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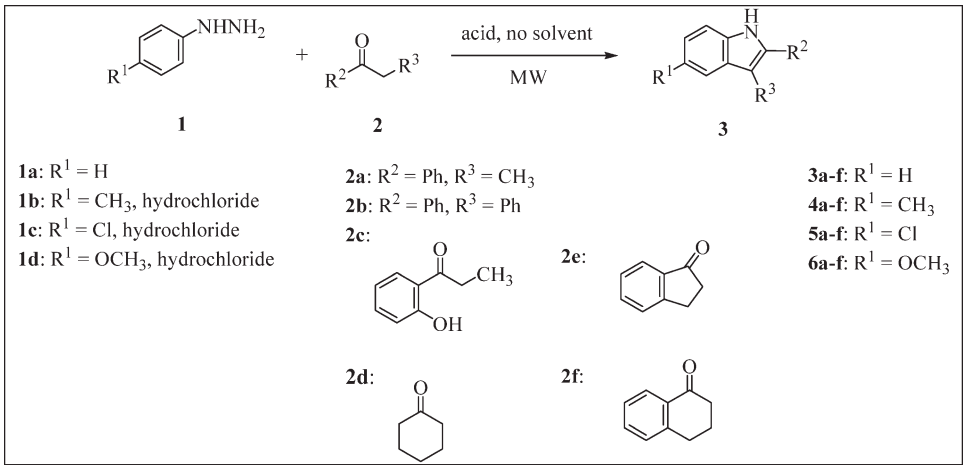

The Fischer indole synthesis was carried out using microwaves instead of conventional heating procedures. When the mixture of phenylhydrazine, cyclohexanone and zinc chloride was irradiated at 600 W for 3 min, 76% of 1,2,3,4-tetrahydrocarbazole was obtained. However, when zinc chloride was replaced with *p*-toluenesulfonic acid (*p*-TSA), the reaction yielded 91% of 1,2,3,4-tetrahydrocarbazole. Thus, a series of indoles were prepared using microwaves in the presence of *p*-TSA catalyst.

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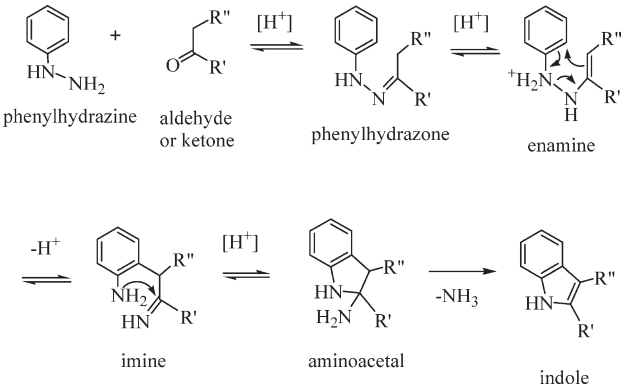
INTRODUCTION

The synthesis of indoles has always been in the frontline of researches because of their many potential uses in the field of medicine [1–3]. Reviews have been written on the diverse methods for the synthesis of indole and its derivatives [3–5]. However, of the many available methods for the synthesis of indoles, the Fischer indole reaction, which was described over a century ago, is still the most versatile and important method for the synthesis of this group of compounds [3,4,6]. The reaction produces the aromatic heterocycle indole from substituted phenylhydrazines and aldehyde or ketone under acidic conditions. Initially, the reaction forms a phenylhydrazone, which undergoes isomerization to the respective enamine (or ene-hydrazine). After protonation, a cyclic [3,3]-sigmatropic rearrangement occurs to produce an imine. The resulting imine then forms a cyclic aminoacetal (or aminal) which, under acid catalysis, eliminates NH_3 to give the energetically favorable indole (Scheme 1).

The choice of acid catalysts is very important. Brønsted acids such as HCl, H_2SO_4, polyphosphoric acid, and *p*-toluenesulfonic acid (*p*-TSA) have been used successfully. Lewis acids, such as boron trifluoride, zinc chloride, iron chloride, and aluminum chloride are also used as catalysts [4,7,8]. More recently, thionyl chloride in ethanol was also experimented for the synthesis of substituted (*N*-acylamino)-2-phenylindoles [9]. New methods for the Fischer indole synthesis have been developed such as the one-pot, multiple component method, which has been reported to give indoles in good yield [10]. The method is convenient because it usually starts from commercially available precursors, thus eliminating the necessity of preparing and isolating the unstable arylhydrazones (Scheme 2) [11].

A number of studies utilizing this method have been reported [12]. The one-pot synthesis (90°C, 3 h) of indoles in acetic acid medium from phenylhydrazine hydrochloride with various acyclic ketones has been reported in literature [7]. To better improve the method, microwave irradiations were used instead of the conventional heating procedures [13]. A number of reports have indicated that the use of microwave radiations with the one-pot method improves the yield of indoles, reduces reaction time, and eliminates the need of solvents for the

Scheme 1. Fischer indole synthesis.



