I. INTRODUCTION

Vibrational spectroscopy is among the foremost experimental tools in the exploration of molecular potential-energy surfaces (PES). Its application to biological systems has so far been severely handicapped, both by experimental difficulties and by the unavailability of adequate computational tools for quantitative interpretation. Recent success in the experimental realization of coherent multidimensional infra-red (IR) spectroscopy provides a new powerful tool to study structure and dynamics of biomolecules with a temporal resolution down to the sub-picosecond regime. Multidimensional IR spectroscopy has the potential to disentangle the congested vibrational spectra of biomolecules to some extent similar to multidimensional NMR but with significantly higher temporal resolution. In nonlinear multidimensional spectra the structural and dynamical information is typically available in terms of diagonal and cross-peak shapes, locations and intensities and their respective temporal evolution. The interpretation of this data in terms of a dynamical model of the biomolecule under investigation requires extensive theoretical modeling.

The calculation of vibrational spectra within the harmonic approximation is very useful, but often has limited significance since many biologically relevant molecules are “floppy” and subject to strong anharmonic effects. Anharmonic effects are even much larger in weakly bound molecular complexes, e.g. hydrogen-bonded complexes with surrounding water. Also, frequently one is interested in the regions of the PES far away from the equilibrium configuration, where the harmonic approximation is even less applicable. The main problem of anharmonic spectroscopic calculations is that different vibrational modes are not mutually separable like in the harmonic approximation. Therefore one has to face the task of calculating wavefunctions and energy levels for systems of many coupled degrees of freedom. Several attempts have been made to overcome this problem. Among others, the discrete variable representation (DVR), diffusion quantum Monte Carlo (DQMC), and vibrational self-consistent-force field (VSCF), methods proved their applicability to study anharmonic effects in systems with varying sizes. The VSCF method is most successful among them to effectively handle large molecular systems.

IR absorption spectra of peptides and proteins are dominated by vibrational bands that can be described approximately in terms of oscillators localized in each repetitive unit and their mutual couplings. The most extensively studied bands are amide-A and amide-B in the region 3000–3500 cm\(^{-1}\) and amide-I and amide-II between 1500–1700 cm\(^{-1}\), which are spectrally well separated from the remaining spectrum and exhibit a strong dependence on the structural motifs present in the investigated biomolecules. The amide-I vibrational mode, which involves mainly the C=O stretch coordinate, has experimentally been the most important mode due to its large transition-dipole moment and because it appears to be mostly decoupled from the remaining vibrational modes in proteins. A detail understanding of these modes is then necessary to understand the structure and dynamics of the protein and peptide. Due to the complex structure of proteins a detailed theoretical understanding of these modes is complicated. A simple small molecule is then necessary for which these exemplar modes and their mutual couplings can be studied in more detail.

In this work Methyl benzoate was chosen as a model for potential vibrational couplings between the carbonyl group and a sidechain C-H moiety, which would allow for a determination of backbone-sidechain dynamics in peptides and proteins. Methyl benzoate has an idealized planar configuration, except for the two hydrogen atoms at the methyl group which are symmetrically out-of-plane.
coupling in proteins is the coupling between the amide-I and a β-hydrogen located in the sidechain. Methyl benzoate also provides a similar structural motif where the ortho hydrogen in the phenyl ring provides the counterpart of a β-hydrogen in protein sidechains. The structural similarities of these two motifs in Methyl benzoate and proteins are depicted in Fig. 1b.

Isotopic substitution is a valuable tool in the identification of molecular structure and dynamics. The C–H or C–D stretch vibrations are particularly important structural probes, because they are very localized, specific, and abundant. Especially the C–D stretching frequency is an excellent structural probe since it is usually spectrally isolated (∼2200 cm⁻¹) even in the spectrum of large proteins. Substitution of β-hydrogen by deuterium provides a probe to obtain a better understanding of the structure and dynamics of protein sidechains with respect to the backbone. It is thus an interesting task to devise new experiments which probe this relative geometry. Methyl benzoate is an ideal candidate model which, once its vibrational Hamiltonian is fully understood, will serve to develop new pulse sequences.

II. COMPUTATIONAL METHODS

A. Quantum Chemistry

Geometry optimization of Methyl benzoate was performed using second order Møller-Plesset perturbation theory26 and employing the augmented correlation-consistent polarized-valence-triple zeta (aug-cc-pVTZ) basis set. Harmonic normal-mode analysis was performed with the density fitting MP2 (DF-MP2) method using an aug-cc-pVTZ regular basis and cc-pVTZ fitting basis sets. All calculations were performed with the MOLPRO quantum chemistry program29.

