Supplementary Informatiomn

Chloroquinoline-acetamide hybrids: A promising series of potential antiprotozoal agent

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Table- Bond lengths [Å] and angles [°] for 2-(4-(7-chloroquinolin-4-yl)piperazine-1-yl)-*N*-(4-fluorophenyl)acetamide (**A7**), for 2-(4-(7-chloroquinolin-4-yl)piperazine-1-yl)-*N*-*p*-tolylacetamide (**A8**)**,** for 2-(4-(7-chloroquinolin-4-yl)piperazine-1-yl)-*N*-*o*-tolylacetamide (**A 12**) and 2-(4-(7-chloroquinolin-4-yl)piperazine-1-yl)-1-(4-(2,3-dichlorophenylpipezin-1-yl)-ethanone (**A21**).

Bond lengths	**A7**	**A8**	**A12**	**A21**
Cl(1)-C(1)	1.7373(11)	1.7404(14)	1.7380(12)	1.7369(11)
Cl(2)-C(15)				1.7257(11)
Cl(3)-C(16)				1.7337(12)
F(1)-C(13)	1.3659(14)			
O(1)-C(9)	1.2212(14)	1.2160(17)	1.2207(15)	1.2255(13)
N(1)-C(5)	1.3994(14)	1.4006(18)	1.4090(14)	1.4054(13)
N(1)-C(6)	1.4613(14)	1.4732(18)	1.4605(15)	1.4655(13)
N(1)-C(21)				1.4748(13)
N(1)-C(17)	1.4751(14)	1.4589(18)	1.4696(15)	
N(2)-C(8)	1.4539(15)	1.4636(18)	1.4564(15)	1.4585(13)
N(2)-C(7)	1.4670(15)	1.4638(18)	1.4588(16)	1.4574(14)

N(2)-C(16)	1.4674(14)	1.4702(18)	1.4625(16)	
N(2)-C(20)				1.4650(13)

Angles	**A7**	**A8**	**A12**	**A21**
C(5)-N(1)-C(6)	115.86(9)	117.11(11)	115.12(10)	115.10(8)
C(5)-N(1)-C(21)				116.43(8)
C(6)-N(1)-C(21)				109.97(8)
C(5)-N(1)-C(17)	114.69(9)	116.95(11)	114.39(9)	
C(6)-N(1)-C(17)	109.46(9)	110.01(11)	110.54(9)	
C(8)-N(2)-C(7)	111.16(9)	110.38(11)	112.00(10)	110.73(8)
C(7)-N(2)-C(20)				109.43(8)
C(8)-N(2)-C(20)				112.45(9)
C(8)-N(2)-C(16)	110.26(9)	110.11(11)	111.66(10)	
C(7)-N(2)-C(16)	109.03(9)	108.47(11)	109.72(10)	

Table - Hydrogen bonds for the compounds 2-(4-(7-chloroquinolin-4-yl)piperazine-1-yl)-*N*-(4-fluorophenyl)acetamide (**A7**), 2-(4-(7-chloroquinolin-4-yl)piperazine-1-yl)-*N*-*p*-tolylacetamide (**A8**) and 2-(4-(7-chloroquinolin-4-yl)piperazine-1-yl)-*N*-*o*-tolylacetamide (**A12**) [Å and °].

A7

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1W)-H(1WA)...N(4)#1	0.831(9)	2.080(10)	2.8965(13)	167.5(16)
O(1W)-H(1WB)...N(2)	0.824(9)	2.137(9)	2.9461(13)	167.3(15)
N(3)-H(3)...O(1W)#2	0.86	2.03	2.8740(13)	165.1

Symmetry transformations used to generate equivalent atoms:

#1 x+1,y+1,z #2 x+1,y,z

A8

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3)-H(3N)...N(2)	0.870(18)	2.248(17)	2.7186(17)	113.8(14)

A12

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3)-H(3N)...N(2)	0.815(17)	2.165(17)	2.6662(15)	119.8(14)

Spectral data of the different substituted chloro acetamides (1-27)

2- chloro-N- phenylacetamide (1): Yield 75%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 8.227 (bs, 1H), 7.567 (d, 2H, *J*=8.1Hz), 7.396-7.344 (m, 2H), 7.207-7.157 (m, 1H), 4.201 (ss, 2H).

