UDC 547.945

DOI: 10.15372/CSD2021321

Amides Based on Fatty Acids and Aminodubamine

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(Received November 12, 2020; revised March 18, 2021)

Abstract

The reaction of 6′-aminodubamine (2-(4′,5′-methylendioxy-2′-aminophenyl)-quinoline) with various aliphatic acids was studied. Amides were obtained in the yields of 23.0–64.9 %. The structure of amides was established on the basis of the analysis of spectral data and X-ray diffraction analysis. The antimicrobial activity of the obtained amides was studied.

Keywords: amides, 6′-aminodubamine (2-(4′,5′-methylenedioxy-2′-aminophenyl)-quinoline), quinoline, aliphatic acids

INTRODUCTION

Amides are extensively used in chemistry, medicine, agricultural chemistry, so their synthesis is an essential direction of organic synthesis. Many pharmaceutical substances applied in modern medicine are amides in the chemical respect. Some examples are acetaminophen with its analgesic properties in combination with antiproliferative, cytotoxic [1, 2] activity, lidocaine (xylocaine) with local anesthetic action and loperamide (Imodium AD) with antidiarrheal effect [3, 4].

It should also be stressed that the quinolone fragment comprises the basis of many natural and pharmacologically active compounds. Preparations based on quinolone exhibit such kinds of activity as antimalarial [5], antibacterial [6], antifungal [7], antiinflammatory [8] and antitumour [9], which makes quinolone alkaloids attractive substrates for the synthesis of amides on their basis.

The goal of the present work was to develop new methods for the synthesis of quinolone amides on the basis of 6-aminodubamine, determination of the spectral characteristics (by means of IR, NMR spectroscopy and X-ray structural analysis) and the biological activity of the synthesised compounds.

EXPERIMENTAL

Methods of investigation

The IR spectra of the compounds were recorded with the help of a System 2000 Fourier Transform spectrometer (Perkin-Elmer, USA) in tablets with KBr. The NMR ^{1}H and ^{13}C spectra were recorded with an Unity-400 spectrometer (Varian, USA, TMS as internal standard, δ-scale), high-resolution mass spectra were recorded with a 6420 Triple quad LC/MS chromatograph (Agilent Technologies, USA).

Reaction progress and the purity of the synthesised compounds were controlled by means of thin layer chromatography (TLC) on Sigma-Aldrich plates, silufol L/W 10 cm × 20 cm (Germany) in the solvent system hexane/chloroform/methanol (5 : 5 : 0.2).

Synthesis procedure

The synthesis of 6′-aminodubamine [10]**.** Dubamine in the amount of 0.5 g (0.002 mol) was dissolved in 5 mL of glacial CH_3COOH. The nitrating mixture composed of 0.14 mL (65 %, d = 1.39 g/mL) HNO_3 and 0.40 mL (d = 1.84 g/mL) H_2SO_4 was added to the solution at room temperature during mixing with a magnetic mixer for 10 min. After the reaction was over, ice was added to the reaction mixture, then it was alkalised by adding NaOH to pH 9–10, extracted with $CHCl_3$ (4 × 15 mL), and the extracts were united. After distillation of the solvent, the precipitate was crumbled with methanol, dried, and crystallised from acetone. The yield of 6′-nitrodubamine was 0.516 g. Then a suspension composed of 0.30 g of 6′-nitrodubamine in 1.44 mL of ethanol and 0.48 mL of HCl (33 %) were added in portions to a mixture of 0.68 g $SnCl_2 \cdot 2H_2O$ and 0.96 mL of HCl (33 %). The reaction mixture was stirred for 30 min, then diluted with water, and alkalised by adding a 20 % solution of NaOH to achieve pH 10. The products were extracted with $CHCl_3$ (3 × 15 mL), the extracts were united, the solvent was distilled. After recrystallisation from methanol, 0.24 g of 6′-aminodubamine **1** was obtained in the total yield of 78.3 %.

The IR spectrum (KBr, ν, cm^{-1}): 3433, 2894, 1599, 1515, 1483, 1464, 1431, 1346, 1277, 1250, 1149, 1118, 1038, 932, 878, 825.

