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Synthesis of fused indoles by sequential palladium-catalyzed Heck reaction and *N*-heteroannulation

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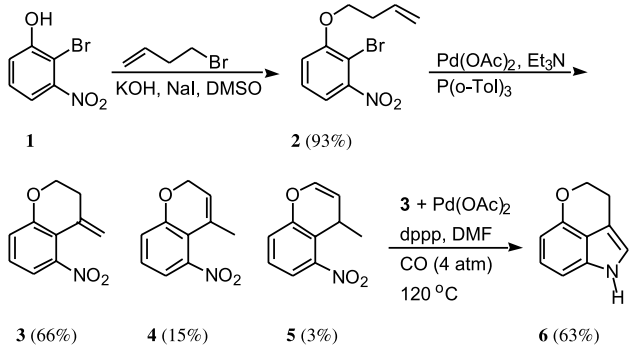
Abstract—A route to 3,4-fused indoles via two consecutive palladium-catalyzed reactions; an intramolecular Heck reaction followed by a reductive *N*-heteroannulation is described. Using this route, a number of indoles have been prepared having a variety of ring sizes anchored to the 3- and 4-position of the indole nucleus. Furthermore, a number of functional groups, both carbon and heteroatom substituents can be introduced in (and on) the additional ring without any detrimental effects on the two reactions.

1. Introduction

The palladium-catalyzed reductive *N*-heteroannulation of 2-(1-alkenyl)nitrobenzenes have been utilized to prepare indoles and carbazoles,[1–7] 2,2′-biindoles,[8] 1*H*-indol-2-yl-1*H*-quinolinones,[9] β-carbolines,[10] and 1,2-dihydro-4(3*H*)-carbazolones.[11,12] We have communicated a novel route to 3,4-fused indoles consisting of two consecutive palladium-catalyzed reactions, an intramolecular Heck reaction followed by a reductive *N*-heteroannulation.[13] For example, compound **2**, prepared by *O*-alkylation of 2-bromo-3-hydroxy-1-nitrobenzene (**1**) with 1-bromo-3-butene, was reacted under standard Heck condition to give a mixture of three isomeric 5-nitro-1-benzopyrans (**3**–**5**) in an 18:4:1 ratio (Scheme 1). Reductive *N*-heteroannulation of **3** using 10 mol % palladium diacetate ($Pd(OAc)_2$), 20 mol % 1,3-bis(diphenylphosphino)propane (dppp) in DMF at 120 °C and 4 atm of carbon monoxide gave an acceptable 63% yield of the fused indole **6** after 70 h.



Scheme 1.

Based on the results shown in Scheme 1, a systematic survey of this reaction sequence to fused indoles was undertaken. The starting materials for the Heck reaction were prepared by benzylic nucleophilic substitution using 2-bromo-3-nitrobenzylbromide (**7**) and a variety of unsaturated alkoxides and phenoxides. Compounds **8**–**15**, prepared in this fashion were used directly in Heck reactions (Table 1). The benzylic bromide **7** was also reacted with allyl amine, allyl sulfide, and the anion of dimethyl malonate to give **16**–**18**, respectively (Scheme 2). Compound **16** was reacted with acetic anhydride to give the amide **20**, the allyl sulfide **17** was oxidized to the sulfoxide **20** using sodium periodate and to the sulfone **21** using a urea–hydrogen peroxide complex. Finally, the malonate adduct **18** was deprotonated and alkylated with allyl bromide to give **22**.

The allylic amide **23** was prepared from 2-bromo-3-nitrobenzoic acid (**24**) via the corresponding acid chloride (Scheme 3). Transformation of **24** to the isocyanate **25** using diphenylphosphoryl azide followed by reaction with sodium methoxide furnished the expected methyl carbamate (Scheme 3). Deprotonation and alkylation using 4-bromo-1-butene gave **26** albeit in low overall yield.

With a number of precursors in hand, the intramolecular Heck reaction was examined.[14] Facile Heck reaction was

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observed in most cases using palladium diacetate, tris-(*o*-tolyl)phosphine (TTP), in triethyl amine (TEA). In some cases, the cyclization afforded products derived from exo to endo double bond migration during the reaction (entries 1, 2, 9, 10, and 12, Table 1). The isomers were readily separated on silica gel and the exocyclic product was always the major isomer. Exclusive or highly selective formation of the exo isomer has been reported in related systems.[15,16] A vinyl-substituted cyclization product was exclusively obtained in one case (entry 3). This result can be explained mechanistically via insertion of the alkene into the oxidative addition intermediate **44** to give a new σ-palladium complex **45** having a *cis*-relationship between the palladium moiety and the newly formed carbon–carbon bond. β-Hydride elimination requires a *cis*-geometry between the metal and the proton. Due to the presence of the sterically demanding nitro group, rotation of the metal is slow compared to the competing β-hydride elimination toward the methyl group forming **31** (Scheme 4). For compounds with two potential directions for the β-hydride elimination, the vinyl-substituted product is usually the major or sole isomer formed.[14] A single stereoisomer was formed upon cyclization of **11** (entry 4). Although the alkene geometry of the product **32** is unknown, the depicted geometry is consistent with a *syn* alkene insertion, σ-bond rotation, and *syn* β-hydride elimination sequence. Trans substituted alkenes related to **11** have previously been shown to give products with the same stereochemistry.[14,17,18]

Non-regioselective Heck reactions forming products derived from insertion into the internal or terminal position of the alkene was observed using a longer tether between the bromide and the alkene (entries 7–8). Both 7-exo and 8-endo (entry 7)[19] and 8-exo and 9-endo (entry 8) cyclizations were observed. The isomers were in both cases inseparable and were used in the next step as a mixture. Compound **13** did not furnish either a 9- or 10-membered cyclization product but gave a complex mixture of unidentified products. Similar results have been reported by Ma and Negishi using 9-membered ring precursors.[20]

Attempted Heck reaction of allylic amine **16** did not produce the anticipated cyclization products but gave, in addition to recovered starting material, a complex mixture of unidentified products. Poor yields of products has previously been reported using *N*-allyl *N*-(2-halo)benzylamines in intramolecular Heck reactions.[21,22] It is not unlikely that the initial σ-complex, formed by oxidative addition of palladium(0) into the aryl-bromine bond in **16**, is coordinated to the pendant amine, forming a relatively stable complex.[23–26] This effectively removes palladium from the catalytic cycle, and the reaction is quenched. The amide **19**, having a substantially lower ability to coordinate to the metal, cyclized to form the expected products **38** and **39**. Finally, unsuccessful cyclizations were observed using sulfide **17**, sulfoxide **20**, and sulfone **21**. Intramolecular Heck reactions of allyl aryl sulfides have been reported. To our knowledge, no examples of allyl benzyl sulfides, sulfones, or sulfoxides have been reported in the literature.

Palladium-catalyzed *N*-heteroannulation of the Heck products having an exocyclic double bond was examined next. We initially studied the reductive *N*-heteroannulation of **3** using conditions previously employed for substituted styrenes. Thus, reaction of **3** with 6 mol % $Pd(OAc)_2$ and 24 mol % PPh_3 in acetonitrile at 70 °C and 3 atm of carbon monoxide for 19.5 h, gave the expected indole **6** in low isolated yield (11%) together with recovered starting material (51%). Reaction of **3** for 70 h at 100 °C, using the same solvent and catalyst system, improved the yield of product (**6**) to 37% but a significant amount of starting material still remained (32%). After some optimization, a catalyst system consisting of 10 mol % $Pd(OAc)_2$, 12 mol % of 1,3-bis(diphenylphosphino)propane in dimethylformamide at 4 atm of CO and 120 °C gave **6** in 63% yield. The last reaction proved to be very clean, and no other organic products was observed by ^1H NMR of the crude reaction mixture. It is interesting to note that no detectable amount (by ^1H NMR at 270 MHz) of isomerization to the endocyclic benzopyranes **4**–**5** was observed in the initial reactions wherein the starting material **3** was not completely consumed. We have recently shown that better yields are obtained in some cases using bis(dibenzylidenacetone)palladium in combination with 1,10-phenanthroline. The reason for the need for two ligands is not clear at this point in time. Most of the reactions presented in Table 1 utilize the latter catalyst system. For the methylene and benzylidene substituted substrates, *N*-heteroannulation to form a 3,4-fused indole was observed in moderate to good yields (33–83%) in all cases examined. Compound **31** did not afford any cyclized product under any of the cyclization conditions described above. Attempts to isomerize the double bond of **31** using basic (potassium *t*-butoxide or triethylamine) or acidic conditions (*p*-toluenesulfonic acids) were fruitless.

The mixtures of tricyclic compounds **34**:**35** and **36**:**37** were also subjected to the reductive *N*-heteroannulation reaction (entries 7–8, respectively). In both cases, a moderate amount of fused indoles was isolated derived from cyclization of the exocyclic isomer. Curiously, reduction of the nitro group to an amine was observed for the two endocyclic compounds **35** and **37**.[27]

In conclusion, a novel route to fused indoles has been developed based on two palladium-catalyzed reactions. This methodology has been used to prepare indoles having a 6–8-membered rings anchored to the 3- and 4-postion of the indole nucleus. Nitrogen- and oxygen-containing rings as well as an example of a carbocyclic ring have been prepared. Applications of this sequence in total synthesis are currently underway in our laboratories.

2. Experimental

2.1. General procedures

All NMR spectra were determined in $CDCl_3$ and the chemical shifts are expressed in δ values relative to Me_4Si (0.0 ppm, ^1H and ^{13}C) or $CDCl_3$ (77.0 ppm, ^{13}C) internal standards. ^1H–^1H coupling constants are reported as calculated from spectra; thus a slight difference between $J_{a,b}$ and $J_{b,a}$ is usually obtained. Results of APT (attached proton test)—^{13}C NMR experiments are shown in

