SOLID-STATE PHOTOREACTION ON AN INCLUSION COMPOUND OF COUMARIN WITH β-CYCLODEXTRIN

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ABSTRACT: β-Cyclodextrin was found to form a crystalline inclusion complex with coumarin. The solid-state photoreaction of the inclusion compound was studied at 25-27°C, and compared with those of coumarin and of a mixture of coumarin with the cyclodextrin. Under irradiation at a wavelength longer than 300 nm, coumarin with or without β-cyclodextrin and in the inclusion complex converted to a photodimer, cis-head-to-head dimer in the solid state. The conversion rate of coumarin was higher than that in the mixture, and the latter was higher than that in the complex. These indicate that β-cyclodextrin retards the photodimerization of coumarin, but does not affect the course of the reaction in the solid state.

1. INTRODUCTION

Cyclodextrins are well known [1] to form a number of crystalline adducts or inclusion complexes with a variety of substances. In the crystalline lattice, cyclodextrins form two types of packing: One is a cage type where the cavity of one cyclodextrin molecule is closed on both sides by ad jacent molecules. The other is a channel-type, in which the cyclodextrin rings are packed on top of each other to produce cylinders with infinite centralcavity. Formation of one or the other type crystal structure depends on the size and molecular character of the guest molecule.

Moreover, cyclodextrins catalyze [1] a number of chemical reactions in solutions. As far as the photoreactions are concerned, such information has been reported by Ohara, et al. [2], who studied the Fries rearrangement of phenyl acetate in an aqueous medium. Yamada, et al. [3] and Uekama, et al. [4] also reported the photolyses of p-benzoquinone and chlorpromazine in aqueous solutions, respectively. However, no photoreaction in the solid state could be found. In connection with our interest in the inclusion complex in the solid state, the use of cyclodextrins has been investigated as inclusion hosts for photoreactions. Previously [5] we have reported a preliminary study on the photolysis of a coumarin inclusion complex with β-cyclodextrin and the present paper

gives details of the reaction.

Substituted coumarins, such as psoralen and a number of its
derivatives, exhibit strong photobiological effects on bactria [6,7],
viruses [8], and mammalian skin [9,10] in presence of light. Coumarin
itself is also known to show interesting photochemical behavior, parti-
cularly dimerization [11-17], in polar and non-polar solvents. In polar
solvents such as ethanol, the cis head-to-head dimer is formed presuma-
bly via interaction of excited singlet coumarin with its groud state,
while in non-polar solvents such as benzene, trans head-to-head dimer is
formed via the triplet state. No detailed study on the photolysis of
coumarin, however, has been done in the solid state [11,18] nor in the
inclusion state.

2. EXPERIMENTAL

2.1. Materials

Coumarin, potassium bromide, and potassium ferrioxalate were reagent
grade and used without further purification. β-Cyclodextrin was pur-
chased from Nichiden Chemical Co. Ltd. and purified by recrystallization
once from 1-propanol and twice from water. Reagent grade organic sol-
vents were purified and dried by standard methods [19]. Cis- and trans-
head-to-head dimers of coumarin were obtained from the irradiation of
coumarin in formic acid and in benzene without or with a small amount of
benzophenone, respectively, by the similar method of Schenck and Krauch
[12,14]. An inclusion complex of coumarin with β-cyclodextrin was ob-
tained as follows: equimolar aounts of coumarin and the cyclodext-
rin were dissolved in hot water at 60-70°C by mixing for 1 hr, and
cooled firstly at room temperature and then in a refrigerator for 2-3
days. A white precipitate was filtered, washed with cold water and
dried under vacuum at room temperature. Coumarin melts at 70°C and eva-
porates at 180°C (b.p., 297-299°C), while this precipitate did not melt
nor evaporate even at 250°C. The expected structure was further veri-
fied by infrared (IR) and ultra-violet (UV) absorption spectra, proton
nuclear magnetic resonance (NMR) and X-ray diffraction spectra, and ele-
mental analysis.

2.2. Test Methods

The exciting light was furnished by an irradiator composed of a 500-W
xenon or 450-W high pressure mercury lamp as the light source and fil-
ters. The irradiation for the measurement of the quantum yields was
performed with a JASCO CRM-FM spectroirradiator composed of a 2000-W xe-
non lamp as the light source and a grating monochromator. The light in-
tensity was measured by potassium ferrioxalate actinometry [20], and the
actinometric estimates were checked with an Eppley thermopile.

