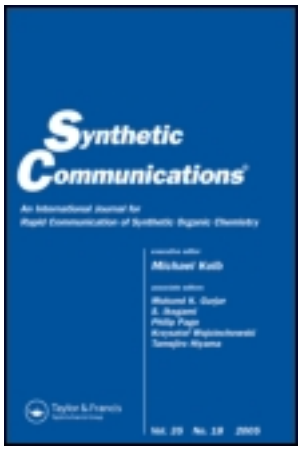


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Microwave-Assisted One-Pot Synthesis of 1,2,3,4-Tetrahydrocarbazoles

Jing Chen [a] & Yongzhou Hu [a]
[a] Department of Medicinal Chemistry, School of Pharmaceutical Science, Zhejiang University, Hangzhou, China
Published online: 21 Aug 2006.

To cite this article: Jing Chen & Yongzhou Hu (2006) Microwave-Assisted One-Pot Synthesis of 1,2,3,4-Tetrahydrocarbazoles, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 36:11, 1485-1494

To link to this article: http://dx.doi.org/10.1080/00397910600588330

Synthetic Communications®, 36: 1485–1494, 2006

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910600588330

Microwave-Assisted One-Pot Synthesis of 1,2,3,4-Tetrahydrocarbazoles

Jing Chen and Yongzhou Hu
Department of Medicinal Chemistry, School of Pharmaceutical Science, Zhejiang University, Hangzhou, China

Abstract: A series of 1,2,3,4-tetrahydrocarbazoles **3a**–**m** were synthesized by the reaction of substituted 2-bromocyclohexanones **2a**–**c** with appropriate anilines **1a**–**i** under microwave irradiation without any other catalysts.

Keywords: Anilines, 2-bromocyclohexanones, microwave, 1,2,3,4-tetrahydrocarbazoles

Substituted 1,2,3,4-tetrahydrocarbazoles have been reported to possess many biological properties, such as central nervous system activity,[1] antihistamine,[2] antidiabetic,[3] and anti-inflammatory properties.[4] Also, they are important as intermediates for the production of pharmaceutically active compounds.[5,6] There are a number of methods available for the construction of this ring system, including the acid-induced Fischer indole synthesis from arylhydrazines and cyclohexanones,[7] palladium-catalyzed coupling of *o*-haloanilines with cyclohexanone,[8] the Bartoli indole synthesis from ortho-substituted nitro-aromatic compounds with vinylmagnesium bromide,[9] Ruthenium complex–catalyzed synthesis from aminoarenes and 1,2-cyclohexanediol,[10] and the Bischler synthesis from α-halocyclohexanones and anilines.[11] Nevertheless, all of them have shortcomings, such as trouble with operation, harsh conditions, difficulty in preparation of

Received in Japan September 13, 2005
Address correspondence to Yongzhou Hu, Department of Medicinal Chemistry, School of Pharmaceutical Science, Zhejiang University, Hangzhou, China. E-mail: huyz@zjuem.zju.edu.cn

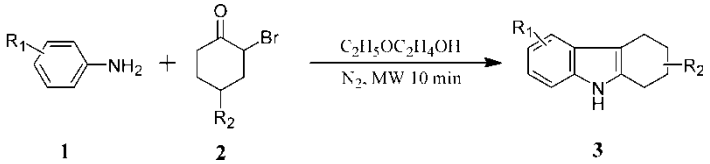
starting materials (arylhydrazines, which are sensitive to air), the need for excess reagents (metal catalysts, acidic catalysts), and longer reaction times. Among these methodologies, the Bischler synthesis applied to the preparation of tetrahydrocarbazoles was a potentially attractive method for us. Ott[12] first mentioned in 1923 that α-halocyclohexanones could be condensed with aromatic amines to give arylaminocyclohexanones and then these could be cyclized to the desired tetrahydrocarbazoles. Although the two-step operation and lower yields limited its use in preparation of tetrahydrocarbazoles, the readily available starting materials made us interested in finding new ways to improve this methodology.

In recent years, the application of microwave (MW) irradiation in organic synthesis has been the focus of considerable attention and is becoming an increasingly popular technology.[13] The prominent features of the microwave approach are rapid reaction, clean reaction conditions, and ease of manipulation. We report herein a microwave-assisted direct coupling of a variety of anilines **1** with 2-bromocyclohexanones **2**, leading to the synthesis of 1,2,3,4-tetrahydrocarbazoles **3** without any other catalysts (Scheme 1).

