

Simple synthesis of a new family of 22- to 28-membered macrocycles containing two chalcone moieties

Rina Mondal, Tapas K. Mandal, and Asok K. Mallik*

Department of Chemistry, Jadavpur University, Kolkata-700 032, India

E-mail: mallikak52@yahoo.co.in

Abstract

A new family of 22- to 28-membered tetrabenzo-macrocycles containing two chalcone moieties has been synthesized from 2-hydroxybenzaldehyde and 2'-hydroxyacetophenone through phenol alkylation with α,ω -dibromoalkanes followed by Claisen-Schmidt reaction under high dilution condition. All the compounds of this family were found to possess both the double bonds in *E*-configuration. An attempt to synthesize another family of isomeric tetrabenzo-macrocycles having opposite alignment of the two chalcone moieties by reaction of 2,2'-dihydroxychalcone with α,ω -dibromoalkanes was not successful, a series of 12- to 14-membered dibenzo-macrocycles with only one chalcone moiety was obtained here.

Keywords: Combinatorial chemistry, macrocycles, bis-chalcones, Claisen-Schmidt reaction, oxygen heterocycles

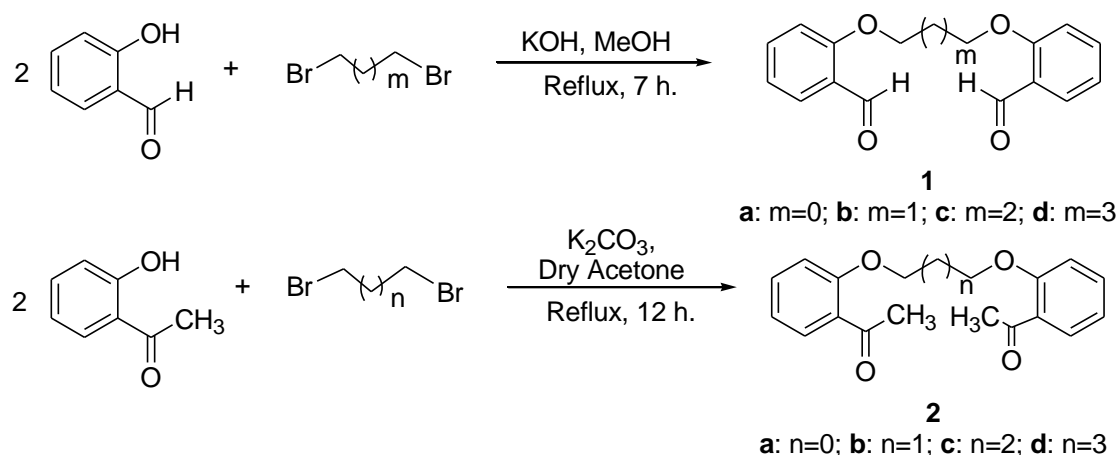
Introduction

The chalcone (1,3-diphenyl-2-propen-1-one) moiety is very easy to construct, and chalcones are reported to possess important biological activities.¹⁻⁷ Moreover, these compounds are known to be transformed into other compounds in a number of ways, many of which are biologically active heterocycles.⁸⁻¹¹ Macrocycles incorporating more than one chalcone moiety have great potential in generating new compounds suitable for molecular recognition¹²⁻¹⁵ and photophysical^{16,17} studies. The chemical literature shows sporadic reports of construction of a few such types of compounds.¹⁸⁻²⁰ Synthesis of other structurally related compounds and their suitable transformations to useful hosts are also reported.^{21,22} Furthermore, very recently several types of macrocycles containing fused heterocyclic or homocyclic moieties have been synthesized²³⁻²⁹ and a good number of them have shown some very interesting properties. It was therefore our endeavour to develop a simple synthesis of macrocycles containing more than one chalcone moiety. The study started with synthesis of target molecules containing two chalcone moieties by exploiting the well-known Claisen-Schmidt reaction which is one of the most simple

and high-yielding organic reactions showing very high atom economy. The outcome of this study is presented herein.

Results and Discussion

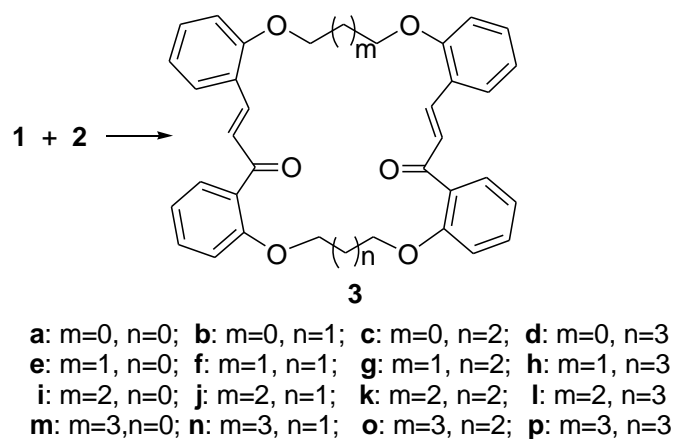
A retrosynthetic analysis of the target macrocycles indicated a very simple approach for their synthesis through the use of commonly available starting materials. It was considered that generation of a bis-aldehyde by joining two benzaldehyde units with a spacer and that of a bis-ketone by joining two acetophenone units with another spacer followed by their Claisen-Schmidt condensation (first step intermolecular and the second step intramolecular) would lead to the target macrocycles. Hydroxybenzaldehydes and hydroxyacetophenones are readily available compounds, and our study began with the *ortho* compounds of these two categories. Reaction of α,ω -dibromoalkanes with 2-hydroxybenzaldehyde in 1:2 mole ratio was used to generate the required bis-aldehydes and analogous reaction involving 2'-hydroxyacetophenone was used to generate the required bis-ketones (Scheme 1). α,ω -Dibromoalkanes containing 2-5 methylene units are commercially available compounds, and so we could readily synthesize the bis-aldehydes **1a-d** and the bis-ketones **2a-d**.³⁰⁻³²



Scheme 1. Synthesis of bis-aldehydes and bis-ketones.

For synthesis of macrocyclic bis-chalcones utilizing the above bis-aldehydes and bis-ketones, reactions of sixteen possible combinations of reactants were performed in aqueous methanolic KOH (Scheme 2), and all of them proved to be successful. An initial study with four examples (**1a+2a**, **1b+2b**, **1c+2c**, **1d+2d**) showed that application of high dilution technique increased the yield of the macrocycles significantly.³³ So the high dilution technique was applied for all the combinations (concentration of each of the two components was in the range 1.5 to 1.9×10^{-3} mol/L). Under this condition the yields of the macrocycles were moderate to good, though they varied widely (Table 1). The configurations of the double bonds of the chalcone moieties present in each macrocyclic system so obtained have been found to be *E* from characteristic coupling

constant values in ^1H NMR spectra ($J_{\alpha,\beta} \sim 16$ Hz). This structural feature was evident also from an X-ray crystallographic study of one of the members (**3f**, Figure 1). It may be mentioned here that under the applied reaction conditions intramolecular aldol condensation of **2** did not take place at all.



Scheme 2. Synthesis of macrocyclic bis-chalcones from **1** and **2**.

