JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.5b01978 • Publication Date (Web): 24 Sep 2015

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Zinc-mediated allylation and benzylation of phenylazocarboxylic esters

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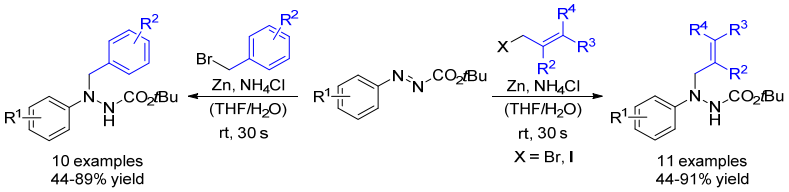
Abstract

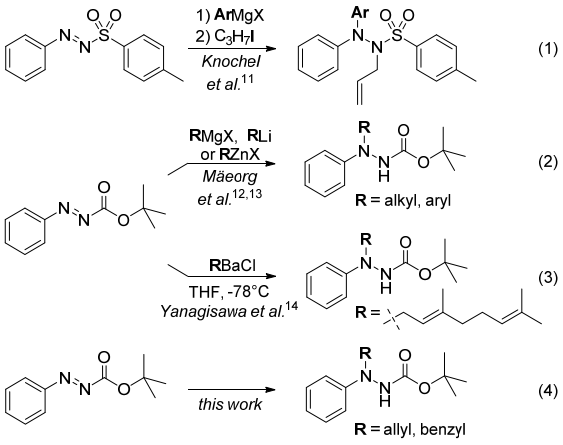
Allylation and benzylation of phenylazocarboxylic *tert*-butyl esters have been achieved under Barbier-type reaction conditions and in very short reactions times using the corresponding allyl and benzyl bromides or iodides in combination with zinc powder. Whereas all reactions occurred exclusively at the β-nitrogen atom of the azocarboxylic esters, the linkage of allyl units was shown to depend on the substitution pattern at the double bond of the allyl halide. The hydrazines obtained are useful precursors for indoles or indazoles.



The formation of carbon-nitrogen bonds is mainly achieved by three general strategies: reactions of nucleophilic organometallic compounds or carbanions with nitrogen-centered electrophiles,[1] transition-metal mediated cross-coupling reactions[2,3] and C-H aminations,[4] as well as classical amination reactions proceeding via nucleophilic substitution of electrophilic

carbon residues with amines, phthalimides or azides.[5] Regarding the organometallic approach, research has focused on nitrogen-centered electrophiles such as substituted hydroxylamines,[6] in which the hydroxyl group was turned into a suitable leaving group, and on additions of organometallics to nitro compounds,[7] nitroso compounds[8] and oximes.[9] Nucleophilic additions to azo compounds preferably occur if the azo compound is suitably activated by ring-strain or at least one electron-withdrawing group. Only a few reactions have been reported with azobenzenes[10a] or diazirines,[10b] whereas organometallic additions to dialkyl azodicarboxylates are more frequent.[10c-f] Over the last decade, nucleophilic additions to unsymmetrical azo compounds (Scheme 1), such as phenylazosulfones (1)[11] and phenylazocarboxylic esters (2,3),[12-14] have gained more interest. In these transformations, however, mainly aryl and only few alkyl residues have so far been coupled to the azo compounds (2).[15] For allylation reactions, in particular, there is currently only one example by Yanagisawa[14] (3) who reported the addition of a geranyl-barium chloride onto *tert*-butyl phenylazocarboxylate.

Scheme 1. Addition of organometallic reagents to phenylazosulfones and phenylazocarboxylic esters.



Our interest in the functionalization of phenylazocarboxylic esters by organometallic reagents was due to recent studies showing that the aromatic core of such reagents is highly activated

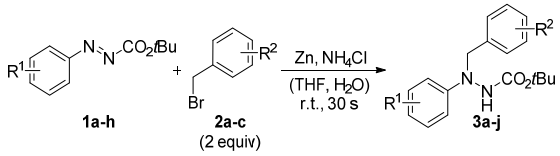
towards nucleophilic aromatic substitution with diverse reagents such as phenols, aromatic and aliphatic amines[16] as well as [^{18}F]fluoride.[17] The combination of this aromatic substitution with modifications at the azo moiety[18] could in turn allow a quick two-step access to a broad variety of products. Thereby, it would be particularly useful if the generation of the organometallic reagent and its addition onto the azocarboxylic ester were feasible under simple reaction conditions, as they have been reported for Barbier-type reactions[19,20] of allyl- and benzylzinc reagents[21] with wide range of carbonyl compounds. In case that the nucleophilic addition could be conducted in short overall reaction times, it might also be applicable in radiosyntheses starting from ^{18}F-labelled phenylazocarboxylic esters.[17]

In this article, we now present the first examples for zinc-mediated allylations and benzylations of phenylazocarboxylic esters, which are shown to be versatile and exceptionally fast reactions to access functionalized hydrazines (Scheme 1, (4)).

Against the background that phenylazocarboxylic esters were readily reduced to their corresponding hydrazines by metallic zinc powder,[22] we decided to add the benzyl bromide and zinc powder – after a short mixing time in which no reaction should occur – simultaneously to the azocarboxylic ester.[23] A mixture of benzyl bromide (**2a**) and an equivalent amount of commercially available zinc powder in tetrahydrofuran was thus stirred for 1 minute before being added to a solution of phenylazocarboxylic *tert*-butyl ester (**1a**) in tetrahydrofuran and saturated aqueous ammonium chloride under air (Table 1).[24] As the characteristic orange color of the phenylazocarboxylate **1a** disappeared after a reaction time of only 30 seconds, the reaction was quenched by the addition of water. Analysis of the crude reaction mixture by ^{1}H-NMR revealed the formation of the desired adduct **3a** in 89% yield and showed no detectable amounts of the hydrazine resulting from the reduction of **1a**. Furthermore, the homo-coupling of benzyl bromide (**2a**) during the short premixing phase had indeed not occurred, as no dibenzyl was found as by-product. After the high yield of hydrazine **3a** was confirmed through

isolation and purification by column chromatography (Table 1, entry 1), we directly turned to evaluate scope and limitations of the benzylation reaction.

Table 1. Zinc-mediated benzylation of phenylazocarboxylic *tert*-butyl esters



entry	azocarboxylate **1**: R^1 =	benzyl bromide **2**: R^2 =	hydrazine **3** (%)[a]
1	**1a**: H	**2a**: H	**3a**: 87
2	**1b**: 4-F	**2a**: H	**3b**: 88
3	**1c**: 4-Br	**2a**: H	**3c**: 80
4	**1d**: 4-I	**2a**: H	**3d**: 89
5	**1e**: 4-CN	**2a**: H	**3e**: 73
6	**1f**: 4-OMe	**2a**: H	**3f**: 82
7	**1g**: 2,4-Cl_2	**2a**: H	**3g**: 82
8	**1h**: 4-F, 2-Me	**2a**: H	**3h**: 75
9	**1c**: 4-Br	**2b**: 2-Br	**3i**: 62[b]
10	**1c**: 4-Br	**2c**: 2-I	**3j**: 44[b]

[a]Yields determined after purification by column chromatography. [b]*tert*-Butyl 2-(4-bromophenyl)hydrazinecarboxylate detected as by-product (ca. 20-40%).

Good to high yields were obtained for all combinations of phenylazocarboxylic esters **1a**-**h** with benzyl bromide (**2a**) (entries 1-8) irrespective of the presence of an electron-withdrawing (R^1 = 4-CN, entry 5) or an electron-donating group (R^1 = 4-OMe, entry 6). Moreover, all types of halogen atoms, including iodine,[25] on the aromatic core of the azocarboxylate were tolerated, and even *ortho*-substitution, as in azocarboxylates **1g** and **1h** (entries 7 and 8), did not have remarkably negative effects on the product formation. The two attempts with the *ortho*-substituted benzyl bromides **2b** and **2c** gave lower yields (entries 9 and 10), which can be attributed to slower benzylation reactions and a consequently increased reduction of the azo compound **1c** to its corresponding hydrazine.

