Asian Journal of Chemistry Vol. 22, No. 10 (2010), 8185-8191

Synthesis of Intermediates for the Synthesis of Pyrido[3,2-c]carbazole Derivatives

GUNDUZ TASKIRAN, SIBEL GULLE and YAVUZ ERGUN*
Department of Chemistry, Faculty of Arts and Sciences, Dokuz Eylul University, Kaynaklar Campus, 35160 Buca-Izmir, Turkey
E-mail: yavuz.ergun@deu.edu.tr

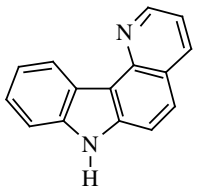
The synthesis of an effective intermediates **7** and **11** for the synthesis of pyrido[3,2-c]carbazole derivatives were accomplished with different synthetic pathways. In this study, new tetrahydrocarbazole derivatives (3, 4, 5, 6, 9 and 10) were also synthesized.

Key Words: Carbazole alkaloids, Pyridocarbazoles, Pyrido[3,2-c]carbazole.

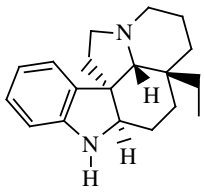
INTRODUCTION

The discovery of antitumor activity of ellipticine and 9-methoxyellipticine, two naturally occurring 6*H*-pyrido[4,3-b]carbazole alkaloids, has led to an explosion of activities toward synthesis and biological evaluation of pyridocarbazoles[1-5]. Many efforts have revealed that pyridocarbazoles show marked anticancer and anti-HIV activities[6,7].

When examining the structure of the pyridocarbazoles, it is observed that the fusion of the carbazole nucleus at the a, b and c positions with the pyridine ring at the 2,3- and 3,4-positions results in 12 isomeric pyridocarbazoles, six belonging to the quinoline and six to the isoquinoline series. The synthesis of both the quinoline and the isoquinoline series was achieved previously[8-13].



