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Data Article

Design and one-pot synthesis of 2H (methyl)-3-alkyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamides

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ABSTRACT

2H(Methyl)-3-alkylquinazolin-4(3H)-ones were synthesized by reactions of 2H(methyl)quinazolin-4(3H)-ones with alkyl halides. The obtained 2H(methyl)-3-alkylquinazolin-4(3H)-ones were subjected to one-pot synthesis in the presence of chlorosulfonic acid and ammonia, primary sulfonamides among bicyclic quinazolines were synthesized and were characterized by ^{1}H NMR, ^{13}C NMR, IR and mass spectral data. The crystal structure of 2-methyl-3-butyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide was determined by the single-crystal X-ray diffraction method at 293 K.

Specifications Table

Subject area	*Organic Chemistry, Spectroscopy*
Compounds	*2H(Methyl)−3-alkylquinazoline-4-one-6-sulfonamides*
Data category	*Synthesized, spectral, crystallographic data*
Data acquisition format	*NMR, IR, Mass spectra, CIF for Crystallography*
Data type	*Experimental*
Procedure	*The title compound was synthesis and characterized by NMR, IR, Mass spectra crystallographic studies.*
Data accessibility	*Data is within the article, crystallographic data was in Cambridge Crystallographic Data center with CCDC 2190885 (refcode: XEJRIR) for* ***7d;*** *CCDC 2345709 for* ***8d***

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1. Rationale

At present, in the world medical practice, the number of drugs based on synthetic - heterocyclic compounds is growing every year. Such heterocyclic compounds include bicyclic quinazolines. If we look at the work of scientists conducting research in the field of chemistry and pharmacy, we can see that serious attention is paid to the synthesis of these potential heterogeneous - candidate compounds and a comprehensive study of their pharmacological activity.

Quinazoline derivatives are of great interest to pharmaceutical chemists because this heterocyclic skeleton serves as the basis for the development of several potent anti-cancer drugs. The Food and Drug Administration (FDA) has approved several quinazoline derivatives: gefitinib, erlotinib, lapatinib, and vandetanib as effective anti-cancer drugs [1,2].

Sulfonamides were the first antimicrobial drugs which lead to the antibiotic revolution in medicine. For the medicinal chemist, the $–SO_2NH_2$ moiety has become privileged building block, found in many drug molecules [3]. Sulfonamides represent an important class of drugs which exhibit various biological activities like antimicrobial [4], antidiabetics [5], anti-inflammatory [6], antihypertensive [7,8], and antileishmanial [9] activities. Further, these derivatives are used as angiogenesis inhibitors for the treatment of cancer [10], in the treatment of Alzheimer's disease [11], as antiviral-HIV protease inhibitors (amprenavir), and anti-hepatitis C virus (HCV) agents [12].

Fig. 1 presents preparations based on primary sulfonamides, for example: the antibacterial Prontosil, for epilepsy (Acetazolamide), high blood pressure (Hydrochlorothiazide), arthritis (Celecoxib) and glaucoma (Methazolamide).

In addition, there are many articles on the synthesis, chemical properties and biological activities of sulfonamides [13–16].

Based on the above data, it is interesting to study the synthesis and biological activity of primary sulfonamides using bicyclic derivatives of quinazoline. The crystal structure of the 3-butyl-2-methyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide is reported here (Fig. 3).

2. Procedure

2.1. Experimental

Freshly distilled solvents: chloroform, hexane, cyclohexane, benzene, ethanol, methanol, isopropanol were used in the work. The IR spectra of the compounds were recorded on a Perkin Elmer (USA) FTIR System 2000 spectrometer on KBr tablets, ^{1}H and ^{13}C NMR spectra on JNM-ECZ400R (Jeol, Japan) with operating frequencies of 400 MHz, TMS (0 ppm) as an internal standard) and obtained in solutions of deuterochloroform ($CDCl_3$), dimethylsulfoxide (DMSO-d_6). Mass spectra was recorded using CAMAG TLC-MS equipped with an ACQUITY Q detector. Thin layer chromatography (TLC) was performed on Sigma-Aldrich, Silufol L/W 20cm20cm UV-254 and Whatman® UV-254 (Germany) plates, and the eluents were benzene:acetone −2:1, chloroform:methanol - 10:1. The melting points of the synthesized compounds were determined on the equipment «BIOBASE BMP-M70» (China) and «MEL-TEMP» (USA).

General procedure for preparation of 2H(methyl)−3-alkylquinazoline-4(3H)-ones (**3a-h, 4a-h**) [17–19].

