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Synthesis of Natural Products on Solid Phases via Copper-Mediated Coupling: Synthesis of the Aristogin Family, Spiraformin A, and Hernandial

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The formation of natural products on solid phases via diaryl ether coupling is presented herein. Starting with either commercially-available or easily-producible benzoic, cinnamic, or propionic acids, all immobilized on Merrifield resin via a pentane linker, copper-mediated couplings yielded solid phase diaryl ethers in good yields. Both, phenol and resins containing aryl halides were used for these Ullmann-type couplings to generate resin-bound natural product derivatives. Through cleavage from the resin, eight naturally occurring substances isolated from *Aristolochia elegans, Hernandia nymphaeifolia*, *Spiraea formosana*, and *Kandelia candel* were prepared. To the best of our knowledge, four of these compounds, namely Aristogin D and F as well as Spiraformin A and compound **12** have never previously been synthesized. Gaining access to these natural products on solid supports, demonstrated the utility of diaryl ether formation for the development of combinatorial syntheses. Our approach to diaryl ethers on solid support offers the possibility of synthesizing libraries of natural product derivatives via combinatorial syntheses.

Introduction

Diaryl ethers are important lead structures because, on the one hand, they form polymers that are under investigation such as thermoplasts[1] and because, on the other hand, diaryl ethers are a common motif in many natural products like vancomycin,[2–4] teicoplanin[5] and piperazinomycin.[6–7]

Natural products bearing a diaryl ether moiety can be classified into acyclic and cyclic. Acyclic diaryl ethers are found as structural motifs in bisbenzylisoquinoline alkaloids,[8–11] in perrottetines,[12–14] quinoline alkaloids,[15] tetrahydroisoquinolines,[16] aporphines,[17–20] dibenzopyrans,[21] neolignans,[22] and biphenyl ethers.[23–26] Cyclic diaryl ethers can be found as a component of bis(benzoquinolines),[27,28] benzylisoquinoline alkaloids,[29,27] bis(bibenzyls),[30,31] cularines,[32] bastadines,[33,34] several peptidic diaryl ethers[35–38] and macrocyclic heptanoids,[39,40] as well as acerogenins[41,42] and curcumins (Figure 1).[43] Various methods were established for the formation of diaryl ethers in solution phase. The most popular of these reactions are either the palladium- and copper-catalyzed (Cu-mediated) ones or the diaryl ether formations via nucleophilic aromatic substitution (S_NAr).[44]

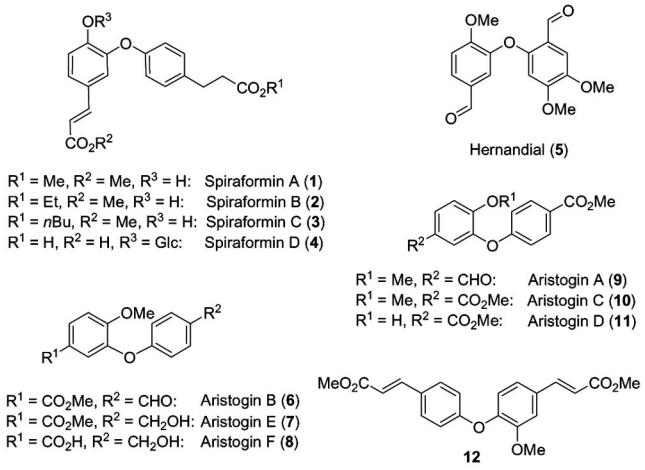

Figure 1. Selected natural products with diaryl ether motif (for other natural products with diaryl ether motif see references[45–50]).

Whereas synthetic procedures involving metal-catalyzed transformations make no special demands on the nature of the aromatic system, successful nucleophilic aromatic substitutions require the presence of strongly electron-withdrawing substituents on the aryl moiety. Very often, the synthesis of these diaryl ethers involves the conversion of aryls that contain at least one, or better two nitro functionalities.

Some macrocyclic natural products such as vancomycin or teicoplanin have been synthesized via nucleophilic aromatic substitution.[51–53] In fact, this concept has even been

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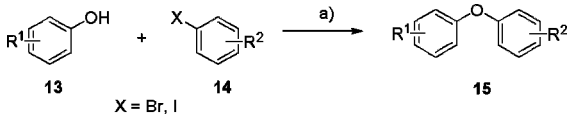
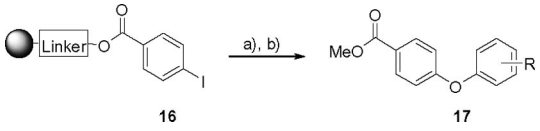
transferred successfully to solid-phase reactions (for natural product syntheses on solid supports see references[54–59]). The disadvantage of these substitution reactions is that one has to carry out additional steps to remove the activating functional group after diaryl ether formation. Thus, other synthetic methods have been investigated in order to identify a universally applicable synthetic procedure. Regarding this matter, the development of new catalysts and ligands for copper-[60–62] as well as palladium-catalyzed reactions have gained special attention.[63–65] In addition, several other methods[66–70] have been elaborated, such as the reaction of phenols with electrophiles like arylboronic acids which facilitate diaryl ether synthesis at room temperature under mild conditions.[71–73]

Among these methods, our group has investigated procedures in order to synthesize diaryl ethers on solid supports. We have recently developed a synthesis based on triazene-linked aryl fluorides and proceeding through the coordination of phenols and a copper species derived from $CuBr{\cdot}SMe_2$.[74] Moreover, in subsequent studies on non-triazene-linked aromatic systems, the copper-catalyzed transformations of halogenated phenyls as well as those with arylboronic acids were of special interest.[75] We found that phenols can be converted into diaryl ethers in excellent yields when reacted with solid-supported halogenated aryls,[76] under conditions similar to the syntheses first published by Song et al. (Scheme 1).[77–79]



Scheme 1. Diaryl ether formation in solution. *Reagents and conditions*: a) CuCl, Cs_2CO_3, TMHD, NMP, 80–120 °C, 12 h.[77–80]

Similar transformations have been successful through the reaction of boronic acids with phenols according to published procedures (known for solution phase chemistry). However, given the low number of commercially-available boronic acids and the necessity of repeating the coupling procedure several times, we have concentrated our research on the diaryl ether synthesis through aryl halogens (Scheme 2).

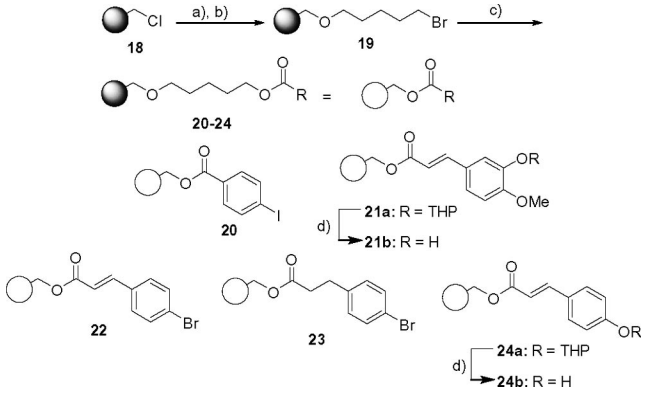


Scheme 2. Diaryl ether formation on solid supports. *Reagents and conditions*: a) phenol, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 120 °C, 12 h; b) KCN, MeOH, 90 °C, 12 h.[76]

The synthetic route to diaryl ethers through solid-phase synthesis described in Scheme 2 was performed with various phenols and halogenated aryls. The resulting resin-bound diaryl ethers were cleaved from the resin through either saponification/methanolysis or ozonolysis in high yields and purities. The success of diaryl ether formation through the reaction of phenols with resin-bound aryl halides encouraged us to apply this methodology to the synthesis of several natural products on solid supports. The advantage of transferring natural product synthesis to solid supports is quite obvious. With the identification of a practicable synthetic procedure on the resin, one can synthesize diverse library members of natural product derivatives in order to study the effect of modification of the original lead structure. Herein, we describe the successful synthesis of diverse structures found in *Hernandia nymphaeifolia*[9] (Hernandial), *Aristolochia elegans*[16,23,24] (Aristogin family), *Spiraea formosana*[22] (Spiraformin A), and *Kandelia candel*[80] (compound **12**) to demonstrate the utility of diaryl ether coupling on solid phases for the synthesis of natural products and their precursors.