Table 1. Intramolecular Heck reaction and *N*-heteroannulation

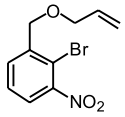
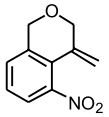
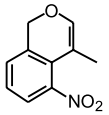
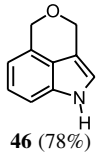
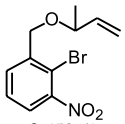
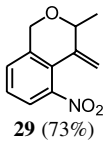
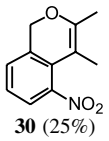
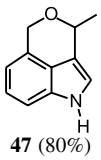
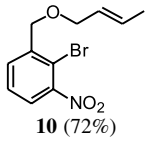
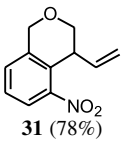
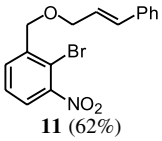
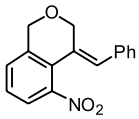
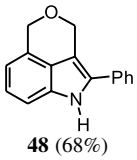
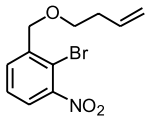
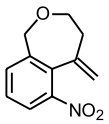
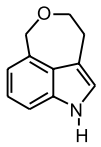
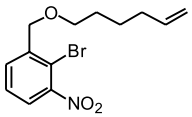
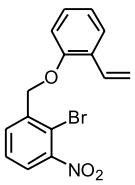
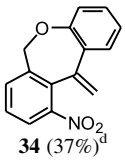
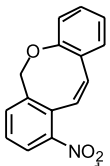
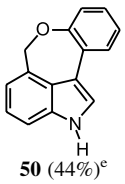
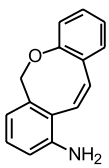
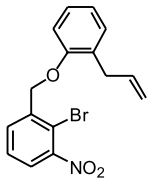
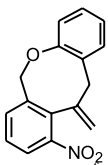
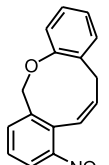
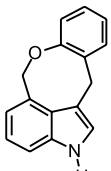
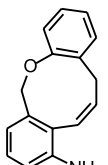
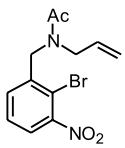
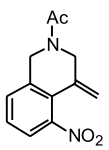
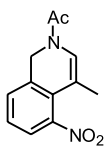
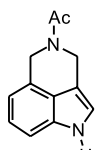
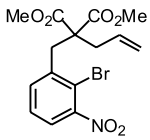
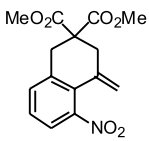
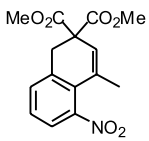
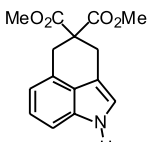
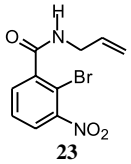
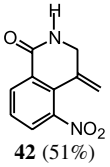
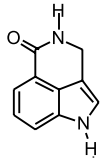
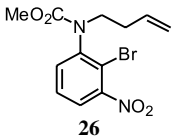
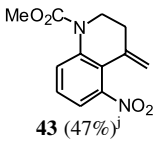
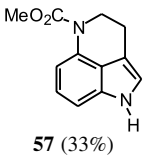
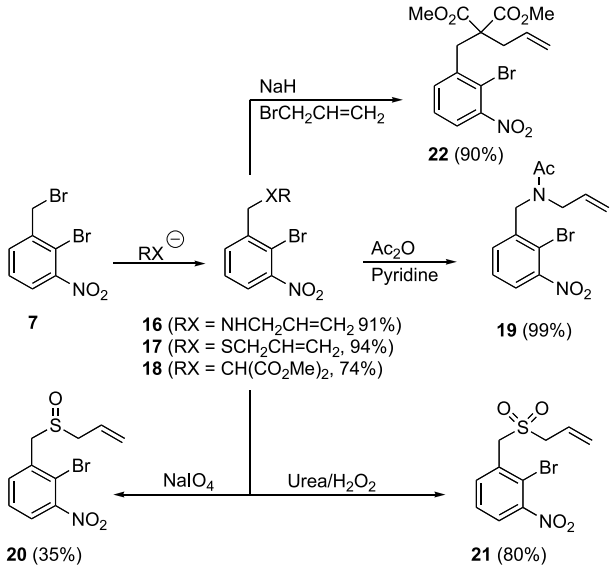
Entry	Bromoalkene[a,b]	Coupling product(s)[a,b]		Indole[a,b]	
1	 **8** (67%)	 **27** (76%)	 **28** (20%)	 **46** (78%)	
2	 **9** (50%)	 **29** (73%)	 **30** (25%)	 **47** (80%)	
3	 **10** (72%)	 **31** (78%)	Complex mixture of products		
4	 **11** (62%)	 **32** (82%)[c]		 **48** (68%)	
5	 **12** (67%)	 **33** (81%)		 **49** (83%)	
6	 **13** (46%)		Complex mixture of products		
7	 **14** (65%)	 **34** (37%)[d]	 **35** (60%)[d]	 **50** (44%)[e]	 **51** (64%)[e]
8	 **15** (91%)	 **36** (18%)[f]	 **37** (13%)[f]	 **52** (44%)[g]	 **53** (15%)[g,h]
9	 **19**	 **38** (69%)	 **39** (26%)	 **54** (41%)	
10	 **22**	 **40** (72%)	 **41** (14%)	 **55** (65%)	

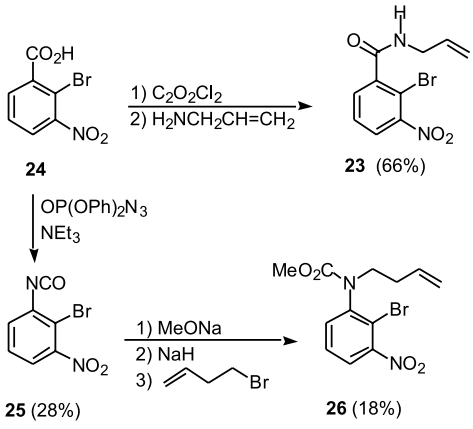
Table 1 (*continued*)

Entry	Bromoalkene[a,b]	Coupling product(s)[a,b]	Indole[a,b]
11	 **23**	 **42** (51%)	 **56** (61%)[i]
12	 **26**	 **43** (47%)[j]	 **57** (33%)

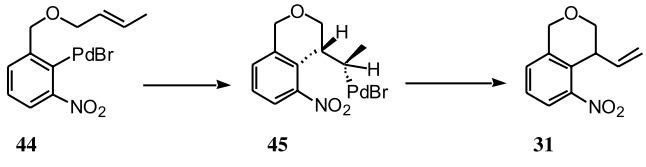
[a] See Section 2 for details.
[b] Isolated yield of pure compound given in parenthesis.
[c] Only one alkene isomer was obtained, however, the stereochemistry is not known.
[d] Calculated yield from an inseparable 1:1.6 mixture of **34** and **35**.
[e] Calculated yields starting from a mixture of **34** and **35**.
[f] Calculated yields from an inseparable 1.37:1 mixture of **36** and **37**.
[g] Calculated yields from a mixture of **36** and **37**.
[h] This product was tentatively assigned from a mixture of **52** and **53**.
[i] Minor amounts of impurity remained after extensive purification.
[j] Minor amount of products tentatively assigned as endocyclic isomers were also isolated.



Scheme 2.



Scheme 3.



Scheme 4.

parentheses, where relative to $CDCl_3$, (+) denotes CH_3 or CH and (−) denotes CH_2 or C.

Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl prior to use. Pyridine, hexanes, acetonitrile, and ethyl acetate were distilled from calcium hydride. Chemicals prepared according to literature procedures have been footnoted first time used; all other reagents were obtained from commercial sources and used as received. All reactions were performed under an argon atmosphere in oven-dried glassware unless otherwise stated. Solvents were removed from reaction mixtures and products on a rotary evaporator at water aspirator pressure. Elemental Analyses were performed by Atlantic Microlab, Inc., Norcross, GA. High Resolution Mass Spectra (HRMS) were performed at University of California Riverside Mass Spectrometry Center.

2.1.1. 2-Bromo-3-nitro-1-(3-butenyloxy)benzene (2). To a solution of 2-bromo-3-nitrophenol[28] (**1**) (1.09 g, 5.00 mmol) in DMSO (31 mL) was added KOH (3.00 g, 20.0 mmol). After 5 min of stirring, 4-bromo-1-butene (2.00 mL, 20.0 mmol) was added to the resulting red solution. After 43 h, water (150 mL) was added, and the

mixture was extracted with diethyl ether (4×150 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed. Purification by chromatography (hexanes/EtOAc, 9:1) gave **2** (1.27 g, 4.67 mmol, 93%) as a pale yellow oil that solidified upon storage in freezer (−20 °C). Mp 27–28 °C; ^{1}H NMR (270 MHz) δ 7.37 (t, J=8.1 Hz, 1H), 7.30 (dd, J=8.1, 1.6 Hz, 1H), 7.05 (dd, J=8.1, 1.6 Hz, 1H), 5.94 (tdd, J=17.0, 10.3, and 6.4 Hz, 1H), 5.21 (dd, J=17.0, 1.4 Hz, 1H), 5.15 (br d, J=10.3 Hz, 1H), 4.12 (t, J=6.5 Hz, 2H), 2.62 (q, J=6.7 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 156.3 (−), 151.4 (−), 133.4 (+), 128.5 (+), 117.4 (−), 116.1 (+), 115.4 (+), 104.3 (−), 69.0 (−), 33.0 (−); IR (neat) 3080, 2935, 1588, 1535, 1456, 1363, 1276, 1040 cm^{-1}; Anal. Calcd for $C_{10}H_{10}BrNO_3$: C, 44.14; H, 3.70. Found: C, 44.43; H, 3.73.

2.1.2. 2-Bromo-3-nitro-1-[(2-propen-1-yloxy)methyl]-benzene (8). In a conical vial was placed 2-propen-1-ol (210 μL, 3.09 mmol) and small pieces of sodium (52 mg, 2.24 mmol). After 3 h, the resulting alkoxide was added via pipette to a solution of 2-bromo-3-bromomethyl-1-nitro-benzene (**7**)[1] (300 mg, 1.02 mmol), tetrabutylammonium iodide (39 mg, 0.11 mmol) in THF (10 mL). The conical vial was rinsed with THF (9 mL total). The resulting mixture was stirred at ambient temperature (27 h), diluted with water (15 mL), and extracted with diethyl ether (3× 15 mL). The combined organic phases were dried ($MgSO_4$), and filtered, and the solvents were removed. Purification by chromatography (hexanes/EtOAc, 4:1) gave **8** (186 mg, 0.68 mmol, 68%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.75 (d, J=7.7 Hz, 1H), 7.64, (d, J=7.9 Hz, 1H), 7.47 (t, J=7.9 Hz, 1H), 5.99 (10 line pattern, J=17.2, 10.3, 5.3 Hz, 1H), 5.37 (dd, J=17.2, 1.6 Hz, 1H), 5.27 (dd, J=10.3, 1.4 Hz, 1H), 4.16 (td, J=5.5, 1.4 Hz, 2H), 4.63 (s, 2H); ^{13}C NMR (67.5 MHz) δ 150.7 (+), 141.1 (+), 133.9 (−), 131.2 (−), 127.8 (−), 123.5 (−), 117.5 (+), 113.1 (+), 71.5 (+), 71.0 (+); IR (neat) 3081, 2858, 1532, 1353, 1102 cm^{-1}; Anal. Calcd for $C_{10}H_{10}BrNO_3$: C, 44.14; H, 3.70. Found: C, 44.14; H, 3.66.

2.1.3. 2-Bromo-3-nitro-1-[(2-buten-1-yloxy)methyl]ben-zene (9). Reaction of sodium (95 mg, 4.11 mmol) with 2-butene-1-ol (1.00 mL, 11.72 mmol) for (3.5 h) followed by reaction of the formed alkoxide with **7** (294 mg, 1.00 mmol) and tetrabutylammonium iodide (40 mg, 0.11 mmol) in THF (total 20 mL) for 66 h, as described for **8**, gave after chromatography (hexanes/EtOAc, 4:1) **9** (206 mg, 0.72 mmol, 72%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.74 (d, J=6.9 Hz, 1H), 7.63, (d, J=7.9 Hz, 1H), 7.45 (t, J=7.9 Hz, 1H), 5.81 (dq, J=15.2, 6.3 Hz, 1H), 6.64 (dtq, J=15.2, 5.9, 1.2 Hz, 1H), 4.60 (s, 2H), 4.08 (dd, J=6.1, 1.0 Hz, 2H), 1.75 (dd, J=6.3, 1.2 Hz, 3H); ^{13}C NMR (67.5 MHz) δ 150.8 (+), 141.3 (+), 131.4 (−), 130.4 (−), 127.8 (−), 126.8 (−), 123.5 (−), 113.2 (+), 71.8 (+), 70.8 (+), 17.8 (−); IR (neat) 1537, 1360 cm^{-1}.

2.1.4. 2-Bromo-3-nitro-1-[(3-buten-2-yloxy)methyl]ben-zene (10). Reaction of sodium (95 mg, 4.12 mmol) with 3-butene-2-ol (0.52 mL, 6.00 mmol) in THF (1 mL) for 66 h followed by addition of the formed alkoxide to a solution of **7** (298 mg, 1.01 mmol) and tetrabutylammonium iodide (38 mg, 0.10 mmol) in THF (total 20 mL), as described for **8**, gave after chromatography (hexanes/EtOAc, 7:3) **10** (144 mg, 0.51 mmol, 50%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.75 (dd, J=7.7, 0.78 Hz, 1H), 7.61 (d, J=7.9 Hz, 1H), 7.45 (t, J=7.9 Hz, 1H), 5.81 (ddd, J=17.4, 10.3, 7.5 Hz, 1H), 5.27 (d, J=18.0 Hz, 1H), 5.21 (d, J=11.1 Hz, 1H), 4.63 (d, J=14.0 Hz, 1H), 4.51 (d, J=14.0 Hz, 1H), 4.01 (pent, J=6.3 Hz, 1H), 1.35 (d, J=6.5 Hz, 3H); ^{13}C NMR (67.5 MHz) δ 150.7 (+), 141.5 (+), 139.4 (−), 131.4 (−), 127.8 (−), 123.4 (−), 116.6 (+), 113.1 (+), 77.4 (−), 69.2 (+), 21.2 (−); IR (neat) 1535, 1361, 1104, 912, 729 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{12}BrNO_3$ 285.0001, found 284.9996.

