NEW ACYLATED DERIVATIVES OF 2-METHYL-4-OXO-QUINAZOLIN-3(4H)-IL-ACETOHYDROXAMIC ACID

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Abstract

In our research of bioactive molecules we synthesized some new substances with 4(3H)-quinazolinone structure that may have similar pharmacological properties to those of other compounds with similar structures. These compounds are acylated derivatives of 2-methyl-4-oxo-quinazolin-3(4H)-il-acetohydroxamic acid. Their chemical structures were confirmed by elemental analysis, infrared (IR) and nuclear magnetic resonance (NMR) spectra.

Rezumat

Cercetările noastre având drept scop obţinerea de molecule bioactive s-au finalizat cu sinteza unor substanţe cu structură 4(3H)-chinazolinonică care pot avea proprietăţi farmacologice asemănătoare cu ale compuşilor cu structură înrudită. Aceste noi substanţe sunt derivaţi acilaţi ai acidului 2-metil-4-oxo-chinazolin-3(4H)-il-acetohidroxamic. Structura chimică a acestor compuşi a fost confirmată cu ajutorul analizei elementale şi al spectrelor în infraroşu (IR) şi de rezonanţă magnetică nucleară (RMN).

Keywords: quinazolones, hydroxamic acid potassium salt, acylation, carbamates.

Introduction

A lot of pharmacological research revealed the therapeutic importance of the compounds having 4(3H)-quinazolinone structure. These substances have valuable biological activities and are used as antidepressants [11], anticonvulsants [15], analgesics, antipyretic, anti-inflammatory agents [2-5, 10, 14] or for their antihypertensive [1, 6], tuberculostatic [13], antimalarial [17], antibacterial, antifungal [9, 12], antiviral and anticancer [16] properties.

On the other hand it is known that the carbamate ester derivatives have different certain therapeutic actions, this class including

physostigmine, neostigmine, pyridostigmine, rivastigmine, methocarbamol, carisoprodol.

In order to obtain new bioactive molecules, we brought together the 4(3H)-quinazolinone structure with carbamic ester moiety.

Materials and Methods

All starting materials and solvents were purchased from common commercial suppliers and were used without purification unless otherwise noted.

Melting points were measured in open capillary tubes on an Electrothermal 9100 apparatus and they are uncorrected. Infrared spectra were recorded on a FT/IR-solid in ATR spectrometer (the signal intensities (height) were denoted by the following abbreviations: w = weak, m = medium, s = strong, v = variable). The NMR spectra were recorded on a Varian 2000 and Bruker Fourier 300 instruments at room temperature, operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. The chemical shifts were recorded in δ units (ppm), relative to residual peak of the deuterated dimethyl sulfoxide (DMSO-d6). tetramethylsilane (TMS) was used as internal standard. The coupling constants values are reported in hertz and the splitting patterns are abbreviated as following: s = singlet; d = doublet; t = triplet; m =multiplet; b = broad. The elemental analyses were performed on a Perkin Elmer CHNS/O Analyser Series II 2400 apparatus and the results were in agreement with the calculated values.

Intermediate synthesis

The main intermediate compound necessary for obtaining the new compounds is the potassium salt of hydroxamic acid with 4(3H)-quinazolinone structure (III). This was obtained by condensation reaction between methyl 2-(2-methyl-4-oxoquinazolin-3(4H)-yl)-acetate (I) with hydroxylammonium chloride (II), in the presence of potassium hydroxide [7,8]. The condensation reaction is presented in Figure 1.