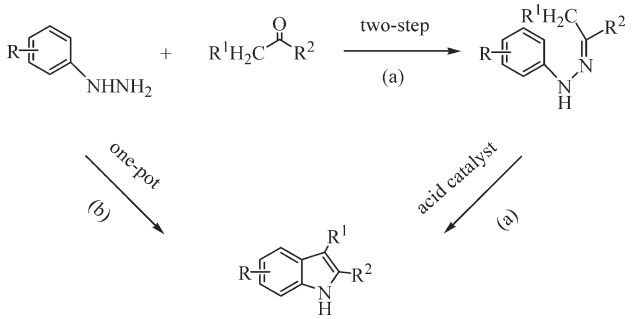
reactions [7,14]. Aside from this, use of solid-support and solid catalysts along with the one-pot, solvent-free microwave-assisted reaction is gaining much attention in the scientific community [1,7,8,15–18].

The goal of this present study is to synthesize indoles by one-pot-one-step, solvent-free, microwave-assisted Fischer indole reaction (Scheme 3). In the course of the study, several protic acids were investigated for their efficiency as catalysts for the reaction. These were used in the model reaction between phenylhydrazine and cyclohexanone and the mixture irradiated with microwaves at 600 W for 3 min. From among the acids investigated (H_2SO_4, HCl, $ZnCl_2$, and *p*-TSA), *p*-TSA gave the highest yield of 1,2,3,4-tetrahydrocarbazole (91%). The conventional Fischer reaction was then carried out using *p*-TSA without a solvent (120°C, 4 h, 15% yield) and with xylene as solvent (120°C, 6 h, 19% yield) [19]. The microwave-assisted reaction gave a better yield at shorter reaction time. This method was applied to various phenylhydrazines and enolizable ketones, and the results are discussed in this article.

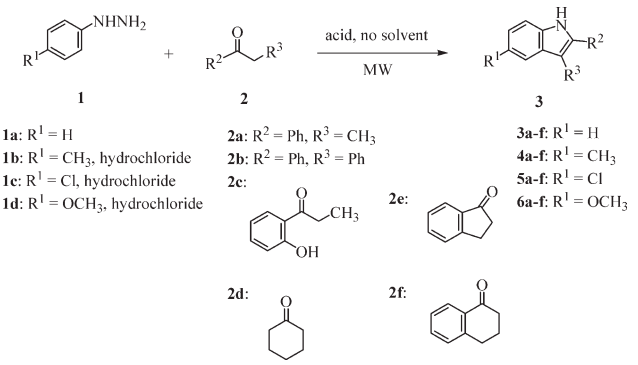
RESULTS AND DISCUSSION

A one-pot-one-step, solvent-free, microwave-assisted Fischer indole synthesis (Scheme 3) is investigated

Scheme 2. Fischer indole synthesis. (a) classical two-step procedure and (b) one-pot-one-step procedure.



Scheme 3. One-pot-one-step, microwave-assisted Fischer indole synthesis.



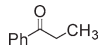
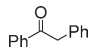
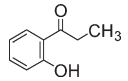
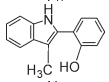
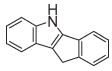
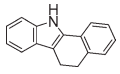
using various readily available substituted phenylhydrazines and enolizable ketones.

Table 1 gives the results of the synthesis of indoles when phenylhydrazine **1a** was reacted with various enolizable ketones **2a–f** (Scheme 4). The results show that the reaction of phenylhydrazine **1a** with the different enolizable ketones **2a–f** gave excellent yields (76–96%) of the corresponding 1*H*-indoles **3a–f**. Liu *et al*. [18] reported 60% yield of 3-methyl-2-phenylindole **3a,** 31% yield of 2,3-diphenylindole **3b** and 54% yield of 1,2,3,4-tetrahydrocarbazole **3d** from phenylhydrazine and α-branched aldehydes via rearrangement of 3,3-disubstituted indolenine intermediates, with the reaction conducted at 110°C for 6 h. Reduction of 2-(2-nitrophenyl)-2-cyclohexene-1-one with Pd/C catalyst and 1 atm H_2 at ambient temperature yielded 22% of 1,2,3,4-tetrahydrocrbazole **3d** [20]. The Fischer reaction of phenylhydrazine and cyclohexanone carried out in the presence of Brønsted acidic ionic liquid gave a comparable yield of 1,2,3,4-tetrahydrocarbazole **3d** (92%, 70°C, 1 h) [11]. The microwave-assisted Bischler reaction of aniline and 2-bromocyclohexanone in ethoxyethanol (325 W, 10 min, N_2 atmosphere) yielded 84% of 1,2,3,4-tetrahydrocarbazole [21] **3d** whereas the microwave-assisted cycloisomerization of 2-alkynylanilines in water without catalysts, acids, or bases, gave 46% of 2-phenylindole (200°C, 90 min) [22].

Table 2 gives the results for the reaction of *p*-methylphenylhydrazine **1b** and various enolizable ketones **2a–f** (Scheme 5). The results show excellent yields (84–97%) of the different 1*H*-indoles **4a–f** from the one-pot-one-step, solvent-free, microwave-assisted method. Chen and Hu [21] reported 83% yield of 6-methyl-1,2,3,4-tetrahydrocarbazole **4d** by irradiating a mixture of 4-methylaniline and 2-bromocyclohexanone at 325 W for 10 min under nitrogen condition. The present method yielded 93% **4d** by irradiating a mixture of 4-methylphenylhydrazine hydrochloride and cyclohexanone at 80 W for 5 min in the presence of *p*-TSA catalyst.

