SYNTHESIS AND ALKYLATION OF SODIUM 4-THIOXO-1,4-DIHYDROQUINOLINE-3-SULFINATE #

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Abstract - Reaction of 4-chloro-3-quinolinesulfonyl chloride (1) with sodium hydrogen sulfide led to sodium 4-thioxo-1,4-dihydro-3-quinolinesulfinate (2). Compound 2 in reactions with alkyl halides was monoalkylated to sodium 4-alkylsulfanyl-3-quinolinesulfinate (3) or double alkylated directly to 4-alkylsulfanyl-3-alkanesulfonylquinolines (4).

INTRODUCTION

3-Sulfonylquinolines including 3-sulfonyl-4(1H)-quinolinones are of considerable interest since they exhibit potent biological activities.1-3 Some of them exert arterial-venous vasodilatory activity, other act as PDE-5 inhibitors or GABA enhancers or show antihypertensive properties.

Several years ago we developed a convenient synthesis of 4-chloro-3-quinolinesulfonyl chloride (1) from quinoline.4 Both chloride-functions of compound 1 as well as reaction at endocyclic nitrogen were engaged in preparation of numerous quinoline derivatives A and B, mainly 3-quinolinesulfonamides. (Scheme 1)5

Scheme 1
In search for preparation of further 4-thioxoderivatives of 3-quinolinesulfonic acid, compound 1 was treated with sodium hydrogen sulfide hydrate. The reaction proceeded simultaneously with both chloride functions and gave sodium salt of 4-thiao-1,4-dihydro-3-quinolinesulfonic acid (2). Salt 2 was used for a new synthesis of 3-alkanesulfonylquinolines 3, 4 and 6, described in this paper.

RESULTS AND DISCUSSION

There are many methods of synthesis of sulfones from compounds containing other thio functional groups.6 However, synthesis of 3-sulfonylquinolines was performed only by the oxidation of 3-methylsulfanylquinoline to 3-methanesulfonylquinoline7 or 3-methylsulfanyl (or methylsulfinyl)-4-quinolinone to 3-methanesulfonyl-4-quinolinones,3 as well as by methylation of sodium 4-(4-phenoxy-3-quinolinylsulfonyl)-3-quinolinesulfinate to 3'-methylsulfonyl-4-phenoxy-3,4'-diquinolinyl sulfide, as recently reported from our laboratory.8

3-Alkanesulfonylquinolines- or 3-arenesulfonylquinolines were most often prepared by cyclization reactions based on the formation of pyridine ring.3,9,10,11

Our approach presented below opens the other route to 4-substituted 3-alkanesulfonylquinolines. Treatment of 4-chloro-3-quinolinesulfonyl chloride (1) with aqueous sodium hydrogen sulfide caused vigorous exothermic reaction with intensive evolution of hydrogen sulfide and led to a complete consumption of substrate 1. Diluting an aqueous solution of products with ethanol precipitated a deep-orange solid with elemental composition C9H6NO2S2Na x 4 H2O assigned to sodium 4-thioxo-1,4-dihydro-3-quinolinesulfinate (2), as presented below.

Scheme 2
Entry data in the structure assignment of 2 tetrahydrate come from $^1$H NMR and UV-Vis spectra. $^1$H NMR spectrum of 2 revealed presence of five aromatic protons with $\delta_H$ values and multiplet shapes both typical for 4(1H)-quinolinethiones. The most diagnostic data come from the spectral position of the H5 proton shifted downfield by 4-thixo function up to $\delta_H = 8.70$ ppm. Very close peri-effect regarding the H-5 proton $\delta_H$ value was observed for other 4(1H)-quinolinethiones 7, 8 and 9 (Scheme 3). Also UV-Vis spectra of the newly prepared compounds 2 and 6 showed very similar absorption bands to those of 4(1H)-quinolinethione (7) both in neutral solution ($\lambda_{max}=384-388$ nm) and in alkaline solution ($\lambda_{max}=344-359$ nm).

Scheme 3. Proton chemical shift values [ppm] (in DMSO-d6) for the H-5 proton of 4(1H)-quinolinethiones 2, 6, 7 and 8, and UV-Vis absorption bands for thiones 2 and 6.

