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Efficient macrocyclization using methylene-tethered terminal dienes and bis(manganese(III)-enolate)s

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ABSTRACT

Macrocyclic compounds, which have two fused dihydrofuran rings, were synthesized with complete control by the oxidation of α,α,ω,ω-tetraaryl-α,(ω-1)-alkadienes $\mathbf{1}_x$ with manganese(III)-oligomethylenebis(enolate) complexes directly formed by the reaction of the oligomethylene bis(3-oxobutanoate)s $\mathbf{2}_y$ with manganese(III) acetate in situ. The oxamethylene-tethered macrodiolides **5** and **7** were also produced in good to moderate yields by a similar oxidation. The key intermediate, an electron donor–acceptor-like complex, was proposed for the efficient macrocyclization reaction.

1. Introduction

Many macrocyclic compounds have been isolated from natural sources, some of which have significant biological activities,[1] for example, the erythromycin and rifamycin antibiotics,[2] while many macrocyclic compounds were synthesized in order to manifest a functionality such as molecular recognition[3] and metal ion transport.[4] Therefore, from the standpoint of the pharmaceutical interests of the natural macrocycles[5] and physicochemical properties of the synthesized macrocyclic compounds,[6] the synthesis of the functionalized macrocyclic compounds and the development of the synthetic method of the macrocycles are very attractive. In general, it is convenient to prepare cyclic compounds using a free-radical cyclization reaction,[7] especially, the radical-based construction of the five and six-membered or smaller ring system is efficient. However, most of the macrocyclic compounds are synthesized according by ionic reactions,[8] and needless to say, the synthesis of more than 10-membered macrocycles is somewhat difficult using radical reactions. Previously, we[9a–t] and other research groups[9u–z] developed the oxidative radical cyclization using manganese(III)-enolate complexes as the carbon radical promoter. The reaction of alkenes with 1,3-dicarbonyl compounds in the presence of manganese(III) acetate selectively gave the corresponding 4,5-dihydrofurans at elevated temperature[9o,10] and 1,2-dioxan-3-ols at ambient temperature in air.[9h,11] When the oxidation of β-ketoesters was carried out in the presence of the α,α,ω,ω-tetraaryl-α,(ω-1)-alkadienes **I** (path a in Scheme 1), the corresponding bis(dihydrofuran)s **II** were produced,[12] while the reaction was applied the methylene-tethered bis(3-oxobutanoate)s in the presence of alkene to give the corresponding oligomethylene bis(dihydrofurancarboxylate)s **IV** during the production of the formal biradicals **III** (path b in Scheme 1).[13a,b] Therefore, we realized that the use of both the oligomethylene-tethered terminal dienes **I** and bis(3-oxobutanoate) radicals **III** in the manganese(III)-oxidation system must lead to the production of macrocyclic compounds (path c in Scheme 1). In fact, the reaction of 1,5-hexadiene with oligomethylene bis(3-oxobutanoate) was preliminarily examined and the desired macrodiolide, such as **V**, was obtained.[13] We now report the full results of the macrocyclization using both oligomethylene-tethered terminal dienes and bis(3-oxobutanoate)s, optimized reaction conditions, and reaction limitations.

2. Results and discussion

2.1. Reaction of 1,5-hexadiene $\mathbf{1}_2$ with bis(3-oxobutanoate) $\mathbf{2}_2$ in the presence of manganese(III) acetate

We initially examined the oxidation of a mixture of 1,1,6,6-tetraphenyl-1,5-hexadiene ($\mathbf{1}_2$) and ethylene bis(3-oxobutanoate) ($\mathbf{2}_2$) with manganese(III) acetate in glacial acetic acid at 100 °C under an argon atmosphere, and fortunately the desired 12-membered macrodiolide $\mathbf{3}_{2,2}$ was obtained in 40% yield together with an intractable

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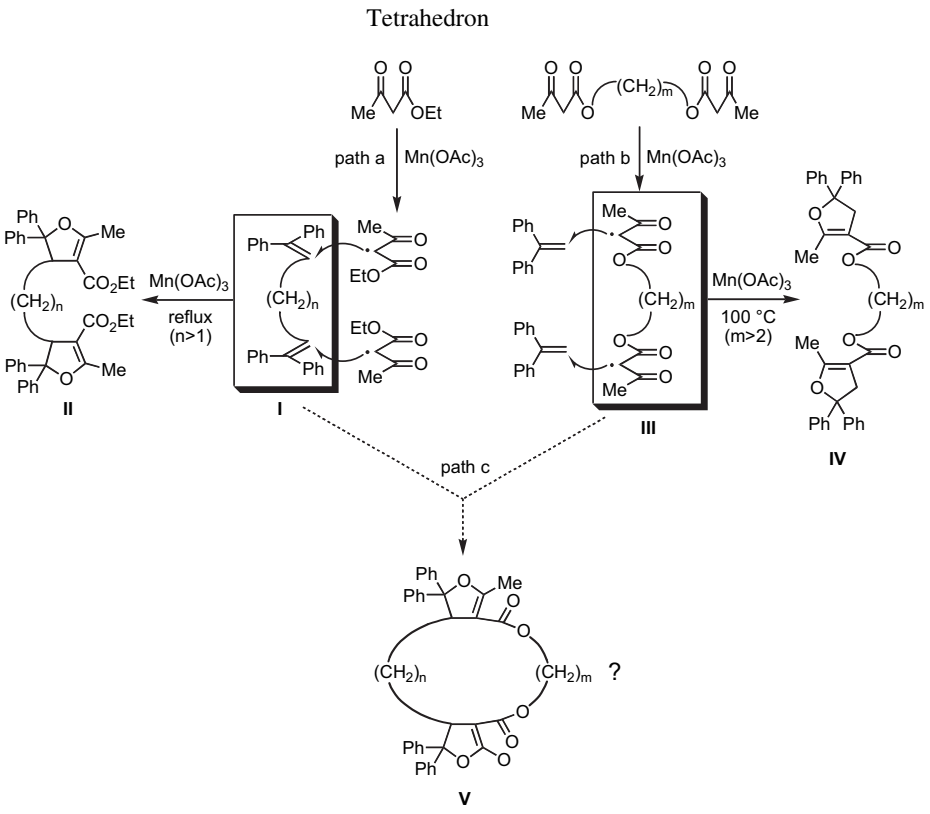
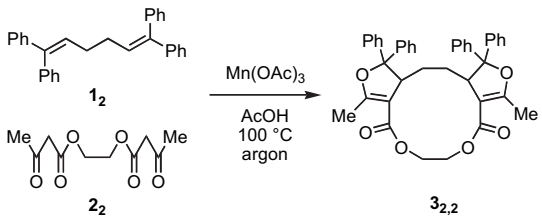


Scheme 1. Strategy of the macrocyclization.

mixture (Scheme 2 and Table 1, entry 1).[13a] We scrutinized the reaction conditions and ascertained that dissolved molecular oxygen in the solvent must complicate the reaction, while the dilution conditions were important for the macrocylization to avoid polymerization.[13b] Therefore, before the reaction, the mixture was sufficiently degassed under reduced pressure for 30 min using an ultrasonicator for exchange with an argon atmosphere. The mixture was then heated at 100 °C until the manganese(III) acetate was completely consumed (entries 2–4). As a result, the yield of the macrodiolide $\mathbf{3_{2,2}}$ increased to 71% (entry 5).



Scheme 2.

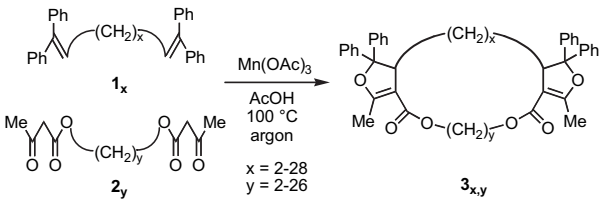
Table 1
Reaction of 1,5-hexadiene $\mathbf{1_2}$ with bis(3-oxobutanoate) $\mathbf{2_2}$ under various concentration[a]

Entry	AcOH/mL	Concn of $\mathbf{1_2}$/mM	*T*/min	$\mathbf{3_{2,2}}$/%[b]
1	30	33.3	45	40
2	60	16.7	60	51
3	150	3.3	30	64
4	250	2.0	40	68
5	500	1.0	25	71

[a] The reaction was carried out at the molar ratio of $\mathbf{1_2}$ (0.5 mmol):$\mathbf{2_2}$:$Mn(OAc)_3$=1:1.5:7 in acetic acid at 100 °C after exchange with an argon atmosphere by ultrasonication except for entry 1.
[b] Isolated yield based on $\mathbf{1_2}$.

2.2. Manganese(III)-based oxidation of a combination of various methylene-tethered terminal dienes $\mathbf{1}_x$ and bis(3-oxobutanoate)s $\mathbf{2}_y$

With the optimized conditions in hand, we applied the reaction to a combination of much longer methylene-tethered terminal dienes $\mathbf{1}_x$ (x=1–28) and bis(3-oxobutanoate)s $\mathbf{2}_y$ (y=2–26), and the desired macrodiolides $\mathbf{3}_{x,y}$ were obtained in good to moderate yields (Scheme 3 and Table 2). Although increasing the ring size tended to decrease the yield, the difference in the methylene chain length of the dienes $\mathbf{1}_x$ and the bis(3-oxobutanoate)s $\mathbf{2}_y$ did not affect the yield of $\mathbf{3}_{x,y}$. When the combination of $\mathbf{1_5}$ and $\mathbf{2_4}$ was used, the best yield of the macrodiolide $\mathbf{3}_{x,y}$ was achieved and the corresponding 17-membered macrodiolide $\mathbf{3_{5,4}}$ was isolated in 86% yield (entry 9). As a result, according to the macrocyclization reaction, the synthesis of various sizes of macrodiolides $\mathbf{3}_{x,y}$ from the smallest (12-membered $\mathbf{3_{2,2}}$; entry 2) to the largest (62-membered $\mathbf{3_{28,26}}$; entry 24) could be accomplished. However, the reaction of the pentadiene $\mathbf{1_1}$ with the bis(3-oxobutanoate) $\mathbf{2_2}$ to give the corresponding 11-membered macrodiolide failed (entry 1), probably due to steric hindrance of the four neighboring phenyl groups.



Scheme 3.

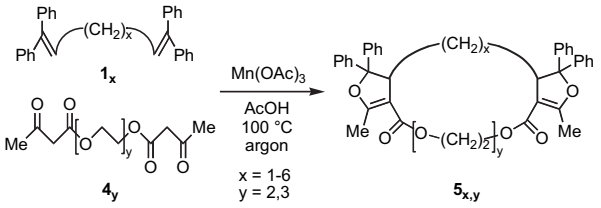
Table 2
Reaction of dienes $\mathbf{1}_x$ with di(3-oxobutanoate)s $\mathbf{2}_y$ in the presence of manganese(III) acetate[a]

Entry	*x*	*y*	$\mathbf{1}_x$:$\mathbf{2}_y$:Mn(III)[b]	*T*/min	$\mathbf{3}_{x,y}$/%[c]	Ring size
1	1	2	1:1.5:7	60	0	11
2	2	2	1:1.3:7	40	68	12
3	2	3	1:1.3:7	50	64	13
4	2	4	1:1.3:7	40	66	14
5	3	3	1:1.3:7	50	67	14
6	4	2	1:1.3:7	70	76	14
7	4	3	1:1.3:7	60	74	15
8	5	3	1:1.3:7	40	57	16
9	5	4	1:1.3:7	80	86	17
10	6	4	1:1.3:7	80	59	18
11	6	6	1:1.3:7	25	60	20
12	6	10	1:1.3:7	18	53	24
13	6	12	1:1.3:7	21	57	26
14	8	6	1:1.3:7	33	54	22
15	8	10	1:1.3:7	24	46	26
16	8	12	1:1.3:7	15	49	28
17	8	20	1:1.3:7	35	49	36
18	16	6	1:1.3:7	60	40	30
19	16	10	1:1.3:7	21	50	34
20	16	12	1:1.3:7	21	50	36
21	16	20	1:1.3:7	46	50	44
22	18	20	1:1.3:7	36	36	46
23	28	6	1:1.3:7	32	40	42
24	28	26	1:1.3:7	82	22	62

[a] The reaction was carried out in acetic acid (0.2 mM for $\mathbf{1}_x$) at 100 °C under an argon atmosphere.
[b] Molar ratio.
[c] Isolated yield based on $\mathbf{1}_x$.