7H-Pyrido(3,2-c)carbazole

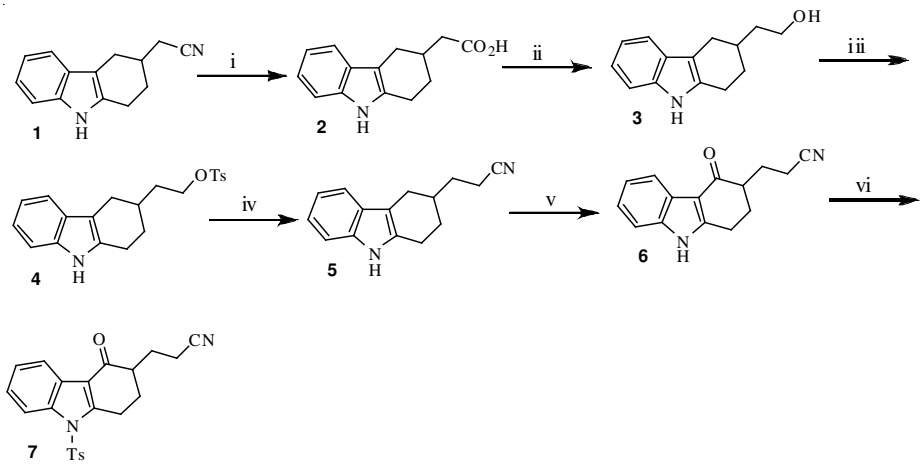


Aspidospermidine

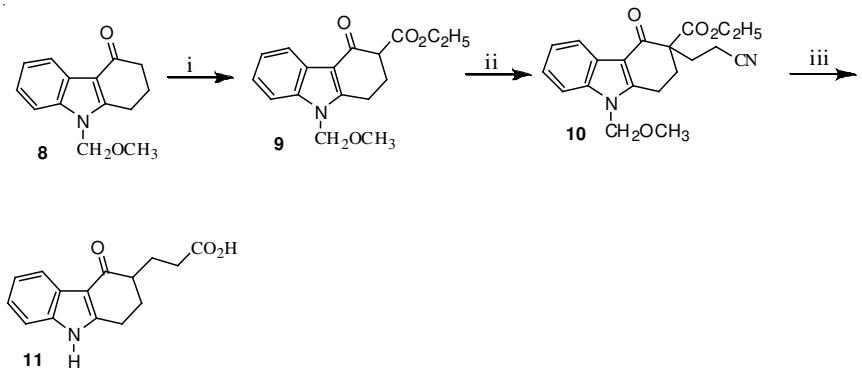
One of them, 7*H*-pyrido[3,2-c]carbazole, was synthesized in two different ways previously. First synthesis of 7*H*-pyrido[3,2-c]carbazole was accomplished *via* aromatization of 8,9,10,11-tetrahydro-7*H*-pyrido[3,2-c]carbazole which obtained from cyclization of 7-quinolylhydrozone of cyclohexanone by Kulka and Manske[13]. Second successful synthesis was realized with photocyclization of 1(2-indolyl)-2-arylethylene derivatives by Silva and Snieckus[14].

Hexahydro and octahydro pyrido[3,2-c]carbazole derivatives which have saturated structure at C and D rings of pyrido[3,2-c]carbazole are very important precursors and synthesized successfully as a core structure of aspidosperma alkaloids in most studies[15,16].

Herein we accomplished the synthesis of two new precursors **7** and **11** for the synthesis of pyrido[3,2-c]carbazole skeleton (**Schemes 1** and **2**).



Scheme-I: (i) NaOH (20 %), methanol-water, THF, reflux, 12 h; (ii) $LiAlH_4$, THF, reflux, 5 h; (iii) *p*-TsCl, pyridine, stirred, 18 h; (iv) NaCN, DMSO, stirred, 18 h; (v) DDQ, THF (90 %), N_2, 0°C, stirred, 5 h; (vi) TBAHS, *p*-TsCl, NaOH (40 %), CH_2Cl_2, stirred, 2 h



Scheme-II: (i) KH, diethyl carbonate, refluxed, 1 h; (ii) $NaOC_2H_5/C_2H_5OH$, acrylonitrile, stirred, overnight; (iii) conc. HCl, dioxane, reflux, 8 h

EXPERIMENTAL

All melting points were measured in sealed tubes using an electrothermal digital melting point apparatus (Gallenkamp) and are uncorrected. IR spectra were recorded

on a Hitachi 270-30 infrared spectrometer. ^{1}H NMR spectra were obtained on a high resolution fourier transform Bruker WH-400 NMR spectrometer with tetramethyl silane as an internal standard. Mass spectra were determined on the electron impact mode by direct insertion at 70 eV with a Micromass UK Platform II LC-MS spectrometer. Combustion analysis of compounds was obtained on a CHNS-932-LECO. Analytical and preparative thin layer chromatography (TLC) was carried out using silica gel 60 HF-254 (Merck). Column chromatography was carried out by using 70-230 mesh silica gel (0.063-0.200 mm, Merck).

2-(1,2,3,4-Tetrahydro-9*H*-carbazol-3-yl)acetic acid (2): Tetrahydrocarbazole nitrile derivative **1** (1 g, 4.76 mmol) was dissolved in tetrahydrofuran (2 mL) and sodium hydroxide (20 mL) (methanol-water) was added. The mixture was refluxed for 12 h and then it was poured in water (150 mL). The mixture was extracted with diethyl ether. Organic layer was dried with anhydrous magnesium sulfate. After the solvent was removed, a yield of 0.86 g (79 %) of 219 was obtained. m.p. 97-98 °C. IR (KBr, ν_{max}, cm^{-1}): 3397 (NH), 3300 (OH-broad band), 1698 (C=O). ^{1}H NMR (DMSO-d_6): δ 1.50-1.60 (m, 1H, CH), 1.94-1.98 (m, 1H, CH), 2.18-2.22 (m, 1H, CH), 2.24-2.31 (m, 1H, CH), 2.34 (d, 2H, J = 7.2 Hz, CH_2), 2.71 (d, 2H, J = 4.8 Hz, CH_2), 2.79 (dd, 1H, J = 14.8 and 4.8 Hz, CH), 6.89 (t, 1H, J = 8 Hz, ArH), 6.96 (t, 1H, J = 7.6 Hz, ArH), 7.22 (d, 1H, J = 8.4 Hz, ArH), 7.29 (d, 1H, J = 8 Hz, ArH), 10.59 (s, 1H, NH), 12.60 (s, 1H, OH). LC-MS (70 eV): m/z % 231 (11.4), 230 (100), 169 (4.9), 143 (4.4). Anal. calcd. (%) for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found. (%): C, 73.25; H, 6.63; N, 6.13.

