Mild Synthesis of Polyfunctional Benzimidazoles and Indoles by the Reduction of Functionalized Nitroarenes with Phenylmagnesium Chloride

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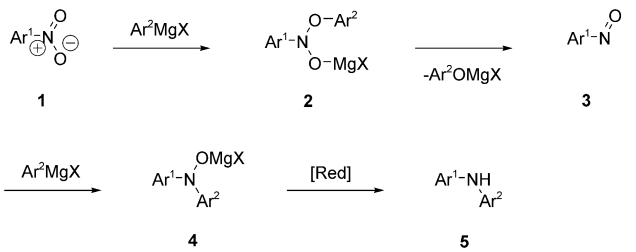
Abstract: Phenylmagnesium chloride has been used for the conversion of selected nitroarenes into nitrenes. Their insertion into a neighboring sp^2 C–H bond yielded functionalized heterocycles. A novel and mild synthesis of polyfunctional benzimidazoles and indoles is described.

Keywords: Grignard reaction · heterocycles · magnesium nitrenoids · nitrenes

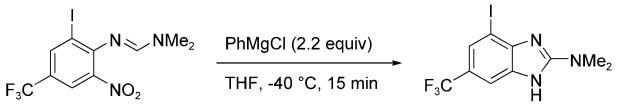
Introduction

The preparation of functionalized heterocycles is an important synthetic objective, since many of these molecules have interesting pharmaceutical properties.[1] Recently, we have studied the reaction of functionalized nitroarenes **1** with arylmagnesium reagents (Ar^2MgX).[2, 3] We have found that nitroarenes react with arylmagnesium reagents, leading first to an intermediate nitrosoarene of type **3**,[4] which reacts with a second equivalent of Ar^2MgX to furnish the magnesiated diarylhydroxylamine of type **4**. Reduction of this gives diarylamines of type **5** in good yields (Scheme 1).[2] This method proved to be quite general and practical.



Scheme 1. Reaction of arylmagnesium halides (Ar^2MgX) with nitroarenes (Ar^1NO_2): formation of diarylamines.

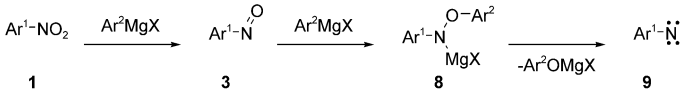
However, *ortho*-iodo-substituted nitroarenes undergo iodine–magnesium exchange reactions with phenylmagnesium chloride and usually no reduction of the nitro group is observed.[5] During our studies the question arose of whether this iodine–magnesium exchange reaction could also be performed in the presence of a nitro group by use of protected amines as directing groups.[6] Therefore, the iodo-substituted nitroarene **6a** (Scheme 2) was prepared and treated with phenylmagnesium chloride. Neither an iodine–magnesium exchange reaction, nor the reduction of the nitro group to the



Scheme 2. Formation of benzimidazole **7a** by treatment of nitroarene **6a** with phenylmagnesium chloride.

corresponding diarylamine was observed, but a clean reductive cyclization reaction occurred, leading to the corresponding benzimidazole **7a**, which was isolated in 75% yield (Scheme 2).

This unexpected result led us to explore the scope of this reaction. Thus, we have noticed that when nitroarenes of type **1** bear bulky substituents (Scheme 3), nitrosoarenes of type **3**



Ar^1 = 2,3-disubstituted aryl group

Scheme 3. Reaction of arylmagnesium halides (Ar^2MgX) with nitroarenes (Ar^1NO_2): formation of nitrenes.

are still formed, but due to steric hindrance the second equivalent of the Grignard reagent does not add—as was previously the case—at the nitrogen atom. Rather, it attacks the more readily available oxygen atom of the nitroso intermediate **3**, leading to the magnesium–nitrenoid **8** (Scheme 3). This behavior is further favored if the aromatic system is electron poor.

Here we report the use of intermediates such as **8** (or nitrenes of type **9** generated in situ) for the preparation of

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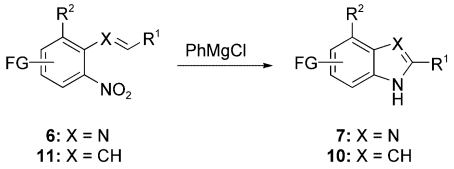
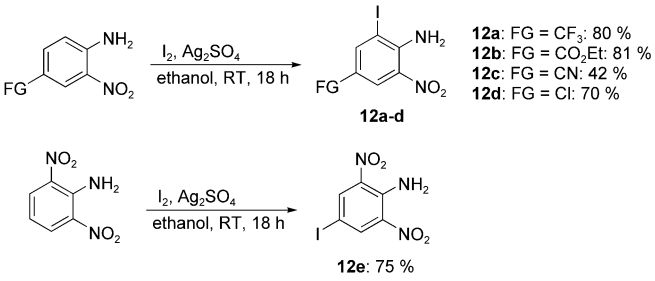
benzimidazoles of type **7** and indoles of type **10** under very mild reaction conditions, starting from *ortho*-nitro-substituted amidine and imine derivatives of type **6** and stilbenes of type **11**, respectively (Scheme 4).



Scheme 4. Preparation of functionalized benzimidazoles and indoles.

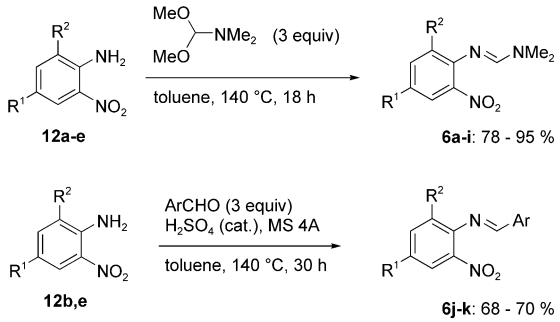
Results and Discussion

Preparation of the starting materials: The anilines **12a–e** were prepared by iodination of *ortho*-nitroanilines with silver sulfate and iodine in ethanol at room temperature (Scheme 5).[7]



Scheme 5. Preparation of iodinated nitroanilines **12a–e**.

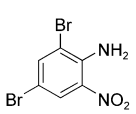
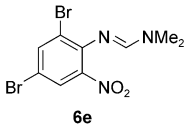
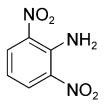
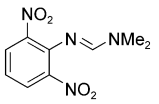
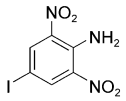
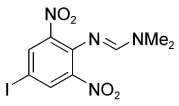
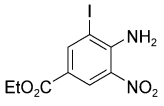
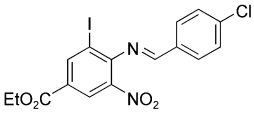
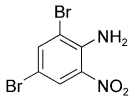
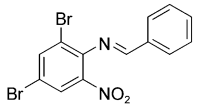
The amidines **6a–i** and the imines **6j–k** were readily prepared from the corresponding anilines of type **12** by treatment either with $(MeO)_2CHNMe_2$ in toluene[8] at 140 °C for 18 h or with ArCHO in the presence of catalytic amounts of conc. H_2SO_4 and MS (4 Å), respectively (Scheme 6 and Table 1).



Scheme 6. Preparation of amidines **6a–i** and imines **6j–k**.

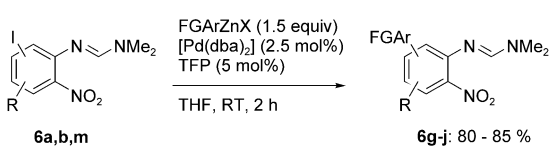
The aryl-substituted compounds **6g–j** were prepared by palladium-catalyzed cross-coupling reactions between **6a–b** and **6k** and the corresponding functionalized arylzinc halide in THF at room temperature (Scheme 7 and Table 2).[9]

Table 1. Preparation of nitro-substituted amidine and imine derivatives **6a–m**.

Entry	Aniline type **12**	Amidine and imine type **6**	Yield [%][a]
1	**12a**: $R^1 = CF_3$	**6a**: $R^1 = CF_3$	95
2	**12b**: $R^1 = CO_2Et$	**6b**: $R^1 = CO_2Et$	91
3	**12c**: $R^1 = CN$	**6c**: $R^1 = CN$	83
4	**12d**: $R^1 = Cl$	**6d**: $R^1 = Cl$	78
5		 **6e**	95
6		 **6f**	94
7	 **12e**	 **6k**	79
8	 **12b**	 **6l**	70
9		 **6m**	68

[a] Isolated yield of analytically pure product.

The *ortho*-nitro-substituted stilbenes **11a–e** were prepared by condensation reactions from the corresponding *ortho*-nitrotolyl derivatives **13a–c** with aromatic aldehydes in the presence of piperidine at elevated temperatures (Scheme 8 and Table 3).[10]

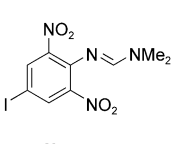
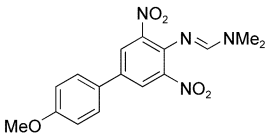
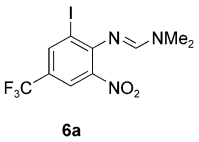
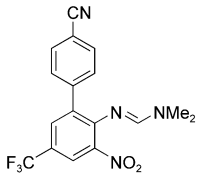


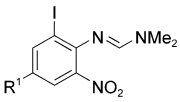
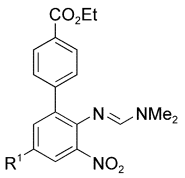
Scheme 7. Preparation of aryl-substituted compounds **6g–j**.

Preparation of the functionalized benzimidazoles 7a–l: The protected *ortho*-nitro-substituted anilines **6a–m** were treated with PhMgCl at −40 °C. (Scheme 9 and Table 4).

The functionalized benzimidazoles **7a–l** were obtained in satisfactory to good yields (42–87 %). Various substituents R^1 and R^2 can be attached to the aromatic ring. The iodo-substituted compounds **6a–d** and **6l** (entries 1–4 and entry 11 in Table 4) undergo the reductive cyclization reaction to

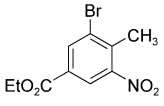
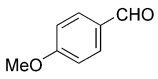
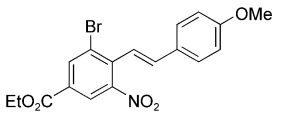
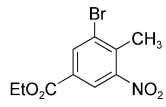
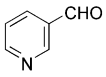
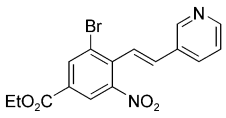
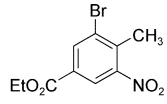
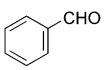
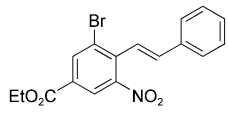
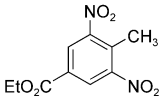
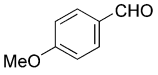
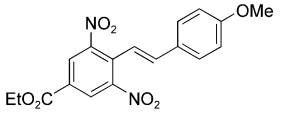
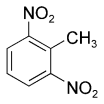
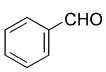
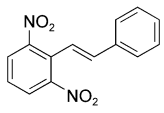
Table 2. Arylfunctionalized nitro-substituted amidines **6g–j** obtained by palladium-catalyzed cross-coupling reactions.

