Efficient Regioselective Synthesis of Novel Condensed Sulfur–Nitrogen Heterocyclic Compounds Based on Annulation Reactions of 2-Quinolinesulfenyl Halides with Alkenes and Cycloalkenes

Vladimir A. Potapov *, Roman S. Ishigeev and Svetlana V. Amosova

A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Division of The Russian Academy of Sciences, 1 Favorsky Str., 664033 Irkutsk, Russia; ishigeev@irioch.irk.ru (R.S.I.); amosova@irioch.irk.ru (S.V.A.)

* Correspondence: v.a.potapov@irioch.irk.ru or v.a.potapov@mail.ru; Tel.: +7-3952-426599

Abstract: The preparation of novel reagents 2-quinolinesulfenyl chloride and bromide based on available 2-mercaptoquinoline has been described. This approach opens up opportunities for the introduction of 2-quinolinesulfenyl chloride and bromide into organic synthesis. Regioselective synthesis of novel 1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium derivatives in high yields has been developed by annulation reactions of 2-quinolinesulfenyl chloride and bromide with alkenes. Condensed tetracyclic products have been obtained by the reactions of 2-quinolinesulfenyl chloride and bromide with cycloalkenes. The opposite regiochemistry in the reactions with styrene, isoeugenol and 1-alkenes was discussed.

Keywords: 1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium derivatives; annulation reactions; 2-quinolinesulfenyl chloride; 2-quinolinesulfenyl bromide; alkenes; cycloalkenes; 2-mercaptoquinoline

1. Introduction

The vast majority of drugs contain heterocyclic fragments in their structures [1]. The sulfur heterocycles are structural parts of many drugs that are used in modern pharmacotherapy [2]. Drugs containing condensed nitrogen and sulfur heterocycles are some of the most commonly used medications [2]. Penicillin and cephalosporin scaffolds contain condensed nitrogen and sulfur heterocycles and represent examples of antibiotics that played an outstanding role in the history and development of pharmaceutical chemistry.

The quinoline derivatives exhibit a variety of biological activities, including antibacterial, antifungal, anticancer, anti-inflammatory, antimalarial and antileishmanial actions [3–9]. The fluoroquinolone antibiotics (ciprofloxacin, levofloxacin, gatifloxacin and moxifloxacin) and antimalarial medications (chloroquine, hydroxychloroquine, amodiaquine and primaquine) took an important place in pharmacotherapy. It is worth noting that some quinoline derivatives (e.g., hydroxychloroquine) have been recently used for the treatment of COVID-19 [10].

The condensed system of quinoline and thiazole heterocycle is very promising in terms of possible manifestation of biological activity. The [1,3]thiazolo[3,2-a]quinolin-10-ium scaffold derivatives represent an important class of condensed heterocyclic compounds exhibiting various types of biological activity including antibacterial [11–21], antitumor [22–24], anti-inflammatory [25] and antitrypanosomal [26] action as well as glycogen synthase kinase 3 inhibitors properties [24,27] (Figure 1).
Figure 1. Known biologically active compounds containing \([1,3]\)thiazolo\([3,2-a]\)quinolin-10-ium scaffold (antibacterial \([11,16,21]\), antitumor \([22,24]\), antitrypanosomal \([26]\) and glycogen synthase kinase 3 inhibitor \([24]\) activities).

The development of the effective synthesis of novel chalcogen condensed compounds and heterocycles by regioselective annulation and cyclization reactions of chalcogen-containing reagents is our favourable area of research \([28–39]\). The annulation reactions of 2-pyridinesulfenyl and 2-pyridineselenenyl halides with functionalized alkenes led to novel 2H,3H-[1,3]thiazolo[3,2-a]pyridin-4-ium and 2H,3H-[1,3]selenazolo[3,2-a]pyridin-4-ium derivatives in high yields \([34–39]\).

Recently we described the annulation reactions of 8-quinolinesulfenyl halides with vinylic heteroatom compounds, including vinylic ethers, sulfides, divinyl selenide and tetravinyl silane \([40]\). Starting 8-quinolinesulfenyl halides were generated in situ from di(8-quinolinyl) disulfide by the action of sulfuryl chloride or bromine and used in further reactions without isolation (Scheme 1).

Scheme 1. The generation of 8-quinolinesulfenyl halides from di(8-quinolinyl) disulfide by the action of sulfuryl chloride or bromine followed by the annulation reactions with vinylic ethers, sulfides, divinyl selenide and tetravinyl silane.
The annulation reactions of 8-quinolinesulfenyl halides with vinylic ethers, sulfides and divinyl selenide proceeded in a regioselective manner affording 3-substituted 2H,3H-[1,4]thiazino[2,3,4-ij]quinolin-4-ium halides in high yields (Scheme 1) [40]. The annulation reaction of 8-quinolinesulfenyl halides with tetravinyl silane was found to occur with opposite regiochemistry leading to 2-trivinylsilyl-2H,3H-[1,4]thiazino[2,3,4-ij]quinolin-4-ium halides in near quantitative yields (Scheme 1).

