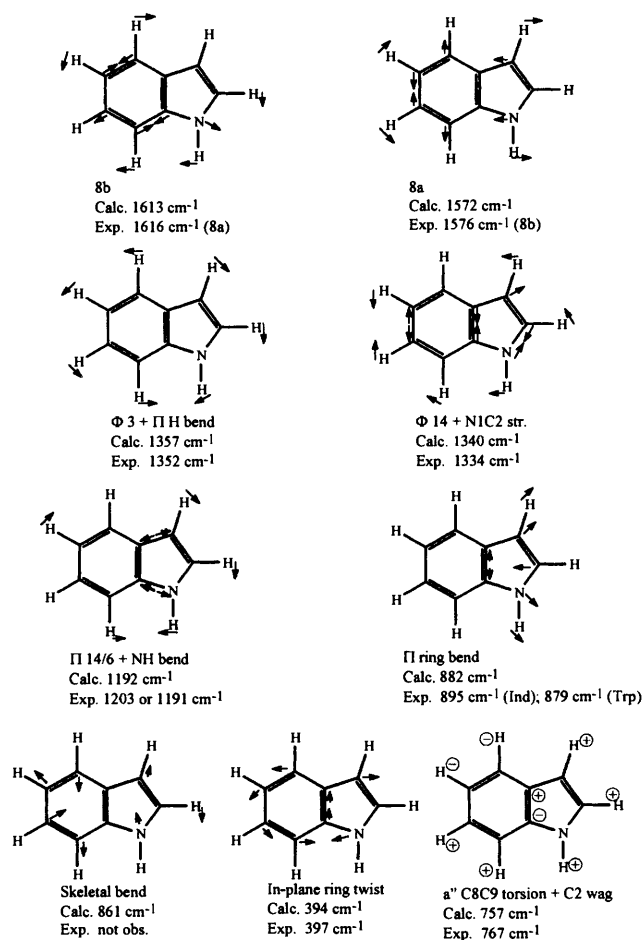
Fig. 1 Illustration of relative atomic displacements for selected fundamentals of indole. Calculated frequencies are from BLYP with 6-31G(d) basis set. Relative arrow lengths are approximately proportional to displacement. For the out-of-plane mode, signs indicate relative direction, but not magnitude of displacement. Experimental frequencies from Ref. 40.

1 cm^{-1}. These experiments could potentially demonstrate the nature of the two strong bands observed for indole and trp in the 1330–1360 cm^{-1} region.

The number of fundamental modes between 1190 and 1210 cm^{-1}. The number of fundamentals occurring in the narrow mid-range frequency region of 1190–1210 cm^{-1} is unsettled among the various experimentalists as 0, 1 and 2 fundamentals have been reported in this region. Table 1 shows the frequencies of the observed bands in this range. All methods employed here for harmonic frequency calculation indicate that only one fundamental occurs in this region, though within the average error of the calculations, we cannot say which of the observed bands at 1203 or 1191 cm^{-1} is the fundamental. While this is contrary to the assignments made by LL,[40] this finding is con-

sistent with the assignments of Collier[30] and of MV,[27] who both designated a band at 1204 cm^{-1} as a fundamental.

Symmetry assignments for three bands of Lautié and co-workers. LL assigned an observed mode at 397 cm^{-1} to an a" Π mode;[40] however, this was subsequently reassigned by Takeuchi and Harada[39] to an a' mode. Collier[30] and MV[27] both observed an a' mode between 385 and 400 cm^{-1}. This vibration, an in-plane ring rock (a' symmetry), is well predicted by all three DFT and HF/DFT methods, including its intensity. The BLYP frequency for this mode is 394 cm^{-1}.

