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Synthesis and Characterization of Carbazolyl-Oxazolones

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In this study, the synthesis of 2-carbazolyl-4-aryl/heteroarylidene-5-oxazolones (**3a-k**) derivatives starting from carbazole glycine ester derivatives (**1a-b**) was described. Thus, we aimed to combine the advantages of carbazole and 5-oxazolone moieties in synthesis of 2-carbazolyl-4-aryl/heteroarylidene-5-oxazolones (**3a-k**). These derivatives (**3a-k**) may have important biological and spectroscopic properties.

Key Words: Carbazole, Oxazolones, Heteroaryl substituted carbazoles.

INTRODUCTION

Carbazole[1-6] and oxazolone[7-10] moieties have great interest by chemist due to their biological properties and technological importance. Oxazolones have considerable pharmacological activities including anticancer, antimicrobial, antifungal, antagonistic, sedative, *etc*.[8]. Oxazolones are quite versatile intermediates used for the synthesis of several organic molecules, including amino acids, peptides, antimicrobial or antitumor compounds, immunomodulators, heterocyclic precursors, for biosensors coupling and/or photosensitive composition devices for proteins.

Carbazoles are well known as a conjugated, good hole-transporting, electron-donor, planar compound and ease to introduce solubilizing groups to rigid ring structure. Moreover many important alkaloids have carbazole moiety[1]. Carbazole derivatives have important roles of optical material due to their special photorefractive, electrical and chemical properties[2-6].

Most heteroarylcarbazoles reported in the literature contain a heteroaryl moiety fused with a carbazole which have received significant attention due to the promising antitumor properties[11]. However, there are few reports where the heteroaryl moiety is substituted with a carbazole unit. The synthesis of heteroaryl substituted carbazoles has begun to attract increasing interest because of their broad spectrum of useful biological activities[12-15].

EXPERIMENTAL

All solvents were of analytical grade and purchased from Merck, Fluka and Riedel. All melting points were measured in sealed tubes using an electrothermal digital melting points apparatus and are uncorrected. Infrared spectra were recorded on a Perkin ELMER FTIR infrared spectrometer (spectrum BX-II). ^{1}H NMR spectra were obtained on a high resolution fourier transform Bruker WH-400 NMR spectrometer with tetramethyl silane as an internal standard. Combustion analysis of compounds was obtained on a CHNS-932-LECO. Analytical and preparative thin layer chromatographies (TLC) were carried out using silica gel 60 F_{254} (Merck). Column chromatography was carried out by using 70-230 mesh silica gel (0.063-0.2 mm, Merck).

General procedure of the synthesis of carbazolyl glycine derivatives (2a and 2b): A solution of **1a** or **1b** (5 mmol) and lithium hydroxide monohydrate (5 mmol) in 25 mL of ethanol was stirred for 2 h. The solvent was removed under reduced pressure and the residue was diluted with water and acidified with conc. HCl. The solution was extracted with ethyl acetate and the organic layer was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the resulting residue was recrystallized from ether to afford **2a**[16] or **2b** as a white solid.

2-(9*H*-Carbazole-3-carboxamido) acetic acid (2b): m.p. 269 ºC; IR (KBr, ν_{max}, cm^{-1}): 3377(NH), 3258 (NH), 2921 (CH), 1705 (C=O), 1631 (C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 3.92 (d, 2H, $CONHCH_2$, J = 6.0 Hz), 7.18 (d, 1H, J = 8.0 Hz, ArH), 7.33 (d, 1H, J = 8.4 Hz, ArH), 7.37-7.44 (m, 1H, ArH) 7.50 (d, 1H, J = 8.4 Hz, ArH), 8.18 (d, 1H, J = 8.4 Hz, ArH), 8.42 (t, 1H, J = 6.0 Hz, $CONHCH_2$), 11.40 (s, 1H, NH), 12.50 (bs,1H, OH). Anal. calcd. (%) for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found (%): C, 67.11; H, 4.48; N, 10.51.

General methods for the synthesis of phenyl carbazole oxazolones (3a-k): Aryl or heteroaryl aldehyde (5 mmol), **2a** or **2b** (5 mmol), acetic anhydride (2.49 mL, 12 mmol) and

sodium acetate (5 mmol) was heated until the mixture just liquefied and then heating was continued for further 2 h. After completion of the reaction (determined by thin-layer chromatography), ethanol (25 mL) was added and mixture was kept at room temperature for 18 h. The solid product thus obtained was purified by washing with cold ethanol, hot water and then a small amount of hexane. The solid was recrystallized from hot ethanol to afford carbazolyl-oxazolones (**3a-k**).