The reactions of 8-quinolinesulfenyl halides with cycloalkenes (cyclopentene, cyclohexene and cyclooctene), depending on the nature of the halogen, led to 1,4-thiazino[2,3,4-ij]quinolin-11-ium derivatives or 8-(2-chlorocycloalkyl)sulfanyl]quinolines in high yields (90–100%) (Scheme 2). The reactions of 8-quinolinesulfenyl chloride with cycloalkenes led to electrophilic addition products, while condensed compounds were obtained in the case of 8-quinolinesulfenyl bromide (Scheme 2) [41].

![Scheme 2](image)

*Scheme 2.* The synthesis of [1,4]thiazino[2,3,4-ij]quinolin-11-ium derivatives and 8-[2-chlorocycloalkyl]sulfanyl]quinolines by the reactions of 8-quinolinesulfenyl chloride and bromide with cycloalkenes.

The aim of this research is the development of the efficient regioselective synthesis of novel condensed [1,3]thiazolo[3,2-a]quinolin-10-ium derivatives with promising biological activity based on annulation reactions of 2-quinolinesulfenyl halides with alkenes and cycloalkenes. The annulation of 5-membered 1,3-thiazole heterocycle to the quinoline ring occurs in the reaction of 2-quinolinesulfenyl halides with alkenes and cycloalkenes, whereas the annulation of 6-membered 1,4-thiazine heterocycle to the quinoline ring is observed in the reactions of 8-quinolinesulfenyl halides with cycloalkenes and vinyl heteroatom compounds [40,41] (Schemes 1 and 2).

2. Results and Discussion

The reactions of 2-quinolinesulfenyl halides are unknown, and the preparation of 2-quinolinesulfenyl chloride and bromide has not yet been described in the literature (the SciFinder database). Previously we generated 8-quinolinesulfenyl halides from di(8-quinoliny1) disulfide by the action of sulfuryl chloride or bromine and involved in further reactions without isolation (Scheme 1). However, di(2-quinoliny1) disulfide is a hard-to-get reagent, whereas 2-mercaptopquinoline is an available compound. It would seem that di(2-quinoliny1) disulfide can be easily prepared by oxidation of 2-mercaptopquinoline. Unfortunately, the oxidation reactions of 2-mercaptopquinoline are complicated by side processes that make it difficult to obtain pure di(2-quinoliny1) disulfide.

We developed a simple and efficient method for the generation of 2-quinolinesulfenyl chloride (2) and bromide (3) by the action of sulfuryl chloride or bromine on 2-mercaptopquinoline (1) in methylene chloride or chloroform. The generated 2-quinolinesulfenyl halides 2 and 3 were involved in further reactions without isolation (Scheme 3).
Scheme 3. The simple and efficient method for generation of 2-quinolinesulfenyl chloride 2 and bromide 3 by the action of sulfuryl chloride or bromine on 2-mercaptoquinoline 1 in methylene chloride or chloroform.

The chemical properties of 2-quinolinesulfenyl chloride 2 and bromide 3 are unknown, and we started studies using simple terminal alkenes (1-hexene, 1-heptene and 1-octene) and cycloalkenes (cyclopentene, cyclohexene and cyclooctene).

We found that the reactions of 2-quinolinesulfenyl chloride 2 with 1-hexene, 1-heptene and 1-octene proceeded in a regioselective fashion at room temperature in methylene chloride or chloroform affording 2-alkyl-1,2-dihydro[1,3]thiazolo[3,2-α]quinolin-10-ium chlorides 4–6 in 95–100% yields (Scheme 4). The electrophilic addition of the sulfur atom of 2-quinolinesulfenyl chloride 2 occurred to the α-carbon atom of the terminal double bond of alkenes in an anti-Markovnikov fashion.

Scheme 4. The synthesis of 2-alkyl-1,2-dihydro[1,3]thiazolo[3,2-α]quinolin-10-ium chlorides 4–6 by the reactions of sulfenyl chloride 2 with 1-hexene, 1-heptene and 1-octene.

Along with the investigation of the chemical properties of sulfenyl chloride 2, the reactions of 2-quinolinesulfenyl bromide 3 with alkenes were studied. The reaction of sulfenyl bromide 3 with 1-heptene also proceeded regioselectively, leading to condensed compound 7 in a 99% yield (Scheme 5).

Scheme 5. The synthesis of 2-pentyl-1,2-dihydro[1,3]thiazolo[3,2-α]quinolin-10-ium bromide 7 by the reactions of sulfenyl bromide 3 with 1-heptene.

However, the reactions of 2-quinolinesulfenyl bromide 3 with alkenes containing an even number of carbon atoms (1-hexene and 1-octene) occurred with loss of regioselectivity giving along with compounds 8 and 9 (bromide analogues of products 4 and 6) minor regioisomers 10 and 11, which were originated from electrophilic addition of the sulfur atom of 2-quinolinesulfenyl bromide 3 to the terminal carbon atom of the double bond of alkenes (Scheme 6). A ratio of regioisomers, compounds 8/10 and 9/11, was found to be approximately 3:1. The total yields of regioisomers 8 + 10 and 9 + 11 are quantitative.
The reactions of 2-quinolinesulfenyl chloride 3 with 1-hexene and 1-octene affording compounds 8–11.

