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ORIGINAL PAPER

(*E*)-2-Benzylidenebenzocyclanones: part XIII—(*E*)/(*Z*)-Isomerization of some cyclic chalcone analogues. Effect of ring size on lipophilicity of geometric isomers

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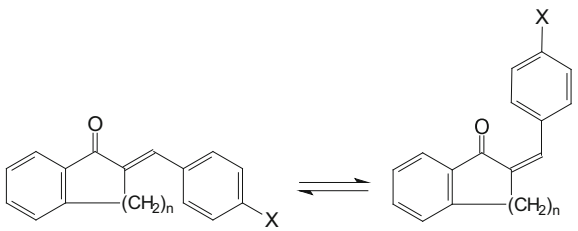
Abstract Optimized isocratic reverse phase high-performance liquid chromatography (RP-HPLC) method was developed for separation of the respective (*E*) and (*Z*) isomers of the cyclic chalcone analogues (*E*)-2-(4′-X-benzylidene)-1-indanones, -tetralones, and -benzosuberones. The method has been applied to monitor progress of the light-induced (*E*)/(*Z*) isomerization process in the three series. Data indicate formation of equilibrium mixtures of the respective geometric isomers. Comparison of the HPLC retention factors of the respective geometric isomers showed the (*Z*) isomers less lipophilic in the benzosuberone and the tetralone but more lipophilic in the indanone series. Data provide experimental evidence of opposite effect of ring size and geometric isomerism on lipophilicity of conformationally restricted (cyclic) analogues of chalcone, an open chain pharmacophore.

Graphical abstract



Keywords Cyclic chalcone analogues · Photochemistry · (*E*)/(*Z*) Isomerization · Equilibrium isomeric mixtures · Lipophilicity

Introduction

Recently, we have reported [2–6] on synthesis and antitumor (cytotoxic) activity of a series of (*E*)-2-(X-benzylidene)-1-indanones **1**, -tetralones **2**, and -benzosuberones **3** (Fig. 1). Structurally, these compounds can be regarded as cyclic analogues of chalcones, a class of flavonoids with a broad range of biological effects [7–9]. Our previous studies have revealed that (*E*)-2-(X-benzylidene)-1-benzosuberones (**3**) are a group of useful cytotoxic agents, and some derivatives can serve as prototypic molecules for subsequent structural modifications [3]. Results of in vitro cell culture studies suggested that noncovalent interaction of the compounds with cellular macromolecules can be the most important contribution to their biologic effects [5, 6]. UV–Vis and fluorescence spectroscopic investigations of such interactions demonstrated how the actual molecular environment affects the spectroscopic characteristics of the compounds [10, 11].

Theoretically, (*E*) and (*Z*) isomers of the investigated 2-(X-benzylidene)-1-benzocycloalkanones can be formed in the reactions used for synthesis of the compounds. The (*Z*) configuration, however, is unfavorable because of a strong steric interaction between the aryl and the carbonyl groups [12]. In practice, synthesis of the compounds yielded the energetically more favored (*E*) isomers in pure form [2–4]. On the other hand, photoisomerization and photodimerization of alkenes and α,β-unsaturated ketones, including chalcones, are well-known phenomena in the literature [13]. UV light-induced (*E*)/(*Z*) isomerization of

For part XII of this series, see Ref. [1].

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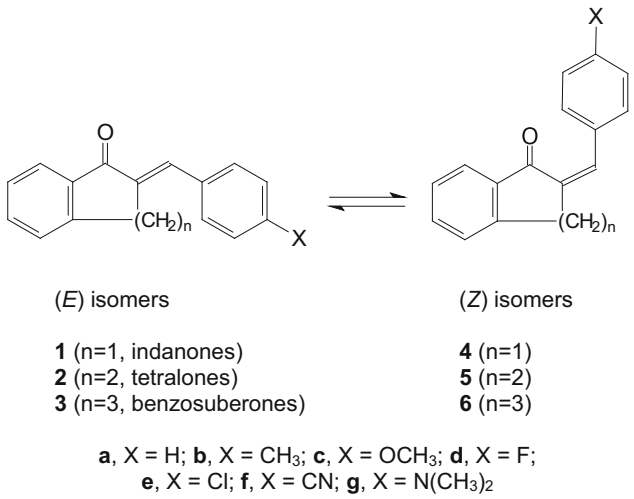

Fig. 1 Structure of the (*E*) (**1–3**) and the (*Z*) (**4–6**) isomers of the investigated 2-(4′-X-benzylidene)-1-benzocycloalkanones

some chalcones [14–16], (*E*)-2-arylidene-1-indanones [17–19], and -tetralones [18, 19] has been published and the respective (*Z*) isomers were structurally characterized.