Ultraviolet spectra measurements were performed with a Shimadzu UV-
200 spectrophotometer equipped with a holder for KBr pellet. To attenu-
ate the scattered light ultraviolet absorption spectra were measured by
the method of an integrating sphere attached to a spectrophotometer.

Infrared absorption spectra were obtained on a Hitachi EPI-G3 spectro-
photometer equipped with NaCl prism. The samples were prepared by the
KBr pellet technique. The X-ray diffraction pattern of the powdered
samples was taken in the region of 3 to 40° by a Rigakudenki Model 3D-F
X-ray diffractometer, using Ni-filtered copper Kα radiation. The proton
nuclear magnetic resonance (NMR) spctra were obtained in the region of 0
to 10 ppm by a JEOL HCL 60 (60 MHz) spectrometer. The samples were dis-
solved in deutero dimethyl sulfoxide (DMSO-d_6) and chemical shifts are
given in ppm relative to the internal reference standard, tetramethylsi-
lane (TMS). The thermal behavior of the specimens was observed with a
Rigakudenki TG-DSC standard analyzer, which has been previously calib-
rated with standard substances. TG-DSC thermograms were obtained at a
fixed heating rate: 10°C/min.

To examine the photoreaction of coumarin, ultraviolet and infrared
absorption spectral changes of the sample were measured during reaction
upon irradiation with filtered light. For this purpose, KBr pellets
containing coumarin with or without β-cyclodextrin and the inclusion
complex were prepared by pressing in an evacuated die at 13-15Kbar for
5 min. KBr pellets made of carefully dried material prepared in this
way were sufficiently transparent down to 220 nm; they exhibited a low
degree of scattering and at low solute concentrations apparently they
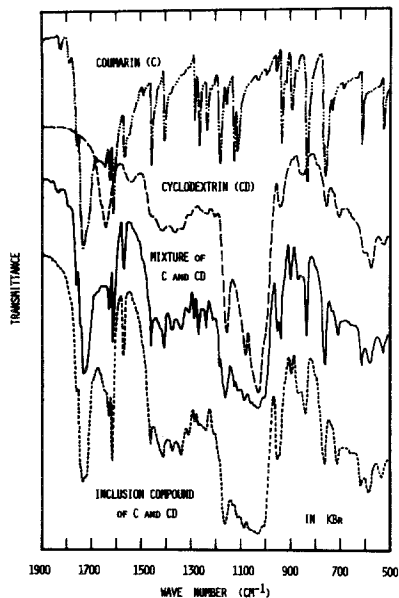obeyed the Lambert-Beer Law.

Fig.1. The IR absorption spec-
tra of coumarin, β-cyclodetrin,
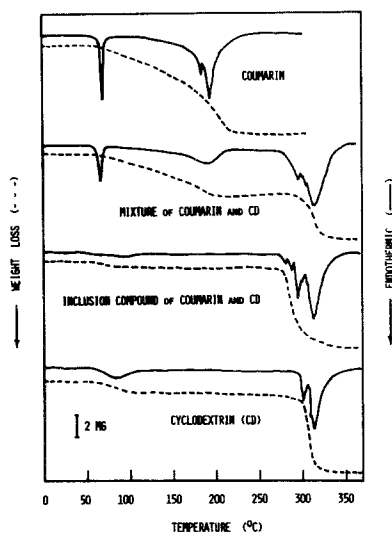their mixture, and the inclu-
sion complex at 25°C

Fig. 2. TGA and DSC curves of
coumarin, β-cyclodextrin, their
mixture, and the inclusion complex
under atmospheric pressure of N_2

3. RESULTS AND DISCUSSION

3.1. An Inclusion Complex

As mentioned in "Experimental", a white precipitate was obtained when equimolar amounts of coumarin and β-cyclodextrin were dissolved in hot water and cooled. To examine the formation of an inclusion complex, IR (Fig.1), DSC-TG (Fig. 2), and X-ray (Fig. 3) spectra of the precipitate were compared with those of coumarin, β-cyclodextrin and their mixture. IR absorption spectrum of the mixture, shown in Fig. 1, can be described with those of coumarin and the cyclodextrin. The precipitate has a similar spectrum to that of the mixture, but some differences are observed between them, especially in the region of 900 - 1000 cm^{-1} and 1200 -1300 cm^{-1}.