A mixture of 2H(methyl)quinazolin-4(3H)-ones (**1, 2**) (1.0 mmol), alkyl halide (1.2 mmol) and KOH (1.2 mmol) was dissolved in ethanol (30 mL). The solution was stirred and refluxed for 6 h. The resulting reaction mixture was cooled and mixed by adding 30 ml of an aqueous solution of NaOH (5 %), and then 70 ml of chloroform was poured over it and was stirred for 5–10 min, and the chloroform layer was separated using a separatory funnel and dried under anhydrous Na_2SO_4. Chloroform was removed, and the resulting substance was filtered off and recrystallized. Some physical parameters and yields of substances **3a-h, 4a-h** are given in the Table 1.

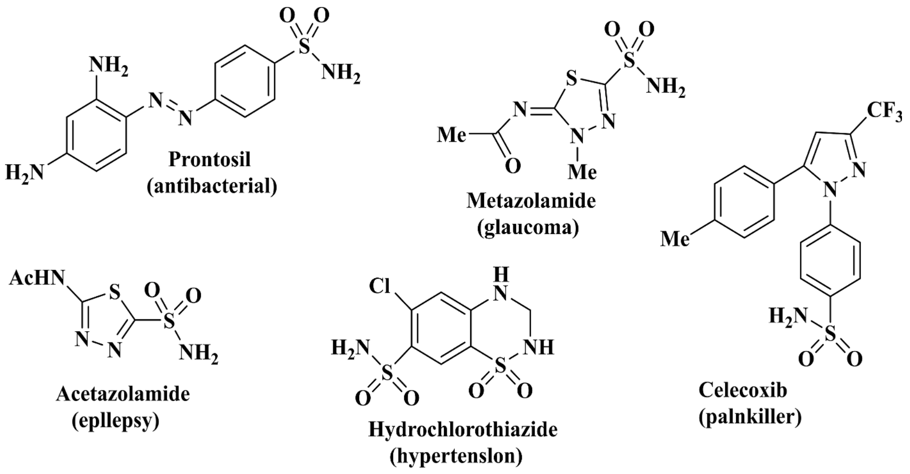


Fig. 1. Primary sulfonamide-containing drugs.

Table 1
Some physical parameters and yields of substances **3a-h, 4a-h**.

Compound	R	R'	X	Chemical formula	Yield,%	R_f	M.p. ^{0}C
3a	H	CH_3	I	$C_9H_8N_2O$	90	0.65	98–96
4a	CH_3	CH_3	I	$C_{10}H_{10}N_2O$	92	0.63	104–106
3b	H	C_2H_5	Br	$C_{10}H_{10}N_2O$	86	0.61	90–92
4b	CH_3	C_2H_5	Br	$C_{11}H_{12}N_2O$	91	0.60	95–97
3c	H	C_3H_7	Br	$C_{11}H_{12}N_2O$	82	0.70	75–77
4c	CH_3	C_3H_7	Br	$C_{12}H_{14}N_2O$	89	0.80	70–72
3d	H	C_4H_9	Br	$C_{12}H_{14}N_2O$	81	0.58	58–60
4d	CH_3	C_4H_9	Br	$C_{13}H_{16}N_2O$	84	0.77	64–66
3e	H	C_5H_{11}	I	$C_{13}H_{16}N_2O$	76	0.60	51–53
4e	CH_3	C_5H_{11}	I	$C_{14}H_{18}N_2O$	77	0.62	50–52
3f	H	C_6H_{13}	I	$C_{14}H_{18}N_2O$	72	0.62	56–58
4f	CH_3	C_6H_{13}	I	$C_{15}H_{20}N_2O$	74	0.62	47–50
3 g	H	C_7H_{15}	Br	$C_{15}H_{20}N_2O$	71	0.72	41–43
4 g	CH_3	C_7H_{15}	Br	$C_{16}H_{22}N_2O$	70	0.76	40–42
3h	H	$CH_2C_6H_5$	Cl	$C_{15}H_{12}N_2O$	74	0.83	112–114
4h	CH_3	$CH_2C_6H_5$	Cl	$C_{16}H_{14}N_2O$	76	0.60	118–120

2.2. *Synthesis of 3-methyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**7a**)*

A mixture consisting of 6.6 ml (0.1 mol, 11.6 g, $d = 1.75$ g/ml) of chlorosulfonic acid and 1.6 g (0.01 mol) of 3-methylquinazolin-4-one was heated for 4–6 h at 120–130 °C. It was then cooled to 0–2 °C and ammonium hydroxide (25 %) was added until the pH reached 8–9 and mixture left for 16 h at 5–6 °C. The resulting precipitate was filtered off and washed with water. As a result, 3-methyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**7a**) is obtained, white crystalline solid, yield 2.15 g (90 %), mp. 243–245°C. IR-spectrum (KBr, ν, cm^{-1}): 3293 (NH_2), 1682 (C = O), 1607 (C = N), 1397 (as-SO_2), 1151 (s-SO_2), 726 (C-S). ^{1}H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, *J*/Hz): 8.54 (1H, d, $J = 2.15$, H-2), 8.37 (1H, s, H-5), 8.10 (1H, dd, J_1=2.19, J_2=8.6, H-7), 7.71 (1H, d, $J = 8.53$, H-8), 7.37 (2H, s, NH_2), 3.51 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-d6+CCl_4, δ, ppm): 31.25 ($N{—}\underline{C}H_3$), 120.60 (C-4a), 121.92 (C-5), 128.33 (C-8), 133.88 (C-7), 138.27 (C-6), 146.79 (C-8a), 152.83 (C-2), 160.53 (C = O); Mass spectrum *m/z* 262.7896 [M+Na]$^+$.