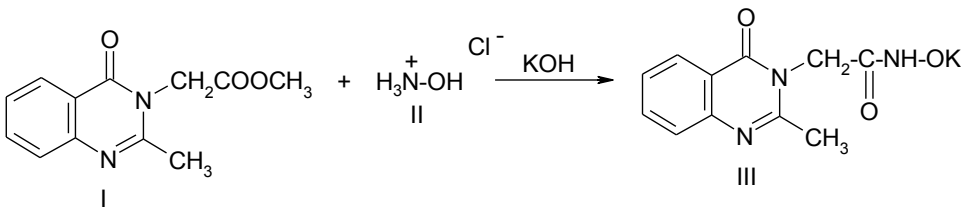


Figure 1
Synthesis of the intermediate compound III

In a round bottom flask equipped with condenser, stirrer and dropping funnel were added 6.95 g (0.10 mol) hydroxylammonium chloride in 36 mL methanol and a solution of 8.37 g (0.15 mol) potassium hydroxide in 21 mL methanol was added dropwise. For total precipitation of potassium chloride, the mixture was kept on an ice bath for ten minutes. Then the mixture was filtered quickly and a solution of 11.5 g(0.05 mol) methyl ester (I) in 20 mL methanol was added under stirring. The reaction mixture was allowed to stand at room temperature, after 30-40 minutes begining the formation of white christals; the concluding of the reaction took place in approx. 48 hours. The precipitate was filtered and washed with absolute ethanol. After drying at room temperature resulted 12.39 g (91.5% yield) white microcrystals.

Final compound synthesis

The parameters of the acylation reaction were tested for obtaining ten original carbamates. These compounds were obtained by treating the potassium hydroxamate former obtained with aromatic acid chlorides in dioxane.

The new carbamates (1-10) were obtained in accordance with the following general procedure described in Figure 2.

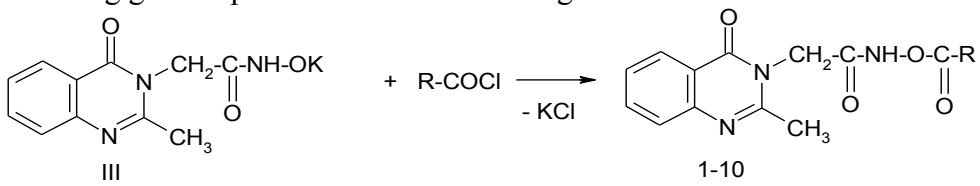


Figure 2

The synthesis of the new carbamates 1-10

The chemical structures of these new compounds are presented in Table I.

The 0.68 g (0.0025 mol) potassium hydroxamate (III) were dissolved in 25 mL dioxane heating gently; then were gradually added 0.0025 mol acid chlorides in 20 mL dioxane; a white precipitate (potassium chloride) appeared. The reaction mixture was refluxed for 3 hours and then was filtered. The filtrate was evaporated to dryness warming up easily at vacuum to give the final crude compound. The new compounds were recrystallized from isopropanol.

Results and Discussion

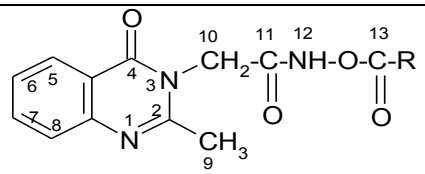
Following the acylation reaction between potassium 2-methyl-4-oxo-quinazolin-3(4H)-il-acetohydroxamate with different carboxylic acid chlorides, we obtained ten new carbamates, using dioxane as reaction medium.

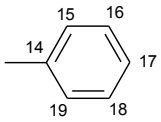
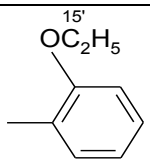
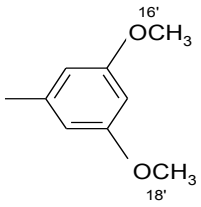
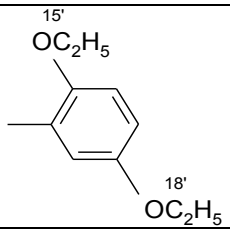
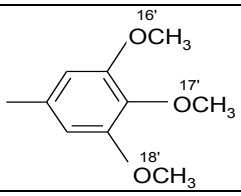
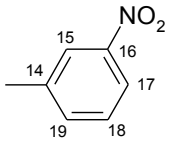
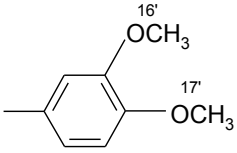
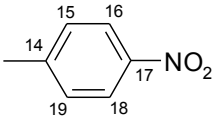
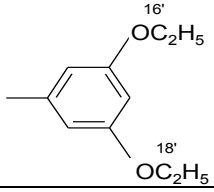
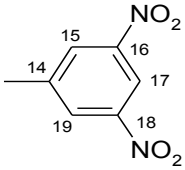
These carbamates are solid, crystalline, white, or slight yellow substances and they were recrystallized from isopropanol. Their structures were confirmed by elemental analysis, IR and NMR spectra. All this data, molecular formula, relative mass (Mr), melting points (m.p.), are further presented.