Table 1

Reaction of phenylhydrazine **1a** and ketones **2a–f**.

Entries		2	Power (W)	Time (min)	Product	3	Yield[a] (%)
1		**2a**	600	3		**3a**	86
2		**2b**	200	4.5		**3b**	76
3		**2c**	200	5		**3c**	94
4		**2d**	600	3		**3d**	91
5		**2e**	600	3		**3e**	83
6		**2f**	600	2.5		**3f**	96

[a] Isolated yield.

The reaction of *p*-chlorophenylhydrazine **1c** and various enolizable ketones **2a–f** conducted under the present method gave excellent product yields (81–95%) of 1*H*-indoles **5a–f** (Table 3, Scheme 6). When the mixture of 4-chloroaniline and 2-bromocyclohexanone was irradiated at 325 W for 10 min under nitrogen condition, yield of 71% 6-chloro-1,2,3,4-tetrahydrocarbazole [21] **5d** was reported. The present method gave 84% **5d** when the mixture of *p*-chlorophenylhydrazine hydrochloride and cyclohexanone was irradiated at 200 W for 1 min in the presence of *p*-TSA catalyst.

Good yields of the products **6a–f** (26–83%) were also obtained from the reaction of *p*-methoxyphenylhydrazine **1d** and various enolizable ketones **2a–f** as shown in Table 4 (Scheme 7). Entry 4 of Table 4 shows that 83% 6-methoxy-1,2,3,4-tetrahydrocabazole **6d** was obtained when the mixture of *p*-methoxyphenylhydrazine hydrochloride and cyclohexanone was irradiated at 200 W for 1 min in the presence of *p*-TSA catalyst. On the other hand, 49% **6d** was obtained when the mixture of 4-methoxyaniline and 2-bromocyclohexanone was irradiated at 325 W for 10 min under nitrogen condition [21].

3*H*-Indoles **3–6g** were also synthesized by the one-pot-one-step, solvent-free, microwave-assisted Fischer reaction using the unsymmetrically-substituted ketone isobutyrophenone **2g** (Scheme 8). The results in Table 5 show that the reactions also gave good product yields (54–78%).

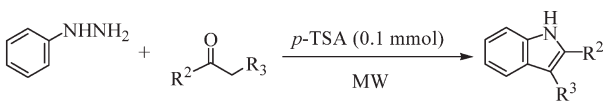
CONCLUSION

The one-pot-one-step, microwave-assisted Fischer indole synthesis is a convenient method for the synthesis of various indoles from substituted phenylhydrazines and enolizable ketones. The method does not require the preparation and isolation of the unstable arylhydrazones because commercially available precursors are used as starting reagents. The results revealed that the one-pot-one-step, solvent-free microwave-assisted Fischer indole reaction gave higher product yields at shorter reaction times as compared with previously reported methods. In summary, the present study describes a method for the synthesis of indoles from substituted phenylhydrazines and enolizable ketones that gives better product yields at shorter reaction times and does not necessitate the use of solvent.

EXPERIMENTAL

The microwave oven used for the reactions was Model YD-17 (W), Yoshii Electric. The reaction vessel was a Pyrex test tube (15 mm i.d. × 17 mm o.d. × 105 mm h) placed in a 50-mL Erlenmeyer flask for support. The melting points are uncorrected. Column chromatography was performed on silica gel (Wakogel C-200). Unless otherwise stated, anhydrous sodium sulfate was used as the drying agent. The IR spectra were measured on a Hitachi Model 270-30 IR spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were measured at 500 and 125 MHz, respectively, on a Varian Unity plus-500W NMR

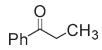
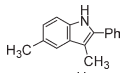
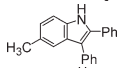
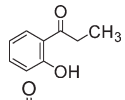
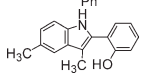
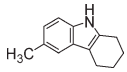
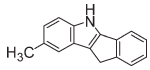
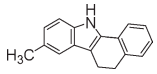
Scheme 4. One-pot-one-step, microwave-assisted reaction of phenylhydrazine **1a** and enolizable ketones **2a-f**.



1a (1.0 mmol) **2a-f** (1.5 mmol) **3a-f**

Table 2

Reaction of *p*-methylhydrazine **1b** and ketones **2a–f**.

Entries		2	Power (W)	Time (min)	Product	4	Yield[a] (%)
1		**2a**	80	5		**4a**	88
2		**2b**	80	5		**4b**	87
3		**2c**	80	6		**4c**	84
4		**2d**	80	5		**4d**	93
5		**2e**	80	5		**4e**	92
6		**2f**	80	5		**4f**	97

[a] Isolated yield.

spectrometer, using tetramethylsilane as the internal standard. The starting materials are available commercially and used as received.

One-pot-one-step, solvent-free, microwave-assisted Fischer indole synthesis. A mixture of phenylhydrazine (1.0 mmol), enolizable ketone (1.5, 2.0 or 3.0 mmol), and *p*-TSA (0.1 mmol) was placed in a test tube, plugged with quartz wool and irradiated with microwaves at a specific power for several minutes. The resulting mixture was then extracted with acetone, filtered, and then concentrated in a rotary evaporator. The residue was subjected to silica gel column chromatography using benzene, benzene:hexane, hexane:ethyl acetate, or hexane:acetone to give the various products.