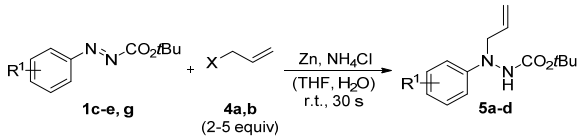
Further experiments demonstrated that the benzylation reaction can also be performed as a one-pot procedure in the way that the azocarboxylic ester **1c** is added as a solid to a mixture of benzylbromide **2a** and zinc powder in tetrahydrofuran and aqueous ammonium chloride to give

3c in 84% yield. Alternatively, and with an even slightly higher yield of 93%, hydrazine **3c** could be obtained by the addition of zinc powder to **1c** and **2a** in the usual solvent mixture, which makes the transformation fully comparable to a Barbier-type reaction.[19]

The replacement of benzyl bromide (**2a**) for 4-chlorobenzyl chloride in a reaction with azocarboxylate **1d** led to no product formation but instead to the complete reduction of the azocarboxylate, thus indicating that the desired reaction pathway is too slow (c.f. Table 1, entries 9 and 10).[26] A control experiment with 2-(4-bromophenyl)hydrazinecarboxylic acid *tert*-butyl ester and benzyl bromide in the absence of zinc, but under otherwise identical conditions, ruled out a reaction course in which the azo compound **1** is first reduced to a hydrazine that does then react with benzyl bromide.

In a second series of experiments we evaluated the transferability of the previously found reaction conditions to allylation reactions (Table 2). The first attempts in this series indicated that two equivalents of allyl bromide (**4a**) or of the more reactive allyl iodide (**4b**) are not sufficient to obtain the desired allylation product **5a** in good yield. By increasing the amounts of **4a** or **4b** and zinc powder to five equivalents, the phenylazocarboxylates **1c-e** and **1g** then underwent allylation in good to high yields (entries 3-7). Similar to the benzylation reactions summarized in Table 2, only the hydrazines arising from reduction of the azocarboxylates **1** were detected as minor by-products. An experiment with the addition of zinc powder to a mixture of **1d** and **4b** (c.f. entry 5, Table 2) provided **5b** in a yield of 92%, thereby showing that the Barbier-type order of addition is possible, too.

Table 2. Zinc-mediated allylation of phenylazocarboxylates.



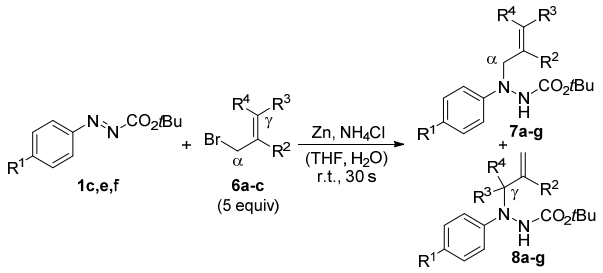
1c-e, g **4a,b** (2-5 equiv) **5a-d**

entry	azocarboxylate **1**: R^1 =	allyl halide **4**: X =	(equiv.)	hydrazine **5** (%)[a]
1	**1c**: 4-Br	**4a**: Br	2[b]	**5a**: 29
2	**1c**: 4-Br	**4b**: I	2[b]	**5a**: 45
3	**1c**: 4-Br	**4a**: Br	5	**5a**: 70
4	**1c**: 4-Br	**4b**: I	5	**5a**: 71
5	**1d**: 4-I	**4b**: I	5	**5b**: 91
6	**1e**: 4-CN	**4b**: I	5	**5c**: 90
7	**1g**: 2,4-Cl_2	**4b**: I	5	**5d**: 66

[a]Yields determined after purification by column chromatography. [b]Reactions conducted with reduced amounts of allyl halide (1.0 mmol) and zinc powder (1.0 mmol).

In widely studied reactions of aldehydes and ketones under aqueous Barbier conditions, using ammonium chloride and tetrahydrofuran as solvents, allyl zinc reagents preferably react at their γ-carbon atom,[24,27] which can be rationalized by a 6-membered zinc-containing transition state.[28] For comparable allylation reactions of azo compounds, only results from a study with allylbarium reagents are so far available (c.f. Scheme 1, (3)).[14] As the allylbarium reagent was thereby found to react with the phenylazocarboxylic ester unselectively at the α- and the γ-position of the allyl unit, two different mechanisms appear to be possible for azobenzenes in contrast to the carbonyls. For further insights, we submitted the substituted allyl bromides **6a-c** to the previously developed conditions (Table 3).

Table 3. Zinc-mediated allylation of phenylazocarboxylates.



entry	azo-carboxylate **1**: R^1 =	allyl bromide **6**: R^2, R^3, R^4 =	hydrazines **7:8** (%:%)[a] preferred attack (α *vs.* γ)	
1	**1c**: Br	**6a**: H, Me, H	**7a**:**8a** (0:86)	γ
2	**1e**: CN	**6a**: H, Me, H	**7b**:**8b** (18:72)	γ
3	**1f**: OMe	**6a**: H, Me, H	**7c:8c** (33:65)	γ
4	**1c**: Br	**6b**: H, Me, Me	**7d**:**8d** (48:32)	α
5	**1e**: CN	**6b**: H, Me, Me	**7e**:**8e (**51:36**)**	α
6	**1f**: OMe	**6b**: H, Me, Me	**7f**:**8f** (57:9)	α
7	**1c**: Br	**6c**: Me, H, H	**7g** (44)	-

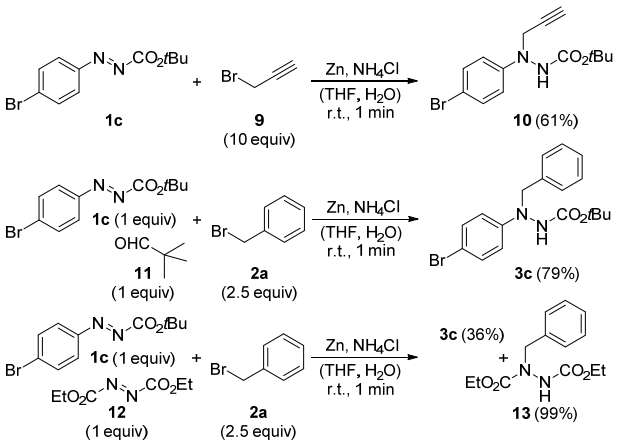
[a]Yields determined after purification by column chromatography.

If only one methyl group is present in γ-position of the allylbromide, as in (*E*)-2-buten-1-yl bromide (**6a**), the addition occurs preferably in γ-position (entries 1-3). This strongly suggests that **6a**, and mostly probably allyl bromide (**4a**) and allyl iodide (**4b**), too, react with phenylazocarboxylic esters **1** via the above mentioned 6-membered transition state, which was also suggested by Fristrup and Madsen.[28b] The acceptor- as well as the donor-substituted azocarboxylates **1e** and **1f** gave lower regioselectivities, which, in case of **1e** (R^1 = CN, entry 2) could be due to an increased electrophilicity of the N=N-moiety. In agreement with the observations previously made with allylbarium reagents,[14] the γ,γ-disubstituted allylbromide **6b** showed C-N bond formation preferably at its α-position, whereby the products **7d-f** resulting from the α-attack were obtained in nearly the same yield for all three azocarboxylates **1c, 1e** and **1f** (R^1 = Br, CN, OMe; entries 4-6). The already less pronounced γ-attack in the reactions with **6b** was found to be especially unfavorable for the donor-substituted azocarboxylate **1f** (R^1 = OMe; entry 7). Unexpectedly, a comparably low yield was obtained with **1c** and the β-substituted allylbromide **6c**, for which the products resulting from α- and γ-attack are identical (entry 7). In conclusion, it appears that the introduction of further substituents in γ-position of

the allyl halide complicates the formation of a 6-membered transition state consisting of the N-N moiety of the azo compound, the zinc ion, and the allyl unit, and therefore more of the non-rearranged product **7** resulting from α-attack is obtained.

Two experiments with azocarboxylate **1c** and propargyl bromide (**9**) demonstrated that the Barbier-type procedure, in which zinc powder is added to **1c** and **9**, is clearly superior for propargylation reactions, as the addition of premixed zinc powder and propargyl bromide **9** gave the desired hydrazine **10** in only 28% yield compared to 61% for the zinc addition (Scheme 2).[29] Although the related allenyl hydrazine resulting from a potential γ-attack on **9** could not be detected,[30] the known instability of comparable compounds[31] could however be an explanation for the formation of several by-products. Two further reactions with competing electrophiles demonstrated that the phenylazocarboxylic ester **1c** is more reactive towards the organozinc reagent formed from **2a** than towards pivalyl aldehyde (**11**),[32] as only hydrazine **3c** was obtained. On the other hand, **1c** is less reactive than diethyl azodicarboxylate (**12**), as evidenced by the individual yields of **3c** (36%) and **13** (99%).

