Development of the Traceless Phenylhydrazide Linker for Solid-Phase Synthesis

Frank Stieber,[a, b] Uwe Grether,[a, b] and Herbert Waldmann*[a, b]

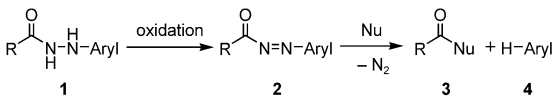
Abstract: The hydrazide group is a new oxidatively cleavable traceless linker for solid-phase chemistry. It can be readily introduced by hydrazide formation between a carboxy-functionalized resin and different substituted hydrazines. In order to achieve high yields in this step, new carboxylic acid resins were developed that are not prone to undesired imide formation upon activation of the carboxylic acid. The polymer-bound acyl hydrazides were successfully employed in various transformations, namely Heck, Suzuki, Sonogashira, and Stille couplings, as well as Wittig and Grignard reactions. Traceless release of the coupling products from the solid support is achieved selectively under mild conditions and in high purity by oxidation of the aryl hydrazides to acyl diazenes with Cu^{II} salts or *N*-bromosuccinimide (NBS) and subsequent nucleophilic attack of the acyl diazene intermediates. Traceless cleavage by oxidation with NBS can be carried out as a two-step process in which stable acyl diazenes are first generated by treatment with NBS in the absence of a nucleophile. After removal of the reagents by simple resin washing, the traceless release is effected by the addition of methanol, which leads to products of high purity without any additional separation steps.

Keywords: combinatorial chemistry · phenylhydrazides · solid-phase synthesis · traceless linker

Introduction

The combinatorial synthesis of small-molecule libraries on polymeric supports is a powerful method for the discovery and development of new molecules with a predetermined profile of properties.[1] Vital to all solid-phase methodologies is the design and utilization of suitable linker groups allowing facile attachment, functionalization, and release of the molecules of interest. Typically, linkage to the polymeric support is achieved through a functionality already present in the target molecule. However, after cleavage from the support at the end of a synthetic sequence, this functional group may have an unwanted effect on the biological or chemical activity of the target compounds. A highly desirable alternative linker would be capable of releasing a product while forming a carbon–hydrogen bond in place of the resin attachment, thus leaving behind no trace of a solid-phase synthesis. Such widely applicable "traceless" linkers introduced so far[1] include aryl silanes,[2a–f] alkyl sulfides and sulfones,[2g] alkyl selenides,[2h,i] and aryl triazenes.[2j]

Oxidative cleavage of aryl hydrazides **1** to give carboxylic acid derivatives **3**, nitrogen, and arenes **4** via a transient acyl diazene **2** has been applied in peptide chemistry both in solution[1] and on a solid support[2] to obtain peptide carboxylic acids, amides, and esters (Scheme 1, R = peptide, Aryl = phenyl or phenyl linked to a polymeric support). Alternatively, this transformation clearly offers the opportunity to cleave aryl compounds from polymeric supports leaving only an aryl–H bond (Scheme 1, R = polymeric support, Aryl = substituted aromatic compound).



Scheme 1. Oxidative cleavage of hydrazides.

In this and the following article,[5] we report in full detail on the development of the aryl hydrazide group as a new traceless linker for solid-phase and combinatorial chemistry.[6]

Results and Discussion

Development of new acid-functionalized resins: In the development of the traceless hydrazide linker group we required

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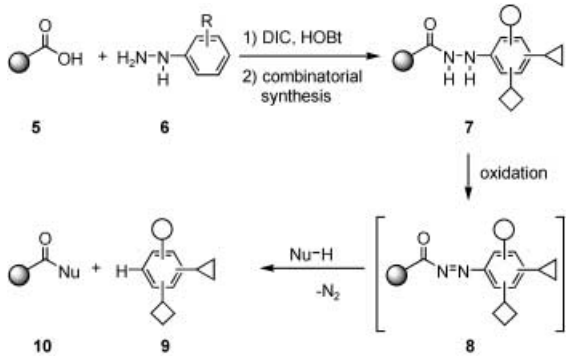
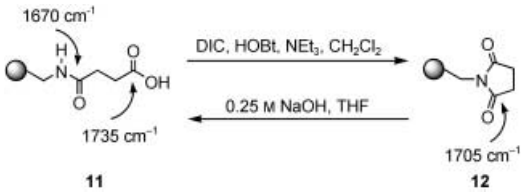
polymeric supports carrying carboxylic acids on their surface to couple different hydrazines to the solid support before subjecting them to combinatorial derivatization and final oxidative traceless cleavage (Scheme 2).



Scheme 2. Principle of the oxidative cleavage of the hydrazide linker.

The initial phase of this investigation was greatly complicated by nonreproducible results that were traced to problems arising during the attachment of the hydrazines to the carboxylic acid-functionalized solid support. Thus, inspection of the resins obtained after activation of the polymer-bound carboxylate with carbodiimide and subsequent treatment with different phenylhydrazines by means of Fourier transform IR spectroscopy consistently revealed a strong band at $\tilde{\nu} = 1705\ cm^{-1}$ that could not be ascribed to the starting material or the product. The commercially available resins employed in these experiments (polystyrene and TentaGel, Rapp Polymere) had been obtained from an amino-functionalized carrier by formation of a succinic acid monoamide, that is, they contained an amide nitrogen and an activatable carboxylic acid separated by a distance suitable for formation of a five-membered ring imide. Thus, in order to explain the above finding it was speculated that, after reaction of the carboxylic acid **11** with the carbodiimide, the activated intermediate is attacked intramolecularly by the nitrogen of the amide group to produce a polymer-bound cyclic imide **12** (Scheme 3).[6b]



Scheme 3. Observed intramolecular imide formation on a solid support.

Such cyclizations are well-known in solution.[7, 8] Formation of imide **12** was readily induced in a model reaction by treatment of carboxy-functionalized resin **11** with a carbodiimide (Scheme 3). The FT-IR spectrum of resin **12** displayed a strong peak at $\tilde{\nu} = 1705\ cm^{-1}$.

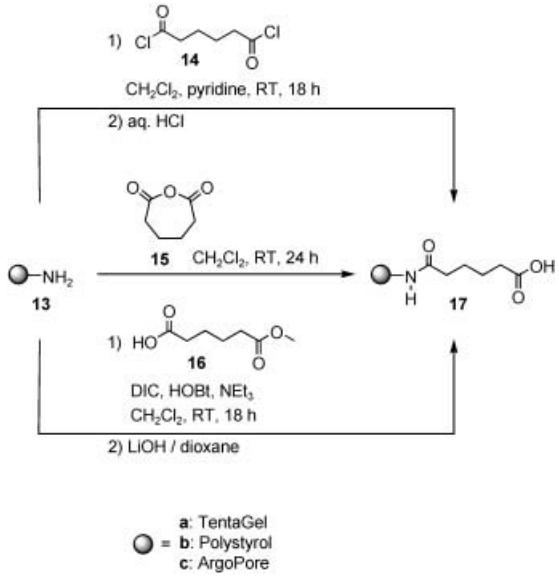
Under basic conditions, the polymer-bound succinimide **12** was readily hydrolyzed to acid **11**. These findings are of general relevance since they point to problems that may arise if commercially available polymeric resins carrying a linker of the type found in **11** are used. They also call for the development of alternative carboxylic acid-functionalized supports which do not undergo this undesired sidereaction.

In attempting to overcome this problem we reasoned that a simple elongation of the carbon chain by two methylene units, namely the use of an adipic acid derivative instead of a succinic acid derivative, might provide a straightforward solution since the formation of a seven-membered ring is unfavorable.

Consequently, different amino resins **13** (polystyrene-NH_2, TentaGel-NH_2, ArgoPore-NH_2) were treated with adipic dichloride (**14**) in dichloromethane and pyridine followed by aqueous work-up. The acid-functionalized resins obtained thereby did not undergo the undesired cyclization upon activation with carbodiimide.

However, the reaction with the dichloride **14** also resulted in substantial crosslinking of the amino groups in the starting material and the level of product loading was only up to 40% of the original loading with amino groups.

This situation was significantly improved if freshly prepared[9] adipic anhydride (**15**) was employed or if first an adipic acid monoamide was formed with adipic methyl ester (**16**) followed by basic saponification of the ester group (Scheme 4). Analysis of the coupling efficiency by means of

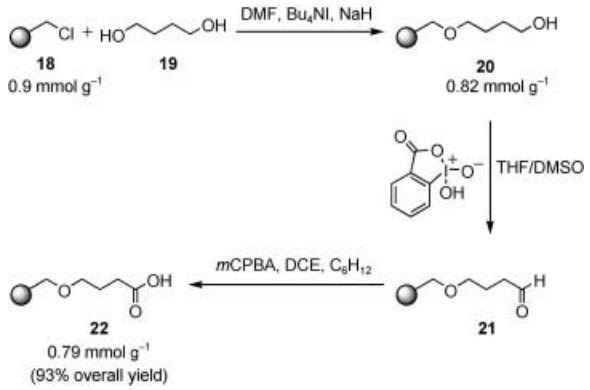


Scheme 4. Synthesis of adipic acid-functionalized resin **17**.

the Kaiser test,[10] which detects remaining free amino groups, revealed that essentially no underivatized amino groups had remained. The loading level was then determined by nucleophilic esterification of the carboxylic acid groups with 2-methoxy-5-nitrobenzyl bromide in DMF and basic saponification of the resulting polymeric esters. The loading was quantified by determining the amount of released 2-methoxy-5-nitrobenzyl alcohol by means of UV spectroscopy (at $\lambda = 307$ nm).[11] These determinations revealed that derivatization of polystyrene-NH_2 (loading level: 1.1 mmol g), TentaGel-NH_2 (loading level: 0.42 mmol g) and ArgoPore-NH_2 (loading level: 1.13 mmol g) had proceeded with yields in the range of

93–98%. Resin **17** was employed in all subsequent transformations (see below).

All the acid-functionalized resins described above contain an amide group. While this function does not interfere with many organic transformations, it would be highly desirable to have an alternative with a different linkage. To this end, resins were synthesized in which the carboxylic acid linker is attached to the solid support by an ether bond. Therefore, butanediol (**19**) was treated with chloromethylated polystyrene **18** and the resulting polymer-bound alcohol **20** was oxidized in two steps: firstly to the aldehyde **21** [employing 1-hydroxy-1,2-benziodoxol-3(1*H*)-one (IBX)] and then to the acid **22** (employing *m*CPBA; see Scheme 5), which was



Scheme 5. Synthesis of the acid-functionalized polystyrene resin **22** with an ether linkage.

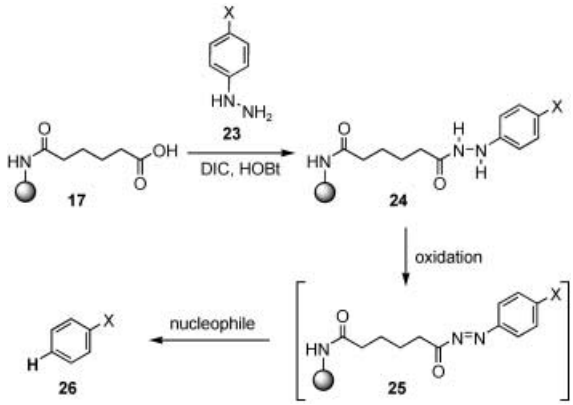
formed with an overall yield of 93%. The loading of polymeric support **20** was determined by acylation with Fmoc-Cl, cleavage of the carbonate, and UV-spectrometric determination of the released fulvene.[12] The loading of resin **22** was determined as described above for polymeric support **17**.

