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Synthesis of 1,2,3,4-tetrahydrocarbazoles and related tricyclic indoles

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Abstract—Reduction of 2-(2-nitrophenyl)-2-cyclohexene-1-ones using palladium on carbon under 1 atm of hydrogen gas at ambient temperature affords 1,2,3,4-tetrahydrocarbazoles in excellent isolated yields. The starting materials were prepared by intermolecular Stille coupling of 2-iodo-2-cyclohexen-1-ones with 2-(tributylstannyl)-1-nitrobenzenes.

1. Introduction

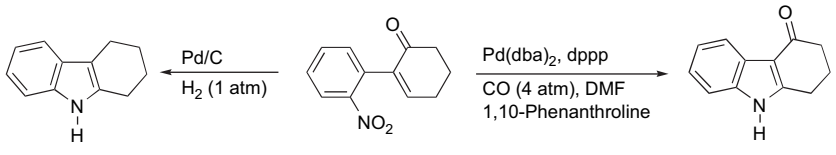
We and others have developed mild and very efficient routes to substituted indoles,[1–10] β-carbolines,[11] carbazoles,[12] and 1,2-dihydro-4(3*H*)-carbazolones[13,14] using a palladium-catalyzed reductive N-heteroannulation as the key step. For example, 1,2-dihydro-4(3*H*)-carbazolone (**2**) was prepared in good isolated yield by reductive cyclization of 2-(2-nitrophenyl)-2-cyclohexene-1-one (**1**) (Scheme 1). A mechanism involving the formation of a palladium-bound nitrene followed by electrocyclization has been proposed for the annulation reaction.[5] The starting 2-(2-nitrophenyl)-2-cyclohexenones were prepared by a Stille-type cross-coupling of the appropriate 2-nitrophenylstannanes with 2-iodo-2-cycloalken-1-ones.

It was perceived that initial reduction of the nitro group of **1**, using palladium on carbon and hydrogen gas, to an amine followed by condensation with the carbonyl moiety would afford a product with a different oxidation state and regiochemistry. This idea was corroborated in our initial experiment wherein **1** was reduced under mild conditions to give 1,2,3,4-tetrahydrocarbazole (**3**) (Scheme 1).[15]

Reduction of 2-nitroarenes having an adjacent saturated cyclohexanone with a variety of reducing agents, such as $TiCl_3$,[16–18] zinc,[19,20] and palladium on carbon–hydrogen gas[21,22] has been described to afford 1,2,3,4-tetrahydrocarbazoles (Scheme 2). In addition, a general method for the formation of *N*-hydroxyindoles was reported using a lead-promoted reductive cyclization of related ketones and aldehydes under transfer hydrogenation conditions.[23]

Scheme 2.

Herein is reported a study of the reduction of 2-(2-nitrophenyl)-2-cycloalkene-1-one to give reduced carbazoles and related tricyclic compounds. It should be noted that while working on this manuscript, Banwell et al. communicated a related methodology involving an Ullman-type coupling of 2-nitro-1-halobenzenes with α-halo-enones and



3 (95%) **1** **2** (83%)

Scheme 1.

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-enals followed by a palladium on carbon catalyzed reductive annulation.[24]

2. Results and discussion

A variety of 2-(2-nitrophenyl)-2-cycloalkenones were prepared using published procedures or modifications thereof. For example, compound **4** was synthesized starting from 4-methylcyclohexanone (**5**) (Scheme 3). Formation of silyl enol ether **6** followed by palladium-catalyzed dehydrosilylation (a Saegusa oxidation)[22] gave 4-methyl-2-cyclohexen-1-one (**7**). The relatively low yield of **7** may be attributed to the volatility of this product. Iodide **8** was prepared in 65% yield employing iodine in a pyridine–carbon tetrachloride mixture as described by Johnson et al.[25] Stille-type cross-coupling of **8** with 2-nitrophenyl-substituted stannane **9**, using bis(benzonitrile)palladium dichloride, triphenylarsine, and copper iodide in *N*-methylpyrrolidinone gave **4** in good yield (80%). Two additional new compounds, **11** and **12** (Table 1), were prepared in a similar fashion by coupling of 2-iodo-5-methylcyclohexenone and 2-iodo-3-methylcyclohexenone with **9**, respectively.

