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Photochromism of Dihydroindolizines. Part III [1]. Synthesis and Photochromic Behavior of Novel Photochromic Dihydroindolizines Incorporating a Cholesteryl Moiety

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Summary. Ten novel photochromic dihydroindolizines (*DHI*s) based on 1,5-electrocyclization and bearing a cholesteryl moiety at 7′-position of the *DHI* skeleton were synthesized. 1D, 2D, N*O*ESY ^{1}H NMR spectra, mass spectrometry, and elemental analysis were used for their characterization. Irradiation of the *DHI*s in CH_2Cl_2 solution with polychromatic light leads to the formation of red to red-violet colored betaines. Most colored betaine forms are notable in CH_2Cl_2 solution at room temperature because of their slow 1,5-electrocyclization except in one case, where the colored betaine could be observed only after cooling with liquid nitrogen due to the fast electrocyclization back reaction. The kinetics of the reverse 1,5-electrocyclization of the colored betaines into the corresponding *DHI*s were detected using both UV/VIS and flash photolysis measurements.

The presence of three isosbestic points in the fading spectrum of the betaines proved that the thermal back reaction to the *DHI*s follows a first order mechanism. Tuning of the photophysical properties of *DHI*s and their colored betaines was achieved by change of substituents in the ester and fluorene regions. A notable increase of the t_{30}-value of some betaines by a factor ranging between 1.01 and 1.57 compared with the betaine form of dicyanopridazine *DHI* standard ($t_{30} = 243$ min) was observed. The high photo-fatigue resistance of these betaines will help to find their applications.

Keywords. Photochromism; Dihydroindolizines; 1,5-Electrocylization; Half-lives; Photo-fatigue.

Introduction

Photochromism, as a branch of photochemistry, is currently attracting a great deal of interest. Its reversibility is the inherent characteristic of this phenomenon, which

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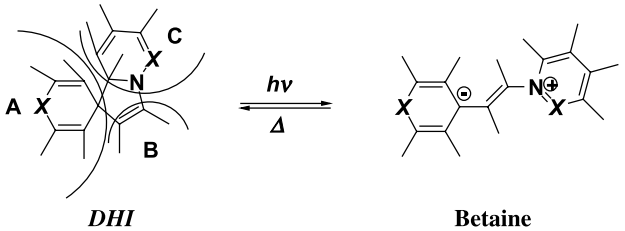
distinguishes it from other photoinduced reactions [2–4]. The applications configure the fascinating ability of modulating given physical properties through an external stimulation, namely, upon light irradiation. Variable transmission materials, optical switches and memories [5–10], and biological sensors are among the most interesting. In the field of these variable-transmission optical materials, the main characteristics strived for, are i) the ability to be activated by sunlight (heliochromism) and bleached through a thermal process, ii) extended absorption in the visible region to provide a neutral color upon irradiation, iii) a suitable fading rate (is related to the stability of the colored state), iv) high efficiency of coloration upon irradiation (colorability), and v) a high resistance to photodegradation (fatigue resistance) [11–13].

Since the discovery of the photochromic dihydroindolizines (*DHI*s) and tetrahydroindolizines (*THI*s) by *Dürr* in 1979 [14, 15], they became a very interesting class of photochromic molecules and have been extensively studied and received particular attention owing to their remarkable photofatigue-resistance and wide broad photochromic properties [16–31]. Due to these important and interesting properties, they have already found their applications in optical technology [32], ophthalmic lenses [33], data storage [34], photoswitches [1, 16, 35, 36], dental filling materials [21, 26, 37], IR-sensitive photoswitchable materials [1, 16, 21], and *DNA* markers [38].

These interesting molecules undergo a photo-induced change of color in solutions and in polymer matrices when exposed to UV radiation or direct sunlight. They return to the initial state when the illumination ceases, normally *via* a thermal pathway. The photochromic behavior of *DHI*s is based on a reversible pyrroline ring opening, induced by light, that converts a colorless form (usually named the 'closed form') to the colored form (betaine form). The thermal back reaction – the 1,5-electrocyclization – from the ring-open betaine to *DHI* shows rates extending from milliseconds to several weeks [19, 21, 31, 39–42] depending on the substituents and structure of the involved molecule. This interesting wide range in the lifetime of the colored form leads these molecules to find many applications [19, 21, 32–38].

In continuation of our pervious work dealing with the synthesis and photochromic properties of dihydroindolizines (*DHI*s) [1, 16–21, 34, 39] we wish to report the synthesis, and photochromism of novel photochromic dihydroindolizines bearing a cholesterol moiety in the region B (Scheme 1) as the first entry to supramolecular photoresponsive self-assembling organogelators based on the photochromic *DHI* skeleton.



DHI **Betaine**

Scheme 1

Results and Discussion

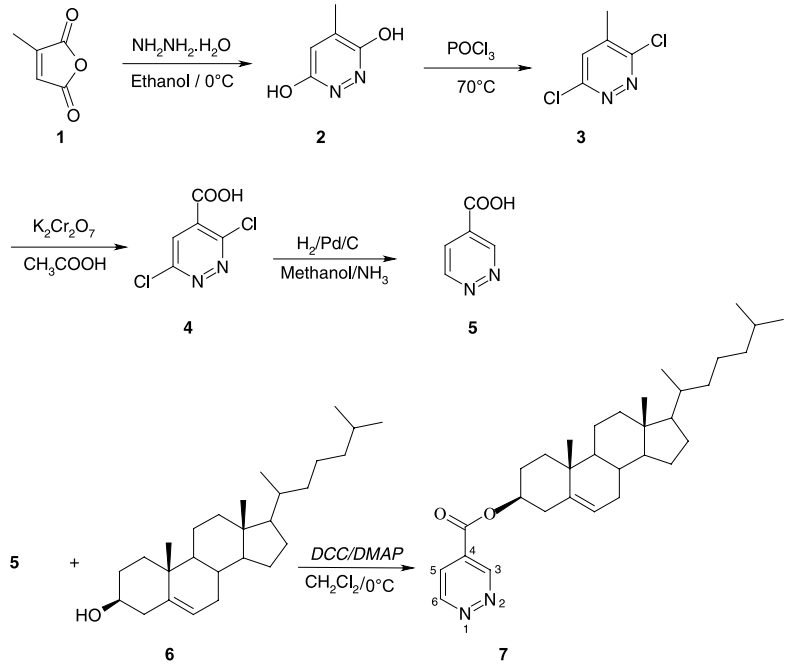
Preparation of Cholesterol Pyridazine Precursor 7

