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The Novel Syntheses of Photoreversible Cyclobutanocrown Ethers by the Intramolecular Photoaddition of α,ω-Dicinnamoyl Polyethylene Glycol Derivatives

Sadatoshi AKABORI,* Yoichi HABATA, Misako NAKAZAWA, Yoko YAMADA, Yoichi SHINDO,
Tokuko SUGIMURA, and Sadao SATO†
Department of Chemistry, Faculty of Science, Toho University, Funabashi, Chiba 274
†Analytical and Metabolic Research Laboratories, Sankyo Co. Ltd., Hiromachi, Shinagawaku, Tokyo 140
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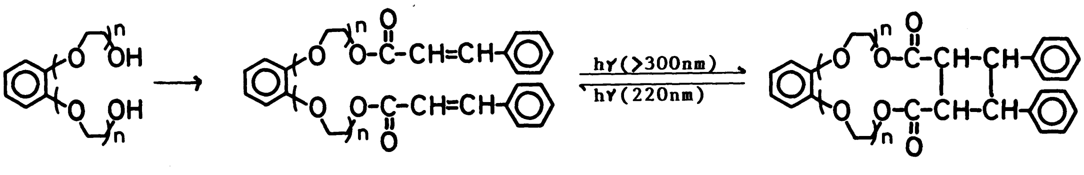
Synopsis. Irradiation of a solution of dicinnamates of *o*-bis(3-hydroxy-1-oxapropyl)benzene and *o*-bis(6-hydroxy-1,4-dioxahexyl)benzene in methanol by Pyrex-filtered UV light gave the corresponding intramolecular pseudophotodimerized crown ethers, and irradiation of the crown ethers in methanol by 220 nm UV light gave the open chain starting dicinnamates in reverse. The structures of the isolated crown ethers were confirmed to be δ-form by the ^{1}H NMR spectra and X-ray analysis.

It is well-known1) that crown ethers can be complexed with alkali, alkaline earth, and other metal cations, despite the poor complexing abilities of the corresponding open chain polyethers. Recently, several kinds of photoresponsive crown ethers have been reported by Shinkai et al.2) and Osa et al.3) For example, the alkali cation-binding abilities of benzocrown ethers containing azo group were enhanced by photoirradiation.2) There are many reports on the photodimerization of cinnamic acid and its derivatives.4) Furthermore, intramolecular photocycloaddition has received attention from the synthetic viewpoints of crown ethers. For example, Mizuno et al.5) obtained cyclobutanocrown ethers (cyclobutane-fused crown ethers) by intramolecular photocycloaddition of the bis(vinyloxy) compounds using a sensitizer. Recently, Egerton et al.6) have suggested that photodimerization of the ethyl cinnamate in solution gives a cyclodimer in high yield. It was further reported that, on irradiation of 210 nm UV light, the cyclodimer regenerated the starting monomer. In connection with the above results, the preparation of polymers having both crown ether moiety as a cation binding site and a cinnamic acid ester moiety as a photodimerizable pendant group has been recently reported by Shirai et al.7) They showed that, in 310 nm UV light, the cinnamoyl groups of these polymers caused dimerization in a dilute solution and the cation extraction abilities of the photoreacted polymers were higher than those of the original polymers. Also, Kimura et al.8) and Hiratani et al.9) reported the preparation of the cyclobutanocrown ethers by photoirradiation of the dicinnamates of the polyethylene glycol derivatives. These findings suggest that dicinnamates of polyethylene glycol and their homologs in solution could be cyclized by intramolecular additions in 310 nm light; then, in 210 nm UV light, the cyclized crown ethers could possibly give the corresponding open chain dicinnamates in reverse. Therefore, the extraction abilities of the crown ether could be controlled by photoaddition. However, these authors did not describe the reversible photocleavage of the cyclobutanocrown ethers. We therefore in this paper report on the syntheses of cyclobutanocrown ethers by intramolecular photocycloaddition of the polyethylene glycol derivatives and their photoreversible reaction.

Catechol (**1a**) reacted with cinnamoyl chloride in the presence of pyridine in benzene to give **2a** in 57.3% yield. Also, the dicinnamates **2b** and **2c** were obtained in 61% yields, respectively by the reaction of cinnamic acid with **1b** and **1c** in the presence of a catalytic amount of *p*-toluenesulfonic acid in benzene.

Irradation of methanol solutions (1 dm^3) of **2b** and **2c** (4×10^{-4} mol) with a 450W high-pressure mercury lamp through a Pyrex filter gave **3b** and **3c** in 27 and 41% yields, respectively. However, **3a** could not be isolated from the photoirradiated products. The thin-layer chromatography of the reaction mixture of **2a** or **2c** showed the presence of several products. However, in both cases, the products, which may be isomers of **3a** or **3c**, could not be separated because of their negligible amounts.

