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

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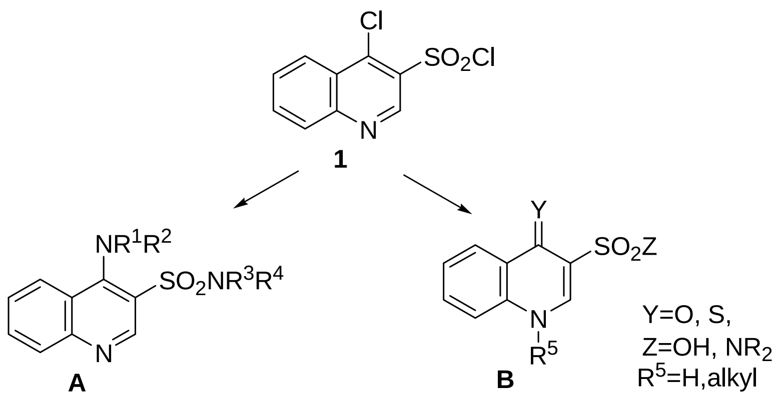
Abstract - Reaction of 4-chloro-3-quinolinesulfonyl chloride (**1**) with sodium hydrogen sulfide led to sodium 4-thioxo-1,4-dihydro-3-quinolinesulfinate (**2**). Compound **2** in reactions with alkyl halides was monoalkylated to sodium 4-alkylsulfanyl-3-quinolinesulfinate (**3**) or double alkylated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

INTRODUCTION

3-Sulfonylquinolines including 3-sulfonyl-4(1*H*)-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-thioxo-1,4-dihydro-3-quinolinesulfinic acid (**2**). Salt **2** was used for a new synthesis of 3-alkanesulfonylquinolines **3**, **4** and **6**, described in this paper.