Cholesterol pyridazine precursor **7** was prepared by five steps as shown in Scheme 2. Treatment of citraconic anhydride (**1**) with hydrazine hydrate in refluxing ethanol led to ring expansion and 3,6-dihydroxy-4-methylpyridazine (**2**) was formed in 93% yield [44–46]. Chlorination of diol **2** with phosphoryl chloride afforded 3,6-dichloro-4-methyl-pyridazine (**3**) in good yield (73%). Oxidation of the methyl group in **3** by $KMnO_4/H_2SO_4$ led to the formation of 3,6-dihydroxypyridazine-4-carboxylic acid (**4**) in moderate yield (44%). Dechlorination of **4** with hydrogen and 10% Pd/C in an ammonia/methanol mixture gave the corresponding pyridazine-4-carboxylic acid **5** in low yield (10%) [47–49].

Esterification of **5** with cholesterol (**6**) in the presence of *DMAP* and *DCC* at low temperature under anhydrous conditions gave the corresponding pyridazine-4-carboxylic acid cholesteryl ester **7** in 18% yield. The constitutions of **1**–**5** as well as the cholesterol pyridazine precursor **7** were established by elemental analysis and spectral data.

*Preparation of Dialkyl 7′-Chloresterylcarbonyl-1′H-spiro[substituted fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylates, DHIs (**11a–11j**)*

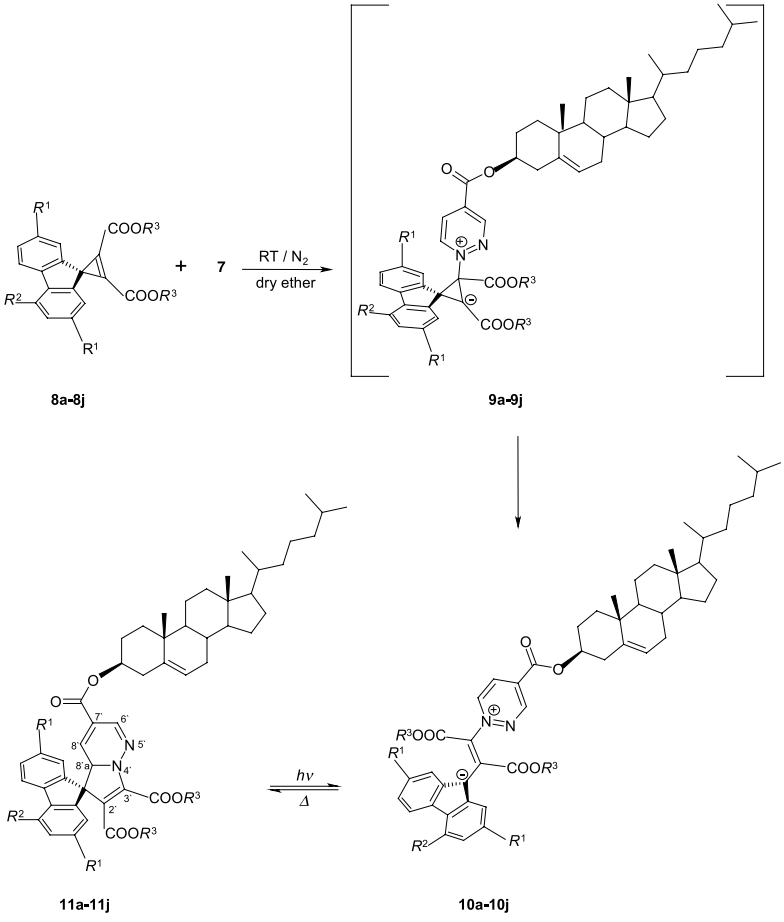
Electrophilic addition of spirocyclopropenes **8a**–**8j** to cholesteric pyridazine precursor **7** using the cyclopropene route (Scheme 2) in dry ethereal solution at room



Scheme 2

temperature under dry nitrogen in the absence of light for 24–40 h (TLC-controlled using CH_2Cl_2 as eluent) led to the formation of the photochromic dialkyl 7′-chloresterylcarbonyl-1′H-spiro[substituted fluorene-9,1′-pyrrolo[1,2-**b**]pyridazine]-2′,3′-dicarboxylates **11a**–**11j** (Scheme 3).

The formation of *DHI*s **11a**–**11j** proceeded by a cyclopropyl-allylanion rearrangement [16, 49] of **9a**–**9j**. The dark colored betaines **10a**–**10j** underwent



10/11	R^1	R^2	R^3	10/11	R^1	R^2	R^3
a	H	H	CH_3	f	H	H	
b	H	H	CH_2CH_3	g	Cl	H	CH_3
c	H	H	$CH(CH_3)_2$	h	Br	H	CH_3
d	H	H	$C(CH_3)_3$	i	NO_2	H	CH_3
e	H	H		j	H	$COOCH_3$	CH_3

Scheme 3

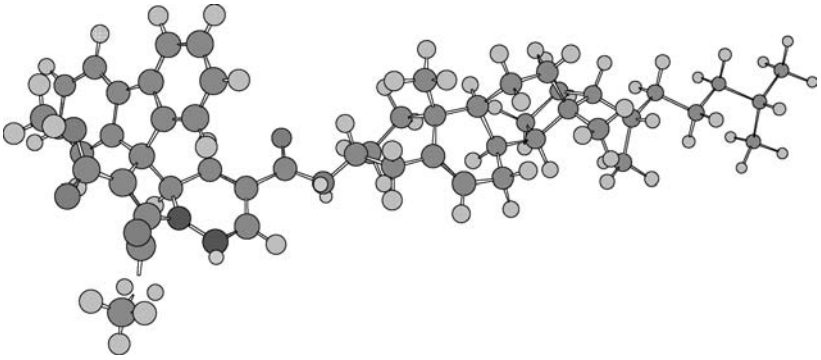


Fig. 1. Representation of the optimized (MM2) structure of *DHI* **11a**

1,5-electrocyclization to give the corresponding *DHI*s **11a**–**11j**. Irradiation of *DHI*s **11a**–**11j** with UV-light gave the dark colored betaine forms **10a**–**10j** with high reaction quantum yield ($\phi \cong 0.4$) [21, 51]. The high colorability as well as high photostability of betaines **10a**–**10j** renders wide applications to this class of photochromic compounds.