2.3. Manganese(III)-based oxidation of a combination of various oxamethylene-tethered terminal dienes $\mathbf{6}_x$ and bis(3-oxobutanoate)s $\mathbf{4}_y$

The results encouraged us to investigate a similar reaction using the oxamethylene-tethered terminal dienes $\mathbf{6}_x$ and bis(3-oxobutanoate)s $\mathbf{4}_y$, which seemed to produce a crown ether-type macrodiolide. The oxamethylene-tethered bis(3-oxobutanoate)s $\mathbf{4}_y$ (y=1–4) were prepared by the reaction of the corresponding glycols with diketene. First of all, we examined the reaction of 1,1,8,8-tetraphenyl-1,7-octadiene ($\mathbf{1}_4$) with 3-oxapentamethylene bis(3-oxobutanoate) ($\mathbf{4}_2$) (Scheme 4). As a result, the expected macrocyclization occurred and the desired 17-membered macrodiolide $\mathbf{5}_{4,2}$ was produced in 86% yield (Table 3, entry 4). A similar reaction of other terminal alkadienes $\mathbf{1}_x$ (x=1–6) with bis(3-oxobutanoate) $\mathbf{4}_y$ (y=2 and 3) also gave the corresponding macrodiolides $\mathbf{5}_{x,y}$ in good to moderate yields (Table 3). The pentadiene $\mathbf{1}_1$ afforded the 14-membered macrodiolide $\mathbf{5}_{1,2}$ in only 27% yield probably due to the crowded tetraphenyl groups.



Scheme 4.

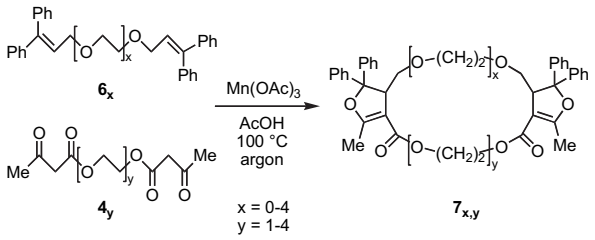
Since the combination of the alkadienes $\mathbf{1}_x$ and the oxamethylene-tethered bis(3-oxobutanoate)s $\mathbf{4}_y$ succeeded for the macrocyclization, we next examined the combination of both the oxamethylene-tethered $\mathbf{6}_x$ (x=0–4) and $\mathbf{4}_y$ (y=1–4) in order to synthesize crown ether-type macrodiolides. The oxamethylene-tethered terminal dienes $\mathbf{6}_x$ (x=1–4) were prepared by the Williamson ether synthesis of the corresponding glycols with 1,1-diphenyl-3-bromopropene. The reaction was carried out under the optimized

Table 3
Reaction of $\mathbf{1}_x$ with $\mathbf{4}_y$ in the presence of manganese(III) acetate[a]

Entry	*x*	*y*	$\mathbf{1}_x$:$\mathbf{4}_y$:Mn(III)[b]	*T*/min	$\mathbf{5}_{x,y}$/%[c]	Ring size
1	1	2	1:1.3:7	60	27	14
2	2	2	1:1.3:7	50	71	15
3	3	2	1:1.3:7	50	77	16
4	4	2	1:1.3:7	30	86	17
5	2	3	1:1.3:7	80	45	18
6	3	3	1:1.3:7	60	56	19
7	4	3	1:1.3:7	70	68	20
8	5	3	1:1.3:7	80	55	21
9	6	3	1:1.3:7	60	56	22

[a] The reaction was carried out in acetic acid (0.2 mM for $\mathbf{1}_x$) at 100 °C under an argon atmosphere.
[b] Molar ratio.
[c] Isolated yield based on $\mathbf{1}_x$.

conditions and the desired macrodiolides $\mathbf{7}_{x,y}$ were produced in moderate yields (Scheme 5 and Table 4). It seemed that the oxamethylene-chain length of $\mathbf{6}_x$ and $\mathbf{4}_y$ might be important since the yield of **7** decreased in the reaction of the shortest $\mathbf{6}_0$ with the longer $\mathbf{4}_y$ (y=3 and 4). In addition, the oxamethylene-tethered alkadienes $\mathbf{6}_x$ were longer, the ionization potential of $\mathbf{6}_x$ was lower, and therefore, the direct oxidation of $\mathbf{6}_x$ with manganese(III) acetate must occur since the decomposed fragments were isolated instead of the recovery of $\mathbf{6}_x$.



Scheme 5.

Table 4
Reaction of $\mathbf{6}_x$ with $\mathbf{4}_y$ in the presence of manganese(III) acetate[a]

Entry	*x*	*y*	$\mathbf{6}_x$:$\mathbf{4}_y$:Mn(III)[b]	*T*/min	$\mathbf{7}_{x,y}$/%[c]	Ring size
1	0	1	1:1.3:7	60	51	13
2	0	2	1:1.3:7	40	67	16
3	0	3	1:1.3:7	60	37	19
4	0	4	1:1.3:7	40	24	22
5	1	1	1:1.3:7	30	66	16
6	1	2	1:1.3:7	50	63	19
7	1	3	1:1.3:7	60	62	22
8	1	4	1:1.3:7	120	29	25
9	2	1	1:1.5:7	30	34	19
10	2	2	1:1.3:6	40	35	22
11	2	3	1:1.3:6	40	33	25
12	2	4	1:1.3:6	40	27	28
13	3	1	1:1.5:7	50	42	22
14	3	2	1:1.3:7	60	42	25
15	3	3	1:1.3:7	40	35	28
16	3	4	1:1.5:7	30	39	31
17	4	1	1:1.3:7	40	40	25
18	4	2	1:1.3:7	70	44	28
19	4	3	1:1.3:7	150	42	31
20	4	4	1:1.3:7	30	30	34

[a] The reaction was carried out in acetic acid (0.2 mM for $\mathbf{6}_x$) at 100 °C under an argon atmosphere.
[b] Molar ratio.
[c] Isolated yield based on $\mathbf{6}_x$.

2.4. Structure determination of macrodiolides

The isolated macrodioides **3**, **5**, and **7** were characterized by a spectroscopic method, combustion analysis as well as FABMS spectrometry, and X-ray crystallography. The ^{13}C NMR spectrum

contained peaks assigned to the ester carbonyl, all the dihydrofuran ring carbons, and the methylene carbon attached to the ester oxygen appeared as two slightly different peaks, due to the diastereomixture of the macrodiolides that contained two asymmetric carbons. For example, in the ^{13}C NMR spectrum of the 20-membered macrodiolide $\mathbf{3_{6,6}}$, the peaks assigned to the ester carbonyl appeared at δ 166.7 and 166.5, the sp^2, and the methine carbons of the dihydrofuran ring at δ 166.1 and 166.0, 108.6 and 108.4, 48.6 and 48.5, the methylene carbons attached to the ester oxygens at δ 63.3 and 63.2 ppm, respectively. However, this phenomenon disappeared in the large macrodiolides of more than 26 members. In addition, energy calculations of the *meso*- and DL-macrodiolides were performed by the MOPAC PM3 program;[14] however, the formation energies were not very different because of the large macrocyclic rings. Fortunately, the macrodiolides $\mathbf{5_{4,2}}$, $\mathbf{5_{3,3}}$, and $\mathbf{7_{0,3}}$ crystallized from dichloromethane/hexane to provide single crystals, which were measured by X-ray diffraction. As a result, it was confirmed that the macrocyclic compounds had two fused dihydrofuran rings, and the two asymmetric carbons of $\mathbf{5_{4,2}}$, $\mathbf{5_{3,3}}$ showed a *meso*-configuration and those of $\mathbf{7_{0,3}}$ had a DL-configuration (Fig. 1 and see Experimental).

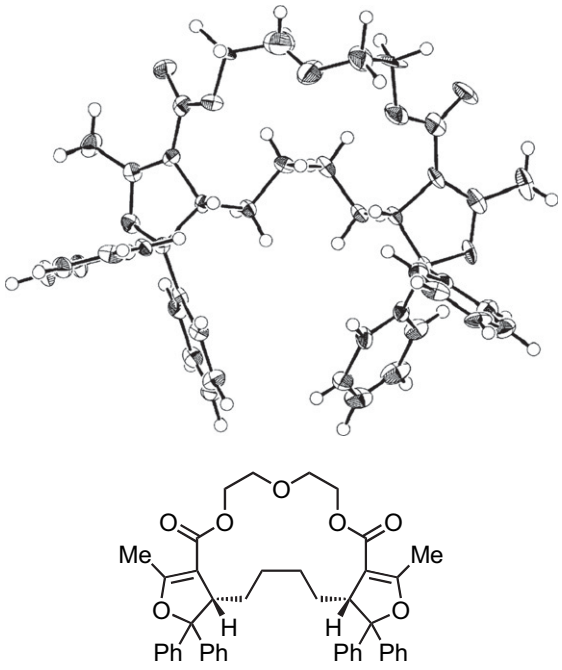


Figure 1. ORTEP drawing of *meso*-macrodiolide $\mathbf{5_{4,2}}$.

2.5. Mechanism of the macrocyclization

The mechanism for the formation of the dihydrofurans by the manganese(III)-based oxidation of alkenes with β-diketoesters could be explained by the well-known oxidation mechanism.[15,16] Hence the manganese(III)-bis(enolate) complexes would be formed by the reaction of the bis(3-oxobutanoate)s $\mathbf{2_y}$ with manganese(III) acetate in situ, and then undergo a one-electron-transfer oxidation to give the formal 3-oxobutanoate biradical such as **III** in Scheme 1, from which the double electrophilic attack on the terminal dienes $\mathbf{1_x}$ would provide the macrodiolides $\mathbf{3_{x,y}}$ via the subsequent oxidation and deprotonation. However, when the reaction of dodecadiene $\mathbf{1_8}$ with hexamethylene bis(3-oxobutanoate) $\mathbf{2_6}$ was carried out using a half stoichiometric amount of manganese(III) acetate, the oxidant was completely consumed within 5 min and the corresponding macrodiolide $\mathbf{3_{8,6}}$ was produced only in 14% yield together with 9-decenyldihydrofurancarboxylate **8** (28%)[16] and the unchanged diene $\mathbf{1_8}$ (26%) (see Experimental section). This suggested that the macrocyclization should follow a stepwise process. Accordingly, in order to demonstrate the stepwise process, the intermediate dihydrofuran **8** was alternatively prepared by the manganese(III)-oxidation of the diene $\mathbf{1_8}$ with THP-protected hexamethylene butanoate **9** followed by esterification with diketene (Scheme 6). The reaction of **8** using a stoichiometric amount of manganese(III) acetate actually gave the macrodiolide $\mathbf{3_{8,6}}$ in 78% yield.

The remaining question was why the intermediate dihydrofuran such as **8** smoothly underwent an intramolecular cyclization to afford large macrocyclic compounds such as the 62-membered macrodiolide $\mathbf{3_{28,26}}$. For example, when the dihydrofuran **8** was produced by the reaction of the diene $\mathbf{1_8}$ with bis(3-oxobutanoate) $\mathbf{2_6}$ during the first stage, each reaction site during the next intramolecular cyclization should be quite far due to the steric repulsion between the decenyl-side chain and the oxadioxoundecyloxycarbonyl-side chain of **8**. This was also supported by the MM2 calculation (see Supplementary data).[14] However, in order to undergo the intramolecular cyclization during the second stage, each reaction site must be closer. Recently, we proposed a unique electron donor–acceptor-like the manganese(III)-enolate intermediate complex (EDA complex) in the manganese(III) oxidation system.[17] The donor alkene would undergo a complex formation with the acceptor enolate in the inner sphere of the oxygen-centered manganese(III)-triangle complex and one-electron-transfer oxidation would result in the carbon–carbon bond formation and finally produce the dihydrofuran. Hence, both the reaction sites of the dihydrofuran **8** should be in close proximity by the formation of a similar intramolecular EDA complex such as **A** in Scheme 7, which seemed to easily cause the oxidative intramolecular cyclization to give radical **B**, and the macrodiolide **3** was finally produced via the oxidative dihydrofuranation reaction (Scheme 7). The formation of other macrodiolides **5** and **7** could also be explained in a similar manner.

