

Palladium Complex-Catalyzed Reductive N-Heterocyclization of Nitroarenes: Novel Synthesis of Indole and 2H-Indazole Derivatives¹

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The dichlorobis(triphenylphosphine)palladium (PdCl₂(PPh₃)₂)-tin(II) chloride (SnCl₂) system shows high catalytic activity for the reductive N-heterocyclization of various 2-nitrostyrene and *N*-(2-nitrobenzylidene)amine derivatives when employed at 100 °C for 16 h under 20 kg cm⁻² of initial carbon monoxide pressure, to give the corresponding indole and 2*H*-indazole derivatives in good yield. For example, 2-phenylindole was obtained in 75% yield from the reductive N-heterocyclization of 2-nitrostilbene. Similarly, 2-propyl-2*H*-indazole was readily prepared in 83% yield by the reductive N-heterocyclization of *N*-(2-nitrobenzylidene)propylamine. A nitrene intermediate for the present reaction is proposed on the basis of deuterium-labeling experiments and the investigation of alkyl rearrangement in the construction of the indole skeleton. Carbon monoxide effectively operates as a deoxygenating agent of the nitro group to afford a nitrene intermediate.

Introduction

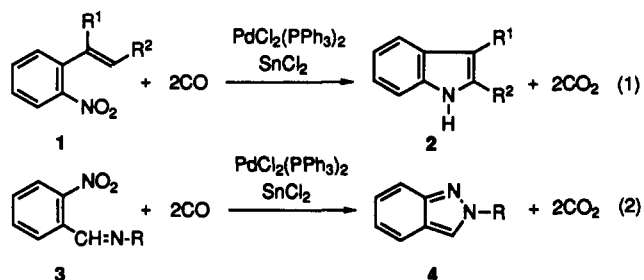
The chemistry of indole and 2*H*-indazole derivatives continues to be of interest because of their industrial and agricultural applications and their biological and analytical importance.² The development of a catalytic synthesis of such compounds by transition-metal complexes is therefore desirable.

For the construction of the indole skeleton, the Fischer indole synthesis is most widely used and has been extensively reviewed.³ Recently, numerous other approaches to the construction of the indole skeleton have been reported, many employing transition-metal catalysts,⁴ and those of palladium in particular.⁵ Hegedus et al. have reported the palladium(II) complex-catalyzed oxidative N-heterocyclization of 2-aminostyrene or 2-allylaniline derivatives to various indoles, including the ergot alkaloids.^{5a,b} Taniguchi et al. have reported the palladium complex-catalyzed isomerization of diphenylazirine to 3-phenylindole.^{5c} Larock et al. recently reported the palladium-catalyzed heteroannulation of internal alkynes with 2-iodoanilines to form indole derivatives.^{5d}

On the other hand, widely adapted syntheses of 2*H*-indazole derivatives employ the reduction of *N*-(2-nitrobenzylidene)amines using triethyl phosphite as a reducing agent^{6a} and the thermal decomposition of *N*-(2-azidobenzylidene)amines.^{6b} Unlike indoles, the catalytic

synthesis of 2*H*-indazoles using transition-metal complexes has never been reported.

Of the various synthetic methods for nitrogen heterocycles, we have been interested in transition-metal complex-catalyzed reductive N-heterocyclization of nitroarenes.⁷ Recently, Cenini et al. reported novel synthetic methods for indole,^{8a,b} benzotriazole,^{8c} and benzazole^{8d} derivatives using transition-metal carbonyl catalysts. However, their reaction conditions were severe (*i.e.*, at 220 °C under 80 kg cm⁻² of CO pressure), and a more effective catalyst is desirable. We have succeeded in developing a new catalyst system, *i.e.*, PdCl₂(PPh₃)₂-SnCl₂, for the efficient and facile syntheses of indoles and 2*H*-indazoles under considerably milder reaction conditions (at 100 °C under 20 kg cm⁻² of CO pressure). In this paper, we report the details of this novel synthetic route to indoles **2** and 2*H*-indazoles **4** via the reductive N-heterocyclizations of 2-nitrostyrenes **1** and *N*-(2-nitrobenzylidene)amines **3** respectively (eqs 1 and 2).