Fig. 2. shows thermogravimetric (TG) and differential scanning calorimetry (DSC) curves for coumarin, β-cyclodextrin, their mixture, and the precipitate. Coumarin melts at 70°C and easily evaporates   at 180°C (b.p., 297 - 299°C [21]). β-Cyclodextrin seems to dehydrate at 80 - 90°C and degrades at 300°C. The mixture has a characteristic curve showing the melting and evaporating phenomena of coumarin as well as the thermal nature of the cyclodextrin. On the other hand, the precipitate does not melt nor evaporate even at 250°C, as a result of the formation
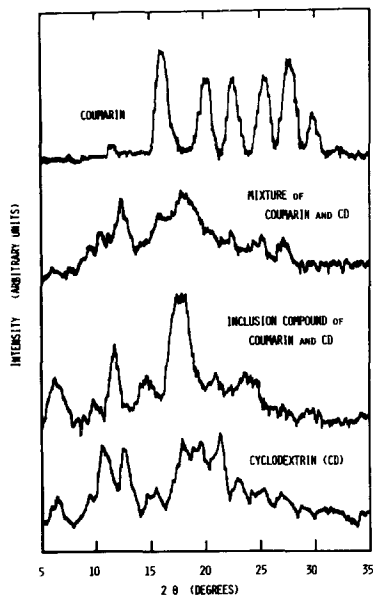

Fig. 3. X-ray diffractograms of powdered samples of coumarin, β-cyclodextrin, their mixture, and the precipitate(the inclusion complex) at 25°C
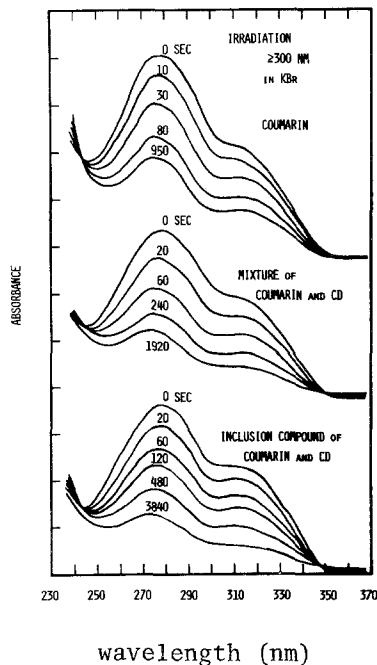

Fig. 4. UV spectra changes of coumarin without or with β-cyclodextrin, and of the inclusion complex on irradiation at wavelength longer than 300 nm

of a complex.

X-Ray diffractogram of the precipitate was compared with those of coumarin, β-cyclodextrin and their mixtrue, as shown in Fig. 3. The diffractogram of the mixture could be described with those of coumarin and the cyclodextrin, while the latter can not explain the spectrum of the precipitate, which should have a different crystal structure from those of coumarin and the cyclodextrin. The elemental analysis and NMR spectrum show the precipitate is composed of 1 mole of coumarin and 1 mole of β-cyclodextrin. This and the data shown in Figs. 1 - 3 indicate that coumarin is fairly strongly bonded to the cyclodextrin to form an inclusion complex at the solid state.

3.2. Solid-State Photoreaction

UV absorption spectra of coumarin with or without β-cyclodextrin and the inclusion complex, and the representative results of photoreaction are shown in Fig. 4. On the irradiation of coumarin with or without the cyclodextrin in KBr pellets at a wavelength longer than 300nm, the UV absorption maximum of coumarin at 280 nm decreased gradually, and finally the spectra were changed into those similar to that of photodimers of coumarin. A similar change of UV absorption spectrum was also observed for the irradiated pellet of the inclusion complex.