2.3. *Synthesis of 3-ethyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**7b**)*

White crystalline solid, Yield: 2.2 g (88 %), mp. 198–200°C. IR-spectrum (KBr, ν, cm^{-1}): 3306 (NH_2), 1671 (C = O), 1605 (C = N), 1382 (as-SO_2), 1175 (s-SO_2), 728 (C-S). ^{1}H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, *J*/Hz): 8.58(1H, d, $J = 2.08$; H-2), 8.39 (1H, d, $J = 2.33$; H-5), 8.12 (1H, d,d; J_1=2.2, J_2=8.4; H-7), 7.71 (1H, d, $J = 8.58$; H-8), 7.35 (2H, s, NH_2), 4.03 (2H, q, J_1=7.15, J_2= 7.14; CH_2), 1.32 (3H, t, J_1=7.01, J_2= 7.28; CH_3); ^{13}C NMR (100 MHz, DMSO-d$_6$+CCl_4, δ, ppm): 13.87 ($N{–}CH_2\underline{C}H_3$), 23.15 ($N{–}\underline{C}H_2CH_3$), 120.22 (C-4a), 125.22 (C-5), 127.54 (C-8), 131.18 (C-7), 142.19 (C-6), 149.43 (C-8a), 156.56 (C-2), 160.83 (C = O). Mass spectrum *m/z* 276.1324 [M+Na]$^+$.

2.4. *Synthesis of 3-propyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**7c**)*

White crystalline solid, Yield: 2.27 g (85 %), mp. 180–182°C. IR-spectrum (KBr, ν, cm^{-1}): 3249 (NH_2), 1664 (C = O), 1609 (C = N), 1389 (as-SO_2), 1163 (s-SO_2), 754 (C-S). ^{1}H NMR spectrum (400 MHz, DMSO-d6, δ, ppm, *J*/Hz): 8.55 (1H, d, $J = 2.29$; H-2), 8.49 (1H, s; H-5), 8.13 (1H, d,d, J_1=2.24, J_2=8.54; H-7), 7.81 (1H, d, $J = 8.6$ H-8), 7.52 (2H, s, NH_2), 3.93 (2H, t, $J = 7.28$; CH_2), 1.69 (2H, m; CH_2); 0.86 (3H, t, $J = 7.45$; CH_3); ^{13}C NMR (100 MHz, DMSO-d$_6$+CCl_4, δ, ppm): 10.79 ($N{—}CH_2CH_2\underline{C}H_3$), 21.83 ($N{—}CH_2\underline{C}H_2CH_3$), 47.70 ($N{—}\underline{C}H_2CH_2CH_3$), 121.29 (C-4a), 124.16 (C-5), 128.29 (C-8), 130.76 (C-7), 142.13 (C-6), 149.88 (C-8a), 150.12 (C-2), 159.78 (C = O); Mass spectrum *m/z* 290.1227 [M+Na]$^+$.

2.5. *Synthesis of 3-butyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**7d**)*

White crystalline solid, Yield: 2.47 g (88 %), mp.: 173–174°C. IR-spectrum (KBr, ν, cm^{-1}): 3309 (NH2), 1663 (C = O), 1605 (C = N), 1376 (as-SO_2), 1175 (SO2), 773 (C-S). ^{1}H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, *J*/Hz): 8.56 (1H, s, $J = 1.8$; H-2), 8.43 (1H, d; $J = 3.7$; H-5), 8.14 (1H, d,d, J_1=2.17, J_2=8.5; H-7), 7.75 (1H, d,d, H-8), 7.43 (2H, s, NH2), 4.0 (2H, t, $J = 7.3$; CH_2), 1.7 (2H, m; CH_2); 1.37 (2H, m; CH_2), 0.95 (3H, t, $J = 7.16$; CH_3). ^{13}C NMR (100 MHz, DMSO-d$_6$+CCl_4, δ, ppm): 14.04 ($N{—}CH_2CH_2CH_2\underline{C}H_3$), 19.95 ($N{—}CH_2CH_2\underline{C}H_2CH_3$), 31.35 ($N{—}CH_2\underline{C}H_2CH_2CH_3$), 46.45 ($N{—}\underline{C}H_2CH_2CH_2CH_3$), 121.89 (C-4a), 125.05 (C-5), 128.27 (C-8), 131.16 (C-7), 142.94 (C-6), 149.73 (C-8a), 150.31 (C-2), 160.11 (C = O); Mass spectrum *m/z* 304.1343 [M+Na]$^+$.

