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SYNTHESIS OF 3-ALKANESULFONYL-4(1*H*)-QUINOLINONES FROM 3-ALKANESULFONYL-4-ALKYLSULFANYLQUINOLINES

Leszek Skrzypek,[a),]* Andrzej Maślankiewicz,[a)] and Kinga Suwińska[b)]

[a)] Department of Organic Chemistry, Medical University of Silesia, Jagiellońska 4, 41-200 Sosnowiec, Poland. [b)] Institute of Physical Chemistry, Polish Academy of Science, Kasprzaka 44/52, 01-224 Warszawa and Faculty of Biology and Environmental Sciences, Cardinal Stefan Wyszynski University in Warsaw, Wóycickiego 1/3, PL-01 938 Warszawa, Poland. E-mail: skrzypek@sum.edu.pl

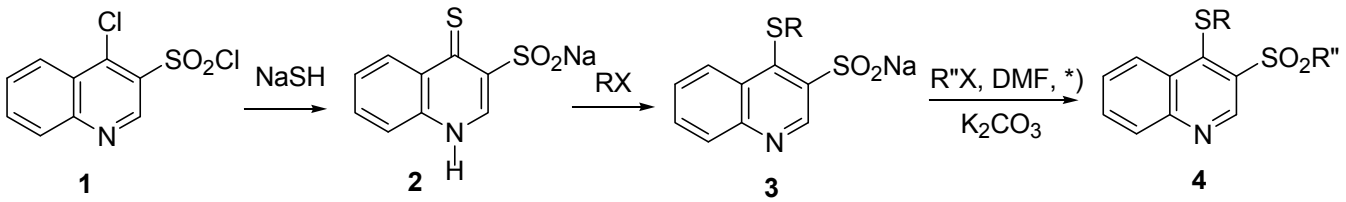
Abstract – 3-Alkanesulfonyl-4-alkylsulfanylquinolines (**4**) were transformed to 3-alkanesulfonyl-4(1*H*)-quinolinones (**5**) and (**6**). 1*H*-Derivatives **5** were obtained by acidic hydrolysis of compounds **4**. 1-Alkyl derivatives **6** were prepared in three ways: a) *via* 1-alkylquinolinium salts **7** followed by their acidic hydrolysis to **6**; b) in one-pot reactions of compounds **4** with alkyl bromides under Phase Transfer Catalysis (PTC) conditions; or c) by alkylation of 1*H*-derivatives **5** with alkyl bromides under PTC conditions.

INTRODUCTION

The discovery of strong antimicrobial 4(1*H*)-quinolinones inspired broad and intensive study on the structure-activity relationship of 4(1*H*)-quinolinone derivatives.[1-3] It is well documented that *N*-alkyl derivatives are more potent than their N-H parent structures.[1-5] The same trends were observed for 3-alkylsulfinyl-4(1*H*)-quinolinones acting as antihypertensive agent[5] and for 3-sulfamoyl-4(1*H*)-quinolinones with antihypertensive,[5,7] or phosphordiesterase-5 inhibitory[6] activity.

N-Alkyl-4(1*H*)-quinolinones were synthesized mainly by cyclisation of the benzene derivatives,[1-7] by hydrolysis of *N*-alkylquinolinium salts [8,9] or by *N*-alkylation of 4(1*H*)-quinolinones.[1-3]

The easy access to the title 4-alkylsulfanyl-3-alkanesulfonylquinolines **4** from 4-chloro-3-quinolinesulfonyl chloride[10] (Scheme 1) prompted us to a study on the transformation of compounds **4** to 3-alkanesulfonyl-4(1*H*)-quinolinones **5** and **6** (Schemes 2-4).