Entry	Amidine type **6**	Cross-coupling product	Yield [%][a]
1	 **6k**	 **6g**	82
2	 **6a**	 **6h**	80
3	**6b**: $R^1 = CO_2Et$	**6i**: $R^1 = CO_2Et$	85
4	**6a**: $R^1 = CF_3$	**6j**: $R^1 = CF_3$	80

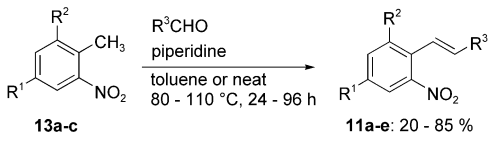
[a] Isolated yield of analytically pure product.

Table 3. Preparation of functionalized *ortho*-nitro stilbenes **11a–e**.

Entry	Nitrotolyl compound type **13**	Aldehyde	Nitrostilbene type **11**	Yield [%][a]
1	 **13a**		 **11a**	73
2	 **13a**		 **11b**	21
3	 **13a**		 **11c**	67
4	 **13b**		 **11d**	59
5	 **13c**		 **11e**	20

[a] Isolated yield of analytically pure product.

give the functionalized benzimidazoles **7a–d** and **7k** much more rapidly than iodine–magnesium exchange, which was not observed under our reaction conditions. These mild reaction conditions, allowing the performance of the ring closures at $-40\,^{\circ}C$, assure broad functional group compatibility, so various functionalities (CN, CO_2Et, CF_3, Br, Cl, OMe; entries 1–5 and entry 7 in Table 4) are tolerated. The substituent R^2 can also contain functionalized aryl substituents (entries 8–10 in Table 4) as well as a second nitro functionality (entries 6–7 in Table 4).



Scheme 8. Preparation of functionalized *ortho*-nitro stilbenes **11a–e**.

Preparation of functionalized indoles 10a–e: This method can also be used for the reductive cyclization of the nitro-substituted stilbenes **11a–e**, furnishing the corresponding indoles **10a–e** in good yields (56–76%; Scheme 10 and Table 5).

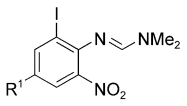
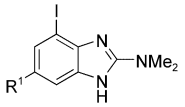
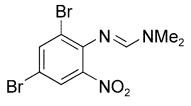
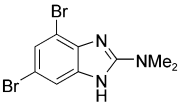
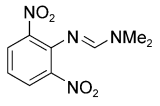
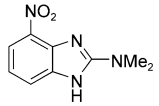
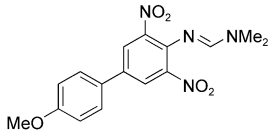
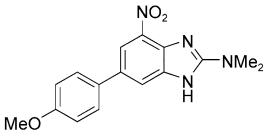
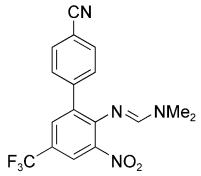
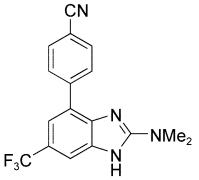
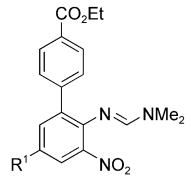
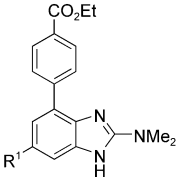
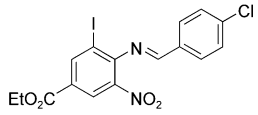
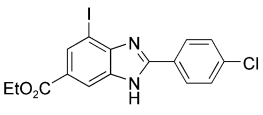
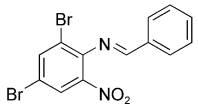
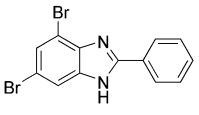
This new indole synthesis shows the same functional group tolerance as the new procedure described above for the preparation of benzimidazoles. Ester, bromo, methoxy, heteroaryl, and also a second nitro functionality can be present in the corresponding *ortho*-nitrostilbene (entries 1–5 in Table 5).

As a tentative mechanism of this reaction we propose nitrenes of type **9** as intermediates (Scheme 3). Closely related reductive cyclization reactions with triethylphosphite as deoxygenation agent proceed under much harsher reaction conditions. This method, which has been described by Cadogan[11] and others,[12] is also proposed to proceed through nitrenes as intermediates. In order to check whether we could compare our method to these known procedures, we also treated 2-nitrobiphenyl with phenylmagnesium chloride at $-40\,^{\circ}C$. As expected, carbazole was formed and could be isolated in 24% yield (Scheme 11).

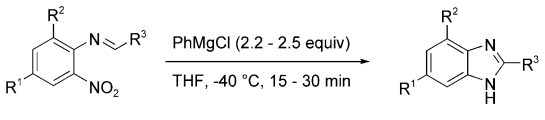
Conclusion

Treatment of phenylmagnesium chloride with various 2-amino-1-nitroaromatics or 2-nitrostilbenes under mild conditions furnishes polyfunctional benzimidazoles of type **7** and indoles of type **10**, respectively, in satisfactory to good yields. The reaction occurs very rapidly under mild conditions and is best explained by the involvement of functionalized nitrenes as intermediates.

Table 4. Functionalized benzimidazoles **7a–l** obtained by treatment of nitro-substituted amidines and imines **6a–m** with phenylmagnesium chloride.

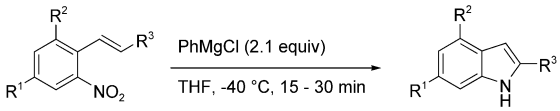
Entry	Amidine and imine type **6**	Benzimidazole type **7**	Yield [%][a]
			
1	**6a**: $R^1 = CF_3$	**7a**: $R^1 = CF_3$	75
2	**6b**: $R^1 = CO_2Et$	**7b**: $R^1 = CO_2Et$	79
3	**6c**: $R^1 = CN$	**7c**: $R^1 = CN$	48
4	**6d**: $R^1 = Cl$	**7d**: $R^1 = Cl$	61
5	 **6e**	 **7e**	70
6	 **6f**	 **7f**	62
7	 **6g**	 **7g**	87
8	 **6h**	 **7h**	45
			
9	**6i**: $R^1 = CO_2Et$	**7i**: $R^1 = CO_2Et$	56
10	**6j**: $R^1 = CF_3$	**7j**: $R^1 = CF_3$	77
11	 **6l**	 **7k**	42
12	 **6m**	 **7l**	77

[a] Isolated yield of analytically pure product.



6a-m **7a-l**: 42 - 87 %

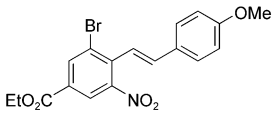
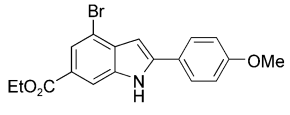
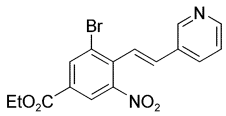
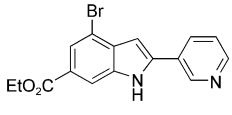
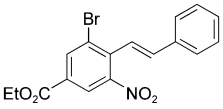
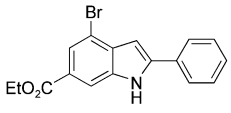
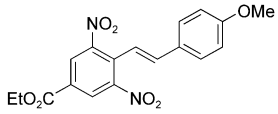
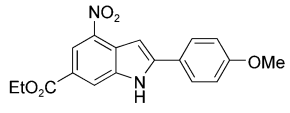
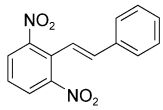
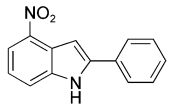
Scheme 9. Preparation of functionalized benzimidazoles **7a–l** by treatment of nitro-substituted amidines and imines **6a–m** with phenylmagnesium chloride.



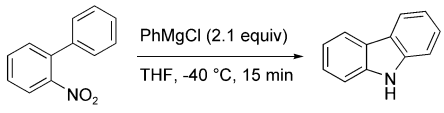
11a-e **10a-e**: 56 - 76 %

Scheme 10. Preparation of functionalized indoles **10a–e** by treatment of nitro-substituted stilbenes **11a–e** with phenylmagnesium chloride.

Table 5. Functionalized indoles **10a–e** obtained by treatment of nitro-substituted stilbenes **11a–e** with phenylmagnesium chloride.

Entry	Nitrostilbene of type **11**	Indole of type **10**	Yield [%][a]
1	 **11a**	 **10a**	76
2	 **11b**	 **10b**	70
3	 **11c**	 **10c**	75
4	 **11d**	 **10d**	56
5	 **11e**	 **10e**	60

[a] Isolated yield of analytically pure product.



14 **15**: 24 %

Scheme 11. Formation of carbazole by treatment of 2-nitrobiphenyl with phenylmagnesium chloride.

Experimental Section

General methods: THF was distilled from sodium/benzophenone and toluene from sodium. Reactions in solution were monitored by thin-layer chromatography (TLC) and gas chromatography (GC) analysis of worked-up reaction aliquots. Analytical TLC was performed on Merck silica gel (60 F-254) plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was carried out on silica gel 60 (70–230 mesh). NMR data were recorded on 300 and 600 MHz NMR spectrometers from Bruker. IR

spectra were performed with a Nicolet 510 FT-IR spectrometer. The ionization method used for mass spectroscopy was electron impact ionization (EI, 70 eV). Melting points were measured on a Büchi B 540 and are uncorrected.