2.6. *Synthesis of 2,3-dimethyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**8a**)*

White crystalline solid, Yield: 2.32 g (92 %), mp.: 264–266°C. IR-spectrum (KBr, ν, cm^{-1}): 3293 (NH_2), 1682 (C = O), 1592 (C = N), 1387 (as-SO_2), 1152 (s-SO_2), 738 (C-S). ^{1}H NMR spectrum (400 MHz, DMSO-d$_6$, δ, ppm, *J*/Hz): 8.52 (1H, d, $J = 2.22$; H-5), 8.09 (1H, d, d; J_1=2.23, J_2=8.59; H-7), 7.64 (1H, d,d; J_1=0.53, J_2=8.6; H-8), 7.37 (2H, s, S-NH_2), 3.57 (3H, s, N—CH_3), 2.61(3H, s; C—CH_3); ^{13}C NMR (100 MHz, DMSO-d_6+CCl_4, δ, ppm): 23.18 (C—$\underline{C}H_3$), 30.57 (N—$\underline{C}H_3$), 119.31 (C-4a), 126.98 (C-5), 127.14 (C-8), 132.12 (C-7), 134.91 (C-6), 149.33 (C-8a), 157.49 (C-2), 160.43 (C = O); Mass spectrum *m/z* 276.0814 $[M+Na]^+$.

2.7. *Synthesis of 3-ethyl-2-methyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**8b**)*

White crystalline solid, Yield: 2.4 g (90 %), mp.: 252–254°C. IR-spectrum (KBr, ν, cm^{-1}): 3304 (NH_2), 1681 (C = O), 1611 (C = N), 1394 (as-SO_2), 1184 (s-SO_2), 732 (C-S). ^1H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, *J*/Hz): 8.49(1H, d, *J* = 2.17; H-5), 8.08 (1H, dd, J_1=2.29, J_2=8.59; H-7), 7.70 (1H, d, *J* = 8.6 H-8), 7.5 (2H, s, NH_2), 4.07 (2H, q, *J* = 7.1, N—CH_2), 2.6 (3H, S; C—CH_3); 1.23 (3H, t, *J* = 7.1; H_2C—CH_3); ^{13}C NMR (100 MHz, DMSO-d_6+CCl_4, δ, ppm): 15.03 (N–$CH_2\underline{C}H_3$), 34.08 (-C-$\underline{C}H_3$), 41.96 (N–$\underline{C}H_2CH_3$), 121.93 (C-4a), 125.04 (C-5), 128.25 (C-8), 131.15 (C-7), 142.96 (C-6), 149.52 (C-8a), 150.37 (C-2), 159.98 (C = O); Mass spectrum *m/z* 290.1555 $[M+Na]^+$.

2.8. *Synthesis of 2-methyl-4-oxo-3-propyl-3,4-dihydroquinazoline-6-sulfonamide (**8c**)*

White crystalline solid, Yield: 2.47 g (88 %), mp.: 216–218°C. IR-spectrum (KBr, ν, cm^{-1}): 3244 (NH_2), 1663 (C = O), 1609 (C = N), 1389 (as-SO_2), 1165 (s-SO_2), 755 (C-S). ^1H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, *J*/Hz): 8.48 (1H, d, *J* = 2.29; H-5), 8.16 (1H, dd, J_1=2.18, J_2=8.6; H-7), 7.69 (1H, d, *J* = 8.02; H-8), 7.55 (2H, s, NH_2), 3.97 (2H, t, *J* = 5.04; CH_2), 2.6 (3H, s, CH_3); 1.64(2H, m, CH_2), 0.9 (3H, t, *J* = 7.33; CH_3); ^{13}C NMR (100 MHz, DMSO-d_6+CCl_4, δ, ppm): 11.6 (N—$CH_2CH_2\underline{C}H_3$), 21.6 (N—$CH_2\underline{C}H_2CH_3$), 23.4 (-C-$\underline{C}H_3$), 46.18 (N—$\underline{C}H_2CH_2CH_3$), 120.05 (C-4a), 124.8 (C-5), 128.1 (C-8), 131.3 (C-7), 141.8 (C-6), 149.4 (C-8a), 158.07 (C-2), 161.2 (C = O); Mass spectrum *m/z* 304.1140 $[M+Na]^+$.