RESULTS AND DISCUSSION

To study the microwave-assisted synthesis of 1,2,3,4-tetrahydrocarbazoles, we investigated the reaction by choosing different solvents, such as toluene, 1,4-dioxane, ethanol, *tert*-butanol, and 2-ethoxyethanol. The object products cannot be obtained in the case of toluene. The reactions proceeded slowly, and the yields were very low with a lot of uncyclized intermediates in ethanol or *tert*-butanol. The yields also cannot be improved in 1,4-dioxane. When the higher boiling solvent, 2-ethoxyethanol, was used the yields were improved greatly.

Thus, 2-bromocyclohexanone **2a** was treated with varying amounts of aniline **1a** in 2-ethoxyethanol under different conditions in a microwave oven (Table 1). The results demonstrated that a microwave power of 325 W was most appropriate. A higher microwave power increased the rate of reaction, but the yields were decreased (entries 9–11). The yields were markedly affected by the molar ratio of **1a** to **2a**. By increasing **1a** from 1



1 2 3

Scheme 1.

Table 1. Microwave-assisted direct coupling **1a** with **2a** under various conditions

Entry	1a:2a[a]	Power (W)	Solvent	Time (min)	Yield (%)[b]
1	1:1	325	Toluene	10	—
2	1:1	325	1,4-Dioxane	10	25
3	1:1	325	Ethanol	10	20
4	1:1	325	*tert*-Butanol	10	11
5	1:1	325	2-Ethoxyethanol	10	34
6	1.5:1	325	2-Ethoxyethanol	10	44
7	2:1	325	2-Ethoxyethanol	10	51
8	2.5:1	325	2-Ethoxyethanol	10	66
9	3:1	325	2-Ethoxyethanol	10	84
10	3:1	455	2-Ethoxyethanol	8	81
11	3:1	650	2-Ethoxyethanol	5	62

[a]Molar ratio of **1a** to **2a**.
[b]Isolated yields.

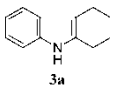
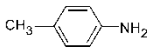
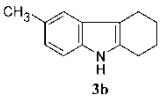
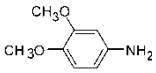
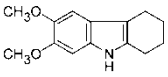
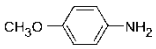
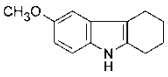
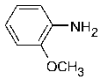
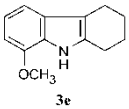
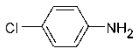
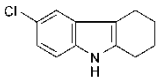
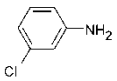
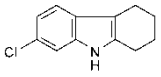
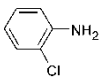
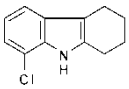
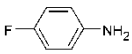
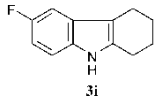
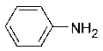
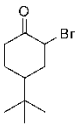
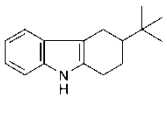
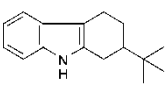
equiv to 3 equiv, the yields would be corresponding improved (entries 5–9). Therefore, the best condition was treating **1a** (3 equiv) with **2a** for 10 min using a microwave power of 325 W in 2-ethoxyethanol. The results of the experiment are summarized in Table 2. Clearly, introducing microwave irradiation to the Bischler synthesis would be of significant benefit for the yields and reaction time. The reaction would also proceed when 2-bromocyclohexanone was replaced with 2-bromocyclopentanone **2d**, but the yield was lower (entry 14). However, the reaction of aniline with 4-*tert*-butyl-2-bromocyclohexanone **2b** or 4-phenyl-2-bromocyclohexanone **2c** led to a mixture of 2- and 3-substituted-1,2,3,4-tetrahydrocarbazoles (entries 10–13). The plausible mechanism of the reaction is showed in Scheme 2.

In summary, we have explored an efficient one-pot route to synthesize a series of 1,2,3,4-tetrahydrocarbazoles from easily available 2-bromocyclohexanones and substituted anilines under microwave-irradiation conditions without any other catalysts. The simple procedure, mild reaction conditions, and shorter reaction times render this method a valuable addition to tetrahydrocarbazole chemistry.

