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ORIGINAL PAPER

Photodimerizations of hydroxy- and benzoylated 4-azachalcones and quantum chemical investigation of the reactions

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Abstract Photodimerization reactions of compounds **4–6** gave four new cyclobutane-containing compounds (**7–9**) with full control over the stereochemistry at the four stereogenic centers. These new cyclobutane-containing compounds had *β*-truxinic (**7a**), *δ*-truxinic (**7b** and **9**), and *ε*-truxillic (**8**) structures. However, *o*-, *m*-, and *p*-hydroxy 4-azachalcones (**1–3**) did not give photochemical cyclization products under any conditions (in solvent or in their solid or molten states). Experimental data suggested the possibility of frontier orbital control over stereochemical behavior, so some theoretical calculations were performed. Full geometrical optimization of compounds **1–9** was performed via DFT B3LYP/6-31^{+}G**, and their electronic structures were also investigated. The geometries of the singlet and triplet states were initially optimized by density functional theory (DFT) and the configuration interaction singles (CIS) B3LYP/3-21^{+}G** level. An additional calculation was performed for the triplet state using the ground-state geometry. The possible photochemical dimerization products of compounds **7–9** (**a–g**) and the intrinsic reaction coordinates (IRCs) of the reactions of compounds **4–6** were calculated theoretically by the DFT/3-21^{+}G** method. The configurations (reactant, transition state, product, and reaction pathway) corresponding to the stationary points (minima or saddle points) were determined. The intrinsic reaction coordinates were followed to verify the energy profiles that connect each TS to the appropriate local minimum. The dimeric products expected from the calculations coincided with the dimers produced experimentally.

Keywords Azachalcones · Theoretical calculations · Photodimerization reactions · IRC

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Introduction

Chalcones comprise one of the most commonly occurring classes of medicinally important natural compounds, since they show various biological activities [1, 2]. Azachalcones are homologs of chalcones with an annular nitrogen atom in the phenyl ring. They have also shown a wide range of biological activities, such as antituberculostatic, antimicrobial, anti-inflammatory, and antibacterial potential [3–10].

Cyclobutane-containing natural products have been reported form *Combretum albopunctatum* [11], *Goniothalamus thwaitesii* [12], *Agelas sceptrum* [13], and *Agelas conifera* [14]. Because of the various biological activities of these natural compounds, the synthesis of the cyclobutane ring is one of the most intensively studied photochemical reactions of chalcone derivatives. Irradiations of different chalcones and azachalcones in solution and in the solid and molten states have been reported [1–10, 15, 16].

The photochemical reactions of compounds **4–6** and the reaction intermediates involved have been studied using quantum-chemical methods [17–23]. It is interesting to investigate the reasons for the regio- and stereoselective

properties of these reactions. In order to carry out a detailed analysis of the formation mechanism and stereochemistry of the product of each reaction, a quantum chemical investigation of the structures and the stabilities of the reaction intermediates appears to be a very important task. The stereo- and regioselectivities of these reactions largely depend on the geometry and the electron structure of the double bonds of the compound. The properties of the substituted group exert the strongest influence on the stability of the structure.

The present work deals with the synthesis of three new *o*-, *m*-, and *p*-benzoyl (*E*)-4-azachalcones (**4–6**), four new dimers (**7–9**), their spectral characterization, and the intrinsic reaction coordinates of the photodimerization reactions of compounds **4–6** (Fig. 1).

Theoretical calculation

All geometrical optimizations were performed using DFT (density functional theory) B3LYP/6-31^{+}G** methods [24–35]. The predicted intermediates formed during the transition states were investigated using the DFT/6-31^{+}G** method. The HOMO and LUMO energies in the ground state and the HSOMO and LSOMO energies in the excited state were calculated using DFT B3LYP (Becke tree-parameter hybrid exchange with Lee–Young–Parr correlation) methods with the 6-31^{+}G* basis set and the configuration interaction singles (CIS) B3LYP/3-21^{+}G** level, respectively . The reaction pathway was calculated using the compounds **4–6**, and the reaction coordinate was obtained via minimum energy path (MEP) computations using the DFT/3-21^{+}G** method. Full geometry optimization was carried out employing the Polak–Ribiere (conjugate gradient) algorithm (convergence of 0.00001 kcal mol^{-1}) and an RMS gradient of 0.001 kcalÅ^{-1}mol^{-1}. The calculations were performed with HyperChem 7.5 and Gaussian 03 software running on an IBM Pentium IV computer.

Results and discussion

In our previous studies, nitro-substituted dimerization reactions of azachalcones gave cyclobutane-containing compounds [5–9]. However, photoaddition reactions of 2-nitro-substituted azachalcones did not give cyclization products [7–9]. Photochemical dimerization reactions of hydroxyazachalcones (**1–3**) did not occur experimentally in solution (ethanol, methanol, acetic acid, chloroform) and in the solid state. Furthermore, an attempt was made to use benzophenone as a source of radicals, but this did not gave any dimerization product. The photochemical behavior of these substrates is similar to that reported for ethyl cinnamate and cinnamonitrile [27], and for α-methyl furyl acrylates [28]. These substrates were also recovered unchanged after a prolonged reaction. The reason for this behavior may be elucidated by theoretical calculations of frontier orbital control in the stereochemical behavior of compounds **1–3** and cycloaddition parameters (Tables 1 and 2). The electron coefficient, the HOMO/LUMO energy in the ground state and the HSOMO/LSOMO energy in the excited state were calculated using the B3LYP/6-31^{+}G** and CIS/3-21^{+}G** methods, respectively, and the results are shown in Table 1. It is clear that the ground-state electron coefficient of the HOMO ($q_i = 2c_i^2$) and the excited triplet and singlet state electron density of the HSOMO ($q_i = 2c_i^2$) are too low to result in any dimerization reaction on the basis of the data obtained for compounds **1–3**, and the superposition of the HOMO and the LSOMO of the singlet state is not allowed (Table 1).

