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Synthesis of chalconoid-like compounds and their [2 + 2] photodimerizations in solution and theoretical calculations

Nurettin Yaylı*, Ahmet Yaşar, Osman Üçüncü, Serpil Ö. Sivrikaya, Canan Güleç, Murat Küçük, Rıza Abbasov

Department of Chemistry, Faculty of Arts and Sciences, Karadeniz Technical University, 61080 Trabzon, Turkey

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Abstract

Chalconoid-like compounds; (2*E*,4*E*)-1,5-diphenylpenta-2,4-diene-1-one (**1**), (2*E*,4*E*)-1-(*p*-ethyl)phenyl-5-phenylpenta-2,4-diene-1-one (**2**), (2*E*,4*E*)-1-(*m*-methyl)phenyl-5-phenylpenta-2,4-diene-1-one (**3**) and (2*E*,4*E*)-1-(*p*-methyl)phenyl-5-phenylpenta-2,4-diene-1-one (**4**) have been synthesized and their (2 + 2) photosensitized cycloaddition reaction gave four new δ-truxinic-type dimers in solution: rel-(1β,2α)-dibenzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane (**5**), rel-(1β,2α)-di-(*p*-ethyl)-benzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane (**6**), rel-(1β,2α)-di-(*m*-methyl)-benzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane (**7**) and rel-(1β,2α)-di-(*p*-methyl)-benzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane (**8**), stereoselectively. The possible dimerization products of compound **1** were calculated theoretically. Experimental and theoretical calculations showed that δ-truxinic-type dimer is the most stable isomer of all.

Keywords: Chalconoids; Alnustone; Photodimerizations; Dimers; Theoretical calculation

1. Introduction

Alnustone is a member of a broad class of naturally occurring compounds [1–3], which has (4*E*,6*E*)-1,7-diphenylhepta-4,6-diene-3-one structure and has been shown to exhibit anti-inflammatory, antihepatotoxic and anti-emetic activities [3–5]. Analogous to alnustone structure, two unknown (**2**, **3**) and two known (**1**, **4**) [6] *p*-ethyl and *m*-, *p*-methyl-substituted chalconoid-like compounds with the structure (2*E*,4*E*)-1,5-diphenylpenta-2,4-diene-1-one were synthesized in the current study.

A fast method to obtain cyclobutane rings is the photochemical dimerization of α,β-unsaturated carbonyl compounds due to intermolecular [2 + 2] photocycloaddition [7–14]. Photodimerizations of various α,β-unsaturated carbonyl compounds, chalcones, and their derivatives in solution and in solid and molten state have been studied [7–14], although the need is still great for unstudied stereoselective photodimerizations of chalconoid-like ((2*E*,4*E*)-1,5-diphenylpenta-2,4-diene-1-one) α,β,γ,δ-unsaturated carbonyl compounds which can undergo intramolecular electrocyclic cyclization [15] and intermolecular dimerization to give cyclobutene and cyclobutane rings, respectively. These reactions are stereospecific, and this stereospecificity has been explained by means of the Woodward–Hoffmann selection rules [16]. Dimerization reactions can be carried out by UV–vis and sunlight irradiation, with variable results in terms of yield and product composition. In the literature, various cyclobutane containing chalcones have been reported to be synthesized [7–14,17,18] and isolated from various plants [19–22] and many showed antibacterial and antimicrobial activities [19–22]. Analogous to these isolated and synthesized dimers of chalcones, four new chiral dimers of chalconoid-like compounds were synthesized stereoselectively in the current study.

As known, [2 + 2] cycloaddition reactions occur via supra–supra or antra–antra photochemical reactions [16].

* Corresponding author. Tel.: +90 462 3772486; fax: +90 462 3253196.
E-mail address: yayli@ktu.edu.tr (N. Yaylı).

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On the other hand, photochemical dimerization of non-symmetrical alkenes, having different R groups, through the head-to-head or head-to-tail positions is also possible. Photochemical reactions of chalcones possessing conjugated double bonds yield dimers of various structures having cyclobutane ring. Theoretical investigations were performed with HYPERCHEM 7.5 program to determine the stability of the dimers [16,23–25] that are possible to form starting from (2*E*,4*E*)-1,5-diphenylpenta-2,4-diene-1-one (**1**) molecule.

2. Experimental

2.1. General and instrumentation

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 spectrometer. Infrared spectra were obtained with a Perkin-Elmer 1600 FT-IR (4000–400 cm^{-1}) spectrometer. Melting points were determined by using a Thermo-var apparatus fitted with a microscope and are uncorrected. UV–vis spectral analyses were carried out on a Unicam UV2-100 at 25 °C. Thin-layer chromatography (TLC) was carried out on Merck precoated 60 Kieselgel F_{254} analytical aluminum plates. PTLC was carried out on Merck precoated 60 Kieselgel F_{254} (20 cm × 20 cm, 0.25 mm) silica gel plates. Analytical HPLC were carried out on an Agilent 1100 series using a UV–vis detector at 254 nm and column was Zorbax-Rx-SIL (i.d. 4.6 mm × 150 mm, 5 μm) with MeOH/H_2O (95:5), flow 0.5 ml/min.