2-(1,2,3,4-Tetrahydro-9*H*-carbazol-3-yl)ethanol (3): A solution of acid **2** (0.5 g, 2.18 mmol) in 15 mL of anhydrous tetrahydrofuran was added to a stirred solution of lithium aluminum hydride (0.34 g, 8.94 mmol) in tetrahydrofuran (15 mL) at 0 °C. The mixture was refluxed for 5 h and then it was cooled. The excess lithium aluminum hydride was decomposed with water (10 mL). The reaction mixture was extracted with ethyl acetate and organic layer was dried anhydrous magnesium sulfate. The solvent was removed under reduced pressure. The reaction product **3** was obtained as yellow oil which on standing set to a glass. IR (KBr, ν_{max}, cm^{-1}): 3401 (NH), 3299 (OH). ^{1}H NMR ($CDCl_3$): δ 1.58-1.65 (m, 1H, CH), 1.70-1.76 (m, 2H, CH_2), 1.96-2.06 (m, 2H, CH and OH), 2.33-2.40 (m, 1H, CH), 2.65-2.72 (m, 2H, CH_2), 2.92 (dd, 2H, J = 15.2 and 4.4 Hz, CH_2), 3.81 (t, 2H, J = 6.8 Hz, CH_2), 7.16-7.27 (m, 3H, ArH), 7.54 (d, 1H, J = 7.2 Hz, ArH), 7.91 (s, 1H, NH). LC-MS (70 eV): m/z % 217 (14.6), 216 (100), 215 (3.9), 198 (21.2). Anal. calcd. (%) for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found. (%): C, 78.28; H, 7.91; N, 6.45.

2-(1,2,3,4-Tetrahydro-9*H*-carbazol-3-yl)ethyl-4-methylbenzenesulfonate (4): A cooled solution of *p*-toluenesulfonyl chloride (0.47 g, 2.46 mmol) in 10 mL of pyridine was added to a cooled solution of **3** (0.47 g, 2.18 mmol) in pyridine (10 mL). The solution was allowed to stand in the cold for 18 h. The mixture was poured into water (200 mL) and then it was extracted with ethyl acetate. Organic layer dried with anhydrous magnesium sulfate. The solvent was evaporated under

reduced pressure and the residue was recrystallized from methanol to yielded 0.35 g (43 %) of **4**. m.p. 108-109 °C. IR (KBr, ν_{max}, cm^{-1}): 3436 (NH), 1356 and 1170 (S=O). ^{1}H NMR (DMSO-d_6): δ 1.35-1.45 (m, 1H, CH), 1.61-1.82 (m, 4H, 2x CH_2), 2.09 (dd, 1H, *J* = 14.4 and 8.8 Hz, CH), 2.36 (s, 3H, Ar-CH_3), 2.56 (dd, 1H, CH, *J* = 10.0 and 3.6 Hz, CH), 2.59-2.64 (m, 2H, CH_2), 4.16 (t, 2H, *J* = 5.6 Hz, CH_2), 6.90 (t, 1H, *J* = 8.0 Hz, ArH), 6.96 (t, 1H, *J* = 6.8 Hz, ArH), 7.21 (d, 2H, *J* = 8.4 Hz, ArH), 7.42 (d, 2H, *J* = 8.0 Hz, ArH), 7.79 (d, 2H, *J* = 8.0 Hz, ArH), 10.56 (s, 1H, NH); LC-MS (70 eV): m/z % 371 (28.7), 370 (100), 369 (10.8), 198 (53.2), 196 (11.7), 173 (3.1), 155 (3.3). Anal. calcd. (%) for $C_{21}H_{23}NO_3S$: C, 68.27; H, 6.27; N, 3.79; S, 8.68. Found. (%): C, 68.16; H, 6.21; N, 3.84; S, 8.65.