General numbering used in NMR spectral data interpretation is presented in Table I.

Table I

General numbering of compounds 1-10



No	R	No	R
1.		6.	
2.		7.	
3.		8.	
4.		9.	
5.		10.	

Compound 1: 3-(Phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methyl-quinazolin-4(3H)-one. $C_{18}H_{15}N_3O_4$ (Mr 337.33).

Elemental analysis: Calculated: C 64.09%, H 4.48%, N 12.46%; Found C 64.27%, H 4.38%, N 12.52%; m.p. 155-156 ºC; yield 57.2%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.56(s, 1H, H-12); 8.12(dd, 1H, H-5, *J= 1.5, J= 7.9*); 8.03(bd, 2H, H-15, H-19, *J= 7.6*); 7.82(td, H-7, *J= 7.9, J= 1.5*); 7.74(tt, 1H, H-17, *J=1.4*, *J= 7.3*); 7.61(dd, 1H, H-8, *J= 1.5*, *J= 7.9*); 7.60(dd, 2H, H-16, H-18, *J= 7.3*, *J= 7.6*); 7.51(td, 1H, H-6, *J= 7.9*, *J= 1.5*); 4.98(s, 2H, H-10); 2.59(s, 3H, H-9).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.90(CO-11); 164.06(CO-13); 161.17(C-4); 155.00(C-2); 146.92(C-1a); 126.47(C-14); 119.53(C-4a); 134.51(C-7); 134.38(C-17); 129.40(C-19, C-15); 129.07(C-16, C-18); 126.48(C-8); 126.38(C-6); 126.17(C-5); 43.86(C-10); 22.57(C-9). 134.64(C-7); 126.62(C-8); 126.49(C-6); 126.26(C-5).

FT-IR (solid in ATR, ν cm^{-1}): 3198m; 3007w; 1781m; 1766m; 1707m; 1688s; 1655vs; 1596vs; 1572m; 1472m; 1449m; 1389m; 1372w; 1238s; 1184w; 1055m; 991m; 970m; 774m; 719w; 702m; 658w.

Compound 2: 3-(3,5-Dimethoxy-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{20}H_{19}N_3O_6$ (Mr 397.39)**.**

Elemental analysis: Calculated: C 60.45%, H 4.82%, N 10.57%; Found C 60.60%, H 4.96%, N 10.65%; m.p. 148-149 ºC; yield 48.1%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.58(s, 1H, H-12); 8.10(dd, 1H, H-5, *J= 7.8 Hz, J=1.6 Hz*); 7.79(td, 1H, H-7, *J= 7.8*, *J= 1.6*); 7.62(bd, 1H, H-8, *J= 7.8*); 7.51(td, 1H, H-6, *J= 7.8, J= 1.5*); 7.11(d, 2H, H-15, H-19, *J= 2.3*); 6.87(t, 1H, H-17, *J= 2.3*); 4.96(s, 2H, H-10); 3.81(s, 6H, H-16', H-18'); 2.58(s, 3H, H-9).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.86(CO-11); 163.74(CO-13); 161.13(C-4); 160.69(C-16, C-18); 155.09(C-2); 147.05(C-1a); 128.33(C-14); 119.61(C-4a); 134.65(C-7); 126.63(C-8); 126.51(C-6); 126.26(C-5); 106.99(C-19, C-15); 106.46(C-17); 55.66(C-16', C-18'); 43.93(C-10); 22.73(C-9).