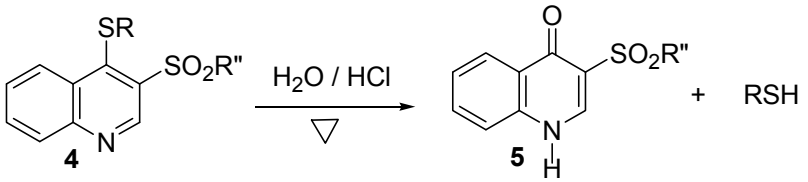


*) when R=R", compounds **4** could be prepared directly by double alkylation of salts **2**

Scheme 1

RESULTS AND DISCUSSION

First experiments on the purification of 4-alkylsulfanyl-3-alkanesulfonylquinolines (**4**) by recrystallization from aqueous ethanolic solutions revealed an instability in the compounds **4**, which partially decomposed to 4-quinolinones **5** accompanied by volatile odorous thioderivatives. Hydrolysis of compounds **4** was performed for preparative purposes in boiling 1% hydrochloric acid for 1 h to give 1,4-dihydro-4-oxo-3-alkanesulfonylquinolines **5a**-**e** as sole products.



4

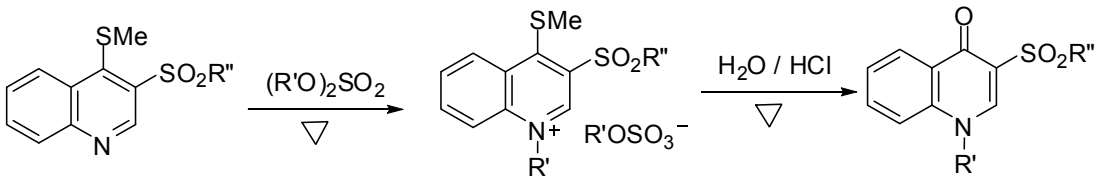
4a, R=R"=Me
4b, R=Me, R"=Et
4c, R=R"=Et
4d, R=Me, R"=Pr
4e, R=R"=Pr
4f, R=Me, R"=i-Pr
4g, R=Me, R"=Allyl
4h, R=Me, R"=Bn

5

5a, R"=Me, (79 %)
5b, R"=Et (75 %) from **4b**; (70 %) from **4c**
5c, R"=Pr, (75 %) from **4d**; (90 %) from **4e**
5d, R"=i-Pr, (75 %)
5e, R"=Allyl, (80 %)
5f, R"=Bn, (88 %)

Scheme 2

We then turned to the synthesis of *N*-alkyl derivatives **6** *via* quinolinium salts **7** applying our previous methodology.[9] For this purpose, compounds **4** were heated with dimethyl or diethyl sulfate which led to *N*-alkylquinolinium salts **7**. Due to instability of salts **7** crude alkylation products were subjected directly to hydrolysis, and *N*-alkyl derivatives **6a**, **b**, **f, g**, **h, i** were obtained as sole products in good yields (70-90%).



4

4a, R"=Me
4b, R"=Et
4c, R"=Pr

7

R'=Me or Et

6

6a, R'=R"=Me, (70 %)
6b, R'=Et, R"=Me, (81 %)
6f, R'=Me, R"=Et, (90 %)
6g, R'=R"=Et (78 %)
6h, R'=Me, R"=Pr, (80 %)
6i, R'=Et, R"=Pr, (71 %)

