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Synthesis of a *para*-quinone macrolactam related to geldanamycin by ring closing metathesis

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Abstract—Model studies conducted with the α,β,γ,δ-unsaturated 3-alkenyl-2,4,5-trimethoxyanilides **11** revealed that a ring closing metathesis (RCM) of these compounds is possible if the ansa chain contains more than 14 atoms. The (*Z*)-configurated products **12c**–**e** were obtained in good yields (77–87%) and with perfect simple diastereoselectivity. Since the oxidation of the 2,4,5-trimethoxyanilides led predominantly to undesired *ortho*-quinones such as **15** or to *para*-azaquinones such as **16** the macrocyclic 2,5-di-*iso*-propoxy-4-methoxyanilide **22** was prepared. The *iso*-propyl protecting groups could be selectively cleaved and the intermediate *para*-hydroquinone oxidized on air to the desired *para*-quinone **2** (86% yield). The compound shows some key features (macrolactam ring with the same ring size, α,β,γ,δ-unsaturated anilide, *para*-quinone) of geldanamycin.

1. Introduction

Geldanamycin (**1**)[1] is an antitumor agent with a medium 50% growth inhibition (GI_{50}) of 180 nM against 60 tumor cell lines tested by the national cancer institute (NCI). The GI_{50} against the most sensitive cell lines was found to be as low as 13 nM.[2] Its antitumor activity is attributed to a binding to the heat shock protein 90 (Hsp 90)[3,4] although other modes of action have been discussed.[5] Structures of Hsp 90–geldanamycin complexes have been elucidated and the most important binding motifs have been identified.[6] Geldanamycin binds to the N-terminal ATP/ADP-binding domain of Hsp 90 and inhibits the ATPase activity which is essential for the function of the enzyme. Based on its molecular structure, geldanamycin can be classified as an ansamycin.[7] It differs from other ansamycins (e.g., herbimycin A) by the additional methoxy substituent at the quinone ring (C-17) and by the substitution in the ansa chain. Early synthetic efforts by Schill et al.[8] established the possibility to construct the macrocycle by C–C bond (C-15/C-16) formation at a suitable arene and subsequent macrolactamization. After the discovery of its antitumor activity geldanamycin was the target of many modification studies from which more active bioavailable compounds derived.[9] The first total synthesis of geldanamycin was recently accomplished by Andrus and co-workers.[10]

We envisioned an access to the geldanamycin macrocycle by ring closing metathesis (RCM)[11] between carbon atoms C-4 and C-5. Preliminary studies revealed that this strategy is feasible.[12] A first target, which contains the same *para*-quinone chromophore, the (*E*,*Z*)-α,β,γ,δ-unsaturated anilide, and an ansa chain identical in chain length to geldanamycin, is compound **2** the synthesis of which was undertaken (Fig. 1).

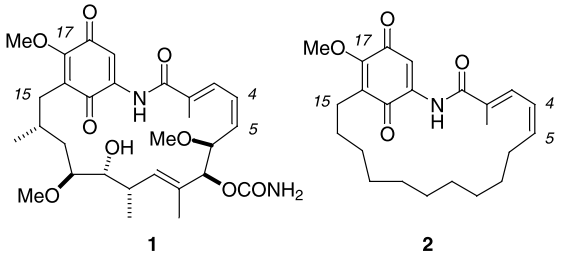

Figure 1. Geldanamycin (**1**) and the *para*-quinone macrolactam **2**.

In this account, we provide full details on the synthesis of appropriate precursors which allowed us to study the RCM for the preparation of macrocycles with different ring sizes. We discuss the oxidation of the initially studied 2,4,5-trimethoxyanilides and report on the structure elucidation of the oxidation products. The mechanism of the oxidation is briefly discussed. Finally, the synthesis of compound **2** is described starting from 1,4-di-*iso*-propoxy-2-methoxybenzene.

Keywords: Ring closing metathesis; Ansa chain; Geldanamycin.
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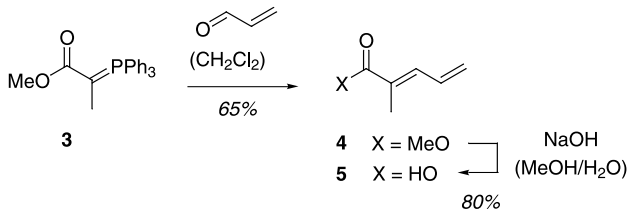


Scheme 1. Preparation of 2-methyl-2,4-pentadienoic acid (**5**).

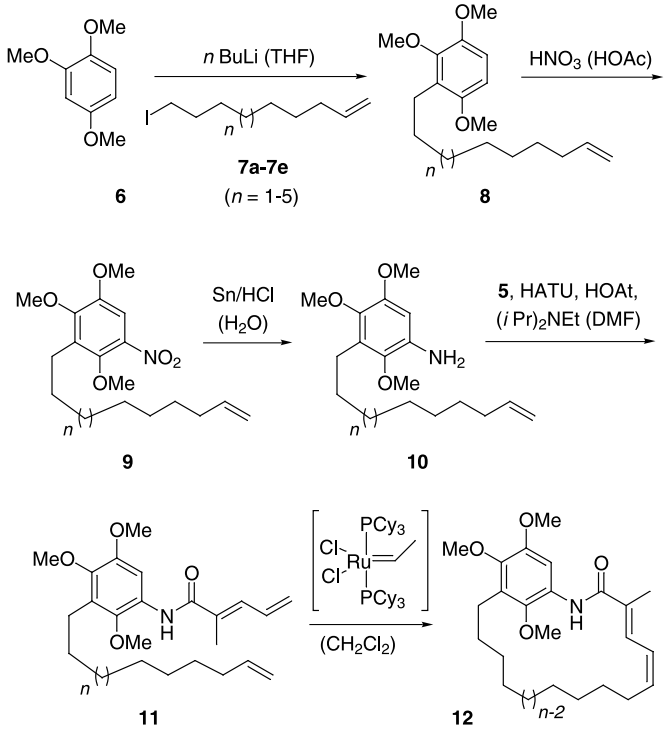
2. Ring closing metathesis

Studies on the RCM commenced with attempts to synthesize suitable 3-ω-alkenyl-2,4,5-trimethoxyanilides of 2-methyl-2,4-pentadienoic acid (**5**). The acid itself was prepared (Scheme 1)[13] from Wittig reagent **3** and acrolein via its methyl ester which was subsequently saponified to the free acid.

The lithiation of 1,2,4-trimethoxybenzene (**6**) with *n*-butyl lithium (1.1 equiv) was optimized by quenching the lithiated intermediate with iodine and by subsequent GLC analysis. The reaction proceeded slowly at −78 °C and at 0 °C in THF as the solvent (<50% conversion after 1 h). At ambient temperature the conversion was rapid and lithiation was complete after less than an hour. Prolonged stirring at room temperature led to decomposition.

Based on the preliminary experiments the lithiation of **6** was conducted by adding *n*-butyl lithium to the arene and keeping the reaction mixture for 45 min at room temperature. After cooling to 0 °C, the corresponding alkyl halide was added. Although Schill et al. had used bromoalkanes in their alkylation experiments[8] we found the iodides superior allowing a smoother and cleaner conversion than the corresponding bromides and—more importantly—avoiding the use of an excess of the halide. The ω-alkenyliodides **7** employed as electrophiles in the alkylation step are literature known and were prepared according to reported procedures.[14–18] The alkylation reaction proceeded nicely and yielded the ω-alkenylarenes **8** (Scheme 2). Regioselective nitration using nitric acid in acetic acid[8] as the solvent furnished the nitro compounds **9** in very good yields. The reduction to the anilines **10** was accomplished by treatment of the nitroarenes with tin in aqueous hydrochloric acid at 60 °C (Table 1).[19]

The acylation of anilines **10** was initially projected with the chloride of acid **5** or via a mixed anhydride. Despite several attempts with $SOCl_2$ or $(COCl)_2$ as reagents, the chloride could not be obtained from **5**. Contrary to that, sorboyl chloride,[20] for example, was readily accessible from sorboic acid using common conditions ($SOCl_2$ in refluxing benzene). The acylation of aniline **10c** with sorboyl chloride was facile but it was not further optimized (56% yield). Upon attempted activation of acid **5** with pivaloyl chloride and subsequent reaction with aniline **10c** the sole product obtained was the corresponding *N*-pivaloyl aniline (63% yield). Experiments to use an in situ activation with common peptide coupling reagents commenced with dicyclohexyl carbodiimide (DCC). Minor product formation (27% yield) was observed when aniline **10c** was treated with DCC and 1-hydroxybenzotriazole (HOBt) in CH_2Cl_2 at ambient temperature for three days. An improvement in yield and in the rate of conversion was achieved upon addition of bases and upon changing the solvent to DMF. The best result was recorded with di-*iso*-propylethylamine (Hünig base) in DMF (36% yield). Further improvements were due to a modification of the additive. Both 1-hydroxy-7-azabenzotriazole (HOAt) and 3-hydroxy-4-oxo-3,4-dihydro-1,2,3-benzotriazole (HOOBt)



Scheme 2. Preparation of the RCM precursors **11** and RCM to products **12** (for yields and further comments see Table 1).

Table 1. Yields of isolated products for the five individual steps in the conversion of arene **6** to the RCM products **12** (cf. Scheme 2)

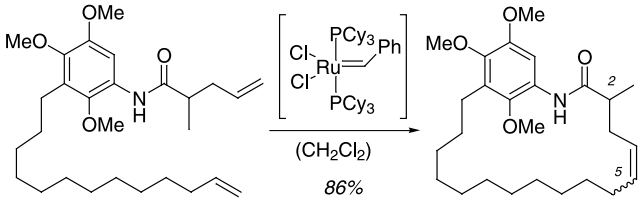
n	Iodide	**8** (%)	**9** (%)	**10** (%)	**11** (%)	**12** (%)
1	**7a**	59	73	82	72	—[a]
2	**7b**	76	95	77	58	—[b]
3	**7c**	76	98	84	66	66[c]
4	**7d**	73	95	79	68	77
5	**7e**	73	94	83	63	87

[a] Only starting material (50%) and dimer/oligomer (25%) were isolated.
[b] Only starting material (84%) and dimer/oligomer (10%) were isolated.
[c] Starting material (14%) was isolated. The yield based on recovered starting material is 77%.

gave better yields than HOBt under otherwise identical conditions (up to 56% yield). Still, the reaction was unsatisfactory being not fully reproducible and sluggish at times. A significant breakthrough was achieved by substituting the activation reagent DCC. *O*-(7-Azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HATU) in the presence of HOAt[21] turned out to be the reagent combination of choice which guaranteed significantly better conversions in a generally applicable reaction. The anilides **11** were so obtained in 58–72% yield.

Details of the RCM have been discussed already in our preliminary paper.[12] Key issues are a low concentration of the substrate (0.5 mM) in CH_2Cl_2 as the solvent, the use of conventional Grubbs I catalyst (10 mol%) with an ethylidene or benzylidene ligand at the ruthenium center, and the alkenyl chain length as the determining factor for the success of the RCM. Indeed, ring sizes of 18–20 (compounds **12c**–**e**) were readily accessible whereas the formation of the 16- or 17-membered ansa compounds **12a** and **12b** could not be achieved. Apparently, the nonenyl and docenyl group do under the given restriction by the α,β,γ,δ-unsaturated anilide not reach the terminal double bond of the diene and an ansa chain with less than 15 atoms does not form. The double bonds which are in the course of the metathesis reaction established between carbon atom C-4 and C-5 of the products **12c**–**e** are uniformly configurated. The coupling constant between the protons H-4 and H-5 in all compounds **12c**–**e** is around $J \cong 10$ Hz. Strong NOE contacts were observed for these protons in compound **12e** supporting the assignment of the double bond configuration as (*Z*). Further ^{1}H NMR NOESY data which are in line with a C-4/C-5 (*Z*)-configuration were obtained from oxidation products of compounds **12c** and **12e** (vide infra).

If the conformational restriction exerted by the C-2/C-3 double bond in the 3-alkenyl-2,4,5-trimethoxyanilide is removed the RCM is not stereoselective any more. When the anilide **13** of 2-methyl-2-pentenoic acid was employed as a substrate the 20-membered ansa compound **14** was obtained as a mixture of (*E*)- and (*Z*)-isomers (Scheme 3). Since the isomers were not separable, configurations could not be assigned to the individual isomers.



13 **14** (d.r. = 66/34)

Scheme 3. RCM of ω-alkenylanilide **13** to a mixture of diastereomeric lactams **14**.

3. Oxidation reactions

Although there is literature precedence for the oxidation of 1,2,4-trimethoxybenzenes to 2-methoxy-*para*-benzoquinones,[19,22] ansa compounds related to **12c**–**e** had earlier been shown to give the 4-methoxy-*ortho*-benzoquinones upon oxidation with concentrated nitric acid in acetic acid solution.[8] This result was corroborated in recent studies by Andrus et al.[10,23] Upon oxidation of an immediate geldanamycin precursor with 70% nitric acid they obtained in 55% yield a 10:1 mixture of the undesired *ortho*- and the desired *para*-geldanamycin. Oxidation with other reagents (Ag_2O or MnO_2 impregnated with nitric acid) led to the formation of a *para*-azaquinone. Subsequent model studies showed that conformationally unrestricted 3-alkyl-2,4,5-trimethoxyanilides yielded predominantly *ortho*-quinones upon oxidation.[23]

Our oxidation experiments were conducted with ceric ammonium nitrate (CAN) and pyridine-2,6-dicarboxylic acid *N*-oxide[24] in acetonitrile/water at 0 °C. They confirmed that an oxidation of either precursor **12c**–**e** to a *para*-quinone was not possible. The reactions with substrates **12c** and **12e** led to well defined oxidation products in moderate yields. Compound **12c** gave *ortho*-quinone **15** (30% yield) and compound **12e** furnished *para*-azaquinone **16** (64% yield). ^{1}H NMR NOESY studies (Fig. 2) revealed that the 18-membered ansa compound **15** is perfectly planar in the region C-16 (arene) to C-6 while the 20-membered ring is somewhat twisted. This fact is indicated by weak NOE contacts between H-3 and H-4 as well as between H-19 and

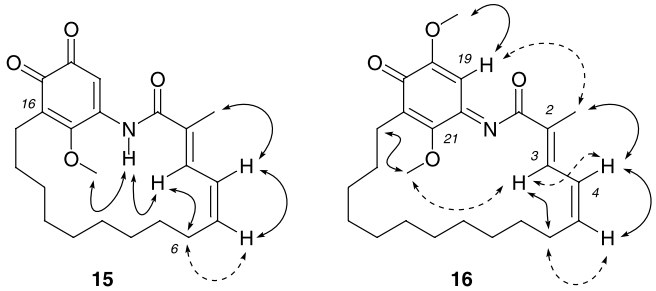


Figure 2. Significant NOE contacts (- - - weak, — strong) recorded in the oxidation products **15** and **16** obtained from anilides **12c** and **12e** by CAN oxidation.

the methyl group at C-2. If the precursor **12e** exhibits a similar conformation the NH proton may be removed by a base in an intermediate radical cation (or cation) which in turn is formed by single electron oxidation. In our opinion, the removal of the NH proton, which competes with the hydroxy-de-methoxylation[24a,25] at carbon atoms C-18 or C-17, governs the chemoselectivity of the oxidation process. In the twisted compound **12e** the deprotonation is facile and accounts for the formation of the azaquinone, in the flat compound **12c** and in other acyclic systems the hydroxy-de-methoxylation is faster and leads to the *ortho*-quinone. The hydroxy-de-methoxylation at the less accessible carbon atom C-21 is slow possibly due to steric reasons.