Development of conditions for the traceless cleavage: Phenylydrazines **23** were attached to carboxy-functionalized resins **17** by means of well-established procedures and reagents for amide bond formation.[13] To this end, resins **17** were activated with *N*,*N*′-diisopropyl carbodiimide (DIC) and 1-hydroxybenzotriazole (HOBt; Scheme 6). The resulting polymer-bound arylhydrazides were then subjected to different oxidative cleavage conditions (Table 1) and the released compounds were analyzed by means of HPLC and GC-MS.

Table 1. Oxidative cleavage of the polymer-bound iodophenylhydrazide with amines and oxygen.

Amine/O_2	Yield [%][a]
ethylene diamine	97
n-propylamine	90
cyclohexylamine	68
tert-butylamine	traces
piperidine	42
triethylamine	traces

[a] Determined by HPLC.



Scheme 6. Oxidative cleavage of the traceless hydrazide linker.

Previous works by Semenov et al.[4a] on the use of polymer-bound phenylhydrazides in solid-phase peptide synthesis had made extensive use of Cu^{II}-mediated oxidative cleavage. Application of the conditions developed in this context led to the release of model aromatic compounds **26** (X = NO_2, I, Br, OCH_3) in 83–95% yield. However, the isolation of the product from a mixture of pyridine and acetic acid in DMF was cumbersome. This problem was overcome by employing the conditions described by Lowe et al.[4b] for the cleavage of polymer-bound peptide phenylhydrazides. It includes the use of catalytic amounts of $[Cu(OAc)_2]$ in the presence of amines or in the presence of alcohols and pyridine (for complexation of Cu^{II}).

Application of 0.5 equiv $[Cu(OAc)_2]$ in *n*-propylamine (Method A) led to quantitative cleavage of the phenylhydrazides from resin **24**. The procedure worked well for Tentagel, polystyrene, or ArgoPore as polymeric carriers and tolerated different substituents in the aromatic ring (**26**: X = NO_2, I, Br, OCH_3). Cu^{I} formed in the course of the reaction can readily be reoxidized with oxygen. Reduction of the amount of copper to 0.1 equiv is possible; however, this results in longer reaction times (10 h instead of 2 h). In cases where the use of primary amines may be problematic (e.g. if reactive carbonyl groups are embedded in the target compounds), 0.5 equiv $[Cu(OAc)_2]$ and 10 equiv pyridine in methanol as the solvent (Method B) proved to be advantageous. Method B worked well with all polymeric supports investigated. However, in the case of the nonpolar polystyrene and ArgoPore supports, THF had to be added to ensure sufficient wetting and swelling of the polymeric carriers.

For subsequent biological testing of compounds prepared employing the hydrazide linker, it is mandatory to remove the copper. This was achieved by partitioning the crude product between ether and 1N HCl. Investigation of the product obtained from the organic layer by means of atom absorption spectroscopy revealed that 99.9% of the copper had been removed. Alternatively, it was possible to remove the copper by means of solid-phase extraction techniques. Filtering a solution of the crude product in an aprotic solvent through a silica gel cartridge led to the removal of 99.9% of the metal salt.

Particularly effective is the use of a polyamine scavenger[14] (tris(2-aminoethyl)amine resin, Novabiochem, 200–

400 mesh). Suspension of the crude product in dichloromethane and trituration with 10 equiv of the polyamine resin at room temperature resulted in the 99.99% removal of the copper.

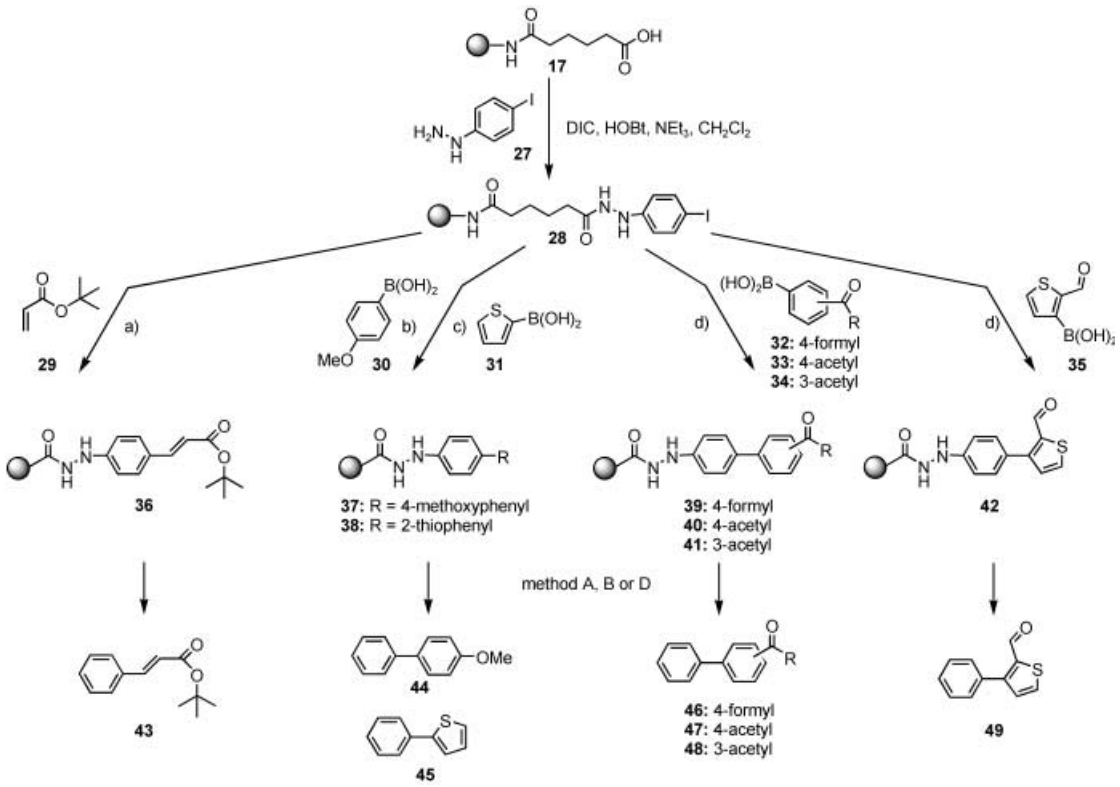
These results demonstrate that the Cu^{II}-mediated oxidative cleavage procedures are mild and efficient methods for the traceless cleavage of the hydrazide linker.

In the course of the experiments mentioned above and subsequent investigations, it was observed that the linker is also sensitive to treatment with amines in the presence of oxygen (probably via intermediary formation of amine oxides). This is particularly the case for primary and secondary amines. Thus, in the presence of ethylenediamine or *n*-propylamine, *p*-iodobenzene was released after 24 h in 97 and 90% yields, respectively. Increasing steric demand of the amine reduces the yield. With cyclohexylamine only 68% of the product was formed, while cleavage was not observed in the presence of *tert*-butylamine. The use of the secondary amine piperidine gave 42% of the product whereas triethylamine did not induce cleavage at all. The presence of oxygen is necessary. Under argon and if oxygen-free solvents and reagents are used cleavage does not occur.

In principle, this observation can be exploited to cleave the linker under very convenient conditions. The resin is simply shaken in the presence of an appropriate amine and in a stream of oxygen. Product isolation is achieved by simple evaporation of the solvent and the amine. For this purpose, *n*-propylamine is particularly advantageous on account of its low boiling point (Method C).

In general, the oxidative cleavage of the phenylhydrazides is a two-step process consisting of oxidation to the activated acyldiazene intermediate and its subsequent nucleophile-induced fragmentation. It would, therefore, be advantageous not to conduct them in a one-pot reaction as in the methods described above. Rather, if oxidation to the acyl diazene could be achieved in the absence of a suitable nucleophile, all reagents could be conveniently removed and fragmentation would then be induced in a separate second operation. This could simplify product isolation since only excess nucleophile and solvent would have to be removed. Phenylhydrazides can be oxidized in solution to acyldiazenes with NBS and pyridine in dichloromethane.[15, 16] They can be isolated and they are reasonably stable in the absence of water and other nucleophiles. Based on these findings, a two-step process as delineated above was developed. Oxidation of polymer-bound hydrazides to acyl diazenes was achieved with 2 equiv NBS and 2 equiv pyridine in dichloromethane. After 5 minutes all reagents were removed by simple filtration and washing steps. Fragmentation was then induced by the addition of methanol and, after shaking for 2 h, the products were isolated by filtration and evaporation of methanol. This procedure (Method D) gave yields $>90\%$ for both electron-rich and electron-poor aromatic compounds (Table 2).

Application of the phenylhydrazide linker in solid-phase syntheses: In order to demonstrate the wide applicability of the hydrazide linker in solid-phase synthesis, different Pd^0-



Scheme 7. Heck and Suzuki reactions employing polymer-bound 4-iodoarylhydrazides **28** and traceless oxidative cleavage of the coupling products from the solid supports. For yields, see Table 3. a) 6 equiv **29**, 3 equiv NaOAc, 1 equiv Bu_4NBr, 0.2 equiv $[Pd(OAc)_2]$, dimethylacetamide, 100 °C, 24 h; b) 10 equiv **30**, 2 equiv K_3PO_4, 0.02 equiv $[Pd(PPh_3)_4]$, dimethylformamide/water 6:1, 80 °C, 24 h; c) 5 equiv **31**, 2 equiv K_2CO_3, 0.1 equiv $[Pd_2(dba)_3]$, dimethylformamide, 90 °C, 24 h; d) 8 equiv **32–35**, 18 equiv K_2CO_3, 10 equiv *N*,*N*-diisopropyl-*N*-ethylamine, 0.2 equiv $[Pd(OAc)_2]$, dioxane/water 6:1, 95 °C, 24 h.

Table 2. Methods for oxidative cleavage of the traceless hydrazide linker.

Method A	$[Cu(OAc)_2]$ (5 mM, 0.5 equiv) in *n*-propylamine, O_2, 2 h
Method B	$[Cu(OAc)_2]$ (5 mM, 0.5 equiv) and pyridine (0.1M) in methanol, O_2, 2 h
Method C	*n*-propylamine, O_2, 24 h
Method D	i) NBS (2 equiv) and pyridine in CH_2Cl_2, 5 min, ii) methanol, 2 h

catalyzed transformations, as well as Wittig and Grignard reactions were investigated and the coupling products were released from the solid support with formation of a C–H bond at the former attachment site.

For the Pd-catalyzed reactions, 4-iodophenylhydrazine (**27**) was coupled to the solid support and iodinated hydrazides **28** were subjected to a Heck reaction with acrylic *tert*-butyl ester (**29**; Scheme 7). For all three polymeric carriers investigated, quantitative conversion was achieved (Table 3) at 80 °C in dimethylacetamide and in the presence of palladium(II) acetate, triphenylphosphine, tetrabutylammonium acetate, and sodium acetate.[17] Oxidative cleavage of polymer-bound hydrazides **36** was carried out employing Methods A, B, and D (Table 2) and cinnamic ester (**43**) was obtained in 83–96% yield (Table 3).