2.1.5. 2-Bromo-3-nitro-1-[(3-phenyl-2-propen1-1yloxy)-methyl]benzene (11). To a slurry of hexane washed sodium hydride (77 mg, 3.22 mmol) in THF (10 mL) was added 3-phenyl-2-propen-1-ol (347 mg, 2.59 mmol) via syringe. The reaction mixture was stirred until no more gas was evolved (1 h). The formed alkoxide was cooled to − 78 °C and added via pipette to a solution of **7** (502 mg, 1.70 mmol) and tetrabutylammonium iodide (64 mg, 0.17 mmol) in THF (10 mL). The resulting mixture was stirred (44 h) in the cold bath while warming to ambient temperature. Workup as described for **8** and purification by chromatography (hexanes/EtOAc, 19:1) gave **11** (369 mg, 1.06 mmol, 62%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.75 (d, J=7.5 Hz, 1H), 7.68, (d, J=8.1 Hz, 1H), 7.50 (t, J=7.9 Hz, 1H), 7.42–7.21 (m, 5H), 6.72 (d, J=15.8 Hz, 1H), 6.38 (dt, J=16.0, 6.1 Hz, 1H), 4.66 (s, 2H), 4.29 (dd, J=5.9, 1.2 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 150.5 (+), 140.9 (+), 136.2 (+), 132.6 (−), 131.1 (−), 128.3 (−), 127.7 (−), 127.6 (−), 126.3 (−), 125.0 (−), 123.3 (−), 112.9 (+), 71.3 (+), 70.9 (+); IR (neat) 1537, 1265, 739 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{14}BrNO_3$ 347.0157, found 347.0161.

2.1.6. 2-Bromo-3-nitro-1-[(3-buten-1-yloxy)methyl]ben-zene (12). Reaction of sodium hydride (118 mg, 4.92 mmol) and 3-butene-1-ol (0.30 mL, 3.49 mmol) in THF (10 mL, 2 h) followed by reaction of the formed alkoxide with **7** (590 mg, 2.00 mmol) in THF (10 mL, 42 h), as described for **11**, gave after workup and chromatography (hexanes then hexanes/EtOAc, 49:1) **12** (345 mg, 1.35 mmol, 67%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.73 (d, J=7.7 Hz, 1H), 7.63 (d, J=7.9 Hz, 1H), 7.46 (t, J=7.7 Hz, 1H), 5.88 (ddt, J=17.0, 10.3, 6.7 Hz, 1H), 5.14 (d, J=17.8 Hz, 1H), 5.09 (d, J=11.3 Hz, 1H), 4.62 (s, 2H), 3.66 (t, J=6.7 Hz, 2H), 2.44 (q, J=6.5 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 150.7 (+), 141.2 (+), 134.8 (−), 131.2 (−), 127.8 (−), 123.5 (−), 116.7(+), 113.1 (+), 71.8 (+), 70.5 (+), 34.1 (+); IR (neat) 1534, 1352, 1119, 796 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{12}BrNO_3$ 285.0001, found 284.9996.

2.1.7. 2-Bromo-3-nitro-1-[(5-hexen-1-yloxy)methyl]ben-zene (13). *t*-Butyl lithium (1.7 M, 2.4 mL, 4.08 mmol) was added to a solution of 5-hexene-1-ol (0.50 mL, 4.16 mmol) in THF (20 mL) and the reaction mixture was stirred until no more gas was evolved (2 h). The formed alkoxide was added to a solution of **7** (598 mg, 2.03 mmol) and tetrabutylammonium iodide (77 mg, 0.21 mmol) in THF (10 mL) that had been stirred for 1 h. The resulting solution was stirred (89.5 h) at ambient temperature. The mixture was diluted with water (30 mL) and extracted with

dichloromethane (4×20 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed on a rotary evaporator at water aspirator pressure. Purification by chromatography (hexanes/EtOAc, 9:1) gave **13** (291 mg, 0.93 mmol, 46%) as a faint yellow oil. ^{1}H NMR (600 MHz) δ 7.72 (d, J=7.8 Hz, 1H), 7.63 (d, J=7.8 Hz, 1H), 7.46 (t, J=7.8 Hz, 1H), 5.82 (ddt, J=17.4, 10.2, 6.6 Hz, 1H), 5.02 (d, J=16.8 Hz, 1H), 4.97 (d, J=10.2, 1H), 4.61 (s, 2H), 3.60 (t, J=6.6 Hz, 2H), 2.10 (q, J=7.2 Hz, 2H), 1.70 (pentet, J=6.6 Hz, 2H), 1.52 (pentet, J=7.2 Hz, 2H); ^{13}C NMR (150 MHz) δ 150.9 (+), 141.5 (+), 138.6 (−), 131.3 (−), 127.9 (−), 123.6 (−), 114.7 (+), 113.3 (+), 71.9 (+), 71.3 (+), 33.5 (+), 29.1 (+), 25.5 (+); IR (neat) 2937, 2863, 1639, 1535, 1117, 733, 643 cm^{-1}; HRMS (DCI, CH_4) calcd for $C_{13}H_{18}BrNO_3$ (MH^+) 314.0392, found 314.0389.

2.1.8. 2-Bromo-3-nitro-1-[(2-ethenyl)phenoxy]methyl]-benzene (14). Reaction of sodium hydride (26 mg, 1.08 mmol) and 2-ethenylphenol (102 mg, 0.76 mmol) in THF (10 mL, 1.5 h) followed by reaction of the formed alkoxide with **7** (128 mg, 0.44 mmol) in THF (10 mL, 44 h), as described for **11**, gave after work up and chromatography (hexanes then hexanes/EtOAc, 9:1) **14** (95 mg, 0.28 mmol, 65%) as a faint yellow solid. Mp 68–71 °C; ^{1}H NMR (270 MHz) δ 7.77 (d with further fine splitting, J=7.7 Hz, 1H), 7.67 (dd, J=7.9, 1.6 Hz, 1H), 7.53 (dd, J=7.5, 1.6 Hz, 1H), 7.47 (t, J=7.9 Hz, 1H), 7.23 (t, J=6.4 Hz, 1H), 7.14 (q, J=17.8, 11.1 Hz, 1H), 6.99 (t, J=7.5 Hz, 1H), 6.86 (d, J=8.1 Hz, 1H), 5.77 (dd, J=17.8, 1.4 Hz, 1H), 5.31 (dd, J=11.3, 1.4 Hz, 1H), 5.18 (s, 2H); ^{13}C NMR (67.5 MHz) δ 154.8 (+), 150.8 (+), 139.7 (+), 131.2 (−), 131.1 (−), 129.0 (−), 128.2 (−), 127.2 (+), 126.6 (−), 124.0 (−), 121.7 (−), 114.9 (+), 113.1 (+), 112.3 (−), 69.5 (+); IR (neat) 1536, 1486, 1361, 1111, 907, 850, 733 cm^{-1}.

2.1.9. 2-Bromo-3-nitro-1-[2-(2-propen-1-ylphenoxy)-methyl]benzene (15). Reaction of sodium hydride (158 mg, 6.56 mmol) with 2-(2-propen-1-yl)phenol in THF (25 mL, 1H) followed by reaction of the formed alkoxide with **7** (1.02 g, 3.44 mmol) and tetrabutylammonium iodide (127 mg, 0.35 mmol) in THF (25 mL, 42.5 h), as described for **11**, gave after work up and chromatography (hexanes/EtOAc, 49:1) **15** (1.09 g, 3.14 mmol, 91%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.78 (d, J=7.7 Hz, 1H), 7.64 (dd, J=7.9, 1.2 Hz, 1H), 7.45 (t, J=7.9 Hz, 1H), 7.20–7.15 (m, 2H), 6.94 (t, J=7.5 Hz, 1H), 6.85 (d, J=8.3 Hz, 1H), 6.03 (ddq, J=17.6, 9.5, 6.5 Hz, 1H), 5.14 (s, 2H), 5.11–5.04 (m, 2H), 3.49 (d, J=6.5 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 155.4 (+), 150.7 (+), 139.8 (+), 136.6 (−), 131.0 (−), 130.1 (−), 128.7 (+), 128.1 (−), 127.4 (−), 123.9 (−), 121.5 (−), 115.6 (+), 112.9 (+), 111.5 (−), 69.1 (+), 34.4 (+); IR (neat) 3078, 1534, 1492, 1364, 1236 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}BrNO_3$ 347.0157, found 347.0170.

2.1.10. 2-Bromo-3-nitro-*N*-(2-propenyl)benzenemethanamine (16). To a solution of **7** (1.00 g, 3.39 mmol) dissolved in THF (15 mL) was added 2-propen-1-ylamine (509 μL, 6.78 mmol) and triethylamine (950 μL, 6.78 mmol) via syringe. The resulting mixture was stirred at ambient temperature (36 h), diluted with water (15 mL), and extracted with diethyl ether (3×25 mL). The combined organic phases were dried ($MgSO_4$) and filtered, and the solvents were removed. Purification by chromatography (hexanes/EtOAc, 9:1) gave **16** (853 mg, 3.15 mmol, 93%) as an orange oil. ^{1}H NMR (270 MHz) δ 7.69 (dd, J=7.5, 1.4 Hz, 1H), 7.58 (dd, J=7.9, 1.6 Hz, 1H), 7.43 (t, J=7.9 Hz, 1H), 5.93 (ddt, J=17.2, 10.3, 5.9 Hz, 1H), 5.22 (dd with further fine splitting, J=17.2, 1.6 Hz, 1H), 5.14 (dd, J=10.3, 1.4 Hz, 1H), 3.94 (s, 2H), 3.29 (d with further fine splitting, J=5.9 Hz, 2H), 1.62 (br s, 1H); ^{13}C NMR (67.5 MHz) δ 151.0 (+), 142.5 (+), 136.1 (−), 132.4 (−), 127.7 (−), 123.1 (−), 116.2 (+), 114.5 (+), 52.7 (+), 51.2 (+); IR (neat) 3324, 1534, 1360 cm^{-1}; Anal. Calcd for $C_{10}H_{11}BrN_2O_2$: C, 44.30; H, 4.09. Found: C, 44.38; H, 4.07.

2.1.11. 2-Propen-1-yl 2-bromo-3-nitrobenzyl sulfide (17). Reaction sodium hydride (60 mg, 2.50 mmol) and 2-propenyl-1-thiol (140 μL mL, 1.81 mmol) in THF (10 mL, 1 h) followed by reaction of the formed thiolate with **7** (587 mg, 1.99 mmol) in THF (10 mL, 25 h), as described for **11**, gave after work up (extracted with dichloromethane (4×15 mL)) and chromatography (hexanes then hexanes/EtOAc, 49:1) a mixture of product (**17**) and starting material. The mixture was dissolved in chloroform (20 mL) and triphenylphosphine (61 mg, 0.23 mmol) was added. The resulting mixture was stirred (21.25 h) at 70 °C. The solvents were removed at reduced pressure and the crude material was purified by chromatography (hexanes/EtOAc, 9:1) to give **17** (425 mg, 1.86 mmol, 94%) as a faint yellow solid. Mp 35–38 °C; ^{1}H NMR (270 MHz) δ 7.59 (dd, J=3.6, 1.6 Hz, 1H), 7.56 (dd, J=3.8, 1.6 Hz, 1H), 7.41 (t, J=7.7 Hz, 1H), 5.83 (ddt, J=16.4, 10.5, 7.1 Hz, 1H), 5.20–5.12 (m, 2H), 3.86 (s, 2H), 3.13 (dt, J=7.1, 1.0 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 151.3 (+), 140.9 (+), 133.5 (−), 133.2 (−), 127.6 (−), 123.1 (−), 117.7 (+), 115.4 (+), 35.3 (+), 34.5 (+); IR (neat) 1535, 1426, 1360, 1225, 990, 649 cm^{-1}; GCMS (EI) *m/z* 288.