3. Materials and methods

Acetophenone, *p*-ethylacetophenone, *m*-methylacetophenone, *p*-methylacetophenone, and cinnamaldehyde were purchased from Aldrich and used without further purification. The solvents (chloroform, *n*-hexane, diethyl ether and ethyl alcohol) used were either of analytical grade or bulk solvents distilled before use.

3.1. (2E,4E)-1-(p-ethyl)phenyl-5-phenylpenta-2,4-diene-1-one (2)

To a cooled solution (∼1–5 °C) of sodium hydroxide (1.2 g, 30 mmol) in 5 ml of 80% EtOH was added *p*-ethylacetophenone (1.2 g, 10 mmol) solution in EtOH dropwise. The resulting mixture was stirred for 10 min then was added cinnamaldehyde (1.32 g, 10 mmol) solution in EtOH dropwise. After addition was completed, the reaction mixture was stirred at room temperature for 1 h. The mixture was neutralized with 10% HCl. The ethanol was evaporated under the vacuum, then the aqueous phase was extracted by $CHCl_3$ (3× 30 ml). The combined organic phases were dried over Na_2SO_4. Removal of the solvent under the reduced pressure gave compound **2** (2.1 g, 92% yield). R_f = 0.6; *n*-hexane–$CHCl_3$ (1:3); Oily; UV $\lambda_{max}^{CHCl_3}$ (nm): 248; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm); 7.03 [d, J = 13.2 Hz, *H*-2], 7.52 [m, *H*-3], 7.10 [d, J = 14.8 Hz, *H*-4], 7.02 [m, *H*-5], 7.92 [d, J = 8.6 Hz, *H*-2′, 6′], 7.34 [m, *H*-3′, 5′], 7.50 [m, *H*-2″, 6″], 7.46 [m, *H*-3″, 5″], 7.34 [m, *H*-4″], 2.71 [q, J = 7.8 Hz, CH_2], 1.27 [t, J = 7.8 Hz, CH_3]. ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm); 189.93 [C=O], 126.96 [*C*-2], 144.36 [*C*-3], 125.39 [*C*-4], 141.57 [*C*-5], 136.07 [*C*-5′], 128.78 [*C*-2′, *C*-6′], 128.06 [*C*-3′, *C*-5′], 149.62 [*C*-4′], 135.76 [*C*-1″], 127.20 [*C*-2″, *C*-6″], 128.58 [*C*-3″, *C*-5″], 129.09 [*C*-4″], 28.92 [CH_2], 15.22 [CH_3]; positive LC–MS/MS *m*/*z* (%); *m*/*z* = 285 (72) $[M + Na]^+$, 262 (8) $[M]^+$, 244 (12), 224 (10), 200 (7), 154 (6), 132 (100), 104 (55); FT-IR (cm^{-1}): 3021, 2968, 1689, 1606, 1416, 755 and 700.

The synthesis of compounds **1**, **3**, and **4** were treated in the same way as compound **2**. The spectral data (^{1}H, ^{13}C, FT-IR, UV and MS) of compounds **1** and **4** were the same as in the literature [6].

3.2. (2E,4E)-1-(3-methyl)phenyl-5-phenylpenta-2,4-diene-1-one (3)

Oily; UV $\lambda_{max}^{CHCl_3}$ (nm): 252, 342; 2.14 g, 87% yield. R_f = 0.55, *n*-hexane–diethyl ether (0.5:1). ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm); 6.98 [d, J = 15.6 Hz, *H*-2], 7.30 [m, *H*-3], 7.02 [d, J = 14.6 Hz, *H*-4], 6.98 [m, [*H*-5], 7.69 [bs, *H*-2′], 7.57 [dd, J = 8.8, 1.8 Hz, *H*-4′], 7.32 [m, *H*-5′], 7.68 [m, *H*-6′], 7.40 [m, *H*-2″, *H*-6″], 7.30 [m, *H*-3″, *H*-5″], 7.24 [m, *H*-4″], 2.36 [s, CH_3]. ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm); 190.14 [C=O], 125.35 [*C*-2], 144.34 [*C*-3], 125.21 [*C*-4], 141.51 [*C*-5], 138.08 [*C*-1′], 128.93 [*C*-2′], 137.92 [*C*-3′], 133.24 [*C*-4′], 128.68 [*C*-5′], 126.68 [*C*-6′], 135.82 [*C*-1″], 127.04 [*C*-2″], 128.58 [*C*-3″], 128.18 [*C*-4″], 128.58 [*C*-5″], 127.04 [*C*-6″], 21.14 [CH_3]; positive LC–MS/MS *m*/*z* (%); *m*/*z* = 249(16) $[M + H]^+$, 248(100) $[M]^+$, 114(16) $[M - 134]^+$; FT-IR (cm^{-1}): 3021, 2962, 1681, 1037, 790, 750, 698 and 658.