Polymer-bound aryl iodides **28** were also employed in Suzuki reactions with boronic acids **30** and **31** (Scheme 7). Coupling of iodide **28** with compound **30** proceeded well in the presence of $[Pd(PPh_3)_4]$ in DMF/water (6:1) and with K_2CO_3 as base.[18] Application of Methods A, B, and D yielded biphenyl **44** in overall yields of 60–93%. Thienylboronic acid (**31**) was used to investigate the compatibility of the oxidative cleavage conditions with oxidation-sensitive compounds. After employing $[Pd(OAc)_2]$ as catalyst and *i*PrNEt$_2$ as base in dioxane/H_2O[19] and oxidative cleavage of the linker, arylated thiophene **45** was obtained in only 20% yield. However, a change of the solvent (DMF) and the base (K_2CO_3) and double coupling in the presence of the more reactive catalyst $[Pd_2(dba)_3]$ served to increase the overall yield. Hydrazide cleavage with Method B delivered thienyl compound **45** in 77% yield.[20] Attack on the thiophene was not observed.

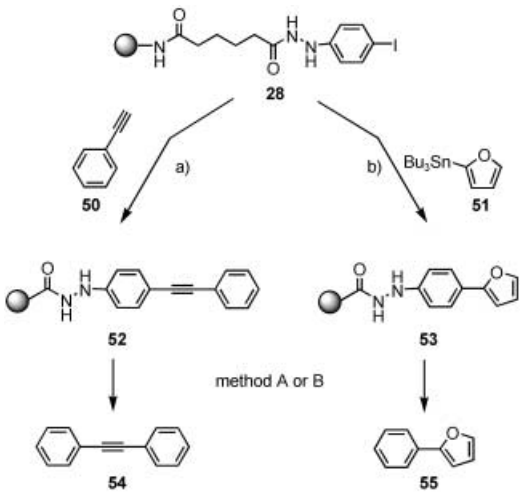
Table 3. Representative results of the three-step reaction sequence on the solid support consisting of hydrazide formation, Pd^0-catalyzed coupling reaction and oxidative cleavage of the hydrazide linker (Methods A, B or D).

Compound	Polymeric support	Method[a]	Yield [%][b] (three steps)
43	TentaGel	D	83
43	polystyrene	A	84
43	polystyrene	B	85
43	ArgoPore	A	89
43	ArgoPore	B	96
44	TentaGel	A	93
44	TentaGel	B	86
44	TentaGel	D	74
44	polystyrene	A	67
44	ArgoPore	A	60
45	polystyrene	B	77
46	polystyrene	B	39
47	polystyrene	B	48
48	polystyrene	B	40
49	polystyrene	B	32
54	polystyrene	A	92
54	polystyrene	B	93
54	ArgoPore	A	86
55	TentaGel	A	86
55	polystyrene	A	79
55	polystyrene	B	79
55	ArgoPore	A	80

[a] Method A: $[Cu(OAc)_2]$, *n*-propylamine, RT, 2 h; Method B: $[Cu(OAc)_2]$ (0.5 equiv), methanol, pyridine (10 equiv, RT, 2 h; Method D: NBS (2 equiv), pyridine (2 equiv), CH_2Cl_2, RT, 45 min.; after filtration addition of methanol. [b] Determined for the unpurified products. All products were >90% pure (HPLC, GCMS, NMR).

Additional Suzuki reactions were carried out with less reactive acetyl and formylboronic acids **32**–**35**. After optimization of the reaction conditions,[20] (see the Experimental Section) acylated biphenyl derivatives **39**–**42** were formed and then tracelessly released from the resin employing Method B to yield compounds **46**–**49** in moderate yields (Scheme 7, Table 3).

Next, a Sonogashira and a Stille coupling were investigated (Scheme 8). On the one hand, iodoaryl resins **28** were treated with phenylacetylene (**50**) and $[Pd(PPh_3)_2Cl_2]/Cu^I$ as catalyst system in dioxane/NEt_3 (2:1) at room temperature.[17] Target compound **54** was then released into solution in yields up to 93% by means of Methods A or B.

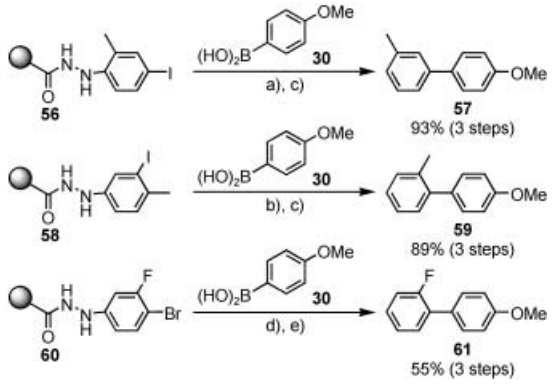


Scheme 8. Sonogashira and Stille reactions employing polymer-bound 4-iodoarylhydrazides **28** and traceless oxidative cleavage of the coupling products from the solid supports. For yields, see Table 3. a) 6 equiv **50**, 0.2 equiv CuI, 0.1 equiv $[Pd(PPh_3)_2Cl_2]$, dioxane/triethylamine 2:1, RT, 24 h; b) 5 equiv **51**, 0.4 equiv $AsPh_3$, 0.1 equiv $[Pd_2(dba)_3]$, dioxane, 60 °C, 24 h.

On the other hand 2-furanyl-tri-*n*-butylstannane (**51**) was coupled quantitatively to aryliodide **28** in the presence of $[Pd_2(dba)_3]/AsPh_3$.[19] Subsequent Cu^{II}-mediated cleavage of phenyl-substituted furan **55** from the solid support proceeded in high yield without undesired attack on the furan.

All Pd-catalyzed C–C bond-formation reactions described above were conducted with polymer-bound 4-iodophenylhyrazide **28**. In order to demonstrate the applicability of the new traceless linker to other derivatives, immobilized arylhydra-

zides **56**, **58**, and **60** were synthesized and subjected to Suzuki reactions with boronic acid (**30**; Scheme 9). The hydrazines required for coupling to the solid support were synthesized from the corresponding anilines by diazotation ($NaNO_2$ in HCl) and reduction of the diazonium salts ($SnCl_2$ in HCl).[21]



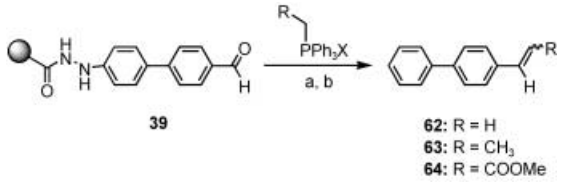
Scheme 9. Pd^0-catalyzed C–C coupling reactions employing polymer-bound 4-iodoarylhydrazide **56** and **58** and 4-bromoarylhydrazide (**60**) with traceless oxidative cleavage of the coupling products from the solid supports. a) 10 equiv **30**, 2 equiv K_3PO_4, 0.02 equiv $[Pd(PPh_3)_4]$, dimethylformamide/water 6:1, 80 °C, 24 h; b) As for a), 95 °C; c) Method A; d) 3 equiv **30**, 0.03 equiv $[Pd(PPh_3)_4]$, dimethylformamide/triethylamine 1:1, 90 °C, 24 h; e) Method D.

Aryliodides **56** and **58** were converted into the corresponding biaryls according to the method used by Piettre et al.[17] Finally, oxidation with $[Cu(OAc)_2]$ in *n*-propylamine (Method A) yielded biaryls **57** and **59** in 93 and 89 % overall yield.

Activation of aryl bromide **60** was not efficient under the conditions developed for the aryl iodides. High yields were obtained, however, in DMF/NEt_3 (1:1) and in the presence of $[Pd(PPh_3)_4]$.[22] Subsequent oxidation with NBS in the presence of pyridine and methanol-induced fragmentation of the intermediary formed diazene (Method D) delivered fluorinated biaryl compound **61** in a very useful overall yield of 55 %.

In addition to the Pd-catalyzed reactions, the phenylhydrazide linker was also investigated in further important C–C bond-forming reactions.

Thus, polymer-bound aldehyde **39** was subjected to Wittig reactions with different phosphonium salts. Application of methyl-, ethyl-, and methoxycarbonylmethyl triphenylphosphonium salts at 60 °C in THF and employing KO*t*Bu as base[23] resulted in complete conversion (Scheme 10). Target



Scheme 10. Wittig reactions employing polymer-bound 4-biphenylaldehyde **39** and traceless oxidative cleavage of the coupling products from the solid supports. For yields, see Table 4. a) 10 equiv alkyl-triphenylphosphonium salt, 10 equiv potassium *tert*-butoxide, THF, 60 °C, 24 h; b) Method A.

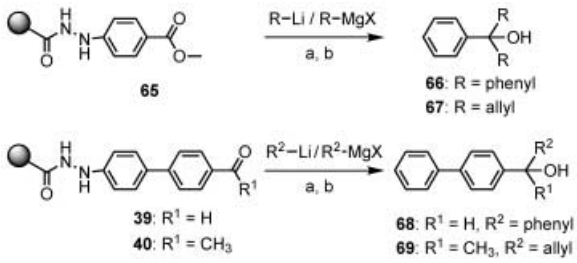
compounds **62**–**64** were obtained in yields of 27–45 % (four steps) and with purities >90 % after cleavage according to Method A and subsequent solid-phase extraction (Table 4).

Table 4. Results of the reaction sequences on the solid support including a Wittig reaction or a reaction with an organometallic reagent.

Compound	Polymeric support	Method	Yield [%][a] (all steps)
62	polystyrene	A	45
63	polystyrene	A	39 (*cis*:*trans* 43:57)
64	polystyrene	A	27
66	polystyrene	A	62
67	polystyrene	A	60
68	polystyrene	A	35
69	polystyrene	A	37

[a] Determined for the unpurified products. All products were >97 % pure (HPLC, GCMS, NMR).

Also, the compatibility of the hydrazide linker with organometallic reagents, namely phenyl lithium and allylmagnesium bromide, was investigated.[24] To this end, polymer-bound ester **65** was synthesized and treated with the organometallic reagents (Scheme 11). Complete conversion



Scheme 11. Reactions with organometallic reagents employing polymer-bound 4-hydrazinobenzoic acid methyl ester **65**, biphenylaldehyde (**39**), and biphenylketone (**40**) with traceless oxidative cleavage of the coupling products from the solid supports. For yields, see Table 4. a) 2 × 20 equiv organometallic reagent, THF, RT, 72 h; b) Method A.

could not be achieved at 0 °C. The temperature had to be raised to room temperature to obtain the desired alcohols **66** and **67** in high yields (60–62 %).[25] Similarly, immobilized aldehyde **39** was converted into a secondary alcohol with phenyl lithium, and ketone **40** yielded tertiary alcohol **69** after treatment with allylmagnesium bromide and subsequent traceless cleavage in overall yields of 35 % and 37 %, respectively, and with high purity.

Conclusion

The results detailed above clearly demonstrate that the traceless hydrazide linker is compatible with several of the most important organic synthesis reactions. It is stable under very different conditions yet it can be removed selectively in a traceless manner with mild oxidative methods that are compatible with various functional groups and oxidation-labile structures. Thus, if Methods A and B are used for cleavage, double and triple bonds remain intact, and thio-

phene and furan groups are not affected. Also cinnamic esters can be formed efficiently. The experimental conditions for cleavage of the linker group can be varied such that the desired products are obtained after simple extraction or even without a further separation step in high overall yields and with excellent purity.

Together with the results described in the accompanying paper,[5] our findings demonstrate that the hydrazide linker can be applied widely and opens up new opportunities to solid-phase and combinatorial chemistry.

Experimental Section

General procedures: ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AC250, DRX400 or DRX500 spectrometers. HPLC were measured on an Agilent 1100 Series equipped with a C18PPN column (Macherey & Nagel). GCMS were measured on a Agilent 6890 Series gas chromatograph connected to a Agilent 5973 Series mass spectrometer. All HPLC was performed with a flow rate of 1 mL min^{-1} and a gradient which changed from H_2O/acetonitrile/formic acid 90:10:0.1 (*v*/*v*/*v*) to H_2O/acetonitrile/formic acid 10:90:0.1 (*v*/*v*/*v*) within 30 min. High-resolution mass spectra (HR-MS) were measured on a Finnigan MAT8200 spectrometer. IR spectra were measured on Bruker IFS88 or Bruker Vector 22 spectrometers with a diffuse reflectance head A527 from Spectra Tech. UV spectra were measured on a Perkin–Elmer Cary50 spectrometer.