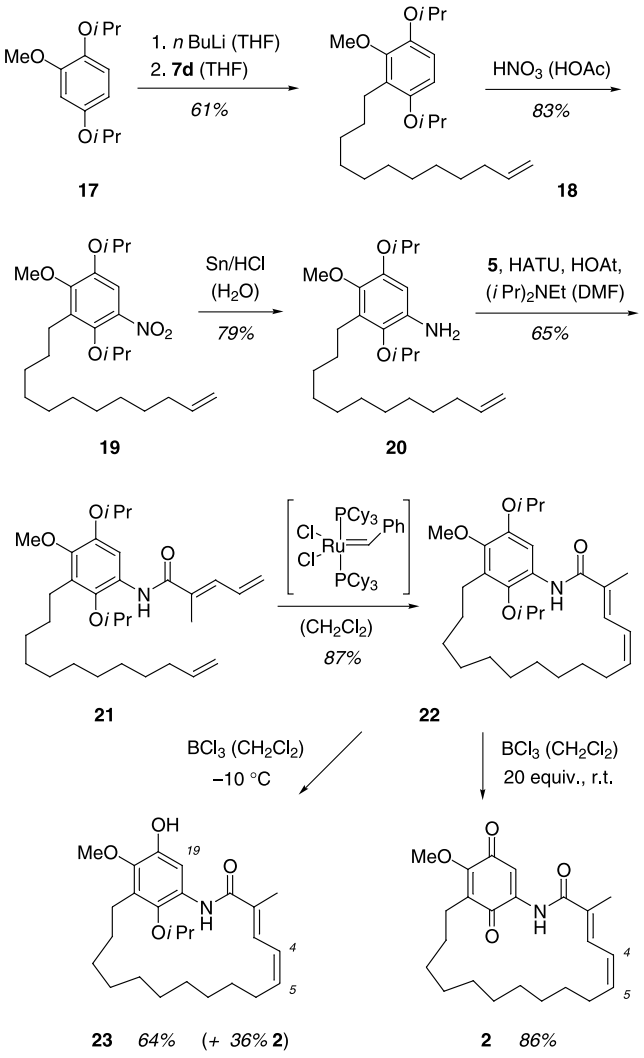
Selective demethylation reactions by strong nucleophiles (LiI) or Lewis acids (BBr_3) were attempted with model compounds but led only to degradation. BCl_3 facilitated a demethylation but the yields and the regioselectivity were not satisfactory. Consequently, we looked for alternative protection strategies for the 1,4-hydroquinone. A minimal change in reactivity and a maximum coincidence with the previous results was expected upon replacing the methyl protecting groups by other alkyl groups. The *iso*-propyl group was considered to be a reasonable choice and work along these line continued.

4. Synthesis of *para*-quinone 2

Model studies proved that 3-alkyl-2,5-di-*iso*-propoxy-4-methoxyanilides are readily deprotected with BCl_3 at -10 °C in CH_2Cl_2 and yield upon work-up without addition of an oxidizing agent the corresponding *para*-quinones.

Based on these results the readily available 1,4-di-*iso*-propoxy-2-methoxybenzene (**17**)[26] was lithiated in 3-position with *n*-butyl lithium and subsequently alkylated with iodide **7d** (Scheme 4). A side product was found (4% yield) which arose from deprotonation at the 6-position. All further reactions starting from arene **18** were conducted in analogy to our previous work. Selective nitration led to nitroarene **19** which was reduced to aniline **20**. After amide bond formation the anilide underwent the RCM smoothly and gave the desired lactam **22** in excellent yield. The deprotection occurred less readily than in the test system. At -10 °C there was a monodeprotection to phenol **23**. After addition of an excess of BCl_3 and by warming to room temperature the deprotection could be driven to completion and the desired compound **2** was isolated as the sole reaction product. The total yield in which *para*-quinone **2** was obtained from arene **17** was 19%.

Both products **23** and **2** were intensively studied by ^1H NMR NOESY experiments. The phenol OH proton in compound **23** showed a strong NOE to H-19 which proves the regioselectivity of the deprotection. The (*Z*)-configuration of the double bond formed in the RCM step was in both products unequivocally proven by the relatively small coupling constants and by strong NOE contacts between H-4 and H-5. The other NOEs in the area C-1 to C-6 were similar to the signals recorded for compound **15** supporting a s-*trans* amide bond (C-1/NH).



Scheme 4. Synthesis of the phenol **23** and the *para*-quinone **2** from 1,4-di-*iso*-propoxy-2-methoxybenzene (**17**).

In conclusion, the study has shown that the construction of *para*-quinones related to geldanamycin is feasible based on a RCM strategy. The *iso*-propyl group was used as a protecting group for the latent *para*-quinone moiety in the corresponding hydroquinone di-*iso*-propyl ether. The amide bond formation between the aniline nitrogen atom and carbon atom C-1 of 2-methyl-2,4-pentadienoic acid was achieved by use of the reagent combination HATU/HOAt. The synthesis of compound **2** was achieved in an overall yield of 19% starting from 1,4-di-*iso*-propoxy-2-methoxybenzene (**17**). There are of course many further challenges ahead if this strategy is to be applied to a successful synthesis to geldanamycin. The selective introduction of the nitro group into a more highly functionalized precursor, the generation of the appropriate stereogenic centers and the protection of the hydroxy groups as well as the carbamate formation before or after *para*-quinone deprotection are among the most important aspects to be addressed. Work along these lines is currently pursued in our laboratory.

5. Experimental

5.1. General

All reactions involving water-sensitive chemicals were carried out in flame-dried glassware with magnetic stirring under Ar. Tetrahydrofuran and diethyl ether were distilled from sodium immediately prior to use. *N*,*N*-Di-*iso*-propylethylamine (DIPEA) and dichloromethane were distilled from calcium hydride. All other chemicals were either commercially available or prepared according to the cited references. TLC: Merck glass sheets (0.25 mm silica gel 60, F_{254}), eluent given in brackets. Detection by UV or coloration with cerium ammonium molybdate (CAM). Optical rotation: Perkin–Elmer 241 MC. NMR: Bruker AC-250, AV-360, AV-500. ^1H and ^{13}C NMR spectra were recorded at ambient temperature. Chemical shifts are reported relative to tetramethylsilane as internal standard. Apparent multiplets which occur as a result of the accidental equality of coupling constants of magnetically non-equivalent protons are marked as virtual (v.). The multiplicities of the ^{13}C NMR signals were determined by DEPT experiments. IR: Perkin–Elmer 1600 FT-IR. MS: Finnigan MAT 8200 (EI). Elemental Analysis: Elementar Vario EL. Flash chromatography was performed on silica gel 60 (Merck, 230–400 mesh) (ca. 50 g for 1 g of material to be separated) with the indicated eluent. Common solvents for chromatography [pentane (P), ethyl acetate (EA), dichloromethane (DCM)] were distilled prior to use.

Procedure A. Alkylation of 1,2,4-trimethoxybenzene. To a solution of 1,2,4-trimethoxybenzene in THF (1 mL/mmol), *n*-butyl lithium (2.5 M in hexane, 1.1 equiv) was slowly added at rt. After 10 min, a white precipitate appeared indicating the formation of the lithiated compound. The mixture was allowed to stir for 30 to 45 min at room temperature and was subsequently cooled to 0 °C. The iodide (1.05–1.1 equiv) was added at this temperature. The mixture was stirred for 14 h at rt. Then, diethyl ether (3 mL/mmol) and water (3 mL/mmol) were added. The aqueous layer was extracted twice with diethyl ether (2×5 mL/mmol). The combined organic layers were washed once with brine (5 mL/mmol), dried (Na_2SO_4) and concentrated under reduced pressure. The product was purified by flash chromatography (P/EA).

Procedure B. General procedure for the nitration of arenas. To a solution of the arene in acetic acid (2.8 mL/mmol), concentrated nitric acid (70% w/w, 0.58 mL/mmol) in acetic acid (1.8 mL/mmol) was slowly added at room temperature. After 5 min the solution takes an orange color, which turns after a few minutes into a yellow color. The mixture was stirred for 60 min at rt. Water (5 mL/mmol) and diethyl ether (5 mL/mmol) were added. $NaHCO_3$ was carefully added and the solution was stirred for 30 min. The layers were separated and the aqueous layer was extracted three times with diethyl ether (3×5 mL/mmol). The combined organic layers were washed once with a saturated solution of $NaHCO_3$ in water (5 mL/mmol), brine (5 mL/mmol), dried (Na_2SO_4) and concentrated under reduced pressure. The product was purified by flash chromatography (P/EA).

Procedure C. General procedure for the reduction of nitroarenes. To the nitroarene and tin powder (8 equiv) under argon atmosphere, concentrated hydrochloric acid (8 equiv, 2.8 mL/mmol) was added. The mixture was heated for 2 h at 60 °C and cooled to 0 °C. The reaction was then quenched by addition of aqueous NaOH (10% w/w). The pH was adjusted to 10. The aqueous layer was extracted three times with DCM (3×5–10 mL/mmol). The combined organic layers were washed once with brine (5–10 mL/mmol), dried (Na_2SO_4) and concentrated in vacuum. The product was purified by flash chromatography (P/EA).

Procedure D. General procedure for the peptide bond formation with HATU/HOAt. To 2-methyl-2,4-pentadienoic acid dissolved in DMF (1.8 mL/mmol) and cooled to 0 °C, DIPEA (2.5 equiv) was added slowly. After being stirred 30 min at this temperature, HOAt (1.0 equiv) dissolved in DMF (0.6 mL/mmol) was added. The mixture was stirred for 30 min at 0 °C and HATU (1.0 equiv) dissolved in DMF (0.6 mL/mmol) was added. After being stirred for 15 min at 0 °C and 15 min at rt, the corresponding aniline (1.0 equiv) dissolved in DMF (3.0 mL/mmol) was added. The mixture was stirred for 48 h at rt. DCM (50 mL/mmol) and water (50 mL/mmol) were added. The aqueous layer was extracted twice with DCM (2×50 mL/mmol). The combined organic layers were washed with a saturated aqueous $NaHCO_3$ solution (5 mL/mmol), brine (5 mL/mmol), dried (Na_2SO_4) and concentrated in vacuo. The product was purified by flash chromatography (P/EA).

Procedure E. General procedure for the macrocyclization. To refluxing CH_2Cl_2 (1.9 L/mmol), a solution of catalyst (0.10 equiv) in CH_2Cl_2 (20 mL/mmol) was added under argon atmosphere. After 5 min a solution of the anilide in CH_2Cl_2 (80.0 mL/mmol) was added. The solution was refluxed until the reaction was complete (TLC). The solvent was removed in vacuo and the product was purified by flash chromatography (P/EA).

Procedure F. Oxidation with CAN. To a solution of the anilide and pyridine-2,6-dicarboxylic acid *N*-oxide (2.5 equiv) in acetonitrile (5.0 mL/mmol) and water (1.5 mL/mmol) cooled to 0 °C, a solution of CAN (2.5 equiv) in acetonitrile (2.5 mL/mmol) and water (2.5 mL/mmol) was slowly added. The resulting solution was stirred at 0 °C until no more starting material remained according to TLC. The mixture was dissolved in water (45 mL/mmol) and extracted three times with DCM (3×75 mL/mmol). The combined organic layers were washed with brine (5 mL/mmol), dried (Na_2SO_4) and concentrated.

Procedure G. Alkylation of 1,4-di-iso-propoxy-2-methoxybenzene. To a solution of 1,4-di-*iso*-propoxy-2-methoxybenzene in THF (1 mL/mmol), *n*-butyl lithium (2.5 M in hexane, 1.1 equiv) was slowly added at rt. The mixture was stirred 30 to 45 min at rt, and was cooled to 0 °C. The iodide (1.05 equiv) was added at this temperature. The mixture was stirred for 14 h at rt. Then, diethyl ether (5 mL/mmol) and water (5 mL/mmol) were added. The aqueous layer was extracted twice with diethyl ether (2×4 mL/mmol). The combined organic layers were washed once with brine (5 mL/mmol), dried (Na_2SO_4) and concentrated under

reduced pressure. The product was purified by chromatography (P/EA).

5.1.1. 1,2,4-Trimethoxy-3-non-8-enylbenzene (8a). Procedure A was performed with 9-iodonon-1-ene (**7a**)[14] (3.32 g, 13.2 mmol) and 1,2,4-trimethoxybenzene (2.02 g, 12.2 mmol). After flash chromatography (P/EA 90/10), the product was obtained (2.09 g, 7.16 mmol, 59%) as a colorless oil. TLC: R_f=0.77 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3075 (w, =CH_2), 2927 (v. s, CH_2), 2854 (s, CH_2), 1639 (m, C=C), 1593 (m, C_{ar}=C_{ar}), 1487 (m, CH_2), 1255 (s, COC), 1224 (m), 1162 (s, COC), 1092 (s, COC), 1024 (m); 909 (m, RCH=CH_2), 789 (w, CH), 718 (w, CH_{ar}); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=6.68 (d, ^3J=8.9 Hz, 1H, C_{ar}H), 6.53 (d, ^3J=8.9 Hz, 1H, C_{ar}H), 5.79 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 5.00–4.97 (m, 1H, H_{trans}CH=CHR), 4.94–4.91 (m, 1H, H_{cis}CH=CHR), 3.82 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.63 (v. t, $^3J\cong$7.7 Hz, 2H, CH_2Ar), 2.08 (v. q, $^3J\cong$6.6 Hz, 2H, CH_2=CHCH_2), 1.53–1.34 (m, 10H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=152.34 (C_{ar}OMe), 148.05 (C_{ar}OMe), 147.14 (C_{ar}OMe), 139.18 (HR*C*=CH_2), 126.07 ($C_{ar}CH_2$), 114.2 (HRC=*C*H_2), 109.6 (C_{ar}H), 105.3 (C_{ar}H), 60.7 (OCH_3), 56.1 (OCH_3), 55.8 (OCH_3), 33.8 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 23.9 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 292 (100) [M^+], 277 (5), 181 (46), 166 (30), 151 (8), 123 (6), 91 (8), 41 (5). Anal. $C_{18}H_{28}O_3$ (292.4): calcd C, 73.93; H, 9.65; found C, 73.95; H: 9.76.

5.1.2. 2-Dec-9-enyl-1,3,4-trimethoxybenzene (8b). Procedure A was performed with 10-iododec-1-ene (**7b**)[15] (2.70 g, 10.2 mmol) and 1,2,4-trimethoxybenzene (1.56 g, 9.30 mmol). After flash chromatography (P/EA 90/10), the product was obtained (2.15 g, 7.03 mmol, 76%) as a colorless oil. TLC: R_f=0.65 (P/EA 9/1) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3075 (w, =CH_2), 2927 (v. s, CH_2), 2854 (s, CH_2), 1639 (m, C=C), 1593 (m, C_{ar}=C_{ar}), 1487 (m, CH_2), 1255 (s, COC), 1224 (m), 1162 (s, COC), 1092 (s, COC), 1024 (m); 909 (m, RCH=CH_2), 789 (w, CH), 718 (w, CH_{ar}); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=6.70 (d, ^3J=8.9 Hz, 1H, C_{ar}H), 6.54 (d, ^3J=8.9 Hz, 1H, C_{ar}H), 5.82 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 5.00–4.95 (m, 1H, H_{trans}CH=CHR), 4.94–4.91 (m, 1H, H_{cis}CH=CHR), 3.83 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 2.64 (v. t, $^3J\cong$7.7 Hz, 2H, CH_2Ar), 2.04 (v. q, $^3J\cong$6.8 Hz, 2H, CH_2=CHCH_2), 1.53–1.31 (m, 12H, CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm)=152.5 (C_{ar}OMe), 148.2 (C_{ar}OMe), 147.3 (C_{ar}OMe), 139.4 (HR*C*=CH_2), 126.4 ($C_{ar}CH_2$), 114.4 (HRC=*C*H_2), 109.7 (C_{ar}H), 105.5 (C_{ar}H), 60.9 (OCH_3), 56.3 (OCH_3), 56.0 (OCH_3), 33.9 (CH_2), 30.1 (CH_2), 30.0 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 24.1 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 306 (100) [M^+], 181 (41), 166 (41), 151 (5); HRMS: *m*/*z* calcd for $C_{19}H_{30}O_3$: 306.2195; found 306.2191.

