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# Photochemical Synthesis of both Strained and Macrocyclic (1,7)Naphthalenophanes

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# Abstract:

Naphthalenophanes are a special type of cyclophanes. While in the past (1,5), (1,6) and (1,8)Naphthaleno-phanes were successfully prepared by using the (Photo)-Dehydro-Diels-Alder (DDA) reaction, the access to (1,7)Naphthalenophanes by this method was hitherto unknown. After numerous unsuccessful attempts to prepare these compounds by thermal DDA, we found that the photoinitiated variant (PDDA) represents a very efficient method to [k](1,7)Naphthalenophanes 13. The scope ranged from highly strained (k = 11, 12) to

macrocyclic products (k = 22, 24). The extraordinary reactivity could be explained by folded ground state geometries of diketones 12 used as reactants of the PDDA. Furthermore, we calculated the ring strain energies with the help of an isodesmic reaction and evaluated structural and spectroscopic (NMR) consequences of ring strain.

# Introduction

Although the arsenal of synthetic methods is enormous today and seemingly every thinkable molecule can be prepared, there is still a number of challenging tasks. One of them is the synthesis of highly strained molecules due to their intrinsic reactivity and pronounced tendency to reduce the strain by rearrangement and decomposition reactions. Another challenge is the efficient synthesis of macrocyclic compounds, which are widely distributed in nature. Here, the difficulties arise mainly from entropically disfavored formation of large rings compared with the competing polymerization. Common strategies to overcome these problems are using either large dilution (*Ruggli-Ziegler* dilution principle) or template effects.

The synthesis of cyclophanes, *i.e.* molecules consisting of an aromatic core and a chain forming a bridge between two nonadjacent atoms of this core, is often associated with one or both of the problems mentioned above.<sup>1</sup> If the aromatic core is a naphthalene scaffold, this type of cyclophanes is called naphthalenophane.<sup>2</sup> There are basically two strategies to synthesize naphthalenophanes: either the bridging chain is tethered at a naphthalene moiety already present, or the naphthalene moiety is formed in the cyclization reaction. Pursuing the latter approach we recently reported on the preparation of a series of naphthalenophanes<sup>3</sup> based on the application of the *Dehydro-Diels-Alder* (DDA) reaction.<sup>4</sup> The DDA reaction differs from the classical *Diels-Alder* (DA) reaction in that at least one double bond of the diene moiety is replaced by a triple bond.





As a result, the DDA reaction proceeds in contrast to the DA reaction stepwise and diradicals and highly strained cycloallenes are assumed to be intermediates of the DDA reaction. Furthermore, the DDA reaction can be initiated both thermally and photochemically (with regard to the mechanistic details we refer to previous publications<sup>4</sup>).

The synthetic strategy toward naphthalenophanes 2 applied in our previous work is outlined in figure 1. Thus, two 3-arylynones 1a (R=alkyl),<sup>3a-c</sup> 3-arylpropiolic esters 1b (R=alkoxy),<sup>3c</sup> or 3-arylpropiolic acids (R=hydroxy)<sup>3c</sup> are connected by a variable linker unit X. Whereas ketones 1a and esters 1b undergo the DDA reaction upon irradiation (*Photo Dehydro-Diels-Alder reaction*, PDDA), the ring closure of carboxylic acids 1c proceeds by preceding formation of cyclic anhydrides 3 mediated by carbodiimides. By this way we already prepared (1,5), (1,6) and (1,8)naphthalenophanes A-C while (1,7)naphthalenophanes D are still a "missing link" in this array (Figure 2).

Figure 2. Structure of (1,5), (1,6), (1,8), and (1,7)Naphthalenophanes A-D.



Herein we report on the efficient synthesis of (1,7)naphthalenophanes as well as on their properties.

# **Results and Discussion**

# **1.** Attempted thermal synthesis of (1,7)Naphthalenophanes.

Based on the good results we previously achieved for the synthesis of other naphthalenophanes (*cf.* figure 1) we first explored the thermal synthesis of (1,7)naphthalenophanes. The established method for mild DDA to arylnaphthalenes comprises the in situ preparation of 3-substituted propiolic anhydrides by treatment with reagents activating the carboxylic group. In most cases carbodiimides were used for this task. In these anhydrides the alkyne moieties are brought in spatial proximity lowering the activation barrier of the DDA. To apply this approach to (1,7)naphthalenophanes we chose a medium linker length (10 atoms) to rule out the prevention of product formation by too small (ring strain) or too large (macrocycles) ring sizes. We started with 3-(4-iodophenyl)propanoic acid **4c**, <sup>5</sup> which was converted into the diester **5i** by treatment with diisopropyl carbodiimide

(DIC)/DMAP<sup>6</sup> in good yield. The subsequent *Sonogashira* coupling with propiolic acid furnished the dicarboxylic acid **6** in nearly quantitative yield.<sup>7</sup>

Surprisingly, all attempts using various reagents and conditions (for details see the SI) failed to convert compound **6** into the desired naphthalenophane **8** via the cyclic anhydride **7** (Scheme 1).

Scheme 1. Attempted thermal synthesis of (1,7)naphthalenophane 8.



i DIC, DMAP, DCM, 50°C, 72h, 70%. ii PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, DMSO, DBU, dppb, propiolic acid, 50°C, 5h, 96%. iii various conditions (see SI).

In cases where DIC was used as activating agent, we always isolated the diureide **9** as main product. The formation of ureides as byproducts upon activation of carboxylic acids with carbodiimides is a long-standing problem. It is the result of a 1,3-acyl migration in the primarily formed O-acyl isourea (the adduct of a carboxylic acid on the carbodimide) that occur if this species does not react fast enough with the nucleophile (in our case the second carboxylate) or no nucleophile is available. From this outcome we concluded that the conformational equilibrium of diacid 6 is dominated by straight conformation with a large distance between the carboxylic groups preventing any reaction to the anhydride 7 and subsequent DDA to 8.

## 2. Photochemical synthesis of (1,7)Naphthalenophanes.

Assuming that the reaction centers point to diametrically oriented directions, we doubted whether a synthesis of (1,7)naphthalenophanes starting from p-substituted arylalkynes such as **6** is possible at all. Nevertheless, the significant mechanistic differences between the thermal and photochemical variant of the DDA<sup>4a</sup> gave rise to the assumption that (1,7)naphthalenophanes could be accessible by the PDDA reaction. To verify this we prepared a library of twelve diketones **12** in a three-step sequence. For this purpose we combined three  $\omega$ -(4-iodophenyl)carboxylic acids **4a-c** with six diols **10a-f**. *Steglich* esterification<sup>6</sup> of **4** with **10** afforded diiodides **5**.

Scheme 2. Synthesis of diketones 13.



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i DIC, DMAP, DCM, 50°C, 72h. ii but-3-yn-2-ol, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, CuI, Et<sub>3</sub>N, THF, r.t., 24h. iii DMSO, Ac<sub>2</sub>O, r.t., 24 h.

	n	m	$N^{a}$	5 <sup>b</sup>	11 <sup>b</sup>	12 <sup>b</sup>
a	0	2	6	95	82	73
b	0	3	7	67	83	57
c	0	4	8	69	85	55
d	0	6	10	70	70	86
e	0	12	18	99	83	71
f	1	2	8	80	77	71
g	1	4	10	70	88	70
h	1	6	12	67	80	68
i	2	2	10	57	70	60
j	2	6	14	82	86	74
k	2	10	18	66	73	78
l	2	12	20	69	63	66

 Table 1. Yields of diiodides 5, diols 11 and diketones 12.

<sup>a</sup> N= m + 2n + 4. <sup>b</sup> Yields in percent.

By subsequent *Sonogashira* coupling with but-3-yn-2-ol we obtained the diols **11**. In the third step compounds **11** were converted into diketones **12** by an *Albright-Goldman* oxidation (Scheme 2).<sup>8</sup> The yields of **5**, **11**, and **12** are summarized in Table 1.

With diketones 12 in hand we investigated the photochemical reactivity of these compounds. The UV spectra of all compounds 12 exhibit a broad structured absorption band with a maximum at 276 nm (log  $\varepsilon = 4.54 - 4.70$ , for details see the SI). Compared with the parent compound 4-phenylbut-3-yn-2-one  $14^{4a, 9}$  the absorption maxima of diones 12 are slightly (3 nm) but significantly red-shifted. Furthermore, the molar extinction coefficients  $\varepsilon$  of 12f-l (n > 0) are consistently higher by 16-30%, compared with 14. (The  $\varepsilon$  values for 12a-e are not directly comparable with 14, because the chromophor is extended by an ester group). These findings strongly suggest an interaction of the two chromophors in **12** in the ground state (see Section 3).

# Scheme 3. PDDA reaction to (1,7)naphthalenophanes 13 and dimerization of the parent compound 14 to 15.



Table 2. Yields of [k](1,7)Naphthalenophanes 13a-l.

	k <sup>a</sup>	Yields [%] <sup>b</sup>		k <sup>a</sup>	Yields [%] <sup>b</sup>
13a	10	0 ( <b>12a</b> : 99)	13g	14	53
13b	11	33 ( <b>12b</b> : 32)	13h	16	70
13c	12	47 ( <b>12c</b> : 23)	13i	14	59
13d	14	70	13j	18	74

# The Journal of Organic Chemistry

13e	22	39	13k	22	66	
13f	12	52	131	24	70	

<sup>a</sup> k = N + 4. <sup>b</sup>Starting concentration for irradiation: 1.0 mM.

To our great surprise most of the diketones **12** exhibit a remarkable photochemical reactivity (excitation wavelength > 300 nm) and smoothly react to the corresponding [k](1,7)naphthalenophanes **13** (Scheme 3, k is the total number of atoms in the linker connecting positions 1 and 7 of naphthalene). As already mentioned above the PDDA reaction proceeds stepwise via biradicals **BR** and cycloallenes **CA**, which are also depicted in Scheme 3 for the reaction from **12** to **13**.

For k > 12 we obtained the target compounds in almost all cases with yields > 50% (except **13e**). With decreasing length of the linker (**13b,c**) the yields decreased and **13a** bearing the shortest linker was not accessible by PDDA of **12a** (Table 2).

The structure of (1,7) naphthalenophanes **13** was unambiguously proven with the x-ray structure of **13i** (Figure 3).<sup>10</sup>

Figure 3. X-ray crystal structure of 13i.



2. Mechanism of the PDDA to (1,7)Naphthalenophanes.

As mentioned above we felt that diketones 12 exhibit an unusually high photochemical reactivity. To substantiate this impression, we compared their photokinetics with previously investigated o- and m-substituted systems. For this purpose we measured the decay rate of 12h as well as of *o*-substituted precursor  $16^{3a}$  and of *m*-substituted precursor  $17^{3b}$ . The degradation curves of these three compounds are depicted in Figure 4. It is clearly discernable that the decay rate of 12h is more than twice the decay rates of 16 and 17 (for  $k_{REL}$  the decay rate of 16 was set to unity). Although the exact cause of the increased reactivity of ketones 12 is still unclear we hypothesized that a "folded" ground-state conformation of 12, which facilitates the PDDA, is responsible for this behavior. In the preceding section we have already mentioned conspicuous changes in the UV spectra of 12 compared with the parent compound 14. Indeed, a comparative conformational analysis of 12h, 16, and 17 (force field MMFF94x<sup>11</sup>, for details see the SI) revealed a folded conformation for **12h** as the global minimum, but not for 16 and 17. The stabilization of this conformation originates from headto-tail dipole-dipole interactions between the ketocarbonyl groups resulting in a relatively short distance between the alkyne moieties. To verify these findings at a higher level of theory we optimized both the folded and the stretched geometry using a DFT method (B3LYP<sup>12</sup>/6- $31G^{*13}$ ). The geometry of the folded conformer is depicted in figure 5. We found that this structure is more stable by about 3 kcal/mol compared with the stretched conformation. A similar result was obtained for 12i. The close proximity of the photoreactive ynone moieties in these folded conformers could be the explanation for the high reactivity of compounds 12.