Characterizations of the new photochromic *DHI*s **11a**–**11j** were done using spectral as well as analytical tools. In addition, the chemical structure of **11h** was assigned by 2D-NMR spectroscopy. The ^{1}H-^{1}H-correlation of **11h** was used to assign the protons of the pyridazine ring (region C) and in the ^{1}H,^{1}H-COSY spectrum both 2′- and 3′- methyl ester groups showed no coupling with other protons and appeared as two singlets at $\delta = 3.39$ and 4.02 ppm. The 8′-CH signal was shifted to high field and appeared as a doublet of triplets at $\delta = 5.00$ ppm showing two coupling systems. The first is due to ^3J-coupling with the 8′a-CH, which appears as doublet at $\delta = 5.70$ ppm, the second is due to ^4J-coupling with the 6′-CH, which appears as a double doublet at $\delta = 6.92$ ppm. Further assignments of 6′-CH, 8′-CH, and 8′a-CH were done by the aid of N*O*ESY spectrum of **11h**. Here we observed that 8′a-CH at $\delta = 5.27$ ppm is close in space to both 8′-CH at $\delta = 5.04$ ppm and 1-CH of the fluorene moiety at $\delta = 7.67$ ppm. This system proves that 8′a-CH is in 8′a-position and not at 6′-position. Additionally, the connectivity between 8′-CH and 8-CH of the fluorene part at $\delta = 7.55$ ppm was observed. This vicinity of 8′-CH with 8-CH proved that the pyridazine moiety is perpendicular to the fluorene skeleton as proved by a molecular modeling calculation [1, 19–21] of **11h**. It showed that the distance between both 8′a-CH, 8′-CH and 1-CH, 8-CH of the fluorene moiety is <3 Å. Probably 6′-CH and 3′-CH_3 of the ester group at $\delta = 4.01$ ppm are also near to each other (Fig. 1).

*Photophysical Properties of New Photochromic DHIs **11a–11j** and their Corresponding Betaines **10a–10j** in Solution*

The UV-Vis spectra of **11a**–**11j** and their corresponding betaines **10a**–**10j** were measured in dichloromethane. All *DHI*s showed a yellow color in solution as well as in the solid state. The intensities (log ε) of these bands were found to be between

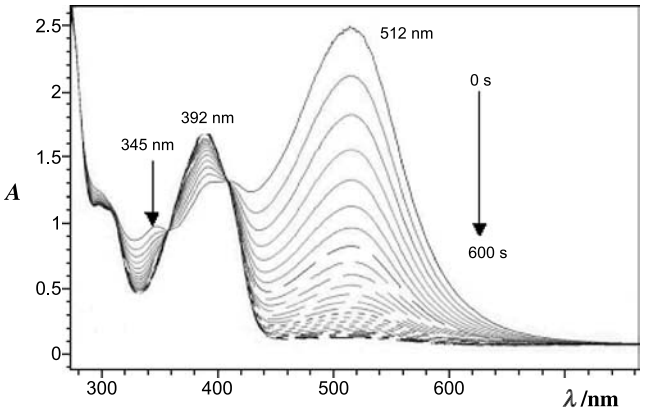


Fig. 2. Kinetic UV-Vis spectrum of the thermal fading of betaine **10a** to *DHI* **11a** (cycle time = 20 s, run time = 600 s) in CH_2Cl_2 ($c = 2 \times 10^{-5}$ mol dm^{-3}) at 296 K

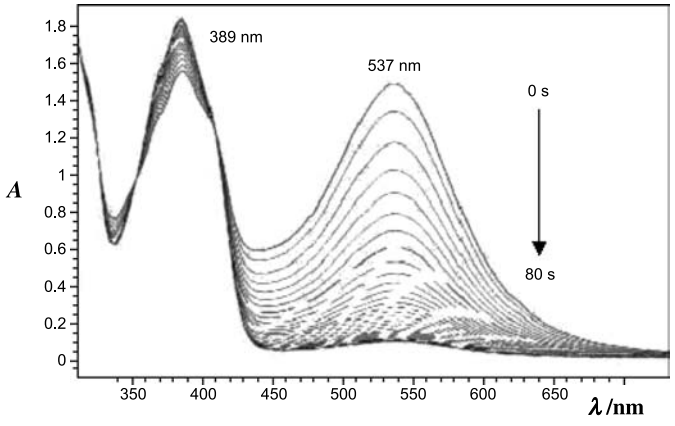


Fig. 3. Kinetic UV-Vis spectrum of the thermal fading of betaine **10h** to *DHI* **11h** (cycle time = 1.5 s, run time = 80 s) in CH_2Cl_2 ($c = 2 \times 10^{-5}$ mol dm^{-3}) at 296 K

3.90 and 4.22. The absorption maxima of *DHI*s **11a–11j** lie between 379–391 nm (Figs. 2, 3). As established previously, these absorption bands can be assigned to the locally excited π–π^*-transition located in the butadienyl-vinyl-amine chromophore [1–3] of the *DHI*s system.

Irradiation of *DHI*s **11a–11j** in CH_2Cl_2 solution with polychromatic light led to the formation of red to red-violet colored betaines **10a–10j**. The colored betaine forms **10a–h** and **10j** (Figs. 2, 3) are obvious in CH_2Cl_2 solution at room temperature because of their slower 1,5-electrocyclization. Only for betaine **10i** the color is observed after cooling with liquid nitrogen due to the fast electrocyclic back reaction. The betaines **10a–10j** revealed absorption spectra in the visible region between 507–537 nm (Table 1). Millisecond flash photolysis (Fig. 4) was used to determine in addition to the λ_{max} (525 ± 12 nm) of betaine **10i**, the kinetics of the thermal back reaction (**10i** → **11i**).