The choice of the computational method and the basis set are not arbitrary. A standard MP2 with aug-cc-pVTZ basis set level of computation is generally a reliable method to generate an anharmonic PES. For a system like Methyl benzoate it is not suitable due to the size of the molecule and the resulting high computational cost. To find a suitable method a comparison of computations employing different basis sets has been performed and is presented in Table I. The standard MP2 calculation employing an aug-cc-pVTZ basis set is given in the first row and provides the reference. It is clear that the standard MP2 method with aug-cc-pVTZ basis is beyond our scope to study all 48 normal modes for Methyl benzoate, as it takes almost one day and a very large memory space for a single-point energy calculation. If no specially optimized fitting basis sets are available for a certain regular AO basis set it is common practice for the DF-MP2 computations to use a fitting basis set one order higher than the regular one. The DF-MP2 with aug-cc-pVTZ regular basis and cc-pVQZ fitting basis speeds up the calculation dramatically (see Table I) without sacrificing quality compared to the standard MP2/aug-cc-pVTZ results. A single-point energy calculation with this method takes only one and a half hours and requires almost 200 times less memory than memory require for regular MP2 calculation with aug-cc-pVTZ basis set. Whereas the DF-MP2 method employing aug-cc-pVTZ regular and cc-pVTZ fitting basis sets gives almost identical energy values in half the time and is a reasonable choice for our purpose. The anharmonic pair couplings are calculated with the DF-MP2 level of theory employing the same cc-pVDZ basis for regular and fitting basis set. For some of the most problematic modes the diagonal potentials are calculated with the local density fitting coupled cluster singles and doubles and perturbative triple correction DF-L-CCSD(T)23-25 method with the cc-pVTZ basis set in a dual-level scheme. All computations were additionally performed using the density fitting spin-component scaled (DF-SCS) MP2 method30 employing different basis sets.

TABLE I. Single point energy, calculation time and the required memory for energy calculation of Methyl benzoate at equilibrium geometry with different basis sets.

| Basis      | Energy in E_h | CPU time | Memory |
|------------|---------------|----------|--------|
| mp2fit     | -457.5104     | -1.7601  | -459.2702 | 85363   | 6799.36 |
| jkfit      | -457.5101     | -1.7601  | -459.2702 | 2822    | 270.39  |
| SCF        | -457.5104     | -1.7601  | -459.2702 | 5829    | 361.65  |
| MP2        | -457.5104     | -1.7601  | -459.2702 | 17132   | 3194.88 |
| Total      | -457.5104     | -1.7601  | -459.2702 | 29014   | 3194.88 |
B. Grid for VSCF

The choice of an appropriate grid size is crucial for anharmonic frequency calculations for both diagonal and pair potentials. The VSCF PES can be expressed in terms of a hierarchical expansion:\textsuperscript{34}

\[
V(q_1, \ldots, q_N) = \sum_{j}^{N} V_j^{(1)}(q_j) + \sum_{i<j}^{N} V_{i,j}^{(2)}(q_i, q_j) + \cdots + \sum_{i<j<k}^{N} V_{i,j,k}^{(3)}(q_i, q_j, q_k) + \cdots
\]

where \( V_j^{(1)}(q_j) \) is the diagonal potential, \( V_{i,j}^{(2)}(q_i, q_j) \) is the pairwise potential, \( V_{i,j,k}^{(3)}(q_i, q_j, q_k) \) is the triple coupling and so on.

The grid was constructed based on the harmonic frequency analysis and PM3 PES cuts. The innermost two points (-h, h) are determined from the second derivative of the PES at equilibrium corresponding to the harmonic frequencies of the normal modes. The outer two points (-a, b) are determined as those points on the 1D-PES cuts along the normal modes for which the PM3 energy reaches six times the harmonic frequency quantum w.r.t. \( V_0 \). The remaining points are calculated dividing the interval with different proportions e.g., \( c = \frac{-a+(-h)\cdot \frac{1}{2}}{2} \), \( d = \frac{b+h\cdot \frac{1}{2}}{2} \), \( e = \frac{c+(-h)\cdot \frac{1}{2}}{2} \), \( f = \frac{d+h\cdot \frac{1}{2}}{2} \), \( i = \frac{-a+c\cdot \frac{1}{2}}{2} \), \( j = \frac{d+h\cdot \frac{1}{2}}{2} \), \( k = \frac{e+(-h)\cdot \frac{1}{2}}{2} \) and \( l = \frac{f+h\cdot \frac{1}{2}}{2} \). Diagonal potentials with 6 points (see Fig. 2a) are insufficient for a reasonable description of the PES in the calculation of anharmonic frequencies. In particular, a denser set of grid points is required near the equilibrium configuration. A comparative study has been carried out with 8 point (see Fig. 2b) and 12 point (see Fig. 2c) 1D grids. It indicates that the 8 point grid PES is a reasonable choice for anharmonic frequency calculations.

All diagonal points were first evaluated on an eight point one-dimensional grid as shown in Fig. 2a, then interpolated to equidistant 16 point grids which were used in the collocation treatment. Pair potentials, calculated at semiempirical PM3 level, were evaluated on 8 \times 8 point direct product grids and then interpolated to 16 \times 16 point grids by two-dimensional cubic spline interpolation.\textsuperscript{35} To lower the computational cost while maintaining high quality pair potentials, we performed DF-MP2/cc-pVDZ computations for selected coupling potentials on irregularly spaced two-dimensional grids, as shown in Fig. 2d. Energies are only calculated for the grid points marked with crosses. The undetermined points (marked with circles in Fig. 2d) are filled by using non-uniform IMLS (interpolating moving list-squares)\textsuperscript{36} interpolation, which provides a potential on 8 \times 8 point direct product grids. The 8 \times 8 point grid is extended to the 16 \times 16 point grid by using 2D cubic-spline interpolation.

