A Reinvestigation of a Sensitized Photochemical Cycloaddition of Coumarin with Cyclopentene[1)]

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Synopsis. A reinvestigation of a sensitized photochemical cycloaddition of coumarin with cyclopentene reported by Hanifin and Cohen indicated that the cycloaddition gives a sterically disfavored cis-cisoid-cis adduct (18%) together with a cis-transoid-cis adduct (25%) and a head-to-head coumarin dimer with a cis-transoid-cis disposition. The two adducts behaved differently in hydrolysis and recyclization.

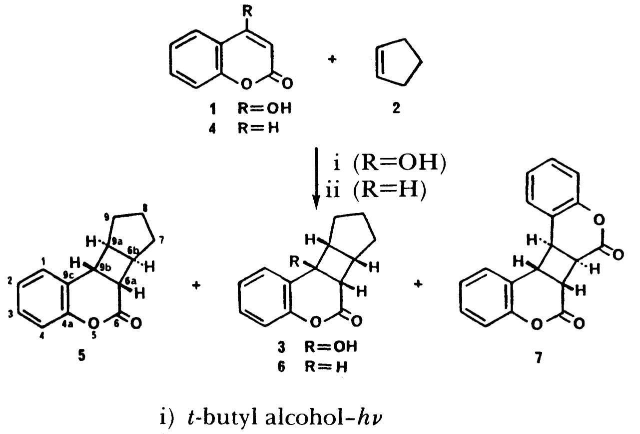
In connection with the program we have designed to explore the potential of the β-scission of the alkoxyl radicals generated from the cyclobutanols obtained by a [2+2]photocycloaddition of 4-hydroxycoumarin and olefins,[2,4)] we have been interested in the distinctly different behavior of coumarin reported by Hanifin and Cohen in 1966[3)] and 4-hydroxycoumarin in their photochemical cycloaddition.[5)]

Thus, while both Reid and his colleagues and we ourselves have found that the [2+2]photoaddition of 4-hydroxycoumarin (**1**) and cyclopentene (**2**) on direct irradiation gives a single [2+2]photocycloadduct **3** having a sterically disfavored cis-cisoid-cis configuration in a good yield (Scheme 1),[2,6)] Hanifin and Cohen[3)] have reported that the photoaddition of coumarin itself and cyclopentene does not give any cycloadducts on direct irradiation but gives single [2+2]photocycloadduct, mp 139 °C, on a sensitized irradiation. According to Hanifin and Cohen,[3)] the cyclopentane ring and the six-membered ring of the photoadduct are probably transoid oriented.

We have therefore reinvestigated the direct and sensitized photocycloadditions of coumarin and cyclopentene. Our results which differ from the previous report[3)] are described in this paper.

Results

A sensitized irradiation of coumarin and cyclopentene carried out according to the procedure of Hanifin and Cohen [**4** (5.6 mmol), **2** (5 ml), benzophenone (1 mmol), and dioxane (1 ml)] through a Pyrex filter with a 500-W high-pressure mercury arc for 5 days gave a mixture of three products, **5** (mp 82—84 °C, 25%), **6** (mp 138—139 °C, 18%), and **7** (mp 175—176 °C, 21%), which were separable by means of preparative TLC.



i) t-butyl alcohol-$h\nu$
ii) $C_6H_5COC_6H_5$-dioxan-$h\nu$

Scheme 1.

^{1}H NMR spectroscopy and their behaviors in hydrolysis and regeneration of the coumarin ring indicated that the stereochemistries of adducts **5** and **6** have cis-transoid-cis for **5** and cis-cisoid-cis for **6**.

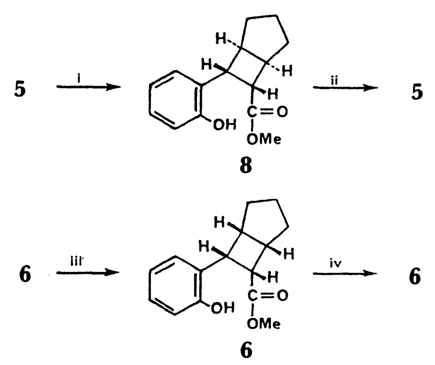
A 500 MHz ^{1}H NMR spectrum of adduct **5** exhibited four signals (each 1H) at δ 2.70, 3.05, 3.14, and 3.19. The signal at δ 3.05 assignable to 6a-H split into a doublet of a doublet with $J_{6a,9b}$=9.28 Hz, $J_{6a,6b}$=4.88 Hz, and $J_{6a,9b}$=0.98 Hz. The signal at δ 3.19 assignable to 9b-H split into a doublet of a doublet with $J_{6a,9b}$=9.28 Hz and $J_{9a,9b}$=3.91 Hz. The signals at δ 3.41 (br. td, J=6.8 and 5.9 Hz) are assigned to the 9a-H and 6b-H. These coupling constants indicated that the cyclobutane-coumarin ring fusion as well as the cyclobutane-cyclopentane ring are cis and that the coumarin and cyclopentane ring are transoid oriented. The structure of the photoadducts **5** was thus established to be 6aα,6bβ,9aβ,9bα-($\pm$)-6b,7,8,9,9a,9b-hexahydrobenzo[*b*]cyclopenta[3,4]cyclobuta [1,2-*d*]pyran-6-(6a*H*)-one (**5**).