Previously, on-plate and in solution light-catalyzed (*E*)/(*Z*) isomerization of some of the title compounds **1–3** has been studied by gas chromatographic (GC) and reverse-phase thin-layer chromatographic (RP-TLC) methods. It was demonstrated that the log*P* values—one of the physico-chemical characteristics affecting the biological effects [20]—of the respective (*E*)- and (*Z*)-2-(X-benzylidene)-1-benzosuberones **3** are different; the (*Z*) isomers are less lipophilic [21].

The main goal of the present work was to develop an easy-to-perform reverse-phase high-performance liquid chromatographic (RP-HPLC) method that can be used to test isomeric purity of the title compounds. Since the 4′-methoxy (**1c–3c**) and the 4′-dimethylamino (**1g–3g**)—previously not investigated—derivatives displayed the most promising in vitro antitumor activities [3, 4], these compounds have also been involved in the present investigation. Because both reactivity [12] and biological activity [15] of the respective (*E*) and (*Z*) isomers are expected to be different, such a chromatographic method is a valuable tool to test isomeric purity of the compounds. The developed RP-HPLC method was used to follow the time-course of the light-catalyzed (*E*)/(*Z*) isomerization of compounds **1–3** and characterize composition of the isomeric mixtures as a function of the ring size and the electronic characteristics of the aromatic substituents. Based on comparison of the isocratic RP-HPLC retention factors (*k*) conclusions could be drawn concerning relative lipophilicity of the respective (*E*) and (*Z*) isomers in all the three series [22].

Results and discussion

Syntheses of the 2-(4′-X-benzylidene)-1-benzocycloalkanones **1a–3g** resulted in isolation of stereohomogeneous (*E*) isomers. Isomeric purity of the compounds was checked by GC and ^{1}H NMR methods [2–4]. Earlier we reported that some (*E*)-(4′-X-benzylidene)-1-benzocycloalkanones **1–3** have been found to undergo light-catalyzed on-plate and in-solution (*E*)/(*Z*) isomerization [21]. As a continuation of these experiments, isomeric composition of dichloromethane and methanol solutions of compounds **1a–3g** exposed to scattered laboratory light was investigated by the previously used GC-FID method [21]. It was found that each benzylidene derivative except the 4′-dimethylamino-substituted **1g–3g** underwent (*E*)/(Z) isomerization on standing on the shelve already for 1 day. This latter observation can be explained by the strong electron-donor capacity of the dimethylamino substituent, which increases the double bound character (i.e., the energy needed for isomerization) of the compounds [23]. Similar result was obtained with 4-hydroxychalcone; the methanol solution of the compound resisted daylight-induced (*E*)/(*Z*) isomerization [15].

According to our earlier observations [21], GC retention time of each of the formed (*Z*)-2-(4′-X-benzylidene)-1-benzocycloalkanones **4a–6f** was found to be shorter than that of the respective (*E*) isomer. This GC characteristic (shorter retention times for the less planar (*Z*) isomers) is in accordance with the results of similar investigations of the related (*E*)- and (*Z*)-dypnones [24]. GC–MS analysis of the (*E*)/(*Z*) mixtures showed the two isomeric compounds to give identical molecular ion peak and fragmentation [21]. Similar results were obtained for the previously non-investigated **1c–3c/4c–6c** isomeric pairs. As an example, GC–MS chromatograms of (*E*) and (*Z*) isomers of the five-membered 2-(4′-methoxybenzylidene)-1-indanone (**1c** and **4c**) (retention times 21.19 min and 20.19 min, respectively) are shown in Fig. 2.

In order to obtain samples with higher fraction of the newly formed (*Z*) isomers, 3.5 mM benzene solution of the pure (*E*) isomers of **1a–3g** were illuminated with 3 × 125 W high-pressure mercury lamps for 4 h as described before [21]. The illuminated solutions were evaporated by nitrogen gas and the solid residues were analyzed by GC and HPLC. Separation of the (*E*) and the (*Z*) isomers could be accomplished by isocratic RP-HPLC method using 330 nm UV detection. The selected wavelength is around the absorption maxima of the pure (*E*) isomers [10] around which the forming (*Z*) isomers are also expected to show (a lower intensity) absorption [21, 25]. HPLC analysis of the illuminated solutions of **1a–3f** showed appearance of a new peak in each chromatogram.