The NMR ^1H spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 5.85 (2H, s, 4′-OCH_2O-5′), 6.18 (2H, br. s, NH_2), 6.28 (1H, s, H-3′), 7.12 (1H, s, H-6′), 7.40 (1H, td, *J* = 8.1, 1.2, H-6), 7.60 (1H, td, *J* = 8.4, 1.5, H-7), 7.62 (1H, d, *J* = 8.9, H-3), 7.69 (1H, dd, J = 8.2, 1.5, H-5),7.92 (1H, d, *J* = 8.4, H-8), 8.06 (1H, d, *J* = 8.9, H-4).

The NMR ^{13}C spectrum (100 MHz, $CDCl_3$), δ, ppm: 98.6 (C-3′), 101.1 (4′-OCH_2-O5′), 108.5 (C-6′), 113.6 (C-2′), 120.2 (C-3), 126.1 (C-10), 125.9 (C-6), 127.6 (C-5), 128.7 (C-8), 129.8 (C-7), 136.7 (C-4), 140.3 (C-1′), 144.3 (C-5′), 147.0 (C-4′), 149.6 (C-9), 159.1 (C-2).

The general procedure of 2a–e synthesis [11]. The acid in the amount of 0.912 mmol was added to the solution of 0.2 g (0.760 mmol) of 6′-aminodubamine in 3 mL of chloroform for the formation of the salt. Chloroform was removed, then the salt was heated with an oil bath for 2–4 h at a temperature of 178–180 °C. After cooling, the reaction mixture was dissolved in 100 mL of chloroform and washed with a 2 % NaOH solution and with water to achieve the neutral reaction of washing water. The chloroform extract was dried with Na_2SO_4, the solvent was evaporated. The residue was crystallised from ethanol.

2-(4′,5′-Methylenedioxy-2′-(N-hexamido)-phenyl)-quinoline (2a). $C_{22}H_{22}N_2O_3$. Synthesised from 0.201 g (0.76 mmol) of amine **1** and 0.105 g (0.91 mmol) of hexanoic acid. The yield is 0.178 g (64.9 %), m.p. 126–129 °C (C_2H_5OH), R_f 0.63.

HR-ESI-MS: *m/z* 363.2025 $[M + H]^+$, calculated for $C_{22}H_{23}N_2O_3$ 363.4375.

The IR spectrum (KBr, ν, cm^{-1}): 2919, 2853, 1671 (C=O), 1625, 1596, 1534, 1476, 1427, 1395, 1354, 1209, 1092, 1032, 962, 920, 873, 820.

The NMR ^1H spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.83 (3H, t, *J* = 7.0, H-6″), 1.31 (4H, m, H-4″, 5″), 1.76 (2H, m, H-3″), 2.44 (2H, t, *J* = 7.5, H-2″), 6.01 (2H, s, 4′-OCH_2O-5′), 7.27 (1H, s, H-6′), 7.57 (1H, td, *J* = 8.1, 1.0, H-6), 7.74 (1H, d, *J* = 8.7, H-3), 7.77 (1H, td, *J* = 8.4, 1.4, H-7), 7.84 (1H, d, *J* = 8.1, H-5), 8.00 (1H, d, *J* = 8.5, H-8), 8.24 (1H, d, *J* = 8.8, H-4), 8.28 (1H, s, H-3′), 13.03 (1H, s, NH).

The ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 14.1 (C-6″), 22.6 (C-5″), 25.6 (C-4″), 31.6 (C-3″), 38.9 (C-2″), 101.7 (C-3′), 103.4 (4′-OCH_2O-5′), 108.3 (C-6′), 118.4 (C-2′), 120.7 (C-3), 126.3 (C-10), 126.8 (C-6), 127.8 (C-5), 128.1 (C-8), 130.4 (C-7), 134.4 (C-1′), 137.6 (C-4), 143.7 (C-5′), 146.1 (C-4′), 149.0 (C-9), 158.0 (C-2), 171.9 (C-1″).

2-(4′,5′-Methylenedioxy-2′-(N-octanamido)-phenyl)-quinoline (2b). $C_{24}H_{26}N_2O_3$. Synthesised from 0.200 g (0.76 mmol) of amine **1** and 0.131 g (0.91 mmol) of octanoic acid. Yield: 0.192 g (64.8 %), m.p. 139–141 °C (C_2H_5OH). R_f 0.63.

HR-ESI-MS: *m/z* 391.2351 $[M + H]^+$, calculated for $C_{24}H_{27}N_2O_3$ 391.4913.