Template-typed photoreaction was also determined, however the yields of **3** were not improved. In the ^{1}H NMR spectra of **3b** and **3c**, the aromatic protons caused by the phenyl moieties shifted upfield (ca. 0.11 ppm), compared with those of the starting materials. Kuzuya et al.10) reported that the signals of the phenyl protons in the δ-truxinate of polymethylene dicinnamates were shifted upfield about 0.13 and 0.35 ppm, compared with those of the starting dicinnamates, respectively. Therefore, there was an upfield shift of ca. 0.11 ppm of the signal of the phenyl moieties when going from the dicinnamates



1a: n=0
1b: n=1
1c: n=2

2a: n=0
2b: n=1
2c: n=2

3a: n=0
3b: n=1
3c: n=2

(**2b** and **2c**) to the crown ethers (**3b** and **3c**). Furthermore, the discovery of the coupling constant (ca. 5.7 Hz) between the Ha and Hb in the cyclobutane ring of **3b** and **3c** is also supported by the above results. Also, the hydrolysis of **3b** and **3c** with dil hydrochloric acid gave δ-truxinic acid quantitatively.[8] In addition, irradiation of **3b** and **3c** with 220 nm UV light gave the starting dicinnamates quantitatively.

In order to investigate in more detail, photocycloaddition was carried out at a concentration of 4×10^{-5} mol dm^{-3} of **2a**—**c** in methanol. These results showed the relationship between the lengths of oxyethylene units and formation rates of photocycloaddition. In specific results, the rate of the decrease of the absorption at 275 nm of the dicinnamates was in the following order (min): **2b**(98.7)>**2c**(105.9)>**2a** (590.7). This finding is explicable when the length of the oxyethylene units in the dicinnamates is considered, because the overlapping of two cinnamoyl groups in **2b** could easily occur due to their suitable bond lengths compared with the longer and shorter chain units of **2c** and **2a**, respectively, although other influences cannot be ruled out.

Photocleavage of **3b** and **3c** was carried out in acetonitrile under irradiation at 220nm UV light using a grating monochromator with a 500W xenon lamp. The solution was measured by UV-VS spectra at appropriate intervals. The absorption band at 275 nm increased with UV irradiation of the solution and a steady state was attained within 7 h. The photoreversible cleavage of **3b** and **3c** proceeded to give **2b** and **2c** in 40 and 60% yields, respectively.

Measurement of the extraction ability was carried out by the method described in a previous paper.[11] The extraction abilities of the compounds **2a**—**c**, **3b**, and **3c** toward alkali metal cations were very low or negligible in values. Also, the differences in the extraction abilities between the **2** and **3** could not be observed in all cases. The low extraction ability of the dicinnamates **2** is explicable by the large steric repulsion between the two terminal cinnamoyl groups when a guest cation is surrounded by the oxygen atoms of the host molecule. Also, the distortion of the structure of the macrocyclic moiety as well as the presence of the ester moiety in **3** seems to be the reason for their low extraction abilities. Therefore, **3b** was further characterized by X-ray crystallographic study. The conformation of **3b** is illustrated in Fig. 1, which also shows the atom labels used. The result confirmed the δ-configuration of the toluxinate moiety in **3b**, indicating that the cyclobutane structure bearing two ester groups largely distorts the macrocyclic structure as shown in Fig. 1. The distances between O(5)–O(15), O(2)–O(15), and O(2)–O(12) are 3.819(5), 3.515(4) and 4.379(4) Å, respectively, although the distances between O(2)–O(5) (2.844(5) Å), O(12)–O(15) (2.740(4) Å) are better located to form the complex. The conformation and the long distances (3.819, 3.515, and 4.379 Å) between those oxgen atoms of the macrocyclic moiety are disadvantageous for forming the complex with a guest cation.

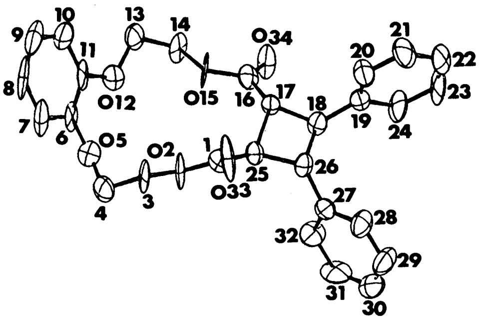


Fig. 1. ORTEP drowing of the molecular structure of **3b**.

In conclusion, the complexing abilities of the cyclobutanocrown ether **3b** with alkali metal cation were decreased by the two factors of long distances between the oxygen atoms of the ether linkage and the presence of the ester moieties in the macrocyclic polyether part. However, the photoreversible reaction between **2** and **3** suggests the possibility of its use as photoresponsive crown ether.

