Preparation and Photochemistry of 3-Methoxyestra-1,3,5(10)-trien-17β-yl cinnamates and 3-O-methylestra-1,3,5(10)-trien-17-one O-cinnamoyl-17-oximes

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Addendum:

Computational optimization of the steroidal *E*-/*Z*-alkoxycinnamates and of methyl *E*-/*Z*-alkoxycinnamates

Calculation of the electronic spectra of the methyl *E*-/*Z*-alkoxycinnamates as model compounds

1- Methods and Basis Sets

For optimizing the structures of the compounds below, the B3LYP method was used first with a 6-31G(d) basis set and then with a 6-311+G(d,p) basis set. For calculating the electronic spectra, the CIS (Nstates=6) method was used, with the 6-31G(d) as a basis set.

2- Compounds:

Figures 1-3 illustrate the chemical structures of the compounds that we have optimized. We have calculated the electronic spectra of methyl cinnamates as the model compounds of the steroidal cinnamates, in which the steroid part was replaced by a methyl group.

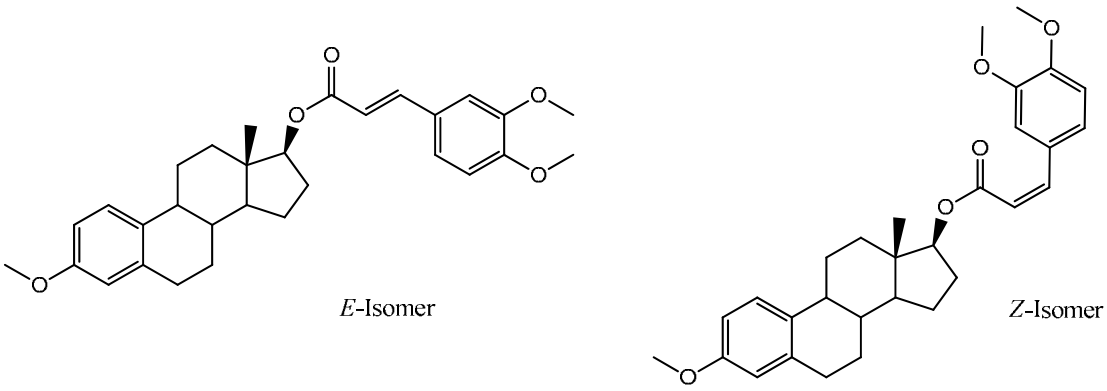

Figure 1: 3-Methoxyestra-1,3,5(10)-trien-17β-yl 3,4-dimethoxycinnamate (abbreviation: 3,4-diMeO-steroid)

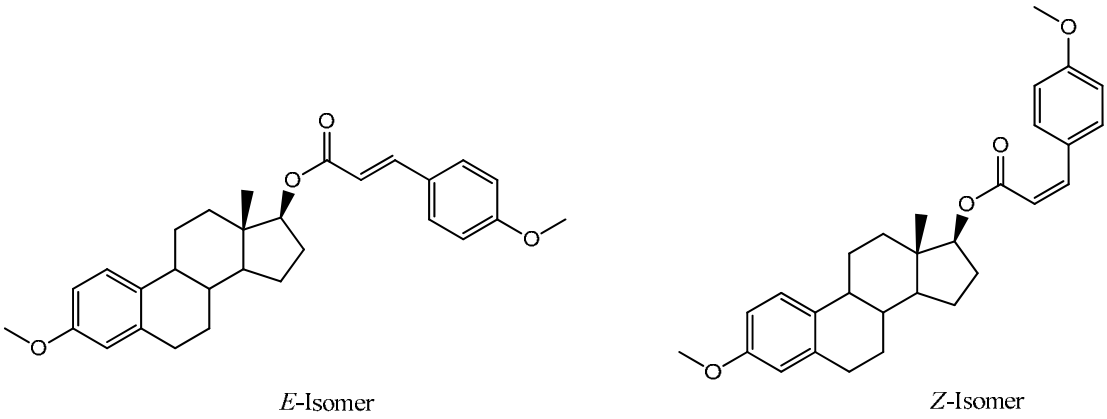

Figure 2: 3-Methoxyestra-1,3,5(10)-trien-3,17β-yl 4-methoxycinnamate (abbreviation: 4-MeO-steroid)

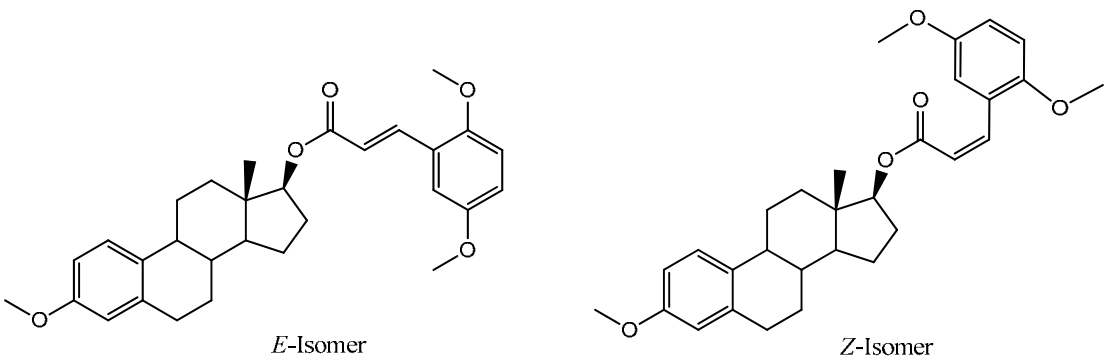

Figure 3: 3-Methoxyestra-1,3,5(10)-trien-17β-yl 2,5-dimethoxycinnamate (abbreviation: 2,5-diMeO-steroid)

Table 1 shows the optimized energies of the compounds for both isomers. Table 2 shows the optimized energies of all model compounds in order to compare the effect of replacing the steroid part by a methyl group. Clearly, the energy difference between the *Z*- and *E*- isomers for the steroidal and the methyl cinnamate model compounds are comparable.

