

HETEROCYCLES, Vol. 85, No. 10, 2012, pp. 2531 - 2541. © 2012 The Japan Institute of Heterocyclic Chemistry  
Received, 24th July, 2012, Accepted, 29th August, 2012, Published online, 11th September, 2012  
DOI: 10.3987/COM-12-12554

## ONE-POT SYNTHESIS OF MACROCYCLIC TETRALACTONES VIA THE SEQUENTIAL INTER- AND INTRAMOLECULAR [2+2] PHOTOCYCLOADDITION REACTIONS OF DI-2-PYRONES WITH POLYETHYLENE GLYCOL DIMETHACRYLATES

Tetsuro Shimo,\* Hideki Matsukubo, and Hui Min Zhang

Department of Chemistry, Biotechnology and Chemical Engineering, Graduate School of Science and Engineering, Kagoshima University, Korimoto 1-21-40, Kagoshima 890-0065, Japan

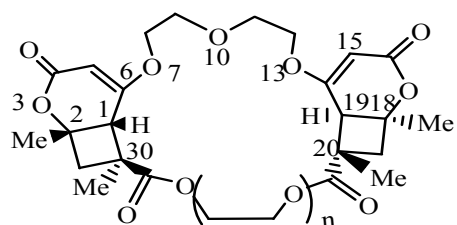
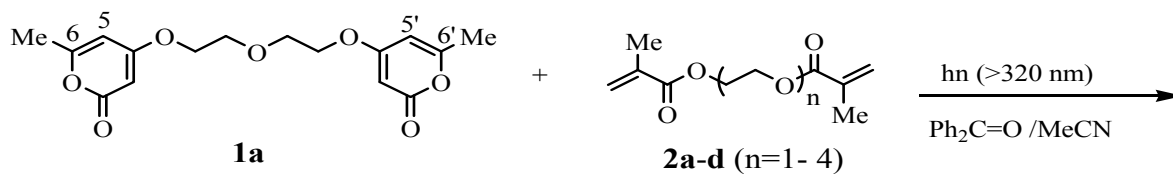
**Abstract** – The sensitized photocycloaddition reactions of 6,6'-dimethyl-4,4'-[1,7-(1,4,7-trioxaheptyl)]-di-2-pyrone (**1a**) and 6,6'-dimethyl-4,4'-[1,10-(1,4,7,10-tetraoxadecyl)]-di-2-pyrone (**1b**) with polyethylene glycol dimethacrylates (**2a-d**) afforded macrocyclic tetralactones containing two cyclobutane rings. The reactions of **1a** with **2a-d** afforded diastereomixtures of macrocyclic crown ether-type structures (**3a-d** and **3a'-d'**) possessing 19- to 28-membered rings across the C5-C6 and C5'-C6' double bonds of **1a**. Similarly, **1b** reacted with **2a-d** to give the corresponding 22- to 31-membered-ring products (**4a-d** and **4a'-d'**). A structure for the key intermediate involved in the formation of compounds **3** and **4** has been proposed.

Significant efforts have been focused on the development of efficient general strategies for the synthesis of macrocyclic ring systems, including thermally and photochemically driven cyclization, capping, and condensation reactions,<sup>1,2</sup> because macrocyclic compounds are involved in natural products and artificial substrates and represent an important area of organic chemistry. The photochemical [2+2] cycloaddition reaction has been used effectively for the synthesis of a variety of macrocyclic compounds containing one or two cyclobutane rings.<sup>3</sup> Recently, we successfully developed a one-pot synthesis of macrocyclic lactones via the sequential inter- and intramolecular [2+2] photocycloadditions of di-2-pyrones with

$\alpha,\omega$ -diolefins.<sup>4</sup> Furthermore, we used MO analysis to clarify the origin of a remarkable change in the regioselectivities of the inter- and intramolecular photocycloaddition reactions.<sup>5,6</sup> We planned to extend this one-pot synthesis of macrocyclic lactones to di-2-pyrone units tethered to each other with ethylene glycol linkers (**1a,b**) to investigate the generality of this sequential inter- and intramolecular photoreaction process with electron-poor  $\alpha,\omega$ -diolefins (**2a-d**). Furthermore, we wanted to explore the potential for controlling the ring-size in the resulting systems.

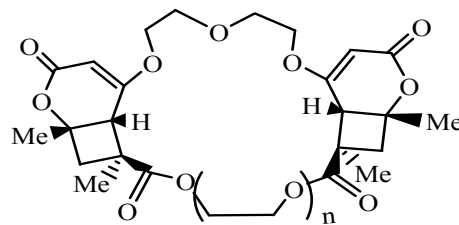
The di-2-pyrones (**1a** and **1b**) were prepared by the dehydrochlorination of 4-hydroxy-6-methyl-2-pyrone with bis(2-chloroethyl) ether and 1,2-bis(2-chloroethoxy)ethane in 57% and 66% yields, respectively, using 1,8-diazabicyclo[5.4.0]-7-undecene. A solution of **1a** and diethylene glycol dimethacrylate (**2b**) in acetonitrile in the presence of benzophenone (sensitizer) was irradiated with a 300 W high-pressure mercury lamp using a UV cutoff filter of less than 320 nm, under a nitrogen atmosphere. The reaction was followed by TLC analysis and required 6 h of irradiation to allow for complete consumption of the starting material **1a**. Compound **2b** polymerized under the reaction conditions and the addition of two equivalents was required to mitigate these losses. Upon completion of the reaction, the solvent was removed *in vacuo* and the resulting oily residue chromatographed on silica gel (eluent: ethyl acetate:hexane = 2:1, v/v) to afford a 1:1 mixture of **3b** and **3b'** (5,6- and 5',6'-[2+2] cycloadducts) in 26% yield (Scheme 1 and Table 1, entry 2) and product **5** (intramolecular [2+2] cycloadduct of **1a**) in 2% yield, together with a complex mixture that we were unable to isolate. The macrocyclic compounds **3b** and **3b'** were determined to be the major products by <sup>1</sup>H NMR analysis of the reaction mixture.