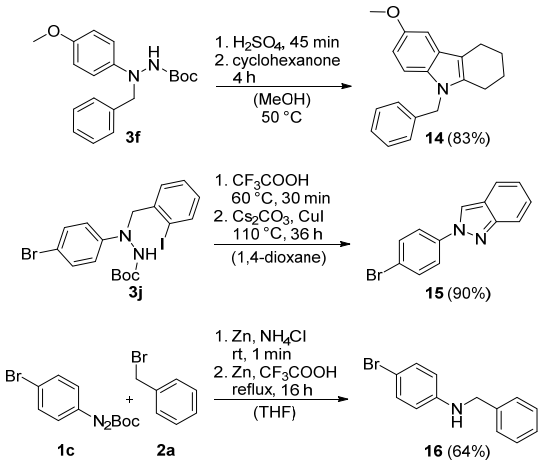
Scheme 2. Propargylation and comparison of reactivity.



The hydrazines **3f** and **3j** (Table 1) obtained as products were finally used for further transformations (Scheme 3). In a one-pot procedure, hydrazine **3f** was first Boc-deprotected by

sulfuric acid in methanol and then converted to indole **14** by the addition of cyclohexanone in an overall yield of 83%.[33] In another one-pot procedure, the removal of the Boc-group from **3j** by trifluoroacetic acid was combined with a copper-mediated intramolecular amination to give indazole **15** in 90% yield.[34] The reductive cleavage of the N-N bond of the hydrazine can be performed directly after benzylation of the azo compound without intermediate work-up.[35] For the purpose of obtaining amine **16** from **1c** and **2a**, however, additional zinc powder, trifluoroacetic acid and elevated temperatures over longer reaction times were required in the second step.

Scheme 3. Synthesis of heterocycles and reductive cleavage of the N-N bond.



In summary, we have shown that *tert*-butyl phenylazocarboxylic esters can efficiently be applied in zinc-mediated allylation and benzylation reactions. All reactions turned out to be robust regarding the order of how the reagents are mixed, whereby the combined addition of zinc and allyl or benzyl halide to the azocarboxylate gave in most cases – with exception of the propargylation - similar results as the Barbier-type procedure, in which zinc powder was finally added to the other reagents In the allylations, benzylations and the propargylation, functionalization selectively occurred at the β-nitrogen atom of the azocarboxylic esters, which is adjacent to the aromatic core. Only allyl halides substituted at their C-C double bond gave

product mixtures, as they were found to undergo C-N bond formation at their α- and γ-position depending on the substitution pattern.

Experimental Section

Solvents and reagents were used as received. ^{1}H NMR spectra were recorded on 360 and 600 MHz spectrometers using $CDCl_3$ as solvent referenced to TMS (0.00 ppm) or $CDCl_3$ (7.26 ppm).^{13}C NMR spectra were recorded at 91 or 151 MHz in $CDCl_3$ (77.0 ppm) as standard. Chemical shifts are reported in parts per million (ppm). Coupling constants are in Hertz (*J* Hz). The following abbreviations are used for the description of signals: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), bs (broad singlet) and mc (centered multiplet). Mass spectra were recorded using electron impact (EI) or electron spray ionization (ESI). A sector field mass analyzer or TOF were used for HRMS measurements.

Analytical TLC was carried out on *Merck* silica gel plates using short wave (254 nm) UV light, $KMnO_4$ [3.0 g $KMnO_4$, 20 g potassium carbonate, 5.0 mL aqueous sodium hydroxide (5% *w*/*w*) in 300 mL H_2O] and ninhydrin [200 mg ninhydrin in 100 mL ethanol] to visualize components. For flash column chromatography silica gel (Kieselgel 60, grain size 40 - 63 μm, *Merck*) was used. The phenylazocarboxylic esters **1a-h** have been previously characterized[18] and were prepared according to established procedures.

General procedures

General procedure for the *N*-benzylation of phenylazocarboxylic esters (GP 1)

A solution of the phenylazocarboxylic ester (1.00 mmol) in tetrahydrofuran (3 mL) and saturated aqueous solution of ammonium chloride (0.5 mL) is treated with a suspension of the

benzyl bromide (2.00 mmol) and zinc (2.00 mmol) in tetrahydrofuran (1 mL). After complete consumption of the phenylazocarboxylate, as monitored by TLC, ethyl acetate (20 mL) is added and the mixture is filtered. The filtrate is washed with water (3 × 15 mL), a saturated aqueous solution of sodium chloride (20 mL) and dried over sodium sulfate. The solvent is removed under reduced pressure and the residue is subjected to column chromatography. Note: Upscaling of the reaction requires external cooling or a slower addition of the reagents due to considerable generation of heat.

General procedure for the *N*-allylation of phenylazocarboxylic esters (GP 2)

A solution of the phenylazocarboxylic ester (1.00 mmol) in tetrahydrofuran (3 mL) and saturated aqueous solution of ammonium chloride (0.5 mL) is treated with a suspension of the allyl bromide/iodide (5.00 mmol) and zinc (5.00 mmol) in tetrahydrofuran (1 mL). After complete consumption of the phenylazocarboxylate, as monitored by TLC, ethyl acetate (20 mL) is added and the mixture is filtered. The filtrate is washed with water (3 × 15 mL), a saturated aqueous solution of sodium chloride (20 mL) and dried over sodium sulfate. The solvent is removed under reduced pressure and the residue is subjected to column chromatography. Note: Upscaling of the reaction requires external cooling or a slower addition of the reagents due to considerable generation of heat.

***tert*-Butyl 2-benzyl-2-phenylhydrazine carboxylate** (**3a**) is prepared from *tert*-butyl 2-phenylazocarboxylate (**1a**) (242 µmol, 50.0 mg) and benzyl bromide (**2a**) (484 µmol, 60 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 10:1) to give the title compound **3a** as a white solid (210 µmol, 62.6 mg, 87%): R_f = 0.4 (hexane / ethyl acetate = 9:1) (UV); mp 97–98 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3302, 2986, 1727, 1599, 1501, 1461, 1362, 1250, 1166, 1033, 757, 684;^{1}H NMR

(600 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 4.73 (bs, 2 H), 6.36 (bs, 1 H), 6.84 (t, *J* = 7.3 Hz, 1 H), 6.89 (d, *J* = 8.0 Hz, 2 H), 7.27-7.34 (m, 7 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 28.3, 56.5, 80.9, 112.9, 119.5, 127.4, 128.0, 128.6, 129.2, 137.1, 149.3. (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 299 [MH^+]; HRMS (ESI) calcd for $C_{18}H_{22}N_2O_2$ [$M^+ + Na^+$]: 321.1573, found: 321.1573. Analytical data is in agreement with those reported in literature ref 35b.

***tert*-Butyl 2-benzyl-2-(4-fluorophenyl)hydrazine carboxylate** (**3b**) is prepared from *tert*-butyl 2-(4-fluorophenyl)azocarboxylate (**1b**) (1.00 mmol, 224 mg) and benzyl bromide (**2a**) (2.00 mmol, 238 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 9:1) to give the title compound **3b** as a pale brown solid (877 µmol, 278 mg, 88%): R_f = 0.4 (hexane / ethyl acetate = 9:1) (UV); mp 95–96 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3313, 2979, 1717, 1508, 1455, 1368, 1228, 1157, 822, 744, 696; ^1H NMR (360 MHz, $CDCl_3$) δ 1.42 (s, 9 H), 4.67 (bs, 2 H), 6.34 (bs, 1 H), 6.84 (dd, J_{HF}= 4.4 Hz, *J* = 9.2 Hz, 2 H), 6.94 (dd, J_{HF}= 8.2 Hz, *J* = 9.2 Hz, 2 H), 7.27-7.37 (m, 5 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 28.2, 57.0, 81.0, 114.4 (d, J_{CF} = 7.6 Hz) 115.5 (d, J_{CF} = 23.0 Hz), 127.5, 128.1, 128.6, 136.8, 145.8, 157.0 (d, J_{CF} = 237.4 Hz). (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 317 [MH^+]; HRMS (ESI) calcd for $C_{18}H_{21}FN_2O_2$ [$M^+ + Na^+$]: 339.1479, found: 339.1474.