$\lambda_{max}=384$ nm (H$_2$O, neutral)
$\lambda_{max}=344$ nm (H$_2$O, alkaline)
$\lambda_{max}$ taken from ref. 15
$\delta_H$ value taken from ref. 12

Both thiofunctional groups of 2 could be stabilized by alkylation. (see Scheme 2) In aqueous alkali solution thiono function of 2 was converted to thiolate one of 2A. Thus, alkylation takes place at the more reactive thiolate function to form sodium 4-alkylsulfanyl-3-quinolinesulfinites (3). The latter could be transformed to 4-alkylsulfanyl-3-alkanesulfonylquinolines (4) after treatment with alkyl halides at rt in DMF. Furthermore, the reaction of thionosulfinate 2 performed under the same reaction conditions (rt, DMF) in the presence of K$_2$CO$_3$ with an excess of alkylating agents led directly to dialkyl derivates 4 with the same alkyl groups.

Due to the ambident nature of the sulfinate anion, reaction of sodium quinoline-3-sulfinate 3a with dimethyl or diethyl sulfates led to alkyl 4-alkylsulfanylquinoline-3-sulfinites (5a or 5b), respectively. This is in agreement with the conclusion of Meek and Fowler regarding the O- and S-regioorientation in the alkylation of benzenesulfinites with methyl iodide and dimethyl sulfate in DMF. IR spectra (strong bands at 1130 cm$^{-1}$ and 1307 cm$^{-1}$ for sulfones 4 and strong bands at 880 cm$^{-1}$ and 1129 cm$^{-1}$ for alkyl sulfinites 5 are in agreement with the regularity observed for the respective benzene derivatives. Both alkyl sulfinites 5a and 5b underwent thermal rearrangement (above 150 °C) to isomeric sulfones 4a and 4b.
CONCLUSIONS

Both chloride-functions of compound 1 were consumed in reactions with sodium hydrogen sulfide. They ran on one hand as nucleophilic substitution of the 4-chlorine substituent with hydrogen sulfide anion to form after tautomerization the 4-thioxo function of 2, and on the other hand as reduction of the chlorosulfonyl moiety to the sulfinate anion. Both types of sulfide anion-induced reactions are separately well documented\textsuperscript{19,20} but their simultaneous application in the treatment of 1 opens a unique route to the title compound 2. Taking into account the one-pot synthesis of 4 by double alkylation of 2, the present study extends previous findings concerning the preparation and transformation of 1\textsuperscript{4} to a four-step, convenient preparation of 4-alkylsulfanyl-3-alkanesulfonylquinolines (4) from quinoline.

Table. Synthesis of 4-alkylsulfanyl-3-alkanesulfonylquinolines (4) by alkylation of sodium 4-alkylsulfanyl-3-quinolinesulfinate (3a) or sodium 4-thioxo-1,4-dihydro-3-quinolinesulfinate (2).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (2)</th>
<th>Alkylation agent</th>
<th>Solvent</th>
<th>Product, yield (%)</th>
</tr>
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<tr>
<td>1</td>
<td>2 MeI</td>
<td>10% NaOH</td>
<td>3a, R\textsuperscript{1} = Me, 89</td>
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<tr>
<td>2</td>
<td>2 EtI</td>
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<td>3b, R\textsuperscript{1} = Et, 81</td>
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<tr>
<td>3</td>
<td>2 i-PrI</td>
<td>10% NaOH</td>
<td>3c, R\textsuperscript{1} = i-Pr, 87</td>
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<tr>
<td>4</td>
<td>2 AllylBr</td>
<td>10% NaOH</td>
<td>3d, R\textsuperscript{1} = Allyl, 87</td>
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<tr>
<td>5</td>
<td>2 BnCl</td>
<td>10% NaOH</td>
<td>3e, R\textsuperscript{1} = Bn, 86</td>
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<td>3a MeI</td>
<td>DMF</td>
<td>4a, R = R\textsuperscript{1} = Me, 88</td>
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<tr>
<td>7</td>
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<tr>
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<tr>
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<td>DMF</td>
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<tr>
<td>11</td>
<td>2 MeI\textsuperscript{[a]}</td>
<td>DMF / K\textsubscript{2}CO\textsubscript{3}</td>
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<td>12</td>
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<td>DMF / K\textsubscript{2}CO\textsubscript{3}</td>
<td>4f, R = R\textsuperscript{1} = Et, 91</td>
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<td>13</td>
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<td>DMF / K\textsubscript{2}CO\textsubscript{3}</td>
<td>4g, R = R\textsuperscript{1} = i-Pr, 57</td>
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<td>2 AllylBr\textsuperscript{[a]}</td>
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<tr>
<td>16</td>
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<td>DMF</td>
<td>5a, R = Me, 60</td>
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<tr>
<td>17</td>
<td>3a\textsuperscript{[b]} (EtO)\textsubscript{2}SO\textsubscript{2}</td>
<td>DMF</td>
<td>5b, R = Et, 63</td>
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\textsuperscript{[a]} 2.1 molar eqvs. of alkylation agent were used.
\textsuperscript{[b]} anhydrous salt 3a was used.
EXPERIMENTAL