This is the first example of a transition-metal complex-catalyzed synthesis of 2*H*-indazole. Further, this process

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(7) We have also reported the transition-metal complex-catalyzed synthesis of several *N*-heterocyclic compounds via reductive N-heterocyclization reactions. For example; (a) Akazome, M.; Kondo, T.; Watanabe, Y. *J. Org. Chem.* 1993, 58, 310. (b) Watanabe, Y.; Suzuki, N.; Tsuji, Y.; Shim, S. C.; Mitsudo, T. *Bull. Chem. Soc. Jpn.* 1982, 55, 1116. (c) Watanabe, Y.; Suzuki, N.; Tsuji, Y. *Ibid.* 1982, 55, 2445.

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Table 1. Catalytic Activities of Several Transition-Metal Complexes^a

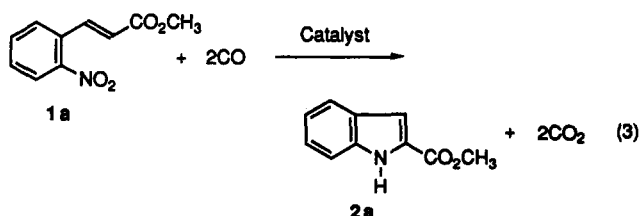
| entry | catalyst | additive | conv of 1a ^b (%) | yield of 2a ^b (%) |
|-----------------|---|-------------------|-----------------------------|------------------------------|
| 1 | PdCl ₂ (PPh ₃) ₂ | SnCl ₂ | 100 | 62 |
| 2 | PdCl ₂ (PPh ₃) ₂ | | 4 | 3 |
| 3 | | SnCl ₂ | 31 | 7 |
| 4 | 2PPh ₃ | SnCl ₂ | 30 | 10 |
| 5 | PdCl ₂ (PhCN) ₂ | SnCl ₂ | 14 | 10 |
| 6 | PdCl ₂ (PhCN) ₂ + 2PPh ₃ | SnCl ₂ | 96 | 52 |
| 7 | Pd(PPh ₃) ₄ | | 52 | 39 |
| 8 | PdCl ₂ (PBu ₃) ₂ | SnCl ₂ | 81 | 61 |
| 9 ^c | PdCl ₂ (dppe) | SnCl ₂ | 31 | 11 |
| 10 ^d | PdCl ₂ (bipy) | SnCl ₂ | 16 | 8 |
| 11 | PtCl ₂ (PPh ₃) ₂ | SnCl ₂ | 44 | 32 |
| 12 | NiCl ₂ (PPh ₃) ₂ | SnCl ₂ | 31 | 8 |
| 13 | RuCl ₂ (PPh ₃) ₃ | SnCl ₂ | 25 | 16 |
| 14 | RhCl(PPh ₃) ₃ | SnCl ₂ | 24 | 15 |

^a 1a (2.0 mmol), catalyst (0.10 mmol), additive (1.0 mmol), 1,4-dioxane (10 mL), CO (20 kg cm⁻²), 100 °C, 16 h. ^b Determined by GLC. ^c dppe = 1,2-bis(diphenylphosphino)ethane. ^d bipy = 2,2'-bipyridine.

is quite attractive since it can be regarded as a nitrogen-nitrogen bond-forming reaction by a transition-metal complex. It is quite different from the iron pentacarbonyl-catalyzed reductive homocoupling of nitroarenes to azo and/or azoxy compounds.⁹

Results and Discussion

Palladium-Catalyzed Synthesis of Indoles from 2-Nitrostyrene Derivatives. Catalytic activities of several transition-metal complexes were measured in the reductive N-heterocyclization of methyl 2-nitrocinnamate (1a) to methyl 2-indolecarboxylate (2a) (eq 3), and the results are summarized in Table 1.



The combination of PdCl₂(PPh₃)₂ and SnCl₂ was essential for catalytic activity (entries 1, 2, and 3). Monodentate phosphorus ligands such as triphenylphosphine and tributylphosphine were also indispensable for high catalytic activity (entries 1, 5, 6, and 8). The catalytic activity of the PdCl₂(PhCN)₂-SnCl₂ system was quite low, but by the addition of triphenylphosphine, the catalytic activity drastically increased (entries 5 and 6). The combination of a platinum complex (PtCl₂(PPh₃)₂) with SnCl₂ also showed moderate catalytic activity (entry 11), but the activities of other group VIII metal complexes were relatively low (entries 12–14).