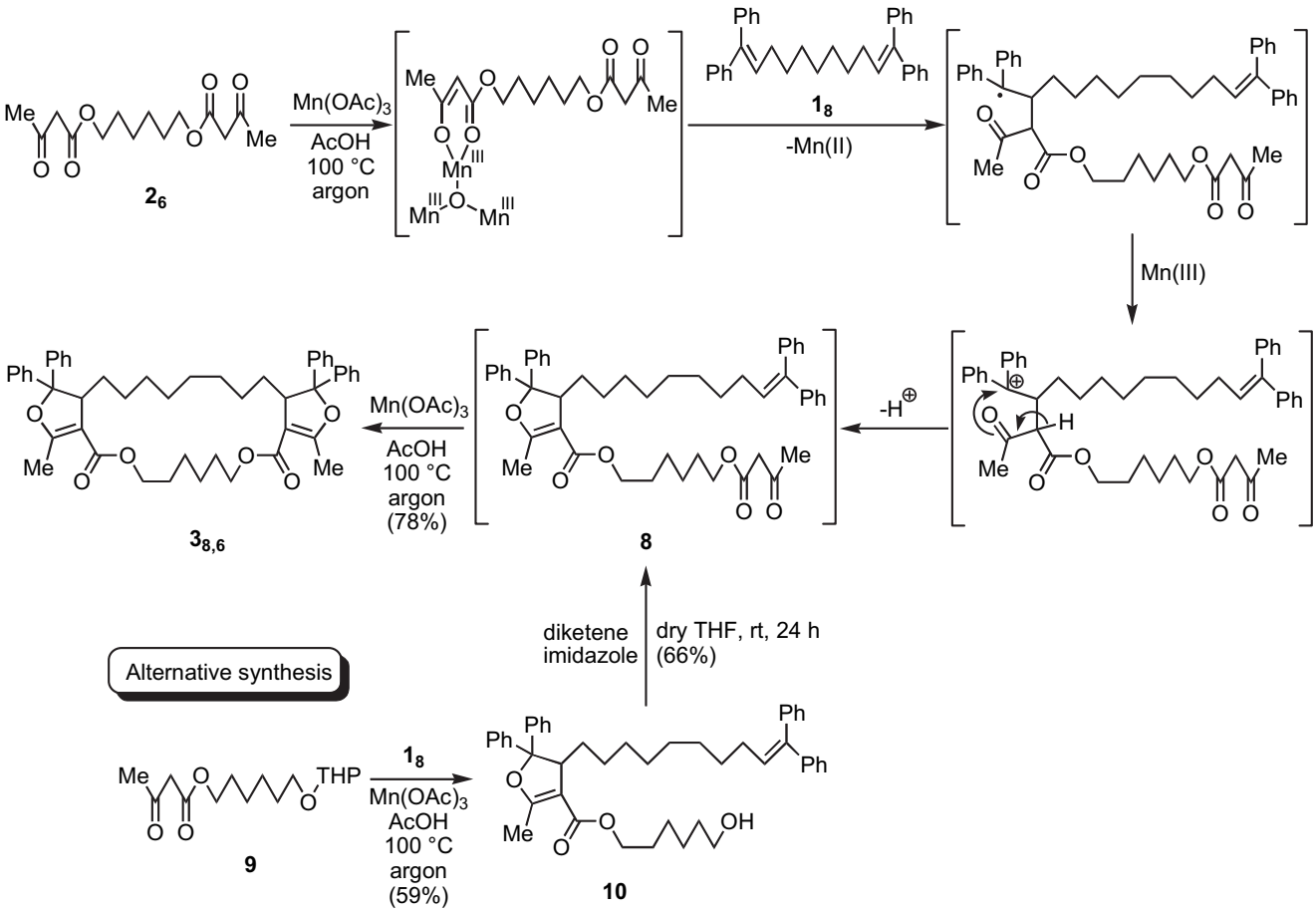
3. Conclusion

We have developed a facile and convenient synthesis of macrocyclic compounds using the manganese(III)-based oxidative radical cyclization. We guarantee the synthesis of macrodiolides from 12 to 62 members having two fused dihydrofurans. We also demonstrated that the macrocyclization using the methylene-tethered terminal dienes and bis(3-oxobutanoate)s proceeded according to a two-step process. In addition to the dilution conditions from the standpoint of the manganese(III)-based macrocyclization, the formation of the EDA complex **A** during the reaction of the intermediate dihydrofuran such as **8** with manganese(III) acetate could play an important role in the manganese(III)-based macrocyclization. Furthermore, the balance of the chain length of the dienes and bis(3-oxobutanoate)s was also important for the standpoint of the yield.

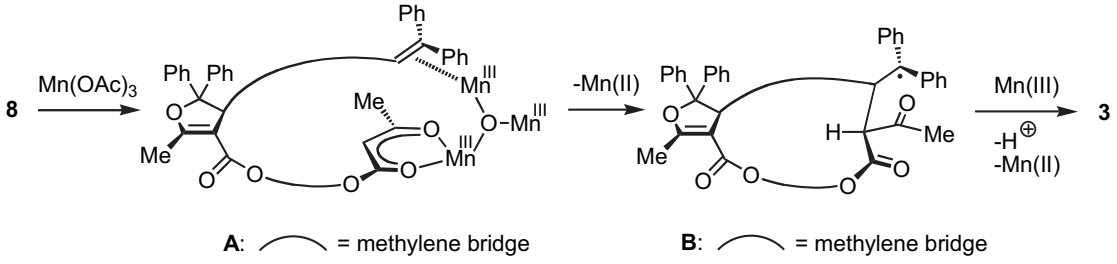
4. Experimental

4.1. General

The melting points are uncorrected. The NMR spectra were measured at 300 MHz for ^1H and at 75 Hz for ^{13}C at 400 MHz for ^1H and at 100 Hz for ^{13}C with tetramethylsilane as the internal standard. The chemical shifts are reported in ™ values (ppm) and the coupling constants in Hertz. The IR spectral data are expressed in cm^{-1}. The EIMS spectra were recorded at the ionizing voltage of 70 eV. The high-resolution mass spectra were measured at the Institute for Materials Chemistry and Engineering, Kyushu University, Fukuoka, Japan, and the Analytical Center of Kumamoto University, Kumamoto, Japan. The elemental analyses were also



Scheme 6.



Scheme 7.

performed at the Analytical Center of Kumamoto University, Kumamoto, Japan.

4.2. Materials

Manganese(III) acetate dihydrate, $Mn(OAc)_3 \cdot 2H_2O$, was prepared according to a literature method.[9] The terminal alkadienes $\mathbf{1}_x$ were synthesized by the reaction of the corresponding 1,ω-alkanedicarboxylates with phenylmagnesium bromide followed by acid-catalyzed dehydration. The oxamethylene-tethered terminal dienes $\mathbf{6}_x$ were prepared by the Williamson ether synthesis of the corresponding glycols with 1,1-diphenyl-3-bromopropene, which was synthesized by the bromination of 1,1-diphenylpropene. The bis(3-oxobutanoate)s $\mathbf{2}_y$ and $\mathbf{4}_y$ were prepared by the esterification of the corresponding 1,ω-alkanediols or glycols with diketene. Commercially available glacial acetic acid was used as received.

4.3. General procedure for the manganese(III)-based oxidation of terminal dienes 1_x and 6_x with bis (3-oxobutanoate)s 2_y and 4_y

To a solution of the terminal alkadiene **1** or **6** (0.2 mmol) and bis(3-oxobutanoate) **2** or **4** (0.26 mmol) in glacial acetic acid (100 mL), manganese(III) acetate dehydrate (1.4 mmol) was added and the mixture was degassed under reduced pressure for 30 min using an ultrasonicator for exchange with an argon atmosphere. The mixture was then heated at 100 °C under an argon atmosphere for the period mentioned in the tables until the brown color of manganese(III) disappeared. The color typically turned a transparent yellow. The solvent was removed in vacuo, and the residue was triturated with 2 M HCl (20 mL), and then extracted with $CHCl_3$ (20 mL×3). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ (30 mL) and water, and then concentrated to dryness. The crude products were separated by silica gel TLC

(Wako B-10 or Whatman K6F 60A) while eluting with $CHCl_3$, $CHCl_3$/MeOH, or Et_2O/hexane. The analytical samples were further purified by recrystallization from the solvent specified in parentheses except for the amorphous products. The molar ratio and product yields are summarized in Tables 1–4. The specific details are given below. The data were shown as a diasteromixture except for **$7_{1,1}$**.

*4.3.1. 9,18-Dimethyl-3,6,10,17-tetraoxa-2,7-dioxo-11,11,16,16-tetraphenyltricyclo[13.3.0.0^{8,12}]octadeca-8,18-diene (**$3_{2,2}$**).* Diastereomer ratio, 43:57. Colorless microcrystals (from CH_2Cl_2/hexane); mp 197–199 °C (lit.[13a] mp 197–199 °C); IR ($CHCl_3$) ν 1699 (C=O), 1648 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–6.88 (20H, m), 4.79–4.09 (4H, m), 3.96–3.52 (2H, m), 2.38–2.14 (6H, m), 1.35–0.60 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 165.6, 145.2, 141.0, 128.1, 127.8, 127.6, 126.9, 126.6, 126.3, 107.8, 94.9, 60.9, 51.2, 26.8, 14.4; FABMS *m*/*z* (rel intensity), 613 (100, M+H). Anal. Calcd for $C_{40}H_{36}O_6$: C, 78.41; H, 5.92. Found: C, 78.32; H, 6.03.

*4.3.2. 10,19-Dimethyl-3,7,11,18-tetraoxa-2,8-dioxo-12,12,17,17-tetraphenyltricyclo[14.3.0.0^{9,13}]nonadeca-9,19-diene (**$3_{2,3}$**).* Colorless microcrystals (from CH_2Cl_2/hexane); mp 259–261 °C (lit.[13a] mp 259–260 °C); IR ($CHCl_3$) ν 1693 (C=O), 1645 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–6.85 (20H, m), 4.78–4.08 (4H, m), 3.85–3.54 (2H, m), 2.40–2.20 (6H, m), 2.11–1.85 (2H, m), 1.39–0.63 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 166.1, 145.1, 141.0, 128.1, 127.8, 127.6, 126.9, 126.7, 126.1, 107.6, 95.2, 63.2, 49.3, 27.9, 27.6, 14.5. Anal. Calcd for $C_{41}H_{38}O_6$: C, 78.57; H, 6.11. Found: C, 78.72; H, 6.17.

*4.3.3. 11,20-Dimethyl-3,8,12,19-tetraoxa-2,9-dioxo-13,13,18,18-tetraphenyltricyclo[15.3.0.0^{10,14}]icosa-10,20-diene (**$3_{2,4}$**).* Diastereomer ratio, 48:52. Colorless microcrystals (from CH_2Cl_2/hexane); mp 125–128 °C (lit.[13a] mp 124–126 °C); IR ($CHCl_3$) ν 1686 (C=O), 1643 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54–6.86 (20H, m), 4.39–4.25 (4H, m), 3.67–3.63 (2H, m), 2.29–2.16 (6H, m), 1.90–1.80 (4H, m), 1.42–0.81 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 165.7, 145.5, 141.1, 128.0, 127.8, 127.6, 126.8, 126.5, 126.1, 107.8, 95.2, 62.8, 50.3, 27.6, 26.1, 14.7. Anal. Calcd for $C_{42}H_{40}O_6$: C, 78.73; H, 6.29. Found: C, 78.35; H, 6.16.

*4.3.4. 10,20-Dimethyl-3,7,11,19-tetraoxa-2,8-dioxo-12,12,18,18-tetraphenyltricyclo[15.3.0.0^{9,13}]icosa-9,20-diene (**$3_{3,3}$**).* Diastereomer ratio, 41:59. Colorless microcrystals (from CH_2Cl_2/hexane); mp 144–146 °C; IR ($CHCl_3$) ν 1699 (C=O), 1648 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54–7.11 (20H, m), 4.57–4.36 (2H, m), 4.23–3.98 (2H, m), 3.88–3.73 (2H, m), 2.35–2.18 (6H, m), 2.10–1.86 (2H, m), 1.55–0.50 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 166.4, 165.9, 165.8, 145.4, 145.2, 140.9, 140.8, 128.1, 128.1, 127.7, 127.0, 126.9, 126.6, 126.4, 126.2, 126.0, 108.5, 107.6, 95.4, 95.0, 59.8, 59.4, 48.5, 47.7, 31.4, 30.1, 26.0, 24.0, 14.5, 14.4. Anal. Calcd for $C_{42}H_{40}O_6$: C, 78.73; H, 6.29. FAB HRMS (acetone/NBA) calcd for $C_{42}H_{40}O_6$ 640.2825 (M^+). Found 640.2811.