2.1.12. Dimethyl 2-(2-bromo-3-nitrophenyl)-1,1-ethanedicarboxylate (18). To slurry of NaH (80% in mineral oil, 0.33 g, 11.0 mmol) in THF (25 mL) was added dimethylmalonate (1.14 mL, 10.0 mmol) via syringe. The reaction mixture was stirred (2H) until no more gas was evolved and a clear red solution was formed. A solution of **7** (2.95 g, 10.0 mmol) in THF (15 mL) was added to the formed anion. The solution slowly turned milky and a yellowish precipitate was formed. The resulting mixture was stirred at ambient temperature (2 h), diluted with H_2O (40 mL) and extracted with diethyl ether (3×50 mL). The combined organic phases were dried ($MgSO_4$) and filtered, and the solvents were removed. Purification by chromatography (hexanesEtOAc, 4:1) gave **18** (2.55 g, 7.37 mmol, 74%) as pale yellow crystals. Mp 68–70 °C; ^{1}H NMR (270 MHz) δ 7.59 (dd, J=7.9, 1.8 Hz, 1H), 7.50 (dd, J=7.7, 1.8 Hz, 1H), 7.37 (t, J=7.9 Hz, 1H), 3.88 (t, J=7.7 Hz, 1H), 3.73 (s, 3H), 3.46 (d, J=7.7 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 168.5 (+), 151.5 (+), 140.2 (+), 134.4 (−), 127.9 (−), 123.6 (−), 115.6 (+), 52.8 (−), 50.7 (−), 35.4 (+); IR (neat) 1749, 1721, 1528, 1231 cm^{-1}; Anal. Calcd for $C_{12}H_{12}BrNO_6$: C, 41.64; H, 3.49. Found: C, 41.75; H, 3.45.

2.1.13. *N*-2-propen-1-yl-*N*-(2-bromo-3-nitrophenyl)-methyl ethanamide (19). To a solution of **16** (0.78 g,

2.88 mmol) in pyridine (1.18 mL, 14.6 mmol) was added acetic anhydride (1.66 mL, 17.4 mmol) via syringe. The yellow mixture was stirred at ambient temperature (overnight) then heated to 100 °C (oil-bath temperature, 1.5 h). The solvent was removed and the crude product was purified by chromatography (hexanes/EtOAc, 9:1) affording **19** (0.89 g, 2.85 mmol, 99%) as a pale yellow solid. Analytical data from a *ca* 3:1 mixture of rotamers. Mp 53–55 °C; ^{1}H NMR (270 MHz) δ 7.71–7.34 (m, 3H), 5.82 (br m), 5.3–5.1 (m), 4.73 (s, major), 4.63 (s, minor), 4.05 (d, J=5.7 Hz, minor), 3.97 (br s, major), 2.23 (s, major), 2.09 (s, minor); ^{13}C NMR (major) δ 171.1 (+), 150.9 (+), 139.4 (+), 131.6 (−), 130.9 (−), 123.2 (−), 117.0 (+), 113.9 (+), 50.8 (+), 48.8 (+), 20.9 (−); ^{13}C NMR (67.5 MHz) (minor) δ 170.6 (+), 151.0 (+), 138.8 (+), 132.0 (−), 129.3 (−), 123.7 (−), 117.9 (+), 113.4 (+), 51.6 (+), 48.0 (+), 21.1 (−); IR (neat) 1650, 1536 cm^{-1}; Anal. Calcd for $C_{12}H_{13}BrN_2O_3$: C, 46.02; H, 4.18. Found: C, 45.98; H, 4.21.

2.1.14. 2-Propen-1-yl 2-bromo-3-nitrobenzyl sulfoxide (20). To a solution of 1:1 water/ethanol solution (4 mL) was added sodium metaperiodate (289 mg, 1.35 mmol) and cooled to 0 °C. Compound **17** (250 mg, 1.10 mmol) dissolved in water/ethanol (1:1, 2 mL) was added to the cooled solution via pipette. The resulting solution was stirred at 0 °C (25 h). The mixture was then extracted with dichloromethane (4×15 mL) and the combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed at reduced pressure. Crude H^1 NMR showed some remaining starting material. Sodium metaperiodate (265 mg, 1.24 mmol) was added to a solution of water/ethanol (1:1, 6 mL) and the crude product at 0 °C. The resulting solution was stirred (69.75 h) while warming from 0 °C to ambient temperature. The mixture was then extracted with dichloromethane (4×15 mL) and the combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed at reduced pressure. Purification by chromatography (in sequence: hexanes/EtOAc, 1:1, hexanes/EtOAc, 3:7, and hexanes/EtOAc, 1:9) gave **20** (117 mg, 0.38 mmol, 35%) as a faint yellow solid. Mp 79–80 °C; ^{1}H NMR (270 MHz) δ 7.71 (dd, J=7.9, 1.8 Hz, 1H), 7.62 (dd, J=7.7, 1.6 Hz, 1H), 7.48 (t, J=7.7 Hz, 1H), 6.00 (ddt, J=17.0, 10.1, 7.5 Hz, 1H), 5.53 (d, J=9.1 Hz, 1H), 5.49 (dd, J=17.0, 1.2 Hz, 1H), 4.42 (d, J=12.9 Hz, 1H), 4.07 (d, J=12.9 Hz, 1H), 3.67 (dd, J=12.9, 7.3 Hz, 1H), 3.52 (dd, J=13.0, 7.5 Hz, 1H); ^{13}C NMR (67.5 MHz) δ 151.4 (+), 135.3 (−), 134.0 (+), 128.2 (−), 125.2 (−), 124.7 (−), 124.2 (+), 116.0 (+), 57.6 (+), 56.0 (+); IR (neat) 1533, 1362, 1038, 930, 805, 733 cm^{-1}; HRMS (DEI) calcd for $C_{10}H_{10}BrNO_3S$ 302.9565, found 302.9557.

2.1.15. 2-Propen-1-yl 2-bromo-3-nitrobenzyl sulfone (21). To a solution of trifluoroacetic anhydride (0.64 mL, 4.53 mmol) and acetonitrile (10 mL) was added urea/hydrogen peroxide[29] (UHP) crystals (565 mg, 6.00 mmol) and the mixture was stirred (20 min) at ambient temperature. To the solution was added **17** (370 mg, 1.62 mmol) and the resulting solution was stirred at ambient temperature (21.5 h). The mixture was diluted with water (10 mL) and extracted with dichloromethane (4×5 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. Purification by chromatography (hexanes/EtOAc, 6:4) gave **21** (337 mg, 1.30 mmol, 80%) as a faint yellow solid. Mp 139–143 °C; ^{1}H NMR (270 MHz) δ 7.79 (dd, J=7.7, 1.6 Hz, 1H), 7.73 (dd, J=8.1, 1.8 Hz, 1H), 7.53 (t, J=7.9 Hz, 1H), 5.93 (ddt, J=16.8, 10.3, 7.3 Hz, 1H), 5.54 (dd with further fine splitting, J=10.3, 0.8 Hz, 1H), 5.51 (dd with further fine splitting, J=16.8, 1.2 Hz, 1H), 4.63 (s, 2H), 3.80 (d, J=7.3 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 151.6 (+), 135.7 (−), 130.8 (+), 128.4 (−), 125.4 (−), 125.4 (+), 123.8 (−), 116.9 (+), 58.1 (+), 57.2 (+); IR (neat) 1737, 1537, 1362, 1122, 942, 737 cm^{-1}; GCMS (EI) m/z 214 ($M^+ - NO_2$); HRMS (DEI) calcd for $C_{10}H_{11}BrNO_4S$ 319.9592, found 319.9603.

2.1.16. Dimethyl 1-(2-bromo-3-nitrophenyl)-2,2-pent-4-ene-dicarboxylate (22). Sodium hydride (80% in mineral oil, 0.21 g, 7.0 mmol) was added, at ambient temperature, to a solution of **18** (2.20 g, 6.36 mmol) in THF (20 mL). The reaction mixture was stirred (1 h) until no more gas was evolved and a clear orange solution was formed. To the solution was added 3-bromo-propene (606 mL, 7.00 mmol), via syringe. The solution slowly turned milky and a yellowish precipitate was formed. The resulting mixture was stirred at ambient temperature (16 h), diluted with H_2O (40 mL) and extracted with diethyl ether (3×50 mL). The combined organic phases were dried ($MgSO_4$) and filtered, and the solvents were removed. Purification by chromatography (hexanes/EtOAc, 9:1 followed by hexanes/EtOAc, 4:1) gave **22** (2.20 g, 5.71 mmol, 90%) as faint yellow crystals. Mp 57–60 °C; ^{1}H NMR (270 MHz) δ 7.59–7.48 (m, 2H), 7.35 (t, J=7.9 Hz, 1H), 5.93 (ddt, J=17.0, 9.9, 7.1 Hz, 1H), 5.2–5.1 (m, 2H), 3.69 (s, 3H), 3.57 (s, 2H), 2.70 (d, J=7.1 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 170.6 (+), 151.8 (+), 139.9 (+), 134.2 (−), 132.2 (−), 127.6 (−), 123.1 (−), 119.6 (+), 116.8 (+), 58.7 (+), 52.6 (−), 38.8 (+), 38.2 (+); IR (neat) 1732, 1536, 1215 cm^{-1}; Anal. Calcd for $C_{15}H_{16}BrNO_6$: C, 46.65; H, 4.18. Found: C, 46.74; H, 4.19.

2.1.17. 2-Bromo-3-nitro-1-(*N*-(2-propen-1-yl)benzenamide (23). To a solution of 2-bromo-3-nitrobenzoic acid (**24**) (1.00 g, 4.07 mmol) in dichloromethane (20 mL) was added oxallyl chloride (1.00 mL, 11.46 mmol) via syringe. The resulting mixture was heated at reflux (3 h) where after the remaining solvent and excess reagent was removed. The crude product was dissolved in dichloromethane (20 mL), pyridine (1.0 mL, 12.36 mmol) was added via pipette, and the resulting mixture was stirred (18 min) at ambient temperature. The solution was cooled (−20 °C) and 2-propen-1-ylamine (440 μL, 5.86 mmol) was added via syringe. The resulting mixture was stirred while warming to ambient temperature (20 h). The solvents were removed on under reduced pressure to give, after chromatography (hexanes/EtOAc, 6:4), **23** (769 mg, 2.70 mmol, 66%) as a faint yellow solid. Mp 120–121 °C; ^{1}H NMR (270 MHz) δ 7.75 (d, J=7.7 Hz, 1H), 7.62 (d, J=7.3 Hz, 1H), 7.51 (t, J=7.9 Hz, 1H), 6.13 (broad s, 1H), 5.93 (ddt, J=16.0, 10.9, 5.7 Hz, 1H), 5.31 (d, J=17.2 Hz, 1H), 5.23 (d, J=10.1 Hz, 1H), 4.09 (broad s, 2H); ^{13}C NMR (67.5 MHz) δ 166.2 (+), 150.6 (+), 141.0 (+), 132.9 (−), 131.2 (−), 128.3 (−), 125.3 (−), 116.8 (+), 111.1 (+), 42.2 (+); IR (neat) 3053,

2986, 1264, 895, 738 cm^{-1}; HRMS (EI) calcd for $C_{10}H_9BrN_2O_3$ 283.9797, found 283.9808.

2.1.18. 2-Bromo-3-nitrophenyl isocyanate (25). To a solution of diphenylphosporyl azide (2.00 mL, 9.28 mmol), triethylamine (2.4 mL, 17.22 mmol), and benzene (40 mL) was added **24** (1.99 g, 8.13 mmol). The resulting solution was stirred at ambient temperature (3 h) followed by stirring at 100 °C (3 h). The mixture was then diluted with ammonium chloride (sat. aqueous. 40 mL) and extracted with dichloromethane (3×30 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. Purification by chromatography (in sequence: hexanes/EtOAc, 8:2, 1:1, and 3:7) gave **25** (558 mg, 2.30 mmol, 28%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ ($CDCl_3$ and DMSO-d_6) 8.12 (d with other fine splitting, J=8.1 Hz, 1H), 8.02 (dd, J=7.9, 1.4 Hz, 0.7H), 7.91 (dd, J=7.9, 1.3 Hz, 0.3H), 7.81 (d, J=7.3 Hz, 1H); ^{13}C NMR (67.5 MHz) δ ($CDCl_3$ and DMSO-d_6) 149.5 (+), 144.6 (+), 133.03 (−), 132.98 (+), 128.1 (−), 125.1 (−), 114.5 (+); IR (neat) 1717, 1540, 1028, 1008, 952, 644 cm^{-1}; HRMS (EI) calcd for $C_7H_3BrN_2O_3$ 241.9327, found 241.9319.