Materials: TLC was performed on Merck silica gel 60F_{254} aluminum sheets. For flash chromatography, silica gel (40–60 μm) was used. The resins were purchased from Rapp Polymere, Advanced Chemtech, and Argonaut Technologies. If not otherwise indicated, all reactions were performed under an argon atmosphere with freshly distilled and dried solvents. All solvents were distilled by means of standard procedures. Commercial reagents were used without further purification.

General procedure for the preparation of acid-functionalized supports 17 with adipic dichloride (Procedure A): Adipic dichloride (30 equiv) was added slowly to a suspension of the appropriate amino-functionalized resin in CH_2Cl_2 and pyridine (5:1, 30 mL g^{-1} resin). The mixture was shaken for 18 h at room temperature and then filtered. The resin washed with THF, THF/1N HCl (1:1), THF, methanol, methylene chloride, and cyclohexane (2× each), and was then dried to constant weight in vacuo.

General procedure for the preparation of acid-functionalized supports 17 with adipic anhydride (Procedure B): Freshly distilled adipic anhydride (10 equiv) was added to a suspension of the appropriate amino-functionalized resin in methylene chloride (30 mL g^{-1} resin). The mixture was shaken for 24 h at room temperature and then filtered. The resin washed with methylene chloride, THF, THF/1N HCl (1:1), THF, methanol, methylene chloride, and cyclohexane (2× each), and was then dried to constant weight in vacuo.

General procedure for the preparation of acid-functionalized supports 17 with adipic acid monomethyl ester (Procedure C): *N*,*N*-Diisopropylcarbodiimide (3 equiv), 1-hydroxybenzotriazole (3 equiv), triethylamine (3 equiv), and adipic acid monomethylester (3 equiv) were added to a suspension of the appropriate amino-functionalized resin in methylene chloride (30 mL g^{-1} resin). The mixture was shaken for 18 h at room temperature and then filtered. The resin washed with methylene chloride, THF, THF/1N HCl (1:1), THF, methanol, methylene chloride, and cyclohexane (2× each), and was then dried to constant weight in vacuo. The resin was suspended in dioxane (20 mL g^{-1} resin). After 15 min, 1% aqueous lithium hydroxide solution (20 mL g^{-1} resin) was added. The mixture was shaken for 18 h at room temperature and filtered. The resin was washed with methylene chloride, THF, THF/1N HCl (1:1), THF, methanol, methylene chloride, and cyclohexane (2× each) and was then dried to constant weight in vacuo.

Acid-functionalized TentaGel (17a): According to Procedure A, TentaGel-HL-NH_2 (5 g, 2.10 mmol, Rapp Polymere, 0.42 mmol g^{-1}, 130 μm) was treated with adipic dichloride (9.0 mL, 63 mmol) in methylene chloride and pyridine (5:1, 150 mL) to yield the off-white resin **17a** (5.18 g). IR (SiO_2): $\tilde{\nu}$ = 3357 (OH), 1739 (C=O), 1667 (C=O), 1109 (C-O-C) cm^{-1}; loading: 0.24 mmol g^{-1} (59%). Preparation of **17a** according to Procedure B: loading: 0.39 mmol g^{-1} (97%). Preparation of **17a** according to Procedure C: loading: 0.37 mmol g^{-1} (92%).

Acid-functionalized polystyrene (17b): According to Procedure A, polystyrene-NH_2 (5 g, 5.50 mmol, Rapp Polymere, 1.1 mmol g^{-1}, 100–200 mesh) was treated with adipic acid dichloride (23.7 mL, 165 mmol) in methylene chloride and pyridine (5:1, 150 mL) to yield the off-white resin **17b** (5.23 g). IR (SiO_2): $\tilde{\nu}$ = 3349 (OH), 1742 (C=O), 1658 (C=O) cm^{-1}; loading: 0.42 mmol g^{-1} (44%). Preparation of **17b** according to Procedure B: loading: 0.93 mmol g^{-1} (96%). Preparation of **17b** according to Procedure C: loading: 0.92 mmol g^{-1} (95%).

Acid-functionalized ArgoPore (17c): According to Procedure A, ArgoPore-NH_2 (5 g, 5.65 mmol, Argonaut Technologies, 1.13 mmol g^{-1}, 60–140 mesh) was treated with adipic acid dichloride (24.3 mL, 169.5 mmol) in methylene chloride and pyridine (5:1, 150 mL) to yield the off-white resin **17c** (5.15 g). IR (SiO_2): $\tilde{\nu}$ = 3412 (OH), 1742 (C=O), 1682 (C=O) cm^{-1}; loading: 0.35 mmol g^{-1} (36%). Preparation of **17c** according to Procedure C: loading: 0.94 mmol g^{-1} (95%).

Polystyrene-bound alcohol (20): Sodium hydride (692 mg, 17.3 mmol, 60% in mineral oil) was added to a solution of butanediol (**19**, 1.54 mL, 17.3 mmol) in dry DMF (100 mL) at 0 °C and the mixture was shaken for 90 min. A suspension of chloromethylated polystyrene **18** (4.81 g, 4.33 mmol, Advanced Chemtech, 0.9 mmol g^{-1}, 100–200 mesh) and tetrabutylammonium iodide (159 mg, 0.433 mmol) in dry DMF (50 mL) was added. The mixture was shaken for 18 h at room temperature and filtered. The resin was washed with DMF, THF, THF/1N HCl (1:1), THF, methanol, methylene chloride, and cyclohexane (2× each), and then dried to constant weight in vacuo to yield the off-white resin **20** (4.82 g). IR (SiO_2): $\tilde{\nu}$ = 3448 (OH), 1099 (C-O-C) cm^{-1}; loading: 0.82 mmol g^{-1} (96%). The loading was determined as follows: to a suspension of **20** (10 mg) in methylene chloride and pyridine (10:1, 3 mL) was added Fmoc-Cl (10 equiv) and the mixture was shaken at room temperature for 2 h. The resin was filtered, washed with methylene chloride, THF and methylene chloride (2× each), and then dried to constant weight in vacuo. The Fmoc-loading of the resin was determined by standard procedures used to calculate the hydroxyl loading.[12]

Polystyrene-bound aldehyde (21): IBX (2.99 g, 11.07 mmol) was added to a suspension of polystyrene-bound alcohol **20** (4.5 g, 3.69 mmol) in THF/DMSO (1:1, 90 mL). The mixture was shaken for 18 h at room temperature and then filtered. The resin was washed with THF/DMSO (1:1), THF, methanol, methylene chloride, and cyclohexane (2× each), and then dried to constant weight in vacuo to yield the off-white resin **21** (4.45 g). IR (SiO_2): $\tilde{\nu}$ = 2717 (CHO), 1727 (C=O) cm^{-1}.

Polystyrene-bound acid (22): To a suspension of the polystyrene-bound aldehyde **21** (4.0 g, 3.28 mmol) in 1,2-dichloroethane/cyclohexane (1:1, 160 mL) was added *m*-chloroperbenzoic acid (*m*-CPBA, 70%, 8.1 g, 32.8 mmol) and the mixture was refluxed for 48 h. After cooling to room temperature, the mixture was filtered. The resin was washed with methylene chloride, THF, THF/1N HCl (1:1), methanol, methylene chloride, and cyclohexane (2× each), and then dried to constant weight in vacuo to yield the off-white resin **22** (3.98 g). IR (SiO_2): $\tilde{\nu}$ = 3325 (OH), 1743 (C=O) cm^{-1}; loading: 0.79 mmol g^{-1} (93% over 3 steps, starting from **18**).

General procedure for the oxidative cleavage of the phenylhydrazide linker with [Cu(OAc)$_2$] and *n*-propylamine (Method A): The resin was suspended in 0.5 equiv [$Cu(OAc)_2$] in *n*-propylamine (5 mM) and was shaken at room temperature for 2 h with oxygen bubbling through the mixture. The solvent was removed under reduced pressure and the work-up was performed using one of the following procedures: i) addition of diethyl ether and 1N HCl (1:1) to the residue. After phase separation, the organic layer was dried over $MgSO_4$. The solvent was removed and the residue was dried in vacuo. ii) The residue was suspended in methylene chloride (50 mL g^{-1} resin) and tris-(2-aminoethyl)amino resin (5 equiv, Novabiochem, 200–400 mesh) was added. The mixture was shaken for 1 h at room temperature and then filtered. The filtrate was evaporated and dried in vacuo. iii) The residue was suspended in cyclohexane/ethyl acetate (10:1) or methylene chloride/cyclohexane (5:1), filtered through a SPE cartridge (SiO_2) and washed with cyclohexane/ethyl acetate (1:1) or methylene chloride (3×). The filtrate was evaporated and dried in vacuo.

General procedure for the oxidative cleavage of the phenylhydrazide linker with [Cu(OAc)$_2$], methanol, and pyridine (Method B): The resin was suspended in 0.5 equiv [Cu(OAc)$_2$] (5 mM) and pyridine (100 nM) in methanol and was shaken at room temperature for 2 h with oxygen bubbling through the mixture. If polystyrene resins were used, the same volume of THF was added. The solvent was removed under reduced pressure and the work-up was performed using one of the procedures described above.

General procedure for the oxidative cleavage of the phenylhydrazide linker with *n*-propylamine (Method C): The resin was suspended in *n*-propylamine (50 mL g^{-1} resin) and shaken at room temperature for 24 h with oxygen bubbling through the mixture. The mixture was filtered, the filtrate was evaporated, and the residue was dried in vacuo.

General procedure for the oxidative cleavage of the phenylhydrazide linker with NBS and pyridine (Method D): The resin was suspended in a solution of 2 equiv NBS (15 mM) and pyridine (15 mM) in dichloromethane, the mixture was shaken at room temperature for 5 min, filtered, and washed with dichloromethane (2 ×). The TentaGel resins were suspended in methanol (5 mL), the polystyrene resins were suspended in methanol/THF (1:1, 5 mL) and shaken for 2 h at room temperature. The mixture was filtered, the filtrate was evaporated to dryness, and the residue was dried in vacuo.

General procedure for the carbodiimide-mediated preparation of polymer-bound phenylhydrazides (Procedure E): To a suspension of the acid-functionalized support **17** in methylene chloride (20 mL g^{-1} resin), were added *N,N*-diisopropylcarbodiimide (3 equiv), 1-hydroxybenzotriazole (3 equiv), triethylamine (3 equiv), and phenylhydrazine (3 equiv). The mixture was shaken for 18 h at room temperature and filtered. The resin was washed with methylene chloride, THF, THF/1N HCl (1:1), THF, methanol, methylene chloride, and cyclohexane (2 × each), and dried to constant weight in vacuo.

TentaGel-bound 4-iodophenylhydrazide (28a): According to Procedure E, TentaGel resin **17a** (1 g, 0.24 mmol) was treated with *N,N*-diisopropylcarbodiimide (111 μL, 0.72 mmol), 1-hydroxybenzotriazole (110 mg, 0.72 mmol), triethylamine (101 μL, 0.72 mmol), and 4-iodophenylhydrazine (**27**, 168 mg, 0.72 mmol) in methylene chloride (20 mL) to yield the yellow resin **28a** (1.03 g). IR (KBr): $\tilde{\nu}$ = 3296 (NH), 1669 (C=O), 1108 (C-O-C) cm^{-1}.