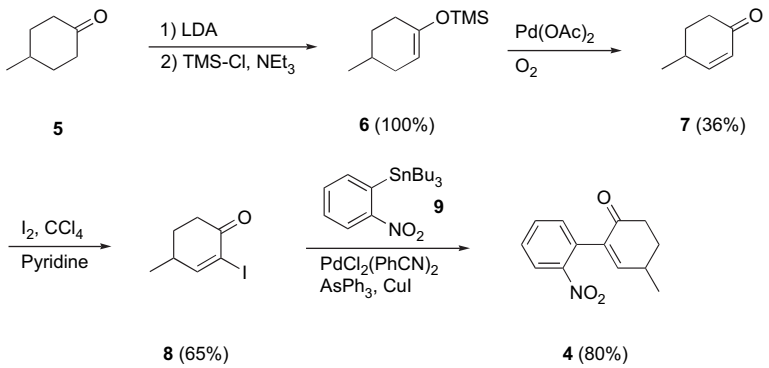
With a variety of substrates readily available, the N-heteroannulation was examined next and the results of the reductive cyclizations are summarized in Table 1. Most of the reductions were performed in methanol using 10% Pd/C (~20 mol % Pd) and hydrogen gas (1 atm) at ambient temperature. The starting materials were completely consumed within 20 min to 2 h as monitored by thin layer chromatography. Compounds related to those described in Table 1 have been shown to be sensitive to oxidation on silica.[26] For compounds where this was a noticeable problem, precautions were taken such as using base-washed glassware, filtering the NMR solvents through potassium carbonate prior to use, and adding a small amount of triethylamine to the eluent (approximately 0.2–1% of triethylamine per 100 mL of eluent) used for chromatography.

For the methyl-substituted starting materials (**10**–**12** and **4**, entries 1–4), excellent yields of methyl-substituted 1,2,3,4-tetrahydrocarbazoles were obtained upon reduction. It should be noted that the connectivity between the indole nitrogen and the reduced six-membered ring is different from that obtained using the palladium–carbon monoxide catalyst system shown in Scheme 1. Thus, by simply changing the reducing agent, carbon monoxide versus hydrogen gas, regioisomeric compounds can be obtained although in different oxidation states.

The inherent regioselectivity in the present methodology is important to stress. For example, preparation of compound **22** is problematic using more conventional methods such as the Fischer indole synthesis. For example, reaction of 3-methylcyclohexanone with phenylhydrazine affords a 10:1 mixture of **20**:**22**.[27] In addition, a more recently developed palladium-catalyzed annulation between 2-iodoaniline and 3-methylcyclohexanone also gave **20** as the major product (8:1 mixture of **20**:**22**).[28] In contrast, both **20** and **22** can readily be prepared in high yields using the present methodology.

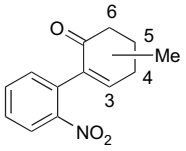
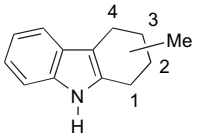
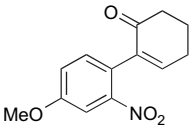
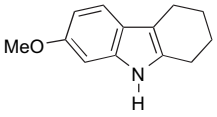
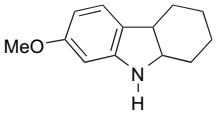
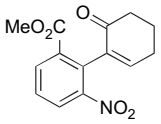
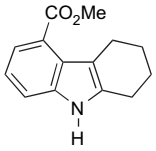
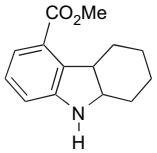
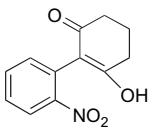
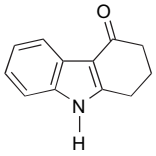
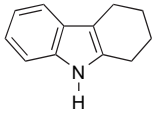
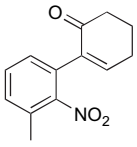
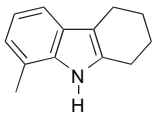
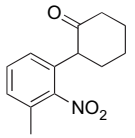
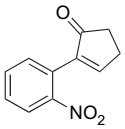
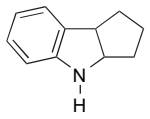
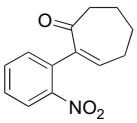
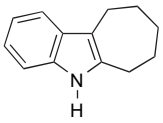
Substitution on the benzene ring affected the oxidation state of products isolated. Upon reduction of compounds **13** and **14**, in addition to the expected tetrahydrocarbazoles (**23** and **25**), hexahydrocarbazoles (**24** and **26**) were formed as well (entries 5 and 6). Over-reduction was observed to give 1,2,3,3a,4,8b-hexahydrocyclopent[*b*]indole (**29**) as the only product upon reaction of 2-(2-nitrophenyl)-2-cyclopenten-1-one (**17**, entry 9). Reduction of 1,2,3,4-tetrahydrocyclopent[*b*]indole to **29** in 69% yield using 5 mol % Pd/C under 3 atm of hydrogen gas has been reported.[29] A related over-reduction of 2-(2,4-dinitrophenyl)cyclopentanone to give 6-amino-hexahydrocyclopent[*b*]indole was reported by Kuehne employing 2.6 mol % palladium.[30] In contrast, the formation of **29** was not observed by Banwell et al. using the same starting material (**17**) and 2 mol % palladium. Interestingly, we did not isolate the over-reduction product from the corresponding cycloheptenone derivative **18**, which smoothly was reduced to the 5,6,7,8,9,10-hexahydrocyclohept[*d*]indole (**30**) (entry 10).