Table 1: The optimized energies of the compounds

Compound	***Z*-Isomer (KJ/mol)**	***E*-Isomer (KJ/mol)**	**$\Delta E = E_Z - E_E$ (KJ/mol)**
3,4-DiMeO-Steroid	-4.0469610×10^6	-4.0469781×10^6	17.1
4-MeO-Steroid	-3.7452178×10^6	-3.7452335×10^6	15.7
2,5-DiMeO-Steroid	-4.0459005×10^6	-4.0459129×10^6	12.4

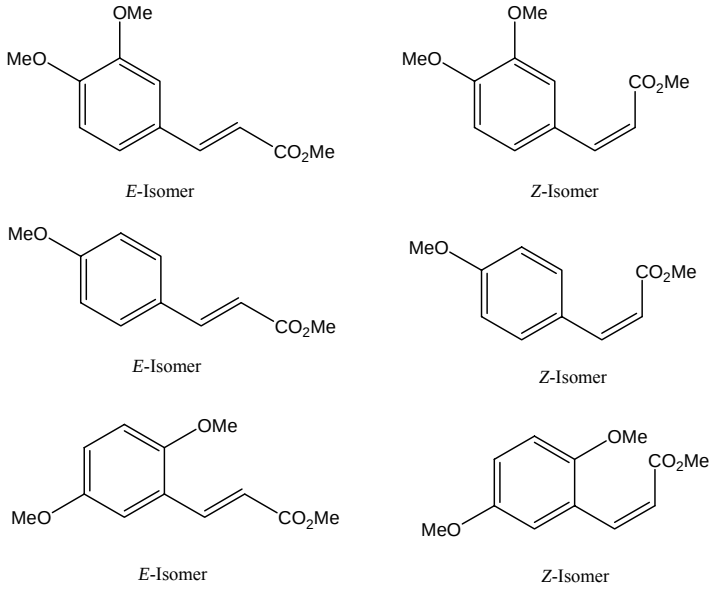

Figure 4: Methyl methoxycinnamates used as model compounds

Table 2: The optimized energies of the model compounds

Compound	***Z*-Isomer (KJ/mol)**	***E*-Isomer (KJ/mol)**	**$\Delta E = E_Z - E_E$ (KJ/mol)**
Methyl 3,4-diMeO-cinnamate	-2.0132622×10^6	-2.0132794×10^6	17.3
Methyl 4-MeO-cinnamate	$-1.7125030E\times10^6$	-1.7125202×10^6	17.2
Methyl 2,5-diMeO-cinnamate	-2.0132718×10^6	-2.0132878×10^6	16.0

Electronic transitions of the *Z*-isomer of methyl 3,4-diMeO-cinnamate

The calculated electronic spectrum of the *Z*-isomer is shown in Figure 4, where there are 5 bands in the region λ = 150 nm – 250 nm, 4 strong bands and one weak band. Table 3 gives the details of the wavelength, intensity and the orbitals involved in each transition.

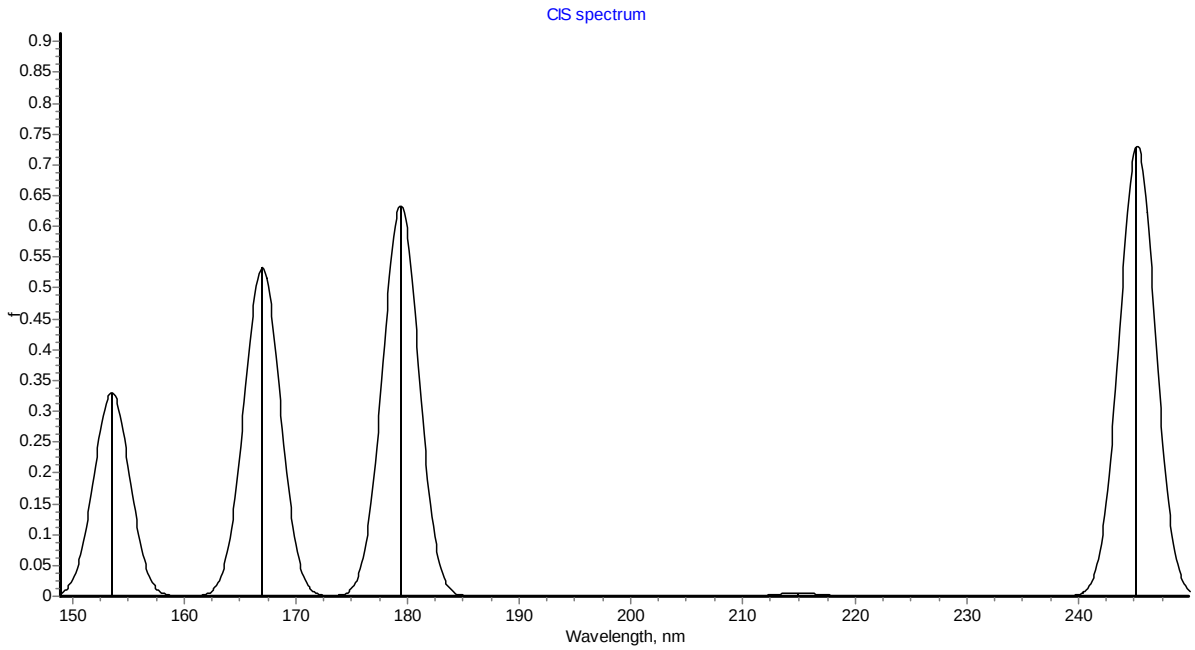

Figure 5: The electronic spectrum of the *Z*-isomer of methyl 3,4-diMeO-cinnamate

Table 3: The wavelengths and intensity of the electronic transitions in methyl (*Z*)-3,4-diMeO-cinnamate

Wavelength (nm)	**Intensity (f)**	**Orbitals**
245.3	0.7303	59→60 (π→π*)
179.38	0.6337	58→61
166.99	0.5332	59→61
153.52	0.3303	57→60

Figure 6 and Figure 7 illustrate the HOMO and LUMO of the model compound methyl (*Z*)-3,4-diMeO-cinnamate. The HOMO and LUMO are π (59) and π*(60), respectively; The HOMO is bonding between C3 and C4, and the LUMO antibonding between C3 and C4: Hence it is proposed that the transition [π(59)→π*(60)] may be involved in the *Z*-/*E*-isomerisation process.