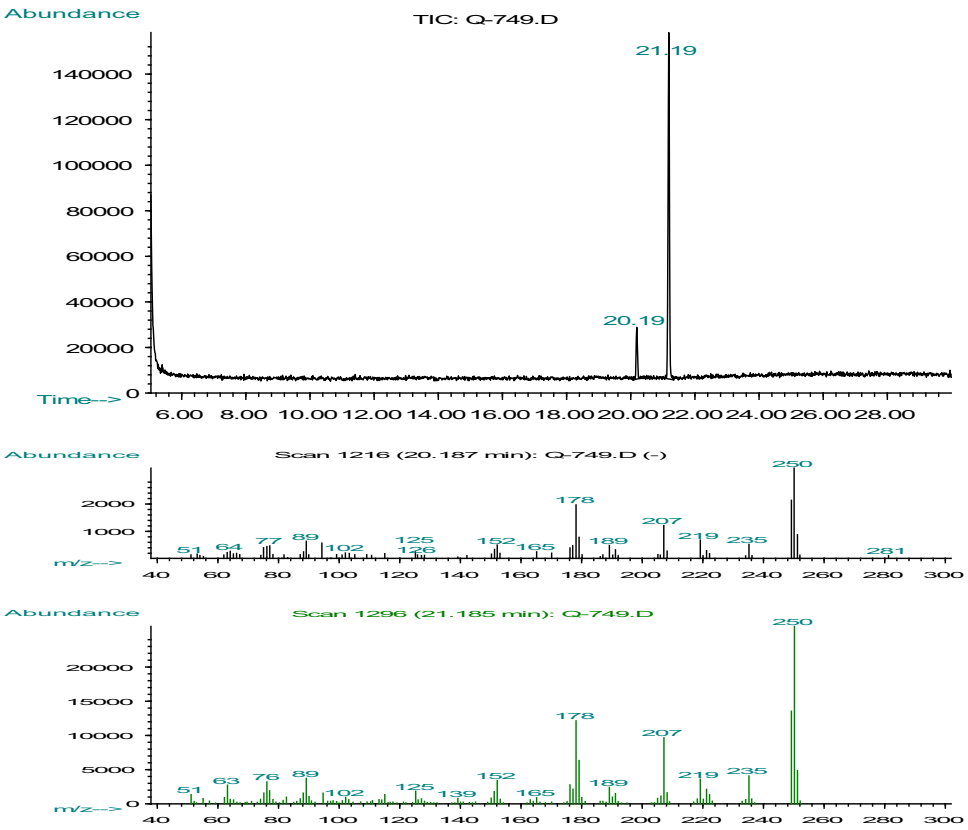

Fig. 2 GC-MS spectrum of (*E*) (**1c**, $t_R = 21.19$ min) and (*Z*) (**4c**, $t_R = 20.19$ min) isomers of 2-(4′-methoxybenzylidene)-1-indanone

These observations are in accordance with the results of the GC investigations of the samples. According to the results of earlier GC–MS investigations, the formed compounds are the respective (*Z*) isomers. As an example, HPLC chromatograms of (*E*) and (*Z*) isomers of the 4′-methoxy-substituted indanone (**1c**, **4c**), tetralone (**2c**, **5c**), and benzosuberone (**3c**, **6c**) derivatives are shown in Fig. 3. Formation of dimers under our experimental conditions could not be observed.

On the contrary, HPLC analysis of illuminated solutions of the 4′-dimethylamino derivatives **1g–3g** indicated appearance of several peaks corresponding to more polar substances than the parent compounds. Similar observation could be made by GC-FID analysis of the samples as well. These results suggest decomposition of the parent compounds. Light-induced isomerization and decomposition of the dimethylamino derivatives **1g–3g** have also been presumed while investigating fluorescence properties of the compounds [26]. The strong electron-donating capacity of the 4′-dimethylamino substituent results in increased electron density of the enone moiety [2]. The intense fluorescence and the pronounced positive solvatochromism (significant charge transfer (CT) character of the transitions) indicate expressed dipolar character of the excited state of the compounds [10, 11, 26]. Furthermore, the open chain analogue 4-dimethylamino-2′-hydroxychalcone has been reported to be highly versatile photoinitiator even under soft irradiation conditions (upon exposure to UV and/or visible light) [27]. Most of the photosensitizers suffer degradation by light [28]. Based on such observations, decomposition of the dimethylamino derivatives can be considered as a result of photosensitized autoxidation (photobleaching).

Retention times (t_R) and retention factors (k) of the respective (*E*) and (*Z*) isomers of the investigated cyclic chalcone analogues (**1a–3g** and **4a–6f**, respectively) are shown in Table 1.