The IR spectrum (KBr, ν, cm^{-1}): 2919, 2851, 1672 (C=O), 1627, 1597, 1537, 1506, 1479, 1428, 1396, 1356, 1224, 1205, 1095, 1033, 959, 921, 872, 819.

The ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.83 (3H, t, *J* = 7.0, H-8″), 1.27 (8H, m, H-4″-7″), 1.75 (2H, m, H-3″), 2.44 (2H, t, *J* = 7.6, H-2″), 6.01 (2H, s, 4′-OCH_2O-5′), 7.26 (1H, c, H-6′), 7.57 (1H, td, *J* = 8.0, 1.1, H-6), 7.74 (1H, d, *J* = 8.8, H-3), 7.76 (1H, td, *J* = 8.3, 1.3, H-7), 7.84 (1H, d, *J* = 8.0, H-5), 8.00 (1H, d, *J* = 8.5, H-8), 8.24 (1H, d, *J* = 8.8, H-4), 8.28 (1H, s, H-3′), 13.03 (1H, s, NH).

The ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 14.2 (C-8″), 22.7 (C-7″), 25.9 (C-6″), 29.1 (C-5″), 29.4 (C-4″), 31.8 (C-3″), 38.9 (C-2″), 101.7 (C-3′), 103.4 (4′-OCH_2O-5′), 108.3 (C-6′), 118.4 (C-2′), 120.7 (C-3), 126.3 (C-10), 126.8 (C-6), 127.8 (C-5), 128.1 (C-8), 130.4 (C-7), 134.4 (C-1′), 137.6 (C-4),

143.7 (C-5′), 146.1 (C-4′), 149.2 (C-9), 158.1 (C-2), 171.9 (C-1″).

2-(4′,5′-Methylenedioxy-2′-(N-hexadecanamido)-phenyl)-quinoline (2c). $C_{32}H_{42}N_2O_3$. Synthesised from 0.200 g (0.76 mmol) of amine **1** and 0.233 g (0.91 mmol) of palmitic (hexadecanoic) acid. Yield: 0.164 g (42 %), m.p. 120–121 °C (C_2H_5OH). R_f 0.75.

HR-ESI-MS: *m/z* 503.3709 $[M+H]^+$, calculated for $C_{32}H_{43}N_2O_3$ 503.7065.

The IR spectrum (KBr, ν, cm^{-1}): 2918, 2848, 1673 (C=O), 1625, 1598, 1538, 1475, 1427, 1397, 1355, 1222, 1094, 1032, 958, 921, 873, 819.

The ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.88 (3H, t, *J* = 6.6, H-16″), 1.19–1.37 (24H, m, H-4″-15″), 1.75 (2H, m, H-3″), 2.44 (2H, t, *J* = 7.5, H-2″), 6.00 (2H, s, 4′-OCH_2O-5′), 7.27 (1H, s, H-6′), 7.55–7.59 (1H, m, H-6), 7.75 (1H, d, *J* = 8.8, H-3), 7.76 (1H, td, *J* = 8.3, 1.2, H-7), 7.84 (1H, d, *J* = 8.1, H-5), 8.01 (1H, d, *J* = 8.4, H-8), 8.24 (1H, d, *J* = 8.7, H-4), 8.28 (1H, s, H-3′), 13.03 (1H, s, NH).

The ^{13}C NMR spectrum (100 MHz, $CDCl_3$, δ, ppm): 14.3 (C-16″), 22.8 (C-15″), 25.9 (C-14″), 29.5 (C-12″, 13″), 29.6 (C-10″, 11″), 29.7 (C-8″, 9″), 29.8 (C-7″), 29.8 (C-4″-6″), 32.1 (C-3″), 38.9 (C-2″), 101.7 (C-3′), 103.4 (4′-OCH_2O-5′), 108.3 (C-6′), 118.4 (C-2′), 120.7 (C-3), 126.3 (C-10), 126.8 (C-6), 127.8 (C-5), 128.2 (C-8), 130.4 (C-7), 134.4 (C-1′), 137.6 (C-4), 143.7 (C-5′), 146.1 (C-4′), 149.0 (C-9), 158.0 (C-2), 171.9 (C-1″).