III. RESULTS AND DISCUSSION

A. Vibrational spectrum of Methyl benzoate

There are not many experimental results (except for the low-resolution IR Raman spectrum of Chattopadhyay\textsuperscript{37}) available for Methyl benzoate. Also, not all modes are resolved and identified experimentally, especially for low-frequency and near-degenerate modes. We therefore choose our best computational result, which agrees comparatively well with the known experimental results\textsuperscript{37–40}, as a reference and then discuss all other levels of computation with respect to that. For this purpose, we choose the non-correlated VSCF results as a reference, where diagonal and pair potentials are calculated using the DF-SCS method employing a cc-pVDZ basis set.

The entire vibrational spectrum of Methyl benzoate can be divided into three different frequency regions. Most interesting high frequency modes are due to the C-H stretching modes. Low frequency (up to \( \sim 1000 \) cm\(^{-1} \)) modes are primarily due to bending motions involving the phenyl ring and the ester group. Between these two extremes there are modes with combinations of bending and stretching motions and also the spectroscopically well-separated C=O band at about 1725 cm\(^{-1} \).

The vibrational frequencies of all modes of Methyl benzoate calculated at different levels of theory are presented in Table I along with their experimentally observed values and full assignment of all modes. The deviation of the vibrational frequencies calculated at different levels of theory with respect to the frequency obtained from the non-correlated VSCF/DF-SCS method are plotted in...
TABLE II. Vibrational frequencies of Methyl-Benzate with different level of theories, where diagonal grids are calculated with the DF-MP2/AVTZ level. Mode numbers are based on normal mode frequencies. The RMSD calculated with respect to the anharmonic frequency calculated with VSCF/DF-SCS method. The modes for which diagonal anharmonicities are observed larger than 10 cm$^{-1}$ are with bold numbers.

| Mode | Harmonic | Diagonal | VSCF | VC-MP2 | VSCF/DF-SCS | Experiment | Isotopomer | Assignment$^a$ |
|------|----------|----------|------|--------|-------------|------------|------------|---------------|
| 1    | 52       | 82       | 147  | 103    | 87          | 112        | D7         | Phenyl-ester opr |
| 2    | 112      | 154      | 178  | 192    | 160         | 196        | D11        | Phenyl opb, ester opb |
| 3    | 185      | 361      | 366  | 316    | 352         | 342        | CH$_3$ asb  |
| 4    | 167      | 170      | 169  | 173    | 169         | 179        | CH$_3$ asb  |
| 5    | 208      | 217      | 236  | 239    | 234         | 242        | Phenyl-ester ipr |
| 6    | 331      | 333      | 326  | 334    | 331         | 340        | Phenyl-ester ipr |
| 7    | 358      | 358      | 356  | 366    | 365         | 363        | O=C-O ipb, phenyl ipb |
| 8    | 404      | 411      | 419  | 416    | 414         | 421        | phenyl ipd |
| 9    | 454      | 458      | 477  | 470    | 466         | 468        | phenyl ipd |
| 10   | 481      | 481      | 481  | 478    | 475         | 477        | phenyl ipd |
| 11   | 617      | 617      | 618  | 612    | 611         | 612        | phenyl ipd |
| 12   | 678      | 679      | 685  | 676    | 673         | 681        | phenyl ipd |
| 13   | 712      | 728      | 788  | 737    | 726         | 754        | phenyl ipd |
| 14   | 795      | 801      | 840  | 808    | 837         | 813        | phenyl ipd |
| 15   | 831      | 830      | 818  | 818    | 812         | 823        | phenyl ipd |
| 16   | 694      | 760      | 759  | 781    | 724         | 731        | phenyl ipd |
| 17   | 863      | 894      | 880  | 856    | 841         | 891        | phenyl ipd |
| 18   | 1003     | 1004     | 1170 | 974    | 971         | 978        | phenyl ipd, ester ipd |
| 19   | 1012     | 1012     | 1052 | 991    | 989         | 979        | phenyl ipd |
| 20   | 1048     | 1049     | 1146 | 1029   | 1025        | 1035       | phenyl ipd |
| 21   | 977      | 1000     | 980  | 978    | 987         | 986        | phenyl ipd |
| 22   | 1097     | 1101     | 1162 | 1082   | 1074        | 1096       | phenyl ipd |
| 23   | 938      | 970      | 951  | 931    | 926         | 958        | phenyl ipd |
| 24   | 1142     | 1144     | 1220 | 1111   | 1103        | 1126       | phenyl ipd |
| 25   | 1174     | 1189     | 1154 | 1153   | 1146        | 1167       | phenyl ipd |
| 26   | 1185     | 1199     | 1074 | 1170   | 1161        | 1182       | phenyl ipd |
| 27   | 1191     | 1198     | 1176 | 1164   | 1156        | 1183       | phenyl ipd |
| 28   | 958      | 994      | 908  | 968    | 982         | 979        | phenyl ipd |
| 29   | 1221     | 1227     | 1164 | 1200   | 1194        | 1214       | phenyl ipd |
| 30   | 1317     | 1321     | 1350 | 1283   | 1262        | 1303       | phenyl ipd |
| 31   | 1330     | 1334     | 1287 | 1301   | 1309        | 1320       | phenyl ipd |
| 32   | 1472     | 1469     | 1318 | 1423   | 1415        | 1342       | phenyl ipd |
| 33   | 1479     | 1482     | 1354 | 1433   | 1411        | 1447       | phenyl ipd |
| 34   | 1471     | 1475     | 1461 | 1436   | 1434        | 1452       | phenyl ipd |
| 35   | 1509     | 1507     | 1420 | 1459   | 1454        | 1453       | phenyl ipd |
| 36   | 1519     | 1517     | 1422 | 1488   | 1488        | 1485       | phenyl ipd |
| 37   | 1518     | 1519     | 1529 | 1478   | 1477        | 1498       | phenyl ipd |
| 38   | 1634     | 1636     | 1750 | 1587   | 1581        | 1606       | phenyl ipd |
| 39   | 1634     | 1634     | 1747 | 1587   | 1580        | 1603       | phenyl ipd |
| 40   | 1766     | 1759     | 1915 | 1724   | 1724        | 1778       | phenyl ipd |
| 41   | 3092     | 3059     | 2909 | 2946   | 2795        | 2974       | phenyl ipd |
| 42   | 3183     | 3255     | 2787 | 2582   | 2492        | 2560       | phenyl ipd |
| 43   | 3205     | 3208     | 2867 | 2809   | 2849        | 2855       | phenyl ipd |
| 44   | 3214     | 3247     | 2867 | 2809   | 2834        | 2852       | phenyl ipd |
| 45   | 3217     | 3213     | 2868 | 2809   | 2834        | 2845       | phenyl ipd |
| 46   | 3222     | 3233     | 2913 | 2955   | 2849        | 2952       | phenyl ipd |
| 47   | 3226     | 3191     | 2932 | 3014   | 3035        | 3064       | phenyl ipd |
| 48   | 3238     | 3161     | 2898 | 2935   | 2928        | 3022       | phenyl ipd |
|      |          |          |      |        |             |            |            |               |
| RMSD | 148      | 151      | 78   | 24     | 45          |            |            |               |