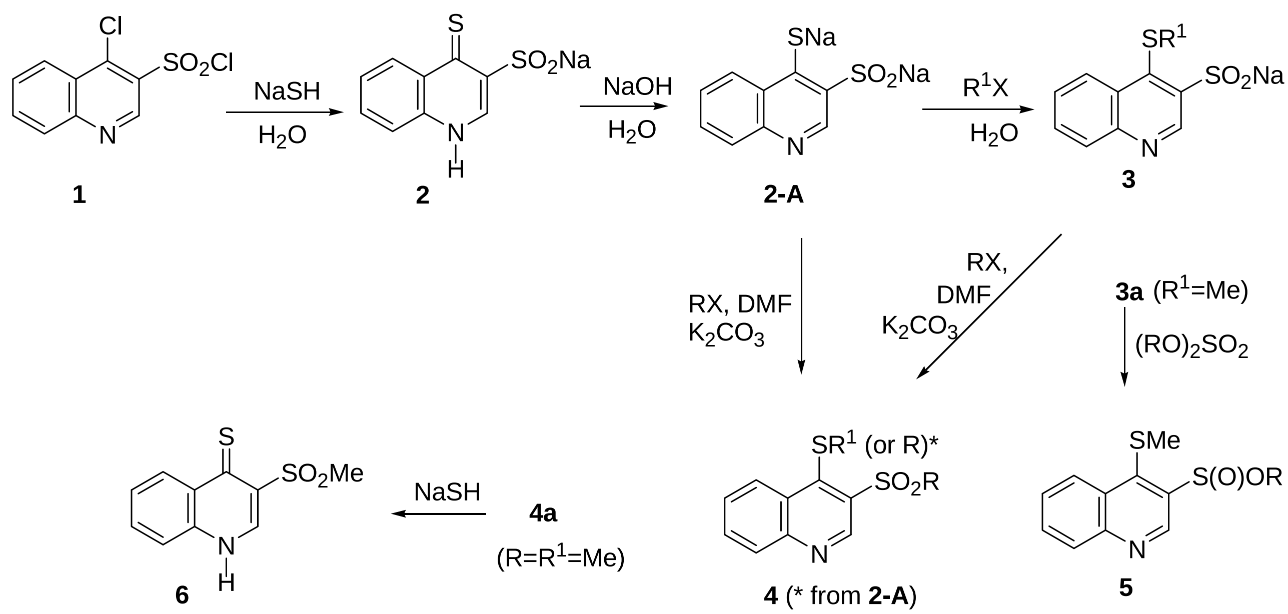
RESULTS AND DISCUSSION

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-methanesulfonylquinoline[7] or 3-methylsulfanyl (or methylsulfinyl)-4-quinolinone to 3-methanesulfonyl-4-quinolinones,[3] as well as by methylation of sodium 4-(4-phenoxy-3-quinolinylsulfanyl)-3-quinolinesulfinate to 3'-methylsulfonyl-4-phenoxy-3,4'-diquinolinyl sulfide, as recently reported from our laboratory.[8]

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

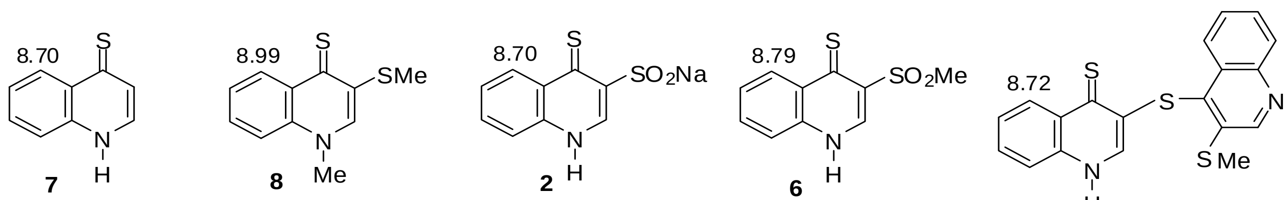
Our approach presented below opens the other route to 4-substituted 3-alkanesulfonylquinolines. Treatment of 4-chloro-3-quinolinesulfonyl chloride (**1**) with aqueous sodium hydrogen sulfide caused vigorous exothermic reaction with intensive evolution of hydrogen sulfide and led to a complete consumption of substrate **1**. Diluting an aqueous solution of products with ethanol precipitated a deep-orange solid with elemental composition $C_9H_6NO_2S_2Na$ x 4 H_2O 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 δ_H values and multiplet shapes both typical for 4(1*H*)-quinolinethiones.[12-14] The most diagnostic data come from the spectral position of the H5 proton shifted downfield by 4-thioxo function up to δ_H = 8.70 ppm. Very close *peri*-effect regarding the H-5 proton δ_H value was observed for other 4(1*H*)-quinolinethiones **7**, **8** and **9** [12-14] (Scheme 3). Also UV-Vis spectra of the newly prepared compounds **2** and **6** showed very similar absorption bands to those of 4(1*H*)-quinolinethione (**7**)[15] both in neutral solution (λ_{max}= 384-388 nm) and in alkaline solution (λ_{max}= 344-359 nm).

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



9

7: λ_{max}=384 nm (H_2O,neutral)
λ_{max}=344 nm (H_2O,alkaline)
λ_{max} taken from ref.[15]
δ_H value taken from ref.[12]

8: ref.[12]

2: λ_{max}=387 nm [a]
λ_{max}=350 nm [b]

6: λ_{max}=388 nm [a]
λ_{max}=359 nm [b]

9: ref.[14]

[a] neutral aqueous or aqueous-ethanol solution
[b] alkaline aqueous or aqueous-ethanol solution

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-quinolinesulfinates (**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_2CO_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,[16,17] reaction of sodium quinoline-3-sulfinate **3a** with dimethyl or diethyl sulfates led to alkyl 4-alkylsulfanylquinoline-3-sulfinates (**5a** or **5b**), respectively. This is in agreement with the conclusion of Meek and Fowler[17] regarding the *O*- and *S*-regioorientation in the alkylation of benzenesulfinates 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 sulfinates **5** are in agreement with the regularity observed for the respective benzene derivatives.[18,16] Both alkyl sulfinates **5a** and **5b** underwent thermal rearrangement (above 150 ºC) 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[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**[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**).

