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Zinc-Mediated Allylation and Benzylation of Phenylazocarboxylic Esters

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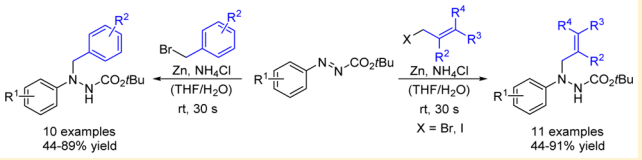
Supporting Information

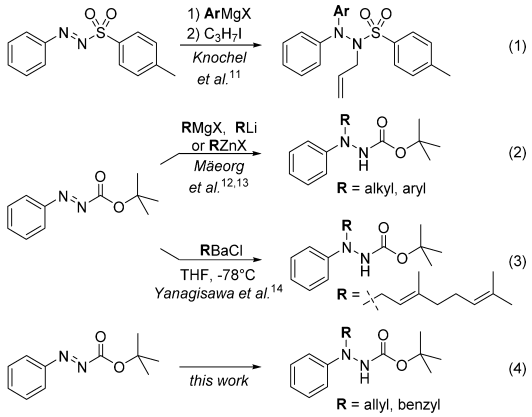
ABSTRACT: Allylation and benzylation of phenylazocarboxylic *tert*-butyl esters have been achieved under Barbier-type reaction conditions and in very short reactions times using the corresponding allyl and benzyl bromides or iodides in combination with zinc powder. Whereas all reactions occurred exclusively 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 and 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 past 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 a 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.

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 toward 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 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 a wide range of carbonyl compounds. In the case that the nucleophilic addition could be conducted in short overall reaction times, it might also be applicable in radiosyntheses starting from ^{18}F-labeled phenylazocarboxylic esters.[17]

Scheme 1. Addition of Organometallic Reagents to Phenylazosulfones and Phenylazocarboxylic Esters



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

Against the background that phenylazocarboxylic esters were readily reduced to their corresponding hydrazines by metallic

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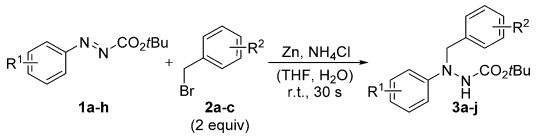
zinc powder,[22] we decided to add the benzyl bromide and zinc powder—after a short mixing time in which no reaction should occur—simultaneously to the azocarboxylic ester.[23] A mixture of benzyl bromide (**2a**) and an equivalent amount of commercially available zinc powder in tetrahydrofuran was thus stirred for 1 min before being added to a solution of phenylazocarboxylic *tert*-butyl ester (**1a**) in tetrahydrofuran and saturated aqueous ammonium chloride under air (Table 1).[24]

Table 1. Zinc-Mediated Benzylation of Phenylazocarboxylic *tert*-Butyl Esters



1a-h **2a-c** (2 equiv) **3a-j**

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 byproduct (~20–40%).

As the characteristic orange color of phenylazocarboxylate **1a** disappeared after a reaction time of only 30 s, the reaction was quenched by the addition of water. Analysis of the crude reaction mixture by ^{1}H NMR revealed the formation of desired adduct **3a** in 89% yield and showed no detectable amounts of the hydrazine resulting from the reduction of **1a**. Furthermore, the homocoupling of benzyl bromide (**2a**) during the short premixing phase had indeed not occurred, as no dibenzyl was found as byproduct. 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 the scope and limitations of the benzylation reaction.

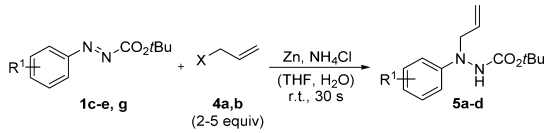
Good to high yields were obtained for all combinations of phenylazocarboxylic esters **1a–h** with benzyl bromide (**2a**) (entries 1–8) irrespective of the presence of an electron-withdrawing (R^1 = 4-CN, entry 5) or an electron-donating group (R^1 = 4-OMe, entry 6). Moreover, all types of halogen atoms, 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 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 azocarboxylic ester **1c** is added as a solid to a mixture of benzyl bromide **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**) with 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 azo compound **1** is first reduced to a hydrazine that then reacts 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

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).

indicated that two equivalents of allyl bromide (**4a**) or of the more reactive allyl iodide (**4b**) are not sufficient to obtain desired allylation product **5a** in good yield. By increasing the amounts of **4a** or **4b** and zinc powder to five equivalents, 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 azocarboxylates **1** were detected as minor byproducts. 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 also possible.