Polystyrene-bound 4-iodophenylhydrazide (28b): According to Procedure E, polystyrene resin **17b** (1 g, 0.42 mmol) was treated with *N,N*-diisopropylcarbodiimide (195 μL, 1.26 mmol), 1-hydroxybenzotriazole (193 mg, 1.26 mmol), triethylamine (176 μL, 1.26 mmol), and 4-iodophenylhydrazine (**27**, 295 mg, 1.26 mmol) in methylene chloride (20 mL) to yield the yellow resin **28b** (1.04 g). IR (KBr): $\tilde{\nu}$ = 3290 (NH), 1661 (C=O) cm^{-1}.

ArgoPore-bound 4-iodophenylhydrazide (28c): According to Procedure E, ArgoPore resin **17c** (1 g, 0.35 mmol) was treated with *N,N*-diisopropylcarbodiimide (162 μL, 1.05 mmol), 1-hydroxybenzotriazole (161 mg, 1.05 mmol), triethylamine (145 μL, 1.05 mmol), and 4-iodophenylhydrazine (**27**, 246 mg, 1.05 mmol) in methylene chloride (20 mL) to yield the yellow resin **28c** (1.02 g). IR (KBr): $\tilde{\nu}$ = 3291 (NH), 1665 (C=O) cm^{-1}.

General procedure for the preparation of the polymer-bound cinnamic *tert*-butyl ester (36; Procedure F): Acrylic *tert*-butyl ester (**29**, 6 equiv) was added to a suspension of the polymer-bound 4-iodophenylhydrazide (**28**), sodium acetate (3 equiv) and tetrabutylammonium bromide (1 equiv) in dimethylacetamide (5–10 mL g^{-1} g^{-1} resin). The mixture was degassed (ultrasound), palladium(II) acetate (0.2 equiv) was added and the mixture was heated to 100 °C for 24 h. The mixture was cooled to room temperature and filtered. The resin was washed with DMF, water, DMF, ethyl acetate, and methylene chloride (3 × each), and was then dried to constant weight in vacuo.

TentaGel-bound cinnamic *tert*-butyl ester (36a): According to Procedure F, TentaGel-bound 4-iodoarylhydrazide (**28a**, 650 mg, 0.15 mmol), sodium acetate (37 mg, 0.45 mmol) and tetrabutylammonium bromide (48 mg, 0.15 mmol) were treated with acrylic *tert*-butyl ester (**29**, 131 μL, 0.9 mmol) and palladium(II) acetate (7 mg, 30 μmol) in dimethylacetamide (3 mL) to yield the black resin **36a** (641 mg). IR (KBr): $\tilde{\nu}$ = 3204 (NH), 1699 (C=O), 1668 (C=O) cm^{-1}.

Cinnamic *tert*-butyl ester (43): According to Method D for the oxidative cleavage of the hydrazide linker, **36a** (266 mg, 34 μmol) was oxidized with NBS and pyridine in methylene chloride and the product was cleaved by addition of methanol to yield yellowish oil (6.0 mg, 29 μmol, 83%). R_f = 0.51 (cyclohexane/ethyl acetate 10:1); HPLC: 91% (260 nm); ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.58 (d, ^3J(H,H) = 14.6 Hz, 1H, Ph-C*H*=CH), 7.55–7.35 (5H, arom. CH), 6.38 (d, ^3J(H,H) = 14.6 Hz, 1H, Ph-CH=C*H*), 1.52 (s, 9H, C(CH$_3$)$_3$); GCMS (70 eV, EI): *m*/*z* (%): 204 (10) [*M*]$^+$, 147 (100), 131 (70), 103 (33), 77 (33), 57 (51), 51 (16), 41 (27), 29 (14). The spectroscopic data are in agreement with reported values.[26]

Polystyrene-bound cinnamic *tert*-butyl ester (36b): According to Procedure F, polystyrene-bound 4-iodoarylhydrazide (**28b**, 800 mg, 0.12 mmol), sodium acetate (30 mg, 0.36 mmol), and tetrabutylammonium bromide (37 mg, 0.12 mmol) were treated with acrylic *tert*-butyl ester (**29**, 105 μL, 0.72 mmol) and palladium(II) acetate (5 mg, 24 μmol) in dimethylacetamide (6 mL) to yield the black resin **36b** (786 mg). IR (KBr): $\tilde{\nu}$ = 3286 (NH), 1704 (C=O), 1670 (C=O) cm^{-1}.

Cinnamic *tert*-butyl ester (43): According to Method A for the oxidative cleavage of the hydrazide linker, **36b** (205 mg, 31 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by extractive work-up to yield the title compound (5.3 mg, 26 μmol, 84%). HPLC: 92% (260 nm). Cleavage according to Method B: Yield: 85%; HPLC: 93% (260 nm).

ArgoPore-bound cinnamic *tert*-butyl ester (36c): According to Procedure F, ArgoPore-bound 4-iodophenylhydrazide (**28c**, 231 mg, 0.04 mmol), sodium acetate (10 mg, 0.12 mmol), and tetrabutylammonium bromide (13 mg, 0.04 mmol) were treated with acrylic acid *tert*-butyl ester (**29**, 35 μL, 0.24 mmol) and palladium(II) acetate (2 mg, 8 μmol) in dimethylacetamide (3 mL) to yield the black resin **36c** (224 mg). IR (KBr): $\tilde{\nu}$ = 3245 (NH), 1700 (C=O), 1670 (C=O) cm^{-1}.

Cinnamic *tert*-butyl ester (43): According to Method A for the oxidative cleavage of the hydrazide linker, **36c** (117 mg, 20 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by extractive work-up to yield the title compound (3.7 mg, 18 μmol, 89%). HPLC: 98% (260 nm). Cleavage according to Method B: Yield: 95%; HPLC: 97% (260 nm).

General procedure for the preparation of polymer-bound 4-methoxybiphenyls (Procedure G): 4-Methoxyphenylboronic acid (**30**, 10 equiv) was added to a suspension of the polymer-bound 4-iodophenylhydrazide (**28**) and potassium phosphate trihydrate (2 equiv) in DMF/water (6:1) and the mixture was degassed (ultrasound). [Pd(PPh$_3$)$_4$] (0.02 equiv) was added and the mixture was heated to 80 °C for 24 h. The mixture was cooled to room temperature and filtered. The resin was washed with DMF, water, DMF, ethyl acetate, and methylene chloride (3 × each), and then dried to constant weight in vacuo.

TentaGel-bound 4-methoxybiphenyl (37a): According to Procedure G, TentaGel-bound 4-iodophenylhydrazide (**28a**, 525 mg, 0.21 mmol) was treated with 4-methoxyphenylboronic acid (**30**, 319 mg, 2.1 mmol), potassium phosphate (112 mg, 0.42 mmol), and [Pd(PPh$_3$)$_4$] (5 mg, 4 μmol) in DMF/water (6:1, 14 mL) to yield the black resin **37a** (507 mg). IR (KBr): $\tilde{\nu}$ = 3323 (NH), 1667 (C=O), 1122 (C-O-C) cm^{-1}.

4-Methoxybiphenyl (44): According to Method A for the oxidative cleavage of the hydrazide linker, **37a** (107 mg, 25 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by extractive work-up to yield the title compound (4.3 mg, 23 μmol, 93%). HPLC: 94% (260 nm); off-white solid. R_f = 0.58 (cyclohexane/ethyl acetate 10:1); m.p. 85 °C; ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.58–7.26 (7H, arom. CH), 6.93 (d, ^3J(H,H) = 8.8 Hz, 2H, arom. CH), 3.82 (s, 3H, OCH$_3$); GCMS (70 eV, EI): *m*/*z* (%): 184 (100) [*M*]$^+$, 169 (46), 141 (46), 115 (38), 63 (10), 44 (10), 32 (38), 28 (91). The spectroscopic data are in agreement with reported values.[27, 29] Cleavage according to Method B: Yield: 86%; HPLC: 95% (260 nm). Cleavage according to Method D: Yield: 74%; HPLC: 91% (260 nm).

Polystyrene-bound 4-methoxybiphenyl (37b): According to Procedure G, polystyrene-bound 4-iodophenylhydrazide (**28b**, 1.35 g, 0.5 mmol) was treated with 4-methoxyphenylboronic acid (**30**, 760 mg, 5.0 mmol), potassium phosphate (266 mg, 1.0 mmol), and [Pd(PPh$_3$)$_4$] (12 mg, 10 μmol) in DMF/water (6:1, 14 mL) to yield the black resin **37b** (1.27 g). IR (KBr): $\tilde{\nu}$ = 3224 (NH), 1678 (C=O) cm^{-1}.

4-Methoxybiphenyl (44): According to Method A for the oxidative cleavage of the hydrazide linker, **37b** (103 mg, 31 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by extractive work-up to yield the title compound (3.9 mg, 21 μmol, 67%); HPLC: 96% (260 nm).

ArgoPore-bound 4-methoxybiphenyl (37c): According to Procedure G, ArgoPore-bound 4-iodophenylhydrazide (**28c**, 3.2 g, 1.13 mmol) was treated with 4-methoxyphenylboronic acid (**30**, 1.71 g, 11.3 mmol), potassium phosphate (599 mg, 2.25 mmol), and $[Pd(PPh_3)_4]$ (26 mg, 23 μmol) in DMF/water (6:1, 14 mL) to yield the black resin **37c** (3.1 g). IR (KBr): $\tilde{\nu}=3195$ (NH), 1679 (C=O) cm^{-1}.

4-Methoxybiphenyl (44): According to Method A for the oxidative cleavage of the hydrazide linker, **37c** (125 mg, 41 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield the title compound (4.6 mg, 25 μmol, 60%); HPLC: 96% (260 nm).

Polystyrene-bound 2-phenylthiophene (38): A suspension of **28b** (400 mg, 73 μmol), 2-thiopheneboronic acid (**31**, 47 mg, 0.37 mmol), and potassium carbonate (20 mg, 0.14 mmol) in dry DMF (6 mL) was degassed (ultrasound). $[Pd_2(dba)_3]\cdot CHCl_3$ (8 mg, 8 μmol) was added and the mixture was heated to 90 °C for 24 h. The mixture was cooled to room temperature and filtered. The resin was washed with THF, THF/1N HCl, THF, methanol, methylene chloride, and cyclohexane (2× each), and then dried to constant weight in vacuo to yield the black resin **38** (387 mg). IR (KBr): $\tilde{\nu}=$ 3144 (NH), 1668 (C=O) cm^{-1}.

2-Phenylthiophene (45): According to Method B for the oxidative cleavage of the hydrazide linker, **38** (170 mg, 30 μmol) was treated with $[Cu(OAc)_2]$ and pyridine in methanol followed by extractive work-up to yield a yellowish oil (3.7 mg, 23 μmol, 77%). HPLC: 93% (260 nm). $R_f=0.37$ (cyclohexane/ethyl acetate 10:1); ^1H NMR ($CDCl_3$, 250 MHz): $\delta=7.53$ (d, $^3J(H,H)=9.1$ Hz, 1H, arom. CH, thiophene), 7.40–7.25 (m, 5H, arom. CH), 7.02 (d + dd, 2H, arom. CH, thiophene); GCMS (70 eV, EI): *m/z* (%): 160 (100) $[M]^+$, 128 (12), 115 (43), 89 (9), 28 (13). The spectroscopic data are in agreement with reported values.[27]

General procedure for the preparation of polymer-bound biphenylaldehydes and -ketones (Procedure H): A suspension of the polymer-bound 4-iodophenylhydrazide (**28**), potassium carbonate (18 equiv), formyl- or acetylphenylboronic acid (8 equiv), and *N,N*-diisopropyl-*N*-ethylamine (10 equiv) in dioxane/water (6:1) was degassed (ultrasound). Palladium(II) acetate (0.2 equiv) was added and the mixture was heated to 95 °C for 24 h. The mixture was cooled to room temperature and filtered. The resin was washed with THF, THF/1N HCl, THF, methanol, methylene chloride, and cyclohexane (2× each), and was then dried to constant weight in vacuo.