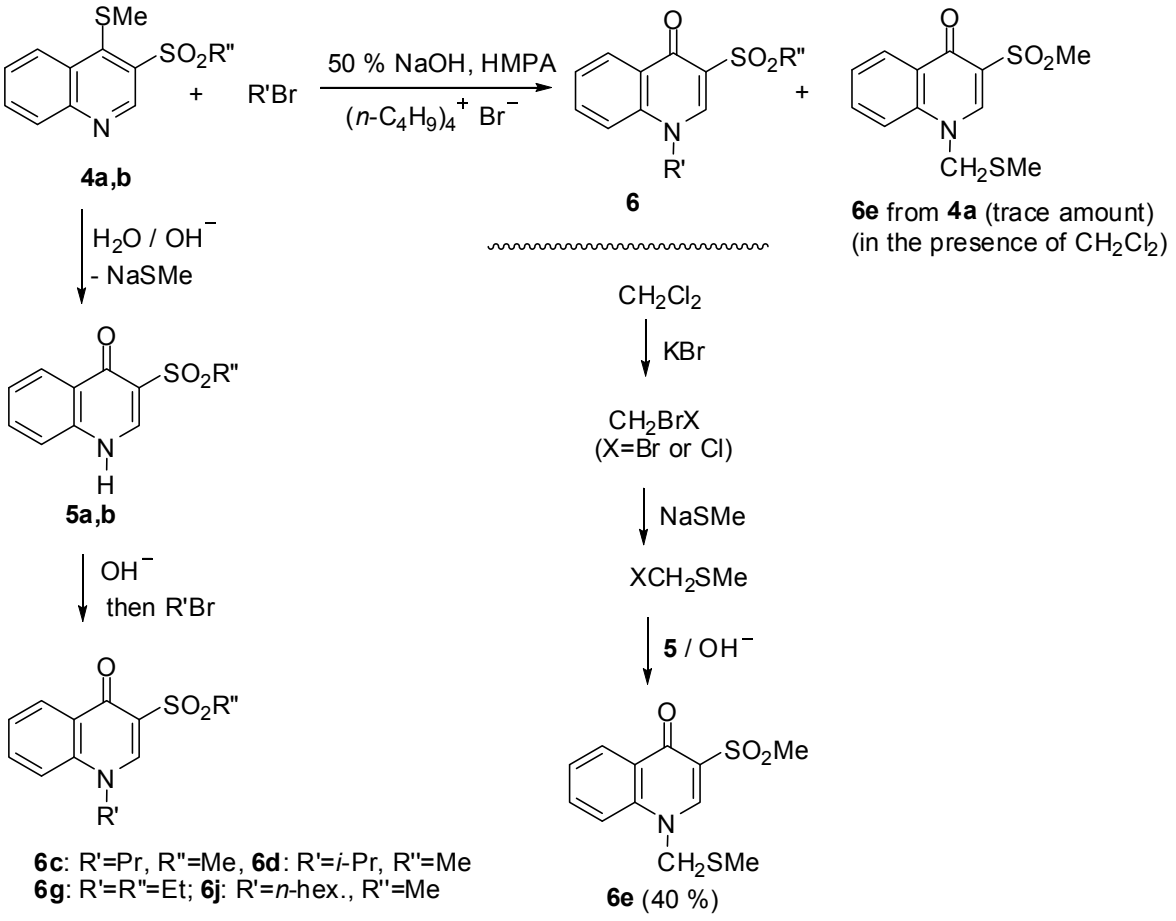
Scheme 3

Hoping to extend the set of alkanesulfonyl derivatives **4**, it was attempted to alkylate compound **4a** at α-alkanesulfonyl carbon using the PTC conditions described for aryl benzylsulfones or sulfonamides.[11] Unexpectedly, the reaction gave the *N*-alkyl-4-quinolinones **6b** and **6e** or **6c** and **6e** in the presence of methylene chloride (Table, entries 2 and 4), but *N*-alkyl-4-quinolinones **6b**, **c**, **d, j** were obtained as sole

products in the absence of methylene chloride and using an excess of alkyl bromide (Scheme 4).

Due to the sensitivity of compounds **4** toward hydrolysis and the rigorous conditions of *N*-alkylation of compounds **4**, we assumed that the hydrolysis of 4-methylsulfanylquinolines **4** to 4(1*H*)-quinolinones **5** is the first step in the reaction sequences involved under PTC conditions. To confirm this assumption, 4(1*H*)-quinolinones **5a**, **b** were isolated from reaction performed under the PTC conditions in the absence of alkylating agents. Then, compounds **5a**, **b** were subjected to *N*-alkylation under the PTC conditions and 1-ethyl-4(1*H*)-quinolinones **6c**, **g** were obtained in good yields. 4-Quinolinone **5a** did not react with methylene chloride under the PTC conditions.