2.9. *Synthesis of 3-butyl-2-methyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**8d**)*

White crystalline solid, Yield: 2.5 g (85 %), mp.: 181–182 °C. IR-spectrum (KBr, ν, cm^{-1}): 3277 (NH_2), 1662 (C = O), 1608 (C = N), 1393 (as-SO_2), 1178 (s-SO_2), 756 (C-S). ^1H NMR spectrum (400 MHz, DMSO-d_6, δ, ppm, *J*/Hz): 8.48 (1H, d, *J* = 1.61; H-5), 8.08 (1H, dd, J_1=2.29, J_2=8.6; H-7), 7.69 (1H, d, *J* = 8.6; H-8), 7.48 (2H, s, NH_2), 4.01 (2H, t, *J* = 7.8; CH_2), 2.61 (3H, s, CH_3); 1.60 (2H, m, CH_2), 1.34(2H, m, CH_2), 0.90 (3H, t, *J* = 7.23; CH_3); ^{13}C NMR (100 MHz, DMSO-d_6+CCl_4, δ, ppm): 14.09 (N—$CH_2CH_2CH_2\underline{C}H_3$), 20.32 (N—$CH_2CH_2\underline{C}H_2CH_3$), 23.27 (-C-$\underline{C}H_3$), 30.65 (N—$CH_2\underline{C}H_2CH_2CH_3$), 44.42 (N—$\underline{C}H_2CH_2CH_2CH_3$), 120.17 (C-4a), 125.22 (C-5), 127.56 (C-8), 131.18 (C-7), 142.17 (C-6), 149.31 (C-8a), 156.71 (C-2), 160.97 (C = O); Mass spectrum *m/z* 218.0726 $[M+Na]^+$.

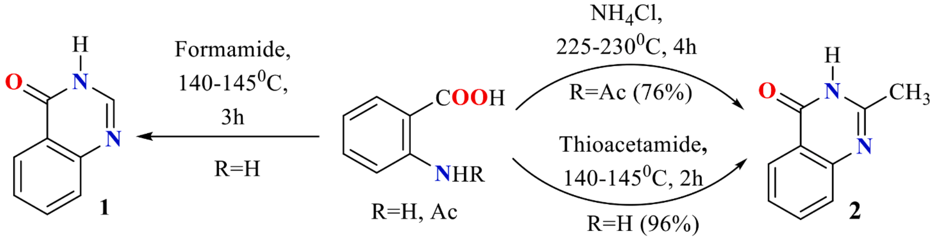
2.10. *Single crystal X-ray diffraction and refinement*

Single crystal diffraction data for *of* 2-methyl-3-butyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**8c**) were collected at a temperature of 294 K on a XtaLAB Synergy, Single source at home/near, HyPix3000 with CuKα radiation from a PhotonJet (Cu) X-ray Source microfocus tube. The structure was solved by direct methods with the program *SHELXS* [20] and refined by full-matrix least squares on F^2 using the *SHELXL* [21] package. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined using the riding model, except for the N—H atoms, which were located by a difference Fourier map and refined isotropically. The H atoms bonded to nitrogen were restrained to a N—H distance of 0.87 Å. Geometrical calculations were carried out using *PLATON* [22]. Crystal data and convergence results have been included to Supplementary in Table S1. Supplementary crystallographic data were deposited in CCDC (Cambridge Crystallographic Data Centre, No: 2,345,709) for (**8c**). The data can be obtained free of charge via http:/www.ccdc.cam.ac.uk/conts/retrieving.html, or e-mail: deposit@ccdc.ac.uk

3. Data, value and validation

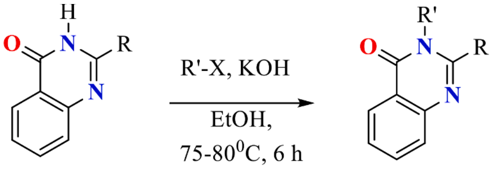
3.1. *Chemistry results and discussion*

Synthesis of quinazolin-4(*3H*)-one (**1**) required for research is carried out by heating a 1:2 mixtures of anthranilic acid and formamide at 140–150 °C for 3 h [17]:



Synthesis of 2-methylquinazolin-4(*3H*)-one (**2**) carried out by two methods [18,19]. According to the first method, N-acetylanthranilic acid is cyclized with ammonium chloride under harsh conditions, and according to the second method, anthranilic acid is cyclized with thioacetamides at a relatively low temperature. Since the second method occurs at a relatively low temperature and in a short time with the formation of product **2** in quantitative yield (96 %), we can say that this method is more effective than the first (yield of **2** 76 %).

