

DFT Study of Alkyl-Substituted Morphine Molecules

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Abstract

In this paper, (5 α ,6 α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol (morphine) as well as alkyl-substituted morphines are studied using density functional theory (DFT) at B3LYP/6-311++g(2d,p) level. The calculated Hartree-Fock (H-F) energies ranged as -1018.0049 to -939.3950 kJ mol⁻¹. Among the three studied molecules, C₁₆H₁₆NO₃-CH₂CH₂CH₃ system represents the minimum vibrational frequency, H-F energy as well as the minimum highest occupied molecular orbital (HOMO)-lowest unoccupied molecular orbital (LUMO) energy gap with 49.939 $\times$ 10¹⁰ Hz, -1018.0049 kJ mol⁻¹ and 0.11257, respectively.

Keywords: DFT, Hartree-Fock, Morphine, HOMO-LUMO.

Introduction

Morphine is an extremely effective opiate analgesic drug, and is believed to be the typical drug among the opiates. It influences directly on central nervous system and is utilized as a pain killer and narcotic in drugs such as laudanum and paregoric. Persons who are Addicted to this chemical usually experience withdrawal symptoms, including anxiety, severe abdominal cramps, diarrhea and vomiting. These can last for 10–14 days unless a further dose of morphine is taken.

Morphine is usually taken by injection to reduce the chronic pain, rapidly [1]. In this investigation morphine and its two alkyl-substituted molecules are studied and their optimized structures, calculated H-F energies, vibrational frequencies and HOMO-LUMO energy levels are reported using theoretical approach.

Computational Details

Inputs were prepared by Gauss View and DFT studies were applied using B3LYP/6-

311++G(2d,p) within the Gaussian 03W program [2].

Results and Discussion

The minimum energy structures of morphine as well as alkyl-substituted morphines obtained from DFT calculations, are exhibited in Figure 1. As can be understood from Table 1, the lowest H-F energy belongs to molecule number 3 with -1018.0049 kJ mol⁻¹. Table 2 exposes the vibrational frequency of the molecules.

According to the table, molecule number 3 has the lowest vibrational frequency, which documents the stability of this substituted molecule against two others. Also, the highest stability of C₁₆H₁₆NO₃-CH₂CH₂CH₃ can be detected from HOMO-LUMO energy levels and molecular orbitals represented in Table 3 and Figure 2, respectively. Molecule number 3 illustrates the lowest HOMO-

LUMO gap as well as three dimensional and orbitals of alkyl groups and morphine. highest interaction between the molecular

Table 1 Calculated H-F energy for morphine and its substituted molecules

NO.	Molecule	H-F (kJ mol^{-1})
1	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_3$	-939.3950
2	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_3$	-939.7004
3	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_2\text{CH}_3$	-1018.0049

Table 2: Calculated Vibrational frequency for morphine and its substituted molecules

No.	Molecule	Vibrational Frequency (Hz)
1	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_3$	148.308×10^{10}
2	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_3$	111.628×10^{10}
3	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_2\text{CH}_3$	49.939×10^{10}

Table 3: HOMO & LUMO energy levels for morphine and its substituted molecules

No..	Molecule	HOMO (eV)	LUMO (eV)	Δ
1	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_3$	-0.20138	-0.02714	0.17424
2	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_3$	-0.16786	-0.05165	0.11621
3	$\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_2\text{CH}_3$	-0.17452	-0.06196	0.11257

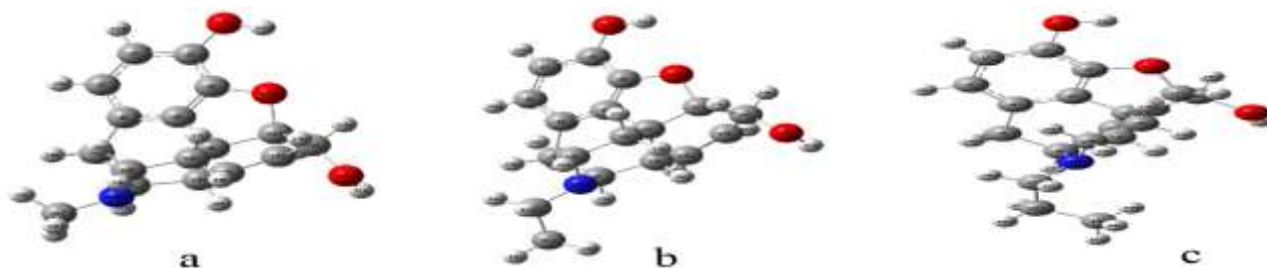


Figure 1: Ball-and-stick representation of structures obtained from B3LYP/6-311++g(2d,p) calculations for a, $\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_3$; b, $\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_3$; c, $\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_2\text{CH}_3$. [Color code: white, H; grey, C; blue, N; red, O].