$^a$ Symbols: R = rotation, r = rocking, ipr = in-plane rotation, opr = out-of-plane rotation, ipb = in-plane bending, opb = out-of-plane bending, ipd = in-plane deformation, opd = out-of-plane deformation, as = asymmetric stretch, ss = symmetric stretch, asb = asymmetric bending, sb = symmetric bending, sipb = symmetric in plane bending, mCH = methyl CH bond, pCH = phenyl CH bond, sy = symmetric.
Figs. 3, 4 and 5. The trend observed for the root mean squared deviation (RMSD) with respect to VSCF/DF-SCS going from harmonic (148 cm$^{-1}$) to the inclusion of only diagonal anharmonic potentials (151 cm$^{-1}$), and finally to the full potential expansion up to pair contributions at PM3 level (78 cm$^{-1}$) and DF-MP2/cc-pVDZ level (24 cm$^{-1}$) shows that a balanced description of diagonal and coupling contributions is of importance in simplified models. Surprisingly, for VC-MP2 the RMSD (45 cm$^{-1}$) deteriorates compared to the non-correlated VSCF treatment. Correlation correction may not be necessary for such a large system, and the VC-MP2 method may suffer from a degeneracy problem due to the high density of states in Methyl benzoate. As seen from Figs. 3a, 3b and 3c, the VC-MP2 vibrational frequencies are in good agreement with the experimental results, respectively. Frequencies calculated with DF-MP2/aug-cc-pVTZ diagonal and DF-MP2/cc-pVDZ pair potentials are surprisingly accurate for the C–H stretch vibrational frequencies. The RMSD calculated for these eight modes is 13 cm$^{-1}$ only.

