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Photochemistry of 4*H*,7*H*-Benzo[1,2-*c*:4,3-*c*′]dipyran-4,7-dione, a Twofold Isocoumarin

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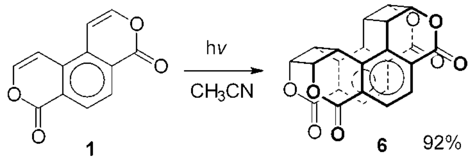
ABSTRACT

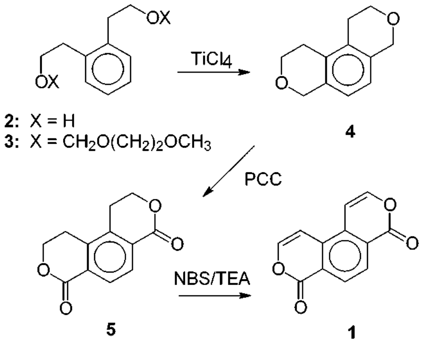


The title compound 1 was synthesized starting from 1,2-bis(2-hydroxyethyl)benzene (2). Irradiation (350 nm) of 1 in CH$_3$CN affords the *all-cis*-dimer 6 in >90% yield. Irradiation (>390 nm) of 1 in the presence of tetrachloroethene leads selectively to the monocyclobuta adduct 8, which on subsequent irradiation is converted to a 4:1 mixture of biscyclobuta derivatives 9 and 10.

Both the intermolecular bis-photocyclodimerization of divinylarenes and the intramolecular [2 + 2]-photocycloaddition of tethered vinylarenes have been successfully used as methods for stereocontrol in cyclophane synthesis.[1] Nevertheless, the yields for this first reaction type are usually low. This is exemplified in the irradiation of 1,2-divinylbenzene which gives only 11% of a biscyclobuta-orthocyclophane.[2] Here we report on the synthesis of the 2-fold isocoumarin **1**, a molecule containing a rigid *o*-divinylbenzene substructure, and on its selective, high-yield photoreactions.

Using a procedure by Corey et al.,[3] 2-(2-hyxdroxyethyl)-phenylethanol (**2**)[4] was converted to bis-methoxyethoxymethyl ether **3** in 96% yield. Bis-cyclization in the presence of TiCl$_4$ in dichloromethane at −50 °C led quantitatively[5] to benzo[1,2-*c*:4,3-*c*′]dipyran **4**, mp 108 °C, which was then oxidized to benzodipyrandione **5**, mp 263 °C, by treatment[6] with PCC in 48% yield. Finally, conversion of **5** to **1** was achieved by a bromination/dehydrobromination sequence (Scheme 1).[7]

Scheme 1



On excitation at 350 nm, tricycle **1** exhibits a strong fluorescence emission band ($\lambda_{max} = 446$ nm in CH$_3$CN). This contrasts the excited state behavior of the parent, isocoumarin or isothiocoumarin, which do not show any luminescence.[8]

Irradiation (350 nm) of **1** in either C$_6$H$_6$ or CH$_3$CN leads to the immediate formation of a precipitate. Analysis of this precipitate by ^{1}H NMR spectroscopy in DMSO-d_6 indicates the formation (Scheme 2) of a 9:1 mixture of **6** and **7** in

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(1) Nishimura, J.; Nakamura, Y.; Hayashida, Y.; Kudo, T. *Acc. Chem. Res.* **2000**, *33*, 679.

(2) Nakamura, Y.; Hayashida, Y.; Wada, Y.; Nishimura, J. *Tetrahedron* **1997**, *53*, 4593.

(3) Corey, E. J.; Gras, J. L.; Ulrich, O. *Tetrahedron Lett.* **1976**, *17*, 809.