3-(1,2,3,4-Tetrahydro-9*H*-carbazol-3-yl)propanenitrile (5): Nitrile **4** (2 g, 5.40 mmol) was dissolved in N,N-dimethylformamide (30 mL) and sodium cyanide (1.33g, 27 mmol) was added. The mixture was heated at 50 °C for 18 h. The mixture was cooled and it was poured into water (150 mL). The mixture was extracted with diethyl ether. The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed. The reaction product **5** was obtained as yellow oil. IR (KBr, ν_{max}, cm^{-1}): 3397 (NH), 2244 (CN). ^{1}H NMR ($CDCl_3$): δ 1.41-1.51 (m, 1H, CH), 1.57-1.68 (m, 2H, CH_2), 1.76-1.84 (m, 1H, CH), 1.89-1.97 (m, 1H, CH), 2.21 (dd, 1H, *J* = 14.8 and 9.6 Hz, CH), 2.49 (t, 2H, *J* = 7.2 Hz, CH_2), 2.73-2.81 (m, 3H, CH and CH_2), 6.99 (t, 1H, *J* = 6.8 Hz, ArH), 7.05 (t, 1H, *J* = 7.2 Hz, ArH), 7.32 (d, 1H, *J* = 7.6 Hz, ArH), 7.38 (d, 1H, *J* = 8.0 Hz, ArH), 10.58 (s, 1H, NH). LC-MS (70 eV): m/z % 226 (11.6), 225 (67.3), 199 (17.2), 198 (100), 182 (4.6), 155 (2.0). Anal. calcd. (%) for $C_{15}H_{16}N_2$: C, 80.32; H, 7.19; N, 12.49. Found. (%): C, 80.24; H, 7.21; N, 12.53.

3-(4-Oxo-1,2,3,4-tetrahydro-9*H*-carbazol-3-yl)propanenitrile (6): A solution of tetrahydrocarbazole nitrile **5** (2 g, 8.92 mmol) was prepared at 0-5 °C in tetrahydrofuran (30 mL) (90 %). A solution of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (4.05 g, 17.83 mmol) was dissolved in tetrahydrofuran (20 mL) and it was added the solution at inert atmosphere. The reaction mixture was stirred 5 h at room temperature then the solution was poured into sodium hydroxide solution (400 mL, 10 %) and the mixture was extracted twice with ethyl acetate. The organic layer was dried with anhydrous magnesium sulfate and the solvent was evaporated under reduced pressure. The residue was purified by chromatography using silica gel and ethyl acetate. After the solvent was evaporated, a yield of 1.15 g (54 %) of **6** was obtained. m.p. 221-222 °C. IR (KBr, ν_{max}, cm^{-1}): 3183 (NH), 2239 (CN), 1612 (C=O). ^{1}H NMR (DMSO-d_6): δ 1.73-1.81 (m, 1H, CH), 1.92-2.01 (m, 1H, CH), 2.17-2.25 (m, 1H, CH), 2.27-2.32 (m, 1H, CH), 2.52-2.58 (m, 1H, CH), 2.69 (t, 2H, *J* = 7.2 Hz, CH_2), 3.05-3.08 (m, 2H, CH_2), 7.15-7.22 (m, 2H, ArH), 7.44 (d, 1H, *J* = 7.2 Hz, ArH), 8.00 (d, 1H, *J* = 6.8 Hz, ArH), 11.90 (s, 1H, NH). LC-MS (70 eV): m/z % 240 (17.2), 239 (100), 186 (0.7), 73 (8.4). Anal. calcd. (%) for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found. (%): C, 75.73; H, 5.86; N, 11.78.