B. High frequency vibrational modes

The high-frequency vibrational modes (41 to 48) are spectrally isolated from all other modes of Methyl benzoate (see Table II). The deviation in frequency for these 8 modes calculated at different levels of theory w.r.t. the VSCF/SCS-VDZ method is plotted in Fig. 3c. Harmonic and diagonal frequencies are too high. The RMSD w.r.t. the VSCF/DF-SCS results for the C–H stretch vibrational modes (41 to 48) alone is 319 cm$^{-1}$ for the harmonic frequency, whereas it is 454 cm$^{-1}$ for the diagonal frequencies. The large RMSDs for these eight modes from the harmonic and the diagonal frequency calculations are mostly due to the mode 42, which shows an unexpected red shift to the frequency $\sim 2550$ cm$^{-1}$ (this is discussed in details later). However, when pair couplings are included, the RMSD is reduced dramatically. Dual level calculations, with DF-MP2/aug-cc-pVTZ diagonal potentials and PM3 pair potentials (see Table II) yield a RMSD of 100 cm$^{-1}$. In this case mode 42 is also quite high but shows a red shift from the conventional C–H stretch vibrational frequency to a frequency of 2787 cm$^{-1}$. Dual level non-correlated VSCF computation with DF-MP2/aug-cc-pVTZ diagonal and DF-MP2/cc-pVDZ pair potentials are surprisingly accurate for the C–H stretch vibrational frequencies. The RMSD calculated for these eight modes is 13 cm$^{-1}$ only.
brational modes is shifted to a much lower frequency than the remaining C–H stretch vibrations. This red shift of the C–H stretch vibrational mode has not been discussed in literature, so far. However, a close investigation of the experimental spectra reveals the presence of an unassigned peak at 2560 cm$^{-1}$, with low intensity. In a recent 1D IR experimental study of deuterated Methyl benzoate by Steinel group, a low intensity peak is observed at 2542 cm$^{-1}$, which matches with the calculated frequency (see Fig. 8).

Closer inspection of this mode reveals that this frequency originates from the combination of anti-symmetric C–H (two out of plane hydrogens) stretch vibration in the methyl group along with the out of plane rotation of the ester group w.r.t. the phenyl ring about the C–C bond (mode 1). The ester group rotational motion pulls in one out-of-plane hydrogen to the plane of molecule and pushes the other from the molecular plane. Such a pull and push force changes the force constant of the anti-symmetric C–H stretch vibration, which unexpectedly lower the vibrational frequency of this band. Their motion is depicted in Fig. 4a. The rotational motion is indicated by a curved arrow. Since this vibrational mode (mode 42) is, in the rectilinear normal mode basis employed here, strongly coupled with the lower frequency mode 1, the harmonic and the diagonal anharmonic analysis fails to describe it, where as pair coupling analysis explain it.

C. C=O band

The spectroscopically most studied vibrational band in peptides is the amide-I band. In the Methyl benzoate spectrum the C=O stretch vibrational band which is analogous to amide-I band, is spectrally isolated from all other vibrational frequencies. Computationally, however, the study of this vibrational mode is not straightforward. The harmonic and the anharmonic diagonal frequencies of the C=O stretch vibration at DF-MP2/aug-cc-pVTZ level are relatively high (1766 cm$^{-1}$ and 1759 cm$^{-1}$ respectively) for this mode, compared to its experimental frequency (1724 cm$^{-1}$) (see Table II). Dual level frequency calculations employing DF-MP2/aug-cc-pVTZ diagonal and the PM3 pair potential is even worse (see Table II). The calculated C=O frequency is improved when dual level calculation are performed replacing the DF-MP2/cc-pVDZ diagonal potential for the C=O vibrational mode alone by a DF-L-CCSD(T)/cc-pVTZ diagonal potential. A perfect match with the experimentally observed frequency (1724 cm$^{-1}$) is obtained. For Methyl benzoate, the non correlated VSCF computation yields the C=O stretch vibrational frequency of 1726 cm$^{-1}$, whereas both V-MP2 and VC-MP2 yield 1727 cm$^{-1}$. For the C=O stretch mode a high level description of the diagonal potential is thus of tantamount importance.

IV. DEUTERATED METHYL BENZOATE

Deuteration of Methyl benzoate in the ortho position of the benzene ring yields the syn- and anti- isomers of ortho-deutero methyl benzoate (o-DMB) shown in Fig. 4. In the potential energy minima the ester group remains in the same plane as the benzene ring. Upon thermal excitation, the conformers interconvert by a rotation of the ester group around the C–C bond axis. The barrier height for the ester group rotation in Methyl benzoate is estimated at $\sim 0.25$ eV, as calculated by the DF-MP2 method with aug-cc-pVTZ basis set. This is rather small and easily accessible even at room temperature and thus the conformers can easily interconvert. Since both conformers have nearly the same equilibrium energy, they are also equally populated. Although both conformers have nearly the same molecular energy, they possess different vibrational C–D frequencies due to the different couplings to the ester group. With the best possible computation (dual level VSCF) a C–D stretch frequency difference for these two conformers of about 10 cm$^{-1}$ is found.

A. Identification of isotope effects by co-diagonalization

The co-diagonalization method finds a convenient application in vibrational spectroscopy to identify the coupling of different modes and isotope effects. When an atom is substituted with its isotope, some of the eigen vectors differ from the non-substituted molecule. In co-diagonalization these are identified by non-zero off-diagonal elements. The frequency shift for the primary isotope effect appears in the diagonal element and secondary effects appear as off-diagonal elements. Fig. 9 (a) and (b) depict the resulting co-diagonalized matrices of the syn- and anti-o-DMB. Fundamental frequencies are plotted on the diagonal and the residual couplings are shown in the upper left triangle on the same scale as the diagonal. The scale is given by the left rainbow color spectrum. Ten times magnified coupling elements...
C–D and methyl group rotation (see Fig. 4b).