A symmetry switch for the 767 cm^{-1} (from a' to a") and 873 cm^{-1} (from a" to a') fundamentals of Lautié and co-workers was suggested by Takeuchi and Harada[39] based on their empirical force-field calculations. This has been adopted by subsequent researchers. All three DFT and HF/DFT methods support the reassignments of the 767 cm^{-1} band, since an out-of-plane mode is predicted to be near 770 cm^{-1} (757 cm^{-1}-BLYP†). The band observed by LL at 873 cm^{-1} may be an in-plane ring bending mode as suggested by Takeuchi and Harada or it may, indeed, be an out-of-plane mode as originally assigned. Our calculations predict both an a' and an a" mode in this vicinity. A very weak in-plane mode is predicted to be near 870 cm^{-1} (861 cm^{-1}-BLYP) and a moderate to weak out-of-plane mode corresponding to Φ CH γ 10b is also calculated in this region (829 cm^{-1}-BLYP). The assignment Φ CH γ 10b is the same as the one given to the 873 cm^{-1} mode by LL. Thus, while our calculations do predict an a' mode near 870 cm^{-1}, they also show an a" mode near the same frequency in accordance with the original assignments made by LL.

The out-of-plane fundamentals between 760 and 910 cm^{-1}. Lautié and co-workers identified two out-of-plane fundamental frequencies in this range,[40] but one additional band which they assigned to an in-plane pyrrole mode was subsequently reassigned to an out-of-plane mode (see above). Thus, there are three a" vibrations in this region. They are assigned by LL to Φ CH γ 10b (873 cm^{-1}), CH γ on C2 (848 cm^{-1}), and the Π mode at 767 cm^{-1}. The BLYP calculations agree quite well with the ordering and assignments: Φ CH γ 10b (829 cm^{-1}), Π CH γ asynchronous (803 cm^{-1}), and the C8–C9 torsion mixed with C2–H γ (757 cm^{-1}). Our calculations from all methods show mixing of the C2–H and C3–H wagging modes, however. The predicted C8–C9 torsion mixed with C2–H γ could easily be attributed to a generic Π mode. Our calculations do not predict out-of-plane fundamentals near 904 cm^{-1} identified as a fundamental only by MV[27] and near 791 cm^{-1} identified as a fundamental by MV and by Collier.[30] We have correlated our calculated mode at 757 cm^{-1} (BLYP) to the experimentally measured mode at 767 cm^{-1} (LL). Based on their scaled calculated frequencies, MV assigned an observed band at 791 cm^{-1} to this same mode from Lautié *et al.*, although they report an observed band at 764 cm^{-1} which they assign to a combination band. Our calculations for the C8–C9 isotopically substituted indole mentioned earlier indicate that the mode at 757 cm^{-1} shifts by approximately 15 cm^{-1} with the ^{13}C substitution. Our calculations in this region support the fundamental frequencies and assignments of Lautié and co-workers with re-assignment of the 767 cm^{-1} (exp.) band as a" symmetry.

Modes identified as fundamentals by only one experimental group. There are five observed vibrations: a' at 505, 1227, 1300 cm^{-1} and a" at 625 and 904 cm^{-1} which have been described as fundamentals by only one group each. Our calculated frequencies and relative intensities imply that none of these five bands is a harmonic fundamental for indole.

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† For consistency calculated B3LYP frequencies are not used during discussions of out-of-plane modes even though their numerical agreement with experiment is better. The same conclusions are reached regardless of method. The B3LYP frequencies may be obtained from Table 5.

Mode Description[a]	Name	Trp (exp) cm⁻¹	IndH (calc.) cm⁻¹
$\Phi\nu'_{8a}$ & ν NC8	W1	1622	1613 (8b)
$\Phi\nu'_{8b}$	W2	1579	1572 (8a)
$\Pi\ \nu$ C2C3	W3	1552	1514
$\Phi\nu'_{19b}$	W4	1496	1492 (19a + δ NH)
$\Phi\nu'_{19a}$	W5	1452	1450 (19b)
NC2C3 sym. str. & δNH	W6	1435	1414
Fermi Doublet	W7	1362/1342	1357/1340[b]
ν C3C9, δ NH	W8	1305	1269/1192
δCH & νC3 C$_{ext}$	W10	1238	na
similar to $\Phi\nu_{9b}$	W13	1127	1119
Φ ring str. (resp)	W16	1012	1012 (Φ 18b)
sim $\Phi\nu_{12}$ & δNH[c]	W17	879	882
Indole breathe	W18	759	753