The results of typical kinetics of the photoreaction in KBr are plotted in Fig. 5, in which the conversion measured by the relative intensity changes at 312 nm are plotted against the irradition time. The conversion of coumarin increased gradual-
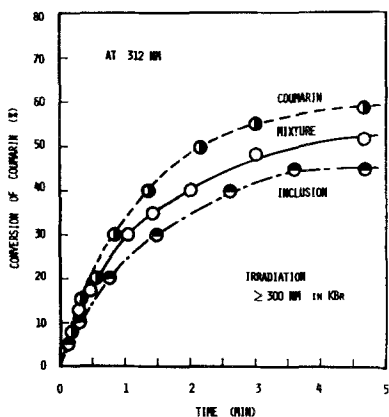

Fig. 5. Kinetics of the photoreaction of coumarin with or without β-cyclodextrin, and the inclusion complex in KBr pellet, measured at 312 nm. The average of the three measurements was used for plot.
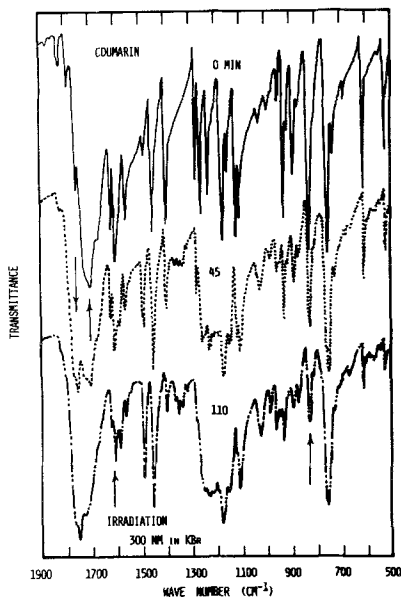

Fig. 6. IR absorption spectrum change of coumarin in KBr on irradiation at a wavelength longer than 300 nm at room temperature.

ly and then reached a constant level in all cases. The relative rate of
photodimerization of coumarin without β-cyclodextrin was found to be
higher than that with the cyclodextrin. The photoreaction of coumarin
in the complex takes place at a much slower rate than in the mixture
    Under these conditions, characteristic infrared absorption bands at
830 and 1610 cm^{-1}, which can be assigned to the out-of-plane hydrogen
deformation mode and to the stretching modes of the carbon-carbon double
bond of olefinic hydrocarbons, respectively, decreased gradually, as
shown in Fig. 6. IR absorption band at 1720 cm^{-1}, which may correspond
to the carbonyl vibrational modes of coumarin, also decreased, while the
similar band at 1760 cm^{-1} due to the carbonyl vibration of a coumarin
photodimer appeared gradually. The IR absorption spectrum of the sample
irradiated for 110 min was almost coincident with that of a head-to-head
dimer of coumarin. Similar changes were found also in the IR absorption
spectra of the irradiated pellets of the mixture and the inclusion com-
plex of coumarin and β-cyclodextrin. Fig. 7 shows changes in IR absorp-
tion spectra of the inclusion complex under irradiation: Absorption
bands at 830, 1560, 1600 and 1720 cm^{-1} gradually decreased, and the band
at 1760 cm^{-1} appeared and increased. These imply that coumarin with or
without β-cyclodextrin and its inclusion complex in the crystals are
converted into a dimer or dimers on irradiation at a wavelength longer
than 300 nm.
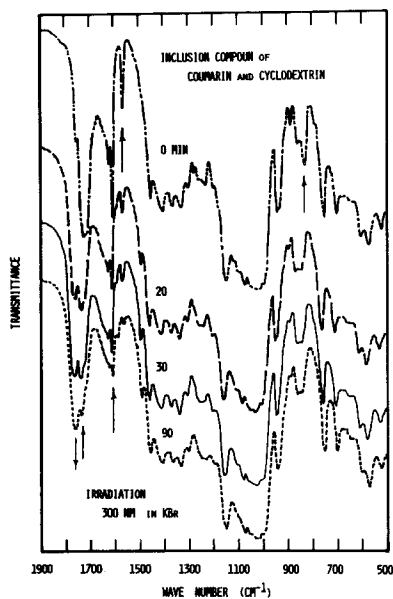   The typical results of the photoreaction kinetics in KBr are shown

Fig. 7. IR absorption spectral
changes of the inclusion complex
in KBr on irradiation at a wave-
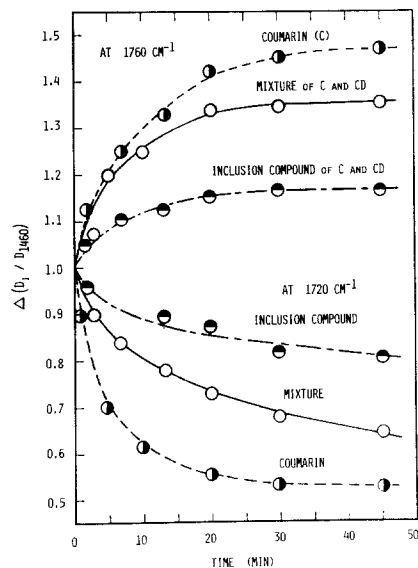length longer than 300 nm at
room temperature.