Melting points were taken in open capillary tubes and are uncorrected. All NMR spectra were recorded on a Bruker AVANS 400 spectrometer operating at 400.22 MHz and 100.64 MHz for $^1$H and $^{13}$C nuclei, respectively, in deuterochloroform (CDCl$_3$) or in hexadeuterodimethylsulfoxide (DMSO-d$_6$) solutions with tetramethysilane ($\delta$ 0.0 ppm) as internal standard. Two-dimensional $^1$H-$^{13}$C HSQC and HMBC experiments were performed using standard Bruker software HSQCGP and HMBCGP, respectively, and the following parameters: the spectral widths in $F_2$ and $F_1$ were ca. 5 kHz for $^1$H and 16.7 kHz for $^{13}$C, the relaxation delay was 1.5 s, the refocusing in the HSQC experiment was 1.7 ms and the delay for long-range evolutions was 50 ms in $^1$H / $^{13}$C HMBC. 2D spectra were acquired as 2048 x 1024 hypercomplex files, with 1-4 transients. EI MS spectra were determined on a Finnigan MAT 95 spectrometer at 70 eV. IR spectra were recorded with a Magma – IR 500 (Nicolet) spectrometer in potassium bromide pellets. The UV-VIS measurements were made using a JASCO UV-VIS spectrophotometer (model V-530) for solutions of salt 2 tetrahydrate in water (0.07 mM / L) or in 0.4% aqueous NaOH (0.1 mM / L) as well as for solutions of thione 6 in a mixture of ethanol-water (4/1, v/v) (0.13 mM/L) or in 0.4% aqueous NaOH (0.1 mM / L). TLC analyses were performed employing Merck’s aluminium oxide 60 F$_{254}$ neutral (type E) plates using chloroform as an eluent.

**Sodium 4-thioxo-1,4-dihydro-3-quinolinesulfinate (2)**

Solution of commercial sodium hydrogen sulfide hydrate containing ca. 1.8 molar eqvs. of water per 1 molar eqv. of NaSH (Aldrich) (4.6 g, 52 mmol) in 6 mL of water was added in one portion to finely powdered sulfochloride 1 (2.3 g, ca. 8.8 mmol) on stirring. This caused an exothermic reaction and a strong evolution of hydrogen sulfide. Stirring was continued at rt until the evolution of hydrogen sulfide ceased (15-25 min). Next the mixture was diluted with EtOH (4 mL) and left for several hours at –18 ºC. The salt 2 in the form of tetrahydrate (2.64 g, 89 %) was filtered off and dried on air. Crude product was used successfully in the reactions with alkylation agents. For analytical purposes salt 2 x 4 H$_2$O was recrystallized from aqueous EtOH.