3.3. Photodimerization of (2E,4E)-1,5-diphenylpenta-2,4-diene-1-one (1)

A solution of compound **1** (250 mg) in 30 ml of diethyl ether, kept in a Pyrex flask, was exposed to UV light (400 W high-pressure Hg lamp). The progress of the reaction was followed by silica gel TLC (*n*-hexane–diethyl ether, 1:1). The reaction was stopped after ∼6 h. The solution was evaporated and the residue purified by PTLC (0.25 mm, 20 cm × 20 cm, two plates) to give compound **5** (10.4 mg, 26% yield, R_f = 0.48, *n*-hexane–diethyl ether, 1:1).

3.4. Photodimerization of (2E,4E)-1-(p-ethyl)phenyl-5-phenylpenta-2,4-diene-1-one (2)

A solution of compound **2** (173 mg) was treated in the same way as compound **1** to give compound **6** (12 mg, 27%

yield, $R_f = 0.72$, *n*-hexane–diethyl ether, 1:1; reaction time ~10 h).

3.5. Photodimerization of (2E,4E)-1-(m-methyl)phenyl-5-phenylpenta-2,4-diene-1-one (3)

A solution of compound **3** (155 mg) was treated in the same way as compound **1** to give compound **7** (14 mg, 36% yield, $R_f = 0.52$, *n*-hexane–diethyl ether, 1:1; reaction time ~13 h).

3.6. Photodimerization of (2E,4E)-1-(p-methyl)phenyl-5-phenylpenta-2,4-diene-1-one (4)

A solution of compound **4** (410 mg) was treated in the same way as compound **1** to give compound **8** (8 mg, 24% yield, $R_f = 0.52$, *n*-hexane–diethyl ether, 1:1; reaction time ~12 h).

3.7. rel-(1β,2α)-Dibenzoyl-rel-(3β,4α)-di-(E)-(2-phenyl)ethenylcyclobutane (5)

Amorphous solid, mp 120–122 °C; UV $\lambda_{max}^{CHCl_3}$ (nm): 251; ^{1}H NMR ($CDCl_3$, 200 MHz) (Table 1) and ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) (Table 2); LC–MS/MS *m/z* (%); *m/z* = 491(28) $[M + Na]^+$, 370(25), 320(22), 304(100), 259 (20), 198(15), 153(52); FT-IR (cm^{-1}): 3065, 3026, 2923, 1668, 1596, 1448, 1320, 1220, 1021, 752 and 693.

3.8. rel-(1β,2α)-Di-(p-ethyl)-benzoyl-rel-(3β,4α)-di-(E)-(2-phenyl)ethenylcyclobutane (6)

Amorphous solid, mp 58–60 °C; UV $\lambda_{max}^{CHCl_3}$ (nm): 260; ^{1}H NMR ($CDCl_3$, 200 MHz) (Table 1) and ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) (Table 2); LC–MS/MS *m/z* (%); *m/z* = 547(13) $[M + Na]^+$, 525(7) $[M + 1]^+$, 370(20), 336(18), 320(52), 318(68), 304(100), 282(28), 153(25), 134(42); FT-IR (cm^{-1}): 3028, 2967, 2932, 1667, 1605, 1566, 1450, 1415, 1230, 1181, 845, 752 and 695.

3.9. rel-(1β,2α)-Di-(m-methyl)-benzoyl-rel-(3β,4α)-di-(E)-(2-phenyl)ethenylcyclobutane (7)

Amorphous solid, mp 109–110 °C; UV $\lambda_{max}^{CHCl_3}$ (nm): 254; ^{1}H NMR ($CDCl_3$, 200 MHz) (Table 1) and ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) (Table 2); LC–MS/MS *m/z* (%); *m/z* = 519(40) $[M + Na]^+$, 497(100) $[M + 1]^+$, 471(35), 379(42), 320(38), 304(100), 282(19), 229(15), 198(18), 153(12), 118(45); FT-IR (cm^{-1}): 3026, 2924,