Fig. 8. Photoreaction kinetics
of coumarin with or without β-cy-
clodextrin and the inclusion com-
plex in KBr, measuring at 1720
and 1760 cm^{-1}.

in Fig. 8, in which the relative intensity changes of 1720 and 1760 cm^{-1} to 1460 cm^{-1}, $\Delta[D(1720)/D(1460)]$ and $\Delta[D(1760)/D(1460)]$, are plotted against the irradiation time. The relative intensity changes of 1720 and 1760 cm^{-1} decreased and increased, respectively, gradually and then reached a constant level in all cases. The relative rate of photoreaction of coumarin without β-cyclodextrin was found to be higher than that with the cyclodextrin. The photodimerization of coumarin in the inclusion complex takes place at a much slower rate than that in the mixture. This suggests that the cyclodextrin retards the photoreaction of coumarin at the solid state.

Krauch and his co-workers [14] have reported the photocleavage of trans-head-to-head dimer to coumarin in dioxane by irradiation at a wave length shorter than 310 nm. In the experiment to confirm this, irradiation of chloroform solutions of trans- and cis-head-to-head dimers of coumarin with monochromatic light of 277 nm gave the original coumarin as a sole product in high yield. Then, the irradiated pellets of coumarin with or without β-cyclodextrin and the inclusion complex were dissolved in chloroform and the solutions were irradiated at 277 nm, resulting in the formation of monomer coumarin in all cases. In Fig. 9 is shown a gradual change of the UV absorption spectrum of a chloroform solution of the irradiated inclusion complex during irradiation at 277 nm. The apparent photocleavage rate decreased with the irradiation time because the absorption band of coumarin produced overlaps with that of the dimer. Thus, the yield of coumarin attains a maximum of only about 60 % under the present experimental conditions.

In order to obtain more amounts of the photoproduct, a suspension of
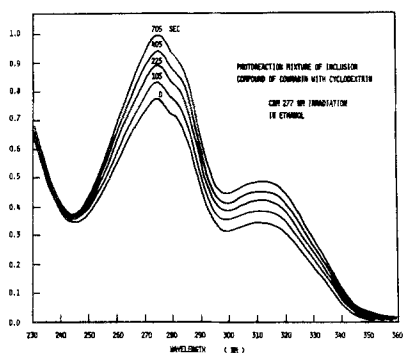

Fig. 9. UV absorption spectral change in photocleavage of the photoproduct(dimer) of the inclusion complex into coumarin by irradiation with light of 277 nm at 25°C.
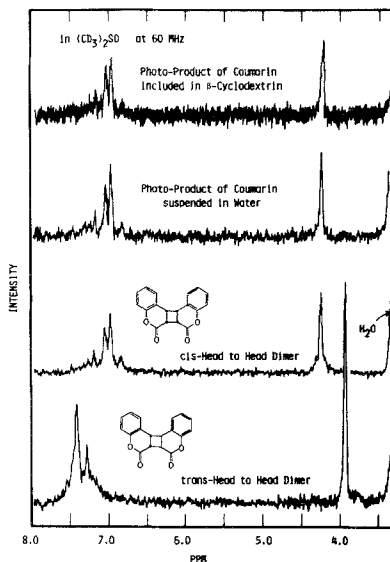

Fig. 10. Proton NMR spectra in DMSO-d$_6$ of trans- and cis-head-to-head dimers and photoproducts from the solid coumarin and inclusion complex at 25°C. TMS is used as the internal reference.

coumarin in water was irradiated at a wavelength longer than 300 nm with a 450-W high pressure mercury lamp. The crystalline powders of the mix-ture of coumarin and β-cyclodextrin, and of their inclusion complex were spread over   a plate in form of thin layer and then irradiated with a 500-W xenon lamp. Reaction mixtures were extracted with chloroform from the irradiated inclusion complex, and the photoproduct was isolated by extraction of unchanged coumarin with diethyl ether from the powdery reaction mixtures.