***tert*-Butyl 2-benzyl-2-(4-bromophenyl)hydrazine carboxylate** (**3c**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (1.00 mmol, 285 mg) and benzyl bromide (**2a**) (2.00 mmol, 238 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 9:1) to give the title compound **3c** as a pale yellow solid (799 µmol, 301 mg, 80%): R_f = 0.4 (hexane / ethyl acetate = 9:1) (UV); mp 96–97 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3308, 2979, 1709, 1591, 1491, 1454, 1392, 1368, 1250, 1213,

1160, 1080, 999, 815, 755, 733, 699; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.43 (s, 9 H), 4.68 (bs, 2 H), 6.38 (bs, 1 H), 6.76 (d, *J* = 8.1 Hz, 2 H), 7.26-7.35 (m, 7 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 28.2, 56.4, 81.2, 111.6, 114.6, 127.6, 127.9, 128.7, 131.9, 136.6, 148.4. (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 379 [^{81}Br-MH^+]; HRMS (ESI) calcd for $C_{18}H_{21}BrN_2O_2$ [$M^+ + Na^+$]: 399.0679, found: 399.0670.

Barbier-type procedure: A mixture of *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (175 µmol, 50.0 mg) and benzyl bromide **2a** (350 µmol, 42.0 µL) in tetrahydrofuran (2.0 mL) and saturated aqueous ammonium chloride (0.5 mL) is treated with zinc (350 µmol, 23.0 mg) and stirred vigorously for 30 seconds. Work up is as described above. The solvent is removed under reduced pressure and the residue is subjected to column chromatography (silica gel, hexane / ethyl acetate = 9:1) to give compound **3c** as a pale yellow solid (167 µmol, 62.9 mg, 93%).

Addition of solid phenylazocarboxylate: A mixture of benzyl bromide **2a** (350 µmol, 42.0 µL) and zinc (350 µmol, 23.0 mg) in tetrahydrofuran (2.0 mL) and saturated aqueous ammonium chloride (0.5 mL) is treated with solid *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (175 µmol, 50.0 mg) and stirred vigorously for 30 seconds. Work up is as described above. The solvent is removed under reduced pressure and the residue is subjected to column chromatography (silica gel, hexane / ethyl acetate = 9:1) to give compound **3c** as a pale yellow solid (147 µmol, 55.4 mg, 84%).

***tert*-Butyl 2-benzyl-2-(4-iodophenyl)hydrazine carboxylate** (**3d**) is prepared from *tert*-butyl 2-(4-iodophenyl)azocarboxylate (**1d**) (602 µmol, 200 mg) and benzyl bromide (**2a**) (1.20 mmol, 150 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 8:1) to give the title compound **3d** as a pale yellow solid (533 µmol, 208 mg, 89%): R_f = 0.4 (hexane / ethyl acetate = 9:1) (UV); mp 97–

98 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3311, 2978, 1717, 1587, 1489, 1454, 1392, 1368, 1250, 1159, 1053, 1028, 10145, 995, 813, 757, 732, 697; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.44 (s, 9 H), 4.68 (bs, 2 H), 6.38 (bs, 1 H), 6.67 (d, *J* = 8.7 Hz, 2 H), 7.26-7.35 (m, 5 H), 7.49 (d, *J* = 8.7 Hz, 2 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 28.2, 56.4, 81.2, 115.1, 127.6, 127.8, 128.7, 136.6, 137.8, 149.1. (Signal of hydrazine carboxylate missing, signal missing); MS (ESI) *m/z* 425 [MH^+]; HRMS (ESI) calcd for $C_{18}H_{21}IN_2O_2$ [$M^+ + Na^+$]: 447.0540, found: 447.0536.

***tert*-Butyl 2-benzyl-2-(4-cyanohenyl)hydrazine carboxylate** (**3e**) is prepared from *tert*-butyl 2-(4-cyanophenyl)azocarboxylate (**1e**) (1.00 mmol, 233 mg) and benzyl bromide (**2a**) (2.00 mmol, 238 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 7:1 → 5:1) to give the title compound **3e** as a white solid (732 µmol, 238 mg, 73%): R_f = 0.3 (hexane / ethyl acetate = 3:1) (UV); mp 122–123 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3302, 2980, 1699, 1604, 1512, 1496, 1455, 1393, 1368, 1352, 1217, 1161, 1029, 1015, 826, 760, 700; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 4.80 (bs, 2 H), 6.47 (bs, 1 H), 6.90 (d, *J* = 9.1 Hz, 2 H), 7.26-7.39 (m, 5 H), 7.50 (d, *J* = 9.1 Hz, 2 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 28.0, 56.0, 81.7, 101.2, 112.2, 119.7, 127.5, 127.7, 128.3, 133.4, 135.6, 152.2. (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 324 [MH^+]; HRMS (ESI) calcd for $C_{19}H_{21}N_3O_2$ [$M^+ + Na^+$]: 346.1526, found: 346.1524.

***tert*-Butyl 2-benzyl-2-(4-methoxyhenyl)hydrazine carboxylate** (**3f**) is prepared from *tert*-butyl 2-(4-methoxyhenyl)azocarboxylate (**1f**) (1.00 mmol, 236 mg) and benzyl bromide (**2a**) (2.00 mmol, 238 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 7:1) to give the title compound **3f** as a pale yellow solid (819 µmol, 269 mg, 82%): R_f = 0.5 (hexane / ethyl acetate = 3:1) (UV); mp 81–82 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3316, 2978, 1718, 1510, 1454, 1392, 1367, 1245, 1160, 1030,

821; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.41 (s, 9 H), 3.75 (s, 3 H), 4.64 (bs, 2 H), 6.28 (bs, 1 H), 6.80-6.92 (m, 4 H), 7.26-7.33 (m, 5 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 28.2, 55.6, 57.3, 80.7, 114.5, 114.9, 127.4, 128.2, 128.5, 137.1, 143.6, 153.5. (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 329 [MH^+]; HRMS (ESI) calcd for $C_{19}H_{24}N_2O_3$ [$M^+ + Na^+$]: 351.1679, found: 351.1675.

***tert*-Butyl 2-benzyl-2-(2,4-dichorohenyl)hydrazine carboxylate** (**3g**) is prepared from *tert*-butyl 2-(2,4-dichlorophenyl)azocarboxylate (**1g**) (1.00 mmol, 275 mg) and benzyl bromide (**2a**) (2.00 mmol, 238 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 8:1) to give the title compound **3g** as a white solid (819 µmol, 269 mg, 82%): R_f = 0.5 (hexane / ethyl acetate = 8:1) (UV); mp 118–119 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3312, 2979, 1717, 1699, 1476, 1456, 1392, 1367, 1250, 1159, 772; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.36 (s, 9 H), 4.62 (bs, 2 H), 6.53 (bs, 1 H), 7.17 (dd, *J* = 2.4 Hz, *J* = 8.6 Hz, 1 H), 7.27-7.42 (m, 7 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 28.2, 56.9, 80.7, 123.5, 127.0, 127.7, 128.5, 128.9, 129.0, 129.4, 130.1, 136.5, 145.2. (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 367 [$^{35}Cl_2$-MH^+]; HRMS (ESI) calcd for $C_{18}H_{20}Cl_2N_2O_2$ [$M^+ + Na^+$]: 389.0794, found: 389.0789.

***tert*-Butyl 2-benzyl-2-(4-fluoro-2-methylphenyl)hydrazine carboxylate** (**3h**) is prepared from *tert*-butyl 2-(4-fluoro-2-methylphenyl)azocarboxylate (**1h**) (1.00 mmol, 238 mg) and benzyl bromide (**2a**) (2.00 mmol, 238 µL) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 8:1) to give the title compound **3h** as a white solid (747 µmol, 247 mg, 75%): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); mp 113–114 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 2977, 1597, 1497, 1457, 1391, 1366, 1245, 1155, 728, 698; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.34 (s, 9 H), 2.38 (s, 3 H), 4.41 (bs, 2 H),

6.09 (bs, 1 H), 7.17 (dt, J = 3.0 Hz, J = 8.4 Hz, J_{HF} = 8.4 Hz, 1 H), 6.87 (dd, J = 3.0 Hz, J = 9.3 Hz, 1 H), 6.99-7.34 (m, 6 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 18.6 (d, J_{CF} = 1.3 Hz), 28.2, 58.8, 80.3, 112.3 (d, J_{CF} = 22.1 Hz), 117.3 (d, J_{CF} = 21.9 Hz), 122.0 (d, J_{CF} = 7.8 Hz), 127.5, 128.4, 129.2, 135.0 (d, J_{CF} = 7.9 Hz), 136.7, 144.5, 159.5 (d, J_{CF} = 242.6 Hz). (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 331 [MH^+]; HRMS (ESI) calcd for $C_{19}H_{23}FN_2O_2$ [$M^+ + Na^+$]: 353.1636, found: 353.1629.