*4.3.5. 9,20-Dimethyl-3,6,10,19-tetraoxa-2,7-dioxo-11,11,18,18-tetraphenyltricyclo[15.3.0.0^{8,12}]icosa-8,20-diene (**$3_{4,2}$**).* Diastereomer ratio, 41:59. Colorless microcrystals (from CH_2Cl_2/hexane); mp 225–228 °C; IR ($CHCl_3$) ν 1693 (C=O), 1643 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55–7.15 (20H, m), 4.64–4.50 (2H, m), 4.24–4.10 (2H, m), 3.81–3.68 (2H, m), 2.37–2.24 (6H, m), 1.35–0.50 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 167.5, 165.7, 165.4, 145.1, 140.8, 140.7, 128.1, 127.8, 127.7, 127.1, 126.8, 126.6, 126.3, 126.2, 108.5, 107.8, 95.6, 95.4, 61.6, 61.3, 48.6, 48.3, 31.6, 31.3, 26.4, 25.2, 14.43, 14.37; FABMS *m*/*z* (rel intensity), 641 (100, M+H). Anal. Calcd for $C_{42}H_{40}O_6$: C, 78.73; H, 6.29. Found: C, 78.55; H, 6.46.

*4.3.6. 10,21-Dimethyl-3,7,11,20-tetraoxa-2,8-dioxo-12,12,19,19-tetraphenyltricyclo[16.3.0.0^{9,13}]henicosa-9,21-diene (**$3_{4,3}$**).* Diastereomer ratio, 41:59. Colorless microcrystals (from CH_2Cl_2/hexane); mp 189–191 °C; IR ($CHCl_3$) ν 1699 (C=O), 1650 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59–7.02 (20H, m), 4.57–4.36 (2H, m), 4.20–3.96 (2H, m), 3.88–3.73 (2H, m), 2.34–2.17 (6H, m), 2.10–1.88 (2H, m), 1.46–0.50 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 166.4, 165.9, 165.8, 145.4, 145.2, 140.9, 140.8, 128.12, 128.07, 127.7, 127.0, 126.9, 126.6, 126.5, 126.2, 126.0, 108.6, 107.6, 95.4, 95.0, 59.8, 59.4, 48.5, 47.7, 31.4, 30.1, 26.5, 26.0, 24.0, 14.5, 14.4. Anal. Calcd for $C_{43}H_{42}O_6$: C, 78.87; H, 6.47. Found: C, 78.83; H, 6.50.

*4.3.7. 10,22-Dimethyl-3,7,11,21-tetraoxa-2,8-dioxo-12,12,20,20-tetraphenyltricyclo[17.3.0.0^{9,13}]icosa-9,22-diene (**$3_{5,3}$**).* Diastereomer ratio, 43:57. Colorless amorphous; IR ($CHCl_3$) ν 1693 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.12 (20H, m), 4.53–4.08 (4H, m), 3.79–3.77 (2H, m), 2.29 (3H, s), 2.26 (3H, s), 2.01–0.63 (12H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 166.5, 165.9, 145.4, 145.2, 140.84, 140.78, 128.5, 128.09, 128.06, 127.6, 127.0, 126.9, 126.7, 126.5, 126.2, 126.1, 108.3, 107.6, 95.2, 95.0, 59.2, 58.8, 49.1, 48.2, 31.3, 30.1, 28.2, 27.94, 27.69, 24.8, 24.2, 14.5, 14.3. FAB HRMS (acetone/NBA) calcd for $C_{44}H_{44}O_6$ 668.3138 (M^+). Found 668.3083.

*4.3.8. 11,23-Dimethyl-3,8,12,22-tetraoxa-2,9-dioxo-13,13,21,21-tetraphenyltricyclo[18.3.0.0^{10,14}]tricosa-10,23-diene (**$3_{5,4}$**).* Diastereomer ratio, 41:59. Colorless microcrystals (from CH_2Cl_2/hexane); mp 127–129 °C; IR ($CHCl_3$) ν 1700 (C=O), 1648 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62–7.02 (20H, m), 4.48–3.81 (4H, m), 3.81–3.58 (2H, m), 2.34–2.21 (6H, m), 1.89–1.64 (2H, m), 1.31–0.57 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.10, 167.01, 166.0, 165.9, 145.2, 145.0, 140.8, 140.7, 128.0, 127.62, 127.58, 127.1, 127.0, 126.8, 126.6, 126.3, 126.2, 108.5, 108.1, 95.4, 95.3, 63.1, 62.7, 48.6, 48.4, 32.5, 32.2, 29.7, 26.9, 26.0, 25.4, 25.35, 14.5, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{45}H_{46}O_6$ 682.3294 (M^+). Found 682.3285.

*4.3.9. 11,24-Dimethyl-3,8,12,23-tetraoxa-2,9-dioxo-13,13,22,22-tetraphenyltricyclo[19.3.0.0^{10,14}]tetracosa-10,24-diene (**$3_{6,4}$**).* Diastereomer ratio, 50:50. Colorless microcrystals (from CH_2Cl_2/hexane); mp 117–119 °C; IR ($CHCl_3$) ν 1699 (C=O), 1648 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64–7.09 (20H, m), 4.43–3.89 (4H, m), 3.80–3.65 (2H, m), 2.34–2.20 (6H, m), 1.82–1.65 (2H, m), 1.39–0.70 (12H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 166.8, 165.9, 165.8, 145.2, 145.1, 140.8, 140.7, 128.0, 127.7, 127.6, 127.0, 126.9, 126.7, 126.2, 108.5, 108.1, 95.28, 95.27, 63.0, 62.9, 49.0, 48.5, 32.1, 31.8, 28.9, 28.8, 26.4, 25.8, 25.7, 25.5, 14.44, 14.40. FAB HRMS (acetone/NBA/NaI) calcd for $C_{46}H_{48}O_6Na$ 719.3374 (M+Na). Found 719.3349.

*4.3.10. 13,26-Dimethyl-3,10,14,25-tetraoxa-2,11-dioxo-15,15,24,24-tetraphenyltricyclo[21.3.0.0^{12,16}]hexacosa-12,26-diene (**$3_{6,6}$**).* Diastereomer ratio, 47:53. R_f=0.27 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1690 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) 7.53–7.19 (20H, m), 4.38–4.24 (2H, m), 4.00–3.90 (2H, m), 3.73 (2H, m), 2.29 (3H, s), 2.27 (3H, s), 1.64–0.82 (20H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.7, 166.5, 166.1, 166.0, 145.1, 140.8, 128.1, 127.7, 127.6, 127.0, 126.83, 126.75, 126.3, 126.2, 108.6, 108.4, 95.2, 63.3, 63.1, 48.6, 48.5, 32.4, 32.2, 30.0, 29.0, 26.9, 26.7, 26.2, 26.1, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{48}H_{53}O_6$ 725.3842 (M+H). Found 725.3821.

*4.3.11. 17,30-Dimethyl-3,14,18,29-tetraoxa-2,15-dioxo-19,19,28,28-tetraphenyltricyclo[23.3.0.0^{12,16}]triaconta-16,30-diene (**$3_{6,10}$**).* R_f=0.59 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1687 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.52–7.16 (20H, m), 4.21 (2H, m), 4.00 (2H, m), 3.68 (2H, m), 2.27 (6H, m), 1.61–0.56 (28H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.5, 166.4, 166.2, 166.1, 145.3, 140.8, 128.0, 127.6, 127.5, 127.0, 126.8, 127.7, 126.22, 126.17, 108.1, 95.0, 63.3, 49.0, 48.9, 31.8, 29.9, 29.7, 29.62, 29.57, 28.9, 26.8,

26.7, 26.4, 26.3, 14.4, 14.3. FAB HRMS (acetone/NBA) calcd for $C_{52}H_{60}O_6$ 780.4390 (M^+). Found 780.4332.

*4.3.12. 19,32-Dimethyl-3,16,20,31-tetraoxa-2,17-dioxo-21,21,30,30-tetraphenyltricyclo[27.3.0.0^{18,22}]dotriaconta-18,32-diene (**3$_{6,12}$**).* R_f=0.61 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1690 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.57–7.07 (20H, m), 4.22–4.13 (2H, m), 4.03–3.96 (2H, m), 3.68 (2H, m), 2.27 (6H, s), 1.61–0.55 (32H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.3, 166.3, 166.1, 145.3, 140.8, 127.99, 127.61, 127.57, 127.02, 126.79, 126.75, 126.2, 108.3, 95.1, 63.4, 63.3, 48.8, 31.9, 29.6, 29.1, 29.06, 29.0, 28.9, 28.6, 26.64, 26.58, 26.02, 25.98, 14.4. FAB HRMS (acetone/NBA/NaI) calcd for $C_{54}H_{64}O_6Na$ 831.4601 (M^++Na). Found 831.4653.

*4.3.13. 13,28-Dimethyl-3,10,14,27-tetraoxa-2,11-dioxo-15,15,26,26-tetraphenyltricyclo[23.3.0.0^{12,16}]octacosa-12,28-diene (**3$_{8,6}$**).* Diastereomer ratio, 49:51. R_f=0.24 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1690 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.53–7.19 (20H, m), 4.30–4.21 (2H, m), 4.02–3.92 (2H, m), 3.73 (2H, m), 2.28 (6H, s), 1.66–0.81 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.64, 166.56, 166.1, 166.0, 145.2, 140.9, 128.0, 127.6, 127.0, 126.8, 126.7, 126.3, 126.2, 108.43, 108.37, 95.2, 63.3, 48.8, 48.7, 32.1, 29.7, 29.1, 28.9, 26.6, 26.4, 26.0, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{50}H_{56}O_6$ 752.4077 (M^+). Found 752.4027.

*4.3.14. 17,32-Dimethyl-3,14,18,31-tetraoxa-2,15-dioxo-19,19,30,30-tetraphenyltricyclo[27.3.0.0^{16,20}]dotriaconta-16,32-diene (**3$_{8,10}$**).* R_f=0.49 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.45–7.11 (20H, m), 4.18–4.13 (2H, m), 3.91–3.88 (2H, m), 3.66 (2H, m), 2.20 (6H, s), 1.55–0.78 (32H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.4, 166.1, 145.3, 140.9, 128.0, 127.6, 127.0, 126.7, 126.2, 108.2, 95.0, 63.2, 49.0, 31.9, 30.1, 29.7, 29.4, 28.9, 26.6, 26.3, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{54}H_{65}O_6$ 809.4781 (M+H). Found 809.4784.

*4.3.15. 19,34-Dimethyl-3,16,20,33-tetraoxa-2,17-dioxo-21,21,32,32-tetraphenyltricyclo[29.3.0.0^{18,22}]-tetratriaconta-18,34-diene (**3$_{8,12}$**).* R_f=0.70 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.53–7.16 (20H, m), 4.20–4.16 (2H, m), 4.03–3.93 (2H, m), 3.74–3.71 (2H, m), 2.24 (6H, s), 1.61–0.75 (36H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.4, 166.1, 145.3, 140.9, 128.0, 127.6, 127.0, 126.8, 126.0, 108.2, 95.0, 63.3, 49.1, 31.9, 29.9, 29.5, 29.4, 28.8, 26.6, 26.3, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{56}H_{68}O_6$ 836.5016 (M^+). Found 836.5013.