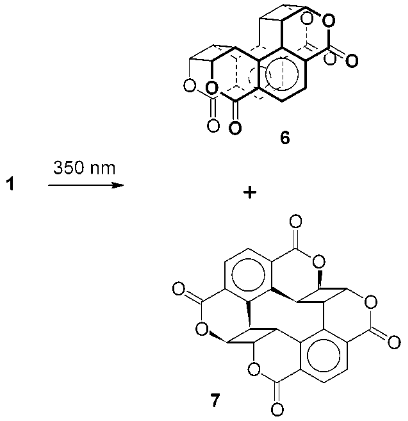
(4) Burns, J. A.; Whitesides, G. M. *J. Am. Chem. Soc.* **1990**, *112*, 6296.

(5) Mohler, D. L.; Thompson, D. W. *Tetrahedron Lett.* **1987**, *28*, 2567.

(6) Bonadies, F.; Di Fabio, R. *J. Org. Chem.* **1984**, *49*, 1647.

10.1021/ol006820y CCC: $19.00

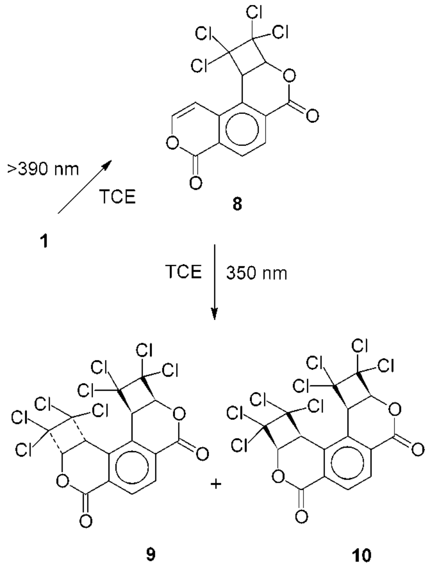
Scheme 2



benzene and the selective formation of **6** in acetonitrile.[9] The spectra show singlets for the aromatic H atoms and AA′XX′ patterns for the cyclobutane H atoms, respectively. The coupling constants for **6** are almost identical to those of the head-to-head *cis-cisoid-cis*-cyclodimer of isothiocoumarin whose structure had additionally been established by X-ray analysis.[10] Separation of the minor product **7** from **6** failed, mainly because of the very low degree of solubilty of both products in common solvents. Its ^{1}H NMR data (from the mixture) is compatible with the proposed, complementary, *HH-cis-transoid-cis* structure.[11] Irradiation of **1** using light $>$ 390 nm proceeds in the same manner as described above. The conversion of **1** to **6** in acetonitrile on irradiation (350 nm) in the presence of naphthalene (0.02 mol/L) occurs with the same efficiency as in the absence of the arene. Finally, irradiation of **1** (350 nm) as a solid suspension in hexane gives an 85:15 mixture of **6** and **7**, very similar to that obtained in benzene solution.

Irradiation ($>$390 nm) of **1** in the presence of a 20-fold molar excess of tetrachloroethene (TCE) in CH_3CN leads to selective formation[12] of **8**. On prolonged irradiation this monocyclobuta derivative reacts further to give a 4:1 mixture of **9** and **10**, respectively (Scheme 3). As attempts to separate the diastereomers by either liquid chromatography or by GC on a chiral stationary phase failed, the structural assignment of these compounds is tentative and based on the assumption that the backside approach of the second alkene molecule to excited **8** will occur with less hindrance than the corresponding front-side attack, thus favoring the formation of the *transoid* biscyclobuta adduct **9**.[13]

Scheme 3



The 2-fold [2 + 2]-photocyclodimerization of **1** to **6** is relevant from the preparative point of view as it represents the first example of a photocyclodimerization of an isocoumarin, not only in solution but also on solid-state irradiation.[8] Regarding the mechanistic aspects of this reaction, it is noteworthy that *all-cis* dimer **6** is formed from **1** selectively, both in solution and as a solid suspension, thus suggesting