The effects of additives on this reaction are summarized in Table 2. As mentioned above, the system of PdCl₂(PPh₃)₂ with SnCl₂ showed the highest catalytic activity (entry 1), and the employment of SnCl₄ instead of SnCl₂ with PdCl₂(PPh₃)₂ was less effective (entry 15). Similarly, a combination of Pd(PPh₃)₄ with SnCl₄ was ineffective (entry 16). Other Lewis acids such as CuCl₂, FeCl₃, ZnCl₂, and MoCl₅ were totally ineffective (entries 17–20). Furthermore, BF₄⁻ and CF₃SO₃⁻ are weakly or noncoordinating anions and the cationic palladium complexes generated

Table 2. Effect of Additives on the Reductive N-Heterocyclization of 1a^a

| entry | catalyst | additive | conv of 1a ^b (%) | yield of 2a ^b (%) |
|-------|--|------------------------------------|-----------------------------|------------------------------|
| 1 | PdCl ₂ (PPh ₃) ₂ | SnCl ₂ | 100 | 62 |
| 15 | PdCl ₂ (PPh ₃) ₂ | SnCl ₄ | 23 | 8 |
| 16 | Pd(PPh ₃) ₄ | SnCl ₄ | 24 | 8 |
| 17 | PdCl ₂ (PPh ₃) ₂ | CuCl ₂ | 4 | 3 |
| 18 | PdCl ₂ (PPh ₃) ₂ | FeCl ₃ | 4 | 2 |
| 19 | PdCl ₂ (PPh ₃) ₂ | ZnCl ₂ | 24 | 2 |
| 20 | PdCl ₂ (PPh ₃) ₂ | MoCl ₅ | 100 | 0 |
| 21 | PdCl ₂ (PPh ₃) ₂ | AgBF ₄ | 11 | 6 |
| 22 | PdCl ₂ (PPh ₃) ₂ | BF ₃ ·Et ₂ O | 7 | 0 |
| 23 | PdCl ₂ (PPh ₃) ₂ | SnBr ₂ | 46 | 23 |
| 24 | PdCl ₂ (PPh ₃) ₂ | SnI ₂ | 35 | 16 |

^a 1a (2.0 mmol), catalyst (0.10 mmol), additive (1.0 mmol), 1,4-dioxane (10 mL), CO (20 kg cm⁻²), 100 °C, 16 h. ^b Determined by GLC.

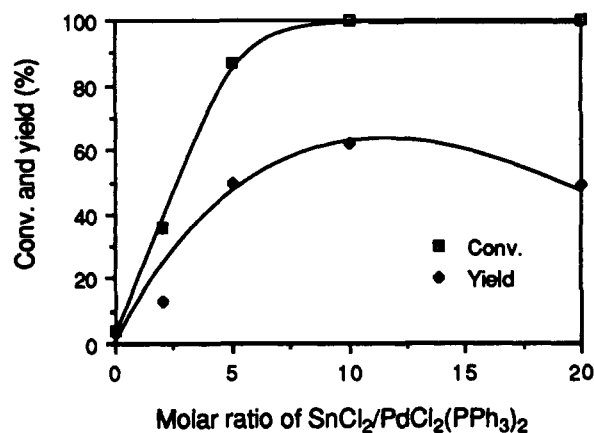


Figure 1. Effect of the molar ratio of SnCl₂/PdCl₂(PPh₃)₂ on the reductive N-heterocyclization of 1a to 2a. Reaction conditions: 1a (2.0 mmol), PdCl₂(PPh₃)₂ (0.10 mmol), and 1,4-dioxane (10 mL) under CO (20 kg cm⁻²) at 100 °C for 16 h.

by addition of these salts are often employed as active catalyst precursors in organic synthesis.¹⁰ However, the addition of BF₃·Et₂O or AgBF₄ did not improve the catalytic activity (entries 21 and 22). When the effect of the halogen in SnX₂ was examined, the catalytic activities dwindled in the order of Cl > Br > I (entries 1, 23, and 24).