**Sodium 4-thioxo-1,4-dihydro-3-quinolinesulfinate (2):**

deep orange solid, mp 304-305 ºC (decomp). $^1$H NMR (D$_2$O): $\delta$ = 7.45-7.49 (m, 1H, H6), 7.72-7.75 (m, 2H, H7 and H8), 8.59 (s, 1H, H2), 8.82-8.86 (m, 1H, H5). $^1$H NMR (DMSO-d$_6$), $\delta$H: $\delta$C for carbons from single bond and long-range proton-carbon correlations: 3.10-3.80 (broad, 9H, 4 x H$_2$O + NH), 7.39 [(ddd, 1H, $^3$J=8.2 Hz, $^3$J=7.0 Hz, $^4$J=1.2 Hz, H-6); 124.9(C-6) / 120.8(C-8), 133.1 (C-4a)], 7.60 [(ddd, 1H, $^3$J=8.3 Hz, $^3$J=7.0 Hz, $^4$J=1.4 Hz, H-7); 131.1(C-7) / 128.0(C-5), 136.8(C-8a)], 7.74 [(dd, 1H, $^3$J=8.3 Hz, $^4$J=1.2 Hz, H-8); 120.8(C-8)/124.9(C-6), 133.1(C-4a)], 8.21 [(s, 1H, H-2); 133.5(C-2)/136.8(C-8a), 149.2(C-3), 186.8(C-4), 8.70 [(ddd, 1H, $^3$J=8.3 Hz, $^3$J=7.0 Hz, $^4$J=1.2 Hz, H-5); 128.0(C-5)/131.1(C-7)]
136.8(C-8a), 186.8(C-4)]. UV/Vis (H2O): \( \lambda_{\text{max}} \) (H2O), (\( \varepsilon \)) = 387 nm (0.9408), \( \lambda_{\text{max}} \) (0.4 % aqueous NaOH) (\( \varepsilon \)) = 350 nm (0.9359). *Anal.* Calcd for C9H6NO2S2Na x 4 H2O: C, 33.85; H, 4.42; N, 4.39. Found: C, 33.99; H, 4.11; N, 4.44.

**Sodium 4-alkythio-3-quinolinesulfinates (3)**

Alkylation agent [alkyl (Me, Et, iPr) iodide, allyl bromide or benzyl chloride (ca. 2.2 mmol)] was dropped on stirring at rt into a solution of salt 2 tetrahydrate (500 mg, 1.48 mmol) in 5 mL of 10 % aqueous NaOH. Vigorous stirring was continued for 1 h. The solid was filtered off, washed with THF (0.5 mL) and air-dried to give salts 3 (81-97%). Ethyl derivative 3b was isolated by outsalting the solution with sodium chloride, as an oil, which solidified on standing. Crude salts 3 were successfully used in the reactions with alkylation agents. For analytical purposes salts 3 were recrystallized from aqueous EtOH.

**Sodium 4-methylsulfanyl-3-quinolinesulfinate (3a):**

mp 282-283 °C (decomp). \(^{1}H\) NMR (D2O): \( \delta = 2.50 \) (s, 3H, SCH3), 7.68-7.73 (m, 1H, H6), 7.79-7.84 (m, 1H, H7), 7.96-7.99 (m, 1H, H8), 8.47-8.49 (m, 1H, H5), 9.00 (s, 1H, H2). *Anal.* Calcd for C10H8NNaO2S2 x 3 H2O: C 38.09, H 4.47, N 4.44. Found: C 37.87, H 4.72, N 4.32.

**Sodium 4-ethylsulfanyl-3-quinolinesulfinate (3b):**

mp 292-293 °C (decomp). \(^{1}H\) NMR (D2O): \( \delta = 1.05 \) (t, J=7.2 Hz, 3H, CH3), 2.92 (q, J=7.2 Hz, 2H, CH2), 7.59-7.64 (m, 1H, H6), 7.71-7.77 (m, 1H, H7), 7.91-7.93 (m, 1H, H8), 8.43-8.45 (m, 1H, H5), 8.98 (s, 1H, H2). *Anal.* Calcd for C11H10NNaO2S2 x 3 H2O: C 40.11, H 4.90, N 4.25. Found: C 39.80, H 4.50, N 4.02.