On the other hand, the results on the ^{1}H NMR spectrum of adduct **6**, the melting point of which is nearly in agreement with that of the adduct reported by Hanifin and Cohen, indicated that the cyclobutane-coumarin ring fusion as well as the cyclobutane-cyclopentane ring fusion are cis while the coumarin and cyclopentane ring are cisoid oriented in the adduct.

Thus, 500 MHz ^{1}H NMR spectrum of adduct **6** exhibited four signals each corresponding to ^{1}H at δ 3.23, 3.41, 3.73, and 3.97. The signal at δ 3.73 assignable to 5a-H split into a doublet of a doublet with $J_{6a,6b}$=11.23 Hz, and $J_{6a,9b}$=10.74 Hz. The signal at δ 3.97 assignable to 9b-H similarly split into a doublet of a doublet with $J_{6a,9b}$=11.23 Hz, and $J_{6b,9a}$=10.74 Hz. The signal at δ 3.97 assiganble to 9b-H similarly split into a doublet of a doublet with $J_{6a,9b}$=10.74 Hz and $J_{9b,9a}$=10.25 Hz. The rest of the signals at 3.23 (dq, J=7.81 and 8.3 Hz) and at δ 3.41 (dt, J=10.25 and 7.81 Hz) can be assigned to the 6b-H and 9a-H.

The spectroscopic analysis of the third photoadduct **7** indicated that it is a head-to-head and cis-transoid-cis dimer of coumarin obtained by Schenck and his colleagues by means of a sensitized irradiation of coumarin in ethanol or in benzene.[7)]

Thus, we conclude that the cycloadduct **6** previously reported by Hanifin and Cohen[3)] has cis-cisoid-cis structure and the cycloadduct **5**, newly isolated in the



i) CH_3COONa-MeOH, r.t.
ii) *p*-toluenesulfonic acid-benzene-r.t. 10 min
iii) CH_3ONa-MeOH, r.t.
iv) concd HCl, r.t. 2 h

Scheme 2.

present work, has cis-transoid-cis structure (Scheme 1).

Irradiation of a solution of coumarin in cyclopentene and dioxane in the absence of a sensitizer for 5 days gave no [2+2]photocycloadducts: this agrees with the observation by Hanifin and Cohen.[3]

We found a clear difference between **5** and **6** in a base-catalyzed hydrolysis. Thus, while the cis-transoid-cis adducts **5** was readily hydrolyzed with sodium acetate in methanol at room temperature no hydrolysis took place when cis-cisoid-cis adduct **6** was exposed to the same conditions of hydrolysis. Hydrolysis of adduct **6** was, however, achieved with sodium methoxide in methanol for 2 h at room temperature (Scheme 2).

The molecular geometry of cis-cisoid-cis adduct **6** can be assumed to be similar to cis-cisoid-cis adduct **3**, whose molecular structure we determined by means of an X-ray crystallographic analysis.[2,3]

The difference in the behavior under hydrolysis of adducts **5** and **6** can be understood by comparing the geometries of these molecules since an inspection of the molecular models of adducts **5** and **6** indicated that the carbonyl carbon of adducts **6** is more shielded from an attacking nucleophile.

We also found a clear difference in the rates of the recyclizations of the hydrolyzed products **7** and **8**; the hydrolyzed product **8** gave the parent adduct **5** after treatment with *p*-toluenesulfonic acid in benzene at room temperature nearly spontaneously while no cyclization of **9** took place under these conditions. The ester **9** gave a more strained parent adduct **6** after treatment with concd HCl at pH 3 in ethanol at room temperature for 2 h (Scheme 2).

In has been reported as generally true that in an adduct of cycloalkenes and monocyclic enones where the cyclobutane ring fusion to the enones and alkene derived ring are cis, the rings are preferentially disposed transoid to each other.[5b]

It is worth noting that the present triplet sensitized photoaddition led to the production of a substantial proportion of the sterically disfavoured cis-cisoid-cis adduct in addition to an expected cis-transoid-cis adduct. The reason for this is not clear but the attractive interaction of an aromatic portion of coumarin and cycloalkene in the triplet exciplex or the biradical intermediate might be partly responsible for the formation of cis-cisoid-cis product.