Starting materials: The following starting materials were prepared by literature procedures: ethyl 4-amino-3-nitrobenzoate[13] and ethyl 3-bromo-4-methyl-5-nitrobenzoate.[14]

Typical procedure A: 2-Iodo-6-nitro-4-(trifluoromethyl)aniline (12a): 4-Trifluoromethyl-2-nitroaniline (6.18 g, 30.0 mmol) was treated with iodine (10.64 g, 42.0 mmol) and Ag_2SO_4 (13.09 g, 42.0 mmol) in ethanol (300 mL) at room temperature for 36 h. The reaction mixture was filtered and the solid was washed with ethyl acetate (3×100 mL). The filtrate was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (250 mL). The organic layer was then washed with aqueous NaOH (5%; 100 mL) and water (100 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **12a** was isolated as a yellow/orange solid (7.99 g, 24.1 mmol, 80%). M.p. 101–102 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta =$ 8.41–8.39 (m, 1H), 8.06 (d, $J = 2.1$ Hz, 1H), 6.96 ppm (brs, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 145.9$, 141.5 (q, $J = 3.3$ Hz), 130.4, 124.7 (q, $J = 4.3$ Hz), 124.2, 120.6, 87.2 ppm; IR (KBr): $\tilde{\nu} = 3463$ (s), 3351 (s), 3096 (w), 1633 (s), 1578 (m), 1519 (m), 1455 (s), 1342 (s), 1298 (s), 1252 (s), 1154 (m), 1123 (s), 906 (m), 765 (w), 720 (w), 658 (m), 467 cm^{-1} (w); MS (EI): m/z (%): 332 $[M]^+$ (100), 286 (14), 274 (10), 159 (84), 140 (14); elemental analysis calcd (%) for $C_7H_4F_3IN_2O_2$ (332.02): C 25.32, H 1.21, N 8.44; found: C 25.54, H 1.03, N 8.32.

Ethyl 4-amino-3-iodo-5-nitrobenzoate (12b): Ethyl 4-amino-3-nitrobenzoate (6.30 g, 30.0 mmol) was treated with iodine (10.65 g, 42.0 mmol) and Ag_2SO_4 (13.10 g, 42.0 mmol) in ethanol (150 mL) at room temperature for 36 h as described in procedure A. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **12b** was isolated as a yellow/orange solid (8.19 g, 24.4 mmol, 81%). M.p. 136 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.83$ (d, $J = 2.1$ Hz, 1H), 8.53 (d, $J = 2.1$ Hz, 1H), 7.01 (brs, 2H), 4.36 (q, $J = 7.2$ Hz, 2H), 1.39 ppm (t, $J =$ 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 163.7$, 146.4, 145.8, 130.8, 129.1, 120.1, 86.5, 61.5, 14.3 ppm; IR (KBr): $\tilde{\nu} = 3459$ (s), 3346 (s), 3084 (m), 2980 (m), 1715 (s), 1620 (s), 1510 (s), 1450 (m), 1398 (m), 1371 (m), 1334 (s), 1268 (vs), 1141 (s), 1026 (m), 867 (m), 756 (s), 717 (m), 677 (m), 478 cm^{-1} (m); MS (EI): m/z (%): 336 $[M]^+$ (100), 308 (53), 291 (95), 262 (12), 245 (25), 135 (10), 118 (14), 90 (21), 63 (11); elemental analysis calcd (%) for $C_9H_9IN_2O_4$ (336.08): C 32.16, H 2.70, N 8.34; found: C 32.42, H 2.51, N 8.29.

4-Amino-3-iodo-5-nitrobenzonitrile (12c): 4-Amino-3-nitrobenzonitrile (3.26 g, 20.0 mmol) was treated with iodine (7.11 g, 28.0 mmol) and Ag_2SO_4 (8.74 g, 28.0 mmol) in ethanol (150 mL) at room temperature as described in procedure A. The reaction was stopped after 4 d (approximately 50% conversion) and worked up. The crude product was purified by flash column chromatography (silica gel, CH_2Cl_2) to yield compound **12c** as a yellow/orange solid (2.43 g, 8.41 mmol, 42%). The starting material was also reisolated (1.47 g, 9.02 mmol, 45%). M.p. 175–176 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.42$ (d, $J = 2.4$ Hz, 1H), 8.04 (d, $J = 2.4$ Hz, 1H), 7.14 ppm (brs, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 146.5$, 145.6, 131.6, 130.4, 116.1, 100.8, 87.2 ppm; IR (KBr): $\tilde{\nu} = 3448$ (m), 3329 (m), 3087 (w), 2229 (s), 1614 (vs) 1535 (s), 1508 (s), 1453 (m) 1402 (w), 1356 (m), 1280 (s), 1204 (w), 1087 (w), 930 (w), 896 (w), 756 (w), 526 cm^{-1} (w); MS (EI): m/z (%): 289 $[M]^+$ (100), 243 (19), 231 (8), 163 (11), 116 (36); HRMS (EI) calcd for $C_7H_4IN_3O_2$ $[M]^+$: 288.9348; found: 288.9349.

4-Chloro-2-iodo-6-nitroaniline (12d): 4-Chloro-2-nitro-aniline (5.16 g, 30.0 mmol) was treated with iodine (10.66 g, 42.0 mmol) and Ag_2SO_4 (13.10 g, 42.0 mmol) in ethanol (300 mL) at room temperature for 36 h as described in procedure A. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **12d** was isolated as an orange solid (6.26 g, 21.0 mmol, 70%). M.p. 132–133 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.04$ (d, $J = 2.4$ Hz, 1H), 7.80 (d, $J =$ 2.4 Hz, 1H), 6.70 ppm (brs, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 144.3$, 142.4, 130.3, 125.3, 120.7, 87.1 ppm; IR (KBr): $\tilde{\nu} = 3462$ (s), 3350 (s), 3090 (w), 1622 (s), 1552 (m), 1498 (s), 1440 (m), 1386 (m), 1345 (m), 1319 (m), 1246 (s), 1130 (m), 1078 (w), 896 (w), 880 (m), 762 (m), 726 (m), 708 (m), 547 (w), 456 cm^{-1} (w); MS (EI): m/z (%): 300/298 $[M]^+$ (32/100), 254/252 (10/32), 127 (38), 90 (10); HRMS (EI) calcd for $C_6H_4ICIN_2O_2$ $[M]^+$: 297.9006; found: 297.8988.

4-Iodo-2,6-dinitroaniline (12e): 2,6-Dinitroaniline (1.83 g, 10.0 mmol) was treated with iodine (3.61 g, 14.2 mmol) and Ag_2SO_4 (4.37 g, 14.0 mmol) in ethanol (30 mL) at room temperature for 18 h as described in procedure A. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **12e** was isolated as a red/orange solid (2.33 g, 7.54 mmol, 75%). M.p. 173–174 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.76$ (s, 2H), 8.45 ppm (brs, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta =$ 141.9, 140.9, 135.8, 71.4 ppm; IR (KBr): $\tilde{\nu} = 3451$ (m), 3353 (m), 3078 (w), 1632 (s), 1513 (s), 1388 (m), 1354 (m), 1259 (s), 898 (m), 769 (m), 539 cm^{-1} (m); MS (EI): m/z (%): 309 $[M]^+$ (100), 263 (6), 217 (5), 90 (14), 78 (9), 63 (9); HRMS (EI) calcd for $C_6H_4IN_3O_4$ $[M]^+$: 308.9247; found: 308.9261.

Typical procedure B: *N*′-[2-Iodo-6-nitro-4-(trifluoromethyl)phenyl]-*N*,*N*-dimethylimidoformamide (6a): Compound **12a** (6.65 g, 20.0 mmol) was treated with *N*,*N*-dimethylformamide dimethylacetal (DMF-DMA, 4.79 g, 40.3 mmol) in toluene (100 mL) at 140 °C for 36 h. After cooling down to room temperature the reaction mixture was filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **6a** was isolated as a yellow/orange solid (7.37 g, 19.0 mmol, 95%). M.p. 85–86 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.18$ (s, 1H), 7.98 (s, 1H), 7.28 (s, 1H), 3.08 ppm (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 154.1$, 150.1, 141.6, 138.8 (q, $J =$ 2.5 Hz), 124.8, 124.3, 122.3 (q, $J = 3.8$ Hz), 98.9, 40.3, 34.5 ppm; IR (KBr): $\tilde{\nu} = 3436$ (w), 3087 (w), 1648 (s), 1604 (s), 1547 (m), 1521 (m), 1436 (m), 1378 (m), 1307 (s), 1272 (m), 1218 (w), 1157 (m), 1132 (m), 1104 (s), 906 (w), 772 (w), 718 (w), 682 cm^{-1} (w); MS (EI): m/z (%): 387 $[M]^+$ (100), 368 (15), 341 (36), 327 (15), 314 (14), 260 (17), 214 (16), 199 (9), 187 (13), 173 (38), 159 (13), 143 (16), 72 (24); elemental analysis calcd (%) for $C_{10}H_9F_3IN_3O_2$ (387.10): C 31.03, H 2.34, N 10.86, I 32.78; found: C 31.08, H 2.32, N 10.84, I 32.75.

Ethyl 4-{[(*E*)-(dimethylamino)methylidene]amino}-3-iodo-5-nitrobenzoate (6b): Compound **12b** (6.72 g, 20.0 mmol) was treated with DMF-DMA (4.77 g, 40.1 mmol) in toluene (100 mL) at 140 °C for 36 h as described in procedure B. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **6b** was isolated as a yellow/orange solid (7.14 g, 18.3 mmol, 91%). M.p. 80 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.58$ (d, $J = 2.1$ Hz, 1H), 8.34 (d, $J =$ 2.1 Hz, 1H), 7.28 (s, 1H), 4.35 (q, $J = 7.2$ Hz, 2H), 3.07 (s, 6H), 1.37 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 163.6$, 153.9, 150.5, 142.9, 141.8, 126.2, 124.7, 98.0, 61.5, 40.3, 34.5, 14.2 ppm; IR (KBr): $\tilde{\nu} =$ 3435 (m), 2923 (w), 1708 (s), 1647 (s), 1588 (s), 1541 (s), 1516 (m), 1386 (m), 1350 (m), 1270 (s), 1136 (m), 1104 (m), 1078 (m), 1024 (m), 759 (m), 716 cm^{-1} (m); MS (EI): m/z (%): 391 $[M]^+$ (100), 345 (25), 317 (18), 290 (15), 264 (12), 190 (9), 145 (12), 72 (16); elemental analysis calcd (%) for $C_{12}H_{14}IN_3O_4$ (391.16): C 36.85, H 3.61, N 10.74, I 32.44; found: C 36.69, H 3.62, N 10.89, I 32.42.