FT-IR (solid in ATR, ν cm^{-1}): 3239w; 3092w; 2949w; 2844w; 1775m; 1676vs; 1600vs; 1500w; 1469m; 1431m; 1390m; 1352m; 1305m; 1212m; 1195m; 1179m; 1165m; 1081w; 1051m; 1016m; 976m; 931w; 877w; 848w; 772m; 747w.

Compound 3: 3-(3,4,5-Trimethoxy-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{21}H_{21}N_3O_7$ (Mr 427.41).

Elemental analysis: Calculated: C 59.01%, H 4.95%, N 9.83%; Found C 58.92%, H 5.05%, N 10.02%; m.p. 152-153 ºC; yield 45.3%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.58(s, 1H, H-12); 8.11(dd, 1H, H-5, *J= 7.3, J= 1.6*); 7.82(td, 1H, H-7, *J= 7.3, J= 1.6*); 7.62(bd, 1H, H-8, *J= 7.3*); 7.51(td, 1H, H-6, *J= 7.3, J= 1.4*); 7.29(s, 2H, H-15, H-19); 4.96(s, 2H, H-10); 3.85(s, 6H, H-16', H-18'); 3.76(s, 3H, H-17'); 2.58(s, 3H, H-9).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.88(CO-11); 163.64(CO-13); 161.13(C-4); 155.10(C-1a); 152.99(C-16, C-18); 147.05(C-17); 142.69(C-14); 121.30(C-14); 119.61(C-4a); 134.65(C-7); 126.63(C-8); 126.51(C-6); 126.26(C-5); 106.83(C-15, C-19); 60.25(C-17'); 56.13(C-16', C-18'); 43.90(C-10); 22.72(C-9).

FT-IR (solid in ATR, ν cm^{-1}): 3200w; 2979w; 1766m; 1680vs; 1601s; 1512m; 1465m; 1416wm; 1405w; 1277m; 1250m; 1209m; 1188m; 1144m; 1071m; 1017m; 972m; 870m; 772m.

Compound 4: 3-(3,4-Dimethoxy-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{20}H_{19}N_3O_6$ (Mr 397.39).

Elemental analysis: Calculated: C 60.45%, H 4.82%, N 10.57%; Found C 60.57%, H 5.05%, N 10.48%; m.p. 180-181 ºC; yield 38.9%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.48(s, 1H, H-12); 8.11(dd, 1H, H-5, *J= 7.8, J= 1.6*); 7.82(td, 1H, H-7, *J= 7.8, J= 1.6*); 7.62(bd, 1H, H-8, *J= 7.8*); 7.51(td, 1H, H-6, *J= 7.8, J= 1.4*); 7.68(dd, 1H, H-19, *J= 2.1, J= 8.5*); 7.46(d, 1H, H-15, *J= 2.1*); 7.13(d, 1H, H-18, J= 8.5); 4.96(s, 2H, H-10); 3.85(s, 3H, H-17' or H-16); 3.82(s, 3H, H-16'or H-17'); 2.58(s, 3H, H-9).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.85(CO-11); 163.75(CO-13); 161.14(C-4); 155.11(C-2); 153.88(C-16); 148.67(C-17); 147.05(C-1a); 119.61(C-4a); 118.25(C-14); 134.64(C-7); 126.62(C-8); 126.49(C-6); 126.26(C-5); 123.90(C-18); 111.67(C-15); 111.44(C-19); 55.84(C-16' or C-17'); 55.62(C-16' or C-17'); 43.90(C-10); 22.72(C-9).

FT-IR (solid in ATR, ν cm^{-1}): 3200w; 2978w; 1766m; 1680vs; 1601s; 1517m; 1465m; 1416w; 1405w; 1386w; 1277m; 1250m; 1209w; 1188m; 1144m; 1071m; 1018m; 972m; 870m; 772m; 750w.

Compound 5: 3-(3,5-Diethoxy-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{22}H_{23}N_3O_6$ (Mr 425.44).