Finally, reductive annulation of dione **15** gave not only the expected carbazolone **2** but also 1,2,3,4-tetrahydrocarbazole (**3**) (Table 1, entry 7). We speculated that **2** was initially formed followed by a second reduction to give **3**, under the reaction conditions.[31] Reduction of carbonyl groups adjacent to the 3-position of the indole ring using palladium on carbon and hydrogen gas has been reported previously.[32] In a control experiment, subjecting carbazolone **2** to the hydrogenation conditions did produce tetrahydrocarbazole **3**, but 39% of the starting material was still present after 3 days. Due to the vastly different reaction kinetics of the reductions described in entry 7 (2 h) and Scheme 4 (3 days), it is unlikely that **2** is a major intermediate to **3**.



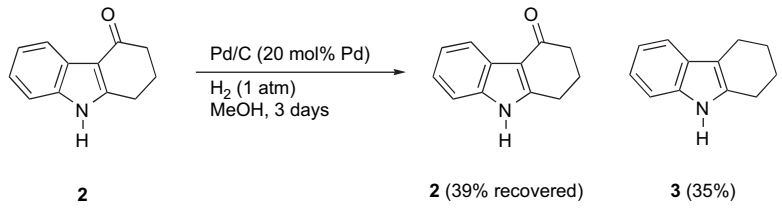
Scheme 3.

Table 1. Synthesis of 1,2,3,4-tetrahydrocarbazoles

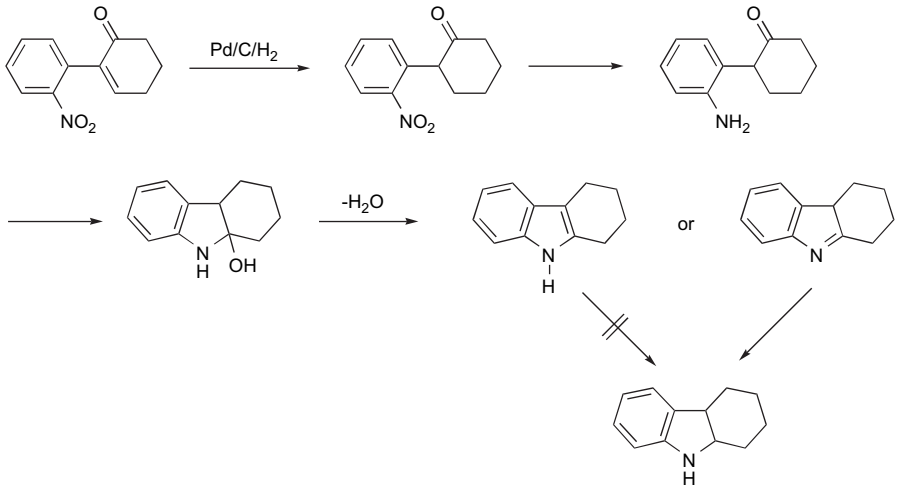
Entry	Nitrobenzene	Carbazole[a,b]	
			
1	**10** (6-Me)	**19** (1-Me, 94%)	
2	**11** (5-Me)	**20** (2-Me, 93%)	
3	**4** (4-Me)	**21** (3-Me, 89%)	
4	**12** (3-Me)	**22** (4-Me, 79%)	
			
5	**13**	**23** (62%)	**24** (10%)[c]
			
6	**14**	**25** (28%)	**26** (41%)
			
7	**15**	**2** (43%)	**3** (22%)
			
8	**16**	**27** (43%)	**28** (0%)
9	**16**	**27** (18%)	**28** (35%)[d]
			
10	**17**	**29** (83%)	
			
11	**18**	**30** (71%)	

[a] For experimental details, see Section 4.
[b] Isolated yields in parenthesis.
[c] As an inseparable mixture with **23**.
[d] Using 2% palladium.

A number of mechanistic pathways wherein the timing of the reductive steps differs can be envisioned. Some details have been obtained in the present study. It is likely that initially the cyclohexenone double bond is reduced. This is supported by the following experiment. Reductive annulation of **16** for 20 min produced the expected tetrahydrocarbazole (**27**, 18%) and 2-(3-methyl-2-nitrophenyl)-1-cyclohexanone (**28**, 36%), the latter derived from reduction of the α,β-unsaturated ketone (entry 8). This type of by-product was also observed in one case by Banwell et al.[24] When we reduced the amount of palladium from 20 mol % to 2 mol %, a 95% yield of **28** was obtained. This result suggests an initial reduction of the cycloalkenone to a cycloalkanone prior to reduction of the nitro group, at least for some substrates. It should be noted that **28** is transformed to **27** (26% yield) upon reaction with Pd/C–H_2 for 2 h.