***N*′-(4-Cyano-2-iodo-6-nitrophenyl)-*N*,*N*-dimethylimidoformamide (6c)**: Compound **12c** (1.73 g, 6.0 mmol) was treated with DMF-DMA (1.40 g, 11.8 mmol) in toluene (20 mL) at 140 °C for 36 h as described in procedure B. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **6c** was isolated as an orange solid (1.72 g, 5.00 mmol, 83%). M.p. 123 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.18$ (d, $J = 1.8$ Hz, 1H), 8.01 (d, $J = 1.8$ Hz, 1H), 7.30 (s, 1H), 3.10 (s, 3H), 3.09 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 153.8$, 150.9, 144.5, 141.4, 128.9, 116.1, 105.7, 99.2, 40.4, 34.6 ppm; IR (KBr): $\tilde{\nu} =$ 3437 (m), 3062 (m), 2921 (m), 2230 (s), 1643 (vs), 1585 (vs), 1540 (s), 1462 (m), 1388 (s), 1254 (m), 1220 (m), 1104 (s), 1085 (s), 982 (m), 894 (w), 790 (w), 769 (m), 720 (m), 599 cm^{-1} (w); MS (EI): m/z (%): 344 $[M]^+$ (100), 298 (28), 284 (18), 271 (14), 217 (11), 171 (16), 144 (10), 130 (31), 116 811), 100 (16), 72 (22); HRMS calcd for $C_{10}H_9IN_4O_2$: 343.9770; found: 343.9766 $[M]^+$.

***N*′-(4-Chloro-2-iodo-6-nitrophenyl)-*N*,*N*-dimethylimidoformamide (6d)**: Compound **12d** (2.38 g, 8.0 mmol) was treated with DMF-DMA (1.94 g, 16.3 mmol) in toluene (30 mL) at 140 °C for 36 h as described in procedure B. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **6d** was isolated as an orange solid (2.23 g, 6.31 mmol, 78%). M.p. 74–75 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.95$ (d, $J = 2.1$ Hz, 1H), 7.72 (d, $J = 2.1$ Hz, 1H), 7.23 (s, 1H), 3.05 ppm (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 164.6$, 146.1, 142.0, 141.8, 126.9, 124.6, 98.8, 40.2, 34.5 ppm; IR (KBr): $\tilde{\nu} = 3436$ (w), 3075 (w), 2927 (w), 1639 (vs), 1590 (s), 1540 (s), 1514 (s), 1463 (m), 1416 (m), 1399 (s), 1376 (s), 1342 (s), 1254 (s), 1212 (m), 1106 (s), 1082 (m), 885 (m),

770 (m), 751 (m), 716 cm^{-1} (m); MS (EI): *m/z* (%): 355/353 $[M]^+$ (32/100), 309/305 (11/33), 293 (15), 280 (12), 226 (11), 180 (14), 153 (10), 139 (21), 124 (12), 109 (10), 72 (19); HRMS (EI) calcd for $C_9H_9ICIN_3O_2$: 352.9428; found: 352.9421 $[M]^+$.

***N′*-(2,4-Dibromo-6-nitrophenyl)-*N*,*N*-dimethylimidoformamide (6e)**: 2,4-Dibromo-6-nitroaniline (1.76 g, 6.0 mmol) was treated with DMF-DMA (1.45 g, 12.2 mmol) in toluene (20 mL) at 140 °C for 36 h as described in procedure B. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **6e** was isolated as a yellow/orange solid (2.30 g, 6.55 mmol, 95%). M.p. 90–91 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.83$ (d, $J = 2.1$ Hz, 1H), 7.78 (d, $J = 2.1$ Hz, 1H), 7.31 (s, 1H), 3.05 (s, 3H), 3.02 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 154.6$, 144.4, 144.3, 138.4, 126.3, 121.2, 112.8, 40.2, 34.3 ppm; IR (KBr): $\tilde{\nu} = 3436$ (m), 2926 (w), 1643 (s), 1582 (m), 1542 (m), 1461 (m), 1397 (m), 1248 (m), 1106 (m), 723 cm^{-1} (w); MS (EI): *m/z* (%): 353/351/349 $[M]^+$ (50/100/51), 321 (5/9/4), 307/305/303 (23/45/25), 280/278/276 (12/21/13), 264/262 (13/11), 183 (27), 170 (10), 155 (12), 88 (9), 72 (21); HRMS (EI) calcd for $C_9H_9Br_2N_3O_2$: 348.9061; found: 348.9070 $[M]^+$.

***N′*-(2,6-Dinitrophenyl)-*N*,*N*-dimethylimidoformamide (6f)**: 2,6-Dinitroaniline (550 mg, 3.0 mmol) was treated with DMF-DMA (723 mg, 6.1 mmol) in toluene (100 mL) at 140 °C for 18 h as described in procedure B. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **6f** was isolated as a yellow/orange solid (673 mg, 2.83 mmol, 94%). M.p. 69 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.85$ (d, $J = 8.1$ Hz, 2H), 7.39 (s, 1H), 7.04 (t, $J = 8.1$ Hz, 1H), 3.05 (s, 3H), 2.96 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 154.6$, 145.4, 141.3, 127.7, 120.2, 40.3, 34.2 ppm; IR (KBr): $\tilde{\nu} = 3436$ (w), 2922 (w), 1648 (s), 1600 (s), 1523 (s), 1404 (m), 1345 (m), 1258 (m), 1106 (m), 1083 (m), 852 (w), 749 (m), 702 cm^{-1} (m); MS (EI): *m/z* (%): 238 $[M]^+$ (100), 192 (23), 178 (19), 165 (22), 149 (11), 146 (11), 133 (10), 119 (16), 103 (16), 90 (23), 75 (20), 72(70), 63 (15); elemental analysis calcd (%) for $C_9H_{10}N_4O_4$ (238.20): C 45.38, H 4.23, N 23.52; found: C 45.58, H 3.96, N 23.72.

Typical procedure C: ***N′*-(4′-Methoxy-3,5-dinitro[1,1′-bi-phenyl]-4-yl)-*N*,*N*-dimethylimidoformamide (6g)**: Compound **6k** (364 mg, 1.0 mmol) was dissolved in a solution of the preformed catalyst {[$Pd(dba)_2$] (14.4 mg, 0.025 mmol) and tris-2-furyl-phosphine (TFP, 12.0 mg, 0.050 mmol) in THF (2 mL)} and treated with 4-methoxyphenylzinc bromide (3.0 mL, 0.5 M in THF, 1.5 mmol) at room temperature for 2 h. The reaction mixture was quenched by the addition of aqueous NH_4Cl solution (5 mL), poured into water (30 mL), and extracted with ethyl acetate (3 × 30 mL). The combined organics were washed with brine (30 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 75:25). Compound **6g** was isolated as an orange solid (425 mg, 1.23 mmol, 82%). M.p. 123–124 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.04$ (s, 2H), 7.52–7.46 (m, 2H), 7.43 (s, 1H), 7.02–6.96 (m, 2H), 3.85 (s, 3H), 3.07 (s, 3H), 2.99 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 160.1$, 154.7, 145.7, 19.4, 133.7, 129.2, 127.7, 125.2, 114.7, 55.4, 40.3, 34.3 ppm; IR (KBr): $\tilde{\nu} = 3436$ (m), 2929 (m), 1652 (vs), 1516 (vs), 1472 (s), 1412 (s), 1376 (s), 1295 (s), 1249 (vs), 1184 (s), 1102 (s), 1069 (s), 1032 (m), 985 (m), 924 (m), 899 (m), 831 (s), 802 (m), 775 (m), 720 (m), 529 cm^{-1} (m); MS (EI): *m/z* (%): 344 $[M]^+$ (100), 312 (7), 298 (10), 196 (17), 135 (13), 72 (24); elemental analysis calcd (%) for $C_{16}H_{16}N_4O_5$ (344.32): C 55.81, H 4.68, N 16.27; found: C 55.96, H 4.57, N 16.48.

Diethyl 6-{[(*E*)-(dimethylamino)methylidene]amino}-5-nitro-[1,1′-biphenyl]-3,4′-dicarboxylate (6i): Compound **6b** (587 mg, 1.5 mmol) was treated with 4-ethoxycarbonylphenylzinc bromide (4.0 mL, 0.56 M in THF, 2.25 mmol) in the presence of [$Pd(dba)_2$] (21.6 mg, 0.037 mmol) and TFP (17.4 mg, 0.075 mmol) in THF (2 mL) at room temperature for 2 h as described in procedure C. After workup, the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 90:10 and 2% NEt_3). Compound **6i** was isolated as a yellow oil (524 mg, 1.27 mmol, 85%); ^{1}H NMR ($CDCl_3$/[D_6]DMSO, 300 MHz): $\delta = 8.35$ (d, $J = 2.1$ Hz, 1H), 8.10 (d, $J = 2.1$ Hz, 1H), 8.05 (d, $J = 8.4$ Hz, 2H), 7.51 (d, $J = 8.4$ Hz, 2H), 7.01 (s, 1H), 4.33 (q, $J = 7.1$ Hz, 2H), 4.32 (q, $J = 7.0$ Hz, 2H), 2.88 (s, 3H), 2.80 (s, 3H), 1.35 (t, $J = 7.1$ Hz, 3H), 1.33 ppm (t, $J = 7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$/[D_6]DMSO, 75 MHz): $\delta = 166.4$, 164.9, 153.8, 147.9, 144.5, 143.0, 136.2, 134.3, 129.8, 129.3, 125.3, 123.6, 61.4, 60.1, 40.0, 34.3, 14.3 ppm; IR (KBr): $\tilde{\nu} = 2982$ (s), 1715 (s), 1651 (s), 1597 (s), 1532 (s), 1369 (s), 1244 (s), 1183 (s), 1106 (s), 1073 (s), 1021 (s), 862 (m), 767 (s), 739 (m), 716 cm^{-1} (s); MS (EI): *m/z* (%): 413 $[M]^+$ (59), 381 (11), 369 (100), 368 (31), 367 (25), 352 (9), 267 (10), 72 (11); HRMS (EI) calcd for $C_{21}H_{23}N_3O_6$: 413.1587; found: 413.1623 $[M]^+$.