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 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).

If only one methyl group is present in the γ-position of the allyl bromide, as in (*E*)-2-buten-1-yl bromide (**6a**), the addition

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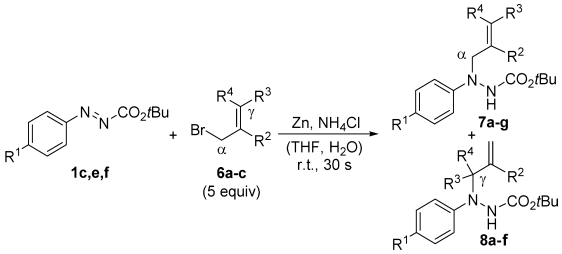
Table 3. Zinc-Mediated Allylation of Phenylazocarboxylates



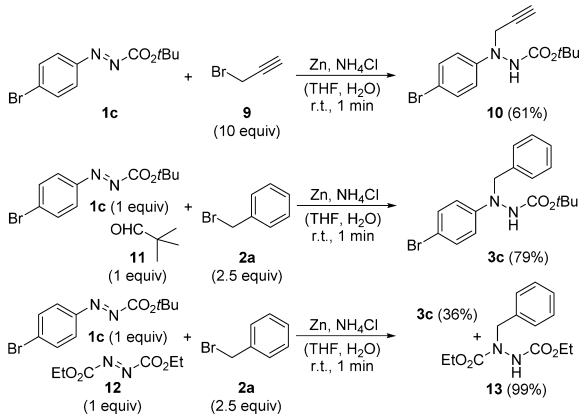
entry	azo-carboxylate **1**: R^1 =	allyl bromide **6**: R^2, R^3, R^4 =	hydrazines **7**:**8** (%:%)[a]	α vs γ[b]
1	**1c**: Br	**6a**: H, Me, H	**7a**:**8a** (0:86)	γ
2	**1e**: CN	**6a**: H, Me, H	**7b**:**8b** (18:72)	γ
3	**1f**: OMe	**6a**: H, Me, H	**7c**:**8c** (33:65)	γ
4	**1c**: Br	**6b**: H, Me, 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. [b]Preferred attack.

occurs preferably in the γ-position (entries 1−3). This strongly suggests that **6a**, and mostly probably allyl bromide (**4a**) and allyl iodide (**4b**), also 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 the case of **1e** (R^1 = CN, entry 2) could be due to increased electrophilicity of the N=N moiety. In agreement with the observations previously made with allylbarium reagents,[14] the γ,γ-disubstituted allyl bromide **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 reaction 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 allyl bromide **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 the 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 nonrearranged 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 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 byproducts. Two further reactions with competing electrophiles demonstrated that phenylazocarboxylic ester **1c** is more reactive toward the organozinc reagent formed from **2a** than toward pivalyl aldehyde (**11**),[32] as only hydrazine **3c** was obtained. Conversely, **1c** is less reactive than diethyl azodicarboxylate

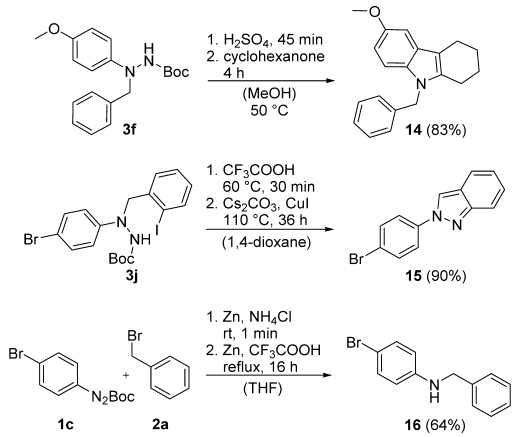
Scheme 2. Propargylation and Comparison of Reactivity



(**12**), as evidenced by the individual yields of **3c** (36%) and **13** (99%).