5.1.3. 1,2,4-Trimethoxy-3-undec-10-enylbenzene (8c). Procedure A was performed with 11-iodoundec-1-ene (**7c**)[16] (1.80 g, 6.42 mmol) and 1,2,4-trimethoxybenzene (1.01 g, 6.00 mmol). After flash chromatography (P/EA 95/05), the product was obtained (1.46 g, 4.56 mmol, 76%) as a colorless oil. TLC: R_f=0.46 (P/EA 95/05) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3075 (w, =CH_2), 2927 (v. s, CH_2), 2854 (s, CH_2), 1639 (m, C=C), 1593 (m, C_{ar}=C_{ar}), 1487 (m, CH_2), 1255 (s, COC), 1224 (m), 1162 (s, COC), 1092 (s, COC), 1024 (m); 909 (m, RCH=CH_2), 789 (w, CH), 718 (w, CH_{ar}); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm)=6.68 (d, ^3J=8.9 Hz, 1H, C_{ar}H), 6.53 (d, ^3J=8.9 Hz, 1H, C_{ar}H), 5.78 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.99–4.94 (m, 1H, H_{trans}CH=CHR), 4.93–4.90 (m, 1H, H_{cis}CH=CHR), 3.81 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.61 (v. t, $^3J\cong$7.6 Hz, 2H, CH_2Ar), 2.04 (v. q, $^3J\cong$6.7 Hz, 2H, CH_2=CHCH_2), 1.51–1.27 (m, 14H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=152.5 (C_{ar}OMe), 148.2 (C_{ar}OMe), 147.3 (C_{ar}OMe), 139.4 (HR*C*=CH_2), 126.4 ($C_{ar}CH_2$), 114.4 (HRC=*C*H_2), 109.7 (C_{ar}H), 105.5 (C_{ar}H), 60.9 (OCH_3), 56.3 (OCH_3), 56.0 (OCH_3), 33.9 (CH_2), 30.1 (CH_2), 30.0 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 24.1 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 320 (100) [M^+], 181 (31), 166 (33). Anal. $C_{20}H_{32}O_3$ (320.5): calcd C, 74.96; H, 10.06; found C, 75.03; H: 10.15.

5.1.4. 2-Dodec-11-enyl-1,3,4-trimethoxybenzene (8d). Procedure A was performed with 12-iodododec-1-ene (**7d**)[17] (956 mg, 3.26 mmol) and 1,2,4-trimethoxybenzene (538 mg, 3.20 mmol). After flash chromatography (P/EA 97/03), the product was obtained (778 mg, 2.33 mmol, 73%) as a colorless oil. TLC: R_f=0.81 (P/EA 9/1) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3075 (w, =CH_2), 2927 (v. s, CH_2), 2854 (s, CH_2), 1639 (m, C=C), 1593 (m, C_{ar}=C_{ar}), 1487 (m, CH_2), 1255 (s, COC), 1224 (m), 1162 (s, COC), 1092 (s, COC), 1024 (m); 909 (m, RCH=CH_2), 789 (w, CH), 718 (w, CH_{ar}); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=6.69 (d, ^3J=8.8 Hz, 1H, C_{ar}H), 6.54 (d, ^3J=8.8 Hz, 1H, C_{ar}H), 5.81 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 5.02–4.97 (m, 1H, H_{trans}CH=CHR), 4.95–4.92 (m, 1H, H_{cis}CH=CHR), 3.83 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.65 (v. t, $^3J\cong$7.7 Hz, 2H, CH_2Ar), 2.05 (v. q, $^3J\cong$7.0 Hz, 2H, CH_2=CHCH_2), 1.56–1.30 (m, 16H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=152.5 (C_{ar}OMe), 148.2 (C_{ar}OMe), 147.3 (C_{ar}OMe), 139.4 (HR*C*=CH_2), 126.3 ($C_{ar}CH_2$), 114.2 (HRC=*C*H_2), 109.7 (C_{ar}H), 105.4 (C_{ar}H), 60.8 (OCH_3), 56.3 (OCH_3), 55.9 (OCH_3), 33.9 (CH_2), 30.1 (CH_2), 30.0 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 24.1 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 334 (100) [M^+], 181 (59), 166 (47), 151 (8), 121(6), 91 (10), 55 (5). Anal. $C_{21}H_{34}O_3$ (334.5): calcd C, 75.41; H, 10.25; found C, 75.63; H: 10.34.

5.1.5. 1,2,4-Trimethoxy-3-tridec-12-enylbenzene (8e). Procedure A was performed with 13-iodotridec-1-ene (**7e**)[18] (765 mg, 2.48 mmol) and 1,2,4-trimethoxybenzene (378 mg, 2.25 mmol). After flash chromatography (P → P/EA 95/05), the product was obtained (570 mg, 1.64 mmol, 73%) as a colorless oil. TLC: R_f=0.40 (P/EA 95/05) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3075 (w, =CH_2), 2927 (v. s, CH_2), 2854 (s, CH_2), 1639 (m, C=C), 1593 (m, C_{ar}=C_{ar}), 1487 (m, CH_2), 1255 (s, COC), 1224 (m), 1162 (s, COC), 1092 (s, COC), 1024 (m); 909 (m, RCH=CH_2), 789 (w, CH), 718 (w, CH_{ar}); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=6.67 (d, ^3J=8.8 Hz, 1H, C_{ar}H), 6.52 (d, ^3J=8.8 Hz, 1H, C_{ar}H), 5.80 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.98–4.93 (m, 1H,

H_{trans}CH=CHR), 4.92–4.89 (m, 1H, H_{cis}CH=CHR), 3.81 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.62 (v. t, $^3J\cong7.7$ Hz, 2H, CH_2Ar), 2.04 (v. q, $^3J\cong7.0$ Hz, 2H, CH_2=CHCH_2), 1.56–1.23 (m, 18H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=152.5 (C_{ar}OMe), 148.2 (C_{ar}OMe), 147.3 (C_{ar}OMe), 139.4 (HR*C*=CH_2), 126.3 ($C_{ar}CH_2$), 114.2 (HRC=*C*H_2), 109.7 (C_{ar}H), 105.4 (C_{ar}H), 60.8 (OCH_3), 56.3 (OCH_3), 55.9 (OCH_3), 33.9 (CH_2), 30.1 (CH_2), 30.1 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 24.1 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 348 (100) [M^+], 181 (32), 166 (25), 121 (3). Anal. $C_{22}H_{36}O_3$ (348.5): calcd C, 75.82; H, 10.41; found C, 75.80; H: 10.30.

5.1.6. 1,2,4-Trimethoxy-5-nitro-3-non-8-enylbenzene (9a). Procedure B was performed with 1,2,4-trimethoxy-3-non-8-enylbenzene (**8a**) (1.97 g, 6.73 mmol). After flash chromatography (P/EA 90/10), the product was obtained (1.66 g, 4.93 mmol, 73%) as a yellow oil. TLC: R_f=0.69 (P/EA90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=2919 (v. s, CH_2), 2854 (s, CH_2), 1640 (m, C=C), 1573 (m, C=C), 1523 (s, NO_2), 1480 (s, C=C_{ar}), 1424 (m, CH_2), 1343 (m, CNO_2), 1246 (m, COC), 1108 (m), 1053 (m), 1004 (w, RCH=CH_2), 964 (m), 909 (w, RCH=CH_2), 847 (w, CH_{ar}), 770 (w, CH_{ar}); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=7.32 (s, 1H, C_{ar}H), 5.76 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.98–4.93 (m, 1H, H_{trans}-CH=CHR), 4.91–4.88 (m, 1H, H_{cis}CH=CHR), 3.89 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.62 (v. t, $^3J\cong7.8$ Hz, 2H, CH_2C_{ar}), (v. q, $^3J\cong6.7$ Hz, 2H, CH_2=CHCH_2), 1.28–1.52 (m, 10H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=152.4 (C_{ar}OCH$_3$), 148.5 (C_{ar}OCH$_3$), 147.4 (C_{ar}OCH$_3$), 139.1 (HR*C*=CH_2), 138.0 (C_{ar}), 132.8 (C_{ar}), 114.1 (HRC=*C*H_2), 106.6 (C_{ar}H), 62.6 (OCH_3), 60.9 (OCH_3), 56.1 (OCH_3), 33.7 (CH_2), 30.1 (CH_2), 29.8 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 24.7 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 337 (100) [M^+], 320 (15), 226 (25), 211 (15), 196 (10), 181 (10), 166 (26), 151 (10), 137 (7), 55 (7). Anal. $C_{18}H_{27}NO_5$ (337.4): calcd C, 64.07; H, 8.07; found C, 64.03; H: 7.99.

5.1.7. 3-Dec-9-enyl-1,2,4-trimethoxy-5-nitrobenzene (9b). Procedure B was performed with 2-dec-9-enyl-1,3,4-trimethoxybenzene (**8b**) (2.07 g, 6.76 mmol). After flash chromatography (P/EA 95/5), the product was obtained (2.28 g, 6.49 mmol, 95%) as a yellow oil. TLC: R_f=0.45 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=2919 (v. s, CH_2), 2854 (s, CH_2), 1640 (m, C=C), 1573 (m, C=C), 1523 (s, NO_2), 1480 (s, C=C_{ar}), 1424 (m, CH_2), 1343 (m, CNO_2), 1246 (m, COC), 1108 (m), 1053 (m), 1004 (w, RCH=CH_2), 964 (m), 909 (w, RCH=CH_2), 847 (w, CH_{ar}), 770 (w, CH_{ar}); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm)=7.34 (s, 1H, C_{ar}H), 5.78 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.98–4.93 (m, 1H, H_{trans}-CH=CHR), 4.92–4.89 (m, 1H, H_{cis}CH=CHR), 3.90 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 2.64 (v. t, $^3J\cong7.8$ Hz, 2H, CH_2C_{ar}), (v. q, $^3J\cong6.7$ Hz, 2H, CH_2=CHCH_2), 1.28–1.52 (m, 12H, CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm)=152.4 (C_{ar}OCH$_3$), 148.5 (C_{ar}OCH$_3$), 147.3 (C_{ar}OCH$_3$), 139.1 (HR*C*=CH_2), 138.5 (C_{ar}), 132.8 (C_{ar}), 114.0 (HRC=*C*H_2), 106.6 (C_{ar}H), 62.6 (OCH_3), 60.9 (OCH_3), 56.1 (OCH_3), 33.7 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 24.7 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 351 (100) [M^+], 334 (15), 226 (25), 211 (15), 196 (10), 181 (15), 166 (28), 151 (10), 137 (7), 55 (7); HRMS: *m*/*z* calcd for $C_{19}H_{29}NO_5$: 351.2046; found 351.2045.

5.1.8. 1,2,4-Trimethoxy-5-nitro-3-undec-10-enylbenzene (9c). Procedure B was performed with 1, 2, 4-trimethoxy-3-undec-10-enylbenzene (**8c**) (1.38 g, 4.31 mmol). The amount of reagents and solvents was adjusted accordingly. After flash chromatography (P/EA 90/10), the product was obtained (1.54 g, 4.22 mmol, 98%) as a yellow oil. TLC: R_f=0.42 (P/EA90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=2919 (v. s, CH_2), 2854 (s, CH_2), 1640 (m, C=C), 1573 (m, C=C), 1523 (s, NO_2), 1480 (s, C_{ar}=C_{ar}), 1424 (m, CH_2), 1343 (m, CNO_2), 1246 (m, COC), 1108 (m), 1053 (m), 1004 (w, RCH=CH_2), 964 (m), 909 (w, RCH=CH_2), 847 (w, CH_{ar}), 770 (w, CH_{ar}); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm)=7.35 (s, 1H, C_{ar}H), 5.78 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.98–4.93 (m, 1H, H_{trans}CH=CHR), 4.92–4.89 (m, 1H, H_{cis}CH=CHR), 3.91 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.65 (v. t, ^3J=7.8 Hz, 2H, CH_2C_{ar}), 2.04 (v. q, $^3J\cong6.7$ Hz, 2H, CH_2=CHCH_2), 1.50 (m, 2H, CH_2), 1.35–1.23 (m, 12H, CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm)=152.4 (C_{ar}OCH$_3$), 148.5 (C_{ar}OCH$_3$), 147.3 (C_{ar}OCH$_3$), 139.1 (HR*C*=CH_2), 138.5 (C_{ar}), 132.8 (C_{ar}), 114.0 (HRC=*C*H_2), 106.6 (C_{ar}H), 62.6 (OCH_3), 60.9 (OCH_3), 56.1 (OCH_3), 33.7 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 24.7 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 365 (100) [M^+], 348 (20), 226 (36), 211 (17), 196 (18), 181 (24), 166 (28), 151 (10), 137 (10), 107 (9), 97 (8), 91 (8), 55 (20), 41 (15); HRMS: *m*/*z* calcd for $C_{20}H_{31}NO_5$: 365.2202; found 365.2202.

5.1.9. 3-Dodec-11-enyl-1,2,4-trimethoxy-5-nitrobenzene (9d). Procedure B was performed with 2-dodec-11-enyl-1,3,4-trimethoxybenzene (**8d**) (415 mg, 1.24 mmol). After flash chromatography (P/EA 90/10), the product was obtained (448 mg, 1.18 mmol, 95%) as a yellow oil. TLC: R_f=0.60 (P/EA90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=2919 (v. s, CH_2), 2854 (s, CH_2), 1640 (m, C=C), 1573 (m, C=C), 1523 (s, NO_2), 1480 (s, C_{ar}=C_{ar}), 1424 (m, CH_2), 1343 (m, CNO_2), 1246 (m, COC), 1108 (m), 1053 (m), 1004 (w, RCH=CH_2), 964 (m), 909 (w, RCH=CH_2), 847 (w, CH_{ar}), 770 (w, CH_{ar}); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=7.32 (s, 1H, C_{ar}H), 5.76 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.98–4.93 (m, 1H, H_{trans}CH=CHR), 4.91–4.88 (m, 1H, H_{cis}CH=CHR), 3.88 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.62 (v. t, $^3J\cong7.8$ Hz, 2H, CH_2C_{ar}), 2.00 (v. q, $^3J\cong6.7$ Hz, 2H, CH_2=CHCH_2), 1.50 (m, 2H, CH_2), 1.35–1.23 (m, 14H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=152.4 (C_{ar}OCH$_3$), 148.5 (C_{ar}OCH$_3$), 147.3 (C_{ar}OCH$_3$), 139.1 (HR*C*=CH_2), 138.5 (C_{ar}), 132.8 (C_{ar}), 114.0 (HRC=*C*H_2), 106.6 (C_{ar}H), 62.6 (OCH_3), 60.9 (OCH_3), 56.1 (OCH_3), 33.7 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 24.7 (CH_2); MS (EI, 70 eV), *m*/*z* (%): 379 (100) [M^+], 362 (20), 334 (15), 320 (15), 306 (8), 290 (8), 226 (23), 211 (10), 196 (10), 181 (16), 166 (14), 151 (11), 137 (9), 121 (5), 107 (8), 97 (8), 91 (8), 83 (5), 55 (14), 41 (14). Anal. $C_{21}H_{33}NO_5$ (379.5): calcd C, 66.68; H, 8.86; found C, 66.46; H: 8.76.