N-Alkylation of 2H(methyl)quinazolin-4(3H)-ones (**1, 2**) are carried out at the boiling temperature of ethanol (78°C) in the ratio of 1:1.2 and 2H(methyl)−3-alkylquinazolin-4(3H)-ones (**3a-h, 4a-h**) were synthesized in good yields [19] (Table 1):



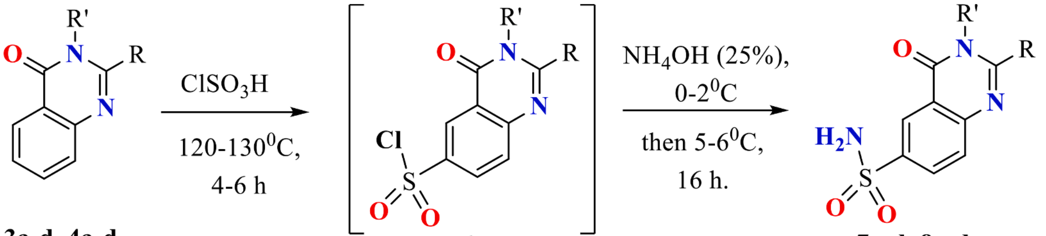
1, R=H;
2, R=CH_3

3a-h, R=H
4a-h, R=CH_3

3a, **4a** R'=Me;
3b, **4b** R'=Et;
3c, **4c** R'=Pr;
3d, **4d** R'=Bu;
3e, **4e** R'=Pe;
3f, **4f** R'=Hex;
3g, **4g** R'=Hep;
3h, **4h** R'=Bn.

It should be noted that during alkylation of compounds **1** and **2**, with an increase in the length of the alkyl chain of alkyl halides, the yield of products decreases. Relatively low yields of alkyl products (3 g (71 %), 4 g (70 %)) are observed when using heptyl bromide as an alkylating agent. This can be explained by a decrease in the electrophilicity of alkylating agents in the CH_3—C_7H_{15} series.

Currently, sulfonamide drugs are widely used in medical practice [23]. Therefore, the creation of convenient methods of synthesis is of great interest among chemists and pharmaceutical scientists. In order to carry out the synthesis of sulfonamides we studied One-pot reactions of 2H(methyl)−3-methyl(ethyl, propyl, butyl)quinazolin-4-ones (**3a-d, 4a-d**) with chlorosulfonic acid ($ClSO_3H$) and ammonium hydroxide (NH_4OH) in two steps:



3a-d, 4a-d **5a-d, 6a-d** **7a-d, 8a-d**

3a-d, **5a-d**, **7a-d** R=H; **4a-d**, **6a-d**, **8a-d** R=CH_3;
3a, **4a**, **5a**, **6a**, **7a**, **8a** R'=Me; **3b**, **4b**, **5b**, **6b**, **7b**, **8b** R'=Et;
3c, **4c**, **5c**, **6c**, **7c**, **8c** R'=Pr; **3d**, **4d**, **5d**, **6d**, **7d**, **8d** R'=Bu

For this, compounds **3a-d, 4a-d** were dissolved in $ClSO_3H$ in cold conditions, and reaction mixture was heated at 120–130°C for 4–6 h. Then, the reaction mixture was first cooled to 0–2°C (ice), and an excess of NH_4OH was slowly added and left in the refrigerator (5–6°C) for up to 16 h. As a result, corresponding 2H(methyl)−3-methyl(ethyl, propyl, butyl)−4-oxo-3,4-dihydroquinazoline-6-sulfonamides (**7a-d, 8a-d**) were synthesized in 80–92 % yields. Thus, a one-reactor two-step synthesis method of sulfonamides was developed. It should be emphasized that the intermediately formed sulfochlorides (**5a-d, 6a-d**) are convenient synthons for the

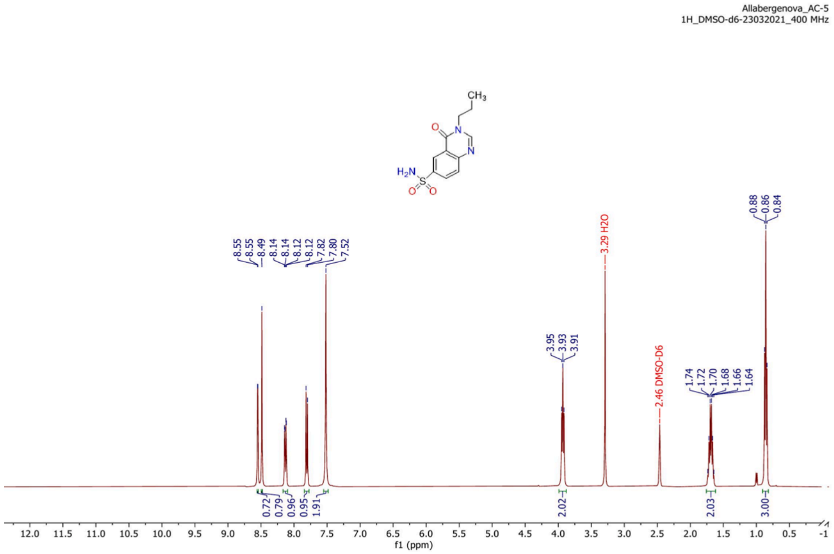


Fig. 2. ^1H NMR spectra of 3-propyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (7c).

synthesis of various sulfonamides.