The hydrazines **3f** and **3j** (Table 1) obtained as products were finally used for further transformations (Scheme 3). In a

Scheme 3. Synthesis of Heterocycles and Reductive Cleavage of the N−N Bond



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 workup.[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.

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 the exception of 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.

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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-positions 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 of potassium carbonate, 5.0 mL of aqueous sodium hydroxide (5% w/w) in 300 mL of H_2O], and ninhydrin [200 mg of ninhydrin in 100 mL of 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 (GP1).* 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 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) and then 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 (GP2). A solution of the phenylazocarboxylic ester (1.00 mmol) in tetrahydrofuran (3 mL) and a saturated aqueous solution of ammonium chloride (0.5 mL) is treated with a suspension of 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) and then 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**).* **3a** is prepared from *tert*-butyl 2-phenylazocarboxylate (**1a**) (242 μmol, 50.0 mg) and benzyl bromide (**2a**) (484 μmol, 60 μL) according to GP1. The crude product is subjected to column chromatography (silica gel, 10:1 hexane/ethyl acetate) to give title compound **3a** as a white solid (210 μmol, 62.6 mg, 87%). R_f = 0.4 (9:1 hexane/ethyl acetate) (UV); mp 97−98 °C; IR (NaCl, cm^{-1}) ν 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 that reported in ref 35b.

*tert-Butyl 2-Benzyl-2-(4-fluorophenyl)hydrazine Carboxylate (**3b**).* **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 GP1. The crude product is subjected to column chromatography (silica gel, 9:1 hexane/ethyl acetate) to give title compound **3b** as a pale brown solid (877 μmol, 278 mg, 88%). R_f = 0.4 (9:1 hexane/ethyl acetate) (UV); mp 95−96 °C; IR (NaCl, cm^{-1}) ν 3313, 2979, 1717, 1508, 1455, 1368, 1228, 1157, 822, 744, 696; ^{1}H 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 GP1. The crude product is subjected to column chromatography (silica gel, 9:1 hexane/ethyl acetate) to give title compound **3c** as a pale yellow solid (799 μmol, 301 mg, 80%). R_f = 0.4 (9:1 hexane/ethyl acetate) (UV); mp 96−97 °C; IR (NaCl, cm^{-1}) ν 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 s. The work up is as described above. The solvent is removed under reduced pressure, and the residue is subjected to column chromatography (silica gel, 9:1 hexane/ethyl acetate) 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 s. Work up is as described above. The solvent is removed under reduced pressure, and the residue is subjected to column chromatography (silica gel, 9:1 hexane/ethyl acetate) 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**).* **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 GP1. The crude product is subjected to column chromatography (silica gel, 8:1 hexane/ethyl acetate) to give title compound **3d** as a pale yellow solid (533 μmol, 208 mg, 89%). R_f = 0.4 (9:1 hexane/ethyl acetate) (UV); mp 97−98 °C; IR (NaCl, cm^{-1}) ν 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 (two signals 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**).* **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 GP1. The crude product is subjected to column chromatography (silica gel, 7:1 → 5:1 hexane/ethyl acetate) to give title compound **3e** as a white solid (732 μmol, 238 mg, 73%). R_f = 0.3 (3:1 hexane/ethyl acetate) (UV); mp 122−123 °C; IR (NaCl, cm^{-1}) ν 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,

