Research Article

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DFT calculations as an efficient tool for prediction of Raman and infra-red spectra and activities of newly synthesized cathinones

https://doi.org/10.1515/chem-2020-0021
received September 14, 2019; accepted February 7, 2020.

Abstract: Initially made for medical treatment for Parkinsonism, obesity, and depression, cathinones have become illegal drugs for the “recreational use”. The mechanism of action of synthetic cathinones consists of the inhibition of monoamine transporters. DFT (Density Functional Theory) calculations on the selected cathinones (3-FMC, 4-FMC, 4-MMC, Buphedrone, Butylone, Ethylone, MDPV, Methcathinone, and Methylone) were performed using B3LYP level of the Gaussian 09 program suite. The unscaled B3LYP/6–31G vibrational wavenumbers are in general larger than the experimental values, so the use of selective scaling was necessary. The calculated spectra of selected cathinones are in good correlation with the experimental spectra which demonstrates that DFT is a good tool for the prediction of spectra of newly synthesized and insufficiently experimentally characterised cathinones. Also, HOMO-LUMO (Highest Occupied Molecular Orbital-Lowest Unoccupied Molecular Orbital) analysis shows that 3-FMC possesses the minimum energy gap of 3.386 eV, and the molecule 4-FMC possesses the maximum energy gap of 4.205 eV among the investigated cathinones. It indicates that 3-FMC would be highly reactive among all the cathinones under investigation.

Keywords: cathinones; DFT; spectra; reactivity.

1 Introduction

The illegal drugs problem has reached an epidemic level with the increased number of registered users and deaths caused by overdoses, with the causes of this phenomenon being numerous.

Usually, illegal drugs are divided into synthetic cannabinoids, synthetic cathinones, phenethylamines, arylcyclohexylamines, and tryptamines [1]. Synthetic cathinones [2, 3] are known as “bath salts” in the USA, and “plant food” or “research chemicals” in Europe. Synthetic cathinones were made in the 1920’s for the medical treatment of parkinsonism, obesity, and depression. Unfortunately, since the beginning of the 21st century, synthetic cathinones have started to be used recreationally with two pioneering representatives: CAT (metcathinone) and 4-MMC (mephedrone, 4-methylmethcathinone), which were followed by methyline (3,4-methylenedioxyn-N-methylcathinone) and MDPV (3,4-methylenedioxypyrvalerone) [3-5]. New cathinones were synthesized as substitute drugs: butylone, ethylone, buphedrone, and its analog pentedrone, and the constitutional isomer of the latter, 4-MEC (4-methyl-N-ethylcathinone), mephedrone derivatives-4-FMC (flephedrone, 4-fluoromethcathinone) and 3-FMC (3-fluoromethcathinone), and α-PVP (α-pyrrolidinopentiophenone) [3, 4, 6].

Considering the potency of cathinones to inhibit dopamine, noradrenaline, and serotonin re-uptake and the ability to liberate these compounds, Simmler et al. [5] classified synthetic cathinones into three groups on the basis of in vitro experiments:

1. Cathinones which act like MDMA and cocaine are “cocaine-MDMA-mixed cathinones”. The mechanism of action of this subgroup of cathinones involves non-selective inhibition of monoamine re-uptake. Representatives of this group are mephedrone, methyline, ethylone, and butylone (similar action to...
cocaine), and naphyrone (similar action to MDMA) [5, 7-11].

2. Cathinones which act like methamphetamine (“methamphetamine-like cathinones”). Their mechanism of action involves the preferential re-uptake inhibition of catecholamines and liberation of dopamine. Methcathinone, flephedrone, and clephedrone (4-chloromethcathinone) belong to this group [5, 7].

3. Synthetic cathinones with structures based on pyrovalerone (“pyrovalerone-cathinones”). The representatives of this group are MDPV and MDPBP, very potent and selective inhibitors of the catecholamine re-uptake demonstrating no neurotransmitter liberating effect [5, 7].