The effect of the molar ratio of SnCl₂/PdCl₂(PPh₃)₂ on the reductive N-heterocyclization of 1a is shown in Figure 1. When the ratio was 10, the indole 2a was obtained in the best yield (62%). Further addition of SnCl₂ did not improve the yield of 2a. In the case when the ratio was 2 and the reaction time was 16 h, the conversion and yield were 36% and 13%, respectively. However, when the reaction time was extended to 48 h, both the conversion and yield increased to 100% and 55%, respectively. This result suggests that a catalytic amount of tin(II) chloride was sufficient in the present reaction.

The effect of solvents is summarized in Table 3. Among the solvents employed, 1,4-dioxane was the most effective (entries 1 and 25–27), since the reaction mixture was completely homogeneous even after the termination of the reaction.

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Table 4. Palladium-Catalyzed Reductive N-Heterocyclization of 2-Nitrostyrene Derivatives^a

| entry | substrate | product | yield ^b (%) |
|-------|-----------|---------|------------------------|
| 30 | | | 62 (60) |
| 31 | | | 75 (74) |
| 32 | | | 57 (41) |
| 33 | | | 50 |
| 34 | | | 52 |
| | | | 34 |
| 35 | | | (23) |
| 36 | | | 0 |

^a Substrate (2.0 mmol), PdCl₂(PPh₃)₂ (0.10 mmol), SnCl₂ (1.0 mmol), 1,4-dioxane (10 mL), CO (20 kg cm⁻²), 100 °C, 16 h. ^b GLC yields (isolated yields).

Although Hegedus et al. reported the palladium-catalyzed intramolecular cyclization of 2-aminostyrenes to indoles,^{5b} when a 2-aminostyrene such as 2-aminostilbene (7), rather than a 2-nitrostyrene, was employed in the present reaction, 2-phenylindole was not produced. This result completely excludes the possibility that the present reductive N-heterocyclization proceeds via a 2-aminostyrene-type intermediate.

During the reductive N-heterocyclization of 1a (entry 30 in Table 4), the evolution of carbon dioxide was detected and the yield of the generated carbon dioxide was 141% on the basis of 1a charged. This result suggests that carbon monoxide actually operates as an efficient deoxygenating agent for 2-nitrostyrenes, generating the corresponding nitrene intermediates. Under hydrogen pressure (20 kg cm⁻²), or water gas shift reaction conditions (H₂O (10 mmol) + CO (20 kg cm⁻²)), the present reaction did not occur.

Palladium-Catalyzed Synthesis of 2H-Indazoles from N-(2-Nitrobenzylidene)amine Derivatives. The reductive N-heterocyclization of N-(2-nitrobenzylidene)amines 3 proceeded smoothly using the same catalyst system to give the corresponding 2H-indazole derivatives 4 in good yields (eq 2).

The results are listed in Table 5. When (2-nitrobenzylidene)amines 3a–i bearing alkyl, aryl, methoxyalkyl, and 3-chlorophenyl substituents on the imino group were employed, the corresponding 2H-indazole derivatives 4a–i

Table 5. Palladium-Catalyzed Reductive N-Heterocyclization of N-(2-Nitrobenzylidene)amines^a

| entry | substrate | product | yield ^b (%) |
|-------|-----------|---------|------------------------|
| 37 | | | 62 (83) |
| 38 | | | 48 (64) |
| 39 | | | 65 |
| 40 | | | 51 |
| 41 | | | 63 |
| 42 | | | 53 |
| 43 | | | 74 |
| 44 | | | 75 |
| 45 | | | 59 |
| 46 | | | 37 |

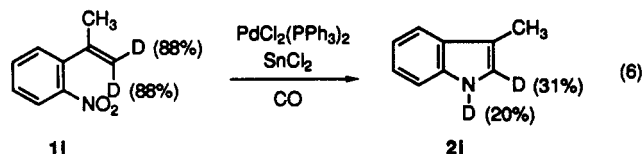
^a Substrate (2.0 mmol), PdCl₂(PPh₃)₂ (0.10 mmol), SnCl₂ (1.0 mmol), THF (10 mL), CO (20 kg cm⁻²), 100 °C, 16 h. ^b Isolated yields (GLC yields).

were obtained in 51–83% yields (entries 37–45). Steric hindrance presented by N-substituents did not affect the reaction (entries 44 and 45). Furthermore, 2H-indazoles having a dioxymethylene substituent on the aromatic ring were also obtained in good yields (entries 39 and 40). Upon employment of 2-nitrobenzaldehyde (8), 2,1-benzisoxazole (9) was obtained in 37% yield (entry 46).