Elemental analysis: Calculated: C 62.11%, H 5.45%, N 9.88%; Found C 62.25%, H 5.58%, N 10.05%; m.p. 158-159 ºC; yield 35.8%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.59(s, 1H, H-12); 8.11(dd, 1H, H-5, *J= 7.8, J= 1.6*); 7.82(td, 1H, H-7, *J= 7.8, J= 1.6*); 7.62(bd, 1H, H-8, *J= 7.8*); 7.51(td, 1H, H-6, *J= 7.8, J= 1.4*); 7.07(d, 2H, H-15, H-19, *J= 2.1*); 6.82(t, 1H, H-17, *J= 2.1*); 4.96(s, 2H, H-10); 4.07(q,

4H(CH_2), H-16', H-18', *J= 6.9*); 2.58(s, 3H, H-9); 1.32(t, 6H(CH_3), H-16', H-18', *J= 6.9*).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 163.78(CO-11); 163.14(CO-13); 161.09(C-4); 159.88(C-16, C-18); 155.03(C-2); 147.01(C-1a); 128.25(C-14); 119.57(C-4a);

134.58(C-7); 126.58(C-8); 126.44(C-6); 126.20(C-5); 107.30(C-16, C-18); 107.21(C-17); 63.64(CH_2-16', CH_2-18'); 43.89(C-10); 22.67(C-9); 14.43(CH_3-16', CH_3-18').

FT-IR (solid in ATR, ν cm^{-1}): 3219w; 2980w; 2937w; 2882w; 1778m; 1675vs; 1602s; 1510w; 1471w; 1451m; 1389m; 1372m; 1355m; 1301m; 1179vs; 1116m; 1086m; 1058s; 976m; 934m; 859m; 829w; 776m; 747m; 708w; 692w; 676w; 658m.

Compound 6: 3-(2-Ethoxy-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{20}H_{19}N_3O_5$ (Mr 381.39).

Elemental analysis: Calculated: C 62.99%, H 5.02%, N 11.02%; Found C 63.15%, H 5.15%, N 10.85%; m.p. 150-151 ºC; yield 40.1%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.49(s, 1H, H-12); 8.11(dd, 1H, H-5, *J= 7.7, J= 1.6*); 7.82(td, 1H, H-7, *J= 7.7, J= 1.6*); 7.73(dd, 1H, H-19, *J= 1.4, J= 8.6*); 7.62(bd, 1H, H-8, *J= 7.7*); 7.60(td, 1H, H-17, *J= 8.6, J= 1.4*); 7.51(td, 1H, H-6, *J= 7.7*, *J= 1.4*); 7.20(bd, 1H, H-16, *J= 8.6*); 7.05(bd, 1H, H-18, *J= 8.6*); 4.94(s, 2H, H-10); 4.13(q, 2H(CH_2), H-15', *J= 6.9*); 2.57(s, 3H, H-9); 1.32(t, 3H(CH_3), H-15', *J= 6.9*).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.74(CO-11); 163.53(CO-13); 161.17(C-4); 158.10(C-15); 155.15(C-2); 147.05(C-1a); 119.64(C-4a); 116.57(C-14); 134.92(C-19); 134.67(C-7); 131.03(C-17); 126.61(C-8); 126.53(C-6); 126.29(C-5); 120.29(C-18); 113.83(C-16); 64.28(CH_2-15'); 43.94(C-10); 22.72(C-9); 14.50(CH_3-15').

FT-IR (solid in ATR, ν cm^{-1}): 3227w; 2981w; 1748m; 1682vs; 1601s; 1486w; 1470m; 1455m; 1402m; 1297m; 1245m; 1219m; 1184w; 1171w; 1122w; 1065m; 1042m; 999w; 971m; 780m; 753s; 712w; 696m; 657w.

Compound 7: 3-(2,5-Diethoxy-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{22}H_{23}N_3O_6$ (Mr 425.44).