EXPERIMENTAL

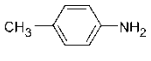
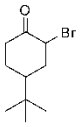
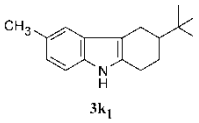
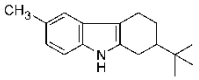
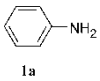
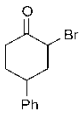
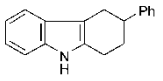
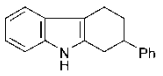
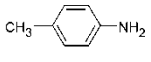
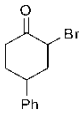
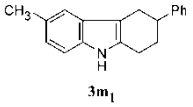
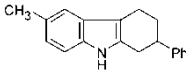
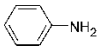
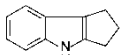
Melting points were obtained on a B-540 Bűchi melting-point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Brucker AM 400-MHz spectrometer with $SiMe_4$ as the internal standard in $CDCl_3$. Element analyses were performed on a EA-1110 instrument. Infrared spectra were recorded on a Bruck Vector 200 spectrophotometer.

Table 2. Synthesis of 1,2,3,4-tetrahydrocarbazoles under microwave irradiation

Entry	**1**	**2**[a]	**3**	Yield[b] (%)
1	 **1a**	 **2a**	 **3a**	84
2	 **1b**	 **2a**	 **3b**	83
3	 **1c**	 **2a**	 **3c**	74
4	 **1d**	 **2a**	 **3d**	49
5	 **1e**	 **2a**	 **3e**	71
6	 **1f**	 **2a**	 **3f**	71
7	 **1g**	 **2a**	 **3g**	71
8	 **1h**	 **2a**	 **3h**	40
9	 **1i**	 **2a**	 **3i**	61
10	 **1a**	 **2b**	 **3j**$_1$	34
			 **3j**$_2$	28

(*continued*)

Table 2. Continued

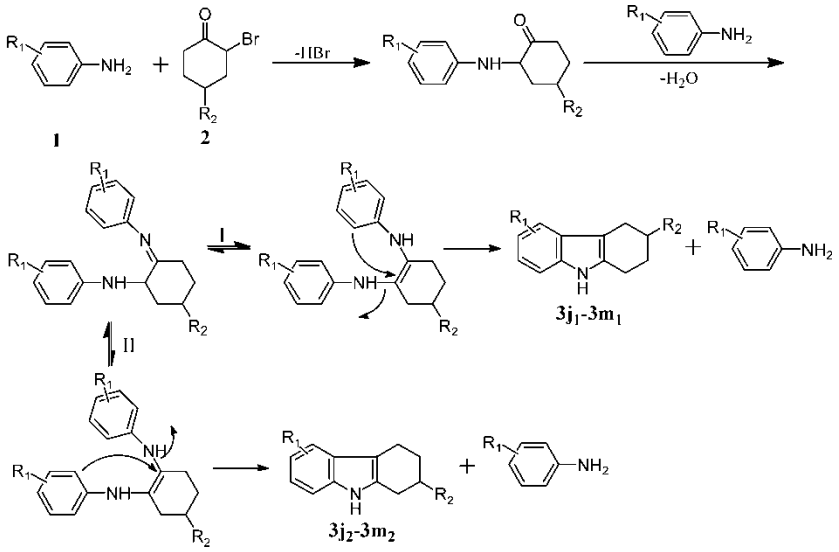
Entry	1	2[a]	3	Yield[b] (%)
11	 1b	 2b	 $3k_1$	34
			 $3k_2$	24
12	 1a	 2c	 $3l_1$	36
			 $3l_2$	17
13	 1b	 2c	 $3m_1$	35
			 $3m_2$	20
14	 1a	 2d	 3n	26

[a]The requisite bromides were prepared from the appropriate cyclohexanone following the method described in the literature.[14]

[b]Isolated yields.

General Procedure for the Preparation of 1,2,3,4-Tetrahydrocarbazoles (3)

A mixture of aniline **1** (0.9 mmol), 2-bromocyclohexanone **2** (0.3 mmol), and 0.5 mL 2-ethoxyethanol were mixed in a round-bottom flask (25 mL). The mixture was irradiated with microwaves (325 W) under nitrogen for 10 min. After completion of the reaction, the solvent was evaporated and the crude residue was extracted with ethyl acetate (3 mL × 2). The extracts were



Scheme 2. Plausible reaction mechanism for the synthesis of 1,2,3,4-tetrahydrocarbazoles.

dried over anhydrous sodium sulfate and concentrated under vacuum. All the products were purified by column chromatography over silica gel, using a different ratio of ethyl acetate and petroleum ether as eluent according to different products.