Ethyl 2′-{[(*E*)-(dimethylamino)methylidene]amino}-3′-nitro-5′-(trifluoromethyl)[1,1′-biphenyl]-4-carboxylate (6j): Compound **6a** (581 mg, 1.5 mmol) was treated with 4-ethoxycarbonylphenylzinc bromide (4.0 mL, 0.56 M in THF, 2.25 mmol) in the presence of [$Pd(dba)_2$] (21.3 mg, 0.037 mmol) and TFP (17.1 mg, 0.074 mmol) in THF (2 mL) at room temperature for 2 h as described in procedure C. After workup, the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 90:10 and 2% NEt_3). Compound **6j** was isolated as a yellow solid (493 mg, 1.21 mmol, 80%). M.p. 123 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.03$ (d, $J = 8.4$ Hz, 2H), 7.97–7.96 (m, 1H), 7.66–7.65 (m, 1H), 7.52 (d, $J = 8.4$ Hz, 2H), 7.02 (s, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.89 (s, 3H), 2.81 (s, 3H), 1.42 ppm (t, $J = 7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 166.3$, 153.9, 146.2, 147.2, 142.5, 137.3, 130.0, 129.8, 129.6, 129.4, 123.8, 123.3 (q, $J = 32.5$ Hz), 121.4, 61.1, 40.0, 34.3, 14.3 ppm; IR (KBr): $\tilde{\nu} =$ 3431 (m), 3069 (w), 2977 (m), 1714 (s), 1646 (s), 1605 (s), 1525 (s), 1441 (m), 1370 (s), 1331 (s), 1290 (s), 1258 (s), 1206 (s), 1181 (s), 1156 (s), 1124 (s), 1071 (s), 1019 (m), 991 (m), 899 (m), 866 (m), 810 (m), 784 (m), 756 (m), 707 (m), 692 (m), 666 cm^{-1} (w); MS (EI): *m/z* (%): 409 $[M]^+$ (49), 390 (9), 366 (20), 365 (100), 364 (20), 363 (20), 337 (24), 319 (10), 292 (11), 291 (20), 275 (10), 249 (11), 246 (12), 235 (10), 72 (22); HRMS (EI) calcd for $C_{19}H_{18}F_3N_3O_4$: 409.1249; found: 409.1258 $[M]^+$.

***N′*-(4-Iodo-2,6-dinitrophenyl)-*N*,*N*-dimethylimidoformamide (6k)**: Compound **12e** (1.85 g, 6.0 mmol) was treated with DMF-DMA (1.45 g, 12.2 mmol) in toluene (30 mL) at 140 °C for 18 h as described in procedure B. After workup, the crude product was purified by flash column chromatography (silica gel, CH_2Cl_2). Compound **6k** was isolated as a yellow/orange solid (1.73 g, 4.75 mmol, 79%). M.p. 137 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.12$ (s, 2H), 7.38 (s, 1H), 3.06 (s, 3H), 2.97 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 154.4$, 145.8, 141.0, 136.0, 79.1, 40.4, 34.3 ppm; IR (KBr): $\tilde{\nu} = 3436$ (m), 3088 (m), 2930 (m), 1639 (vs), 1596 (s), 1535 (s), 1463 (m), 1428 (m), 1412 (s), 1400 (s), 1336 (m), 1250 (m), 1106 (m), 1000 (m), 920 (m), 888 (m), 774 (m), 718 (m), 554 cm^{-1} (w); MS (EI): *m/z* (%): 364 $[M]^+$ (100), 318 (28), 304 (15), 291 (26), 245 (11), 217 (12), 189 (12), 99 (19), 88 (12), 75 (22), 72 (80); HRMS (EI) calcd for $C_9H_9IN_4O_4$: 363.9669; found: 363.9677 $[M]^+$.

2,4-Dibromo-6-nitro-*N*-[(*E*)-phenylmethylidene]aniline (6m): 2,4-Dibromo-6-nitroaniline (1.77 g, 6.0 mmol) was treated with benzaldehyde (1.91 g, 18.0 mmol) in the presence of molecular sieves (4 Å, 400 mg) and 3 drops of conc. H_2SO_4 in toluene (12 mL) at 140 °C for 30 h. The reaction mixture was allowed to cool to room temperature, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 85:15 and 2% NEt_3). Compound **6m** was obtained as a yellow solid (1.56 g, 4.06 mmol, 68%). M.p. 117 °C; ^{1}H NMR (C_6D_6, 300 MHz): $\delta = 7.70–7.65$ (m, 3H), 7.47 (d, $J = 2.1$ Hz, 1H), 7.37 (d, $J = 2.1$ Hz, 1H), 7.12–7.00 ppm (m, 3H); ^{13}C NMR (C_6D_6, 75 MHz): $\delta =$ 166.9, 144.9, 142.1, 140.7, 139.0, 135.1, 132.8, 129.7, 129.0, 126.8, 117.4, 116.0 ppm; IR (KBr): $\tilde{\nu} = 3466$ (s), 3355 (s), 3075 (w), 1624 (s), 1581 (m), 1545 (s), 1505 (s), 1446 (m), 1387 (m), 1346 (s), 1318 (m), 1260 (s), 1192 (m), 1120 (m), 1099 (m), 876 (m), 762 (m), 726 (m), 692 (m), 544 cm^{-1} (w); MS (EI): *m/z* (%): 386/384/382 $[M]^+$ (20/38/21), 178 (13), 177 (21), 151 (19), 150 (12), 106 (11), 105 (100), 89 (17), 77 (17); HRMS (EI) calcd for $C_{13}H_8Br_2N_2O_2$: 381.8952; found: 381.8963 $[M]^+$.

Typical procedure D: **Ethyl 3-bromo-4-[(*E*)-2-(4-methoxyphenyl)ethenyl]-5-nitrobenzoate (11a)**: Compound **13a** (864 mg, 3.00 mmol) was placed in a dry 50 mL round-bottomed flask, equipped with a magnetic stirrer and a reflux condenser, and treated with 4-methoxybenzaldehyde (1.23 g, 9.0 mmol) and piperidine (383 mg, 4.50 mmol) in the presence of molecular sieves (4 Å, 600 mg) in toluene (5 mL) at 100 °C for 4 d. After the mixture had cooled to room temperature, THF (5 mL) was added, the reaction mixture was filtered, and the remaining residue was washed with CH_2Cl_2 (3 × 5 mL). The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (silica gel, pentane/diethyl ether 96:4). A yellow solid was obtained; this still contained some aldehyde, which was mostly removed by Kugelrohr distillation. The remaining residue was washed with diethyl ether, to afford compound **11a** (630 mg, 52%) as a yellow solid. The filtrate was concentrated in vacuo and the residue was purified by Kugelrohr distillation to afford compound **11a** (259 mg, 21%; total yield 889 mg, 2.19 mmol, 73%). M.p. 129 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.43$ (d, $J = 1.8$ Hz, 1H), 8.26 (d, $J =$

1.8 Hz, 1H), 7.44 (dm, J = 8.8 Hz, 2H), 6.98 (d, J = 16.6 Hz, 1H), 6.91 (dm, J = 8.8 Hz, 2H), 6.73 (d, J = 16.6 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 1.42 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 163.3, 160.5, 150.2, 137.1, 136.6, 136.5, 130.4, 128.6, 128.4, 125.4, 123.6, 119.4, 114.2, 62.2, 55.3, 14.2 ppm; IR (KBr): $\tilde{\nu}$ = 3420 (m), 3076 (m), 2982 (m), 2937 (m), 2842 (w), 1718 (vs), 1631 (m), 1600 (s), 1574 (m), 1532 (s), 1513 (s), 1462 (m), 1422 (m), 1362 (s), 1250 (vs), 1178 (s), 1142 (m), 1034 (m), 970 (m), 907 (w), 822 (m), 767 (m), 748 (m), 726 (m), 545 cm^{-1} (w); MS (EI): m/z (%): 407/405 $[M]^+$ (6/7), 390 (14), 388 (14), 362 (14), 360 (15), 271 (13), 269 (13), 243 (17), 241 (11), 216 (11), 214 (10), 164 (24), 163 (41), 152 (14), 136 (64), 135 (100), 134 (31), 121 (48), 77 (10); HRMS (EI) calcd for $C_{18}H_{16}BrNO_5$: 405.0212; found: 405.0219 $[M]^+$.

Ethyl 3-bromo-5-nitro-4-[(*E*)-2-(3-pyridinyl)ethenyl]benzoate (11b): Compound **13a** (864 mg, 3.00 mmol) was treated with nicotinaldehyde (964 mg, 9.00 mmol) and piperidine (383 mg, 4.50 mmol) in the presence of molecular sieves (4 Å, 600 mg) in toluene (5 mL) as described in procedure D. The solution was heated at 110 °C for 4 d. As the conversion, as determined by GC, was still incomplete, the mixture was heated at 140 °C for 1 d, after which the conversion remained still incomplete (43%). After the mixture had cooled to room temperature, THF (5 mL) was added, the reaction mixture was filtered, and the remaining residue was washed with CH_2Cl_2 (3 × 5 mL). The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 65:35) and was subsequently recrystallized to afford compound **11b** as a light yellow solid (238 mg, 0.63 mmol, 21%). M.p. 101 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.72–8.69 (m, 1H), 8.57 (dd, J = 4.9, 1.8 Hz, 1H), 8.48 (d, J = 1.8 Hz, 1H), 8.35 (d, J = 1.8 Hz, 1H), 7.87–7.82 (m, 1H), 7.33 (dd, J = 8.0, 4.9 Hz, 1H), 7.20 (d, J = 16.8 Hz, 1H), 6.75 (d, J = 16.8 Hz, 1H), 4.44 (q, J = 7.1 Hz, 2H), 1.43 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 163.1, 150.2, 150.0, 148.9, 137.0, 135.9, 133.6, 133.3, 131.4, 125.5, 124.2, 123.8, 123.7, 62.3, 14.2 ppm; IR (KBr): $\tilde{\nu}$ = 3410 (w), 3080 (m), 2998 (m), 1729 (s), 1608 (m), 1533 (vs), 1480 (m), 1465 (m), 1384 (m), 1364 (s), 1274 (s), 1206 (m), 1152 (s), 1023 (m), 906 (m), 870 (m), 854 (m), 770 (m), 748 (m), 729 cm^{-1} (m); MS (EI): m/z (%): 378/376 $[M]^+$ (8/8), 361/359 (67/68), 333/331 (64/65), 305/303 (28/27), 271/269 (81/81), 260 (27), 256/254 (26/23), 243/241 (64/65), 226/224 (41/38), 216/214 (70/73), 199/197 (52/54), 178 (70), 177 (55), 166 (35), 151 (66), 150 (78), 139 (28), 125 (18), 106 (74), 92 (100), 78 (53), 75 (42), 63 (19), 51 (15); HRMS (EI) calcd for $C_{18}H_{13}BrN_2O_5$: 376.0059; found: 376.0068 $[M]^+$.