Table 1
^{1}H NMR data of compounds **5**–**8**[a] in $CDCl_3$

H No	δ_H			
	Compound **5**	Compound **6**	Compound **7**	Compound **8**
1, 2	4.99, dd, 8.8, 8.6 Hz	4.98, dd, 8.6, 8.2 Hz	4.97, dd, 8.8, 8.6 Hz	4.98, dd, 8.8, 8.2 Hz
	4.68, dd, 9.0, 8.8 Hz	4.64, dd, 8.6, 8.4 Hz	4.69, dd, 8.8, 8.6 Hz	4.64, dd, 9.2, 8.8 Hz
3, 4	3.82, ddd, 8.6, 8.2, 6.4, 2.0 Hz	3.80, ddd, 8.2, 7.6, 5.2, 2.2 Hz	3.80, ddd, 9.0, 8.4, 6.0, 2.4 Hz	3.80, ddd, 8.6, 8.2, 5.2, 2.0 Hz
1′a, 2′a	6.30, dd, 13.4, 2.4 Hz	6.32, dd, 13.2, 2.2 Hz	6.32, dd, 13.0, 2.4 Hz	6.30, dd, 13.4, 2.6 Hz
1″a, 2″a	6.31, dd, 13.0, 2.0 Hz	6.32, dd, 13.2, 2.2 Hz	6.32, dd, 13.0, 2.4 Hz	6.30, dd, 13.4, 2.6 Hz
2′/2″	8.13, dd, 6.6, 1.4 Hz	8.07, d, 7.8 Hz	7.92, d, 1.6 Hz	8.05, d, 8.2 Hz
	7.88, dd, 6.8, 1.8 Hz	7.80, d, 8.4 Hz	7.68, d, 1.8 Hz	7.78, d, 8.6 Hz
3′/3″	7.50, m	7.28, m	–	7.26, m
	7.48, m	7.22, m		7.20, m
4′/4″	7.18, m	–	7.32, m	–
5′/5″	7.50, m	7.28, m	7.20, m	7.26, m
	7.48, m	7.22, m		7.20, m
6′/6″	8.13, dd, 6.6, 1.4 Hz	8.07, d, 7.8 Hz	7.93, d, 7.8 Hz	8.05, d, 8.2 Hz
	7.88, dd, 6.8, 1.8 Hz	7.80, d, 8.4 Hz	7.67, d, 7.8 Hz	7.78, d, 8.6 Hz
2× *m*-Me	–	–	2.33, s	–
2× *p*-Me	–	–	–	2.38, s
				2.34, s
2× *p*-Et	–	2.67, q, 7.4 Hz	–	–
		2.63, q, 7.6 Hz		
		1.22, t, 7.4 Hz		
		1.19, t, 7.6 Hz		
2‴/2⁗	7.42, m	7.20, m	7.28, m	7.20, m
3‴/3⁗	7.20, m	7.20, m	7.18, m	7.20, m
4‴/4⁗	7.16, m	7.20, m	7.18, m	7.20, m
5‴/5⁗	7.20, m	7.20, m	7.18, m	7.20, m
6‴/6⁗	7.42, m	7.20, m	7.28, m	7.20, m

[a] Assignment based on ^{1}H, ^{1}H—^{1}H COSY, HETCOR and comparison with ACD NMR Program.

Table 2
^{13}C NMR data of compounds **5**–**8**[a,b] in $CDCl_3$

C No.	δ_C			
	5	**6**	**7**	**8**
1, 2	45.94	45.99	45.70	45.87
	45.74	45.72	45.68	45.73
3, 4	44.55	44.35	44.75	44.32
	43.18	42.95	43.39	43.05
1a, 2a	199.48	199.15	199.60	199.11
	197.85	197.44	198.08	197.40
1′a, 2″a	133.42	133.79	133.87	133.78
	133.26	132.56	132.79	132.58
1″a, 2″a	128.00	128.08	128.11	128.23
	125.30	125.60	125.54	125.56
1′/1″	136.71	136.83	136.76	136.78
			136.70	
2′/2″	128.58	126.28	129.72	129.26
	128.46			128.38
3′/3″	129.06	128.07	138.29	126.28
	128.28		138.25	
4′/4″	134.02	150.38	134.13	144.25
	132.80	150.12	133.97	144.02
5′/5″	129.06	128.07	128.74	126.28
	128.28			
6′/6″	128.58	126.28	125.45	129.26
	128.46			128.38
2× *m*-Me	–	–	21.27	21.65
2× *p*-Me	–	–	–	–
2× *p*-Et	–	28.88	–	–
		15.14		
		15.03		
1‴/1⁗	136.13	133.92	136.25	133.64
	135.98	133.62	135.91	133.42
2‴/2⁗	126.28	128.42	126.28	129.26
		128.30	126.24	128.31
3‴/3⁗	128.34	129.29	128.43	129.19
		128.50	128.31	
4‴/4⁗	127.46	127.38	127.43	127.39
	127.37	127.28	127.32	127.30
5‴/5⁗	128.34	129.29	128.43	129.19
		128.50	128.31	
6‴/6⁗	126.28	128.42	126.28	129.26
		128.30	126.24	128.31

[a] Assignment based on APT, ^{1}H—^{1}H COSY, NOESY, HETCOR and comparison with ACD NMR Program.
[b] Some of the phenyl CH peaks may exchange.

2855, 1668, 1585, 1510, 1449, 1252, 966, 787, 751 and 693.

*3.10. rel-(1β,2α)-Di-(p-methyl)-benzoyl-rel-(3β,4α)-di-(E)-(2-phenyl)ethenylcyclobutane (**8**)*

Amorphous solid, mp 132–134 °C; UV $\lambda_{max}^{CHCl_3}$ (nm): 259; ^{1}H NMR ($CDCl_3$, 200 MHz) (Table 1) and ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) (Table 2); LC–MS/MS *m/z* (%); *m/z* = 519(25) $[M + Na]^+$, 497(5) $[M + 1]^+$, 361(100), 320(18), 304(82), 289(12), 198(5), 153(6), 118(45); FT-IR (cm^{-1}): 3027, 2924, 2851, 1667, 1606, 1573, 1449, 1409, 1231, 1180, 966, 819, 753 and 695.