Theoretical results showed that access to the double bond that yields the cyclobutane ring is hindered by the

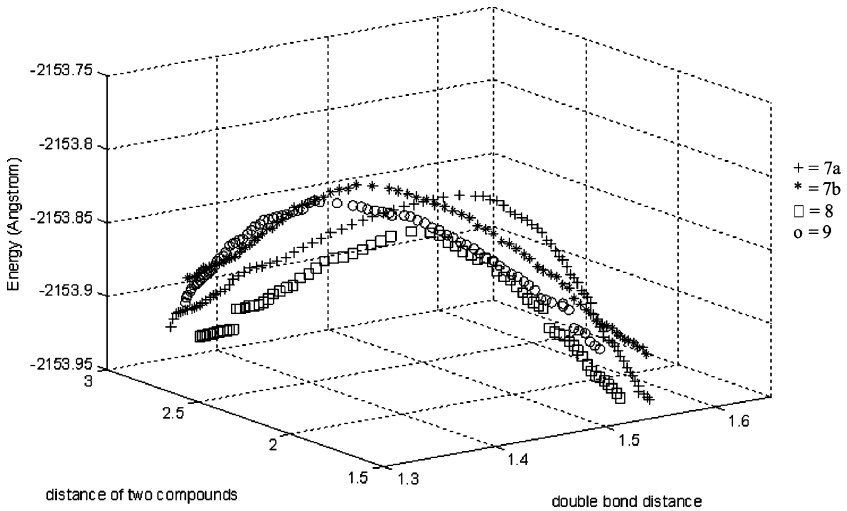


Fig. 1 Plot of intrinsic reaction coordinates for compounds **7–9**

Table 1 HOMO/LUMO and HSOMO/LSOMO energies and electron coefficients of compounds **1–3**

Compounds				1			2			3	
Electronic state	S_0	S_1	T_1	S_0	S_1	T_1	S_0	S_1	T_1		
HOMO (eV)	−6.79			−6.35			−6.49				
C_α	−0.10			−0.08			0.05				
C_β	−0.17			−0.10			0.10				
LUMO (eV)	−2.75			−2.50			−2.56				
C_α	−0.68			−0.40			−0.56				
C_β	0.74			0.35			0.66				
HSOMO (eV)		0.83	−5.86		0.97	−5.71		−8.64	−5.97		
C_α		0.08	0.36		−0.16	0.04		−0.23	0.10		
C_β		0.06	0.57		−0.15	−0.23		−0.10	−0.30		
LSOMO (eV)		−8.55	−9.91		−8.56	−9.66		1.18	−9.66		
C_α		−0.45	0.10		−0.48	0.46		−0.56	0.39		
C_β		0.61	−0.33		0.63	0.51		0.49	0.66		

hydroxy group, and so adjacent molecules cannot dimerize, considering the calculated distances of 4.5 Å, 6.6 Å, and 4.4 Å for compounds **1–3**, respectively (Table 2). In the literature, the molecules form pairs connected by hydrogen bonds that prevent them moving from a distance of about 3.6 Å apart to a distance of 1.5 Å apart, which prohibits the formation of the cyclobutane ring [29]. The hydroxyl groups on the azachalcones were then converted to benzoyl groups, and three new *o*-, *m*-, and *p*-benzoyl-(*E*)-4-azachalcones (**4–6**) were obtained. The photochemical dimerization of compounds **4–6** gave cyclobutane-containing dimers in chloroform solution. Contrary to other reported publications [4–10], the photochemical dimerization of compound **5** gave a *trans* head-to-tail dimer (**8**), which is not very common in the literature.

In order to explain the formation of the dimers, we examined the possibility of frontier orbital control in the stereochemical behavior of compounds **4–6**, and some theoretical calculations were performed in order to investigate synthesized compound optimization. We calculated the HOMO/LUMO energies in the ground state, the HSOMO/LSOMO energies in the excited state and their electron coefficients using density functional theory (DFT) at the B3LYP/6-31$^+$G** level and the CIS/3-21$^+$G** method (Table 3). According to theoretical calculations, total superposition occurs between both the HOMO/LSOMO and the LUMO/HSOMO in the excited singlet state for compounds **5** and **6** and the LUMO/HSOMO in the excited triplet state for compound **4**. The electron densities of the HSOMO and LSOMO ($qi = 2c_i{}^2$) for the double bonds are too low to permit any dimerization reaction to occur in the excited triplet state for compound **6** and the singlet state for compound **4**. The superposition of the HOMO and the LSOMO of the triplet state is not allowed for compound **5** (Table 3). Thus, the photodimerization reactions of compounds **5** and **6** occur with stereo- and regioselectivity and give one product, while the photodimerization reaction of compound **4** gives two products because of a lack of regioselectivity.

Table 2 The mutual orientation parameter for compounds **1–6**

Compounds	*d* (Å)	α	τ	Ø	κ
1	4.5				
2	6.6				
3	4.4				
4	2.5	89.8	7.0	0	89.9
5	2.6	95.7	9.4	0	87.3
6	2.9	86.1	6.6	0	96.8
Ideal values	<4.2	90.0	0	0	90.0

d, the distance between carbon atoms in the C=C bonds of adjacent molecules; α, the angle C=C...C formed by two C=C bonds of adjacent molecules; τ, the torsion angle C=C...C=C formed by adjacent molecules; *Ø*, the angle between planes of >C=C< fragments of adjacent molecules; κ, the angle between the >C=C< plane of one molecule and the plane of the four C atoms from two C=C bonds [26]

Transition states play a very important role in photodimerization reactions. The photochemical reactions of compounds **4–6** could give eleven different possible isomers according to kinetic theory [28]. We calculated possible head-to-head isomers for compounds **4** and **6** and head-to-head and head-to-tail isomers for compound **5** by means of the DFT B3LYP/6-31$^+$G** level and CIS/3-21+G** methods to show how the dimers of compounds **4–6** are formed, and investigate the energy of the transition state of the ring-closure reactions from the biradical *syn* and *anti* forms [28] (Table 4). According to the results obtained with DFT, the stablest of the possible dimers (i.e., that has the lowest strain energy and heat of formation) is a head-to-head isomer that has R_1 and R_2 groups in the cyclobutane

Table 3 HOMO/LUMO and HSOMO/LSOMO energies and electron coefficients of compounds **4–6**