3-(4-Oxo-9-tosyl-1,2,3,4-tetrahydro-9*H*-carbazol-3-yl)propanenitrile (7): A solution of **6** (0.75 g, 3.15 mmol) in 20 mL of chloroform was cooled to 0 ºC. After that 2 mL of sodium hydroxide solution (40 %), tetrabutyl ammonium hydrogen sulfate (100 mg) and *p*-toluenesulfonyl chloride (0.90 g, 4.72 mmol) were added. The mixture was stirred for 2 h at 0 °C, washed with hydrochloric acid (20 mL, 10 %) and the organic layer was dried with anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure. The residue was recrystallized from methanol to yielded 0.81 g (65 %) of **7**. m.p. 135-136 °C. IR (KBr, ν_{max}, cm^{-1}): 2931(CH), 2245 (CN), 1668 (C=O), 1363 and 1169 (S=O). ^{1}H NMR ($CDCl_3$): δ 1.73-1.82 (m, 1H, CH), 1.95-2.06 (m, 1H, CH), 2.19-2.25 (m, 1H, CH), 2.26-2.35 (m, 1H, CH), 2.38 (s, 3H, Ar-CH_3), 2.52-2.63 (m, 2H, CH_2), 2.64-2.73 (m, 1H, CH), 3.15-3.24 (m, 1H, CH), 3.57 (dt, 1H, *J* = 18.8 and 4.8 Hz, CH), 7.27 (d, 2H, *J* = 8.4 Hz, ArH), 7.31-7.37 (m, 2H, ArH), 7.74 (d, 2H, *J* = 8.8 Hz, ArH), 8.12-8.18 (m, 2H, ArH). LC-MS (70 eV): m/z % 394 (3.5), 393 (10.2), 392 (42), 339 (66), 237 (24), 184 (58), 156 (67), 128 (47), 91 (100). Anal. calcd. (%) for $C_{22}H_{20}N_2O_3S$: C, 67.33; H, 5.14; N, 7.14; S, 8.17. Found. (%): C, 67.21; H, 5.09; N, 7.23; S, 8.15.

Ethyl-4-oxo-1,2,3,4-tetrahydro-9-methoxymethyl-carbazole-3-carboxylate (9): A solution of 4-oxo-1,2,3,4-tetrahydro-9-methoxymethyl carbazole **8** (1.15 g, 5 mmol) in diethyl carbonate (25 mL) was added dropwise at 0 °C to a mixture of potassium hydride (35 % dispersion in mineral oil, 1.18 g, 10 mmol) in diethyl carbonate (25 mL). The mixture was heated at reflux temperature (150 °C) for 1 h and the reaction mixture was poured into ice-water (100 mL). The aqueous layer was extracted three times with dichloromethane. The combined organic phases were dried with magnesium sulfate and filtered and the solvents were evaporated. The residue was purified by column chromatography using silica gel and ethyl acetate/hexane (1:1). The solvent was evaporated and the residue was recrystallized form methanol to afford 1.20 g (79 %) of **9**. m.p. 85-86 °C. IR (KBr, ν_{max}, cm^{-1}): 2939 (CH), 1727 (C=O), 1654 (C=O). ^{1}H NMR (DMSO-d_6): δ 1.20 (t, 3H, *J* = 6.8 Hz, CH_3), 2.35-2.41 (m, 2H, CH_2), 3.02-3.19 (m, 2H, CH_2), 3.22 (s, 3H, OCH_3), 3.65 (t, 1H, *J* = 7.2 Hz, CH), 4.14 (q, 2H, *J* = 7.2 Hz, CH_2), 5.56 (s, 2H, NCH_2O), 7.20-7.29 (m, 2H, ArH), 7.64 (d, 1H, *J* = 6.8 Hz, ArH), 7.98 (d, 1H, *J* = 6.8 Hz, ArH). LC-MS (70 eV): m/z % 303 (18.6), 302 (100), 286 (8.0), 271 (1.0), 270 (6.1). Anal. calcd. (%) for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.35; N, 4.65. Found. (%): C, 67.69; H, 6.33; N, 4.71.

Ethyl-3-(cyanoethyl)-4-oxo-1,2,3,4-tetrahydro-9-methoxymethylcarbazole-3-carboxylate (10): A solution of **9** (1 g, 3.3 mmol) in absolute ethanol-tetrahydrofuran (1:1) (20 mL) was added to a solution of sodium ethoxide in absolute ethanol which was prepared from metallic sodium (0.2 g) and absolute ethanol (25 mL), at 0 °C under nitrogen atmosphere. The reaction mixture was stirred 0.5 h at 0 °C and then acrylonitrile (0.23 g, 3.3 mmol) was added. The reaction mixture was stirred overnight at room temperature. Then the reaction mixture was poured into hydrochloric acid solution (50 mL, 5 %) and extracted with ethyl acetate. The solvent was evaporated