Methyl 2-(2-chloroacetamido) benzoate (2): Yield 72%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 11.906 (bs, 1H), 8.741 (d, 1H, *J*=8.1Hz), 8.105 (d, 1H, J=6.6Hz), 7.624-7.574 (m, 1H), 7.205-7.158 (m, 1H), 4.236 (ss, 2H), 1.74 (s, 3H).

2-chloro-N-(2, 4-difluorophenyl)acetamide (3): Yield 70%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 9.359 (bs, 1H), 8.543 (m, 2H), 7.995 (s, 1H), 4.105 (ss, 2H).

***N*-(3-acetylphenyl)-2-chloroacetamide (4)**: Yield 71%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm) : 8.400 (bs, 1H) , 8.066 (s , 1H) , 7.946 (d, 1H, J=8.1 Hz) ,7.793 (d ,1H, J=7.8 Hz), 7.521 (t, 1H, J=7.8 Hz), 4.236 (s, 2H , CH_2), 2.638 (ss, 3H ,CH_3).

***N*-(4-acetylphenyl)-2-chloroacetamide (5)**: Yield 73%, H[1]NMR (300MHz, $CDCl_3$) δ(ppm) : 8.398 (bs, 1H) , 7.996-7.959 (m , 2H ,) ,7.694 (d, 2H, J=8.7 Hz) , 4.220 (ss, 2H) , 2.595 (ss, 3H)

2-chloro-N-(2-fluorophenyl)acetamide (6): Yield 78%,[1]HNMR (300MHz, $CDCl_3$) δ(ppm): 8.548 (bs, 1H) ,8.330-8.274(m , 1H) , 7.214-7.125(m , 3H) , 4.240 (ss ,2H)

2-chloro-N-(4-fluorophenyl)acetamide (7): Yield 80%,[1]HNMR (300MHz, $CDCl_3$) δ(ppm) : 8.242 (bs, 1H) , 7.558-7.514 (m , 2H) ,7.109-7.051 (m, 2H) , 4.341(ss,2H)

2-chloro-N-*p*-tolylacetamide (8): Yield 82%,[1]HNMR (300MHz, $CDCl_3$) δ(ppm) : 8.190 (bs, 1H) , 7.458 (d , 2H, *J*=8.4 Hz) , 7.198 (d , 2H, *J*=8.4 Hz), 4.205 (ss, 2H), 2.356 (ss, 3H).

2-chloro-N-*m*-tolylacetamide (9): Yield 84%,[1]HNMR (300MHz, $CDCl_3$) δ(ppm): 8.201(bs,1H) , 7.400 (s ,1H) , 7.37 (d , 1H , *J*=8.1 Hz) , 7.28-7.24 (m, 1H), 7.02 (d , 1H , *J*=7.2Hz) , 4.20 (ss ,2H), 2.38 (ss ,3H)

2-chloro-*N*-(3-chlorophenyl)acetamide (10): Yield 77%, [1]HNMR (300MHz, $CDCl_3$) δ(ppm): 8.275 (bs, 1H), 7.702 (bs, 1H), 7.440 (d, 1H, J= 6.9Hz), 7.348-7.281 (m, 1H), 7.199-7.170 (m, 1H), 4.210 (ss, 2H).

2-chloro-N-(4-bromophenyl)acetamide (11): Yield 65%,[1]HNMR (300MHz, $CDCl_3$) δ(ppm) : 9.278 (bs, 1H), 6.910-6.881 (m, 2H), 6.768 (d, 2H, *J*=8.4Hz), 3.486 (ss, 2H).

2-chloro-N-*o*-tolylacetamide (12): Yield 79%, [1]HNMR (300MHz, $CDCl_3$) δ(ppm): 8.262 (bs, 1H), 7.904 (d, 1H, J=7.8Hz), 7.284-7.323 (m, 2H), 7.146 (d, 1H, J=7.2Hz), 4.288 (ss, 2H), 3.327 (ss, 3H).

2-chloro-*N*-(naphthalene-1-yl)acetamide (13): Yield 76%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 8.800 (bs, 1H), 8.021 (d, 1H, *J*=7.5Hz), 7.932 (t, 2H, *J*=8.1Hz), 7.795 (d, 1H, J=8.1Hz), 7.631-7.54 (m, 3H), 4.371 (ss, 2H).