Scheme 4.



Scheme 5.

Submitting indole **23** to the reaction conditions did not result in reduction to the hexahydroindole **24**, even after prolonged reaction time, indicating that hexahydroindoles are formed via a different intermediate. Based on the experiments described above, we propose the following series of events for the reductive annulation of 2-(2-nitrophenyl)-2-cyclohexene-1-ones. The alkene is initially reduced to an alkane, which is followed by a reduction of the nitro group to an amine (Scheme 5). Subsequently an aminal is formed that eliminates water forming either a (9*H*)-1,2,3,4-tetrahydrocarbazole or an isomeric (4a*H*)-1,2,3,4-tetrahydrocarbazole (an imine). Further reduction of the imine would give a hexahydroindole, the product observed in some cases.

3. Conclusion

A short synthetic sequence to 1,2,3,4-tetrahydrocarbazoles and related tricyclic indoles employing a Stille-type cross-coupling and a palladium-catalyzed reductive annulation as the key steps has been described. Over-reduction is observed at times affording the corresponding fused indoline.

4. Experimental section

4.1. General procedures

NMR spectra were determined in $CDCl_3$ at 270 MHz or 600 MHz (^{1}H NMR) and 67.5 MHz or 150 MHz (^{13}C NMR). The chemical shifts are expressed in δ values relative to Me_4Si (0.0 ppm, ^{1}H and ^{13}C) or $CDCl_3$ (77.0 ppm, ^{13}C) as internal standards. ^{1}H–^{1}H 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 parentheses where, relative to $CDCl_3$, (−) denotes CH_3 or CH and (+) denotes CH_2 or C.

Tetrahydrofuran (THF), 1,4-dioxane, and diethyl ether were distilled from sodium benzophenone ketyl prior to use. Toluene, pyridine, hexanes, acetonitrile, methanol, 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. Chromatography was performed on silica gel 60 (35–75 μm, VWR). Melting points were determined on a MelTemp and are uncorrected. Elemental analyses were performed in the Department of Chemical Engineering, College of Engineering and Mineral Resources, West Virginia University.

4.1.1. Trimethyl[(4-methyl-1-cyclohexen-1-yl)oxy]silane (6).[16] *n*-Butyllithium (20 mL of a 2.5 M solution in hexanes, 50.0 mmol) was added dropwise to a −78 °C cold solution of diisopropylamine (8.15 mL, 58.2 mmol) in THF (160 mL) under an argon atmosphere. The reaction mixture was stirred (10 min) and a solution of 4-methylcyclohexanone (5.01 g, 44.6 mmol) in THF (40 mL) was added slowly to the

reaction mixture. The reaction was stirred for 30 min, followed by slow addition of trimethylsilyl chloride (6.80 mL, 53.6 mmol) and triethylamine (12.5 mL, 89.7 mmol). The reaction mixture was allowed to warm to room temperature over 1 h. The mixture was diluted with diethyl ether (400 mL), washed with water (3×100 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by chromatography (hexanes–EtOAc, 9:1) to give **6** (8.23 g, 44.6 mmol, 100%) as a colorless oil. Spectral data (^{1}H NMR) were in complete accordance with literature values.[33]

4.1.2. 4-Methyl-2-cyclohexen-1-one (7).[34] To a solution of **6** (3.14 g, 17.0 mmol) in dimethylsulfoxide (100 mL) was added palladium diacetate (366 mg, 1.63 mmol). The reaction flask was flushed with O_2 for 5 min and the mixture was stirred at 40 °C under O_2 (1 atm, 24 h). The reaction mixture was allowed to cool, diluted with EtOAc (400 mL), and washed with water (3×100 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by chromatography (hexanes–EtOAc, 9:1) to give **7** (676 mg, 6.14 mmol, 36%) as a colorless oil. Spectral data (^{1}H NMR) were in complete accordance with literature data.[35]

4.1.3. 2-Iodo-4-methyl-2-cyclohexen-1-one (8). A solution of iodine (2.97 g, 11.7 mmol) in CCl_4 (10 mL) and pyridine (10 mL) was added dropwise to a solution of **7** (628 mg, 5.70 mmol) in CCl_4 (10 mL) and pyridine (10 mL) at 0 °C. The reaction mixture was allowed to warm to ambient temperature overnight. The mixture was diluted with ether (100 mL) and washed successively with water (40 mL), HCl (5%-aq, 2×40 mL), water (40 mL), and $Na_2S_2O_3$ (20%-aq, 40 mL). The organic phase was dried ($MgSO_4$), filtered, and the solvents were removed at reduced pressure. The crude product was purified by chromatography (hexanes–EtOAc, 9:1) to give **8** (873 mg, 3.70 mmol, 65%) as a yellow oil. IR (neat) 2958, 2870, 1686, 1585, 1454 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.19 (d, J=7.2 Hz, 3H), 1.76 (dddd, J=13.8, 13.2, 9.0, 3.6 Hz, 1H), 2.17 (ddq, J=14.4, 4.8, 1.2 Hz, 1H), 2.55 (ddd, J=16.8, 12.6, 4.8 Hz, 1H), 2.66–2.71 (m, 1H), 2.77 (dt, J=16.8, 4.8 Hz, 1H), 7.60 (dd, J=3.0, 1.2 Hz, 1H); ^{13}C NMR (150 MHz) δ 19.9 (+), 30.8 (−), 35.7 (+), 35.8 (−), 103.2 (−), 164.7 (+), 192.2 (−). Anal. Calcd for C_7H_9IO: C, 35.62; H, 3.84. Found: C, 35.28; H, 4.07.