Figure 4. Degradation curves of the irradiation of 12h, 16, 17.





Figure 5. DFT-optimized ground-state geometry of 12h.



3. Ring strain and structural strain indicators.

Some of the (1,7)naphthalenophanes **13** should be considerably strained<sup>14</sup> and we were interested in the corresponding ring strain energies as well as possible structural and spectroscopic consequences of the strain.

For the determination of strain energy by means of quantum chemical calculations, the definition of an isodesmic reaction is the method of choice.<sup>15</sup> This is understood to be a hypothetic reaction in which the type and number of bonds cleaved in the reactants are the same as the type and number of bonds formed in the products. Recently, we successfully applied this approach for calculating the ring strain of (1,5)naphthalenophanes.<sup>3a</sup> In analogy to this work we defined the isodesmic reaction shown in Scheme 4 for even values of m (this applies to all cases except **13b** where two different cuts from **E** to **G** are possible, for details see the SI). Starting from the naphthalenophane **E** the central C-C bond of the diol linker is cleaved to the 1-arylnaphthalene **G**, releasing potential ring strain. The simultaneous cleavage of a C-C bond and the formation of two C-H bonds are compensated by the reaction between two alkyl acetates **F** to diol diacetate **H**. Here, the value of p is given in eq. 1 and the strain energy  $E_{STR}$  is defined by eq. 2 (Scheme 4).

# Scheme 4. Isodesmic reaction for the calculation ring strain of (1,7)Naphthalenophanes 13.



## The Journal of Organic Chemistry

$$p = \frac{m}{2} - 1 \tag{1}$$

 $E_{STR} = E(\boldsymbol{G}) + E(\boldsymbol{H}) - E(\boldsymbol{E}) - 2E(\boldsymbol{F}) \qquad (2)$ 

The resulting strain energies are summarized in Table 3 (3<sup>rd</sup> col.). The highest value (25.4 kcal/mol) was obtained for the inaccessible compound **13a** (k = 10). **13b** with the next larger linker (k = 11), which was obtained with 33% yield, exhibits a ring strain energy of 19.3 kcal/mol. Obviously, products with strain energies above about 20 kcal/mol cannot be obtained with this method. The strain energies of [12](1,7)naphthalenophanes **13c** and **13f** are quite different (13.2 kcal/mol *vs*. 3.7 kcal/mol). This can be explained by the conjugation of the ester groups with the  $\pi$ -systems of the aromatic rings (n = 0) in the case of **13c**, resulting in conformational stiffening. Most of the other (1,7)naphthalenophanes are only moderately strained and the strain energies range from 1 to 4 kcal/mol (Table 3).

In our previous work on (1,5)naphthalenophanes we observed an increasing twist of naphthalene moiety with increasing ring strain.<sup>3a</sup>

Table 3. Strain energy  $E_{STR}$ , deformation angle  $\gamma_{Ph}$  (see Figure 6) and selected <sup>1</sup>H-NMR shifts of [k](1,7)Naphthalenophanes 13.

13	k <sup>a</sup>	E <sub>STR</sub> <sup>b</sup>	γ <sub>Ph</sub> <sup>c</sup>	δ(H-8) <sup>d</sup>	$\delta(\text{Ac-2})^{e}$
a	10	25.4	29.01	-	-
b	11	19.3	25.63	6.34	2.60
с	12	13.2	19.16	6.74	2.55
d	14	6.0	10.03	7.46	2.41
e	22	3.5	1.74	- <sup>f</sup>	2.08
f	12	3.7	9.46	6.83	2.37
g	14	1.0	3.75	-f	2.14
h	16	1.1	1.23	f	2.09

i	14	3.0	4.76	7.04	2.11
j	18	2.7	1.71	_f	2.08
k	22	3.9	1.36	_f	2.09
l	24	3.7	1.78	_f	2.08

 $^{a}k = N+4 = m + 1n + 8$ . <sup>b</sup>Strain energy in kcal/mol. <sup>c</sup>deformation angle of the phenyl ring in °. <sup>d</sup>Chemical shift of

H-8 in ppm. <sup>e</sup>Chemical shift of Ac-2. <sup>f</sup>signal could not be unambiguously determined due to superposition of signals in NMR spectra.

Figure 6. (a) Definition of the deformation angle  $\gamma_{Ph}$ . (b) Effects of increasing ring strain on the chemical shifts of H-8 (blue) and the methyl group of Ac-2 (red).



In order to find out whether in the case of (1,7) naphthalophanes **13** the naphthalene part is also the "weakest link" we carefully explored the optimized geometries. The first striking detail was the nearly perpendicular orientation of the phenyl ring relative to the naphthalene system in all cases (*cf.* figure 3). In contrast to the previously investigated (1,5) naphthalenophanes the naphthalene moiety is virtually planar even for highly strained cases.

### The Journal of Organic Chemistry

By contrast, the two C-C bonds connecting the phenyl ring with the rest of the naphthalenophane are considerably inclined from the  $\pi$ -plane in these cases. This effect can be expressed by a deformation angle  $\gamma_{Ph}$ , which is defined by the difference between 180 and the arithmetic average of two pseudo-valance angles,  $\alpha$  and  $\beta$  (Figure 6a). The values for  $\gamma_{Ph}$ , which correlate well with  $E_{STR}$ , are listed in Table 3 (4<sup>th</sup> col.).

The bending of the phenyl ring should significantly influence the <sup>1</sup>H NMR spectra of compounds **13**. Caused by the aromatic ring current in a static magnetic field, each phenyl ring exhibits an anisotropy cone. The chemical shift values of all protons inside this cone are decreased (upfield), whereas signals of protons outside the cone are shifted downfield.<sup>16</sup> Looking at the geometries of naphthalenophanes **13** the positions both of H-8 (blue) and of the methyl group of Ac-2 (red) regarding the anisotropy cone (green) are altered upon bending of the phenyl ring (Figure 6). Whereas H-8 is moved towards the interior of the cone, the aforementioned methyl group is moved out of the cone. The measured <sup>1</sup>H NMR shift values of H-8 and Ac-2, which are also summarized in Table 3, excellently reflect the forecasted trend. Comparing highly strained **13b** and moderately strained **13i**, the signal of H-8 is downfield-shifted by 0.70 ppm and the signal of Ac-2 is upfield-shifted by 0.49 ppm.

# Conclusion

Based on our previous successful synthesis of naphthalenophanes<sup>3c</sup> by thermal DDA reaction we first examined whether this approach is also an appropriate way to (1,7)naphthalenophanes. Unfortunately, all attempts in this direction failed. On the other hand, the photochemical variant (PDDA reaction) using diketones **12** smoothly provided the [k](1,7)naphthalenophanes **13** even in highly strained (k = 11, 12) and macrocyclic (k up to 24) cases. The photochemical reactivity of compounds **12** is unusually high, compared with previously investigated systems, and could be explained by folded ground state geometries of the reactants bringing the ynone moieties in close proximity. The ring strain energies  $E_{STR}$  of naphthalenophanes **13** were determined with the help of an isodesmic reaction. The most strained product **13b** (k = 11) exhibits a strain energy of about 19 kcal/mol, whereas **13a** (k = 10,  $E_{STR} = 25.4$  kcal/mol) was not accessible. The most conspicuous change in the geometry of highly strained (1,7)naphthalenophanes is a bending of the phenyl ring, expressed by the deformation angle  $\gamma_{Ph}$ . This bending causes distinct changes of the NMR signals of protons, which are located near the anisotropy cone of the phenyl ring. Finally, it should be noted that, according to our experience, the cyclization of diketones **12** to (1,7)naphthalenophanes **13** is one of the most efficient PDDA systems known to date. Currently, we are investigating applications as peptide mimetic and in supramolecular assemblies.

# **Experimental Section**

General Information. All reactions were conducted in heat-gun-dried and nitrogen flushed glassware using Schlenk techniques. Solvents and reagents were purchased in highest available purity and used without additional purification, if not stated elsewhere. Solvents were dried and distilled prior to use. Reaction monitoring was performed by thin layer chromatography (TLC) until the starting material was completely consumed indicated at the appropriate sections. Crude mixtures were purified by flash column chromatography (FSC). For the visualization of the products UV- and/or dark light (254/366 nm) was used. The individual solvent mixtures for the elution of the product and the corresponding retardation factors  $(R_t)$  were noted in the appropriate sections. Melting points of solids were recorded and not corrected. NMR spectra were recorded on a 300 MHz spectrometer with appropriate deuterated solvents and used as internal standard: CDCl<sub>3</sub> (<sup>1</sup>H:  $\delta$  = 7.26 ppm, <sup>13</sup>C:  $\delta = 77.2$  ppm); CD<sub>3</sub>OD (<sup>1</sup>H:  $\delta = 3.31$  ppm, 13C:  $\delta = 49.0$  ppm). Coupling constants (*J*) are given in Hertz (Hz). Fine structure analysis was performed and multiplicities were abbreviated as follows: broad singlet (br s), doublet (d), triplet (t), quartet (q), multiplet (m). FT-IR measurements were performed on ATR crystals and the characteristic intensities of absorption bands ( $\tilde{v}$ , cm<sup>-1</sup>) were abbreviated as follows: weak (w), medium (m), strong (s), very strong (vs). High resolution mass spectrometry (HRMS) was performed with impact ionization (EI) and were recorded on a Mass spectrometer equipped with a quadrupol. UV-Vis spectra were recorded in a two-cuvette spectrometer in the range of 200-500 nm. Phosphorescence spectra were recorded in an EPA (diethyl ether, iso-pentane, ethanol, 5:5:2, v/v/v) matrix at 77 K. Photochemical reactions were performed in a standard (semi)preparative batch apparatus equipped with an internal cooling jacket (quartz) and

## The Journal of Organic Chemistry

external pyrex vessel water cooling system. For efficient stirring of the reaction medium a gentle stream of nitrogen was needed and bubbled 15 min before the reaction was initiated with a high-pressure mercury arc lamp (150 W; excitation  $\lambda > 300$  nm). 2-(4-Iodophenyl)acetic acid<sup>17</sup> and 3-(4-Iodophenyl)propionic<sup>5</sup> acid were synthesized according to literature.

#### **General Procedures**

General procedure 1 (GP1) for the synthesis of diiodides 5: To a suspension containing the diol 10 (1.0 equiv) and the carboxylic acid 4 (2.67 equiv) in dry DCM (10 mL/mmol) were added  $N,N^{\epsilon}$ -diisopropyl-carbodiimide (DIC, 2.5 equiv) and DMAP (20 mol%). Stirring at 50 °C was continued until TLC indicated the complete consumption of the starting material. The heterogeneous reaction mixture was washed three times with brine and the combined organic phases were dried with magnesium sulfate. Before removing the solvent under reduced pressure the suspension was filtered over Celite<sup>®</sup>. The purification of compounds 5 was accomplished by FSC.