Table 1. Macrocyclic bis-chalcones synthesized from **1** and **2**

Bis-aldehyde	Bis-ketone	Product	Ring size	Isolated yield (%)
1a	2a	3a	22	64
1a	2b	3b	23	72
1a	2c	3c	24	54
1a	2d	3d	25	57
1b	2a	3e	23	70
1b	2b	3f	24	72
1b	2c	3g	25	60
1b	2d	3h	26	58
1c	2a	3i	24	54
1c	2b	3j	25	43
1c	2c	3k	26	56
1c	2d	3l	27	68
1d	2a	3m	25	73
1d	2b	3n	26	62
1d	2c	3o	27	74
1d	2d	3p	28	51

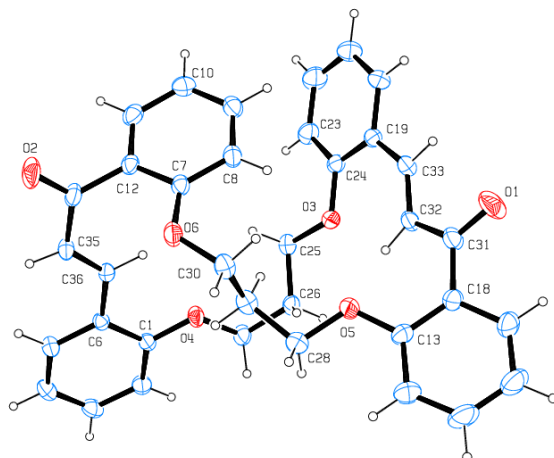
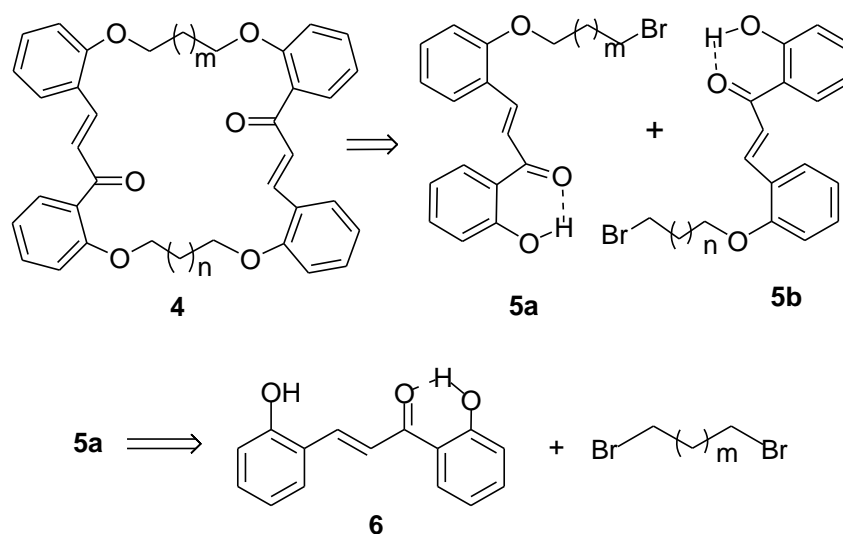


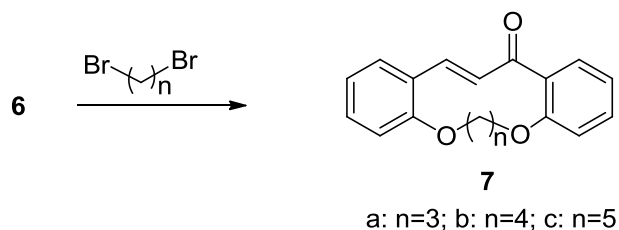
Figure 1. ORTEP diagram of **3f** showing thermal ellipsoids at 25% probability.

In all the macrocycles **3a-p**, the two α,β -unsaturated ketone moieties are aligned in the same way. There is a possibility of getting the corresponding isomeric macrocycles where these two moieties are aligned in the opposite way, *i.e.*, the macrocycles being of the type **4**. Such macrocycles also would be structurally interesting, and for their synthesis etherification involving **5a** and **5b** (through occurrence of an intermolecular process first and then an intramolecular process) was conceived as one of the plausible routes. Anticipating that reaction at the free OH of 2,2'-dihydroxychalcone (**6**) would be faster than that at its chelated OH, the mono ethers **5a** and **5b** would be expected to be the products of the first step of its reaction with α,ω -dibromoalkanes. It was our consideration that if it is possible to bring about the second step of the reaction in the same pot, any target compound of the series **4** with $m=n$ may be reached readily (Scheme 3). With this synthetic planning, **6** was refluxed separately



Scheme 3. Retrosynthetic analysis for construction of **4**.

with each of the α,ω -dibromoalkanes, Br-(CH₂)₂-Br, Br-(CH₂)₃-Br, Br-(CH₂)₄-Br and Br-(CH₂)₅-Br in dry acetone with K₂CO₃ using the reactants at the concentration 0.067 mol/L. It was observed that reaction took place in last three of these cases yielding nonphenolic products. However, the spectral data of the products thus obtained showed that, instead of the desired compounds **4** (with m=n), cyclic compounds of general structure **7** were formed (Yield: **7a**-50%, **7b**-49%, **7c**-54%) (Scheme 4). Thus, it may be concluded that even by using the reactants in relatively higher concentration as mentioned above, the intramolecular reactions are more facile than intermolecular ones in these cases.



Scheme 4. Alkylation of **6** with α,ω -dibromoalkanes.

A careful examination of the chemical shifts of H- α and H- β of the enone system of **3a-p** showed that the former proton appeared in the range δ 7.01 - 7.55 while the latter in the range δ 7.52 - 7.73 (*vide* Experimental), and the variation of chemical shift values of each of these two protons did not show any regular trend. In case of the compounds **7a-c**, the variation of chemical shifts of H- β and the Ar-H *ortho* to carbonyl is very conspicuous (Table 2) and here also no regular trend of chemical shift values was observed. The large δ -value for H- β of **7b** indicated that in the preferred conformation of this compound the said proton experiences remarkable anisotropic deshielding.

Table 2. Chemical shift values (δ) of some protons of **7a-c**

Compound	H- α	H- β	Ar-H <i>ortho</i> to C=O
7a	7.52	7.60	7.72
7b	7.64	8.95	8.08
7c	7.70	8.20	7.68

Some initial work towards synthesis of macrocyclic bis-chalcones of the type **8-10** by including 3-hydroxybenzaldehyde and 3'-hydroxyacetophenone also as starting materials could be done so far. Thus, attempts towards synthesis of **8a** (from **11** and **2b**), **9a** (from **1c** and **12**) and **10a** (from **11** and **12**) were found to be successful in the first two cases, though the yields were somewhat lower [**8a** (ring size 26) - 35%; **9a** (ring size 28) - 38%]. It is being planned to undertake a separate program for synthesis of these categories of macrocycles.

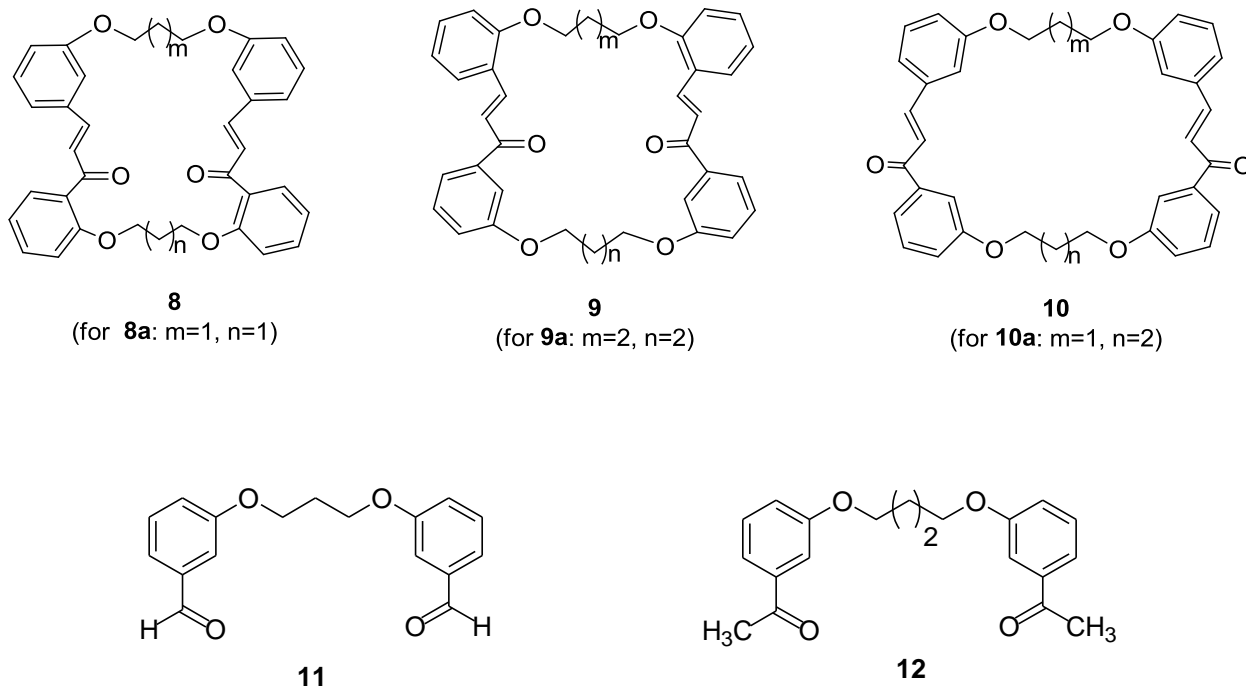


Figure 2. Some possible macrocyclic bis-chalcones starting from **1c**, **2b**, **11** and **12**.