4-(4-Methoxybenzylidene)-2-(4-methyl-9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3a): m.p. 230 ºC; IR (KBr, ν_{max}, cm^{-1}): 3331 (NH), 1773 (-O-C=O), 1647 (-C=N-), 1163 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 3.30 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 7.04 (d, 2H, *J* = 7.4 Hz, ArH), 7.15 (s, 1H, Ar-CH=C), 7.21-7.25 (m, 1H, ArH), 7.41-7.50 (m, 2H, ArH), 7.51-7.59 (m, 1H, ArH), 7.96 (d, 1H, *J* = 7.2 Hz, ArH), 7.81 (d, 2H, *J* = 7.6 Hz, ArH), 8.24-8.27 (m, 1H, ArH), 11.79 (s, 1H, NH). Anal. calcd. (%) for $C_{24}H_{18}N_2O_3$: C, 75.38; H, 4.74; N, 7.33; found (%): C, 75.23; H, 4.81; N, 7.37.

4-(4-Acetoxybenzylidene)-2-(4-methyl-9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3b): m.p. 248 ºC; IR (KBr, ν_{max}, cm^{-1}): 3374 (NH), 1796 (-OC=O), 1745 ($OCOCH_3$), 1651 (-C=N-), 1162 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 2.29 (s, 3H, $COCH_3$), 3.30 (s, 3H, CH_3), 7.22 (s, 1H, Ar-CH=C), 7.23-7.29 (m, 3H, ArH), 7.45-7.56 (m, 3H, ArH), 8.00 (d, 1H, *J* = 8.4 Hz, ArH), 8.28-8.32 (m, 3H, ArH), 11.83 (s, 1H, NH). Anal. calcd. (%) for $C_{25}H_{18}N_2O_4$: C, 73.16; H, 4.42; N, 6.83; found (%): C, 73.04; H, 4.49; N, 6.91.

4-(4-*tert*-Butylbenzylidene)-2-(4-methyl-9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3c): m.p. 254 ºC; IR (KBr, ν_{max}, cm^{-1}): 3300 (NH), 1771 (-OC=O), 1646 (-C=N-), 1167 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 1.31 (s, 9H, $C(CH_3)_3$), 3.35 (s, 3H, CH_3), 7.20 (s, 1H, Ar-CH=C), 7.27 (t, 1H, *J* = 7.2 Hz, ArH), 7.45-7.60 (m, 5H, ArH), 8.01 (d, 1H, *J* = 8.8 Hz, ArH), 8.21 (d, 2H, *J* = 8.0 Hz, ArH), 8.31 (d, 1H, *J* = 7.6 Hz, ArH), 11.85 (s, 1H, NH). Anal. calcd. (%) for $C_{27}H_{24}N_2O_2$: C, 79.39; H, 5.92; N, 6.86; found (%): C, 79.25; H, 6.05; N, 6.96.

4-(4-Methylbenzylidene)-2-(4-methyl-9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3d): m.p. 173 ºC; IR (KBr, ν_{max}, cm^{-1}): 3248 (NH), 1774 (-OC=O), 1643 (-C=N-), 1164 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 2.40 (s, 3H, CH_3) 3.39 (s, 3H, CH_3), 7.24 (s, 1H, Ar-CH=C), 7.29 (t, 1H, *J* = 8.0 Hz, ArH), 7.36 (d, 2H, *J* = 7.6 Hz, ArH), 7.48 (d, 1H, *J* = 6.8 Hz, ArH), 7.52 (d, 1H, *J* = 8.8 Hz, ArH), 7.59 (d, 1H, *J* = 8.0 Hz,ArH), 8.04 (d, 1H, *J* = 8.8 Hz, ArH), 8.20 (d, 2H, *J* = 8.4 Hz, ArH), 8.35 (d, 1H, *J* = 7.6 Hz, ArH), 11.87 (s, 1H, NH). Anal. calcd. (%) for $C_{24}H_{18}N_2O_2$: C, 78.67; H, 4.95; N, 7.65; found (%): C, 78.50; H, 5.01; N, 7.73.