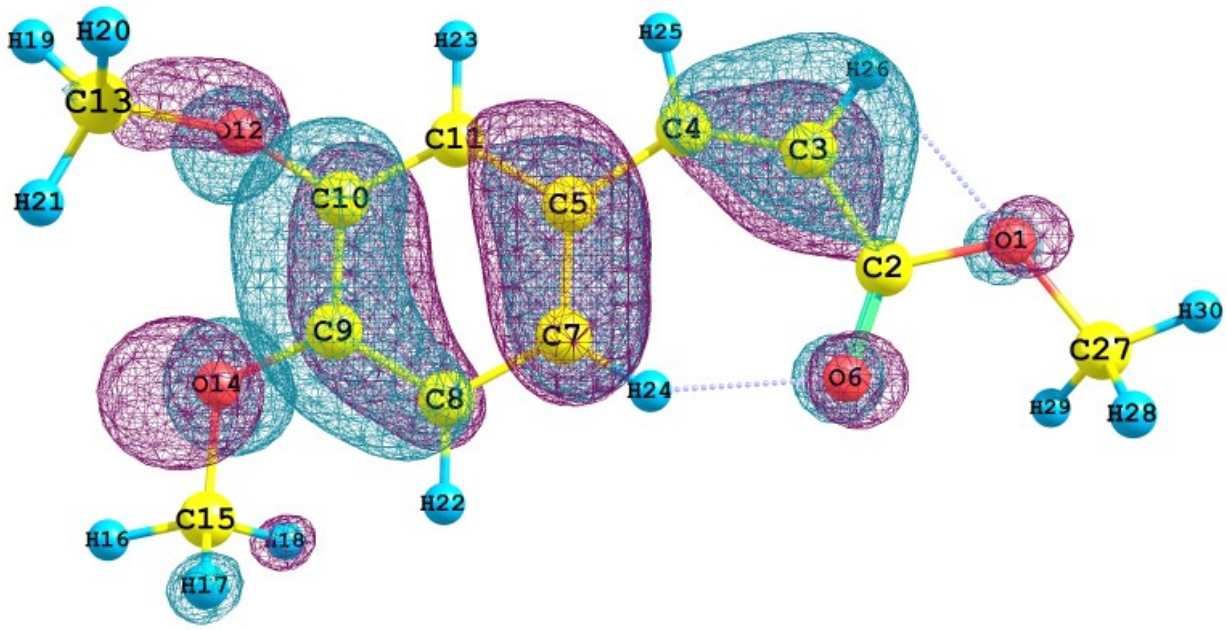

Figure 6: HOMO of the *Z*-isomer of methyl 3,4-diMeO-cinnamate

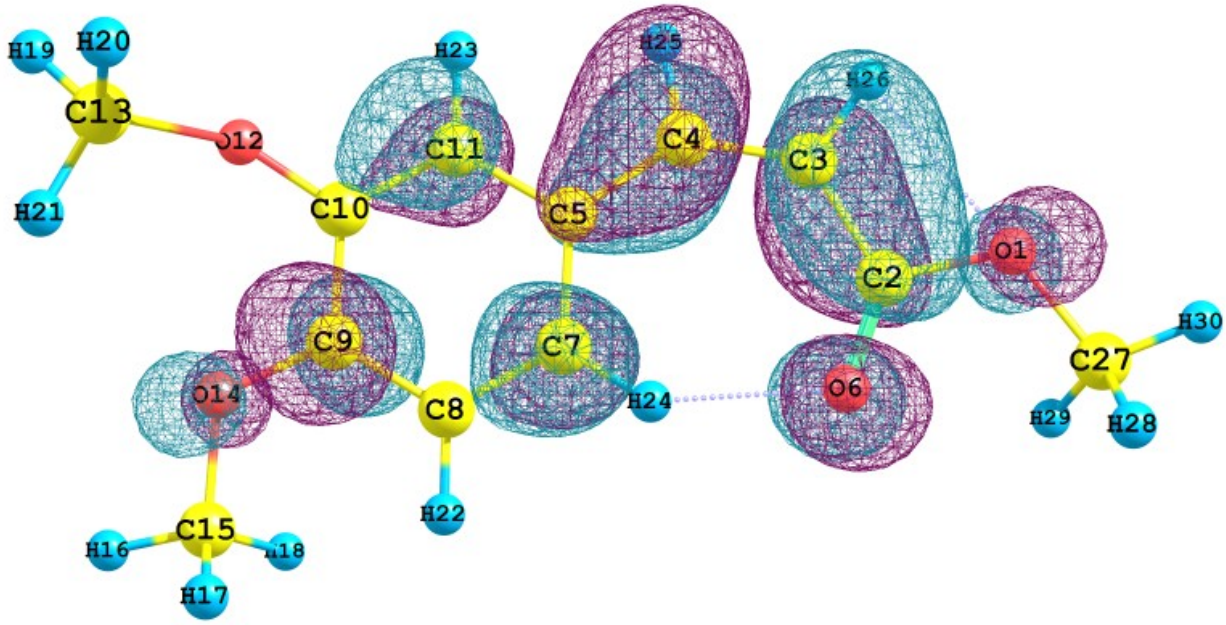

Figure 7: LUMO of the *Z*-isomer of methyl 3,4-diMeO-cinnamate

Calculated electronic transitions in methyl (*E*)-3,4-diMeO-cinnamate

Table 4 summarizes the data of the calculated electronic transitions in methyl (*E*)-3,4-diMeO-cinnamate.