Although compound **3b** was isolated by recrystallization of the product mixture from ethanol, it was difficult to obtain the material as a single crystal. The structure of **3b** was estimated to be the regioselective [2+2] cycloadduct, 2,18,20,30-tetramethyl-3,7,10,13,17,22,25,28-octaoxapentacyclo-[28.1<sup>2,30</sup>.1<sup>18,20</sup>.0.0<sup>1,6</sup>.0<sup>14,19</sup>]triaconta-5,14-dien-4,16,21,29-tetraone (20-*exo*, 30-*exo* adduct, C<sub>2</sub> symmetry), based on a comparison of its <sup>1</sup>H NMR spectrum with those from similar macrocyclic structures (**6** and **6'**) previously described in the literature (Figure 1).<sup>6</sup> That is, the chemical shifts of the cyclobutane protons of **3b** showed similar values to those of the compound **6** (**3b**:  $\delta$  2.31, 2.73 (CH<sub>2</sub>), 3.42 (CH); **6**:  $\delta$  2.32, 2.64 (CH<sub>2</sub>), 3.45 (CH)). Product **3b'** was characterized as the facially selective isomer (C<sub>s</sub> symmetry) from the addition of the C5-C6 and C5'-C6' double bonds of **1a** to those in **2b** because it possessed NMR spectral properties similar to those of compound **3b**.



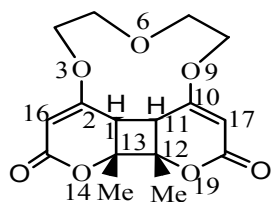
$C_2$  symmetry

**3a**:  $n=1$  (12.5%)  
**3b**:  $n=2$  (13%)  
**3c**:  $n=3$  (12%)  
**3d**:  $n=4$  (12%)

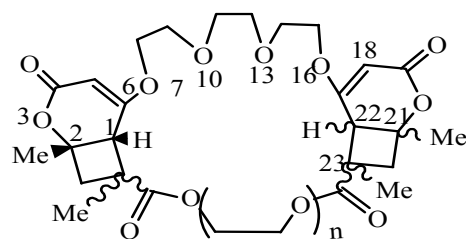
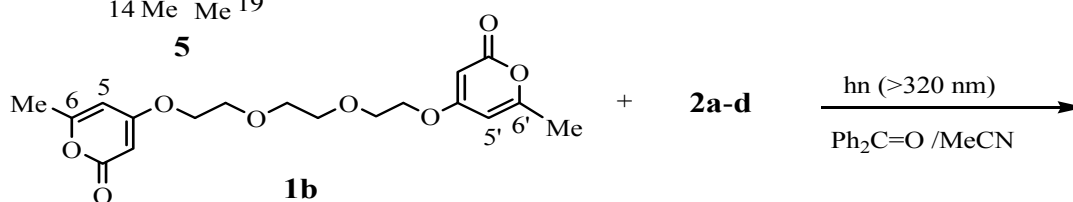


$C_s$  symmetry

**3a'**:  $n=1$  (12.5%)  
**3b'**:  $n=2$  (13%)  
**3c'**:  $n=3$  (12%)  
**3d'**:  $n=4$  (12%)

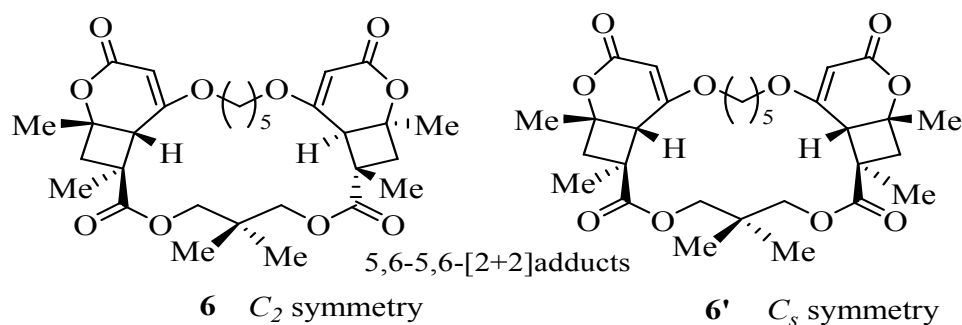


**5**

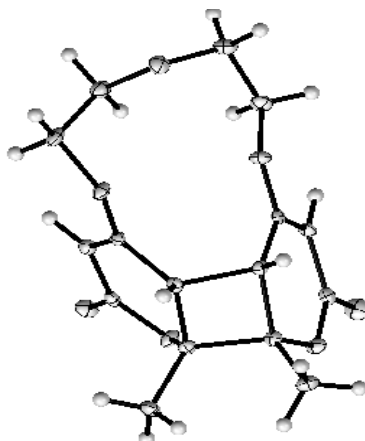


**4a**:  $n=1$  (9.5%), **4a'**:  $n=1$  (9.5%)  
**4b**:  $n=2$  (9.5%), **4b'**:  $n=2$  (9.5%)  
**4c**:  $n=3$  (9.5%), **4c'**:  $n=3$  (9.5%)  
**4d**:  $n=4$  (5.5%), **4d'**:  $n=4$  (5.5%)