Entry	Substrate	Alkylating agent	Solvent	Product, yield (%)
1	**2**	MeI	10% NaOH	**3a**, R^1 = Me, 89
2	**2**	EtI	10% NaOH	**3b**, R^1 = Et, 81
3	**2**	*i*-PrI	10% NaOH	**3c**, R^1 = *i*-Pr, 87
4	**2**	AllylBr	10% NaOH	**3d**, R^1 = Allyl, 87
5	**2**	BnCl	10% NaOH	**3e**, R^1 = Bn, 86
6	**3a**	MeI	DMF	**4a**, R = R^1 = Me, 88
7	**3a**	EtI	DMF	**4b**, R = Et, R^1 = Me, 67
8	**3a**	*i*-PrI	DMF	**4c**, R =*i*-Pr, R^1 = Me, 72
9	**3a**	AllylBr	DMF	**4d**, R = Allyl, R^1 = Me, 89
10	**3a**	BnCl	DMF	**4e**, R = Bn, R^1 = Me, 90
11	**2**	MeI [a]	DMF / K_2CO_3	**4a**, R = R^1 = Me, 89
12	**2**	EtI [a]	DMF / K_2CO_3	**4f**, R = R^1 = Et, 91
13	**2**	*i*-PrI [a]	DMF / K_2CO_3	**4g**, R = R^1 = *i*-Pr, 57
14	**2**	AllylBr [a]	DMF / K_2CO_3	**4h**, R = R^1 = Allyl, 71
15	**2**	BnCl [a]	DMF / K_2CO_3	**4i**, R = R^1 = Bn, 61
16	**3a** [b]	$(MeO)_2SO_2$	DMF	**5a**, R = Me, 60
17	**3a** [b]	$(EtO)_2SO_2$	DMF	**5b**, R = Et, 63

[a] 2.1 molar eqvs. of alkylating agent were used.
[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 ^1H and ^{13}C nuclei, respectively, in deuterochloroform ($CDCl_3$) or in hexadeuterodimethylsulfoxide (DMSO-d6) solutions with tetramethylsilane (δ 0.0 ppm) as internal standard. Two-dimensional ^1H-^{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 ^1H 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 ^1H / ^{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 alkylating agents. For analytical purposes salt **2** x 4 H_2O was recrystallized from aqueous EtOH.

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

deep orange solid, mp 304-305 °C (decomp). ^1H NMR (D_2O): δ = 7.45-7.49 (m, 1H, **H**6), 7.72-7.75 (m, 2H, **H**7 and **H**8), 8.59 (s, 1H, **H**2), 8.82-8.86 (m, 1H, **H**5). ^1H NMR (DMSO-d6), δ_H: [δ_C for carbons from single bond and/long-range proton-carbon correlations]: 3.10-3.80(broad, 9H, 4 x **H**$_2$O + N**H**), 7.39 [(ddd, 1H, ^3J=8.2 Hz, ^3J=7.0 Hz, ^4J=1.2 Hz, **H**-6); 124.9(**C**-6) / 120.8(**C**-8), 133.1 (**C**-4a)], 7.60 [(ddd, 1H, ^3J=8.3 Hz, ^3J=7.0 Hz, ^4J=1.4 Hz, **H**-7); 131.1(**C**-7) / 128.0(**C**-5), 136.8(**C**-8a)], 7.74 [(dd, 1H, ^3J=8.3 Hz, ^4J=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, ^3J=8.3 Hz, ^3J=7.0 Hz, ^4J=1.2 Hz, **H**-5); 128.0(**C**-5)/131.1(**C**-7)

136.8(**C**-8a), 186.8(**C**-4)]. UV/Vis (H_2O): λ_{max} (H_2O), (ε) = 387 nm (0.9408), λ_{max} (0.4 % aqueous NaOH) (ε) = 350 nm (0.9359). *Anal.* Calcd for $C_9H_6NO_2S_2Na$ x 4 H_2O: C, 33.85; H, 4.42; N, 4.39. Found: C, 33.99; H, 4.11; N, 4.44.