Previously we found that the reactions of 8-quinolinesulfenyl bromide with cycloalkenes led to condensed compounds, while in the case of 8-quinolinesulfenyl chloride electrophilic addition, products were obtained (Scheme 2). Unlike this trend, the reactions of cyclopentene with both sulfenyl chloride 2 and bromide 3 at room temperature in methylene chloride afforded condensed tetracyclic products 12 and 13 in 81% and quantitative yields, respectively (Scheme 7).

The reactions of cyclohexene with both 2-quinolinesulfenyl chloride 2 and bromide 3 were accompanied by the formation of by-products, and it was difficult to separate the desired condensed compounds.

Unlike the reactions of cyclopentene with both 2-quinolinesulfenyl halides 2 and 3 giving condensed tetracyclic products 12 and 13, the reaction of 2-quinolinesulfenyl chloride 2 with cyclooctene at room temperature led to electrophilic addition product 14 in quantitative yield (Scheme 8). When sulfenyl bromide 3 was involved in the reaction with cyclooctene under similar conditions, tetracyclic condensed compound 15 was obtained in quantitative yield (Scheme 8).

\[ \text{Hal} = \text{Cl} (12), \text{Br} (13) \]

**Scheme 7.** The reactions of 2-quinolinesulfenyl chloride 2 and bromide 3 with cyclopentene leading to condensed tetracyclic compounds 12 and 13.

\[ \text{Hal} = \text{Cl} (8, 10), \text{Hex} (9, 11) 24-26\% 74-75\% \]

**Scheme 6.** The reactions of 2-quinolinesulfenyl bromide 3 with 1-hexene and 1-octene affording compounds 8–11.

\[ \text{Hal} = \text{Cl}, 81\% \]

\[ \text{Hal} = \text{Br}, \sim 100\% \]

**Scheme 8.** The reactions of 2-quinolinesulfenyl chloride 2 and bromide 3 with cyclooctene affording compounds 14 and 15.
The formation of an intermediate bromine analogue of compound 14 is accompanied by intramolecular cyclization at room temperature with the formation of a condensed product 15, while chloro derivative 14 is less reactive under these conditions and remains uncyclized. It is known that the bromine atom is leaving group better than the chlorine atom in nucleophilic substitution reactions, and intramolecular cyclization with the bromine analogue of compound 14 proceeds easier than with chloro derivative 14.

Finally, we obtained condensed compounds from 2-quinolinesulfonyl chloride 2 and alkenes containing a benzene ring (Scheme 9). The reactions of 2-quinolinesulfonyl chloride 2 with styrene and natural product isoeugenol proceeded at room temperature in methylene chloride in a regioselective manner but with opposite regiochemistry compared to the reactions of sulfonyl chloride 2 with terminal alkenes (Scheme 4). The electrophilic addition of the sulfur atom of sulfonyl chloride 2 occurred to the β-carbon atom of the double bond of styrene and isoeugenol in a Markovnikov fashion. Condensed products 16 and 17 based on styrene and isoeugenol were obtained in quantitative and 80% yields, respectively (Scheme 9).

![Scheme 9](image)

**Scheme 9.** The reactions of 2-quinolinesulfonyl chloride 2 with styrene and isoeugenol giving compounds 16 and 17.

Why do annihilation reactions of quinolinesulfonyl chloride 2 with styrene, isoeugenol and terminal alkenes proceed with opposite regiochemistry? Supposed reaction pathways can be regarded in order to explain this trend (Scheme 10). The reactions of sulfonyl chloride 2 with compounds containing a double bond conjugated with the benzene ring (styrene, isoeugenol) proceeded regioselectively via electrophilic addition of the sulfur atom to the β-carbon atom of the double bond. The regioselectivity is due to the formation of intermediate linear carbocation A, which is stabilized by the benzene ring (the relatively stable benzyl cation) (Scheme 10).

![Scheme 10](image)

**Scheme 10.** The supposed pathways of the reactions of sulfonyl chloride 2 with styrene and 1-alkenes.
Addition reactions of sulfenyl halides to alkenes are well understood [42–53], and it is known that the reactions of arylsulfenyl halides with styrene and its derivatives also afforded Markovnikov adducts [42,43].

It is worth noting that electrophilic addition of arylsulfenyl halides to linear 1-alkene afforded predominantly anti-Markovnikov products, and thiiranium cations were regarded as intermediates in these reactions [44–47]. Taking into account these data, we suppose that the reactions of quinolinesulfenyl chloride with terminal alkenes proceeded via intermediates thiiranium cation and nucleophilic attack of the nitrogen atom of the quinoline ring occurred at the least substituted carbon atom of thiiranium ion leading to the formation of products 4–6 in an anti-Markovnikov fashion (Scheme 10).