In order to explain the formation of methylthiomethyl derivative **6e**, 3-methanesulfonyl-4-methylsulfanyl-quinoline (**4a**) was subjected to the reaction with methylene chloride under the PTC conditions. The reaction gave only traces of **6e**. However, the same reaction performed in the presence of potassium bromide (2 molar equivalents) produced compound **6e** (~40%). This suggests that bromide anion activated the methylene chloride molecule to form bromomethylene derivatives (CH_2BrCl or CH_2Br_2), which then reacted with sodium methanethiolate to give methylthiomethyl halogenide (X=Br or Cl). The latter acted as an alkylating agent toward the quinolinone **5a** anion (see Scheme 3).



Scheme 4

Table. Synthesis of 3-alkanesulfonyl-1-alkyl-4(1*H*)-quinolines **6** from 3-alkanesulfonyl-4-alkylsulfanyl-quinolines **4** under the PTC conditions (Scheme 4)

Entry	Substrate	Alkylating agent	Temp. / Time	Product(s), yield (%)
1	**4a**	EtBr [a]	40 °C/24h	**6b**, R'=Et, R"=Me, 69
2	**4a**	EtBr [b]	20 °C/48	**6b**, 51; **6e**, R'=$MeSCH_2$, R"=Me, 15
3	**4a**	PrBr [c]	70 °C/7h	**6c**, R'=Pr, R"=Me, 74
4	**4a**	PrBr [b]	20 °C/48	**6c**, 56; **6e**, R'=$MeSCH_2$, 13
5	**4a**	*i*-PrBr [c]	60 °C/7h	**6d**, R'= *i*-Pr, R"=Me, 22
6	**4a**	HexBr [c]	70 °C/7h	**6j**, R'=Hex, R"=Me, 87
7	**4a**	CH_2Cl_2/KBr (2mM)	40 °C/24h	**6e**, R'=$MeSCH_2$, R"=Me, 40
8	**4b**	EtBr [a]	40 °C/24h	**6g**, R'=R"=Et, 70
9	**5a**	PrBr [c]	70 °C/7h	**6c**, R'=Pr, R"=Me, 72
10	**5b**	EtBr [a]	40 °C/24h	**6g**, R'=R"=Et, 71

[a] 20 molar eqvs.; [b] reaction was performed in the presence of CH_2Cl_2 and 2 molar eqvs. of EtBr were used,; [c] 11 molar eqvs.

X-Ray analysis

Products obtained by the hydrolysis of compounds **4** may formally exist as the 1,4-dihydro-4-oxo or 4-hydroxy tautomer, as it was observed for 4(1*H*)-quinolinone derivatives with a strong electron-withdrawing group, like 4-hydroxy- or 4-mercapto-3-quinolinesulfonic acids.[12,13]

Therefore, in order to evaluate tautomeric preferences of hydrolysis products of compounds **4**, *n*-propyl derivative **5c** was subjected to X-ray examination. It was proved that compound **5c** exists as the 4-oxo form in the solid state with hydrogen atom located at the N1 atom (Figure 1a).

Molecules in crystal form 1D polymer *via* bifurcated N-H···O1(O2) hydrogen bonds (Figure 1b). Two molecules related by center of symmetry are arranged in "dimers", in which the quinolone aromatic rings are parallel one to each other and are separated by 3.527 Å indicating π-π interaction (Figure 1c). There are also one C-H··· π·and one C=O···π interactions to the quinolone aromatic rings with distances to the ring 2.895 and 3.286 Å, respectively (Figure 1d).