Ethyl 3-bromo-5-nitro-4-[(*E*)-2-phenylethenyl]benzoate (11c): Compound **13a** (720 mg, 2.50 mmol) was treated with benzaldehyde (795 mg, 7.50 mmol) and piperidine (319 mg, 3.75 mmol) in the presence of molecular sieves (4 Å, 600 mg) in toluene (5 mL) at 80 °C for 4 d as described in procedure D. After the mixture had cooled to room temperature, THF (5 mL) was added, the reaction mixture was filtered, and the remaining residue was washed with CH_2Cl_2 (3 × 5 mL). The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 96:4), which afforded compound **11c** as a yellow solid (629 mg, 1.67 mmol, 67%). M.p. 124 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.46 (d, J = 1.8 Hz, 1H), 8.30 (d, J = 1.8 Hz, 1H), 7.54–7.48 (m, 2H), 7.43–7.31 (m, 3H), 7.13 (d, J = 16.4 Hz, 1H), 6.78 (d, J = 16.4 Hz, 1H), 4.44 (q, J = 7.1 Hz, 2H), 1.43 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 163.3, 150.3, 137.4, 136.7, 136.4, 135.6, 130.8, 129.2, 128.8, 127.1, 125.5, 123.6, 121.9, 62.2, 14.2 ppm; IR (KBr): $\tilde{\nu}$ = 3428 (w), 3080 (w), 1721 (s), 1539 (m), 1366 (m), 1279 (m), 1257 (m), 1149 (m), 1024 (w), 974 (w), 758 (m), 727 (w), 694 cm^{-1} (w); MS (EI): m/z (%): 377/375 $[M]^+$ (5/5), 360/358 (43/43), 332/330 (51/51), 304/302 (28/28), 271/269 (42/42), 243/241 (39/39), 226 (20), 224 (27), 216/214 (38/41), 199/197 (27/28), 177 (40), 176 (100), 165 (38), 163 (21), 151 (33), 134 (10), 105 (33), 91 (69), 88 (38), 77 (31); HRMS (EI) calcd for $C_{17}H_{14}BrNO_4$: 375.0106; found: 375.0092 $[M]^+$.

Ethyl 4-[(*E*)-2-(4-methoxyphenyl)ethenyl]-3,5-dinitrobenzoate (11d): Compound **13b** (2.54 g, 10.0 mmol) was treated with 4-methoxybenzaldehyde (4.08 g, 30.0 mmol) and piperidine (1.28 g, 15.0 mmol) in the presence of molecular sieves (4 Å, 2.00 g) in toluene (25 mL) at 80 °C for 1 d as described in procedure D. After the mixture had cooled to room temperature, THF (25 mL) was added, the reaction mixture was filtered, and the remaining residue was washed with CH_2Cl_2 (3 × 25 mL). The filtrate was concentrated in vacuo and the crude product was purified by flash chromatography (silica gel, pentane/ethyl acetate 95:5) to afford compound **11d** as a yellow solid (2.19 g, 5.89 mmol, 59%). M.p. 108 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.59 (s, 2H), 7.41 (dm, J = 8.8 Hz, 2H), 7.17 (d, J = 16.8 Hz, 1H), 6.90 (d, J = 8.8 Hz, 2H), 6.67 (d, J = 16.8 Hz, 1H), 4.47 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 1.44 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 162.5, 160.9, 150.2, 137.6, 131.7, 130.7, 128.9, 128.1, 127.7, 114.7, 114.3, 62.7, 55.34, 14.2 ppm; IR (KBr): $\tilde{\nu}$ = 3431 (w), 2977 (w), 1715 (s), 1604 (s), 1539 (s),1515 (s), 1460 (m), 1425 (w), 1353 (m), 1286 (s), 1255 (s), 1179 (s), 1033 (m), 978 (m), 918 (w), 834 (m), 768 (w), 749 (m), 723 (m), 540 cm^{-1} (w); MS (EI): m/z (%): 372 $[M]^+$ (9), 163 (15), 152 (10), 137 (27), 136 (75), 135 (100), 121 (17); HRMS (EI) calcd for $C_{18}H_{16}N_2O_7$: 372.0958; found: 372.0915 $[M]^+$; elemental analysis calcd (%) for $C_{18}H_{16}N_2O_7$ (372.34): C 58.06, H 4.33, N 7.52; found: C 58.05, H 4.54, N 7.56.

1,3-Dinitro-2-[(*E*)-2-phenylethenyl]benzene (11e):[10a,10e] Compound **13c** (1.82 g, 10.0 mmol) with benzaldehyde (3.18 g, 30.0 mmol) and piperidine (1.28 g, 15.0 mmol) in the presence of molecular sieves (4 Å, 2.00 g) at 110 °C for 4 d was treated as described in procedure D. After the mixture had cooled to room temperature, THF (25 mL) was added, the reaction mixture was filtered, and the remaining residue was washed with CH_2Cl_2 (3 × 25 mL). The filtrate was concentrated in vacuo and the crude product was purified by flash chromatography (silica gel, pentane/ethyl acetate 95:5) to afford compound **11e** as a yellow solid (540 mg, 2.0 mmol, 20%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.99 (d, J = 7.8 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.45–7.40 (m, 2H), 7.37–7.28 (m, 4H), 6.58 ppm (d, J = 16.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 150.3, 135.9, 135.5, 129.0, 128.7, 128.5, 128.1, 127.3, 127.0, 118.3 ppm.

Typical procedure E: ***N,N*-Dimethyl-4-iodo-6-(trifluoromethyl)-1*H*-benzimidazole-2-amine (7a)**: Compound **6a** (387 mg, 1.0 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (1.20 g, 25% in THF, 2.2 mmol). After 15 min the reaction was quenched by the addition of methanol (0.5 mL), and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 50:50). Compound **7a** was isolated as a white solid (266 mg, 0.75 mmol, 75%). M.p. 226 °C; ^{1}H NMR ($CDCl_3$/[D$_6$]DMSO, 300 MHz): δ = 9.60 (br s, 1H), 7.54 (s, 1H), 7.28 (s, 1H), 3.10 ppm (s, 6H); ^{13}C NMR ($CDCl_3$/[D$_6$]DMSO, 75 MHz): δ = 157.6, 146.2, 134.5, 126.1 (q, J = 3.9 Hz), 125.8, 122.5, 122.1, 106.9, 38.1 ppm; IR (KBr): $\tilde{\nu}$ = 3435 (w), 2933 (m), 1637 (s), 1606 (s), 1570 (m), 1433 (s), 1370 (m), 1317 (vs), 1269 (m), 1238 (m), 1189 (m), 1153 (s), 1118 (s), 1074 (m), 963 (w), 924 (m), 863 (m), 758 (w), 687 (m), 664 (w), 452 cm^{-1} (w); MS (EI): m/z (%): 355 $[M]^+$ (100), 340 (62), 326 (49), 213 (22), 186 (15); elemental analysis calcd (%) for $C_{10}H_9F_3IN_3$ (355.10): C 33.82, H 2.55, N 35.74; found: C 33.85, H 2.61, N 35.81.

Ethyl 2-(dimethylamino)-4-iodo-1*H*-benzimidazole-6-carboxylate (7b): Compound **6b** (391 mg, 1.0 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (1.20 g, 25% in THF, 2.2 mmol) for 15 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 50:50). Compound **7b** was isolated as a white solid (285 mg, 0.79 mmol, 79%). M.p. 250–251 °C; ^{1}H NMR ($CDCl_3$/[D$_6$]DMSO, 300 MHz): δ = 7.87 (d, J = 1.5 Hz, 1H), 7.55 (d, J = 1.5 Hz, 1H), 4.09 (q, J = 7.2 Hz, 2H), 2.94 (s, 6H), 1.14 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$/[D$_6$]DMSO, 75 MHz): δ = 165.6, 157.6, 148.2, 133.1, 130.9, 121.7, 110.2, 59.9, 37.6, 13.8 ppm; IR (KBr): $\tilde{\nu}$ = 3429 (m), 2930 (w), 1687 (m), 1636 (s), 1601 (s), 1558 (m), 1432 (m), 1368 (m), 1293 (s), 1228 (m), 1181 (m), 1096 (w), 1020 (w), 925 (w), 862 (w), 767 cm^{-1} (w); MS (EI): m/z (%): 359 $[M]^+$ (100), 344 (22), 330 (29), 316 (25), 302 (17), 286 (11), 144 (8); HRMS (EI) calcd for $C_{12}H_{14}IN_3O_2$: 359.0131; found: 359.0138 $[M]^+$; elemental analysis calcd (%) for $C_{12}H_{14}IN_3O_2$ (359.16): C 40.13, H 3.93, N 35.33; found: C 40.06, H 3.81, N 35.46.

2-(Dimethylamino)-4-iodo-1*H*-benzimidazole-6-carbonitrile (7c): Compound **6c** (344 mg, 1.0 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (1.20 g, 25% in THF, 2.2 mmol) for 15 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 50:50). Compound **7c** was isolated as a white solid (151 mg, 0.48 mmol, 48%). M.p. 261 °C; ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 7.91 (d, J = 1.5 Hz, 1H), 7.61 (d, J = 1.5 Hz, 1H), 3.13 ppm (s, 6H); ^{13}C NMR ([D$_6$]DMSO, 300 MHz): δ = 156.9, 146.1, 134.7, 130.7, 120.3, 118.6, 104.0, 95.7, 37.6 ppm; IR (KBr): $\tilde{\nu}$ = 3435 (m), 2924 (w), 2229 (m), 1642 (s), 1592 (vs), 1544 (s), 1481 (w), 1423 (m), 1376 (s), 1197 (w), 1114 (m), 832 (w), 781 cm^{-1} (w); MS (EI): m/z (%): 312 $[M]^+$ (100), 297 (63), 283 (54), 170 (20), 143 (14); HRMS (EI) calcd $C_{10}H_9IN_4$ 311.9872; found: 311.9881 $[M]^+$; elemental analysis calcd

(%) for $C_{10}H_9IN_4$ (312.11): C 38.48, H 2.91, N 17.95; found: C 38.30, H 2.75, N 18.10.