[a] These mode descriptions and experimental frequencies are taken from ref. 9, except where noted. Π = pyrrole ring localized; Φ = benzene ring localized. The Φ modes are from Wilson (refs. 47 and 48). The calculated mode assignments were verified using the XVIBS and XMOL computer programs (ref. 75). [b] Calculated to be two fundamentals. [c] This description is from Takuechi and Harada's empirical force field calculation (ref. 39). From Hirakawa et al. (ref. 38) ¹⁵N- and N-D substitution spectra the 882 cm⁻¹ band of trp ¹⁴NH is shown to be pyrrole bending coupled with NH bending, as our calculations predict.

The frequency of the NH wagging mode and its mixing with Φ 16b for monomeric indole. The NH out-of-plane bending mode (γ NH) has been reported at frequencies ranging from 516.0 cm⁻¹ (ref. 27) to 403 cm⁻¹ (ref. 52) and seems to present particular difficulties for both experiment and computation. The experimental difficulties are believed to arise from the formation of NH $\cdots$ π hydrogen-bond-like interactions in solution, other than very dilute, or condensed phases. The bathochromic shift of the N-H stretching frequency has been used as an indicator of this autoassociation of indole.[40,52,53] The existence of two discernible dimeric species was proposed[52] after evaluating concentration and solvent effects on other vibrational frequencies of indole, notably certain skeletal motions and the NH wag.[52] Based on the bathochromic shift observed for the γ ND mode in CCl₄ solution, Lautié and co-workers suggested that the γ NH mode decreases in frequency by approximately 50 cm⁻¹ (from 487 cm⁻¹ to ca. 437 cm⁻¹) in going from liquid to gas-phase as the degree of self-association decreases. This suggestion was verified by Barraza et al. who observed[52] that a band at 500 cm⁻¹ in the solid shifted to 403 cm⁻¹ in a dilute, non-hydrogen bonding, solution and also exhibited decreases in intensity and breadth characteristic of spectroscopic changes for bending modes resulting from decreases in H-bonding. Although previously observed as a strongly absorbing mode, the γ NH mode was assigned by Majoube and Vergoten to a moderately intense absorbance observed at 516.0 cm⁻¹. They also observed an absorbance of unspecified intensity at 403 cm⁻¹ but assigned it to an overtone of a lower frequency vibration. Lautié et al. comment that the γ ND mode of 1-[²H]indole was studied for H-bonding effects because the γ NH of [¹H₇]indole involved too much mixing, though they do not specify with which mode it is mixed.

The basis for the computational difficulties with this mode is less clear since no calculations included dimerization. There seems to be some basis set dependence as previous Hartree–Fock type calculations with the 3-21G basis set predict the γ NH mode at a much higher frequency than where it has been measured.[27,28] Using the larger 6-31G(d) basis set with polarization functions on the heavy atoms, however, our UHF, HF/DFT and DFT (except SVWN) and published MP2[43] calculations predict the mode at a much lower frequency than the experimentally observed band. The only published MO calculations including a potential energy distribution[27] (MV) and our own BLYP, B3LYP and UHF calculations also predict this

mode to be a nearly pure γ NH mode. Only the local density approximation method SVWN indicates that the γ NH is mixed with another out-of-plane mode and places it near the frequency expected.

The two gradient-corrected methods agree with each other by predicting a weak purely Φ/16b mode at ca. 430 cm⁻¹ and a very strong purely γ NH mode at 360 cm⁻¹ (B3LYP) or 330 cm⁻¹ (BLYP). SVWN predicts two fundamentals at 432 and 415 cm⁻¹, with strong and very strong IR intensities, respectively, which are each derived approximately 50:50 from Φ16b (a benzene ring torsion mode) and γ NH. Lautié et al. report a very strong absorbance at 423 cm⁻¹ attributed to the Φ16b mode and observed the strong γ NH mode at 487 cm⁻¹ but postulated the gas-phase frequency to be near 437 cm⁻¹. Thus, for the NH wagging mode the SVWN method seems to correlate by frequency and relative intensity much better with experiment than the gradient-corrected or molecular orbital methods and supports the conclusions of LL and Barraza et al. that this mode appears between 437 and 403 cm⁻¹. Perhaps this agreement is related to the mixing predicted by SVWN but not by the other methods.