The structural assignments of synthesized compounds were made using 1H and 13C-NMR spectroscopy (see Supplementary Materials), including proton-coupled 13C-NMR spectra, and confirmed by elemental analysis.

The products of opposite regiochemistry exhibit characteristic signals of the carbon atoms bonded with charged nitrogen (N+), sulfur atom and with one or two protons in 13C-NMR spectra of the obtained compounds (the number of protons is determined by NMR experiments). The CHS moiety and the CH2N+ methylene group manifest themselves in the regions of 44–48 ppm and 58–62 ppm, respectively, in 13C-NMR spectra of compounds 4–9 (the products derived from anti-Markovnikov addition of the sulfur electrophile to the double bond). Signals of the CH2S group and containing one proton CHN+ moiety are observed in the regions of 31–38 ppm and 66–71 ppm, respectively, in 13C-NMR spectra of compounds 10, 11 and 16 (the products derived from Markovnikov addition of the sulfur electrophile to the double bond).

Stereochemistry of compound 17 is determined based on the value of the spin–spin coupling constant (JH-H = 8.2 Hz) of protons in the N-(Ar)CH-CH(Me)-S fragment. This value corresponds to the trans-disposition of methyl and aryl groups relative to the plane of the ring (trans-configuration) [39,54,55].

3. Experimental Section

3.1. General Information

1H (400.1 MHz) and 13C (100.6 MHz) NMR spectra were recorded on a Bruker DPX-400 spectrometer (Bruker BioSpin GmbH, Rheinstetten, Germany) in 2–5% solution in D2O. 1H and 13C chemical shifts (δ) are reported in parts per million (ppm), relative to tetramethylsilane (external) or to the residual solvent peaks of D2O (δ = 4.79), acetone-d6 (δ = 2.05 and 29.84 ppm) and DMSO-d6 (δ = 2.50 and 39.52 ppm for 1H and 13C NMR, respectively). Elemental analysis was performed on a Thermo Scientific FLASH 2000 Organic Elemental Analyzer (Thermo Fisher Scientific Inc., Milan, Italy). Melting points were determined on a Kofler Hot-Stage Microscope PolyTherm A apparatus (Wagner & Munz GmbH, München, Germany). Absolute solvents were used in the reactions.

3.2. Synthesis of Compounds 4–11 by the Reactions of 2-Quinolinesulfenyl Chloride 2 and Bromide 3 with Alkenes

2-Butyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium chloride (4). A solution of sulfuryl chloride (0.074 g, 0.55 mmol) in methylene chloride (5 mL) was added dropwise to a solution of 2-mercaptoquinoline (0.089 g, 0.55 mmol) in methylene chloride (5 mL), and the mixture was stirred for 15 min at room temperature. The obtained solution of 2-quinolinesulfenyl chloride was added dropwise to a solution of 1-hexene (0.093 g, 1.1 mmol) in methylene chloride (5 mL), and the reaction mixture was stirred for 20 h at room temperature. The solvent was removed by a rotary evaporator. The residue was washed with CCl4 and dried in vacuum, giving product 4 (0.146 g, 95% yield) as a yellow oil.

1H-NMR (400 MHz, D2O): δ 0.81 (t, J 7.1 Hz, 3H, CH3), 1.25–1.40 (m, 4H, CH2), 1.77–1.88 (m, 1H, CH2), 1.89–1.99 (m, 1H, CH2), 3.79 (tt, J 8.7, 6.4 Hz, 1H, SCH2), 5.00 (dd, J 13.0, 6.4 Hz, 1H, NCH2), 5.25 (dd, J 13.0, 8.7 Hz, 1H, NCH2), 5.66–5.72 (m, 2H, Cquin), 7.86–7.88 (m, 1H, Cquin), 7.93–7.98 (m, 1H, Cquin), 8.00–8.02 (m, 1H, Cquin), 8.50–8.52 (m, 1H, Cquin).
13C-NMR (101 MHz, D2O): \( \delta \) 11.82 (CH\(_3\)), 20.27, 27.17, 32.72 (CH\(_2\)), 45.44 (SCH), 59.82 (NCH\(_2\)), 116.27 (C\(_{\text{quino}}\)), 116.84 (C\(_{\text{quino}}\)), 124.96 (C\(_{\text{quino}}\)), 127.06 (C\(_{\text{quino}}\)), 128.85 (C\(_{\text{quino}}\)), 133.87 (C\(_{\text{quino}}\)), 136.51 (C\(_{\text{quino}}\)), 143.49 (C\(_{\text{quino}}\)), 163.60 (C\(_{\text{quino}}\)).

Anal. Calcd for C\(_{15}\)H\(_{18}\)NClS: C 66.32, H 7.20, Cl 11.52, N 4.55, S 10.90. Found: C 66.68, H 7.39, Cl 11.88, N 4.72, S 10.90.