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$CDCl_3$) 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**).* **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 GP1. The crude product is subjected to column chromatography (7:1 silica gel, hexane/ethyl acetate) to give title compound **3f** as a pale yellow solid (819 μmol, 269 mg, 82%). R_f = 0.5 (3:1 hexane/ethyl acetate) (UV); mp 81−82 °C; IR (NaCl, cm^{-1}) v 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**).* **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 GP1. The crude product is subjected to column chromatography (silica gel, hexane/ethyl acetate =8:1) to give title compound **3g** as a white solid (819 μmol, 269 mg, 82%). R_f = 0.5 (8:1 hexane/ethyl acetate) (UV); mp 118−119 °C; IR (NaCl, cm^{-1}) v 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**).* **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 GP1. The crude product is subjected to column chromatography (silica gel, 8:1 hexane/ethyl acetate) to give title compound **3h** as a white solid (747 μmol, 247 mg, 75%). R_f = 0.3 (9:1 hexane/ethyl acetate) (UV); mp 113−114 °C; IR (NaCl, cm^{-1}) v 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**).* **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 GP1. The crude product is subjected to column chromatography (silica gel, 8:1 hexane/ethyl acetate) to give title compound **3i** as a viscous yellow oil (312 μmol, 142 mg, 62%). R_f = 0.3 (9:1 hexane/ethyl acetate) (UV); IR (NaCl, cm^{-1}) v 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**).* **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 GP1. The crude product is subjected to column chromatography (silica gel, 10:1 hexane/ethyl acetate) to give title compound **3j** as an orange oil (440 μmol, 221 mg, 44%). R_f = 0.3 (9:1 hexane/ethyl acetate) (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). Because of the low stability of **3j**, the compound was immediately used for the synthesis of **15**.

*tert-Butyl 2-Allyl-2-(4-bromophenyl)hydrazine Carboxylate (**5a**).* **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 GP2. The crude product is subjected to column chromatography (silica gel, 8:1 hexane/ethyl acetate) to give title compound **5a** as a white solid (356 μmol, 117 mg, 71%). R_f = 0.2 (9:1 hexane/ethyl acetate) (UV); mp 105−106 °C; IR (NaCl, cm^{-1}) v 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**).* **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 GP2. The crude product is subjected to column chromatography (silica gel, 10:1 hexane/ethyl acetate) to give title compound **5b** as a white solid (456 μmol, 171 mg, 91%). R_f = 0.3 (9:1 hexane/ethyl acetate) (UV); mp 97−98 °C; IR (NaCl, cm^{-1}) v 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 s. Work up is as described above. The solvent is removed under reduced pressure, and the residue is subjected to column chromatography (silica gel, 9:1 hexane/ethyl acetate) to give compound **5b** as a white solid (139 μmol, 52.1 mg, 92%).

*tert-Butyl 2-Allyl-2-(4-cyanophenyl)hydrazine Carboxylate (**5c**).* **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 GP2. The crude product is subjected to column chromatography (silica gel, 10:1 hexane/ethyl acetate) to give title compound **5c** as a white solid (456 μmol, 171 mg, 91%). R_f = 0.4 (3:1 hexane/ethyl acetate) (UV); mp 106−107 °C; IR (NaCl, cm^{-1}) v 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**).* **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 GP2. The crude product is subjected to column chromatography (silica gel, 8:1 hexane/ethyl acetate) to give title compound **5d** as a white solid (658 μmol, 209 mg, 66%). R_f = 0.5 (9:1 hexane/ethyl acetate) (UV); mp 52−53 °C; IR (NaCl, cm^{-1}) v 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