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(7) **Preparative Details.** A solution of **5** (1.09 g, 5 mmol), NBS (2.67 g, 15 mmol), and AIBN (5 mg) in $CHCl_3$ (50 mL) is refluxed for 3 h. The solvent is evaporated, then triethylamine (25 mL) is added, and the mixture is heated at reflux for 2 h. After evaporation of excess amine, 2 N HCl (50 mL) and CH_2Cl_2 (50 mL) are added, the layers are separated, the aqueous layer is extracted twice with CH_2Cl_2 (50 mL), and the combined organic phases are dried ($MgSO_4$). After evaporation of the solvent, the residue is redissolved in $CHCl_3$ and the bromination/dehydrobromination sequence is repeated as described. The final residue is then purified by chromatography (SiO_2, CH_2Cl_2) to afford 4*H*,7*H*-benzo[1,2-*c*:4,3-*c*′]dipyran-4,7-dione (**1**) (482 mg, 45%), mp 297 °C: ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.39 (d, J = 5.9 Hz, 2H), 7.81 (d, J = 5.9 Hz, 2H), 8.23 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 102.5, 124.9, 127.7, 132.7, 147.2, 160.7; mass spectrum m/z 214 (M^+, 100%), 186 [$(M - CO)^+$, 60%]; UV (CH_3CN) λ_{max} 373 nm (log ϵ = 3.80), 270 nm (log ϵ = 4.40). Compounds **1**, **4**, and **5** gave satisfactory elemental analyses.

(8) Kinder, M. A.; Kopf, J.; Margaretha, P. *Tetrahedron* **2000**, *56*, 6763.

(9) **Preparative Details.** An Ar-degassed solution of **1** (107 mg, 0.5 mmol) in CH_3CN (100 mL) is irradiated in a Rayonet RPR-100 photoreactor equipped with 350 nm lamps for 24 h. The precipitate (70 mg) is filtered, the filtrate is concentrated to a volume of 10 mL, and the new precipitate is filtered. The combined precipitates are washed with cold CH_3CN and dried. One obtains 98.5 mg (92%) of spectroscopically pure 7α,8α,17α,18α,22α,23α,26α,27α-6,9,16,19-tetraoxanonacyclo[12.6.4.4^{4,11}0.^{7,26}0.^{8,27}.0.^{17,23}0.^{18,22}0.^{21,25}0^{24,28}]octaeicosa-1,3,11,13,21(25),24(28)-hexaene-5,10,15,20-tetraone (**6**), mp $>$360 °C (dec): ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.46 and 5.65 (AA′XX′, $J_{AA'}$ = 9.4 Hz, J_{AX} = 8.0 Hz, $J_{XX'}$ = −5.7 Hz, $J_{XX'}$ = 1.5 Hz, 8H), 7.79 (s, 4H); ^{13}C NMR NMR (125 MHz, DMSO-d_6) δ 36.2, 73.6, 126.5, 127.8, 136.3, 160.9; mass spectrum m/z 428 (M^+, 1%), 384 [$(M - CO_2)^+$, 2%], 214 (100%). An analytically pure sample is obtained by recrystallization from acetonitrile.

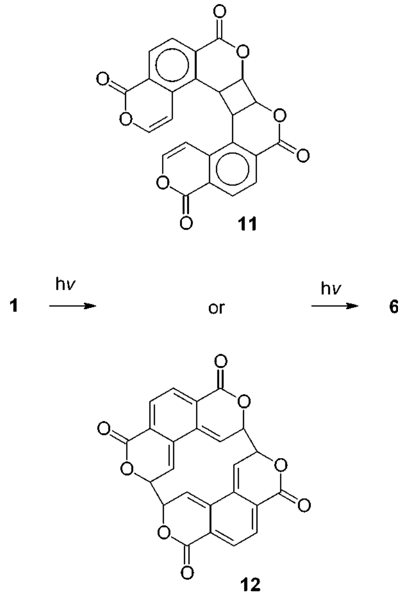
(10) Bethke, J.; Kopf, J.; Margaretha, P.; Pignon, B.; Dupont, L.; Christiaens, L. E. *Helv. Chim. Acta* **1997**, *80*, 1865.