A typical N-(2-aminobenzylidene)amine such as N-(2-aminobenzylidene)propylamine was not transformed into the corresponding 2H-indazole under the present reaction conditions.

Mechanism of the Reductive N-Heterocyclization of Nitroarenes. In order to investigate the mechanism, we carried out the following deuterium labeling experiments. First, 2-(2,2-dideuterio-1-methylvinyl)nitrobenzene (1i) was prepared by a Wittig reaction (see Experimental Section); the level of deuteriation in the β-positions of 1i was 88%. N-Heterocyclization of 1i afforded 3-methylindole 2i with 20% and 31% deuterium at the 1- and 2-positions respectively (eq 6).¹² This result clearly indicates that the deuterium at the β-position of the starting 2-nitrostyrene 1i is directly abstracted by the

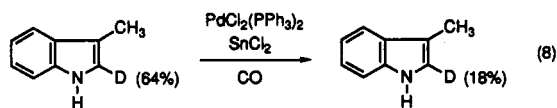
nitrogen atom (probably of a nitrene intermediate) in the construction of the indole skeleton.



Recently, Leconte et al. reported the generation of a metallacyclic intermediate in the reductive N-carbonylation of nitrobenzene.¹³ In the present reaction, however, carbon monoxide operates only as a reducing agent for the nitro group (*vide supra*) and is not incorporated into the product. Therefore, the generation of isocyanate or metallacyclic intermediates as postulated by Leconte et al. is unlikely in the present reaction. From the results of the deuterium labeling experiments and the reaction features mentioned previously, we now assume a nitrene intermediate,¹⁴ which would strongly coordinate to the metal as postulated for many traditional reductive N-carbonylations of nitroarenes¹⁵ and reductions of nitroso compounds.¹⁶ Accordingly, the most plausible route for the reductive N-heterocyclization of nitroarenes is illustrated in Scheme 1. Firstly, deoxygenation of the nitro group of the nitroarene by carbon monoxide would occur to give the corresponding nitrene intermediate, along with the generation of CO₂ (*vide supra*). In the case of indole synthesis, this electrophilic nitrene could attack the olefinic carbon, followed by a hydrogen transfer via a [1,5]-sigmatropic rearrangement, to give the corresponding indole.

The reductive N-heterocyclization of β,β -disubstituted 2-nitrostyrenes (eq 4) can also be rationalized by a similar mechanism (Scheme 2). Namely, the nitrene intermediate would also attack the olefinic carbon to form a nitrogen-carbon bond. Following [1,5]-sigmatropic rearrangement

(12) The reason that the deuterium content of the β -position of the starting 2-nitrostyrene 11 was reduced from 88% to 31% in the generated 3-methylindole 21 (at the 2 position) could be explained by the following additional experiment. Namely, 3-methylindole labeled by deuterium at the 2 position (64%) was separately prepared and treated under the present reaction conditions (eq 8). In the presence of both PdCl₂(PPh₃)₂ and SnCl₂, the deuterium content at the 2 position was drastically reduced to 18%, although the deuterium content at the 2 position did not change at all in the absence of both PdCl₂(PPh₃)₂ and SnCl₂. These results suggest that the deuterium on the indole ring would easily exchange with the other hydrogens on the indole ring, solvent, and/or triphenylphosphine ligand.



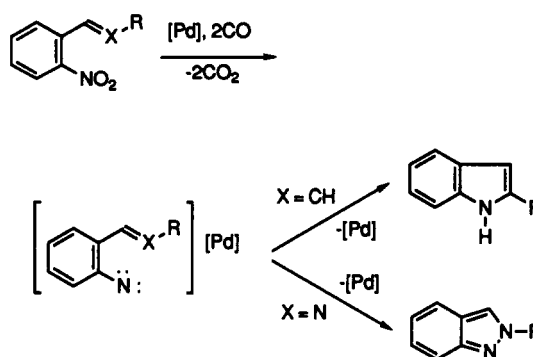
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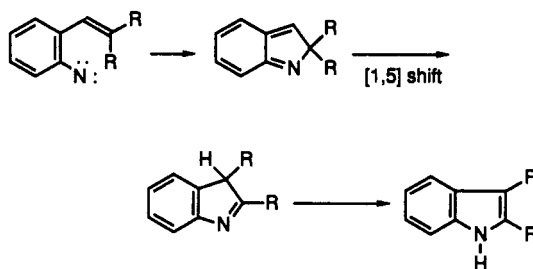
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Scheme 1