Table 4: The wavelength, intensity and orbitals involved in the electronic spectrum of *E*-isomer of methyl 3,4-diMeO-cinnamate

Wavelength (nm)	Intensity (f)	Orbitals
242.21	0.8345	59→60 (π→π*)
179.91	0.8257	58→61
165.04	0.5098	58→60
151.61	0.3578	57→60

In the region λ = 150 nm – 250 nm, methyl (*E*)-3,4-diMeO-cinnamate exhibits 5 calculated electronic transitions (4 strong, 1 weak), similar to those of the *Z*-isomer, but they are shifted to slightly higher energy. HOMO and LUMO are shown in Figures 8 and 9, respectively. Again, HOMO and LUMO are π (59) and π*(60), respectively, and according to the calculations, again, the transition [π(59)→π*(60)] may be involved in the *E*-/*Z*-isomerisation process.

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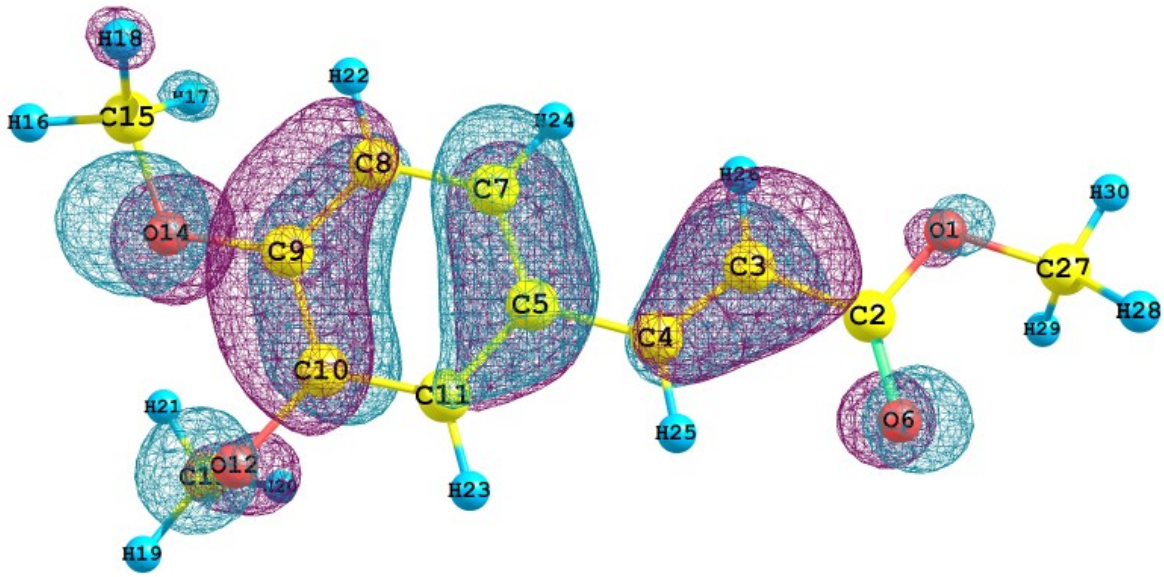

Figure 8: HOMO of the *E*-isomer of methyl 3,4-diMeO-cinnamate

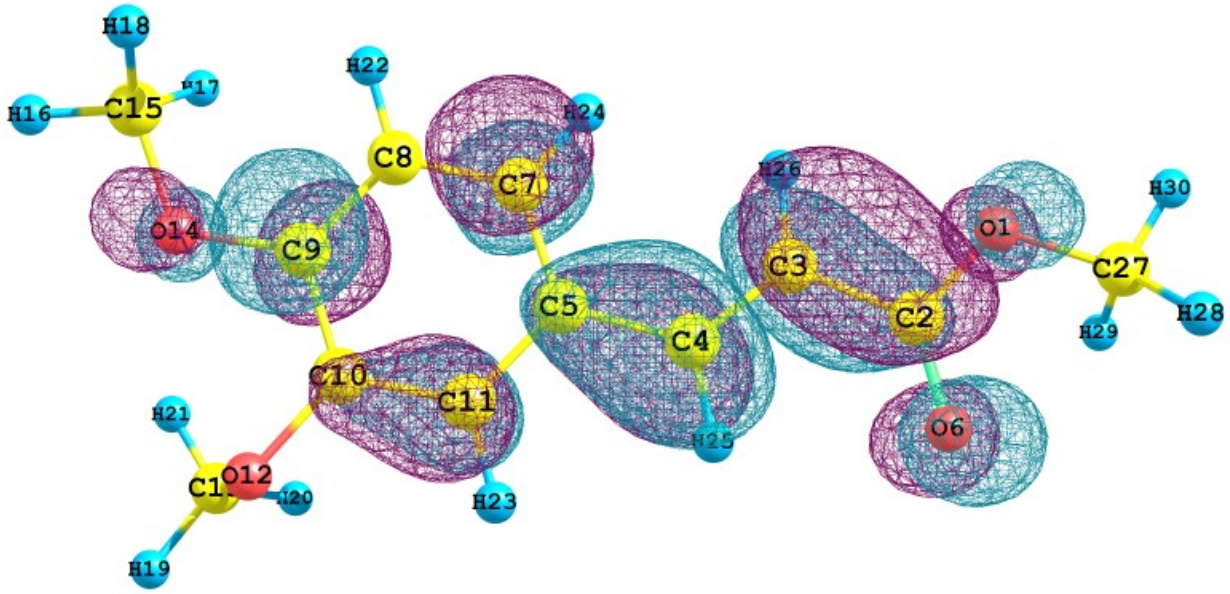

Figure 9: LUMO of the *E*-isomer methyl 3,4-diMeO-cinnamate

Calculated electronic transitions in methyl (*Z*)-4-MeO-cinnamate

Table 5 summarizes the data of the calculated electronic transitions in methyl (*Z*)-4-MeO-cinnamate.

Table 5: The wavelength, intensity and orbitals involved in the transitions of the electronic spectrum of *Z*-isomer methyl 4-MeO-cinnamate

Wavelength (nm)	**Intensity (f)**	**Orbitals**
244.05	0.7798	51→52 (π→π*)
177.07	0.3837	50→53
165.03	0.5849	50→52
152.45	0.3922	49→62

As with the earlier compounds, in the region λ = 150 nm – 250 nm, methyl (*Z*)-4-MeO-cinnamate exhibits 5 calculated electronic transitions (4 strong, 1 weak). HOMO and LUMO are shown in Figures 10 and 11, respectively. HOMO and LUMO are π (51) and π*(52),

respectively, and according to the calculations the transition [π(51)→π*(52)] should contribute to the *Z*-/*E*-isomerisation process.