***N*-(6-Chloro-4-iodo-1*H*-benzimidazol-2-yl)-*N*,*N*-dimethylamine (7d)**: Compound **6d** (354 mg, 1.0 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (1.20 g, 25% in THF, 2.2 mmol) for 15 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 50:50). Compound **7d** was isolated as a light brownish solid (197 mg, 0.61 mmol, 61%). M.p. 228–229 °C; ^{1}H NMR ([D$_6$]DMSO, 600 MHz): $\delta = 7.29$ (d, $J = 1.8$ Hz, 1H), 7.13 (d, $J = 1.8$ Hz, 1H), 3.07 ppm (s, 6H); ^{13}C NMR ([D$_6$]DMSO, 150 MHz): $\delta = 157.0$, 144.8, 133.3, 127.6, 122.5, 108.3, 80.7, 37.7 ppm; IR (KBr): $\tilde{\nu} =$ 3435(m), 1630(s), 1593(s), 1565(m), 1430(s), 1315(m), 1266(m), 1180(w), 923(m), 838(w), 744 cm^{-1} (w); MS (EI): *m*/*z* (%): 323/321 $[M]^+$ (32/100), 308/306 (17/53), 294/292 (19/58), 179 (13), 152 (12); HRMS (EI) calcd for $C_9H_9ICIN_3$: 320.9530; found: 320.9507 $[M]^+$; elemental analysis calcd (%) for $C_9H_9ICIN_3$ (321.55): C 33.62, H 2.82, N 13.07; found: C 33.54, H 2.70, N 13.21.

4,6-Dibromo-*N*,*N*-dimethyl-1*H*-benzimidazole-2-amine (7e): Compound **6e** (349 mg, 1.0 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (1.20 g, 25% in THF, 2.2 mmol) for 15 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 50:50). Compound **7e** was isolated as a light brownish solid (223 mg, 0.70 mmol, 70%). M.p. 214 °C; ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO, 300 MHz): $\delta = 10.40$ (br s, 1H), 7.16 (s, 2H), 3.07 ppm (s, 6H); ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO, 75 MHz): $\delta = 157.1$, 143.5, 134.4, 127.6, 124.3, 120.7, 110.9, 38.0 ppm; IR (KBr): $\tilde{\nu} = 3434$(m), 1630(m), 1597(m), 1434(m), 1317(w), 1267(w), 922 cm^{-1} (w); MS (EI): *m*/*z* (%): 321/319/317 $[M]^+$ (50/100/52), 306/304/302 (39/80/41), 292/290/280 (41/85/41), 278/276/274 (10/20/10), 223 (10), 196 (19), 144 (9); HRMS (EI) calcd for $C_9H_9Br_2N_3$: 316.9163; found: 316.9166 $[M]^+$; elemental analysis calcd (%) for $C_9H_9Br_2N_3$ (319.00): C 33.89, H 2.84, N 13.17; found: C 33.63, H 2.70, N 13.28.

***N*,*N*-Dimethyl-*N*-(4-nitro-1*H*-benzimidazole-2-yl)amine (7f)**: Compound **6f** (239 mg, 1.0 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (1.20 g, 25% in THF, 2.2 mmol) for 15 min. After workup, the crude product was purified by flash column chromatography (silica gel, ethyl acetate/methanol 90:10). Compound **7f** was isolated as a red/orange solid (129 mg, 0.62 mmol, 62%). M.p. 168–170 °C; ^{1}H NMR (CDCl$_3$, 300 MHz): $\delta = 10.13$ (br s, 1H), 7.68 (d, $J = 8.4$ Hz, 1H), 7.55–7.48 (m, 1H), 7.06–6.98 (m, 1H), 3.16 ppm (s, 6H); ^{13}C NMR (CDCl$_3$, 75 MHz): $\delta = 157.1$, 146.3, 128.9, 121.1, 120.2, 113.7, 37.9 ppm; IR (KBr): $\tilde{\nu} = 3398$(m), 1648(s), 1610(s), 1583(m), 1512(m), 1433(m), 1334(m), 1297(m), 1247(m), 924(m), 809(w), 738(m), 560 cm^{-1} (w); MS (EI): *m*/*z* (%): 206 $[M]^+$ (100), 191 (39), 189 (30), 177 (33), 159 (71), 144 (24), 130 (14), 119 (12); HRMS (EI) calcd for $C_9H_{10}N_4O_2$: 206.0804; found: 206.0811 $[M]^+$.

6-(4-Methoxyphenyl)-*N*,*N*-dimethyl-4-nitro-1*H*-benzimidazol-2-ylamine (7g): Compound **6g** (172 mg, 0.5 mmol) in THF (1 mL) was treated at −40 °C with PhMgCl (0.60 g, 25% in THF, 1.1 mmol) for 15 min. After workup, the crude product was purified by flash column chromatography (silica gel, ethyl acetate). Compound **7g** was isolated as a red/orange solid (137 mg, 0.44 mmol, 87%). M.p. 179–180 °C; ^{1}H NMR (CDCl$_3$, 300 MHz): $\delta = 7.99$ (s, 1H), 7.75 (s, 1H), 7.60 (d, $J = 8.7$ Hz, 2H), 7.04 (d, $J = 8.7$ Hz, 2H), 3.87 (s, 3H), 3.27 ppm (s, 6H); ^{13}C NMR (CDCl$_3$, 75 MHz): $\delta = 161.1$, 156.1, 146.3, 141.0, 139.9, 139.0, 136.1, 129.8, 120.2, 112.4, 110.8, 55.3, 37.8 ppm; IR (KBr): $\tilde{\nu} = 3400$(m), 2934(m), 1651(m), 1610(s), 1513(s), 1430(m), 1304(m), 1246(s), 1179(m), 1037(m), 922(m), 830(m), 762(w), 558 cm^{-1} (m); MS (EI): *m*/*z* (%): 312 $[M]^+$ (100), 297 (29), 283 (20), 265 (19), 250 (25), 207 (81); HRMS (EI) calcd for $C_{16}H_{16}N_4O_3$: 312.1222; found: 312.1235 $[M]^+$.

Ethyl 2-(dimethylamino)-4-[4-(ethoxycarbonyl)phenyl]-1*H*-benzimidazole-6-carboxylate (7i): Compound **6i** (207 mg, 0.5 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (617 mg, 25% in THF, 1.1 mmol). After 30 min the reaction mixture was quenched by the addition of methanol (0.5 mL), poured into water, and extracted with ethyl acetate (4 × 20 mL). The combined organics were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 75:25). Compound **7i** was isolated as a white solid (107 mg, 0.28 mmol, 56%). M.p. 223–224 °C; ^{1}H NMR ([D$_6$]DMSO, 300 MHz): $\delta =$ 8.27 (d, $J = 8.1$ Hz, 2H), 8.04 (d, $J = 8.1$ Hz, 2H), 7.96 (d, $J = 1.3$ Hz, 1H), 7.75 (d, $J = 1.3$ Hz, 1H), 4.34 (q, $J = 7.2$ Hz, 2H), 4.32 (q, $J = 7.2$ Hz, 2H), 3.14 (s, 6H), 1.35 (t, $J = 7.2$ Hz, 3H), 1.34 ppm (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ([D$_6$]DMSO, 75 MHz): $\delta = 166.3$, 165.6, 158.9, 142.8, 136.6, 129.0, 128.2, 127.8, 123.5, 121.1, 109.3, 60.6, 60.2, 37.6, 14.2, 14.1 ppm; IR (KBr): $\tilde{\nu} =$ 3432(m), 1840(w), 1709(m), 1663(w), 1608(s), 1505(w), 1394(m), 1378(m), 1367(m), 1352(w), 1322(m), 1306(w), 1248(m), 1162(w), 1104(m), 1053(w), 1022(w), 957(w), 926(w), 910(w), 765 cm^{-1} (w); MS (EI): *m*/*z* (%): 381 $[M]^+$ (100), 367 (20), 352 (28), 336 (14), 324 (11), 308 (7), 265 (5), 192 (4); HRMS (EI) calcd for $C_{21}H_{23}N_3O_4$: 381.1689; found: 381.1657 $[M]^+$.

Ethyl 4-[2-(dimethylamino)-6-(trifluoromethyl)-1*H*-benzimidazol-4-yl]-benzoate (7j): Compound **6j** (205 mg, 0.5 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (602 mg, 25% in THF, 1.1 mmol). After 30 min the reaction mixture was quenched by the addition of methanol (0.5 mL), poured into water, and extracted with ethyl acetate (4 × 20 mL). The combined organics were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel, pentane/ethyl acetate 85:15). Compound **7j** was isolated as a white solid (145 mg, 0.38 mmol, 77%). M.p. 191 °C; ^{1}H NMR (CDCl$_3$, 300 MHz): $\delta = 8.03$ (d, $J = 8.4$ Hz, 2H), 7.84 (d, $J = 8.4$ Hz, 2H), 7.47 (s, 1H), 7.40 (s, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 3.17 (s, 6H), 1.41 ppm (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz): $\delta = 166.5$, 157.6, 142.5, 129.9, 129.2, 128.3, 126.8, 124.5, 123.2, 117.3, (q, $J =$ 32.5 Hz), 108.9, 61.1, 38.3, 14.3 ppm; IR (KBr): $\tilde{\nu} = 3350$(m), 2983(m), 1698(s), 1638(s), 1609(s), 1581(s), 1421(s), 1395(s), 1368(m), 1335(s), 1263(s), 1237(s), 1165(s), 1109(s), 1022(m), 969(w), 926(m), 857(m), 783(m), 707(m), 620 cm^{-1} (w); MS (EI): *m*/*z* (%): 377 $[M]^+$ (100), 362 (28), 348 (33), 334 (15), 332 (13), 320 (13), 158 (10); HRMS (EI) calcd for $C_{19}H_{18}F_3N_3O_2$: 377.1351; found: 377.1359 $[M]^+$.

4,6-Dibromo-2-phenyl-1*H*-benzimidazole (7l): Compound **6m** (384 mg, 1.0 mmol) in THF (2 mL) was treated at −40 °C with PhMgCl (1.22 g, 25% in THF, 2.2 mmol). After 30 min the reaction mixture was quenched by the addition of methanol (0.5 mL) and poured into water (15 mL), and saturated NH_4Cl solution (15 mL) was added. The mixture was extracted with ethyl acetate (4 × 30 mL). The combined organics were washed with brine (30 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was transferred onto silica gel and purified by flash column chromatography (silica gel, pentane/ethyl acetate 90:10). Compound **7l** was isolated as a light brownish solid (271 mg, 0.77 mmol, 77%). M.p. 177–178 °C; ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO, 300 MHz): $\delta = 8.19–8.15$ (m, 2H), 7.51 (d, $J = 1.9$ Hz, 1H), 7.42 (d, $J = 1.3$ Hz, 1H), 7.37–7.35 ppm (m, 3H); ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO, 75 MHz): $\delta = 149.0$, 134.6, 130.2, 128.7, 128.2, 127.6, 127.5, 115.3, 113.4, 111.4 ppm; IR (KBr): $\tilde{\nu} = 3432$(m), 1618(m), 1570(m), 1447(m), 1397(m), 1286(m), 946(m), 842(m), 751(m), 691(m), 583 cm^{-1} (m); MS (EI): *m*/*z* (%): 354/352/350 $[M]^+$ (50/100/51), 192 (19); HRMS (EI) calcd for $C_{13}H_8Br_2N_2$: 349.9054; found: 349.8982 $[M]^+$.