2-(4′,5′-Methylenedioxy-2′-(N-heptadecanamido)-phenyl)-quinoline (2d). $C_{33}H_{44}N_2O_3$. Synthesised from 0.200 g (0.76 mmol) of amine **1** and 0.205 g (0.91 mmol) of margaric acid. Yield: 0.103 g (26 %), m.p. 119–122 °C (C_2H_5OH). R_f 0.75.

HR-ESI-MS: *m/z* 517.3869 $[M + H]^+$, calculated for $C_{33}H_{45}N_2O_3$ 517.7334.

The IR spectrum (KBr, ν, cm^{-1}): 2919, 2849, 1674 (C=O), 1626, 1597, 1542, 1478, 1430, 1396, 1356, 1224, 1097, 1034, 960, 921, 870, 820.

The ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.88 (3H, t, *J* = 6.7, H-17″), 1.19–1.30 (26H, m, H-4″-16″), 1.75 (2H, m, H-3″), 2.44 (2H, t, *J* = 7.5, H-2″), 6.02 (2H, s, 4′-OCH_2O-5′), 7.26 (1H, s, H-6′), 7.57 (1H, td, *J* = 8.1, 1.0, H-6), 7.74 (1H, d, *J* = 8.7, H-3), 7.76 (1H, td, *J* = 8.4, 1.3, H-7), 7.84 (1H, d, *J* = 8.1, H-5), 8.01 (1H, d, *J* = 8.4, H-8), 8.24 (1H, d, *J* = 8.8, H-4), 8.28 (1H, s, H-3′), 13.04 (1H, s, NH).

The ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 14.3 (C-17″), 22.6 (C-16″), 25.9 (C-15″), 28.9 (C-14″), 29.0 (C-13″), 29.1 (C-12″), 29.2 (C-11″), 29.3 (C-10″), 29.5 (C-9″), 30.2 (C-7″, 8″), 30.3 (C-5″, 6″), 30.4 (C-4″), 32.1 (C-3″), 38.9 (C-2″), 101.7 (C-3′), 103.4 (4′-OCH_2O-5′), 108.3 (C-6′), 118.4 (C-2′), 120.7 (C-3), 126.3 (C-10), 126.8 (C-6), 127.6 (C-5), 128.2 (C-8), 130.4 (C-7), 134.4 (C-1′), 137.6 (C-4), 143.7 (C-5′), 146.1 (C-4′), 149.0 (C-9), 158.0 (C-2), 171.9 (C-1″).

2-(4′5′-Methylenedioxy-2′-(N-docosanamido)-phenyl)quinoline (2e). $C_{38}H_{54}N_2O_3$. Synthesised from 0.200 g (0.76 mmol) of amine **1** and 0.310 g (0.91 mmol) of begenic (docosanoic) acid. Yield: 0.103 g (23 %), m.p. 112–114 °C (C_2H_5OH). R_f 0.75.

HR-ESI-MS: *m/z* 587.4717 $[M + H]^+$, calculated for $C_{38}H_{55}N_2O_3$ – 587.8679.

The IR spectrum (KBr, ν, cm^{-1}): 2918, 2849, 1674 (C=O), 1626, 1598, 1540, 1477, 1429, 1397, 1357, 1224, 1097, 1034, 960, 923, 872, 820.

The ^1H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.87 (3H, t, *J* = 6.7, H-22″), 1.19–1.25 (36H, m, H-4″-21″), 1.75 (2H, m, H-3″), 2.44 (2H, t, *J* = 7.5, H-2″), 6.02 (2H, s, 4′-OCH_2O-5′), 7.27 (1H, s, H-6′), 7.57 (1H, td, *J* = 8.0, 1.0, H-6), 7.74-7.79 (2H, m, H-3, H-7), 7.85 (1H, d, *J* = 8.2, H-5), 8.01 (1H, d, *J* = 8.5, H-8), 8.25 (1H, d, *J* = 8.8, H-4), 8.28 (1H, s, H-3′), 13.03 (1H, s, NH).