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

Alkylating 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 alkylating 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 (D_2O): δ = 2.50 (s, 3H, SC**H**$_3$), 7.68-7.73 (m, 1H, **H**6), 7.79-7.84 (m, 1H, **H**7), 7.96-7.99 (m, 1H, **H**8), 8.47-8.49 (m, 1H, **H**5), 9.00 (s, 1H, **H**2). *Anal.* Calcd for $C_{10}H_8NNaO_2S_2$ x 3 H_2O: 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 (D_2O) δ: 1.05 (t, *J*=7.2 Hz, 3H, C**H**$_3$), 2.92 (q, *J*=7.2 Hz, 2H, C**H**$_2$). 7.59-7.64 (m, 1H, **H**6), 7.71-7.77 (m, 1H, **H**7), 7.91-7.93 (m, 1H, **H**8), 8.43-8.45 (m, 1H, **H**5), 8.98 (s, 1H, **H**2). *Anal.* Calcd for $C_{11}H_{10}NNaO_2S_2$ x 3 H_2O: 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 (D_2O) δ: 1,18 (d, *J*=6.6 Hz, 6H, (C**H**$_3$)$_2$), 3.40-3.53 (m, 1H, C**H**). 7.56-7.61 (m, 1H, **H**6), 7.71-7.76 (m, 1H, **H**7), 7.91-7.94 (m, 1H, **H**8), 8.39-8.41 (m, 1H, **H**5), 9.06 (s, 1H, **H**2). *Anal.* Calcd for $C_{12}H_{12}NNaO_2S_2$ x 3 H_2O: 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 (D_2O): δ: 3.49 (d, *J* = 7.5 Hz, 2H, –C**H**$_2$–), 4.47-4.68 (m, 1H, –C**H**=), 5.60-5.76 (m, 2H, =C**H**$_2$), 7.55-7.60 (m, 1H, **H**6), 7.67-7.73 (m, 1H, **H**7), 7.87-7.90 (m, 1H, **H**8), 8.35-8.38 (m, 1H, **H**5), 8.96 (s, 1H, **H**2). *Anal.* Calcd for $C_{12}H_{10}NNaO_2S_2$ x 2 H_2O: 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 (D_2O) δ: 4.00 (s, 2H, C**H**$_2$), 6.77-6.79 (m, 2H, **H**$_{arom}$), 6.95-6.99 (m, 3H, **H**$_{arom}$), 7.42-7.46 (m, 1H, **H**6), 7.63-7.67 (m, 1H, **H**7), 7.857.87 (m, 1H, **H**8), 8.19-8.21 (m, 1H, **H**5), 8.90 (s, 1H, **H**2). *Anal.* Calcd for $C_{16}H_{12}NNaO_2S_2$ x H_2O: 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-alkanesulfonylquinolines (**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^+]. ^{1}H NMR ($CDCl_3$) δ: 2.60 (s, 3H, SC**H**$_3$), 3.53 (s, 3H, C**H**$_3$), 7.75-7.81 (m, 1H, **H**6), 7.89-7.95 (m, 1 H, **H**7), 8.23-8.25 (m, 1H, **H**8), 8.70-8.73 (m, 1H, **H**5), 9.52 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 1130 cm^{-1} and 1307 cm^{-1}. *Anal.* Calcd for $C_{11}H_{11}NO_2S_2$: 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^+]. ^{1}H NMR ($CDCl_3$) δ: 1.34 (t, *J*=7.5 Hz, 3H, C**H**$_3$), 2.59 (s, 3H, SC**H**$_3$), 3.72 (q, *J*=7.5 Hz, 2H, C**H**$_2$), 7.77-7.81 (m, 1H, **H**6), 7.91-7.95 (m, 1H, **H**7), 8.23-8.25 (m, 1H, **H**8), 8.71-8.73 (m, 1H, **H**5), 9.48 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 1130 cm^{-1} and 1305 cm^{-1}. *Anal.* Calcd for $C_{12}H_{13}NO_2S_2$: 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^+]. ^{1}H NMR ($CDCl_3$) δ: 1.38 (d, *J*=6.8 Hz, 6H, (C**H**$_3$)$_2$), 2.59 (s, 3H, SC**H**$_3$), 4.19-4.28 (m, 1H, CH), 7.78-7.81 (m, 1H, **H**6), 7.90-7.94 (m, 1H, **H**7), 8.23-8.25 (m, 1H, **H**8), 8.70-8.72 (m, 1H, **H**5), 9.45 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 1128 cm^{-1} and 1307 cm^{-1}. *Anal.* Calcd for $C_{13}H_{15}NO_2S_2$: 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^+]. ^{1}H NMR ($CDCl_3$) δ: 2.56 (s, 3H, SC**H**$_3$), 4.38 (d, *J*=7.2 Hz, 2H, –C**H**$_2$-, 5.68-5.82 (m, 1H, –C**H**=), 5.14-5.24 (m, 2H, =C**H**$_2$), 7.69-7.74 (m, 1H, **H**6), 7.83-7.88 (m, 1H, **H**7), 8.14-8.17 (m, 1H, **H**8), 8.61-8.74 (m, 1H, **H**5), 9.32 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 1130 cm^{-1} and 1305 cm^{-1}. *Anal.* Calcd for $C_{13}H_{13}NO_2S_2$: 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^+]. ^{1}H NMR ($CDCl_3$) δ: 2.66 (s, 3H, SC**H**$_3$), 4.94 (s, 2H, C**H**$_2$), 7.22-7.26 (m, 5H, **H**$_{arom}$), 7.75-7.80 (m, 1H, **H**6), 7.87-7.92 (m, 1H, **H**7), 8.14-8.17 (m, 1H, **H**8), 8.70-8.73 (m, 1H, **H**5), 9.07 (s, 1H, H2). IR (KBr pellet): ν (O=S=O) = 1129 cm^{-1} and 1304 cm^{-1}. *Anal.* Calcd for $C_{17}H_{15}NO_2S_2$: 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-alkanesulfonyl-quinolines (**4**) with the same alkyl groups.