Polystyrene-bound biphenylaldehyde (39): According to Procedure H, polystyrene-bound 4-iodophenylhydrazide (**28b**, 400 mg, 0.3 mmol) was treated with 4-formylphenylboronic acid (**32**, 360 mg, 2.4 mmol), potassium carbonate (504 mg, 5.4 mmol), *N,N*-diisopropyl-*N*-ethylamine (420 μL, 3 mmol), and palladium(II) acetate (15 mg, 0.06 mmol) in dioxane/water (6:1, 10 mL) to yield the black resin **39** (396 mg). IR (SiO_2): $\tilde{\nu}=3307$ (NH), 2851 (CHO), 1680 (C=O) cm^{-1}.

Biphenyl-4-carbaldehyde (46): According to Method B for the oxidative cleavage of the hydrazide linker, **39** (164 mg, 126 μmol) was treated with $[Cu(OAc)_2]$ and pyridine in methanol followed by work-up with SPE. to yield an off-white solid (9.0 mg, 49 μmol, 39%); HPLC: 93% (260 nm). $R_f=0.30$ (cyclohexane/ethyl acetate 10:1); m.p. 55 °C; ^1H NMR ($CDCl_3$, 400 MHz): $\delta=10.07$ (s, 1H, CHO), 7.96 (dd, $^3J(H,H)=6.4$, $^4J(H,H)=$ 1.8 Hz, 2H, arom. CH), 7.77 (dd, $^3J(H,H)=6.4$, $^4J(H,H)=1.6$ Hz, 2H, arom. CH), 7.65 (dd, $^3J(H,H)=6.8$, $^4J(H,H)=1.4$ Hz, 2H, arom. CH), 7.50–7.44 (m, 3H, arom. CH); GCMS (70 eV, EI): *m/z* (%): 182 (100) $[M]^+$, 152 (92), 127 (5), 102 (8), 76 (37), 63 (13), 51 (14). The spectroscopic data are in agreement with reported values.[28]

Polystyrene-bound biphenylketone (40): According to Procedure H, polystyrene-bound 4-iodophenylhydrazide (**28b**, 400 mg, 0.3 mmol) was treated with 4-aceylphenylboronic acid (**33**, 394 mg, 2.4 mmol), potassium carbonate (504 mg, 5.4 mmol), *N,N*-diisopropyl-*N*-ethylamine (420 μL, 3 mmol), and palladium(II) acetate (15 mg, 0.06 mmol) in dioxane/water (6:1, 10 mL) to yield the black resin **40** (392 mg). IR (SiO_2): $\tilde{\nu}=3412$ (NH), 1684 (C=O) cm^{-1}.

Biphenyl-4-acetaldehyde (47): According to Method B for the oxidative cleavage of the hydrazide linker, **40** (183 mg, 141 μmol) was treated with $[Cu(OAc)_2]$ and pyridine in methanol followed by work-up with SPE to yield an off-white solid (13.4 mg, 68 μmol, 48%); HPLC: 96% (260 nm). $R_f=0.34$ (cyclohexane/ethyl acetate 10:1); m.p. 117 °C; ^1H NMR ($CDCl_3$, 400 MHz): $\delta=8.05$ (d, $^3J(H,H)=8.2$ Hz, 2H, arom. CH), 7.70 (d, $^3J(H,H)=8.2$ Hz, 2H, arom. CH), 7.64 (d, $^3J(H,H)=7.0$ Hz, 2H, arom. CH), 7.51–7.42 (m, 3H, arom. CH), 2.65 (s, 3H, C(=O)-CH_3); GCMS (70 eV, EI): *m/z* (%): 196 (60) $[M]^+$, 181 (100), 152 (63), 127 (11), 91 (4), 76 (11), 63 (3), 51 (3). The spectroscopic data are in agreement with reported values.[29]

Polystyrene-bound biphenylketone (41): According to Procedure H, polystyrene-bound 4-iodophenylhydrazide (**28b**, 400 mg, 0.3 mmol) was treated with 3-aceylphenylboronic acid (**34**, 394 mg, 2.4 mmol), potassium carbonate (504 mg, 5.4 mmol), *N,N*-diisopropyl-*N*-ethylamine (420 μL, 3 mmol), and palladium(II) acetate (15 mg, 0.06 mmol) in dioxane/water (6:1, 10 mL) to yield the black resin **41** (388 mg). IR (SiO_2): $\tilde{\nu}=3395$ (NH), 1687 (C=O) cm^{-1}.

Biphenyl-3-acetaldehyde (48): According to Method B for the oxidative cleavage of the hydrazide linker, **41** (147 mg, 113 μmol) was treated with $[Cu(OAc)_2]$ and pyridine in methanol followed by work-up with SPE to yield a yellow oil (8.9 mg, 45 μmol, 40%); HPLC: 95% (260 nm). $R_f=0.35$ (cyclohexane/ethyl acetate 10:1); ^1H NMR ($CDCl_3$, 400 MHz): $\delta=8.19$ (s, 1H, arom. CH), 7.95 (d, $^3J(H,H)=7.7$ Hz, 1H, arom. CH), 7.80 (d, $^3J(H,H)=6.4$ Hz, 2H, arom. CH), 7.65–7.39 (m, 5H, arom. CH), 2.69 (s, 3H, C(=O)-CH_3)$_3$; GCMS (70 eV, EI): *m/z* (%): 196 (85) $[M]^+$, 181 (100), 152 (89), 127 (14), 90 (11), 76 (31), 63 (10), 51 (9). The spectroscopic data are in agreement with reported values.[30]

Polystyrene-bound thiophenealdehyde (42): According to Procedure H, polystyrene-bound 4-iodophenylhydrazide (**28b**, 400 mg, 0.3 mmol) was treated with 2-formylthiophene-3-boronic acid (**35**, 394 mg, 2.4 mmol), potassium carbonate (504 mg, 5.4 mmol), *N,N*-diisopropyl-*N*-ethylamine (420 μL, 3 mmol), and palladium(II) acetate (15 mg, 0.06 mmol) in dioxane/water (6:1, 10 mL) to yield the black resin **42** (396 mg). IR (SiO_2): $\tilde{\nu}=3304$ (NH), 2714 (CHO), 1679 (C=O) cm^{-1}.

3-Phenylthiophene-2-carbaldehyde (49): According to Method B for the oxidative cleavage of the hydrazide linker, **42** (140 mg, 107 μmol) was treated with $[Cu(OAc)_2]$ and pyridine in methanol followed by work-up with SPE to yield a colorless oil (6.3 mg, 34 μmol, 32%), HPLC: 93% (260 nm). $R_f=0.31$ (cyclohexane/ethyl acetate 10:1); ^1H NMR ($CDCl_3$, 400 MHz): $\delta=9.90$ (s, 1H, CHO), 7.75 (d, $^3J(H,H)=5.1$ Hz, 1H, thiophene-C(5)H), 7.56–7.42 (m, 5H, arom. CH), 7.24 (d, $^3J(H,H)=5.1$ Hz, 1H, thiophene-C(5)H); GCMS (70 eV, EI): *m/z* (%): 188 (60) $[M]^+$, 187 (100), 159 (9), 115 (41), 89 (9), 63 (6), 51 (3). The spectroscopic data are in agreement with reported values.[31]

General procedure for the preparation of polymer-bound diphenylacetylenes 52 (Procedure J): A suspension of the polymer-bound 4-iodophenylhydrazide (**28**) and phenylacetylene (**50**, 6 equiv) in dioxane/triethylamine (2:1) was degassed (ultrasound), copper(I) iodide (0.2 equiv) and $[Pd(PPh_3)_2Cl_2]$ (0.1 equiv) were added. The mixture was shaken at room temperature for 24 h and then filtered. The resin was washed with DMF, water, DMF, methanol, ethyl acetate, and methylene chloride (3× each), and then dried to constant weight in vacuo.

Polystyrene-bound diphenylacetylene (52b): According to Procedure J, polystyrene-bound 4-iodophenylhydrazide (**28b**, 600 mg, 0.24 mmol) was treated with phenylacetylene (**50**, 158 μL, 1.44 mmol), copper(I) iodide (9 mg, 48 μmol) and $[Pd(PPh_3)_2Cl_2]$ (17 mg, 24 μmol) in dioxane/triethylamine (2:1, 9 mL) to yield the brown resin **52b** (589 mg). IR (KBr): $\tilde{\nu}=$ 3122 (NH), 2213 (C≡C), 1669 (C=O) cm^{-1}.

Diphenylacetylene (54) from 52b: According to Method A for the oxidative cleavage of the hydrazide linker, **52b** (161 mg, 37 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield the title compound (6.1 mg, 34 μmol, 92%); HPLC: 97% (260 nm); $R_f=0.72$ (cyclohexane/ethyl acetate 10:1); m.p. 56 °C; ^1H NMR ($CDCl_3$, 250 MHz): $\delta=7.53$ (d, $^3J(H,H)=8.2$ Hz, 4H, arom. CH), 7.38–7.28 (m, 6H, arom. CH); GCMS (70 eV, EI): *m/z* (%): 178 (100) $[M]^+$, 152 (12), 127 (15), 89 (12), 76 (15), 63 (6), 51 (4). The spectroscopic data are in agreement with reported values.[27] Cleavage according to Method B: Yield: 93%; HPLC: 90% (260 nm).

ArgoPore-bound diphenylacetylene (52c): According to Procedure J, ArgoPore-bound 4-iodoarylhydrazide (**28c**, 1.0 g, 0.20 mmol) was treated phenylacetylene (**50**, 132 μL, 1.2 mmol), copper(I) iodide (8 mg, 40 μmol) and $[Pd(PPh_3)_2Cl_2]$ (14 mg, 20 μmol) in dioxane/triethylamine (2:1, 9 mL) to yield the brown resin **52c** (979 mg). IR (KBr): $\tilde{\nu}=3103$ (NH), 2214 (C≡C), 1672 (C=O) cm^{-1}.

Diphenylacetylene (54) from 52c: According to Method A for the oxidative cleavage of the hydrazide linker, **52c** (135 mg, 25 μmol) was

treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield the title compound (3.9 mg, 22 μmol, 86 %); HPLC: 97 % (260 nm).

General procedure for the preparation of polymer-bound 2-phenylfurans 53 (Procedure K): A suspension of polymer-bound 4-iodophenylhydrazide (**28**), triphenylarsane (0.4 equiv), and 2-(tributylstannyl)furan (**51**, 5 equiv) in dioxane was degassed (ultrasound). $[Pd(dba)_3]\cdot CHCl_3$ (0.1 equiv) was added and the mixture was heated to 60 °C for 24 h. Subsequently, the mixture was filtered. The resin was washed with DMF, water, DMF, methanol, ethyl acetate, and methylene chloride (3 × each), and then dried to constant weight in vacuo.