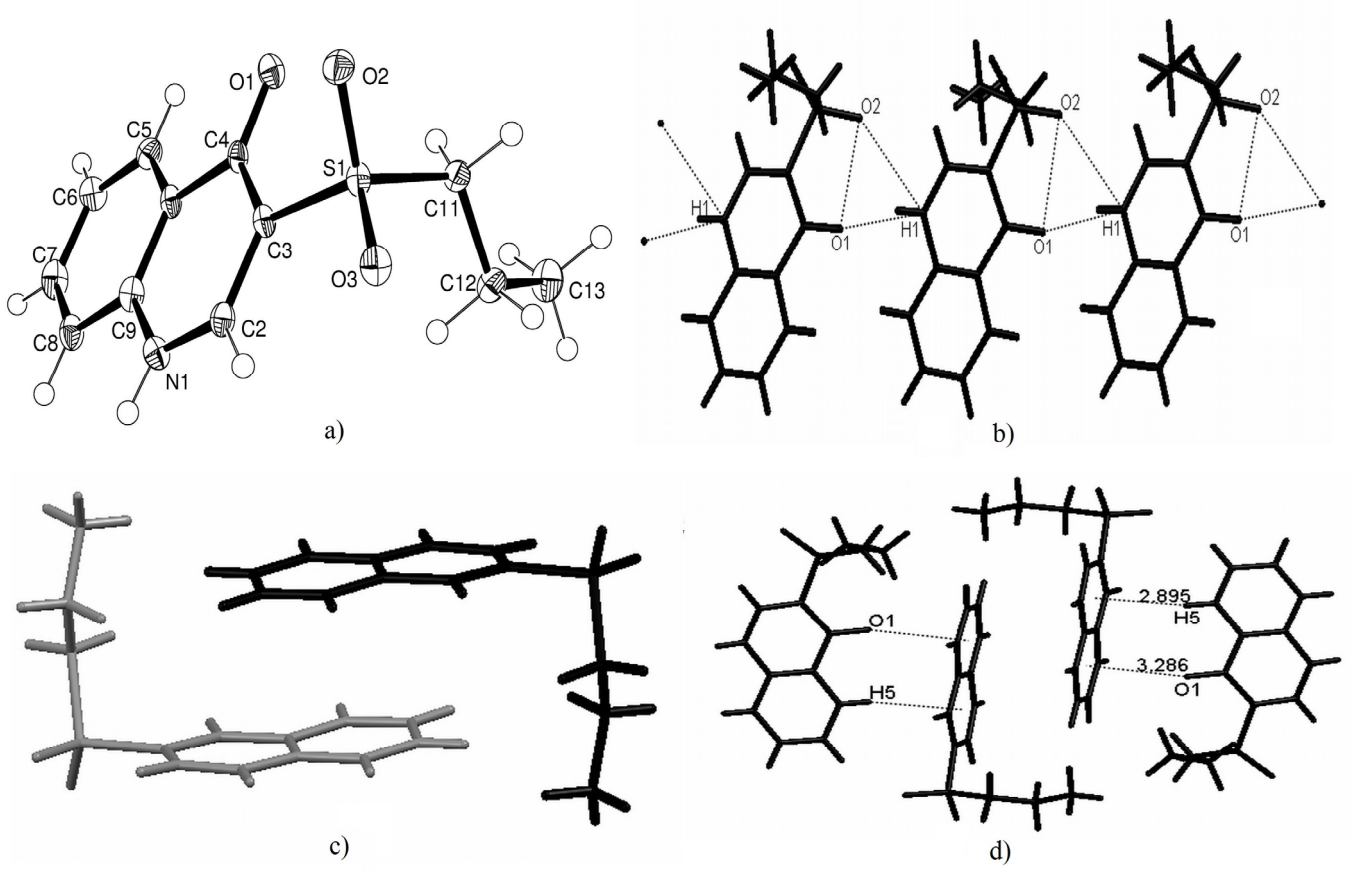


Figure 1. Graphical presentations deduced from X-ray diffraction study of 3-(1-propanesulfonyl)-4(1*H*)-quinolinone (**5c**): a) ORTEP drawing with the atom labeling scheme. Displacement ellipsoids are drawn at the 50% probability level. b) hydrogen bonds, c) π- π stacking interactions, d) C-H···π·and C=O···π interactions to the quinolone aromatic rings.