Data

1,2,3,4-Tetrahydrocarbazole (3a): mp 113–114°C (lit.[15] 115–116°C); IR (KBr): ν 3400 (NH), 3050 (ArH), 2927, 2849, 1589, 1469, 738 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.69 (br, NH), 7.50 (d, $J = 7.6$ Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 1H), 7.17–7.09 (m, 2H), 2.78–2.74 (m, 4H), 1.96–1.91 (m, 4H); anal. calcd. for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found C, 84.57; H, 7.34; N, 7.97.

6-Methyl-1,2,3,4-tetrahydrocarbazole (3b): mp 138–140°C (lit.[16] 138°C); IR (KBr): ν 3393 (NH), 3022 (ArH), 2925, 2846, 1589, 796 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.57 (br, NH), 7.24 (s, 1H), 7.16 (d, $J = 8.0$ Hz, 1H), 6.93 (d, $J = 8.0$ Hz, 1H), 2.72–2.66 (m, 4H), 2.17 (s, 3H), 1.92–1.84 (m, 4H); anal. calcd. for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found C, 84.12; H, 8.37; N, 7.19

6,7-Dimethoxyl-1,2,3,4-tetrahydrocarbazole (3c): mp 100–102°C (lit.[17] 101–103°C); IR (KBr): ν 3390 (NH), 3075 (ArH), 2923, 2834, 1596, 1487,

832 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.51 (br, NH), 6.92 (s, 1H), 6.84 (s, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 2.70–2.67 (m, 4H), 1.89–1.88 (m, 4H); anal. calcd. for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found C, 72.51; H, 7.05; N, 5.89.

6-Methoxyl-1,2,3,4-tetrahydrocarbazole (3d): mp 91–92°C (Lit.[11] 92–103°C); IR (KBr): ν 3388 (NH), 2951, 2850, 1592, 1485, 801 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.56 (br, NH), 7.16 (d, $J = 8.0$ Hz, 1H), 6.93 (s, 1H), 6.77 (d, $J = 8.0$ Hz, 1H), 3.86 (s, 3H), 2.72–2.67 (m, 4H), 1.92–1.87 (m, 4H); anal. calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found C, 77.94; H, 7.82; N, 6.82.

8-Methoxyl-1,2,3,4-tetrahydrocarbazole (3e): compound **3e** was obtained as an oil; IR (KBr): ν 3404 (NH), 3062 (ArH), 2926, 2850, 1572, 1467, 774 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.99 (br, NH), 7.15 (d, $J = 8.0$ Hz, 1H), 7.05 (t, $J = 8.0$ Hz, 1H), 6.66 (d, $J = 8.0$ Hz, 1H), 3.99 (s, 3H), 2.76–2.70 (m, 4H), 1.97–1.91 (m, 4H); anal. calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found C, 77.35; H, 7.84; N, 6.78.

6-Chloro-1,2,3,4-tetrahydrocarbazole (3f): mp 140–141°C (lit.[16] 138–140°C); IR (KBr): ν 3404 (NH), 2937, 2846, 1580, 1467, 800 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.71 (br, NH), 7.43 (d, $J = 2.0$ Hz, 1H), 7.19 (d, $J = 8.0$ Hz, 1H), 7.07 (dd, $J = 8.0$, 2.0 Hz, 1H), 2.75–2.66 (m, 4H), 1.96–1.85 (m, 4H); anal. calcd. for $C_{12}H_{12}ClN$: C, 70.07; H, 5.88; N, 6.81. Found C, 69.80; H, 5.99; N, 6.68.

7-Chloro-1,2,3,4-tetrahydrocarbazole (3g): mp 178–180°C (lit.[18] 128–130°C); IR (KBr): ν 3392 (NH), 2941, 2853, 1539, 1469, 801 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.66 (br, NH), 7.34 (d, $J = 8.0$ Hz, 1H), 7.24 (d, $J = 1.6$ Hz, 1H), 7.03 (dd, $J = 8.0$, 1.6 Hz, 1H), 2.72–2.66 (m, 4H), 1.94–1.83 (m, 4H); anal. calcd. for $C_{12}H_{12}ClN$: C, 70.07; H, 5.88; N, 6.81. Found C, 70.24; H, 6.01; N, 6.54.