General procedure 2 (GP2) for the synthesis of diols 11: The diiodide 5 (1.0 equiv) was dissolved in a mixture of triethylamine (Et<sub>3</sub>N) and THF (10 mL/ mmol, 3:1, v/v). The solution was degassed three times and flushed with nitrogen. Bis(triphenylphosphine) palladium(II)dichloride (Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, 10 mol%) and copper iodide (CuI, 5 mol%) were added and stirred for five minutes. 3-Butyne-2-ol (97%, 4.0 equiv) was added and the reaction mixture was stirred until TLC indicated complete consumption of the starting material. The heterogeneous mixture was poured into diethyl ether and washed subsequently (each two times) with water, aq tartaric acid (20%), sodium bicarbonate and brine. The combined organic phases were dried with magnesium sulfate and filtered over Celite<sup>®</sup>. After removing the solvent under reduced pressure the crude product 11 was purified by FSC.

**General procedure 3 (GP3) for the synthesis of diketones 12:** The diol **11** (1.0 equiv) was dissolved in anhyd DMSO (10 mL/mmol). Acetic anhydride (10.0 equiv) was added and stirring was continued until TLC indicated the complete consumption of the starting material. The solvent was removed in vacuo. The pure product **12** was isolated after FSC.

General procedure 4 (GP4) for the PDDA reaction to (1,7)Naphthalenophanes 13. The diketone 12 was dissolved in DCM (380 mL) using a standard photochemical batch apparatus for (semi)preparative scale reactions. The solution was purged 15 min with nitrogen and irradiated with a high-pressure mercury arc lamp until TLC indicated the complete consumption of the starting material. The solvent was removed under reduced pressure. The crude material 13 was purified by FSC.

**3,3'-{Ethane-1,2-diylbis[oxy(3-oxopropane-3,1-diyl)benzene-4,1-diyl]}bisprop-2-ynoic acid 6**. Bis-(3-(4-Iodophenyl)propionic acid)-ethane-1,2-diyl-ester (0.60 g, 1.04 mmol) (**5i**) was dissolved in dry DMSO (40 mL) and DBU (1.60 mL, 10.38 mmol), 1,4-Bis(diphenylphosphino)butane (dppb, 0.089 g, 0.21 mmol) and bis(triphenylphosphine)palladium (II)dichloride (Pd(PPh\_3)\_2Cl\_2, 0.057 g, 0.10 mmol) were added subsequently. Before adding propiolic acid (0.13 mL, 2.08 mmol) dropwise the heterogenous reaction mixture was degassed

three times and flushed with nitrogen. Stirring at 50 °C was continued until TLC indicated the complete consumption of the starting material (5h). The dark mixture was diluted with ethyl acetate (100 mL) and extracted three times (3 x 80) with saturated aq NaHCO<sub>3</sub> solution. The combined aq phases were acidified with ice-cold HCl (aq, 6 M, 50 mL) up to pH 2. The resulting precipitate was extracted five times (5 x 50 mL) with DCM. The combined phases were dried over magnesium sulfate and the solvent was removed under reduced pressure. After FSC compound **6** was isolated as light yellowish solid (0.46 g, 96%). *R*<sub>f</sub> 0.48 (EtOAc + 1% formic acid); m.p. 159-160 °C; <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>OD, ppm):  $\delta$  7.48 (d, *J* = 8.2 Hz, 4H), 7.27 (d, *J* = 8.2 Hz, 4H), 4.20 (s, 4H), 2.92 (t, *J* = 7.4 Hz, 4H, 2.61 (t, *J* = 7.4 Hz, 4H; <sup>13</sup>C NMR (75 MHz, MeOD, ppm):  $\delta$  173.9, 156.7, 145.3, 134.0, 130.0, 118.8, 86.7, 63.5, 35.9, 31.7; IR: 3436 (w), 2972 (m), 2569 (m), 2201 (s), 1681 (vs), 1606 (m), 1367 (m), 1282 (m), 1216 (s), 1173 (s), 830 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>26</sub>H<sub>22</sub>O<sub>8</sub> 462.1315; found 462.1320.

**Ethane-1,2-diyl bis[3-(4-{3-oxo-3-[propan-2-yl(propan-2-ylcarbamoyl)amino]prop-1-yn-1-yl}phenyl)propanoate] (9).** According to table SI-1 (see conditions), the Diureide 9 was isolated as a vitreous oil,  $R_f$  0.60 (PE/EtOAc 1:1); <sup>1</sup>H NMR 300 MHz, CDCl<sub>3</sub>) δ 8.48 (br s, 2H), 7.53 (d, J = 8.1 Hz, 4H), 7.32 – 7.25 (m, 4H), 4.98 (dt, J = 13.7, 6.8 Hz, 2H), 4.29 (s, 4H), 4.03 (dq, J = 13.3, 6.6 Hz, 2H), 3.02 (t, J = 7.5 Hz, 4H), 2.69 (t, J = 7.6 Hz, 4H), 1.59 (d, J = 6.8 Hz, 12H, 1.24 (d, J = 6.5 Hz, 12H; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm) δ 172.2, 156.9, 152.9, 143.7, 132.9, 128.9, 118.0, 93.8, 82.3, 62.4, 51.9, 42.7, 35.2, 30.9, 22.8, 21.2. HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>40</sub>H<sub>50</sub>N<sub>4</sub>O<sub>8</sub> 714.3629; found 714.3634.

**Bis-(4-Iodobenzoic acid)-ethane-1,2-diyl-ester (5a)**. 1,2-Ethanediol (0.77 mL, 13.69 mmol) and 4-Iodobenzoic acid (9.07 g, 36.56 mmol), were subjected to the reaction conditions described in **GP1**. The reaction was finished after 43 h, yielding the title compound as colorless solid (6.79 g, 95%).  $R_f$  = 0.38 (PE/EtOAc 1:1); m.p. 142 – 143 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.81 – 7.72 (m 8H), 4.64 (s, 4H; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  166.0, 137.9, 131.2, 129.3, 101.3, 63.0; IR ( $\tilde{\upsilon}$ ): 3077 (w), 2857 (w), 1713 (vs), 1581 (s), 1454 (m), 1393 (m), 1291 (m), 1255 (s), 1176 (m), 1101 (s), 1009 (s), 837 (m), 751 (s), 680 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>16</sub>H<sub>12</sub>I<sub>2</sub>O<sub>4</sub> 521.8820; found 521.8821.

**Bis-(4-iodobenzoic acid)-propane-1,3-diyl-ester (5b).** 1,3-Propanediol (0.67 mL, 9.25 mmol) and 4-Iodobenzoic acid (6.12 g, 24.68 mmol) were subjected to the reaction conditions described in **GP1**. The reaction was finished after 38 h, yielding the title compound as colorless solid (3.31 g, 67%).  $R_f$  0.58 (PE/EtOAc 3:1); m.p. 116-117 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.79 – 7.69 (m, 8H), 4.48 (t, J = 6.2 Hz, 4H), 2.24 (p, J = 6.1 Hz, 2H; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  166.1, 137.9, 131.1, 129.6, 101.0, 62.1, 28.3; IR ( $\tilde{\upsilon}$ ): 2980 (m), 1709 (vs), 1586 (s), 1393 (s), 1272 (vs), 1122 (vs), 1008 (s), 840 (m), 748 (s)cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>17</sub>H<sub>14</sub>I<sub>2</sub>O<sub>4</sub> 535.8982; found 535. 8985.

**Bis-(4-Iodobenzoic acid)-butane-1,4-diyl-ester (5c).** 1,4-Butanediol (1.0 g, 11.1 mmol) and 4-Iodobenzoic acid (7.35 g, 29.63 mmol), were subjected to the reaction conditions described in **GP1**. The reaction was finished after 47 h yielding the title compound as colorless solid (4.2 g, 69%).  $R_f$  0.25 (PE/EtOAc 10:1); m.p. 134-135 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.80 – 7.71 (m, 8H, H-Ar), 4.38 (s, 4H,  $CH_2$ ), 1.92 (s, 4H, 18

CH<sub>2</sub>);<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  166.2 (C=O), 137.9 (C<sub>Ar</sub>H), 131.1 (C<sub>Ar</sub>H), 129.8 (C<sub>Ar</sub>), 100.9 (C<sub>Ar</sub>), 64.8 (CH<sub>2</sub>), 25.6 (CH<sub>2</sub>); IR ( $\tilde{\upsilon}$ ): 1703 (vs), 1585 (m), 1267 (vs), 1102 (s), 915 (m), 757 (m), 745 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>18</sub>H<sub>16</sub>I<sub>2</sub>O<sub>4</sub> 549.9138; found 549.9150.

**Bis-(4-Iodobenzoic acid)-hexane-1,6-diyl-ester (5d)**. 1,6-Hexanediol (0.71 g, 6.0 mmol) and 4-Iodobenzoic acid (3.97 g, 16.02 mmol), were subjected to the reaction conditions described in **GP1**. The reaction was finished after 44 h yielding the title compound as colorless solid (2.41 g, 70%).  $R_f$  0.61 (PE/EtOAc 1:1); m.p. 85-86 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.83 – 7.67 (m, 8H), 4.31 (t, J = 6.6 Hz, 4H), 1.88 – 1.68 (m, 4H), 1.56 – 1.44 (m, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  166.2, 137.8, 131.1, 130.0, 100.8, 65.3, 28.7, 25.9; IR ( $\tilde{\upsilon}$ ): 2941 (m), 1710 (s), 1584 (s), 1264 (vs), 1103 (s), 1004 (s), 753 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>20</sub>H<sub>20</sub>I<sub>2</sub>O<sub>4</sub> 577.9446; found 577.9436.

**Bis-(4-Iodobenzoic acid)-dodecane-1,12-diyl-ester (5e)**. 1,12-Dodecanediol (1.00 g, 4.94 mmol) and 4-Iodobenzoic acid (3.27 g, 13.20 mmol) were subjected to the reaction conditions described in **GP1**. The reaction was finished after 65 h yielding the title compound as colorless solid (3.27 g, 99%).  $R_f$  0.51 (PE/EtOAc 10:1); m.p. 55-57 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.76 (q, J = 8.5 Hz, 8H), 4.30 (t, J = 6.7 Hz, 4H), 1.89 – 1.60 (m, 4H, H-7), 1.51 – 1.10 (m, 16H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  166.3, 137.8, 131.1, 130.1, 100.7, 65.5, 29.6,29.4, 28.8, 26.1; IR ( $\tilde{v}$ ): 2916 (s), 2849 (s), 1716 (vs), 1584 (m), 1392 (m), 1314 (m), 1272 (m), 1181 (m), 1104 (m), 1007 (m), 845 (m), 750 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>26</sub>H<sub>32</sub>I<sub>2</sub>O<sub>4</sub> 662.0385; found 662.0395.

**Bis-(2-(4-Iodophenyl)acetic acid)-ethane-1,2-diyl-ester (5f).** 1,2-Ethanediol (0.46 mL, 8.22 mmol) and 2-(4-Iodophenyl)acetic acid (5.76 g, 21.96 mmol) were subjected to the reaction conditions described in **GP1**. The reaction was finished after 48 h yielding the title compound as colorless solid (3.62 g, 80%).  $R_f$  0.47 (PE/EtOAc 1:1); m.p.: 60-61 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.65 (d, J = 8.3 Hz, 4H), 7.01 (d, J = 8.2 Hz, 4H), 4.29 (s, 4H), 3.54 (s, 4H; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  170.8, 137.8, 133.4, 131.4, 92.9, 62.6, 40.7; IR ( $\tilde{\upsilon}$ ): 2982 (w), 2921 (w), 1729 (vs), 1483 (s), 1338 (m), 1251 (s), 1159 (s), 1136 (vs), 1043 (s), 1007 (s), 976 (s),737(s), 485 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>18</sub>H<sub>16</sub>I<sub>2</sub>O<sub>4</sub> 549.9138; found 549.9136.