CONCLUSIONS

Both functions of compounds **4** were engaged in reactions with alkylating agents under the PTC conditions. They participated, on one hand, in nucleophilic substitution of the 4-alkylsulfanyl substituent with hydroxy anion to form, after tautomerization the 4-oxo function of **5**, which was then alkylated at the *endocyclic* nitrogen atom to afford the final *N*-alkyl-3-alkanesulfonyl-4(1*H*)-quinolinones **6**. Taking into account the easy access to the title 3-alkanesulfonyl-4-alkylsulfanylquinolines **4** and the one-pot synthesis of **6** from compounds **4**, the present study opens a unique route to the title compounds **6** and is therefore more general and more convenient than previous findings concerning the preparation of 3-methanesulfonyl-1-methyl-4(1*H*)-quinolinone (**6a**) derivatives by cyclizations or oxidation of the respective 3-thioderivatives.[7]

EXPERIMENTAL

Melting points were taken in open capillary tubes and are uncorrected. All NMR spectra were recorded on

a Bruker AVANCE 400 spectrometer operating at 400.22 MHz for ^{1}H nuclei, in deuterochloroform or in hexadeuterodimethyl sulfoxide solutions with tetramethylsilane (δ 0.0 ppm) as internal standard.

EI MS spectra were determined on a Finnigan MAT 95 spectrometer at 70 eV. TLC analyses were performed employing Merck's aluminium oxide 60 F_{254} neutral (type E) plates and using chloroform as an eluent.

3-Alkanesulfonyl-4-alkylsulfanylquinolines **4** were prepared as described previously.[10] In the same way were prepared 3-(1-propanesulfonyl)-4-methylsulfanylquinoline (**4d**) (82% from salt **3a**, R=Me) and 3-(1-propanesulfonyl)-4-propylsulfanylquinoline (**4e**) (90% from salt **2**) required for this paper.

3-(1-Propanesulfonyl)-4-methylsulfanylquinoline (**4d**):

Oil. MS (EI, 70 eV): m/z (%) = 281 (M^+, 100). ^{1}H NMR ($CDCl_3$) δ: 1.04 (t, *J*=7.5 Hz, 3H, **CH**$_3$), 1.78-1.84 (m, 2H, C**H**$_2$CH$_3$), 3.66-3.70 (m, 2H, SO_2C**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), 8.70-8.73 (m, 1H, **H**5), 9.48 (s, 1H, **H**2). *Anal*. Calcd for $C_{13}H_{15}NO_2S_2$: C 55.49, H 5.37, N 4.98. Found: C 55.79, H 5.67, N 5.12.

3-(1-Propanesulfonyl)-4-propylsulfanylquinoline (**4e**):

Mp 66-67 °C. MS (EI, 70 eV): m/z (%) = 309 (M^+, 51), ^{1}H NMR ($CDCl_3$) δ: 1.01-1.05 (m, 6H, 2 x **CH**$_3$), 1.68-1.73 (m, 4H, 2x C**H**$_2$), 3.05-3.08 (m, 2H, SC**H**$_2$), 3.66-3.70 (m, 2H, SO_2C**H**$_2$), 7.75-7.79 (m, 1H, **H**6), 7.92-7.94 (m, 1H, **H**7), 8.22-8.24 (m, 1H, **H**8), 8.71-8.73 (m, 1H, **H**5), 9.48 (s, 1H, **H**2). *Anal*. Calcd for $C_{15}H_{19}NO_2S_2$: C 58.22, H 6.19, N 4.53. Found: C 58.41, H 6.41, N 4.30.

Hydrolysis of 3-alkanesulfonyl-4-alkylsulfanylquinolines (**4**) to 3-alkanesulfonyl-4(1*H*)-quinolinones (**5**)

A mixture of 3-alkanesulfonyl-4-alkylsulfanylquinolines (**4**) (1.5 mM), 8 mL of 1% HCl aq. and 2 mL of EtOH was kept at the boiling state for 1 h. The mixture was cooled down to rt. The solid was filtered off and recrystallized from aqueous EtOH to give 3-alkanesulfonyl-4(1*H*)-quinolinones **5**.