8-Chloro-1,2,3,4-tetrahydrocarbazole (3 h): mp 136–139°C (lit.[18] 138–140°C); IR (KBr): ν 3443 (NH), 2927, 2853, 1588, 1464, 773 cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 7.94 (br, NH), 7.36 (d, $J = 8.0$ Hz, 1H), 7.11 (d, $J = 8.0$ Hz, 1H), 7.01 (t, $J = 8.0$ Hz, 1H), 2.78–2.69 (m, 4H), 1.96–1.80 (m, 4H); anal. calcd. for $C_{12}H_{12}ClN$: C, 70.07; H, 5.88; N, 6.81. Found C, 69.75; H, 6.05; N, 6.72.

6-Fluoro-1,2,3,4-tetrahydrocarbazole (3i): mp 106–108°C (lit.[19] 103–104°C); IR (KBr): ν 3407 (NH), 2930, 2852, 1583, 1482, 795 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.65 (br, NH), 7.17 (m, 1H), 7.10 (dd, $J = 9.2$, 2.8 Hz, 1H), 6.86–6.81 (m, 1H), 2.73–2.64 (m, 4H), 1.94–1.84 (m, 4H); anal. calcd. for $C_{12}H_{12}FN$: C, 76.17; H, 6.39; N, 7.40. Found C, 76.54; H, 6.02; N, 7.76.

3-*tert*-Butyl-1,2,3,4-tetrahydrocarbazole ($3j_1$): mp 126–127°C (lit.[20] 129–131°C); IR (KBr): ν 3409 (NH), 3022 (ArH), 2959, 2920, 2862, 2842,

1468, 742 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.66 (br, NH), 7.48 (d, $J = 8.0$ Hz, 1H), 7.27 (d, $J = 8.0$ Hz, 1H), 7.14–7.08 (m, 2H), 2.85–2.75 (m, 3H), 2.45–2.38 (m, 1H), 2.13–2.10 (m, 1H), 1.55–1.53 (m, 2H), 0.99 (s, 9H); anal. calcd. for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found C, 84.59; H, 9.01; N, 6.18.

2-*tert*-Butyl-1,2,3,4-tetrahydrocarbazole (3j$_2$): mp 129–131°C; IR (KBr): ν 3407 (NH), 3048 (ArH), 2956, 2920, 2867, 1591, 1469, 738 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.63 (br, NH), 7.46 (d, $J = 8.0$ Hz, 1H), 7.27 (d, $J = 8.0$ Hz, 1H), 7.13–7.05 (m, 2H), 2.89–2.84 (m, 1H), 2.77–2.72 (m, 1H), 2.60–2.53 (m, 2H), 2.14–2.10 (m, 1H), 1.66–1.64 (m, 1H), 1.44–1.40 (m, 1H), 1.00 (s, 9H); anal. calcd. for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found C, 84.49; H, 9.58; N, 6.34.

3-*tert*-Butyl-6-methyl-1,2,3,4-tetrahydrocarbazole (3k$_1$): mp 122–123°C; IR (KBr): ν 3401 (NH), 3009 (ArH), 2960, 2920, 2855, 1595, 1474, 793 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.51 (br, NH), 7.22 (s, 1H), 7.12 (d, $J = 8.0$ Hz, 1H), 6.90 (d, $J = 8.0$ Hz, 1H), 2.79–2.74 (m, 3H), 2.40 (s, 3H), 2.38–2.31 (m, 1H), 2.08–2.04 (m, 1H), 1.51–1.45 (m, 2H), 0.97 (s, 9H); anal. calcd. for $C_{17}H_{23}N$: C, 84.59; H, 9.60; N, 5.80. Found C, 84.67; H, 9.52; N, 6.07.