4.1.4. 4-Methyl-2-(2-nitrophenyl)-2-cyclohexen-1-one (4) and 1-nitro-2-(2-nitrophenyl)benzene. A solution of 2-iodo-4-methyl-2-cyclohexen-1-one (**8**) (405 mg, 1.72 mmol), 1-(tributylstannyl)-2-nitrobenzene (**9**)[36] (854 mg, 2.07 mmol), $PdCl_2(PhCN)_2$ (32.9 mg, 0.0858 mmol), $AsPh_3$ (52.6 mg, 0.172 mmol), and CuI (32.7 mg, 0.172 mmol), in NMP (4 mL) was heated at 80 °C (2 d). The reaction mixture was diluted with EtOAc (100 mL) and washed successively with NH_4OH (10%-aq, 3×30 mL) and H_2O (2×30 mL). The aqueous portions were combined and extracted with EtOAc (50 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated at reduced pressure. The crude product was purified by chromatography (hexanes–EtOAc, 9:1) to give an 11:1 mixture of **4** and 1-nitro-2-(2-nitrophenyl)benzene (318 mg) as a faint yellow oil.[37] Data from the mixture of **4** and 1-nitro-2-(2-nitrophenyl)benzene: IR (neat) 2960, 2871, 1682, 1525, 1352 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.26 (d, J=7.1 Hz, 3H), 1.74–1.91 (m, 1H), 2.14 (m, 1H), 2.46–2.84 (m, 3H), 6.81 (s, 1H), 7.25 (d, J=5.9 Hz, 1H), 7.47 (t, J=6.3 Hz, 1H), 7.60 (t, J=7.9 Hz, 1H), 8.02 (d, J=8.1 Hz, 1H); ^{13}C NMR (67.5 MHz) δ 20.2 (−), 30.5 (+), 31.6 (−), 37.0 (+), 124.1 (−), 128.7 (−), 131.6 (−), 131.9 (+), 133.2 (−), 138.1 (+), 148.5 (+), 152.1 (−), 196.4 (+).

4.1.5. 5-Methyl-2-(2-nitrophenyl)-2-cyclohexen-1-one (11). Reaction of 2-iodo-5-methyl-2-cyclohexen-1-one[13] (241 mg, 1.02 mmol), **9** (455 mg, 1.10 mmol), $PdCl_2(PhCN)_2$ (20.6 mg, 0.0537 mmol), $AsPh_3$ (31.6 mg, 0.103 mmol), and CuI (19.1 mg, 0.100 mmol) in NMP (1 mL), as described for **4** (80 °C, 2 d), gave after chromatography (hexanes–EtOAc, 9:1) **11** (175 mg, 0.757 mmol, 75%) as a pale yellow solid. Mp 107–109 °C; IR (neat) 1672, 1517, 1340 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.13 (d, J=6.0 Hz, 3H), 2.20 (dd, J=16.8, 12.6 Hz, 1H), 2.34 (ddd, J=18.6, 10.8, 2.4 Hz, 1H), 2.42–2.54 (m, 2H), 2.59 (dd, J=16.8, 4.2 Hz, 1H), 5.98 (d, J=2.4 Hz, 1H), 7.30 (dd, J=7.2, 1.2 Hz, 1H), 7.56 (dt, J=8.4, 0.6 Hz, 1H), 7.67 (dt, J=7.2, 0.6 Hz, 1H), 8.10 (dd, J=8.4, 1.2 Hz, 1H); ^{13}C NMR (150 MHz) δ 21. 0 (+), 30.8 (+), 38.9 (−), 45.5 (−), 124.9 (+), 127.3 (+), 129.5 (+), 129.7 (+), 133.8 (+), 136.6 (−), 146.6 (−), 159.8 (−), 199.1 (−). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 66.65; H, 6.12; N, 5.67.[38] HRMS calcd for $C_{13}H_{14}NO_3$ (M+H$^+$) 232.0974, found 232.0969.