2-chloro-N-(2,6-dimethylphenyl)acetamide (14) : Yield 79%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 7.875 (bs, 1H), 7.199-7118 (m, 3H), 4.281 (ss, 2H), 2.269 (ss, 6H).

2-chloro-N-(3-chloro,4-fluorophenyl)acetamide (15): Yield 72%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 8.249 (bs, 1H), 7.771-7.742 (m, 1H), 7.432-7.372 (m, 1H), 7.283 (s, 1H), 4.214 (m, 2H).

1-(4-benzylpiperazin-1-yl)-2-chloroethanone (16): Yield 55%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 7.289-7.150 (m, 2H), 7.090-6.991 (m, 3H), 4.012 (ss, 2H), 3.994-3.850 (m, 4H), 3.830 (ss, 2H), 3.654-3.590 (m, 4H).

2-chloro-1-(4-(3-chlorophenyl)piperazin-1-yl)ethanone (17): Yield 42%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 7.190 (s, 1H), 7.154 (t, 1H, *J*=8.1Hz), 6.821 (d, 1H, J= 8.4Hz), 6.750 (d, 1H, J= 7.8Hz), 4.041 (ss, 2H), 3.795-3.661 (m, 4H), 3.170-3.125 (m, 4H).

1-(4-tert-butylpiperazin-1-yl)-2-chloroethanone (18): Yield 69%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 4.022 (ss, 2H), 3.522-3.430 (m, 4H), 3.395-3.310 (m, 4H), 1.400 (ss, 9H).

1-(4-(benzo[1,3]dioxol-5-ylmethyl)piperazine-1yl)-2-chloroethanone (19): Yield 52%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 6.861 (s, 1H), 6.750 (bs, 2H), 5.957 (ss, 2H), 4.069 (ss, 2H), 3.642 (bs, 2H), 3.526 (bs, 2H), 3.455 (bs, 2H), 2.470-2.453 (m, 4H).

2-chloro-1-1(4-phenylpiperazin-1-yl)ethanone (20): Yield 55%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 7.950-7.824 (m, 2H), 7.431-7.330 (m, 2H), 6.981 (m, 1H), 4.021 (ss, 2H), 3.951-3.820 (m, 4H), 3.350-3.249 (m, 4H).

2-chloro-1-(4-(2,3-dichlorophenyl)piperazine-1-yl)ethanone (21): Yield 55%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 7.281-7.137 (m, 2H), 6.956-6.932 (m, 1H), 4.125 (ss, 2H), 3.824-3.811 (m, 2H), 3.723-3.710 (m, 2H), 3.106-3.038 (m, 4H)

2-chloro-N-(4-hydroxypiperidin-1-yl)acetamide (22): Yield 55%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 5.248 (bs, 1H), 5.148-5.116 (m, 1H), 4.112-4.011 (m, 4H), 3.832-3.720 (m, 2H), 2.016-1.775 (m, 4H).

2-chloro-*N*-cyclohexylacetamide (23): Yield 82%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 6.450 (bs, 1H), 4.041 (ss, 2H), 3.861-3.750 (m, 1H), 1.969-1.922 (m, 2H), 1.780-1.626 (m, 4H), 1.470-1.342 (m, 2H), 1.288-1.150 (m, 2H).

2-chloro-N-isopropylacetamide (24): Yield 75%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 6.419 (bs, 1H) , 4.289-4.093 (m ,1H), 4.031 (s, 2H), 1.223 (ss ,6H) .

2-chloro-N-cyclopropylacetamide (25): Yield 70%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm) 12.078 (bs, 1H), 3.618 (s, 2H), 1.870-1.654 (m, 1H), 1.453-1.404 (m, 4H).

2-chloro-*N*-cyclopentylacetamide (26): Yield 78%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 6.520 (bs, 1H), 4.271-4.170 (m, 1H), 4.012 (ss, 2H), 2.030-1.971(m, 2H), 1.730-1.569 (m, 4H), 1.469-1.400 (m, 2H).

N-butyl-2-chloroacetamide (27): Yield 74%, ^{1}HNMR (300MHz, $CDCl_3$) δ(ppm): 7.354 (bs, 1H), 3.452-3.349 (m, 2H), 3.190 (ss, 2H), 2.145-2.059 (m, 2H), 2.045-1.990 (m, 2H), 1.210-1.115 (m, 3H).