3-Methanesulfonyl-4(1*H*)-quinolinone (**5a**):

mp 319-320 °C. MS (EI, 70 eV): m/z (%) = 223 (M^+, 100). ^{1}H NMR (DMSO-d_6), δ: 3.26 (s, 3H, SO_2C**H**$_3$), 7.48-7.52 (m, 1H, **H**6),7.70-7.72 (m, 1H, **H**8), 7.78-7.81 (m, 1H, **H**7), 8.18-8.20 (m, 1H, **H**5), 8.53 (s, 1H, **H**2), 12.69 (s, 1H, N**H**). *Anal*. Calcd for $C_{10}H_9NO_3S$: C 53.80, H 4.06, N 6.27, S 14.36. Found: C 54.04, H 4.36, N 6.40, S 14.51.

3-Ethanesulfonyl-4(1*H*)-quinolinone (**5b**):

mp 216-217 °C. MS (EI, 70 eV): m/z (%) = 237 (M^+, 100). ^{1}H NMR (DMSO-d_6), δ: 1.12 (t, *J*=7.3 Hz, 3H, CH_2C**H**$_3$), 3.41 (q, *J*=7.3 Hz, 2H, C**H**$_2$CH$_3$), 7.48-7.52 (m, 1H, **H**6),7.70-7.72 (m, 1H, **H**8), 7.78-7.80 (m, 1H, **H**7), 8.17-8.19 (m, 1H, **H**5), 8.50 (s, 1H, **H**2), 12.71 (s, 1H, N**H**). *Anal*. Calcd for $C_{11}H_{11}NO_3S$: C 55.68, H 4.67, N 5.90, S 13.51. Found: C 55.47, H 4.88, N 6.11, S 13.72.

3-(1-Propanesulfonyl)-4(1*H*)-quinolinone (**5c**):

mp 206-209 °C. MS (EI, 70 eV): m/z (%) = 251 (M^+, 79), (M-$SO_2CH_2CH_2CH_3$ +1, 100). ^{1}H NMR (DMSO-d_6), δ: 0.94 (t, *J*=7.5 Hz, 3H, $CH_2CH_2CH_3$), 1.54-1.64 (m, 2H, $CH_2CH_2CH_3$), 3.40-3.44 (m, 2H, $CH_2CH_2CH_3$), 7.48-7.52 (m, 1H, **H**6) 7.70-7.72 (m, 1H, **H**8), 7.77-7.82 (m, 1H, **H**7), 8.17-8.19 (m, 1H, **H**5). 8.51 (s, 1H, **H**2), 12.71 (s, 1H, N**H**). *Anal*. Calcd for $C_{12}H_{13}NO_3S$: C 57.35, H 5.21, N 5.57, S 12.76. Found: C 57.64, H 5.09, N 5.50, S 12.97.

3-(1-Methylethanesulfonyl)-4(1*H*)-quinolinone (**5d**):

mp 295-296 °C. MS (EI, 70 eV): m/z (%) = 251 (M^+, 82), 191(M-SO_2, 100). ^{1}H NMR (DMSO-d_6), δ: 1.20 (d, 6H, *J*=7.3 Hz, $(CH_3)_2$), 3.81-3.91 (m, 1H. C**H**), 7.48-7.51 (m, 1H, **H**6), 7.71-7.73 (m, 1H, **H**8), 7.78-7.81 (m, 1H, **H**7), 8.16-8.18 (m, 1H, **H**5), 8.59 (s, 1H, **H**2), 12.71 (s, 1H, N**H**). *Anal*. Calcd for $C_{12}H_{13}NO_3S$: C 57.35, H 5.21, N 5.57, S 12.76. Found: C 57.47, H 5.55, N 5.32, S 12.81.