Earlier lipophilicity of the respective (*E*)/(*Z*) isomeric pairs of 2-(X-benzylidene)-1-benzosuberones (**3/6a**, **b**, **d**, **e**, **f**) was characterized by their log*P* determined by RP-TLC. It was found that the least planar (*Z*) isomers were less lipophilic [21]. According to these earlier results, the RP-HPLC retention times of the newly formed (*Z*) isomers were found to be shorter than those of the corresponding (*E*) ones in the benzosuberone (**3/6**) series (Table 1). Similar observation was made in the case of the respective isomeric pairs of the tetralone series (**2/5**). In these cases, however, the two peaks appear closer than those of the corresponding benzosuberone (**3/6**) pairs. Isocratic RP-HPLC studies of the respective open chain (*E*)-s-*cis* and (*Z*)-s-*cis* chalcones also showed the (*Z*) isomers to have shorter retention times (lower retention factors) [29]. On

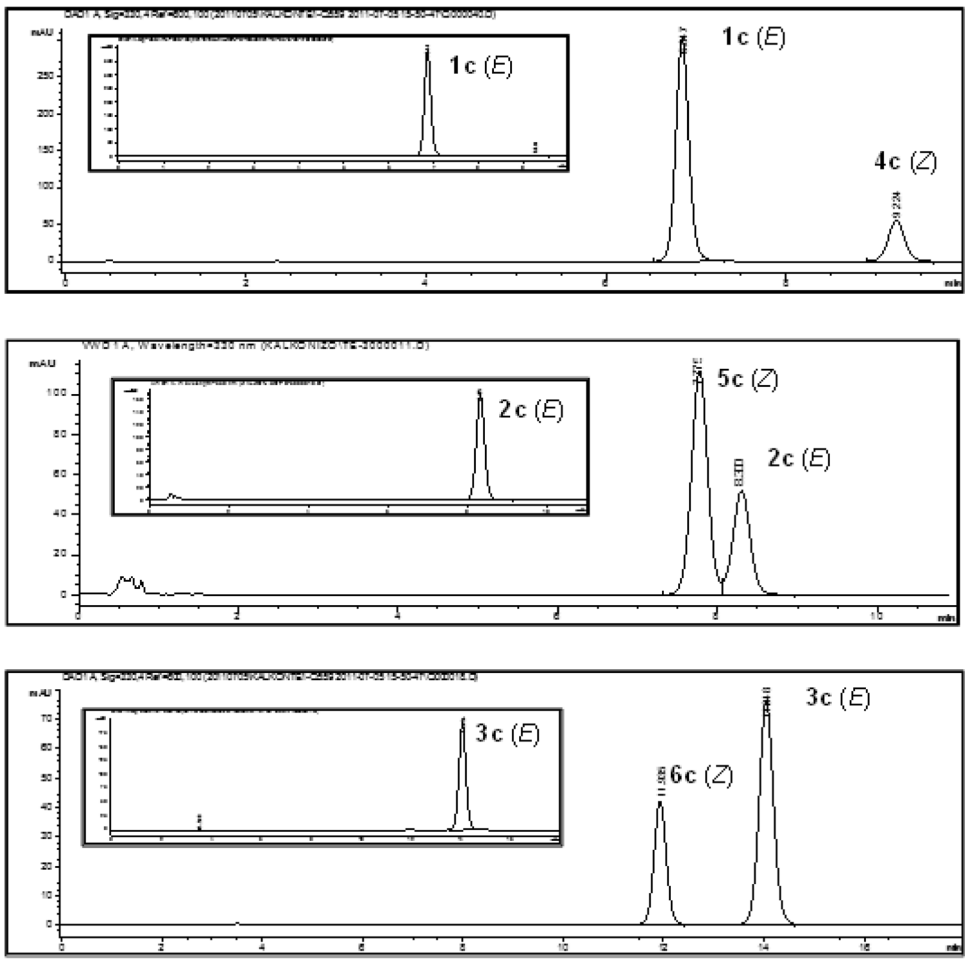

Fig. 3 HPLC chromatograms of the (*E*) (**1c–3c**) and the (*Z*) isomers (**4c–6c**) of the investigated 2-(4′-methoxybenzylidene)-1-benzocycloalkanones

Table 1 RP-HPLC retention times (t_R/min) and retention factors (k) of the (*E*)- and (*Z*)-2-(4′-X-benzylidene)-1-indanones **1**,**3**, -tetralones **2**,**5**, and -benzosuberones **3**,**6**