**Bis-(2-(4-Iodophenyl)acetic acid)-butane-1,4-diyl-ester (5g).** 1,4-Butanediol (0.99 mL, 11.15 mmol) and 2-(4-Iodophenyl)acetic acid (7.8 g, 29.77 mmol), were subjected to the reaction conditions described in **GP1**. The reaction was finished after 63 h yielding the title compound as colorless solid (4.53 g, 70%).  $R_f$  0.35 (PE/EtOAc 1:1); m.p. 71–72 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.65 (d, J = 8.4 Hz, 4H), 7.02 (d, J = 8.4 Hz, 4H), 4.08 (t, J = 5.6 Hz, 4H), 3.55 (s, 4H), 1.69 – 1.59 (m, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  171.0, 137.8, 133.7, 131.4, 92.7, 64.5, 41.0, 25.3; IR ( $\tilde{v}$ ): 2956 (w), 1722 (vs), 1485 (m), 1348 (m), 1216 (m), 1164 (m), 800 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>20</sub>H<sub>20</sub>I<sub>2</sub>O<sub>4</sub> 577.9451, found 577.9442.

**Bis-(2-(4-Iodophenyl)acetic acid)-hexane-1,6-diyl-ester (5h)**. 1,6-Hexanediol (0.86 g, 8.46 mmol) and 2-(4-Iodophenyl)acetic acid (5.0 g, 19.08 mmol) were subjected to the reaction conditions described in **GP1**. The

reaction was finished after 71 h yielding the title compound as colorless solid (2.94 g, 67%).  $R_f$  0.52 (PE/EtOAc 3:1); m.p. 97-98 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.64 (d, J = 8.2 Hz, 4H), 7.03 (d, J = 8.2 Hz, 4H), 4.06 (t, J = 6.6 Hz, 4H), 3.55 (s, 4H, 4H), 1.57 (d, J = 6.5 Hz, 4H), 1.35 – 1.21 (m, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  171.2, 137.8, 133.9, 131.4, 92.7, 65.0, 41.1, 28.5, 25.5; IR ( $\tilde{0}$ ): 2935 (w), 2886 (w), 1723 (vs), 1484 (m), 1218 (m), 1170 (s), 981 (m), 800 (m), 733 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>22</sub>H<sub>24</sub>I<sub>2</sub>O<sub>4</sub> 605.9764; found 605.9745.

**Bis-(3-(4-Iodophenyl)propionic acid)-ethane-1,2-diyl-ester (5i).** Ethyleneglycol (0.31 mL, 5.55 mmol) and 3-(4-Iodophenyl)propionic acid (4.0 g, 14.49 mmol) were subjected to the reaction conditions described in **GP1**. The reaction was finished after 46 h yielding the title compound as colorless solid (1.84 g, 57%).  $R_f$  0.38 (PE/EtOAc 1:1); m.p. 55-56 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.59 (d, J = 8.3 Hz, 4H), 6.95 (d, J = 8.4 Hz, 4H), 4.24 (s, 4H), 2.88 (t, J = 7.6 Hz, 4H), 2.61 (t, J = 7.7 Hz, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  172.3, 140.1, 137.6, 130.5, 91.6, 62.3, 35.4, 30.4; IR ( $\tilde{v}$ ): 2932 (w), 1745 (m), 1726 (vs), 1484 (m), 1152 (s), 1006 (m), 805 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>20</sub>H<sub>20</sub>I<sub>2</sub>O<sub>4</sub> 577.9451; found 577.9446.

**Bis-(3-(4-Iodophenyl)propionic acid)-hexane-1,6-diyl-ester (5j)**. 1,6-Hexanediol (1.00 g, 8.46 mmol) and 3-(4-Iodophenyl)propionic acid (6.24 g, 22.59 mmol) were subjected to the reaction conditions described in **GP1**. The reaction was finished after 48 h yielding the title compound as colorless solid (4.41 g, 82%).  $R_f$  0.50 (PE/EtOAc 3:1); m.p. 77-78 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.59 (d, J = 8.3 Hz, 4H), 6.95 (d, J = 8.3 Hz, 4H), 4.04 (t, J = 6.6 Hz, 4H), 2.88 (t, J = 7.6 Hz, 4H), 2.59 (t, J = 7.6 Hz, 4H), 1.58 (dd, J = 11.6, 4.9 Hz, 4H), 1.30 (d, J = 7.0 Hz, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  172.8, 140.3, 137.6, 130.6, 91.5, 64.6, 35.7, 30.6, 28.6, 25.7; IR ( $\tilde{v}$ ): 2935 (m), 2854 (w), 1721 (vs), 1484 (m), 1288 (m), 1172 (s), 981 (m), 834 (m), 801 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>24</sub>H<sub>28</sub>I<sub>2</sub>O<sub>4</sub> 634.0077; found 634.0089.

**Bis-(3-(4-Iodophenyl)propionic acid)-decane-1,10-diyl-ester (5k)**. 1,10-Decanediol (0.50 g, 2.87 mmol) and 3-(4-Iodophenyl)propionic acid (11.64 g, 7.66 mmol) were subjected to the reaction conditions described in **GP1**. The reaction was finished after 66 h yielding the title compound as colorless solid (1.32 g, 66%).  $R_f$  0.35 (PE/EtOAc 5:1); m.p. 56-57 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.59 (d, J = 8.1 Hz, 4H), 6.95 (d, J = 8.0 Hz, 4H), 4.04 (t, J = 6.7 Hz, 4H), 2.89 (t, J = 7.6 Hz, 4H), 2.59 (t, J = 7.6 Hz, 4H), 1.72 – 1.43 (m, 4H), 1.23 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  172.8, 140.3, 137.6, 130.6, 91.5, 64.8, 35.7, 30.6, 29.5, 28.7, 26.0; IR ( $\tilde{\upsilon}$ ):  $\tilde{\upsilon}$  2958 (m), 2928 (m), 2852(m), 1731 (vs), 1480 (m), 1356 (m), 1203 (m), 1193 (s), 1176 (m), 1040 (w), 1007 (m), 947 (w), 806 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>36</sub>I<sub>2</sub>O<sub>4</sub> 690. 0703; found 690.0708.

**Bis-(3-(4-Iodophenyl)propionic acid)-dodecane-1,12-diyl-ester (5l).** 1,12-Dodecanediol (1.00 g, 4.94 mmol) and 3-(4-Iodophenyl)propionic acid (3.64 g, 13.20 mmol) were subjected to the reaction conditions described in **GP1**. The reaction was finished after 72 h yielding the title compound as colorless solid (3.52 g, 99%).  $R_f$  0.63 (PE/EtOAc 3:1); m.p. 59-61 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.59 (d, J = 8.2 Hz, 4H), 6.95 (d, J = 8.2

Hz, 4H), 4.04 (t, J = 6.7 Hz, 4H), 2.89 (t, J = 7.6 Hz, 4H), 2.59 (t, J = 7.6 Hz, 4H), 1.58 (dd, J = 12.2, 6.0 Hz, 4H), 1.22 (m, 16H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  172.8, 140.3, 137.6, 130.6, 91.5, 64.9, 35.7, 30.6, 29.7, 29.4, 28.7, 26.0; IR ( $\tilde{\upsilon}$ ): 2958 (w), 2919 (m), 2850 (m), 1731 (vs), 1480 (m), 1358 (m), 1204 (m), 1193 (m), 1149 (s), 1007 (m), 806 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>30</sub>H<sub>40</sub>I<sub>2</sub>O<sub>4</sub> 718.1016; found 718.0992.

Bis (4-(2-(3-hydroxybut-1-inyl)benzoic acid))-ethane-1,2-diyl-ester (11a). Bis-(4-Iodobenzoic acid)-ethane-1,2-diyl-ester (5a) (2.46 g, 4.71 mmol) was subjected to the reaction conditions described in GP2. The reaction was finished after 24 h yielding the title compound as light brown solid (1.58 g, 82%).  $R_f$  0.5 (PE/EtOAc 1:1); m.p. 136-138 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.96 (d, J = 8.2 Hz, 4H), 7.45 (d, J = 8.2 Hz, 4H), 4.76 (q, J = 6.6 Hz, 2H), 4.64 (s, 4H), 2.28 (br s, 2H), 1.55 (d, J = 6.6 Hz, 6H; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  165.9, 131.7, 129.7, 129.3, 127.8, 94.3, 83.3, 63.0, 58.9, 24.3; IR ( $\tilde{\upsilon}$ ): 3296 (m), 2977 (w), 1714 (vs), 1605 (m), 1466 (w), 1407 (w), 1343 (m), 1271 (s), 1176 (m), 1097 (m), 1077 (m), 1033 (m), 1018 (m), 935 (w), 859 (m), 767 (m), 696 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>24</sub>H<sub>22</sub>O<sub>6</sub> 406.1411; found 406.1421.

**Bis(4-(3-hydroxybut-1-inyl)benzoic acid)-propane-1,3-diyl-ester (11b)**. Bis-(4-Iodobenzoic acid)-propane-1,3-diyl-ester (**5b**) (2.27 g, 4.24 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 23 h yielding the title compound as light brown solid (1.48 g, 83%).  $R_f$  0.43 (PE/EtOAc 1:2); m.p. 140-141 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.93 (d, J = 8.3 Hz, 4H), 7.43 (d, J = 8.3 Hz, 4H), 4.78 (q, J = 6.6 Hz, 2H), 4.50 (t, J = 6.1 Hz, 4H), 2.34 – 2.15 (m, 2H), 1.94 (br s, 2H), 1.57 (d, J = 6.6 Hz, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 165.9, 131.5, 129.5, 129.4, 127.6, 94.0, 83.2, 62.2, 58.8, 28.2, 24.2; IR ( $\tilde{\upsilon}$ ): 3324 (m), 2979 (m), 1706 (vs), 1607 (m), 1470 (m), 1407 (m), 1275 (vs), 1094 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>25</sub>H<sub>24</sub>O<sub>6</sub> 420.1573; found 420.1565.

**Bis-(4-(3-hydroxybut-1-inyl)benzoic acid)-butane-1,4-diyl-ester (11c)**. Bis-(4-Iodobenzoic acid)-butane-1,4-diyl-ester (**5c**) (2.73 g, 4.96 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 23 h yielding the title compound as light brown solid (1.83 g, 85%).  $R_f$  0.35 (PE/EtOAc 1:1); m.p. 119-120 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 (d, J = 8.4 Hz, 4H), 7.45 (d, J = 8.4 Hz, 4H), 4.77 (q, J = 6.6 Hz, 2H), 4.38 (s, 4H), 2.18 (br s, 2H), 1.93 (s, 4H), 1.56 (d, J = 6.6 Hz, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  166.1, 131.7, 129.8, 129.5, 127.5, 94.1, 64.8, 58.9, 25.6, 24.4; IR ( $\tilde{\nu}$ ): 3353 (w), 2977 (w), 1713 (vs), 1606 (m), 1266 (s), 1255 (s), 1099 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>26</sub>H<sub>26</sub>O<sub>6</sub> 434.1729; found 434.1745.

