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SYNTHESIS AND REACTIONS OF 3-(6-AMINO-2-PYRIDYL)-2-METHYL-4(3H)-QUINAZOLINONE

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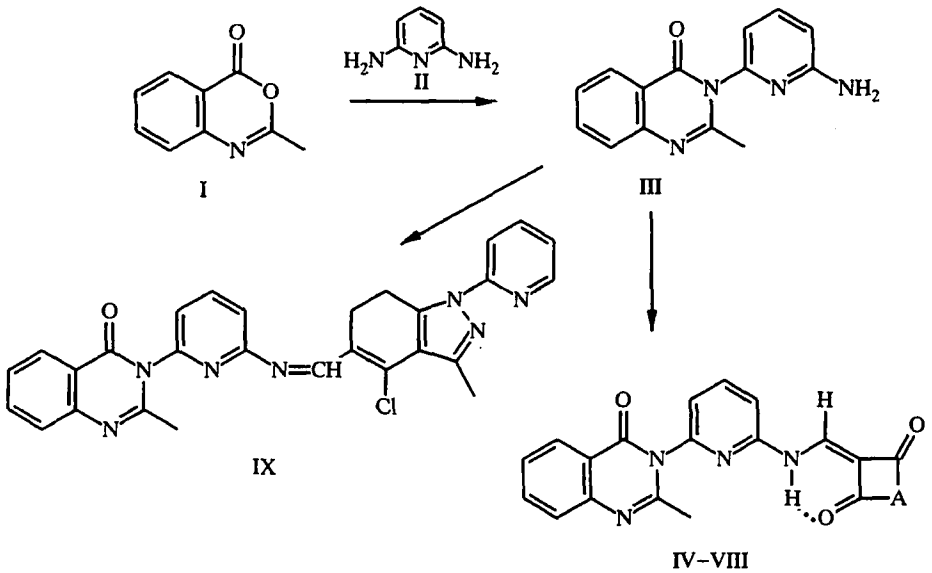
Taking into account the varied biological activity of 2,3-substituted 4(3H)-quinazolinones [1] and in the development of the work of [2-6], we have synthesized 3-(6-amino-2-pyridyl)-2-methyl-4(3H)-quinazolinone (III) and subjected it to reaction with some formyl derivatives. The quinazolinone III was synthesized by the fusion of 2-methylbenz-3,1-oxazin-4(H)-one (I) with 2,6-diaminopyridine (II) at 140°C. Reaction of the amine III with 2-formyldimedone, 2-formyl-5-phenyl-1,3-cyclohexanedione, the potassium salt of 2-formyl-1,3-cyclohexanedione, 2-formyl-1,3-indandione, and 5-ethoxymethylene-2,2-dimethyl-1,3-dioxane-4,6-dione leads to the 2-aminomethylene-1,3-cyclanediones IV-VIII. The reaction with 4-chloro-5-formyl-3-methyl-1-(2-pyridyl)-6,7-dihydroindazole [7] afforded the Schiff base IX.

The structure of the compounds III-IX was confirmed by IR and PMR spectral data. Thus, the primary amino group of compound III is characterized by stretching vibration frequencies of 3350 and 3250 cm^{-1} and the chemical shift δ 6.29 ppm. The =CH–NH– portion in the compounds IV-VIII is characterized by low-intensity absorption at 3180-3100 cm^{-1} and doublet signals with the characteristic SSCC J = 12.5-13.0 Hz in the regions of 8.81-9.11 ppm (=CH–) and 11.14-12.95 ppm (NH).



I II III IX IV–VIII

A = IV CH_2—$C(CH_3)_2$—CH_2; V CH_2—$CH(C_6H_5)$—CH_2; VI $(CH_2)_3$; VII C_6H_4-1,2; VIII O—$C(CH_3)_2$—O

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3-(6-Amino-2-pyridyl)-2-methyl-4(3H)-quinazolinone (III). The mixture of the benz-3,1-oxazine I (8.06 g, 50 mmol) and the diamine II (6.00 g, 5.5 mmol) is heated for 1.5 h at 140°C. The reaction mass is recrystallized from water prior to the isolation of 1.87 g (15%) of colorless crystals; mp 196-198°C. IR spectrum: 3350, 3250, 1682, 1654, 1606, 1558, 1508 cm^{-1}. PMR spectrum (DMSO-d_6): 2.18 (3H, s, CH_3); 6.29 (2H, br. s, NH_2); 6.55-8.04 ppm (7H, m, C_6H_4, C_5H_3N). Found, %: C 66.50; H 4.90; N 22.12. $C_{14}H_{12}N_4O$. Calculated, %: C 66.66; H 4.79; N 22.21.