	1		**4**		**2**		**5**		**3**		**6**	
	t_R	k	t_R	k	t_R	k	t_R	k	t_R	k	t_R	k
a	6.25	8.83	7.43	10.70	10.08	14.45	8.73	12.39	12.95	18.68	9.95	14.12
b	9.69	14.41	11.82	17.80	15.80	23.19	13.80	20.14	20.31	30.16	15.22	22.34
c	6.85	9.72	9.22	13.44	8.30	11.67	7.78	10.87	14.05	20.41	11.94	17.19
d	6.32	8.94	8.29	12.03	10.25	14.75	9.81	14.06	13.32	19.21	10.94	15.60
e	10.75	16.03	13.56	20.49	17.32	25.48	15.53	22.74	22.61	33.68	17.07	25.19
f	4.24	5.62	5.19	7.09	6.40	8.87	6.06	8.33	8.15	11.52	6.94	9.66
g	8.92	8.83	–	–	14.62	–	–	–	20.61	18.68	–	–

Data represent average of three parallel experiments

the contrary, the order of the two isomeric peaks of the five-membered indanones (**1/4**) is opposite (Table 1). Since isocratic RP-HPLC retention factors (k) represent a relative scale of lipophilicity [21], this observation indicates the formed (*Z*) isomers in the indanone series (**4**) to be more lipophilic than the corresponding (*E*) ones (Table 1).

The effect of geometric isomerism on lipophilicity is a relatively unexplored field of medicinal chemistry [30]. Changing configuration of the chalcone core induces changes in molecular volume, surface area, polarizability, and dipole moments of the respective isomers. Investigation of effectiveness of transmission of substituent effects of the respective (*E*) and (*Z*) isomers of the compounds by ^{1}H and ^{13}C NMR methods showed the enone moiety to be the most planar in the indanone series (**1** and **4**). Deviation from the planar structure is more pronounced in the six-

membered (**2** and **5**) and seven-membered (**3** and **6**) cyclic chalcone analogues [21, 31, 32]. Cumulative effect of difference in geometry (and conjugation) on the above mentioned molecular characteristics is likely to be responsible for the observed effect of ring size on lipophilicity of the (*E*) and (*Z*) isomers (**1–3/4–6**). To the best of our knowledge, this is the first example of opposite effect of ring size and geometric isomerism on lipophilicity of conformationally restricted (cyclic) analogues of an open-chain pharmacophore.

By means of the optimized HPLC method time-course of isomerization of selected compounds of the three series (**1a–3d**) was followed. Isomeric composition of the solutions illuminated by mercury lamps was analyzed at the 0-, 30-, 60-, 90-, 120-, 180-, and 240-min timepoints over the 4-h illumination period of solutions of the pure (*E*) isomers. Composition of the samples was characterized by (a) the ratio of the integrated peak areas (*A*) of the starting (*E*) isomers at $t = t$ (A_t) and $t = 0$ (A_o) times; and (b) by the ratio of those of the formed (*Z*) isomers at $t = t$ (A_t) and $t = 240$ min (A_{240}) timepoints. The numerical values of the respective ratios are summarized in Tables 2 and 3. Graphical representation of the data obtained for compounds **3c** and **6c** is shown on Fig. 4. The two asymptotic graphs indicate formation of equilibrium mixtures of the corresponding (*E*) and (*Z*) isomers.

According to the obtained data, formation of the (*Z*) isomers was found to be the most pronounced over the first 30-min period in each case. At the 60-min timepoints compositions of the photostationary mixtures are very close to those measured at the endpoint (240 min) of the experiments. Although only qualitative analysis, the ring size seems to affect composition of the equilibrium mixtures: contribution of the (*Z*) isomers is lower in case of the indanones **1** than in the respective mixtures of the tetralones **2** and the benzosuberones **3**. This observation can be explained by proximity of the carbonyl and the benzylidene moieties in the (*Z*) isomers, which is more dominant in the most planar indanones **4** than in the series of **5** and **6**, where the enone moiety is deviated from planarity [21]. Pronounced substituent effect—lowering the fraction of the (*Z*) isomer in the photostationary mixtures—could only be observed in the case of **1c** (Table 2). This observation can be rationalized by the electron-donor capacity of the 4′-methoxy substituent (**c**), which is the most effective in the most planar (most strongly conjugated) indanone (**1/4**) series [31, 32].

Experimental

Synthesis of (*E*)-2-(4′-X-benzylidene)-1-benzocycloalkanones **1a–3g** was performed by base-catalyzed Claisen-Schmidt condensation as published before [2–4]. Each sample was purified by column chromatography over silica gel (0.2–0.5 mm; Reanal, Hungary) using toluene or toluene-methanol (99:1, v/v) as mobile phases. The compounds had melting points in accord with their literature values [3]. Structure of the investigated samples was verified by IR (Nicolet Impact 400 FT IR spectrometer) [2], ^{1}H NMR [2, 31, 32], and ^{13}C NMR spectroscopy [31, 32] (Varian Unity Inova, 400 MHz spectrometer). IR spectra were recorded in KBr pellets. ^{1}H and ^{13}C NMR spectra were run in $CDCl_3$ solutions using TMS as internal standard. Structure of compounds **3b**, **3c**, and **3g** was also verified by X-ray crystallography [3].