Experimental

The melting points are uncorrected. The ^{1}H NMR spectra were obtained on Hitachi R-90 and GEOL GX400 spectrometers, with TMS as an internal standard. The UV spectra were obtained on a Hitachi 330 Spectrometer. The IR spectra were measured on a JASCO IRA-2 Diffraction Grating Infrared Spectrometer. For irradiation of **2** on a preparative scale, a solution charged in a vessel fitted with a Pyrex cooling jacket was purged with dry nitrogen for 10 min and internally irradiated with an Ushio High-pressure mercury lamp (HPL) (UM-452). Also, photocleavage of **3** to **2** was carried out by means of a 220 nm UV light using a grating monochromater (Model JASCO CT-10) with a 500 W xenon lamp(JASCO PS-X500) and 0.5 nm band width.

2a. Dry pyridine (40 cm^3) was added dropwise to a solution of chatechol (1.65 g, 15 mmol) and cinnamoyl chloride (5.0 g, 30 mmol) in benzene (100 cm^3) and the mixture was stirred for 3 h at room temperature. Water (100 cm^3) was then added dropwise to the mixture, and an aqueous layer was separated. The organic layer was then washed with dil hydrochloric acid, water, 10% aq sodium hydrogencarbonate solution and water, and then dried over anhyd. sodium sulfate. After evaporation of the solvent under reduced pressure, the residue was recrystallized from ethanol to give **2a** as colorless crystals in 57.3% yield. Mp 123.5—124.5 °C. Found: C, 77.80, H, 4.99%. Calcd for $C_{24}H_{18}O_4$: C, 77.82, H, 4.90%. MS (70 eV) *m/z* 370 (M$^+$). IR(KBr) 1720 cm^{-1} (C=O). UV (in MeOH) 275 nm (ε 9000). ^{1}H NMR (CDCl$_3$) δ=6.58 (d, *J*=16.0 Hz, 2H, C$_\alpha$–H), 7.86(d, *J*=16.0 Hz, 2H, C$_\beta$–H), 7.58—7.31 (m, 10H, aromatic H), and 7.31(s, 4H, aromatic H).

2b. A solution of **lb** (0.68 g, 3.5 mmol), cinnamic acid (2.1 g, 14 mmol), and a trace of *p*-toluenesulfonic acid in toluene (80 cm^3) was refluxed for 26 h. The reaction mixture was cooled to room temperature and washed with a 0.01% aq sodium hydroxide solution and water, and then evaporated. The residual solid was recrystallized from hexane to give **2b** as colorless needles in 61% yield. Mp 59.0—59.5 °C. Found: C, 73.03, H, 5.86%. Calcd for $C_{28}H_{26}O_6$: C, 73.35, H, 5.72%. MS (70 eV) *m/z* 458 (M$^+$). UV (in MeOH) 277 (ε 49000). IR (KBr) 1720 cm^{-1} (C=O). ^{1}H NMR (CDCl$_3$) δ=4.64—4.25 (m, 8H, CH$_2$), 6.45 (d, *J*=16.0 Hz, 2H, C$_\alpha$–H), 7.69 (d, *J*=16.0 Hz, 2H, C_β–H), 7.48—7.32 (m, 10H, aromatic H), 6.98 (s, 4H, aromatic H).

2c. A solution of **1c** (1.03 g, 3.64 mmol), cinnamic acid (2.16 g, 15 mmol) and a trace of *p*-toluenesulfonic acid in toluene (80 cm^3) was refluxed for 44 h. The reaction mixture was cooled, evaporated in vacuo and the residue was dissolved in chloroform. The solution was washed with a 10% aq sodium hydrogencarbonate solution and water, and evaporated. The residue was chromatographed on silica gel using a benzene–acetone (12:1) solution as an eluent. The evaporation of the second fraction gave **2c** as pale yellow viscous oil in 61.0% yield. Found: C, 70.12, H, 6.33%. Calcd for $C_{32}H_{34}O_8$: C, 70.31, H, 6.27%. MS (70 eV) m/z 546 (M^+). IR (KBr) 1720 cm^{-1} (C=O). UV (in MeOH) 277 nm (ε 49000). ^{1}H NMR ($CDCl_3$) δ=4.45—4.10 (m, 8H, CH_2), 3.95—3.72 (m, 8H, CH_2), 6.45 (d, J=16.0 Hz, 2H, C_α–H), 7.70 (d, J=16.0 Hz, 2H, C_β–H), 7.52—7.32 (m, 10H, aromatic H), 6.92(s, 4H, aromatic H).