3.2. Spectra description

The structures of all compounds (**7a-d, 8a-d)** were characterized by IR, ^{1}H, ^{13}C NMR spectroscopy and mass-spectrometry. The details are provided in the experimental section and supporting information (Table S1). For example, in the ^{1}H NMR spectrum of **7c** (Fig. 2), the chemical shift (CS) in δ 7.56 ppm appeared as a singlet and assigned to the NH_2 protons. The CS at 8.59–7.86 ppm appeared as doublet, singlet, doublet-doublet and doublet correspond to the four aromatic protons. The methyl protons resonated as a triplet at 0.86 ppm. The methylene protons resonated as a multiplet at 1.69 ppm and triplet at 3.93 ppm (Table 2).

In addition, the crystallographic data of 3-butyl-4-oxo-3,4-dihydroquinazoline-6-sulfonamide (**7d**) and the results of Hirschfeld surface analysis are detailed in this article [24]. Supplementary crystallographic data were deposited in CCDC (Cambridge Crystallographic Data Centre, No: 2190885).

3.3. Single crystal structure description of **8d**

The title compound, $C_{13}H_{17}N_3O_3S$, crystallizes in the triclinic space group *P-1*. A displacement ellipsoid plot and the numbering scheme are provided in Fig. 3. The central aromatic quinazoline moiety is near planar with r.m.s. deviation 0.0233 Å, the largest deviation of 0.0527 Å from the that plane by an N3 atom (Fig. S1a). A comparative analysis the geometry of planarity of the title molecule with the similar structure (refcode CCDC: XEJRIR) [24] showed that the planarity has close values (for molecule of XEJRIR the r.m.s. is 0.0258 Å)(Fig. S2b).

In the crystal revealed an intramolecular C7—H7•••O2, C10—H10B•••O1 interactions, and molecules are linked by intermolecular N2—H2A···O1, N2—H2B···N1 and C12—H12A···O3 hydrogen bonds (Table 3), forming infinity chains propagating along the (*103*)-direction and give rise to $R_2^2(16)$, $C_2^2(8)$, $C_2^2(16)$ and $C_4^4(24)$ graph-set motifs [25] (Fig. 4).

The molecules in adjacent chains interact C—O···π stacking and S—O···π contacts (Fig. S2) along *b*-axis. They amount to C4—O1···*Cg1* (1-*x*, 1-*y*, 1-*z*) = 3.396(3) Å and S1—O2···*Cg*1 (1-*x*, 2-*y*, 1-*z*) = 3.720(3) Å. *Cg*1 correspond to the ring centroid N1/C2/N3/C4/C4A/C8A.

4. Conclusions

The primary sulfonamides of bicyclic quinazolines of high practical importance were synthesized for the first time through the chemical transformations of 2H(methyl)−3-alkylquinazolin-4-ones in the presence of chlorosulfonic acid and ammonium hydroxide. The structure of the synthesized compounds was proved using modern physical research methods: IR-, ^{1}H, ^{13}C NMR-spectroscopy and mass-spectrometry. In the crystal of 2-methyl-4-oxo-3-propyl-3,4-dihydroquinazoline-6-sulfonamide (**8c**), the intermolecular N—H•••O hydrogen bonds lead to the formation of an infinity chain with $C_4^4(24)$ graph-set notation.

CRediT authorship contribution statement

Sevara M. Allabergenova: Validation, Resources, Investigation, Formal analysis. **Fazliddin A. Zulpanov:** Validation, Investigation, Formal analysis. **Nasiba B. Pirnazarova:** Validation, Investigation, Formal analysis. **Ubaydulla M. Yakubov:** Writing – original draft, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kosim O. Zokhidov:** Investigation, Formal analysis. **Sirojiddin S. Abdullayev:** Investigation, Formal analysis. **Azimjon A. Mamadrakhimov:** Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Jamshid M. Ashurov:** Validation, Formal analysis. **Akmaljon G. Tojiboev:** Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Burkhon Zh. Elmuradov:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing

Table 2
Some physical parameters and yields of substances **7a-d, 8a-d**.