Results and Discussion

For the synthesis of diaryl ethers on solid supports, an appropriate linker system had to be immobilized to guarantee minimized steric hindrance for the coupling reaction and the final cleavage step. The pentanediol linker[81] has been identified as an adequate spacer unit that—after transformation into a bromine-linker—allows the attachment of diverse benzoic, cinnamic and propanoic acids. In contrast to the direct linkage of acids to Merrifield resin, the resulting esters were stable under the conditions optimized for diaryl ether coupling on solid phases. Scheme 3 summarizes the previously published synthesis of the bromine-linker and the subsequent attachment of carboxylic acids to give resin-bound esters.[76]

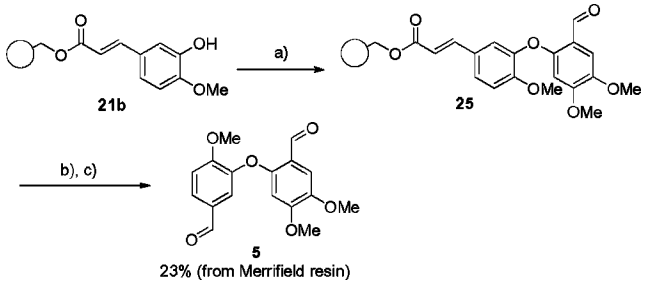


Scheme 3. Linker syntheses and immobilization of the first aryl moiety. *Reagents and conditions*: a) pentane-1,5-diol, DMF, NaH, 80 °C; b) CBr_4, PPh_3, CH_2Cl_2, 0 °C to room temp., 12 h; c) carboxylic acid, DMF, Cs_2CO_3, 80 °C, 12 h; d) PPTS, toluene, 90 °C, 3 h.

Crucial for the successful synthesis of resins **21** and **24** (Scheme 3) was the use of THP-protected cinnamic acids for the on-bead ester formation. The desired free phenols **21b** and **24b** had to be generated via the addition of PPTS and reaction in toluene. The immobilization of carboxylic acids yielded resins **20**–**24**, which could be used for diaryl ether formation with either aromatic halides or phenols.

Synthesis of Hernandial. The synthesis of Hernandial (**5**) was performed on resin **21b** through coupling with 2-bromo-4,5-dimethoxybenzaldehyde under conditions pre-

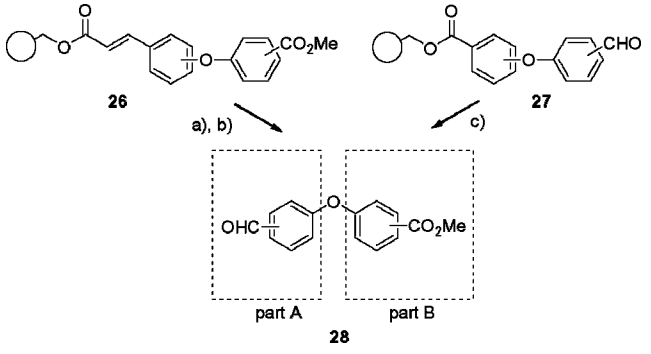
viously described by our group (Scheme 4).[76] The chosen linkage via a cinnamic ester yields resin-bound Hernandial precursor **25**, which can be cleaved from the solid support by ozonolysis in 20 s.



Scheme 4. Synthesis of Hernandial. *Reagents and conditions*: a) 2-bromo-4,5-dimethoxybenzaldehyde, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 12 h, 120 °C; b) O_3, CH_2Cl_2, room temp., 20 s; c) Me_2S, room temp., 30 min.

Syntheses of Aristogins A–F. Aristogins A, B, C, and E have been synthesized in liquid phase,[82–84] but to the best of our knowledge there is no synthetic protocol for the syntheses of Aristogins D and F, neither referring to liquid nor to solid-phase syntheses.

Due to the structure of the Aristogins A–F, namely the presence of either an aldehyde/alcohol group on one of the aromatic rings or that of an ester functionality, the formation of these natural products on solid phases can be performed via ozonolytic cleavage or alternatively via cleavage of an ester linker by transesterification to give the desired products. Precursors for the attachment of part A (containing the aldehyde) on the solid phases (Scheme 5) are cinnamic acid derivatives, which enable the oxidative cleavage of the double bond, whereas the corresponding immobilized part B (containing the ester functionality) can be formed via the attachment of benzoic acids.

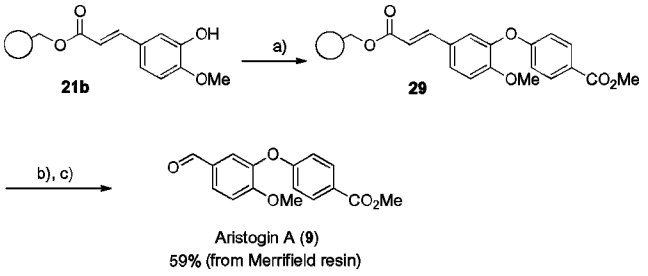


Scheme 5. Alternative procedures for the cleavage of diaryl ethers from solid supports. *Reagents and conditions*: a) O_3, CH_2Cl_2, room temp., 20 s; b) Me_2S, room temp., 30 min; c) KCN, MeOH, 90 °C, 12–15 h.

Both concepts for the cleavage from the solid support (ozonolysis and methanolysis) have been applied to generate Aristogins using the advantages of each method for the syntheses on solid phases.

The syntheses starting with compounds **27** were preferred in cases where the starting material (mostly iodobenzoic acid) was easily accessible. In all other cases, the syntheses via compounds **26** were favored because of the use of less toxic, volatile reagents and the rapid synthetic protocol (referring especially to the cleavage conditions). The removal of solvents as well as reagents through simple evaporation makes this procedure very attractive. Both methodologies lead to the target compounds in high purities and yields.

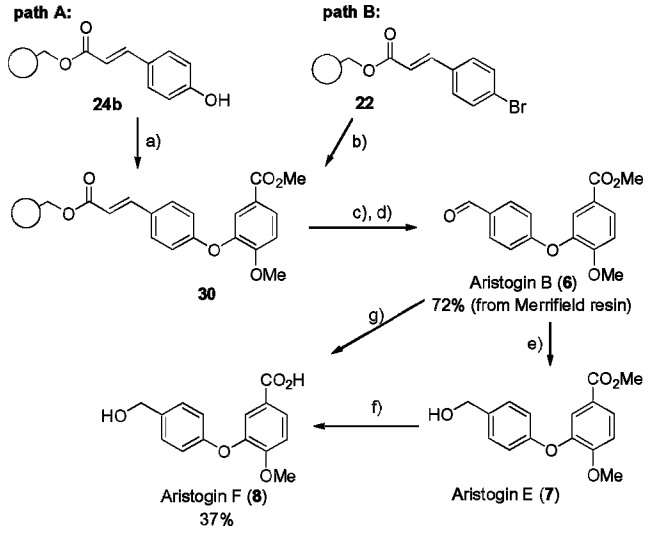
The immobilized cinnamic acid derivative **21b** has been further used to generate a member of the recently-isolated Aristogin family. As shown in Scheme 6, the formation of a diaryl ether from resin **21b** and methyl 4-iodobenzoate produced the resin-bound Aristogin A precursor **29**. Ozonolysis was used for the cleavage of the natural product, generating Aristogin A in 59% yield over six steps on solid phases starting from Merrifield resin.