Summary. In summary, our calculations for fundamental vibrations of indole exhibit much closer agreement with the experimentally derived assignments of Lautié and co-workers than with subsequent assignments based on empirical or scaled molecular orbital calculations. The gradient-corrected DFT method BLYP with the 6-31G(d) basis set yields unscaled harmonic fundamentals in excellent *overall* agreement with the experiment. Yet, of the methods applied here, the hybrid HF/DFT method B3LYP compares best with experiment for the out-of-plane modes, except for the NH wagging mode, for which SVWN shows better agreement. The two most significant differences between our calculations and previous molecular orbital calculations are in the assignment of two fundamentals, rather than a Fermi doublet, near 1350 cm⁻¹ and the frequency and mixing of the NH wagging mode. Additionally we have addressed the issue of varying sets of fundamental frequencies for indole, which if taken all together would yield $3N + 3$ normal modes.

Not only do our assignments for [¹H₇]indole predominately agree with those of Lautié and co-workers, we have calculated the vibrational frequencies for the series of deuterium-substituted indoles studied by them and have found that the differences between calculated (BLYP) and experiment are less than 2% for a' modes and less than 5% for a" modes. (The XH stretching frequencies which are not included in Lautié's paper and the γ NH were not included.)

Comparisons with indole derived vibrational modes of tryptophan
Although indole lacks tryptophan's substituent at the C-3 position, Table 7 indicates that our calculations show excellent agreement with the frequencies and slight variations from the assignments of the tryptophan vibrational bands used in protein spectroscopy.[9]

A marker for hydrogen bonding, the frequency of the W17 mode is relatively linear with respect to hydrogen-bonding strength. This mode was described through empirical force-field analysis[39] to be phenyl ring bending similar to Φ 12 mixed with NH δ. This empirical description is similar to the predicted very weak band at 861 cm⁻¹ which our calculations show includes those vibrations as well as Π ring bends and C2-H and C3-H bends. A stronger band predicted at 882 cm⁻¹ does not contain the phenyl vibrations but does have Π ring bending, NH δ and C3-H δ. This mode is consistent with descriptions derived from spectra of ¹⁵N- and N-D substituted tryptophan.[38] The frequencies calculated for the 882 cm⁻¹ mode for isotopically substituted indole are different only by 6 cm⁻¹ for the ¹⁵N-substitution and 0 cm⁻¹ for the D-substitution from those experimentally measured for the W17 mode of the substituted tryptophans. Thus, assuming indole's vibrations are a good

model for those of trp, W17 is not phenyl ring bending mixed with NH bending, but is instead pyrrole ring bending mixed with NH and C3–H bending vibrations.

Three other modes also exhibit a frequency shift which is linear with respect to hydrogen-bond strength as measured by the frequency of the NH stretch. These modes are W2, W4 and W6. Our predicted assignment of Π 14/6 ‡[54] mixed with NH δ for the 1414 cm^{-1} fundamental correlates very well with W6, previously assigned by empirical force-field analysis to N1–C2–C3 symmetric stretching mixed with NH δ. The band designated W4 at 1496 cm^{-1}, assigned via the empirical force-field calculations to Φ 19b, also shows a correlation between frequency shift and hydrogen-bond strength. Our calculations identify this band as Φ 19a mixed with NH δ and some C5–H δ at 1491 cm^{-1}. Of the 19a/19b pair the lower frequency band is more intense experimentally and in our calculations. Our assignment of the lower frequency band (trp exp. 1452 cm^{-1}; BLYP 1450 cm^{-1}) to Φ 19b and the higher frequency band to Φ 19a is the same as Lautié and co-workers' original assignment for indole. Likewise the vibration W2 was assigned to Φ 8b via the empirical force-field analysis, yet our calculations show it to be the Φ 8a vibration. We do show Φ 8a, at 1572 cm^{-1}, to be mixed with NH bending motion which would be affected by hydrogen bonding. Thus, for W2 and W4 our calculations show NH bend character, as indicated experimentally, but the mixing 'partners' are different from those from empirical calculations.[39]