Compound	R	R'	Chemical formula	Yield,%	R_f	Mp, ^{0}C
7a	H	CH_3	$C_9H_{11}N_3O_3S$	90	0.25	243–245
7b	H	C_2H_5	$C_{10}H_{13}N_3O_3S$	88	0.28	198–200
7c	H	C_3H_7	$C_{11}H_{15}N_3O_3S$	85	0.42	180–182
7d	H	C_4H_9	$C_{12}H_{17}N_3O_3S$	80	0.61	173–174
8a	CH_3	CH_3	$C_{10}H_{13}N_3O_3S$	92	037	264–266
8b	CH_3	C_2H_5	$C_{11}H_{15}N_3O_3S$	90	0.56	252–254
8c	CH_3	C_3H_7	$C_{12}H_{17}N_3O_3S$	88	0.47	216–218
8d	CH_3	C_4H_9	$C_{13}H_{19}N_3O_3S$	85	0.55	179–181

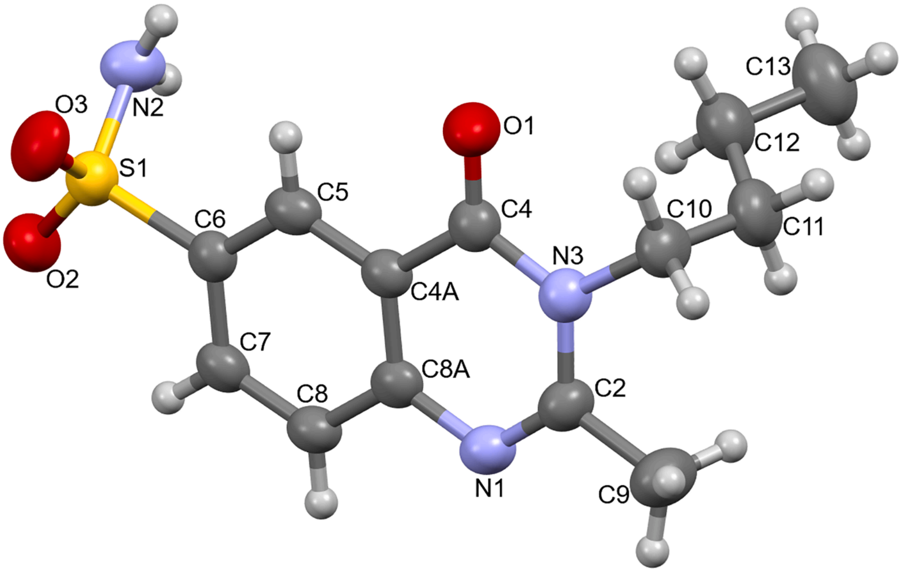


Fig. 3. Displacement ellipsoid plot of 8d and atom-labeling scheme ellipsoids drawn at 50 % probability, H atoms shown as fixed-size spheres.

Table 3
Intermolecular and intramolecular hydrogen-bond interactions geometries (Å, °) for title compound.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2*A*···O1^{i}	0.87(3)	2.12(3)	2.975(4)	170(4)
N2—H2*B*···N1^{ii}	0.88(3)	2.27(3)	3.102(4)	160(3)
C12—H12A···O3 ^{i}	0.97	2.51	2.444(6)	162
C7—H7···O2 (intra)	0.93	2.50	2.888(5)	105
C10—H10B···O1(intra)	0.97	2.34	2.742(5)	104

Symmetry codes: (i) -*x*, -*y* + 1, -*z* + 1; (ii) 1-*x*, 2-*y*, 1-*z*.

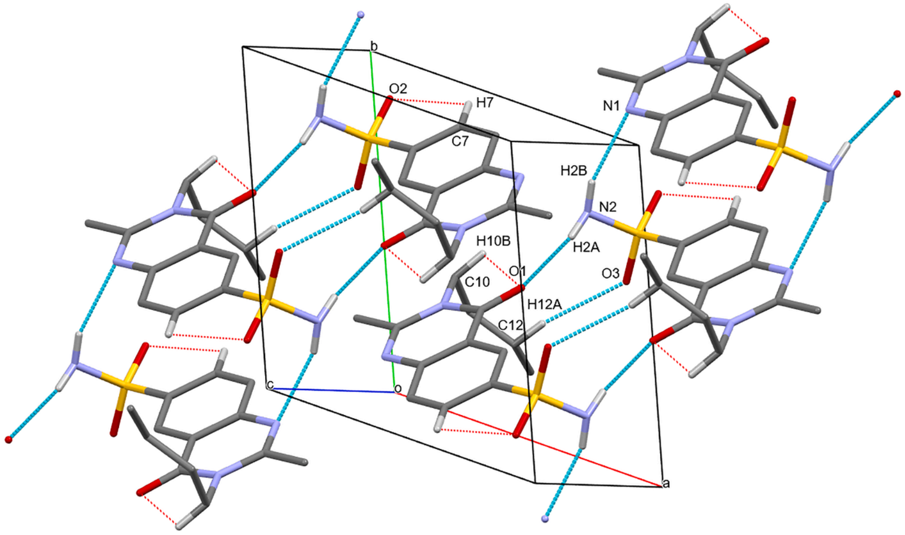


Fig. 4. Intramolecular C7—H7•••O2 and C10—H10B•••O1 hydrogen bonds (red dashed lines) and intermolecular N2—H2A···O1, N2—H2B···N1 and C12—H12A···O3 hydrogen bonds (blue dashed lines).

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Data availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cdc.2024.101160.

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