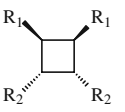
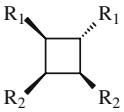
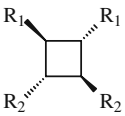
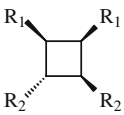
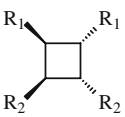
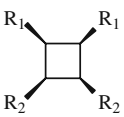
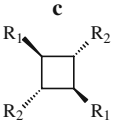
Compounds		4			5			6	
Electronic state	S_o	S_1	T_1	S_o	S_1	T_1	S_o	S_1	T_1
HOMO (eV)	−6.49			−6.71			−6.66		
C_α	−0.04			0.18			−0.26		
C_β	−0.03			0.21			−0.22		
LUMO (eV)	−2.44			−2.38			−2.51		
C_α	0.52			−0.51			−0.52		
C_β	−0.45			0.61			0.40		
HSOMO (eV)		1.01	2.26		−0.78	2.01		1.01	−5.88
C_α		−0.01	0.33		−0.42	−0.23		−0.52	0.05
C_β		0.12	−0.31		0.51	0.04		0.58	−0.26
LSOMO (eV)		−9.29	−7.36		−9.20	−7.33		−9.20	−9.88
C_α		−0.02	0.04		0.29	−0.70		−0.24	0.02
C_β		−0.01	−0.09		0.22	0.81		−0.21	0.07

ring in a *trans–trans–trans–trans* configuration for compounds **7b** and **9** and a *cis–trans–cis–trans* configuration for compound **7a**, while it is a head-to-tail isomer that has R_1 and R_2 groups in the cyclobutane ring in a *trans–trans–trans–trans* configuration for compound **8g**. The results showed that isomers **7a**, **7b**, **8g** and **9b** were the most stable isomers according to this method (Table 4).

Intrinsic reaction coordinate analyses of the relations between the reactant, transition state, and product in the dimerization reactions (Fig. 1) were performed using the DFT/3-21$^+$G** method, and results are shown in Tables 5 and 6. The IRCs were followed to confirm the energy profiles that connect each TS to the appropriate local minimum.

In order to investigate the meaning of differences between the orientations of neighboring molecules in the photochemical reactions of compounds **1–6**, we also considered the mutual orientation parameters for compounds that undergo [2+2] photodimerization, and the results are shown in Table 2. The mutual orientation of neighboring molecules in a photodimerization reaction is one of the main factors that influences whether a photochemical reaction will occur [29].

Table 4 The total electronic energies of head-to-head dimers (excluding **8g**), and the transition state energies for the ring closure reaction for isomers of **7–9**, respectively (kcal mol^{-1})

Isomers [a])	-E (a.u.)	Biradicals $\Delta H^{\neq}$ (kcal/mol)	Isomers	-E (a.u.)	Biradicals $\Delta H^{\neq}$ (kcal/mol)
	2179.44(**7**)	23.21(**7**)		2179.40(**7**)	34.54(**7**)
	2179.46(**8**)	18.72(**8**)		2179.44(**8**)	17.54(**8**)
	2179.46(**9**)	20.87(**9**)		2179.45(**9**)	22.58(**9**)
a			**d**		
	2179.44(**7**)	15.03(**7**)		2179.39(**7**)	29.53(**7**)
	2179.45(**8**)	12.45(**8**)		2179.43(**8**)	19.71(**8**)
	2179.47(**9**)	12.95(**9**)		2179.39(**9**)	20.80(**9**)
b			**e**		
	2179.43(**7**)	38.67(**7**)		2179.42(**7**)	34.65(**7**)
	2179.42(**8**)	12.36(**8**)		2179.44(**8**)	30.85(**8**)
	2179.42(**9**)	17.67(**9**)		2179.44(**9**)	26.80(**9**)
c			**f**		
	2179.47(**8**)	12.12(**8**)			
g					

[a]) R_1= o, *m*- and *p*-PhCOO-PhCO-, R_2= 4-Pyridyl

Table 5 Calculated bond lengths (Å) in compounds **7–9**

Compounds	Reactants		Transition state		Products	
	C_1–C_2	C_3–C_4	C_1–C_2	C_3–C_4	C_1–C_2	C_3–C_4
7a	2.75	2.64	2.27	2.09	1.56	1.58
7b	2.75	2.64	2.28	1.89	1.55	1.55
9	2.70	2.53	2.35	1.86	1.55	1.58
8	2.62		2.12		1.58	

Full geometrical optimization of the reactants was carried out with ab initio SCF and DFT/B3LYP methods using the 6-31$^+$G** basis set, and the structure of the molecule was also investigated in detail. The values of the distances C_1–C_2 (the distance between the two carbon atoms in cyclobutane that are attached to benzoyl groups), C_3–C_4 (the distance between carbon atoms of C=C bonds in adjacent molecules) and C_1–C_4 (the distance between the two carbon atoms in cyclobutane that are attached to pyridinyl groups) were determined (Tables 5 and 6).

Scheme 1 illustrates the synthetic approach chosen for the preparation of *o*-, *m*-, and *p*-benzoyl-(*E*)-4-azachalcones (**4–6**) and dimerization products (**7–9**) [5–10]. The most noticeable feature of the structural characterization of *o*-, *m*-, and *p*-hydroxy-substituted (*E*)-4-azachalcones (**1–3**) is the assignment of the proton resonances of the α,β-unsaturated moiety, which was achieved by carefully analyzing their ^{1}H and 2D-COSY NMR spectra. Using the values of the vicinal coupling constants (^3J H_α–H_β δ16.4/15.8/15.8 Hz, respectively), it was possible to establish the *trans* configuration of these two protons [3–10]. When exposed to UV light (from a 400 W high-pressure Hg lamp) in chloroform, *o*-, *m*- and *p*-benzoyl-(*E*)-4-azachalcones (**4–6**) were converted to their respective cyclobutanes (**7a**, **7b**, **8**, and **9**) with yields (chromatographed product, PTLC) of 13%, 17%, 23% and 20%, respectively.