**Scheme 1**



**Figure 1.**



**Figure 2.** ORTEP drawing of **5**

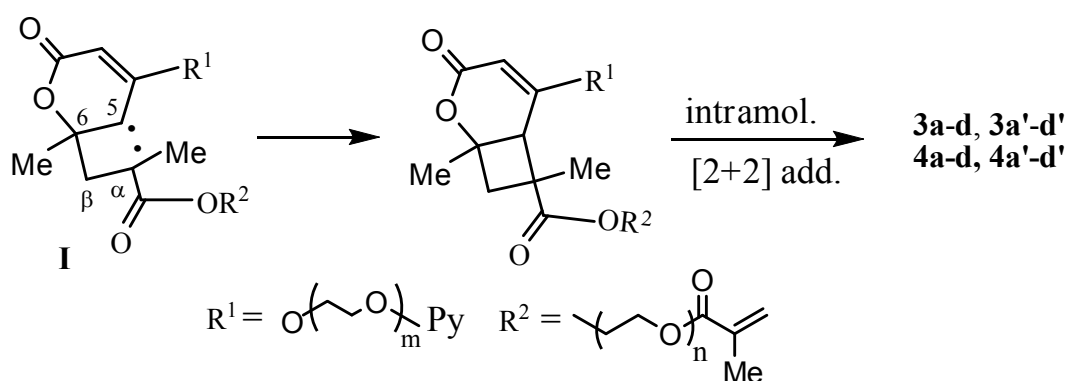
The structure of product **5** was confirmed by X-ray crystallographic analysis to be the intramolecular [2+2] cycloadduct of **1a**, 12,13-dimethyl-3,6,9,14,19-ntaoxatetracyclo[9.3<sup>2,13</sup>.3<sup>10,12</sup>.2.0]nanodecan-2(16), 10(17)-dien-15,18-dione (syn head-to-head adduct), which was formed by addition across the C5-C6 and C5'-C6' double bonds of **1a** (Figure 2). The results of the similar photoreactions of **1a** with **2a**, **c**, and **d**, and **1b** with **2a-d** are summarized in Table 1. Unfortunately, despite the screening of many different crystallization conditions, the mixtures of the other [2+2] cycloadducts (**3a/3a'**, **3c/3c'**, **3d/3d'**, **4a/4a'**, **4b/4b'**, **4c/4c'**, and **4d/4d'**) could not be separated from each other.

**Table 1.** The photoreaction of the di-2-pyrones (**1a** and **1b**) with diolefins (**2a-d**)

Entry	Di-2-pyrones	Diolefins	Irradiation time (h)	Conversion of <b>1</b> (%) <sup>a</sup>	Product (yield, %) <sup>a</sup>		Ring size	Other product
					5,6-5,6-[2+2] Adducts			
1	<b>1a</b>	<b>2a</b>	6	100	<b>3a</b> (12), <b>3'a</b> (12)	19	-	
2	<b>1a</b>	<b>2b</b>	6	100	<b>3b</b> (13), <b>3'b</b> (13)	22	<b>5</b> (2)	
3	<b>1a</b>	<b>2c</b>	6	100	<b>3c</b> (12), <b>3'c</b> (12)	25	-	
4	<b>1a</b>	<b>2d</b>	12	100	<b>3d</b> (12), <b>3'd</b> (12)	28	-	
5	<b>1b</b>	<b>2a</b>	6	100	<b>4a</b> (9.5), <b>4'a</b> (9.5)	22	-	
6	<b>1b</b>	<b>2b</b>	6	100	<b>4b</b> (9.5), <b>4'b</b> (9.5)	25	-	
7	<b>1b</b>	<b>2c</b>	6	100	<b>4c</b> (9.5), <b>4'c</b> (9.5)	28	-	
8	<b>1b</b>	<b>2d</b>	12	100	<b>4d</b> (5.5), <b>4'd</b> (5.5)	31	-	

<sup>a</sup> Estimated from the NMR spectra using an internal standard (fumaronitrile).