Table 1. UV-Vis absorption data of *DHI*s **11a–11j** and their corresponding betaines **10a–10j** in CH_2Cl_2 solution (23°C, $c = 2 \times 10^{-4}$ mol dm^{-3})

10/11	λ_{max} *DHI*/nm	log ε *DHI*	λ_{max} betaine/nm	color of betaine
a	392	4.00	345, 512	red
b	389	3.98	346, 511	red
c	388	3.97	346, 509	red
d	386	3.94	348, 509	red
e	389	3.92	346, 507	red
f	388	3.90	344, 512	red
g	385	3.90	531	red-violet
h	389	3.93	537	red-violet
i	379	4.22	525 ± 12	red
j	388	3.94	344, 510	red

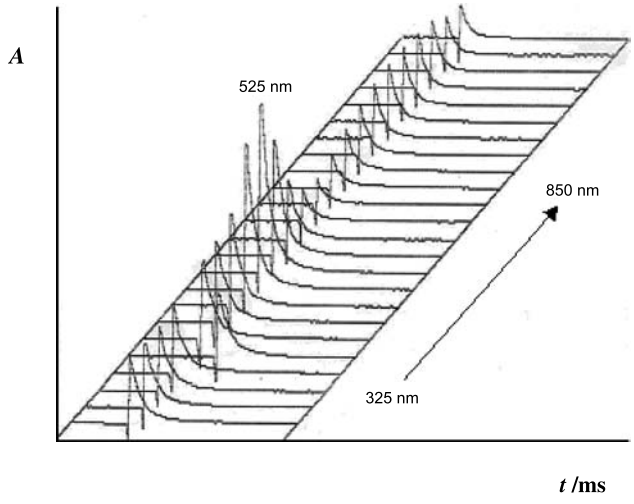


Fig. 4. Millisecond flash photolysis spectrum of **10i** for determination of the absorption maxium of the betaine form at different wavelengths (325–850 nm every 25 nm) in CH_2Cl_2 at 296 K

*Effect of Substituents on the λ_{max} of Photochromic DHIs **11a–11j***

Effect of Substituents in the Fluorene Part (Region A)

A hypsochromic shift in the absorption maxima from 3 to 7 nm was observed in 2,7-disubstituted fluorene *DHI*s **11h** and **11g** compared with the unsubstituted *DHI* **11a**. A more significant hypsochromic shift by 11 nm in 2,7-dinitrofluorene *DHI* **11i** compared with the unsubstituted *DHI* **11a** was recorded (Table 1). These results were in good agreement with former studies on pyridazine *DHI*s [18, 21, 42].

Effect of Substituents in the Double Bond Part (Region B)

Generally, changing the alkyl ester group has resulted in very small influence or no effect on the λ_{max} of *DHI*s [3, 19]. A small hypsochromic shift of 6 nm was observed by changing the alkyl ester from a methyl to a *tert*-butyl group.

*Effect of Substituents on λ_{max} and Colors of Betaine **10a–10j***

Substitution in the Fluorene Part (Region A)

Interestingly, the absorption maxima of 2,7-dichloro- and 2,7-dibromosubstituted fluorene betaines **10g** and **10h** were shifted bathochromically by 19–25 nm compared with betaine **10a**, so that the color changes from red to red-violet. In addition, a pronounced bathochromic shift was observed in the absorption maxima of the betaine form of 2,7-dinitrosubstituted fluorene *DHI* **10i** by 13 nm compared with betaine **10a**. This large shift due to the delocalization of betaine charges (CT) was affected by the electron attracting nitro group [1, 3, 14, 15, 19, 39]. A notable bathochromic shift by 6 nm from 2,7-dichlorosubstituted betaine **10g** to 2,7-dibromosubstituted betaine **10h** was also recorded.

Substitution in the Double Bond Part (Region B)

The change of the alkyl ester group in a fixed betaine system generally has no pronounced influence on the λ_{max} of the betaine form as well as on the color [1, 3, 19, 21]. In betaines **10a–10f**, a small bathochromic shift was observed upon changing the alkyl ester group from methyl to cyclohexyl by 5 nm while the norbornyl betaine **10f** showed no absorption change compared with betaine **10a**.

*Kinetics of the 1,5-Electrocyclization of Betaines **10a–10j** to DHIs **11a–11j***

Irradiation of *DHI*s **11a–11h** and **11j** with long-wavelength UV or visible light ($\lambda_{max} = 400$–450 nm) at room temperature afforded the colored betaines **10a–10h** and **10i**. The kinetics of the reverse 1,5-electrocyclization of the colored betaines **10a–10j** into the corresponding *DHI*s **11a–11j** were detected using both UV-Vis (in the case of **10a–10h** and **10j**) and flash photolysis measurements (in the case **10i**). The presence of three isosbestic points in the fading spectrum of betaines **10** (*e.g.* Fig. 2) proved that the thermal back reaction to *DHI*s **11** follows a first order

Table 2. Kinetic data of the thermal 1,5-electrocyclization of betaines **10a–10j** to their corresponding *DHI*s **11a–11j** in CH_2Cl_2 solution (23°C, $c = 2 \times 10^{-4}$ mol dm^{-3})

10/**11**	k (1/s) $\times 10^{-3}$	$t_{1/2}$/s
a	9.9	70
b	13.3	52
c	16.9	41
d	21.7	32
e	11.0	63
f	12.8	54
g	49.5	14
h	99.0	7
i	3872	0.179
j	10.0	68

mechanism [1, 3, 4, 21]. The decrease in absorption of the colored betaine with time was measured at six different wavelengths at the same time. The cyclization rate constant (k) and the half-lives ($t_{1/2}$) are listed in Table 2.