While W4 and W6 are not significantly enhanced in resonance Raman spectra, the W1 and W2, or Φ 8a and 8b, pair of frequencies are significant in trp analysis because both exhibit resonance enhancement in resonance Raman experiments at different wavelengths.[9,38,55–58] The assignment of Φ 8a for the higher frequency W1 band has been based on the empirical force-field calculations of Takeuchi and Harada[39] and rationalizations of vibrational mode symmetry compared to the transition moment vectors for electronic transitions and the resulting resonance Raman enhancement.[57] Our assignment of Φ 8b for the 1613 cm^{-1} vibration (calcd.) does not necessarily contradict the previous arguments based on the transition moment vectors, because atomic displacements in Φ 8b (Fig. 1) are more symmetric than the displacements of Φ 8a to a transition moment vector through C6, as the B_b electronic transition has been described.[59]

The W3 mode, a C2–C3 stretching fundamental, is considered indicative of the C2–C3–C_β–C_α torsional angle.[9,60] Our calculated frequency is not very different from that for indole (1509 cm^{-1} LL) at 1514 cm^{-1}, but is considerably more different from the W3 mode of trp at 1552 cm^{-1}. For trp, the stretch involves a carbon (C3) with an exocyclic carbon bonded to it, whereas in indole C3 of course has a hydrogen on it.

The pair of frequencies postulated to be a Fermi doublet has been examined as a measure of the hydrophobic environment of trp residues.[9,61,62] As mentioned in the earlier section, our calculations, and others including electron correlation, predict two fundamentals in this region. The isotopic substitution experiments suggested, when addressing indole frequencies near 1350 cm^{-1}, could potentially demonstrate the nature of these two strong bands observed for indole and trp in the 1330–1360 cm^{-1} region and help explain observed effects of protein environment on them. Both fundamentals exhibit delocalized motion which could be affected by pH and solvent polarity.

In summary, while our assignment for W17 does not agree with the empirical force-field analysis which has been used in the past for descriptions of the trp vibrational modes, our assignment and isotopically induced frequency shifts do agree with previous ones based on experimental investigations. We have calculated two fundamentals near 1350 cm^{-1} where the

empirical force-field calculations (and other calculations not including electron correlation effects) only predict one, leading to our suggestion that the postulated Fermi doublet is actually two fundamentals. The two pairs of frequencies resulting from the Φ 19 and Φ 8 degenerate pairs are reordered in our calculations relative to the ordering from the earlier empirical calculations. Finally, since there is no exocyclic carbon in indole, we naturally have no fundamental to compare with the C3–C_{ext} stretch and our calculated frequency for the C2–C3 stretch is within 5 cm^{-1} for indole experiments, but is 38 cm^{-1} lower than the trp experimental frequency.

Conclusions

For computational resources comparable to Hartree–Fock calculations, a geometry was calculated for indole using the B3LYP method and a 6-31G(d) basis set with an absolute average difference from a geometry from CASSCF calculations of only 0.005 Å. Our B3LYP calculations not only show excellent agreement with the geometry from CASSCF calculations, but also with an averaged X-ray structure of 3-alkylindoles used in our earlier report for comparison[37] and the rotational constants measured by microwave spectroscopy. The bond distances from SVWN and BLYP are not as accurate as B3LYP, but still exhibit average absolute differences of only 0.009 and 0.011 Å, respectively. The rotational constants from SVWN are nearly as accurate as those from B3LYP, but the rotational constants from BLYP do not agree as well with experiment.