under reduced pressure and the resulting residue was chromatographed using silica gel and ethyl acetate-hexane (1:1). The solvent was removed and then the product was recrystallized from ether to afford 0.72 g (61 %) of 10, m.p. 97-98 ºC. IR (KBr, ν_{max}, cm^{-1}): 2956 (CH), 2249 (CN), 1713 (C=O), 1647 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.20 (t, 3H, *J* = 6.8 Hz, CH_3), 2.24-2.40 (m, 3H, CH and CH_2), 2.60-2.64 (m, 2H, CH_2), 2.73-2.79 (m, 1H, CH), 3.05-3.11 (m, 1H, CH), 3.18-3.24 (m, 1H, CH), 3.31 (s, 3H, OCH_3), 4.17 (q, 2H, *J* = 7.2 Hz, CH_2), 5.44 (s, 2H, NCH_2O), 7.30-7.33 (m, 2H, ArH), 7.44-7.47 (m, 1H, ArH), 8.21-8.24 (m, 1H, ArH). LC-MS (70 eV): m/z % 357 (3.3), 356 (22), 355 (100), 325 (6.3), 323(8.2). Anal. calcd. (%) for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.90. Found.: C, 67.86; H, 6.30; N, 7.83.

3-(4-Oxo-1,2,3,4-tetrahydro-9*H*-carbazol-3-yl)propanoic acid (11): A solution of **10** (1 g, 2.8 mmol) in dioxane (20 mL) was refluxed with concentrated hydrochloric acid (10 mL) for 8 h. Then the reaction mixture was poured into water and extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the resulting residue was recrystallized from ether to afford 110 mg (15 %) of **11**, m.p. 260-261 ºC. IR (KBr, ν_{max}, cm^{-1}): 3250 (NH), 2958 (CH), 1711(C=O), 1625 (C=O). ^{1}H NMR (DMSO-d_6): δ 1.59-1.67 (m, 1H, CH), 1.81-1.90 (m, 1H, CH), 1.98-2.08 (m, 1H, CH), 2.16-2.22 (m, 1H, CH), 2.30-2.42 (m, 3H, CH and CH_2), 2.92-2.98 (m, 2H, CH_2), 7.08-7.15 (m, 2H, ArH), 7.36 (dd, 1H, *J* = 6.8 and 2.4 Hz, ArH), 7.91 (d, 1H, *J* = 6.8 Hz, ArH), 11.75 (s, 1H, NH), 11.98 (s, 1H, OH). LC-MS (70 eV): m/z % 258 (100), 256 (2.5), 255 (5.9), 241 (11.7), 240 (68.7), 230 (21.7), 201 (4.4), 200 (31.6). Anal. calcd. (%) for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found. (%) C, 69.90; H, 5.81; N, 5.49.

RESULTS AND DISCUSSION

In this study we accomplished the synthesis of a precursor **7** for the synthesis of pyrido[3,2-c]carbazole in a different pathway starting from carbazolone **1**[17] (**Scheme-I**). Compound **1** was hydrolyzed in basic conditions to give acid **2**[18,19]. Acid **2** was reduced to alcohol **3** with lithium aluminum hydride[17,19]. Alcohol **3** was converted into sulfonate ester derivative **4** with *p*-toluene sulfonyl chloride[20]. Compound **4** was reacted with sodium cyanide in dimethyl sulfoxide yielded compound **5**[17,18]. Then compound **5** selectively oxidized at **4** position using dichloro dicyano-*p*-benzoquinone in tetrahydrofuran (90 %) gave compound **6**[21]. Nitrogen atom of compound **6** was protected with *p*-toluene sulfonyl chloride using phase transfer catalyst tetrabutyl hydrogensulfate and sodium hydroxide (50 %) in dichloromethane and gave compound **7**[22].

Pyrido[3,2-c]carbazole can be easily synthesized with the aromatization of the octahydropyrido[3,2-c]carbazole which is synthesized from catalytic hydrogenation and cyclization of compound **7** in the light of literature[23,24].