Scheme 2



of an *alkyl* group from the 2 position to the 3 position on the indole ring, and subsequent hydrogen migration, the corresponding more stable indoles would be obtained. A similar rearrangement of alkyl substituents has been reported by Sundberg et al. in the synthesis of indoles from β,β -disubstituted 2-nitrostyrenes using an excess of triethyl phosphite as the reducing agent.¹⁷ In the case of pyrrole analogs, Chiu and Sammes have reported that a 2,2-disubstituted 2*H*-pyrrole can be reversibly interconverted to give the more stable 1*H*-pyrrole via [1,5]-sigmatropic rearrangement.¹⁸

In the case of the formation of 2*H*-indazole derivatives, the electrophilic nitrene could attack the nitrogen atom of the imino substituent to give the corresponding 2*H*-indazole derivatives.

In summary, this paper reports the discovery of a new palladium-catalyzed reductive N-heterocyclization of nitroarenes for the synthesis of indole and 2*H*-indazole derivatives. We anticipate that this reductive N-heterocyclization will be applicable to the construction of other N-heterocyclic ring systems.

Experimental Section

General. The GLC analyses were carried out on gas chromatographs equipped with glass columns (3 mm i.d. \times 3 m) packed with Silicone OV-17 (2% on Chromosorb W(AW-DMCS), 80-100 mesh) and PEG-HT (5% on Uniport HP, 60-80 mesh). In the case of gas-phase analysis, gaseous products were collected in a gas buret and analyzed on a gas chromatograph equipped with a thermal conductivity detector and a stainless column (3 mm i.d. \times 3 m) packed with active carbon (60-80 mesh). The ¹H-NMR spectra were recorded at 90 and/or 270 MHz. ¹³C-NMR spectra were recorded at 25.05 and/or 67.80 MHz. Samples were analyzed in CDCl₃, and the chemical shift values are expressed relative to Me₄Si as internal standard. Elemental analyses were performed at Microanalytical Center of Kyoto University.

Materials. The reagents employed in this study were dried and purified before use by the usual procedures. Carbon monoxide (>99.9%) was used without further purification.

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Transition-metal complexes such as $\text{PdCl}_2(\text{PPh}_3)_2$,¹⁹ $\text{Pd}(\text{PPh}_3)_4$,²⁰ $\text{PdCl}_2(\text{PBu}_3)_2$,²¹ $\text{PdCl}_2(\text{dppe})$,²² $\text{PdCl}_2(\text{bipy})$,²³ $\text{PdCl}_2(\text{PhCN})_2$,²⁴ $\text{PtCl}_2(\text{PPh}_3)_2$,²⁵ $\text{NiCl}_2(\text{PPh}_3)_2$,²⁶ $\text{RuCl}_2(\text{PPh}_3)_3$,²⁷ and $\text{RhCl}(\text{PPh}_3)_3$ ²⁸ were prepared by the literature methods. SnCl_2 , SnBr_2 , SnI_2 , and AgBF_4 were commercially available and were used without further purification. Starting materials were prepared by the following procedure. Methyl 2-nitrocinnamate (**1a**) was prepared by esterification of 2-nitrocinnamic acid with dimethyl sulfate according to the literature.²⁹ 2-Nitrostilbene (**1b**), 2-(2-methyl-1-propenyl)nitrobenzene (**1g**), and (2-nitrobenzylidene)cyclopentane (**1h**) were prepared by the Wittig-Horner reaction of 2-nitrobenzyl bromide with triethyl phosphite.³⁰ 2-Isopropenylnitrobenzene (**1c**) was prepared by a Wittig reaction.³¹ 2-Nitrostyrene (**1d**) was prepared by decarboxylation of 2-nitrocinnamic acid using copper powder in quinoline according to the literature.³² 2-Nitrochalcone (**1e**) was prepared by the condensation of 2-nitrobenzaldehyde with acetophenone under basic conditions.³³ 2-(2,2-Dideuterio-1-methylvinyl)nitrobenzene (**1i**) was prepared by the Wittig reaction of 2-nitroacetophenone with (methyl-*d*₃)triphenylphosphonium iodide.³¹ 2-Aminostilbene (**7**) was prepared by reduction of 2-nitrostilbene with iron powder in acetic acid and ethanol.⁵⁴ *N*-(2-Nitrobenzylidene)amines **3a**–**i** were readily obtained by a condensation of 2-nitrobenzaldehyde and the corresponding amines using MgSO_4 as a dehydrating reagent in ether.