4-(4-Fluorobenzylidene)-2-(4-methyl-9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3e): m.p. 251 ºC; IR (KBr, ν_{max}, cm^{-1}): 3474 (NH), 1781 (-OC=O), 1653 (-C=N-), 1159 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 3.38 (s, 3H, CH_3), 7.26 (s, 1H, Ar-CH=C), 7.29 (d, 1H, *J* = 8.0 Hz, ArH), 7.38 (t, 2H, *J* = 8.8 Hz, ArH), 7.47 (d, 1H, *J* = 7.6 Hz, ArH), 7.51 (d, 1H, *J* = 8.4 Hz, ArH), 7.59 (d, 1H, *J* = 8.0 Hz, ArH), 8.03 (d, 1H, *J* = 8.4 Hz, ArH), 8.32 (d, 1H, *J* = 8.4 Hz, ArH), 8.34-8.39 (m, 2H, ArH), 11.87 (s, 1H, NH). Anal. calcd. (%) for $C_{23}H_{15}N_2O_2F$: C, 74.59; H, 4.08; N, 7.56; found (%): C, 74.48; H, 4.13; N, 7.63.

4-(4-Chlorobenzylidene)-2-(4-methyl-9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3f): m.p. 263 ºC; IR (KBr, ν_{max}, cm^{-1}): 3455 (NH), 1781(-OC=O), 1646 (-C=N-), 1164 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 3.37 (s, 3H, CH_3), .22 (s, 1H, Ar-CH=C), 7.26 (t, 1H, *J* = 7.6 Hz, ArH), 7.44-7.59 (m, 5H, ArH), 8.01 (d, 1H, *J* = 9.2 Hz, ArH), 8.26-8.31 (m, 3H, ArH), 11.88 (s, 1H, NH). Anal. calcd. (%) for $C_{23}H_{15}N_2O_2Cl$: C, 71.41; H, 3.91; N, 7.24; found (%): C, 71.32; H, 3.95; N, 7.31.

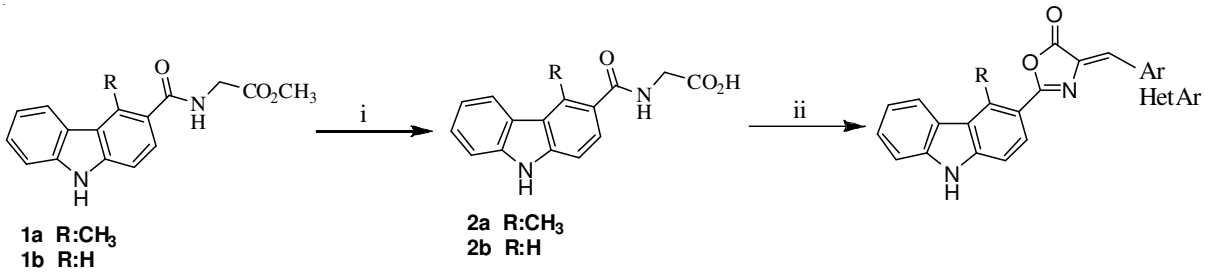
4-(4-Bromobenzylidene)-2-(4-methyl-9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3g): m.p. 276 ºC; IR (KBr, ν_{max}, cm^{-1}): 3449 (NH), 1779 (-OC=O), 1644 (-C=N-), 1163 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 3.37 (s, 3H, CH_3), 7.21 (s, 1H, Ar-CH=C), 7.28 (d, 1H, *J* = 7.6 Hz, ArH), 7.47 (d, 1H, *J* = 8.0 Hz, ArH), 7.51 (d, 1H, *J* = 8.4 Hz, ArH), 7.58 (d, 1H, *J* = 8.0 Hz, ArH), 7.72 (d, 2H, *J* = 8.0 Hz, ArH), 8.03 (d, 1H, *J* = 8.4 Hz, ArH), 8.20 (d, 2H, *J* = 8.8 Hz, ArH), 8.31 (d, 1H, *J* = 7.6 Hz, ArH), 11.92 (s, 1H, NH). Anal. calcd. (%) for $C_{23}H_{15}N_2O_2Br$: C, 64.05; H, 3.51; N, 6.50; found (%): C, 63.91; H, 3.57; N, 6.56.

2-(9*H*-Carbazol-3-yl)-4-((9-methyl-9*H*-carbazol-3-yl)methylene)oxazol-5(4*H*)-one (3h): m.p. 344 ºC; IR (KBr, ν_{max}, cm^{-1}): 3331 (NH), 1780 (-OC=O), 1648 (-C=N-), 1169 (-O-C=O); 1H NMR (dimethyl sulfoxide-d_6): δ 3.95 (s, 3H, NCH_3), 7.29 (t, 1H, *J* = 7.2 Hz, ArH), 7.34 (t, 1H, *J* = 7.3 Hz, ArH), 7.44 (s, 1H, Ar-CH=C), 7.50 (t, 1H, *J* = 8.0 Hz, ArH), 7.54 (d, 1H, *J* = 7.6 Hz, ArH), 7.59 (d, 1H, *J* = 8.0 Hz, ArH), 7.66 (d, 1H, *J* = 8.0 Hz, ArH), 7.75 (t, 2H, *J* = 8.4 Hz, ArH), 8.29 (d, 2H, *J* = 8.8 Hz, ArH), 8.37 (d, 1H, *J* = 8.0 Hz, ArH), 8.59 (d, 1H, *J* = 8.4 Hz, ArH), 8.93 (s, 1H, ArH), 9.08 (s, 1H, ArH), 11.86 (s, 1H, NH). Anal. calcd. (%) for $C_{29}H_{19}N_3O_2$: C, 78.90; H, 4.34; N, 9.52; found (%): C, 78.79; H, 4.40; N, 9.56.