*4.3.16. 27,42-Dimethyl-3,24,28,41-tetraoxa-2,25-dioxo-29,29,40,40-tetraphenyltricyclo[37.3.0.0^{26,30}]dotetraconta-26,42-diene (**3$_{8,20}$**).* R_f=0.56 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.46–7.10 (20H, m), 4.04–3.98 (4H, m), 3.67–3.66 (2H, t, J=5.4 Hz), 2.20 (6H, m), 1.58–0.70 (52H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 165.98, 165.95, 145.4, 140.9, 128.0, 127.6, 126.99, 126.8, 126.2, 108.4, 95.0, 63.5, 49.1, 31.7, 29.7, 29.1, 29.04, 28.99, 28.9, 28.6, 26.2, 26.0, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{64}H_{84}O_6$ 948.6268 (M^+). Found 948.6271.

*4.3.17. 13,36-Dimethyl-3,10,14,35-tetraoxa-2,11-dioxo-15,15,34,34-tetraphenyltricyclo[31.3.0.0^{12,16}]-hexatriaconta-12,36-diene (**3$_{16,6}$**).* R_f=0.70 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.55–7.19 (20H, m), 4.15–4.04 (4H, m), 3.78 (2H, t, J=5.9 Hz), 2.28 (6H, s), 1.68–0.96 (40H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.0, 166.0, 145.3, 141.0, 128.1, 127.7, 127.0, 126.7, 126.3, 108.5, 95.2, 63.4, 48.7, 31.8, 29.3, 29.2, 29.1, 28.9, 28.8, 25.9, 25.8, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{58}H_{72}O_6$ 864.5329 (M^+). Found 864.5263.

*4.3.18. 17,40-Dimethyl-3,14,18,39-tetraoxa-2,15-dioxo-19,19,38,38-tetraphenyltricyclo[35.3.0.0^{16,20}]tetraconta-16,40-diene (**3$_{16,10}$**).* R_f=0.80 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.47–7.12 (20H, m), 4.11–4.05 (2H, m), 3.98–3.92 (2H, m), 3.69 (2H, t, J=5.5 Hz), 2.20 (6H, m), 1.60–0.87 (48H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.2, 166.1, 145.3, 140.9, 128.0, 127.6, 127.0, 126.7, 126.2, 108.4, 95.1, 63.6, 48.7, 31.8, 29.7, 29.5, 29.4, 29.2, 29.1, 28.9, 26.3, 26.1, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{62}H_{80}O_6$ 920.5955 (M^+). Found 920.5958.

*4.3.19. 19,42-Dimethyl-3,16,20,41-tetraoxa-2,17-dioxo-21,21,40,40-tetraphenyltricyclo[37.3.0.0^{18,22}]dotetraconta-18,42-diene (**3$_{16,12}$**).* R_f=0.78 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.54–7.20 (20H, m), 4.20–4.15 (2H, m), 4.03–3.97 (2H, m), 3.74 (2H, m), 2.28 (6H, m), 1.64–0.94 (52H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.4, 166.1, 145.4, 140.9, 128.1, 127.7, 127.0, 126.68, 126.3, 108.4, 95.1, 63.6, 48.8, 31.9, 29.9, 29.6, 29.5, 29.3, 28.9, 26.4, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{64}H_{84}O_6$ 948.6268 (M^+). Found 948.6199.

*4.3.20. 27,50-Dimethyl-3,24,28,49-tetraoxa-2,25-dioxo-29,29,48,48-tetraphenyltricyclo[45.3.0.0^{26,30}]pentaconta-26,50-diene (**3$_{16,20}$**).* R_f=0.59 ($CHCl_3$:hexane=8:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.47–7.12 (20H, m), 4.13–4.10 (2H, m), 3.95–3.93 (2H, m), 3.68 (2H, m), 2.20 (6H, m), 1.56–0.85 (68H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.2, 166.1, 145.3, 140.9, 128.0, 127.6, 127.0, 126.7, 126.2, 108.3, 95.0, 63.5, 49.0, 31.9, 29.9, 29.7, 29.6, 29.4, 29.3, 28.8, 26.4, 26.3, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{72}H_{101}O_6$ 1061.7598 (M+H). Found 1061.7598.

*4.3.21. 27,52-Dimethyl-3,24,28,51-tetraoxa-2,25-dioxo-29,29,50,50-tetraphenyltricyclo[47.3.0.0^{26,30}]dopentaconta-26,52-diene (**3$_{18,20}$**).* R_f=0.49 ($CHCl_3$:hexane=8:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1686 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.55–7.17 (20H, m), 4.23–4.15 (2H, m), 4.04–3.98 (2H, m), 3.76 (2H, m), 2.28 (6H, s), 1.66–0.93 (72H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.2, 166.0, 145.3, 140.9, 128.0, 127.6, 127.0, 126.8, 126.2, 108.3, 95.0, 63.5, 49.0, 31.9, 29.83, 29.79, 29.7, 29.6, 29.4, 29.3, 28.8, 26.4, 26.3, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{74}H_{104}O_6$ 1088.7833 (M^+). Found 1088.7826.

*4.3.22. 13,48-Dimethyl-3,10,14,47-tetraoxa-2,11-dioxo-15,15,46,46-tetraphenyltricyclo[43.3.0.0^{12,16}]-octatetraconta-12,48-diene (**3$_{28,6}$**).* R_f=0.63 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1684 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.56–7.21 (20H, m), 4.14–4.07 (4H, m), 3.78 (2H, m), 2.28 (6H, m), 1.67–0.95 (64H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 165.9, 165.9, 145.4, 140.9, 128.1, 127.6, 127.0, 126.8, 126.2, 108.4, 95.1, 63.4, 49.1, 31.7, 29.7, 29.4, 29.0, 28.7, 26.2, 25.8, 14.7. FAB HRMS (acetone/NBA) calcd for $C_{70}H_{96}O_6$ 1032.7207 (M^+). Found 1032.7115.

*4.3.23. 33,68-Dimethyl-3,30,34,67-tetraoxa-2,31-dioxo-35,35,66,66-tetraphenyltricyclo[63.3.0.0^{32,36}]octahexaconta-32,68-diene (**3$_{28,26}$**).* R_f=0.74 ($CHCl_3$); colorless amorphous; IR ($CHCl_3$) ν 1684 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.55–7.20 (20H, m), 4.14 (2H, m), 4.04–4.02 (2H, m), 3.76 (2H, m), 2.28 (6H, s), 1.66–0.93 (104H, m); ^{13}C NMR (75 MHz, $CDCl_3$™) 166.1, 166.1, 145.4, 140.9, 128.0, 127.6, 127.0, 126.8, 126.2, 108.4, 95.0, 63.6, 49.0, 31.8, 29.8, 29.7, 29.6, 29.3, 28.8, 26.3, 26.2, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{90}H_{136}O_6$ 1313.0337 (M^+). Found 1313.0259.

*4.3.24. 12,20-Dimethyl-3,6,9,13,19-pentaoxa-2,10-dioxo-14,14,18,18-tetraphenyltricyclo[15.3.0.0^{11,15}]icosa-11,20-diene (**5$_{1,2}$**).* Diastereomer ratio, 50:50. Colorless microcrystals (from CH_2Cl_2/hexane); mp

132–135 °C; IR ($CHCl_3$) ν 1689 (C=O), 1643 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78–6.97 (20H, m), 4.60–3.45 (10H, m), 2.32–2.13 (6H, m), 1.37–0.85 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 166.5, 166.0, 165.2, 145.0, 144.8, 140.6, 128.1, 127.9, 127.7, 127.4, 127.0, 126.4, 126.3, 125.9, 111.2, 110.3, 96.1, 95.4, 69.9, 69.6, 64.4, 64.3, 45.7, 44.1, 36.4, 14.6, 14.4. FAB HRMS (acetone/NBA/NaI) calcd for $C_{41}H_{38}O_7Na$ 665.2515 (M^++Na). Found 665.2566.

*4.3.25. 12,21-Dimethyl-3,6,9,13,20-pentaoxa-2,10-dioxo-14,14,19,19-tetraphenyltricyclo[16.3.0.0^{11,15}]henicosa-11,21-diene (**5$_{2,2}$**).* Diastereomer ratio, 48:52. Colorless microcrystals (from CH_2Cl_2/hexane); mp 163–165 °C; IR ($CHCl_3$) ν 1691 (C=O), 1642 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55–6.90 (20H, m), 4.40–4.00 (4H, m), 3.76–3.32 (6H, m), 2.20–2.00 (6H, m), 1.34–0.88 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 166.4, 165.7, 165.5, 145.1, 144.9, 140.9, 140.8, 128.0, 127.63, 127.6, 127.5, 126.9, 126.74, 126.5, 126.0, 125.8, 107.2, 107.0, 94.9, 94.8, 69.3, 69.2, 62.5, 61.9, 49.4, 49.3, 28.7, 27.9, 14.43, 14.39. FABMS *m*/*z* (rel intensity) 657 (32, M+H). Anal. Calcd for $C_{42}H_{40}O_7$: C, 76.81; H, 6.14. Found: C, 76.73; H, 6.16.

*4.3.26. 12,22-Dimethyl-3,6,9,13,21-pentaoxa-2,10-dioxo-14,14,20,20-tetraphenyltricyclo[17.3.0.0^{11,15}]docosa-11,22-diene (**5$_{3,2}$**).* Diastereomer ratio, 49:51. Colorless microcrystals (from CH_2Cl_2/hexane); mp 258–260 °C (lit.[13b] mp 258–260 °C); IR ($CHCl_3$) ν 1690 (C=O), 1644 (C=C); ^1H NMR ($CDCl_3$) δ 7.34–7.01 (20H, m), 4.37–4.34 (2H, m), 4.01–3.91 (2H, m), 3.64–3.53 (6H, m), 2.19 (3H, s), 2.17 (3H, s), 1.20–0.67 (6H, m); ^{13}C NMR ($CDCl_3$) δ 166.0, 166.0, 164.8, 164.7, 144.4, 144.3, 139.9, 139.8, 127.0, 126.7, 126.6, 125.93, 125.88, 125.6, 125.5, 125.2, 125.1, 107.1, 106.6, 94.3, 94.2, 68.3, 68.2, 61.6, 61.5, 48.5, 48.1, 31.1, 30.8, 23.1, 22.3, 13.4, 13.3. FABMS *m*/*z* (rel intensity) 671 (100, M+H). Anal. Calcd for $C_{43}H_{42}O_7$: C, 76.99; H, 6.31. Found: C, 76.69; H, 6.31.

*4.3.27. 12,23-Dimethyl-3,6,9,13,22-pentaoxa-2,10-dioxo-14,14,21,21-tetraphenyltricyclo[18.3.0.0^{11,15}]tricosa-11,23-diene (**5$_{4,2}$**).* Diastereomer ratio, 38:62. Colorless microcrystals (from CH_2Cl_2/hexane); mp 253–254 °C; IR ($CHCl_3$) ν 1690 (C=O), 1642 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.56–7.11 (20H, m), 4.56–4.46 (2H, m), 4.11–4.02 (2H, m), 3.82–3.64 (6H, m), 2.32–2.23 (6H, m), 1.32–0.58 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 166.0, 145.4, 145.1, 140.9, 140.8, 128.1, 128.0, 127.7, 127.6, 127.0, 126.9, 126.6, 126.4, 126.3, 126.0, 108.4, 108.0, 95.4, 95.3, 69.8, 69.6, 63.0, 62.9, 48.3, 48.1, 32.0, 30.9, 26.1, 25.1, 14.45, 14.40. FABMS *m*/*z* (rel intensity), 685 (100, M+H). Anal. Calcd for $C_{44}H_{44}O_7$: C, 77.17; H, 6.48. Found: C, 76.98; H, 6.55.

*4.3.28. 15,24-Dimethyl-3,6,9,12,16,23-hexaoxa-2,13-dioxo-17,17,22,22-tetraphenyltricyclo[19.3.0.0^{14,18}]tetracosa-14,24-diene (**5$_{2,3}$**).* Diastereomer ratio, 50:50. Colorless microcrystals (from CH_2Cl_2/hexane); mp 169–171 °C; IR ($CHCl_3$) ν 1694 (C=O), 1650 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50–7.08 (20H, m), 4.40–4.06 (4H, m), 3.80–3.53 (10H, m), 2.15–1.89 (6H, m), 1.22–0.90 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 166.5, 165.5, 145.2, 144.9, 140.8, 140.7, 127.9, 127.6, 127.4, 127.0, 126.8, 126.3, 126.1, 125.9, 107.4, 106.7, 95.1, 70.5, 70.4, 69.3, 69.2, 62.6, 62.1, 48.7, 47.3, 29.0, 26.8, 14.6, 14.1. Anal. Calcd for $C_{44}H_{44}O_8$: C, 75.41; H, 6.33. Found: C, 75.63; H, 6.42.