***tert*-Butyl 2-(4-bromophenyl)-2-(2-bromobenzyl)hydrazine carboxylate** (**3i**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (500 µmol, 143 mg) and 2-bromobenzyl bromide (**2b**) (1.00 mmol, 250 mg) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 8:1) to give the title compound **3i** as a viscous yellow oil (312 µmol, 142 mg, 62%): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); ; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3303, 2979, 1708, 1590, 1441, 1392, 1368, 1344, 1250, 1215, 1158, 1026, 999, 815, 750; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.43 (s, 9 H), 4.73 (bs, 2 H), 6.45 (bs, 1 H), 6.71 (d, J = 9.2 Hz, 2 H), 7.16 (dt, J = 1.8 Hz, J = 7.5 Hz, J = 7.7 Hz, 1 H), 7.24-7,41 (m, 4 H), 7.59 (dd, J = 1.2 Hz, J = 7.9 Hz, 1 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 28.3, 57.5, 81.5, 111.8, 114.5, 123.4, 127.7, 129.2, 129.8, 131.9, 133.0, 135.6, 148.0, 154.6; MS (ESI) *m/z* 459 [$^{81}Br_2$-MH^+], 457 [$^{81}Br^{79}Br$-MH^+]; HRMS (ESI) calcd for $C_{18}H_{20}Br_2N_2O_2$ [$M^+ + Na^+$]: 478.9764, found: 478.9751.

***tert*-Butyl 2-(4-bromophenyl)-2-(2-iodobenzyl)hydrazine carboxylate** (**3j**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (1.00 mmol, 285 mg) and 2-iodobenzyl bromide (**2c**) (2.00 mmol, 540 mg) according to general procedure GP 1. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 10:1) to give the title compound **3j** as an orange oil (440 µmol, 221 mg, 44%): R_f = 0.3 (hexane / ethyl acetate = 9:1)

(UV); ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 4.68 (bs, 2 H), 6.65 (bs, 1 H), 6.72 (d, *J* = 8.9 Hz, 2 H), 6.99-7.02 (m, 1 H), 7.29-7.37 (m, 4 H), 7.88 (dd, *J* = 1.2 Hz, *J* = 7.9 Hz, 1 H). Due to low stability of **3j** the compound was immediately used for the synthesis of **15**.

***tert*-Butyl 2-allyl-2-(4-bromophenyl)hydrazine carboxylate** (**5a**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (500 µmol, 140 mg) and allyl iodide (**4b**) (2.50 mmol, 225 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 8:1) to give the title compound **5a** as a white solid (356 µmol, 117 mg, 71%): R_f = 0.2 (hexane / ethyl acetate = 9:1) (UV); mp 105–106 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3295, 2979, 1673, 1644, 1593, 1488, 1393, 1365, 1304, 1288, 1254, 1152, 913, 821, 771; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.39 (s, 9 H), 4.07 (d, *J* = 5.9 Hz, 2 H), 5.15-5.21 (m, 2 H), 5.82-5.93 (m, 1 H), 6.62 (d, *J* = 8.9 Hz, 2 H), 7.30 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 28.2, 52.4, 81.4, 112.5, 114.6, 118.1, 131.9, 132.7, 146.9, 155.7; MS (ESI) *m/z* 327 [^{79}Br-MH^+]; HRMS (ESI) calcd for $C_{14}H_{19}BrN_2O_2$ [$M^+ + Na^+$]: 349.0522, found: 349.0516.

***tert*-Butyl 2-allyl-2-(4-iodophenyl)hydrazine carboxylate** (**5b**) is prepared from *tert*-butyl 2-(4-iodophenyl)azocarboxylate (**1d**) (500 µmol, 166 mg) and allyl iodide (**4b**) (2.50 mmol, 225 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 10:1) to give the title compound **5b** as a white solid (456 µmol, 171 mg, 91%): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); mp 97–98 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3312, 2978, 1699, 1592, 1485, 1384, 1367, 1250, 1175, 1150, 998, 816, 771; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.39 (s, 9 H), 4.07 (d, *J* = 5.8 Hz, 2 H), 5.15-5.21 (m, 2 H), 5.82-5.93 (m, 1 H), 6.52 (d, *J* = 8.9 Hz, 2 H), 7.49 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR

(151 MHz, $CDCl_3$) δ 28.2, 52.5, 81.4, 82.1, 115.1, 118.1, 132.7, 137.8, 147.8, 155.7; MS (ESI) *m/z* 375 [MH^+]; HRMS (ESI) calcd for $C_{14}H_{19}IN_2O_2$ [$M^+ + Na^+$]: 397.0383, found: 397.0376.

Barbier-type procedure: A mixture of *tert*-butyl 2-(4-iodophenyl)azocarboxylate (**1d**) (151 µmol, 50.0 mg) and allyl iodide **4b** (755 µmol, 70.0 µL) in tetrahydrofuran (3.0 mL) and saturated aqueous ammonium chloride (0.5 mL) is treated with zinc (755 µmol, 50.0 mg) and stirred vigorously for 30 seconds. Work up is as described above. The solvent is removed under reduced pressure and the residue is subjected to column chromatography (silica gel, hexane / ethyl acetate = 9:1) to give compound **5b** as a white solid (139 µmol, 52.1 mg, 92%).

***tert*-Butyl 2-allyl-2-(4-cyanophenyl)hydrazine carboxylate** (**5c**) is prepared from *tert*-butyl 2-(4-iodophenyl)azocarboxylate (**1e**) (500 µmol, 166 mg) and allyl iodide (**4b**) (2.50 mmol, 225 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 10:1) to give the title compound **5c** as a white solid (456 µmol, 171 mg, 91%): R_f = 0.4 (hexane / ethyl acetate = 3:1) (UV); mp 106–107 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3310, 2979, 1701, 1596, 1515, 1392, 1368, 1275, 1250, 1170, 1151, 925, 831, 762; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.41 (s, 9 H), 4.09 (bs, 2 H), 5.19-5.24 (m, 2 H), 5.85-5.92 (m, 1 H), 6.20 (bs, 1 H), 6.75 (d, *J* = 8.8 Hz, 2 H), 7.51 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 28.1, 52.7, 81.4, 81.8, 102.5, 112.4, 118.5, 119.6, 132.2, 133.6, 151.3, 155.4; MS (ESI) *m/z* 274 [MH^+]; HRMS (ESI) calcd for $C_{15}H_{19}N_3O_2$ [$M^+ + Na^+$]: 296.1369, found: 296.1367.

***tert*-Butyl 2-allyl-2-(2,4-dichlorophenyl)hydrazine carboxylate** (**5d**) is prepared from *tert*-butyl 2-(2,4-dichlorophenyl)azocarboxylate (**1g**) (1.00 mmol, 275 mg) and allyl iodide (**4b**) (5.00 mmol, 450 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 8:1) to give the title compound **5d**

as a white solid (658 µmol, 209 mg, 66%): R_f = 0.5 (hexane / ethyl acetate = 9:1) (UV); mp 52–53 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3341, 2979, 1710, 1595, 1577, 1496, 1457, 1368, 1269, 1248, 1152, 1103, 1049, 993, 928, 855, 812, 759; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.39 (s, 9 H), 4.10 (d, *J* = 5.3 Hz, 2 H), 5.20-5.26 (m, 2 H), 5.86-5.97 (m, 1 H), 6.35 (bs, 1 H), 6.75 (d, *J* = 8.7 Hz, 1 H), 7.13 (dd, *J* = 2.3 Hz, *J* = 8.7 Hz, 1 H), 7.27-7.29 (m, 1 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 28.1, 52.7, 81.6, 114.0, 118.6, 119.1, 124.8, 127.7, 129.0, 132.5, 142.6, 155.4; MS (ESI) *m/z* 317 [MH^+]; HRMS (ESI) calcd for $C_{14}H_{18}Cl_2N_2O_2$ [$M^+ + Na^+$]: 339.0638, found: 339.06356.