Elemental analysis: Calculated: C 62.11%, H 5.45%, N 9.88%; Found C 62.28%, H 5.38%, N 9.70%; m.p. 153-154 ºC; yield 39.4%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.51(s, 1H, H-12); 8.11(dd, 1H, H-5, *J= 7.8, J=1.6*); 7.82(td, 1H, H-7, *J=7.8, J= 1.6*); 7.62(bd, 1H, H-8, *J= 7.8*); 7.51(td, 1H, H-6, *J= 7.8, J= 1.4*); 7.20(d, 1H, H-19, *J= 2.4*); 7.16(d, 1H, H-16, *J= 8.6*); 7.13(dd, 1H, H-17, *J= 2.4, J= 8.6*); 4.95(s, 2H, H-10); 4.06(q, 2H(CH_2), H-15' or H-18', *J= 6.9*); 3.99(q,

2H(CH_2), H-18' or H-15', *J= 6.9*); 2.57(s, 3H, H-9); 1.29(t, 6H(CH_3), H-15', H-18', *J= 6.9*).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.67(CO-11); 163.20(CO-13); 161.09(C-4); 155.07(C-2); 155.07(C-15); 152.10(C-18); 151.78(C-14); 146.99(C-1a); 119.58(C-4a); 134.58(C-19); 126.55(C-8); 126.44(C-6); 126.22(C-5); 121.18(C-19); 115.93(C-16); 115.66(C-17); 64.97(CH_2, C-15' or C-18'); 64.74(CH_2, C-18' or C-15'); 43.88(C-10); 22.67(C-9); 14.58(CH_3, C-15'or C-18'); 14.54(CH_3, C-18' or C-15').

FT-IR (solid in ATR, ν cm^{-1}): 3201w; 2979w; 2932w; 1752m; 1683vs; 1602s; 1501m; 1472m; 1420m; 1391m; 1338w; 1283m; 1265m; 1234s; 1189s; 1111w; 1066m; 1042s; 976m; 934m; 873w; 813m; 769s; 711w; 694m; 658w.

Compound 8: 3-(3-Nitro-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{18}H_{14}N_4O_6$ (Mr 382.33).

Elemental analysis: Calculated: C 56.55%, H 3.69%, N 14.65%; Found: C 56.73%, H 3.85%, N 14.38%; m.p. 163-164 ºC; yield 41.2%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.88(s, 1H, H-12); 8.67(t, 1H, H-15*, J= 1.1*); 8.57(dt, 1H, H-17, *J= 8.2, J= 1.1*); 8.44(bd, 1H, H-19, *J= 8.2*); 8.12(dd, 1H, H-5, *J= 7.8, J= 1.6*); 7.90(t, 1H, H-18, *J= 8.2*); 7.83(td, 1H, H-7, *J= 7.8, J= 1.6*); 7.63(bd, 1H, H-8, *J= 7.8*); 7.53(td, 1H, H-6*, J= 7.8, J= 1.4*); 5.00(s, 2H, H-10); 2.61(s, 3H, H-9).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.91(CO-11); 162.47(CO-13); 161.01(C-4); 155.46(C-2); 148.07(C-16); 146.51(C-1a); 127.97(C-14); 119.50(C-4a); 135.55(C-19); 134.83(C-7); 131.22(C-18); 128.93(C-17); 126.71(C-8); 126.35(C-6); 126.27(C-5); 124.01(C-15); 44.01(C-10); 22.60(C-9).

FT-IR (solid in ATR, ν cm^{-1}): 3178w; 3010w; 1767w; 1675vs; 1598m; 1526s; 1474w; 1390w; 1353m; 1254m; 1236m; 1218w; 1108w; 978w; 766w; 713m.

Compound 9: 3-(4-Nitro-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{18}H_{14}N_4O_6$ (Mr 382.33).

Elemental analysis: Calculated: C 56.55%, H 3.69%, N 14.65%; Found: C 56.78%, H 3.56%, N 14.84%; m.p. 183-184 ºC; yield 38.7%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 12.84(s, 1H, H-12); 8.39(d, 2H, H-16, H-18, *J= 9.4*); 8.27(d, 2H, H-15, H-16, *J= 9.2*); 8.11(dd, 1H, H-5, *J= 7.8*, *J= 1.6*); 7.82(td, 1H, H-7, *J= 7.8, J= 1.6*); 7.61(bd, 1H, H-8, *J= 7.8*); 7.51(td, 1H, H-6, *J= 7.8, J= 1.4*); 4.98(s, 2H, H-10); 2.58(s, 3H, H-9).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 164.99(CO-11); 162.69(CO-13); 161.13(C-4); 155.11(C-2); 150.87(C-17); 146.97(C-1a); 131.86(C-14);

119.57(C-4a); 134.71(C-7); 131.13(C-16, C-18); 126.60(C-8); 126.56(C-6); 126.28(C-5); 124.26(C-15, C-19); 43.96(C-10); 22.73(C-9).