*4.3.29. 15,25-Dimethyl-3,6,9,12,16,24-hexaoxa-2,13-dioxo-17,17,23,23-tetraphenyltricyclo[20.3.0.0^{14,18}]pentacosa-14,25-diene (**5$_{3,3}$**).* Diastereomer ratio, 44:56. Colorless microcrystals (from CH_2Cl_2/hexane); mp 253–255 °C; IR ($CHCl_3$) ν 1698 (C=O), 1657 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55–7.04 (20H, m), 4.35–4.14 (4H, m), 3.82–3.52 (10H, m), 2.30–2.16 (6H, m), 1.10–0.48 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.5, 165.5, 145.3, 145.2, 140.7, 140.6, 128.0, 127.6, 126.8, 126.7, 126.6, 126.2, 126.1, 108.05, 95.2, 95.1, 70.8, 70.6, 69.5, 69.4, 62.7, 62.1, 48.5, 48.0, 31.6, 31.1, 23.0, 14.6, 14.4. Anal. Calcd for $C_{45}H_{46}O_8$: C, 75.61; H, 6.49. Found: C, 75.34; H, 6.62.

*4.3.30. 15,26-Dimethyl-3,6,9,12,16,25-hexaoxa-2,13-dioxo-17,17,24,24-tetraphenyltricyclo[21.3.0.0^{14,18}]hexacosa-14,26-diene (**5$_{4,3}$**).* Colorless microcrystals (from CH_2Cl_2/hexane); mp 155–157 °C; IR ($CHCl_3$) ν 1692 (C=O), 1646 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.52–7.13 (20H, m), 4.49–4.33 (2H, m), 4.14–4.02 (2H, m), 3.76–3.56 (10H, m), 2.25 (6H, m), 1.20–1.00 (6H, m), 0.70–0.50 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 166.8, 165.8, 165.7, 145.3, 140.7, 140.6, 128.0, 127.7, 127.6, 127.0, 126.5, 126.1, 108.12, 108.06, 95.1, 70.6, 70.3, 69.7, 69.5, 62.7, 62.2, 49.0, 48.8, 31.6, 31.4, 26.7, 26.4, 14.5, 14.4. Anal. Calcd for $C_{46}H_{48}O_8$: C, 75.80; H, 6.64. Found: C, 75.57; H, 6.71.

*4.3.31. 15,27-Dimethyl-3,6,9,12,16,26-hexaoxa-2,13-dioxo-17,17,25,25-tetraphenyltricyclo[22.3.0.0^{14,18}]heptacosa-14,27-diene (**5$_{5,3}$**).* Colorless microcrystals (from CH_2Cl_2/hexane); mp 137–139 °C; IR ($CHCl_3$) ν 1693 (C=O), 1646 (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.56–7.11 (20H, m), 4.49–4.38 (2H, m), 4.12–4.01 (2H, m), 3.81–3.55 (10H, m), 2.28 (6H, m), 1.39–1.09 (6H, m), 0.78–0.59 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 165.8, 165.7, 145.3, 140.8, 128.0, 127.7, 127.5, 127.0, 126.7, 126.2, 107.9, 95.20, 95.18, 70.4, 70.3, 69.8, 62.6, 62.5, 49.0, 48.9, 31.8, 30.2, 30.1, 26.43, 26.37, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{47}H_{51}O_8$ 743.3584 (M+H). Found 743.3561.

*4.3.32. 15,28-Dimethyl-3,6,9,12,16,27-hexaoxa-2,13-dioxo-17,17,26,26-tetraphenyltricyclo[23.3.0.0^{14,18}]octacosa-14,28-diene (**5$_{6,3}$**).* Colorless microcrystals (from CH_2Cl_2/hexane); mp 126–128 °C; IR ($CHCl_3$) ν 1699 (C=O), 1648 (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.61–7.06 (20H, m), 4.51–4.38 (2H, m), 4.12–4.02 (2H, m), 3.83–3.55 (10H, m), 2.28 (6H, m), 1.41–1.14 (4H, m), 0.94–0.64 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 166.9, 165.83, 165.79, 145.3, 140.9, 128.1, 127.6, 127.0, 126.72, 126.67, 126.21, 126.17, 108.01, 107.97, 95.20, 95.18, 70.3, 69.8, 62.6, 48.8, 48.7, 31.8, 29.8, 29.7, 26.4, 26.3, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{48}H_{52}O_8$ 756.3662 (M^+). Found 756.3669.

*4.3.33. 9,19-Dimethyl-3,6,10,14,18-pentaoxa-2,7-dioxo-11,11,17,17-tetraphenyltricyclo[14.3.0.0^{8,12}]nonadeca-8,19-diene (**7$_{0,1}$**).* Colorless microcrystals (from CH_2Cl_2/hexane); mp 122–125 °C; IR ($CHCl_3$) ν 1703 (C=O), 1652 (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.55–7.05 (20H, m), 4.72 (2H, d, *J*=9.0 Hz), 4.13–3.90 (4H, m), 3.05–2.93 (2H, m), 2.88–2.77 (2H, m), 2.27 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 165.7, 144.6, 140.0, 128.2, 127.8, 127.1, 126.3, 126.0, 106.7, 94.5, 72.1, 60.9, 48.4, 14.2. FAB HRMS (acetone/NBA) calcd for $C_{40}H_{37}O_7$ 629.2539 (M+H). Found 629.2495.

*4.3.34. 12,22-Dimethyl-3,6,9,13,17,21-hexaoxa-2,10-dioxo-14,14,20,20-tetraphenyltricyclo[17.3.0.0^{11,15}]docosa-11,22-diene (**7$_{0,2}$**).* Colorless microcrystals (from CH_2Cl_2/hexane); mp 208–210 °C; IR ($CHCl_3$) ν 1698 (C=O), 1636 (C=C9); ^1H NMR (300 MHz, $CDCl_3$) δ 7.62–6.96 (20H, m), 4.48–4.25 (2H, m), 4.20–4.05 (3H, m), 3.93–3.83 (1H, m), 3.78–3.55 (4H, m), 3.45–3.30 (2H, m), 3.11–3.00 (1H, m), 2.89–2.78 (1H, m), 2.36 (3H, s), 2.32 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 168.7, 165.5, 145.3, 145.1, 140.5, 140.4, 128.1, 127.7, 127.53, 127.49, 127.0, 126.93, 126.86, 126.7, 126.3, 102.9, 102.7, 95.3, 94.8, 70.4, 70.1, 69.2, 68.9, 62.5, 62.0, 52.4, 51.9, 14.5, 14.3. Anal. Calcd for $C_{42}H_{40}O_8$: C, 74.98; H, 5.99. Found: C, 74.69; H, 5.77.

*4.3.35. 15,25-Dimethyl-3,6,9,12,16,20,24-heptaoxa-2,13-dioxo-17,17,23,23-tetraphenyltricyclo[20.3.0.0^{14,18}]-pentacosa-14,25-diene (**7$_{0,3}$**).* Colorless microcrystals (from CH_2Cl_2/hexane); mp 199–201 °C; IR ($CHCl_3$) ν 1698 (C=O), 1648 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.63–6.96 (20H, m), 4.40–4.15 (4H, m), 3.94–3.54 (10H, m), 3.26–3.17 (2H, m), 2.84–2.73 (2H, m), 2.34 (3H, s), 2.32 (3H,

s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 168.3, 165.5, 165.3, 145.3, 145.2, 140.5, 140.4, 128.2, 128.0, 127.7, 127.6, 127.3, 127.23, 127.16, 127.1, 126.9, 126.4, 126.3, 103.2, 102.9, 94.9, 94.8, 70.7, 70.5, 69.4, 69.3, 62.6, 62.3, 51.8, 51.0, 14.5. Anal. Calcd for $C_{44}H_{44}O_9$: C, 73.73; H, 6.19. Found: C, 73.80; H, 6.22.

*4.3.36. 18,28-Dimethyl-3,6,9,12,15,19,23,27-octaoxa-2,16-dioxo-20,20,26,26-tetraphenyltricyclo[23.3.0.0^{17,21}]octacosa-17,28-diene (**7$_{0,4}$**).* Colorless amorphous; IR ($CHCl_3$) ν 1695 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63–7.16 (20H, m), 4.60–2.87 (22H, m), 2.33 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 165.2, 145.6, 145.9, 128.1, 127.6, 127.5, 127.3, 127.2, 127.1, 126.9, 126.8, 126.7, 126.6, 126.4, 103., 94.9, 70.7, 70.6, 69.4, 69.1, 61.7, 51.5, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{46}H_{49}O_{10}$ 761.3326 (M+H). Found 761.3328.

*4.3.37. 9,22-Dimethyl-3,6,9,10,14,17,21-heptaoxa-2,7-dioxo-11,11,20,20-tetraphenyltricyclo[17.3.0.0^{8,12}]docosa-8,22-diene (**7$_{1,1}$**).* R_f=0.49 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1705 (C=O), 1639 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.58–7.17 (20H, m), 4.41 (2H, m), 4.30 (2H, m), 3.95 (2H, br dd, J=8.1, 2.4 Hz), 3.59 (2H, dd, J=9.0, 2.2 Hz), 3.11 (2H, dd, J=9.0, 8.1 Hz), 2.66 (2H, m), 2.51 (2H, m), 2.35 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 169.0, 165.4, 144.9, 140.5, 128.1, 127.8, 127.15, 127.1, 127.0, 126.5, 102.6, 94.9, 70.7, 70.3, 61.8, 51.5, 14.6. FAB HRMS (acetone/NBA) calcd for $C_{42}H_{41}O_8$ 673.2801 (M+H). Found 673.2804.

Diastereoisomer. R_f=0.49 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1697 (C=O), 1643 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.62–7.17 (20H, m), 4.54 (2H, m), 4.21 (2H, m), 4.04 (2H, br dd, J=7.8, 2.1 Hz), 3.43 (2H, dd, J=9.0, 2.1 Hz), 3.07 (2H, dd, J=9.0, 7.8 Hz), 2.83–2.77 (2H, m), 2.35–2.28 (2H, m), 2.31 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.7, 165.3, 144.8, 140.4, 128.1, 127.8, 127.1, 127.0, 126.5, 102.9, 94.9, 69.4, 69.4, 61.7, 51.4, 14.6. FAB HRMS (acetone/NBA) calcd for $C_{42}H_{41}O_8$ 673.2801 (M+H). Found 673.2808.

*4.3.38. 12,25-Dimethyl-3,6,9,13,17,20,24-heptaoxa-2,10-dioxo-14,14,23,23-tetraphenyltricyclo[20.3.0.0^{11,15}]-pentacosa-11,25-diene (**7$_{1,2}$**).* Diastereomer ratio, 50:50. R_f=0.44 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1697 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.59–7.20 (20H, m), 4.44–4.30 (2H, m), 4.20–3.97 (4H, m), 3.78–3.67 (4H, m), 3.54 (1H, dd, J=9.5, 2.9 Hz), 3.34 (1H, dd, J=9.5, 2.9 Hz), 3.09–3.02 (2H, m), 2.65–2.52 (4H, m), 2.37 (3H, s), 2.30 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.5, 168.4, 165.4, 145.0, 144.9, 140.5, 140.4, 128.11, 128.1, 127.8, 127.22, 127.19, 127.16, 127.10, 126.98, 126.96, 126.4, 103.6, 103.1, 94.8, 94.7, 70.3, 69.8, 69.6, 69.5, 61.9, 51.5, 50.8, 14.47, 14.46. HRMS (acetone/NBA) calcd for $C_{44}H_{45}O_9$ 717.3064 (M+H). Found 717.3078.