(*E*)-2-(4′-X-Benzylidene)-1-benzocycloalkanones **1a–3g** were subjected to light-induced isomerization either in 2 mg/cm^3 methanol or dichloromethane solution allowing the solutions to be exposed by scattered laboratory light for 1 week, or in 1 mg/cm^3 benzene solutions illuminating them with 3 × 125 W high-pressure mercury lamps

Table 2 Ratios of integrated peak areas (A_t/A_0) of (*E*)-2-(4′-X-benzylidene)-1-benzocyloalkanones **1–3** in the UV-light illuminated solution of (*E*)-2-(4′-X-benzylidene)-1-benzocyloalkanones **1–3** as a function of time of illumination

	A_t/A_0^a											
	1 ($n = 5$)				**2** ($n = 6$)				**3** ($n = 7$)			
	30′	60′	120′	240′	30′	60′	120′	240′	30′	60′	120′	240′
a	0.362	0.287	0.278	0.278	0.195	0.153	0.153	0.178	0.208	0.172	0.173	0.156
b	0.550	0.482	0.422	0.366	0.279	0.233	0.200	0.215	0.287	0.192	0.192	0.180
c	0.842	0.783	0.748	0.621	0.297	0.220	0.169	0.162	0.391	0.265	0.233	0.209
d	0.456	0.444	0.428	0.377	0.226	0.211	0.219	0.204	0.206	0.193	0.193	0.198
e	0.527	0.444	0.409	0.374	0.221	0.175	0.172	0.175	0.232	0.189	0.184	0.163

A_t integrated peak area at $t = t$min, A_0 integrated peak area at $t = 0$

[a] Average of three parallel experiments

Table 3 Ratios of integrated peak areas (A_t/A_{240}) of (*Z*)-2-(4′-X-benzylidene)-1-benzocyloalkanones **4–6** in the UV-light illuminated solution of (*E*)-2-(4′-X-benzylidene)-1-benzocyloalkanones **1–3** as a function of time of illumination

	A_t/A^a_{240}											
	4 ($n = 5$)				**5** ($n = 6$)				**6** ($n = 7$)			
	30′	60′	120′	240′	30′	60′	120′	240′	30′	60′	120′	240′
a	0.913	0.971	1.011	1.000	1.031	1.122	1.125	1.000	0.965	1.057	1.054	1.000
b	0.872	1.076	1.095	1.000	0.970	1.070	1.057	1.000	0.989	1.093	1.098	1.000
c	0.651	0.964	0.931	1.000	0.907	0.970	1.023	1.000	0.844	1.003	1.058	1.000
d	1.013	1.033	1.097	1.000	0.957	1.020	1.085	1.000	0.987	1.051	1.041	1.000
e	0.879	1.0073	1.001	1.000	0.960	1.0457	1.048	1.000	1.011	1.055	1.081	1.000

A_t integrated peak area at $t = t$min, A_{240} integrated peak area at $t = 240$ min