A noticeable feature of the methyl vibrational modes, respectively. The primary isotope effect is observed in the C–D stretching vibration as expected. The secondary isotope effects are mainly due to the coupling with the C–D vibrational mode. These appear in the low frequency region. A noticeable feature of the isotope effect is that both isotopomers show secondary isotope effects for the same normal modes (modes 8, 13, 14, 17, 18, 19, 20, 23, 27 and 31), where as primary isotope effects are observed for different normal modes. A strong secondary isotope effect is observed at the upper left corner of Fig. 6 (a) and (b), due to the coupling of C–D and methyl group rotation (see Fig. 6b).

The secondary isotope effects are mainly due to the coupling with the C–D vibrational mode. These appear in the low frequency region. A noticeable feature of the isotope effect is that both isotopomers show secondary isotope effects for the same normal modes (modes 8, 13, 14, 17, 18, 19, 20, 23, 27 and 31), where as primary isotope effects are observed for different normal modes. A strong secondary isotope effect is observed at the upper left corner of Fig. 6 (a) and (b), due to the coupling of C–D and methyl group rotation (see Fig. 6b).

B. Vibrational frequencies of anti-o-DMB

For the deuterated species, the overall RMSD shows a similar behavior as in undeuterated Methyl benzoate. Calculated harmonic and anharmonic diagonal frequencies are quite offset from the reference frequencies and give high RMSD values of 137 cm$^{-1}$ and 130 cm$^{-1}$, respectively. Non-correlated VSCF dual level frequency calculations based on MP2/aug-cc-pVTZ diagonal and PM3 pair potentials also deviate considerably from the reference frequencies (RMSD = 76 cm$^{-1}$). The non-correlated VSCF frequencies employing DF-MP2/cc-pVDZ pair and DF-MP2/aug-cc-pVTZ diagonal potentials show good agreement with the reference frequencies and yield a very low RMSD of 14 cm$^{-1}$, for all 48 modes. Figs. 7a, 7b, and 7c depict the general features of the different computational methods for the deuterated Methyl benzoate and Table II presents the vibrational frequencies for the anti-o-deutero-methyl-benzoate. Dual level frequency calculation employing DF-MP2/aug-cc-pVTZ diagonal potentials and PM3 pair potentials for all 48 low frequency modes are not reliable, but for the high frequency modes it yields quite reasonable results. The harmonic and the diagonal anharmonic frequencies are also too high in the low frequency region as well as the high frequency region. For the low frequency modes (40 modes) the non-correlated VSCF employing DF-MP2/aug-cc-pVTZ diagonal and DF-MP2/cc-pVDZ pair potentials are in good agreement with the reference frequencies, yielding a RMSD of 13 cm$^{-1}$. This level of computation is also adequate for the high frequency region and yields a RMSD for the 8 C–H stretch vibrational modes of 17 cm$^{-1}$.

C. C–D band

The harmonic C–D vibrational frequencies at DF-MP2/aug-cc-pVTZ level are rather large, they are 2384 cm$^{-1}$ and 2392 cm$^{-1}$ for the syn- and anti-o-DMB, respectively. The anharmonic diagonal frequency calculation at DF-MP2/aug-cc-pVTZ level improved the results over harmonic calculation by about 70 cm$^{-1}$. It is noteworthy that the C–D stretching frequency is significantly improved by using the pair potentials calculated at DF-MP2/cc-pVDZ level. The non-correlated dual level VSCF method yields C–D vibrational frequencies of 2171 cm$^{-1}$ and 2161 cm$^{-1}$, for the two isotopomers.

An interesting result is observed when the dual level calculations are performed with systematically improved diagonal PES for the C–D stretch vibrational mode. With the improved basis set (for all atoms same basis sets are used) for the diagonal PES, the C–D anharmonic vibrational frequency exhibits a red shift. The frequency change is rather large for the DZ to TZ basis sets, and it converges quickly for larger basis sets. For example, when the diagonal potential for C–D (in anti-o-DMB) vibrational mode is calculated with augmented ba-
sis sets, a 32 cm\(^{-1}\) frequency shift is observed going from AVDZ to AVTZ. On the other hand, a basis set improvement from AVTZ to AVQZ shows just 1 cm\(^{-1}\) frequency shift (Table III column SCF). The C–D shows also a

TABLE III. The C–D vibrational frequency for anti-o-DMB. The diagonal potential for the C–D stretch vibrational mode is calculated at different level of theory and employing different size of basis sets. All other diagonal and pair coupling potentials are calculated at DF-MP2/cc-pVDZ level.