The aim of this study was to perform numerous calculations in order to predict spectra and properties of selected cathinones.

2 Materials and Methods

The selected molecules were treated quantum mechanically by applying DFT method using the Gaussian 09 program suite [12] at the Becke-3-Lee-Yang-Par (B3LYP) level [13, 14] combined with the standard 6-31G basis set. During the optimization procedure all the parameters were set in order to obtain a stable structure with minimum energy. The global minimum energy of the title compound was determined from the structure optimization procedure. The Natural bonding orbital (NBO) analysis was performed using the NBO 5.1 program [15] as implemented in the Gaussian 09 package at DFT/B3LYP level. The hyperconjugation and the interaction energy within the molecule were obtained from the second-order perturbation approach [16-18].

Ethical approval: The conducted research is not related to either human or animal use.

3 Results and discussion

3.1 Molecular geometry

The optimized structures of the title compounds along with numbering of atoms are shown in Figure 1. The global minimum energy obtained by the DFT structure optimization procedure for the investigated compounds is summarised in Table 1. All the calculated vibrational wavenumbers using the optimized geometry were found to be positive for the title compounds. The bond lengths, bond angles and the optimized parameters calculated using the DFT method are shown in the Supplementary material (Tables A1-A9).
Table 1: Optimized energies of the investigated cathinones.

| Drug          | Optimized energy (Hartree) |
|---------------|---------------------------|
| methcathinone | -518.720208               |
| 4-MMC         | -558.030047               |
| methylene     | -707.174321               |
| MDPV          | -902.472357               |
| Butylene      | -746.478171               |
| Ethylene      | -746.481312               |
| buphedrone    | -558.024529               |
| 4-FMC         | -617.934012               |
| 3-FMC         | -617.932918               |

In 3-FMC, the bond lengths of C1-C6, C3-C4, C5-C6, C6-C8, C8-C10, C10-C11 were found to be elongated to 1.407 Å, 1.401 Å, 1.409 Å, 1.493 Å, 1.529 Å, 1.562 Å, respectively compared to their default values of 1.39 Å. In the structurally similar 4-FMC, the bond lengths of C1-C6, C5-C6, C6-C8, C8-C10, and C10-C11 were found to be elongated to 1.409 Å, 1.410 Å, 1.489 Å, 1.541 Å, 1.538 Å, respectively, compared to their default values of 1.39 Å. In both cases, C10-H18 and C13-H24 were found to be elongated to 1.1 Å (3-FMC, 4-FMC) and 1.016 Å (3-FMC) and 1.04 Å (4-FMC) compared to their default values of 1.08 Å (3-FMC) and 1.09 Å (4-FMC). This elongation may be due to their proximity to the electronegative oxygen, fluorine and nitrogen atoms [19, 20]. It also indicates the extensive charge delocalization that takes place within the molecule.

In 4-MMC, the bond lengths of C3-C7, C6-C8, C8-C9, and C9-C10 were found to be elongated to 1.506 Å, 1.515 Å, 1.553 Å and 1.524 Å, respectively, compared to their default value of 1.39 Å. Similarly, the bond lengths of C9-H21, C10-H23, and C12-H26 were found to be elongated to 1.097 Å, 1.097 Å and 1.096 Å, respectively, compared to their default value of 1.08 Å. This elongation may be due to their proximity to the electronegative oxygen (O13) and nitrogen (N13) atoms [19, 20] indicating the extensive charge delocalization inside the molecule.