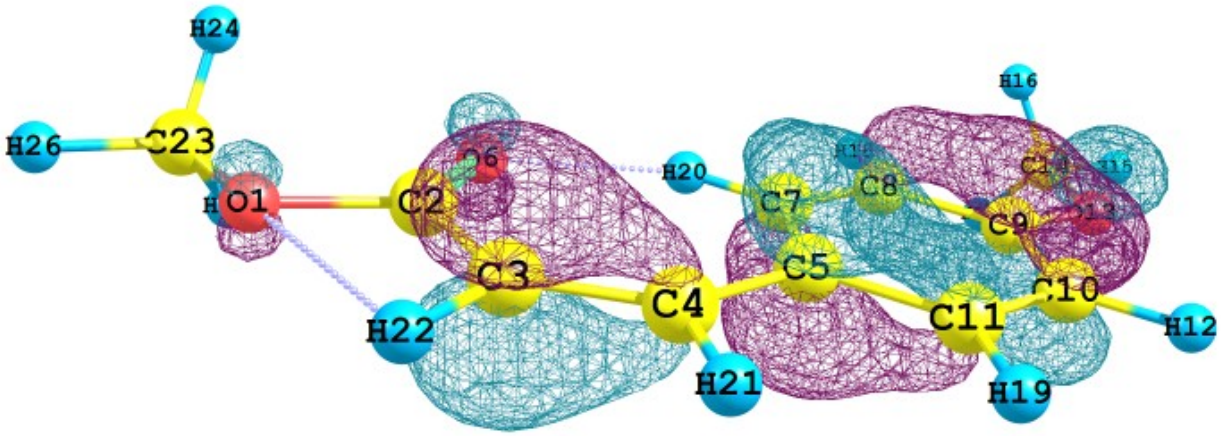

Figure 10: HOMO of the *Z*-isomer of methyl 4-MeO-cinnamate

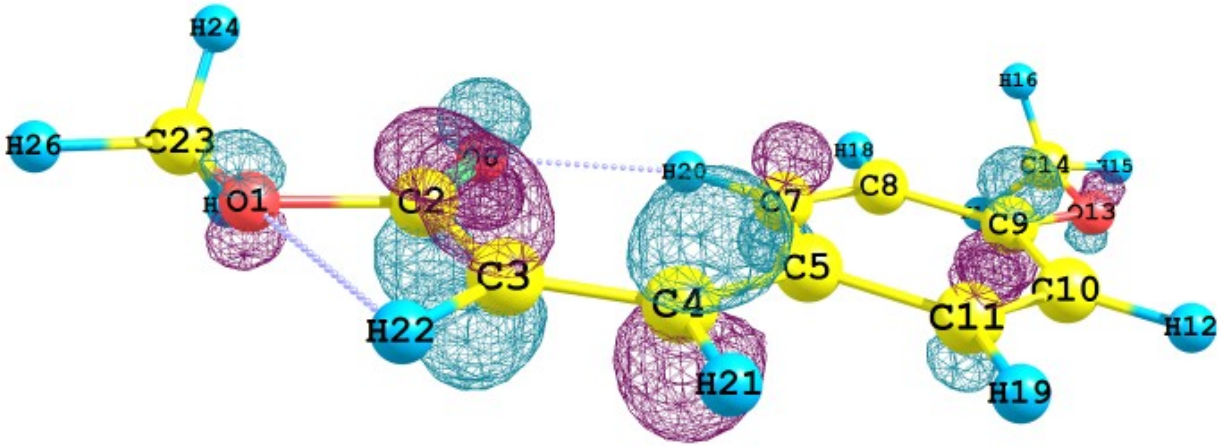

Figure 11: The LUMO of the *Z*-isomer of methyl 4-MeO-cinnamate

Calculated electronic transitions in methyl (*E*)-4-MeO-cinnamate

Table 6: The wavelength, intensity and orbitals involved in the calculated transitions in the electronic spectrum of *E*-isomer of methyl 4-MeO-cinnamate.

Wavelength (nm)	Intensity (f)	Orbitals
241.65	0.8837	51→52 (π→π*)
176.88	0.592	50→53
162.96	0.5189	50→52
150.54	0.403	49→52

The calculated electronic spectrum of the *E*-isomer of methyl 4-MeO-cinnamate shows that there are 5 bands, 4 strong and 1 weak, at 250 nm > λ > 150 nm, similar to that of the *Z*-isomer of methyl 4-MeO-cinnamate, but shifted to slightly higher energy. The HOMO π (51) and LUMO π* (52) are illustrated in Figure 12 and Figure 13, respectively. Again, the HOMO – LUMO transition is suggested to be involved in the *E*-/*Z*-isomerization of the molecule.