Experimental

For the instruments and the experimental procedures see Ref. 2.

Photochemical Cycloaddition of Coumarin with Cyclopentene in the Presence of Benzophenone. Coumarin (820 mg, 6.5 mmol), cyclopentene (5 ml), benzophenone (180 mg, 1 mmol), and dioxane (1 ml) were irradiated through a Pyrex filter with a 500-W high-pressure Hg arc at room temperature for 5 days. After the removal of an excess of cyclopentene and dioxane under a reduced pressure, the product was subjected to preparative TLC with a 1:3 ethyl acetate and hexane to give three cycloadducts **5**, **6**, and **7** in the order of their mobility on the TLC plate. The most mobile adduct **5** (300 mg, 25%) was recrystallized from hexane to yield a specimen for analysis. Mp 82—84 °C. (Found: *m/z* 214.0989. Calcd for $C_{14}H_{14}O_2$: M, 214.0992). IR (Nujol) 1752 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ=1.57—1.67 (2H, m, 8-H), 1.86—2.02 (4H, m, 7-H and 9-H), 2.70 (1H, br. td, J=7.3 and 3.91 Hz, 9a-H), 3.50 (1H, ddd, J=9.28, 4.88, and 0.98 Hz, 6a-H), 3.14 (1H, br. td, J=6.8 and 5.9 Hz, 6b-H), 3.19 (1H, dd, J=9.28 and 3.91 Hz, 9b-H), and 7.00—7.31 (4H, m, 1,2,3,4-H); MS *m/z* (rel intensity), 214 (M$^+$, 4.6%), and 146 (100).

The second mobile adduct **6** (219 mg, 18%) was recrystallized from hexane. Mp 138—139 °C (lit,[3] mp 139 °C): (Found: *m/z* 214.0983. Calcd for $C_{14}H_{14}O_2$: M, 214.0992); IR (Nujol) 1746 cm^{-1} (C=O), 1172, amd 772; ^{1}H NMR (500 MHz), δ= 1.71—1.27 (1H, m), 1.34—1.62 (4H, m), 1.88 (1H, dd, J=13.67 and 6.35 Hz), 3.23 (1H, br. dq, J=7.81 and 8.3 Hz, 6b-H), 3.42 (1H, dt, J=10.25 and 7.81 Hz, 9a-H), 3.73 (1H, dd, J= 11.23 and 10.74 Hz, 6a-H), 3.97 (1H, dd, J=10.74 and 10.25 Hz, 9b-H), and 6.96—7.31 (4H, m, 1,2,3,4-H); MS *m/z* (rel intensity) 214 (M$^+$, 3.3%) and 146 (100).

The most polar adduct **7** (173 mg, 21%) was recrystallized from hexane. Mp 175—176 °C (lit,[6] mp 176.5 °C).

A Base-Catalyzed Hydrolysis of the Adduct 5. Adduct **5** (52 mg, 0.24 mmol) in methanol (1 ml) containing sodium acetate (20 mg, 0.24 mmol) was stirred overnight at room temperature. Examination of the solution by TLC (1 : 3 ethyl acetate-hexane) indicated the disappearance of the starting material. To this solution, dichloromethane (10 ml) was added and the solution was washed first with aq. saturated ammonium chloride and then with brine and dried over anhydrous magnesium sulfate. After the usual work-up, the product was dissolved in benzene (2 ml) containing *p*-toluenesulfonic acid (10 mg, 0.05 mmol). The solution was stirred for 10 min. at room temperature, washed with aq. sodium hydrogencarbonate and dried over anhydrous magnesium sulfate. The usual work-up of the solution gave the residue which was subjected to preparative TLC with a 1 : 3 ethyl acetate and hexane to yield the starting adduct **5** (31 mg, 60%).

A Base-Catalyzed Hydrolysis of Adduct 6. (a) Adduct **6** (26 mg, 0.12 mmol) in methanol (1 ml) containing sodium acetate (10 mg, 0.12 mmol) was stirred overnight at room temperature. The usual work-up of the solution gave the starting adduct **6** nearly quantitatively.

(b) To adduct **6** (54 mg, 0.25 mmol) in methanol (5 ml), a small amount of sodium metal was added. The solution was then stirred for 2 h at room temperature. Examination of the solution by means of TLC (a 1 : 3 ethyl acetate-hexane) indicated the disappearance of the starting adduct **6**. The solution was neutralized with concd hydrochloric acid (pH 3) and was stirred for another 2 h. After the removal of methanol under reduced pressure the residue was extracted with diethyl ether. The ethereal extract was washed first with aq.

sodium sulfate. The product was subjected to preparative TLC with a 1:3 ethyl acetate-hexane to yield the starting adduct **6** (41 mg, 76%).

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