Conclusions

Thus, a simple method for synthesis of a new family of 22- to 28-membered macrocycles of general structure **3**, all containing two chalcone moieties with *E* double bonds, has been developed. As an offshoot of this study, another group of 12- to 14-membered macrocycles (**7**) containing one *E* chalcone unit has also been synthesized. The yields of the compounds **3** which are of major interest here, have been found to be much better than those for some related compounds reported by other groups.^{18,19} This category of compounds has the potential to find wide applicability as two of their spacers can be varied independently and widely and the two α,β -unsaturated ketone moieties present in each of them can be made to undergo condensation with varieties of suitable heteroatom containing condensing agents leading to interesting heterocycle fused macrocycles. Some works in this direction are being done currently.

Experimental Section

General. Melting points were recorded on a K ofler block. IR spectra were recorded on a Perkin Elmer FT-IR Spectrometer (Spectrum RX 1) in KBr pellets. ¹H and ¹³C NMR spectra were recorded in CDCl₃ on a Bruker AV-300 (300 MHz) spectrometer. Mass spectra were measured in the following ways: ESIMS(+) [Waters Micromass Q-ToF micro], FAB-MS [Jeol M Station

JMS.700], DI-EIMS and GCMS [Shimadzu-QP5050A], and GCMS [Q star XL hybrid instrument]. Analytical samples were routinely dried *in vacuo* at room temperature. Microanalytical data were recorded on four Perkin-Elmer 2400 Series II C, H, N analyzers. Column chromatography was performed with silica gel (100-200 mesh) and TLC with silica gel G made of SRL Pvt. Ltd. Petroleum ether had the boiling range 60-80 °C. X-ray single crystal data collection for **3f** was performed with a “Bruker SMART” diffractometer (details given at the end of this section).

1,m-Bis(2-/3-formylphenoxy)alkanes 1a-d and 11. General procedure

A mixture of 2-/3-hydroxybenzaldehyde (20 mmol) and α,ω -dibromoalkane (10 mmol) was refluxed in methanolic KOH (5%, 25mL) for 7 h. Removal of methanol by distillation, addition of water followed by extraction with ethyl acetate gave crude alkylation product which was purified by rapid column chromatography followed by crystallization from CHCl_3 -petroleum ether. They were characterized from their melting points (given below) and ^1H NMR spectral features (data given where necessary).

1,2-Bis-(2-formylphenoxy)ethane (1a). Colourless needles, mp 128-129 °C (lit.^{8a} 128-130 °C).

1,3-Bis-(2-formylphenoxy)propane (1b). Colourless needles, mp 98-99 °C (lit.^{8a} 99-100 °C).

1,4-Bis-(2-formylphenoxy)butane (1c). Colourless needles, mp 145-146 °C (lit.^{8a} 146-148 °C).

1,5-Bis-(2-formylphenoxy)pentane (1d). Colourless needles, mp 57 °C (lit.^{8b} 50-53 °C).

1,3-Bis-(3-formylphenoxy)propane (11). Colourless needles, mp 68 °C; ^1H NMR (300 MHz, CDCl_3): δ_{H} 2.32 (quintet, 2H, J 6 Hz), 4.24 (t, 4H, J 6 Hz), 7.17-7.20 (m, 2H), 7.41-7.47 (m, 6H), 9.97 (br. s, 2H, 2 \times -CHO).

1,n-Bis-(2-/3-acetylphenoxy)alkanes 2a-d and 12. General procedure

A mixture of 2’-/3’-hydroxyacetophenone (20 mmol), α,ω -dibromoalkane (10 mmol) and anhyd. K_2CO_3 (3g.) was refluxed in dry acetone for 12 h. Usual work-up followed by purification of the resulting crude material by column chromatography over silica gel afforded pure product. They were characterized from their melting points (given below) and ^1H NMR spectral features (data given where necessary).

1,2-Bis-(2-acetylphenoxy)ethane (2a). Colourless needles, mp 126 °C (lit.^{8c} 125 °C).

1,3-Bis-(2-acetylphenoxy)propane (2b). Colourless needles, mp 104-106 °C (lit.^{8c} 107 °C).

1,4-Bis-(2-acetylphenoxy)butane (2c). Colourless needles, mp 148-150 °C; ^1H NMR (300 MHz, CDCl_3): δ 2.07 (br. s, 4H, $w_{1/2}\approx 13.0$ Hz), 2.61 (s, 6H, 2 \times -COCH₃), 4.14 (br. s, 4H, $w_{1/2}\approx 13.0$ Hz), 6.95 (br. d, 2H, J 8.4 Hz), 7.00 (br. t, 2H, J 7.6 Hz), 7.45 (ddd, 2H, J 8.4, 7.7 and 1.8 Hz), 7.73 (dd, 2H, J 7.7 and 1.8 Hz).

1,5-Bis-(2-acetylphenoxy)pentane (2d). Colourless needles, mp 106 °C (lit.^{8b} 105-106 °C).

1,4-Bis-(3-acetylphenoxy)butane (12). Colourless needles, mp 105 °C; ^1H NMR (300 MHz, CDCl_3): δ 2.01 (br. s, 4H, $w_{1/2}\approx 13.0$ Hz), 2.59 (s, 6H, 2 \times -COCH₃), 4.09 (br. s, 4H, $w_{1/2}\approx 13.0$ Hz), 7.10 (br. d, 2H, J 8.0 Hz), 7.36 (t, 2H, J 7.9 Hz), 7.48 (br. s, 2H) and 7.53 (br. d, 2H, J 7.7 Hz).

General procedure for macrocyclisation using the bis-aldehydes 1 and the bis-ketones 2. A mixture of bis-aldehyde (**1**) (0.25 mmol) and bis-ketone (**2**) (0.25 mmol) was dissolved in a KOH solution (10%, 130-160 mL) in MeOH-H₂O (3:1) and the mixture was stirred at room temperature. A precipitate began to be formed after *ca.* 5 h. of stirring. The stirring was continued for 72 h., the volume of the solvent was reduced to nearly half of the original by distillation under reduced pressure. The product obtained as precipitate was collected by careful filtration. The solid thus obtained was almost pure and it was further purified by column chromatography over silica gel followed by crystallization from CHCl₃-petroleum ether. The analytical and spectral data of the macrocyclic products **3a-p** were as follows:

(2E,22E)-11,14,30,33-Tetraoxapentacyclo[32.4.0.0^{5,10}.0^{15,20}.0^{24,29}]octatriaconta-1(38),2,5,7,9,-15,17,19,22,24,26,28,34,36-tetradecaene-4,21-dione (3a). Eluent: petroleum ether-EtOAc (6:4, v/v), light yellow cubes, mp 225-227 °C; IR (KBr): 1628 (CO), 1597, 1487, 1472, 1455 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 4.17 (s, 4H, -CH₂-CH₂-), 4.22 (s, 4H, -CH₂-CH₂-), 6.52 (d, 2H, *J* 8.2 Hz), 6.81 (d, 2H, *J* 8.3 Hz), 6.88 (t, 2H, *J* 7.4 Hz), 6.99 (t, 2H, *J* 7.4 Hz), 7.14 (t, 2H, *J* 8.1 Hz), 7.14 (d, 2H, *J* 16.3 Hz, 2 × H-α), 7.34 (t, 2H, *J* 7.5 Hz), 7.38 (dd, 2H, *J* 7.8 and 1.5 Hz), 7.57 (d, 2H, *J* 7.5 Hz), 7.59 (d, 2H, *J* 16.4 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 66.89, 67.35, 112.14, 112.65, 120.92, 121.38, 123.96, 128.13, 128.46, 129.44, 129.67, 131.40, 131.97, 139.56, 156.55, 157.32, 195.07 (CO); FABMS: *m/z* 533 (M+H)⁺; Anal. Calcd for C₃₄H₂₈O₆ (532.19): C, 76.68; H, 5.30%. Found C, 76.48; H 5.43%.