Since these photoreactions were sensitized by triplet sensitizer, they were inferred to go through two-step radical paths via a 1,4-biradical intermediate **I** (Figure 3) because the reactions of **1a** and **1b** with compounds **2a-d** afforded the macrocyclic crown ether-type compounds **3a-d** and **4a-d** by addition of the C5-C6 and C5'-C6' double bonds in **1a** and **1b** to the two olefin moieties in **2a-d**. Furthermore, this suggestion was strongly supported by the MO calculation of the C6 (HSOMO, 2-pyrone)-C $\beta$  (LUMO, olefin) interaction from the consideration of the narrow energy gap and large coefficients of two frontier orbitals between 2-pyrone and olefin.<sup>6</sup>



**Figure 3.** Intermediate structure

The macrocyclic tetralactones, **3** and **4**, containing 19– to 31–membered rings, were obtained from a one-pot synthesis via sequential inter- and intramolecular photocycloaddition reactions. In the <sup>1</sup>H NMR spectra of the compounds, the resonance of the methyl group attached to the cyclobutane ring (20-Me in **3** and **3'**, 23-Me in **4** and **4'**) appeared as two slightly different peaks because of the diastereomixture of the macrocyclic lactones, which contained six asymmetric carbons. For example, in the <sup>1</sup>H NMR spectrum of the 19–membered macrocyclic lactones **3a** and **3a'**, the peaks assigned to the methyl groups at the 20- and 20'-positions appeared at  $\delta$  1.326 and 1.314, respectively ( $\Delta\delta = 0.012$ ). This phenomenon was not present in the larger macrocyclic lactones that contained more than 28 members in their macrocyclic ring system. The data for compounds **3a-d**, **3a'-d'**, **4a-d** and **4a'-d'** are summarized in Table 2.

**Table 2.** Difference in the chemical shifts ( $\Delta\delta$ , ppm) of the two methyl groups (20, 20'-Me and 23, 23'-Me) of the diastereomixtures (**3/3'** and **4/4'**)

Compounds	<b>3a, 3a'</b>	<b>3b, 3b'</b>	<b>3c, 3c'</b>	<b>3d, 3d'</b>
Ring size	19	22	25	28
$\Delta\delta$ (x 10 <sup>3</sup> ppm)	12	8	5	0
Compounds	<b>4a, 4a'</b>	<b>4b, 4b'</b>	<b>4c, 4c'</b>	<b>4d, 4d'</b>
Ring size	22	25	28	31
$\Delta\delta$ (x 10 <sup>3</sup> ppm)	8	2	0	0

Results similar to these were recently reported for macrocyclic compounds containing two fused dihydrofuran rings.<sup>7</sup> It was assumed that other stereoisomers of macrocycles and by-products, such as oxetanes formed from the di-2-pyrones and benzophenone (triplet sensitizer)<sup>8</sup> and inter- or intramolecular [2+2] cycloadducts formed from the di-2-pyrones, must have been formed, because the yields of the macrocyclic tetralactones **3** and **4** were low (11–26%) compared to the high levels of conversion observed for **1a** and **1b**. Furthermore, the intramolecular [2+2] cycloadduct of **1a** (**5**) was isolated.

In summary, the photocycloaddition reactions of polyethylene glycol-di-2-pyrones (**1**) with polyethylene glycol dimethacrylates (**2**) afforded macrocyclic crown ether-type compounds (**3** and **4**) by the [2+2] addition of the C5-C6 and C5'-C6' double bonds of **1** to the two olefin moieties of **2**, generating 19- to 31-membered rings. We have demonstrated that this sequential inter- and intramolecular [2+2] photocycloaddition reaction process is an efficient method for the synthesis of macrocyclic compounds from the reactions of di-2-pyrones with electron-rich or electron-poor  $\alpha,\omega$ -diolefins.<sup>4-6</sup>

## EXPERIMENTAL

All melting points were measured on Yanagimoto Melt-temp apparatus and uncorrected. NMR spectra were measured at 400 MHz on the JNM GSX-400 (TMS as an internal standard). IR spectra were recorded with a JASCO IR Report-100 spectrometer. Mass spectra were recorded with a JEOL JMS-HX110A (FABMS) using *m*-nitrobenzyl alcohol as matrix. Elemental analysis was made using a Yanaco MT-5. Single crystal X-ray diffraction analysis of **5** was performed on a Rigaku RAXIS-RAPID imaging plate diffractometer with graphite monochromated Mo K $\alpha$  radiation. Lorentz and polarization

corrections were applied to the intensity data. The structures were solved by direct methods using SIR 92<sup>9</sup> and refined by a full-matrix least-squares method. The non-hydrogen atoms were refined anisotropically. All calculations were performed using the Crystal Structure crystallographic software package.<sup>10,11</sup> Photoirradiations were carried out in the Pyrex tube using 300 W high-pressure mercury lamp. Wakogel C200 was used for preparative column chromatography.

**6,6'-Dimethyl-4,4'-[1,7-(1,4,7-trioxaheptyl)]-di-2-pyrone (1a)** ..... To a refluxing MeCN (45 mL) solution of 4-hydroxy-6-methyl-2-pyrone (12.7 g, 101 mmol) and DBU (18.4 g, 121 mmol) was slowly added bis(2-chloroethyl) ether (6.0 g, 42 mmol) and refluxing was continued for 40 h. After cooling to room temperature, the reaction mixture was evaporated *in vacuo* and the resulting oily residue was dissolved in CHCl<sub>3</sub> (100 mL). To the concentrate was added acetic acid and water, and the CHCl<sub>3</sub> part was separated. The solution was evaporated to give white solid which was recrystallized from MeCN to afford **1a** (7.72 g, 57%).