4. Results and discussion

In this study, two unknown (**2**, **3**) and two known (**1**, **4**) [6] alnustone/chalconoid-like *p*-ethyl, *m*- and *p*-methyl derivatives of (2*E*,4*E*)-1,5-diarylpenta-2,4-diene-1-one were prepared by Claisen–Schmidt condensation of an appropriate aromatic ketone with cinnamaldehyde according to the route indicated in Scheme 1. The most noticeable feature of the structural characterization of compounds **1**–**4** is the assignment of the proton resonances of their α,β,γ,δ-unsaturated moiety, which was made by a careful analysis of their ^{1}H, 2D-COSY and by the help of ACD NMR program. From the values of the vicinal coupling constants ($^3J_{H\alpha—H\beta} \sim 15$ Hz) it was possible to establish the *trans* configuration of these two protons.

These chalconoid-like compounds (**1**–**4**), when exposed to UV light (400 W high-pressure Hg lamp), were converted to the respective cyclobutanes **5**–**8** with the yields (chromatographed products, PTLC) of 26% (**5**), 27% (**6**), 36% (**7**), and 24% (**8**). The yields of these types of reactions have been usually low as in our case or even lower [7–14]. Purity of the synthetic compounds **5**–**8** was controlled by analytical HPLC which showed a single compound for each.

In our previous work [17,18] and literature research [7–14], dimerization of chalconoid compounds showed 1/2 of the total carbon resonance peak in their ^{13}C NMR spectra as expected due to the symmetry of structures. But, in this study, photochemical dimerization of compounds **1**–**4** yielded δ-truxinic-type compounds **5**–**8**. We saw some of the carbon resonances to be two peaks for each symmetrical carbon such as C_{1a}/C_{2a} at $\delta \sim 199/197$ ppm in their ^{13}C NMR spectra. This could be formation of partial twisting of cyclobutyl ring (Fig. 1, calculated structure for compound **5** by PM3 semi-empirical method) with phenylethenyl substitution for compounds **5**–**8** (Tables 1 and 2) which causes the loss of symmetry of these molecules.

The structures of the cyclobutyl rings of products **5**–**8** were elucidated from their ^{1}H NMR spectra, which showed highly shielded CH proton signals for H_1 to H_4 at $\delta_H \sim 4.99$, 4.68 and 3.82 ppm, respectively (Table 1). Stereochemistry of the compounds **5**–**8** were determined from NMR spectrometry information and literature data [7–14,17–18]. Two symmetrical doublet-doublets at δ-H_1 4.99 (dd, $J = 8.8$, 8.6 Hz, δ-C_1 45.94) and δ-H_2 4.68 (dd, $J = 9.0$, 8.8 Hz, δ-C_2 45.74) for compound **5**, at δ-H_1 4.98 (dd, $J = 8.6$, 8.2 Hz, δ-C_1 45.99) and δ-H_2 4.64 (dd, $J = 8.6$, 8.4 Hz, δ-C_2 45.72) for compound **6**, at δ-H_1 4.97 (dd, $J = 8.8$, 8.6 Hz, δ-C_1 45.70) and δ-H_2 4.69 (dd, $J = 8.8$, 8.6 Hz, δ-C_2 45.68) for compound **7** and at δ-H_1 4.98 (dd, $J = 8.8$, 8.2 Hz, δ-C_1 45.87) and δ-H_2 4.64 (dd, $J = 9.2$, 8.8 Hz, δ-C_2 45.73) for compound **8** were observed for the cyclobutyl protons in ^{1}H NMR spectra. The chemical shift differences on the ^{1}H NMR data for H_1 ($\delta \sim 4.99$) and H_2 ($\delta \sim 4.68$) are due to again partial twisting of cyclobutyl ring (Fig. 1 for compound **5**) for compounds **5**–**8** (Table 1). NMR patterns allowed the calculation of the coupling constants of the cyclobutyl protons. The obtained values for J are in agreement with a *trans* relationship between the A and B part of cyclobutane, while the values of J_A and J_B (∼9 Hz) are in good agreement with a *trans* relationship between A and A′ and B and B′, respectively (Table 1). The values of these coupling constants suggest that **5**–**8** were formed by the head-to-head coupling *anti* stereochemistry. A more accurate structural determination was attained from NOESY spectra and literature data [7–14,17–18]. The important NOESY interactions in compounds **5**–**8** were seen between H_1 and H_3 and between H_2 and H_4. Thus the presence of cyclobutane ring was established. The chemical shifts of compounds **5**–**8** are in total agreement with those of similar structures in the literature with δ-truxinic-type structure [7–14].

The structural connectivities of compounds **5**–**8** were established as individual parts from ^{1}H–^{1}H COSY NMR spectra. It was found that for the most down field for the cyclobutyl ring had correlation through H_1 to H_4 in compounds **5**–**8**. The close similarity of the ^{1}H and ^{13}C NMR patterns of the cyclobutyl moieties with δ-truxinic structure strongly suggests that the formation of cyclobutane ring occurs by *anti* head-to-head junction in compounds **5**–**8**.