(2E,23E)-11,15,31,34-Tetraoxapentacyclo[33.4.0.0^{5,10}.0^{16,21}.0^{25,30}]nonatriaconta-1(39),2,5,7,-9,16,18,20,23,25,27,29,35,37-tetradecaene-4,22-dione (3b). Eluent: petroleum ether-EtOAc (6:4, v/v), light yellow cubes, mp 227-229 °C; IR (KBr): 1633 (CO), 1582, 1486, 1469, 1387 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 2.00 (quintet, 2H, *J* 5.1 Hz, -CH₂-CH₂-CH₂-), 3.85 (t, 4H, *J* 5.1 Hz, -CH₂-CH₂-CH₂-), 4.08 (s, 4H, -CH₂-CH₂-), 6.21 (d, 2H, *J* 8.1 Hz), 6.69-6.75 (m, 4H), 6.85 (br. t, 2H, *J* 7.6 Hz), 7.01 (dd, 2H, *J* 16.5 and 1 Hz, 2 × H-α), 7.08 (t, 2H, *J* 7.5 Hz), 7.18 (br. d, 2H, *J* 7.1 Hz), 7.38 (br. t, 2H, *J* 7.7 Hz), 7.52 (d, 2H, *J* 16.3 Hz, 2 × H-β), 7.64 (br. d, 2H, *J* 7.6 Hz); ¹³C NMR (75 MHz, CDCl₃) δ_C: 28.40, 63.94, 68.12, 112.10, 113.65, 121.03, 121.34, 124.04, 128.56, 129.56, 130.12, 131.04, 131.21, 132.27, 140.01, 156.70, 157.45, 194.53 (CO); FABMS: *m/z* 547 (M+H)⁺; Anal. Calcd for C₃₅H₃₀O₆ (546.61): C, 76.91; H, 5.53%. Found C, 76.63; H, 5.61%.

(2E,24E)-11,16,32,35-Tetraoxapentacyclo[34.4.0.0^{5,10}.0^{17,22}.0^{26,31}]tetraconta-1(40),2,5,7,9,17,-19,21,24,26,28,30,36,38-tetradecaene-4,23-dione (3c). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 198-200 °C; IR (KBr): 1626 (CO), 1597, 1485, 1447, 1385 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 1.68 (br. s, 4H, *w*_{1/2} ≈ 12.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 3.56 (br. s, 4H, *w*_{1/2} ≈ 12.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 4.21 (s, 4H, -CH₂-CH₂-), 6.37 (d, 2H, *J* 8.4 Hz), 6.85 (d, 2H, *J* 8.4 Hz), 6.95 (t, 2H, *J* 7.5 Hz), 7.04 (t, 2H, *J* 7.5 Hz), 7.12 (d, 2H, *J* 16.4 Hz, 2 × H-α), 7.24 (t, 2H, partially merged with CHCl₃ peak), 7.38 (dd, 2H, *J* 7.5 and 1.5 Hz), 7.43 (br. t, 2H, *J* 8.1 Hz), 7.57 (d, 2H, *J* 16.4 Hz, 2 × H-β), 7.62 (br. d, 2H, *J* 7.5 Hz); ¹³C NMR (75 MHz, CDCl₃) δ_C: 25.18, 66.16, 67.00, 111.84, 111.94, 120.53, 121.47, 123.78, 128.29, 128.71, 129.31,

129.50, 131.58, 131.72, 139.98, 156.64, 157.00, 196.37 (CO); TOFMSES⁺: *m/z* 583.08 (M+Na)⁺. Anal. Calcd for C₃₆H₃₂O₆ (560.64): C, 77.12; H, 5.75%. Found C, 77.18; H, 5.93%.

(2E,25E)-11,17,33,36-Tetraoxapentacyclo[35.4.0.0^{5,10}.0^{18,23}.0^{27,32}]juntetraconta-1(41),2,5,7,9,-18,20,22,25,27,29,31,37,39-tetradecaene-4,24-dione (3d). Eluent: petroleum ether-EtOAc (6:4, v/v), light yellow cubes, mp 218-220 °C; IR (KBr): 1634 (CO), 1596, 1488, 1473, 1456 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 1.36-1.46 (m, 6H, -CH₂-CH₂-CH₂-CH₂-), 3.47 (t, 4H, *J* 5.2 Hz, -CH₂-CH₂-CH₂-CH₂-), 4.26 (br. s, 4H, -CH₂-CH₂-), 6.57 (d, 2H, *J* 8.2 Hz), 6.81 (d, 2H, *J* 8.2 Hz), 7.00 (t, 2H, *J* 7.4 Hz), 7.03 (t, 2H, *J* 7.5 Hz), 7.29-7.36 (m, 4H), 7.37 (d, 2H, *J* 16.2 Hz, 2 × H-α) and 7.46 (br. d, 2H, *J* 7.5 Hz), 7.56 (d, 2H, *J* 7.6 Hz), 7.66 (d, 2H, *J* 16.2 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 23.38, 29.05, 67.66, 68.08, 112.01, 112.81, 120.47, 121.54, 124.28, 129.01, 129.65, 130.02, 130.30, 131.42, 132.05, 139.39, 157.11, 157.66, 195.69 (CO); TOFMSES⁺: *m/z* 597.00 (M+Na)⁺; Anal. Calcd for C₃₇H₃₄O₆ (574.24): C 77.33, H, 5.96%. Found C, 77.09; H, 6.14%.

(2E,22E)-11,14,30,34-Tetraoxapentacyclo[33.4.0.0^{5,10}.0^{15,20}.0^{24,29}]nonatriaconta-1(39),2,5,7,-9,15,17,19,22,24,26,28,35,37-tetradecaene-4,21-dione (3e). Eluent: petroleum ether-EtOAc (6:4, v/v), light yellow cubes, mp 186-188 °C; IR (KBr): 1625 (CO), 1598, 1486, 1470, 1310 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 2.19 (quintet, 2H, *J* 6.0 Hz, -CH₂-CH₂-CH₂-), 4.09 (t, 4H, *J* 6.0 Hz, -CH₂-CH₂-CH₂-), 4.27 (s, 4H, -CH₂-CH₂-), 6.78 (d, 2H, *J* 8.1 Hz), 6.80 (d, 2H, *J* 8.1 Hz), 6.91 (t, 2H, *J* 7.4 Hz), 6.99 (t, 2H, *J* 7.3 Hz), 7.26 (br. t, 4H, *J* 7.2 Hz), 7.43-7.47 (m, 4H), 7.48 (d, 2H, *J* 16.5 Hz, 2 × H-α), 7.64 (d, 2H, *J* 16.2 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 28.41, 63.94, 68.17, 112.11, 113.67, 121.03, 121.55, 124.05, 128.90, 129.96, 130.25, 131.05, 131.21, 132.28, 140.15, 156.71, 157.43, 194.73 (CO); FABMS: *m/z* 547 (M+H)⁺; Anal. Calcd for C₃₅H₃₀O₆ (546.61): C, 76.91; H, 5.53%. Found C, 77.02; H, 5.66%.