**1a**: mp 198 – 200 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.22 (6H, s, Me), 3.86, 4.10 (each 4H, dd, *J* = 4.8, 2.8 Hz, CH<sub>2</sub>), 5.39, 5.81 (each 2H, d, *J* = 2.0 Hz, CH). IR (KBr) 1714, 1645 cm<sup>-1</sup>. LR MS *m/z* 323 (MH<sup>+</sup>). *Anal.* Calcd for C<sub>16</sub>H<sub>18</sub>O<sub>7</sub>: C, 59.62, H, 5.63. Found: C, 59.17, H, 5.66.

**6,6'-Dimethyl-4,4'-[1,10-(1,4,7,10-tetraoxadecyl)]-di-2-pyrone (1b)** ..... **1b** was prepared by a similar method to that of **1a** by using 4-hydroxy-6-methyl-2-pyrone (7.26 g, 57.6 mmol), 1,2-bis(2-chloroethoxy)ethane (4.49g, 24.0 mmol), and DBU (9.65 g, 63.4 mmol). **1b** (5.82 g, 66%).

**1b**: mp 134–136 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.22 (6H, s, Me), 3.70 (4H, s, CH<sub>2</sub>), 3.83, 4.10 (each 4H, dd, *J* = 5.2, 3.2 Hz, CH<sub>2</sub>), 5.40, 5.81 (each 2H, d, *J* = 2.0 Hz, CH). IR (KBr) 1720, 1638 cm<sup>-1</sup>. LR MS *m/z* 367 (MH<sup>+</sup>). *Anal.* Calcd for C<sub>18</sub>H<sub>22</sub>O<sub>8</sub>: C, 59.01, H, 6.05. Found: C, 58.55, H, 6.04.

**2,18,20,27-Tetramethyl-3,7,10,13,17,22,25-heptaioxapentacyclo[25.1<sup>2,27</sup>.1<sup>18,20</sup>.0.0<sup>1,6</sup>.0<sup>14,19</sup>]heptacos-5,14-dien-4,16,21,26-tetraone (3a, 3a')** ..... To a solution of **1a** (0.644 g, 2.00 mmol) with ethylene glycol dimethacrylate (**2a**) (0.793 g, 4.00 mmol) in MeCN (200 mL) was irradiated in the presence of benzophenone (0.364 g, 2.00 mmol) for 6 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc/hexane = 3:1, v/v) to afford a mixture of **3a** and **3a'** (1:1) (0.250 g, 25% yield), whose compounds were difficult to separate each other by recrystallization.

**3a** and **3a'** (1:1 mixture): oil. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.31, 1.33 (each 6H, s, Me), 1.54, 1.55 (each 6H, s, Me), 2.32 (4H, d, *J* = 13.2 Hz, CH<sub>2</sub>), 2.69, 2.70 (each 2H, dd, *J* = 13.2, 2.4 Hz CH<sub>2</sub>), 3.44, 3.48 (each 2H, d, *J* = 2.4 Hz, CH), 3.78 (8H, m, CH<sub>2</sub>), 4.05 (8H, m, CH<sub>2</sub>), 4.36 (4H, m, CH<sub>2</sub>), 4.51 (4H, m, CH<sub>2</sub>), 5.27,

5.28 (each 2H, s, =CH). IR (neat) 1720, 1680, 1620  $\text{cm}^{-1}$ . LR MS  $m/z$  521 ( $\text{MH}^+$ ). HR MS ( $\text{MH}^+$ ) calcd for  $\text{C}_{26}\text{H}_{33}\text{O}_{11}$  521.2023. found: 521.2025.

**2,18,20,30-Tetramethyl-3,7,10,13,17,22,25,28-octaoxapentacyclo[28.1<sup>2,30</sup>.1<sup>18,20</sup>.0.0<sup>1,6</sup>.0<sup>14,19</sup>]triaconta-5,14-dien-4,16,21,29-tetraone (20-*exo*, 30-*exo* adduct) (3b) ( $\text{C}_2$  symmetry), (3b') ( $\text{C}_s$  symmetry) and 12,13-dimethyl-3,6,9,14,19-pentaoxatetracyclo[9.3<sup>2,13</sup>.3<sup>10,12</sup>.2.0]nanodecan-2(16),10(17)-dien-15,18-dione (5) (syn head-to-head adduct)....** To a solution of **1a** (1.29g, 4.00 mmol) with diethylene glycol dimethacrylate (**2b**) (1.93 g, 8.00 mmol) in MeCN (400 mL) (**1a**: 10 mM solution) was irradiated in the presence of benzophenone (0.730 g, 4.00 mmol) for 6 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc/hexane = 2:1, v/v) to afford a mixture of **3b** and **3b'** (1:1) (0.586 g, 26% yield) and **5** (0.128 g, 2% yield). Compound **3b** was separated by recrystallization from EtOH, and compound **5** was recrystallized from a mixture of MeCN and  $\text{CHCl}_3$  (5:1).