**Bis-(4-(3-hydroxybut-1-inyl)benzoic acid)-hexane-1,6-diyl-ester (11d)**. Bis-(4-Iodobenzoic acid)-hexane-1,6-diyl-ester (**5d**) (1.88 g, 3.25 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 24 h yielding the title compound as light yellowish solid (1.41 g, 88%).  $R_f$  0.5 (PE/EtOAc 1:1); m.p. 80-82 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.95 (d, J = 8.6 Hz, 4H), 7.44 (d, J = 8.6 Hz, 4H), 4.77 (q, J = 6.6 Hz, 2H), 4.32 (t, J = 6.5 Hz, 4H), 2.14 (br s, 2H), 1.89 – 1.68 (m, 4H), 1.56 (d, J = 6.6 Hz, 6H), 1.53 – 1.44 (m, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 166.2, 131.7, 130.0, 129.5, 127.4, 94.0, 83.4, 65.3, 58.9, 28.7, 26.0, 24.4; IR ( $\tilde{\upsilon}$ ): 3327 (m) , 2950 (m), 2906 (m), 2852 (m), 1707 (vs), 1606 (m), 1271 (s), 1096 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>30</sub>O<sub>6</sub> 462.2042 ; found 462.2044 .

Bis-(4-(3-hydroxybut-1-inyl)benzoic acid)-dodecane-1,12-diyl-ester (11e). Bis-(4-Iodobenzoic acid)dodecane-1,12-diyl-ester (5e) (2.00 g, 3.02 mmol) was subjected to the reaction conditions described in GP2. The reaction was finished after 24 h yielding the title compound as light brown solid (1.37 g, 83%).  $R_f$  0.47 (PE/EtOAc 1:1); m.p. 94-96 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.96 (d, J = 8.3 Hz, 4H), 7.45 (d, J = 8.2Hz, 4H), 4.76 (q, J = 9.9 Hz, 2H), 4.30 (t, J = 6.6 Hz, 4H), 2.21 (bs, 2H), 1.83 – 1.66 (m, 4H), 1.54 (t, J = 10.7Hz, 6H), 1.44 – 1.19 (m, 16H<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 166.3, 131.7, 130.1, 129.5, 127.3, 94.0, 83.4, 65.5, 58.8, 29.5, 28.8, 26.1, 24.4; IR ( $\tilde{v}$ ): 3332 (m), 2913 (vs), 2848 (s), 1706 (vs), 1605 (m), 1470 (m), 1407 (m), 1316 (m), 1273 (s), 1175 (m), 1097 (s), 1019 (m), 933 (w), 862 (m), 769 (m), 697 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>34</sub>H<sub>42</sub>O<sub>6</sub> 546.2976; found 546.2978.

**Bis-(2-(4-(3-hydroxybut-1-inyl)phenyl) acetic acid-ethane-1,2-diyl-ester (11f).** Bis-(2-(4-Iodophenyl)acetic acid)-ethane-1,2-diyl-ester (**5f**) (2.50 g, 4.55 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 19 h yielding the title compound as light brown solid (1.52 g, 77%).  $R_f$  0.53 (PE/EtOAc 1:2); m.p. 71-73 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm) δ 7.36 (d, J = 8.0 Hz, 4H), 7.17 (d, J = 8.0 Hz, 4H), 4.74 (q, J = 6.5 Hz, 2H), 4.27 (s, 4H), 3.57 (s, 4H), 2.33 (br s, 2H), 1.54 (d, J = 6.6 Hz, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm) δ 171.0, 134.0, 132.0, 129.3, 121.7, 91.4, 83.7, 62.6, 58.9, 41.1, 24.5; IR ( $\tilde{\nu}$ ): 3391 (m), 2984 (w), 1730 (vs), 1511 (w), 1353 (m), 1215 (m), 1158 (m), 1102 (m), 1035 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>34</sub>H<sub>42</sub>O<sub>6</sub> 546.2976; found 546.2978.

**Bis-(2-(4-(3-hydroxybut-1-inyl)phenyl)acetic acid)-butane-1,4-diyl-ester (11g).** Bis-(2-(4-Iodophenyl)acetic acid)-butane-1,4-diyl-ester (**5g**) (2.00 g, 3.46 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 26 h yielding the title compound as light brown solid (1.41 g, 88%).  $R_f$  0.28 (PE/EtOAc 1:1); m.p. 75-76 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.37 (d, J = 8.2 Hz, 4H), 7.20 (d, J = 8.2 Hz, 4H), 4.74 (q, J = 6.6 Hz, 2H), 4.14 – 3.99 (m, 4H), 3.59 (s, 4H), 2.20 (br s, 2H), 1.65 – 1.58 (m, 4H), 1.54 (d, J = 6.6 Hz, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  171.2, 134.4, 132.0, 129.3, 121.6, 91.3, 83.8, 64.5, 58.9, 41.4, 25.2, 24.5; IR ( $\tilde{\nu}$ ): 3322 (m), 2981 (m), 1726 (vs), 1510 (m), 1318 (m), 1296 (m), 1239 (m), 1098 (m), 1039 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>30</sub>O<sub>6</sub> 462.2042; found 462.2026.

**Bis-(2-(4-(3-hydroxybut-1-inyl)phenyl)acetic acid)-hexane-1,6-diyl-ester (11h)**. Bis-(2-(4-Iodophenyl)acetic acid)-hexane-1,6-diyl-ester (**5h**) (2.00 g, 3.30 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 23 h yielding the title compound as highly viscous oil (1.28 g, 80%).  $R_f$  0.48 (PE/EtOAc 1:2); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.37 (d, J = 8.1 Hz, 4H), 7.21 (d, J = 8.0 Hz, 4H), 4.74 (q, J = 6.5 Hz, 2H), 4.05 (t, J = 6.5 Hz, 4H), 3.59 (s, 4H), 2.14 (br s, 2H), 1.55 (s, 6H, H-1), 1.53 (s, 4H), 1.24 (s, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  171.2, 124.4, 131.8, 129.2, 121.4, 91.2, 83.7, 64.9, 58.8, 41.4, 28.4, 25.4, 24.4; IR ( $\tilde{0}$ ): 3416 (m), 2934 (m), 1729 (vs), 1510 (m), 1250 (m), 1157 (s), 1103 (m), 1034 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>30</sub>H<sub>34</sub>O<sub>6</sub> 490.2355; found 490.2366.

**Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic** acid)-ethane-1,2-diyl-ester (11i). Bis-(3-(4-I00)) Bis-(3-(4

## The Journal of Organic Chemistry

conditions described in **GP2**. The reaction was finished after 23 h yielding the title compound as light brown solid (0.39 g, 70%).  $R_f$  0.23 (PE/EtOAc 1:1); m.p. 48-49 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.31 (d, J = 8.0 Hz, 4H), 7.10 (d, J = 8.0 Hz, 4H), 4.72 (q, J = 6.5 Hz, 2H), 4.21 (s, 4H), 2.90 (t, J = 7.6 Hz, 4H), 2.60 (t, J = 7.6 Hz, 4H), 2.50 (br s, 2H), 1.52 (d, J = 6.6 Hz, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  172.5, 140.9, 131.9, 128.4, 120.7, 91.0, 83.9, 62.3, 58.9, 35.4, 30.7, 24.5; IR ( $\tilde{v}$ ): 3414 (m), 2980 (m), 1733 (vs), 1509 (m), 1371 (m), 1254 (m), 1147 (s), 1104 (s), 1034 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>30</sub>O<sub>6</sub> 462.2042; found 462.2063.

**Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic** acid)-hexane-1,6-diyl-ester (11j). Bis-(3-(4-Iodophenyl)propionic acid)-hexane-1,6-diyl-ester (5j) (2.05 g, 3.23 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 24 h yielding the title compound as light brown solid (1.44 g, 86%).  $R_f$  0.6 (PE/EtOAc 1:2); m.p. 32-33 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.33 (d, J = 8.1 Hz, 4H), 7.13 (d, J = 8.0 Hz, 4H), 4.73 (q, J = 6.5 Hz, 2H), 4.04 (t, J = 6.5 Hz, 4H), 2.93 (t, J = 7.5 Hz, 4H), 2.6 (t, J = 7.5 Hz, 4H), 2.27 (br s, 2H), 1.54 (s, 4H, H-14), 1.52 (s, 6H), 1.23 (s, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 173.0, 141.0, 131.9, 128.4, 120.7, 90.9, 83.9, 64.7, 58.9, 35.7, 31.0, 28.6, 25.7, 24.5; IR ( $\tilde{v}$ ): 3423 (m), 2933 (m), 1729 (vs), 1509 (m), 1180 (m), 1155 (m), 1104 (s), 1034 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>32</sub>H<sub>38</sub>O<sub>6</sub> 518.2668; found 518.2685.

**Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic** acid)-decane-1,10-diyl-ester (11k). Bis-(3-(4-Iodophenyl)propionic acid)-decane-1,10-diyl-ester (5k) (0.388 g, 0.562 mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 23 h yielding the title compound as light brown solid (0.234 g, 73%).  $R_f$  0.5 (PE/EtOAc 1:1); m.p. 48-50 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  7.33 (d, J = 8.0 Hz, 4H), 7.13 (d, J = 8.0 Hz, 4H), 4.74 (q, J = 6.6 Hz, 2H), 4.04 (t, J = 6.7 Hz, 4H), 2.93 (t, J = 7.7 Hz, 4H), 2.60 (t, J = 7.7 Hz, 4H), 2.04 (br s, 2H), 1.57 – 1.45 (m, 10H), 1.26 (s, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$ 173.0, 141.2, 131.9, 128.4, 120.6, 90.8, 84.0, 64.9, 58.9, 35.7, 31.0, 29.4, 28.7, 26.0, 24.6, 24.0; IR ( $\tilde{v}$ ): 3326 (m), 2959 (m), 2922 (s), 2855 (m), 1726 (vs), 1510 (w), 1478 (w), 1446 (w), 1428 (w), 1369 (m), 1323 (m), 1296 (m), 1169 (m), 1152 (m), 1106 (m), 1078 (m), 1037 (m), 931 (w), 832 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>36</sub>H<sub>46</sub>O<sub>6</sub> 574.3294; found 574.3300.

**Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic** acid)-dodecane-1,12-diyl-ester (111). Bis-(3-(4-Iodophenyl)propionic acid)-dodecane-1,12-diyl-ester (2.5 g, 3.48mmol) was subjected to the reaction conditions described in **GP2**. The reaction was finished after 20 h yielding the title compound as light brown solid (1.32 g, 63%).  $R_f$  0.48 (PE/EtOAc 1:1); m.p. 59-61 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.32 (d, J = 8.1 Hz, 4H), 7.12 (d, J = 8.0 Hz, 4H), 4.73 (q, J = 6.6 Hz, 2H), 4.04 (t, J = 6.7 Hz, 4H), 2.92 (t, J = 7.7 Hz, 4H), 2.59 (t, J = 7.7 Hz, 4H), 2.27 (br s, 2H), 1.62 – 1.46 (m, 10H), 1.25 (s, 16H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  173.0, 141.1, 131.9, 128.4, 120.6, 90.8, 84.0, 64.9, 58.8, 35.7, 30.9, 29.6, 29.3, 28.7, 26.0, 24.5, 24.0; IR ( $\tilde{v}$ ): 3340 (m), 2916 (vs), 2851 (s), 1725 (vs), 1510 (w), 1472 (w), 1445 (w), 1419 (w), 1396 (w), 1320 (m), 1296 (m), 1266 (m), 1178 (m), 1169 (m), 1106 (m), 1077 (m), 1037 (m), 933 (w), 833 (m) cm<sup>-1</sup>; HRMS (m/z): [M<sup>+</sup>] calcd for C<sub>38</sub>H<sub>50</sub>O<sub>6</sub> 602.3602; found 602.3600. Bis-(4-(3-oxobut-1-inyl)benzoic acid)-ethane-1,2-diyl-ester (12a). Bis(4-(3-hydroxybut-1-inyl)benzoic acid))ethane-1,2-diyl-ester (11a) (1.00 g, 2.46 mmol) was subjected to the reaction conditions described in GP3. The reaction was finished after 23 h yielding the title compound as light yellowish solid (0.72 g, 73%). R<sub>f</sub> 0.6 (PE/EtOAc 1:1); m.p. 160-162 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 8.04 (d, J = 8.2 Hz, 4H), 7.62 (d, J = 8.2Hz, 4H), 4.68 (s, 4H), 2.46 (s, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.3, 165.4, 133.0, 131.3, 129.9, 124.9, 90.1, 88.3, 63.1, 32.9; IR ( $\tilde{\upsilon}$ ): 2962 (w), 2200 (s), 1711 (vs), 1664 (s), 1604 (m), 1403 (m), 1366 (m), 1258 (vs), 1178 (m), 1118 (s), 1106 (s), 1010 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>24</sub>H<sub>18</sub>O<sub>6</sub> 402.1103; found 402.1100 ; UV-Vis (ACN):  $\lambda_{max}$  (nm) = 276 (ε = 42506 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(4-(3-oxobut-1-inyl)benzoic** acid)-propane-1,3-diyl-ester (12b). Bis-(4-(3-hydroxybut-1-inyl)benzoic acid)-propane-1,3-diyl-ester (11b) (1.00 g, 2.38 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 24 h yielding the title compound as light yellowish solid (0.72 g, 73%).  $R_f$  0.32 (PE/EtOAc 3:1); m.p. 118-119 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 8.01 (d, J = 8.2 Hz, 4H), 7.59 (d, J = 8.2 Hz, 4H), 4.51 (t, J = 6.1 Hz, 4H), 2.46 (s, 6H), 2.27 (d, J = 5.8 Hz, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.4, 165.5, 132.9, 131.6, 129.7, 124.7, 90.0, 88.4, 62.3, 32.9, 28.2; IR ( $\tilde{v}$ ): 2914 (w), 2205 (s), 1710 (s), 1668 (vs), 1405 (w), 1361 (s), 1269 (vs), 1178 (s), 1123 (s), 1108 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>25</sub>H<sub>20</sub>O<sub>6</sub> 416.1260; found 416.1266; UV-Vis (ACN):  $\lambda_{max}$  (nm) = 276 (ε = 48978 M<sup>-1</sup>·cm<sup>-1</sup>),

**Bis-(4-(3-oxobut-1-inyl)benzoic acid)-butan-1,4-diyl-ester (12c)**. Bis-(4-(3-hydroxybut-1-inyl)benzoic acid)butane-1,4-diyl-ester (**11c**) (1.5 g, 3.45 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 23 h yielding the title compound as light yellowish solid (0.82 g, 55%). *R*<sub>f</sub> 0.15 (PE/EtOAc 3:1); m.p. 127.128 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 8.03 (d, *J* = 8.4 Hz, 4H), 7.61 (d, *J* = 8.4 Hz, 4H), 4.41 (s, 4H), 2.46 (s, 6H), 1.95 (s, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.4, 165.6, 132.9, 131.9, 129.7, 124.6, 90.0, 88.5, 65.0, 32.9, 25.6; IR ( $\tilde{\upsilon}$ ): 2959 (w), 2198 (s), 1714 (s), 1667 (s), 1266 (vs), 1239 (s), 1108 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>26</sub>H<sub>22</sub>O<sub>6</sub> 430.1416; found 430.1408; UV-Vis (ACN): λ<sub>max</sub> (nm) = 276 (ε = 47245 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(4-(3-oxobut-1-inyl)benzoic acid)-hexane-1,6-diyl-ester (12d)**. Bis-(4-(3-hydroxybut-1-inyl)benzoic acid)-hexane-1,6-diyl-ester (11d) (0.935 g, 2.02 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 20 h yielding the title compound as light yellowish solid (0.78 g, 86%). *R*<sub>f</sub> 0.43 (PE/EtOAc 3:1); m.p. 101-102 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 8.02 (d, *J* = 8.7 Hz, 4H), 7.60 (d, *J* = 8.7 Hz, 4H), 4.33 (t, *J* = 6.6 Hz, 4H), 2.45 (s, 6H), 1.92 – 1.69 (m, 4H), 1.58 – 1.45 (m, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.3, 165.7, 132.9, 132.1, 129.7, 124.4, 89.9, 88.6, 65.4, 32.8, 28.7, 25.8; IR ( $\tilde{0}$ ): 2945 (w), 2205 (m), 1707 (s), 1668 (s), 1269 (vs), 1105 (s), 771 (s), 697 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>26</sub>O<sub>6</sub> 458.1729; found 458.1725; UV-Vis (ACN): λ<sub>max</sub> (nm) = 276 (ε = 47904 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(4-(3-oxobut-1-inyl)benzoic acid)-dodecane-1,12-diyl-ester (12e).** Bis-(4-(3-hydroxybut-1-inyl)benzoic acid)-dodecane-1,12-diyl-ester (11e) (1.10 g, 2.01 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 22 h yielding the title compound as orange solid (0.77 g, 71%).  $R_f$  0.5

(PE/EtOAc 3:1); m.p. 78-79 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  8.04 (d, J = 8.3 Hz, 4H, H-Ar), 7.61 (d, J = 8.3 Hz, 4H, H-Ar), 4.31 (t, J = 6.7 Hz, 4H, CH<sub>2</sub>), 2.46 (s, 6H, CH<sub>3</sub>), 1.87 – 1.64 (m, 4H, CH<sub>2</sub>), 1.53 – 1.16 (m, 16H, CH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  184.4, 165.7, 132.9, 132.2, 129.7, 124.4, 89.9, 88.6, 65.7, 32.9, 29.9 – 29.2, 28.8, 26.1; IR ( $\tilde{\upsilon}$ ): 2918 (s), 2850 (m), 2208 (m), 1709 (vs), 1670 (s), 1604 (w), 1408 (w), 1359 (w), 1271 (s), 1181 (m), 1122 (m), 1015 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>34</sub>H<sub>38</sub>O<sub>6</sub> 542.2668; found 542.2641; UV-Vis (ACN):  $\lambda_{max}$  (nm) = 276 ( $\varepsilon$  = 50282 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(4-(2-(3-oxobut-1-inyl)phenyl)acetic** acid)-ethane-1,2-diyl-ester (12f). Bis-(2-(4-(3-hydroxybut-1-inyl)phenyl)acetic acid)-ethane-1,2-diyl-ester (11f) (1.00 g, 2.3 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 24 h yielding the title compound as light yellowish solid (0.7 g, 71%).  $R_f$  0.55 (PE/EtOAc 1:1); m.p. 79-80 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.52 (d, J = 8.1 Hz, 4H), 7.27 (d, J = 8.2 Hz, 4H), 4.30 (s, 4H), 3.62 (s, 4H), 2.44 (s, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.6, 170.5, 136.7, 133.4, 129.8, 119.0, 90.0, 88.6, 62.7, 41.1, 32.8; IR ( $\tilde{v}$ ): 2986 (w), 200 (vs), 1738 (vs), 1664 (vs), 1362 (m), 1149 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>26</sub>H<sub>22</sub>O<sub>6</sub> 430.1416; found 430.1424; UV-Vis (ACN):  $\lambda_{max}$  (nm) = 276 ( $\varepsilon$  = 37840 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(4-(2-(3-oxobut-1-inyl)phenyl)acetic acid)-butane-1,4-diyl-ester (12g).** Bis-(2-(4-(3-hydroxybut-1-inyl)phenyl)acetic acid)-butane-1,4-diyl-ester (**11g**) (0.20 g, 0.432 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 23 h yielding the title compound as light yellowish solid (0.14 g, 70%). *R*<sub>f</sub> 0.67 (PE/EtOAc 1:1); m.p. 62-63 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.53 (d, *J* = 8.3 Hz, 4H), 7.30 (d, *J* = 8.4 Hz, 4H), 4.09 (t, *J* = 5.0 Hz, 4H), 3.64 (s, 4H), 2.44 (s, 6H), 1.67 – 1.61 (m, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.7, 170.8, 137.1, 133.5, 129.8, 118.9, 90.1, 88.6, 64.6, 41.4, 32.9, 25.3; IR ( $\tilde{\nu}$ ): 2962 (w), 2201 (vs), 1721 (vs), 1670 (vs), 1224 (s), 1146 (s), 970 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>26</sub>O<sub>6</sub> 458.1729; found 413.1726; UV-Vis (ACN): λ<sub>max</sub> (nm) = 276 (ε = 35073 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(4-(2-(3-oxobut-1-inyl)phenyl)acetic** acid)-hexane-1,6-diyl-ester (12h). Bis-(2-(4-(3-hydroxybut-1-inyl)phenyl)acetic acid)-hexane-1,6-diyl-ester (11h) (1.14 g, 2.32 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 24 h yielding the title compound as light yellowish solid (0.77 g, 68%).  $R_f$  0.35 (PE/EtOAc 3:1); m.p. 52-53 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.53 (d, J = 8.2 Hz, 4H), 7.30 (d, J = 8.1 Hz, 4H), 4.07 (t, J = 6.6 Hz, 4H), 3.63 (s, 4H), 2.44 (s, 6H), 1.67 – 1.49 (m, 4H), 1.29 (t, J = 10.1 Hz, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.7, 170.9, 137.2, 133.4, 129.8, 118.8, 90.2, 88.6, 65.1, 41.5, 32.9, 28.5, 25.5; IR ( $\tilde{v}$ ): 2958 (w), 2199 (s), 1730 (vs), 1668 (vs), 1215 (m), 1153 (s), 986 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>30</sub>H<sub>30</sub>O<sub>6</sub> 486.2042; found 486.2044; UV-Vis (ACN):  $\lambda_{max}$  (nm) = 276 ( $\varepsilon$  = 37412 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)-ethane-1,2-diyl-ester (12i).** Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic acid)-ethane-1,2-diyl-ester (**11i**) (1.00 g, 2.16 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 22 h yielding the title compound as light yellowish solid (0.6 g, 60%).  $R_f$  0.4 (PE/EtOAc 3:1); m.p. 54-55 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm):  $\delta$  7.49 (d, J = 8.2 Hz, 4H), 7.21 (d, J = 8.1 Hz, 4H), 4.24 (s, 4H), 2.96 (t, J = 7.6 Hz, 4H), 2.63 (t, J = 7.6 Hz, 4H), 2.43 (s, 6H);