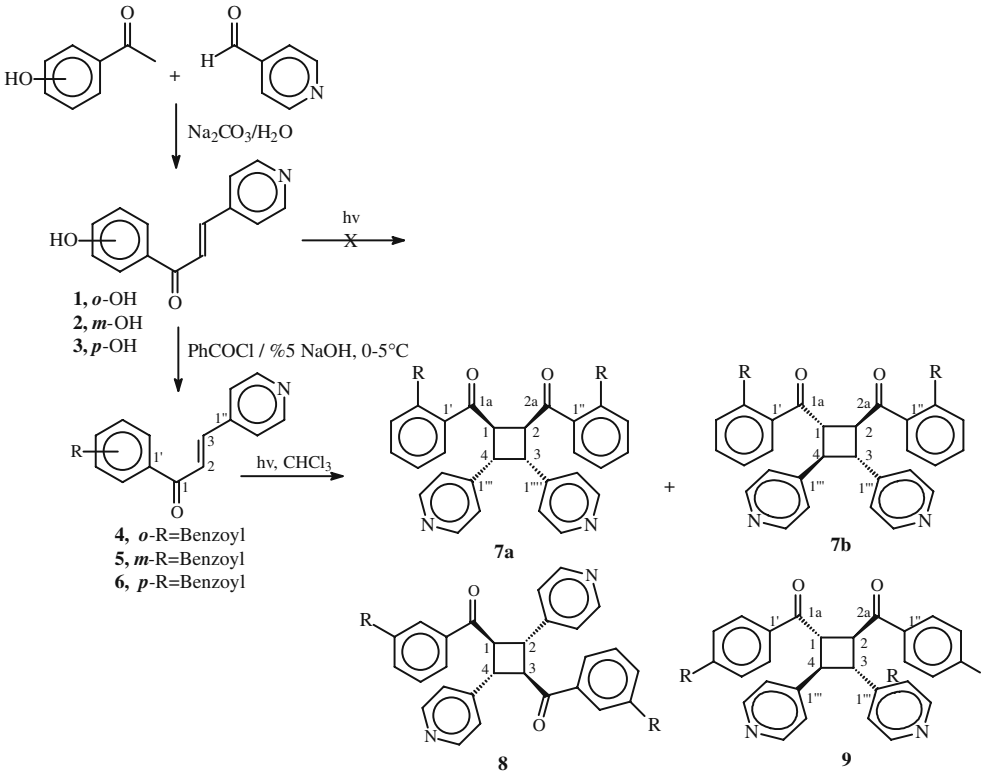
The structures of the cyclobutyl rings of products **7–9** were elucidated from their ^{1}H NMR spectra, which show two symmetrical highly shielded CH proton signals at δH 4.72 (H_{1-2})/4.58 (H_{3-4}) for **7a**, δH 4.50 (H_{1-2})/3.91 (H_{3-4}) for **7b**, δH 4.86 (H_{1-4}) for **8**, and δH 4.59 (H_{1-2})/4.03 (H_{3-4}) for **9**, respectively [3–10]. The stereochemistry of the dimers (**7–9**) was established on the basis of their ^{1}H NMR spectra and by comparing with literature data [3–10, 27, 28, 30, 31]. The values for *J* suggest a *cis* relationship for **7a**, and a *trans* relationship for **7b** and **9** between A and A′ and B and B′, because the values are 6.8, 8.8, and 8.8, respectively. Although the values of these coupling constants suggest that **7a**, **7b** and **9** were formed by head-to-head coupling, they do not allow certain assignment with respect to *syn*/*anti* stereochemistry. J_A and J_B values were not determined for compound **8** due to the symmetry of the molecule. Simulating the NMR patterns allowed the coupling constants of the cyclobutyl protons to be calculated ($J_{AA'}$=6.8/8.8/8.8, J_{AB}=5.0/4.0/5.4, $J_{AB'}$ = 2.4/2.2/3.4, $J_{BB'}$=6.8/8.8/8.8, respectively) [5–10, 29, 32–34]. The values of these coupling constants and the ^{1}H and ^{13}C NMR patterns of the cyclobutyl moieties of compound **7a** suggest that the formation of the cyclobutane ring occurs via a *cis* head-to-head junction to give a β-truxinic structure, while compounds **7b** and **9** are created by a *trans* head-to-head junction to give a δ-truxinic structure [32–35]. A singlet peak was observed at δ 4.86 ppm (4H) in the ^{1}H NMR spectrum for the cyclobutyl ring of compound **8**, which indicates that the dimerization of compound **5** occurred by a *trans* head-to-tail junction to give a ε-truxillic structure for **8**.

Positive-mode LC–MS/MS gave [*M*+H]+ at *m*/*z* 225 (100%) for **1–3**, [*M*+H]+ at *m*/*z* 329 (100, 63, and 63%) for **4–6**, and [*M*+H]+ at *m*/*z* 659 (62, 52, 83, 52%) for **7–9**, which were consistent with the molecular formulae of $C_{14}H_{11}NO_2$ for **1–3**, $C_{21}H_{15}NO_3$ for **4–6**, and $C_{42}H_{30}N_2O_6$ for **7-9**. Compounds **1–9** were characterized based on evaluations of spectral data (^{1}H, ^{13}C, ^{1}H–^{1}H COSY NMR, FT-IR, UV-vis, and LC–MS/MS), and the results of these evaluations were in agreement with the proposed structures.

As a result, the kinetically favorable photoadducts (**7–9**) were formed based upon the above observations, and the complete chemical shift assignments for **7–9** were found to be (1β,2β)-di-[(2-O-benzoyl)benzoyl]-(3α,4α)-di-(4-pyridinyl) cyclobutane (**7a**), (1α,2β)-di-[(2-O-benzoyl)benzoyl]-(3α,4β)-di-(4-pyridinyl)cyclobutane (**7b**), (1β,3β)-di-[(3-O-benzoyl)benzoyl]-(2α,4α)-di-(4-pyridinyl)cyclobutane (**8**), and (1α,2β)-di-[(4-O-benzoyl)benzoyl]-(3α,4β)-di-(4-pyridinyl)cyclobutane (**9**).

Table 6 Calculated C_1–C_4 bond lengths (Å) for the reactants, transition states and products in the dimerization reactions

Compounds	Reactants	Transition state	Products
	C_1–C_4	C_1–C_4	C_1–C_4
7a	1.31	1.39	1.55
7b	1.31	1.40	1.55
8	1.32	1.40	1.55
9	1.32	1.42	1.57



Scheme 1 Synthetic approach chosen to prepare compounds **1–9**

Conclusions

Experimentally obtained results showed that two dimerization products (**7a** and **7b**) were obtained from compound **4**, and one dimer product (**8** and **9**, respectively) was obtained from each of the compounds **5** and **6**. According to theoretical calculations, only one dimerization product can be obtained from compounds **5** and **6** due to the superposition of the HOMO/LSOMO and the LUMO/HSOMO frontier orbitals, while two stereochemical dimerization products can be obtained from compound **4** via the superposition of the one frontier orbital of the LUMO/HSOMO. Photoaddition of hydroxy-4-azachalcones did not give any product. Theoretical calculations indicate that three of the 4-azachalcone ground-state HOMOs and both of the excited-state LSOMOs, the singlet and triplet states, do not have enough electron density to yield any dimerization product. Also, the superposition of the ground-state and excited-state HOMO/LSOMO and LUMO/HSOMO is allowed in the triplet state, but is not allowed in the singlet state (thus ruling out any dimerization reaction).