5.1.10. 1,2,4-Trimethoxy-5-nitro-3-tridec-12-enylbenzene (9e). Procedure B was performed with 1,2,4-trimethoxy-3-tridec-12-enylbenzene (**8e**) (458 mg, 1.31 mmol). After flash chromatography (P/EA 90/10), the product was obtained (484 mg, 1.23 mmol, 94%) as a yellow oil. TLC: R_f=0.67 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=2919 (v. s, CH_2), 2854 (s, CH_2), 1640 (m, C=C), 1573 (m, C=C), 1523 (s, NO_2), 1480 (s, C_{ar}=C_{ar}), 1424 (m, CH_2), 1343 (m, CN), 1246 (m, COC), 1108 (m), 1053 (m), 1004 (w, RCH=CH_2), 964 (m), 909 (w, RCH=CH_2), 847 (w, CH_{ar}), 770 (w, CH_{ar}); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=7.32 (s, 1H, $C_{ar}H$), 5.79 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.98–4.93 (m, 1H, H_{trans}CH=CHR), 4.92–4.89 (m, 1H, H_{cis}CH=CHR), 3.89 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 2.62 (v. t, $^3J\cong$7.8 Hz, 2H, CH_2C_{ar}), 2.00 (v. q, $^3J\cong$6.7 Hz, 2H, CH_2=CHCH_2), 1.50 (m, 2H, CH_2), 1.35–1.23 (m, 16H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=152.4 ($C_{ar}OCH_3$), 148.5 ($C_{ar}OCH_3$), 147.5 ($C_{ar}OCH_3$), 139.2 (HR*C*=CH_2), 138.5 (C_{ar}), 132.9 (C_{ar}), 114.0 (HRC=*C*H_2), 106.7 ($C_{ar}H$), 62.7 (OCH_3), 61.0 (OCH_3), 56.2 (OCH_3), 33.8 (CH_2), 30.2 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 24.7 (CH_2); MS (EI, 70 eV), *m/z* (%): 393 (100) [M^+], 376 (20), 359 (15), 348 (8), 226 (21), 196 (10), 181 (14), 166 (8), 151 (8), 123 (6), 95 (5), 69 (5), 55 (14), 41 (8). Anal. $C_{22}H_{35}NO_5$ (393.5): calcd C, 67.15; H, 9.05; found C, 67.58; H: 8.96.

5.1.11. 2,4,5-Trimethoxy-3-non-8-enylphenylamine (10a). Procedure C was performed using the nitro arene **9a** (215 mg, 0.64 mmol). After flash chromatography (P/EA 90/10), the product was obtained (162 mg, 0.52 mmol, 82%) as a colorless oil. TLC: R_f=0.16 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3430 (w, NH_2), 3358 (m, NH_2), 3095 (w, =CH_2), 2926 (v. s, CH_2), 2854 (s, CH_2), 1614 (m, N–H), 1490 (m, CH_2), 1363 (s, COC), 1224 (s), 1120 (m, COC), 1058 (m), 1011 (m, RCH=CH_2), 909 (w, RCH=CH_2), 821 (w, CH); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm)=6.18 (s, 1H, $C_{ar}H$), 5.76 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.98–4.93 (m, 1H, H_{trans}CH=CHR), 4.92–4.89 (m, 1H, H_{cis}CH=CHR), 3.74 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.50 (br. s, 2H, NH_2), 2.53 (v. t, $^3J\cong$7.9 Hz, 2H, CH_2C_{ar}), 2.00 (v. q, $^3J\cong$6.9 Hz, 2H, CH_2=CHCH_2), 1.52 (m, 2H, CH_2), 1.33–1.25 (m, 8H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=149.5 ($C_{ar}OCH_3$), 139.5 (HR*C*=CH_2), 139.1 ($C_{ar}OCH_3$), 138.9 ($C_{ar}OCH_3$), 135.6 (C_{ar}), 130.3 (C_{ar}), 114.0 (HRC=*C*H_2), 98.5 ($C_{ar}H$), 60.8 (OCH_3), 59.9 (OCH_3), 55.7 (OCH_3), 33.7 (CH_2), 30.6 (CH_2), 29.9 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 24.7 (CH_2); MS (EI, 70 eV), *m/z* (%): 307 (100) [M^+], 292 (87), 208 (5), 192 (8), 182 (17), 167 (25), 152 (10), 138 (17), 122 (10), 55 (7). Anal. $C_{18}H_{29}NO_3$ (307.4): calcd C, 70.32; H, 9.51; found C, 69.99; H: 9.46.

5.1.12. 2,4,5-Trimethoxy-3-dec-9-enylphenylamine (10b). Procedure C was performed using the nitro arene **9b** (1.99 g, 5.67 mmol). After flash chromatography (P/EA 75/25), the product was obtained (1.40 g, 4.37 mmol, 77%) as a light brown oil. TLC: R_f=0.47 (P/EA 75/25) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3430 (w, NH_2), 3358 (m, NH_2), 3095 (w, =CH_2), 2926 (v. s, CH_2), 2854 (s, CH_2), 1614 (m, N–H), 1490 (m, CH_2), 1363 (s, COC), 1224 (s), 1120 (m, COC), 1058 (m), 1011 (m, RCH=CH_2), 909 (w, RCH=CH_2), 821 (w, CH); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm)=6.21 (s, 1H, $C_{ar}H$), 5.80 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.97–4.92 (m, 1H, H_{trans}CH=CHR), 4.91–4.88 (m, 1H, H_{cis}CH=CHR), 3.77 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.63 (br. s, 2H, NH_2), 2.58 (v. t, $^3J\cong$7.9 Hz, 2H, CH_2C_{ar}), 2.02 (v. q, $^3J\cong$6.9 Hz, 2H, CH_2=CHCH_2), 1.52 (m, 2H, CH_2), 1.33–1.25 (m, 10H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=150.0 ($C_{ar}OCH_3$), 139.9 ($C_{ar}OCH_3$), 138.6 ($C_{ar}OCH_3$), 139.3 (HR*C*=CH_2), 136.0 (C_{ar}), 130.8 (C_{ar}), 114.4 (HRC=*C*H_2), 98.8 ($C_{ar}H$), 61.3 (OCH_3), 60.4 (OCH_3), 56.2 (OCH_3), 34.2 (CH_2), 31.2 (CH_2), 30.4 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 25.1 (CH_2); MS (EI, 70 eV), *m/z* (%): 321 (100) [M^+], 306 (90), 192 (5), 182 (28), 167 (18), 152 (12), 138 (12), 122 (9). Anal. $C_{19}H_{31}NO_3$ (321.4): calcd C, 70.99; H, 9.72; found C, 71.00; H: 9.70.

5.1.13. 2,4,5-Trimethoxy-3-undec-10-enylphenylamine (10c). Procedure C was performed using the nitro arene **9c** (2.30 g, 6.30 mmol). The amount of reagents and solvents was adjusted accordingly. After flash chromatography (P/EA 90/10), the product was obtained (1.77 g, 5.29 mmol, 84%) as a light brown oil. TLC: R_f=0.16 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3430 (w, NH_2), 3358 (m, NH_2), 3095 (w, =CH_2), 2926 (v. s, CH_2), 2854 (s, CH_2), 1614 (m, N–H), 1490 (m, CH_2), 1363 (s, COC), 1224 (s), 1120 (m, COC), 1058 (m), 1011 (m, RCH=CH_2), 909 (w, RCH=CH_2), 821 (w, CH); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm)=6.19 (s, 1H, $C_{ar}H$), 5.75 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.97–4.92 (m, 1H, H_{trans}CH=CHR), 4.91–4.88 (m, 1H, H_{cis}CH=CHR), 3.75 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.49 (br. s, 2H, NH_2), 2.56–2.54 (m, 2H, CH_2C_{ar}), 2.00 (v. q, $^3J\cong$6.9 Hz, 2H, CH_2=CHCH_2), 1.53–1.51 (m, 2H, CH_2), 1.35–1.26 (m, 12H, CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm)=150.0 ($C_{ar}OCH_3$), 139.9 ($C_{ar}CH_3$), 139.6 (HR*C*=CH_2), 139.3 ($C_{ar}OCH_3$), 136.0 (C_{ar}), 130.8 (C_{ar}), 114.6 (HRC=*C*H_2), 98.8 ($C_{ar}H$), 61.3 (OCH_3), 60.4 (OCH_3), 56.2 (OCH_3), 34.2 (CH_2), 31.2 (CH_2), 30.5 (CH_2), 29.9 (2CH_2), 29.8 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 25.1 (CH_2); MS (EI, 70 eV), *m/z* (%): 335 (100) [M^+], 306 (78), 182 (18), 167 (20), 152 (10), 138 (10), 122 (9). Anal. $C_{20}H_{33}NO_3$ (335.5): calcd C, 71.60; H, 9.91; found C, 71.53; H: 9.86.

5.1.14. 2,4,5-Trimethoxy-3-dodec-11-enylphenylamine (10d). Procedure C was performed using the nitro arene **9d** (448 mg, 1.18 mmol). After flash chromatography (P/EA 90/10), the product was obtained (326 mg, 0.93 mmol, 79%) as a transparent oil. TLC: R_f=0.15 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3450 (w, NH_2), 3358 (m, NH_2), 3095 (w, =CH_2), 2926 (v. s, CH_2), 2854 (S, CH_2), 1614 (m, NH), 1490 (m, CH_2), 1363 (S, COC), 1224 (S), 1120 (m, COC), 1058 (m), 1011 (m, RCH=CH_2), 909 (w, RCH=CH_2), 821 (w, CH); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=6.19 (s, 1H, $C_{ar}H$), 5.79 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 4.99–4.94 (m, 1H, H_{trans}CH=CHR), 4.92–4.89 (m, 1H, H_{cis}CH=CHR), 3.75 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.60 (br. s, 2H, NH_2), 2.58–2.56 (m, 2H, CH_2C_{ar}), 2.00 (v. q,

$^3J \cong 6.9$ Hz, 2H, CH_2=CHCH_2), 1.53–1.51 (m, 2H, CH_2), 1.35–1.25 (m, 14H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 149.6 ($C_{ar}OCH_3$), 139.6 ($C_{ar}OCH_3$), 139.2 (HR*C*=CH_2), 139.0 ($C_{ar}OCH_3$), 135.6 (C_{ar}), 130.4 (C_{ar}), 114.0 (HRC=*C*H_2), 98.5 (C_{ar}H), 60.9 (OCH_3), 59.7 (OCH_3), 55.8 (OCH_3), 33.7 (CH_2), 30.7 (CH_2), 30.0 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (2 CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.1 (CH_2); MS (EI, 70 eV), *m/z* (%): 349 (100) [M^+], 334 (66), 182 (18), 167 (12), 152 (6), 138 (6), 122 (6). Anal. $C_{21}H_{35}NO_3$ (349.5): calcd C, 72.17; H, 10.09; found C, 72.28; H: 10.06.

5.1.15. 2,4,5-Trimethoxy-3-tridec-12-enylphenylamine (10e). Procedure C was performed using the nitro arene **9e** (210 mg, 0.53 mmol). After flash chromatography (P/EA 80/20), the product was obtained (159 mg, 0.44 mmol, 83%) as a transparent oil. TLC: R_f = 0.21 (P/EA 80/20) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1}) = 3450 (w, NH), 3358 (m, NH), 3095 (w, =CH_2), 2926 (v. s, CH_2), 2854 (s, CH_2), 1614 (m, N–H), 1490 (m, CH_2), 1363 (s, COC), 1224 (s), 1120 (m, COC), 1058 (m), 1011 (m, RCH=CH_2), 909 (w, RCH=CH_2), 821 (w, CH); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 6.19 (s, 1H, C_{ar}H), 5.79 (ddt, ^3J = 17.1 Hz, ^3J = 10.2 Hz, ^3J = 6.7 Hz, 1H, CH_2=C*H*R), 4.99–4.94 (m, 1H, H_{trans}CH=CHR), 4.93–4.90 (m, 1H, H_{cis}CH=CHR), 3.73 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 3.60 (br. s, 2H, NH_2), 2.57–2.55 (m, 2H, CH_2C_{ar}), 2.00 (v. q, $^3J \cong 6.9$ Hz, 2H, CH_2=CHCH_2), 1.53–1.51 (m, 2H, CH_2), 1.35–1.26 (m, 16H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 149.6 ($C_{ar}OCH_3$), 139.7 ($C_{ar}OCH_3$), 139.2 (HR*C*=CH_2), 139.0 ($C_{ar}OCH_3$), 135.6 (C_{ar}), 130.5 (C_{ar}), 114.0 (HRC=*C*H_2), 98.5 (C_{ar}H), 60.9 (OCH_3), 60.0 (OCH_3), 55.8 (OCH_3), 33.8 (CH_2), 30.7 (CH_2), 30.1 (CH_2), 29.7 (CH_2), 29.6 (2 CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 24.8 (CH_2); MS (EI, 70 eV), *m/z* (%): 363 (100) [M^+], 348 (54), 182 (18), 167 (12), 152 (8), 138 (8), 122 (8), 55 (6), 41 (6) [$C_3H_4^+$]. Anal. $C_{22}H_{37}NO_3$ (363.5): calcd C, 72.69; H, 10.26; found C, 72.57; H: 10.28.

5.1.16. 2-Methylpenta-2,4-dienoic acid (2,4,5-trimethoxy-3-non-8-enylphenyl)-amide (11a). Procedure D was performed with the aniline **10a** (50 mg, 163 μmol). After flash chromatography (P/EA 80/20), the product was obtained (47 mg, 117 μmol, 72%) as a light yellow oil. TLC: R_f = 0.32 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1}) = 3436 (m, NH), 2926 (v. s, CH_2), 2854 (s, CH_2), 1673 (s, C=O), 1600 (m, C=C), 1514 (s), 1455 (s), 1410 (s), 1221 (s, CN), 1171 (m), 1104 (s), 1058 (s), 1007 (s, RCH=CH_2), 909 (m, RCH=CH_2), 851 (m, CH); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 8.07 (s, 1H, NH), 8.00 (s, 1H, C_{ar}H), 7.01 [d, ^3J = 10.2 Hz, 1H, CH_2=CH–C*H*=C(CO)], 6.68 (ddd, ^3J = 16.7 Hz, ^3J = 10.2 Hz, ^3J = 10.0 Hz, 1H, CH_2=C*H*–CH=C), 5.80 (ddt, ^3J = 17.1 Hz, ^3J = 10.2 Hz, ^3J = 6.7 Hz, 1H, CH_2=C*H*R), 5.56 (d, ^3J = 16.7 Hz, 1H, H_{trans}CH=CH–CH=C), 5.45 (d, ^3J = 10.2 Hz, 1H, H_{cis}-CH=CH–CH=C), 4.99–4.93 (m, 1H, H_{trans}CH=CHR), 4.91–4.88 (m, 1H, H_{cis}CH=CHR), 3.86 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 2.62 (v. t, $^3J \cong 6.4$ Hz, 2H, CH_2C_{ar}), 2.09 (d, ^4J = 0.9 Hz, 3H, =CCH_3), 2.03 (v. q, $^3J \cong 7.0$ Hz, 2H, CH_2=CHCH_2), 1.57–1.31 (m, 10H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 166.6 (C=O), 149.2 ($C_{ar}OCH_3$), 143.5 ($C_{ar}OCH_3$), 141.0 ($C_{ar}OCH_3$), 139.2 (HR*C*=CH_2), 134.5 (C_{olef}H), 131.9 (C_{olef}H), 131.3 (C_{ar}), 129.5 (C_{ar}), 127.4 (=*C*CH_3), 123.5 (=CH–HC=*C*H_2), 114.1 (HRC=*C*H_2), 102.8 (C_{ar}H), 61.4 (OCH_3), 60.8 (OCH_3), 55.9 (OCH_3), 33.8 (CH_2), 30.5 (CH_2), 29.9 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 24.7 (CH_2), 13.0 (CH_3); MS (EI, 70 eV), *m/z* (%): 401 (100) [M^+], 386 (8), 370 (10), 153 (7), 95 (66), 67 (20); HRMS: *m/z* calcd for $C_{24}H_{35}NO_4$: 401.2566; found 401.2566.