TentaGel-bound 2-phenylfurans 53a: According to Procedure K, TentaGel-bound 4-iodophenylhydrazide (**28a**, 539 mg, 0.22 mmol) was treated with triphenylarsane (26 mg, 86 μmol), 2-(tributylstannyl)furan (**51**, 339 μL, 1.1 mmol) and $[Pd(dba)_3]\cdot CHCl_3$ (22 mg, 22 μmol) in dioxane (5 mL) to yield the black resin **53a** (512 mg). IR (KBr): $\tilde{\nu} = 3122$ (NH), 1666 (C=O), 1108 (C-O-C) cm^{-1}.

2-Phenylfuran (55) from 53a: According to Method A for the oxidative cleavage of the hydrazide linker, **53a** (152 mg, 36 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield a yellow oil (4.6 mg, 34 μmol, 86 %), HPLC: 97 % (260 nm). $R_f = 0.61$ (cyclohexane/ethyl acetate 10:1); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 7.82 - 7.33$ (m, 6H, arom. CH), 6.60 – 6.39 (m, 2H, arom. CH); GCMS (70 eV, EI): *m*/*z* (%): 144 (45) $[M]^+$, 115 (71), 89 (7), 63 (7), 32 (28), 28 (100). The spectroscopic data are in agreement with reported values.[27]

Polystyrene-bound 2-phenylfurans 53b: According to Procedure K, polystyrene-bound 4-iodophenylhydrazide (**28b**, 1.6 g, 0.4 mmol) was treated with triphenylarsane (49 mg, 0.16 mmol), 2-(tributylstannyl)furan (**51**, 634 μL, 2.0 mmol), and $[Pd(dba)_3]\cdot CHCl_3$ (42 mg, 40 μmol) in dioxane (8 mL) to yield the black resin **53b** (1.55 g). IR (KBr): $\tilde{\nu} = 3183$ (NH), 1663 (C=O) cm^{-1}.

2-Phenylfuran (55) from 53b: According to Method A for the oxidative cleavage of the hydrazide linker **53b** (85 mg, 33 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield the title compound (3.8 mg, 26 μmol, 79 %); HPLC: 94 % (260 nm). Cleavage according to Method B: Yield: 79 %; HPLC: 91 % (260 nm).

ArgoPore-bound 2-phenylfurans (53c): According to Procedure K, polystyrene-bound 4-iodoarylhydrazide (**28c**, 1.0 g, 0.2 mmol) was treated with triphenylarsane (25 mg, 0.08 mmol), 2-(tributylstannyl)furan (**51**, 315 μL, 1.0 mmol), and $[Pd(dba)_3]\cdot CHCl_3$ (21 mg, 20 μmol) in dioxane (5 mL) to yield the black resin **53c** (975 mg). IR (KBr): $\tilde{\nu} = 3173$ (NH), 1671 (C=O) cm^{-1}.

2-Phenylfuran (55) from 53c: According to Method A for the oxidative cleavage of the hydrazide linker, **53c** (234 mg, 44 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield the title compound (5.1 mg, 35 μmol, 80 %); HPLC: 93 % (260 nm).

Polystyrene-bound 4-iodo-2-methylphenylhydrazide (56): According to Procedure E, polystyrene resin **17b** (700 mg, 0.20 mmol) was treated with *N*,*N*-diisopropylcarbodiimide (93 μL, 0.60 mmol), 1-hydroxybenzotriazole (92 mg, 0.60 mmol), triethylamine (84 μL, 0.60 mmol), and 4-iodo-2-methylphenylhydrazine (149 mg, 0.60 mmol) in methylene chloride (20 mL) to yield the yellow resin **56** (712 mg). IR (KBr): $\tilde{\nu} = 3305$ (NH), 1673 (C=O) cm^{-1}.

4′-Methoxy 3-methylbiphenyl (57): According to Procedure G, 4-iodo-2-methylphenylhydrazide (**56**, 400 mg, 0.16 mmol) was treated with 4-methoxyphenylboronic acid (**30**, 244 mg, 1.6 mmol), potassium phosphate (86 mg, 0.32 mmol), and $[Pd(PPh_3)_4]$ (4 mg, 4 μmol) in DMF/water (6:1, 8 mL) to yield a black resin (378 mg). IR (KBr): $\tilde{\nu} = 3245$ (NH), 1667 (C=O) cm^{-1}. According to Method A for the oxidative cleavage of the hydrazide linker, the resin prepared above (313 mg, 37 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield the title compound (6.8 mg, 34 μmol, 93 %), HPLC: 90 % (260 nm); yellow oil. $R_f = 0.57$ (cyclohexane/ethyl acetate 10:1); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 7.46$ (d, $^3J(H,H) = 9.3$ Hz, 2H, arom. CH), 7.44 – 7.30 (m, 3H, arom. CH), 7.07 (d, $^3J(H,H) = 8.2$ Hz, 1H, arom. CH), 6.91 (d, $^3J(H,H) = 9.3$ Hz, 2H, arom. CH), 3.80 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3); GCMS (70 eV, EI): *m*/*z* (%): 198 (100) $[M]^+$, 183 (54), 155 (37), 128 (14), 115 (12), 63 (8). The spectroscopic data are in agreement with reported values.[32]

Polystyrene-bound 3-iodo-4-methylphenylhydrazide (58): According to Procedure E, polystyrene resin **17b** (700 mg, 0.29 mmol) was treated with *N*,*N*-diisopropylcarbodiimide (135 μL, 0.87 mmol), 1-hydroxybenzotriazole (133 mg, 0.87 mmol), triethylamine (122 μL, 0.87 mmol), and 3-iodo-4-methylphenylhydrazine (216 mg, 0.87 mmol) in methylene chloride (20 mL) to yield the off-white resin **58** (704 mg). IR (KBr): $\tilde{\nu} = 3304$ (NH), 1676 (C=O) cm^{-1}.

4′-Methoxy-2-methylbiphenyl (59): According to Procedure G, polystyrene-bound 4-iodo-2-methylphenylhydrazide (**58**, 548 mg, 0.22 mmol) was treated with 4-methoxyphenylboronic acid (**30**, 333 mg, 2.2 mmol), potassium phosphate (117 mg, 0.44 mmol), and $[Pd(PPh_3)_4]$ (5 mg, 4 μmol) in DMF/water (6:1, 7 mL) at 95 °C to yield a black resin (526 mg). IR (KBr): $\tilde{\nu} = 3244$ (NH), 1673 (C=O) cm^{-1}. According to Method A for the oxidative cleavage of the hydrazide linker, the resin prepared above (254 mg, 100 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by extractive work-up to yield the title compound (17.8 mg, 89 μmol, 89 %), HPLC: 91 % (260 nm); yellow oil. $R_f = 0.58$ (cyclohexane/ethyl acetate 10:1); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 7.32 - 7.21$ (m, 7H, arom. CH), 6.97 (d, $^3J(H,H) = 9.0$ Hz, 1H, arom. CH), 3.87 (s, 3H, OCH_3), 2.29 (s, 3H, CH_3); GCMS (70 eV, EI): *m*/*z* (%): 198 (100) $[M]^+$, 183 (27), 165 (24), 155 (26), 128 (19), 115 (17), 55 (15). The spectroscopic data are in agreement with reported values.[33]

TentaGel-bound 4-bromo-3-fluorphenylhydrazide (60): According to Procedure E, TentaGel resin **17a** (800 mg, 0.13 mmol) was treated with *N*,*N*-diisopropylcarbodiimide (60 μL, 0.39 mmol), 1-hydroxybenzotriazole (60 mg, 0.39 mmol), triethylamine (54 μL, 0.39 mmol), and 4-bromo-3-fluorophenylhydrazine (82 mg, 0.39 mmol) in methylene chloride (20 mL) to yield the off-white resin **60** (811 mg). IR (KBr): $\tilde{\nu} = 3240$ (NH), 1666 (C=O), 1108 (C-O-C) cm^{-1}.

4′-Methoxy-2-fluorobiphenyl (61): A suspension of the TentaGel-bound 4-bromo-3-fluorophenylhydrazide (**60**, 400 mg, 62 μmol) and 4-methoxyphenylboronic acid (**30**, 28 mg, 0.19 mmol) in DMF/triethylamine (1:1, 4 mL) was degassed (ultrasound), $[Pd(PPh_3)_4]$ (2 mg, 2 μmol) was added and the mixture was heated to 90 °C for 24 h. The mixture was cooled to room temperature and filtered. The resin was washed with DMF, water, DMF, ethyl acetate, and methylene chloride (3 × each), and then dried to constant weight in vacuo to yield a brown resin (379 mg). IR (KBr): $\tilde{\nu} =$ 3298 (NH), 1665 (C=O), 1109 (C-O-C) cm^{-1}. According to Method D for the oxidative cleavage of the hydrazide linker, the resin (178 mg, 27 μmol) was oxidized with NBS and pyridine in methylene chloride and the product was cleaved with methanol to yield a yellow solid (3.0 mg, 15 μmol, 55 %), HPLC: 93 % (260 nm). $R_f = 0.51$ (cyclohexane/ethyl acetate 10:1); m.p. 44 °C; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 7.65 - 7.15$ (m, 6H, arom. CH), 6.92 (d, $^3J(H,H) = 9.1$ Hz, 2H, arom. CH), 3.79 (s, 3H, OCH_3); GCMS (70 eV, EI): *m*/*z* (%): 202 (100) $[M]^+$, 187 (44), 159 (56), 133 (36). The spectroscopic data are in agreement with reported values.[34]

General procedure for the Wittig reaction of the polymer-bound biphenyaldehyde 39 (Procedure L): A suspension of the polymer-bound biphenyl aldehyde (**39**), alkyl-triphenyl-phosphonium salt (10 equiv), and potassium *tert*-butoxide (10 equiv) in THF was heated to 60 °C for 24 h. Subsequently, the mixture was filtered. The resin was washed with THF, THF/1N HCl (1:1), THF, methanol, methylene chloride, and cyclohexane (2 × each), and then dried in vacuo.