2.1.19. Methyl *N*-(2-bromo-3-nitrophenyl) carbamate. To a solution of **25** (191 mg, 0.78 mmol) in methanol (5 mL) was added via pipette a solution of sodium methoxide prepared from sodium (20 mg, 0.86 mmol) and methanol (5 mL). The resulting mixture was stirred at ambient temperature (91 h). The mixture was diluted with HCl (aqueous 5%, 20 mL) and extracted with dichloromethane (3×20 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. Purification by chromatography (hexanes/EtOAc, 8:2) gave methyl *N*-(2-bromo-3-nitrophenyl)-carbamate (153 mg, 0.56 mmol, 71%) as a faint yellow solid. Mp 96–98 °C; ^{1}H NMR (270 MHz) δ (DMSO-d_6) 9.43 (bs, 1H), 7.78 (dd, J=3.6, 1.6 Hz, 1H), 7.75 (dd, J=3.8, 1.4 Hz, 1H), 7.58 (t, J=7.9 Hz, 1H), 3.68 (s, 3H); ^{13}C NMR (67.5 MHz) δ 153.4 (+), 150.7 (+), 137.9 (+), 128.6 (−), 122.8 (−), 119.1 (−), 104.2 (+), 52.9 (−); IR (neat) 3401, 3278, 1746, 1530, 1225, 1077, 957, 796 cm^{-1}; GCMS (EI) m/z 275; HRMS (EI) calcd for $C_8H_7BrN_2O_4$ 273.9589, found 273.9589.

2.1.20. Methyl *N*-(2-bromo-3-nitrophenyl)-*N*-3-buten-1-yl carbamate (26). To a slurry of hexane washed sodium hydride (50 mg, 2.06 mmol) in THF (20 mL) was added methyl *N*-(2-bromo-3-nitrophenyl) carbamate (299 mg, 1.09 mmol). The reaction mixture was stirred until no more gas was evolved (1 h). To the resulting solution was added 4-bromo-1-butene (170 μL, 1.68 mmol) and the mixture was heated at reflux (80 °C, 138 h). The mixture was diluted with water (20 mL) and extracted with dichloromethane (4×15 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed on a rotary evaporator at water aspirator pressure. Purification by chromatography (in sequence: hexanes/EtOAc, 95:5 then 9:1) gave **26** (93 mg, 0.28 mmol, 26%) as a faint yellow oil. ^{1}H NMR (600 MHz) δ 7.71 (d, J=7.8 Hz, 1H), 7.48 (t, J=8.4 Hz, 1H), 7.45 (d, J=7.2 Hz, 1H), 5.76 (dt, J=16.2, 6.6 Hz, 1H), 5.12–5.06 (m, 2H), 4.00 (pentet, J=7.2 Hz, 1H), 3.80 (br s, 1H), 3.65 (s, 3H), 3.40 (pentet, J=6.9 Hz, 1H), 2.41–2.29 (m, 2H); ^{13}C NMR (150 MHz, APT at 67.5 MHz) δ 155.2 (+), 151.8 (+), 143.0 (+), 134.7 (−), 133.9 (−), 128.4 (−), 124.0 (−), 117.3 (+), 116.9 (+), 53.3 (−), 49.3 (+), 32.5 (+); IR (neat) 1712, 1537, 1383, 908, 650 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{13}BrN_2O_4$ 328.0059, found 328.0055.

2.1.21. Dihydro-4-methylene-5-nitro-2*H*-1-benzopyrane (3), 4-methyl-5-nitro-2*H*-1-benzopyrane (4), and 4-methyl-5-nitro-4*H*-1-benzopyrane (5). A solution of **2** (1.27 g, 4.67 mmol), $Pd(OAc)_2$ (52 mg, 0.23 mmol), and tri(*o*-tolyl)phosphine (TTP, 142 mg, 0.47 mmol) in triethylamine (TEA, 23 mL) was heated at 125 °C (1.5 h). The reaction mixture was filtered (Celite), the filtrate was diluted with CH_2Cl_2 (50 mL), and the resulting solution was washed with HCl (10% aqueous, 3×50 mL). The organic phase was dried ($MgSO_4$), filtered, and the solvents were removed by evaporation. Purification of the crude product by chromatography (hexanes/EtOAc, 19:1) gave, in order of elution, **5** (30 mg, 0.17 mmol, 3%), a mixture of **4** and **5** (1:1 mixture by ^{1}H NMR, 257 mg, 1.34 mmol, 29%), as yellow oils and **3** (462 mg, 2.42 mmol, 52%) as pale yellow crystals. Data for **3**. Mp 30–32 °C; ^{1}H NMR (270 MHz) δ 7.20 (t, J=8.1 Hz, 1H), 7.00 (dd, J=7.7, 1.0 Hz, 1H), 6.74 (dd, J=8.3, 1.2 Hz, 1H), 5.14 (s, 1H), 5.08 (s, 1H), 4.35 (t, J=5.7 Hz, 2H), 2.69 (t, J=5.8 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 155.1 (+), 149.1 (+), 132.3 (+), 128.7 (−), 120.1 (−), 115.2 (−), 114.7 (+), 114.1 (+), 68.0 (+), 31.7 (+); IR (neat) 1527, 1308, 1248, 1042, 811 cm^{-1}; Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74. Found: C, 62.72; H, 4.72.

Data for **4** from a 1:1 mixture of **4** and **5**: ^{1}H NMR δ 7.26–7.17 (m, 2H), 7.08 (dd, J=6.5, 2.8 Hz, 1H), 5.83 (m, 1H), 4.48 (m, 2H), 1.93 (s, 3H); ^{13}C NMR δ 128.4 (−), 122.7 (−), 116.7 (−), 64.7 (+), 17.8 (−); ^{13}C NMR δ 156.1 (+), 148.3 (+), 128.6 (+), 128.3 (−), 122.6 (−), 119.9 (−), 118.8 (+), 116.7 (−), 64.5 (+), 17.5 (−); IR (neat) 1525, 1468, 1444, 1360, 1301, 1253 cm^{-1}; MRMS (EI) m/z 191.0575 (191.0582 calcd for $C_{10}H_9NO_3$).

Data for **5**. ^{1}H NMR (270 MHz) δ 7.52 (dd, J=8.1, 1.4 Hz, 1H), 7.19 (t, J=8.1 Hz, 1H), 7.06 (dd, J=8.3, 1.4 Hz, 1H), 6.46 (d, J=6.1 Hz, 1H), 5.00 (t, J=5.7 Hz, 1H), 4.05 (dq, J=6.7, 5.3 Hz, 1H), 1.18 (d, J=6.7 Hz, 3H); ^{13}C NMR (67.5 MHz) δ 152.3 (+), 149.0 (+), 139.0 (−), 127.2 (−), 121.6 (−), 121.1 (+), 119.8 (−), 107.2 (−), 25.0 (−), 24.8 (−); IR (neat) 1673, 1526, 1352, 1298, 1264, 1191, 1046 cm^{-1}; Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74. Found: C, 63.07; H, 4.93.

2.1.22. 3,4-Dihydro-4-methylene-5-nitro-1*H*-2-benzopyrane (27), and 4-methyl-5-nitro-1*H*-2-benzopyrane (28). Reaction of **8** (630 mg, 2.32 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and TTP (71 mg, 0.23 mmol) in TEA (12 mL), as described for **2** (125 °C, 1.5 h), gave after chromatography (hexanes/EtOAc, 19:1) in order of elution, **28** (90 mg, 0.47 mmol, 20%) and **27** (338 mg, 1.77 mmol, 76%) both as yellow crystals.

Analytical data for **27**. Mp 67–70 °C; ^{1}H NMR (270 MHz) δ 7.44 (d, J=7.9 Hz, 1H), 7.33 (t, J=7.7 Hz, 1H), 7.22 (d, J=7.7 Hz, 1H), 5.33 (s, 1H), 5.32 (s, 1H), 4.81 (s, 2H), 4.45

(s, 2H); ^{13}C NMR (67.5 MHz) δ 148.6 (+), 138.1 (+), 133.3 (+), 127.8 (−), 127.4 (−), 125.1 (+), 122.1 (−), 115.2 (+), 70.61 (+), 67.8 (+); IR (CCl_4) 3084, 2845, 1523, 1361, 1094, 917 cm^{-1}; Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74. Found: C, 62.69; H, 4.82.

Analytical data for **28**. Mp 58–61 °C; ^{1}H NMR δ 7.39 (dd, J=7.5, 2.0 Hz, 1H), 7.26–7.17 (m, 2H), 6.63 (q, J=1.4 Hz, 1H), 4.96 (s, 2H), 1.81 (d, J=1.4 Hz, 3H); ^{13}C NMR δ 147.3 (−), 145.7 (+), 132.7 (+), 126.7 (−), 126.6 (−), 123.1 (−), 124.8 (+), 109.4 (+), 68.1 (+), 12.8 (−); IR (neat) 1518 cm^{-1}; Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74. Found: C, 62.53; H, 4.84.

2.1.23. 3-Methyl-4-methylene-5-nitro-isochroman (29) and 3,4-dimethyl-5-nitro-1*H*-isochromene (30). Reaction of **9** (108 mg, 0.38 mmol), $Pd(OAc)_2$ (6 mg, 0.03 mmol), and TTP (34 mg, 0.11 mmol) in TEA (13 mL), as described above for **2** (120 °C, 24 h), gave after chromatography (hexanes/EtOAc, 9:1) in order of elution **30** (19 mg, 0.09 mmol, 25%) and **29** (56 mg, 0.27 mmol, 73%) as faint yellow oils.

Analytical data for **29**: ^{1}H NMR (270 MHz) δ 7.50 (d, J=7.9 Hz, 1H), 7.33 (t, J=7.7 Hz, 1H), 7.25 (d, J=10.7 Hz, 1H), 5.30 (s, 1H), 5.26 (s, 1H), 4.77 (d, J=14.6 Hz, 1H), 4.66 (d, J=14.6 Hz, 1H), 4.57 (pent, J=6.3 Hz, 1H), 1.46 (d, J=6.5 Hz, 3H); ^{13}C NMR (67.5 MHz) δ 148.9 (+), 139.1 (+), 138.6 (+), 127.5 (−), 127.3 (−), 126.7 (+), 122.4 (−), 113.9 (+), 73.9 (−), 66.2 (+), 20.2 (−); IR (neat) 1529, 1369, 1090, 909, 732 cm^{-1}.

Spectral data for **30**: ^{1}H NMR (270 MHz) δ 7.48 (dd, J=7.1, 2.6 Hz, 1H), 7.23–7.15 (m, 2H), 4.87 (s, 2H), 2.01 (d, J=0.8 Hz, 3H), 1.81 (d, J=0.8 Hz, 3H); ^{13}C NMR (67.5 MHz) δ 156.3 (+), 145.3 (+), 133.6 (+), 127.4 (+), 126.7 (−), 125.4 (−), 123.7 (−), 104.7 (+), 68.0 (+), 17.0 (−), 13.0 (−); IR (neat) 1625, 1525, 1361, 1183, 1056; GCMS (EI) m/z 159 (M^+).

2.1.24. 4-Ethenyl-5-nitroisochroman (31). Reaction of **10** (436 mg, 1.53 mmol), Pd(OAc)2(26 mg, 0.12 mmol), and TTP (135 mg, 0.44 mmol) in TEA (13 mL), as described for **2** (120 °C, 23 h), gave after chromatography (hexanes/EtOAc, 8:2) **31** (242 mg, 1.19 mmol, 78%) as a faint yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$ and DMSO-d_6) δ 7.73 (d, J=7.7 Hz, 1H), 7.35 (t, J=7.7 Hz, 1H), 7.26 (d, J=7.5 Hz, 1H), 5.94 (ddd, J=17.4, 10.3, 7.5 Hz, 1H), 5.10 (d, J=10.3 Hz, 1H), 4.95–4.78 (m, 3H), 4.24–4.21 (m, 1H), 3.96 (d, J=11.5 Hz, 2H); ^{13}C NMR (67.5 MHz) δ ($CDCl_3$ and DMSO-d_6) 148.0 (+), 135.9 (−), 135.6 (+), 127.9 (−), 127.1 (+), 125.6 (−), 121.3 (−), 114.9 (+), 67.2 (+), 65.8 (+), 35.8 (−); IR (neat) 1526, 1352, 1113, 924 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{11}NO_3$ 205.0739, found 205.0739.