Experimental part

General NMR spectra were recorded on a Varian Mercury NMR at 200 MHz in $CDCl_3$. The mass spectral analyses were carried out on a Micromass Quattro LC–MS/MS spectrophotometer. The elemental analyses were performed on a Leco CHNS 932 instrument. Infrared spectra were obtained with a Perkin-Elmer 1600 FT-IR (4000–400 cm^{-1}) spectrometer. Melting points were determined using a Thermovar apparatus fitted with a microscope and are uncorrected. UV-vis spectral analyses were carried out on a Unicam UV2-100 spectrophotometer at 25 °C. Thin-layer chromatography (TLC) was carried out on Merck precoated 60 Kieselgel F254 analytical aluminum plates. PTLC was carried out on Merck precoated 60 Kieselgel F254 (20 mm × 20 mm×0.25 mm) silica gel plates. The known compounds **1–3** were prepared according to the literature [4–10].

General procedure for benzoylation The 2-, 3-, and 4-hydroxy-4-azachalcones (300 mg each) (**1–3**) were dissolved in 5% NaOH solution (5 ml) in an Erlenmeyer flask (125 ml) and then cooled in an ice bath. To this, benzoylchloride (187 mg mmol) was added dropwise over the course of 10 min. The solution was warmed to room temperature and stirred for an additional 1 h. The reactions were monitored by analytical TLC and extractions were performed with chloroform. The residue was purified by column chromatography (column, length 30 cm, diameter 2 cm) on silica gel (25 g, Merck, 230–400 mesh). The column was eluted successively with the following solvent and solvent mixture:

n-hexane (20 ml) and hexane–ethyl acetate (20:1, 50 ml; 20:2, 50 ml; 20:5, 40 ml; and 20:10, 50 ml). Fractions (10–15 ml each) were collected and monitored by analytical TLC. The desired products **4–6** were obtained from fractions 6–10, 7–12, and 6–13 (44%, 80%, and 85% yield, R_f=0.56, 0.81, and 0.46, hexane:ethyl acetate, 1:1), respectively.

General procedure for irradiation A solution of compounds **4–6** (0.45 g, each) in 35 ml of chloroform, kept in a beaker, was exposed to UV light (from a 400 W high-pressure Hg lamp). The progress of the reaction was followed by silica gel TLC (ethyl acetate:methanol, 3:1). The reaction was stopped after 24 h. The solution was evaporated and a portion of the residue purified by prep. TLC (200 mg, 0.5 mm, 20 × 20 cm, 2 plates) to give compounds **7a**, **7b**, **8g** and **9b**.

1-[(2-O-Benzoyl)-phenyl]-(2E)-3-(4-pyridinyl)-2-propen-1-one (4) Yield 44%, UV λ_{max}^{CHCl3} nm: 242 (ε, 16645), 266 (ε, 9578), 302 (ε, 8384); ^{1}H NMR ($CDCl_3$, 200 MHz): 7.42 (s, H-2, H-3), 7.80 (dd, *J* =9.4 and 1.8, H-3′), 7.61 (t, H-4′), 7.24 (t, H-5′), 7.33 (d, *J*= 8.8, H-6′), 7.20 (d,d *J*= 6.0 and 1.5, H-2″, H-6″), 8.55 (dd, *J*= 6.0 and 1.6, H-3″, H-5″), 8.11 (dd, *J*= 9.8 and 1.4, H-2‴, H-6‴), 7.45 (t, H-3‴, H-5‴), 7.53 (t, H-4‴); ^{13}C NMR ($CDCl_3$, 50 MHz) & (ppm): 190.63 (C-1), 121.74 (C-2), 141.54 (C-3), 128.69 (C-1′), 149.10 (C-2′), 126.30 (C-3′), 133.17 (C-4′), 123.62 (C-5′), 130.10 (C-6′), 141.58 (C-1″), 128.58 (C-2″, C-6″), 150.37 (C-3″, C-5″), 131.77 (C-1‴), 130.14 (C-2‴, C-6‴), 129.28 (C-3‴, C-5‴), 133.89 (C-4‴); MS(+): 330(58) $[M+1]^+$, 329 (63) $[M]^+$, 248(60) $[M-81]^+$, 247(77) $[M-82]^+$, 232(56) $[M-97]^+$, 230(100) $[M-99]^+$, 215(48) $[M-114]^+$, 213(59) $[M-116]^+$, 185(48) $[M-144]^+$; Anal. calc. for $C_{21}H_{15}NO_3$ (329.11): C 76.58, H 4.59, N 4.25; found: C 76.567; H 4.589, N 4.274.

1-[(3-O-Benzoyl)-phenyl]-(2E)-3-(4-pyridinyl)-2-propen-1-one (5) Yield 80%, UV λ_{max}^{CHCl3} nm: 285 (ε, 22900), 242 (ε, 16549); ^{1}H NMR ($CDCl_3$, 200 MHz): 7.67 (s, H-2, H-3), 7.59 (s, H-2′), 7.51 (d, *J*= 7.8, H-4′), 7.41 (t, H-5′), 7.47 (d, *J* =7.8, H-6′), 7.45 (d, *J* = 5.8, H-2″, H-6″), 8.66 (d, *J* = 5.8, H-3″, H-5″), 8.20 (d, *J* = 8.4, H-2‴, H-6‴), 7.91 (dd, *J* = 8.4 and 1.0, H-3‴,H-5‴), 7.59 (dd, *J* = 8.4 and 3.0, H-4‴); ^{13}C NMR ($CDCl_3$, 50 MHz) & (ppm): 188.51 (C-1), 125.97 (C-2), 141.81 (C-3), 138.74 (C-1′), 125.74 (C-2′), 150.11 (C-3′), 126.77 (C-4′), 150.11 (C-5′), 128.17 (C-6′), 142.14 (C-1″), 129.99 (C-2″), 122.16 (C-3″), 129.90 (C-4″, C-5″, C-6″), 131.77 (C-1‴), 130.14 (C-2‴, C-6‴), 129.28 (C-3‴, C-5‴), 133.86 (C-4‴); FT-IR: 3423, 3062, 2443, 1723, 1668, 1595, 1273, 1226, 1167, 1065, 1024, 793, 708; MS(+): 332(100) $[M+3]^+$, 330(75) $[M+1]^+$, 329(63) $[M]^+$, 295(65) $[M-34]^+$, 294(60) $[M-35]^+$, 284(90) $[M-45]^+$, 283 (71) $[M-46]^+$, 229(58) $[M-100]^+$, 191(55) $[M-138]^+$; Anal. calc. for $C_{21}H_{15}NO_3$ (329.11): C 76.58, H 4.59, N 4.25; found: C 76.551; H 4.570, N 4.217.