2-*tert*-Butyl-6-methyl-1,2,3,4-tetrahydrocarbazole (3k$_2$): mp 167–168°C; IR (KBr): ν 3398 (NH), 3018 (ArH), 2961, 2919, 2867, 2842, 1596, 1467, 798 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.53 (br, NH), 7.23 (s, 1H), 7.15 (d, $J = 8.0$ Hz, 1H), 6.92 (d, $J = 8.0$ Hz, 1H), 2.84–2.79 (m, 1H), 2.73–2.68 (m, 1H), 2.59–2.46 (m, 2H), 2.43 (s, 3H), 2.12–2.08 (m, 1H), 1.68–1.58 (m, 1H), 1.45–1.34 (m, 1H), 0.97 (s, 9H); anal. calcd. for $C_{17}H_{23}N$: C, 84.59; H, 9.60; N, 5.80. Found C, 84.46; H, 9.79; N, 6.10.

3-Phenyl-1,2,3,4-tetrahydrocarbazole (3l$_1$): mp 121–123°C; IR (KBr): ν 3391 (NH), 3026 (ArH), 2915, 1493, 1468, 743, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.73 (br, NH), 7.44 (d, $J = 8.0$ Hz, 1H), 7.34–7.32 (m, 4H), 7.30 (d, $J = 8.0$ Hz, 1H), 7.26–7.22 (m, 1H), 7.15–7.06 (m, 2H), 3.10–3.06 (m, 2H), 2.92–2.88 (m, 1H), 2.85–2.78 (m, 2H), 2.24–2.10 (m, 2H); anal. calcd. for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found C, 87.71; H, 7.15; N, 5.43.

2-Phenyl-1,2,3,4-tetrahydrocarbazole (3l$_2$): mp 159–161°C; IR (KBr): ν 3396 (NH), 3028 (ArH), 2912, 2842, 1492, 1470, 741, 698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.69 (br, NH), 7.50 (d, $J = 8.0$ Hz, 1H), 7.37–7.29 (m, 5H), 7.27–7.24 (m, 1H), 7.17–7.09 (m, 2H), 3.19–3.11 (m, 1H), 3.01–2.77 (m, 4H), 2.23–2.19 (m, 1H), 2.08–2.00 (m, 1H); anal. calcd. for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found C, 87.63; H, 7.23; N, 5.93.

3-Phenyl-6-methyl-1,2,3,4-tetrahydrocarbazole (3m$_1$): mp 68–70°C; IR (KBr): ν 3403 (NH), 3025 (ArH), 2915, 2848, 1593, 1453, 793, 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.63 (br, NH), 7.30–7.16 (m, 6H), 7.14 (d, $J = 8.0$ Hz, 1H), 7.05 (d, $J = 8.0$ Hz, 1H), 3.13–3.08 (m, 2H), 2.95–2.85 (m, 3H), 2.44

(s, 3H), 2.25–2.02 (m, 2H); anal. calcd. for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found C, 87.00; H, 7.65; N, 5.72.

2-Phenyl-6methyl-1,2,3,4-tetrahydrocarbazole (3 m$_2$): mp 146–149°C; IR (KBr): ν 3403 (NH), 3025 (ArH), 2915, 2848, 1592, 1451, 792, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.59 (br, NH), 7.36–7.22 (m, 6H), 7.17 (d, $J = 8.0$ Hz, 1H), 6.95 (d, $J = 8.0$ Hz, 1H), 3.17–3.09 (m, 1H), 2.98–2.76 (m, 4H), 2.44 (s, 3H), 2.21–2.17 (m, 1H), 2.05–1.98 (m, 1H); anal. calcd. for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found C, 87.53; H, 7.18; N, 5.01.

1,2,3,4-Tetrahydrocyclopenta[*b*]indole (3n): mp 102–104°C (lit.[15] 102–104°C); IR (KBr): ν 3405 (NH), 3050 (ArH), 2930, 2867, 1460, 745 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.83 (br, NH), 7.46 (dd, $J = 6.0$, 4.0 Hz, 1H), 7.33–7.30 (m, 1H), 7.13–7.08 (m, 2H), 2.91–2.83 (m, 4H), 2.60–2.53 (m, 2H); anal. calcd. for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91. Found C, 84.31; H, 7.35; N, 9.03.