*4.3.39. 15,28-Dimethyl-3,6,9,12,16,20,23,27-octaoxa-2,13-dioxo-17,17,26,26-tetraphenyltricyclo[23.3.0.0^{14,18}]-octacosa-14,28-diene (**7$_{1,3}$**).* Diastereomer ratio, 50:50. R_f=0.41 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1697 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.18 (20H, m), 4.41–4.36 (2H, m), 4.13–4.01 (4H, m), 3.77–3.61 (9H, m), 2.52 (1H, dd, J=9.6 Hz, 3.0 Hz), 3.02–2.96 (2H, m), 2.69–2.65 (2H, m), 2.54–2.52 (2H, m), 2.36, 2.33 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.7, 168.6, 165.44, 165.39, 144.95, 144.90, 140.5, 128.1, 127.8, 127.25, 127.22, 127.20, 127.14, 127.06, 127.0, 126.48, 126.45, 103.1, 103.0, 94.9, 94.8, 71.0, 70.9, 70.1, 69.83, 69.77, 69.5, 69.47, 63.4, 63.3, 51.5, 51.3, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{46}H_{49}O_{10}$ 761.3326 (M+H). Found 761.3352.

*4.3.40. 18,31-Dimethyl-3,6,9,12,15,19,23,26,30-nonaoxa-2,16-dioxo-20,20,29,29-tetraphenyltricyclo[26.3.0.0^{17,21}]-hentriaconta-17,31-diene (**7$_{1,4}$**).* Diastereomer ratio, 50:50. R_f=0.39 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1695 (C=O), 1645 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.65–7.19 (20H, m), 4.39–4.33 (2H, m), 4.20–4.14 (2H, m), 4.07 (1H, m), 4.00 (1H, m), 3.73–3.62 (12H, m), 3.58–3.52 (2H, m), 3.00–2.92 (2H, m), 2.82–2.72 (2H, m), 2.61–2.56 (1H, m), 2.49–2.46 (1H, m), 2.35 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.60, 168.57, 165.42, 165.38, 145.1, 145.0, 140.6, 140.5, 128.1, 127.7, 127.3, 127.1, 127.07, 126.55, 126.48, 102.9, 102.8, 95.0, 94.9, 70.9, 70.8, 70.7, 69.7, 69.6, 69.38, 69.3, 69.2, 63.0, 51.8, 51.6, 14.5, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{48}H_{53}O_{11}$ 805.3588 (M+H). Found 805.3583.

*4.3.41. 9,25-Dimethyl-3,6,10,14,17,20,24-heptaoxa-2,7-dioxo-11,11,23,23-tetraphenyltricyclo[20.3.0.0^{8,12}]-pentacosa-8,25-diene (**7$_{2,1}$**).* Diastereomer ratio, 42:58. R_f=0.35 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1697 (C=O), 1645 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.18 (20H, m), 4.41–4.37 (2H, m), 4.31–4.27 (2H, m), 4.03–4.02 (2H, m), 3.51–3.21 (8H, m), 2.86–2.74 (4H, m), 2.35 (3H, s), 2.31 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.7, 168.5, 165.3, 165.2, 145.0, 140.53, 140.48, 128.1, 127.8, 127.2, 127.17, 127.12, 127.06, 127.0, 126.4, 102.9, 102.8, 94.8, 94.7, 70.62, 70.58, 70.4, 69.1, 69.0, 62.0, 61.8, 51.4, 51.1, 14.8. FAB HRMS (acetone/NBA) calcd for $C_{44}H_{45}O_9$ 717.3064 (M+H). Found 717.3068.

*4.3.42. 12,28-Dimethyl-3,6,9,13,17,20,23,27-octaoxa-2,10-dioxo-14,14,26,26-tetraphenyltricyclo[23.3.0.0^{11,15}]-octacosa-11,28-diene (**7$_{2,2}$**).* R_f=0.27 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1695 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.60–7.17 (20H, m), 4.36–4.31 (2H, m), 4.19–4.14 (2H, m), 4.06–4.04 (2H, m), 3.74–3.71 (4H, m), 3.50–3.42 (2H, m), 3.35–3.23 (4H, m), 3.20–3.14 (2H, m), 3.00–2.88 (4H, m), 2.34 (3H, s), 2.31 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.2, 165.4, 145.0, 140.5, 128.1, 128.0, 127.3, 127.1, 126.4, 103.4, 94.7, 70.3, 70.1, 69.74, 69.70, 69.3, 69.2, 62.64, 62.55, 51.1, 51.0, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{46}H_{49}O_{10}$ 761.3326 (M+H). Found 761.3339.

*4.3.43. 15,31-Dimethyl-3,6,9,12,16,20,23,26,30-nonaoxa-2,13-dioxo-17,17,29,29-tetraphenyltricyclo[26.3.0.0^{14,18}]-hentriaconta-14,31-diene (**7$_{2,3}$**).* R_f=0.27 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1701 (C=O), 1651 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.19 (20H, m), 4.41–4.36 (2H, m), 4.13–4.04 (4H, m), 3.74–3.67 (8H, m), 3.58–3.49 (2H, m), 3.30–3.21 (4H, m), 3.14–2.95 (4H, m), 2.81–2.73 (2H, m), 2.33 (3H, s), 2.32 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.4, 165.4, 145.0, 140.4, 128.1, 127.7, 127.1, 126.4, 103.1, 94.8, 70.7, 70.2, 69.9, 69.61, 69.55, 69.3, 63.0, 51.2, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{48}H_{53}O_{11}$ 805.3588 (M+H). Found 805.3615.

*4.3.44. 18,34-Dimethyl-3,6,9,12,15,19,23,26,29,33-decaoxa-2,16-dioxo-20,20,32,32-tetraphenyltricyclo-[29.3.0.0^{17,21}]tetratriaconta-17,34-diene (**7$_{2,4}$**).* R_f=0.25 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1695 (C=O), 1645 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.19 (20H, m), 4.39–4.34 (2H, m), 4.15–4.05 (4H, m), 3.71–3.55 (14H, m), 3.26–3.16 (4H, m), 3.10–3.00 (4H, m), 2.74–2.65 (2H, m), 2.33 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.6, 165.4, 145.0, 140.5, 128.1, 127.7, 127.2, 127.1, 126.5, 102.9, 94.8, 70.71, 70.66, 70.62, 70.3, 70.2, 69.94, 69.87, 69.56, 69.51, 69.33, 69.30, 63.0, 51.3, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{50}H_{57}O_{12}$ 849.3850 (M+H). Found 849.3837.

*4.3.45. 9,28-Dimethyl-3,6,10,14,17,20,23,27-octaoxa-2,7-dioxo-11,11,26,26-tetraphenyltricyclo[23.3.0.0^{8,12}]-octacosa-8,28-diene (**7$_{3,1}$**).* R_f=0.22 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1701 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.59–7.19 (20H, m), 4.41–4.28 (4H, m), 4.07–4.05 (2H, m), 3.57–3.44 (8H, m), 3.39–3.19 (4H, m), 3.01–2.89 (4H, m), 2.33 (3H, s), 2.31 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.4, 168.2, 165.2, 145.0, 144.9, 140.5, 128.1, 127.8, 127.2, 127.1, 127.0, 126.4, 103.2, 103.1, 94.8, 70.7, 70.6, 70.5, 70.4,

70.3, 70.1, 69.4, 69.3, 61.8, 61.7, 51.2, 14.7. FAB HRMS (acetone/NBA) calcd for $C_{46}H_{49}O_{10}$ 761.3326 (M+H). Found 761.3344.

*4.3.46. 12,31-Dimethyl-3,6,9,13,17,20,23,26,30-nonaoxa-2,10-dioxo-14,14,29,29-tetraphenyltricyclo-[26.3.0.0^{11,15}]hentriaconta-11,31-diene (**7$_{3,2}$**).* Diastereomer ratio, 49:51. R_f=0.30 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1699 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.60–7.16 (20H, m), 4.37–4.28 (2H, m), 4.20–4.16 (2H, m) 4.06 (2H, m), 3.74–3.68 (4H, m), 3.54–3.46 (6H, m), 3.41–3.29 (4H, m), 3.18–3.10 (2H, dd, J=15.6, 7.5 Hz), 2.97–2.85 (4H, m), 2.33 (3H, s), 2.32 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.2, 168.1, 165.4, 144.9, 140.5, 128.1, 127.8, 127.3, 127.11, 127.07, 126.4, 103.42, 103.35, 94.7, 70.6, 70.4, 70.3, 70.21, 70.16, 69.64, 69.56, 69.2, 62.74, 61.65, 51.1, 14.6, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{48}H_{53}O_{11}$ 805.3588 (M+H). Found 805.3597.

*4.3.47. 15,34-Dimethyl-3,6,9,12,16,20,23,26,29,33-decaoxa-2,13-dioxo-17,17,32,32-tetraphenyltricyclo-[29.3.0.0^{14,18}]tetratriaconta-14,34-diene (**7$_{3,3}$**).* R_f=0.30 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1695 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.19 (20H, m), 4.35–4.30 (2H, m), 4.17–4.10 (2H, m), 4.06–4.04 (2H, m), 3.73–2.78 (24H, m), 2.33 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.4, 165.4, 144.9, 140.5, 128.1, 127.8, 127.2, 127.1, 127.1, 126.5, 103.1, 94.8, 70.7, 70.6, 70.26, 70.23, 70.0, 69.5, 69.3, 62.9, 51.2, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{50}H_{57}O_{12}$ 849.3850 (M+H). Found 849.3851.

*4.3.48. 18,37-Dimethyl-3,6,9,12,15,19,23,26,29,32,36-undecaoxa-2,16-dioxo-20,20,35,35-tetraphenyltricyclo-[32.3.0.0^{17,21}]heptatriaconta-17,37-diene (**7$_{3,4}$**).* R_f=0.18 ($CHCl_3$:MeOH=95:5 v/v); colorless amorphous; IR ($CHCl_3$) ν 1693 (C=O), 1645 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.18 (20H, m), 4.36–4.31 (2H, m), 4.18–4.05 (4H, m), 3.72–3.51 (18H, m), 3.31–3.23 (4H, m), 3.11–3.03 (4H, m), 2.78–2.74 (2H, m), 2.33 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.5, 165.4, 144.9, 140.5, 128.1, 127.8, 127.23, 127.21, 127.1, 126.5, 103.0, 94.8, 70.7, 70.62, 70.61, 70.56, 70.54, 70.19, 70.16, 69.85, 69.83, 69.54, 69.51, 69.3, 62.9, 51.3, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{52}H_{61}O_{13}$ 893.4112 (M+H). Found 893.4117.

*4.3.49. 9,31-Dimethyl-3,6,10,14,17,20,23,26,30-nonaoxa-2,7-dioxo-11,11,29,29-tetraphenyltricyclo[26.3.0.0^{8,12}]-hentriaconta-8,31-diene (**7$_{4,1}$**).* Diastereomer ratio, 49:51. R_f=0.11 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1701 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.58–7.19 (20H, m), 4.42–4.27 (4H, m), 4.04 (2H, m), 3.65–3.46 (10H, m), 3.38–3.30 (4H, m), 3.21–3.13 (2H, m), 3.00–2.87 (4H, m), 2.311(3H, s), 2.308 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.34, 168.26, 165.11, 165.09, 144.94, 144.92, 140.5, 128.1, 127.8, 127.3, 127.12, 127.06, 126.4, 103.14, 103.10, 94.8, 70.72, 70.69, 70.41, 70.39, 70.2, 69.5, 62.60, 61.56, 51.22, 51.17, 14.74, 14.72. FAB HRMS (acetone/NBA) calcd for $C_{48}H_{53}O_{11}$ 805.3588 (M+H). Found 805.3588.

*4.3.50. 12,34-Dimethyl-3,6,9,13,17,20,23,26,29,33-decaoxa-2,10-dioxo-14,14,32,32-tetraphenyltricyclo-[29.3.0.0^{11,15}]tetratriaconta-11,34-diene (**7$_{4,2}$**).* R_f=0.11 ($CHCl_3$:MeOH=98:2 v/v); colorless amorphous; IR ($CHCl_3$) ν 1699 (C=O), 1651 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.18 (20H, m), 4.35–4.29 (2H, m), 4.21–4.16 (2H, m) 4.06 (2H, m), 3.74–3.48 (14H, m), 3.35–3.31 (4H, m), 3.17–3.10 (2H, m), 2.98–2.93 (2H, m), 2.87–2.82 (2H, m), 2.322 (3H, s), 2.318 (3H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.04, 168.0, 165.2, 144.8, 140.4, 128.0, 127.7, 127.2, 127.1, 127.0, 126.4, 103.2, 103.1, 94.7, 70.69, 70.67, 70.62, 70.3 70.1, 70.0, 69.54, 69.50, 69.2, 62.6, 51.1, 14.5. FAB HRMS (acetone/NBA) calcd for $C_{50}H_{57}O_{12}$ 849.3850 (M+H). Found 849.3847.