1-[(4-O-Benzoyl)-phenyl]-(2E)-3-pyridin-(4-pyridinyl)-2-propen-1-one (6) Yield 85%, UV λ_{max}^{CHCl3} nm: 286 (ε, 18219); ^{1}H NMR ($CDCl_3$, 200 MHz): 7.71 (s, H-2, H-3), 8.22 (d, *J* = 9.2 and 6.2, H-2′, H-6′), 7.55 (d, *J* = 9.2, H-3′, H-5′), 7.49 (dd, *J* = 6.0 and 3.0, H-2″, H-6″), 8.70 (dd, *J* = 6.0 and 3.0, H-3″, H-5″), 8.13 (dd, *J* = 8.8 and 5.2, H-2‴, H-6‴), 7.40 (d, *J* = 8.8 , H-3‴, H-5‴), 7.66 (dd, *J* = 8.8 and 3.0, H-4‴); ^{13}C NMR ($CDCl_3$, 50 MHz) & (ppm): 188.33 (C-1), 125.57 (C-2), 141.54 (C-3), 134.87 (C-1′), 131.17 (C-2′, C-6′), 122.05 (C-3′, C-5′), 154.69 (C-4′), 141.80 (C-1″), 121.93 (C-2″, C-6″), 150.45 (C-3″, C-5″), 128.74 (C-1‴), 130.10 (C-2‴, C-6‴), 128.58 (C-3‴, C-5‴), 133.86 (C-4‴); FT-IR: 3057, 2907, 2721, 1731, 1663, 1597, 1416, 1302, 1269, 1220, 1170, 1023, 801, 713; MS(+): 358(22) $[M+29]^+$, 344(15) $[M+15]^+$, 330.98(26) $[M+1]^+$, 329.98(100) $[M]^+$, 247(15) $[M-82]^+$, 231(17) $[M-98]^+$, 225(16) $[M-104]^+$, 167(11) $[M-132]^+$, 162(12) $[M-167]^+$, 104(18) $[M-225]^+$; Anal. calc. for $C_{21}H_{15}NO_3$ (329.11): C 76.58, H 4.59, N 4.25; found: C 76.591; H 4.578, N 4.244.

(1β,2β)-Di-[(2-O-benzoyl)benzoyl]-(3α,4α)-di-(4-pyridinyl)cyclobutane (7a) Yield 13%, UV λ_{max}^{CHCl3} nm: 260 (ε, 94974), 242 (ε, 75650); ^{1}H NMR ($CDCl_3$, 200 MHz): 4.72 (AA′BB′, *J* = 6.8, 5.0, 2.4, H-1, H-2), 4.58 (AA′BB′, *J* = 6.8, 5.0, 2.4, H-3, H-4), 7.20 (d, *J* = 7.8, H-3′, H-3″), 7.07 (t, *J* = 7.8 ,1.8, H-4′, H-4″), 7.63 (t, *J* = 7.8, 3, H-5′, H-5″), 7.79 (d, *J* = 7.8, H-6′), 6.83 (d, *J* = 6.4, H-2‴, H-2⁗, H-6‴, H-6⁗), 8.24 (d, *J* = 6.4, H-3‴, H-3⁗, H-5‴, H-5⁗), 8.046 (d, *J* = 8.8, H-2⁗′, H-2⁗′′, H-6⁗′, H-6⁗′′), 7.48 (dt, *J* = 8.8, 3, H-3⁗′, H-3⁗′′, H-5⁗′, H-5⁗′′), 7.12 (t, *J* = 8.8, 2.4, H-4⁗′, H-4⁗′′); ^{13}C NMR ($CDCl_3$, 50 MHz) & (ppm): 51.55 (C-1, C-2), 55.19 (C-3, C-4), 199.22 (C-1a, C-2a), 173.08 (C-3a, C-4a), 133.28 (C-1′, C-1″), 150.76 (C-2′, C-2″), 128.78 (C-3′, C-3″), 123.50 (C-4′, C-4″), 128.41 (C-5′, C-5″), 128.89 (C-6′, C-6″), 126.09 (C-1‴, C-1⁗), 130.22 (C-2‴, C-2⁗, C-6‴, C-6⁗), 129.65 (C-3‴, C-3⁗, C-5‴, C-5⁗), 158.01 (C-1⁗′, C-1⁗′′), 134.37 (C-2⁗′, C-2⁗′′, C-6⁗′, C-6⁗′′), 150.76 (C-3⁗′, C-3⁗′′, C-5⁗′, C-5⁗′′), 125.76 (C-4⁗′, C-4⁗′′); FT-IR: 3031, 2925, 2854, 2482, 1739, 1687, 1601, 1449, 1264, 1201, 1060; MS(+): 688(62) $[M+30]^+$, 687(66) $[M+29]^+$, 673(92) $[M+15]^+$, 659(62) $[M+1]^+$, 584(35) $[M-74]^+$, 550(66) $[M-108]^+$, 522 (51) $[M-136]^+$, 494(32) $[M-164]^+$, 248(98) $[M-410]^+$, 247 (100) $[M-410]^+$, 230(67) $[M-428]^+$, 219(82) $[M-439]^+$; Anal. calc. for $C_{42}H_{30}N_2O_6$ (658.21): C 76.58, H 4.59, N 4.25; found: C 76.557; H 4.545, N 4.290.

