SYNTHESIS OF 2-N-R-AMINOMETHYL-3-BENZYLQUINOLIN-4-ONES AS POTENTIAL NEUROTROPIC AGENTS

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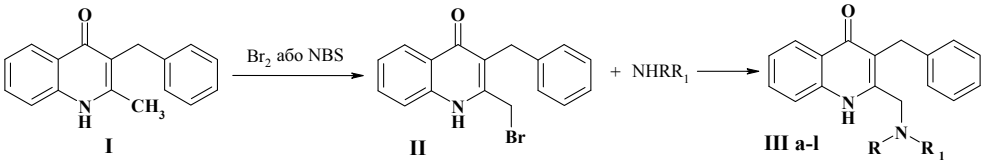
Halogenation of heterocycles is a powerful tool for their further modification. In order to expand the chemical diversity of derivatives based on quinolin-4-one scaffold we have investigated 3-alkyl-2-methylquinoline-4-ones bromination.

Bromination of 3-substituted 2-methylquinoline-4-ones was performed with molecular bromine and N-bromosuccinimide in such solvents as glacial acetic acid and chloroform respectively, in the presence of catalytic amounts of benzoyl peroxide or without it.

According to the obtained results it has been shown that in the case of 3-benzyl-2-methylquinoline-4-one **I** halogenation takes place with the methyl group in C-2 position of quinolone ring, and 3-benzyl-2-brommetylquinolin-4-one **II** was isolated as the main product with yields 63% (Br_2) and 73% (NBS) respectively.



III a R=C_6H_{13}, R'=H; **b** R=*cyclo*-C_6H_{11}, R'=H; **c** R=C_6H_5, R'=H; **d** R=*o*-$CH_3C_6H_4$, R'=H; **e** R=*m*-$CH_3C_6H_4$, R'=H; **f** R=*p*-$CH_3C_6H_4$, R'=H; **g** R=*o*-$CH_3OC_6H_4$, R'=H; **h** R=*p*-$CH_3OC_6H_4$, R'=H; **i** R=*m*-ClC_6H_4, R'=H; **j** R=C_2H_5, R'=C_2H_5; **k** R+R'=piperidine; **l** R+R'=morpholine.

Also it has been shown that bromination of 2-methylquinoline-4-ones with other alkyl substituents (methyl, propyl, butyl) at C-3 position occurs with low regioselectivity, which does not allow to use this reaction as a preparative method for the synthesis of corresponding 2-brommetylderivatives.

Synthesized 3-benzyl-2-brommetylquinolin-4-one **II** was used in reactions with various amines. Alkylation of corresponding amines by 3-benzyl-2-brommetylquinolin-4-one **II** via heating in DMSO/K_2CO_3 leads to formation of target 2-N-R-aminomethyl-3-benzylquinolin-4-ones **III a-l** rapidly and with high yields.

This direction is a logical continuation of the research of quinoline-4-one derivatives with aminoalkyl substituents, because these structural determinants should impart a neurotropic orientation of pharmacological action to these molecules through structural similarity to known ligands of 5-HT receptors.