Irradiation of 2b. Dicinnamate **2b** (0.137 g, 0.3 mmol) dissolved in methanol (1 dm^3) was irradiated internally with HPL (450 W) through a Pyrex filter at running water temperature for 5 h. The solvent was evaporated and the residue was recrystallized from methanol resulting in **3b** as colorless crystals. Yield 20%, Mp 142.0—143.0 °C. Found: C, 73.05, H, 5.68%. Calcd for $C_{28}H_{26}O_6$: C, 73.33, H, 5.72%. MS (70 eV) m/z 458(M^+). UV (in MeOH) 275 nm (ε 2300); ^{1}H NMR ($CDCl_3$) δ=7.29 (s, 10H), 6.97 (s, 4H), 4.92—4.50(m, 2H), 4.50—4.03 (m, 6H), 4.00—3.80 (m, 2H), 3.50—3.31 (m, 2H).

Irradiation of 2c. Dicinnamate **2c** (0.109 g, 0.2 mmol) dissolved in methanol (1 dm^3) was irradiated as described above. After irradiation, the solvent was evaporated. An oily residue was chromatographed on silica gel. Elution with benzene–ethyl acetate (4:1) gave pure **3c** as an oily product. Yield 24%. Found: C, 69.93, H, 6.40%. Calcd for $C_{32}H_{34}O_8$; C, 70.30, H, 6.28%. MS (70 eV) m/z 546 (M^+). UV (in MeOH) 275 nm (ε 2400), ^{1}H NMR($CDCl_3$) δ=7.28 (s, 10H), 6.91 (s, 4H), 4.57—4.01 (m, 8H), 4.01—3.58 (m, 10H), 3.53—3.36 (m, 2H).

Irradiation of 3b and 3c. An acetonitrile solution of **3** (ca. 2.0×10^{-5} mol dm^{-3}) was placed in a quartz cell (1×1×4 cm) and was irradiated at room temperature with a 220 nm UV light for 6—7 h. The UV spectra during irradiation were recorded with a Hitachi 330 spectrometer. The photoreversible yields of **2b** and **2c** were calculated from the intensity of the absorption band at 275 nm in the stead state. After irradiation, the solvent was evaporated in vacuo and the residue was chromatographed on silica-gel TLC using chloroform as an eluent. The main fraction was extracted with chloroform and the solution was then evaporated in vacuo to give **2c** or **2b**. The structures of **2b** and **2c** were confirmed by comparison with R_f values of TLC, the melting point (for **2b**) and spectral data of the authentic samples.

Hydrolysis of 3b and 3c. A solution of **3b** (0.107 g, 0.23 mmol) in methanol (20 cm^3) containing dil hydrochloric acid (10 cm^3) was refluxed for 4.5 h. After the solution has been cooled to room temperature, aq sodium hydroxide solution was added. The resulting alkaline solution was extracted with chloroform. To the aqueous solution was added dil hydrochloric acid until it became acidic and then the solution was extracted with chloroform. The extract was dried over anhyd. sodium sulfate and concentrated. To the residue was added an ether solution (50 cm^3) of diazomethane. Evaporation of the solvent gave dimethyl δ-toluxinate in 33% yield. Mp 78.0—79.5 °C(lit,[12] 77 °C). ^{1}H NMR (in $CDCl_3$) δ=7.24 (s, 10H), 3.94—3.29 (m, A_2B_2 pattern, 4H), 3.82 (s, 6H).

δ-Toluxinate was also obtained from **3c** by the same method.

X-Ray Crystallography. Crystal of dimensions 0.4×0.2×0.1 mm was used for the X-ray crystallography. Crystal data are as follows: $C_{28}H_{26}O_6$, Mw=450.5. Monoclinic, $P2_1/n$, a=19.325(5), b=5.323(1), c=22.838(5) Å, β=95.14(2)°, U=2339.9 Å^3, Z=4, Dx=1.30 g cm^{-3}, ν(Cu $K\alpha$)=7.6 cm^{-1}. Intensity data for $2\theta\leqslant128°$ were recorded on a Rigaku AFC-5R with graphite monochromatized Cu$K\alpha$ radiation. A total of 3898 independent reflections were corrected for Lorentz and polarization factors but not for absorption. The structure was solved by direct methods using MULTAN84,[13] and refined by block diagonal least-squares methods. The positions of the hydrogen atoms were estimated using standard geometry. The final refinements with anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms were lowered R values 0.079 (R_w=0.050, $w=1/\sigma^2(F_o)$, 2646 observed reflections with $F_o\geqslant2\sigma(F_o)$). Parameters for bond lengths, angles and structure factors (observed and calculated) are kept at the Chemical Society of Japan (Document No.8751).

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