3-Methyl-2-phenylindole (3a). Colorless crystals from hexane: m.p. 91°C (lit.[23] m.p. 90–92°C); IR (KBr): 3420 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.47 (s, 3H), 7.15 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.21 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.35–7.38 (m, 2H), 7.48 (dd, J = 7.5 Hz, 7.5 Hz, 2H), 7.57–7.62 (m, 3H), 8.01 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.6 (q), 108.7 (s), 110.6 (d), 118.9 (d), 119.5 (d), 122.3 (d), 127.3 (d), 127.7 (d), 128.8 (d), 130.0 (s), 133.3 (s), 134.0 (s), 135.8 (s).

2,3-Diphenylinddole (3b). Colorless crystals from hexane: m.p. 122–124°C (lit.[24] m.p. 122–124°C); IR (KBr): 3392 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 7.15 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.25 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.27–7.35 (m, 4H), 7.38 (dd, J = 7.5 Hz, 7.5 Hz, 2H), 7.41–7.46 (m, 5H), 7.69 (d, J = 7.5 Hz, 1H), 8.24 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 110.9 (d), 115.0 (s), 119.7 (d), 120.4 (d), 122.7 (d), 126.2 (d), 127.7 (d), 128.1 (d), 128.5 (d), 128.6 (d), 128.7 (d), 130.1 (s), 132.7 (s), 134.1 (s), 135.0 (s), 135.9 (s).

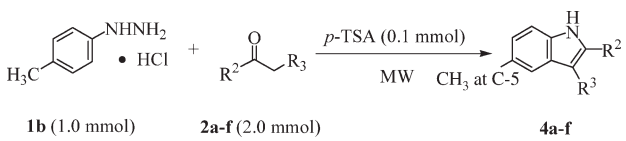
2-(2′-Hydroxyphenyl)-3-methylindole (3c). Yellow liquid [25]: IR (neat): 3364 cm^{-1} (O—H); ^1H NMR ($CDCl_3$): δ 2.32 (s, 3H), 5.54 (br s, 1H), 6.99–7.05 (m, 2H), 7.18 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.25 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.32 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.35–7.41 (m, 2H), 7.62 (d, J = 7.5 Hz, 1H), 8.06 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.3 (q), 110.6 (s), 110.9 (d), 115.8 (d), 119.0 (d), 119.1 (s), 119.8 (d), 120.7 (d), 122.7 (d), 129.3 (s), 129.4 (s), 130.0 (d), 130.4 (d), 136.4 (s), 153.3 (s).

1,2,3,4-Tetrahydrocarbazole (3d). Pale yellow crystals from hexane: m.p. 115–116°C (lit.[26] m.p. 115–116°C); IR (KBr) [21]: 3400 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 1.85–1.95 (m, 4H), 2.69–2.74 (m, 4H), 7.06 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.10 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.26 (d, J = 7.5 Hz, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.65 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 20.9 (t), 23.1 (t), 23.1 (t), 23.2 (t), 110.1 (s), 110.3 (d), 117.7 (d), 119.0 (d), 120.9 (d), 127.7 (s), 134.0 (s), 135.6 (s).

5,10-Dihydroindeno[1,2-b]indole (3e). Colorless crystals from benzene: m.p. 209°C (lit.[27] m.p. 208–210°C); IR (KBr): 3412 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 3.73 (s, 2H), 7.14–7.24 (m, 3H), 7.33 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.42–7.47 (m, 2H), 7.54 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 8.29 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 30.3 (t), 112.0 (d), 117.3 (d), 119.0 (d), 120.2 (d), 121.7 (d), 121.8 (s), 124.7 (s), 124.8 (d), 125.5 (d), 126.5 (d), 135.0 (s), 140.6 (s), 143.3 (s), 147.8 (s).

6,11-Dihydro-5H-benzo[a]carbazole (3f). Colorless crystals from hexane/benzene: m.p. 161°C (lit.[28] m.p. 160–161°C); IR (KBr): 3404 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.96–3.00 (m, 2H), 3.05–3.09 (m, 2H), 7.12 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.17 (dd, J = 7.5 Hz, 7.5 Hz, 2H), 7.24–7.29 (m, 2H), 7.33 (d, J = 7.5 Hz, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.55 (d, J = 7.5 Hz, 1H), 8.19 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 19.6 (t), 29.5 (t), 111.1 (d), 112.6 (s), 118.7 (d), 119.7 (d), 119.8 (d),

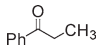
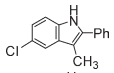
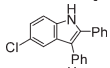
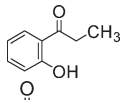
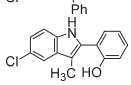
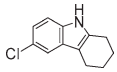
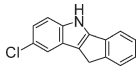
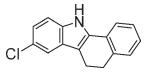
Scheme 5. One-pot-one-step, microwave-assisted reaction of phenylhydrazine **1b** and enolizable ketones **2a–f.**



1b (1.0 mmol) **2a-f** (2.0 mmol) **4a-f**

Table 3

Reaction of *p*-chlorophenylhydrazine **1c** and ketones **2a–f**.