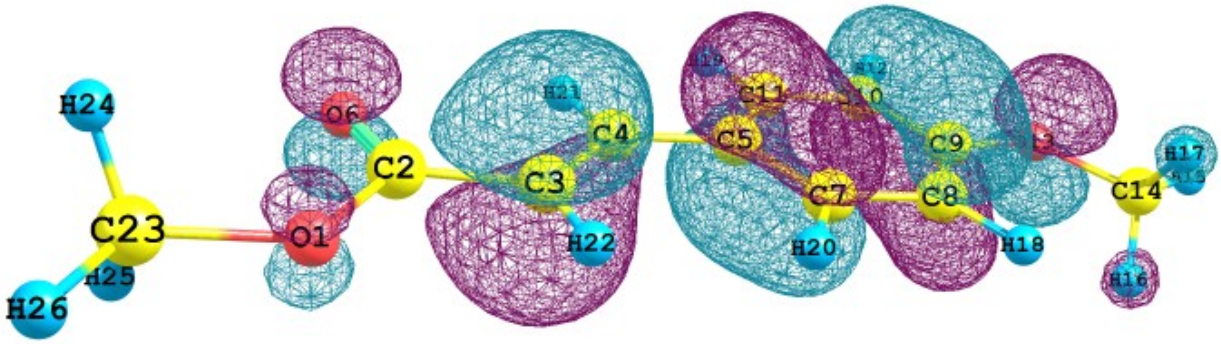

Figure 12: HOMO of the *E*-isomer of methyl 4-MeO-cinnamate

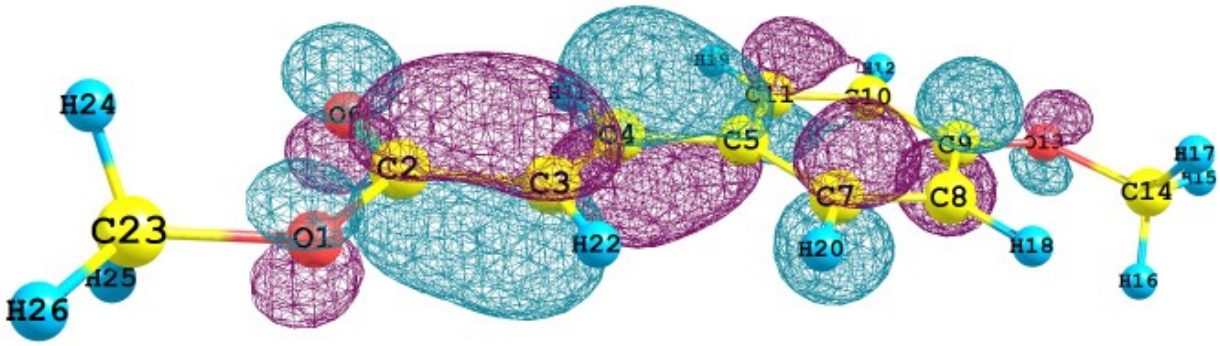

Figure 13: LUMO of the *E*-isomer of methyl 4-MeO-cinnamate

The electronic spectrum of the *Z*-isomer of methyl 2,5-diMeO-cinnamate

The calculated electronic transitions of the *Z*-isomer of methyl 2,5-diMeO-cinnamate are giben in Table 7.

Table 7: The wavelength, intensity and orbitals involved in the transitions of the electronic spectrum of the *Z*-isomer of methyl 2,5-diMeO-cinnamate

Wavelength (nm)	Intensity (f)	Orbitals
254.71	0.6636	59→60
226.27	0.0868	58→60
182.72	0.2863	59→62
164.83	0.2929	59→61
151.34	0.5934	57→60

The HOMO and LUMO molecular orbitals of the *Z*-isomer of methyl 2,5-diMeO-cinnamate are shown in Figure 14 and Figure 15. The HOMO-1 orbital is shown in Figure 16. The HOMO does not contribute to C3-C4 bonding, but the LUMO is clearly antibonding between C3-C4. In this case, and it is the HOMO-1 → LUMO transition [π(58)→π*(60)] that is expected to weaken the C4-C4 bond and assist in isomerization.