[a] Average of three parallel experiments

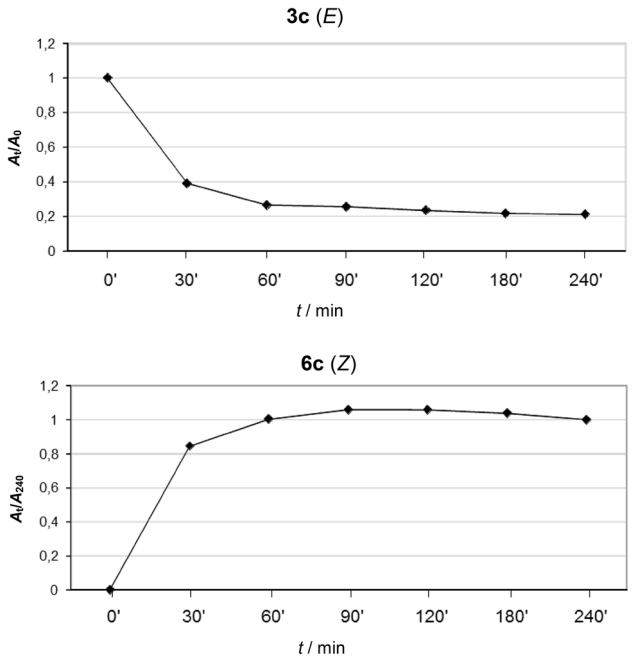

Fig. 4 Ratios of integrated peak areas of (*E*)-2-(4′-methoxybenzylidene)-1-benzosuberone (**3c**) (*upper panel*) and (*Z*)-2-(4′-methoxybenzylidene)-1-benzosuberone (**6c**) (*lower panel*) in UV-light illuminated solution of (*E*)-2-(4′-methoxybenzylidene)-1-benzosuberone (**3c**) as a function of time of illumination (data points represent average of three parallel experiments. A_t integrated peak area at $t = t$min; A_0 integrated peak area at $t = 0$; A_{240} integrated peak area at $t = 240$ min

(Tungsram, Hungary) for 4 h. The solutions were analyzed by GC and HPLC as described below. Evaporation of the solutions illuminated by the mercury lamps resulted in yellowish solids, which were analyzed by GC and HPLC. Three parallel experiments were performed in each case. In case of the previously non-investigated **1c–3c/4c–6c** (*E*)/(*Z*) pairs the solids were also analyzed by GC–MS.

GC and GC–MS methods for investigation of (*E*)/(*Z*) isomerization

GC investigations of the pure (*E*) isomers **1a–3g** and the (*E*)/(*Z*) mixtures of **1a–3g/4a–6g** were performed on HP 5890 Series II gas chromatograph equipped with flame ionization detector (FID) as described before [21]. Briefly, the conditions were as follows: column: 25 m × 0.32 mm × 0.17 μm HP-5 capillary column; inj. temp.: 280 °C; det. temp.: 280 °C; oven temp. progr.: 100 °C (1 min) to 200 °C at 5 °C/min (0.5 min) to 250 °C at 15 °C/min (1 min). Carrier: helium, 1.8 cm^3/min, constant flow. Injection: 1 mm^3, split 40 cm^3/min. Retention data of the previously non-investigated **1c/4c**, **2c/5c**, and **3c/6c** isomeric pairs were 13.15/12.30, 13.58/12.62, and 13.74/12.55 min, respectively. Retention times of compounds **1g**, **2g**, and **3g** were 16.99, 17.10, and 17.28 min, respectively.

GC–MS investigations of the previously non-investigated pure (*E*) isomers **1c–3c** and the (*E*)/(*Z*) mixtures of **1c–3c/4c–6c** were performed on HP 5890 Series II gas chromatograph coupled with a HP-5971A mass selective detector as described before [21]. Briefly, the conditions were as follows: column: 30 m × 0.32 mm × 1.00 μm RTX-5 capillary column; inj. temp.: 280 °C; det. temp.: 280 °C; oven temp. progr.: 50 °C (1 min) to 300 °C at 20 °C/min (16.5 min). Carrier: helium, 1.0 cm^3/min, constant flow. Injection: 1 mm^3, split 30 cm^3/min. The mass selective detector was operated in scan mode (50–650 *m*/*z*). Retention times and the main fragment peaks of compounds **1c–3c/4c–6c** were as follows. **1c/3c**: 21.19/20.19 min; $m/z = 250, 249, 235, 219, 207,189, 178, 152, 125, 102, 89, 76$. **2c/4c**: 21.64/20.58 min; $m/z = 264, 263, 249, 233, 221, 203, 178, 121, 103, 90, 77$. **3c/6c**: 21.91/20.52 min; $m/z = 278, 277, 263, 250, 247, 235, 219, 207, 131, 121, 103, 91, 77$.

HPLC method for investigation of (*E*)/(*Z*) isomerization

HPLC investigations of the pure (*E*) isomers **1a–3g** and the (*E*)/(*Z*) mixtures of **1a–3g/4a–6g** were performed on an Agilent 1100 integrated high-performance liquid chromatography system equipped with a quaternary pump, a degasser, an autosampler, an injector with a 100-mm^3 sample loop, a column oven, and an ultraviolet–visible (UV–Vis) detector. Data were recorded and evaluated using Agilent ChemStation (Rev.B.03.02-SR2) software. Separation of the isomers was performed on a 4.6 × 150 mm, 5 μm particle size Waters Spherisorb ODS-2 (Method A) or on a 3.0 × 125 mm, 5 mm particle size Macharey-Nagel CC 125/3 LiChrospher 100 RP 18 column (Method B) using isocratic mobile phase consisting of acetonitrile (WWR HiPerSolv Chromanorm) and water (Merck Lichrosolv) (1:1, v/v). Chromatography was performed at room temperature. Flow rate: 2.0 cm^3/min. Detection wavelength: $\lambda = 330$ nm. Injected volume: 20 mm^3.