4-Vinyl biphenyl (62): According to Procedure L, the polymer-bound biphenylaldehyde (**39**, 150 mg, 0.117 mmol) was treated with methyltriphenylphosphonium bromide (418 mg, 1.17 mmol) and potassium *tert*-butoxide in THF (10 mL) to yield an off-white resin (153 mg). IR (KBr): $\tilde{\nu} = 3272$ (NH), 1682 (C=O), 1602 (C=C) cm^{-1}. According to Method A, the resin (124 mg, 96 μmol) was treated with $[Cu(OAc)_2]$ in *n*-propylamine followed by work-up with solid-phase extraction. Yield: 7.8 mg (43 μmol, 45 %), HPLC: 98 % (260 nm); white solid. $R_f = 0.57$ (cyclohexane/ethyl acetate 10:1); m.p. 117 °C; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 7.62 - 7.57$ (m, 4H, arom. CH), 7.51 – 7.44 (m, 4H, arom. CH), 7.39 – 7.35 (m, 1H, arom. CH), 6.79 (dd, $^3J_{trans}(H,H) = 17.6$, $^3J_{cis}(H,H) = 10.9$ Hz, 1H, Ar-C*H*=CH_2), 5.82 (d, 1H, $^3J_{trans}(H,H) = 17.6$ Hz, Ar-C*H*=CH_2), 5.30 (d, 1H, $^3J_{cis}(H,H) =$ 10.9 Hz, Ar-C*H*=CH_2); GCMS (70 eV, EI): *m*/*z* (%): 180 (100) $[M]^+$, 165 (36), 152 (26), 115 (9), 89 (13), 76 (19). The spectroscopic data are in agreement with the reported values.[35]

4-Propenyl biphenyl (63):According to Procedure L, the polymer-bound biphenylaldehyde (**39**, 150 mg, 0.117 mmol) was treated with ethyltriphe-

nylphosphonium iodide (489 mg, 1.17 mmol) and potassium *tert*-butoxide (131 mg, 1.17 mmol) in THF (10 mL) to yield an off-white resin (148 mg). IR (KBr): $\tilde{\nu}$ = 3313 (NH), 1671 (C=O), 1607 (C=C) cm^{-1}. According to Method A, the resin (133 mg, 102 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by work-up with solid-phase extraction to yield a yellowish solid (7.8 mg, 40 μmol, 43%, *cis*:*trans* 43:57), HPLC: 99% (260 nm). R_f = 0.52 (cyclohexane/ethyl acetate 10:1); m.p. 93 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64 – 7.53 (m, 4H, arom. CH), 7.47 – 7.31 (m, 5H, arom. CH), 6.50 – 6.43 (m, 1H, Ar-C*H*=CH-CH$_3$, *cis* + *trans* isomers), 6.30 (dq, 1H, $^3J_{trans}$(H,H) = 15.8, ^3J(H,H) = 6.5 Hz, Ar-C*H*=CH-CH$_3$, *trans*), 5.84 (dq, 1H, $^3J_{cis}$(H,H) = 11.6, ^3J(H,H) = 7.3 Hz, Ar-C*H*=CH-CH$_3$, *cis*), 1.97 (dd, 3H, ^3J(H,H) = 7.3, ^4J(H,H) = 1.8 Hz, Ar-CH=CH-C*H*$_3$, *cis*), 1.92 (dd, 3H, ^3J(H,H) = 6.5, ^4J(H,H) = 1.8 Hz, Ar-CH=CH-C*H*$_3$, *trans*); GCMS (70 eV, EI): *m*/*z* (%): 194 (100) [*M*]$^+$, 178 (46), 165 (30), 152 (15), 115 (14), 89 (3), 63 (3). The spectroscopic data are in agreement with reported values.[36]

4-Phenyl-cinnamic methyl ester (64): According to Procedure L, the polymer-bound biphenylaldehyde (**39**, 150 mg, 0.117 mmol) was treated with methoxycarbonylmethyl-triphenylphosphonium bromide (486 mg, 1.17 mmol) and potassium *tert*-butoxide (131 mg, 1.17 mmol) in THF (10 mL) to yield an off-white resin (151 mg). IR (KBr): $\tilde{\nu}$ = 3309 (NH), 1673 (C=O), 1609 (C=C) cm^{-1}. According to Method A for the oxidative cleavage of the hydrazide linker, the resin prepared above (142 mg, 109 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by work-up with solid-phase extraction. Yield: 6.8 mg (29 μmol, 27%), HPLC: 96% (260 nm); yellow solid. R_f = 0.24 (cyclohexane/ethyl acetate 10:1); m.p. 147 °C; ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.75 (d, $^3J_{trans}$(H,H) = 16.0 Hz, 1H, Ar-CH=C*H*-OCH$_3$), 7.63 – 7.61 (m, 5H, arom. CH), 7.48 – 7.44 (m, 4H, arom. CH), 6.49 (d, $^3J_{trans}$(H,H) = 16.0 Hz, 1H, Ar-C*H*=CH), 3.83 (s, 3H, -OCH$_3$); GCMS (70 eV, EI): *m*/*z* (%): 238 (100) [*M*]$^+$, 207 (66), 178 (95), 165 (44), 152 (41), 89 (24), 76 (19). The spectroscopic data are in agreement with reported values.[37]

4-Hydrazinobenzoic methyl ester: To a solution of 4-hydrazinobenzoic acid (10 g, 66 mmol) in methanol (300 mL) was added slowly conc. H_2SO_4 (3.5 mL, 66 mmol). The mixture was refluxed for 15 h, cooled to room temperature, and the solvent was removed under reduced pressure. The residue was suspended in methylene chloride (700 mL), washed 3 × with a saturated solution of $NaHCO_3$ (150 mL) and a saturated solution of NaCl (100 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to yield the 4-hydrazino benzoic acid methyl ester as an off-white solid (6.8 g, 51%). M.p. 227 °C; ^{1}H NMR (DMSO, 400 MHz): δ = 10.40 (b, 2H, NH), 8.93 (b, 1H, NH), 7.90 (d, ^3J(H,H) = 8.8 Hz, 2H, arom. CH), 7.00 (d, ^3J(H,H) = 8.8 Hz, 2H, arom. CH), 3.82 (s, 3H, OCH$_3$); ^{13}C NMR (DMSO, 100.6 MHz): δ = 166.2 (-*C*OOCH$_3$), 150.1 (C-N), 130.9, 113.4 (4 arom. CH), 52.1 (O*C*H$_3$); GCMS (70 eV, EI): *m*/*z* (%): 166 (97) [*M*]$^+$, 135 (100), 119 (11), 107 (14), 90 (17), 77 (9), 63 (10). HRMS (70 eV, EI): calcd for $C_8H_{10}N_2O_2$ [*M*]$^+$: 166.0742, found: 166.0746.

Polystyrene-bound 4-hydrazinobenzoic methyl ester (65): According to Procedure E, polystyrene resin **17b** (5.0 g, 5.05 mmol) was treated with *N*,*N*-diisopropylcarbodiimide (2.4 mL, 15.2 mmol), 1-hydroxybenzotriazole (2.3 g, 15.2 mmol), triethylamine (2.1 mL, 15.2 mmol), and 4-hydrazinobenzoic acid methyl ester (3.1 g, 15.2 mmol) in methylene chloride (100 mL) to yield the off-white resin **65** (5.12 g). IR (KBr): $\tilde{\nu}$ = 3298 (NH), 1740 (C=O), 1666 (C=O) cm^{-1}.

General procedure for the addition of organometallic reagents to a polymer-bound ester, aldehyde, or ketone (Procedure M): The corresponding Grignard reagent (20 equiv) was added to a suspension of polymer-bound ester, aldehyde, or ketone in THF and the mixture was shaken at room temperature for 24 h. Subsequently, the addition of Grignard reagent (20 equiv) was repeated. The mixture was shaken for further 48 h at room temperature and filtered. The resin was washed with THF, THF/1N NH_4Cl (1:1), THF/water (1:1), THF, methanol, methylene chloride, and cyclohexane (2 × each), and then dried in vacuo.

Triphenylmethanols (66): According to Procedure M, the polymer-bound 4-hydrazinobenzoic acid methyl ester (**65**, 300 mg, 0.26 mmol) was treated with phenyl lithium (2 × 2.6 mL, 2M in cyclohexane/diethyl ether (7:3), 5.2 mmol) in THF (10 mL) to yield an off-white resin (295 mg). IR (KBr): $\tilde{\nu}$ = 3298 (OH, NH), 1682 (C=O) cm^{-1}. According to Method A for the oxidative cleavage of the hydrazide linker, the resin prepared above (155 mg, 96 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by work-up with solid-phase extraction to yield a white solid (15.4 mg, 60 μmol, 62%), HPLC: 99% (260 nm). R_f = 0.42 (cyclohexane/ethyl acetate 10:1); m.p. 159 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.35 – 7.26 (m, 15H, arom. CH), 2.79 (s, 1H, OH); GCMS (70 eV, EI): *m*/*z* (%): 260 (29) [*M*]$^+$, 207 (21), 183 (100), 165 (20), 154 (32), 105 (97), 77 (54). The spectroscopic data are in agreement with reported values[38]

4-Phenylhepta-1,6-dien-4-ols (67): According to Procedure M, the polymer-bound 4-hydrazinobenzoic acid methyl ester (**65**, 200 mg, 0.17 mmol) was treated with allylmagnesium bromide (2 × 1.7 mL, 2M in THF, 3.4 mmol) in THF (10 mL) to yield an off-white resin (199 mg). IR (KBr): $\tilde{\nu}$ = 3308 (OH, NH), 1681 (C=O) cm^{-1}. According to Method A for the oxidative cleavage of the hydrazide linker, the resin prepared above (113 mg, 97 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by work-up with solid-phase extraction to yield a yellowish oil (10.9 mg, 58 μmol, 60%), HPLC: 97% (260 nm). R_f = 0.33 (cyclohexane/ethyl acetate 10:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.35 – 7.09 (m, 5H, arom. CH), 5.51 (m, 2H, CH$_2$-C*H*=CH$_2$), 5.02 (m, 4H, CH$_2$-CH=C*H*$_2$), 2.65 – 2.34 (m, 4H, C*H*$_2$-CH=CH$_2$); GCMS (70 eV, EI): *m*/*z* (%): 147 (57) [*M* – allyl], 105 (100), 91 (22), 77 (75), 51 (16), 63 (3). The spectroscopic data are in agreement with reported values.[39]

4-Biphenyl-phenyl-methanol (68): According to Procedure M, the polymer-bound 4-biphenylaldehyde (**39**, 200 mg, 0.14 mmol) was treated with phenyllithium (2 × 1.4 mL, 2M in cyclohexane/diethyl ether (7:3), 2.8 mmol) in THF (10 mL) to yield an off-white resin (204 mg). IR (KBr): $\tilde{\nu}$ = 3315 (OH, NH), 1676 (C=O) cm^{-1}. According to Method A for the oxidative cleavage of the hydrazide linker, the resin prepared above (125 mg, 85 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by work-up with solid-phase extraction to yield a white solid (7.7 mg, 30 μmol, 35%), HPLC: 98% (260 nm). R_f = 0.17 (cyclohexane/ethyl acetate 5:1); m.p. 91 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.60 – 7.56 (m, 4H, arom. CH), 7.48 – 7.30 (m, 10H, arom. CH), 5.91 (s, 1H, benzyl-CH); GCMS (70 eV, EI): *m*/*z* (%): 260 (100) [*M*]$^+$, 181 (52), 155 (80), 105 (54), 77 (34). The spectroscopic data are in agreement with reported values.[40]

2-Biphenyl-pent-4-en-2-ol (69): According to Procedure M, the polymer-bound 4-biphenylketone (**40**, 200 mg, 0.14 mmol) was treated with allylmagnesium bromide (2 × 1.4 mL, 2M in THF, 2.8 mmol) in THF (10 mL) to yield the off-white resin (201 mg). IR (KBr): $\tilde{\nu}$ = 3333 (OH, NH), 1681 (C=O) cm^{-1}. According to Method A for the oxidative cleavage of the hydrazide linker, the resin prepared above (158 mg, 108 μmol) was treated with [Cu(OAc)$_2$] in *n*-propylamine followed by work-up with solid-phase extraction to yield a colorless oil (9.5 mg, 40 μmol, 37%), HPLC: 97% (260 nm). R_f = 0.15 (cyclohexane/ethyl acetate 10:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.72 – 7.69 (m, 1H, arom. CH), 7.62 (dd, ^3J(H,H) = 8.4 Hz, 2H, arom. CH), 7.51 – 7.42 (m, 5H, arom. CH), 7.38 – 7.34 (m, 1H, arom. CH), 5.75 – 5.64 (m, 1H, CH$_2$-C*H*=CH$_2$), 5.21 – 5.13 (m, 2H, CH$_2$-CH=C*H*$_2$), 2.60 – 2.53 (m, 2H, C*H*$_2$-CH=CH$_2$), 2.1 (b, 1H, OH), 1.62 (s, 3H, CH$_3$); GCMS (70 eV, EI): *m*/*z* (%): 238 (1) [*M*]$^+$, 197 (100), 181 (17), 165 (7), 152 (39). The spectroscopic data are in agreement with reported values.[41]

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