Ethyl 4-bromo-2-(4-methoxyphenyl)-1*H*-indole-6-carboxylate (10a): Compound **11a** (406 mg, 1.0 mmol) in THF (1 mL) was treated at −40 °C with PhMgCl (1.9 M in THF, 1.1 mL, 2.1 mmol) for 30 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (pentane/ethyl acetate 80:20 to 50:50). Compound **10a** was isolated as a yellow solid (285 mg, 0.76 mmol, 76%). M.p. 230 °C; ^{1}H NMR ([D$_5$]pyridine, 300 MHz,): $\delta = 8.30$ (s, 2H), 8.01 (d, $J = 8.8$ Hz, 2H), 7.18–7.16 (m, 1H), 7.10 (d, $J = 8.8$ Hz, 2H), 4.33 (q, $J = 7.1$ Hz, 2H), 3.70 (s, 3H), 1.22 ppm (t, $J = 7.1$ Hz, 3H); ^{13}C NMR ([D$_5$]pyridine, 75 MHz): $\delta = 166.5$, 160.6, 143.7, 137.4, 134.1, 127.9, 124.8, 124.7, 123.7, 115.0, 113.6, 113.0, 99.3, 61.0, 55.3, 14.4 ppm; IR (KBr): $\tilde{\nu} = 3346$(s), 2985(w), 2837(w), 1690(s), 1610(s), 1566(m), 1543(m), 1495(s), 1440(m), 1368(m), 1311(s), 1254(s), 1228(s), 1180(s), 1096(w), 1026(m), 980(w), 878(w), 832(m), 794(m), 766(m), 598 cm^{-1} (m); MS (EI): *m*/*z* (%): 375/373 (100/97), 347/345 (37/35), 330 (42), 302 (17), 221(8), 206 (12); HRMS (EI) calcd for $C_{18}H_{16}BrNO_3$: 373.0314; found: 373.0292 $[M]^+$; elemental analysis calcd (%) for $C_{18}H_{16}BrNO_3$ (374.23): C 57.77, H 4.31, N 3.74; found: C: 57.74, H 4.28, N 3.72.

Ethyl 4-bromo-2-(3-pyridinyl)-1*H*-indole-6-carboxylate (10b): Compound **11b** (195 mg, 0.52 mmol) in THF (1 mL) was treated at −40 °C with PhMgCl (1.9 M in THF, 0.77 mL, 1.47 mmol) for 30 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (pentane/ethyl acetate 80:20 to 50:50). Compound **10b** was isolated as a yellow solid (124 mg, 0.36 mmol, 70%). M.p. 264 °C;

^{1}H NMR ([D$_5$]pyridine, 300 MHz): $\delta = 13.03$ (br s, 1H), 9.35 (s, 1H), 8.68–8.62 (m, 1H), 8.27–8.21 (m, 2H), 8.20–8.14 (m, 1H), 7.34–7.26 (m, 1H), 7.15 (s, 1H), 4.34 (q, $J = 7.1$ Hz, 2H), 1.24 ppm (t, $J = 7.1$ Hz, 3H); ^{13}C NMR ([D$_5$]pyridine, 75 MHz): $\delta = 166.4$, 148.1, 140.4, 138.0, 133.8, 133.4, 128.4, 126.3, 124.1, 114.4, 113.5, 101.7, 89.2, 61.2, 14.5 ppm; IR (KBr): $\tilde{\nu} = 3350$ (w), 2984 (w), 1701 (m), 1567 (w), 1366 (w), 1315 (m), 1279 (w), 1230 (m), 1094 (w), 1024 (w), 790 (w), 764 cm^{-1} (w); MS (EI): m/z (%): 346/344 (99/100), 318/316 (30/32), 301/299 (46/44), 273/271 (14/15), 192 (31), 164 (8); HRMS (EI) calcd for $C_{16}H_{13}BrN_2O_3$: 344.0160; found: 344.0151 $[M]^+$.

Ethyl 4-bromo-2-phenyl-1*H*-indole-6-carboxylate (10c): Compound **11c** (282 mg, 0.75 mmol) in THF (1 mL) was treated at $-40\,^\circ$C with PhMgCl (1.9 M in THF, 1.21 mL, 1.58 mmol) for 30 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (pentane/ethyl acetate 90:10 to 75:25). Compound **10c** was isolated as a yellow solid (194 mg, 0.57 mmol, 75%). M.p. 216 °C; ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO, 300 MHz): $\delta = 11.39$ (br s, 1H), 7.76–7.73 (m, 1H), 7.52–7.45 (m, 3H), 7.09 (t m, $J = 7.4$ Hz, 2H), 6.99 (t m, $J = 7.4$ Hz, 1H), 6.48–6.45 (m, 1H), 4.00 (q, $J = 7.4$ Hz, 2H), 1.05 ppm (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO, 75 MHz): $\delta = 165.4$, 141.3, 135.7, 132.0, 130.5, 128.0, 127.6, 124.9, 123.3, 122.1, 112.2, 112.1, 98.3, 59.9, 13.5 ppm; IR (KBr): $\tilde{\nu} =$ 3328 (m), 2977 (w), 1692 (m), 1618 (w), 1566 (w), 1487 (w), 1367 (m), 1316 (m), 1276 (m), 1231 (s), 1177 (w), 1027 (w), 877 (w), 762 (m), 734 (w), 691 cm^{-1} (w); MS (EI): m/z (%): 345/343 (97/100), 317/315 (38/40), 300/298 (44/46), 272/270 (16/14), 207 (25), 192 (10), 191 (41), 190 (38), 177 (36), 163 (16), 96 (10); HRMS (EI) calcd for $C_{17}H_{14}NO_2$: 343.0208; found: 343.0180 $[M]^+$; elemental analysis calcd (%) for $C_{17}H_{14}NO_2$ (264.31): C 59.32, H 4.10, N 4.07; found: C 59.61, H 4.21, N 4.05.

Ethyl 2-(4-methoxyphenyl)-4-nitro-1*H*-indole-6-carboxylate (10d): Compound **11d** (372 mg, 1.0 mmol) in THF (2 mL) was treated at $-40\,^\circ$C with PhMgCl (1.9 M in THF, 1.11 mL, 2.1 mmol) for 30 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (pentane/ethyl acetate 75:25). Compound **10d** was isolated as a yellow solid (190 mg, 0.56 mmol, 56%). M.p. 245–246 °C; ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO, 300 MHz): $\delta = 11.73$ (br s, 1H), 8.65 (s, 1H), 8.28–8.22 (m, 1H), 7.77–7.71 (m, 2H), 7.40–7.34 (m, 1H), 6.94–6.86 (m, 2H), 4.34 (q, $J = 7.1$ Hz, 2H), 3.84 (s, 3H), 1.24 ppm (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO, 75 MHz): $\delta = 165.6$, 160.5, 146.2, 138.8, 138.2, 131.5, 127.5, 126.1, 123.0, 121.5, 118.4, 114.1, 98.6, 60.8, 55.0, 14.0 ppm; IR (KBr): $\tilde{\nu} = 3351$ (m), 2982 (w), 1712 (m), 1688 (s), 1630 (m), 1609 (s), 1501 (s), 1484 (s), 1369 (m), 1332 (s), 1256 (vs), 1182 (s), 1028 (m), 835 (w), 798 cm^{-1} (w); MS (EI): m/z (%): 340 (3), 322 (100), 250 (18), 236 (8); HRMS (EI) calcd for $C_{18}H_{16}N_2O_5$: 340.1059; found: 340.1072 $[M]^+$; elemental analysis calcd (%) for $C_{18}H_{16}N_2O_5$ (340.33): C 63.52, H 4.74, N 8.23; found: C 63.41, H 4.64, N 8.31.

4-Nitro-2-phenyl-1*H*-indole (10e):[10a] Compound **11e** (242 mg, 0.9 mmol) in THF (2 mL) was treated at $-40\,^\circ$C with PhMgCl (1.9 M in THF, 1.0 mL, 1.9 mmol) for 30 min as described in procedure E. After workup, the crude product was purified by flash column chromatography (pentane/ethyl acetate 80:20). Compound **10e** was isolated as an orange solid (129 mg, 0.54 mmol, 60%); ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO, 300 MHz): $\delta = 11.59$ (br s, 1H), 8.00 (d, $J = 8.1$ Hz, 1H), 7.84–7.80 (m, 2H), 7.69 (d, $J = 8.4$ Hz, 1H), 7.48–7.37 (m, 3H), 7.34–7.27 (m, 1H), 7.12 ppm (t, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO, 75 MHz): $\delta = 142.4$, 139.1, 138.9, 130.8, 128.3, 128.0, 125.3, 122.6, 119.5, 117.6, 116.7, 98.6 ppm.

9*H*-Carbazole (15):[15] 2-Nitrobiphenyl **14** (199 mg, 1.0 mmol) was treated with phenylmagnesium chloride (0.67 M in THF, 3.15 mL, 2.1 mmol) as described in procedure E. The reaction mixture was quenched by the addition of methanol (0.5 mL). The solvent was removed, and the residue was dissolved in ethyl acetate and poured into saturated NH_4Cl solution (25 mL). Water (25 mL) was added, and the aqueous layer was extracted with ethyl acetate (2×50 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (pentane/diethyl ether = 85:15). Compound **15** was isolated as a white, crystalline solid (41 mg, 0.24 mmol, 24%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.12$ (d, $J =$ 7.7 Hz, 2H), 7.51 (d, $J = 8.0$ Hz, 2H), 7.39 (dd, $J = 8.0$, 7.2 Hz, 2H), 7.20 ppm (dd, $J = 7.7$, 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 139.6$, 125.2, 122.8, 120.1, 118.6, 110.9 ppm.

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