4.1.6. 3-Methyl-2-(2-nitrophenyl)-2-cyclohexen-1-one (12). Reaction of 2-iodo-3-methyl-2-cyclohexen-1-one[25] (404 mg, 1.71 mmol), **9** (850 mg, 2.06 mmol), $PdCl_2(PhCN)_2$ (32.9 mg, 0.0858 mmol), $AsPh_3$ (52.4 mg, 0.171 mmol), CuI (32.8 mg, 0.172 mmol), in NMP (4 mL) as described for **4** (80 °C, 20 h), gave after chromatography (hexanes–EtOAc, 9:1) **12** (309 mg, 1.33 mmol, 78%) as a pale yellow solid. Mp 75–77 °C; IR (neat) 2943, 2873, 1663, 1622, 1522, 1356 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.78 (s, 3H), 2.03–2.09 (m, 2H), 2.10–2.18 (m, 2H), 2.46–2.59 (m, 2H), 7.17 (dd, J=7.8, 1.2 Hz, 1H), 7.47 (dt, J=8.4, 1.8 Hz, 1H), 7.60 (dt, J=7.8, 1.8 Hz, 1H), 8.07 (dd, J=8.4, 1.2 Hz, 1H); ^{13}C NMR (150 MHz) δ 21.8 (−), 22.4 (+), 32.3 (−), 37.5 (−), 124.4 (+), 128.4 (+), 131.7 (+), 132.5 (+), 133.0 (−), 135.1 (−), 148.8 (−), 156.4 (−), 196.6 (−). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67. Found: C, 67.33; H, 5.99.

4.1.7. 1,2,3,4-Tetrahydrocarbazole (3).[39] Hydrogen gas was bubbled through a mixture of 2-(2-nitrophenyl)-2-cyclohexen-1-one (**1**)[13] (54 mg, 0.25 mmol) and Pd/C (10%-Pd, 51 mg, 0.048 mmol) in MeOH (10 mL) for 5 min. The reaction was stirred under H_2 (1 atm, ambient temperature, 2 h). The mixture was filtered through Celite, the solvent was removed under reduced pressure, and the resulting crude product was purified by chromatography (hexanes–EtOAc, 8:2) to give **3** (41 mg, 0.24 mmol, 96%) as a white solid. Mp 116–118 °C (Aldrich Chem. Co. 118–120 °C).

Reaction of 2-(2-nitrophenyl)-1,3-cyclohexanedione (**15**)[40] (53 mg, 0.23 mmol) and Pd/C (10%, 52 mg, 0.049 mmol) in MeOH (10 mL), as described above (1 atm H_2, ambient temperature, 2 h), gave after chromatography

(hexanes–EtOAc, 8:2 followed by 1:1) in order of elution **3** (8.5 mg, 0.049 mmol, 22%) and **2**[13] (19 mg, 0.10 mmol, 43%).

Reaction of **5** (18 mg, 0.10 mmol) and Pd/C (10%, 19 mg, 0.018 mmol) in MeOH (5 mL), as described above (1 atm H_2, ambient temperature, 3 d), gave after chromatography (hexanes–EtOAc, 19:1 followed by 1:1) in order of elution **3** (6.0 mg, 0.035 mmol, 35%) and **5** (7.3 mg, 0.039 mmol, 39%).

4.1.8. 1-Methyl-1,2,3,4-tetrahydrocarbazole (19).[41] Reaction of 6-methyl-2-(2-nitrophenyl)-2-cyclohexen-1-one (**10**)[13] (37 mg, 0.16 mmol), and Pd/C (10%, 37 mg, 0.035 mmol) in MeOH (10 mL), as described for **3** (2 h), gave after chromatography (hexanes–EtOAc, 19:1) **19** (27 mg, 0.15 mmol, 94%) as a white solid. Mp 56–62 °C (lit.[41] mp 63–65 °C).

4.1.9. 2-Methyl-1,2,3,4-tetrahydrocarbazole (20).[28] Reaction of 5-methyl-2-(2-nitrophenyl)-2-cyclohexen-1-one (**11**)[13] (100 mg, 0.43 mmol) and Pd/C (10%, 100 mg, 0.094 mmol) in MeOH (10 mL), as described for **3** (2 h), gave after chromatography (hexanes–EtOAc–Et_3N, 490:10:1) **20** (74 mg, 0.40 mmol, 93%) as a white solid. Mp 98.5–99.5 °C (lit.[42] mp 98–100 °C).

4.1.10. 3-Methyl-1,2,3,4-tetrahydrocarbazole (21).[27] Reaction of **4** (150 mg, 0.65 mmol) and Pd/C (10%, 175 mg, 0.16 mmol) in MeOH (10 mL), as described for **3** (30 min), gave after chromatography (hexanes–EtOAc–Et_3N, 490:10:1) **21** (107 mg, 0.58 mmol, 89%) as a white solid. Mp 109–110 °C (lit.[27] 108–111 °C).