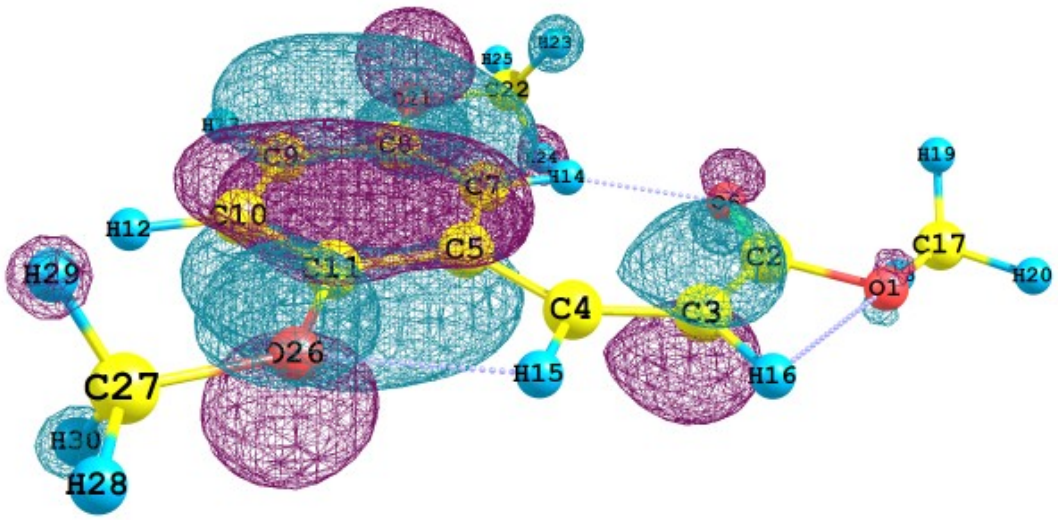

Figure 14: The HOMO orbital of the *Z*-isomer of methyl 2,5-diMeO-cinnamate

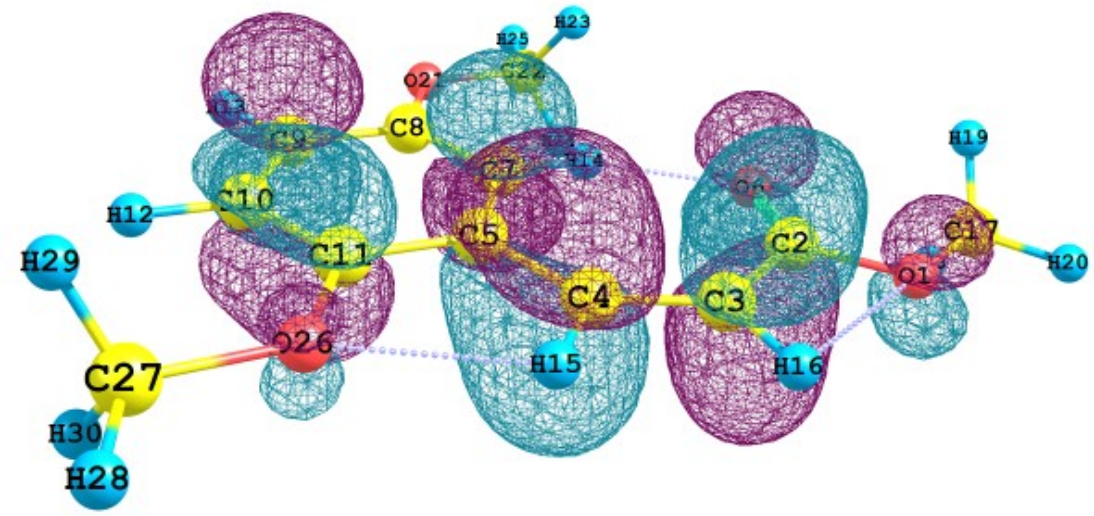

Figure 15: The LUMO orbital of the *Z*-isomer of methyl 2,5-diMeO-cinnamate

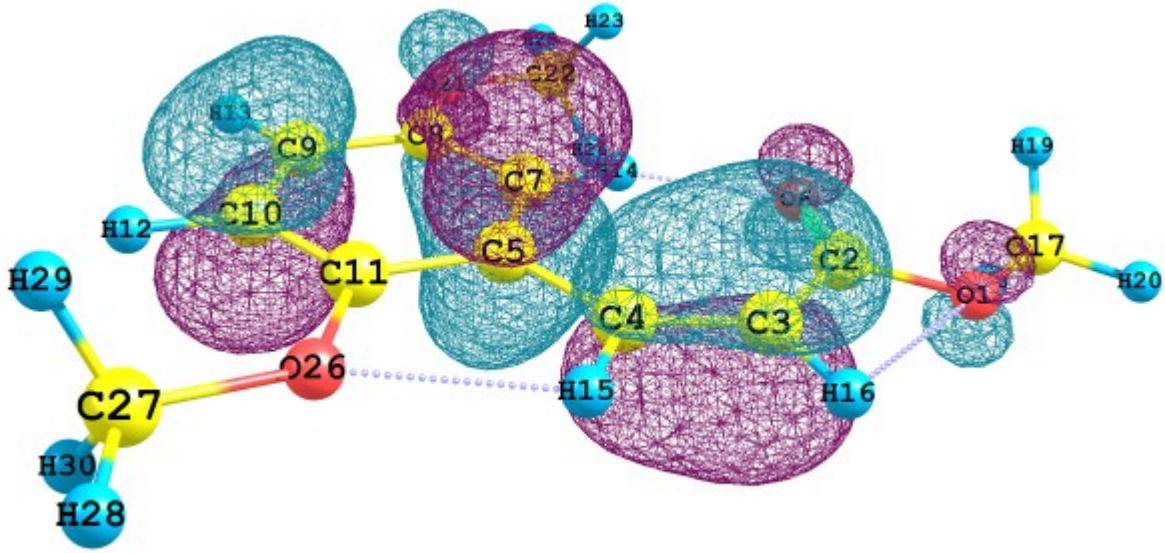

Figure 16: The HOMO-1 orbital of the *Z*-isomer of methyl 2,5-diMeO-cinnamate

The electronic spectrum of the *E*-isomer of methyl 2,5-diMeO-cinnamate

The calculated electronic transitions of the *E*-isomer of methyl 2,5-diMeO-cinnamate are given in Table 8.

Table 8: The wavelength, intensity and orbitals involved in the transitions of the electronic spectrum of *E*-isomer of methyl 2,5-diMeO-cinnamate

Wavelength (nm)	Intensity (f)	Orbitals
252.12	0.7235	59→60
220.64	0.0903	58→60
180.92	0.5109	59→62
162.94	0.4615	59→61
149.15	0.3748	57→60

The electronic spectrum of *E*-isomer of methyl 2,5-diMeO-cinnamate is similar to that of the Z-isomer, with transition energies shifted slightly to higher energy. Figure 17 and Figure 18 illustrate the HOMO and LUMO molecular orbitals of the *E*-isomer of methyl 2,5-diMeO-cinnamate, respectively. The HOMO-1 molecular orbital is shown in Figure 19. As with the Z-isomer, the LUMO is clearly antibonding between C3-C4, but the HOMO does not contribute significantly to C3-C4 bonding. As observed for the Z-isomer, it is the HOMO-1→ LUMO [$\pi(58)\rightarrow\pi^*(60)$] transition that would be expected to contribute to photoisomerization.