Entries		2	Power (W)	Time (min)	Product	5	Yield[a] (%)
1		**2a**	80	5		**5a**	95
2		**2b**	80	5		**5b**	81
3		**2c**	80	4		**5c**	90
4		**2d**	200	1		**5d**	84
5		**2e**	80	5		**5e**	89
6		**2f**	80	5		**5f**	91

[a] Isolated yield.

122.3 (d), 126.6 (d), 126.7 (d), 127.4 (s), 128.4 (d), 128.8 (s), 133.0 (s), 136.5 (s), 136.9 (s).

3,3-Dimethyl-2-phenyl-3H-indole (3g). Orange liquid [29]: IR (neat): 2956 cm^{-1} (C—H); ^1H NMR ($CDCl_3$): δ 1.59 (s, 6H), 7.27 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.32–7.38 (m, 2H), 7.46–7.52 (m, 3H), 7.70 (d, J = 7.5 Hz, 1H), 8.14 (dd, J = 7.5 Hz, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 24.7 (q), 53.5 (s), 120.8 (d), 125.8 (d), 127.7 (d), 128.2 (d), 128.3 (d), 128.5 (d), 130.4 (d), 133.3 (s), 147.5 (s), 153.0 (s), 183.2 (s).

3,5-Dimethyl-2-phenylindole (4a). Yellow needles from hexane: m.p. 80–82°C (lit.[30] m.p. 80–82°C); IR (KBr): 3384 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.44 (s, 3H), 2.48 (s, 3H), 7.02 (d, J = 7.5 Hz, 1H), 7.25 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.38 (s, 1H), 7.46 (dd, J = 7.5 Hz, 7.5 Hz, 2H), 7.57 (d, J = 7.5 Hz, 2H), 7.90 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.6 (q), 21.5 (q), 108.2 (s), 110.3 (d), 118.6 (d), 118.7 (s), 123.8 (d), 127.1 (d), 127.6 (d), 128.6 (d), 128.7 (s), 130.2 (s), 133.4 (s), 134.1 (s).

5-Methyl-2,3-diphenylindole (4b). Colorless needles from hexane: m.p. 153–154°C (lit.[31] m.p. 153–155°C); IR (KBr): 3360 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.44 (s, 3H), 7.07 (d, J = 7.5 Hz, 1H), 7.26–7.34 (m, 5H), 7.35–7.47 (m, 7H), 8.24 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 21.5 (q), 110.5 (d), 114.6 (s), 119.2 (d), 124.3 (d), 126.1 (d), 127.5 (d), 128.1 (d), 128.5 (d), 128.6 (d), 129.0 (s), 129.7 (s), 130.2 (d), 132.8 (s), 134.1 (s), 134.2 (s), 135.2 (s).

2-(2′-Hydroxyphenyl)-3,5-dimethylindole (4c). Yellow liquid: IR (neat): 3364 cm^{-1} (O—H); ^1H NMR ($CDCl_3$): δ 2.29 (s, 3H), 2.49 (s, 3H), 5.61 (br s, 1H), 6.99–7.05 (m, 2H), 7.07 (d, J = 7.5 Hz, 1H), 7.27 (d, J = 7.5 Hz, 1H), 7.31 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.36 (d, J = 7.5 Hz, 1H), 7.40 (s, 1H, s), 7.98 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.2 (q), 21.5 (q), 110.1 (s), 110.6 (d), 115.8 (d), 118.7 (s), 119.3 (s), 120.6 (d), 124.3 (d), 128.3 (d), 129.1 (s), 129.6 (s), 129.9 (d), 130.3 (d), 134.8 (s), 153.3 (s).

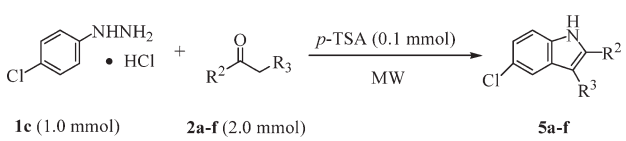
6-Methyl-1,2,3,4-tetrahydrocarbazole (4d). Colorless crystals from hexane: m.p. 140°C (lit.[21] m.p. 138–140°C); IR (KBr): 3388 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 1.80–1.93 (m, 4H), 2.43 (s, 3H), 2.65–2.72 (m, 4H), 6.92 (d, J = 7.5 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 7.24 (s, 1H), 7.53 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 20.9 (q), 21.5 (t), 23.2 (t), 23.2 (t), 23.3 (t), 109.6 (s), 110.0 (d), 117.4 (d), 122.3 (d), 128.0 (s), 128.1 (s), 133.9 (s), 134.2 (s).

8-Methyl-5,10-dihydroindeno[1,2-b]indole (4e). Colorless crystals from benzene: m.p. 225°C (lit.[32] m.p. 225°C); IR (KBr): 3388 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.47 (s, 3H), 3.73 (s, 2H), 7.00 (d, J = 7.5 Hz, 1H), 7.20 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.29–7.35 (m, 2H), 7.41–7.47 (m, 2H), 7.52 (d, J = 7.5 Hz, 1H), 8.29 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 21.5 (q), 30.3 (t), 111.7 (d), 117.2 (d), 118.8 (d), 121.4 (s), 123.2 (d), 124.6 (d), 124.9 (s), 125.5 (d), 126.5 (d), 129.5 (s), 135.1 (s), 140.0 (s), 143.5 (s), 147.8 (s).