Scheme 6. Synthesis of Aristogin A. *Reagents and conditions*: a) methyl 4-iodobenzoate, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 120 °C, 12 h; b) O_3, CH_2Cl_2, room temp., 20 s; c) Me_2S, room temp., 30 min.

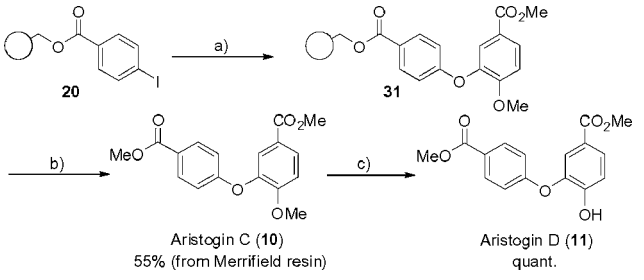
For the synthesis of Aristogin B and F, we used *para*-substituted cinnamic acids for the immobilization of the first aryl moiety on solid phases. Both the hydroxy derivative **24b** as well as the bromo derivative **22** were examined as starting material. The preparation of resin **24b** required one additional step on solid phases because of the introduction of the cinnamic ester in the form of the THP-protected derivative **24a**. This method was investigated because the reaction of iodo-substituted aryls (e.g. methyl 3-iodo-4-methoxybenzoate) with phenols is generally faster than that with bromo-substituted aryls. In the end, the formation of bromo-aryl resin **22** was deemed more advantageous, because the aforementioned synthesis of protected cinnamic acid derivatives (in solution) was not necessary and the resin could be synthesized in just three steps starting from Merrifield resin.

In the following step, the resins **22** and **24b** were treated with a phenol derivative (for resin **22**) or an iodo-aryl derivative (for resin **24b**) to yield the same resin-bound diaryl ether **30** (Scheme 7). Cleavage of the target substrate from the solid support via ozonolysis generated Aristogin B (72% over six steps) and in combination with the one pot reduction and saponification of the cleavage product, Aristogin F could be isolated in 37% yield (path g). Through another strategy, the aldehyde functionality of compound **6** was first reduced with $NaBH_4$ to give Aristogin E (not characterized) as intermediate. Saponification of the crude compound **7** produced Aristogin F (**8**).



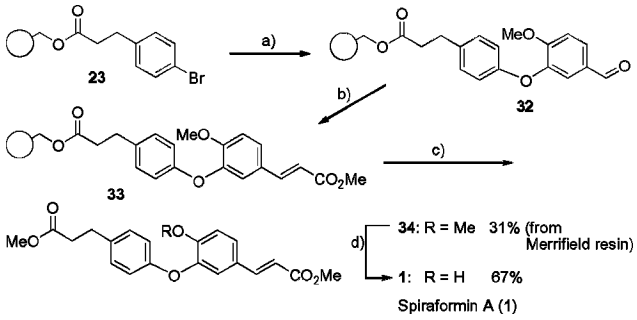
Scheme 7. Synthesis of Aristogin B and F. *Reagents and conditions*: a) methyl 3-iodo-4-methoxybenzoate, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 120 °C, 12 h; b) methyl 3-hydoxy-4-methoxybenzoate, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 120 °C, 12 h; c) O_3, CH_2Cl_2, room temp., 20 s; d) Me_2S, room temp., 30 min; e) $NaBH_4$, EtOH, room temp., 1 h; f) KOH, H_2O/EtOH, room temp.; g) KOH, EtOH/H_2O, room temp., 5 h.

As there was no need to perform ozonolysis for the preparation of Aristogin C and Aristogin D on solid supports, the latter compounds were synthesized through the use of resin **20** and subsequent diaryl ether coupling with methyl 3-hydroxy-4-methoxybenzoate (Scheme 8). The iodine resin **20** was chosen as starting material because of prior discouraging results regarding resin-bound hydroxy-substituted benzoic acid derivatives that do not withstand the coupling conditions. The desired naturally-occurring Aristogin C was obtained in 55% yield (from Merrifield resin) after cleavage from the resin via transesterification. The related Aristogin D is accessible via the same procedure, in combination with additional treatment of the crude cleavage product with BBr_3 in dichloromethane.



Scheme 8. Synthesis of Aristogin C and D. *Reagents and conditions*: a) methyl 3-hydroxy-4-methoxybenzoate, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 120 °C, 12 h; b) KCN, MeOH, 90 °C, 15 h; c) BBr_3, CH_2Cl_2, room temp., 24 h.

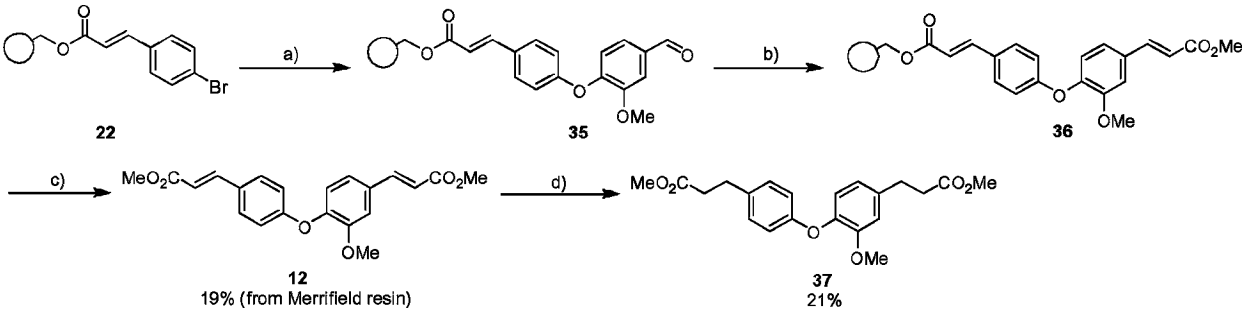
Spiraformin A. Beyond the use of cinnamic acids as starting resins for diaryl ether coupling, we investigated the use of commercially available 3-(4-bromophenyl)propanoic acid for the formation of natural products on solid supports. The attachment of the first aryl moiety was performed similarly to the previously described synthesis of ester resins. In a subsequent coupling step, the diaryl ether formation was successful when isovanillin was used as the phenolic part. The latter conversion has been chosen to introduce an aldehyde that allows for further conversion into cinnamic acid derivatives via Wittig-type reactions. Though former studies had shown that the diaryl ether coupling step is generally less successful in the presence of strong electron-withdrawing substituents, we used this method to generate the precursor **33** for Spiraformin A on solid phases (Scheme 9). The alternative transformation of resin **23** into an iodine-containing diaryl ether has also been performed, but the successive cross-coupling to give resin **33** could not be accomplished with good results.



Scheme 9. Synthesis of Spiraformin A. *Reagents and conditions*: a) 3-hydroxy-4-methoxybenzaldehyde, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 120 °C, 12 h; b) $(Ph)_3PCHCO_2Me$, toluene, 90 °C, 12 h; c) KCN, MeOH, 90 °C, 15 h; d) BBr_3, CH_2Cl_2, room temp., 24 h.

The formation of a resin-bound Spiraformin precursor has been conducted through the reaction of aldehyde-containing resin **32** with methyl (triphenylphosphoranylidene) acetate in toluene at 90 °C. After complete conversion of the solid-supported aldehyde (degree of conversion of the Wittig reaction has been checked by ^{13}C-NMR gel spectroscopy), the natural product precursor was cleaved by transesterification in a KCN/methanol mixture, giving Spiraformin A-precursor **34** in 31% yield over six steps on solid phases. The subsequent deprotection of compound **34** was achieved through the addition of BBr_3 and generated the target compound **1** in 67% yield.