REFERENCES

1. Mooradian, A.; Dupont, P. E.; Hlavac, A. G.; Aceto, M. D.; Pearl, J. 3-Amino-tetrahydrocarbazoles as a new series of central nervous system agents. *J. Med. Chem.* **1977**, *20*, 487–492.
2. Jean, C. F.; Rangisetty, J. B.; Dukat, M.; Setola, V.; Raffay, T.; Roth, B.; Glennon, R. A. 1,2,3,4-Tetrahydrocarbazoles as 5-HT_6 serotonin receptor ligands. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1961–1964.
3. Helmut, B.; Clemens, R.; Hanns, A.; Eberard, S.; Wolfgang, L.; Olaf, L.; Ekkehard, S. Antidiabetic 1,2,3,4-tetrahydrocarbazole derivatives. DE patent 2,226,702, Dec. 13, 1973.
4. Bernard, L. Antiinflammatory 1,2,3,4-tetrahydrocarbazole-2-carboxylic acid derivatives. DE patent 2,141,640, Feb. 24, 1972.
5. Haan, H. B.; Wuppertal, U. R.; Leverkusen, F. L.; Cologne, H. O.; Seuter F. Perzborn, E.; Fiedler, V. B. Cycloalkano(1,2-*b*)indole-sulponamides. US patent, 4,988,820, Jan. 29, 1991.
6. Atsuo, S.; Shigehiro, I.; Takao, N.; Kazuo, S.; Kazuo, O. 1,2,3,4-Tetrahydro-carbazole derivative. JP patent 49027583, Jul. 18, 1974.
7. Robinson, B. *The Fischer Indole Synthesis*; Wiley-Interscience: New York, 1982.
8. Chen, C. Y.; Lieberman, D. R.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. Syntheses of indoles via a palladium-catalyzed annulation between iodoanilines and ketones. *J. Org. Chem.* **1997**, *62*, 2676–2677.
9. Dobbs, A. Total synthesis of indoles from tricholoma species via Bartoli/hetero-aryl radical methodologies. *J. Org. Chem.* **2001**, *66*, 638–641.
10. Tsuji, Y.; Huh, K. T.; Watanabe, Y. Ruthenium complex–catalyzed *N*-heterocyclization: Syntheses of quinolines and indole derivatives from aminoarenes and 1,3-propanediol of glycols. *J. Org. Chem.* **1987**, *52*, 1673–1680.
11. Campaigne, E.; Lake, R. D. Synthesis of tetrahydrocarbazoles and carbazoles by the Bischler reaction. *J. Org. Chem.* **1959**, *24*, 478–487.
12. Ott, K. Tetrahydrocarbazoles. DE patent 374,098, April 19, **1923**.

13. Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. Microwave–assisted organic synthesis—a review. *Tetrahedron* **2001**, *57*, 9225–9283.
14. Tanemura, K.; Suzuki, T.; Nishida, Y.; Satsumabayashi, K.; Horaguchi, T. A mild and efficient procedure for α-bromosuccinimide catalysed by ammonium acetate. *Chem. Commun.* **2004**, 470–471.
15. Wender, P. A.; White, A. W. Methodology for the facile and region-controlled synthesis of indoles. *Tetrahedron* **1983**, *39*, 3767–3776.
16. Rebeiro, G. L.; Khadilkar, B. M. Chloroaluminate ionic liquid for Fischer indole synthesis. *Synthesis* **2001**, *3*, 370–372.
17. Haruko, T.; Minoru, M.; Yuichi, K. Photochemistry of the phthalimide system, XLII: Intermolecular photoreactions of phthalimide-alkene systems: Regio- and stereoselective oxetane formation from *N*-methylphthalimide and *N*-acetylindole derivatives. *Chem. Pharm. Bull.* **1988**, *36*, 3770–3779.
18. Neil, C.; McCall, E. B. Preparation of tetrahydrocarbazoles from 2-chloro-cyclohexanone. *J. Chem. Soc. Abstr.* **1950**, 2870–2874.
19. Allen, F. L.; Suschitzky, H. Heterocyclic fluorine compounds, I: Monofluoro-1,2,3,4-tetrahydrocarbazoles and monofluorocarbazoles. *J. Chem. Soc. Abstr.* **1953**, 3845–3849.
20. Canas-Rodriguez, A.; Mateo, B. A. Tetrahydrocarbazoles, part II: Tricyclic inhibitors of gastric acid secretion. *Anales de Quimica, Serie C: Quimica Organicay Bioquimica* **1985**, *81*, 254–257.