Preparation of 2-Deuterio-3-methylindole (2i). *N*-(Phenylsulfonyl)-2-lithio-3-methylindole was prepared by the literature method,³⁴ and it was decomposed by the addition of deuterium oxide to give *N*-(phenylsulfonyl)-2-deuterio-3-methylindole. Subsequently, the sulfonyl substituent as a *N*-protecting group was removed by hydrolysis to afford the corresponding indole.³⁵

General Procedures for Palladium-Catalyzed Reductive *N*-Heterocyclization of Nitroarenes. A mixture of nitroarene derivative (2.0 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (0.10 mmol), SnCl_2 (1.0 mmol), and solvent (10 mL) was placed in a 50-mL stainless steel autoclave equipped with a glass liner and a magnetic stirring bar. The unit was sealed and then purged three times with 10 kg cm^{-2} pressurization–depressurization cycles of carbon monoxide. The reactor was then pressurized to 20 kg cm^{-2} with carbon monoxide (at rt), heated to 100 °C within 10 min with stirring, and held at this temperature for 16 h. The reaction was terminated by rapid cooling, and gaseous products were discharged. The resulting brown solution was analyzed by GLC and FT-IR. The products were isolated by Kugelrohr distillation and/or medium pressure column chromatography (absorbent, silica gel; eluent, a mixture of hexane and ethyl acetate). The identification of the products was confirmed by FT-IR, ¹H- and ¹³C-NMR, elemental analyses, and GC-MS.

Reductive *N*-Heterocyclization Products. Methyl 2-indolecarboxylate (**2a**)³⁶ (mp 148.0–148.4 °C), 2-phenylindole

(**2b**)³⁷ (mp 187.8–188.5 °C), 3-methylindole (**2c**)³⁸ (mp 92.5–93.4 °C), 2-benzoylindole (**2e**)³⁹ (mp 152.2–153.0 °C), 2,3-dimethylindole (**2g**)⁴⁰ (mp 105.5–106.5 °C), 1,2,3,4-tetrahydrocarbazole (**2h**)⁴¹ (mp 114–117 °C), 2-phenylquinoline (**6a**)⁴² (mp 82.0–82.5 °C), 2-phenyl-2*H*-indazole (**4b**)⁴³ (mp 81.5–81.8 °C), 5,6-(methylenedioxy)-2-phenyl-2*H*-indazole (**4d**)⁴⁴ (mp 173–175 °C), 2-isopropyl-2*H*-indazole (**4e**)⁴⁵ (bp 130 °C/0.4 mmHg (Kugelrohr distillation)), and 2-*tert*-butyl-2*H*-indazole (**4h**)⁴⁶ (mp 56.5–57.5 °C), 2,1-benzisoxazole (**9**)⁴⁷ (bp 150 °C/13 mmHg (Kugelrohr distillation)) were identical in all respects with authentic samples.

2-Propyl-2*H*-indazole (4a): colorless liquid; bp 160 °C/0.9 mmHg (Kugelrohr distillation); ¹H NMR (CDCl_3 , 90 MHz) δ 0.90 (t, 3H), 1.99 (sextet, 2H), 4.31 (t, 2H), 6.95–7.76 (m, 4H), 7.86 (s, 1H); ¹³C NMR (CDCl_3 , 25.05 MHz) δ 11.2, 24.0, 55.2, 117.3, 120.0, 121.4, 121.6, 122.5, 125.6, 148.8; MS, *m/z* (relative intensity) 160 (*M*⁺, 44.3), 131 (*M*⁺ – Et, 96.1), 118 (*M*⁺ – Pr, 100). Anal. Calcd for $\text{C}_{10}\text{H}_{12}\text{N}_2$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.72; H, 7.59; N, 17.36.