The ^{13}C NMR spectrum (100 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 14.3 (C-22″), 22.8 (C-21″), 25.9 (C-20″), 29.2 (C-19″), 29.5 (C-18″), 29.7 (C-17″), 29.8 (C-7″-16″), 30.1 (C-6″), 30.3 (C-5″), 30.4 (C-4″), 32.1 (C-3″), 38.9 (C-2″), 101.7 (C-3′), 103.4 (4′-OCH_2O-5′), 108.3 (C-6′), 118.4 (C-2′), 120.7 (C-3), 126.3 (C-10), 126.8 (C-6), 127.8 (C-5), 128.1 (C-8), 130.4 (C-7), 134.4 (C-1′), 137.6 (C-4), 143.7 (C-5′), 146.1 (C-4′), 149.0 (C-9), 158.0 (C-2), 171.9 (C-1″).

The X-ray diffraction analysis

The unit cell parameters for the crystals of **1** and **2a** were determined and refined by means of X-ray diffraction analysis (XRD) using a CCD Xcalibur Ruby diffractometer (Oxford Diffraction) with CuK_α-radiation (*T* = 288 K) [12]. The crystal space groups are *Pbca* (rhombic) and *P*-1 (triclinic), respectively. A three-dimensional set of reflections for the crystals was recorded using this diffractometer. A correction for absorption was introduced with the help of the SADABS software [13]. The main parameters of XRD experiments and calculations for refinement of the structures of crystals **1** and **2a** are shown in Table 1.

The structures of **1** and **2a** were decoded using the direct methods with the help of SHELXS-97 software [14] and refined with the help of SHELXL-2014/7 software [15]. The positions of hydrogen atoms were determined geometrically and refined with fixed parameters of

TABLE 1

The main crystallographic parameters and characteristics of the crystals of **1** and **2a** according to the data of X-ray diffraction analysis

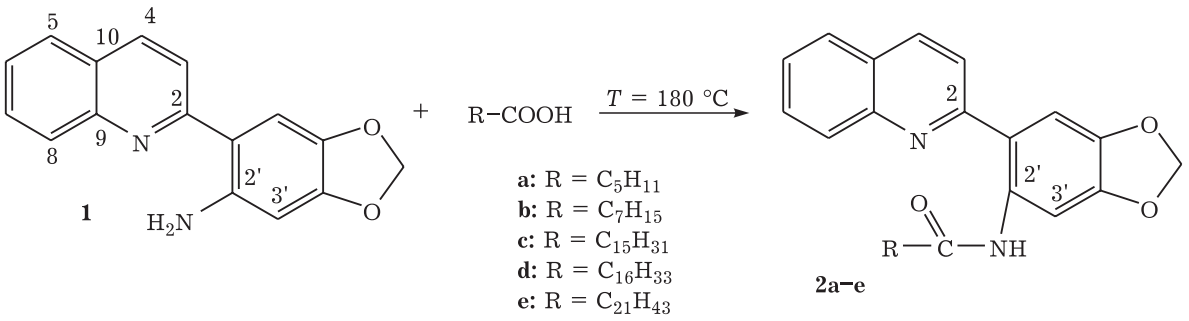
Parameter	**1**	**2a**
Molecular formule	$C_{16}H_{12}N_2O_2$	$C_{22}H_{22}N_2O_3$
M_r	264.28	362.41
a, Å	11.5545(2)	5.2905(8)
b, Å	8.0063(2)	10.850(1)
c, Å	26.7980(5)	16.471(2)
α, deg	90	89.623(9)
β, deg	90	82.54(1)
γ, deg	90	85.20(1)
V, Å^3	2479.05(9)	934.2(2)
ρ, g/cm^3	1.416	1.288
Crystal size, mm	0.75 × 0.25 × 0.25	0.80 × 0.30 × 0.03
Scanning region θ, deg	3.3–76.0°	4.1–76.2°
Number of independent reflections	2572	3797
Number of reflections with $I > 2\sigma(I)$	2125	1602
R_1 ($I > 2\sigma(I)$ and total)	0.042 (0.053)	0.063 (0.153)
wR_2	0.107 (0.116)	0.121 (0.164)
GOOF	1.05	0.96
Difference peaks of EA (*e*Å^{-3})	0.15 и −0.29	0.18 и −0.27
CCDC	2043865	2043866

the isotropic thermal shift $U_{iso} = nU_{eq}$, where n = 1.5 for methyl groups and 1.2 for other groups, and U_{eq} is the equivalent isotropic parameter of thermal shift for the corresponding carbon atoms. The data obtained by means of XRD are deposited in the form of CIF file in the Cambridge Crystallographic Data Centre (CCDC).