2.1.25. 3,4-Dihydro-4-phenylmethylene-5-nitro-1*H*-2-benzopyrane (32). Reaction of **11** (244 mg, 0.70 mmol), Pd(OAc)2(11 mg, 0.05 mmol), and TTP (60 mg, 0.20 mmol) in TEA (13 mL), as described for **2** (120 °C, 43 h), gave after chromatography (hexanes/EtOAc 9:1) **32** (153 mg, 0.57 mmol, 82%) as a faint yellow solid. Mp 79–81 °C; ^{1}H NMR (270 MHz) δ 7.56 (d, J=7.7 Hz, 1H), 7.38–7.17 (m, 7H), 6.69 (s, 1H), 4.82 (s, 2H), 4.57 (s, 2H); ^{13}C NMR (67.5 MHz) δ 148.7 (+), 140.0 (+), 135.3 (+), 131.0 (−), 129.3 (−), 128.4 (+), 128.3 (−), 128.0 (−), 127.7 (+), 127.3 (−), 127.1 (−), 123.1 (−), 67.1 (+), 66.2 (+); IR (neat) 1529, 1359, 908, 732 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{13}NO_3$ 267.0895, found 267.0894.

2.1.26. 5-Methylene-6-nitro-1,3,4,5-tetrahydrobenzo-[*cd*]oxepine (33). Reaction of **12** (870 mg, 3.04 mmol), $Pd(OAc)_2$ (48 mg, 0.22 mmol), and TTP (260 mg, 0.85 mmol) in TEA (13 mL), as described for **2** (120 °C, 22.5 h), gave after chromatography (hexanes/EtOAc, 9:1) **33** (506 mg, 2.47 mmol, 81%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.60 (dd, J=7.9, 1.4 Hz, 1H), 7.38 (dd, J=7.3, 1.4 Hz, 1H), 7.31 (t, J=7.7 Hz, 1H), 5.26 (s, 1H), 4.99 (s, 1H), 4.65 (s, 2H), 4.07 (t, J=5.2 Hz, 2H), 2.66 (t, J=5.4 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 149.9 (+), 143.9 (+), 139.8 (+), 137.4 (+), 131.1 (−), 127.5 (−), 122.6 (−), 116.3 (+), 75.4 (+), 74.3 (+), 38.3 (+); IR (neat) 1530, 1362, 908, 733 cm^{-1}; GCMS (EI) m/z 159 (M^+); HRMS (EI) calcd for $C_{11}H_{11}NO_3$ 205.0739, found 205.0740.

2.1.27. 11-Methylene-10-nitro-6,11-dihydro-dibenzo-[*b*,*e*]oxepine (34) and 10-nitro-6*H*-5-oxa-dibenzo[*a*,*e*]-cyclooctene (35). Reaction of **14** (202 mg, 0.61 mmol), $Pd(OAc)_2$ (10 mg, 0.04 mmol), and TTP (53 mg, 0.18 mmol) in TEA (13 mL), as described for **2** (120 °C, 18.5 h), gave after chromatography (hexanes/EtOAc, 9:1) a 1.7:1 ratio (^{1}H NMR) of an inseparable mixture of **35** and **34** (149 mg, 0.59 mmol, 97%) as a faint yellow solid. Analytical data for the inseparable mixture of **34** and **35**. Mp 142–153 °C; ^{1}H NMR (270 MHz) δ 8.01 (d, J=8.3 Hz), 7.74 (d, J=7.9 Hz), 7.55 (d, J=7.5 Hz), 7.45–7.38 (m), 7.21 (d, J=7.3 Hz), 7.08–6.97 (m), 6.88–6.74 (m), 5.63 (s), 5.46 (s), 5.15 (s); ^{13}C NMR (67.5 MHz) δ 155.1 (+), 154.5 (+), 142.3 (+), 137.4 (+), 136.9 (+), 136.0 (−), 134.3 (+), 133.7 (−), 133.0 (−), 131.4 (−), 130.6 (−), 130.3 (−), 129.0 (−), 128.3 (−), 128.1 (−), 125.1 (−), 124.3 (+), 124.0 (−), 123.7 (−), 122.3 (+), 121.8 (−), 121.0 (−), 120.1 (−), 119.0 (−), 118.4 (+), 70.1 (+), 69.6 (+); IR (neat) 1524, 1481, 1345, 758.

2.1.28. 11-Methylene-10-nitro-11,12-dihydro-6*H*-5-oxa-dibenzo[*a*,*e*]cyclooctene (36) and 6,13-dihydro-10-nitro-5-oxa-dibenzo[*a*,*e*]cyclononene (37) and 3-[2-(2-propen-1-yl)phenoxymethyl]-1-nitrobenzene. Reaction of **15** (454 mg, 1.30 mmol), $Pd(OAc)_2$ (21 mg, 0.09 mmol), and TPP (114 mg, 0.37 mmol) in TEA (13 mL), as described for **2** (120 °C, 20.5 h), gave after chromatography (hexanes/EtOAc, 9:1) a 1.37:1 ratio (by ^{1}H NMR) of an inseparable mixture of **36** and **37** (106 mg, 0.40 mmol, 31%) and 3-[2-(2-propen-1-yl)phenoxymethyl]-1-nitrobenzene (30 mg, 0.11 mmol, 8%) as faint yellow solids. Analytical data for the inseparable mixture of **36** and **37**. Mp 116–119 °C; ^{1}H NMR (270 MHz) δ 7.89–6.95 (m, 14H, major and minor), 6.41 (d, J=11.1 Hz, 1H, minor), 6.26 (dt, J=10.9, 7.7 Hz, 1H, minor), 5.31–4.91 (m, 6H, major and minor), 4.01 (s, 2H, major), 3.43 (d, J=7.3 Hz, 2H, minor); ^{13}C NMR (67.5 MHz) δ 156.8 (+), 156.6 (+), 151.1 (+), 149.9 (+), 144.9 (+), 140.1 (+), 138.5 (+), 136.5 (+), 134.1 (+), 133.3 (+), 133.1 (−), 131.4 (−), 130.3 (−), 130.2 (−), 129.2 (−), 128.9 (−), 128.6 (+), 128.2 (−), 127.8 (−), 127.0 (−), 125.7 (−), 124.9 (−), 124.7 (−),

123.6 (−), 123.3 (−), 121.5 (−), 119.9 (−), 114.1 (+), 75.8 (+, major), 74.8 (+, minor), 41.0 (+, major), 31.1 (+, minor); IR (neat) 1530, 1489, 1359, 1104, 1013.

Spectral data for 3-[2-(2-propen-1-yl)phenoxymethyl]-1-nitrobenzene. Mp 43–46 °C; ^{1}H NMR (270 MHz) δ 8.33 (s, 1H), 8.19 (d, J=8.3 Hz, 1H), 7.78 (dd, J=7.5, 0.6 Hz, 1H), 7.57 (t, J=7.9 Hz, 1H), 7.23–7.16 (m, 2H), 6.96 (dt, J=7.3, 1.0 Hz, 1H), 6.88 (d, J=8.3 Hz, 1H), 6.02 (ddt, J=17.6, 9.5, 6.5 Hz, 1H), 5.17 (s, 2H), 5.10–5.09 (m, 1H), 5.06–5.03 (m, 1H), 3.47 (d, J=6.5 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 155.8 (+), 148.4 (+), 139.5 (+), 136.7 (−), 132.8 (−), 130.2 (−), 129.5 (−), 128.9 (+), 127.4 (−), 122.7 (−), 121.9 (−), 121.4 (−), 115.6 (+), 111.5 (−), 68.6 (+), 34.4 (+); IR (neat) 3055, 1733, 1532, 1493, 1049; HRMS (EI) calcd for $C_{16}H_{15}NO_3$ 269.1052, found 269.1044.

2.1.29. 2-Acetyl-4-methylene-5-nitro-1,2,3,4-tetrahydroisoquinoline (38), and 2-acetyl-4-methyl-5-nitro-1,2-dihydroisoquinoline (39). A solution of **19** (2.13 g, 6.80 mmol), $Pd(OAc)_2$ (76 mg, 0.34 mmol), and TTP (207 mg, 0.68 mmol) in TEA (25 mL) was heated at 100 °C (1.5 h). The reaction mixture was filtered (Celite) and the solvent was removed. The residue was dissolved in CH_2Cl_2 (30 mL), and the resulting solution was washed with HCl (10% aqueous, 4×25 mL). The organic phase was dried ($MgSO_4$), filtered, followed by removal of solvent. Purification of the crude product by chromatography (hexanes/EtOAc, 3:7) gave, in order of elution, **39** (410 mg, 1.77 mmol, 26%) and **38** (1.093 g, 4.71 mmol, 69%) both as yellow crystals.

Analytical data for **38**. Mp 89–92 °C; ^{1}H NMR δ 7.6–7.3 (m, 3H), 5.47 (s, minor), 5.45 (major), 5.29 (s, 1H), 4.72 (s, major), 4.57 (s, minor), 4.40 (s, minor), 4.33 (s, major), 2.20 (s, minor), 2.17 (major); ^{13}C NMR δ 169.5, 137.6 (+), 133.6 (+), 133.5, 129.6 (−), 128.7 (−), 128.4 (−), 128.2 (−), 128.1, 122.8 (−), 122.5 (−), 117.6 (+), 117.2 (+), 51.2 (+), 48.0 (+), 47.7 (+), 43.5 (+), 21.8 (−), 21.7 (−); IR (neat) 1647, 1528, 1420 cm^{-1}; Anal. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 52.06. Found: C, 61.93; H, 5.21.

Analytical data for **39**. Mp 103–105 °C; ^{1}H NMR δ 7.45–7.24 (m, 3H), 6.69 (s, 1H), 4.86 (s, 2H), 2.21 (s, 3H), 1.96 (s, 3H); ^{13}C NMR δ 168.1 (+), 147.1 (+), 135.1 (+), 128.6 (−). 128.5 (−), 127.3 (−), 125.5 (+), 122.9 (−), 114.8 (+), 44.0 (+0, 21.1 (−), 15.6 (−); IR (neat) 1672, 1624, 1524, 1397, 1347 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{12}N_2O_3$ 232.0848, found 232.0843.

2.1.30. Dimethyl 3,4-dihydro-4-methylene-5-nitro-2,2,(1*H*)-naphthalenedicarboxylate (40), and dimethyl 4-methyl-5-nitro-2,2,(1*H*)-naphthalenedicarboxylate (41). A solution of **22** (1.16 g, 3.00 mmol), $Pd(OAc)_2$ (34 mg, 0.15 mmol), and TTP (91 mg, 0.30 mmol) in TEA (10 mL) was heated at 100 °C (2 h). The reaction mixture was filtered (Celite), the filtrate was diluted with CH_2Cl_2 (50 mL), and the resulting solution was washed with HCl (10% aqueous, 3×50 mL). The organic phase was dried ($MgSO_4$), and filtered, followed by solvent evaporation. Purification of the crude product by chromatography (hexanes/EtOAc, 9:1) gave, in order of elution, a mixture of **41**:**40** and **40** (367 mg, 1.20 mmol, 40%) both as yellow crystals. The mixture was repurified by chromatography (hexanes/EtOAc, 9:1) affording **41** (94 mg, 0.31 mmol, 10%), a mixture of **41**:**40** (71 mg, 23 mmol, 8%, *endo–exo*, 1:1) and **40** (261 mg, 0.85 mmol, 28%).

Analytical data for **40**. Mp 97–100 °C; ^{1}H NMR δ 7.38 (dd, J=7.3, 1.6 Hz, 1H), 7.34 (d with further fine splitting, J=5.9 Hz, 1H), 7.28 (t, J=7.7 Hz, 1H), 5.25 (s, 1H), 5.17 (s, 1H), 3.72 (s, 6H, 3.35 (s, 2H), 3.11 (s, 2H); ^{13}C NMR δ 170.5 (+), 148.8 (+), 136.8 (+), 134.7 (+), 131.4 (−), 128.0 (+), 127.8 (−), 121.7 (−), 117.4 (+), 54.8 (+), 52.9 (−, 2C), 37.8 (+), 34.9 (+); IR (neat) 1735, 1528, 1259 cm^{-1}; Anal. Calcd for $C_{15}H_{15}NO_6$: C, 59.02; H, 4.95. Found: C, 59.08; H, 5.01.