5.1.17. 2-Methylpenta-2,4-dienoic acid (3-dec-9-enyl-2,4,5-trimethoxyphenyl)-amide (11b). Procedure D was performed with the aniline **10b** (122 mg, 380 μmol). After flash chromatography (P/EA 95/05), the product was obtained (92 mg, 221 μmol, 58%) as a light brown oil. TLC: R_f = 0.32 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1}) = 3436 (m, NH), 2926 (v. s, CH_2), 2854 (s, CH_2), 1673 (s, C=O), 1600 (m, C=C), 1514 (s), 1455 (s), 1410 (s), 1221 (s, CN), 1171 (m), 1104 (s), 1058 (s), 1007 (s, RCH=CH_2), 909 (m, RCH=CH_2), 851 (m, CH); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 8.07 (s, 1H, NH), 8.00 (s, 1H, C_{ar}H), 7.01 [d, ^3J = 11.1 Hz, 1H, CH_2=CH–C*H*=C(CO)], 6.68 (ddd, ^3J = 16.8 Hz, ^3J = 11.1 Hz, ^3J = 10.1 Hz, 1H, CH_2=C*H*–CH=C), 5.80 (ddt, ^3J = 17.1 Hz, ^3J = 10.2 Hz, ^3J = 6.7 Hz, 1H, CH_2=C*H*R), 5.56 (d, ^3J = 16.8 Hz, 1H, H_{trans}CH=CH–CH=C), 5.45 (d, ^3J = 10.2 Hz, 1H, H_{cis}-CH=CH–CH=C), 4.98 (m, 1H, H_{trans}CH=CHR), 4.90 (m, 1H, H_{cis}CH=CHR), 3.86 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 2.62 (t, ^3J = 6.4 Hz, 2H, CH_2C_{ar}), 2.09 (br. s, 3H, =CCH_3), 2.03 (v. q, $^3J \cong 7.0$ Hz, 2H, CH_2=CHCH_2), 1.58–1.53 (m, 2H, CH_2), 1.37–1.30 (m, 10H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 166.6 (C=O), 149.2 ($C_{ar}OCH_3$), 143.5 ($C_{ar}OCH_3$), 141.0 ($C_{ar}OCH_3$), 139.2 (HR*C*=CH_2), 134.5 (C_{olef}H), 131.9 (C_{olef}H), 131.3 (C_{ar}), 129.5 (C_{ar}), 127.3 (=*C*CH_3), 123.5 (=CH–HC=*C*H_2), 114.1 (HRC=*C*H_2), 102.7 (C_{ar}H), 61.4 (OCH_3), 60.8 (OCH_3), 55.9 (OCH_3), 33.8 (CH_2), 30.5 (CH_2), 30.0 (CH_2), 29.4 (2 CH_2), 29.1 (CH_2), 28.9 (CH_2), 24.7 (CH_2), 13.0 (CH_3); MS (EI, 70 eV), *m/z* (%): 415 (100) [M^+], 384 (10), 332 (5), 166 (6), 95 (57), 67 (17). Anal. $C_{25}H_{37}NO_4$ (415.6): calcd C, 72.26; H, 8.97; found C, 72.15; H: 8.85.

5.1.18. 2-Methylpenta-2,4-dienoic acid (2,4,5-trimethoxy-3-undec-10-enylphenyl)-amide (11c). Procedure D was performed with the aniline **10c** (200 mg, 597 μmol). After flash chromatography (P/EA 90/10), the product was obtained (169 mg, 393 μmol, 66%) as a light brown oil. TLC: R_f = 0.33 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1}) = 3436 (m, NH), 2926 (v. s, CH_2), 2854 (s, CH_2), 1673 (s, C=O), 1600 (m, C=C), 1514 (s), 1455 (s), 1410 (s), 1221 (s, CN), 1171 (m), 1104 (s), 1058 (s), 1007 (s, RCH=CH_2), 909 (m, RCH=CH_2), 851 (m, CH); ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) = 8.08 (s, 1H, NH), 7.99 (s, 1H, C_{ar}H), 7.02 [d, ^3J = 11.1 Hz, 1H, CH_2=CH–C*H*=C(CO)], 6.67 (ddd, ^3J = 16.8 Hz, ^3J = 11.1 Hz, ^3J = 10.1 Hz, 1H, CH_2=C*H*–CH=C), 5.80 (ddt, ^3J = 17.1 Hz, ^3J = 10.2 Hz, ^3J = 6.7 Hz, 1H, CH_2=C*H*R), 5.55 (d, ^3J = 16.8 Hz, 1H, H_{trans}CH=CH–CH=C), 5.46 (d, ^3J = 10.2 Hz, 1H, H_{cis}-CH=CH–CH=C), 4.97 (m, 1H, H_{trans}CH=CHR), 4.91 (m, 1H, H_{cis}CH=CHR), 3.86 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 2.61 (t, ^3J = 6.4 Hz, 2H, CH_2C_{ar}), 2.09 (br. s, 3H, =CCH_3), 2.02 (v. q, $^3J \cong 7.0$ Hz, 2H, CH_2=CHCH_2), 1.60–1.54 (m, 2H, CH_2), 1.35–1.27 (m,

12H, CH_2); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm)=166.9 (C=O), 149.6 ($C_{ar}OCH_3$), 143.9 ($C_{ar}OCH_3$), 141.4 ($C_{ar}OCH_3$), 139.6 (HR*C*=CH_2), 135.0 ($C_{olef}H$), 132.3 ($C_{olef}H$), 131.7 (C_{ar}), 130.0 (C_{ar}), 127.7 (=*C*CH_3), 124.0 (=CH–HC=*C*H_2), 114.4 (HRC=*C*H_2), 103.1 ($C_{ar}H$), 61.8 (OCH_3), 61.3 (OCH_3), 56.2 (OCH_3), 34.2 (CH_2), 31.0 (CH_2), 30.4 (CH_2), 29.9 (2 CH_2), 29.8 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 25.1 (CH_2), 13.4 (CH_3); MS (EI, 70 eV), *m*/*z* (%): 429 (95) [M^+], 414 (15), 398 (10), 346 (9), 320 (9), 167 (6), 95 (100), 67 (26), 41 (6). Anal. $C_{26}H_{39}NO_4$ (429.6): calcd C, 72.69; H, 9.15; found C, 72.59; H: 9.01.

5.1.19. 2-Methylpenta-2,4-dienoic acid (2,4,5-trimethoxy-3-dodec-11-enylphenyl)-amide (11d). Procedure D was performed with the aniline **10d** (191 mg, 547 μmol). The amount of reagents and solvents was adjusted accordingly. After flash chromatography (P/EA 90/10), the product was obtained (165 mg, 372 μmol, 68%) as a light brown oil. TLC: R_f=0.38 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3436 (m, NH), 2926 (v. s, CH_2), 2854 (s, CH_2), 1673 (s, C=O), 1600 (m, C=C), 1514 (s), 1455 (s), 1410 (s), 1221 (s, CN), 1171 (m), 1104 (s), 1058 (s), 1007 (s, RCH=CH_2), 909 (m, RCH=CH_2), 851 (m, CH); ^1H NMR (360 MHz, $CDCl_3$): δ (ppm)=8.03 (s, 1H, NH), 7.96 (s, 1H, $C_{ar}H$), 6.97 [d, ^3J=11.1 Hz, 1H, CH_2=CH–C*H*=C(CO)], 6.66 (ddd, ^3J=16.8 Hz, ^3J=11.1 Hz, ^3J=10.1 Hz, 1H, CH_2=C*H*–CH=C), 5.78 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 5.55 (d, ^3J=16.8 Hz, 1H, H_{trans}CH=CH–CH=C), 5.46 (d, ^3J=10.2 Hz, 1H, H_{cis}-CH=CH–CH=C), 4.97–4.91 (m, 1H, H_{trans}CH=CHR), 4.89–4.86 (m, 1H, H_{cis}CH=CHR), 3.82 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 2.58 (v. t, $^3J\cong$6.4 Hz, 2H, CH_2C_{ar}), 2.06 (br. s, 3H, =CCH_3), 2.02 (v. q, $^3J\cong$7.0 Hz, 2H, CH_2=CHCH_2), 1.53 (m, 2H, CH_2), 1.35–1.27 (m, 14H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=166.4 (C=O), 149.2 ($C_{ar}OCH_3$), 143.5 ($C_{ar}OCH_3$), 141.0 ($C_{ar}OCH_3$), 139.1 (HR*C*=CH_2), 134.4 ($C_{olef}H$), 131.9 ($C_{olef}H$), 131.3 (C_{ar}), 129.4 (C_{ar}), 127.3 (=*C*CH_3), 123.4 (=CH–HC=*C*H_2), 114.0 (HRC=*C*H_2), 102.7 ($C_{ar}H$), 61.3 (OCH_3), 60.7 (OCH_3), 55.8 (OCH_3), 33.7 (CH_2), 30.4 (CH_2), 29.9 (CH_2), 29.5 (CH_2), 29.4 (2 CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 24.7 (CH_2), 12.9 (CH_3); MS (EI, 70 eV), *m*/*z* (%): 443 (100) [M^+], 428 (10), 95 (80), 67 (12), 40 (6). Anal. $C_{27}H_{41}NO_4$ (443.6): calcd C, 73.10; H, 9.32; found C, 73.05; H: 9.41.

5.1.20. 2-Methylpenta-2,4-dienoic acid (2,4,5-trimethoxy-3-tridec-12-enylphenyl)-amide (11e). Procedure D was performed with the aniline **10e** (131 mg, 361 μmol). After flash chromatography (P/EA 90/10), the product was obtained (105 mg, 229 μmol, 63%) as a light brown oil. TLC: R_f=0.33 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3436 (m, NH), 2926 (v. s, CH_2), 2854 (s, CH_2), 1673 (s, C=O), 1600 (m, C=C), 1514 (s), 1455 (s), 1410 (s), 1221 (s, C–N), 1171 (m), 1104 (s), 1058 (s), 1007 (s, RCH=CH_2), 909 (m, RCH=CH_2), 851 (m, CH); ^1H NMR (360 MHz, $CDCl_3$): δ (ppm)=8.05 (s, 1H, NH), 7.98 (s, 1H, $C_{ar}H$), 6.98 [d, ^3J=11.1 Hz, 1H, CH_2=CH–C*H*=C(CO)], 6.67 (ddd, ^3J=16.8 Hz, ^3J=11.1 Hz, ^3J=10.1 Hz, 1H, CH_2=C*H*–CH=C), 5.80 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.7 Hz, 1H, CH_2=C*H*R), 5.55 (d, ^3J=16.8 Hz, 1H, H_{trans}CH=CH–CH=C), 5.46 (d, ^3J=10.2 Hz, 1H, H_{cis}-CH=CH–CH=C), 4.99–4.93 (m, 1H, H_{trans}CH=CHR), 4.92–4.88 (m, 1H, H_{cis}CH=CHR), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 2.61 (t, ^3J=6.4 Hz, 2H, CH_2C_{ar}), 2.08 (d, ^4J=1.1 Hz, 3H, =CCH_3), 2.02 (v. q, $^3J\cong$7.0 Hz, 2H, CH_2=CHCH_2), 1.56–1.49 (m, 2H, CH_2), 1.35–1.27 (m, 16H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=166.6 (C=O), 149.3 ($C_{ar}OCH_3$), 143.6 ($C_{ar}OCH_3$), 141.1 ($C_{ar}OCH_3$), 139.2 (HR*C*=CH_2), 134.5 ($C_{olef}H$), 132.0 ($C_{olef}H$), 131.4 (C_{ar}), 129.6 (C_{ar}), 127.4 (=*C*CH_3), 123.5 (=CH–HC=*C*H_2), 114.0 (HRC=*C*H_2), 102.8 ($C_{ar}H$), 61.4 (OCH_3), 60.9 (OCH_3), 55.9 (OCH_3), 33.8 (CH_2), 30.6 (CH_2), 30.0 (CH_2), 29.7 (CH_2), 29.6 (2 CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 24.8 (CH_2), 13.0 (CH_3); MS (EI, 70 eV), *m*/*z* (%): 457 (100) [M^+], 442 (10), 426 (8), 374 (5), 167 (6), 149 (8), 95 (74), 67 (12), 57 (6), 40 (6). Anal. $C_{28}H_{43}NO_4$ (457.6): calcd C, 73.48; H, 9.47; found C, 73.53; H: 9.30.

5.1.21. (4*E*,6*Z*)-18,19,21-Trimethoxy-4-methyl-2-azabicyclo[15.3.1]henicosa-1(21),4,6,17,19-pentaen-3-one (12c). Procedure E was performed with the anilide **11c** (50 mg, 116 μmol) and Grubbs catalyst (9.5 mg, 11.5 μmol, 10 mol%) in DCM (230 mL). After flash chromatography (P/EA 90/10), the product was obtained (31 mg, 77 μmol, 66%) as a white solid. Starting material was isolated (7 mg, 16 μmol, 14%). TLC: R_f=0.32 (P/EA 90/10) [CAM, UV]; ^1H NMR (360 MHz, $CDCl_3$): δ (ppm)=8.35 (s br, 1H, NH), 8.01 (s, 1H, $C_{ar}H$), 7.01 [d, ^3J=11.3 Hz, 1H, CH=CH–C*H*=C(CO)], 6.28 [v. t, $^3J\cong$10.9 Hz, 1H, CH=C*H*–CH=C(CO)], 5.97 [v. q, $^3J\cong$9.1 Hz, 1H, C*H*=CH–CH=C(CO)], 3.85 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 2.61 (br, 1H, CH_2), 2.09 (br, 1H, CH_2), 2.02 (br. s, 3H, =CCH_3), 1.58–1.10 (m, 16H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=168.6 (C=O), 149.5 ($C_{ar}OCH_3$), 142.8 ($C_{ar}OCH_3$), 141.2 ($C_{ar}OCH_3$), 138.5 ($C_{olef}H$), 133.2 (C_{ar}), 128.8 (C_{ar}), 127.9 (=*C*CH_3), 127.4 ($C_{olef}H$), 123.7 ($C_{olef}H$), 100.7 ($C_{ar}H$), 61.3 (OCH_3), 61.0 (OCH_3), 55.9 (OCH_3), 30.1 (CH_2), 30.0 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 28.7 (CH_2), 28.0 (CH_2), 27.4 (CH_2), 25.9 (CH_2), 22.1 (CH_2), 12.4 (CH_3); MS (EI, 70 eV), *m*/*z* (%): 401 (100) [M^+], 386 (22), 370 (50), 206 (6), 182 (7), 167 (8), 152 (7). Anal. $C_{24}H_{35}NO_4$ (401.5): calcd C, 71.79; H, 8.79; found C, 71.77; H: 8.66.