Determination of antimicrobial activity

To determine the antimicrobial activity, we used the following strains of microorganisms: gram-positive bacterial – *Staphylococcus aureus* (ATCC 25923), *Bacillus subtilis* (RKMUz-5); gram-negative bacterial – *Escherichia coli* (RKMUz-221), *Pseudomonas aeruginosa* (ATCC 27879), opportunistic fungi *Candida albicans* (RKMUz-247) and yeast *Pichia anomala* (RKMUzb). The RKMUz strains were obtained from the collection of the Institute of Microbiology, Academy of Sciences of the Republic of Uzbekistan.

The modified agar-diffusion method was used [16, 17]. A suspension of bacterial cells was prepared from the daily subculture of a corresponding strain, with $1 \cdot 10^6$ colonies per 1 mL. Sterile nutritive agar (LB Agar, Invitrogen, USA, 25 g agar/L distilled water) was inoculated with bacterial cells (200 μL of bacterial cells in 2 mL of 0.9 % NaCl suspension, 20 mL medium) and poured in Petri dishes to obtain a solid phase. *C. albicans* and *P. anomala* ($1 \cdot 10^5$ CFU/mL) were inoculated in sterile Mueller-Hinton-agar in agreement with CLSI for agar disc diffusion methods [16]. Test materials in the volume of 40 μL (which is equivalent to 0.2 mg/disc concentration of an individual compound in chloroform) were deposited on sterile paper discs (6 mm in diameter, Whatman No. 1). Ampicillin, ceftriaxone and fluconazole (Himedia Laboratories Pvt. Limited) were used as a positive reference, while the solvent was used as a negative one. The solvent was evaporated in air flow at room temperature. Then the discs were deposited on the surface of inoculated agar dishes and kept for 2 h in a refrigerator (+4 °C) for prediffusion of the substances in agar. The dishes with bacteria were incubated at 37 °C for 24 h, fungi and yeast – for 48 h at 29 °C. The zone of inhibition (including disc diameter) was measured and recorded after incubation time was over. The average values of inhibition were calculated after the procedure was repeated three times.



Scheme 1.

RESULTS AND DISCUSSION

Many modern methods of heteroamide synthesis are known, but the traditional method based on the interaction of carboxylic acids and amines is still relevant. Using the previously described procedure involving preliminary formation of salts [11], we synthesised amides **2a–e** in the yields of 23.0–64.9 %, starting from previously synthesised 6′-aminodubamine **1** [10, 18] and a series of aliphatic acids (Scheme 1). The structures of the compounds were confirmed with the help of spectral data. There are some specific features in the ^{1}H NMR spectra of amides **2a–e**. First of all, the signal from H-3′ proton is shifted to the weak field by 2 ppm (δ 8.24 ppm) in comparison with the signal for the initial amine **1** (δ 6.28 ppm). Second, in the absence of absorption and related to NH and intramolecular hydrogen bonds in the IR spectra of products **2a–e** (which is possible if chelates are formed) the amide NH-proton in the ^{1}H NMR spectrum also underwent a significant shift to the weak field (δ 13.03 ppm). In the ^{1}H NMR spectrum of 6′-aminodubamine (**1**, (2-(4′,5′-methylenedioxy-2′-aminophenyl)-quinoline)) NH_2 signal appears at δ 6.18 ppm as a two-proton broadened singlet.

Rotation around the amide bond is known to be hindered in the amide group because of conjugation between the unshared electron pair of nitrogen atom and C=O group, however, this fact does not explain the discovered features in full. So, we studied the structures of **1** and (as example) **2a** by means of XRD. The spatial structure of the molecules of **1** and **2a** according to XRD data is shown in Fig. 1. One can see that the mutual positions (rotation) of the flat fragments of quinolone core and the next dicycle in the molecules of **1** and **2a** are practically the same. The torsion angle C13–C12–C6–C7, characterising the mutual positions of flat fragments in the molecules of **1** and **2a**, is equal to 17.8 and 17.0°, respectively. This position of the flat fragments is favourable for the formation of intramolecular hydrogen bond N10-H...N11. Comparing the parameters of these intramolecular hydrogen bonds, one may see that H-bond is pronounced stronger in molecule **2a** (see Fig. 1, the distances N10...N11 2.639(3) Å, H...N11 1.81(3) Å and the angle N10–H...N11 146(2)°) than in molecule **1** (the distances N10...N11