(1α,2β)-Di-[(2-O-benzoyl)benzoyl]-(3α,4β)-di-(4-pyridinyl)cyclobutane (7b) Yield 17%, UV λ_{max}^{CHCl3} nm: 261

(ε, 116334), 241 (ε, 104419); ^{1}H NMR ($CDCl_3$, 200 MHz): 4.50 (AA′BB′, *J* = 8.8, 4.0, 2.2, H-1, H-2), 3.91 (AA′BB′, *J* = 8.8, 4.0, 2.2, H-3, H-4), 7.23 (d, *J* = 7.8, H-3′, H-3″), 7.12 (t, *J* = 7.8 ,2.0, H-4′, H-4″), 7.59 (t, *J* = 7.8 , 1.6, H-5′, H-5″), 7.73 (d, *J* = 7.8, H-6′), 7.17 (d, *J* = 6.4, H-2‴, H-2⁗, H-6‴, H-6⁗), 8.48 (d, *J* = 6.4, H-3‴, H-3⁗, H-5‴, H-5⁗), 8.25 (d, *J* = 8.4, H-2⁗′, H-2⁗″, H-6⁗′, H-6⁗″), 7.49, (dt, *J* = 8.4, 3, H-3⁗′, H-3⁗″, H-5⁗′, H-5⁗″), 7.08 (t, *J* = 8.4, 1.6, H-4⁗′, H-4⁗″); ^{13}C NMR ($CDCl_3$, 50 MHz) & (ppm): 44.71 (C-1, C-2), 48.43 (C-3, C-4), 199.25, 198.22 (C-1a, C-2a), 158.03 (C-3a, C-4a), 128.04 (C-1′, C-1″), 149.22 (C-2′, C-2″), 123.63 (C-3′, C-3″), 129.78 (C-4′, C-4″), 126.09 (C-5′, C-5″), 129.23 (C-6′, C-6″), 133.78 (C-1‴, C-1⁗), 122.57 (C-2‴, C-2⁗, C-6‴, C-6⁗), 149.59 (C-3‴, C-3⁗, C-5‴, C-5⁗), 150.45 (C-1⁗′, C-1⁗″), 130.33 (C-2⁗′, C-2⁗″, C-6⁗′, C-6⁗″), 128.84 (C-3⁗′, C-3⁗″, C-5⁗′, C-5⁗″), 134.08 (C-4⁗′, C-4⁗″); FT-IR: 3031, 2926, 2854, 2475, 1733, 1682, 1601, 1449, 1266, 1201, 1062; MS(+): 687(73) $[M+29]^+$, 673(73) $[M+15]^+$, 659(52) $[M+1]^+$, 550(74) $[M-108]^+$, 522(71) $[M-136]^+$, 494(28) $[M-164]^+$, 230(32) $[M-428]^+$, 109(43) $[M-549]^+$, 104(100) $[M-554]^+$; Anal. calc. for $C_{42}H_{30}N_2O_6$ (658.21): C 76.58, H 4.59, N 4.25; found: C 76.527; H 4.550, N 4.293.

(1β,3β)-Di-[(3-O-benzoyl)benzoyl]-(2α,4α)-di-(4-pyridinyl)cyclobutane (8) Yield 23%, UV λ_{max}^{CHCl3} nm: 284 (ε, 47558), 262 (ε, 136063); ^{1}H NMR ($CDCl_3$, 200 MHz): 4.86 (s, H-1, H-2), 4.86 (s, H-3, H-4), 7.90 (s, H-2′, H-2″), 7.62 (d, *J* = 4.6, H-4′, H-4″), 7.66 (t, H-5′, H-5″), 7.52 (d, *J* = 4.6, H-6′, H-6″), 8.38 (d, *J* = 6.0, H-2‴, H-2⁗, H-6‴, H-6⁗), 7.12 (dd, *J* = 6.0 and 3.0, H-3‴, H-3⁗, H-5‴, H-5⁗), 8.19 (d, *J* = 8.8, H-2⁗′, H-2⁗″, H-6⁗′, H-6⁗″), 7.57 (d, *J* = 8.8, H-3⁗′, H-3⁗″, H-5⁗′, H-5⁗″), 7.36 (t, H-4⁗′, H-4⁗″); ^{13}C NMR ($CDCl_3$, 50 MHz) & (ppm): 41.47 (C-1, C-2), 48.84 (C-3, C-4), 196.47 (C-1a, C-2a), 164.77 (C-3a, C-4a), 137.14 (C-1′, C-1″), 121.55 (C-2′, C-2″), 151.03 (C-3′, C-3″), 125.42 (C-4′, C-4″), 129.84 (C-5′, C-5″), 127.08 (C-6′, C-6″), 146.84 (C-1‴, C1⁗), 122.92 (C-2‴, C-2⁗, C-6‴, C-6⁗), 149.77 (C-3‴, C-3⁗, C-5‴, C-5⁗), 128.84 (C-1⁗′, C-1⁗″), 130.18 (C-2⁗′, C-2⁗″, C-6⁗′, C-6⁗″), 128.67 (C-3⁗′, C-3⁗″, C-5⁗′, C-5⁗″), 133.89 (C-4⁗′, C-4⁗″) ; FT-IR: 3436, 3065, 2923, 2466, 1732, 1677, 1598, 1266, 1237, 1062, 706; MS(+): 688(46) $[M+30]^+$, 687(72) $[M+29]^+$, 660(81) $[M+2]^+$, 659(83) $[M+1]^+$, 550(62) $[M-108]^+$, 522(65) $[M-136]^+$, 388(52) $[M-270]^+$, 248(100) $[M-410]^+$, 230(77) $[M-428]^+$, 229(74) $[M-429]^+$; Anal. calc. for $C_{42}H_{30}N_2O_6$ (658.21): C 76.58, H 4.59, N 4.25; found: C 76.588; H 4.555, N 4.286.