***tert*-Butyl 2-(4-bromophenyl)-2-(but-3-en-2-yl)hydrazine carboxylate** (**8a**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (500 µmol, 140 mg) and crotyl bromide (**6a**) (2.50 mmol, 260 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 8:1) to give the title compound **8a** as a white solid (429 µmol, 146 mg, 86%): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); mp 100–101 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3316, 2978, 1701, 1596, 1490, 1368, 1318, 1253, 1164, 820; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.28 (d, *J* = 6.8 Hz, 3 H), 1.37 (s, 9 H), 4.69-4.85 (m, 1 H), 5.10-5.19 (m, 2 H), 5.87 (ddd, *J* = 6.5 Hz, *J* = 10.4 Hz, *J* = 17.1 Hz, 1 H), 6.67 (d, *J* = 8.9 Hz, 2 H), 7.29 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 17.3, 28.1, 56.1, 81.4, 112.1, 114.7, 115.8, 131.7, 138.0, 148.2, 155.8; MS (ESI) *m/z* 343 [^{81}Br-MH^+], 341 [^{79}Br-MH^+]; HRMS (ESI) calcd for $C_{15}H_{21}BrN_2O_2$ [$M^+ + Na^+$]: 363.0679, found: 363.0670.

***tert*-Butyl 2-(4-cyanophenyl)-2-(but-3-en-2-yl)hydrazine carboxylate (8b) and *tert*-butyl 2-(but-2-en-1-yl)-2-(4-cyanophenyl)hydrazine carboxylate (7b)** are prepared from *tert*-butyl 2-(4-cyanophenyl)azocarboxylate (**1e**) (500 µmol, 117 mg) and croytl bromide (**6a**) (2.50 mmol, 260 µL) according to general procedure GP 2. The crude product is subjected to

column chromatography (silica gel, hexane / ethyl acetate = 6:1) to give compound **8b** (360 µmol, 103 mg, 72%) and **7b** (90.0 µmol, 25.9 mg, 18%) as white solids. *Tert*-butyl 2-(4-cyanophenyl)-2-(but-3-en-2-yl)hydrazine carboxylate (**8b**): R_f = 0.4 (hexane / ethyl acetate = 9:1) (UV); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.29 (mc, 3 H), 1.39 (s, 9 H), 4.84 (bs, 1 H), 5.08-5.33 (m, 2 H), 5.86 (ddd, *J* = 6.4 Hz, *J* = 10.4 Hz, *J* = 17.1 Hz, 1 H), 6.81 (d, *J* = 8.6 Hz, 2 H), 7.49 (d, *J* = 8.6 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 17.8, 28.1, 55.4, 81.9, 112.4, 112.7, 116.1, 119.7, 133.5, 137.4, 152.8. (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 343 [^{81}Br-MH^+], 341 [^{79}Br-MH^+]; HRMS (ESI) calcd for $C_{16}H_{21}N_3O_2$ [M^+ + Na^+]: 310.1526, found: 310.1522. *Tert*-butyl 2-(but-2-en-1-yl)-2-(4-cyanophenyl)hydrazine carboxylate (**7b**): R_f = 0.4 (hexane / ethyl acetate = 9:1) (UV); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.49 (s, 9), 1.74 (d, *J* = 6.4 Hz, 3 H), 3.83-4.32 (m, 2 H), 5.48-5.57 (m, 1 H), 5.78-6.10 (m, 1 H), 6.86 (mc, 2 H), 7.51 (mc, 2 H); MS (ESI) *m/z* 343 [^{81}Br-MH^+], 341 [^{79}Br-MH^+]; HRMS (ESI) calcd for $C_{16}H_{21}N_3O_2$ [M^+ + Na^+]: 310.1526, found: 310.1522.

***tert*-Butyl 2-(4-methoxyphenyl)-2-(but-3-en-2-yl)hydrazine carboxylate (8c)** and ***tert*-butyl 2-(but-2-en-1-yl)-2-(4-methoxyphenyl)hydrazine carboxylate (7c)** are prepared from *tert*-butyl 2-(4-methoxyphenyl)azocarboxylate (**1f**) (500 µmol, 118 mg) and croytl bromide (**6a**) (2.50 mmol, 260 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 6:1) to give compound **8c** (325 µmol, 95.9 mg, 65%) and **7c** (165 µmol, 48.2 mg, 33%) as highly viscous oils. *Tert*-butyl 2-(4-methoxyphenyl)-2-(but-3-en-2-yl)hydrazine carboxylate (**8c**): R_f = 0.5 (hexane / ethyl acetate = 6:1) (UV); IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3322, 2978, 1697, 1510, 1456, 1367, 1316, 1240, 1164, 1107, 1038, 825; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.29 (d, *J* = 6.8 Hz, 3 H), 1.35 (s, 9 H), 3.74 (s, 3 H), 4.76 (mc, 1 H), 5.07-5.11 (m, 1 H), 5.13-5-18 (m, 1 H), 5.86-5.95 (m, 1 H), 6.71-6.78 (m, 4 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 17.5, 28.2, 55.6, 56.2, 81.0, 114.3, 114.4, 115.4, 138.5,

143.5, 153.5, 156.3; MS (ESI) *m/z* 293 [MH^+]; HRMS (ESI) calcd for $C_{16}H_{24}N_2O_3$ [$M^+ + Na^+$]: 315.1679, found: 315.1683. *Tert*-butyl 2-(but-2-en-1-yl)-2-(4-methoxyphenyl)-hydrazine carboxylate (**7c**): R_f = 0.4 (hexane / ethyl acetate = 6:1) (UV); IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3306, 2979, 1717, 1510, 1456, 1367, 1244, 1161, 1040, 822; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.44 (s, 9 H), 1.68-1.72 (m, 3 H), 3.75 (s, 3 H), 3.89-4.14 (m, 2 H), 5.47-5.59 (m, 1 H), 5.65-5.77 (m, 1 H), 6.20 (bs, NH), 6.79-6.89 (m, 4 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 17.8, 28.3, 55.5, 55.6, 80.6, 114.3, 114.4, 115.2, 125.2, 130.3, 143.5, 153.5; MS (ESI) *m/z* 293 [MH^+]; HRMS (ESI) calcd for $C_{16}H_{24}N_2O_3$ [$M^+ + Na^+$]: 315.1679, found: 315.1678.

***tert*-Butyl 2-(4-bromophenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (8d)** and ***tert*-butyl 2-(4-bromophenyl)-2-(3-methylbut-2-en-1-yl)hydrazine carboxylate (7d)** are prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (500 µmol, 142 mg) and 3,3-dimethylallyl bromide (**6b**) (2.50 mmol, 288 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 9:1) to give the title compounds **8d** (160 µmol, 56.8 mg, 32%) and **7d** (240 µmol, 85.3 mg, 48%) as a pale yellow oils. *Tert*-butyl 2-(4-bromophenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (**8d**): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3332, 2979, 1699, 1596, 1489, 1456, 1368, 1339, 1289, 1255, 1164, 1073, 818, 772; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.34 (s, 9 H), 1.44 (s, 3 H), 1.51 (s, 3 H), 5.01 (dd, *J* = 0.7 Hz, *J* = 10.8 Hz, 1 H), 5.06 (dd, *J* = 0.7 Hz, *J* = 17.5 Hz, 1 H), 6.19 (dd, *J* = 10.8 Hz, *J* = 17.5 Hz, 1 H), 6.68 (d, *J* = 8.9 Hz, 2 H), 7.30 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 26.7, 27.0, 28.2, 62.8, 81.5, 110.5, 111.9, 114.3, 131.8, 144.7, 148.8, 155.9; MS (ESI) *m/z* 358 [^{81}Br-MH^+]; HRMS (ESI) calcd for $C_{16}H_{23}BrN_2O_2$ [$M^+ + Na^+$]: 377.0835, found: 377.0827. *Tert*-butyl 2-(4-bromophenyl)-2-(3-methylbut-2-en-1-yl)hydrazine carboxylate (**7d**): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.47 (s, 9 H), 1.71 (s, 3 H), 1.75 (s, 3 H), 4.05 (bs, 2 H), 5.24

(mc, 1 H), 6.75 (d, *J* = 8.5 Hz, 2 H), 7.31 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 17.9, 25.8, 28.2, 62.8, 81.5, 110.4, 111.9, 114.3, 137.8, 144.7, 148.8, 155.9; MS (ESI) *m/z* 358 [^{81}Br-MH^+]; HRMS (ESI) calcd for $C_{16}H_{23}BrN_2O_2$ [$M^+ + Na^+$]: 377.0835, found: 377.0827.