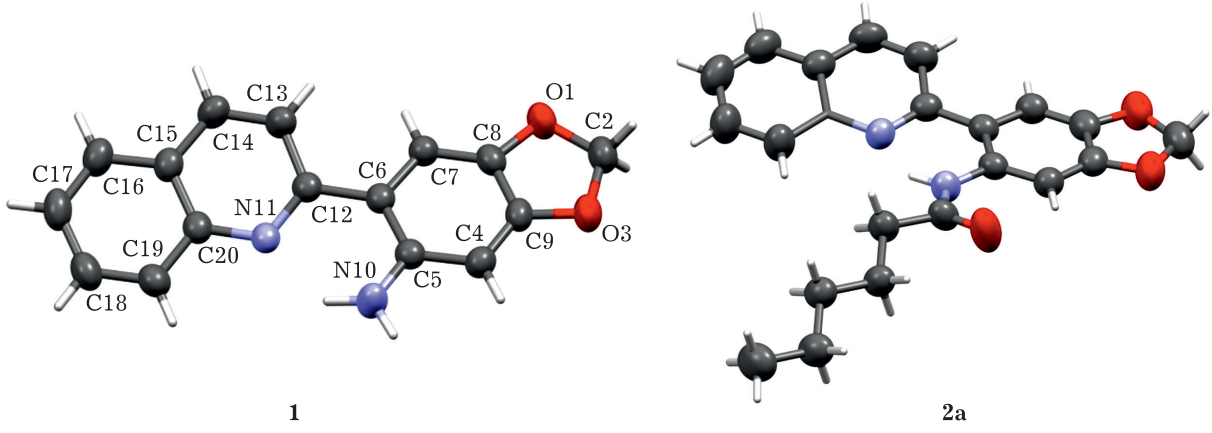


Fig. 1. Spatial structure of the molecules of **1** and **2a**.

2.703(2) Å, H...N11 2.02(2) Å and the angle N10–H...N11 132(1)°).

The nitrogen atom N10 in the aryl fragment takes sp^2-configuration, which is evidenced by the experimentally determined positions of H atoms and the sums of internal valence angles of nitrogen atoms in the aminophenyl ring 356 and 360° for **1** and **2a**, respectively. This value is quite predictable for **2a**, but for the molecule of **1** the sp^2-configuration is somewhat unexpected because nitrogen atom in phenylamines (with NH_2 group) is usually in sp^3-hybridization and takes the tetrahedral configuration.

According to quantum chemical calculations carried out using semi-empirical PM7 method [19] in MOPAC2016 software (www.openmopac.net), compounds **1** and **2a** have an intramolecular hydrogen bond N11....H–N10 with the energy 1.16 and 1.49 eV and the distance 2.125 and 1.960 Å, respectively. The nitrogen atom N10 in **2a** takes planar geometry (the sum of valence angles for N10 is 359.8° for **2a** and 354.8° for **1**), which is explained by the more active participation of the unshared electron pair of nitrogen in compound **2a** in π-interaction within the molecule and confirms the results of XRD.

To evaluate antibacterial and antifungal activity of amides **2a–e**, we used the modified method of diffusion into agar with the application of discs; the concentration of the substances under tests was 0.2 mg/disc [16, 17, 20]. The results of *in vitro* screening showed that the compounds **2a–e** do not exhibit antimicrobial activity against *S. aureus* (ATCC 25923), *B. subtilis* (RKMUz-5), *E. coli* (RKMUz-221), *P. aeruginosa* (ATCC 27879), *C. albicans* and *P. anomala* strains of microorganisms.

CONCLUSION

Five new amides were synthesised on the basis of the amino derivative of quinolone alkaloid dubamine and a series of fatty acids. A comparative investigation of the structure of aminodubamine and 2-(4′,5′-methylenedioxy-2′-(N-hexanamido)-phenyl)-quinoline synthesised from the former compound was carried out by means of NMR spectroscopy, XRD and quantum chemistry. A strong descreening effect of the intramolecular hydrogen bond on the protons H-3′, NH-2′ of the amide was revealed, and sp^2-configuration of nitrogen atom in aminodubamine (2-(4′,5′-methylenedioxy-2′-aminophenyl)-quinoline) was confirmed.

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