Symmetric and Asymmetric Photocleavage of the Cyclobutane Rings in Head-to-head Coumarin Dimers and Their Lactone-opened Derivatives

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The photochemical behaviour of fifteen derivatives of head-to-head coumarin dimers has been investigated. The photocleavage of the cyclobutane rings in these compounds in solution occurs on irradiation with light of wavelength 277 ± 10 nm to give two molecules of coumarin derivatives *via* symmetric fission and/or 2,2'-dihydroxystilbene and fumaric (and maleic) acid derivatives *via* asymmetric fission. The direction of these photofissions is primarily affected by the basic structure of the coumarin dimer derivative, the photocleavage proceeding exclusively with retention of the ring structure when the derivative has a stable five- or six-membered ring fused to its cyclobutane ring. A secondary influence is the steric repulsion between the substituents attached to the cyclobutane ring.

It is well known that olefins form cyclobutane compounds *via* photochemical dimerization and that the resulting cyclobutane compounds revert to the starting olefins on irradiation with light of shorter wavelength.[1] In the case of a head-to-head type dimer, there are two possible routes for the photocleavage of the cyclobutane ring; one is symmetric fission giving the two original olefins and the other is asymmetric fission giving two different olefins, as shown in Scheme 1.

Although a few reports had dealt with asymmetric fission of cyclobutane derivatives,[2,3] a clear-cut example of exclusive asymmetric fission was first described by one of the present authors in the photocleavage of *t*-3,*c*-4-bis(2-hydroxyphenyl)-cyclobutane-*r*-1,*t*-2-dicarboxylic acid.[4] The reaction was extended to a synthetic study of a new type of photoreactive polyamide.[5,6] Thereafter, naphthalene *peri*-fused cyclobutane compounds were reported to be cleaved asymmetrically by photoirradiation.[7] The competition between symmetric and asymmetric fission was observed in the photocleavage of some dimethyl truxinates[8] and dimethyl *t*-3,*t*-4-di(2-naphthyl)-cyclobutane-*r*-1,*c*-2-dicarboxylate *via* the exciplex with triethylamine.[9]

We have recently investigated in detail the lactone-opening reaction of *anti* and *syn* head-to-head coumarin dimers with nucleophiles such as amines and alcohols.[10] This reaction made available a number of coumarin dimer derivatives for the study of the photocleavage modes of cyclobutane rings.†

In this paper we report the photocleavage of the cyclobutane rings in *anti* and *syn* head-to-head coumarin dimers and their lactone-opened derivatives, and discuss the effect of the basic structure, and/or the steric effect of the four substituents on the cyclobutane rings, on the mode of photocleavage.

Results and Discussion

In this study, irradiation of a solution of the coumarin dimer derivatives was carried out with light of wavelength 277 ± 10 nm since all these derivatives have absorption maxima in the range 270—285 nm. The non-conjugated ester and amide carbonyl groups hardly absorb light of wavelength 277 ± 10 nm, as shown by the u.v. spectra of ethyl acetate, acetamide, *N*-methylacetamide, and *N*,*N*-dimethylacetamide, so that the photocleavage reactions should be induced by the excitation
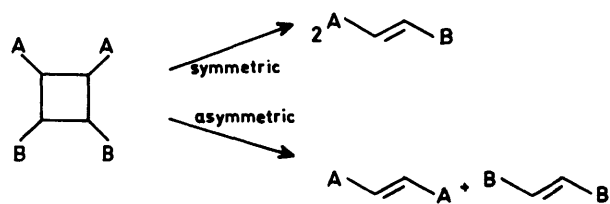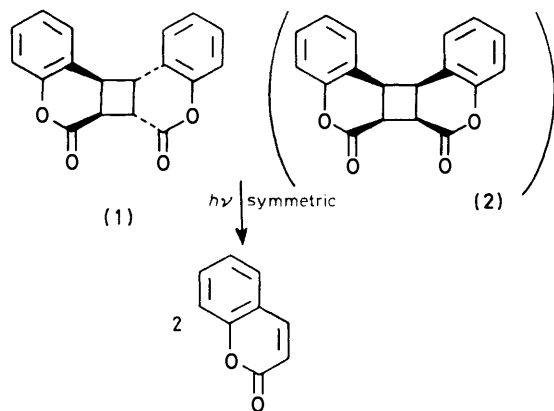