2-Hexyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium chloride (6). A solution of sulfuryl chloride (0.052 g, 0.39 mmol) in methylene chloride (5 mL) was added dropwise to a solution of 2-mercaptoquinoline (0.063 g, 0.39 mmol) in methylene chloride (5 mL), and the mixture was stirred for 15 min at room temperature. The solution of 2-quinolinesulfonyl chloride was added dropwise to a solution of 1-octene (0.096 g, 0.78 mmol) in methylene chloride (5 mL), and the reaction mixture was stirred for 20 h at room temperature. The solvent was removed by a rotary evaporator. The residue was washed with CCl\(_4\) and dried in vacuum, giving product 6 (0.097 g, 100% yield) as a light-yellow oil.

1H-NMR (400 MHz, D2O): \( \delta \) 0.79–0.82 (m, 3H, CH\(_3\)), 1.21–1.24 (m, 4H, CH\(_2\)), 1.29–1.32 (m, 2H, CH\(_2\)), 1.40–1.45 (m, 2H, CH\(_2\)), 1.82–1.89 (m, 1H, CH\(_2\)), 1.92–1.99 (m, 1H, CH\(_2\)), 4.49–4.53 (m, 1H, SCH), 5.00 (dd, \( J \) 13.0, 6.3 Hz, 1H, NCH\(_2\)), 5.25 (dd, \( J \) 13.0, 8.7 Hz, 1H, NCH\(_2\)), 7.74–7.79 (m, 2H, C\(_{\text{quino}}\)), 7.94–7.96 (m, 1H, C\(_{\text{quino}}\)), 8.00–8.03 (m, 1H, C\(_{\text{quino}}\)), 8.09–8.11 (m, 1H, C\(_{\text{quino}}\)), 8.59–8.61 (m, 1H, C\(_{\text{quino}}\)).

13C-NMR (101 MHz, D2O): \( \delta \) 12.03 (CH\(_3\)), 20.55, 24.90, 26.60, 29.49, 33.03 (CH\(_2\)), 45.47 (SCH), 59.86 (NCH\(_2\)), 116.31 (C\(_{\text{quino}}\)), 116.87 (C\(_{\text{quino}}\)), 124.98 (C\(_{\text{quino}}\)), 128.94 (C\(_{\text{quino}}\)), 133.79 (C\(_{\text{quino}}\)), 137.84 (C\(_{\text{quino}}\)), 143.59 (C\(_{\text{quino}}\)), 165.00 (C\(_{\text{quino}}\)).

Anal. Calcd for C\(_{17}\)H\(_{22}\)NClS: C 66.32, H 7.20, Cl 11.52, N 4.55, S 10.42. Found: C 66.58, H 7.39, Cl 11.88, N 4.72, S 10.90.
2-Butyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium bromide (8) and 1-butyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium bromide (10). A solution of bromide (0.048 g, 0.30 mmol) in methylene chloride (5 mL) was added dropwise to a solution of 2-mercaptoquinoline (0.097 g) of products in methylene chloride (5 mL), and the mixture was stirred for 15 min at room temperature. The obtained solution of 2-quinolinesulfenyl bromide was added dropwise to a solution of 1-hexene (0.050 g, 0.60 mmol) in methylene chloride (5 mL), and the reaction mixture was stirred for 20 h at room temperature. The solvent was removed by a rotary evaporator. The residue was washed with CCl₄ and dried in vacuum, giving a mixture (0.097 g) of products 8 (0.073 g, 75% yield) and 10 (0.024 g, 24% yield) as a yellow oil.

2-Butyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium bromide (8). ¹H–NMR (400 MHz, D₂O): δ 0.80–0.87 (m, 3H, CH₃), 1.28–1.52 (m, 4H, CH₂), 1.83–1.92 (m, 1H, CH₂), 1.94–2.01 (m, 1H, CH₂), 4.52 (dd, J 8.3, 6.4 Hz, 1H, SCH), 5.05 (dd, J 13.0, 6.4 Hz, 1H, NCH₂), 5.30 (dd, J 13.0, 8.3 Hz, 1H, NCH₂), 7.71–7.79 (m, 2H, C quino), 7.91–7.93 (m, 1H, C quino), 7.97–8.02 (m, 1H, C quino), 8.05–8.07 (m, 1H, C quino), 8.54–8.56 (m, 1H, C quino).

2-Butyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium bromide (10). ¹H–NMR (400 MHz, D₂O): δ 0.80–0.87 (m, 3H, CH₃), 1.28–1.52 (m, 4H, CH₂), 1.58–1.67 (m, 1H, CH₂), 1.94–2.01 (m, 1H, CH₂), 3.79 (d, J 12.1 Hz, 1H, SCH), 5.02 (dd, J 12.1, 8.3 Hz, 1H, S CH₂), 5.96 (t, J 9.4 Hz, 1H, NCH), 7.71–7.79 (m, 2H, C quino), 8.00–8.04 (m, 2H, C quino), 8.05–8.07 (m, 1H, C quino), 8.54–8.56 (m, 1H, C quino).