(11) ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.32 and 5.43 (AA′XX′, $J_{AA'}$ = 9.3 Hz, J_{AX} = 8.9 Hz, $J_{XX'}$ = −2.0 Hz, $J_{XX'}$ = 1.6 Hz, 8H), 8.05 (s, 4H).

(12) **Preparative Details.** An Ar-degassed solution of **1** (107 mg, 0.5 mmol) and tetrachloroethene (1.66 g, 10 mmol) in CH_3CN (100 mL) is irradiated with a medium-pressure Hg lamp using aqueous $NaNO_2$ as liquid filter (cutoff: $<$390 nm) for 1 h. Traces of precipitate are filtered and washed with cold CH_3CN. The combined filtrates are evaporated, and the residue is purified by chromatography (SiO_2, CH_2Cl_2) to afford 133 mg (35%) 2aα,10cα-1,1,2,2-tetrachloro-1,2-dihydro-2a*H*,4*H*,7*H*,10c*H*-cyclobuta[*a*]benzo[1,2-*c*:4,3-*c*′]dipyran-4,7-dione (**8**), mp 218 °C: ^{1}H NMR (500 MHz, CD_3CN) δ 5.22 (d, J = 7.9 Hz), 5.85 (d, J = 7.9 Hz), 6.81 (d, J = 5.8 Hz), 7.55 (d, J = 5.8 Hz), 8.27 (d, J = 8.5 Hz), 8.38 (d, J = 8.5 Hz); ^{13}C NMR (125 MHz, CD_3CN) δ 47.3, 81.5, 90.1, 92.3, 104.2, 129.5, 131.4, 132.3, 133.4, 136.9, 148.3, 161.7, 164.9. An analytically pure sample is obtained by recrystallization from acetonitrile.

(13) Major product (*transoid*, **9**): ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.17 (d, J = 7.5 Hz, 2H), 5.94 (d, J = 7.5 Hz, 2H), 8.38 (s, 2H). Minor product (*cisoid* **10**): ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.63 (d, J = 7.1 Hz, 2H), 5.69 (d, J = 7.1 Hz, 2H), 8.40 (s, 2H).

Scheme 4



in solution the association of an excited molecule of **1** to a ground-state molecule, i.e., excimer formation, prior to dimerization.

In contrast to the photocycloaddition of **1** to TCE which affords first cyclobutane **8** and then, in a subsequent reaction step, the mixture of bis-cycloadducts **9** and **10**, no intermediate product is observed in the bis-photocyclodimerization of **1**. Indeed, monitoring the long wavelength (>390 nm) irradiation of **1** by ^{1}H NMR analysis of both the CD_3CN solution and the precipitate shows no additional signal to those of **1** and **6** at any stage of the reaction, a result which in turn does not necessarily prove that the four new C−C bonds are formed in a concerted-like process. The only piece of evidence regarding the possible intermediates **11** or **12** stems from the finding that the conversion of **1** to **6** is not slowed by the addition of naphthalene as potential triplet quencher, which implies that the second step in the prospective sequence **1** → **11** or **12** → **6** (Scheme 4) does not involve triplet states of **11** or **12** with E_T > 255 kJ/mol, i.e., the triplet energy of naphthalene.[14] Although E_T values for isocoumarins have not been reported, they can be expected to be equivalent to those of isothiocoumarins, and indeed the photocycloaddition of isothiocoumarin to tetrachloroethene is quenched by the addition of naphthalene.[10] Further studies with various isocoumarins and isothiocoumarins are now in progress.

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(14) Murov, S. L. *Handbook of Photochemistry*; M.Dekker: New York, 1973; p 4.