**3b**: mp 145–146 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.33, 1.53 (each 6H, s, Me), 2.31 (2H, d,  $J = 13.2$  Hz,  $\text{CH}_2$ ), 2.73 (2H, dd,  $J = 13.2, 2.4$  Hz,  $\text{CH}_2$ ), 3.42 (2H, d,  $J = 2.4$  Hz, CH), 3.73, 3.83, 4.05, 4.22, 4.40 (each 2H, m,  $\text{CH}_2$ ), 5.29 (2H, s, =CH). IR (neat) 1724, 1694, 1623  $\text{cm}^{-1}$ . LR MS  $m/z$  565 ( $\text{MH}^+$ ). *Anal.* Calcd for  $\text{C}_{28}\text{H}_{36}\text{O}_{12}$ ; C, 59.57, H, 6.43. Found: C, 59.63, H, 6.62.

**3b'**: mixture with **3b**.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.31 (6H, s, Me), 1.55 (6H, s, Me), 2.31 (2H, d,  $J = 13.2$  Hz,  $\text{CH}_2$ ), 2.69 (2H, dd,  $J = 13.2, 2.4$  Hz,  $\text{CH}_2$ ), 3.48 (2H, d,  $J = 2.4$  Hz, CH), 3.73, 3.83, 4.05, 4.22 (2H, m,  $\text{CH}_2$ ), 4.40 (2H, m,  $\text{CH}_2$ ), 5.28 (2H, s, =CH).

**5**: mp 206–208 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.54 (6H, s, Me), 3.20 (2H, s, CH), 3.63 (2H, ddd,  $J = 12.4, 9.6, 2.4$  Hz  $\text{CH}_2$ ), 3.93 (2H, dt,  $J = 11.6, 2.4$  Hz,  $\text{CH}_2$ ), 4.08 (2H, dt,  $J = 11.6, 2.4$  Hz,  $\text{CH}_2$ ), 4.19 (2H, ddd,  $J = 12.4, 9.6, 2.4$  Hz  $\text{CH}_2$ ), 5.28 (2H, s, CH). IR (KBr) 1694, 1623  $\text{cm}^{-1}$ . LR MS  $m/z$  323 ( $\text{MH}^+$ ). *Anal.* Calcd for  $\text{C}_{16}\text{H}_{18}\text{O}_7$ : C, 59.62, H, 5.63. Found: C, 59.65, H, 5.65.

X-Ray crystal data for **5** ( $\text{C}_{16}\text{H}_{18}\text{O}_7$ ):  $M = 322.31$ , crystal dimensions  $0.20 \times 0.20 \times 0.20$   $\text{mm}^3$ , monoclinic, space group  $P2_1/n$  (#14),  $a = 8.0978(19)$  Å,  $b = 16.974(4)$  Å,  $c = 10.616(3)$  Å,  $\beta = 90.371(3)^\circ$ ,  $V = 1439.7(6)$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calc}} = 1.487$  g/cm<sup>3</sup>,  $2\theta_{\text{max}} = 55.0^\circ$ ,  $T = -150 \pm 1$  °C,  $R = 0.0948$ ,  $R_w = 0.2593$ , GOF = 1.467. Deposition number CCDC-895655 for compound No. **5**. Free copies of the data can be obtained via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

**2,18,20,33-Tetramethyl-3,7,10,13,17,22,25,28,31-nonaoxapentacyclo[31.1<sup>2,33</sup>.1<sup>18,20</sup>.0.0<sup>1,6</sup>.0<sup>14,19</sup>]tritia-**

**conta-5,14-dien-4,16,21,32-tetraone (3c, 3c')** ..... To a solution of **1a** (0.644 g, 2.00 mmol) with triethylene glycol dimethacrylate (**2c**) (1.11 g, 4.00 mmol) in MeCN (200 mL) was irradiated in the presence of benzophenone (0.364 g, 2.00 mmol) for 6 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc/hexane = 3:1, v/v) to afford a mixture of **3c** and **3c'** (1:1) (0.292 g, 24% yield), whose compounds were difficult to separate each other by recrystallization.

**3c** and **3c'**: (1:1 mixture): oil.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.33, 1.34 (each 6H, s, Me), 1.53, 1.54 (each 6H, s, Me), 2.28 (4H, d,  $J = 13.2$  Hz,  $\text{CH}_2$ ), 2.75, 2.76 (each 2H, dd,  $J = 13.2, 2.0$  Hz  $\text{CH}_2$ ), 3.40 (4H, d,  $J = 2.0$  Hz, CH), 3.63, 3.72, 3.83, 4.05 (each 8H, m,  $\text{CH}_2$ ), 4.23, 4.37 (each 4H, m,  $\text{CH}_2$ ), 5.30, 5.31 (each 2H, s, =CH). IR (neat) 1723, 1698, 1627  $\text{cm}^{-1}$ . LR MS  $m/z$  609 ( $\text{MH}^+$ ). HR MS ( $\text{MH}^+$ ) calcd for  $\text{C}_{30}\text{H}_{41}\text{O}_{13}$  609.2547. found: 609.2582.

**2,18,20,36-Tetramethyl-3,7,10,13,17,22,25,28,31,34-decaoxapentacyclo[34.1<sup>2,36</sup>.1<sup>18,20</sup>.0.0<sup>1,6</sup>.0<sup>14,19</sup>]-hexatriaconta-5,14-dien-4,16,21,35-tetraone (3d, 3d')** ..... To a solution of **1a** (0.644 g, 2.00 mmol) with tetraethylene glycol dimethacrylate (**2d**) (1.32 g, 4.00 mmol) in MeCN (200 mL) was irradiated in the presence of benzophenone (0.364 g, 2.00 mmol) for 12 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc/hexane = 3:1, v/v) to afford a mixture of **3d** and **3d'** (1:1) (0.248 g, 24% yield), whose compounds were difficult to separate each other by recrystallization.