Analytical data for **41**. Mp 104–106 °C; ^{1}H NMR δ 7.5–7.2 (m, 3H), 6.25 (s, 1H), 3.73 (s, 6H), 3.36 (s, 2H), 2.00 (s, 3H); ^{13}C NMR δ 169.7 (+), 148.5 (+), 136.5 (+), 131.8 (+), 130.9 (−), 127.9 (−), 127.3 (+), 127.1 (−), 122.6 (−), 53.9 (+), 53.1 (−, 2C), 34.9 (+), 18.8 (−); IR (neat) 1736, 1528, 1274, 1235 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{15}NO_6$ 305.0899, found 305.0887.

2.1.31. 4-Methylene-5-nitro-3,4-dihydro-2*H*-isoquinolin-1-one (42). Reaction of **23** (287 mg, 1.01 mmol), $Pd(OAc)_2$ (17 mg, 0.07 mmol), and TTP (87 mg, 0.29 mmol) in TEA (13 mL), as described for **2** (ambient temp. 5.5 h then 120 °C, 74 h), gave after chromatography (in sequence hexanes/EtOAc, 6:4, 1:1, and 3:7) **42** (105 mg, 0.52 mmol, 51%) as a faint yellow solid. Mp 185–187 °C; ^{1}H NMR (270 MHz) δ 8.25 (d, J=7.5 Hz, 1H), 7.70 (d, J=7.7 Hz, 1H), 7.48 (t, J=7.3 Hz, 1H), 7.20 (s, 1H), 5.44 (s, 1H), 5.28 (s, 1H), 4.16 (s, 2H); ^{13}C NMR (67.5 MHz) δ 163.2 (+), 148.0 (+), 131.6 (+), 131.4 (−), 130.3 (+), 129.8 (+), 128.8 (−), 127.1 (−), 119.5 (+), 47.5 (+); IR (neat) 2962, 1678, 1534, 1261, 907, 650.

2.1.32. 4-Methylene-5-nitro-3,4-dihydro-2*H*-quinoline-1-carboxylic acid methyl ester (43) and 4-methyl-5-nitro-4*H*-quinoline-1-carboxylic acid methyl ester and 4-methyl-5-nitro-2*H*-quinoline-1-carboxylic acid methyl ester. Reaction of **26** (93 mg, 0.28 mmol), $Pd(OAc)_2$ (5 mg, 0.02 mmol), and TTP (26 mg, 0.09 mmol) in TEA (13 mL), as described for **2** (120 °C, 39.75 h), gave after chromatography (hexanes/EtOAc, 95:5) 4-methyl-5-nitro-4*H*-quinoline-1-carboxylic acid methyl ester (4 mg, 0.02 mmol, 6%), 4-methyl-5-nitro-2*H*-quinoline-1-carboxylic acid methyl ester (4 mg, 0.02 mmol, 6%), and **43** (33 mg, 0.13 mmol, 47%) as a faint yellow oil.

Spectral data for **43**: ^{1}H NMR (270 MHz) δ 7.83 (dd, J=6.2, 3.6 Hz, 1H), 7.33–7.31 (m, 2H), 5.23 (t, J=1.4 Hz, 1H), 5.19 (s, 1H), 3.85 (t, J=6.9 Hz, 2H), 3.81 (s, 3H), 2.85 (t, J=7.1 Hz, 2H); ^{13}C NMR (150 MHz, APT at 67.5 MHz) δ 154.8 (+), 148.7(+), 140.1 (+), 134.3 (+), 127.5 (−), 127.0 (−), 124.5 (+), 119.1 (−), 115.6 (+), 53.3 (−), 44.8 (+), 32.9 (+); IR (neat) 1708, 1528, 1439, 1376, 1218, 909; GCMS (EI) m/z 248 (M^+).

Analytical data for 4-methyl-5-nitro-4*H*-quinoline-1-carboxylic acid methyl ester. ^{1}H NMR (270 MHz) δ 8.21 (d, J=8.5 Hz, 1H), 7.66 (dd, J=8.1, 1.2 Hz, 1H), 7.35 (t, J=8.3 Hz, 1H), 6.96 (d, J=7.3 Hz, 1H), 5.48 (t, J=6.9 Hz,

1H), 3.92 (pent, $J=6.9$ Hz, 1H), 3.91 (s, 3H), 1.30 (d, $J=6.9$ Hz, 3H); ^{13}C NMR (150 MHz) δ 152.9, 148.6, 138.2, 128.6, 126.4, 126.4, 125.8, 120.8, 116.0, 53.7, 28.6, 22.0.

Analytical data for 4-methyl-5-nitro-2*H*-quinoline-1-carboxylic acid methyl ester. ^{1}H NMR (270 MHz) δ 7.83 (d, $J=7.7$ Hz, 1H), 7.42 (dd, $J=7.9$, 1.2 Hz, 1H), 7.32 (t, $J=8.1$ Hz, 1H), 6.04 (dt, $J=5.3$, 1.6 Hz, 1H), 4.25 (dd, $J=5.2$, 1.4 Hz, 2H), 3.82 (s, 3H), 1.94 (d, $J=1.4$ Hz, 3H); ^{13}C NMR (150 MHz) δ 154.2, 148.4, 139.4, 130.1, 127.7, 127.1, 126.8, 124.6, 120.1, 53.7, 42.6, 18.0.

2.1.33. 3,5-Dihydro-2*H*-pyrano[4,3,2-*cd*]indole (6). To an oven-dried threaded ACE glass pressure tube was added **3** (81 mg, 0.42 mmol), $Pd(OAc)_2$ (10 mg, 0.042 mmol), dppp (42 mg, 0.10 mmol), and DMF (3 mL). The tube was fitted with a pressure head where after the solution was saturated with CO (four cycles to 4 atm of CO), and the reaction mixture was heated to 120 °C (oil bath temperature) under CO (4 atm, 70 h). The black reaction mixture was diluted with HCl (10% aqueous, 10 mL), and extracted with Et_2O (3×10 mL). The combined organic phases were washed with HCl (10% aqueous, 10 mL), and dried ($MgSO_4$), and the solvents were removed. The crude product was purified by chromatography using hexanes/EtOAc (19:1) as eluent to give **6** (42 mg, 0.265 mmol, 63%) as faint yellow crystals.

A similar reaction of **3** (345 mg, 1.80 mmol), $Pd(OAc)_2$ (24 mg, 0.11 mmol), and triphenylphosphine (112 mg, 0.43 mmol) in MeCN (4 mL) under CO (4 atm, 100 °C, 70 h) gave after work up and chromatography, in order of elution, **3** (110 mg, 0.57 mmol, 32%), and **6** (107 mg, 0.67 mmol, 37%) as faint yellow crystals. Mp 54–57 °C; ^{1}H NMR (270 MHz) δ 8.04 (br s, 1H), 7.19 (t, $J=7.9$ Hz, 1H), 6.96 (d, $J=8.1$ Hz, 1H), 6.78 (br s, 1H), 6.64 (d, $J=7.5$ Hz, 1H), 4.48 (t, $J=5.5$ Hz, 2H), 3.13 (t, $J=4.9$ Hz, 2H); ^{13}C NMR δ 150.9 (+), 135.1 (+), 123.6 (−), 117.9 (+), 116.0 (−), 107.6 (+), 103.7 (−), 101.9 (−), 68.2 (+), 23.2 (+); IR (neat) 3406, 1631, 1610, 1504, 1341, 1267, 1234 cm^{-1}; Anal. Calcd for $C_{10}H_9NO$: C, 75.45; H, 5.70. Found: C, 75.24; H, 5.78.

2.1.34. 1,5-Dihydro-3*H*-pyrano[3,4,5-*cd*]indole (46). Reaction of **27** (109 mg, 0.57 mmol), $Pd(OAc)_2$ (13 mg, 0.058 mmol), dppp (136 mg, 0.14 mmol) in DMF (5 mL), as described for **6** (4 atm CO, 120 °C, 120 h), gave after chromatography (hexanes/EtOAc, 19:1 followed by 9:1) **46** (71 mg, 0.45 mmol, 78%) as faint pink crystals. Mp 168–170 °C; ^{1}H NMR (270 MHz) δ 7.96 (br s, 1H), 7.19 (d, $J=8.1$ Hz, 1H), 7.15 (t, $J=6.5$ Hz, 1H), 6.87 (s, 1H), 6.82 (d, $J=6.7$ Hz, 1H), 5.04 (s, 2H), 4.95 (s, 2H); ^{13}C NMR (67.5 MHz) δ 133.5 (+), 129.4 (+), 124.1 (−), 115.6 (−), 112.6 (−), 111.3 (+), 109.1 (−), 66.7 (+), 64.5 (+); IR (neat) 3308, 1445, 1086 cm^{-1}; HRMS (EI) calcd for $C_{10}H_9NO$ 159.0684, found 159.0678.

2.1.35. 1,5-Dihydro-2-methyl-3*H*-pyrano[3,4,5-*cd*]indole (47). Reaction of **29** (141 mg, 0.69 mmol), $Pd(dba)_2$ (25 mg, 0.04 mmol), dppp (18 mg, 0.04 mmol), and 1,10-phenanthroline monohydrate (16 mg, 0.09 mmol) in DMF (5 mL), as described for **6** (6 atm CO, 120 °C, 29 h), gave after chromatography (hexanes/EtOAc, 9:1) **47** (95 mg, 0.55 mmol, 80%) as a faint yellow solid. Mp 127–130 °C; ^{1}H NMR (270 MHz) δ 8.08 (broad s, 1H), 7.16–7.09 (m, 2H), 6.81–6.70 (m, 1H), 6.76 (t, $J=1.8$ Hz, 1H), 5.07 (dq, $J=6.4$, 1.2 Hz, 1H) overlapping peak centered at 5.01 (m, 2H), 1.63 (d, $J=6.5$ Hz, 3H); ^{13}C NMR (67.5 MHz) δ 133.6 (+), 129.6 (+), 124.2 (+), 123.0 (−), 117.0 (+), 115.4 (−), 112.6 (−), 109.0 (−), 70.5 (−), 66.6 (+), 20.5 (−); IR (neat) 3293, 1448, 1340, 1016, 908, 731; GCMS (EI) *m/z* 173; HRMS (EI) calcd for $C_{11}H_{11}NO$ 173.0842, found 173.0842.

2.1.36. 1,5-Dihydro-2-phenyl-3*H*-pyrano[3,4,5-*cd*]indole (48). Reaction of **32** (105 mg, 0.39 mmol), $Pd(dba)_2$ (14 mg, 0.03 mmol), dppp (12 mg, 0.03 mmol), and 1,10-phenanthroline monohydrate (10 mg, 0.05 mmol) in DMF (5 mL), as described for **6** (6 atm CO, 120 °C, 22 h), gave after purification by chromatography (hexanes/EtOAc, 8:2) **48** (63 mg, 0.27 mmol, 68%) as a faint yellow solid. Mp 189–192 °C; ^{1}H NMR (600 MHz) δ 8.13 (broad s, 1H), 7.47–7.41 (m, 4H), 7.32 (dt, $J=6.6$, 2.4 Hz, 1H), 7.22 (d, $J=7.8$ Hz, 1H), 7.16 (dt, $J=7.8$, 1.2 Hz, 1H), 6.83 (d, $J=6.6$ Hz, 1H), 5.21 (s, 2H), 4.98 (s, 2H); ^{13}C NMR (150 MHz) δ 134.0, 132.5, 129.7, 129.6, 129.2, 127.3, 125.8, 125.6, 123.3, 113.0, 109.1, 109.0, 66.6, 65.0; IR (neat) 1601, 1448, 864, 737, 692 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{13}NO$ 235.0997, found 235.0998.