*Effect of Substituents on the Half-lives of the Colored Betaines **10a–10j***

Effect of Substitution in the Fluorene Region (Region A)

It should be noted that substitution in the fluorene part leads to a decrease in the half-lives of the corresponding betaines by a factor of 106 [1, 21]. To obtain a stable betaine, the negative charge on C-1′-atom should be delocalized by mesomerism [3]. In our case (Table 2) the half-life of the 2,7-disubstituted fluorene betaines **10g–10i** showed a decrease in the half-lives by a factor of 5–10 in the case of 2,7-dihalosubstituted fluorene **10g** and **10h** and by a factor of 391 in case of the dinitrosubstituted fluorene **10i** [27, 28] compared with the unsubstituted betaine **10a**. This is mainly attributed to the highly electron attracting nitro groups. The 2,7-dichlorosubstituted betaine **10g** showed a higher $t_{1/2}$ than 2,7-dibromofluorene betaine **10h** by a factor of 2 while betaine **10g** showed a higher half-life than the dinitrosubstituted fluorene **10i** by a factor of 78. These interesting results reflect well the tuning of the photophysical properties by changing the substitutions in the *DHI* system, which may lead to tunable systems for applications.

Effect of Substitution in the Double Bond Part (Region B)

Changing of the alkyl group of the ester from methyl to ethyl and isopropyl or *tert*-butyl leads to a decrease in the half-life time by a factor of 0.7–2.2. This may be due to the strong electron donation of the *tert*-butyl group compared with the methyl group. The norbornyl ester betaine **10f** showed a smaller $t_{1/2}$ by a factor of 1.3 than the betaine **10a**, in which the bulky norbornyl groups might attribute with an electron donating effect.

*Photo-Fatigue Resistance of Photochromic DHIs **11a–11h** and **11j** and their Corresponding Betaines **10a–10h** and **10j***

In studying the quality of a photochromic system or in other terms, the thermal full reversibility of a specific photochromic molecule, the problem of carrying out a large number of colorization–decolorization cycles arises frequently. The gradual loss of the ability to change color by exposure to visible or ultraviolet light in this context has been termed fatigue [2]. *Gautron* [52] has advanced a quantitative approach to measure the fatigue in photochromic systems.

Irradiation of spirodihydroindolizines **11a–11h** and **11j** with polychromatic light ($\lambda = 200$–400 nm) produced the colored betaines **10a–10h** and **10j**. Upon continued irradiation they decomposed after some time. Betaine **10i** was not measured under these conditions due to its fast thermal bleaching to *DHI* **11i**. However, if oxygen is excluded, these systems are notably more stable. It is possible that in the presence of oxygen, the betaines **10a–10h** and **10j** act as sensitizers towards singlet oxygen [3].

From the photodegradation data represented in Table 3 and Fig. 5, it is clear that the betaine form of the dimethyl ester pyridazine *DHI* **11a** ($t_{30} = 276$ min) is more

Table 3. Photodegradation of betaines **10a**–**10h** and **10j** in dichloromethane ($c = 2 \times 10^4$ mol dm^{-3}) at 23°C

	$t_{1/2}$/s	t_{30}-betaine-*DHI*/min	*F*
a	70	276	1.14
b	52	264	1.09
c	41	259	1.07
d	32	246	1.01
e	63	213	0.87
f	54	195	0.80
g	14	462	1.93
h	7	381	1.57
j	68	278	1.14
Standard	56.2	243	1.0

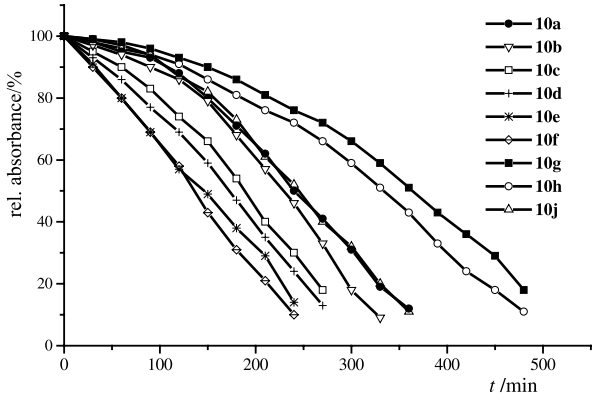


Fig. 5. Time-relative absorbance relationship for the photodegradation experiment for determination of the t_{30}-value of betaines **10a**–**10h** and **10j**

stable than the standard dicyanopyridazine *DHI* (($t_{30} = 243$ min) by a factor of 1.14. This is due to the high electron attraction of cyano groups in the reference compound. The betaine forms with *tert*-butyl, cyclohexyl, and norbornyl ester groups **10d**–**10f** showed a lower stability than dimethyl substituted betaine **10a** probably due to the steric hindrance of the bulky ester groups [28]. Interestingly, the 2,7-dichloro betaine **10g** showed a highly pronounced increase in photostability ($t_{30} = 462$ min) by a factor of 1.7 compared with unsubstituted betaine **10a** and by a factor of 1.9 compared with the standard betaine. On the other hand, the 2,7-dibromo betaine **10h** showed a lower t_{30}-value ($t_{30} = 381$ min) (Fig. 5) than the 2,7-dichloro betaine **10g**, which may be due to the larger size of the bromine atom. Betaine **10j** showed no photostability difference from the unsubstituted betaine **10a**.

In conclusion, the main motivation behind this work was to synthesize, develop, and tune the photophysical properties of novel photochromic *DHI*s based on 1,5-electrocylization bearing a cholesteryl moiety at the 7′-position of the *DHI* skeleton. The red to red-violet colored betaines produced by UV irradiation

returned back through 1,5-electrocyclization to the corresponding *DHI*s **11a–11j** with different rate constants depending on the subsituents in both the fluorene and ester regions. Substituent effects on the absorption maxima of *DHI*s **11** and betaines **10** as well as on the half-lives of betaines **10** were investigated. Tuning of the photophysical properties of *DHI*s **11a–11j** and their colored betaines **10a–10j** by change of substituents in the ester and fluorene regions was clearly achieved. A notable increase of the t_{30}-values of betaines **10a–10h** and **10j** by a factor ranging between 1.01 and 1.57 compared with the betaine form of dicyanopridazine *DHI* used in former studies as standard ($t_{30} = 243$ min) was observed. The high photo-fatigue resistance of these betaines will help to find applications. This study can be considered as the key step for the preparation of a photoresponsive self-assembling network based on the *DHI* skeleton, which will be discussed in details in the forthcoming paper.