The LC–MS/MS of compounds **5**–**8** gave $[M + Na]^+$ at *m*/*z* 491(28%), 547 (13%), 519(40%) and 519(25%), which

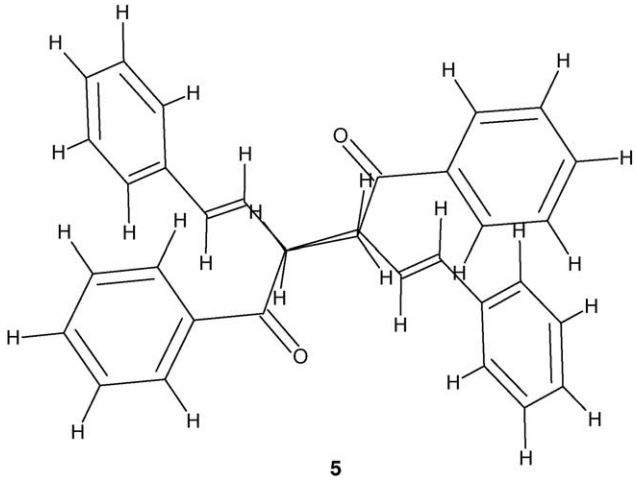
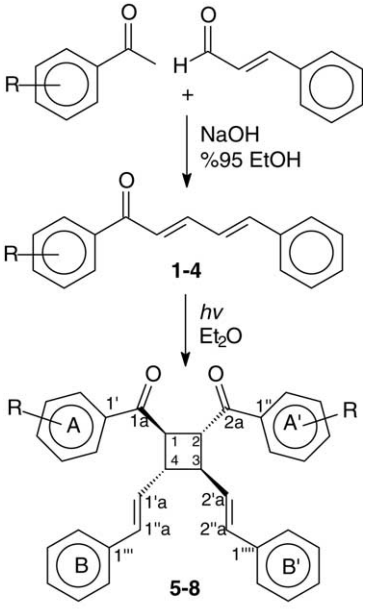


Fig. 1. Calculated structure of compound **5** (PM3 semi-empirical method).



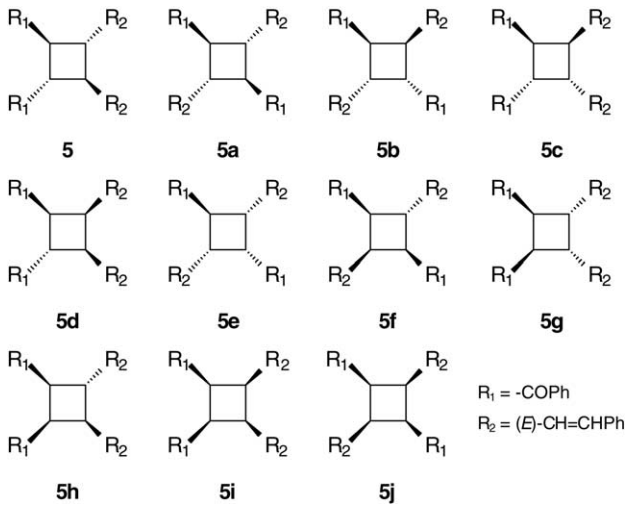
1:	R= H	**5:**	R= H
2:	R= p-Et	**6:**	R= p-Et
3:	R= m-Me	**7:**	R= m-Me
4:	R= p-Me	**8:**	R= p-Me

Scheme 1.

were consistent with the molecular formulas $C_{34}H_{28}O_2$, $C_{38}H_{36}O_2$, $C_{36}H_{32}O_2$ and $C_{36}H_{32}O_2$ requiring dimeric structures, respectively.

Based upon the above observations, the complete chemical shift assignments for **5**–**8** were deduced and listed in Tables 1 and 2. Compounds **5**–**8** were, thus, shown to be rel-(1β,2α)-dibenzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane, rel-(1β,2α)-di-(*p*-ethyl)-benzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane, rel-(1β,2α)-di-(*m*-methyl)-benzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane and rel-(1β,2α)-di-(*p*-methyl)-benzoyl-rel-(3β,4α)-di-(*E*)-(2-phenyl)ethenylcyclobutane, respectively. These four chiral compounds were synthesized and identified for the first time in this work.

A theoretical calculation was done in order to see the most stable isomer of compound **5**. The total geometric optimization of the dimers (**5**, **5a**–**j**, Scheme 2) was made with molecular mechanical MM2 method [23], and their strain energies were calculated. Moreover, the total geometric optimization of the dimers was also made with AM1 [24] and PM3 [25] semi-empirical methods and the heats of formation and other properties of the molecules were calculated. All the calculations were performed with HYPERCHEM 7.5 program on an IBM PC Pentium IV Computer, and the results are given in Tables 3 and 4. According to the results obtained with molecular mechanical and semi-empirical methods, the most stable of the dimers possible to form, having the lowest strain energy and heat of formation, is head-to-head isomer [16] (Scheme 2 and Fig. 1) that has R_1 and R_2 groups in cyclobutane ring at *trans–trans–trans–trans* configuration. The contribution of van der Walls and angle bonding energies to the strain energy of the main isomeric product of the dimerization reaction is highest (Table 3).



Scheme 2.