2-Hexyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium bromide (9) and 1-hexyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium bromide (11). A solution of bromide (0.063 g, 0.39 mmol) in methylene chloride (5 mL) was added dropwise to a solution of 2-mercaptoquinoline (0.063 g, 0.39 mmol) in methylene chloride (5 mL), and the mixture was stirred for 15 min at room temperature. The obtained solution of 2-quinolinesulfenyl bromide was added dropwise to a solution of 1-octene (0.096 g, 0.78 mmol) in methylene chloride (5 mL), and the reaction mixture was stirred for 20 h at room temperature. The solvent was removed by a rotary evaporator. The residue was washed with CCl₄ and dried in vacuum, giving a mixture (0.12 g) of products 9 (0.089 g, 74% yield) and 11 (0.031 g, 26% yield) as a yellow oil.

2-Hexyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium bromide (9). ¹H–NMR (400 MHz, DMSO-d₆): δ 0.80–0.84 (m, 3H, CH₃), 1.26–1.32 (m, 6H, CH₂), 1.36–1.51 (m, 2H, CH₂), 1.84–1.99 (m, 2H, CH₂), 4.59–4.63 (m, 1H, SCH), 5.30–5.34 (m, 1H, NCH₂), 5.45–5.49 (m, 1H, NCH₂), 7.85–7.89 (m, 1H, C quino), 8.12–8.15 (m, 1H, C quino), 8.20–8.25 (m, 1H, C quino), 8.28–8.30 (m, 1H, C quino), 8.32–8.37 (m, 1H, C quino), 8.96–8.98 (m, 1H, C quino).

¹C–NMR (101 MHz, DMSO-d₆): δ 13.93 (CH₃), 21.99, 26.40, 28.23, 31.02, 34.21 (CH₂), 46.57 (SCH), 61.17 (NCH₂), 118.80 (C quino), 119.03 (C quino), 126.28 (C quino), 128.16 (C quino), 130.06 (C quino), 134.78 (C quino), 137.90 (C quino), 144.62 (C quino), 164.46 (C quino).
The text contains a detailed account of the synthesis of various quinoline derivatives. It describes the preparation of compounds through reactions involving quinolinesulfenyl chloride and different cycloalkenes. The synthesis involves the use of methylene chloride and solvolysis with vinyl isobutyl ether. The compounds synthesized include 1-Hexyl-1,2-dihydro[1,3]thiazolo[3,2-α]quinolin-11-ium bromide (11), 8,9,10,10a-Tetrahydro-7aH-cyclopenta[4,5][1,3]thiazolo[3,2-α]quinolin-11-ium chloride (13), and others. The text includes NMR spectral data and analytical calcd values for the compounds. The synthesis process is described step by step, detailing the reagents used, the conditions, and the yields obtained. The compounds are characterized by their distinctive spectral and analytical data, reflecting their unique structures.
0.98 mmol) in methylene chloride (5 mL) was added dropwise, and the reaction mixture was stirred for 100 h at room temperature. The solvent was removed by a rotary evaporator. The residue was washed with CCl\textsubscript{4} and dried in vacuum, giving product 14 (0.119 g, 100% yield) as a light-yellow oil.

1H–NMR (400 MHz, acetone-d\textsubscript{6}): \(\delta \) 1.53–1.72 (m, 4H, CH\textsubscript{4}), 1.76–1.87 (m, 3H, CH\textsubscript{2}), 1.93–1.99 (m, 1H, CH\textsubscript{2}), 2.08–2.16 (m, 2H, CH\textsubscript{2}), 2.28–2.41 (m, 2H, CH\textsubscript{2}), 4.51–4.54 (m, 1H, S\textsubscript{CH}), 4.73–4.78 (m, 1H, CHCL), 7.44–7.45 (m, 1H, C\textsubscript{quino}), 7.55–7.57 (m, 1H, C\textsubscript{quino}), 7.75–7.79 (m, 1H, C\textsubscript{quino}), 7.92–7.94 (m, 1H, C\textsubscript{quino}), 8.09–8.13 (m, 1H, C\textsubscript{quino}), 8.25–8.27 (m, 1H, C\textsubscript{quino}).

13C–NMR (101 MHz, acetone-d\textsubscript{6}): \(\delta \) 24.10 (CH\textsubscript{2}), 26.00 (CH\textsubscript{2}), 26.80 (CH\textsubscript{2}), 27.87 (CH\textsubscript{2}), 32.14 (CH\textsubscript{2}), 32.73 (CH\textsubscript{2}), 53.10 (S\textsubscript{CH}), 66.44 (CHCL), 122.16 (C\textsubscript{quino}), 127.03 (C\textsubscript{quino}), 128.02 (C\textsubscript{quino}), 128.99 (C\textsubscript{quino}), 130.77 (C\textsubscript{quino}), 131.17 (C\textsubscript{quino}), 131.64 (C\textsubscript{quino}), 138.50 (C\textsubscript{quino}), 139.57 (C\textsubscript{quino}).