| isotope | Method | Basis | Diagonal | SCF | Y-MP2 | VC-MP2 |
|---------|--------|-------|----------|-----|-------|--------|
| MP2     | DZ     | 2367  | 2233     | 2243| 2247  |
| syn MP2 | TZ     | 2336  | 2187     | 2210| 2210  |
| o-DMB   | MP2    | 2198  | 2180     | 2202| 2201  |
| CCSD(T) | TZ     | 2308  | 2161     | 2185| 2184  |
| MP2     | DZ     | 2374  | 2242     | 2257| 2257  |
| MP2     | TZ     | 2343  | 2196     | 2220| 2219  |
| MP2     | QZ     | 2338  | 2190     | 2214| 2214  |
| MP2     | ADZ    | 2359  | 2221     | 2239| 2239  |
| anti MP2| ATZ    | 2235  | 2189     | 2212| 2212  |
| o-DMB   | MP2    | 2335  | 2188     | 2212| 2211  |
| Ext     | AVXZ   | 2331  | 2183     | 2208| 2207  |
| CCSD(T) | TZ     | 2315  | 2171     | 2194| 2194  |
| CCSD(T) | T/QZ   | 2310  | 2166     | 2190| 2189  |
| PM3     | selected triple | 2172 | 2197 | 2197 |

red shift when highly correlated methods are used. A non-correlated VSCF calculation where the diagonal potential for the C–D vibrational mode is calculated at the DF-L-CCSD(T)/cc-pVTZ level, yields C–D frequencies of 2161 cm\(^{-1}\) and 2171 cm\(^{-1}\) for the syn- and anti-o-DMB respectively. When the DF-L-CCSD(T) calculation is performed using cc-pVQZ basis only for the deuterium and the directly connected carbon (for all other atoms cc-pVTZ basis are used), the frequency is lowered further by 5 cm\(^{-1}\) with respect to the DF-L-CCSD(T)/cc-pVTZ result (Table III).

A detailed analysis of the coupling pattern shows that only a few modes are coupled with the C–D stretch vibrational mode. It is observed that modes 17 and 19 which correspond to the C–D bending modes, are strongly coupled with the C–D stretching mode. Also some other modes like 12, 13, 14, 15, 16, 18, 21, 24, have some weak coupling with the C–D stretch vibrational mode (see supplemental information). All these modes are involved with some kind of C–D bending motions (see Table II).

One might expect that higher order terms in the many-body expansion of the PES have a significant influence on the vibrational frequency of the anharmonic system. The PM3 triple coupling potentials were used for such an analysis. Selected PM3 level triple couplings were added to the DF-MP2/cc-pVDZ pair coupling. This lowers the C–D stretching frequency negligibly (see supplemental information) indicating a minor influence of triple couplings for this particular mode.

There are two significant peaks observed in the linear IR absorption spectra (see lower right magnified region in Fig. 8) which are equally separated from the calculated C–D stretch frequency at 2189 cm\(^{-1}\). It seems that the C–D vibrational stretching mode is coupled with some low vibrational modes and due to the Fermi resonance it split up into two bands. Vibrational CI calculation may be necessary to describe this feature.
D. C=O band

Due to the structural arrangement, there is a possibility to form a strained five membered ring between the ester and the phenyl ring, which may induce an additional coupling between the C=O and the C–D band. The possible structure is shown in Fig. 5c. Both the oxygen atoms in the ester group may take part in five membered rings along with the ortho and β-hydrogens of the phenyl ring. The calculated possible non-bounded distances are

\[
\begin{array}{cccc}
\text{Isotope} & \text{SCF} & \text{V-MP2} & \text{VC-MP2} \\
\text{syn-o-DMB} & 1724.5 & 1724.4 & 1724.5 \\
\text{anti-o-DMB} & 1724.3 & 1724.1 & 1724 \\
\text{MB} & 1725.6 & 1727.2 & 1727.2 \\
\end{array}
\]

2.499 Å and 2.397 Å for the syn- and anti- positions, respectively, which are much larger than the required bond length to form a true five membered ring. Therefore, isotopic substitution at the ortho position in the phenyl ring does not have any influence on the C=O vibrational frequency. The C=O vibrational frequency remains largely unchanged for both syn- and anti-o-DMB. Calculated anharmonic frequencies in dual level calculations yield the same frequency of 1724 cm\(^{-1}\) for both syn- and anti-conformers, which is in agreement with the experimental results.

E. Anharmonicity observed in the VSCF calculations

The diagonal anharmonicities in frequency calculations are presented in Table V where mode numbers are based on the harmonic normal mode analysis. The diagonal anharmonicities are very high for the high frequency C–H stretch vibrational modes, up to a few hundred wavenumbers. Especially mode 42, which is unexpectedly red shifted, shows maximum anharmonicity. Other than the C–H stretch vibrational modes, diagonal anharmonicities are rather small (< 10 cm\(^{-1}\)). Few low frequency modes show anharmonicities slightly higher than 10 cm\(^{-1}\). These vibrational modes are mostly involved with C–H bending motions (see Table III). For the first three modes the calculated vibrational frequencies are not reliable and for that reason anharmonicities are also unreliable.