In buphedrone, the bond lengths of C6-C7, C7-C9, C9-C10, and C10-C11 were found to be elongated to 1.518 Å, 1.549 Å, 1.538 Å and 1.52 Å, respectively, compared to their default value of 1.39 Å. The bond lengths of C10-H20, C10-H21, and C13-H26 were found to be elongated to 1.098 Å, 1.099 Å and 1.096 Å, respectively, compared to their default value of 1.08 Å. Our assumption is that the phenomenon is caused by the presence of electronegative oxygen (O8) and nitrogen (N12) atoms [19, 20], which causes the delocalization inside the molecule.
3.2 Molecular vibrations and simulated spectra

The well-known excellent performance of density functional theory for the estimation of vibrational spectra of organic compounds can also be observed for the studied compounds. The unscaled B3LYP/6–31G vibrational wavenumbers are generally somewhat larger than the experimental values. This phenomenon is due to the over-estimation of the basis set and methodology used. However, the use of selective scaling is necessary to obtain reliable information on the vibrational properties. The calculated wavenumbers were scaled using a scale factor [21, 22]. The scaling procedure results in overcoming the anharmonicity and over-estimation. The calculated vibrational wavenumbers, IR intensities, Raman activities along with their assignments for all the title molecules are shown in Tables A10-A18. As shown by the data presented in Table 2 and Tables A10-A18 the theoretical results compare well to the experimental values.

### Table 2: Spectral data of the investigated cathinones.

| cathinone | UV spectra | FTIR spectra, wavenumbers of the characteristic bands (cm⁻¹) | FT Raman spectra, wavenumbers of the characteristic bands (cm⁻¹) |
|-----------|------------|-------------------------------------------------------------|-------------------------------------------------------------|
| methcathinone | 239 | 2708.62; 2454.76; 1691.62; 1597.20; 1469.31; 1360.72; 1244.90; 975.99; 700.19 [23] | 1001.5 (ν₁₂, mode-benzene in-plane ring deformation) [24] |
| 4-MMC | 259.5 (257.5) (ethanol) [25] 263.5 (water) [25] | 2715.5; 1685.9; 1606.3 [25] | 517.9; 637.8; 804.8; 1248.8; 1605.7 (ν₁₂ mode) [24] |
| methylene | Not available | (as hydrochloride): 1676; 1450; 1253; 1091; 740 [26] | 589.8; 809.7; 1250.8; 1604.3; 1622.4 [24] |
| MDPV | 233; 282; 315 (methanol) [27] | 2715.7; 1687.17; 1609.53; 1486.95; 1433.83; 1356.19; 1294.94; 1102.84; 1029.28; 935.30; 869.92; 837.23; 743.25; 571.62; 477.64; 428.60 [27] | 428.7; 582.5; 716.8; 809.0; 1252.1; 1352.4; 1601.0; 1611.0 [24] |
| butylene | Not available | 1666; 1456; 1253; 1120; 742 [26] | 589.0; 720.6; 805.9; 1245.5; 1606.6; 1624.8 [24] |
| ethylene | Not available | Polymorph A: 1673; 1605; 1556; 1452; 1256; 1038 [28] | Polymorph A: 3079.0; 3036.4; 2991.6; 2950.2; 2937.3; 2900.1; 2891.7; 2803.5; 2748.8; 2705.7; 1672.6; 1620.7; 1607.3; 1558.8; 1509.0; 1447.8; 1428.0; 1404.0; 1363.6; 1299.7; 1286.5; 1250.7; 1217.6; 1209.7; 1176.1; 1137.2; 1119.8; 1090.8; 1045.8; 994.1; 935.8; 908.8; 863.1; 826.1; 804.7; 731.0; 720.7; 715.1; 584.1; 521.4; 438.6; 411.5; 383.1; 335.8; 285.9; 238.9; 128.2 [28] |
| buphedrone | Not available | 1681; 1356; 1237; 1117; 760 [29] | Exact values are not available |
| 4-FMC | Not available | 2459; 1686; 1594; 1513; 1471; 1410; 1363; 1301; 1238; 1208; 1166; 1113; 1029; 1006; 980; 902; 847; 819; 765; 748; 684 [30] | 498.2; 1250.8; 1597.0 [24] |
| 3-FMC | Not available | 2947; 2685; 2439; 1698; 1589; 1478; 1433; 1382; 1364; 1259; 1230; 1218; 1189; 1167; 1096; 1043; 1016; 993; 896; 830; 796; 757; 723; 674 [30] | 502.9; 1001.5; 1257.5; 1607.0 [24] |
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### 3.3 Frontier Molecular Orbital Analysis