Scheme 1.

of a 2-hydroxyphenyl group and/or chroman-2-one moiety attached directly to the cyclobutane ring. However, the photocleavage of compounds having a phenyl group other than 2-hydroxyphenyl or chroman-2-one [(5), (7), and (12)] could occur *via* two excited species because such a group does absorb light of this wavelength.

The photocleavage reactions were initially monitored by u.v. spectral changes. In all cases, new absorption peaks, which could be attributed to the newly formed conjugated system, appeared gradually at 300—340 nm. However, it was difficult to identify the photoproducts from the u.v. spectra since they showed very similar absorption patterns to each other and, in addition, underwent *cis–trans* isomerization. The conversion and the photocleavage mode and ratio were determined by h.p.l.c., based on the following considerations. The starting material and the products were confirmed by comparing their retention times with those of authentic samples. Asymmetric photocleavage always affords 2,2'-dihydroxystilbene together with an equimolar amount of fumaric (or maleic) acid derivatives, while symmetric scission gives coumaric acid derivatives and/or coumarin, and *cis*-coumaric acid derivatives isomerized to the *trans*-isomer or lactonized to the coumarin with elimination of alcohol or amine after 1 day in the dark at room temperature. Consequently, the two photocleavage modes can be distinguished on the basis of the quantities of 2,2'-dihydroxystilbene and the sum of the amounts of *trans*-coumaric acid derivatives and coumarin produced.

All the derivatives investigated are classified into five groups (Type I—V) depending on the basic structure and the mode of the photocleavage.
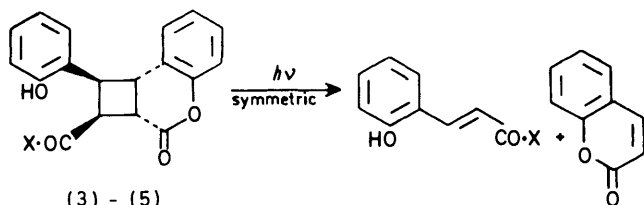
Type I: *anti* and *syn* head-to-head coumarin dimers (1) and (2) gave coumarin as a sole product *via* symmetric photocleavage in dioxan.

Type II: monolactone derivatives of the *anti*-dimer (1), 2-ethoxycarbonyl-, 2-butylcarbamoyl-, and 2-phenylcarbamoyl-1-(2-hydroxyphenyl)-1α,2α,2aβ,8bβ-tetrahydro-3*H*-cyclobuta-

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† The isolation of the ring-opened dicarboxylic acid derived from the *syn*-dimer (2) was unsuccessful by the literature method (R. Anet, *Can. J. Chem.*, 1962, **40**, 1249). The dianilide derivative and the monolactone derivatives of the *syn*-dimer (2) could not be isolated either.

(1) Dioxan, λ_{max}. 271 (ϵ 4 100) and 278 nm (ϵ 3 800)
(2) Dioxan, λ_{max}. 271 (ϵ 7 100) and 279 nm (ϵ 6 800)

Scheme 2. Type I

(3; X = OEt) Dioxan, λ_{max}. 272 (ϵ 4 000) and 278 nm (ϵ 4 300)
(4; X = NHBu^n) Dioxan, λ_{max}. 271 (ϵ 3 700) and 278 nm (ϵ 3 700)
(5; X = NHPh) Dioxan, λ_{max}. 244 (ϵ 17 000), 272 (ϵ 6 800), and 280 nm (ϵ 4 400)