Experimental

All reactions were carried out under N_2 with the use of standard *Schlenk* techniques, but no special precautions were taken to exclude O_2 during work up. Solvents were pre-dried and distilled from appropriate drying agents and stored over molecular sieve (5 Å) in brown bottles under a N_2 atmosphere. All chemicals were obtained from commercial sources, unless otherwise stated, and used as received. Spirocyclopropene derivatives **8a–8i** were obtained *via* photolysis of the corresponding pyrazoles prepared according to reported procedures [13, 14]. Photolysis was carried out in the photochemical reactor of *Schenck* [54] made from Pyrex ($\lambda > 290$ nm). The source of irradiation was a high-pressure mercury lamp Philips HPK 125 W. Solutions to be photolyzed were flushed with dry N_2 for 30 min before switching on the UV lamp.

The progress of the reaction and the purity of the products isolated were monitored using TLC. Separation and purification of all synthesized photochromic materials were carried out using column chromatography (1 m × 2 cm) on silica gel and CH_2Cl_2 as eluent. Melting points were measured on a Gallenkamp or a Büchi (Smp-20) melting point apparatus. ^{1}H NMR spectra were measured in $CDCl_3$ with a JOEL EX270 400 MHz FT-NMR spectrometer, with chemical shift (δ) relative to *TMS* in ppm. IR spectra were measured on a JASCO FT/IR-230 infrared spectrometer FTS 3000. Fast atom bombardment (FAB) mass spectra were recorded with a Finnigan MAT SSQ710 mass spectrometer. UV-spectra were recorded on a FT-UV-Vis HP 6543 computer-spectrometer. Millisecond flash photolysis was carried out with a 12V (50 W) halogen lamp, Photoflash (METZ 32 Z-1). Molecular modeling calculations (MM2) were carried out using version 5 of Hyperchem program.

For photodegradation experiments (photo-fatigue), the initial absorbance of pyridazine *DHI*s **11a–11h** and **11j** was measured using a 3 cm^3 quartz cell in degassed CH_2Cl_2 ($c = 2 \times 10^{-4}$ mol dm^{-3}) solution. Before the beginning of the degradation experiment, the degassed *DHI*s **11a–11h** and **11j** solutions were irradiated for two minutes to achieve equilibrium between *DHI*s and betaines. The extinction was set as 100% at the beginning. The analysis was carried out from absolute destruction time (every 30 min). At the fixed point recommended, the absorbance of the betaine form decreased through irradiation to 30% of the beginning extinction (Fig. 5). This time is called in our work the t_{30}-value and the stability factor (F) can be calculated from the ratio of each t_{30}-value and the t_{30}-value of dicyanopyridazine betaine, which has been used as standard [21, 53].

Pyridazine-4-carboxylic acid cholesteryl ester (**7**, $C_{32}H_{48}N_2O_2$)

To a solution of 0.039 g of **5** (0.32 mmol) and 0.124 g of cholesterol (**6**) (0.32 mmol) in 20 cm^3 of dry CH_2Cl_2 at 5°C under N_2 0.11 g of DCC (0.56 mmol) and 0.03 g of DMAP (0.22 mol) were added. The

reaction mixture was stirred at this temperature and monitored by TLC until completion of the reaction (9 h). The eliminated dicyclohexyl urea was filtered off, the filtrate was evaporated under reduced pressure, and the ester was purified by column chromatography on silica gel and CH_2Cl_2:CH_3OH (9:1) as eluent yielding 28 mg (18%) as white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.86$ (s, 3-CH-pyridazine), 9.47 (d, $J = 8.4$ Hz, 6-CH pyridazine), 8.15 (d, $J = 8.4$ Hz, 5-CH-pyridazine), 5.47 (d, $J = 7.90$ Hz, CH=cholesteryl), 4.56 (m, CH-cholesteryl), 0.68–2.51 (m, 43H, cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3132$ (C–H, pyridazine), 2836–2989 (C–H, cholesteryl), 1727 (4′-C=O), 1608 (C=N), 1532 (C=C), 1262, 1210, 1027, 946, 850, 733 cm^{-1}; MS: $m/z = 493$ [M$^+$].

General Procedure for the Preparation of Dialkyl 7′-Chloresterylcarbonyl-1′H-spiro[substituted fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11a–j**)

A mixture of 1 mmol of spirocyclopropenes **8a–8j** in dry ether (50 cm^3) and 0.387 g of cholesteryl pyridazine **7** (1 mmol) was stirred at room temperature under dry N_2 with exclusion of light for 24–40 h (TLC-controlled). Ether was evaporated under reduced pressure and the pure products were separated by at least twice column chromatography on silica gel using CH_2Cl_2 as eluent. The pure product was recrystallized from a suitable solvent to give white to yellow needles.

Dimethyl 7′-chloresterylcarbonyl-1′H-spiro[fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11a**, $C_{51}H_{62}N_2O_6$)

Yield 68% as white needles; mp 152°C (ether:pentane = 8:2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.73$–7.74 (dd, $J = 7.50$ Hz, CH-arom), 7.53–7.55 (d, $J = 7.50$ Hz, CH-arom), 7.26–7.33 (m, CH-arom), 7.18–7.20 (dd, $J = 7.50$ Hz, CH-arom), 5.80–5.83 (t, $J = 2.2$ Hz, 6′-CH), 5.34–5.36 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.27–5.28 (t, $J = 2.2$ Hz, 8′a-CH), 4.92–4.94 (dt, $J = 2.2$ Hz, 8′-CH), 4.42–4.45 (m, CH-cholesteryl), 4.03 (s, 2′-CH_3), 3.30 (s, 3′-CH_3), 0.68–2.51 (m, CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3032$ (C–H, arom), 2855–2979 (C–H, aliph), 1752 (3′-C=O), 1728 (7′-C=O), 1706 (2′-C=O), 1604 (C=N), 1543 (C=C), 1445, 1322, 1254, 1232, 1123, 1039, 930, 849, 741 cm^{-1}; MS: $m/z = 799$ [M$^+$].