**3d** and **3d'**: (1:1 mixture): oil.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.34 (12H, s, Me), 1.53 (12H, s, Me), 2.29 (4H, d,  $J = 13.2$  Hz,  $\text{CH}_2$ ), 2.74 (4H, bd,  $J = 13.2$  Hz  $\text{CH}_2$ ), 3.46 (4H, s, CH), 3.62 (8H, m,  $\text{CH}_2$ ), 3.71 (8H, m,  $\text{CH}_2$ ), 3.84, 4.05 (each 8H, m,  $\text{CH}_2$ ), 4.28, 4.35 (each 4H, m,  $\text{CH}_2$ ), 5.31 (4H, s, =CH). IR (neat) 1724, 1700, 1626  $\text{cm}^{-1}$ . LR MS  $m/z$  653 ( $\text{MH}^+$ ). HR MS ( $\text{MH}^+$ ) calcd for  $\text{C}_{32}\text{H}_{45}\text{O}_{14}$  653.2809. found: 653.2803.

**2,21,23,30-Tetramethyl-3,7,10,13,16,20,25,28-octaoxapentacyclo[28.1<sup>2,30</sup>.1<sup>21,23</sup>.0.0<sup>1,6</sup>.0<sup>17,22</sup>]-triaconta-5,17-dien-4,19,24,29-tetraone (4a, 4a')** ..... To a solution of **1b** (0.732 g, 2.00 mmol) with ethylene glycol dimethacrylate (**2a**) (0.792 g, 4.00 mmol) in MeCN (200 mL) was irradiated in the presence of benzophenone (0.364 g, 2.00 mmol) for 6 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc/hexane = 3:1, v/v) to afford a mixture of **4a** and **4a'** (1:1) (0.214 g, 19% yield), whose compounds were difficult to separate each other by recrystallization.

**4a** and **4a'**: (1:1 mixture): oil.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.34, 1.35 (each 6H, s, Me), 1.51, 1.52 (each 6H, s, Me), 2.32 (4H, bd,  $J = 13.2$  Hz,  $\text{CH}_2$ ), 2.70, 2.73 (each 2H, d,  $J = 13.2$  Hz  $\text{CH}_2$ ), 3.39, 3.42 (each 2H, s, CH), 3.66, 3.78, 4.03, 4.35 (each 8H, m,  $\text{CH}_2$ ), 5.29 (4H, s, =CH). IR (neat) 1725, 1697, 1626  $\text{cm}^{-1}$ . LR

MS  $m/z$  565 ( $MH^+$ ). HR MS ( $MH^+$ ) calcd for  $C_{28}H_{37}O_{12}$  565.2285. found: 565.2286.

**2,21,23,33-Tetramethyl-3,7,10,13,16,20,25,28,31-nonaoxapentacyclo[31.1<sup>2,33</sup>.1<sup>21,23</sup>.0.0<sup>1,6</sup>.0<sup>17,22</sup>]tritiaconta-5,17-dien-4,19,24,32-tetraone (4b, 4b')** ..... To a solution of **1b** (0.732 g, 2.00 mmol) with diethylene glycol dimethacrylate (**2b**) (0.792 g, 4.00 mmol) in MeCN (200 mL) was irradiated in the presence of benzophenone (0.364 g, 2.00 mmol) for 6 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc/hexane = 3:1, v/v) to afford a mixture of **4b** and **4b'** (1:1) (0.232 g, 19% yield), whose compounds were difficult to separate each other by recrystallization.

**4b** and **4b'** (1:1 mixture): oil.  $^1H$  NMR ( $CDCl_3$ )  $\delta$  1.35 (12H, s, Me), 1.52 (12H, s, Me), 2.29 (4H, d,  $J = 13.2$  Hz,  $CH_2$ ), 2.73, 2.74 (each 2H, dd,  $J = 13.2, 2.0$  Hz  $CH_2$ ), 3.41 (4H, bs, CH), 3.62, 3.71, 3.78, 4.03 (each 8H, m,  $CH_2$ ), 4.24, 4.35 (each 2H, m,  $CH_2$ ), 5.29 (4H, s, =CH). IR (neat) 1724, 1700, 1626  $cm^{-1}$ . LR MS  $m/z$  609 ( $MH^+$ ). HR MS ( $MH^+$ ) calcd for  $C_{30}H_{41}O_{13}$  609.2547. found: 609.2543.

**2,21,23,36-Tetramethyl-3,7,10,13,16,20,25,28,31,34-decaoxapentacyclo[34.1<sup>2,36</sup>.1<sup>21,23</sup>.0.0<sup>1,6</sup>.0<sup>17,22</sup>]hexatriaconta-5,17-dien-4,19,24,35-tetraone (4c, 4c')** ..... To a solution of **1b** (0.732 g, 2.00 mmol) with triethylene glycol dimethacrylate (**2c**) (1.11 g, 4.00 mmol) in MeCN (200 mL) was irradiated in the presence of benzophenone (0.364 g, 2.00 mmol) for 6 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc) to afford a mixture of **4c** and **4c'** (1:1) (0.248 g, 19% yield), whose compounds were difficult to separate each other by recrystallization.