Anal. Calcd for C\textsubscript{17}H\textsubscript{20}NClS: C 66.76, H 6.59, Cl 11.59, N 4.58, S 10.48. Found: C 66.93, H 6.71, Cl 11.93, N 4.79, S 12.00.

7a,8,9,10,11,12,13a-Octahydrocyclocta[4,5][1,3]thiazolo[3,2-a]quinolin-14-ium bromide (15). A solution of bromide (0.074 g, 0.46 mmol) in methylene chloride (5 mL) was added dropwise to a solution of 2-mercaptoquinoline (0.056 g, 0.34 mmol) in methylene chloride (5 mL), and the mixture was stirred for 15 min at room temperature. The obtained solution of 2-quinolinesulfenyl bromide was added dropwise to a solution of cyclooctene (0.102 g, 0.92 mmol) in methylene chloride (5 mL), and the reaction mixture was stirred for 20 h at room temperature. The solvent was removed by a rotary evaporator. The residue was washed with CCl\textsubscript{4} and dried in vacuum, giving product 15 (0.120 g, 77% yield) as a light-yellow oil.

1H–NMR (400 MHz, D\textsubscript{2}O): \(\delta \) 1.24–1.39 (m, 3H, CH\textsubscript{2}), 1.59–1.71 (m, 3H, CH\textsubscript{2}), 1.81–1.91 (m, 3H, CH\textsubscript{2}), 1.99–2.08 (m, 1H, CH\textsubscript{2}), 2.11–2.25 (m, 1H, CH\textsubscript{2}), 2.35–2.44 (m, 1H, CH\textsubscript{2}), 4.61–4.67 (m, 1H, S\textsubscript{CH}), 5.87–5.92 (m, 1H, N\textsubscript{CH}), 7.66–7.72 (m, 2H, C\textsubscript{quino}), 7.70–7.83 (m, 1H, C\textsubscript{quino}), 7.96–8.01 (m, 1H, C\textsubscript{quino}), 8.03–8.06 (m, 1H, C\textsubscript{quino}), 8.50–8.52 (m, 1H, C\textsubscript{quino}).

13C–NMR (101 MHz, D\textsubscript{2}O): \(\delta \) 23.20, 23.76, 24.10, 25.66, 26.11, 27.75 (CH\textsubscript{2}), 50.93 (S\textsubscript{CH}), 71.74 (N\textsubscript{CH}), 117.64 (C\textsubscript{quino}), 117.72 (C\textsubscript{quino}), 126.78 (C\textsubscript{quino}), 127.96 (C\textsubscript{quino}), 130.37 (C\textsubscript{quino}), 134.98 (C\textsubscript{quino}), 136.63 (C\textsubscript{quino}), 144.54 (C\textsubscript{quino}), 162.63 (C\textsubscript{quino}).

Anal. Calcd for C\textsubscript{17}H\textsubscript{20}NB\textsubscript{r}S: C 58.28, H 5.75, Br 22.81, N 4.00, S 9.15. Found: C 58.61, H 6.02, Br 23.14, N 4.31, S 9.71.

3.4. Synthesis of Compounds 16 and 17 by the Reactions of Quinolinesulfenyl Chloride 2 with Styrene and Isoeugenol

1-Phenyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium chloride (16). A solution of sulfuryl chloride (0.047 g, 0.34 mmol) in methylene chloride (5 mL) was added dropwise to a solution of 2-mercaptoquinoline (0.056 g, 0.34 mmol) in methylene chloride (5 mL), and the mixture was stirred for 15 min at room temperature. The obtained solution of 2-quinolinesulfenyl chloride was added dropwise to a solution of styrene (0.072 g, 0.68 mmol) in methylene chloride (5 mL), and the reaction mixture was stirred for 20 h at room temperature. The solvent was removed by a rotary evaporator. The residue was washed with CCl\textsubscript{4} and dried in vacuum, giving product 16 (0.104 g, 100% yield) as a yellow oil.

1H–NMR (400 MHz, D\textsubscript{2}O): \(\delta \) 3.50–3.54 (m, 1H, S\textsubscript{CH}), 4.31–4.36 (m, 1H, S\textsubscript{CH}), 4.34–4.38 (m, 1H, S\textsubscript{CH}), 4.60–4.64 (m, 1H, S\textsubscript{CH}), 5.87–5.92 (m, 1H, N\textsubscript{CH}), 7.04–7.12 (m, 3H, Ar), 7.40–7.44 (m, 1H, C\textsubscript{quino}), 7.49–7.56 (m, 2H, C\textsubscript{quino}), 7.78–7.82 (m, 1H, C\textsubscript{quino}), 7.85–7.90 (m, 1H, C\textsubscript{quino}), 8.52–8.56 (m, 1H, C\textsubscript{quino}).

13C–NMR (101 MHz, D\textsubscript{2}O): \(\delta \) 37.87 (S\textsubscript{CH}), 71.06 (N\textsubscript{CH}), 118.10 (C\textsubscript{quino}), 118.30 (C\textsubscript{quino}), 125.39 (Ar), 126.73 (C\textsubscript{quino}), 128.42 (C\textsubscript{quino}), 129.51 (Ar), 129.65 (Ar), 130.47 (C\textsubscript{quino}), 135.07 (C\textsubscript{quino}), 135.21 (C\textsubscript{quino}), 137.12 (Ar), 145.88 (C\textsubscript{quino}), 166.15 (C\textsubscript{quino}).