8-Methyl-6,11-dihydro-5H-benzo[a]carbazole (4f). Colorless crystals from hexane/benzene: m.p. 184–186°C; IR (KBr): 3400 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.47 (s, 3H), 2.92–2.97 (m, 2H), 3.03–3.07 (m, 2H), 7.01 (d, J = 7.5 Hz, 1H), 7.16 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.22–7.29 (m, 3H), 7.31 (d, J = 7.5 Hz, 1H), 7.34 (s, 1H), 7.90 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 19.6 (t), 21.5 (q), 29.5 (t), 110.7 (d), 112.3 (s), 118.4 (d), 118.5 (s), 119.7 (d), 123.9 (d), 126.5 (d), 127.6 (d), 128.4 (d), 129.0 (s), 129.1 (s), 133.1 (s), 135.3 (s), 136.4 (s).

3,3,5-Trimethyl-2-phenyl-3H-indole (4g). Orange liquid: IR (neat): 2912 cm^{-1} (C—H); ^1H NMR ($CDCl_3$): δ 1.58 (s, 6H), 2.44 (s, 3H), 7.13–7.19 (m, 2H), 7.45–7.52 (m, 3H), 7.57 (d, J = 7.5 Hz, 1H), 8.14 (dd, J = 7.5 Hz, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 21.6 (q), 24.7 (q), 53.3 (s), 120.4 (d), 121.6 (d),

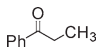
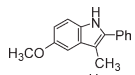
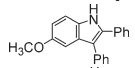
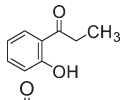
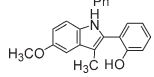
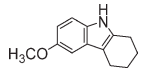
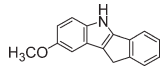
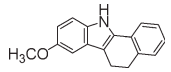
Scheme 6. One-pot-one-step, microwave-assisted reaction of phenylhydrazine **1c** and enolizable ketones **2a–f.**



1c (1.0 mmol) **2a-f** (2.0 mmol) **5a-f**

Table 4

Reaction of *p*-methoxyphenylhydrazine **1d** and ketones **2a–f**.

Entries		2	Power (W)	Time (min)	Product	6	Yield[a] (%)
1		**2a**	80	6		**6a**	74
2		**2b**	80	4		**6b**	41
3		**2c**	80	11		**6c**	26
4		**2d**	200	1		**6d**	83
5		**2e**	80	5		**6e**	70
6		**2f**	80	4		**6f**	79

[a] Isolated yield.

128.1 (d), 128.2 (d), 128.5 (d), 130.3 (d), 133.4 (s), 135.7 (s), 147.7 (s), 150.9 (s), 182.3 (s).

5-Chloro-3-methyl-2-phenylindole (5a). Colorless needles [33] from hexane: m.p. 134–136°C; IR (KBr): 3388 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.41 (s, 3H), 7.14 (d, J = 7.5 Hz, 1H), 7.27 (d, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.48 (dd, J = 7.5 Hz, 7.5 Hz, 2H), 7.54–7.59 (m, 3H), 8.02 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.5 (q), 108.3 (s), 111.6 (d), 118.4 (d), 122.4 (d), 125.1 (d), 127.6 (s), 127.7 (d), 128.8 (d), 131.1 (s), 132.7 (s), 134.1 (s), 135.4 (s).

5-Chloro-2,3-diphenylindole (5b). Yellow crystals from hexane: m.p. 126–127°C (lit.[34] m.p. 124–126°C); IR (KBr): 3412 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 7.19 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.27–7.37 (m, 6H), 7.37–7.44 (m, 5H), 7.63 (d, J = 1.5 Hz, 1H), 8.24 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 111.9 (d), 114.8 (s), 119.1 (d), 122.9 (d), 126.2 (s), 126.5 (s), 128.0 (d), 128.1 (d), 128.6 (d), 128.7 (d), 129.9 (d), 130.0 (d), 132.1 (s), 134.1 (s), 134.3 (s), 135.4 (s).

5-Chloro-2-(2′-hydroxyphenyl)-3-methylindole (5c). Yellow liquid [33]: IR (neat): 3328 cm^{-1} (O—H); ^1H NMR ($CDCl_3$): δ 2.29 (s, 3H), 5.47 (br s, 1H), 6.99–7.05 (m, 2H), 7.17 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.26 (d, J = 7.5 Hz, 1H), 7.31 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.57 (d, J = 1.5 Hz, 1H), 8.01 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.4 (q), 109.7 (s), 111.8 (d), 116.0 (d), 118.3 (d), 118.8 (s), 120.7 (d), 122.6 (d), 125.1 (d), 129.8 (s), 130.3 (d), 130.4 (s), 131.3 (s), 134.4 (s), 153.3 (s).