Compound 12. The synthesis of a natural product isolated from *Kandelia candel*[80] is shown in Scheme 10. Similarly to the synthesis of Spiraformin A, the diaryl ether was formed by coupling a phenol derivative with an immobilized aryl halide. The resulting aldehyde-containing precursor was transformed via Wittig reaction into a twofold unsaturated diaryl ether. After cleavage from the resin, compound **12** was obtained in 19% yield over six steps on solid phases. The natural product **12** was hydrogenated over Pd/C to give the corresponding saturated diaryl ether **37**. This compound is known as Apteniol C, isolated from *Aptenia cordifolia*.[85] Comparison of the analytical data of Apteniol C[86] and compound **37** showed slight differences, which allowed us to presume that the real structure of the isolated compound is a derivative of compound **37** (Scheme 10).



Scheme 10. Synthesis of natural product **12**. *Reagents and conditions*: a) 4-hydroxy-3-methoxybenzaldehyde, CuCl, Cs_2CO_3, TMHD, DMF/MeCN (2:1), 120 °C, 12 h; b) $(Ph)_3PCHCO_2Me$, toluene, 90 °C, 12 h; c) KCN, MeOH, 90 °C, 15 h; d) Pd/C (10% Pd), H_2, EtOAc, room temp., 12 h.

Conclusions

In conclusion, we were applied the recently published method of diaryl ether coupling on solid phases for the synthesis of several natural products with diaryl ethers as structural motifs. We were able to demonstrate that the formation of diaryl ethers on solid supports is an interesting feature in order to obtain natural products, especially with respect to the fact that the formation of derivatives of these naturally-occurring substances via combinatorial exchange of one or two of the aryl moieties should be possible by following the synthetic pathway presented herein.

Experimental Section

Instrumentation and Reagents: ^{1}H NMR spectra were recorded on Bruker spectrometers (AM 250, AM 400, and AM 500). Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (δ =7.26 ppm) or acetone[d_6] (δ =2.09 ppm) as internal standard. All coupling constants are absolute values and *J* values are expressed in Hertz [Hz]. The description of signals include: s = singlet, d = doublet, br. d = broad doublet, t = triplet, dd = doublet of doublets, dt doublet of triplets, m = multiplet. The spectra were analyzed according to first order. ^{13}C NMR spectra were recorded on Bruker spectrometers [AM 250 (62.5 MHz), AM 400 (100 MHz), and AM 500 (125 MHz)]. Chemical shifts are expressed in parts per million (ppm, δ values) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (δ = 77.0 ppm) or [D_6]acetone (δ = 30.8 ppm) as internal standard. For measurement of ^{13}C-NMR gel spectra, 60–100 mg of the resin were swollen in a NMR tube with the appropriate amount of $CDCl_3$. The NMR spectrometer was run with pulse program zgpg30 (relaxation delay D1 = 0.2 s, line broadening LB = 9.0 Hz, 5120 scans). MS (EI) (electron-impact mass spectrometry): Finnigan MAT 90 (70 eV). The molecular fragments are quoted as the relation between mass and charge (*m*/*z*), the intensities as a percentage value relative to the intensity of the base signal (100%). The abbreviation [M^+] refers to the molecule ion. IR: FTIR Bruker IFS 88. IR spectra of solids were recorded in KBr, and as thin films on KBr for oils and liquids. The deposit of the absorption band was given in wave numbers in cm^{-1}. The forms and intensities of the bands were characterized as follows: m = medium 40–70% T, w = weak 70–90% T, vw = very weak 90–100% T. Routine monitoring of reactions was performed using silica-gel-coated aluminium plates (Merck, silica gel 60, F_{254}) which were analyzed under UV light (λ = 254 nm) and/or dipped into a solution of molybdatophosphate (5% phosphormolybdic acid in ethanol, dipping solution) and heated with a heat gun. Solvent mixtures are understood as volume/volume. Solid materials were powdered. Solvents, reagents, and chemicals were purchased from Aldrich, Fluka, and Acros. Tetrahydrofuran was distilled from sodium/benzophenone under argon prior to use. Dichloromethane, ethyl acetate, and diethyl ether were distilled from calcium hydride. All reactions involving moisture-sensitive reactants were executed under an argon atmosphere using oven- and/or flame-dried glassware, all other solvents, reagents, and chemicals were used as purchased unless stated otherwise. Merrifield resin was purchased from Polymer Laboratories (PL-CMS Resin, 0.97 mmol/g, 75–150 μm, 1% cross-linked, CMS 161 Lot 1). If not stated otherwise, vials from Macherey–Nagel were used for all reactions beyond room temperature (size 20–20 und 20–10, in combination with N20 oA and N20 TB/oA-M septum).

General Procedures and Analytical Data for Resins: All compounds not mentioned in the experimental procedure have been prepared according to known literature procedures. Data for cleaved products is given for selected examples that could be determined via NMR of the crude products after cleavage or via TLC chromatography. Signals referring to the linker-unit in the ^{13}C-NMR gel spectroscopic data are marked with an asterisk (*).

Immobilization of Benzoic/Cinnamic Acids (GP1): The Merrifield resin functionalized with a bromoalkyl linker (1.00 g) was swollen in 10.0 mL of DMF, then 5.00 mmol of Cs_2CO_3 and 5.00 mmol of benzoic acid were added at room temp. The mixture was shaken for 1 h at room temp. and then for 10 h at 80 °C. The resin was isolated by filtration and washed two times with acetone, methanol, water, acetone, and three times with dichloromethane.

Cleavage by Transesterification with KCN (GP2): The resin (100 mg) was swollen in methanol (2.00 mL), then KCN (2.00 mg, 30.7 mmol) was added. The reaction vessel was heated at 90 °C for 12–14 h. The reaction mixture was treated with K_2CO_3 (150 mg, 1.09 mmol), 50 mL of H_2O, and 50 mL of ethyl acetate. This mixture was filtered and the filtrate was separated in a separating funnel. The organic layer was washed again with 50 mL of H_2O. The aqueous layer was reextracted with ethyl acetate (100 mL) and washed with 50 mL of H_2O. The combined organic layers were dried with Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was analyzed via GC-MS.

Coupling of Immobilized Phenols with Iodobenzenes (GP3): To 150 mg of resin in 1.50 mL of MeCN and 3.00 mL of DMF were added 600 mg (1.84 mmol) of Cs_2CO_3, 40.0 mg (404 μmol) of CuCl, and 50.0 mg (271 μmol) of 2,2,6,6-tetramethyl-3,5-heptanedione. Then, 2.00 mmol of iodobenzene was added and the reaction

was shaken at 120 °C for 12–36 h. The resin was isolated by filtration and washed with water and acetone. The crude resin was washed with a saturated solution of sodium diethyldithiocarbamic acid trihydrate in DMF. Following, the resin was washed with acetone until no further coloring of the filtrate could be detected. Finally, the resin was washed with methanol and three times with dichloromethane.

Coupling of Immobilized Iodobenzenes with Phenols (GP4): To 150 mg resin in 1.50 mL of MeCN and 3.00 mL of DMF were added 600 mg (1.84 mmol) of Cs_2CO_3, 40.0 mg (404 μmol) of CuCl, and 50.0 mg (271 μmol) of 2,2,6,6-tetramethyl-3,5-heptanedione. Then, 2.00 mmol of phenol was added and the reaction was shaken at 120 °C for 12–36 h. The resin was isolated by filtration and washed with water and acetone. The crude resin was washed with a saturated solution of sodium diethyldithiocarbamic acid trihydrate in DMF. Then the resin was washed with acetone until no further coloring of the filtrate could be detected. Finally, the resin was washed with methanol and three times with dichloromethane.