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.7, 172.3, 143.7, 133.4, 128.8, 118.0, 90.5, 88.4, 62.4, 35.1, 32.9, 30.9; IR ( $\tilde{\upsilon}$ ): 2919 (w), 2197 (vs), 1733 (s), 1657 (vs), 1605 (w), 1356 (m), 1282 (m), 1150 (s), 978 (m), 836 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>26</sub>O<sub>6</sub> 458.1729; found 458.1714; UV-Vis (ACN): λ<sub>max</sub> (nm) = 276 (ε = 36700 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)-hexane-1,6-diyl-ester (12j).** Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic acid)-hexane-1,6-diyl-ester (**11j**) (1.00 g, 2.62 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 23 h yielding the title compound as orange solid (1.0 g, 74%).  $R_f$  0.45 (PE/EtOAc 3:1); m.p. 62-63 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.48 (d, J = 8.1 Hz, 4H), 7.22 (d, J = 8.1 Hz, 4H), 4.04 (t, J = 6.6 Hz, 4H), 2.95 (d, J = 7.6 Hz, 4H), 2.62 (t, J = 7.6 Hz, 4H), 2.43 (s, 6H), 1.57 (m, 4H), 1.28 (s, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.7, 172.6, 144.0, 133.4, 128.8, 117.9, 90.6, 88.4, 64.6, 35.4, 32.8, 31.0, 28.6, 25.6; IR ( $\tilde{v}$ ): 2929 (w), 2197 (vs), 1718 (s), 1670 (vs), 1355 (m), 1278 (m), 1151 (s) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>32</sub>H<sub>34</sub>O<sub>6</sub> 514.2355; found 514.2363; UV-Vis (ACN):  $\lambda_{max}$  (nm) = 276 ( $\varepsilon$  = 36707 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)-decane-1,10-diyl-ester (12k)**. Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic acid)-decane-1,10-diyl-ester (**11k**) (0.211 g, 0.367 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 25 h yielding the title compound as light yellowish solid (0.163 g, 78%). *R<sub>f</sub>* 0.25 (PE/EtOAc 3 : 1); m.p. 38-40 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm) δ 7.49 (d, *J* = 8.0 Hz, 4H), 7.22 (d, *J* = 8.0 Hz, 4H), 4.04 (t, *J* = 6.7 Hz, 4H), 2.97 (t, *J* = 7.6 Hz, 4H), 2.62 (t, *J* = 7.6 Hz, 4H), 2.43 (s, 6H), 1.63 – 1.49 (m, 4H), 1.26 (s, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm) δ 184.7, 172.6, 144.0, 133.4, 128.8, 117.9, 90.6, 88.3, 64.9, 35.4, 32.8, 31.1, 29.4, 28.7, 26.0; IR ( $\tilde{v}$ ): 2958(m), 2920 (m), 2850 (m), 2202 (s), 1725 (vs), 1668 (vs), 1509 (w), 1413 (w), 1360 (m), 1281 (m), 1180 (m), 1152 (s), 983 (w), 834 (w), 641 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>36</sub>H<sub>42</sub>O<sub>6</sub> 570.2981; found 570.2983; UV-Vis (ACN): λ<sub>max</sub> (nm) = 276 (ε = 37243 M<sup>-1</sup>·cm<sup>-1</sup>).

**Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)-dodecane-1,12-diyl-ester (12l)**. Bis-(3-(4-(3-hydroxybut-1-inyl)phenyl)propionic acid)-dodecane-1,12-diyl-ester (**11l**) (1.08 g, 1.79 mmol) was subjected to the reaction conditions described in **GP3**. The reaction was finished after 23 h yielding the title compound as light yellowish solid (0.71 g, 66%). *R*<sub>f</sub> 0.32 (PE/EtOAc 3 : 1); m.p. 51-53 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.49 (d, *J* = 8.1 Hz, 4H), 7.22 (d, *J* = 8.1 Hz, 4H), 4.04 (t, *J* = 6.7 Hz, 4H), 2.97 (t, *J* = 7.6 Hz, 4H), 2.62 (t, *J* = 7.6 Hz, 4H), 2.43 (s, 6H), 1.67 – 1.46 (m, 4H), 1.25 (s, 16H).; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 184.7, 172.6, 144.0, 133.4, 128.8, 117.9, 90.6, 88.4, 64.9, 35.4, 32.8, 31.1, 29.6, 29.3, 28.7, 26.0; IR (õ): 2960 (m), 2921 (m), 2851 (m), 2203 (vs), 1725 (vs), 1668 (s), 1510 (w), 1426 (w), 1360 (m), 1282 (m), 1185 (s), 1151 (s), 1051 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>38</sub>H<sub>46</sub>O<sub>6</sub> 598.3294; found 598.3307; UV-Vis (ACN):  $\lambda_{max}$  (nm) = 276 (ε = 39223 M<sup>-1</sup>·cm<sup>-1</sup>).

Bis-(4-(3-oxobut-1-inyl)benzoic acid)-ethane-1,2-diyl-ester (12a) (0.132 g, 0.32 mmol) was subjected to the reaction conditions described in GP4. The starting material was recovered completely (0.131 g, 99%).

**14,15-Diacetyl-6,7-dihydro-5***H***,9***H***-2,17-(ethanediylidene)-10,13-etheno-4,8 benzodioxacyclopenta-decine-<b>3,9-dione (13b)**. Bis-(4-(3-oxobut-1-inyl)benzoic acid)-propane-1,3-diyl-ester (12b) (0.141 g, 0.34 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 70 min yielding the title compound as yellowish solid (0.047 mg, 33%). The starting material **12b** was recovered (45 mg, 32%).  $R_f$  0.39 (PE/EtOAc 1:1); m.p. 200-201 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.41 (s, 1H), 8.04 – 7.91 (m, 2H), 7.74 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 6.34 (s, 1H), 4.38 (t, J = 7.0 Hz, 2H), 4.28 – 4.16 (m), 2.79 (s, 3H), 2.60 (s, 3H), 2.11 – 1.97 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  204.1, 198.3, 169.6, 164.9, 141.0, 136.8, 136.5, 136.0, 135.1, 133.8, 132.5, 131.0, 130.1, 129.1, 127.7, 126.5, 66.9, 62.9, 32.5, 29.5, 27.1; IR ( $\tilde{0}$ ): 2925 (w), 1720 (vs), 1703 (vs), 1677 (s), 1383 (m), 1259 (s), 1237 (s), 1125 (m), 1100 (m), 1076 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>25</sub>H<sub>20</sub>O<sub>6</sub> 416.1260; found 416.1279.

#### 15,16-Diacetyl-5,6,7,8-tetrahydro-10H-2,18-(ethanediylidene)-11,14-etheno-4,9-benzodioxacyclohexa-

decine-3,10-dione (13c). Bis-(4-(3-oxobut-1-inyl)benzoic acid)-butane-1,4-diyl-ester (12c) (0.124 g, 0.27 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 60 min yielding the title compound as yellowish solid (0.058 g, 47%). The starting material 12c was recovered (0.029 g, 23%).  $R_f$  0.43 (PE/EtOAc 1:1); m.p. 216-217 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.42 (s, 1H), 8.07 (dd, J = 10.8, 4.6 Hz, 3H), 7.98 (d, J = 8.5 Hz, 1H), 7.41 (d, J = 8.2 Hz, 2H), 6.74 (s, 1H), 4.56 – 4.34 (m, 2H), 4.17 – 4.06 (m, 2H), 2.79 (s, 3H), 2.55 (s, 3H), 1.87 – 1.76 (m, 2H), 1.70 – 1.57 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  204.6, 198.5, 179.7, 168.7, 166.0, 141.4, 137.5, 136.9, 135.6, 134.2, 133.2, 132.2, 131.4, 130.7, 129.9, 129.7, 129.5, 127.2, 66.6, 66.0, 32.8, 29.5, 27.4, 26.3; IR ( $\tilde{v}$ ): 2965 (w), 1709 (vs), 1673 (s), 1382 (m), 1262 (s), 1239 (s), 1111 (m), 1092 (s),1016 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>26</sub>H<sub>22</sub>O<sub>6</sub> 430.1416; found 430.1424.

**17,18-Diacetyl-5,6,7,8,9,10-hexahydro-12***H***-2,20-(ethanediylidene)-13,16-etheno-4,11** benzodioxacyclooctadecine-3,12-dione (13d). Bis-(4-(3-oxobut-1-inyl)benzoic acid)-hexane-1,6-diyl-ester (12d) (0.106 g, 0.23 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 50 min yielding the title compound as yellowish solid (0.074 g, 70%).  $R_f$  0.50 (PE/EtOAc 1:1); m.p. 169-170 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.44 (s, 1H), 8.21 – 8.10 (m, 3H), 8.02 (d, J = 8.5 Hz, 1H), 7.46 (s, 1H), 7.40 (d, J = 8.1 Hz, 2H), 4.53 (t, J = 5.2 Hz, 2H), 4.24 – 4.11 (m, 2H), 2.79 (s, 3H), 2.41 (s, 3H), 1.87 – 1.76 (m, 2H), 1.59 – 1.46 (m, 4H), 1.40 – 1.29 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  204.7, 198.3, 166.5, 166.0, 140.7, 136.7, 134.7, 134.4, 134.0, 131.3, 131.1, 130.7, 129.6, 129.5, 129.0, 127.2, 66.7, 32.4, 30.4, 29.5, 29.1, 28.2, 27.2; IR ( $\tilde{0}$ ): 2930 (m), 2857 (w), 1715 (vs), 1681 (s), 1383 (m), 1266 (vs), 1101 (s), 1018 (m), 761 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>26</sub>O<sub>6</sub> 458.1729; found 458.1734.

#### 23,24-Diacetyl-5,6,7,8,9,10,11,12,13,14,15,16-dodecahydro-18H-2,26-(ethanediylidene)-19,22-etheno-4,17-

**benzodioxacyclotetracosine-3,18-dione (13e).** Bis-(4-(3-oxobut-1-inyl) benzoic acid)-dodecane-1,12-diyl-ester (0.130 g, 0.24 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 60 min yielding the title compound as yellowish solid (0.051 g, 39%).  $R_f$  0.52 (PE/EtOAc 1:1); m.p. 95-97 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.44 (s, 1H), 8.21 (dd, J = 12.6, 8.4 Hz, 4H), 8.08 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 8.0 Hz, 2H), 4.51 – 4.39 (m, 2H), 4.24 (t, J = 6.2 Hz, 2H), 2.76 (s, 3H), 2.08 (s, 3H), 1.56 (ddd, J = 20.9, 12.9, 6.7 Hz, 4H), 1.38 – 1.15 (m, 16H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  205.2,

198.5, 166.4, 166.1, 140.4, 140.0, 136.8, 135.2, 134.3, 133.1, 131.2, 131.1, 129.8, 129.6, 128.4, 127.5, 65.5, 65.5, 64.9, 31.9, 28.7, 28.6, 28.4, 28.1, 27.8, 27.5, 27.3, 27.0, 25.6, 24.9; IR ( $\tilde{\upsilon}$ ): 2926 (s), 2855 (m), 1716 (vs), 1684 (s), 1383 (m), 1266 (vs), 1177 (m), 1106 (m), 1019 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>34</sub>H<sub>38</sub>O<sub>6</sub> 542.2668; found 542.2640.

#### 15,16-Diacetyl-6,7-dihydro-2,18-(ethanediylidene)-11,14-etheno-5,8-benzodioxacyclohexadecine-

**4,9(3***H***,10***H***)-dione (13f). Bis-(2-(4-(3-oxobut-1-inyl)phenyl)acetic acid)-ethane-1,2-diyl-ester (12f) (0.121 g, 0.28 mmol) was subjected to the reaction conditions described in <b>GP4**. The reaction was finished after 50 min yielding the title compound as yellowish solid (0.063 g, 52%).  $R_f$  0.24 (PE/EtOAc 1:1); m.p. 219-220 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.39 (s, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.43 – 7.30 (m, 3H), 7.20 (d, J = 8.0 Hz, 2H), 6.83 (s, 1H), 4.41 – 4.24 (m, 2H), 4.16 – 4.01 (m, 2H), 3.80 (s, 2H), 3.66 (s, 2H), 2.75 (s, 3H), 2.37 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  205.4, 198.2, 170.8, 170.7, 138.1, 135.9, 135.6, 134.4, 132.6, 131.3, 131.1, 130.8, 129.6, 126.5, 129.4, 125.3, 64.3, 62.2, 42.0, 41.7, 32.5, 26.9; IR ( $\tilde{v}$ ): 2924 (w), 1728 (vs), 1699 (s), 1675 (s), 1427 (m), 1309 (m), 1260(m), 1232 (s), 1134 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>26</sub>H<sub>22</sub>O<sub>6</sub> 430.1416; found 430.1411.