4-[(1-Acetyl-1*H*-indol-3-yl)methylene]-2-(9*H*-carbazol-3-yl)oxazol-5(4*H*)-one (3i): m.p. 276 ºC; IR (KBr, ν_{max}, cm^{-1}): 3316 (NH), 1771 (-OC=O), 1716 (C=O), 1649 (-C=N-), 1184 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 2.84 (s, 3H, indole $NCOCH_3$), 7.27 (t, 1H, *J* = 7.6 Hz, ArH), 7.42-7.49 (m, 4H, 3xArH and Ar-CH=C), 7.55 (d, 1H, *J* = 7.6 Hz, ArH), 7.68 (d, 1H, *J* = 8.8 Hz, ArH), 8.20 (dd, 1H, *J* = 8.8 and 1.6 Hz, ArH), 8.27 (d, 1H, *J* = 8.0 Hz, ArH), 8.32-8.38 (m, 2H, ArH), 8.84 (s, 1H, ArH), 8.86 (d, 1H, *J* = 1.6 Hz, ArH), 11.85 (s, 1H, NH). Anal. calcd. (%) for $C_{26}H_{17}N_3O_3$: C, 74.45; H, 4.09; N, 10.02; found (%): C, 74.31; H, 4.13; N, 10.11.

2-(9*H*-Carbazol-3-yl)-4-(furan-3-ylmethylene)oxazol-5(4H)-one (3*j*): m.p. 281 ºC; IR (KBr, ν_{max}, cm^{-1}): 3376 (NH), 1755 (-OC=O), 1649 (-C=N-), 1157 (-O-C=O); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 6.84-6.86 (dd, 1H, *J* = 3.2 and 2.0 Hz, FuranH), 7.11 (s, 1H, Ar-CH=C), 7.27 (t, 1H, *J* = 7.6 Hz, ArH), 7.49 (t, 1H, *J* = 8.4 Hz, ArH), 7.58 (d, 1H, *J* = 8.4 Hz, ArH), 7.67 (t, 2H, *J* = 8.8 Hz, ArH), 8.06 (d, 1H, *J* = 1.6 Hz, ArH), 8.19 (dd, 1H, *J* = 8.4 and 1.6 Hz, ArH), 8.34 (d, 1H, *J* = 8.4 Hz, ArH), 8.90 (d, 1H, *J* = 1.6 Hz, ArH), 11.86 (s, 1H, NH). Anal. calcd. (%) for $C_{20}H_{12}N_2O_3$: C, 73.16; H, 3.68; N, 8.53; found (%): C, 73.02; H, 3.72; N, 8.61.

2-(9*H*-Carbazol-3-yl)-4-(thiophen-3-ylmethylene)-oxazol-5(4H)-one (3k): m.p. 253 ºC; IR (KBr, ν_{max}, cm^{-1}): 3370 (NH), 1753 (-OC=O), 1649 (-C=N-), 1159 (-O-C=O); ^{1}H NMR



	R	Ar (HetAr)		R	Ar (HetAr)
3a	CH_3	*p*-methoxyphenyl	**3g**	CH_3	*p*-bromophenyl
3b	CH_3	*p*-acetoxyphenyl	**3h**	H	N-methyl carbazol-3-yl
3c	CH_3	*p*-*tert*-butylphenyl	**3i**	H	N-acetyl indol-3-yl
3d	CH_3	*p*-methylphenyl	**3j**	H	furan-2-yl
3e	CH_3	*p*-florophenyl	**3k**	H	thiophen-2-yl
3f	CH_3	*p*-chlorophenyl			