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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**).* **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 GP2. The crude product is subjected to column chromatography (silica gel, 8:1 hexane/ethyl acetate) to give title compound **8a** as a white solid (429 μmol, 146 mg, 86%). R_f = 0.3 (9:1 hexane/ethyl acetate) (UV); mp 100−101 °C; IR (NaCl, cm^{-1}) v 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**).* The title compounds 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 GP2. The crude product is subjected to column chromatography (silica gel, 6:1 hexane/ethyl acetate) 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 (9:1 hexane/ethyl acetate) (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 (9:1 hexane/ethyl acetate) (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**).* The title compounds 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 GP2. The crude product is subjected to column chromatography (silica gel, 6:1 hexane/ethyl acetate) 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 (6:1 hexane/ethyl acetate) (UV); IR (NaCl, cm^{-1}) v 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 (6:1 hexane/ethyl acetate) (UV); IR (NaCl, cm^{-1}) v 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**).* The title compounds 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 GP2. The crude product is subjected to column chromatography (silica gel, 9:1 hexane/ethyl acetate) to give title compounds **8d** (160 μmol, 56.8 mg, 32%) and **7d** (240 μmol, 85.3 mg, 48%) as pale yellow oils. *tert*-Butyl 2-(4-bromophenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (**8d**): R_f = 0.3 (9:1 hexane/ethyl acetate) (UV); IR (NaCl, cm^{-1}) v 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 (9:1 hexane/ethyl acetate) (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**).* The title compounds 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 GP2. The crude product is subjected to column chromatography (silica gel, 2:1 hexane/ethyl acetate) to give an inseparable mixture of title compounds **8e** and **7e** with a total yield of 87% (435 μmol, 131 mg) 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 (6:1 hexane/ethyl acetate) (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 (6:1 hexane/ethyl acetate) (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**).* The title compounds are prepared from *tert*-butyl 2-(4-methoxyphenyl)-azocarboxylate (**1f**) (500 μmol, 118 mg) and 3,3-dimethylallyl bromide (**6b**) (2.50 mmol, 288 μL) according to GP2. The crude product is subjected to column chromatography (silica gel, 5:1 hexane/ethyl acetate) to give title compounds **8f** (45.0 μmol, 13.8 mg, 9%) and **7f** (285 μmol, 87.3 mg, 57%) as pale yellow oils. *tert*-Butyl 2-(4-methoxyphenyl)-2-(2-methylbut-3-en-2-yl)hydrazine carboxylate (**8f**): R_f = 0.3 (9:1 hexane/ethyl acetate) (UV); IR (NaCl, cm^{-1}) v 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 (9:1 hexane/ethyl acetate) (UV); IR (NaCl, cm^{-1}) v 3311, 2977, 1717, 1510, 1456, 1367, 1245, 1161, 1036, 822;

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J. Org. Chem. 2015, 80, 10412−10420

^{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**).* **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 GP2. The crude product is subjected to column chromatography (silica gel, 5:1 hexane/ethyl acetate) to give title compound **7g** as a pale brown solid (219 μmol, 74.9 mg, 44%). R_f = 0.4 (9:1 hexane/ethyl acetate) (UV); mp 105−106 °C; IR (NaCl, cm^{-1}) ν 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 at 80% in toluene (2.50 mmol) **9** according to GP2 for allylation reactions. The crude product is subjected to column chromatography (silica gel, 6:1 hexane/ethyl acetate) to give title compound **10** (140 μmol, 45.7 mg, 28%) as a yellow oil: R_f = 0.4 (3:1 hexane/ethyl acetate) (UV); IR (NaCl, cm^{-1}) ν 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**) is prepared from 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) that is saturated with aqueous ammonium chloride (0.5 mL), treated with zinc (875 μmol, 57.2 mg), and stirred vigorously for 4 min. Work up is as described above. The solvent is removed under reduced pressure, and the residue is subjected to column chromatography (silica gel, 6:1 hexane/ethyl acetate) 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 1 min, 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, 9:1 hexane/ethyl acetate) 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 1 min, 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 of 1,3,5-trimethoxybenzene. Diethyl 1-benzylhydrazine-1,2-dicarboxylate (**13**): R_f = 0.3 (9:1 hexane/ethyl acetate) (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 that reported in ref 36.

*9-Benzyl-6-methoxy-2,3,4,9-tetrahydro-1H-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 min 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 4 h. 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, 12:1 hexane/ethyl acetate) to give title compound **14** as a white solid (253 μmol, 73.7 mg, 83%). R_f = 0.5 (9:1 hexane/ethyl acetate) (UV); mp 87−88 °C; IR (NaCl, cm^{-1}) ν 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)-2H-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 min 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 h. 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 (9:1 hexane/ethyl acetate) (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 data is in agreement with that reported in ref 37.

*N-Benzyl-4-bromoaniline (**16**).* **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 GP1. The reaction is stirred for 2 min 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 4 h, 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, 7:1 hexane/ethyl acetate) to give title compound **16** as a yellow oil (310 μmol, 81.3 mg, 62%). R_f = 0.4 (6:1 hexane/ethyl acetate) (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 that reported in ref 38.

■ ASSOCIATED CONTENT

Supporting Information

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Copies of ^{1}H and ^{13}C NMR spectra of all new compounds **3a−3j**, **5a−5d**, **7b−7g**, **8a−8f**, and **14** (PDF)

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Notes

The authors declare no competing financial interest.

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