A mixture of salt **2** tetrahydrate (200 mg, 0.59 mM), alkylating 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$^+$]. ^{1}H NMR (CDCl$_3$) δ: 1.24 (t, *J*=7.5 Hz, 3H, SCH$_2$C**H**$_3$), 1.29 (t, *J*=7.5 Hz, 3H, SO$_2$CH$_2$C**H**$_3$), 3.12 (q, *I*=7.5 Hz, 2H, SC**H**$_2$CH$_3$), 3.72 (q, *J*=7.5 Hz, 2H, SO$_2$C**H**$_2$CH$_3$), 7.75-7.79 (m, 1H, **H**6), 7.90-7.94 (m, 1H, **H**7), 8.21-8.24 (m, 1H, **H**8), 8.71-8.74 (m, 1H, **H**5), 9.49 (s, 1H, 2). IR (KBr pellet): ν (O=S=O) = 1129 cm^{-1} and 1307 cm^{-1}. *Anal*. Calcd for C$_{13}$H$_{15}$NO$_2$S$_2$: 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$^+$]. ^{1}H NMR (CDCl$_3$) δ: 1.27 (d, *J*=6.9Hz, 6H, SCH(C**H**$_3$)$_2$), 1.35 (d, *J*=6.6Hz, 6H, SO$_2$CH(C**H**$_3$)$_2$), 3.81-4.23 (m, 2H, 2 x C**H**(CH$_3$)$_2$) 7.73-7.78 (m, 1H, **H**6), 7.90-7.94 (m, 1H, **H**7), 8.21-8.24 (m, 1H, **H**8), 8.72-8.75 (m, 1H, **H**5), 9.47 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 1128 cm^{-1} and 1304 cm^{-1}. *Anal*. Calcd for C$_{15}$H$_{19}$NO$_2$S$_2$: C 58.22, H 6.19, N 4.53, S 20.72. Found: C 58.41, H 5.89, N 4.70, S 20.51.