*4.3.51. 15,37-Dimethyl-3,6,9,12,16,20,23,26,29,32,36-undecaoxa-2,13-dioxo-17,17,35,35-tetraphenyltricyclo-[32.3.0.0^{14,18}]heptatriaconta-14,37-diene (**7$_{4,3}$**).* R_f=0.17 ($CHCl_3$:MeOH=95:5 v/v); colorless amorphous; IR ($CHCl_3$) ν 1701 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.61–7.16 (20H, m), 4.34–4.32 (2H, m), 4.30–4.14 (2H, m) 4.06 (2H, m), 3.72–3.47 (18H, m), 3.34–3.30 (4H, m), 3.12 (2H, t, J=8.4 Hz), 3.03–2.98 (2H, m), 2.84–2.79 (2H, m), 2.33 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.1, 165.2, 144.8, 140.4, 128.0, 127.6, 127.1, 127.03, 126.92, 126.3, 103.0, 94.6, 70.6, 70.53, 70.51, 70.2, 69.9, 69.4, 69.2, 62.6, 51.2, 14.4. FAB HRMS (acetone/NBA) calcd for $C_{52}H_{61}O_{13}$ 893.4112 (M+H). Found 893.4118.

*4.3.52. 18,40-Dimethyl-3,6,9,12,15,19,23,26,29,32,35,39-dodecaoxa-2,16-dioxo-20,20,38,38-tetraphenyltricyclo-[35.3.0.0^{17,21}]tetraconta-17,40-diene (**7$_{4,4}$**).* R_f=0.09 ($CHCl_3$:MeOH=95:5 v/v); colorless amorphous; IR ($CHCl_3$) ν 1695 (C=O), 1647 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$™) 7.62–7.17 (20H, m), 4.36–4.20 (2H, m), 4.19–4.13 (2H, m) 4.06 (2H, m), 3.72–3.49 (22H, m), 3.33–3.30 (4H, m), 3.12–2.99 (4H, m), 2.81–2.76 (2H, m), 2.27 (6H, s); ^{13}C NMR (75 Hz, $CDCl_3$™) 168.3, 165.4, 145.0, 140.5, 128.1, 127.8, 127.2, 126.5, 103.1, 94.8, 70.6, 70.2, 69.9, 69.5, 69.3, 62.8, 51.3, 14.6. FAB HRMS (acetone/NBA) calcd for $C_{54}H_{65}O_{14}$ 937.4374 (M+H). Found 937.4384.

4.4. Reaction of diene 1$_8$ with bis(3-oxobutanoate) 2$_6$ in the presence of manganese(III) acetate

A mixture of the diene **1$_8$** (0.2 mmol) and the bis(3-oxobutanoate) **2$_6$** (0.4 mmol) was allowed to react with manganese(III) acetate (0.4 mmol) in acetic acid (50 mL) at 100 °C under an argon atmosphere for 5 min. After the usual work-up, the macrodiolide **3$_{8,6}$** (14%), the dihydrofuran **8** (28%), and the unchanged diene **1$_8$** (26%) were isolated.

*4.4.1. 7-Oxa-8,10-dioxoundecyl 2-methyl-4-(10,10-diphenyl-9-decenyl)-5,5-diphenyl-4,5-dihydrofuran-3-carboxylate (**8**).* R_f=0.36 (Et_2O:hexane=5:5); colorless liquid; IR ($CHCl_3$) ν 1735, 1717, 1686 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54–7.15 (20H, m), 6.06 (1H, t, J=7.5 Hz), 4.15–4.06 (4H, m), 3.75 (1H, m), 3.43 (2H, s), 2.27, 2.25 (6H, s), 2.10–0.81 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6, 167.2, 165.93, 165.86, 145.4, 142.9, 141.3, 140.9, 140.29, 130.3, 129.9, 128.1, 127.7, 127.2, 127.1, 126.8, 126.7, 126.2, 108.4, 108.3, 95.0, 65.3, 63.4, 50.1, 49.1, 31.8, 31.6, 29.9, 29.8, 29.7, 29.25, 29.18, 29.1, 28.6, 28.4, 26.25, 26.15, 25.8, 25.7, 25.5, 30.2, 14.7. FAB HRMS (acetone/NBA/NaI) calcd for $C_{50}H_{58}O_6Na$ 777.4131 (M^++Na). Found 777.4196.

4.5. Alternative synthesis of dihydrofurancarboxylate 8

3,4-Dihydro-2*H*-pyran (0.4205 g, 5 mmol) was dropwise added to a mixture of hexanediol (0.591 g, 5 mmol) and a catalytic amount of *p*-toluenesulfonic acid in dry THF (20 mL), and the reaction mixture was stirred overnight. The reaction was quenched with water and the aqueous solution was extracted with $CHCl_3$. The extract was washed with brine (20 mL) and a saturated aqueous solution of Na_2CO_3 (20 mL), dried over anhydrous $MgSO_4$, and concentrated to dryness. The residue was separated by silica gel column chromatography eluting with Et_2O/hexane (8:2), giving 6-(2-tetrahydropyranyl)oxyhexan-1-ol (0.474 g, 47%) as a colorless oil. To a solution of 6-(2-tetrahydropyranyl)oxyhexan-1-ol (1.672 g, 8.2 mmol) and imidazole (1.28 g, 18.8 mmol) in dry THF (30 mL), diketene (1.46 mL, 18.8 mmol) was then added dropwise at 0 °C. After the addition, the reaction mixture was stirred for 2 h at room temperature. The reaction was quenched with water and the aqueous mixture was extracted with $CHCl_3$. The extract was washed with brine (20 mL) and a saturated aqueous solution of Na_2CO_3 (20 mL), dried over anhydrous $MgSO_4$, and concentrated to dryness. The crude products were separated by silica gel column chromatography eluting with $CHCl_3$, affording the THP-protected hexamethyl 3-oxobutanoate **9** (1.472 g, 62%) as a colorless oil.

A mixture of the diene $\mathbf{1_8}$ (0.2 mmol) and the butanoate **9** (0.13 mmol) was allowed to react with manganese(III) acetate (0.6 mmol) in acetic acid (50 mL) at 100 °C under an argon atmosphere for 15 min. After the usual work-up, the dihydrofuran **10** (59%) was obtained. The dihydrofuran **10** was treated with diketene in dry THF at room temperature for 24 h in the presence of imidazole to give the corresponding dihydrofurancarboxylate **8** in 66% yield.

*4.5.1. 6-Hydroxyhexyl 2-methyl-4-(10,10-diphenyl-9-decyl)-5,5-diphenyl-4,5-dihydrofuran (**10**).* R_f=0.44 ($CHCl_3$); colorless liquid; IR ($CHCl_3$) ν 1724 (C=O), 1686 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54–7.14 (20H, m), 6.06 (1H, t, J=7.5 Hz), 4.14–4.06 (2H, m), 3.76 (1H, t, J=7.5 Hz), 3.61 (2H, t, J=6.3 Hz), 2.27 (3H, s), 2.10–2.03 (2H, m), 1.68–0.90 (22H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6, 167.2, 166.0, 165.7, 145.4, 142.7, 141.3, 140.9, 140.3, 130.3, 130.0, 128.0, 127.6, 127.2, 127.0, 126.8, 126.2, 108.3, 95.0, 63.4, 62.8, 32.6, 31.6, 29.9, 29.8, 29.7, 29.25, 29.18, 29.1, 28.7, 26.2, 25.9, 25.4, 14.7. FAB HRMS (acetone/NBA/NaI) calcd for $C_{46}H_{54}O_4Na$ 693.3920 (M^++Na). Found 693.3953.

4.6. Manganese(III)-based intramolecular cyclization of dihydrofurancarboxylate 8

The dihydrofurancarboxylate **8** (0.2 mmol) was oxidized with manganese(III) acetate (0.44 mmol) in acetic acid (100 mL) at 100 °C for 7 min under an argon atmosphere. After the usual work-up, the macrodiolide $\mathbf{3_{8,6}}$ was isolated in 78% yield.

4.7. X-ray analysis of macrodiolides $\mathbf{5_{4,2}}$, $\mathbf{5_{3,3}}$, and $\mathbf{7_{0,3}}$

All measurements were made using an imaging plate diffractometer with graphite monochromated Mo Kα radiation (λ=0.71069 Å). The data reductions were carried out by the PROCESS-AUTO program package, and Lorentz and polarization corrections were performed. Corrections for the secondary extinctions were applied. The structures were solved by the direct method and were refined on SIR-92.[18] The refinements were done by the least-squares full matrix method, with anisotropic displacement parameters for all non-hydrogen atoms. The hydrogen atoms were included but not refined. All calculations were performed using the teXsan[19] crystallographic software package of Molecular Structure Corporation. The crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 751794 for $\mathbf{5_{4,2}}$ (Fig. 1), 751795 for $\mathbf{7_{0,3}}$ (Fig. 3), and 751796 for $\mathbf{5_{3,3}}$ (Fig. 2). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk.

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Supplementary data

Synthetic procedure and spectroscopic data of the substrates $\mathbf{1}_x$, $\mathbf{2}_y$, $\mathbf{4}_y$, $\mathbf{6}_x$, the result of the MM2 calculation of the intermediate from the reaction of $\mathbf{1_4}$ with $\mathbf{4_2}$, and copies of ^{1}H NMR, ^{13}C NMR, IR, and MS spectra for the new products. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.02.022.

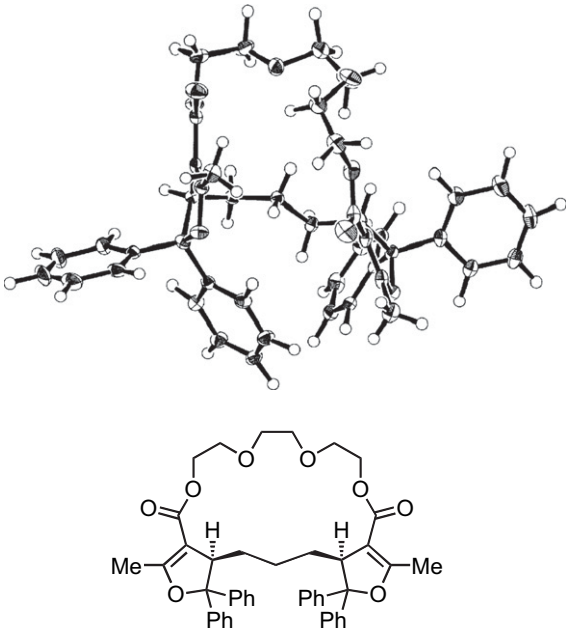

Figure 2. ORTEP drawing of *meso*-macrodiolide $\mathbf{5_{3,3}}$.

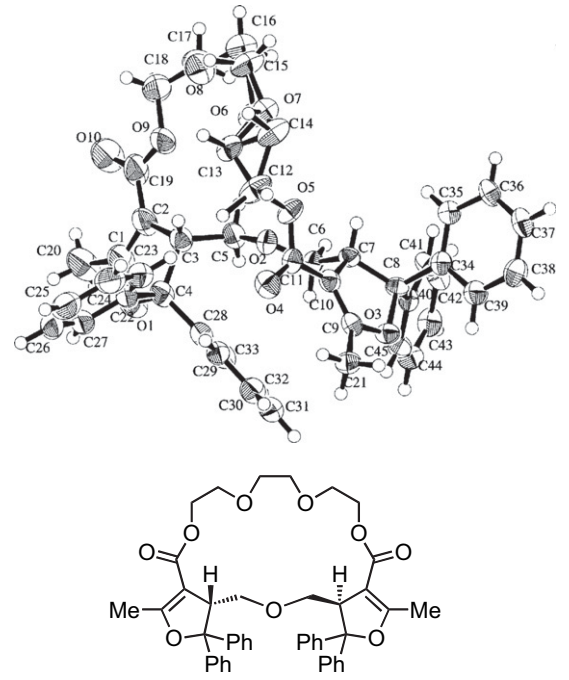

Figure 3. ORTEP drawing of DL-macrodiolide $\mathbf{7_{0,3}}$.

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