F. Off-diagonal anharmonicity

Off-diagonal anharmonicities calculated for the few spectroscopically most important modes are presented in Table VI. Calculated off-diagonal anharmonicities for the C=O vs. C–D coupling modes for both the isotopomers are less than a wave number. Such a negligibly small off-diagonal anharmonicity also indicates that there is negligible direct coupling between the C=O and the C–D vibrational modes.
V. CONCLUSIONS

It has been observed that harmonic frequencies are very poor approximation to assign the vibrational frequencies of Methyl benzoate and its two isotopomers. Anharmonic diagonal frequencies show some improvements but were still not sufficient to reach a reasonable assignment. The fundamental transition frequencies calculated with the VSCF method from a pair potential energy surface expansion seem promising, especially when the 2D PES are calculated at a sufficiently high ab initio level. The success of the VSCF frequency calculations depends upon the accuracy of the PES, in particular near the equilibrium where denser grid points are required. Dual level computations in which the diagonal anharmonic potential along a single vibrational mode is calculated using higher level ab initio methods than for coupling potentials provide an efficient route to the computation of the PES expansion in the VSCF framework. Such a dual level VSCF calculation with DF-L-CCSD(T)/cc-pVTZ diagonal and DF-MP2/cc-pVDZ pair coupling potentials provided a nearly perfect agreement of the C=O vibrational frequency with respect to the experimental result.

Carrying out a systematic study, we have shown that not all pair couplings are necessary to describe a particular vibrational band. Using only 14 coupling potentials for the C–D stretch vibrational mode the computed frequency is in good agreement with the result based on the full set of 1128 couplings. Non-uniform IMLS interpolation has been successfully used to reduce the computational cost for potential energy surface generation even further.

An unexpected red shift has been observed for a C–H stretch vibrational mode when the VSCF calculation has been performed with pair coupling potentials. The inability to find this mode in harmonic and diagonal anharmonic calculations indicates that this is a concerted anharmonic effect and pair and higher order couplings are in fact necessary to understand this feature. Our investigations for the C–H(D) stretch vibrational modes with selected triple couplings at PM3 level do not improve the results much over the ab initio pair coupling calculations. This could indicate that either PM3 triple coupling potentials are in sufficient or that higher order coupling effects are negligible in this model.

The correct assignment of the C–D stretch frequency still poses a problem to both the theoretician and experimentalist. The calculated C–D stretch frequency just sits between the two strong peaks observed in the linear IR absorption spectra at the expected C–D frequency region. It seems that the C–D stretch frequency mode is coupled with some low vibrational frequency modes and thus is shifted equally in both directions and appears as two peaks. Vibrational CI calculation may be necessary to describe this feature.

The diagonal and the off-diagonal anharmonicities have been calculated by non-correlated VSCF method. Other than for a few low frequency modes, which are involved in the C–H bending modes, diagonal anharmonicities are very small. The negligible off-diagonal anharmonicity for C=O and C–D coupling modes indicates that these modes are mostly decoupled.

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Vibrational Spectroscopy of Methyl benzoate

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I. SUPPLEMENTARY INFORMATION

TABLE I. Strongly coupled modes with C–D vibrational mode for anti-o-deutero-methyl-benzoate. Although the frequency differ a little amount, but the qualitative result does not depend upon the isotopomers.

| Coupled modes | SCF V-MP2 | VC-MP2 |
|---------------|-----------|--------|
| all decoupled | 2316.4    | 2316.4 |
| 17            | 2287.4    | 2295.9 |
| 19            | 2294.8    | 2294.7 |
| 17,19         | 2265.6    | 2274.5 |
| 12,17,19      | 2243.1    | 2258.7 |
| 12,14,17,19   | 2212.3    | 2249.8 |
| 12,14,15,17,19| 2206.4    | 2244.3 |
| 12,14,15,17,19,21| 2219.9 | 2238.8 |
| 12,14,15,17,19,21,24| 2215.6 | 2234.1 |
| 12,13,14,15,17,19,21,24| 2211.4 | 2230.3 |
| 12,13,14,15,16,17,19,21,24| 2204.5 | 2244.8 |
| 7,8,12,13,14,15,16,17,18,19,21,24| 2199.2 | 2220.2 |
| 7,8,12,13,14,15,16,17,18,19,21,24,30| 2192.3 | 2214.1 |

TABLE II. Strongly coupled PM3 triple contributions for C–D vibrational mode of anti-o-deutero-methyl-benzoate. Although the frequency differ a little amount, but the qualitative result does not depend upon the isotopomers.

| Triple coupled modes | SCF V-MP2 | VC-MP2 |
|----------------------|-----------|--------|
| No triples           | 2003.2    | 2038.9 |
| 17,40 19             | 2167.9    | 2192.1 |
| 17,40 12,19          | 2168.4    | 2192.4 |
| 17,40 12,14,19       | 2168.0    | 2192.0 |
| 17,40 12,14,15,19    | 2172.6    | 2196.7 |
| 17,40 12,14,15,19,21| 2172.2    | 2196.2 |
| 17,40 12,14,15,19,21,24| 2173.9 | 2198.9 |
| 17,40 12,13,14,15,19,21,24| 2173.1 | 2198.6 |
| 17,40 12,13,14,15,16,19,21,24| 2172.5 | 2198.0 |

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