Scheme 3. Type II

[c]-chromen-3-one [(3), (4), and (5)], gave coumarin and cou-maric acid derivatives via exclusively symmetric photocleavage of the cyclobutane rings in a dioxan solution.
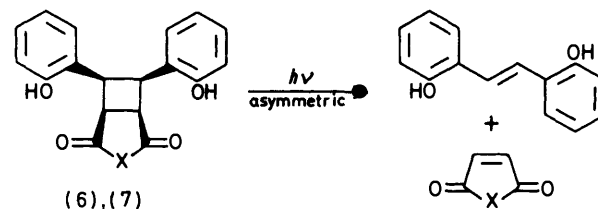
Type III: the photocleavage of the imide derivatives pre-pared from syn-dimer (2), N-butyl- and N-phenyl-c-3,c-4-bis(2-hydroxyphenyl)cyclobutane-r-1,c-2-dicarboximides [(6) and (7)], in a methanol solution proceeded via exclusively asymmetric photocleavage to give 2,2'-dihydroxystilbene and N-substituted maleimides.

Type IV: the cyclobutane rings in both lactone-opened derivatives of the anti-dimer (1), t-3,c-4-bis(2-hydroxyphenyl)-cyclobutane-r-1,t-2-dicarboxylic acid (8), diethyl t-3,c-4-bis-(2-hydroxyphenyl)cyclobutane-r-1,t-2-dicarboxylate (9), N,N'-dibutyl- and N,N,N',N'-tetrabutyl-t-3,c-4-bis(2-hydroxy-phenyl)cyclobutane-r-1,t-2-dicarboxamides [(10) and (11)], and t-3,c-4-bis(2-hydroxyphenyl)cyclobutane-r-1,t-2-dianilide (12), underwent exclusively asymmetric photocleavage in an aqueous methanol or dioxan solution to yield 2,2'-dihydroxy-stilbene and fumaric acid derivatives.

Type V: symmetric and asymmetric photocleavages oc-curred competitively in diethyl c-3,c-4-bis(2-hydroxyphenyl)-cyclobutane-r-1,c-2-dicarboxylate (13), N,N'-dibutyl-c-3,c-4-bis(2-hydroxyphenyl)cyclobutane-r-1,c-2-dicarboxamide (14), and N,N,N',N'-tetrabutyl-c-3,c-4-bis(2-hydroxyphenyl)cyclo-butane-r-1,t-2-dicarboxamide (15).†
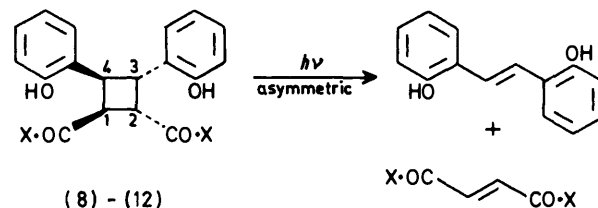
The results are summarized in Schemes 2—6 and the Table. Though there is complete antithesis between the modes of

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† Compound (15) was also obtained by the nucleophilic lactone-opening reaction of the syn-dimer (2).
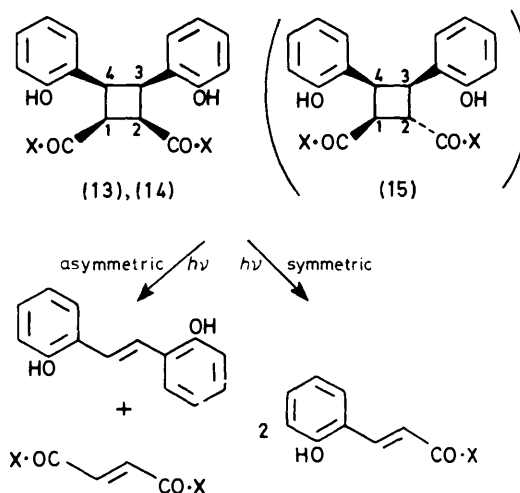

(6; X = NBu^n) MeOH, λ_{max}. 224 (ϵ 14 000), 275 (ϵ 5 000), and 282 nm (ϵ 4 600)
(7; X = NPh) MeOH, λ_{max}. 222 (ϵ 3 700), 275 (ϵ 6 100), and 281 nm (ϵ 5 500)