**Sodium 4-isopropylsulfanyl-3-quinolinesulfinate (3c):**

mp >320 °C (decomp). \(^{1}H\) NMR (D2O): \( \delta = 1.18 \) (d, J=6.6 Hz, 6H, (CH3)2), 3.40-3.53 (m, 1H, CH), 7.56-7.61 (m, 1H, H6), 7.71-7.76 (m, 1H, H7), 7.91-7.94 (m, 1H, H8), 8.39-8.41 (m, 1H, H5), 9.06 (s, 1H, H2). *Anal.* Calcd for C12H12NNaO2S2 x 3 H2O: C 41.97, H 5.28, N 4.08. Found: C 41.81, H, 5.60, N 4.31.

**Sodium 4-allylthio-3-quinolinesulfinate (3d):**

mp 205-207 °C (decomp). \(^{1}H\) NMR (D2O): \( \delta = 3.49 \) (d, J= 7.5 Hz, 2H, –CH=), 4.47-4.68 (m, 1H, –CH), 5.60-5.76 (m, 2H, =CH2), 7.55-7.60 (m, 1H, H6), 7.67-7.73 (m, 1H, H7), 7.87-7.90 (m, 1H, H8), 8.35-8.38 (m, 1H, H5), 8.96 (s, 1H, H2). *Anal.* Calcd for C12H12NNaO2S2 x 2 H2O: C 44.57, H 4.36, N 4.33. Found: C 44.54, H 3.86, N 4.51.

**Sodium 4-benzylsulfanyl-3-quinolinesulfinate (3e):**

mp 314-315 °C (decomp). \(^{1}H\) NMR (D2O): \( \delta = 4.00 \) (s, 2H, CH2), 6.77-6.79 (m, 2H, H6), 7.45-6.99 (m, 3H, H6), 7.42-7.46 (m, 1H, H6), 7.63-7.67 (m, 1H, H7), 7.857.87 (m, 1H, H8), 8.19-8.21 (m, 1H, H5), 8.90 (s, 1H, H2). *Anal.* Calcd for C16H12NNaO2S2 x H2O: C 54.07, H 3.97, N 3.94. Found: C 54.37, H 3.59, N 4.10.

Alkylation of sodium 4-methylsulfanyl-3-quinolinesulfinate (3a) to 4-methylsulfanyl-3-alkanesulfonyl-
quinolines (4).

A solution of salt 3a trihydrate (410 mg, 1.30 mM) and alkylating agent (1.25-1.30 mM) in DMF (2 mL) was stirred at rt for 24 h (or 72 h for the reaction with isopropyl iodide). The mixture was diluted with 20 mL of water and the solid deposited was filtered off. Crude sulfone 4 was recrystallized from EtOH or from aqueous EtOH.

4-Methylsulfanyl-3-methanesulfonylquinoline (4a):

Yellow solid, mp 125-126°C. MS (EI, 70 eV): m/z (%) = 253 (100) [M+]. 1H NMR (CDCl3) δ: 2.60 (s, 3H, SCH3), 3.53 (s, 3H, CH3), 7.75-7.81 (m, 1H, H6), 7.89-7.95 (m, 1H, H8), 8.70-8.73 (m, 1H, H5), 9.52 (s, 1H, H2). IR (KBr pellet): ν (O=S=O) = 1130 cm⁻¹ and 1307 cm⁻¹. Anal. Calcd for C11H11NO2S2: C 52.15, H 4.38, N 5.53, S 25.31. Found: C 52.08, H 4.63, N 5.69, S 25.11.

4-Methylsulfanyl-3-ethanesulfonylquinoline (4b):

mp 72-73°C. MS (EI, 70 eV): m/z (%) = 267 [M+]. 1H NMR (CDCl3) δ: 1.34 (t, J=7.5 Hz, 3H, CH3), 2.59 (s, 3H, SCH3), 3.72 (q, J=7.5 Hz, 2H, CH2), 7.77-7.81 (m, 1H, H6), 7.91-7.95 (m, 1H, H7), 8.23-8.25 (m, 1H, H8), 8.71-8.73 (m, 1H, H2). IR (KBr pellet): ν (O=S=O) = 1130 cm⁻¹ and 1305 cm⁻¹. Anal. Calcd for C12H13NO2S2: C 53.91, H 4.90, N 5.24, S 23.98. Found: C 53.62, H 5.01, N 5.08, S 23.78.