(2E,23E)-11,15,31,35-Tetraoxapentacyclo[34.4.0.0^{5,10}.0^{16,21}.0^{25,30}]tetraconta-1(40),2,5,7,9,16,-18,20,23,25,27,29,36,38-tetradecaene-4,22-dione (3f). Eluent: petroleum ether-EtOAc (6:4, v/v), light yellow cubes, mp 173-175 °C; IR (KBr): 1634 (CO), 1594, 1482, 1471, 1310 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 2.08-2.17(m, 4H, 2 × -CH₂-CH₂-CH₂-), 3.96 (t, 4H, *J* 5.9 Hz, -CH₂-CH₂-CH₂-), 4.02 (t, 4H, *J* 5.9 Hz, -CH₂-CH₂-CH₂-), 6.38 (d, 2H, *J* 8.1 Hz), 6.76 (br. d, 2H, *J* 8.2 Hz), 6.92 (t, 2H, *J* 7.2 Hz), 7.00 (t, 2H, *J* 7.5 Hz), 7.10 (dt, 2H, *J* 6.9 and 1.5 Hz), 7.28 (dt, 2H, *J* 7.2 and 1.4 Hz), 7.35 (d, 2H, *J* 16.2 Hz, 2 × H-α), 7.42 (dd, 2H, *J* 7.8 and 1.6 Hz), 7.56 (br. d, 2H, *J* 7.8 Hz), 7.67 (d, 2H, *J* 16.2 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 28.93, 29.36, 63.71, 64.89, 111.89, 112.36, 120.60, 121.20, 123.96, 128.76, 129.67, 129.72, 130.57, 131.52, 132.23, 140.40, 156.42, 157.47, 195.69 (CO); TOFMSES⁺: *m/z* 583 [M+Na]⁺; Anal. Calcd for C₃₆H₃₂O₆ (560.22): C, 77.12; H, 5.75%. Found C, 76.85, H, 5.71%.

(2E,24E)-11,16,32,36-Tetraoxapentacyclo[35.4.0.0^{5,10}.0^{17,22}.0^{26,31}]juntetraconta-1(41),2,5,7,9,-17,19,21,24,26,28,30,37,39-tetradecaene-4,23-dione (3g). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 156-158 °C; IR (KBr): 1630 (CO), 1484, 1448, 1387, 1308 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 1.67 (br. s, 4H, w_{1/2} ≈ 13.0 Hz, -CH₂-CH₂-CH₂-CH₂-), 2.21 (quintet, 2H, *J* 5.9 Hz, -CH₂-CH₂-CH₂-), 3.63 (br. s, 4H, w_{1/2} ≈ 13.0 Hz, -CH₂-CH₂-CH₂-CH₂-), 4.15 (t, 4H, *J* 5.9 Hz, -CH₂-CH₂-CH₂-), 6.61 (d, 2H, *J* 8.2 Hz), 6.84 (d, 2H, *J* 8.2 Hz), 6.93-7.03 (m,

4H), 7.24-7.36 (m, 4H), 7.36 (d, 2H, J 16.2 Hz, $2 \times$ H- α), 7.49 (dd, 2H, J 7.2 and 1.5 Hz), 7.52 (dd, 2H, J 7.5 and 1.6 Hz), 7.62 (d, 2H, J 16.2 Hz, $2 \times$ H- β); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 26.13, 28.76, 63.85, 68.17, 112.19, 112.38, 120.80, 120.94, 124.16, 129.38, 129.65, 130.02, 130.46, 131.29, 132.34, 139.12, 157.12, 157.46, 194.82 (CO); TOFMSSES⁺: m/z 596.97 (M+Na)⁺; Anal. Calcd for $\text{C}_{37}\text{H}_{34}\text{O}_6$ (574.24): C, 77.33; H, 5.96%. Found C, 77.09; H, 6.15%.

(2E,25E)-11,17,33,37-Tetraoxapentacyclo[36.4.0.0^{5,10}.0^{18,23}.0^{27,32}]dotetraconta-1(42),2,5,7,9,-18,20,22,25,27,29,31,38,40-tetradecaene-4,24-dione (3h). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 182-184 °C; IR (KBr): 1630 (CO), 1586, 1530, 1485, 1407 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.14 (quintet, 2H, J 6.0 Hz, -CH₂-CH₂-CH₂-CH₂-CH₂-), 1.30 (br. s, 4H, $w_{1/2} \approx 24.0$ Hz, -CH₂-CH₂-CH₂-CH₂-CH₂-), 2.13 (quintet, 2H, J 5.1 Hz, -CH₂-CH₂-CH₂-), 3.29 (br. t, 4H, J 5.0 Hz, -CH₂-CH₂-CH₂-CH₂-CH₂-), 4.06 (br. t, 4H, J 5.4 Hz, -CH₂-CH₂-CH₂-), 6.67 (d, 2H, J 8.4 Hz), 6.76 (d, 2H, J 8.2 Hz), 6.97 (t, 2H, J 7.5 Hz), 7.04 (t, 2H, J 7.3 Hz), 7.27 (br. t, 2H, J 8.1 Hz), 7.32 (d, 2H, J 16.1 Hz, $2 \times$ H- α), 7.46 (dt, 2H, J 7.6 and 1.4 Hz), 7.53 (br. d, 2H, J 8.4 Hz), 7.56 (dd, 2H, J 7.6 and 1.5 Hz), 7.62 (d, 2H, J 16.1 Hz, $2 \times$ H- β); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 23.23, 29.00, 29.37, 63.50, 67.64, 112.06, 112.14, 120.54, 120.92, 124.08, 129.45, 129.58, 130.15, 130.21, 131.31, 132.21, 138.95, 157.12, 157.57, 195.18 (CO); TOFMSSES⁺: m/z 611.24 (M+Na)⁺; Anal. Calcd for $\text{C}_{38}\text{H}_{36}\text{O}_6$ (588.69): C, 77.53; H, 6.16%. Found C, 77.36; H, 6.37%.

(2E,22E)-11,14,30,35-Tetraoxapentacyclo[34.4.0.0^{5,10}.0^{15,20}.0^{24,29}]tetraconta-1(40),2,5,7,9,-15,17,19,22,24, 26,28,36,38-tetradecaene-4,21-dione (3i). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 148-150 °C; IR (KBr): 1625 (CO), 1486, 1448, 1387, 1310 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.83 (br. s, 4H, $w_{1/2} \approx 12.5$ Hz, -CH₂-CH₂-CH₂-CH₂-), 3.94 (br. s, 4H, $w_{1/2} \approx 12.5$ Hz, -CH₂-CH₂-CH₂-CH₂-), 4.27 (s, 4H, -CH₂-CH₂-), 6.74 (d, 2H, J 8.1 Hz), 6.89 (d, 2H, J 8.1 Hz), 6.98 (t, 2H, J 8.4 Hz), 7.03 (t, 2H, J 7.5 Hz), 7.19 (dt, 2H, J 7.5 and 1.8 Hz), 7.38 (dt, 2H, J 7.8 and 1.5 Hz) and 7.41 (d, 2H, J 16.5 Hz, $2 \times$ H- α), 7.45 (dd, 2H, J 7.8 and 1.8 Hz), 7.61 (dd, 2H, J 7.8 and 1.8 Hz), 7.70 (d, 2H, J 16.5 Hz, $2 \times$ H- β); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 26.11, 67.04, 67.94, 111.87, 113.30, 121.01, 121.37, 123.65, 128.64, 129.78, 130.28, 130.62, 131.57, 131.91, 140.69, 156.19, 157.92, 195.43 (CO); FABMS: m/z 561 (M+H)⁺, 583 (M+Na)⁺; Anal. Calcd for $\text{C}_{36}\text{H}_{32}\text{O}_6$ (560.64): C, 77.12; H, 5.75%. Found C, 76.88; H, 6.02%.