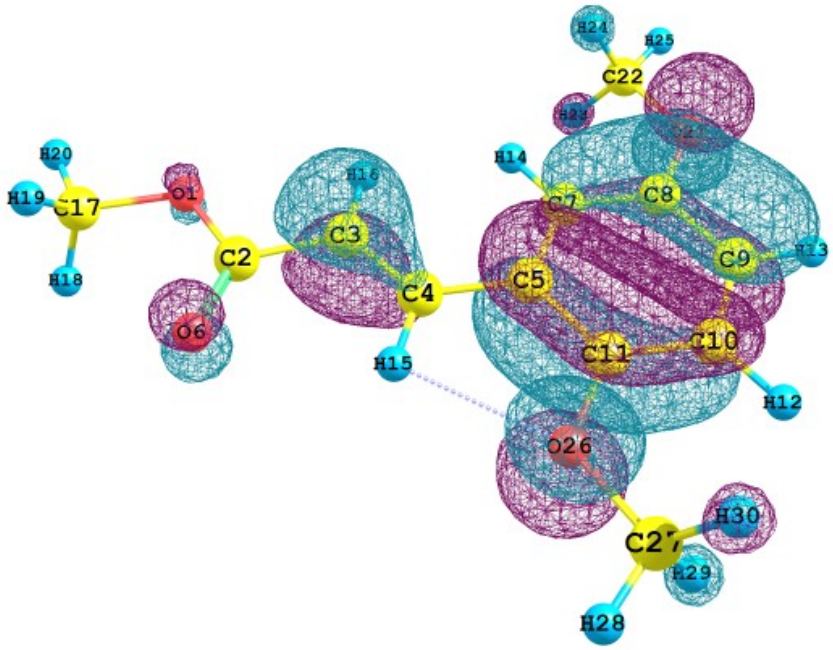

Figure 17: The HOMO orbital of the *E*-isomer of methyl 2,5-diMeO-cinnamate

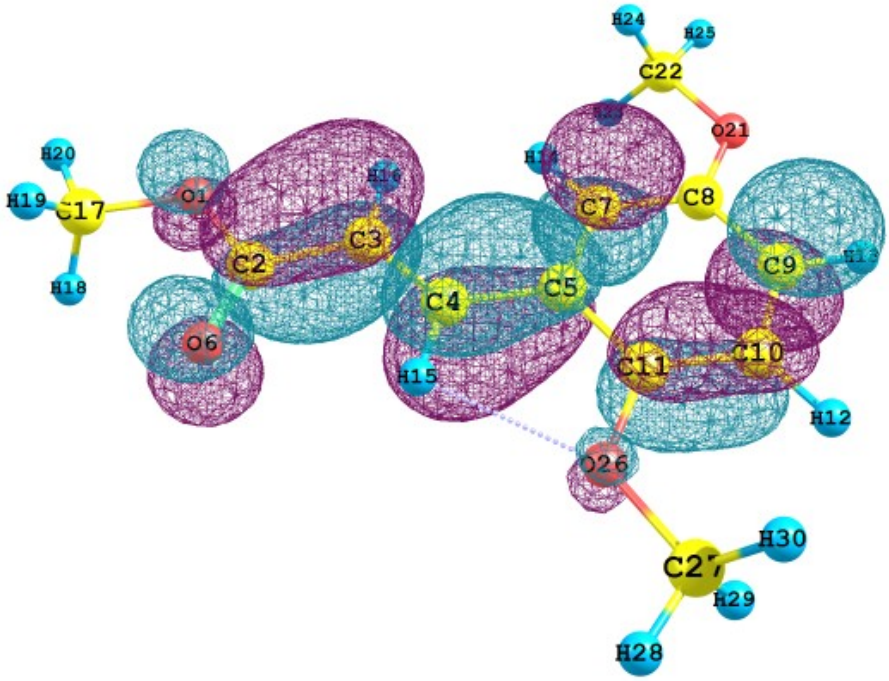

Figure 18: The LUMO orbital of the *E*-isomer of methyl 2,5-diMeO-cinnamate

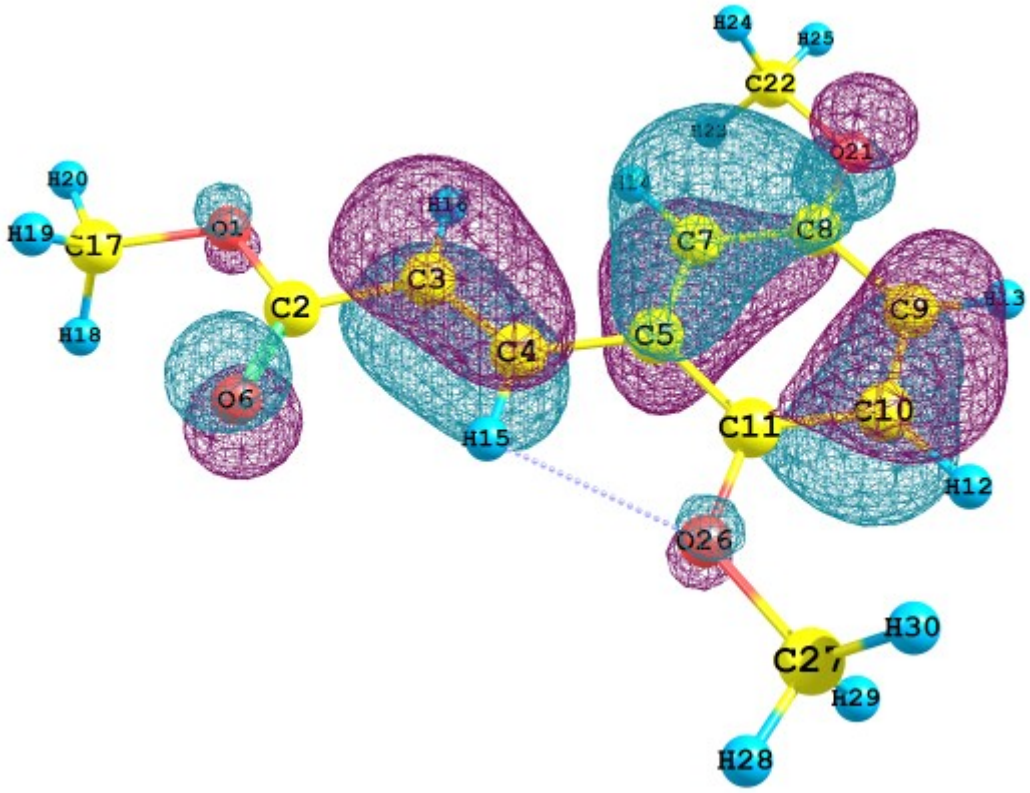

Figure 19: The HOMO-1 orbital of the *E*-isomer of methyl 2,5-diMeO-cinnamate

Conclusion:

The steroidal alkoxycinnamate structures were optimized using the B3LYP/6-31G(d) method followed by re-optimization and total energy calculations using B3LYP/6-311+G(d,p). It was noted that the *E*-isomers are energetically more stable than the *Z*-isomers. Methyl alkoxycinnamates were used as model compounds for the steroidal alkoxycinnamates in the calculation of electronic spectra. The spectra of all the studied compounds show a similar pattern, in which all of them have 4 strong bands and 1 band of low intensity. Moreover, in each case the bands of the spectrum of the *Z*-isomer correspond to lower energy transitions than those for the *E*-isomer. It is interesting to note that while the transition from calculated HOMO to calculated LUMO appears to be involved in the *E*-/*Z*-isomerisation process in the 4-methoxy- and the 3,4-dimethoxycinnamates, the HOMO-1 to LUMO transition seems to be involved in the *E*/*Z*-isomerisation process of *E*- and *Z*-2,5-dimethoxycinnamates. According to our calculation the HOMOs of the 2,5-dimethoxycinnamates do not contribute to bonding between C3 and C4.