4-Methylsulfanyl-3-(1-methylethanesulfonyl)quinoline (4c):

mp 106-107°C. MS (EI, 70 eV): m/z (%) = 281 (76) [M+]. 1H NMR (CDCl3) δ: 1.38 (d, J=6.8 Hz, 6H, (CH3)2), 2.59 (s, 3H, SCH3), 4.19-4.28 (m, 1H, CH), 7.78-7.81 (m, 1H, H6), 7.90-7.94 (m, 1H, H7), 8.23-8.25 (m, 1H, H8), 8.70-8.72 (m, 1H, H5), 9.45 (s, 1H, H2). IR (KBr pellet): ν (O=S=O) = 1128 cm⁻¹ and 1307 cm⁻¹. Anal. Calcd for C13H15NO2S2: C 55.49, H 5.37, N 4.98, S 22.79. Found: C 55.34, H 5.46, N 5.09, S 22.49.

4-Methylsulfanyl-3-(propene-3-sulfonyl)quinoline (4d):

mp 70-71°C. MS (EI, 70 eV): m/z (%) = 279 [M+]. 1H NMR (CDCl3) δ: 2.56 (s, 3H, SCH3), 4.38 (d, J=7.2 Hz, 2H, –CH2=, 5.68-5.82 (m, 1H, –CH=), 5.14-5.24 (m, 2H, =CH2), 7.69-7.74 (m, 1H, H6), 7.83-7.88 (m, 1H, H7), 8.14-8.17 (m, 1H, H8), 8.61-8.74 (m, 1H, H5), 9.32 (s, 1H, H2). IR (KBr pellet): ν (O=S=O) = 1130 cm⁻¹ and 1305 cm⁻¹. Anal. Calcd for C13H13NO2S2: C 55.89, H 4.69, N 5.01, S 22.95. Found: C 55.71, H 4.32, N 5.11, S 22.63.

4-Methylsulfanyl-3-phenylmethanesulfonylquinoline (4e):

mp 117-118°C. MS (EI, 70 eV): m/z (%) = 329 [M+]. 1H NMR (CDCl3) δ: 2.66 (s, 3H, SCH3), 4.94 (s, 2H, CH2), 7.22-7.26 (m, 5H, H arom), 7.75-7.80 (m, 1H, H6), 7.87-7.92 (m, 1H, H7), 8.14-8.17 (m, 1H, H8), 8.70-8.73 (m, 1H, H5), 9.07 (s, 1H, H2). IR (KBr pellet): ν (O=S=O) = 1129 cm⁻¹ and 1304 cm⁻¹. Anal. Calcd for C17H15NO2S2: C 61.98, H 4.59, N 4.25, S 19.46. Found: C 62.10, H 4.32, N 4.35, S 19.23.
Alkylation of sodium 4-thioxo-1,4-dihydro-3-quinolinesulfinate (2) to 4-alkylsulfanyl-3-alkanesulfonylquinolines (4) with the same alkyl groups.

A mixture of salt 2 tetrahydrate (200 mg, 0.59 mM), alkylation agent (1.3 mM), anhydrous potassium carbonate (200 mg, 1.5 mM) and DMF (1mL) was stirred at rt for 24 h (in the case of isopropyl iodide for 72 h). It was then poured to 15 water (15 mL) and the product 4 was filtered off and recrystallized from EtOH to give pure 4 (60-80 %).

4-Ethylsulfanyl-3-ethanesulfonylquinoline (4f):
mp 57-58 °C. MS (EI, 70 eV): m/z (%) = 281 (100) [M⁺]. ¹H NMR (CDCl₃) δ: 1.24 (t, J=7.5 Hz, 3H, SCH₂C₃H₃), 1.29 (t, J=7.5 Hz, 3H, SO₂CH₂C₃H₃), 3.12 (q, J=7.5 Hz, 2H, SCH₂), 3.72 (q, J=7.5 Hz, 2H, SO₂C₂H₄C₂H₃), 7.75-7.79 (m, 1H, H₆), 7.90-7.94 (m, 1H, H₇), 8.21-8.24 (m, 1H, H₈), 8.71-8.74 (m, 1H, H₅), 9.49 (s, 1H, 2). IR (KBr pellet): ν (O=S=O) = 1129 cm⁻¹ and 1307 cm⁻¹.