Alternatively, intermediate **11** was synthesized starting from N protected 4-oxo tetrahydrocarbazole **8** (**Scheme-II**). Compound **8** was refluxed with diethyl carbonate in the presence of potassium hydride and gave **9**[25]. Then compound **9** was treated

with acrylonitrile and sodium ethoxide in ethanol and gave **10**. Compound **10** was hydrolyzed using concentrated hydrochloric acid in dioxane. Deprotection and decarboxylation occurred as a result of hydrolysis and yielded **11**[26,27]. Octahydro pyrido[3,2-c]carbazole structure can be synthesized by using Magnus' precedure[23].

ACKNOWLEDGEMENT

The authors wish to express their gratitude to Scientific Research Founds of Dokuz Eylul University (2007.KB.FEN.30) for financial support.

REFERENCES

1. H.J. Knolker and K.R. Reddy, *Chem. Rev*., **102**, 4303 (2002).
2. G.W. Gribble, In ed.: A. Brossi, The Alkaloids, Academic Press, New York, Vol. 39, p. 239 (1990).
3. V.K. Kansal and P. Potier, *Tetrahedron*, **32**, 2389 (1986).
4. Y. Ergun, S. Patir and G. Okay, *J. Heterocycl. Chem*., **35**, 1445 (1998).
5. N. Haider, *J. Heterocyclic Chem*., **39**, 511 (2002).
6. K. Hirata, C. Ito, H. Furukawa, M. Itogiawa, L. Mark Cosentino and K.H. Lee, *Bioorg. Med. Chem. Lett*., **9**, 119 (1999).
7. V. M. Hedin, T. Tabka, L. Poulin, T. Godard. M. Lachevrel, C. Saturnino, J.C. Lancelot, J.Y. Le Talaer and P. Gauduchon, *Anti Cancer Drug Des*., **15**, 109 (2000).
8. G.R. Clemo and D.G.I. Felton, *J. Chem. Soc*., 671 (1951).
9. S.J. Dewar, *J. Chem. Soc*., 615 (1944).
10. R. Von Huisgen, *Ann*, **559**, 101 (1948).
11. R.H.F. Manske and M. Kulka, *Can. J. Res*., **B27**, 291 (1949).
12. R.H.F. Manske and M. Kulka, *J. Am. Chem. Soc*., **72**, 4997 (1950).
13. M. Kulka and R.H.F. Manske, *Can. J. Chem*., **30**, 711 (1952).
14. O. DeSilva and V. Snieckus, *Synthesis*, **5**, 254 (1971).
15. A. Urrutia and J.G. Rodriquez, *Tetrahedron*, **55**, 11095 (1999).
16. Y. Ergun, *J. Heterocyclic Chem*., **44**, 539 (2007).
17. L.J. Dolby and S.J. Nelson, *J. Org. Chem*., **38**, 2282 (1973).
18. Y. Harrak, G. Rosell, G. Diadone, S. Plescia, D. Schillaci and M.D. Pujol, *Bioorg. Med. Chem*., **15**, 4876 (2007).
19. L.M. Rice and K.R. Scott, *J. Med. Chem*., **13**, 308 (1970).
20. Y. Kitano, T. Ito, T. Suzuki, Y. Nogato, K. Shinsima, E. Yoshimura, K. Chiba, M. Tada and I. Sakaguchi, *J. Chem. Soc. Perkin Trans. I*, 2251 (2002).
21. P. Magnus, N.L. Sear, C.S. Kim and N. Vicker, *J. Org. Chem*., **57**, 70 (1992).
22. Y. Ergun, S. Patir and G. Okay, *J. Heterocycl. Chem*., **39**, 315 (2002).
23. D. Desmaele and J. d'Angelo, *Tetrahedron Lett*., **31**, 883 (1990).
24. M.J.E. Hewlins, A.M. Oliveira-Campos and P.V.R. Shannon, *Synthesis*, 289 (1984).
25. F. Maertens, S. Toppet, G.J. Hoornaert and F. Compernolle, *Tetrahedron*, **61**, 1715 (2005).
26. H. Ping and F. Guoping, Assignee: Shanghai Hualian Pharmaceutical Co., Peop. Rep. China, Patent No: CN 1145902, Pub. Date: March 26 (1997).
27. J. Sperry, C.S.P. McErlean, A.M.Z. Slawin and C.J. Moody, *Tetrahedron Lett*., **48**, 231 (2007).

(*Received*: 23 April 2010; *Accepted*: 5 August 2010) AJC-8955