(2E,23E)-11,15,31,36-Tetraoxapentacyclo[35.4.0.0^{5,10}.0^{16,21}.0^{25,30}]untetraconta-1(41),2,5,7,9,-16,18,20, 23, 25,27,29,37,39-tetradecaene-4,22-dione (3j). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 198-200 °C; IR (KBr): 1633 (CO), 1596, 1488, 1473, 1390 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.67 (br. s, 4H, $w_{1/2} \approx 12.0$ Hz, -CH₂-CH₂-CH₂-CH₂-), 2.06 (quintet, 2H, J 5.4 Hz, -CH₂-CH₂-CH₂-), 3.81 (br. s, 4H, $w_{1/2} \approx 12.0$ Hz, -CH₂-CH₂-CH₂-CH₂-), 4.00 (t, 4H, J 5.4 Hz, -CH₂-CH₂-CH₂-), 6.48 (d, 2H, J 8.1 Hz), 6.86 (d, 2H, J 8.4 Hz), 6.88 (t, 2H, J 7.5 Hz), 6.99 (d, 2H, J 1.7 Hz), 7.04 (t, 2H, J 7.5 Hz), 7.28 (d, 2H, J 16.5 Hz, $2 \times$ H- α), 7.30 (dd, 2H, J 7.1 and 1.8 Hz), 7.39 (dt, 2H, J 8.6 and 1.5 Hz), 7.61 (d, 2H, J 1.5 Hz), 7.66 (d, 2H, J 16.4 Hz, $2 \times$ H- β); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 26.00, 29.34, 64.49, 67.78, 111.92, 112.41, 120.26, 121.07, 123.72, 128.69, 128.92, 129.92, 130.04, 131.38, 131.73, 140.93, 156.27, 157.88,

196.66 (CO); FABMS: m/z 596.97 (M+Na)⁺; Anal. Calcd for C₃₇H₃₄O₆ (574.24): C, 77.33; H, 5.96%. Found C, 77.11; H, 6.18%.

(2E,24E)-11,16,32,37-Tetraoxapentacyclo[36.4.0.0^{5,10}.0^{17,22}.0^{26,31}]dotetraconta-1(42),2,5,7,9,-17,19,21,24, 26,28,30,38,40-tetradecaene-4,23-dione (3k). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 162-164 °C; IR (KBr): 1631 (CO), 1489, 1448, 1387, 1309 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 1.74 (br. s, 8H, w_{1/2}≈12.5 Hz, 2 × -CH₂-CH₂-CH₂-CH₂-), 3.78 (br. s, 4H, w_{1/2}≈ 12.0 Hz, -CH₂-CH₂-CH₂-CH₂-), 3.97 (br. s, 4H, w_{1/2}≈ 12.0 Hz, -CH₂-CH₂-CH₂-CH₂-), 6.60 (d, 2H, *J* 8.4 Hz), 6.91 (d, 2H, *J* 8.4 Hz), 6.96 (t, 2H, *J* 7.5 Hz), 6.98 (t, 2H, *J* 7.5 Hz), 7.18 (d, 2H, *J* 16.2 Hz, 2 × H-α), 7.25 (dt, 2H, partially merged with CHCl₃ peak), 7.37 (dt, 2H, *J* 7.5 and 1.5 Hz), 7.38 (dd, 2H, *J* 7.5 and 1.5 Hz), 7.59 (dd, 2H, *J* 7.8 and 1.2 Hz), 7.66 (d, 2H, *J* 16.2 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 25.12, 25.98, 66.98, 67.70, 111.94, 112.33, 120.52, 120.99, 123.83, 128.39, 129.16, 129.43, 129.92, 131.54, 131.73, 140.43, 156.58, 157.58, 196.02 (CO); TOFMSSES⁺: m/z 611.24 (M+Na)⁺; Anal. Calcd for C₃₈H₃₆O₆ (588.25): C, 77.53; H, 6.16%. Found C, 77.40; H, 6.06%.

(2E,25E)-11,17,33,38-Tetraoxapentacyclo[37.4.0.0^{5,10}.0^{18,23}.0^{27,32}]tritetraconta-1(43),2,5,7,9,-18,20,22,25,27,29,31,39,41-tetradecaene-4,24-dione (3l). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 173-175 °C; IR (KBr): 1630 (CO), 1586, 1483, 1446, 1389 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 1.26-1.33 (m, 2H, -CH₂-CH₂-CH₂-CH₂-CH₂-), 1.53 (quintet, 4H, *J* 6.9 Hz, -CH₂-CH₂-CH₂-CH₂-CH₂-), 1.86 (br. s, 4H, w_{1/2}≈ 12.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 3.69 (t, 4H, *J* 5.7 Hz, -CH₂-CH₂-CH₂-CH₂-CH₂-), 3.99 (br. s, 4H, w_{1/2}≈ 12.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 6.71 (d, 2H, *J* 8.3 Hz), 6.85 (d, 2H, *J* 8.2 Hz), 6.92 (t, 2H, *J* 7.5 Hz), 7.00 (t, 2H, *J* 7.4 Hz), 7.24 (t, 2H, *J* ≈ 8.4 Hz), 7.30 (d, 2H, *J* 16.3 Hz, 2 × H-α), 7.35 (t, 2H, *J* 7.5 Hz), 7.48 (d, 2H, *J* 7.4 Hz), 7.53 (d, 2H, *J* 7.6 Hz), 7.73 (d, 2H, *J* 16.1 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 22.70, 26.11, 28.56, 68.05, 68.40, 112.13, 112.53, 120.51, 120.97, 124.19, 128.62, 129.57, 129.77, 130.01, 131.53, 132.04, 139.47, 157.03, 157.89, 195.30 (CO); GCMS: m/z 602(M⁺). Anal. Calcd for C₃₉H₃₈O₆ (602.27): C, 77.72; H, 6.35%. Found C, 77.48; H, 6.40%.

(2E,22E)-11,14,30,36-Tetraoxapentacyclo[35.4.0.0^{5,10}.0^{15,20}.0^{24,29}]untetraconta-1(41),2,5,7,9,-15,17,19,22,24,26,28,37,39-tetradecaene-4,21-dione (3m). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 212-214 °C; IR (KBr): 1634 (CO), 1597, 1488, 1473, 1390 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 1.54 (quintet, 2H, *J* 6.6 Hz, -CH₂-CH₂-CH₂-CH₂-CH₂-), 1.69-1.78 (m, 4H, -CH₂-CH₂-CH₂-CH₂-CH₂-), 3.88 (t, 4H, *J* 5.5 Hz, -CH₂-CH₂-CH₂-CH₂-CH₂-), 4.20 (s, 4H, -CH₂-CH₂-), 6.56 (d, 2H, *J* 8.4), 6.88 (d, 2H, *J* 8.3 Hz), 6.97 (t, 2H, *J* 7.8 Hz), 7.00 (t, 2H, *J* 7.7 Hz), 7.18 (dt, 2H, *J* 7.2 and 1.5 Hz), 7.36 (dt, 2H, *J* 7.2 and 1.4 Hz), 7.55 (br. d, 4H, *J* 7.5 Hz), 7.57 (d, 2H, *J* 16.2 Hz, 2 × H-α), 7.67 (d, 2H, *J* 16.2 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 23.99, 29.30, 67.49, 68.40, 112.29, 113.55, 121.01, 121.59, 124.02, 129.20, 130.20, 130.36, 131.07, 131.33, 132.50, 139.60, 156.80, 158.19, 194.45 (CO); EIMS: m/z 574 (M⁺); Anal. Calcd for C₃₇H₃₄O₆ (574.24): C, 77.33; H, 5.96%. Found C, 77.23; H, 6.12%.