2.1.37. 2,6,8,9-Tetrahydro-7-oxa-2-aza-benzo[*cd*]azulene (49). Reaction of **33** (412 mg, 2.01 mmol), $Pd(dba)_2$ (74 mg, 0.13 mmol), dppp (52 mg, 0.13 mmol), 1,10-phenanthroline monohydrate (45 mg, 0.25 mmol) in DMF (5 mL), as described for **6** (6 atm CO, 120 °C, 24 h), gave after chromatography (hexanes/EtOAc, 9:1) **49** (287 mg, 1.66 mmol, 83%) as a faint yellow solid. Mp 115–116 °C; ^{1}H NMR (270 MHz) δ 8.35 (broad s, 1H), 7.09–6.98 (m, 2H), 6.79–6.67 (m, 2H), 5.07 (s, 2H), 4.02 (t, $J=4.9$ Hz, 2H), 3.03 (t, $J=5.5$ Hz, 2H); ^{13}C NMR (67.5 MHz) δ 136.5 (+), 134.0 (+), 124.8 (+), 121.3 (−), 121.2 (−), 114.3 (−), 113.7 (+), 109.3 (−), 76.4 (+), 73.3 (+), 29.7 (+); IR (neat) 3413, 2934, 1432, 908, 731 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{11}NO$ 173.0841, found 173.0836.

2.1.38. 2,6-Dihydro-7-oxa-2-aza-dibenzo[*cd*,*h*]azulene (50) and 6*H*-5-oxa-dibenzo[*a*,*e*]cyclooctene-10-ylamine (51). Reaction of a 1.7:1 mixture (estimated by ^{1}H NMR) of **34** and **35** (266 mg, 1.05 mmol), $Pd(dba)_2$ (37 mg, 0.06 mmol), dppp (27 mg, 0.07 mmol), and 1,10-phenanthroline monohydrate (24 mg, 0.13 mmol) in DMF (5 mL), as described for **6** (6 atm CO, 120 °C, 20.5 h), gave after chromatography (hexanes/EtOAc acetate, 9:1 then hexanes/EtOAc, 1:1) two fractions containing **50** and **51**, respectively. However, both fractions contained residual DMF. The fraction containing **51** was each dissolved in diethyl ether (10 mL) and washed with water (4×10 mL). The organic phase was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure to give **51** (98 mg, 0.42 mmol, 64%) as a faint yellow solid. The fraction containing **50** was dissolved in diethyl ether (10 mL) and washed with water (4×10 mL). The organic phase was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The residue was purified by chromatography (hexanes/EtOAc, 7:3) affording **50** (38 mg, 0.17 mmol, 44%) as a faint yellow solid.

Analytical data for **50**. Mp 197–198 °C; ^{1}H NMR (600 MHz) δ 8.35 (broad s, 1H), 7.70 (dd, J=6.6, 1.8 Hz, 1H), 7.54 (d, J=2.4 Hz, 1H), 7.34 (d, J=7.8 Hz, 1H), 7.21–7.12 (m, 4H), 6.95 (d, J=6.6 Hz, 1H), 5.28 (s, 2H); ^{13}C NMR (150 MHz, APT at 67.5 MHz) δ 158.3 (+), 136.0 (+), 133.5 (+), 128.0 (+), 126.5 (−), 126.1 (−), 124.6 (−), 124.2 (−), 122.8 (−), 122.3 (−), 120.2 (−), 116.6 (−), 115.3 (+), 110.7 (+), 75.2 (+); IR (neat) 908, 732, 650; HRMS (EI) calcd for $C_{15}H_{11}NO$ 221.0841, found 221.0837.

Analytical data for **51**. Mp 99–102 °C; ^{1}H NMR (270 MHz) δ 7.12–6.98 (m, 4H), 6.90–6.79 (m, 3H), 6.64–6.49 (m, 1H), 6.27 (d, J=12.7 Hz, 1H), 5.25 (s, 2H), 3.68 (broad s, 2H); ^{13}C NMR (67.5 MHz) δ 156.1 (+), 144.6 (+), 135.2 (+), 134.2 (−), 131.3 (−) 128.5 (−), 128.4 (−), 124.3 (+), 123.1 (+), 122.9 (−), 120.60 (−), 120.58 (−), 120.3 (−), 115.6 (−), 71.4 (+); IR (neat) 3373, 2955, 1618, 1486, 1437, 1255, 1114, 909; GCMS (EI) m/z 223; HRMS (EI) calcd for $C_{15}H_{13}NO$ 223.0997, found 223.1001.

2.1.39. Compound 52 and 10-amino-6*H*-dibenz[*b*,*f*]-oxocine (53). Reaction of a 1.37:1 mixture (estimated by ^{1}H NMR) of **36** and **37** (106 mg, 0.40 mmol), Pd(dba)$_2$ (13 mg, 0.02 mmol), dppp (10 mg, 0.02 mmol), and 1,10-phenanthroline monohydrate (10 mg, 0.05 mmol) in DMF (5 mL), as described for **6** (6 atm CO, 120 °C, 98 h), gave after chromatography (in sequence: hexanes/EtOAc, 9:1, 1:1, 0:1) a mixture of **52** and **53**. The mixture was purified by chromatography (hexanes/EtOAc, 98:2 followed by hexanes/EtOAc, 95:5) to give **52** (20 mg, 0.09 mmol, 37%) as a faint yellow solid followed by a 1:1.7 mixture of **52** to **53** (10 mg, ca. 0.02 mmol **52**, 0.03 mmol **53**, 7% **52**, 15% **53**) as a faint yellow solid.

Analytical data for **52**. Mp 173–175 °C; ^{1}H NMR (270 MHz) δ 7.88 (broad s, 1H), 7.20–6.94 (m, 7H), 6.80 (dd, J=7.3, 1.2 Hz, 1H), 5.71 (s, 2H), 4.11 (s, 2H); ^{13}C NMR (67.5 MHz) δ 158.3 (+), 138.4 (+), 135.0 (+), 132.7 (+), 129.2 (−), 127.8 (−), 123.8 (−), 123.5 (+), 122.0 (−), 121.6 (−), 120.6 (−), 117.2 (+), 116.1 (−), 109.9 (−), 76.7 (+), 31.0 (+); IR (neat) 911, 728, 650 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}NO$ 234.0919, found 234.0914.

Analytical data for **53** from the mixture of **52** and **53**: ^{1}H NMR (270 MHz) δ 6.37 (d, J=11.3 Hz, 1H), 6.07 (dt, J=11.1, 8.1 Hz, 1H), 5.21 (broad s, 2 Hz, 1H), 3.76 (broad s, 2H), 3.21 (d, J=7.7 Hz, 2H).

2.1.40. 4-Acetyl-1,3,4,5,-tetrahydropyrrolo[4,3,2-*de*]isoquinoline (54).[30] Reaction of **38** (350 mg, 1.51 mmol), Pd(OAc)$_2$ (34 mg, 0.151 mmol), dppp (124 mg, 0.302 mmol) in MeCN (5 mL), as described for **6** (4 atm CO, 120 °C, 2 h), gave after chromatography (EtOAc) **54** (124 mg, 0.62 mmol, 41%) as a light yellow crystals followed by **38** (21 mg, 0.092 mmol, 9%) Analytical data for **54**. Mp 207–209 °C, ^{1}H NMR (270 MHz) δ 8.02 (br s, 1H), 7.22–7.13 (overlapping m, 2H), 6.94 (s, 1H), 6.88 (d, J=6.9 Hz, 1H), 5.02 (d, J=1.8 Hz, 2H), 4.83 (s, 1H), 4.82 (s, 1H), 2.20 (s, 3H); ^{13}C NMR (67.5 MHz) δ 169.2 (+), 133.0 (+), 132.9 (+), 126.6 (+), 125.8 (+), 124.7 (+), 124.6 (+), 121.9 (−), 121.6 (−), 116.8 (−), 116.3 (−), 112.9 (−), 112.2 (−), 109.1 (−), 108.6 (−), 108.1 (+), 107.7 (+), 46.8 (+), 43.6 (+), 41.9 (+), 38.8 (+), 21.6 (−), 21.5 (−); IR (neat) 3294, 1626, 1606, 1444, 1441, 1248, 767 cm^{-1}. The compound decompose relatively fast at ambient temperature forming highly colored products.

2.1.41. Dimethyl 1,3-dihydro-4,4(5*H*)-benz[*cd*]indole-5,5-dicarboxylate (55). Reaction of **40** (225 mg, 0.74 mmol), Pd(OAc)$_2$ (17 mg, 0.074 mmol), and dppp (75 mg, 0.18 mmol) in MeCN (5 mL), as described for **6** (4 atm CO, 120 °C, 48 h), gave after chromatography (hexanes/EtOAc, 9:1) gave **55** (131 mg, 0.48 mmol, 65%) as a white solid. Mp 154–155 °C; ^{1}H NMR (270 MHz) δ 7.94 (br s, 1H), 7.08–6.92 (m, 2H), 6.78 (d, J=6.4 Hz, 1H), 6.68 (s, 1H), 3.53 (s, 6H), 3.45 (s, 2H), 3.38; ^{13}C NMR (67.5 MHz) δ 171.6 (+), 133.4 (+), 127.5 (+), 125.4 (+), 122.8 (−), 118.3 (−), 115.9 (−), 109.4 (+), 108.7 (−), 56.2 (+), 52.7 (−), 33.8 (+), 28.7 (+); IR (neat) 3391, 1721 cm^{-1}; Anal. Calcd for $C_{15}H_{15}O_4$: C, 65.92; H, 5.53. Found: C, 65.81; H, 5.59.

2.1.42. 3,4-Dihydro-1*H*-pyrrolo[4,3,2-de]isoquinoline-5-one (56). Reaction of **42** (145 mg, 0.71 mmol), Pd(dba)$_2$ (26 mg, 0.05 mmol), dppp (20 mg, 0.05 mmol), and 1,10-phenanthroline monohydrate (16 mg, 0.09 mmol) in DMF (5 mL), as described for **6** (6 atm, 120 °C, 26.5 h), gave after purification by chromatography (hexanes/EtOAc, 2:8 followed by EtOAc) **56** (74 mg, 0.43 mmol, 61%) as a faint yellow solid. Mp 207–210 °C; ^{1}H NMR (270 MHz, $CDCl_3$ and DMSO-d_6) δ 10.81 (broad s, 1H), 7.47 (d, J=2.8 Hz, 1H), 7.44 (d, J=4.0 Hz, 1H), 7.33 (s, 1H), 7.17 (t, J=7.3 Hz, 1H), 7.05 (s, 1H), 4.90 (s, 2H); ^{13}C NMR δ ($CDCl_3$ and DMSO-d_6) 163.9 (+), 132.1 (+), 127.5 (+), 120.9 (−), 119.2 (+), 117.6 (−), 114.2 (−), 113.4 (−), 103.9 (+), 41.0 (+); IR (neat) 1657, 1054, 911, 644; HRMS (EI) calcd for $C_{10}H_7N_2O$ 171.0558, found 171.0555.

2.1.43. 3,4-Dihydro-1*H*-pyrrolo[4,3,2-*de*]quinoline-5-carboxylic acid methyl ester (57). Reaction of **43** (36 mg, 0.15 mmol), Pd(dba)$_2$ (5 mg, 0.01 mmol), dppp (4 mg, 0.01 mmol), and 1,10-phenanthroline monohydrate (3 mg, 0.02 mmol) in DMF (5 mL), as described for **6** (6 atm CO,120 °C, 43.5 h), gave after chromatography (hexanes/EtOAc, 9:1) **57** (10 mg, 0.05 mmol, 33%) as a faint yellow oil. ^{1}H NMR (270 MHz) δ 7.98 (broad s, 1H), 7.36 (broad s, 1H), 7.15 (t, J=7.9 Hz, 1H), 7.5 (d, J=8.1 Hz, 1H), 6.84 (s, 1H), 4.11 (t, J=5.5 Hz, 2H), 3.86 (s, 3H), 3.01 (dt, J=6.3, 1.0 Hz, 2H); ^{13}C NMR (67.5 MHz) δ 155.4 (+), 134.5 (+), 132.7 (+), 123.1 (−), 120.6 (+), 116.9 (−), 110.3 (+), 109.9 (−), 106.0 (−), 52.9 (−), 45.6 (+), 22.9 (+); IR (neat) 1696, 1439, 1385, 1215, 907, 732, 650; GCMS (EI) m/z 216; HRMS (EI) calcd for $C_{12}H_{12}N_2O_2$ 216.0899, found 216.0896.

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Supplementary data

^{1}H NMR and ^{13}C NMR spectra of all new compounds are available.

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2005.02.033

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