The excitation energy of a molecule can be calculated by finding the energy difference between the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO), and it is an excellent indicator of electronic transition absorption in the molecular systems [31, 32]. These molecular orbitals provide insight into the reactivity nature and the physical and structural properties of molecules. The positive and negative phase was represented in red and green color. The HOMO, LUMO energies and the energy gap for the investigated compounds were calculated using B3LYP/6-31G method. Owing to the HOMO–LUMO orbital interaction, LP-LP, and LP-bond pair type interactions were observed to be predominant in the investigated compounds according to the molecular orbital theory. The calculated HOMO, LUMO energies, and the energy gap are shown in Table 3.

The molecular orbital analysis for the investigated compounds based on their optimized geometry indicates that the frontier molecular orbitals are mainly composed of $p$ type-atomic orbitals. An electronic system with larger HOMO-LUMO gap should be less reactive than one with a smaller gap. Moreover, the HOMO–LUMO energy gap clearly explains the eventual charge transfer taking place within the molecule.

The power of an electronegative atom in a compound to attract an electron towards it was introduced by Pauling. The parameters such as hardness ($\eta$), ionization potential ($I$), electronegativity ($\chi$), chemical potential ($\mu$), electron affinity ($A$), global softness ($\sigma$) and global electrophilicity ($\omega$) are defined as follows:

$$\chi = -\mu = -\left(\frac{\partial E}{\partial N}\right)_{N_0}$$  \hspace{1cm} (1)

$$I = -E_{\text{HOMO}}$$  \hspace{1cm} (2)

$$A = -E_{\text{LUMO}}$$  \hspace{1cm} (3)

$$\chi = (I+A)/2$$  \hspace{1cm} (4)

$$\eta = (I - A)/2$$  \hspace{1cm} (5)

$$\sigma = 1/\eta$$  \hspace{1cm} (6)

$$\omega = (\mu^2/2\eta)$$  \hspace{1cm} (7)

The ionization energy (IE) can be expressed through HOMO orbital energies, and electron affinity (EA) can be expressed through LUMO orbital energies. The hardness ($\eta$) corresponds to the gap between HOMO and LUMO orbital energies. The hardness has been associated with the stability of the chemical system. All the calculated values of quantum chemical parameters of the investigated molecules using the B3LYP method with 6-31G basis set are summarised in Table 3.

From the results in Table 3 it is clear that for the molecules investigated 3-FMC has the minimum energy gap of 3.386 eV and 4-FMC has the maximum energy gap of 4.205 eV. These facts further indicate that 3-FMC would be highly reactive among all the cathinones under investigation.

### 3.4 Mulliken Population Analysis

The Mulliken population analysis [33, 34] of the title compounds was performed at DFT-B3LYP/6-31G level to obtain the values of the atomic charges and the results are shown in Table 4.
| Compound            | Atoms | Charges (e) |
|---------------------|-------|-------------|
| C1                  | 0.1099| -0.1038     |
| C2                  | 0.2316| 0.0975      |
| C3                  | 0.2769| -0.1256     |
| C4                  | 0.3012| 0.0943      |
| C5                  | 0.3215| -0.0895     |
| C6                  | 0.3523| 0.0888      |
| C7                  | 0.3956| -0.0794     |
| C8                  | 0.4430| 0.0794      |
| C9                  | 0.4839| -0.0695     |
| C10                 | 0.5265| 0.0695      |
| C11                 | 0.5649| -0.0595     |
| C12                 | 0.6034| 0.0595      |
| C13                 | 0.6421| -0.0495     |
| C14                 | 0.6819| 0.0495      |
| C15                 | 0.7213| -0.0395     |
| C16                 | 0.7609| 0.0395      |
| C17                 | 0.8005| -0.0295     |
| C18                 | 0.8402| 0.0295      |
| C19                 | 0.8797| -0.0195     |
| C20                 | 0.9194| 0.0195      |
| C21                 | 0.9590| -0.0095     |
| C22                 | 0.9986| 0.0095      |
Continued Table 4: Results obtained in Mullikan population analysis.