Scheme 4. Type III

(8; X = OH) H$_2$O, λ_{max}. 224 (ϵ 10 600), 271 (ϵ 4 500), and 279 nm (ϵ 4 200)
(9; X = OEt) MeOH, λ_{max}. 274 (ϵ 5 500) and 280 nm (ϵ 5 300)
(10; X = NHBu^n) MeOH, λ_{max}. 274 (ϵ 5 600) and 280 nm (ϵ 5 400); dioxan, λ_{max}. 273 (ϵ 4 200) and 279 nm (ϵ 3 900)
(11; X = NBu$^n_2$) MeOH, λ_{max}. 278 (ϵ 6 300) and 282 nm (ϵ 6 000)
(12; X = NHPh) MeOH, λ_{max}. 245 (ϵ 27 000), 273 (ϵ 9 200), and 281 nm (ϵ 5 800)

Scheme 5. Type IV

(13; X = OEt) EtOH, λ_{max}. 273 (ϵ 6 200) and 280 nm (ϵ 7 200)
(14; X = NHBu^n) MeOH, λ_{max}. 276 (ϵ 5 200) and 282 nm (ϵ 4 900)
(15; X = NBu$^n_2$) MeOH, λ_{max}. 277 (ϵ 6 500) and 284 nm (ϵ 5 900)

Scheme 6. Type V

photocleavage of Type I and II compounds (symmetric) and Type III compounds (asymmetric), all three types have stable five- or six-membered ring(s) fused to the cyclobutane ring (imide or lactone) and undergo photocleavage with retention of the ring structure. These results mean that the mode of cyclo-butane fission is primarily determined by the basic structure of

Table. Photocleavage of coumarin dimers and their lactone-opened derivatives

Compound	Solvent	Irradiation Time (min)	(%)	Ratio of symmetric : asymmetric
(1)	Dioxan	16	25	100 : 0
(2)	Dioxan	21	100	100 : 0
(3)	Dioxan	35	71	100 : 0
(4)	Dioxan	15	ca. 100	100 : 0
(5)	Dioxan	30	ca. 45	100 : 0
(6)	MeOH	15	100	0 : 100
(7)	MeOH	30	ca. 75	0 : 100
(8)	H₂O	44	ca. 40	0 : 100
(9)	MeOH	3		0 : 100
(10)	MeOH	6	ca. 90	0 : 100
	Dioxan	15	ca. 85	0 : 100
(11)	MeOH	3	ca. 50	0 : 100
(12)	MeOH	11	100	0 : 100
(13)	EtOH	60	100	36 : 64
(14)	MeOH	10	78	69 : 31
(15)	MeOH	20	100	68 : 32

the coumarin dimer derivatives, *i.e.* the photocleavage proceeds exclusively with retention of the ring structure when the coumarin dimer derivative has a stable five- or six-membered ring fused to its cyclobutane ring. This principle is also applicable to the photolysis of naphthalene *peri*-fused cyclobutane derivatives;[7] these compounds photocleave to give acenaphthene and ethylene-1,2-dicarboxylic acid derivatives *via* asymmetric fission.

In the derivatives without a fused ring system (Types IV and V), the photocleavage of the cyclobutane ring is strongly influenced by the presumed steric repulsions between the *cis*-substituents on the cyclobutane ring. Considering the steric repulsions around the cyclobutane rings in Type IV compounds, the C(1)−C(4) and C(2)−C(3) bonds are much more strained than the C(1)−C(2) and C(3)−C(4) bonds, and consequently the asymmetric photocleavage is exclusively of the former releasing this strain. Thus, photocleavage occurs exclusively symmetrically or asymmetrically when the four substituents on the cyclobutane rings are in *cis-anti-cis* positions, which is consistent with the photocleavage of dimethyl β- and μ-truxinates.[8]

In the case of Type V compounds having three or four substituents on the same side of the cyclobutane ring, however, it is necessary to take account of the hydroxyphenyl–hydroxyphenyl repulsion (and the carbonyl–carbonyl repulsion) in addition to the hydroxyphenyl–carbonyl repulsion(s). Neighbouring repulsions influence the mode of photocleavage, resulting in competition between symmetric and asymmetric modes.