3-[6-(4,4-Dimethyl-2,6-dioxocyclohexylidenemethylamino)-2-pyridyl]-, 3-[6-(4-Phenyl-2,6-dioxocyclohexylidenemethylamino)-2-pyridyl]-, 3-[6-(2,6-Dioxocyclohexylidenemethylamino)-2-pyridyl]-, 3-[6-(1,3-Dioxoindan-2-ylidenemethylamino)-2-pyridyl]-, and 3-[6-(2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-ylidenemethylamino)-2-pyridyl]-4-(3H)-quinazolinones IV-VIII. These compounds were obtained by the boiling of the amine III (2 mmol) and the equimolar amount of the corresponding 2-formyl-1,3-cyclanedione in methanol (15 ml) for 15-20 min. The mixture is cooled, and the compounds IV-VIII are filtered off and recrystallized. In the case of compound VI, the reaction is performed with the potassium salt of 2-formyl-1,3-cyclohexanedione in water. The product is isolated by the acidification of the solution with dilute hydrochloric acid.

Compound IV. Yield 50%; mp 219-221° (methanol). IR spectrum: 3100, 1694, 1674, 1592, 1562, 1552 cm^{-1}. PMR spectrum ($CDCl_3$): 1.06 (6H, s, $2CH_3$); 2.24 (3H, s, CH_3); 2.39 (2H, s, CH_2); 2.43 (2H, s, CH_2); 7.11-8.32 (7H, m, C_6H_4, C_5H_3N); 9.08 (1H, d, J = 12.5 Hz, =CH–); 12.91 ppm (1H, d, J = 12.5 Hz, NH). Found, %: C 68.51; H 5.39; N 13.81. $C_{23}H_{22}N_4O_3$. Calculated, %: C 68.64; H 5.51; N 13.92.

Compound V. Yield 60%; mp 223-224°C (toluene). IR spectrum: 3180, 1689, 1680, 1600, 1551 cm^{-1}. PMR spectrum (DMSO-d_6): 2.18 (3H, s, CH_3); 2.76-3.52 (5H, m, $2CH_2$, CH); 7.33 (5H, m, C_6H_5); 7.51-8.27 (7H, m, C_6H_4, C_5H_3N); 8.93 (1H, d, J = 13.0 Hz, =CH); 12.59 ppm (1H, d, J = 13.0 Hz, NH). Found, %: C 71.81; H 4.79; N 12.30. $C_{27}H_{22}N_4O_3$. Calculated, %: C 71.99; H 4.92; N 12.44.

Compound VI. Yield 72%; mp 242-243°C (toluene). IR spectrum: 3100, 1695, 1675, 1600, 1560, 1540 cm^{-1}. PMR spectrum ($CDCl_3$): 2.01-2.52 (6H, m, $3CH_2$); 2.21 (3H, s, CH_3); 7.06-8.34 (7H, m, C_6H_4, C_5H_3N); 9.11 (1H, d, J = 12.5 Hz, =CH–); 12.5 ppm (1H, d, J = 12.5 Hz, NH). Found, %: C 67.16; H 4.77; N 14.81. $C_{21}H_{18}N_4O_3$. Calculated, %: C 67.37; H 4.85; N 14.96.

Compound VII. Yield 78%; mp 240-241°C (toluene). IR spectrum: 1717, 1685, 1663, 1580, 1576, 1570, 1540 cm^{-1}. PMR spectrum ($CDCl_3$): 2.25 (3H, s, CH_3); 6.75-8.05 (11H, m, $2C_6H_4$, C_5H_3N); 8.79 (1H, d, J = 13.0 Hz, =CH–); 10.87 ppm (1H, d, J = 13.0 Hz, NH). Found, %: C 70.33; H 3.77; N 13.49. $C_{24}H_{16}N_4O_3$. Calculated, %: C 70.58; H 3.95; N 13.72.

Compound VIII. Yield 51%; mp 226-227°C (toluene). IR spectrum: 1748, 1690, 1684, 1624, 1616, 1569 cm^{-1}. PMR spectrum ($CDCl_3$): 1.73 (6H, s, $2CH_3$); 2.27 (3H, s, CH_3); 7.13-8.31 (7H, m, C_6H_4, C_6H_3N); 9.27 (1H, d, J = 13.0 Hz, =CH–); 11.43 ppm (1H, d, J = 13.0 Hz, NH). Found, %: C 61.85; H 4.40; N 13.70. $C_{21}H_{18}N_4O_5$. Calculated, %: C 62.06; H 4.46; N 13.79.

3-(6-[4-Chloro-3-methyl-1-(2-pyridyl)-6,7-dihydroindazol-5-ylmethenal]amino-2-pyridyl)-2-methyl-4(3H)-quinazoline (IX). The amine III (2 mmol) and 4-chloro-5-formyl-3-methyl-1-(2-pyridyl))-6,7-dihydroindazole (2 mmol) are boiled for 15 min in methanol (15 ml). The mixture is cooled, and the residue of quinazoline IX is filtered off and recrystallized from methanol. Yield 75%; mp 198-200°C. IR spectrum: 1695, 1615, 1570, 1530 cm^{-1}. PMR spectrum ($CDCl_3$): 2.30 (3H, s, CH_3); 2.57 (3H, s, CH_3); 3.05-3.53 (4H, m, $2CH_2$); 7.18-8.47 (11H, m, C_6H_4, C_5H_3N); 9.34 ppm (1H, s, =CH–). Found, %: C 66.06; H 4.30; Cl 6.98; N 19.30. $C_{28}H_{22}ClN_7O$. Calculated, %: C 66.20; H 4.37; Cl 6.98; N 19.30.

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