Ozonolysis of Immobilized Olefins (GP5): 200 mg of immobilized olefin in 5.00 mL of CH_2Cl_2 was treated for 20 s at room temp. with a stream of O_2/O_3. The reaction mixture was shaken in the presence of 0.20 mL of dimethyl sulfide for 30 min and the crude resin was separated by filtration and washed two times with acetone. The solvent of the combined filtrates was removed under reduced pressure and the residue was analyzed by GC-MS.

Methyl 3-{4′-Hydroxy-3′-[4′′-(3-methoxy-3-oxopropyl)phenoxy]-phenyl}acrylate [Spiraformin A (1)]: To 4.0 mg (10.9 μmol) of compound **34** was added 1.50 mL (1.50 mmol, 138 equiv.) of BBr_3 solution (1 M in CH_2Cl_2) at room temp. and the resulting mixture was stirred for 12 h at room temp. Methanol (5.00 mL) was added and the solvent was removed under reduced pressure. The procedure of adding methanol and removal under reduced pressure was repeated twice; 2.6 mg of the target compound could be isolated after purification by preparative TLC (*n*-hexane/ethyl acetate, 10:1→3:1) in 67% yield; R_f = 0.57 (*n*-hexane/ethyl acetate, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.65 (t, ^3J = 7.6 Hz, 2 H, $CH_2CH_2CO_2Me$), 2.96 (t, ^3J = 7.6 Hz, 2 H, $CH_2CH_2CO_2Me$), 3.69 (s, 3 H, CO_2CH_3), 3.76 (s, 3 H, CO_2CH_3), 6.17 (d, ^3J = 16.0 Hz, 1 H, $CHCHCO_2Me$), 6.97 (d, ^3J = 8.2 Hz, 2 H, 3′′-H), 6.99 (s, 1 H, 2′-H), 7.03 (d, ^3J = 8.3 Hz, 1 H, 5′-H), 7.20 (d, ^3J = 8.3 Hz, 1 H, 6′-H), 7.52 (d, ^3J = 16.0 Hz, 1 H, $CHCHCO_2Me$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 29.7 ($CH_2CH_2CO_2Me$), 35.7 ($CH_2CH_2CO_2Me$), 51.6 (CO_2CH_3), 51.7 (CO_2CH_3), 115.8 ($CHCHCO_2Me$), 116.3 (C-2), 116.9 (C-6), 118.7 (2 C, C-2′), 125.0 (C-5), 127.4 (C-1), 129.9 (2 C, C-3′), 136.6 (C-4′), 144.2 ($CHCHCO_2Me$), 144.4 (C-1′), 149.1 (C-3), 154.3 (C-4), 167.5 ($CHCHCO_2Me$), 173.2 ($CH_2CH_2CO_2Me$) ppm. EI-MS (70 eV, 130 °C): *m*/*z* (%) = 356 (100) $[M]^+$, 297 (32), 283 (51). HRMS ($C^{20}H_{20}O_6$): calcd. 356.1260; found 356.1264.

2-(5′-Formyl-2′-methoxyphenoxy)-4,5-dimethoxybenzaldehyde [Hernandial (5)]: According to general procedure 5, 100 mg of resin **25** was suspended in 5.00 mL of CH_2Cl_2 and the mixture was ozonized for 20 s at room temp. The crude product could be purified by preparative TLC (*n*-hexane/ethyl acetate, 1:1); 5.0 mg of hernandial was isolated as colorless solid in 23% yield starting from Merrifield resin; R_f = 0.27 (*n*-hexane/ethyl acetate, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 3.99 (s, 3 H, OCH_3), 6.40 (s, 1 H, 3-H), 7.14 (d, ^3J = 8.5 Hz, 1 H, 3′-H), 7.39 (d, ^4J = 1.7 Hz, 1 H, 6′-H), 7.40 (s, 1 H, 6-H), 7.68 (d, ^3J = 8.5 Hz, 1 H, 4′-H), 9.83 (s, 1 H, C*H*O), 10.28 (s, 1 H, C*H*O) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 56.3 (OCH_3), 56.4 (2 C, OCH_3), 102.3, 108.4, 112.1, 117.9, 120.0, 128.6, 130.2, 146.3, 147.2, 154.6, 155.5, 155.6, 187.6 (*C*HO), 190.1 (*C*HO) ppm. FTIR (KBr film): $\tilde{\nu}$ = 3418 (vw), 2926 (w), 2855 (w), 1726 (w), 1687 (w), 1605 (m), 1510 (m), 1439 (w), 1409 (w), 1358 (w), 1278 (m), 1221 (m) cm^{-1}. EI-MS (70 eV, 160 °C): *m*/*z* (%) = 316 (100) $[M]^+$, 285 (9) $[M - OCH_3]^+$, 279 (15), 180 (49), 165 (10), 149 (39). HRMS ($C_{17}H_{16}O_6$): calcd. 316.0947; found 316.0945.

Methyl 3-(4′-Formylphenoxy)-4-methoxybenzoate [Aristogin B (6)]: According to general procedure 5, 150 mg of resin **30** was suspended in 5.00 mL of CH_2Cl_2 and were ozonized at room temp. for 20 s. The crude product was purified by column chromatography (*n*-hexane/ethyl acetate, 10:1–2:1) and 22.0 mg of Aristogin B could be isolated in 72% yield starting from Merrifield resin; R_f = 0.75 (*n*-hexane/ethyl acetate, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 3.88 (s, 3 H, CO_2CH_3), 6.98 (br. d, ^3J = 8.8 Hz, 2 H, 2′-H), 7.06 (d, ^3J = 8.6 Hz, 1 H, 5-H), 7.78 (d, ^4J = 2.1 Hz, 1 H, 2-H), 7.83 (br. d, ^3J = 8.8 Hz, 2 H, 3′-H), 7.96 (dd, ^3J = 8.6, ^4J = 2.1 Hz, 1 H, 6-H), 9.91 (s, 1 H, C*H*O) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 52.1 (CO_2CH_3), 56.1 (OCH_3), 112.1, 116.3 (2 C, C-2′), 123.4, 123.8, 128.5, 131.2, 131.9 (2 C, C-3′), 142.6, 155.5, 163.0, 166.0 (CO_2CH_3), 190.8 (*C*HO) ppm. EI-MS (GC, 120 °C): *m*/*z* (%) = 286 (100) $[M]^+$, 255 (75) $[M - OCH_3]^+$, 183 (7), 127 (16). HRMS ($C_{16}H_{14}O_5$): calcd. 286.0841; found 286.0844.

3-[4′-(Hydroxymethyl)phenoxy]-4-methoxybenzoic Acid [Aristogin F (8)]: To a solution of 10.0 mg (34.9 μmol) Aristogin B (**6**) in 5.00 mL of ethanol and H_2O (1:1) was added 28.0 mg (0.50 mmol, 14.3 equiv.) of KOH. The mixture was shaken for 5 h at room temp., was then neutralized with 1 N HCl and the solvent was removed under reduced pressure. The crude product was dissolved in a mixture of ethyl acetate and water (1:1); after separation of the organic layer, the aqueous layer was extracted two times with ethyl acetate. The solvent was removed under reduced pressure and 3.5 mg of Aristogin F could be isolated in 37% yield by preparative TLC in CH_2Cl_2/methanol (9:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 4.60 (s, 2 H, CH_2OH), 6.89 (d, ^3J = 8.6 Hz, 2 H, 2′-H), 6.98 (d, ^3J = 8.6 Hz, 1 H, 5-H), 7.26 (d, ^3J = 8.6 Hz, 2 H, 3′-H), 7.58 (d, ^4J = 2.1 Hz, 1 H, 2-H), 7.84 (dd, ^3J = 8.6, ^4J = 2.1 Hz, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 56.6 (OCH_3), 64.8 (CH_2OH), 113.2, 117.8 (2 C), 123.4, 128.3, 129.7 (2 C), 136.9, 145.5, 155.8, 158.6, 169.4, 176.5 ppm. FAB-MS (3 NBA): *m*/*z* (%) = 391.3 (100) $[M + 3K]^+$, 352.4 (19) $[M + 2K]^+$.