Anal. Calcd for C₁₃H₁₅NO₂S₂: C 55.49, H 5.37, N 4.98, S 22.79. Found: C 55.48, H 5.20, N 5.08, S 22.44.

4-Isopropylsulfanyl-3-(1-methylethanesulfonyl)quinoline (4g):
mp 101-102 °C. MS (EI, 70 eV): m/z (%) = 309 (37) [M⁺]. ¹H NMR (CDCl₃) δ: 1.27 (d, J=6.9Hz, 6H, SCH(C₃H₃)₂), 1.35 (d, J=6.6Hz, 6H, SO₂CH(C₃H₃)₂), 3.81-4.23 (m, 2H, 2 x C₆H₅(CH₃)₂) 7.73-7.78 (m, 1H, H₆), 7.90-7.94 (m, 1H, H₇), 8.21-8.24 (m, 1H, H₈), 8.72-8.75 (m, 1H, H₅), 9.47 (s, 1H, H₂). IR (KBr pellet): ν (O=S=O) = 1128 cm⁻¹ and 1304 cm⁻¹.


4-Allylsulfanyl-3-(propene-3-sulfonyl)quinoline (4h):
an oil. MS (EI, 70 eV): m/z (%) = 305 [M⁺]. ¹H NMR (CDCl₃) δ: 3.76 (d, J=7.5Hz, 2H, -C₆H₂-), 4.38 (d, J=7.2 Hz, 2H, SO₂C₂H₂), 4.92-4.97 (m, 2H, CH=CH₂), 5.21-5.31 (m, 1H –SO₂CH₂C₆H₅= CH₂), 5.72-5.93 (m, 2H, 2 x –C=), 7.75-7.80 (m, 1H, H₆), 7.90-7.95 (m, 1H, H₇), 8.21-8.23 (m, 1H, H₈), 8.70-8.72 (m, 1H, H₅), 9.41 (s, 1H, H₂). IR (KBr pellet): ν (O=S=O) = 1129 cm⁻¹ and 1310 cm⁻¹. Anal. Calcd for C₁₅H₁₅NO₂S₂: C, 58.99, H 4.95, N 4.59, S 20.99. Found: C 58.74, H 4.59, N 4.50, S 20.63.

4-Benzylsulfanyl-3-phenylmethanesulfonylquinoline (4i):
mp 120-121 °C. MS (EI, 70 eV): m/z (%) = 405 (37) [M⁺]. ¹H NMR (CDCl₃) δ: 4.08 (s, 2H, SCH₂C₆H₅), 4.36 (s, 2H, SO₂CH₂C₆H₅), 7.12-7.25 (m, 10H, H₉, H₆), 7.62-7.67 (m, 1H, H₆), 7.83-7.88 (m, 1H, H₇), 8.12-8.14 (m, 1H, H₈), 8.56-8.59 (m, 1H, H₅), 9.12 (s, 1H, H₂). IR (KBr pellet): ν (O=S=O) = 1129 cm⁻¹ and 1310 cm⁻¹. Anal. Calcd for C₂₃H₁₉NO₂S₂: C 68.12, H 4.72, N 3.45, S 15.81. Found: C 68.33, H 4.91, N 3.39, S 15.62.

Preparation of 4-thioxo-1,4-dihydro-3-methanesulfonylquinoline (6) from 4-methylsulfanyl-3- methanesulfonylquinoline (4a):
A solution of methylsulfanyl derivative 4a (100 mg, ca. 0.4 mM) in EtOH (3 mL), hydrate of sodium
hydrogen sulfide (180 mg, ca. 2 mM) and water (2 mL) was boiled for 2 h. It was then cooled down to rt, acidified with diluted hydrochloric acid (up to pH 5) and evaporated to dryness under vacuum from water bath. The residue was triturated with 5 water (5 mL) and the product 6 was filtered off and finally recrystallized from 50% EtOH.