5.1.22. (4*E*,6*Z*)-19,20,22-Trimethoxy-4-methyl-2-azabicyclo[16.3.1]docosa-1(22),4,6,18,20-pentaen-3-one (12d). Procedure E was performed with the anilide **11d** (50 mg, 112 μmol) and Grubbs catalyst (9.0 mg, 11.2 μmol, 10 mol%) in DCM (220 mL). After flash chromatography (P/EA 90/10), the product was obtained (35 mg, 86 μmol, 77%) as a transparent to light green transparent oil. TLC: R_f=0.29 (P/EA/DCM 50/10/50) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3428 (br, NH), 2974 (s, CH_3), 2926 (v. s, CH_2), 2854 (v. s, CH_2), 1667 (s, C=O), 1592 (m, C=C), 1504 (s, NH), 1434 (s, C=C), 1229 (m), 1105 (s, C–O–C), 1027 (m), 954 (w), 909 (w), 852 (w), 734 (w); ^1H NMR (360 MHz, $CDCl_3$): δ (ppm)=8.23 (br. s, 1H, NH), 7.95 (s, 1H, $C_{ar}H$), 6.99 [d, ^3J=11.3 Hz, 1H, CH=CH–C*H*=C(CO)], 6.32 [v. t, $^3J\cong$10.9 Hz, 1H, CH=C*H*–CH=C(CO)], 5.96 [v. q, $^3J\cong$9.1 Hz, 1H, C*H*=CH–CH=C(CO)], 3.87 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 2.70 (t, ^3J=6.5 Hz, 2H, CH_2), 2.21 (v. q, $^3J\cong$8.0 Hz, 2H, CH_2), 2.04 (d, ^4J=0.7 Hz, 3H, =CCH_3), 1.68–1.65 (m, 2H, CH_2), 1.47–1.10 (m, 14H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ

(ppm) = 168.4 (C=O), 149.4 ($C_{ar}OCH_3$), 143.3 ($C_{ar}OCH_3$), 141.2 ($C_{ar}OCH_3$), 137.9 ($C_{olef}H$), 133.5 (C_{ar}), 128.8 (C_{ar}), 127.6 (=CCH_3), 126.7 ($C_{olef}H$), 124.1 ($C_{olef}H$), 101.4 ($C_{ar}H$), 61.3 (OCH_3), 60.9 (OCH_3), 55.9 (OCH_3), 29.7 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 28.5 (CH_2), 28.1 (CH_2), 27.4 (CH_2), 27.2 (CH_2), 22.1 (CH_2), 12.6 (CH_3); MS (EI, 70 eV), *m/z* (%): 415 (100) [M^+], 400 (22), 384 (23), 182 (6), 167 (8), 152 (6). Anal. $C_{25}H_{37}NO_4$ (415.6): calcd C, 72.26; H, 8.97; found C, 72.42; H: 9.11.

5.1.23. (4*E*,6*Z*)-20,21,23-Trimethoxy-4-methyl-2-aza-bicyclo[17.3.1]tricosa-1(23),4,6,19,21-pentaen-3-one (12e). Procedure E was performed with the anilide **11e** (50 mg, 109 μmol) and first generation of Grubbs catalyst (8.3 mg, 11.0 μmol, 10 mol%) in DCM (200 mL). After flash chromatography (P/EA 90/10), the product was obtained (41 mg, 96 μmol, 87%) as a white solid. TLC: R_f = 0.57 (P/EA/DCM 50/10/50) [CAM, UV]; ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 8.29 (s br, 1H, NH), 7.99 (s, 1H, $C_{ar}H$), 7.03 [d, ^3J = 11.1 Hz, 1H, CH=CH–C*H*=C(CO)], 6.33 [v. t, $^3J \cong$ 11.0 Hz, 1H, CH=C*H*–CH=C(CO)], 5.90 [v. q, $^3J \cong$ 9.0 Hz, 1H, C*H*=CH–CH=C(CO)], 3.87 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 2.65 (t, ^3J = 7.1 Hz, 2H, CH_2), 2.27 (v. q, $^3J \cong$ 7.1 Hz, 2H, CH_2), 2.04 (s, 3H, =CCH_3), 1.61–1.57 (m, 2H, CH_2), 1.47–1.27 (m, 16H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 167.5 (C=O), 149.4 ($C_{ar}OCH_3$), 143.0 ($C_{ar}OCH_3$), 141.1 ($C_{ar}OCH_3$), 138.4 ($C_{olef}H$), 133.0 (C_{ar}), 129.4 (C_{ar}), 127.7 (=CCH_3), 126.2 ($C_{olef}H$), 123.7 ($C_{olef}H$), 101.6 ($C_{ar}H$), 61.1 (OCH_3), 61.0 (OCH_3), 55.9 (OCH_3), 29.6 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.5 (CH_2), 28.0 (CH_2), 27.9 (CH_2), 27.7 (CH_2), 27.7 (CH_2), 27.2 (CH_2), 22.7 (CH_2), 12.6 (CH_3); MS (EI, 70 eV), *m/z* (%): 429 (100) [M^+], 414 (21), 398 (22), 386 (8), 365 (7), 335 (7), 322 (7), 292 (14), 280 (10), 249 (8), 236 (5), 206 (6), 182 (8), 167 (8), 152 (7), 95 (6), 40 (7). Anal. $C_{26}H_{39}NO_4$ (429.6): calcd C, 72.69; H, 9.15; found C, 72.79; H: 8.98.

5.1.24. 2-Methylpent-2-enoic acid (2,4,5-trimethoxy-3-tridec-12-enylphenyl)-amide (13). To 2-methylpent-2-enoic acid (30 mg, 263 μmol) dissolved in THF (0.3 mL), HOBt (42 mg, 322 μmol) and DCC (66 mg, 322 μmol) were added. The mixture was placed under argon atmosphere and stirred for 5 min at rt. Aniline **10e** (30 mg, 83 μmol) dissolved in THF (0.2 mL) was added. The mixture was stirred for 48 h at rt. Diethyl ether (5 mL) and water (5 mL) were added. The aqueous layer was extracted twice with diethyl ether (2×5 mL). The combined organic layers were washed with saturated $NaHCO_3$ (10 mL), brine (10 mL), dried (Na_2SO_4) and concentrated in vacuo. After flash chromatography (P/EA 90/10), the product was obtained (26 mg, 57 μmol, 69%) as a transparent oil. TLC: R_f = 0.39 (P/EA 90/10) [CAM, UV]; ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 7.92 (s, 1H, $C_{ar}H$), 7.68 (s, 1H, NH), 5.82 (m, 2H, CH_2=C*H*), 5.13 (d, ^3J = 17.2 Hz, 1H, H_{trans}CH=CH), 5.06 (d, ^3J = 10.2 Hz, 1H, H_{cis}CH=CH), 4.98 (br. d, ^3J = 17.2 Hz, 1H, H_{trans}CH=CH), 4.91 (br. d, ^3J = 10.2 Hz, 1H, H_{cis}CH=CH_2), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 2.61 (v. t, $^3J \cong$ 6.4 Hz, 2H, C*H*$_2C_{ar}$), 2.52–2.47 (m, 2H, CH_2=CHC*H*$_2$), 2.28–2.22 [m, 1H, CH_2C*H*(CO)CH_3], 2.02 (v. q, $^3J \cong$ 7.0 Hz, 2H, CH_2=CHC*H*$_2$), 1.56–1.50 (m, 2H, CH_2), 1.36–1.26 (m, 19H, CH_3, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 174.0 (C=O), 149.3 ($C_{ar}O$), 143.5 ($C_{ar}O$), 140.1 ($C_{ar}O$), 139.4 (H*C*=CH_2), 135.6 (CH_2H*C*=CH_2), 129.5 (C_{ar}), 127.3 (C_{ar}), 117.4 (HRC=*C*H$_2$), 114.2 (HC=*C*H$_2$), 102.9 ($C_{ar}H$), 61.5 (OCH_3), 61.0 (OCH_3), 56.0 (OCH_3), 42.7 [C*H*(CO)CH_3], 38.5 [C*H*$_2$CH(CO)CH_3], 33.9 (CH_2), 30.7 (CH_2), 30.1 (CH_2), 29.8 (CH_2), 29.7 (2 CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 24.9 (CH_2), 17.6 (CH_3); MS (ESI), *m/z* (%): 460.9 (100) [M+H^+].

5.1.25. 20,21,23-Trimethoxy-4-methyl-2-aza-bicyclo-[17.3.1]tricosa-1(23),6,19,21-tetraen-3-one (14). Procedure E was performed with anilide **13** (26 mg, 57 μmol) and Grubbs catalyst (4.7 mg, 5.7 μmol, 10 mol%) in DCM (113 mL). After flash chromatography (P/EA 90/10), the product was obtained (21 mg, 49 μmol, 86%) as a white solid. The d.r. of the product was 66:34. It was not possible to determine which isomer was the major product. TLC: R_f = 0.62 (P/EA/DCM 50/10/50) [CAM, UV]; ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 7.96 (br. s, 0.33H, NH-minor), 7.93 (br. s, 0.66H, NH-major), 7.72 (s, 0.33H, C_{ar}H-minor), 7.66 (s, 0.66H, $C_{ar}H$), 5.50 (m, 2H, CH=CH), 3.85 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 2.65–1.97 (m, 6H, CH_2), 1.63–1.58 (m, 2H, CH_2), 1.30–1.27 (m, 20H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 174.2 (C=O, major), 174.1 (C=O, minor), 149.3 (C_{ar}-OCH_3, major), 149.3 ($C_{ar}OCH_3$, minor). 143.6 ($C_{ar}OCH_3$), 141.3 ($C_{ar}OCH_3$), 134.2 ($C_{olef}H$, major), 133.3 ($C_{olef}H$, minor). 129.3 (C_{ar}), 129.4 (C_{ar}), 127.3 (=CCH_3), 126.7 ($C_{olef}H$, major), 126.0 ($C_{olef}H$, minor), 102.9 ($C_{ar}H$, major), 102.5 ($C_{ar}H$, minor), 61.2 (OCH_3 minor), 61.1 (OCH_3, major), 61.0 (OCH_3 minor), 61.0 (OCH_3, major), 56.0 (OCH_3), 43.7 (CH_2), 43.3 (CH_2), 37.8 (CH_2), 32.5 (CH_2), 32.2 (CH_2, major), 29.5 (CH_2), 28.9 (CH_2), 28.7 CH_2), 28.6 CH_2), 28.6 (CH_2), 28.5 (CH_2), 28.3 (CH_2), 28.1 (CH_2), 27.8 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 24.2 (CH_2), 23.6 (CH_2), 22.7 (CH_2), 18.1 (CH_3, major), 17.1 (CH_3, minor); MS (EI, 70 eV), *m/z* (%): 431 (100) [M^+], 416 (21), 400 (5), 208 (5), 182 (8), 167 (10), 149 (10), 71 (6), 57 (12), 41 (7); HRMS: *m/z* calcd for $C_{26}H_{41}NO_4$: 431.3036; found 431.3033.

5.1.26. (4*E*,6*Z*)-21-Methoxy-4-methyl-2-aza-bicyclo-[15.3.1]henicosa-1(21),4,6,17,18(21)-tetraen-3,18,19-trione (15). General procedure F was performed with compound **12c** (28 mg, 69 μmol). The product was purified by flash chromatography (P/EA 75/25). The *ortho*-quinone (8.0 mg, 21 μmol, 30%) was isolated as a red film. TLC: R_f = 0.22 (P/EA 75/25) [CAM, UV]. ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm) = 8.57 (s br, 1H, NH), 7.31 (s, 1H, $C_{quin}H$), 7.05 [d, ^3J = 11.1 Hz, 1H, CH=CH–C*H*=C(CO)], 6.33 [v. t, $^3J \cong$ 10.9 Hz, 1H, CH=C*H*–CH=C(CO)], 6.12 [v. q, $^3J \cong$ 9.1 Hz, 1H, C*H*=CH–CH=C(CO)], 3.94 (s, 3H, OCH_3), 2.66 (br, 1H, CH_2), 2.29 (br, 2H, CH_2), 2.19 (s, 3H, =CCH_3), 1.58–1.24 (m, 16H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 180.3 (C_{quin}=O), 179.4 (C_{quin}=O), 168.2 (C=O), 159.3 (C-20), 144.1 (C_{quin}), 140.9 (C-5), 131.9 (C-2), 129.5 (C_{quin}), 129.2 (C-3), 123.3 (C-4), 107.1 (C-18), 62.6 (OCH_3), 29.6 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 28.6 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 27.4 (CH_2), 26.0 (CH_2), 21.8 (CH_2), 12.3 (CH_3); MS (EI, 70 eV), *m/z* (%): 371 (100) [M^+], 354 (22), 340 (10), 328 (12), 274 (6), 244 (6), 178 (5), 152 (24), 138 (14), 110 (44), 95 (30), 79

(32), 67 (40), 55 (22), 41 (36); HRMS: *m/z* calcd for $C_{22}H_{29}NO_4$: 371.2097; found 371.2086.

5.1.27. (*4E,6Z*)-21,23-Dimethoxy-4-methyl-2-aza-bicyclo[17.3.1]tricosa-1,4,6,19(23),21-pentaen-3,20-dione (16). General procedure F was performed with compound **12e** (38 mg, 89 μmol). The amount of reagents and solvents was adjusted accordingly. The mixture was stirred at −10 °C during 40 min. After the work-up, the product was purified by flash chromatography (P/EA 90/10). The aza-quinone (24 mg, 57 μmol, 64%) was isolated as a yellow film. TLC: R_f=0.67 (P/EA 50/50) [CAM, UV]; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm)=7.28 (d, ^3J=11.1 Hz, 1H, CH=CH–C*H*=C(CO)], 6.36 [v. t, $^3J\cong$10.9 Hz, 1H, CH=C*H*–CH=C(CO)], 5.92 [v. q, $^3J\cong$9.1 Hz, 1H, C*H*=CH–CH=C(CO)], 5.80 (s, 1H, $C_{quin}H$), 4.01 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 2.55 (v. t, $^3J\cong$7.0 Hz, 1H, $C_{quin}CH_2$), 2.20 (v. q, $^3J\cong$7.9 Hz, 2H, CH_2), 2.04 (s, 3H, =CCH_3), 1.52–1.24 (m, 20H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=182.3 (C_{quin}=O), 182.3 (C_{quin}=N), 158.7 (C=O), 159.3 (C-20), 155.7 (C_{quin}), 153.8 (C_{quin}), 141.9 (C-5), 136.0 (C-3), 132.5 (C-2), 131.0 (C_{quin}), 123.9 (C-4), 107.1 ($C_{quin}H$), 62.6 (C-22-O*C*H_3), 56.1 (C-19-O*C*H_3) 28.8 (CH_2), 28.5 (CH_2), 28.3 (CH_2), 28.0 (CH_2), 28.0 (CH_2), 27.9 (CH_2), 27.6 (CH_2), 27.6 (CH_2), 27.0 (CH_2), 26.9 (CH_2), 23.0 (CH_2), 11.6 (CH_3); MS (EI, 70 eV), *m/z* (%): 413 (100) [M^+], 398 (22), 382 (24), 354 (14), 318 (5), 274 (10), 242 (11), 229 (10), 180 (20), 164 (14), 136 (10), 110 (14), 95 (25), 79 (42), 67 (40), 55 (36), 41 (50); HRMS: *m/z* calcd for $C_{25}H_{35}NO_4$: 413.2566; found 413.2582.