In Fig. 10, are shown the proton NMR spectra of trans- and cis-head-to-head dimers, and photoproducts from the mixture and the complex, men-tioned above. The spectra of the photoproduct show the peaks of protons attached to the cyclobutane ring near 4.2 - 4.3 ppm. Comparison with the spectra of the authentic dimers suggests that the photoproducts of coumarin with or without β-cyclodextrin, and of the complex, obtained in the solid, are different from trans-head-to-head dimer which has the peaks of protons attached to the cyclobutane ring near 3.7 - 3.9 ppm, but the cis-dimer. The corresponding proton peaks of the latter are found to appear near 4.2 - 4.3 ppm.

The quantum yields for the dimerization of coumarin with or without and the inclusion complex were measured. The quantum yield, Ψ, is de-fined by the equation: $\Psi = -[d(\text{coumarin})/dt]/I(\text{abs})$
where $-[d(\text{coumarin})/dt]$ is the disappearing rate of coumarin per unit of volume, and $I(\text{abs})$ is the rate at which the incident light is absorbed per unit of volume of a pellet containing the sample. The former was estimated by measuring the intensity changes at 312 nm in the UV spectra or at 1720 and 1760 cm^{-1} to 1460 cm^{-1} in the IR spectra of the samples during irradiation at 304 $\pm$ 10 nm.

UV and IR absorption coefficients of coumarin were exactly deter-mined from the calibration curves of the intensity vs. the reactant con-centration in the pellets. $I(\text{abs})$ could not be precisely evaluated be-cause of the ambiguity in the amount of scattered light, and should be equal to the intermediate value between two extreme ones calculated on the assumption that the scattered light is either all lost or not lost at all [22]. The extreme values are calculated as the difference bet-ween the intensity of the radiation transmitted through a pure KBr pe-let [I(KBr)] and a pellet containing the sample [I(samp)] in the former case, and between the incident light intensity (Io) and I(samp) in the latter case. I(KBr) was about 80 - 90 % of Io at 312 nm under these conditions. The substitution of the upper limit of $I(\text{abs})$, Io - I(samp) in the denominator of the equation gives the quantum yield at the low limit, and vice versa.

The initial quantum yields for the dimerization at the lower limit are 0.5, 0.3 and 0.2 without and with β-cyclodextrin, and in the cavity of the cyclodextrin at the solid state, respectively, at 312 nm. This indicates that these photodimerizations all belong to one and the same type of reaction and they proceed more efficiently than that in solution : The quantum efficiencies for formation of cis- and trans-head-to-head dimers were determined as 4.4 X 10^{-4} in acetonitrile; and 4.4-35 X 10^{-4} in various solvents such as acetonitrile, dioxane and carbon tetrachlo-ride, respectively [17]. The reason for the difference between the quantum yields in the solid and the solutions [15,17] could not be ex-

plained until more detailed studies on the photochemical behavior and the crystal structures of coumarin and its inclusion complex are made.

If association species such as ground-state complexes were suggested to be involved in the dimerization mechanism for coumarin, the rate and the product yield would require that association be much more favored in the solid coumarin than in the inclusion complex, which may be more favorable for the aggregation than the isotropic solution.

Ramasubbu, et al. [23] have recently reported that photodimerization of 7-methoxycoumarin occurs in the solid state to give high yield of a syn- or cis-head-to-tail dimer although the potentially reactive double bonds are not favorably oriented in the crystal of the monomer. This seems to show one of the few instances where simple crystal engineering principles [24] do not hold. Formation of cis-head-to-head dimer at the solid state without β-cyclodextrin is coincident with the results of Schönberg, et al. [18] and Anet [11] but inconsistent with that of Ramasubbu et al. [23] who reported that coumarin itself was photostable in the solid state. Morrison et al. [15] observed that irradiation of solid coumarin, deposited from dichloromethane, le d to a larger conversion to trans- than cis-head-to-head dimer, even though frozen solutions produced [14] good yields of cis-head-to-head dimer. These may indicate the distribution of the photoproducts could be described to be state and crystalline structure dependent. β-Cyclodextrin exerts a dramatic influence on the efficiency of dimerization, but play little or no role in determining the stereochemical course of the photoreaction of coumarin in solid state with or without KBr matrix.

4. REFERENCES

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