**4c** and **4c'** (1:1 mixture): oil.  $^1H$  NMR ( $CDCl_3$ )  $\delta$  1.35 (12H, s, Me), 1.52 (12H, s, Me), 2.29 (4H, d,  $J = 13.6$  Hz,  $CH_2$ ), 2.74 (4H, bd,  $J = 13.6$  Hz,  $CH_2$ ), 3.43 (4H, bs, CH), 3.64 (8H, m,  $CH_2$ ), 3.67, 3.72, 3.80, 4.05 (each 8H, m,  $CH_2$ ), 4.24, 4.39 (each 2H, m,  $CH_2$ ), 5.29 (4H, s, =CH). IR (neat) 1722, 1698, 1625  $cm^{-1}$ . LR MS  $m/z$  653 ( $MH^+$ ). HR MS ( $MH^+$ ) calcd for  $C_{32}H_{44}O_{14}$  653.2809. found: 653.2818.

**2,21,23,39-Tetramethyl-3,7,10,13,16,20,25,28,31,34,37-undecaaxapentacyclo[37.1<sup>2,39</sup>.1<sup>21,23</sup>.0.0<sup>1,6</sup>.0<sup>17,22</sup>]nonatriaconta-5,17-dien-4,19,24,38-tetraone (4d, 4d')** ..... To a solution of **1b** (0.732 g, 2.00 mmol) with tetraethylene glycol dimethacrylate (**2d**) (1.32 g, 4.00 mmol) in MeCN (200 mL) was irradiated in the presence of benzophenone (0.364 g, 2.00 mmol) for 6 h. After removal of the solvent, the oily residue was chromatographed by silica gel (eluent: EtOAc to acetone) to afford a mixture of **4d** and **4d'** (1:1) (0.154 g, 11% yield), whose compounds were difficult to separate each other by recrystallization.

**4d** and **4d'** (1:1 mixture): oil.  $^1H$  NMR ( $CDCl_3$ )  $\delta$  1.34 (12H, s, Me), 1.53 (12H, s, Me), 2.30 (4H, bd,  $J = 13.2$  Hz,  $CH_2$ ), 2.72 (4H, bd,  $J = 13.2$  Hz,  $CH_2$ ), 3.46 (4H, bs, CH), 3.63, 3.67, 3.72, 3.80, 4.06 (each

8H, m, CH<sub>2</sub>), 4.25, 4.36 (each 4H, m, CH<sub>2</sub>), 5.30 (4H, s, =CH). IR (neat) 1725, 1698, 1626 cm<sup>-1</sup>. LR MS *m/z* 697 (MH<sup>+</sup>). HR MS (MH<sup>+</sup>) calcd for C<sub>34</sub>H<sub>49</sub>O<sub>15</sub> 697.3071. found: 697.3082.

## ACKNOWLEDGEMENT

The authors are grateful to Dr. Kazunobu Igawa (Institute for Materials Chemistry and Engineering, Kyushu University) for the measurement of the single crystal X-ray diffraction.

## REFERENCES

1. B. Dietrich, P. Viout, and J.-M. Lehn, *Macrocyclic Chemistry*, VCH:Weinheim, 1993.
2. A. G. Griesbeck, A. Henz, and J. Hirt, *Synthesis*, 1996, 126.
3. S. Inokuma, M. Takezawa, H. Satoh, Y. Nakamura, T. Sasaki, and J. Nishimura, *J. Org. Chem.*, 1998, **63**, 5791; S. Inokuma, T. Ide, T. Yonekura, T. Funaki, S. Kondo, S. Shinobara, T. Yoshihara, S. Tobita, and J. Nishimura, *J. Org. Chem.*, 2005, **70**, 1698.
4. T. Shimo, M. Kawamura, E. Fukushima, M. Yasutake, T. Shinmyozu, and K. Somekawa, *Heterocycles*, 2003, **60**, 23.
5. H. Miyauchi, C. Ikematsu, T. Shimazaki, S. Kato, T. Shinmyozu, T. Shimo, and K. Somekawa, *Tetrahedron*, 2008, **64**, 4108.
6. H. M. Zhang, K. Kawabata, H. Miyauchi, and T. Shimo, *Heterocycles*, 2012, **85**, 333.
7. Y. Ito, T. Yoshinaga, and H. Nishino, *Tetrahedron*, 2010, **66**, 2683.
8. W. Wang, T. Shimo, H. Hashimoto, and K. Somekawa, *Tetrahedron*, 2007, **63**, 12367.
9. A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. Burla, G. Polidori, and M. Camalli, *J. Appl. Crystallogr.*, 1994, **27**, 435.
10. Crystal Structure 3.8: Crystal Structure Analysis Package, Rigaku and Rigaku Americas (2000-2007). 9009 New Trails Dr. The Woodlands TX 77381 USA.
11. CRYSTAL Issue 11. J. R. Carruthers, J. S. Rollett, P. W. Betteridge, D. Kinna, L. Pearce, A. Larsen, and E. Gabe, Chemical Crystallography Laboratory, Oxford, UK. (1999).