***tert*-Butyl 2-(4-cyanophenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (8e)** and ***tert*-butyl 2-(4-cyanophenyl)-2-(3-methylbut-2-en-1-yl)hydrazine carboxylate (7e)** are prepared from *tert*-butyl 2-(4-cyanophenyl)azocarboxylate (**1e**) (500 µmol, 116 mg) and 3,3-dimethylallyl bromide (**6b**) (2.50 mmol, 288 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 2:1) to give an inseparable mixture of the title compounds **8e** and **7e** with a total yield of (435 µmol, 131 mg, 87%) as a pale yellow oil. The ratio of the two isomers is determined by ^{1}H NMR. *Tert*-butyl 2-(4-cyanophenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (**8e**): R_f = 0.2 (hexane / ethyl acetate = 6:1) (UV); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.35 (s, 9 H), 1.44 (s, 3 H), 1.51 (s, 3 H), 5.03 (d, *J* = 10.8 Hz, 1 H), 5.08 (d, *J* = 17.4 Hz, 1 H), 6.16 (dd, *J* = 10.8 Hz, *J* = 17.4 Hz, 1 H), 6.79 (d, *J* = 8.8 Hz, 2 H), 7.49 (d, *J* = 8.8 Hz, 2 H). *Tert*-butyl 2-(4-cyanophenyl)-2-(3-methylbut-2-en-1-yl)hydrazine carboxylate (**7e**): R_f = 0.2 (hexane / ethyl acetate = 6:1) (UV); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.48 (s, 9 H), 1.72 (s, 3 H), 1.77 (s, 3 H), 4.13 (bs, 2 H), 5.22-5.26 (m, 1 H), 6.85 (d, *J* = 8.8 Hz, 2 H), 7.49 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$, mixture of **8e** and **7e**) δ 25.6, 25.7, 26.8, 28.0, 28.1, 63.0, 81.6, 81.9, 100.9, 102.3, 110.9, 112.3, 112.3, 112.3, 117.5, 119.6, 119.9, 133.4, 133.5, 133.5, 133.5, 144.0, 152.1, 153.1, 155.5, one signal missing due to overlap; MS (ESI) *m/z* 302.2 [MH^+]; HRMS (ESI) calcd for $C_{17}H_{23}N_3O_2$ [$M^+ + Na^+$]: 324.1682, found: 324.1688.

***tert*-Butyl 2-(4-methoxyphenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (8f)** and ***tert*-butyl 2-(4-methoxyphenyl)-2-(3-methylbut-2-en-1-yl)hydrazine carboxylate (7f)** are

prepared *tert*-butyl 2-(4-methoxyphenyl)azocarboxylate (**1f**) (500 µmol, 118 mg) and 3,3-dimethylallyl bromide (**6b**) (2.50 mmol, 288 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 5:1) to give the title compounds **8f** (45.0 µmol, 13.8 mg, 9%) and **7f** (285 µmol, 87.3 mg, 57%) as a pale yellow oils. *Tert*-butyl 2-(4-methoxyphenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (**8f**): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3332, 2977, 1699, 1510, 1456, 1367, 1332, 1240, 1163, 1078, 1036, 825; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.34 (s, 9 H), 1.46 (s, 3 H), 1.52 (s, 3 H), 3.76 (3 H), 5.01 (dd, *J* = 0.8 Hz, *J* = 10.8 Hz, 1 H), 5.06 (dd, *J* = 0.8 Hz, *J* = 17.5 Hz, 1 H), 6.19 (dd, *J* = 10.8 Hz, *J* = 17.5 Hz, 1 H), 6.74 (d, *J* = 9.1 Hz, 2 H), 6.80 (d, *J* = 9.1 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 25.7, 27.1, 28.2, 55.7, 62.6, 81.1, 110.0, 113.9, 114.5, 143.5, 145.2, 153.8, 156.2; MS (ESI) *m/z* 307 [MH^+]; HRMS (ESI) calcd for $C_{17}H_{26}N_2O_3$ [$M^+ + Na^+$]: 329.1836, found: 329.1840. *Tert*-butyl 2-(4-methoxyphenyl)-2-(3-methylbut-2-en-1-yl)hydrazine carboxylate (**7f**): R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3311, 2977, 1717, 1510, 1456, 1367, 1245, 1161, 1036, 822; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 1.70 (s, 3 H), 1.74 (s, 3 H), 3.75 (3 H), 4.02 (bs, 2 H), 5.26 (mc, 1 H), 6.21 (bs, NH), 6.80-6.90 (m, 4 H); ^{13}C NMR (91 MHz, $CDCl_3$) δ 18.0 (CH_3), 25.9, 28.3, 50.9, 55.7, 80.5, 114.5, 115.3, 118.5, 137.3, 143.6, 153.5. (Signal of hydrazine carboxylate missing); MS (ESI) *m/z* 307 [MH^+]; HRMS (ESI) calcd for $C_{17}H_{26}N_2O_3$ [$M^+ + Na^+$]: 329.1836, found: 329.1834.

***tert*-Butyl 2-(4-bromophenyl)-2-(2-methylallyl)hydrazine carboxylate** (**7g**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (500 µmol, 143 mg) and 3-bromo-2-methylpropene (**6c**) (2.50 mmol, 252 µL) according to general procedure GP 2. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 5:1) to give the title compound **7g** as a pale brown solid (219 µmol, 74.9 mg, 44%): R_f = 0.4 (hexane / ethyl

acetate = 9:1) (UV); mp 105–106 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3304, 2977, 1696, 1595, 1488, 1456, 1435, 1392, 1367, 1289, 1253, 1164, 1132, 1073, 900, 856, 819, 767; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.42 (s, 9 H), 1.76 (s, 3 H), 4.03 (bs, 2 H), 4.79 (mc, 1 H), 4.92 (mc, 1 H), 6.62 (d, *J* = 8.8 Hz, 2 H), 7.32 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 20.3, 28.2, 55.2, 81.4, 112.5, 112.8, 114.6, 132.0, 140.6, 146.6, 155.9; MS (ESI) *m/z* 343 [^{81}Br-MH^+]; HRMS (ESI) calcd for $C_{15}H_{21}BrN_2O_2$ [$M^+ + Na^+$]: 363.0679, found: 363.0675.

Description of experiments (Scheme **2**)

Propargylation: ***tert*-butyl 2-(4-bromophenyl)-2-(prop-2-yn-1-yl)hydrazine carboxylate** (**10**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (500 µmol, 142 mg) and propargyl bromide, 80% in toluene (2.50 mmol) **9** according to general procedure GP 2 for allylation reactions. The crude product is subjected to column chromatography (silica gel, hexane / ethyl acetate = 6:1) to give the title compound **10** (140 µmol, 45.7 mg, 28%) as a yellow oil: R_f = 0.4 (hexane / ethyl acetate = 3:1) (UV); IR (NaCl, cm^{-1}) $\tilde{\nu}$ 3300, 2979, 1701, 1697, 1594, 1489, 1426, 1368, 1249, 1162, 1133, 1073, 851, 821, 635; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.41 (s, 9 H), 2.27 (s 1 H), 4.28 (bs, 2 H), 6.00 (bs, NH), 6.69 (d, *J* = 8.9 Hz, 2 H), 7.31 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 28.1, 72.2, 78.6, 82.3, 112.7, 114.8, 131.9, 146.6, 155.3. One signal missing; MS (ESI) *m/z* 325.2 [^{79}Br-MH^+]; HRMS (ESI) calcd for $C_{15}H_{23}BrN_2O_2$ [$M^+ + Na^+$]: 365.0835, found: 365.0836.