Eleven different isomers are possible to obtain in the dimerization reaction of compound **1** according to kinetic

Table 3
Calculated strain energies (kcal/mol) for isomers of **5** (MM2)

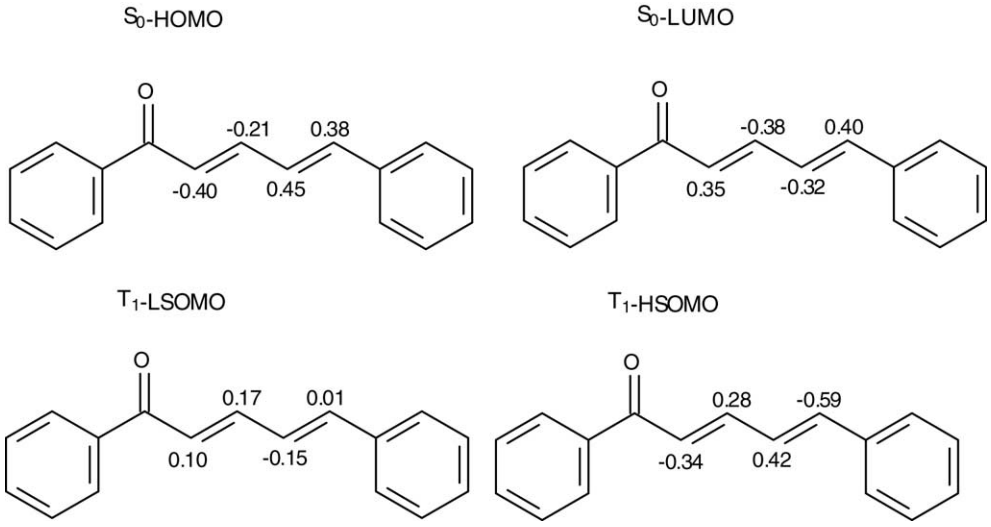
Isomers	Total	Bond	Angle	Torsional	Van Der Walls	Stretch bend	Electrostatic
5	46.71	3.34	34.80	−29.35	38.36	−0.43	0.00
5a	51.76	2.95	33.60	−22.29	38.04	−0.40	−0.15
5b	51.01	3.03	33.85	−21.66	36.35	−0.41	−0.16
5c	50.62	3.02	34.23	−21.87	36.09	−0.42	−0.44
5d	51.97	3.04	33.90	−21.81	38.22	−0.29	0.03
5e	53.05	3.08	35.10	−21.69	37.12	−0.41	−0.14
5f	52.08	2.95	34.73	−22.26	36.28	−0.41	0.78
5g	54.41	3.06	35.85	−21.78	38.03	−0.37	−0.38
5h	55.46	3.15	36.80	−22.91	39.14	−0.36	−0.35
5i	56.40	3.31	37.90	−23.00	38.93	−0.36	−0.39
5j	64.89	3.44	42.55	−17.91	36.89	−0.19	0.11

Table 4
Heat of formation ΔH_f° (in kcal/mol), frontier MO energies, ε_{HOMO}, ε_{LUMO} (in eV), and dipole moment μ_D (in Debye) for isomers of **5**

Isomers	AM1					PM3			
	Point groups	ΔH	ε_{HOMO}	ε_{LUMO}	μ_D	ΔH	ε_{HOMO}	ε_{LUMO}	μ_D
5	C_2	76.23	−8.89	−0.34	1.62	68.10	−9.06	−0.42	1.22
5a	C_2	77.41	−9.05	−0.30	3.75	69.47	−9.21	−0.46	4.15
5b	C_1	79.16	−8.91	−0.32	0.0	71.42	−9.11	−0.36	0.0
5c	C_2	79.19	−8.82	−0.31	0.99	71.52	−9.05	−0.40	1.30
5d	C_1	79.20	−8.84	−0.49	2.39	71.93	−8.99	−0.43	1.22
5e	C_1	80.21	−8.88	−0.33	0.89	73.76	−9.06	−0.35	0.77
5f	C_1	81.17	−8.90	−2.27	4.52	72.87	−9.08	−0.38	4.47
5g	C_1	83.09	−8.94	−0.34	4.69	75.19	−9.06	−0.41	4.58
5h	C_1	84.81	−8.68	−0.37	4.98	77.62	−8.92	−0.46	4.83
5i	C_1	88.61	−8.70	−2.29	4.84	80.55	−8.95	−0.20	4.51
5j	C_1	91.32	−8.86	−0.32	4.16	81.41	−9.03	−0.29	3.67

Table 5
HOMO and LUMO for compound **1**

Electronic state	HOMO (eV)	LUMO (eV)	LSOMO (eV)	HSMO (eV)
S_0	−8.845	−0.916		
T_1			−7.980	−0.392



Scheme 3.

theory [26]. Although the ring closure is a kinetic process, it is not dependent on the thermodynamic stability of the products [26]. However, our major product (**5**), resulting from head-to-head addition, was found to be thermodynamically more stable compared to the others. In order to explain the formation of dimers, we examined the possibility of frontier orbital control in the stereochemical behaviour of compound **1**. We have estimated the HOMO and LUMO energies for this compound by using AM1-UHF semi-empirical method and the results are listed in Table 5.