Methyl 4-(5′-Formyl-2′-methoxyphenoxy)benzoate [Aristogin A (9)]: According to general procedure 5, 100 mg of resin **29** was suspended in 5.00 mL of CH_2Cl_2 and ozonized at room temp. for 20 s. The target compound could be isolated in 59% yield (12.0 mg) starting from Merrifield resin. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.90 (s, 3 H, OCH_3), 3.90 (s, 3 H, CO_2CH_3), 6.93 (d, ^3J = 8.9 Hz, 2 H, 3-H), 7.14 (d, ^3J = 8.4 Hz, 1 H, 3′-H), 7.59 (d, ^4J = 2.0 Hz, 1 H, 6′-H), 7.75 (dd, ^3J = 8.4, ^4J = 2.0 Hz, 1 H, 4′-H), 8.00 (d, ^3J = 8.9 Hz, 2 H, 2-H), 9.87 (s, 1 H, C*H*O) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.0 (CO_2CH_3) 56.2 (OCH_3), 112.4, 116.3 (2 C, C-3), 121.8, 124.7, 129.1, 130.4, 131.7 (2 C, C-2), 144.3, 156.7, 161.3, 166.5 (CO_2CH_3), 190.1 (*C*HO) ppm. EI-MS (GC-MS, 120 °C): *m*/*z* (%) = 286 (100) $[M]^+$, 255 (100) $[M - OCH_3]^+$, 127 (24).

Methyl 4-Methoxy-3-[4′-(methoxycarbonyl)phenoxy]benzoate [Aristogin C (10)]: According to general procedure 2, 150 mg of resin **31** was suspended in MeOH, then 2.00 mg of KCN was added and the mixture was heated for 20 h at 90 °C. The target compound could be isolated in quantitative yield over two steps (19.1 mg) and 55% yield starting from Merrifield resin. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 6.90 (br. d, ^3J = 8.7 Hz, 2 H, 2′-H), 7.04 (d, ^3J = 8.7 Hz, 1 H, 5-H), 7.74 (d, ^4J = 2.0 Hz, 1 H, 2-H), 7.93 (dd, ^3J = 8.7, ^4J =

2.0 Hz, 1 H, 6-H), 7.98 (br. d, ^3J = 8.7 Hz, 2 H, 3-H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 52.0 (CO_2CH_3), 52.1 (CO_2CH_3), 56.0 (OCH_3), 112.0, 115.9, 123.3, 123.4, 124.3, 128.1, 131.6 (2 C, C-3), 143.1, 155.5, 161.7, 166.1 (CO_2CH_3), 166.6 (CO_2CH_3) ppm. EI-MS (70 eV, 90 °C): *m*/*z* (%) = 316 (100) $[M]^+$, 285 (70) $[M - OCH_3]^+$. HRMS ($C_{17}H_{16}O_6$): calcd. 316.0947; found 316.0950.

Methyl 4-Hydroxy-3-[4′-(methoxycarbonyl)phenoxy]benzoate [Aristogin D (11)]: To 12.0 mg (37.9 μmol) of Aristogin C (**10**) was added 2.00 mL of BBr_3 solution (1 M in CH_2Cl_2, 51.3 equiv.) at room temp. The mixture was stirred for 12 h, then 5.00 mL of methanol was added. The solvent was removed under reduced pressure; the procedure of adding methanol and removal under reduced pressure was repeated. The target compound could be isolated in quantitative yield (11.5 mg); R_f = 0.61 (*n*-hexane/ethyl acetate, 1:1). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, CO_2CH_3), 3.87 (s, 3 H, CO_2CH_3), 6.98 (d, ^3J = 8.0 Hz, 2 H, 2′-H), 7.06 (d, ^3J = 7.9 Hz, 1 H, 5-H), 7.59 (s, 1 H, 2-H), 7.79 (d, ^3J = 7.9 Hz, 1 H, 6-H), 7.97 (d, ^3J = 8.0 Hz, 2 H, 3′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.2 (CO_2CH_3), 52.3 (CO_2CH_3), 116.4, 117.0 (2 C, C-2′), 121.2, 123.0, 125.4, 127.7, 131.9 (2 C, C-3′), 141.9, 151.8, 160.2, 166.0 (CO_2CH_3), 166.3 (CO_2CH_3) ppm. EI-MS (70 eV, 120 °C): *m*/*z* (%) = 302 (2) $[M]^+$, 298 (2), 270 (3), 43 (100). HRMS ($C_{16}H_{14}O_6$): calcd. 302.0790; found 302.0792.

Methyl 3-{4′-[2′′-Methoxy-4-(3-methoxy-3-oxoprop-1-enyl)phenoxy]-phenyl}acrylate (12): According to general procedure 2, 100 mg of resin **36** was suspended in 3.00 mL of MeOH, then 1.00 mg of KCN was added. The crude product was purified by preparative TLC; 5.0 mg of the target compound could be isolated in 19% yield starting from Merrifield resin. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 3.82 (s, 3 H, CO_2CH_3), 3.86 (s, 3 H, CO_2CH_3), 6.34 (d, ^3J = 16.0 Hz, 1 H, ArCHC*H*CO_2Me), 6.40 (d, ^3J = 16.0 Hz, 1 H, ArCHC*H*CO_2Me), 6.95 (d, ^3J = 8.7 Hz, 2 H, 3′-H), 7.00 (d, ^3J = 8.2 Hz, 1 H, 6′′-H), 7.12 (dd, ^3J = 8.2, ^4J = 1.8 Hz, 1 H, 5′′-H), 7.15 (d, ^4J = 1.8 Hz, 1 H, 3′′-H), 7.48 (d, ^4J = 8.7 Hz, 2 H, 2′-H), 7.66 (d, ^3J = 16.0 Hz, 1 H, ArC*H*$CHCO_2$Me), 7.68 (d, 1 H, ArC*H*$CHCO_2$Me) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 51.7 (CO_2CH_3), 51.8 (CO_2CH_3), 56.0 (OCH_3), 111.7, 116.4, 117.4, 117.5 (2 C, C-2′), 121.3 (CH*C*HCO_2Me), 121.8 (CH*C*HCO_2Me), 129.2, 129.7 (2 C, C-3′), 131.7, 144.1 (2 C, *C*$HCHCO_2$Me), 146.2, 151.5, 159.2, 167.3 (CO_2Me), 167.6 (CO_2Me) ppm. EI-MS (GC-MS, 120 °C): *m*/*z* (%) = 368 (100) $[M]^+$, 337 (8), 281 (9), 207 (38) $[C_{11}H_{11}O_4]^+$, 153 (12).

5-Polystyrenemethyloxypentyl 3-(4-Bromophenyl)propanoate (23): According to general procedure 1, 4.00 g of resin **19** was dissolved in 40.0 mL of DMF, then 5.56 g (20.0 mmol) of 3-(4-bromophenyl)-propionic acid and 6.54 g (20.0 mmol) of cesium carbonate were reacted over a period of 12 h. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7*, 28.5*, 29.4*, 30.3 ($CH_2CH_2CO_2R$), 35.6 ($CH_2CH_2CO_2R$), 64.5*, 69.8*, 72.8*, 120.0 (C-4), 130.0 (2 C, C-2), 131.5 (2 C, C-3), 139.4 (C-1), 172.6 (*C*OOR) ppm. FTIR: $\tilde{\nu}$ = 3648 (vw), 3620 (vw), 3454 (vw), 3033 (w), 2845 (w), 2338 (vw), 2312 (vw), 2247 (w), 1946 (w), 1875 (w), 1804 (w), 1744 (w), 1667 (w), 1602 (w), 1453 (w) cm^{-1}.