5.1.28. 1,4-Di-*iso*-propoxy-2-methoxy-3-dodec-11-enyl-benzene (18). Procedure G was performed with 12-iodododec-1-ene (**7d**) (633 mg, 2.15 mmol) and 1,4-di-*iso*-propoxy-2-methoxy-benzene (**17**)[26] (3.06 g, 3.06 mmol). After flash chromatography (P/EA 99/01), the product was isolated (517 mg, 1.32 mmol, 61%) as a light yellow oil. A by product 2,5-di-*iso*-propoxy-1-methoxy-3-dodec-11-enyl benzene was also isolated (33mg, 0.08 mmol, 4%) as a colorless oil. TLC: R_f=0.51 (P/EA 95/5) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3075 (w, =CH_2), 2929 (v. s, CH_2), 2856 (s, CH_2), 1640 (m, C=C), 1587 (w, C_{ar}=C_{ar}), 1478 (s, CO), 1251 (s, COC), 1118 (s, COC), 983 (m, RCH=CH_2), 909 (m, RCH=CH_2), 787 (m), 775 (w, CH); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=6.68 (d, ^3J=8.9 Hz, 1H, $C_{ar}H$), 6.51 (d, ^3J=8.9 Hz, 1H, $C_{ar}H$), 5.82 (ddt, ^3J=17.1 Hz, ^3J=10.2 Hz, ^3J=6.2 Hz, 1H, CH_2=C*H*R), 5.03–4.98 (m, 1H, H_{trans}CH=CHR), 4.96–4.93 (m, 1H, H_{cis}-CH=CHR), 4.43 [sept., ^3J=6.2 Hz, 2H, OC*H*$(CH_3)_2$], 3.84 (s, 3H, OCH_3), 2.61 (t, ^3J=7.7 Hz, 2H, CH_2Ar), 2.04 (v. q, $^3J\cong$7.0 Hz, 2H, CH_2=CHCH_2), 1.55–1.49 (m, 2H, CH_2), 1.33–1.29 [m, 26H, CH_2, OCH(CH_3)$_2$]; ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=151.0 (C_{ar}O*i*Pr), 150.0 (C_{ar}O*i*Pr), 144.8 (C_{ar}OMe), 139.4 (HR*C*=CH_2), 127.5 ($C_{ar}CH_2$), 114.7 ($C_{ar}H$), 114.2 (HRC=*C*H_2), 108.4 ($C_{ar}H$), 71.9 [O*C*H$(CH_3)_2$], 70.5 [O*C*H$(CH_3)_2$], 60.7 (OCH_3), 34.0 (CH_2), 30.1 (CH_2), 30.1 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 24.3 (CH_2), 22.5 [CH(*C*H_3)$_2$], 22.4 [CH(*C*H_3)$_2$]; MS (EI, 70 eV), *m/z* (%): 390 (70) [M^+], 348 (22), 306 (100), 195 (6), 153 (47), 141 (6), 125 (14), 107 (10), 75 (6), 55 (10), 43 (13). Anal. $C_{25}H_{42}O_3$ (390.6): calcd C, 76.87; H, 10.74; found C, 76.86; H: 10.79.

5.1.29. 1,4-Di-*iso*-propoxy-3-dodec-11-enyl-2-methoxy-5-nitrobenzene (19). Procedure B was performed with 1,4-di-*iso*-propoxy-2-methoxy-3-dodec-11-enylbenzene (**18**) (507 mg, 1.30 mmol). After flash chromatography (P/EA 98/02), the product was obtained (472 mg, 1.08 mmol, 83%) as a yellow oil. TLC: R_f=0.43 (P/EA 95/05) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3075 (w, =CH), 2977 (s, CH_3), 2926 (v. s, CH_2), 2853 (s, CH_2), 1640 (m, C=C), 1570 (m, C_{ar}=C_{ar}), 1522 (s, NO_2), 1471 (s, C_{ar}=C_{ar}), 1383 (m, CH_3), 1371 (m, CH_3), 1345 (s, CN), 1241 (s, COC), 1122 (s, COC), 974 (w, RCH=CH_2), 910 (m, RCH=CH_2), 787 (w, CH); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=7.28 (s, 1H, $C_{ar}H$), 5.81 (ddt, ^3J=17.0 Hz, ^3J=10.1 Hz, ^3J=6.8 Hz, 1H, CH_2=C*H*R), 5.01–4.97 (m, 1H, H_{trans}CH=CHR), 4.94–4.91 (m, 1H, H_{cis}-CH=CHR), 4.52 [sept., ^3J=6.1 Hz, 1H, OC*H*$(CH_3)_2$], 4.11 [sept., ^3J=6.1 Hz, 1H, OC*H*$(CH_3)_2$], 3.91 (s, 3H, OCH_3), 2.63 (t, ^3J=7.9 Hz, 2H, CH_2Ar), 2.04 (v. q, $^3J\cong$7.0 Hz, 2H, CH_2=CHCH_2), 1.55–1.49 (m, 2H, CH_2), 1.38–1.26 [m, 26H, CH_2, OCH(CH_3)$_2$]; ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=153.4 (C_{ar}O*i*Pr), 146.2 (C_{ar}O*i*Pr), 144.6 (C_{ar}OMe), 139.5 (C_{ar}), 139.4 (HR*C*=CH_2), 133.7 (C_{ar}), 114.2 (HRC=*C*H_2), 109.4 ($C_{ar}H$), 78.1 [O*C*H$(CH_3)_2$], 71.8 [O*C*H$(CH_3)_2$], 61.0 (OCH_3), 34.0 (CH_2), 30.2 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 25.5 (CH_2), 22.4 [CH(*C*H_3)$_2$], 22.1 [CH(*C*H_3)$_2$]; MS (EI, 70 eV), *m/z* (%): 435 (22) [M^+], 393 (100), 351 (8), 334 (26), 316 (56), 284 (20), 256 (5), 198 (24), 180 (22), 168 (30), 153 (18), 139 (9), 123 (12), 95 (12), 69 (18), 55 (32), 43 (60). Anal. $C_{25}H_{41}NO_5$ (435.6): calcd C, 68.93; H, 9.49; found C, 69.05; H: 9.55.

5.1.30. 1,4-Di-*iso*-propoxy-3-dodec-11-enyl-2-methoxy-phenyl amine (20). Procedure C was performed with 1,4-di-*iso*-propoxy-3-dodec-11-enyl-2-methoxy-5-nitrobenzene (**19**) (200 mg, 460 μmol). After flash chromatography (P/EA 90/10), the product was obtained (147 mg, 363 μmol, 79%) as a yellow oil. TLC: R_f=0.17 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3450 (w, NH_2), 3360 (w, NH_2), 3075 (w, =CH), 2973 (S, CH_3), 2925 (v. s, CH_2), 2853 (s, CH_2), 1640 (s, C=C), 1613 (s, N–H), 1483 (s, C_{ar}=C_{ar}), 1381 (m, CH_3), 1371 (m, CH_3), 1222 (s, COC), 1110 (s, COC), 1025 (s), 949 (w, RCH=CH_2), 910 (m, RCH=CH_2), 816 (w, CH); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=6.19 (s, 1H, $C_{ar}H$), 5.80 (ddt, ^3J=17.0 Hz, ^3J=10.2 Hz, ^3J=6.6 Hz, 1H, CH_2=C*H*R), 5.01–4.96 (m, 1H, H_{trans}CH=CHR), 4.94–4.91 (m, 1H, H_{cis}CH=CHR), 4.39 [sept., ^3J=6.1 Hz, 1H, OC*H*$(CH_3)_2$], 4.16 [sept., ^3J=6.1 Hz, 1H, OC*H*$(CH_3)_2$], 3.75 (s, 3H, OCH_3), 3.38 (br. s, 2H, NH_2), 2.56 (t, ^3J=8.0 Hz, 2H, CH_2Ar), 2.04 (v. q, $^3J\cong$7.0 Hz, 2H, CH_2=CHCH_2), 1.55–1.49 (m, 2H, CH_2), 1.36–1.28 [m, 26H, CH_2, OCH(CH_3)$_2$]; ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=147.3 (C_{ar}O*i*Pr), 141.4 (C_{ar}O*i*Pr), 139.3 (HR*C*=CH_2), 137.3 (C_{ar}), 136.3 (C_{ar}), 131.2 (C_{ar}), 114.2 (HRC=*C*H_2), 102.2 ($C_{ar}H$), 75.0 [O*C*H$(CH_3)_2$], 71.1 [O*C*H$(CH_3)_2$], 60.8 (OCH_3), 33.9 (CH_2), 30.3 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 25.7 (CH_2), 22.9 [CH(*C*H_3)$_2$], 22.4 [CH(*C*H_3)$_2$]; MS (EI, 70 eV), *m/z* (%): 405 (60) [M^+], 362 (30), 320 (100), 288 (8), 178 (6), 167 (10), 152 (20), 138 (10), 123 (8), 55 (6), 43 (10). Anal. $C_{25}H_{43}NO_3$ (405.6): calcd C, 74.03; H, 10.73; found C, 73.99; H: 10.69.

5.1.31. 2-Methyl-penta-2,4-dienoic acid (1,4-di-*iso*-propoxy-3-dodec-11-enyl-2-methoxyphenyl)-amide (21). Procedure D was performed with the aniline **20** (116 mg, 286 μmol). After flash chromatography (P/EA 95/05), the product was obtained (93 mg, 186 μmol, 65%) as a light yellow oil. TLC: R_f=0.38 (P/EA 90/10) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3432 (m, NH), 2974 (s, CH_2), 2926 (v. s, CH_2), 2853 (s, CH_2), 1673 (s, C=O), 1600 (m, C=C), 1514 (s), 1468 (m), 1434 (m), 1420 (s), 1381 (m, CH_3), 1371 (m, CH_3), 1222 (s, C–N), 1110 (s, COC), 1031 (w), 1007 (s, RCH=CH_2), 914 (m, RCH=CH_2); ^{1}H NMR (360 MHz, $CDCl_3$): δ (ppm)=8.14 (s, 1H, NH), 8.01 (s, 1H, C_{ar}H), 7.03 [d, ^3J=10.2 Hz, 1H, CH_2=CH–C*H*=C(CO)], 6.66 (ddd, ^3J=16.9 Hz, ^3J=10.6 Hz, ^3J=10.2 Hz, 1H, CH_2=C*H*–CH=C), 5.80 (ddt, ^3J=17.2 Hz, ^3J=10.2 Hz, ^3J=6.8 Hz, 1H, CH_2=C*H*R), 5.54 (d, ^3J=16.9 Hz, 1H, H_{trans}-CH=CH–CH=C), 5.43 (d, ^3J=10.2 Hz, 1H, H_{cis}-CH=CH–CH=C), 5.01–4.95 (m, 1H, H_{trans}CH=CHR), 4.93–4.90 (m, 1H, H_{cis}CH=CHR), 4.57 [sept., ^3J=6.1 Hz, 1H, OC*H*(CH_3)$_2$], 4.13 [sept., ^3J=6.1 Hz, 1H, OC*H*(CH_3)$_2$], 3.81 (s, 3H, OCH_3), 2.58 (t, ^3J=7.9 Hz, 2H, CH_2Ar), 2.09 (d, ^4J=0.9 Hz, 3H, =CC*H*$_3$), 2.03 (v. q, $^3J\cong$7.0 Hz, 2H, CH_2=CHC*H*$_2$), 1.55–1.50 (m, 2H, CH_2), 1.33–1.29 [m, 26H, CH_2, OCH(C*H*$_3$)$_2$]; ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=166.3 (C=O), 147.0 (C_{ar}-O*i*Pr), 144.8 (C_{ar}OCH$_3$), 139.3 (HR*C*=CH_2), 138.6 (C_{ar}-O*i*Pr), 134.6 (C_{olef}H), 132.2 (C_{olef}H), 131.5 (=*C*CH$_3$), 130.1 ($C_{ar}CH_2$), 128.3 (C_{ar}NH), 123.4 (=CH–HC=*C*H$_2$), 114.2 (HRC=*C*H$_2$), 105.3 (C_{ar}H), 76.7 [O*C*H(CH_3)$_2$], 70.9 [O*C*H(CH_3)$_2$], 60.8 (OCH_3), 33.9 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 25.6 (CH_2), 22.8 [CH(*C*H$_3$)$_2$], 22.4 [CH(*C*H$_3$)$_2$], 13.2 (CH_3); MS (EI, 70 eV), *m*/*z* (%): 499 (40) [M^+], 456 (16), 414 (20), 362 (5), 320 (14), 95 (100), 67 (23), 41 (6). Anal. $C_{31}H_{49}NO_4$ (499.7): calcd C, 74.51; H, 9.87; found C, 74.60; H: 9.88.

5.1.32. (4*E*,6*Z*)-20,22-Di-*iso*-propoxy-19-methoxy-4-methyl-2-aza-bicyclo[16.3.1]docosa-1(22),4,6,18,20-pentaen-3-one (22). Procedure E was performed with the anilide **21** (50 mg, 100 μmol) and Grubbs catalyst (8.2 mg, 10.1 μmol, 10 mol%) in DCM (200 mL). After flash chromatography (P/EA 90/10), the product was obtained (41 mg, 87 μmol, 87%) as a light green transparent oil. TLC: R_f=0.85 (P/EA/DCM 50/10/50) [CAM, UV]; IR (film): $\tilde{\nu}$ (cm^{-1})=3428 (br, NH), 2974 (s, $\tilde{\nu}$ CH_3), 2926 (v. s, CH_2), 2854 (v. s, CH_2), 1667 (s, C=O), 1592 (m, C=C), 1504 (s, NH), 1434 (s, C=C), 1382 [s, $(CH_3)_2$CH], 1332 [m, $(CH_3)_2$CH], 1229 (m), 1105 (s, C–O–C), 1027 (m), 954 (w), 909 (w), 852 (w), 734 (w); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm)=8.24 (br. s, 1H, NH), 7.93 (s, 1H, C_{ar}H), 6.98 [d, ^3J=11.3 Hz, 1H, CH=CH–C*H*=C(CO)], 6.31 [v. t, $^3J\cong$10.9 Hz, 1H, CH=C*H*–CH=C(CO)], 5.94 [v. q, $^3J\cong$9.0 Hz, 1H, C*H*=CH–CH=C(CO)], 4.58 [sept., ^3J=6.1 Hz, 1H, OC*H*(CH_3)$_2$], 4.01 [sept., ^3J=6.1 Hz, 1H, OC*H*(CH_3)$_2$], 3.81 (s, 3H, OCH_3), 2.74–2.70 (m, 2H, CH_2), 2.04 (br, 3H, =CC*H*$_3$), 1.70–0.85 [m, 30H, CH_2, CH(C*H*$_3$)$_2$]; ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=168.1 (C=O), 147.2 (C_{ar}O), 144.6 (C_{ar}O), 139.0 (C_{ar}O), 137.9 (C_{olef}H), 133.9 (C_{ar}), 129.3 (C_{ar}), 128.4 (=*C*CH$_3$), 126.7 (C_{olef}H), 124.3 (C_{olef}H), 104.0 (C_{ar}H), 76.9 [O*C*H(CH_3)$_2$], 71.0 [O*C*H(CH_3)$_2$], 60.8 (OCH_3), 30.1 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 28.9 (CH_2), 28.7 (CH_2), 28.6 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 27.4 (CH_2), 23.3 (CH_2), 22.9 [CH(*C*H$_3$)$_2$], 22.5 [CH(*C*H$_3$)$_2$], 22.4 [CH(*C*H$_3$)$_2$], 22.4 [CH(*C*H$_3$)$_2$], 12.8 (CH_3); MS (EI, 70 eV), *m*/*z* (%): 471 (72) [M^+], 428 (38), 386 (100), 358 (21), 152 (12), 150 (11), 123 (9), 95 (18), 67 (11), 55 (6), 41 (6); HRMS: *m*/*z* calcd for $C_{29}H_{45}NO_4$: 471.3349; found 471.3357.