For indole, the matching of calculated frequencies and assignments to experimental assignments is extremely complicated, due in part to a paucity of experimentally based assignments, in part to disagreements among experimentalists regarding which frequencies are fundamentals, and in part to the nature of the molecule with extensive mixing of vibrations. However, as evidenced by the RMSDs of the unscaled, calculated vibrational frequencies, density functional and hybrid Hartree–Fock/density-functional methods yield considerably more accurate vibrational frequencies than Hartree–Fock calculations. Ironically, and possibly through a fortuitous cancellation of errors, the BLYP with 6-31G(d) basis set yields harmonic fundamental frequencies for indole in better agreement with experiment than does B3LYP with the better geometry. One mode, the NH wagging mode, has historically been over-estimated with Hartree–Fock calculations with the 3-21G basis set, but is underestimated by UHF, MP2, BLYP and B3LYP with the 6-31G(d) basis set. Only the local density approximation SVWN with 6-31G(d) basis set has thus far accurately predicted the frequency and mixing of this mode.

A unique feature of our calculations is the prediction of two fundamentals in the 1350 cm^{-1} region, where earlier empirical calculations and experiments indicated a Fermi resonance pair. We propose isotopic substitution studies incorporating ^{13}C at the C8 and C9 positions as an experimental test of our suggestion that these two bands are fundamentals.

Beyond support for our calculations from experimental data on indole and deuterium substituted indole, tryptophan vibrational bands also agree with our calculations. Of the 13 tryptophan Raman bands that are considered to arise from the indole side-chain, our frequencies and assignments agree with experiment for most. Apart from the assignment of the purported Fermi doublet as two fundamentals, our disagreements involve a or b designators for phenyl modes and the assignment of W17. While these differences could be the result of not including the alanyl chain in the calculations, that omission should not extensively affect these primarily benzene ring vibrations.

The density functional and hybrid Hartree–Fock/density functional methods have been relatively untested in heteroaromatic molecules. We have shown that density-functional, gradient-corrected density-functional, and hybrid Hartree–Fock/gradient-corrected density-functional methods with a

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‡ The symbolism Π 14/6 refers to a combination of modes 14 and 6 as described by Lord and Miller.[54]

moderately sized basis set can be employed to predict accurately the geometry, rotational constants and the vibrational spectrum for the bicyclic, heteroaromatic indole molecule. It is hoped that the geometry and the complete set of unscaled frequencies and assignments will be advantageous to experimentalists for answering remaining questions about vibronically coupled spectra of indole and the vibrations of tryptophan arising from the indole side-chain. With accurate vibrational assignments, time-resolved vibrational spectroscopy can be used to study complexations and reactions of indole.

Acknowledgements

Appendix: computational methods

The geometry optimizations and frequency calculations were accomplished with the computer programs GAUSSIAN92/DFT[63] to solve the Hartree–Fock[51,64] and Kohn–Sham[65,66] equations. The density-functional methods utilized embody the local density approximation for exchange of Slater[67] with the local correlation functional of Vosko, Wilk and Nusair[68] (SVWN) and Becke's gradient-corrected exchange functional[69] with the gradient-corrected functional of Lee, Yang and Parr (BLYP).[70] These two methods are collectively referred to as DFT methods. In addition, the three parameter, hybrid Hartree–Fock/density-functional (HF/DFT) method derived from the BLYP, known as B3LYP,[21] was also employed. Unrestricted Hartree–Fock ab initio calculations (UHF) were also performed for comparison. All calculations were performed with the spin-unrestricted formalism and the 6-31G(d) basis set.[71] A geometry optimization was also made with the 6-311G(d,p) basis set and the B3LYP method to compare with the smaller basis set.

The starting geometry employed for all optimizations resulted from a semi-empirical MNDO[72] optimization, calculated using the program MOPAC 6.0.[73] Initially, the geometry was optimized in UHF and SVWN without any symmetry constraints. Because these resulted in a C_s symmetry optimized structure, subsequent calculations designated C_s symmetry for the molecule. Berny's optimization algorithm[74] in internal coordinates was used to fully optimize the geometries for each method before frequency calculations were performed. Analytical first derivatives and analytical or numerical second derivatives of the energy were computed for calculating harmonic force constants. The mode assignments were made through visualization of the atomic displacements with the program XMOL.[75]

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