5,6-(Methylenedioxy)-2-propyl-2*H*-indazole (4c): yellow solid; mp 98.7–99.5 °C; ¹H NMR (CDCl_3 , 90 MHz) δ 0.92 (t, 3H), 1.97 (sextet, 2H), 4.24 (t, 2H), 5.92 (s, 2H), 6.84 (s, 1H), 6.98 (s, 1H), 7.66 (s, 1H); ¹³C NMR (CDCl_3 , 25.05 MHz) δ 11.1, 23.8, 54.9, 93.9, 94.7, 100.7, 116.6, 121.8, 144.9, 145.6, 148.4; MS, *m/z* (relative intensity) 204 (*M*⁺, 46.6), 175 (*M*⁺ – Et, 100), 162 (*M*⁺ – Pr, 62.8). Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2$: C, 64.69; H, 5.95; N, 13.72; O, 15.67. Found: C, 64.61; H, 5.88; N, 13.67.

2-(3-Methoxypropyl)-2*H*-indazole (4f): colorless liquid; bp 190 °C/0.2 mmHg (Kugelrohr distillation); ¹H NMR (CDCl_3 , 270 MHz) δ 1.99 (m, 2H), 3.31 (t, *J* = 5.9 Hz, 2H), 3.31 (s, 3H), 4.50 (t, *J* = 6.8 Hz, 2H), 7.06 (ddd, *J* = 0.7, 6.6, 8.3 Hz, 1H), 7.26 (ddd, *J* = 0.7, 6.6, 8.8 Hz, 1H), 7.63 (ddd, *J* = 0.7, 1.0, 8.3 Hz, 1H), 7.71 (ddd, *J* = 0.7, 1.0, 8.8 Hz, 1H), 7.89 (s, 1H); ¹³C NMR (CDCl_3 , 25.05 MHz) δ 30.5, 50.4, 58.7, 68.8, 117.2, 120.1, 121.5, 122.4, 123.2, 125.8, 148.8; MS, *m/z* (relative intensity) 190 (*M*⁺, 27.2), 175 (*M*⁺ – Me, 26.9), 132 (64.4), 131 (*M*⁺ – $\text{CH}_2\text{CH}_2\text{OCH}_3$, 100), 119 (30.0). Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$: C, 69.45; H, 7.42; N, 14.72. Found: C, 69.41; H, 7.53; N, 14.74.

2-(3-Chlorophenyl)-2*H*-indazole (4g): white solid; mp 102.5–104.0 °C; ¹H NMR (CDCl_3 , 90 MHz) δ 7.07–7.97 (m, 8H), 8.35 (s, 1H); ¹³C NMR (CDCl_3 , 25.05 MHz) δ 117.7, 118.4, 120.1, 120.9, 121.1, 122.5, 126.9, 127.5, 130.2, 135.1, 141.0, 149.5; MS, *m/z* (relative intensity) 230 ($[\text{M}^{37}\text{Cl}]^+$, 33.2), 228.0 ($[\text{M}^{35}\text{Cl}]^+$, 100), 192 (20.2). Anal. Calcd for $\text{C}_{13}\text{H}_9\text{N}_2\text{Cl}$: C, 68.28; H, 3.97; N, 12.25. Found: C, 68.44; H, 3.75; N, 12.29.

2-(2,6-Dimethylphenyl)-2*H*-indazole (4i): white solid; mp 92.3–93.0 °C; ¹H NMR (CDCl_3 , 270 MHz) δ 1.97 (s, 6H), 7.10–7.35 (m, 5H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.80 (dd, *J* = 0.7, 8.8 Hz, 1H), 7.95 (s, 1H); ¹³C NMR (CDCl_3 , 25.05 MHz) δ 17.2, 118.0, 120.3, 121.9, 122.7, 124.4, 126.1, 129.3, 135.4, 139.6, 149.1. Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2$: C, 81.05; H, 6.35; N, 12.60. Found: C, 81.28; H, 6.47; N, 12.70.

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