5-Polystyrenemethyloxypentyl 3-[3-(2-Formyl-4,5-dimethoxyphenoxy)-4-methoxyphenyl]acrylate (25): According to general procedure 3, 300 mg of resin **21b**, 490 mg (2.00 mmol) of 6-bromoveratraldehyde, 100 mg (542 μmol) of TMHD, 80.0 mg (808 μmol) of copper(I) chloride, and 1.20 g (3.68 mmol) of Cs_2CO_3 in DMF/MeCN (3.00 mL/1.50 mL) were reacted at 120 °C over a period of 12 h. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6*, 28.5*, 29.3*, 56.1 (3 C, OCH_3), 64.3*, 69.9*, 72.8*, 101.5, 108.1, 110.3, 116.8, 118.3, 119.3, 121.6, 143.3, 145.8 (*C*$HCHCO_2$R), 152.1, 155.4, 166.9 (CO_2R), 187.7 (*C*HO) ppm.

Methyl 4-{5-[3-(5-Polystyrenemethyloxypentyloxy)-3-oxoprop-1-enyl]-2-methoxyphenoxy}benzoate (29): According to general procedure 3, 150 mg of resin **21b** were converted with 162 mg (1.00 mmol) of methyl 4-iodobenzoate, 50.0 mg (271 μmol) of TMHD, 40.0 mg (404 μmol) of copper(I) chloride, and 600 mg (1.84 mmol) of Cs_2CO_3 in DMF/MeCN (3.00 mL/1.50 mL) at 120 °C over a period of 12 h. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7*, 28.5*, 29.4*, 51.9 (CO_2CH_3), 55.9 (OCH_3), 64.4*, 69.8*, 72.5*, 112.8, 115.8 (2 C, C-2), 116.9, 121.0, 124.2, 131.5 (2 C, C-3), 143.4 (*C*$HCHCO_2$R), 153.2, 161.5 (CO_2CH_3), 166.5 (CHCH*C*O_2R) ppm. FTIR: $\tilde{\nu}$ = 3649 (vw), 3025 (w), 2840 (w), 2602 (w), 2337 (w), 2312 (w), 1945 (w), 1876 (w), 1806 (w), 1732 (w), 1600 (w), 1506 (w), 1455 (w) cm^{-1}.

Methyl 3-{4-[3-(5-Polystyrenemethyloxypentyloxy)-3-oxoprop-1-enyl]phenoxy}-4-methoxybenzoate (30). A: According to general procedure 3, 300 mg of resin **24b** was treated with 584 mg (2.00 mmol) of methyl 3-iodo-4-methoxybenzoate, 100 mg (542 μmol) of TMHD, 80.0 mg (808 μmol) of copper(I) chloride, and 1.20 g (3.68 mmol) of Cs_2CO_3 in DMF/MeCN (3.00 mL/1.50 mL) at 120 °C over a period of 12 h.

B: According to general procedure 4, 300 mg of resin **22** was treated with 364 mg (2.00 mmol) of methyl 3-hydroxy-4-methoxybenzoate, 100 mg (542 μmol) of TMHD, 80 mg (808 μmol) of copper(I) chloride, and 1.20 g (3.68 mmol) of Cs_2CO_3 in DMF/MeCN (3.00 mL/1.50 mL) at 120 °C over a period of 12 h. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7*, 28.6*, 29.3*, 52.0 (CO_2CH_3), 55.9 (OCH_3), 64.4*, 69.7*, 73.0*, 111.9, 116.8 (2 C, C-3′), 122.9, 145.3 (*C*$HCHCO_2$R), 166.0 (CO_2R), 167.6 (CO_2R) ppm. FTIR: $\tilde{\nu}$ = 3334 (vw), 3076 (vw), 2838 (vw), 2248 (vw), 1944 (vw), 1871 (vw), 1801 (vw), 1497 (w), 1369 (w) cm^{-1}.

Methyl 3-{4-[(5-Polystyrenemethyloxypentyloxy)carbonyl]phenoxy}-4-methoxybenzoate (31): According to general procedure 4, 150 mg of resin **20** was treated with 182 mg (1.00 mmol) of methyl 3-hydroxy-4-methoxybenzoate, 50.0 mg (271 μmol) of TMHD, 40 mg (404 μmol) of copper(I) chloride, and 600 mg (1.84 mmol) of Cs_2CO_3 in DMF/MeCN (3.00 mL/1.50 mL) at 120 °C over a period of 12 h. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.8*, 28.6*, 29.4*, 52.0 (CO_2CH_3), 56.0 (OCH_3), 64.8*, 69.8*, 72.7*, 112.0, 115.9, 123.3 (2 C, C-3′), 1316 (2 C, C-2′), 143.0, 155.4, 161.4 (CO_2R), 166.0 (CO_2CH_3) ppm. FTIR: $\tilde{\nu}$ = 3407 (vw), 3059 (w), 3027 (w), 2928 (w), 2849 (w), 2603 (vw), 2247 (vw), 1944 (vw), 1871 (vw), 1718 (vw), 1603 (w), 1493 (w), 1452 (w), 1278 (w) cm^{-1}.

Polystyrenemethyloxypentyl 3-[4-(5-Formyl-2-methoxyphenoxy)-phenyl]propanoate (32): According to general procedure 4, 300 mg of resin **23** was treated with 304 mg (2.00 mmol) of 3-hydroxy-4-methoxybenzaldehyde, 100 mg (542 μmol) of TMHD, 80 mg (808 μmol) of copper(I) chloride, and 1.20 g (3.68 mmol) of Cs_2CO_3 in DMF/MeCN (3.00 mL/1.50 mL) at 120 °C over a period of 15 h. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6*, 28.4*, 29.3*, 30.3 ($CH_2CH_2CO_2R$), 35.5 ($CH_2CH_2CO_2R$), 56.2 (OCH_3), 64.5*, 69.8*, 72.8*, 111.9, 118.2, 126.2, 129.6, 130.0, 131.4, 139.4, 155.0, 156.1, 172.4 (CO_2R), 190.2 (*C*HO) ppm. FTIR: $\tilde{\nu}$ = 3648 (vw), 3450 (vw), 3162 (vw), 3082 (vw), 3057 (w), 3027 (w), 2910 (w), 2849 (w), 2602 (vw), 2337 (vw), 2311 (vw), 1944 (w), 1874 (w), 1804 (w), 1740 (w), 1695 (w), 1601 (w), 1494 (w), 1453 (w) cm^{-1}.

Methyl 3-(3-{4-[3-(5-Polystyrenemethyloxypentyloxy)-3-oxopropyl]-phenoxy}-4-methoxyphenyl)acrylate (33): 200 mg of carbonyl resin **32** was suspended in toluene, then 334 mg (1.00 mmol) of (methoxycarbonylmethylene)triphenylphosphorane was added. The mix-

ture was heated for 12 h at 90 °C. The resin was separated from the supernatant solution by filtration and washed two times with MeOH, acetone, H_2O, acetone, and CH_2Cl_2. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6*, 28.4*, 29.3*, 30.3 (*C*H_2CH$_2$COOR), 35.5 (CH$_2$*C*H$_2$COOR), 51.5 (COO*C*H$_3$), 56.0 (O*C*H$_3$), 64.4*, 69.8*, 72.8*, 112.4, 116.0, 117.6 (CH*C*HCOOMe), 119.0, 119.9, 172.9 (*C*OOR) ppm. FTIR: $\tilde{\nu}$ = 3454 (vw), 3084 (w), 3031 (w), 2945 (w), 2851 (w), 2603 (vw), 2338 (vw), 2311 (vw), 2247 (vw), 1946 (w), 1875 (w), 1805 (w), 1743 (w), 1727 (w), 1691 (w), 1602 (w) cm^{-1}.