|   | 3-FMC |   | 4-FMC |   | Butylone |   | Ethylene |   | MDPV |   | Methcathinone |   | 4-MMC |   | Buphedrone |   | Methylone |
|---|-------|---|-------|---|----------|---|----------|---|------|---|---------------|---|-------|---|-----------|---|---------|
|   | Atoms | Charges (e) | Atoms | Charges (e) | Atoms | Charges(e) | Atoms | Charges(e) | Atoms | Charges(e) | Atoms | Charges(e) | Atoms | Charges(e) | Atoms | Charges(e) |
| H23 | 0.1456 | H23 | 0.1495 | H23 | 0.1522 | H23 | 0.1483 | H23 | 0.1749 | H23 | 0.1479 | H23 | 0.1539 | H23 | 0.1433 | H23 | 0.3067 |
| H24 | 0.1138 | H24 | 0.1258 | H24 | 0.1411 | H24 | 0.1493 | H24 | 0.0969 | H24 | 0.1233 | H24 | 0.1260 | H24 | 0.1285 | H24 | 0.1439 |
| H25 | 0.1370 | H25 | 0.1436 | H25 | 0.1395 | H25 | 0.1358 | H25 | 0.1666 | H25 | 0.1429 | H25 | 0.3128 | H25 | 0.2859 | H25 | 0.1122 |
| H26 | 0.1301 | H26 | 0.3017 | H26 | 0.3017 | H26 | 0.1258 | H26 | 0.1432 | H26 | 0.1461 | H26 | 0.1353 |
| H27 | 0.1435 | H27 | 0.1066 | H27 | 0.1066 | H27 | 0.1834 | H27 | 0.1084 | H27 | 0.1297 | H27 | 0.1838 |
| H28 | 0.2892 | H28 | 0.1271 | H28 | 0.1271 | H28 | 0.1831 | H28 | 0.1370 | H28 | 0.1385 | H28 | 0.1843 |
| H29 | 0.1462 | H29 | 0.1278 | H29 | 0.1278 | H29 | 0.1479 |
| H30 | 0.1225 | H30 | 0.1502 | H30 | 0.1502 | H30 | 0.1063 |
| H31 | 0.1407 | H31 | 0.1325 | H31 | 0.1325 | H31 | 0.1561 | H32 | 0.1019 |
| H33 | 0.1503 |
| H34 | 0.1259 |
| H35 | 0.1391 |
| H36 | 0.1338 |
| H37 | 0.1190 |
| H38 | 0.1391 |
| H39 | 0.1392 |
| H40 | 0.1292 |
| H41 | 0.1300 |
All calculated values indicate the extensive charge delocalization in the investigated molecules [19, 20]. The positive charges are localized over the hydrogen atoms.

### 3.5 Natural Bond Orbital (NBO) Analysis

The intramolecular interactions, delocalization of electrons and stabilization energy of the investigated compounds was performed with NBO analysis using the NBO 5.1 program [15] implemented in the Gaussian 09W package at the DFT-B3LYP/6-31G level. The energy arising from hyperconjugative interactions was deduced from the second-order perturbation approach [17]. The large values of $E^{(2)}$ indicate the tendency of an electron to donate, and therefore, the greater extent of conjugation within the system.

The strength of the delocalization interaction can be estimated by the second-order energy lowering $E^{(2)}$,

\[
E^{(2)} = \Delta E_q = q \cdot F(i,j)^2 / E_{ij}E_i
\]

Where $E^{(2)}$ is the stabilization energy, $q$ is the donor orbital occupancy, $E_i$ and $E_j$ are the diagonal elements and $F(i,j)$ is the off diagonal NBO Fock matrix element reported [35].