4.1.11. 4-Methyl-1,2,3,4-tetrahydrocarbazole (22). Reaction of **12** (155 mg, 0.67 mmol) and Pd/C (10%, 151 mg, 0.14 mmol) in MeOH (10 mL), as described for **3** (30 min), gave after chromatography (hexanes–EtOAc–Et_3N, 490:10:1) **22** (98 mg, 0.53 mmol, 79%) as an unstable solid.[43] ^{1}H NMR (270 MHz) δ 7.55 (d, J=6.3 Hz, 1H), 7.49 (br s, 1H), 7.21–7.16 (m, 1H), 7.11–7.04 (m, 2H), 3.13–3.04 (m, 1H), 2.61 (apparent t, J=5.3 Hz, 2H), 2.03–1.88 (m, 2H), 1.83–1.72 (m, 1H), 1.59–1.50 (m, 1H), 1.34 (d, J=6.9 Hz, 3H); lit.[16] δ 7.64 (br s, 1H), 7.57 (d, J=7.5 Hz, 1H), 7.28 (d, J=7.5 Hz, 1H), 7.11–7.06 (m, 2H), 3.13–3.11 (m, 1H), 2.69–2.70 (m, 2H), 2.00–1.95 (m, 2H), 1.83–1.79 (m, 1H), 1.59–1.55 (m, 1H), 1.37 (d, J=7.0 Hz, 3H).

4.1.12. 7-Methoxy-1,2,3,4-tetrahydrocarbazole (23)[24] **and 7-methoxy-1,2,3,4,4a,9a-hexahydrocarbazole (24).**[44] Reaction of 2-(4-methoxy-2-nitrophenyl)-2-cyclohexen-1-one (**13**)[13] (105 mg, 0.42 mmol) and Pd/C (10%, 104 mg, 0.098 mmol) in MeOH (10 mL), as described for **3** (20 min), gave after chromatography (hexanes–EtOAc–Et_3N, 490:10:1) an inseparable mixture of **23** (52.5 mg, 0.26 mmol, 62%) and **24** (7.9 mg, 0.04 mmol, 10%). The yields were estimated from the ^{1}H NMR spectrum of the mixture. Spectral data (^{1}H and ^{13}C NMR) of **23**[24] were in complete agreement with literature values. Compound **24** was identified based on the following comparison with literature data from the mixture of compounds. ^{1}H NMR (600 MHz) δ 6.95 (d, J=9.0 Hz), 6.28 (dd, J=7.8, 2.4 Hz), 6.27 (br s), 3.75 (s), 3.75–3.69 (m), 3.04 (q, J=6.0 Hz), 1.74–1.30 (m); ^{13}C NMR (150 MHz) δ 159.6, 152.0, 126.1, 123.3, 103.3, 97.2, 60.0, 55.3, 40.1, 29.3, 27.2, 22.4, 21.6; lit.[44] ^{1}H NMR (300 MHz) δ 6.90 (d, J=8.0 Hz, 1H), 6.30–6.15 (m, 2H), 3.70 (s, 3H), 3.76–3.56 (m, 1H), 3.36 (br s, 1H), 2.98 (dd, J=13.0, 12.0 Hz, 1H), 1.87–1.20 (m, 8H).

4.1.13. Methyl 2,3,4,9-tetrahydro-1*H*-carbazole-5-carboxylate (25)[45] **and methyl 2,3,4,4a,9,9a-hexahydro-1*H*-carbazole-5-carboxylate (26).** Reaction of 2-(6-carbomethoxy-2-nitrophenyl)-2-cyclohexen-1-one (**14**)[13] (50.8 mg, 0.18 mmol) and Pd/C (10%, 54.9 mg, 0.052 mmol) in MeOH (10 mL), as described for **3** (2 h), gave after chromatography (hexanes–EtOAc, 19:1) in order of elution **26** (16.8 mg, 0.073 mmol, 41%) and **25** (10.7 mg, 0.05 mmol, 28%) as white solids.[46] Spectral data for **25**: IR: 3414, 2930, 1692, 1644 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.77–1.93 (m, 4H), 2.75 (t, J=5.9 Hz, 2H), 2.88 (t, J=5.7 Hz, 2H), 3.94 (s, 3H), 7.11 (t, J=7.7 Hz, 1H), 7.43 (dd, J=8.1, 1.7 Hz, 1H), 7.64 (dd, J=7.4, 1.7 Hz, 1H), 7.93 (s, 1H).

Partial spectral data for **26**: ^{1}H NMR (270 MHz) δ 1.58–1.77 (m, 4H), 1.89–2.06 (m, 2H), 3.51 (p, J=6.2 Hz, 1H), 3.80–3.87 (m, 2H), 3.88 (s, 3H), 6.84 (d, J=7.9 Hz, 1H), 7.07 (t, J=7.9 Hz, 1H), 7.36 (d, J=7.9 Hz, 1H).