Methyl 3-{4′-Methoxy-3′-[4′′-(3-methoxy-3-oxopropyl)phenoxy]-phenyl}acrylate (34): According to general procedure 2, 150 mg of resin **33** was suspended in 3.00 mL of MeOH, then 2.00 mg of KCN was added. After purification via preparative TLC (*n*-hexane/ethyl acetate, 10:1→3:1) 12.0 mg of the target compound could be isolated in 31% yield starting from Merrifield resin. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.63 (t, ^3J = 7.8 Hz, 2 H, CH$_2$C*H*$_2$COOMe), 2.93 (t, ^3J = 7.8 Hz, 2 H, C*H*$_2$CH$_2$COOMe), 3.67 (s, 3 H, COOC*H*$_3$), 3.77 (s, 3 H, COOC*H*$_3$), 3.88 (s, 3 H, OC*H*$_3$), 6.20 (d, ^3J = 16.0 Hz, 1 H, C*H*CHCOOCH$_3$), 6.89 (br. d, ^3J = 8.5 Hz, 2 H, 3′′-H), 6.98 (d, ^3J = 8.5 Hz, 1 H, 5′-H), 7.10 (d, ^4J = 2.0 Hz, 1 H, 2′-H), 7.14 (br. d, ^3J = 8.5 Hz, 2 H, 2′′-H), 7.70 (d, ^4J = 2.0, ^3J = 8.5 Hz, 1 H, 6′-H), 7.56 (d, ^3J = 16.0 Hz, 1 H, C*H*CHCOOCH$_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.2 (CH$_2$*C*H$_2$COOCH$_3$), 35.8 (*C*H$_2$CH$_2$COOCH$_3$), 51.6 (2 C, CO-O*C*H$_3$), 56.1 (O*C*H$_3$), 112.5, 116.1 (CH*C*HCOOCH$_3$), 117.8 (2 C, C-2′′), 119.0, 125.3, 127.7, 129.5 (2 C, C-3′′), 135.2, 144.0 (*C*HCHCOOCH$_3$), 145.9, 153.0, 155.6, 167.5 (CHCH*C*OOCH$_3$), 173.3 (CH$_2$CH$_2$*C*OOCH$_3$) ppm. EI-MS (GC-MS, 120 °C): *m*/*z* (%) = 370 (100) [M]$^+$, 339 (9) [M – OCH$_3$]$^+$, 310 (21), 297 (85), 281 (14). HRMS ($C_{21}H_{22}O_6$): calcd. 370.1416; found 370.1418.

5-Polystyrenemethyloxypentyl 3-[4-(4-Formyl-2-methoxyphenoxy)-phenyl]acrylate (35): According to general procedure 4, 200 mg of resin **22** was treated with 152 mg (1.00 mmol) of 4-hydroxy-3-methoxybenzaldehyde, 100 mg (542 μmol) of TMHD, 80 mg (808 μmol) of copper(I) chloride, and 1.20 g (3.68 mmol) of Cs_2CO_3 in DMF/MeCN (3.00 mL/1.50 mL) at 120 °C over a period of 12 h. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7*, 28.5*, 29.4*, 56.0 (O*C*H$_3$), 64.5*, 69.8*, 72.7*, 110.9, 118.1, 118.5, 118.8, 119.5, 125.5, 128.79, 132.0, 143.1 (*C*HCHCOOR), 165.6 (*C*OOR), 290.7 (*C*HO) ppm. FTIR: $\tilde{\nu}$ = 3649 (vw), 3035 (w), 2843 (w), 2338 (vw), 23112 (vw), 2248 (w), 1947 (w), 1877 (w), 1804 (w), 1691 (w), 1641 (w), 1602 (w), 1451 (w) cm^{-1}.

5-Polystyrenemethyloxypentyl-3-{4-[2-methoxy-4-(3-methoxy-3-oxoprop-1-enyl)phenoxy]phenyl}acrylate (36): 200 mg of carbonyl resin **35** was suspended in toluene, then 334 mg (1.00 mmol) of (methoxycarbonylmethylene)triphenylphosphorane was added. The mixture was heated for 12 h at 90 °C, the resin was separated from the supernatant solution by filtration. The resulting resin was washed two times with MeOH, acetone, H_2O, acetone, and CH_2Cl_2. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7*, 28.5*, 29.4*, 51.7 (CO$_2$*C*H$_3$), 55.9 (O*C*H$_3$), 64.5*, 69.7*, 72.8*, 111.6, 117.4, 118.2, 118.9, 121.7, 128.8 132.0, 143.2, 144.0 (*C*HCHCO$_2$R), 151.4, 167.0 (*C*O$_2$R) ppm. FTIR: $\tilde{\nu}$ = 3028 (w), 2850 (w), 2633 (vw), 2603 (vw), 2387 (vw), 2338 (vw), 2312 (vw), 2248 (w), 1946 (w), 1877 (w), 1805 (w), 1724 (w), 1679 (w), 1641 (w), 1601 (w) cm^{-1}.

Methyl 3-{4′-[2′′-Methoxy-4′′-(3-methoxy-3-oxopropyl)phenoxy]-phenyl}propanoate (37): 28.0 mg of crude compound **12** was dissolved in 10 mL of methanol and catalytic amounts of Pd/C (10%) were added. The mixture was stirred for 15 h at room temp. under an H_2 atmosphere. After filtration and removal of the solvent under reduced pressure, the target compound was purified by preparative TLC and isolated in 21% yield (6 mg). ^1H NMR (500 MHz, $CDCl_3$): δ = 2.60–2.66 (m, 2 H, CH$_2$C*H*$_2$CO$_2$Me), 2.69–2.63 (m, 2 H, CH$_2$C*H*$_2$CO$_2$Me), 2.92–2.88 (m, 2 H, C*H*$_2$CH$_2$CO$_2$Me), 2.96–2.92 (m, 2 H, C*H*$_2$CH$_2$CO$_2$Me), 3.67 (s, 3 H, CO$_2$C*H*$_3$), 3.69 (s, 3 H, CO$_2$C*H*$_3$), 3.82 (s, 3 H, OC*H*$_3$), 6.73 (d, ^3J = 7.4 Hz, 1 H, 6′′-H), 6.87–6.82 (m, 4 H, 5′′-H, 2′-H, 2′′-H), 7.10 (d, ^3J = 8.4 Hz, 2 H, 3′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.2 (*C*HCHCO$_2$Me), 30.8 (*C*HCHCO$_2$Me), 35.8 (CH*C*HCO$_2$Me), 35.9 (CH*C*HCO$_2$Me), 51.6 (COO*C*H$_3$), 51.7 (CO$_2$*C*H$_3$), 56.0 (O*C*H$_3$), 112.9, 117.2 (2 C, C-2′), 120.6, 120.8, 129.3 (2 C, C-3′), 134.4, 137.2, 143.5, 151.2, 156.4, 173.3 (*C*O$_2$CH$_3$), 173.4 (*C*O$_2$CH$_3$) ppm. EI-MS (70 eV, 100 °C): *m*/*z* (%) = 372 (100) [M]$^+$, 299 (40). HRMS ($C_{21}H_{24}O_6$): calcd. 372.1573; found 372.1577.

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