FT-IR (solid in ATR, ν cm^{-1}): 3164m; 3077w; 3017w; 2976m; 1783s; 1711m; 1642vs; 1597vs; 1528vs; 1473m; 1416w; 1386w; 1347s; 1233m; 1066m; 975m; 873w; 844w; 774m; 710m; 658w.

Compound 10: 3-(3,5-Dinitro-phenyl-carbonyl-oxi-carbamoyl-methyl)-2-methylquinazolin-4(3H)-one. $C_{18}H_{13}N_5O_8$ (Mr 427.33).

Elemental analysis: Calculated: C 50.59%, H 3.07%, N 16.39%; Found: C 50.72%, H 3.15%, N 16.25%; m.p. 135-136 ºC; yield 35.2%.

^{1}H-NMR (dmso-d_6, δ ppm, *J* Hz, T=308K): 13.04(s, 1H, H-12); 9.09(t, 1H, H-17, *J= 2.1*); 8.97(d, 2H, H-15, H-19, *J= 2.1*); 8.11(dd, 1H, H-5*, J= 7.8, J= 1.6*); 7.83(td, 1H, H-7, *J= 7.8, J= 1.6*); 7.62(bd, 1H, H-8, *J= 7.8*); 7.52(td, 1H, H-6, *J= 7.8, J= 1.4*); 5.00(s, 2H, H-10); 2.59(s, 3H, H-9).

^{13}C-NMR (dmso-d_6, δ ppm, T=308K): 165.15(CO-11); 162.38(CO-13); 161.11(C-4); 155.13(C-2); 148.56(C-16, C-18); 146.94(C-1a); 134.76(C-14); 119.56(C-4a); 134.74(C-7); 129.24(C-15, C-19); 126.58(C-8); 126.56(C-6); 126.28(C-5); 123.54(C-17); 43.97(C-10); 22.74(C-9).

FT-IR (solid in ATR, ν cm^{-1}): 34.66w; 3167w; 3086w; 2970w; 1785m; 1717m; 1664s; 1598s; 1543vs; 1472m; 1390m; 1346vs; 1257m; 1133m; 1078m; 976w; 947w; 921w; 770m; 718m; 696w.

Conclusions

We have synthesized a series of ten carbamates in the series of 4(3H)-quinazolinones compounds. We followed an acylation reaction between potassium 2-methyl-4-oxo-quinazolin-3(4H)-il-acetohydroxamate and different aromatic carboxylic acid chlorides. The chemical structures of these have been confirmed by elemental analysis and spectrometric methods (IR, ^{1}H-NMR and ^{13}C-NMR).

References

1. Alagarsamy V., Pathak U.S., Synthesis and antihypertensive activity of novel 3-benzyl-2-substituted-3H-[1,2,4]triazolo[5,1-b]quinazolin-9-ones. *Bioorg. and Med. Chem*., 2007; 15: 3457–3462.
2. Alagarsamy V., Murugesan S., Synthesis and pharmacological evaluation of some 3-(4-methoxyphenyl)-2-substitutedamino-quinazolin-4(3H)-ones as analgesic and anti-inflammatory agents. *Chem. Pharm. Bull*., 2007; 55: 76-80.
3. Alagarsamy V., Solomon V.R., Dhanabal K., Synthesis and pharmacological evaluation of some 3-phenyl-2-substituted-3H-quinazolin-4-one as analgesic anti-inflammatory agents. *Bioorg. Med. Chem*., 2007; 7: 235-241.
4. Aly M.M., Mohamad Y.A., Ei-Bayoki Kam, Basyouni W.M., Abbas S.Y., Synthesis of some new 4(3H)-quinazolinone 2-carboxaldehyde thiosemicarbazones and their anticonvulsant, analgesic, cytotoxic and antimicrobial activities. *Eur. J. Med. Chem*., 2010; 45: 3365-3373.