Total superposition occurs between both LSOMO/HOMO and HSOMO/LUMO of the reagents. Dimerization occurs at unsaturated α–β bond but not at unsaturated γ–δ bond. In excited triplet state, electron density of LSOMO ($q_i = 2c_i^2$) of unsaturated γ–δ bond is too low to have any dimerization reaction occur. So, the regioselective dimerization reaction of **1** forms unsaturated α–β bond. In our reaction, the dimer occurs as a result of head-to-head dimerization reaction but not head-to-tail. The data in Scheme 3 can explain the formation of only head-to-head dimers, because in case of head-to-tail dimers, the same superposition is not allowed due to the frontier orbital control.

In conclusion, the theoretical calculations, similar to the experimental results, showed that the major product of the dimerization reaction is head-to-head isomer (**5**) having δ-truxinic-type *trans-trans-trans-trans* configuration (Schemes 1–3).

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References

[1] G.M. Keseru, M. Nogradi, Stud. Nat. Prod. Chem. 17 (1994) 509–521.
[2] T. Suga, N. Iwata, Y. Asakawa, Bull. Chem. Soc. Jpn. 45 (1972) 2058–2060.
[3] S. Göksu, H. Çelik, H. Seçen, Turk. J. Chem. 27 (2003) 31–34.
[4] P. Claeson, U. Pongprayoon, T. Sematong, P. Tuchinda, V. Reutrakul, P. Soontornsaratune, W.C. Taylor, Planta Med. 62 (1996) 236–240.
[5] Y. Yang, K. Kinoshita, K. Koyama, K. Takahashi, S. Kondo, K. Watanabe, Phytomedicine 9 (2002) 146–152.
[6] D.C.G.A. Pinto, A.M.S. Silva, A. Levai, J.A.S. Cavaleiro, T. Patonay, J. Elguero, Eur. J. Org. Chem. 14 (2000) 2593–2599.
[7] M. D'Auria, L. Emanuele, G. Mauriello, R. Racioppi, J. Photochem. Photobiol. A: Chem. 134 (2000) 147–154.
[8] M. D'Auria, Heterocycles 54 (2001) 475–496.
[9] D. Cesarin-Sobrinho, J. Netto-Ferreira, C. Quim. Nova 1 (2002) 62–68.
[10] F. Toda, K. Tanaka, M. Kato, J. Chem. Soc., Perkin Trans. 1 (1998) 1315–1318.
[11] T. Ishikawa, N. Koseki, T. Furukawa, E. Sakurada, C. Koseki, Y. Saito, K. Ogata, T. Harayama, H. Ishii, Tetrahedron 50 (31) (1994) 9287–9302.
[12] D.M.S. Atkinson, J.M. Almond, P. Hollins, S. Jenkins, Spectrochim. Acta, Part A 59 (2003) 629–635.
[13] I. Turowska-Tryk, K. Grzesniak, E. Trzop, T. Zych, J. Solid State Chem. 174 (2003) 459–465.

[14] B. Montaudo, S. Caccamese, J. Org. Chem. 38 (1973) 710–716.
[15] S.Ö. Sivrikaya, Synthesis of chalconoid-like compounds and 4π photocyclization reactions, Ph.D. Thesis, Karadeniz Technical University, 2004.
[16] R.B. Woodward, R. Hoffmann, The Conservation of Orbital Symmetry, Verlag Chemie Academic Press, 1970.
[17] N. Yaylı, O. Üçüncü, E. Aydın, Y. Gök, A. Yaşar, C. Baltacı, N. Yıldırım, M. Küçük, J. Photochem. Photobiol. A: Chem. 169 (2004) 228–233.
[18] N. Yaylı, O. Üçüncü, A. Yaşar, Y. Gök, M. Küçük, S. Kolaylı, Turk. J. Chem. 28 (2004) 515–521.
[19] V. Seidel, F. Bailleul, G.P. Waterman, Phytochemistry 55 (2000) 439–446.
[20] R.D. Katerere, I.A. Gray, R.A. Kennedy, J.R. Nash, D.R. Waigh, Phytochemistry 65 (2004) 433–438.
[21] M. D'Auria, R. Racioppi, J. Photochem. Photobiol. A: Chem. 112 (1998) 145–148.
[22] V.S. Parmar, S.C. Jain, K.S. Bisht, R. Jajni, P. Yaneja, A. Jha, O.D. Tyagi, A.K. Prasad, J. Wengel, C.R. Olsen, P.M. Boll, Phytochemistry 46 (1997) 597–673.
[23] N.L. Allinger, J. Am. Chem. Soc. 99 (1977) 8127–8134.
[24] M.J.S. Dewar, E.G. Zoebisch, E.F. Healy, J.P.S. Stewart, J. Am. Chem. Soc. 105 (1985) 3902–3909.
[25] J.J.P. Stewart, J. Comput. Chem. 101 (1989) 209–220.
[26] M. D'Auria, L. Emanuele, V. Esposito, R. Racioppi, Arkivoc XI (2002) 65–78.