(1α,2β)-Di-[(4-O-benzoyl)benzoyl]-(3α,4β)-di-(4-pyridinyl)cyclobutane (9) Yield 20%, UV λ_{max}^{CHCl3} nm: 259 (ε, 95147), 246 (ε, 79688); ^{1}H NMR ($CDCl_3$, 200 MHz): 4.59 (AA′BB′, *J* = 8.8, 5.4, and 3.4 , H-1, H-2), 4.03 (AA′BB′, *J* = 8.8, 5.6, and 3.4, H-3, H-4), 7.90 (dd, *J* = 9.0 and 5.0, H-2′, H-2″, H-6′, H-6″), 7.24 (d, *J* = 9.0, H-3′, H-3″, H-5′, H-5″), 7.23 (d, *J* = 6.0 , H-2‴, H-2⁗, H-6‴, H-6⁗), 8.59 (dd, *J* = 6.0 and 3.0, H-3‴, H-3⁗, H-5‴, H-5⁗), 8.14 (d, *J* = 8.4, H-2⁗′, H-2⁗″, H-6⁗′, H-6⁗″), 7.52 (d, *J* = 8.4, H-3⁗′, H-3⁗″, H-5⁗′, H-5⁗″), 7.65 (m, H-4⁗′, H-4⁗″); ^{13}C NMR ($CDCl_3$, 50 MHz) & (ppm): 45.33 (C-1, C-2), 46.77 (C-3, C-4), 196.59 (C-1a, C-2a), 132.41 (C-1′, C-1″), 130.48 (C-2′, C-2″, C-6′, C-6″), 128.64 (C-3′, C-3″, C-5′, C-5″), 155.44 (C-4′, C-4″), 122.24 (C-2‴, C-2⁗, C-6‴, C-6⁗), 150.33 (C-3‴, C-3⁗, C-5‴, C-5⁗), 128.76 (C-1⁗′, C-1⁗″), 130.20 (C-2⁗′, C-2⁗″, C-6⁗′, C-6⁗″), 128.64 (C-3⁗′, C-3⁗″, C-5⁗′, C-5⁗″), 133.96 (C-4⁗′, C-4⁗″); FT-IR: 3055, 2405, 1740, 1670, 1597, 1412, 1264, 1205, 1162, 1055, 710; MS(+): 687(73) $[M+29]^+$, 673(73) $[M+15]^+$, 659(52) $[M+1]^+$, 550(74) $[M-108]^+$, 522(71) $[M-136]^+$, 494(28) $[M-164]^+$, 230(32) $[M-428]^+$, 109(43) $[M-549]^+$, 104(100) $[M-554]^+$; Anal. calc. for $C_{42}H_{30}N_2O_6$ (658.21): C 76.58, H 4.59, N 4.25; found: C 76.537; H 4.550, N 4.293.

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References

1. Harborne JB (1988) The flavonoids: advances in research since 1980. Chapman & Hall, London, pp 329–388
2. Marais JPJ, Ferreira D, Slade D (2005) Phytochemistry 66:2145–2176
3. Nowakowska Z, Wyrzykiewicz E, Kedzia B (2001) II Farmaco 56:325–329
4. Usta A, Yaşar A, Yılmaz N, Güleç C, Yaylı N, Karaoğlu ŞA, Yaylı N (2007) Helv Chim Acta 90:1482–1490
5. Yaylı N, Yaşar A, Üçüncü O, Sivrikaya SÖ, Güleç C, Küçük M, Abbasov R (2005) J Photoch Photobio A 175:291–298
6. Yaylı N, Üçüncü O, Yaşar A, Gök Y, Küçük M, Kolaylı S (2004) Türk J Chem 28:515–521
7. Yaylı N, Küçük M, Üçüncü O, Yaşar A, Yaylı N, Karaoğlu ŞA (2007) J Photoch Photobio A 188:161–168
8. Yaylı N, Üçüncü O, Yaşar A, Küçük M, Yaylı N, Akyüz E, Karaoğlu ŞA (2006) Türk J Chem 30:505–514
9. Yaylı N, Üçüncü O, Yaşar A, Yaylı N, Burnaz NA, Karaoğlu ŞA, Küçük M (2009) J Photoch Photobio A 203:85–91
10. Nowakowska Z (2000) Magn Reson Chem 38:382–383
11. Katerere DR, Gray AI, Kennedy AR, Nash RJ, Waigh RD (2004) Phytochemistry 65:433–438
12. Seidel V, Bailleul F, Waterman PG (2000) Phytochemistry 55:439–446
13. Walker RP, Faulkner DJ, Van Engen D, Clardy J (1981) J Am Chem Soc 103:6772–6773
14. Shen X, Perry TL, Dunbar CD, Borges MK, Hamann MT (1998) J Nat Prod 61:1302–1303
15. Tsukamoto S, Cha BC, Ohta T (2002) Tetrahedron 58:1667–1671
16. D'Auria M, Racioppi R (1998) J Photoch Photobio A 112:145–148

17. Kyne SH, Schiesser CH, Matsubara H (2008) J Org Chem 73:427–434
18. Alonso R, Campos PJ, Rodriguez MA, Sampedro D (2008) J Org Chem 73:2234–2239
19. Belbruno JJ (1997) J Phys Org Chem 10:113–120
20. Andre LS, Mercha M, Borin AC (2006) Proc Natl Acad Sci USA 103:8691–8696
21. Hrovat DA, Borden WT (1992) J Am Chem Soc 114:5879–5881
22. Bearpark MJ, Bernard F, Olivucci M, Robb MA (1996) Int J Quantum Chem 60:505–512
23. Smith DA, Bitar J (1993) J Org Chem 58:6–8
24. Hehre WJ, Ditchfield R, Pople JA (1972) J Chem Phys 56:2257–2261
25. Lee C, Yang W, Parr RG (1988) Phys Rev B 37:785–789
26. Becke AD (1993) J Chem Phys 98:1372–1377
27. D'Auira M, Racioppi R (1997) Tetrahedron 53:17307–17316
28. D'Auira M, Emanuele L, Esposito V, Racioppi R (2002) Arkivoc XI:65–78
29. Tyrk IT, Grzes'niak K, Trzop E, Zych T (2003) J Solid State Chem 174:459–465
30. D'Auira M (2000) Heterocycles 54:475–496
31. D'Auria M, Emanuele L, Mauriello G, Racioppi R (2000) J Photoch Photobio A 134:147–154
32. Jovanovi'c BZ, Vukovi'c MM, Marinkovi'c AD, Csan'adi J (1999) J Mol Struct 482–483:371–374
33. Woodward RB, Hoffmann R (1970) The conservation of orbital symmetry. Verlag Chemie, Weinheim
34. Edwards ML, Stemarick DM, Sabol JS, Diekema KA, Dinerstein RJ (1994) J Med Chem 37:4357–4362
35. Sobrinho DC, Ferreira JCN (2002) Quim Nova 25:62–68