Diethyl 7′-chloresterylcarbonyl-1′H-spiro[fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11b**, $C_{53}H_{66}N_2O_6$)

Yield 55% as white needles; mp 134°C (ether:pentane = 7:3); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.76$–7.79 (dd, $J = 7.50$ Hz, CH-arom), 7.52–7.55 (d, $J = 7.50$ Hz, CH-arom), 7.25–7.34 (m, CH-arom), 7.15–7.19 (dd, $J = 7.50$ Hz, CH-arom) 5.82–5.85 (t, $J = 2.2$ Hz, 6′-CH), 5.37–5.39 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.29–5.31 (t, $J = 2.2$ Hz, 8′a-CH), 4.90–4.94 (dt, $J = 2.2$ Hz, 8′-CH), 4.49–4.53 (m, 2′-CH_2), 4.40–4.43 (m, CH-cholesteryl), 3.70–3.73 (m, 3′-CH_2), 0.66–2.46 (m, 2′,3′CH_3 + CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3059$ (C–H, arom), 2846–2992 (C–H, aliph), 1749 (3′-C=O), 1724 (7′-C=O), 1704 (2′-C=O), 1611 (C=N), 1539 (C=C), 1443, 1321, 1262, 1227, 1127, 1037, 935, 841, 747 cm^{-1}; MS: $m/z = 827$ [M$^+$].

Diisopropyl 7′-chloresterylcarbonyl-1′H-spiro[fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11c**, $C_{55}H_{70}N_2O_6$)

Yield 53% as white needles; mp 127°C (ether:pentane = 6:4); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.70$–7.73 (dd, $J = 7.50$ Hz, CH-arom), 7.55–7.57 (d, $J = 7.50$ Hz, CH-arom), 7.22–7.33 (m, CH-arom), 7.24–7.27 (dd, $J = 7.50$ Hz, CH-arom), 5.80–5.83 (t, $J = 2.2$ Hz, 6′-CH), 5.37–5.39 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.29–5.35 (m, 3′-CH + 8′a-CH), 4.92–4.95 (dt, $J = 2.2$ Hz, 8′-CH), 4.48–4.54 (m, CH-cholesteryl), 4.40–4.43 (m, 2′-CH), 0.52–2.53 (m, 2′,3′$(CH_3)_2$ + CH_2-cholesteryl) ppm; IR

(KBr): $\bar{\nu} = 3057$ (C–H, arom), 2835–2997 (C–H, aliph), 1746 (3′-C=O), 1722 (7′-C=O), 1703 (2′-C=O), 1609 (C=N), 1540 (C=C), 1447, 1320, 1264, 1229, 1125, 1031, 937, 839, 749 cm^{-1}; MS: $m/z = 855$ [M^+].

Di-tert-butyl 7′-chloresterylcarbonyl-1′H-spiro[fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11d**, $C_{57}H_{74}N_2O_6$)

Yield 47% as white needles; mp 107°C (ether:pentane = 5:5); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.78$–7.83 (dd, $J = 7.50$ Hz, CH-arom), 7.52–7.55 (d, $J = 7.50$ Hz, CH-arom), 7.25–7.32 (m, CH-arom), 7.23–7.28 (dd, $J = 7.50$ Hz, CH-arom), 5.82–5.85 (t, $J = 2.2$ Hz, 6′-CH), 5.35–5.37 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.30–5.33 (m, 8′a-CH), 4.94–4.96 (dt, $J = 2.2$ Hz, 8′-CH), 4.50–4.54 (m, CH-cholesteryl), 0.56–2.69 (m, 2′,3′(CH_3)$_3$ + CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3054$ (C–H, arom), 2846–2990 (C–H, aliph), 1748 (3′-C=O), 1721 (7′-C=O), 1707 (2′-C=O), 1612 (C=N), 1547 (C=C), 1442, 1318, 1264, 1227, 1129, 1037, 932, 842, 745 cm^{-1}; MS: $m/z = 883$ [M^+].

Dicyclohexyl 7′-chloresterylcarbonyl-1′H-spiro[fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11e**, $C_{61}H_{78}N_2O_6$)

Yield 49% as white needles; mp 118°C (ether:pentane = 6:4); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.76$–7.80 (dd, $J = 7.50$ Hz, CH-arom), 7.54–7.59 (d, $J = 7.50$ Hz, CH-arom), 7.24–7.36 (m, CH-arom), 7.22–7.29 (dd, $J = 7.50$ Hz, CH-arom) 5.80–5.84 (t, $J = 2.2$ Hz, 6′-CH), 5.34–5.36 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.35–5.39 (m, 8′a-CH), 5.11–5.15 (m, 3′-OCH), 4.92–4.95 (dt, $J = 2.2$ Hz, 8′-CH), 4.49–4.55 (m, CH-cholesteryl), 4.40–5.48 (m, 2′-OCH), 0.58–2.78 (m, 2′,3′-cyclohexyl + CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3052$ (C–H, arom), 2844–2998 (C–H, aliph), 1747 (3′-C=O), 1720 (7′-C=O), 1701 (2′-C=O), 1613 (C=N), 1542 (C=C), 1445, 1315, 1264, 1229, 1128, 1038, 932, 843, 746 cm^{-1}; MS: $m/z = 935$ [M^+].

Di-exo-norbonyl 7′-chloresterylcarbonyl-1′H-spiro[fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11f**, $C_{63}H_{78}N_2O_6$)

Yield 42% as white needles; mp 127°C (ether:pentane = 6:4); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.77$–7.85 (dd, $J = 7.50$ Hz, 2H, CH-arom), 7.57–7.61 (d, $J = 7.50$ Hz, CH-arom), 7.24–7.35 (m, CH-arom), 7.27–7.32 (dd, $J = 7.50$ Hz, CH-arom), 5.81–5.84 (t, $J = 2.2$ Hz, 6′-CH), 5.32–5.36 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.29–5.33 (m, 8′a-CH), 5.00–5.06 (m, 3′-OCH), 4.92–4.95 (dt, $J = 2.2$ Hz, 8′-CH), 4.56–4.59 (m, CH-cholesteryl), 4.34–5.39 (m, 2′-OCH), 0.62–2.72 (m, 2′,3′-exo-norbonyl + CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3050$ (C–H, arom), 2849–2995 (C–H, aliph), 1746 (3′-C=O), 1721 (7′-C=O), 1703 (2′-C=O), 1617 (C=N), 1541 (C=C), 1447, 1312, 1267, 1230, 1129, 1037, 934, 847, 744 cm^{-1}; MS: $m/z = 959$ [M^+].