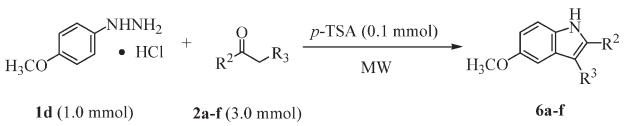
6-Chloro-1,2,3,4-tetrahydrocarbazole (5d). Pale yellow crystals from hexane: m.p. 141°C (lit.[21,35] m.p. 140–141°C); IR (KBr): 3396 cm^{-1} (N—H); ^1H NMR ($CDCl_3$)[21]: δ 1.85–1.95 (m, 4H), 2.63–2.67 (m, 2H), 2.70–2.74 (m, 2H), 7.05 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.17 (d, J = 7.5 Hz, 1H), 7.41 (d, J = 1.5 Hz, 1H), 7.65 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 20.7 (t), 23.0 (t), 23.1 (t), 23.2 (t), 110.0 (s), 111.2 (d), 117.3 (d), 120.9 (d), 124.7 (s), 128.9 (s), 133.9 (s), 135.7 (s).

8-Chloro-5,10-dihydroindeno[1,2-b]indole (5e). Pale orange crystals from benzene: m.p. 223–225°C (lit.[36] m.p. 223–223.5°C); IR (KBr): 3392 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 3.70 (s, 2H), 7.13 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.24 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.31–7.38 (m, 2H), 7.47 (d, J = 7.5 Hz, 1H), 7.54 (d, J = 7.5 Hz, 1H), 7.60 (d, J = 1.5 Hz, 1H), 8.33 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 30.3 (t), 112.9 (d), 117.6 (d), 118.5 (d), 121.1 (s), 121.7 (d), 125.3 (d), 125.6 (d), 125.7 (s), 125.9 (s), 126.7 (d), 134.5 (s), 138.9 (s), 144.7 (s), 147.8 (s).

8-Chloro-6,11-dihydro-5H-benzo[a]carbazole (5f). Colorless crystals from hexane/benzene: m.p. 163–165°C; IR (KBr): 3380 cm^{-1} (N—H); ^1H NMR ($CDCl_3$): δ 2.90–2.95 (m, 2H), 3.03–3.08 (m, 2H), 7.12 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.19 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.24–7.30 (m, 3H), 7.32 (d, J = 7.5 Hz, 1H), 7.50 (d, J = 1.5 Hz, 1H), 8.21 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 19.5 (t), 29.3 (t), 112.0 (d), 112.1 (s), 118.2 (d), 119.9 (d), 122.4 (d), 125.5 (s), 126.6 (d), 127.1 (d), 128.3 (s), 128.5 (d), 128.6 (s), 134.4 (s), 135.2 (s), 136.6 (s).

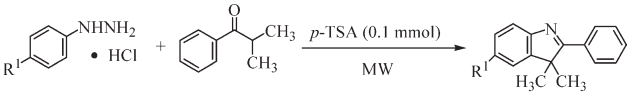
5-Chloro-3,3-dimethyl-2-phenyl-3H-indole (5g). Orange liquid: IR (neat): 2924 cm^{-1} (C—H); ^1H NMR ($CDCl_3$): δ 1.59 (s, 6H), 7.30–7.35 (m, 2H), 7.47–7.52 (m, 3H), 7.60 (d, J =

Scheme 7. One-pot-one-step, microwave-assisted reaction of phenylhydrazine **1d** and enolizable ketones **2a–f.**



1d (1.0 mmol) **2a-f** (3.0 mmol) **6a-f**

Scheme 8. One-pot-one-step, microwave-assisted reaction of phenylhydrazine **1a–d** and isobutyrophenone **2g.**



1 (1.0 mmol) **2g**

1a: R^1 = H
1b: R^1 = CH_3, hydrochloride
1c: R^1 = Cl, hydrochloride
1d: R^1 = OCH_3, hydrochloride

3g: R^1 = H
4g: R^1 = CH_3
5g: R^1 = Cl
6g: R^1 = OCH_3

Table 5

Reaction of phenylhydrazines **1a–d** and isobutyrophenone **2g**.

Entries	1	Power (W)	Time (min)	Product	Yield[a] (%)
1[b]	**1a**	600	3	**3g**	54
2[b]	**1b**	80	7	**4g**	78
3[b]	**1c**	80	7	**5g**	75
4[c]	**1d**	80	4	**6g**	69

[a] Isolated yield.
[b] **2**: 2.0 mmol.
[c] **2**: 3.0 mmol.

7.5 Hz, 1H), 8.12 (dd, J = 7.5 Hz, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 24.6 (q), 53.9 (s), 121.7 (d), 127.9 (d), 128.2 (s), 128.3 (d), 128.6 (d), 130.7 (d), 131.5 (d), 132.9 (s), 149.3 (s), 151.6 (s), 183.5 (s).

5-Methoxy-3-methyl-2-phenylindole (6a). Colorless crystals from hexane: m.p. 114–116°C (lit.[10,37] m.p. 116°C); IR (KBr): 3408 cm^{-1} (N—H); ^{1}H NMR ($CDCl_3$): δ 2.44 (s, 3H), 3.89 (s, 3H), 6.87 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.04 (d, J = 1.5 Hz, 1H), 7.26 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.47 (dd, J = 7.5 Hz, 7.5 Hz, 2H), 7.57 (d, J = 7.5 Hz, 2H), 7.90 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.7 (q), 55.9 (q), 100.8 (d), 108.4 (s), 111.5 (d), 112.4 (d), 127.2 (d), 127.6 (d), 128.7 (d), 130.4 (s), 131.0 (s), 133.3 (s), 135.0 (s), 154.1 (s).