5. Balakumar C., Lamba P., Pran Kishore D., Lakshmi Narayana B., Venkat Rao K., Rajwinder K., Raghuram Rao A., Shireesha B., Narsaiah B., Synthesis, anti-inflammatory evaluation and docking studies of some new fluorinated fused quinazolines. *Eur. J. Med. Chem*., 2010; 45 issue 11 November: 4904-4913.
6. Chaudhary M., Bhattachary S., Ahmad Y., Synthesis of some novel triazolo-quinazolinone derivatives and investigation of their antihypertensive agents. *Der Pharmacia Sinica*, 2012; 3(4): 479-487.
7. Cioroianu D.M. , Moruşciag L., Căproiu M.T., Limban C., Chiriţă I.C., Nuţă D.C., Synthesis and characterization of new acyl-oximines derivatives with potential pharmacological activity. *Farmacia*, 2013; 61(3): 469- 480.
8. Cioroianu D.M., Nuţă D.C., Moruşciag L., Căproiu M.T., Chiriţă I.C., Limban C., The synthesis of some new acyloximines compounds with potential pharmacological activity. *Farmacia*, 2013; 61(2): 298- 312.
9. Deshmukh M.B., Patil S., Patil S.S., Jadhav S.D., Synthesis and antimicrobial screening of pyrzolo-3-aryl-quinazolin-4(3H)ones. *Indian J. Pharm. Sci*., 2010; 72(4): 500-504.
10. Georgey K.H., Abdel-Gawad H., Abbas S., Synthesis and anticonvulsant activity of some quinazolin-4-(3H)-one derivatives. *Molecules*, 2008; 13: 2557-2569.
11. Kashaw S.K., Kashaw V., Mishra P., Jain N.K., Stables J.P., Synthesis, anticonvulsant and CNS depressant activity of some new bioactive 1-(4-substituted-phenyl)-3-(4-oxo-2-phenyl/ethyl-4H-quinazolin-3-yl)-urea. *Eur. J. Med. Chem*., 2009; 44: 4335-4343.
12. Khodarhmi G.A., Khajouei M.R., Hakimelahi G.H., Abedi D., Jafari E., Hassanzadeh F., Antibacterial, antifungal and cytotoxic evaluation of some new 2,3-disubstituted 4(3H)-quinazolinone derivatives. *Res. Pharm. Sci*., 2012; 7(3): 151-158.
13. Kwnes J., Bazant J., Pour M., Waisser K., Slosarek M., Janota J., Quinazolines derivatives with antitubercular activity. *Il Farmaco*, 2000; 55: 725-729.
14. Laddha S.S., Bhatnagar S.P., A new therapeutic approach in Parkinson's disease: Some novel quinazoline derivatives as dual selectivphosphodiesterase 1 inhibitors and antinflammatory agents. *Bioorg. Med. Chem*., 2009; 1: 6796-6802.
15. Paneersalvam P., Raj T., Ishar M.P.S., Singh B., Sharma V., Rather B.A., Anticonvulsant activity of Schiff bases of 3-amino-6,8-dibromo-2-phenyl-quinazolin 4(3H)-ones. *Indian J. Pharm. Sci*., 2010; 7: 375-378.
16. Selvam P., Murugesh N., Chandramohan M., Pannecouque C., De Clercq E., Synthesis Antiviral and Cytotoxic Activities of 2-(2-Phenyl carboxylic acid)-3-Phenylquinazolin-4(3H)-one Derivatives. *Indian J. Pharm. Sci*., 2010; 72(6): 806-809.
17. Zhu S., Wang J., Chandrashekar G., Smith E., Liu X., Zhang Y., Synthesis and evaluation of 4-quinazolinone compounds as potential antimalarial agents. *Eur. J. Med. Chem*., 2010; 45(9): 3864-3869.

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