5.1.33. (4*E*,6*Z*)-20-Hydroxy-22-*iso*-propoxy-19-methoxy-4-methyl-2-aza-bicyclo[16.3.1]docosa-1(21),4,6,18(22),19-pentaen-3-one (23). To a solution of the macrocyclic compound **22** (24.0 mg, 51.0 μmol) in DCM (4.0 mL) cooled to −10 °C under argon atmosphere, BCl_3 (1.0 mL, 1.0 mmol, 1.0 M in hexane) was slowly added. The resulting solution was stirred at −10 °C for 40 min. No more starting material remained according to TLC (P/EA 75/25). The mixture was then quenched by the careful addition of 3.0 mL of NaOH (4.0 M in water). Separation of the organic layer was followed by further extraction of the aqueous layer with DCM (2×5 mL). The combined organic layers were washed, dried over Na_2SO_4 and concentrated. After flash chromatography (P/EA 80/20), the *para*-quinone was obtained (7.0 mg, 18.2 μmol, 36%) as a yellow oil. The mono-deprotected (14.0 mg, 32.6 μmol, 64%) compound was isolated as a white solid. TLC: R_f=0.29 (P/EA 75/25) [CAM, UV]; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm)=8.29 (br. s, 1H, NH), 8.03 (s, 1H, CarH), 7.18 (s, 1H, OH), 6.97 [d, $^3J\cong$11.3 Hz, 1H, CH=CH–C*H*=C(CO)], 6.31 [v. t, $^3J\cong$10.9 Hz, 1H, CH=C*H*–CH=C(CO)], 5.95 [v. q, $^3J\cong$9.1 Hz, 1H, C*H*=CH–CH=C(CO)], 4.00 [sept., ^3J=6.1 Hz, 1H, OC*H*(CH_3)$_2$], 3.83 (s, 3H, OCH_3), 2.76–2.70 (m, 2H, CH_2), 2.37–2.35 (m, 1H, CH_2), 2.06–2.05 (m, 3H, =CCH_3), 1.70–0.85 [m, 23H, CH_2, CH(C*H*$_3$)$_2$]; ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm)=168.8 (C=O), 146.2 (C_{ar}OH), 142.2 (C_{ar}OCH$_3$), 138.7 (C_{ar}O*i*Pr), 138.1 (C_{olef}H), 133.7 (C_{ar}), 128.7 (C_{ar}), 127.1 (C_{olef}H), 124.2 (C_{olef}H), 104.8 (C_{ar}H), 77.1 [O*C*H(CH_3)$_2$], 60.9 (OCH_3), 30.0 (CH_2), 29.6 (CH_2), 28.9 (CH_2), 28.6 (CH_2), 28.4 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 27.3 (CH_2), 23.4 (CH_2), 22.8 [CH(*C*H$_3$)$_2$], 22.3 [CH(*C*H$_3$)$_2$], 12.9 (CH_3).

5.1.34. 19-Methoxy-4-methyl-2-aza-bicyclo[16.3.1]dodocosa-1(21),4,6,18-tetraene-3,20,22-trione (2). To a solution of the macrocyclic compound **22** (45.0 mg, 106 μmol) in DCM (10.4 mL) cooled to −10 °C under argon atmosphere, BCl_3 (1.0 mL, 1.0 mmol, 1.0 M in hexane, 10 equiv) was slowly added. The resulting solution was stirred at −10 °C for 2 h. Some mono deprotected material remained according to TLC (P/EA 75/25). BCl_3 (1.0 mL, 1.0 mmol, 1.0 M in hexane, 10 equiv) was slowly added. The mixture was then allowed to warm up to rt and stirred for 4 h. After a TLC control showing the completion of the reaction, the mixture was quenched by the careful addition of 5.0 mL of NaOH (4.0 M in water). Separation of the organic layer was followed by further extraction of the aqueous layer with DCM (2×10 mL). The combined organic layers were washed, dried over Na_2SO_4 and concentrated. After flash chromatography (P/EA 75/25), the *para*-quinone was obtained (31.0 mg, 90.9 μmol, 86%) as a yellow orange microcrystalline solid. TLC: R_f=0.84 (P/EA 75/25) [CAM, UV]; IR: $\tilde{\nu}$ (cm^{-1})=3557 (br, NH), 2917 (s, CH_2), 2847 (v. s, CH_2), 1695 (s, C=O), 1649 (s, C=O), 1607 (s, C=O), 1497 (s, NH), 1361 (s), 1320 (s), 1247 (m), 1194 (s, COC), 1042 (m), 962 (w), 864 (m), 798

(w), 737 (w), 691 (m); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.86 (s, 1H, NH), 7.25 (s, 1H, C_{quin}H), 7.07 [d, ^3J = 11.3 Hz, 1H, CH=CH–C*H*=C(CO)], 6.30 [v. t, $^3J \cong 11.0$ Hz, 1H, CH=C*H*–CH=C(CO)], 6.04 [v. q, $^3J \cong 9.1$ Hz, 1H, C*H*=CH–CH=C(CO)], 4.12 (s, 3H, OCH_3), 2.52 (t, $^3J = 6.7$ Hz 2H, $C_{quin}CH_2$), 2.24 (v. q, $^3J \cong 8.0$ Hz 2H, =CHCH_2), 1.98–1.96 (m, 3H, =CCH_3), 1.55–1.23 (m, 30H, CH_2); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ (ppm) = 184.5 (C_{quin}=O), 183.8 (C_{quin}=O), 168.8 (C=O), 156.9 (C_{quin}OMe), 140.2 (CH_2CH=CH), 138.1 (C_{quin}NH), 132.0 [CH=*C*(CO)], 129.2 *C*H=C(CO)], 128.6 (C_{quin}-CH_2), 123.8 (CH_2CH=*C*H), 111.3 (C_{quin}H), 61.7 (OCH_3), 29.6 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 28.2 (CH_2), 27.9 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 20.8 (CH_2), 12.5 (CH_3); MS (EI, 70 eV), *m*/*z* (%): 385 (100) [M^+], 368 (38), 342 (10), 314 (5), 300 (3), 274 (8), 272 (7), 244 (5), 152 (20), 121 (14), 110 (31), 95 (30), 67 (32), 55 (30), 41 (30). Anal. $C_{23}H_{31}NO_4$ (385.5): calcd C, 71.66; H, 8.11; found C, 71.78; H: 8.10.

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References and notes

1. (a) De Boer, C.; Meulman, P. A.; Wnuk, R. J.; Peterson, D. H. *J. Antibiot.* **1970**, *23*, 442–447. (b) Sasaki, K.; Rinehart, K. J.; Slomp, G.; Grostic, M. F.; Olson, E. C. *J. Am. Chem. Soc.* **1970**, *92*, 7591–7593.
2. Supko, J. G.; Hickman, R. L.; Grever, M. R.; Malspeis, L. *Cancer Chemother. Pharmacol.* **1995**, *36*, 305–315.
3. Reviews: (a) Buchner, J.; Walter, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1098–1113. (b) Buchner, J.; Richter, K. *J. Cell. Phys.* **2001**, *188*, 281–290. (c) Buchner, J. *Trends Biochem. Sci.* **1999**, *24*, 136–141.
4. Whitesell, L.; Mimnaugh, E. G.; De Costa, B.; Myers, C. E.; Neckers, L. M. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 8324–8328.
5. (a) Dolinski, K. J.; Cardenas, M. E.; Heitman, J. *Mol. Cell Biol.* **1998**, *18*, 7344–7352. (b) Webb, C. P.; Hose, C. D.; Koochekpour, S.; Jeffers, M.; Oskarsson, M.; Sausville, E.; Monks, A.; Vande Wourde, G. F. *Cancer Res.* **2000**, *60*, 342–349.
6. (a) Stebbins, C. E.; Russo, A. A.; Schneider, C.; Rosen, N.; Hartl, F. U.; Pavletich, N. P. *Cell* **1997**, *89*, 239–250. (b) Roe, S. M.; Prodromou, C.; O'Brien, R.; Ladbury, J. E.; Piper, P. W.; Pearl, L. H. *J. Med. Chem.* **1999**, *42*, 260–266.
7. Review: Funayama, S.; Cordell, G. A. *Stud. Nat. Prod. Chem.* **2000**, *23*, 51–106.
8. Schill, G.; Merkel, C.; Zürcher, C. *Liebigs Ann. Chem.* **1977**, 288–296.
9. (a) Schnur, R. C.; Corman, M. L.; Gallaschun, R. J.; Cooper, B. A.; Dee, M. F.; Doty, J. L.; Muzzi, M. L.; DiOrio, C. I.; Barbacci, E. G.; Miller, P. E.; Morin, M. J.; Foster, B. A.; Pollack, V. A.; Savage, D. M.; Sloan, D. E.; Pustilnik, L. R.; Moyer, J. D.; Moyer, M. P. *J. Med. Chem.* **1995**, *38*, 3806–3812. (b) Schnur, R. C.; Corman, M. L.; Gallaschun, R. J.; Cooper, B. A.; Dee, M. F.; Doty, J. L.; Muzzi, M. L.; DiOrio, C. I.; Barbacci, E. G.; Miller, P. E.; Pollack, V. A.; Savage, D. M.; Sloan, D. E.; Pustilnik, L. R.; Moyer, J. D.; Moyer, M. P. *J. Med. Chem.* **1995**, *38*, 3813–3820. (c) Kuduk, S. D.; Zheng, F. F.; Sepp-Lorenzino, L.; Ouerfelli, Q.; Rosen, N.; Danishefsky, S. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1233–1238. (d) Kuduk, S. D.; Harris, C. R.; Zheng, F. F.; Sepp-Lorenzino, L.; Ouerfelli, Q.; Rosen, N.; Danishefsky, S. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1025–1028. (e) Kasuya, Y.; Lu, Z.-R.; Kopeckova, P.; Kopeček, J. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1303–1306. (f) Kasuya, Y.; Lu, Z.-R.; Kopeckova, P.; Kopeček, J. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2089–2091. (g) Hargreaves, R.; Davis, C. L.; Whitesell, L.; Skibo, E. B. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3075–3078.
10. (a) Andrus, M. B.; Meredith, E. L.; Simmons, B. L.; Soma Sekhar, B. B. V.; Hicken, E. J. *Org. Lett.* **2002**, *4*, 3549–3552. (b) Andrus, M. B.; Meredith, E. L.; Hicken, E. J.; Simmons, B. L.; Glancey, R. R.; Ma, W. *J. Org. Chem.* **2003**, *68*, 8162–8169.
11. Recent reviews: (a) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29. (b) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043. (c) Maier, M. E. *Angew. Chem., Int. Ed.* **2000**, *39*, 2073–2077. (d) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450. (e) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed.* **1997**, *36*, 2036–2056.
12. Bach, T.; Lemarchand, A. *Synlett* **2002**, 1302–1304.
13. (a) House, H. O.; Rasmusson, G. R. *J. Org. Chem.* **1961**, *26*, 4278–4281. (b) Piers, E.; Jung, G. L.; Ruediger, E. H. *Can. J. Chem.* **1987**, *65*, 670–682. (c) Elemes, Y.; Foote, C. S. *J. Am. Chem. Soc.* **1992**, *114*, 6044–6050. (d) Jefford, C. W.; Wang, Y.; Houk, K. N. *J. Org. Chem.* **1991**, *56*, 856–858.
14. (a) Takahashi, S.; Kusumi, T.; Sato, Y.; Inouye, Y.; Kakisawa, H. *Bull. Chem. Soc. Jpn* **1981**, *54*, 1777–1780. (b) Stefani, H. A.; Costa, I. M.; Zeni, G. *Tetrahedron Lett.* **1999**, *40*, 9215–9218.
15. Paquette, L. A.; Fabris, F.; Tae, J.; Gallucci, J. C.; Hofferberth, J. E. *J. Am. Chem. Soc.* **2000**, *122*, 3391–3398.
16. Garelli, N.; Vierling, P. *J. Org. Chem.* **1992**, *57*, 3046–3051.
17. (a) Nokami, J.; Ohtsuki, H.; Sakamoto, Y.; Mitsuoka, M.; Kunieda, N. *Chem. Lett.* **1992**, 1647–1650. (b) Dhillon, R. S.; Nayar, K.; Singh, J. *Tetrahedron Lett.* **1992**, *33*, 6015–6016.
18. (a) Chuit, P.; Boelsing, F.; Hausser, J.; Malet, G. *Helv. Chim. Acta* **1927**, *10*, 113–121. (b) Dabideen, D.; Blumenstein, M.; Mootoo, D. R. *Tetrahedron* **2000**, *56*, 9203–9211. (c) Mori, K.; Nishio, H. *Liebigs Ann. Chem.* **1991**, 253–257.
19. (a) Kitahara, Y.; Nagaoka, Y.; Matsumura, T.; Kubo, A. *Heterocycles* **1994**, *38*, 659–678. (b) Kitahara, Y.; Nakahara, S.; Shimizu, M.; Yonezawa, T.; Kubo, A. *Heterocycles* **1993**, *36*, 1909–1924.
20. Lee, V. J.; Branfman, A. R.; Herrin, T. R.; Rinehart, K. L. *J. Am. Chem. Soc.* **1978**, *100*, 4225–4236.
21. (a) Carpino, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 4397–4398. (b) Carpino, L. A.; El-Fayam, A. *J. Org. Chem.* **1994**, *59*, 695–698.
22. (a) Cameron, D. W.; Feutrill, G. I.; Patti, A. F.; Perlmutter, P.; Sefton, M. A. *Aust. J. Chem.* **1982**, *35*, 1501–1508. (b) Witiak, D. T.; Loper, J. T.; Ananthan, S.; Almerico, A. M.; Verhoef,

V. L.; Fillpi, J. A. *J. Med. Chem.* **1989**, *32*, 1636–1642. (c) Kozuka, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2415–2423. (d) Cheng, A. C.; Castagnoli, N. *J. Med. Chem.* **1984**, *27*, 513–518. (e) Michael, J. P.; Cirillo, P. F.; Denner, L.; Hosken, G. D.; Howard, A. S.; Tinkler, O. S. *Tetrahedron* **1990**, *46*, 7923–7932. (f) Luly, J. R.; Rapoport, H. *J. Org. Chem.* **1981**, *46*, 2745–2752. (g) Carreño, M. C.; Garcia Ruano, J. L.; Toledo, M. A.; Urbano, A. *Tetrahedron: Asymmetry* **1997**, *8*, 913–922.

23. Andrus, M. B.; Hicken, E. J.; Meredith, E. L.; Simmons, B. L.; Cannon, J. F. *Org. Lett.* **2003**, *5*, 3859–3862.
24. (a) Jacob, P.; Callery, P. S.; Shulgin, A. T.; Castagnoli, N. *J. Org. Chem.* **1976**, *41*, 3627–3629. (b) Syper, L.; Kloc, K.; Mlochowski, J.; Szulc, Z. *Synthesis* **1979**, 521–523. (c) Fanchiang, Y.-T.; Thomas, J. C.; Heh, J. C. K.; Gould, E. S. *Inorg. Chem.* **1977**, *16*, 1942–1945.
25. Snyder, C. D.; Rapoport, H. *J. Am. Chem. Soc.* **1972**, *94*, 227–231.
26. (a) Sala, T.; Sargent, M. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2593–2598. (b) Iinuma, M.; Iwashima, K.; Matsuura, S. *Chem. Pharm. Bull.* **1984**, *32*, 4935–4941.