(2E,23E)-11,15,31,37-Tetraoxapentacyclo[36.4.0.0^{5,10}.0^{16,21}.0^{25,30}]dotetraconta-1(42),2,5,7,9,-16,18,20,23,25, 27,29,38,40-tetradecaene-4,22-dione (3n). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 148-150 °C; IR (KBr): 1631 (CO), 1491, 1482, 1347, 1308 cm⁻¹; ¹H

NMR (300 MHz, CDCl₃) δ_{H} : 1.42-1.50 (m, 2H, -CH₂-CH₂-CH₂-CH₂-CH₂-), 1.57-1.65 (m, 4H, -CH₂-CH₂-CH₂-CH₂-), 1.96 (quintet, 2H, *J* 5.1 Hz, -CH₂-CH₂-CH₂-), 3.74 (t, 4H, *J* 5.2 Hz, -CH₂-CH₂-CH₂-CH₂-), 3.84 (t, 4H, *J* 5.2 Hz, -CH₂-CH₂-CH₂-), 6.22 (d, 2H, *J* 8.2 Hz), 6.90 (2H, d, *J* 8.2 Hz), 6.98 (t, 2H, *J* 7.5 Hz), 7.06 (t, 2H, *J* 7.5 Hz), 7.19 (dt, 2H, *J* 7.2 and 1.7 Hz), 7.42 (dt, 2H, *J* 7.2 and 1.4 Hz), 7.49 (dd, 2H, *J* 7.5 and 1.7 Hz), 7.50 (d, 2H, *J* 16.2 Hz, 2 × H- α), 7.58 (dd, 2H, *J* 7.8 and 1.2 Hz), 7.65 (d, 2H, *J* 16.1 Hz, 2 × H- β); ¹³C NMR (75 MHz, CDCl₃) δ_{C} : 24.37, 29.62, 29.65, 64.19, 68.44, 111.64, 112.36, 120.50, 120.96, 123.88, 129.77, 129.94, 129.97, 131.21, 131.25, 132.28, 139.37, 156.75, 158.25, 195.36 (CO); TOFMSSES⁺: *m/z* 611.03 (M+Na)⁺; Anal. Calcd for C₃₈H₃₆O₆ (588.25): C, 77.53; H, 6.16%. Found C, 77.29; H, 6.31%.

2E,24E)-11,16,32,38-Tetraoxapentacyclo[37.4.0.0^{5,10}.0^{17,22}.0^{26,31}]tritetraconta-1(43),2,5,7,9,-17,19,21,24,26, 28,30,39,41-tetradecaene-4,23-dione (3o). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 205-207 °C; IR (KBr): 1632 (CO), 1487, 1448, 1308, 1246 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_{H} : 1.35-1.42 (m, 2H, -CH₂-CH₂-CH₂-CH₂-), 1.59 (br. s, 4H, *w*_{1/2} ≈ 12.0 Hz, -CH₂-CH₂-CH₂-CH₂-), 1.67-1.74 (m, 4H, -CH₂-CH₂-CH₂-CH₂-), 3.40 (br. s, 4H, *w*_{1/2} ≈ 12.0 Hz, -CH₂-CH₂-CH₂-CH₂-), 3.96 (s, 4H, *w*_{1/2} ≈ 12.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 6.44 (d, 2H, *J* 8.1 Hz), 6.96-7.01 (m, 6H), 7.10 (d, 2H, *J* 16.3 Hz, 2 × H- α), 7.32 (t, 2H, *J* 7.2 Hz), 7.38-7.42 (m, 4H), 7.62 (d, 2H, *J* 6.9 Hz), 7.63 (d, 2H, *J* 16.6 Hz, 2 × H- β); ¹³C NMR (75 MHz, CDCl₃) δ_{C} : 23.47, 25.05, 28.90, 66.00, 68.25, 111.77, 111.94, 120.67, 121.09, 123.79, 128.33, 128.53, 129.64, 131.66, 131.79, 133.65, 139.42, 156.49, 157.59, 196.26 (CO); GCMS: *m/z* 602(M⁺); Anal. Calcd for C₃₉H₃₈O₆ (602.27): C, 77.72; H, 6.35%. Found C, 77.65; H, 6.60%.

(2E,25E)-11,17,33,39-Tetraoxapentacyclo[38.4.0.0^{5,10}.0^{18,23}.0^{27,32}]tetraetraconta-1(44),2,5,7,-9,18,20,22,25,27,29,31,40,42-tetradecaene-4,24-dione (3p). Eluent: petroleum ether-EtOAc (1:1, v/v), light yellow cubes, mp 212-214 °C; IR (KBr): 1633 (CO), 1488, 1445, 1386, 1304 cm⁻¹; ¹H NMR (CDCl₃) δ_{H} : 1.24-1.29 (m, 2H, -CH₂-CH₂-CH₂-CH₂-), 1.34-1.41 (m, 4H, -CH₂-CH₂-CH₂-CH₂-), 1.52-1.59 (m, 2H, -CH₂-CH₂-CH₂-CH₂-), 1.71-1.78 (m, 4H, -CH₂-CH₂-CH₂-CH₂-), 3.48 (t, 4H, *J* 5.2 Hz, -CH₂-CH₂-CH₂-CH₂-), 3.93 (t, 4H, *J* 5.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 6.64 (d, 2H, *J* 8.3 Hz), 6.84 (d, 2H, *J* 8.3 Hz), 6.94 (2H, t, *J* 7.4 Hz), 7.01 (t, 2H, *J* 7.4 Hz), 7.29 (d, 2H, *J* 7.3 Hz), 7.33 (d, 2H, *J* 16.2 Hz, 2 × H- α), 7.39 (dt, 2H, *J* 7.9 and 1.2 Hz), 7.50 (br. d, 2H, *J* 8.2 Hz), 7.52 (dt, 2H, *J* 7.4 Hz and 1.5 Hz), 7.70 (d, 2H, *J* 16.2 Hz, 2 × H- β); ¹³C NMR (75 MHz, CDCl₃) δ_{C} : 18.46, 19.06, 24.16, 24.45, 63.27, 63.86, 107.39, 107.70, 116.01, 116.24, 119.62, 124.65, 125.30, 125.48, 126.76, 127.60, 134.61, 152.66, 153.61, 190.51 (CO); FABMS: *m/z* 617.4 (M+H)⁺; Anal. Calcd for C₄₀H₄₀O₆ (616.74): C, 77.90; H, 6.54%. Found C, 77.77; H, 6.69%.

General method for reaction of 2,2'-dihydroxychalcone (6) with α,ω -dibromoalkanes. To a solution of 2,2'-dihydroxychalcone (6) (1 mmol) in dry acetone (15 mL), α,ω -dibromoalkane (1 mmol) and anhydrous K₂CO₃ (1.5 g) were added and the mixture was refluxed for 10 hr. Usual work-up of the reaction mixture followed by purification of the resulting material by column

chromatography and crystallization from CHCl_3 -petroleum ether afforded the cyclic compounds **7**. The analytical and spectral data of **7a-c** were as follows:

(2E)-11,15-Dioxatricyclo[14.4.0.0^{5,10}]eicosa-1(20),2,5,7,9,16,18-heptaene-4-one (7a). Eluent: petroleum ether-EtOAc (8:2, v/v), light yellow cubes, mp 96 °C; IR (KBr): 1625 (CO), 1616, 1454, 1294, 1280 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 2.25 (quintet, 2H, J 5.4 Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 4.14 (t, 2H, J 5.5 Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 4.38 (t, 2H, J 5.5 Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 7.04 - 7.18 (m, 4H), 7.31 (t, 1H, J 8.6 Hz), 7.36 (d, 1H, J 7.6 Hz), 7.49 (t, 1H, J 7.8 Hz), 7.52 (d, 1H, J 16.2 Hz, H- α), 7.60 (d, 1H, J 16.2 Hz, H- β), 7.72 (br. d, 1H, J 7.5 Hz, proton *ortho* to CO); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 29.40, 66.60, 69.38, 115.98, 120.45, 122.30, 123.85, 128.90, 130.35, 130.56, 130.72, 131.54, 132.62, 133.23, 138.26, 158.12, 158.20, 193.01 (CO); GCMS: m/z 280 (M^+); Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{O}_3$ (280.31): C, 77.12; H, 5.75%. Found C, 76.95; H, 5.91%.