The most predominant electron donor-acceptor interactions are shown in Tables A19-A27 for the investigated compounds.

In 3-FMC, the electron transfer was predominantly observed from the bond pair to bond pairs and lone pair of oxygen and fluorine atoms to bond pairs. A strong hyperconjugative interaction was observed due to $\pi^*(C_2-C_3)$-- $\pi^*(C_4-C_5)$, $\pi^*(C_8-O_9)$-- $\pi^*(C_{10}-C_{11})$, $\pi(C_1-C_6)$-- $\pi^*(C_2-C_3)$, LP3 (F7) -- $\pi^*(C_{22}-C_{23})$ and LP2 (O9) -- $\pi^*(C_{6}-C_8)$, and values were found to be 159.50 kcal/mol, 97.88 kcal/mol, 22.11 kcal/mol, 1724 kcal/mol and 1709 kcal/mol, respectively, which also leads to the stability of the molecule. Although quite similar to 3-MFC, in 4-FMC, the electron transfer was predominantly observed only from the bond pair to bond pairs. A strong hyperconjugative interaction was observed due to $\pi(C_1-C_6)$-- $\pi^*(C_2-C_3)$, $\sigma(C_1-C_2)$-- $\sigma^*(C_2-C_3)$, $\sigma(C_1-C_2)$-- $\sigma^*(C_3-C_4)$, $\sigma(C_6-C_8)$ and $\sigma(C_1-C_6)$-- $\sigma^*(C_5-C_6)$, and values were found to be 19.27 kcal/mol, 22.11 kcal/mol, 3.97 kcal/mol, 3.37 kcal/mol and 3.82 kcal/mol, respectively.

The electron transfer in 4-MMC was predominantly observed from the bond pair to bond pairs and lone pair of oxygen and nitrogen atoms to bond pairs. A strong hyperconjugative interaction was observed due to $\pi^*(C_1-C_6)$-- $\pi^*(C_2-C_3)$, $\pi(C_1-C_2)$-- $\pi^*(C_3-C_4)$, $\pi(C_1-C_2)$-- $\pi^*(C_6-C_8)$, LP (2) $O_{12}$ -- $\pi^*(C_1-C_4)$ and LP (2) $O_{12}$ -- $\pi^*(C_1-C_4)$, and values were found to be 21.90 kcal/mol, 19.15 kcal/mol, 73.73 kcal/mol, 16.53 kcal/mol and 17.25 kcal/mol, respectively.

In Buphedrone, the electron transfer was predominantly observed from the bond pair to bond pairs and lone pair of oxygen atoms to bond pairs. A strong hyperconjugative interaction was observed due to $\pi^*(C_{15}-O_{15})$-- $\pi^*(C_{27}-C_{26})$, $\pi(C_{15}-C_{27})$-- $\pi^*(C_{15}-C_{26})$, $\pi(C_{15}-C_{27})$-- $\pi^*(C_{15}-O_{15})$, LP (2) $O_{15}$-- $\sigma^*(C_{15}-C_{27})$ and LP (2) $O_{15}$-- $\sigma^*(C_{15}-C_{26})$, and the values were 65.53 kcal/mol, 20.09 kcal/mol, 21.33 kcal/mol, 16.55 kcal/mol and 17.01 kcal/mol, respectively.

In Butylone, similarly to 4-MMC, the electron transfer was predominantly observed from the bond pair to bond pairs and lone pair of oxygen and nitrogen atoms to bond pairs. A strong hyperconjugative interaction appeared due to $\pi(C_{53}-C_{54})$-- $\pi^*(C_{54}-C_{55})$, $\pi(C_{53}-C_{54})$-- $\pi^*(C_{53}-C_{55})$, $\pi(C_{53}-C_{54})$-- $\pi^*(C_{54}-C_{55})$, LP (2) $O_{10}$-- $\pi^*(C_{15}-C_{14})$ and LP (2) $O_{12}$-- $\pi^*(C_{15}-C_{14})$, and values were found to be 21.41 kcal/mol, 21.38 kcal/mol, 22.06 kcal/mol, 26.68 kcal/mol and 24.92 kcal/mol, respectively.