Anal. Calcd for C\textsubscript{18}H\textsubscript{14}NClS: C 68.10, H 4.71, Cl 11.82, N 4.67, S 10.70. Found: C 68.34, H 4.97, Cl 12.12, N 4.81, S 11.20.

trans-1-(Hydroxy-3-methoxyphenyl)-2-methyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium chloride (17). A solution of sulfuryl chloride (0.078 g, 0.57 mmol) in methylene chloride (5 mL)
was added dropwise to a solution of 2-mercaptoquinoline (0.093 g, 0.57 mmol) in methylene chloride (5 mL), and the mixture was stirred for 15 min at room temperature. The obtained solution of 2-quinolinesulfenyl chloride was added dropwise to a solution of isoeugenol (0.189 g, 1.15 mmol) in methylene chloride (5 mL), and the reaction mixture was stirred for 20 h at room temperature. After filtration, the solvent was removed by a rotary evaporator, and the residue was washed with CCl₄ and dried in vacuum, giving product 17 (0.166 g, 80% yield) as an orange oil.

1H-NMR (400 MHz, D₂O): δ 1.70 (d, J 7.0 Hz, 3H, CH₃), 3.76 (s, 3H, OCH₃), 4.07–4.12 (m, 1H, SCH), 6.21 (d, J 8.2 Hz, 1H, NCH), 6.56–6.60 (m, 1H, Ar), 6.66 (s, 1H, Ar), 6.91 (s, 1H, Ar), 7.62–7.66 (m, 1H, C₄₈), 7.74–7.79 (m, 2H, C₄₈), 7.93–7.96 (m, 1H, C₄₈), 8.08–8.11 (m, 1H, C₄₈), 8.72–8.75 (m, 1H, C₄₈).

13C-NMR (101 MHz, D₂O): δ 22.38 (CH₃), 50.80 (SCH), 55.77 (OCH₃), 77.37 (NCH), 109.61 (Ar), 115.50 (Ar), 117.48 (Ar), 118.08 (C₄₈), 118.51 (C₄₈), 126.83 (C₄₈), 126.94 (Ar), 128.42 (C₄₈), 130.42 (C₄₈), 134.97 (C₄₈), 137.59 (C₄₈), 145.78 (Ar), 145.86 (C₄₈), 148.07 (Ar), 164.96 (C₄₈).

Anal. Calcd for CₙH₂₈NClO₂S: C 63.41, H 5.04, Cl 9.85, N 3.89, S 8.91. Found: C 63.63, H 5.21, Cl 10.17, N 4.00, S 9.27.

4. Conclusions

Novel reagents 2-quinolinesulfenyl chloride and bromide have been involved in the preparation of condensed heterocyclic sulfur–nitrogen compounds. The simple and efficient method for generation of 2-quinolinesulfenyl chloride and bromide is based on the action of sulfuryl chloride or bromine on available 2-mercaptoquinoline. Regioselective synthesis of novel 2-alkyl-1,2-dihydro[1,3]thiazolo[3,2-a]quinolin-10-ium derivatives in 95–100% yields has been developed by annulation reactions of 2-quinolinesulfenyl chloride and bromide with 1-alkenes. Condensed tetracyclic products have been obtained by the reactions of 2-quinolinesulfenyl chloride and bromide and cycloalkenes.

The reactions of cyclopentene with both 2-quinolinesulfenyl chloride and bromide at room temperature afforded condensed tetracyclic products in high yields. The reaction of 2-quinolinesulfenyl chloride with cyclooctene led to an electrophilic addition product in quantitative yield. When 2-quinolinesulfenyl bromide was involved in the reaction with cyclooctene under similar conditions, the tetracyclic condensed compound was obtained in quantitative yield.

The reactions of 2-quinolinesulfenyl chloride with styrene and natural compound isoeugenol proceeded in a regioselective manner but with opposite regiochemistry compared to the reactions of 2-quinolinesulfenyl chloride with terminal alkenes. The electrophilic addition of the sulfur atom of 2-quinolinesulfenyl chloride occurred to the β-carbon atom of the double bond of styrene and isoeugenol in a Markovnikov fashion.

The reaction of 2-quinolinesulfenyl chloride with terminal alkenes was supposed to proceed via intermediate thiranium cation, and nucleophilic attack of the nitrogen atom of the quinoline ring occurred at the least substituted carbon atom of thiranium ion, leading to the formation of condensed products in an anti-Markovnikov fashion.

The obtained condensed sulfur–nitrogen heterocycles are novel water-soluble functionalized compounds with potential biological activity.

**Supplementary Materials:** The following are available online. Supporting Information file: examples of 1H- and 13C-NMR spectra of the obtained compounds.

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