1,4-Dihydro-4-thioxo-3-methanesulfonylquinoline (6):
deep orange solid, mp 247-248 °C (decomp). MS (EI, 70 eV): m/z (%) = 239 (100) [M +]. 1H NMR (DMSO-d6) δ: 3.50 (s, 3H, C\textsubscript{H}3), 7.58-7.61 (m, 1H, H6), 7.79-7.81 (m, 1H, H8), 7.85-7.88 (m, 1H, H7), 8.61 (s, 1H, H2), 8.78-8.80 (m, 1H, H5), 13.63 (s, 1H, NH). UV/Vis (EtOH/H\textsubscript{2}O): λ\textsubscript{max} (ε) = 388 nm (1.19629), UV/Vis (0.5% NaOH): λ\textsubscript{max} (ε) = 359 nm (0.25436). Anal. Calcd for C\textsubscript{10}H\textsubscript{9}NO\textsubscript{2}S\textsubscript{2}: C 50.19, H 3.79, N 5.85, S 26.79. Found: C 49.90, H 4.01, N 5.70, S 26.50.

Alkylation of sodium 4-methylsulfanyl-3-quinolinesulfinate (3a) with dimethyl or diethyl sulfates

3a Trihydrate was dried at 110 °C under vacuum to constant weight. Anhydrous 3a (100 mg, ca. 0.38 mM) and dimethyl or diethyl sulfate (0.05 mM) and of DMF (1 mL) were stirred at rt for 24 h. The mixture was diluted with water (20 mL) and the solid deposit was filtered off. Products 5 were recrystallized from EtOH. Sulfinates 5a, 5b (upper Rf value) underwent complete thermal rearrangement (over 150 °C) to the respective isomeric sulfones 4a or 4b (lower Rf value).

Methyl 4-methylsulfanyl-3-quinolinesulfinate (5a):

mp - underwent rearrangement to sulfone 4a over 67 °C. 1H NMR (CDCl\textsubscript{3}) δ: 2.51 (s, 3H, S\textsubscript{CH}3), 3.73 (s, 3H, OCH\textsubscript{3}), 7.73-7.77 (m, 1H, H6), 7.86-7.90 (m, 1H, H7), 8.22-8.24 (m, 1H, H8), 8.54-8.56 (m, 1H, H5), 9.34 (s, 1H, H2). IR (KBr pellet): ν (O=S=O) = 877 cm\textsuperscript{-1} and 1130 cm\textsuperscript{-1}. Anal. Calcd for C\textsubscript{11}H\textsubscript{11}NO\textsubscript{2}S\textsubscript{2}: C 52.15, H 4.38, N 5.53, S 25.31. Found: C 51.78, H 4.23, N 5.31, S 25.01.

Ethyl 4-methylsulfanyl-3-quinolinesulfinate (5b):

mp 72-73 °C. 1H NMR (CDCl\textsubscript{3}) δ: 1.37-1.43 (m, 3H, CH\textsubscript{2}CH\textsubscript{3}), 2.51 (s, 3H, S\textsubscript{CH}3), 3.98-4.05 (m, 1H, OCH\textsubscript{2}CH\textsubscript{3}), 4.28-4.36 (m, 1H, OCH\textsubscript{2}CH\textsubscript{3}), 7.72-7.76 (m, 1H, H6), 7.85-7.89 (m, 1H, H7), 8.22-8.24 (m, 1H, H8), 8.53-8.56 (m, 1H, H5), 9.36 (s, 1H, H2). IR (KBr pellet): ν (O=S=O) = 880 cm\textsuperscript{-1} and 1130 cm\textsuperscript{-1}. Anal. Calcd for C\textsubscript{12}H\textsubscript{13}NO\textsubscript{2}S\textsubscript{2}: C 53.91, H 4.90, N 5.24, S 23.98. Found: C 53.72, H 5.00, N 5.02, S 23.68.

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REFERENCES AND NOTES

# Part CX in the Series of Azinyl Sulfides