In Ethylone, similarly to butylone and 4-MMC, the electron transfer was predominantly observed from the bond pair to bond pairs and lone pair of oxygen and nitrogen atoms to bond pairs. A strong hyperconjugative interaction appeared due to $\pi(C_1-C_2)$-- $\pi^*(C_5-C_6)$, $\pi(C_5-C_6)$-- $\pi^*(C_5-C_6)$, $\pi(C_3-C_6)$-- $\pi^*(C_5-C_6)$, $\pi(C_5-C_6)$-- $\pi^*(C_5-C_6)$, LP (2)(O12)-- $\pi(C_1-C_2)$ and LP (2)(O10)-- $\sigma^*(C_3-C_4)$, and values were 228.68 kcal/mol, 229.07 kcal/mol, 20.93 kcal/mol, 25.00 kcal/mol and 26.65 kcal/mol, respectively.

In MDPV (similarly to ethylone, butylone and 4-MMC), the electron transfer was predominantly observed from the bond pair to bond pairs and lone pair of oxygen and nitrogen atoms to bond pairs. A strong hyperconjugative interaction was noticed due to $\pi(C_1-C_6)$-- $\pi^*(C_1-C_6)$, $\pi(C_1-C_6)$-- $\pi^*(C_1-C_6)$, $\pi(C_1-C_6)$-- $\pi^*(C_1-C_6)$, LP (2) $O_{12}$-- $\pi^*(C_2-C_5)$ and LP (2) $O_{12}$-- $\pi^*(C_2-C_5)$, and values were found to be 21.12 kcal/mol, 21.02 kcal/mol, 21.44 kcal/mol, 26.57 kcal/mol and 24.74 kcal/mol, respectively.

In Methcathinone, the electron transfer was predominantly observed from the bond pair to bond pairs and lone pair of oxygen and nitrogen atoms to bond pairs. A strong hyperconjugative interaction was observed due to $\pi(C_1-C_6)$-- $\pi^*(C_2-C_5)$, $\pi(C_1-C_6)$-- $\pi^*(C_2-C_5)$, $\pi(C_1-C_6)$-- $\pi^*(C_2-C_5)$, LP (2) $O_{12}$-- $\pi^*(C_2-C_5)$ and LP (2) $O_{12}$-- $\pi^*(C_2-C_5)$, and LP (2) $O_{12}$-- $\pi^*(C_2-C_5)$, $\pi(C_1-C_6)$-- $\pi^*(C_2-C_5)$, LP (2) $O_{12}$-- $\pi^*(C_2-C_5)$ and LP (2) $O_{12}$-- $\pi^*(C_2-C_5)$, the values...
Table 5: Thermodynamic parameters of the title compounds computed using DFT/B3LYP/6-31G methodology.