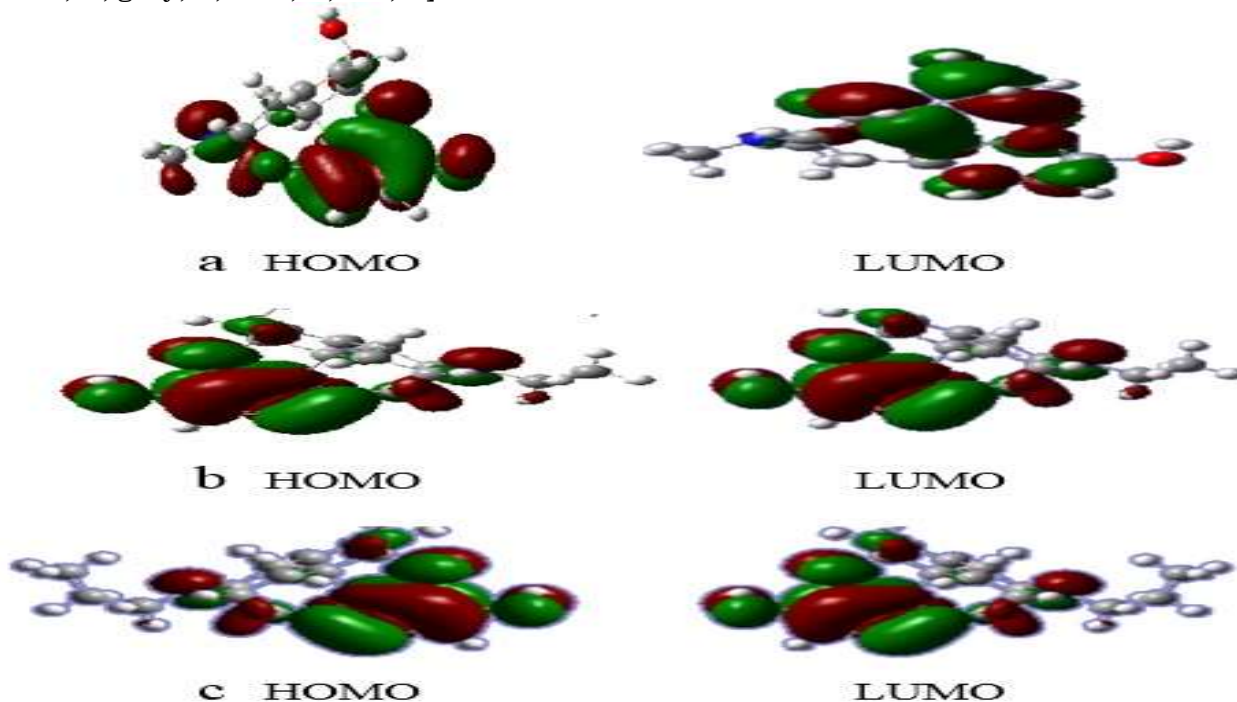


Figure 2: HOMO and LUMO molecular orbitals of a, $\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_3$; b, $\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_3$; c, $\text{C}_{16}\text{H}_{16}\text{NO}_3\text{-CH}_2\text{CH}_2\text{CH}_3$.

Conclusion

Results obtained from DFT at B3LYP/6-311++g(2d,p) level for morphine and alkyl-substituted morphines indicates the lowest H-F energy, HOMO-LUMO energy gap and vibrational frequency for $C_{16}H_{16}NO_3-CH_2CH_2CH_3$. Hence, it can be suggested that morphine molecule stability follows the

molar weight of substituted alkyl groups:
 $C_{16}H_{16}NO_3-CH_3 < C_{16}H_{16}NO_3-CH_2CH_3 < C_{16}H_{16}NO_3-CH_2CH_2CH_3$.

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References

- 1 Dewick PM (2002) Medicinal natural products: a biosynthetic approach. John Wiley & Sons, USA.
- 2 Gaussian, Revision B01, (Gaussian, Inc, Pittsburgh, PA, USA) 2003.
- 3 Taneka H, Yoshioka T, Shimauchi Y, Matsuzawa Y, Oki T, Inui TJ (1980) Antibiot. 133:1323-1330.