4-Allylsulfanyl-3-(propene-3-sulfonyl)quinoline (**4h**):

an oil. MS (EI, 70 eV): m/z (%) = 305 [M$^+$]. ^{1}H NMR (CDCl$_3$) δ: 3.76 (d, *J*=7.5Hz, 2H, -C**H**$_2$-), 4.38 (d, *J*=7.2 Hz, 2H, SO$_2$C**H**$_2$-), 4.92-4.97 (m, 2H, CH=C**H**$_2$), 5.21-5.31 (m, 1H –SO$_2$CH$_2$C**H**= CH$_2$), 5.72-5.93 (m, 2H, 2 x –C**H**=), 7.75-7.80 (m, 1H, **H**6), 7.90-7.95 (m, 1H, **H**7), 8.21-8.23 (m, 1H, **H**8), 8.70-8.72 (m, 1H, **H**5), 9.41 (s, 1H, **H**2). *Anal*. Calcd for C$_{15}$H$_{15}$NO$_2$S$_2$: 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$^+$]. ^{1}H NMR (CDCl$_3$) δ: 4.08 (s, 2H, SC**H**$_2$C$_6$H$_5$), 4.36 (s, 2H, SO$_2$C**H**$_2$C$_6$H$_5$), 7.12-7.25 (m, 10H, **H**$_{arom}$), 7.62-7.67 (m, 1H, **H**6), 7.83-7.88 (m, 1H, **H**7), 8.12-8.14 (m, 1H, **H**8), 8.56-8.59 (m, 1H, **H**5), 9.12 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 1129 cm^{-1} and 1310 cm^{-1}. *Anal*. Calcd for C$_{23}$H$_{19}$NO$_2$S$_2$: 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- methane-sulfonylquinoline (**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^+]. ^{1}H NMR ($DMSO-d_6$) δ: 3.50 (s, 3H, C**H**$_3$), 7.58-7.61 (m, 1H, **H**6), 7.79-7.81 (m, 1H, **H**8), 7.85-7.88 (m, 1H, **H**7), 8.61 (s, 1H, **H**2), 8.78-8.80 (m, 1H, **H**5), 13,63 (s, 1H, N**H**). UV/Vis (EtOH\H_2O): λ_{max} (ε) = 388 nm (1.19629), UV/Vis (0.5% NaOH): λ_{max} (ε) = 359 nm (0.25436). *Anal.* Calcd for $C_{10}H_9NO_2S_2$: 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 ºC 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 ºC) 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. ^{1}H NMR ($CDCl_3$) δ: 2.51 (s, 3H, SC**H**$_3$), 3.73 (s, 3H, OCH_3), 7.73-7.77 (m, 1H, **H**6), 7.86-7.90 (m, 1H, **H**7), 8.22-8.24 (m, 1H, **H**8), 8.54-8.56 (m, 1H, **H**5), 9.34 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 877 cm^{-1} and 1130 cm^{-1}. *Anal.* Calcd for $C_{11}H_{11}NO_2S_2$: 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. ^{1}H NMR ($CDCl_3$) δ: 1.37-1.43 (m, 3H, CH_2C**H**$_3$), 2.51 (s, 3H, SC**H**$_3$), 3.98-4.05 (m, 1H, OC**H**HCH_3), 4.28-4.36 (m, 1H, OCH**H**CH_3), 7.72-7.76 (m, 1H, **H**6), 7.85-7.89 (m, 1H, **H**7), 8.22-8.24 (m, 1H, **H**8), 8.53-8.56 (m, 1H, **H**5), 9.36 (s, 1H, **H**2). IR (KBr pellet): ν (O=S=O) = 880 cm^{-1} and 1130 cm^{-1}. *Anal.* Calcd for $C_{12}H_{13}NO_2S_2$: 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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