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References

1. Veliká B, Tomecková V, Fodor K, Kron I, Perjési P (2015) Spectr Anal Rev 3:1
2. Perjési P, Nusser T, Tarczay Gy, Sohár P (1999) J Mol Struct 479:13
3. Dimmock JR, Kandepu NM, Nazarali AJ, Kowalchuk TP, Motaganahalli N, Quail JW, Mykytiuk PA, Audette GF, Prasad L, Perjési P, Allen TM, Santos CL, Szydlowski J, De Clercq E, Balzarini J (1999) J Med Chem 42:1358
4. Dimmock JR, Zello GA, Oloo EO, Quail JW, Kraatz H-B, Perjési P, Aradi F, Takács-Novák K, Allen TM, Santos CL, Balzarini J, De Clerq E, Stables JP (2002) J Med Chem 45:3103
5. Rozmer Zs, Berki T, Perjési P (2006) Toxicol In Vitro 20:1354
6. Rozmer Zs, Berki T, Maász G, Perjési P (2014) Toxicol In Vitro 28:1359
7. Dimmock JR, Elias DW, Beazely MA, Kandepu NM (1999) Curr Med Chem 6:1125
8. Ni L, Meng CQ, Sikorski JA (2004) Expert Opin Ther Pat 14:1669
9. Go ML, Wu X, Liu XL (2005) Curr Med Chem 12:483
10. Fodor K, Tomeckova V, Kőszegi T, Kron I, Perjési P (2011) Monatsh Chem 142:463
11. Tomeckova V, Stefanisinova VM, Velika B, Fodor K, Perjési P, Stupak M, Guzy J, Tóth S Jr, Pekarova T (2013) Spectr Anal Rev 1:1
12. Dhar DN (1981) The chemistry of chalcones and related compounds. John Wiley and Sons, New York, p 168
13. Schuster DI (1989) The photochemistry of enones. In: Patai S, Rappoport Z (eds) The chemistry of enones. John Wiley and Sons, Chichester, p 623
14. Miquel JF (1961) Bull Soc Chim Fr 1369
15. Iwata S, Nishino T, Inoue H, Nagata N, Satomi Y, Nishino H, Shibata S (1977) Biol Pharm Bull 20:1266
16. Schleuder M, Am Ali F, Otto HH (2003) Pharmazie 58:308
17. Imbach JL, Pohland AE, Weiler ED, Cromwell NH (1967) Tetrahedron 23:3931
18. Kevill DN, Weiler ED, Cromwell NH (1964) J Org Chem 29:1276
19. Azzolina O, Desimoni G, Di Toro V, Gishlandi V, Tacconi G (1975) Gazz Chim Ital 105:971
20. Pliska V (1996) The role of lipophilicity in biological response to drugs and endogenous ligands. In: Pliska V, Testa B, van de Waterbeemd H (eds) Lipophilicity in drug action and toxicology. VCH Publishers, Weinheim, p 263
21. Perjési P, Takács M, Ősz E, Pintér Z, Vámos J, Takács-Novák K (2005) J Chromatogr Sci 43:289
22. Giaginis C, Tsantili-Kakoulidou JA (2008) Liq Chrom Rel Technol 31:79
23. Dugave C, Demange L (2003) Chem Rev 103:2475
24. Gelsomini N, Mazza LJ, Guarna A (1974) J Chromatogr 101:182
25. Shin DM, Song DM, Jung KH, Moon JH (2001) J Photosci 8:9
26. Tomeckova V, Poskrobova M, Stefanisinova M, Perjési P (2009) Spectrochim Acta Part A Mol Biomol Spectr 74:1242
27. Tehfe MA, Dumur F, Xiao P, Delgove M, Graff B, Fouassier J-P, Gigmes D, Lalevée J (2014) Polym Chem 5:382
28. Stratonnikov AA, Meerovich GA, Loschenov VB (2000) Proc SPIE 3909:81
29. Walczak B, Lafosse M, Chrétien JR, Dreux M, Morin-Allory L (1986) J Chrom 369:27
30. Testa B, Carrupt PA, Gaillard P, Tsaiin R-S (1996) Intramolecular interactions encoded in lipophilicity: Their nature and significance. In: Pliska V, Testa B, van de Waterbeemd H (eds) Lipophilicity in drug action and toxicology. VCH Publishers, Weinheim, p 49
31. Perjési P, Perjessy A, Kolehmainen E, Ősz E, Samalikova M, Virtanen E (2004) J Mol Struct 697:41
32. Perjési P, Linnanto J, Kolehmainen E, Ősz E, Virtanen E (2005) J Mol Struct 740:81