4.1.14. 8-Methyl-1,2,3,4-tetrahydrocarbazole (27).[47] Reaction of 2-(3-methyl-2-nitrophenyl)-2-cyclohexen-1-one (**16**)[13] (24.5 mg, 0.106 mmol) and Pd/C (10%, 22.1 mg, 0.0208 mmol) in MeOH (5 mL), as described for **3** (2 h), gave after chromatography (hexanes–EtOAc–Et_3N, 95:5:1) **27** (9.1 mg, 0.049 mmol, 46%) as a white solid. Mp 85–88 °C (lit.[48] 92–94.5 °C).

Alternative method. Reaction of 2-(3-methyl-2-nitrophenyl)-cyclohexan-1-one (**28**, see below) (45.1 mg, 0.193 mmol) and Pd/C (10%, 41.7 mg, 0.0391 mmol) in MeOH (10 mL), as described for **3** (2 h), gave after chromatography (hexanes–EtOAc, 7:3) **27** (9.3 mg, 0.050 mmol, 26%) as a white solid.

4.1.15. 8-Methyl-1,2,3,4-tetrahydrocarbazole (27) and 2-(3-methyl-2-nitrophenyl)-1-cyclohexanone (28). Reaction of **16** (90.7 mg, 0.39 mmol) and Pd/C (10%, 90.5 mg, 0.085 mmol) in MeOH (10 mL), as described for **3** (20 min), gave after chromatography (hexanes–EtOAc–Et_3N, 490:10:1) in order of elution **27** (12.7 mg, 0.07 mmol, 18%) as a white solid and **28** (31.9 mg, 0.14 mmol, 36%) as a white solid. Analytical data for **28**: mp 113–114 °C; IR (neat) 2934, 1707, 1516, 1370 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.74–1.86 (m, 2H), 1.94–2.05 (m, 2H), 2.15–2.22 (m, 1H), 2.33 (overlapping s and m, 4H), 2.41–2.49 (m, 1H), 2.51–2.57 (m, 1H), 3.64 (dd, J=12.6, 4.8 Hz, 1H), 7.16 (d, J=7.8 Hz, 1H), 7.21 (d, J=7.8 Hz, 1H), 7.38 (t, J=7.8 Hz, 1H); ^{13}C NMR (150 MHz) δ 17.8 (−), 25.5 (+), 27.7 (+), 35.3 (+), 42.2 (+), 52.6 (−), 127.5 (−), 129.7 (−), 130.0 (−), 130.0 (+), 130.9 (+), 151.5 (+), 207.8 (+). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 67.34; H, 6.79; N, 5.73.

4.1.16. 2-(3-Methyl-2-nitrophenyl)-1-cyclohexanone (28). Reaction of **16** (141 mg, 0.61 mmol) and Pd/C (10%,

13.4 mg, 0.013 mmol) in MeOH (10 mL), as described above (80 min) gave **28** (136 mg, 0.58 mmol, 95%).

4.1.17. 1,2,3,3a,4,8b-Hexahydrocyclopent[*b*]indole (29).[29,49] Reaction of 2-(2-nitrophenyl)-2-cyclopenten-1-one (**17**)[13] (117 mg, 0.58 mmol) and Pd/C (10%, 115 mg, 0.11 mmol) in MeOH (10 mL), as described for **3** (20 min), gave after solvent removal **29** (76.1 mg, 0.48 mmol, 83%) as a colorless oil.[50] ^{1}H NMR (600 MHz) δ 7.02 (d, J=7.3 Hz, 1H), 6.97 (t, J=7.5 Hz, 1H), 6.66 (dt, J=7.3, 1.0 Hz, 1H), 6.51 (d, J=7.3 Hz, 1H), 4.34 (ddd, J=8.5, 5.7, and 2.6 Hz, 1H), 3.76 (dt, J=8.7 and 2.6 Hz, 1H), 3.68 (br s, 1H), 2.02–1.44 (m, 6H); ^{13}C NMR (150 MHz) δ 151.3, 133.2, 127.2, 124.4, 118.1, 108.3, 63.3, 47.1, 36.8, 34.8, 24.3.

4.1.18. 5,6,7,8,9,10-Hexahydrocyclohept[*b*]indole (30).[24] Reaction of 2-(2-nitrophenyl)-2-cyclohepten-1-one (**18**)[13] (66 mg, 0.28 mmol) and Pd/C (10%, 66 mg, 0.06 mmol) in MeOH (10 mL), as described for **3** (2.5 h), gave after chromatography (hexanes–EtOAc, 95:5) **30** (38 mg, 0.20 mmol, 71%) as a white solid. Mp 134–136 °C (lit.[24] 135–138 °C).

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