#### 17,18-Diacetyl-6,7,8,9-tetrahydro-2,20-(ethanediylidene)-13,16-etheno-5,10-benzodioxacycloocta-decine-

**4,11(3***H***,12***H***)-dione (13g). Bis-(2-(4-(3-oxobut-1-inyl)phenyl)acetic acid)-butane-1,4-diyl-ester (12g) (0.137 g, 0.29 mmol) was subjected to the reaction conditions described in <b>GP4**. The reaction was finished after 40 min yielding the title compound as yellowish solid (0.072 g, 53%).  $R_f$  0.54 (PE/EtOAc 1:1); m.p. 186-187 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  8.40 (s, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.45 (dd, J = 12.4, 5.8 Hz, 4H), 7.26 (d, J = 8.1 Hz, 2H), 4.22 (t, J = 5.4 Hz, 2H), 3.95 (t, J = 7.0 Hz, 2H), 3.72 (s, 4H), 2.76 (s, 3H), 2.16 (s, 3H), 1.60 (dt, J = 10.0, 5.7 Hz, 2H), 1.51 – 1.37 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  205.8, 198.5, 171.1, 170.6, 139.5, 135.8, 135.1, 134.6, 133.0, 131.1, 129.8, 129.5, 129.4, 125.5, 65.0, 63.9, 42.4, 41.9, 32.1, 27.1, 25.5, 25.4; IR ( $\tilde{v}$ ): 2959 (w), 1728 (vs), 1699 (s), 1678 (s), 1426 (m), 1246 (s), 1155 (m), 1140 (m), 1020 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>26</sub>O<sub>6</sub> 458.1729; found 458.1732.

**19,20-Diacetyl-6,7,8,9,10,11-hexahydro-2,22-(ethanediylidene)-15,18-etheno-5,12-benzodioxacycloico-sine-4,13(3***H***,14***H***)-dione (13h). Bis-(2-(4-(3-oxobut-1-inyl)phenyl)acetic acid)-hexane-1,6-diyl-ester (12h) (0.119 g, 0.24 mmol) was subjected to the reaction conditions described in <b>GP4**. The reaction was finished after 40 min yielding the title compound as yellowish solid (0.084 g, 70%).  $R_f$  0.54 (PE/EtOAc 1:1); m.p. 149-150 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.38 (s, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.47 – 7.41 (m, 3H), 7.25 (d, J = 7.6 Hz, 2H), 4.18 (t, J = 5.4 Hz, 2H), 3.97 (t, J = 5.5 Hz, 2H), 3.67 (d, J = 7.3 Hz, 4H), 2.73 (s, 3H), 2.09 (s, 3H), 1.62 (dd, J = 11.7, 5.8 Hz, 2H), 1.52 – 1.42 (m, 2H), 1.41 – 1.33 (m, 2H), 1.31 – 1.22 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  205.9, 198.5, 171.4, 170.9, 139.6, 135.9, 135.8, 135.0, 134.6, 134.5, 133.1, 131.2, 131.1, 129.8, 129.5, 129.3, 127.1, 65.2, 64.2, 42.4, 32.0, 28.6, 28.3, 27.1, 25.6, 25.3; IR ( $\tilde{v}$ ): 2926 (m), 2858 (m), 1733 (s), 1715 (vs), 1698 (vs), 1682 (vs), 1431 (m), 1381 (m), 1301 (m), 1247 (s), 1133 (m), 983 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>30</sub>H<sub>30</sub>O<sub>6</sub> 486.2042; found 486.2059.

#### 17,18-Diacetyl-3,4,7,8,11,12-hexahydro-5H,10H-2,20-(ethanediylidene)-13,16-etheno-6,9-

**benzodioxacyclooctadecine-5,10-dione** (13i). Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)-ethane-1,2diyl-ester (12i) (0.115 g, 0.25 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 55 min yielding the title compound as yellowish solid (0.068 g, 59%). *R*<sub>f</sub> 0.40 (PE/EtOAc 1:1); m.p. 186-187 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm) δ 8.34 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.04 (s, 1H), 4.32 (dd, *J* = 5.1, 2.7 Hz, 2H), 4.05 – 3.96 (m, 2H), 3.19 – 3.10 (m, 2H), 3.05 (dd, *J* = 7.6, 4.4 Hz, 2H), 2.81 – 2.75 (m, 2H), 2.73 (s, 3H), 2.70 – 2.64 (m, 2H), 2.11 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm) δ 206.1, 198.6, 172.9, 172.3, 141.5, 140.3, 139.4, 136.0, 134.9, 134.5, 132.6, 131.0, 130.9, 130.6, 129.4, 129.2, 128.8, 122.9, 63.8, 62.1, 36.4, 32.0, 31.6, 29.9, 29.5, 27.1; IR ( $\tilde{v}$ ): 2921 (w), 1727 (vs), 1676 (s), 1434 (w), 1345 (w), 1294 (m), 1243 (m), 1196 (m), 1148 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>28</sub>H<sub>26</sub>O<sub>6</sub> 458.1729; found 458.1711.

#### 21,22-Diacetyl-3,4,7,8,9,10,11,12,15,16-decahydro-5H,14H-2,24-(ethanediylidene)-17,20-etheno-6,13-

**benzodioxacyclodocosine-5,14-dione (13j).** Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)-hexane-1,6-diylester (**12j**) (0.114 g, 0.22 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 45 min yielding the title compound as yellowish solid (0.084 g, 74%).  $R_f$  0.38 (PE/EtOAc 1:1); m.p. 146-147 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm) δ 8.35 (s, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.34 (d, J = 7.8 Hz, 2H), 7.26 (s, 1H), 7.19 (d, J = 7.9 Hz, 2H), 4.08 (t, J = 6.4 Hz, 2H), 4.01 (t, J = 5.5 Hz, 2H), 3.11 – 2.94 (m, 4H), 2.81 – 2.74 (m, 2H), 2.72 (s, 3H), 2.66 – 2.55 (m, 2H), 2.08 (s, 3H), 1.68 – 1.49 (m, 4H), 1.37 (d, J = 3.3 Hz, 4H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm) δ 206.3, 198.6, 173.0, 172.3, 141.7, 140.8, 139.5, 136.0, 134.7, 134.1, 132.8, 131.0, 130.9, 130.8, 129.7, 128.7, 128.2, 125.4, 64.7, 64.0, 35.4, 35.4, 31.9, 30.4, 28.2, 28.0, 27.1, 25.6, 25.0; IR ( $\tilde{v}$ ): 2923 (m), 2855 (m), 1717 (vs), 1698 (s), 1678 (vs), 1432 (m), 1388 (m), 1353 (m), 1289 (m), 1248 (s), 1150 (s), 1105 (m) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>32</sub>H<sub>34</sub>O<sub>6</sub> 514.2355; found 514.2365.

### 25,26-Diacetyl-3,4,7,8,9,10,11,12,13,14,15,16,19,20-tetradecahydro-5H,18H-2,28-(ethanediylidene)-21,24-

etheno-6,17-benzodioxacyclohexacosine-5,18-dione (13k). Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)decane-1,10-diyl-ester (12k) (0.093 g, 0.16 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 30 min yielding the title compound as yellowish solid (0.061 g, 66%).  $R_f$  0.6 (PE/EtOAc 1:1); m.p. 126-128 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  8.34 (s, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.34 – 7.27 (m, 3H), 7.20 (d, J = 7.9 Hz, 2H), 4.15 (t, J = 5.6 Hz, 2H), 4.01 (t, J = 6.2 Hz, 2H), 3.04 (dt, J = 11.1, 8.3 Hz, 4H), 2.74 (d, J = 11.5 Hz, 5H), 2.61 – 2.54 (m, 2H), 2.09 (s, 3H), 1.66 – 1.51 (m, 4H), 1.37 – 1.19 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  206.2, 198.6, 173.0, 172.6, 142.0, 140.8, 139.5, 135.8, 134.7, 134.1, 132.8, 131.1, 130.8, 129.7, 128.7, 128.4, 125.0, 65.0, 64.9, 36.2, 35.5, 31.9, 31.6, 30.9, 29.2, 28.8, 28.7, 28.5, 28.2, 27.12, 26.3, 25.8; IR ( $\tilde{v}$ ): 2924 (s), 2851 (m), 1731 (vs), 1699 (s), 1670 (s), 1621 (w), 1435 (m), 1350 (m), 1256 (m), 1229 (m), 1135 (m), 1104 (m), 1048 (w), 1022 (m), 965 (w), 929 (w), 836 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>36</sub>H<sub>42</sub>O<sub>6</sub> 570.2981; found 570.2968.

27,28-Diacetyl-3,4,7,8,9,10,11,12,13,14,15,16,17,18,21,22-hexadecahydro-5*H*,20*H*-2,30-(ethanediylidene)-23,26-etheno-6,19-benzodioxacyclooctacosine-5,20-dione (131). Bis-(3-(4-(3-oxobut-1-inyl)phenyl)propionic acid)-dodecane-1,12-diyl-ester (**12**I) (0.127 g, 0.21 mmol) was subjected to the reaction conditions described in **GP4**. The reaction was finished after 60 min yielding the title compound as yellowish solid (0.089 g, 70 %).  $R_f$  0.55 (PE/EtOAc 1:1); m.p. 108-110 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  8.35 (s, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.32 (d, J = 6.2 Hz, 3H), 7.21 (d, J = 7.9 Hz, 2H), 4.16 (t, J = 5.6 Hz, 2H), 4.02 (t, J = 6.5 Hz, 2H), 3.16 – 2.90 (m, 4H), 2.85 – 2.66 (m, 5H, CH<sub>2</sub>), 2.64 – 2.53 (m, 2H), 2.08 (s, 3H,), 1.63 (dd, J = 12.4, 6.2 Hz), 1.58 – 1.48 (m, 2H), 1.27 (s, 16H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$  206.3, 198.6, 173.0, 172.6, 142.1, 140.7, 139.6, 135.8, 134.6, 134.1, 132.9, 131.1, 131.0, 130.8, 129.8, 128.6, 128.4, 125.3, 64.9, 64.8, 36.1, 35.9, 31.9, 31.8, 31.0, 29.1, 29.0, 28.8, 28.6, 27.2, 25.9; IR ( $\tilde{v}$ ): 2924 (s), 2852 (m), 1728 (vs), 1671 (s), 1622 (w), 1435 (m), 1350 (m), 1299 (m), 1255 (s), 1140 (m), 1104 (w), 1022 (w) cm<sup>-1</sup>; HRMS (m/z) [M<sup>+</sup>] calcd for C<sub>38</sub>H<sub>46</sub>O<sub>6</sub> 598.3294; found 598.3288.

# **Supporting Information.**

Copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra. Details of quantum chemical calculations, X-ray structure analysis of **13i**. This information is available free of charge via the Internet at http://pubs.acs.org/.

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