Dimethyl 7′-chloresterylcarbonyl-1′H-spiro[2,7-dichlorofluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11g**, $C_{51}H_{60}Cl_2N_2O_6$)

Yield 56% as pale yellow needles; mp 189°C (ether:methanol = 9:1); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.64$–7.66 (d, $J = 3.56$ Hz, CH-arom), 7.61–7.63 (d, $J = 4.40$ Hz, CH-arom), 7.54–7.55 (d, $J = 1.76$ Hz, CH-arom), 7.43–7.44 (d, $J = 1.76$, CH-arom), 7.37–7.39 (m, CH-arom), 5.86–5.89 (t, $J = 2.2$ Hz, 6′-CH), 5.35–5.37 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.24–5.26 (t, $J = 2.2$ Hz, 8′a-CH), 4.93–4.95 (dt, $J = 2.2$ Hz, 8′-CH), 4.44–4.48 (m, CH-cholesteryl), 4.09 (s, 2′-CH_3), 3.33 (s, 3′-CH_3), 0.61–2.70 (m, CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3062$ (C–H, arom), 2854–2992 (C–H, aliph), 1745 (3′-C=O), 1720 (7′-C=O), 1708 (2′-C=O), 1614 (C=N), 1540 (C=C), 1448, 1315, 1269, 1230, 1132, 1034, 938, 849, 743 cm^{-1}; MS: $m/z = 868$ [M^+].

Dimethyl 7′-chloresterylcarbonyl-1′H-spiro[2,7-dibromofluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11h**, $C_{51}H_{60}Br_2N_2O_6$)

Yield 51% as yellow needles; mp 176°C (ether:methanol = 8:2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.33$–7.35 (d, $J = 2.2$ Hz, CH-arom), 7.20–7.26 (m, CH-arom), 6.98–6.99 (d, $J = 0.88$ Hz, CH-arom), 5.87–5.89 (t, $J = 2.2$ Hz, 6′-CH), 5.34–5.36 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.26–5.28 (t, $J = 2.2$ Hz, 8′a-CH), 4.94–4.95 (dt, $J = 2.2$ Hz, 8′-CH), 4.42–4.46 (m, CH-cholesteryl), 4.07 (s, 2′-CH_3), 3.31 (s, 3′-CH_3), 0.64–2.74 (m, CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3068$ (C–H, arom), 2850–2998 (C–H, aliph), 1744 (3′-C=O), 1721 (7′-C=O), 1707 (2′-C=O), 1617 (C=N), 1545 (C=C), 1443, 1309, 1272, 1229, 1135, 1031, 937, 852, 747 cm^{-1}; MS: $m/z = 959$ [M^{+2}].

Dimethyl 7′-chloresterylcarbonyl-1′H-spiro[2,7-dinitrofluorene-9,1′-pyrrolo[1,2-b]pyridazine]-2′,3′-dicarboxylate (**11i**, $C_{51}H_{60}N_4O_{10}$)

Yield 42% as yellow needles; mp 199°C (ether:methanol = 5:5); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.54$–8.56 (d, $J = 2.2$ Hz, CH-arom), 8.33–8.38 (m, CH-arom), 8.29–8.30 (d, $J = 2.24$ Hz, CH-arom), 7.91–7.93 (q, $J = 3.96$ Hz, CH-arom), 6.78–6.79 (d, $J = 2.20$ Hz, 6′-CH), 5.59–5.62 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.30–5.32 (t, $J = 2.2$ Hz, 8′a-CH), 4.99–5.01 (dt, $J = 2.2$ Hz, 8′-CH), 4.58–4.60 (m, CH-cholesteryl), 4.11 (s, 2′-CH_3), 3.37 (s, 3′-CH_3), 0.60–2.71 (m, CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3070$ (C–H, arom), 2851–2997 (C–H, aliph), 1744 (3′-C=O), 1720 (7′-C=O), 1709 (2′-C=O), 1617 (C=N), 1547 (C=C), 1440, 1303, 1272, 1231, 1137, 1039, 938, 853, 749 cm^{-1}; MS: m/z 889 [M^+].

Trimethyl 7′-chloresterylcarbonyl-1′H-spiro[fluorene-9,1′-pyrrolo[1,2-b]pyridazine]-4,2′,3′-tricarboxylate (**11j**, $C_{53}H_{64}N_2O_8$)

Yield 44% as white needles; mp 141°C (ether:pentane = 5:5); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.70$–7.72 (d, $J = 7.50$ Hz, CH-arom), 7.51–7.53 (d, $J = 7.50$ Hz, CH-arom), 7.24–7.30 (m, CH-arom), 7.16–7.18 (dd, $J = 7.50$ Hz, CH-arom), 5.79–5.81 (t, $J = 2.2$ Hz, 6′-CH), 5.32–5.34 (d, $J = 7.50$ Hz, CH=cholesteryl), 5.23–5.27 (t, $J = 2.2$ Hz, 8′a-CH), 4.90–4.92 (dt, $J = 2.2$ Hz, 8′-CH), 4.44–4.46 (m, CH-cholesteryl), 4.01 (s, 2′-CH_3), 3.56 (s, 4-CH_3), 3.31 (s, 3′-CH_3), 0.63–2.70 (m, CH_2-cholesteryl) ppm; IR (KBr): $\bar{\nu} = 3070$ (C–H, arom), 2843–2987 (C–H, aliph), 1745 (3′-C=O), 1720 (7′-C=O), 1713 (4-C=O), 1705 (2′-C=O), 1611 (C=N), 1547 (C=C), 1440, 1311, 1269, 1220, 1137, 1028, 938, 856, 747 cm^{-1}; MS: $m/z = 857$ [M^+].

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