| THERMODYNAMIC PARAMETERS | 3-FMC | 4-FMC | 4-MMC | Buphedrone | Butylone | Ethylene | MDPV | Methcathinone | Methylene |
|---------------------------|-------|-------|-------|------------|----------|----------|------|---------------|-----------|
| SCF energy (a.u.)         | -617.91085 | -617.91247 | -558.00786 | -558.024529 | -746.4466 | -746.44940 | -902.4378 | -518.6984 | -707.14215 |
| Zero-point Vibrational energy (kcal/mol) | 128.68 | 128.810 | 151.39073 | 152.34868 | 161.600 | 161.33857 | 220.3078 | 134.1173 | 141.31 |
| Rotational constant (GHz) | A 1.5066 | 1.5066 | 2.08900 | 1.24361 | 0.9810 | 1.32847 | 0.4538 | 1.705 | 1.455 |
| B 0.4254 | 0.4254 | 0.37158 | 0.49817 | 0.2795 | 0.22354 | 0.1930 | 0.589 | 0.291 |
| C 0.3561 | 0.3561 | 0.33783 | 0.45433 | 0.2668 | 0.20383 | 0.1626 | 0.462 | 0.255 |
| Dipole moment (Debye) | X -0.6280 | -1.8776 | -2.5985 | 2.2172 | -2.8881 | 2.1312 | -2.0092 | -0.144 | 2.121 |
| Y 0.6230 | 2.1335 | -2.4918 | 0.8253 | -1.2119 | -2.3338 | -1.3365 | 2.658 | -2.304 |
| Z 0.9345 | -0.4624 | -0.6694 | 1.8148 | 0.8815 | 0.7541 | -2.7348 | -0.637 | 0.789 |
| Total 1.2868 | 2.8794 | 3.6618 | 2.9817 | 3.3257 | 3.2492 | 3.6472 | 2.736 | 3.230 |
| Total energy (kcal/mol) | 136.61 | 136.745 | 159.949 | 160.585 | 171.26 | 170.992 | 232.289 | 141.523 | 152.13 |
| C_v (cal/mol K) | 47.04 | 46.33 | 49.725 | 48.386 | 57.16 | 57.369 | 71.048 | 43.756 | 52.64 |
| S (cal/mol K) | 111.99 | 112.783 | 118.098 | 116.006 | 126.990 | 126.612 | 148.769 | 108.494 | 119.05 |
| Electronic Total Energy (kcal/mol) | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| C_v (cal/mol K) | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| S (cal/mol K) | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Translational Total Energy (kcal/mol) | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 |
| C_v (cal/mol K) | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 |
| S (cal/mol K) | 41.48 | 41.48 | 41.422 | 41.422 | 42.083 | 42.083 | 42.735 | 41.176 | 41.88 |
| Rotational Total Energy (Kcal/mol) | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 | 0.889 |
| C_v (cal/mol K) | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 | 2.981 |
| S (cal/mol K) | 31.62 | 31.60 | 31.483 | 31.413 | 32.752 | 32.940 | 34.377 | 30.916 | 32.36 |
| Vibrational Total Energy (kcal/mol) | 134.83 | 134.967 | 158.171 | 158.808 | 161.48 | 169.215 | 230.512 | 139.745 | 150.35 |
| C_v (cal/mol K) | 41.07 | 40.87 | 43.763 | 42.424 | 51.20 | 51.407 | 65.087 | 37.795 | 46.67 |
| S (cal/mol K) | 38.98 | 39.68 | 45.193 | 43.171 | 52.15 | 51.589 | 71.656 | 36.402 | 44.80 |
were found to be 20.88 kcal/mol, 20.93 kcal/mol, 21.33 kcal/mol, 16.76 kcal/mol and 26.64 kcal/mol, respectively.

3.6 Thermodynamic Parameters

The thermodynamic parameters, namely, heat capacity, entropy, rotational constants, dipole moments, vibrational zero-point energies, of the molecules under investigation have also been computed at DFT-B3LYP level using 6-31G basis set and are presented in Table 5. The thermodynamic data provides useful information for further studies of the investigated compounds [36]. These standard thermodynamic functions can be used as reference thermodynamic values to calculate changes of entropies ($\Delta S_{r}^0$), changes of enthalpies ($\Delta H_{r}^0$) and changes of Gibbs free energies ($\Delta G_{r}^0$) of the reaction. The dipole moment and its principal inertial axes are strongly dependent upon the conformation of the molecule.

4 Conclusions

The use of DFT calculations has been shown to be a useful method for predicting vibrational and infra-red spectra of selected cathinones, particularly using the appropriate scaling. Therefore, this method can be used to predict the spectra of newly synthesized and not fully characterised cathinones which would be useful in forensics.

Conflict of interest The authors declare that they have no conflict of interest.

Acknowledgements Dr Biljana Arsic would like to thank the Ministry of Science, Education and Technological Development of the Republic of Serbia for the financial support for this work (Project No. 174007).

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