Reagent and conditions: (i) $LiOH{\cdot}H_2O$, ethanol; (ii) NaOAc, Ac_2O, ArCHO

Scheme-I

(dimethyl sulfoxide-d_6): δ 7.25-7.30 (m, 2H, ArH and Ar-CH=C), 7.49 (t, 1H, *J* = 8.4 Hz, ArH), 7.58 (d, 1H, *J* = 8.4 Hz, ArH), 7.63 (s, 1H, ArH), 7.70 (d, 1H, *J* = 8.4 Hz, ArH), 7.84 (d, 1H, *J* = 4.8 Hz, ArH), 8.04 (d, 1H, *J* = 4.8 Hz, ArH), 8.20 (dd, 1H, *J* = 8.8 and 2 Hz, ArH), 8.33 (d, 1H, *J* = 8.0 Hz, ArH), 8.55 (d, 1H, *J* = 1.6 Hz, ArH), 11.87 (s, 1H, NH). Anal. calcd. (%) for $C_{20}H_{12}N_2O_2S$: C, 69.75; H, 3.51; N, 8.13; S, 9.31; found (%): C, 69.68; H, 3.57; N, 8.18; S, 9.27.

RESULTS AND DISCUSSION

2-Aryl-4-carbazolylidene-5-oxazolones were synthesized firstly *via* Erlenmeyer reaction of the carbazole aldehyde derivatives with several N-benzoyl glycine derivatives and their optical properties were studied[17,18]. A few 2-carbazolyl-4-arylidene-5-oxazolones were also synthesized and carried out their spectroscopic properties[16].

Herein, a new 2-carbazolyl-4-arylidene-5-oxazolones (**3a-k**) derivatives are synthesized. The carbazole glycine ester derivatives **1a** and **1b** were used as starting materials, in which **1a** was synthesized previously[19]. The hydrolysis of carbazole glycine ester **1a-b** in basic conditions gave glycine derivatives of carbazole (**2a-b**)[20]. Finally, 2-carbazolyl-4-arylidene-5-oxazolones (**3a-k**) were synthesized with carbazole glycine derivatives **2a-b** and several aryl or heteroaryl aldehydes by Erlenmeyer reaction. Thus, it is aimed to combine the advantages of carbazole and 5-oxazolone moieties.

REFERENCES

1. H.J. Knölker and K.R. Reddy, *Chem. Rev*., **102**, 4303 (2002).
2. K.R. Yoon, S.-O. Ko, S.M. Lee and H. Lee, *Dyes Pigm*., **75**, 567 (2007).
3. Q. Ying, *Dyes Pigm*., **76**, 277 (2008).
4. Y. Xing, X. Xu, P. Zhang, W. Tian, G. Yu, P. Lu Y. Liu and D. Zhu, *Chem. Phys. Lett*., **408**, 169 (2005).
5. A.K. Mishra, J. Jacob and K. Müllen, *Dyes Pigm*., **75**, 1 (2007).
6. G. Bai, J. Li, D. Li, C. Dong, X. Han and P. Lin, *Dyes Pigm*., **75**, 93 (2007).
7. M. Grigoras and N.C. Antonoaia, *Eur. Polym. J*., **41**, 1079 (2005).
8. K.M. Khan, U.R. Mughal, M.T.H. Khan, Z. Ullah, S. Perveenb, M.I. Choudhary, *Bioorg. Med. Chem*., **14**, 6027 (2006).
9. G. Ozturk, S. Alp and K. Ertekin, *Dyes Pigm*., **72**, 150 (2007).
10. G. Ozturk, S. Alp and Y. Ergun, *Tetrahedron Lett*., **48**, 7347 (2007).
11. H.-J. Knölker and K.R. Reddy, *Chem. Rev*., **102**, 4303 (2002).
12. G.H. Kirsch, *Curr. Org. Chem*., **5**, 507 (2001).
13. R. Meesala and R. Nagarajan, *Tetrahedron Lett*., **47**, 7557 (2006).
14. T.K. Chaitanya and R. Nagarajan, *Tetrahedron Lett*., **48**, 2489 (2007).
15. Z. Li, Y. Xing, X. Ma, S. Xiao and Z. Lu, *Synth. Commun*., **36**, 3287 (2006).
16. C. Gündogdu, D. Topkaya, G. Öztürk, S. Alp and Y. Ergün, *J. Heterocycl. Chem*. **47**, 1450 (2010).
17. J.L. Diaz, B. Villacampa, F. Lopez-Calahorra, D. Velasco, *Chem. Mater*., **14**, 2240 (2002).
18. J.L. Diaz, B. Villacampa, F. Lopez-Calahorraa and D. Velascoa, *Tetrahedron Lett*., **43**, 4333 (2002).
19. Y. Ergün, S. Gülle, A.B. Çagdas, M. Göçmentürk and G. Okay, *Asian J. Chem*., **22**, 1853 (2010).
20. V. Sharma, T.A. Lansdell, G. Jin and J.J. Tepe, *J. Med. Chem*., **47**, 3700 (2004).