5-Methoxy-2,3-diphenylindole (6b). Orange crystals from hexane: m.p. 155°C (lit.[38] m.p. 155°C); IR (KBr): 3404 cm^{-1} (N—H); ^{1}H NMR ($CDCl_3$): δ 3.82 (s, 3H), 6.90 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.12 (d, J = 1.5 Hz, 1H), 7.26–7.34 (m, 5H), 7.36–7.45 (m, 6H), 8.12 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 55.9 (q), 101.2 (d), 111.7 (d), 113.0 (d), 114.9 (s), 126.2 (d), 127.6 (d), 128.0 (d), 128.5 (d), 128.6 (d), 129.2 (s), 130.1 (d), 131.0 (s), 132.7 (s), 134.9 (s), 135.2 (s), 154.8 (s).

2-(2′-Hydroxyphenyl)-5-methoxy-3-methylindole (6c). Brownish liquid: IR (neat): 3328 cm^{-1} (O—H); ^{1}H NMR ($CDCl_3$): δ 2.28 (s, 3H), 3.88 (s, 3H), 5.68 (br s, 1H), 7.07 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 6.98–7.02 (m, 2H), 7.04 (d, J = 1.5 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 7.29 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.99 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.4 (q), 55.9 (q), 108.4 (d), 110.1 (s), 111.7 (d), 112.6 (d), 112.7 (s), 115.8 (d), 119.3 (s), 120.5 (d), 129.8 (d), 130.3 (d), 130.4 (s), 131.6 (s), 153.3 (s), 154.1 (s).

6-Methoxy-1,2,3,4-tetrahydrocarbazole (6d). Pale orange crystals from hexane: m.p. 95–97°C (lit.[39] m.p. 96–97°C); IR (KBr): 3388 cm^{-1} (N—H); ^{1}H NMR ($CDCl_3$) [21]: δ 1.84–1.93 (m, 4H), 2.65–2.73 (m, 4H), 3.85 (s, 3H), 6.76 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 6.92 (d, J = 1.5 Hz, 1H), 7.15 (d, J = 7.5 Hz, 1H), 7.55 (br s, 1H) NH; ^{13}C NMR ($CDCl_3$): δ 20.9 (t), 20.9 (t), 23.2 (t), 23.3 (t), 55.9 (q), 100.2 (d), 109.9 (s), 110.4 (d), 110.9 (d), 128.1 (s), 130.7 (s), 135.1 (s), 153.8 (s).

8-Methoxy-5,10-dihydroindeno[1,2-b]indole (6e). Colorless crystals from benzene: m.p. 208°C (lit.[32] m.p. 207°C); IR (KBr): 3404 cm^{-1} (N—H); ^{1}H NMR ($CDCl_3$): δ 3.70 (s, 2H), 3.88 (s, 3H), 6.84 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.09 (d, J = 1.5 Hz, 1H), 7.21 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.28–7.34 (m, 2H), 7.44 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 7.5 Hz, 1H), 8.17 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 30.3 (t), 55.8 (q), 101.1 (d), 111.5 (d), 112.6 (d), 117.3 (d), 121.5 (s), 124.8 (d), 125.1 (s), 125.5 (d), 126.5 (d), 135.0 (s), 135.7 (s), 144.1 (s), 147.7 (s), 154.5 (s).

8-Methoxy-6,11-dihydro-5H-benzo[a]carbazole (6f). Pale orange needles from hexane/benzene: m.p. 166°C (lit.[40] m.p. 167–168°C); IR (KBr): 3400 cm^{-1} (N—H); ^{1}H NMR ($CDCl_3$): δ 2.92–2.97 (m, 2H), 3.03–3.07 (m, 2H), 3.86 (s, 3H), 6.84 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 6.99 (d, J = 1.5 Hz, 1H), 7.18 (dd, J = 7.5 Hz, 7.5 Hz, 1H), 7.22–7.29 (m, 3H), 7.31 (d, J = 7.5 Hz, 1H), 8.08 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 19.7 (t), 29.5 (t), 55.9 (q), 100.6 (d), 111.8 (d), 112.3 (s), 112.4 (d), 119.7 (d), 126.5 (d), 126.6 (d), 127.8 (s), 128.4 (d), 128.9 (s), 132.1 (s), 133.9 (s), 136.4 (s), 154.3 (s).

5-Methoxy-3,3-dimethyl-2-phenyl-3H-indole (6g). Orange liquid [41]: IR (neat): 2956 cm^{-1} (C—H); ^{1}H NMR ($CDCl_3$): δ 1.58 (s, 6H), 3.87 (s, 3H), 6.86–6.92 (m, 2H), 7.43–7.51 (m, 3H), 7.60 (d, J = 7.5 Hz, 1H), 8.11 (dd, J = 7.5 Hz, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 24.8 (q), 53.7 (s), 55.7 (q), 107.5 (d), 112.4 (d), 121.2 (d), 127.9 (d), 128.5 (d), 130.1 (d), 133.4 (s), 146.8 (s), 149.3 (s), 158.5 (s), 181.2 (s).

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