(2E)-11,16-Dioxatricyclo[15.4.0.0^{5,10}]juncosa-1(21),2,5,7,9,17,19-heptaene-4-one (7b). Eluent: petroleum ether-EtOAc (8:2, v/v), light yellow cubes, mp 123 °C; IR (KBr): 1631 (CO), 1610, 1452, 1291, 1282 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 2.18 (br. s, 4H, $w_{1/2} \approx 12.0$ Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 4.12 (br. s, 4H, $w_{1/2} \approx 13.5$ Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 6.88 (d, 1H, J 8.3 Hz), 6.93 (d, 1H, J 8.3 Hz), 6.98 (t, 1H, J 7.5 Hz), 7.04 (t, 1H, J 7.5 Hz), 7.29 (dt, 1H, J 8.1 and 1.5 Hz), 7.42 (br. d, 1H, J 7.7 Hz), 7.47 (dt, 1H, J 7.5 and 1.5 Hz), 7.64 (d, 1H, J 16.0 Hz, H- α), 8.08 (dd, 1H, J 8.4 and 1.5 Hz, proton *ortho* to CO), 8.95 (dd, 1H, J 15.9 and 0.8 Hz, H- β); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 25.93, 26.91, 68.33, 69.07, 111.65, 112.21, 120.55, 120.63, 124.45, 127.54, 130.41, 131.66, 131.97, 134.06, 134.34, 138.79, 159.01, 159.42, 190.49 (CO). GCMS: m/z 294 (M^+); Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_3$ (294.34): C, 77.53; H, 6.16%. Found C, 77.28; H, 6.30%.

(2E)-11,17-Dioxatricyclo-[16.4.0.0^{5,10}]docosa-1(22),2,5,7,9,18,20-heptaene-4-one (7c). Eluent: petroleum ether-EtOAc (8:2, v/v), light yellow cubes, mp 112 °C; IR (KBr): 1628 (CO), 1610, 1459, 1301, 1294 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.91-2.00 (m, 6H, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 4.15 (t, 2H, J 4.9 Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 4.22 (t, 2H, J 4.9 Hz, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 6.89 (d, 1H, J 8.3 Hz), 6.96 (t, 1H, J 7.4 Hz), 6.99 (d, 1H, J 8.3 Hz), 7.01 (t, 1H, J 7.4 Hz), 7.27 (dt, 1H, J 7.3 and 1.5 Hz), 7.40-7.44 (m, 2H), 7.68 (dd, 1H, J 8.1 and 1.5 Hz, proton *ortho* to CO), 7.70 (d, 1H, J 15.9 Hz, H- α), 8.20 (d, 1H, J 15.9 Hz, H- β); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 21.07, 25.96, 26.58, 64.58, 68.22, 111.60, 112.21, 120.60, 120.70, 124.14, 129.70, 130.17, 130.76, 131.01, 132.82, 134.81, 139.60, 157.53, 159.37, 193.49 (CO); TOFMS/ES: m/z 331 ($\text{M}+\text{Na}^+$); Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{O}_3$ (308.37): C, 77.90; H, 6.54%. Found C, 78.04; H, 6.78%.

Macrocyclisation leading to **8a and **9a****. The combinations of bis-aldehydes and bis-ketones **11+2b**, **1c+12** and **11+12** (1:1 mole ratio in each case) were treated with aqueous methanolic KOH in the same way as in the case of condensation of **1** and **2** described above. Macrocyclization was successful in the first two cases yielding the products **8a** and **9a**. The analytical and spectral data of these two compounds were as follows:

(2E,23E)-11,15,30,34-Tetraoxapentacyclo[33.3.1.0^{5,10}.0^{16,21}.1^{25,29}]tetraconta-1(39),2,5,7,9,16,-18,20,23,25,27,29(40),35,37-tetradecaene-4,22-dione (8a). Eluent: petroleum ether-EtOAc (4:6, v/v), light yellow cubes, mp 206-208 °C; IR (KBr): 1635 (CO), 1586, 1489, 1446, 1305 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 2.18-2.26 (m, 4H, 2 × -CH₂-CH₂-CH₂-), 4.10-4.17 (m, 8H, 2 × -CH₂-CH₂-CH₂-), 6.85-6.91 (m, 4H), 6.94-7.00 (m, 4H), 7.11 (br. s, 2H), 7.18-7.22 (m, 2H), 7.31 (d, 2H, *J* 15.6 Hz, 2 × H-α), 7.37 (dt, 2H, *J* 7.5 and 1.8 Hz), 7.54 (d, 2H, *J* 15.6 Hz, 2 × H-β), 7.56-7.59 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ_C: 29.02, 29.64, 64.46, 66.08, 110.88, 112.79, 117.22, 121.32, 123.69, 127.10, 129.71, 130.02, 130.53, 133.17, 136.49, 141.65, 157.37, 159.16, 192.49 (CO); TOFMSES⁺: *m/z* 583.49 (M+Na)⁺; Anal. Calcd for C₃₆H₃₂O₆ (560.22): C, 77.12; H, 5.75%. Found C, 76.85, H, 5.71%.

(2E,22E)-10,15,30,35-Tetraoxapentacyclo[34.4.0.1^{5,9}.1^{16,20}.0^{24,29}]dotetraconta-1(40),2,5,7,-9(41),16,18,20(42),22,24,26,28,36,38-tetradecaene-4,21-dione (9a). Eluent: petroleum ether-EtOAc (4:6, v/v), light yellow cubes, mp 184-186 °C; IR (KBr): 1629 (CO), 1588, 1487, 1446, 1310 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ_H: 2.03 (br. s, 4H, *w*_{1/2} ≈ 11.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 2.17 (br. s, 4H, *w*_{1/2} ≈ 11.5 Hz, -CH₂-CH₂-CH₂-CH₂-), 4.09-4.16 (m, 8H, 2 × -CH₂-CH₂-CH₂-CH₂-), 6.92 (br. d, 2H, *J* 8.4 Hz), 7.00 (br. t, 2H, *J* 7.5 Hz), 7.05 (dd, 2H, *J* 8.1 and 2.2 Hz), 7.28-7.57 (m, 10H, Ar-H), 7.66 (d, 2H, *J* 16.0 Hz, 2 × H-α), 7.93 (d, 2H, *J* 16.0 Hz, 2 × H-β); ¹³C NMR (75 MHz, CDCl₃) δ_C: 25.45, 25.67, 66.75, 67.44, 111.88, 114.85, 118.50, 120.83, 120.93, 123.90, 124.27, 129.69, 131.22, 131.50, 139.74, 141.44, 158.14, 158.69, 191.71 (CO); TOFMSES⁺: *m/z* 611.53 (M+Na)⁺; Anal. Calcd for C₃₈H₃₆O₆ (588.25): C, 77.53; H, 6.16%. Found C, 77.40; H, 6.06%.

Crystallographic data collection and refinement

A suitable single crystal of compound **3f** (crystallized from acetone and n-hexane) was mounted on a thin glass fiber with commercially available super glue. X-ray single crystal data collection was performed at room temperature using “Bruker SMART” diffractometer, equipped with a normal focus, sealed tube X-ray source with graphite monochromated Mo-Kα radiation (λ 0.71073 Å). The structure was solved by SHELXS 97. Structure refinement was carried out using SHELXL 97. The relevant data are given in Table 3. “CCDC 887597” contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

Table 3. Important crystallographic data for compound **3f**

Molecular formula	C ₃₆ H ₃₂ O ₆
FW (g. mol ⁻¹)	560. 62
Space group	<i>P</i> 2 ₁ / <i>c</i>
Temperature	293 °K
μ (Mo-Kα)	0.085mm ⁻¹
F (000)	1200

Table 3. Continued

a	19.407(3)A°	α	90°
b	10.6494 (17) A°	β	107.18°
c	14.905 (2) A°	γ	90°
Theta	Min-Max		2.20, 25.37
Vol	[Å ³]		2943.1 (8)
Z			4
D _{calc}	(g.cm ⁻³)		1.265
Index range			-22 < h < 22 -12 < k < 12 -17 < l < 17
Number of data measured			13600
Number of unique data			4962
Goodness-of-fit			1.038
Final R indices			R1 0.0517, wR2 0.1580

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