Propargylation (Barbier-type procedure): ***tert*-butyl 2-(4-bromophenyl)-2-(prop-2-yn-1-yl)hydrazine carboxylate** (**10**). A mixture of *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (175 µmol, 50.0 mg) and propargyl bromide, 80% in toluene (1.75 mmol) **9** in tetrahydrofuran (3.0 mL) and saturated aqueous ammonium chloride (0.5 mL) is treated with zinc (875 µmol, 57.2 mg) and stirred vigorously for 4 minutes. Work up is as described above. The solvent is

removed under reduced pressure and the residue is subjected to column chromatography (silica gel, hexane / ethyl acetate = 6:1) to give compound **10** as a pale yellow oil (107 µmol, 35.0 mg, 61%).

Competition experiment with pivaldehyde: A mixture of *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (105 µmol, 30.0 mg) and pivaldehyde **11** (105 µmol, 11.0 µL) in tetrahydrofuran (2.0 mL) and saturated aqueous ammonium chloride (0.5 mL) is treated with a suspension of benzyl bromide (**2a**) (263 µmol, 31.2 µL) and zinc (263 µmol, 17.0 mg) in tetrahydrofuran (0.5 mL). After stirring for one minute the reaction mixture is diluted with water (5 mL) and extracted with dichloromethane (3 × 15 mL). The combined organic phases are washed with a saturated aqueous solution of sodium chloride (5 mL) and dried over sodium sulfate. The solvent is removed under reduced pressure and the residue is subjected to column chromatography (silica gel, hexane / ethyl acetate = 9:1) to give **3c** as a pale yellow solid (83.2 µmol, 31.4 mg, 79%).

Competition experiment with diethyl azodicarboxylate: A mixture of *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (175 µmol, 50.0 mg) and diethyl azodicarboxylate **12** (175 µmol, 52 µL, 40% in toluene) in tetrahydrofuran (2.0 mL) and saturated aqueous ammonium chloride (0.5 mL) is treated with a suspension of benzyl bromide (**2a**) (438 µmol, 52.0 µL) and zinc (438 µmol, 29.0 mg) in tetrahydrofuran (0.5 mL). After stirring for one minute the reaction mixture is diluted with water (5 mL) and extracted with dichloromethane (3 × 15 mL). The combined organic phases are washed with a saturated aqueous solution of sodium chloride (5 mL) and dried over sodium sulfate. The solvent is removed under reduced pressure. The yields of **3c** (63.0 µmol, 36%) and **13** (174 µmol, 99%) were determined with an internal standard 1,3,5-trimethoxybenzene. Diethyl 1-benzylhydrazine-1,2-dicarboxylate (**13**):

R_f = 0.3 (hexane / ethyl acetate = 9:1) (UV); ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.27 (m, 6 H), 4.20 (m, 4 H), 4.69 (bs, 2 H), 7.26-7.40 (m, 5 H). Analytical data is in agreement with those reported in literature ref 36.

9-Benzyl-6-methoxy-2,3,4,9-tetrahydro-1*H*-carbazole (14). A solution of *tert*-butyl 2-benzyl-2-(4-methoxyphenyl)hydrazine carboxylate (**3f**) (305 µmol, 100 mg) in methanol (1.8 mL) is treated with one droplet of concentrated sulfuric acid and stirred for 45 minutes at 50 °C. After complete consumption of **3f**, as monitored by TLC, cyclohexanone (763 µmol, 80.0 µL) is added and the reaction is stirred for four hours. The mixture is diluted with water (4.0 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic phases are washed with a saturated aqueous solution of sodium chloride (10 mL) and dried over sodium sulfate. The solvent is removed under reduced pressure and the residue is subjected to column chromatography (silica gel, hexane / ethyl acetate = 12:1) to give the title compound **14** as a white solid (253 µmol, 73.7 mg, 83%): R_f = 0.5 (hexane / ethyl acetate = 9:1) (UV); mp 87–88 °C; IR (NaCl, cm^{-1}) $\tilde{\nu}$ 2933, 2834, 1622, 1585, 1481, 1453, 1426, 1356, 1309, 1291, 1260, 1223, 1167, 1149, 1054, 1030, 883, 793, 752, 731, 695; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.84-1.92 (m, 4 H), 2.62 (t, *J* = 6.1 Hz, 2 H), 2.73 (t, *J* = 6.0 Hz, 2 H), 3.85 (s, 3 H), 5.21 (s, 2 H), 6.75 (dd, *J* = 2.4 Hz, *J* = 8.8 Hz, 1 H), 6.97 (d, *J* = 2.4 Hz, 1 H), 6.98-6.99 (m, 2 H), 7.07 (d, *J* = 8.8 Hz, 1 H), 7.19-7.27 (m, 4 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 21.2, 22.2, 23.2, 46.3, 56.0, 100.3, 109.5, 109.6, 110.3, 126.1, 127.1, 127.7, 128.6, 131.8, 136.3, 138.4, 153.8; MS (ESI) *m/z* 292 [MH^+], HRMS (ESI) calcd for $C_{20}H_{21}NO$ [$M^+ + Na^+$]: 314.1515, found: 314.1516.

2-(4-Bromophenyl)-2*H*-indazole (15). *tert*-Butyl 2-(2-iodobenzyl)-2-(4-bromophenyl)-hydrazine carboxylate (**3j**) (100 µmol, 50.0 mg) is treated with trifluoroacetic acid (100 µmol,

77.0 µL) in dioxane (2 mL) and stirred for 30 minutes at 60 °C in a pressure tube. Cesium carbonate (300 µmol, 98.0 mg) and copper(I) iodide (10.0 µmol, 19.0 mg) are added and the reaction is heated to 110 °C and stirred for 36 hours. The mixture is diluted with water (5 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic phases are washed with a saturated aqueous solution of sodium chloride (5 mL) and dried over sodium sulfate. The solvent is removed under reduced pressure to obtain **15** as a yellow solid (89.7 µmol, 24.5 mg, 90%): R_f = 0.5 (hexane / ethyl acetate = 9:1) (UV); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (ddd, *J* = 0.8 Hz, *J* = 6.6 Hz, *J* = 8.5 Hz, 1 H), 7.34 (ddd, *J* = 1.1 Hz, *J* = 6.6 Hz, *J* = 8.8 Hz, 1 H), 7.66 (d, *J* = 8.9 Hz, 2 H), 7.71 (td, *J* = 1.1 Hz, *J* = 8.5 Hz, 1 H), 7.78 (qd, *J* = 1.0 Hz, *J* = 8.8 Hz, 1 H), 7.82 (d, *J* = 8.9 Hz, 2 H), 8.40 (d, *J* = 1.0 Hz, 1 H). ^{1}H NMR spectrum is in agreement with those reported in literature ref 37.

***N*-Benzyl-4-bromoaniline** (**16**) is prepared from *tert*-butyl 2-(4-bromophenyl)azocarboxylate (**1c**) (500 µmol, 142 mg) and benzyl bromide (**2a**) (1.00 mmol, 170 µL) according to general procedure GP 1. The reaction is stirred for two minutes followed by the addition of zinc (5.00 mmol, 325 mg) and trifluoroacetic acid (1.0 mL). The reaction is heated to reflux overnight. After four hours additional zinc (5.00 mmol, 325 mg) is added. After cooling to room temperature, the reaction is extracted with ethyl acetate (3 × 25 mL). The combined organic phases are washed with a saturated aqueous solution of sodium chloride (10 mL) and dried over sodium sulfate. The solvent is removed under reduced pressure and the residue is subjected to column chromatography (silica gel, hexane / ethyl acetate = 7:1) to give the title compound **16** as a yellow oil (310 µmol, 81.3 mg, 62%): R_f = 0.4 (hexane / ethyl acetate = 6:1) (UV); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.31 (s, 2 H), 6.52 (d, *J* = 9.0 Hz, 2 H), 7.22 (d, *J* = 9.0 Hz, 2 H), 7.27-7.36 (m, 5 H). ^{1}H NMR spectrum is in agreement with those reported in literature ref 38.

Acknowledgments

The authors would like to thank the Deutsche Forschungsgemeinschaft (DFG) for financial support of this project within the grants HE5413/3-3 and GRK1910/B3.

Supporting Information

Copies of ^{1}H and ^{13}C-NMR spectra of all new compounds **3a-3j**, **5a-5d**, **7b-7g**, **8a-8f** and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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