As described above, the photocleavage of the cyclobutane rings in coumarin dimers and their lactone-opened derivatives is interpreted in terms of the basic structure of the compound and the steric effect of the substituents. These correlations between photochemical fission and chemical structure are widely applicable to the photocleavage of cyclobutane compounds.

Experimental

Irradiation was carried out with a JASCO CRM-FA spectro-irradiator at room temperature. U.v. spectra were recorded on a HITACHI Model 100-60 spectrophotometer. H.p.l.c. analyses were performed on a steel column (4 mm × 250 mm) packed with LiChrosorb SI 60 (5 μm, Merck and Co.) and the

absorbance at 254 or 280 nm was monitored on a TOYO SODA UV8 Model II spectrophotometer at a flow rate of 0.5—0.8 ml/min using dichloromethane or benzene–ethyl acetate (1 : 1 v/v) as eluant.

Spectrograde solvents were used for reaction and u.v. measurement without further purification.

The *anti*-dimer (1) and the *syn*-dimer (2) was prepared by the method of Krauch *et al.*[11] The lactone-opened derivatives [(3)—(15)] were synthesized according to the procedure in ref. 10. Authentic samples, for h.p.l.c. analysis, of coumaric acid,[12] ethyl coumarate,[13] N-butyl- and N,N-dibutylcoumaramides,[14] N-phenylmaleimide,[15] and coumaranilide,[16] were prepared according to literature methods.

Preparation of 2,2'-Dihydroxystilbene.—An aqueous solution of dicarboxylic acid (8) (180 mg in 100 ml) was irradiated with light of wavelength 277 ± 10 nm for 40 h. The white precipitates were filtered off (49 mg, 49%) and recrystallized from EtOH–H₂O (38 mg, 38%). (The present procedure is much simpler and gives a higher yield than the method reported by Kopp.[17]) M.p. 202—203 °C (lit.,[17] 197 °C) (Found: C, 79.4; H, 5.7. Calc. for C₁₄H₁₂O₂: C, 79.23; H, 5.70%); ν_max. (KBr) 1 585, 980, and 760 cm⁻¹; δ [(CD₃)₂SO] 6.6—7.5 (10 H, m, HC=CH and ArH) and 9.44 (2 H, s, OH); λ_max. (EtOH) 278 (ε 13 500) and 321 nm (ε 14 500).

Photolysis of Compounds (1)—(15).—Through a solution of compounds (1)—(15) (*ca.* 5 × 10⁻⁵M) in a quartz cell, anhydrous nitrogen was bubbled for *ca.* 1 min. The photocleavage was monitored by the u.v. spectrophotometer during irradiation. When the new absorption reached a maximum, the irradiation was stopped, and the solution was concentrated under reduced pressure. Then the residue was dissolved in dichloromethane or benzene–ethyl acetate (1 : 1 v/v) and analyzed by h.p.l.c. The products were confirmed by comparing their retention times with those of authentic samples. The conversions were estimated on the basis of the area of an elution band and the molar absorptivity of the starting material. When two modes of photocleavage were observed, the ratios were calculated on the basis of the area of an elution band recorded by the u.v. detector at 280 nm and the molar absorptivity of the corresponding compound at this wavelength, as shown in the following equation:

symmetric fission/asymmetric fission

$$= \Sigma(S_s/\varepsilon_s)/[2(S_a/\varepsilon_a)]$$

where S = the area of the elution band
ε = the molar absorptivity
s = *o*-coumaric acid derivative or coumarin *via* symmetric photocleavage
a = 2,2'-dihydroxystilbene *via* asymmetric photocleavage

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