3-(Propene-3-sulfonyl)-4(1*H*)-quinolinone (**5e**):

mp 224-226 °C. MS (EI, 70 eV): m/z (%) = 249 (M^+, 43), (M- $SO_2CH_2CH=CH_2$, 100). ^{1}H NMR (DMSO-d_6), δ: 4.22 (d, *J*=7.6 Hz, 2H, $CH_2CH=CH_2$), 5.21-5.27 (m, 2H, $CH_2CH=CH_2$), 5.66-5.77 (m, 1H, $CH_2CH=CH_2$), 7.48-7.52 (m, 1H, **H**6) 7.70-7.72 (m, 1H, **H**8), 7.80-7.82 (m, 1H, **H**7), 8.18-8.20 (m, 1H, **H**5). 8.47 (s, 1H, **H**2), 12.72 (s, 1H, N**H**). *Anal*. Calcd for $C_{12}H_{11}NO_3S$: C 57.82, H 4.45, N 5.62, S 12.86. Found: C 57.68, H 4.59, N 5.38, S 12.65.

3-Phenylmethanesulfonylquinolinone (**5f**):

mp 283-285 °C. MS (EI, 70 eV): m/z (%) = 299 (M^+, 22), 91 (CH_2Ph, 100). ^{1}H NMR (DMSO-d_6), δ: 4.78 (s, 2H, CH_2Ph), 7.20-7.22 (m, 2H, H_{arom}), 7.27-7.29 (m, 3H, H_{arom}), 7.51-7.55 (m, 1H, **H**6) 7.69-7.71 (m, 1H, **H**8), 7.78-7.82 (m, 1H, **H**7), 8.24-8.26 (m, 2H, **H**5 and **H**2). 12.74 (s, 1H, N**H**). *Anal*. Calcd for $C_{16}H_{13}NO_3S$: C 64.20, H 4.38, N 4.68, S 10.71. Found: C 64.36, H 4.62, N 4.70, S 11,01.

Alkylation of 3-alkanesulfonyl-4-alkylsulfanylquinolines **4** to 3-alkanesulfonyl-1-alkyl-4-alkylsulfanyl-quinolinium salts **7** and hydrolysis of salts **7** to 3-alkanesulfonyl-1-alkyl-4(1*H*)-quinolinones **6**

3-Alkanesulfony-4-alkylsulfanylquinoline **4** (1 mM) was dissolved in 0.7 mL of freshly distilled dialkyl sulfate and kept at 100 ºC for 2 h (dimethyl sulfate) or 24 h (diethyl sulfate). The mixture was cooled down to rt and triturated three times with dry Et_2O (4 mL) followed by decantation. The residue was kept at rt under vacuum to give quinolinium salt **7** as syrupy semi-solid material. Due to instability of quinolinium methyl (or ethyl) sulfate **7**, they could not be isolated in a pure state, and crude salts **7** were used directly for the preparation of compounds **6**.

For purpose of hydrolysis, salt **7** (*ca.* 1 mM) was dissolved in water (8 mL) and refluxed for 1 h. The mixture was then cooled down to rt. The solid was filtered off, washed with cold water and dried on air. It was recrystallized from EtOH to give 3-alkanesulfonyl-1-alkyl-4(1*H*)-quinolinones **6**.

Reaction of 3-alkanesulfonyl-4-alkylsulfanylquinolines **4** performed under the PTC conditions

a) In the absence of CH_2Cl_2

4-Methylsulfanylquinoline **4** (1 mM) was suspended with stirring in a mixture of 50% aqueous NaOH (2 mL), tetrabutylammonium bromide (50 mg), HMPA (0.2 mL) and then alkyl bromide (11-20 mM) was added. The mixture was stirred for 6 h up to 72 h at rt or at appropriate temperature (for details – see Table). The mixture was then cooled down to rt and diluted with water (20 mL) to precipitate solid, which was filtered off, washed with cold water and dried on air. It was recrystallized from EtOH to give 3-alkanesulfonyl-1-alkyl-4(1*H*)-quinolinone **6**.

b) In the presence of CH_2Cl_2

The reaction performed in the presence of CH_2Cl_2 (2 mL) and using the 2 mM of alkyl bromide led to a mixture of 3-alkanesulfonyl-1-alkyl-4(1*H*)-quinolinone **6b** or **6c** and 1-methylthiomethyl derivative **6e**. The mixture was separated by column chromatography (aluminium oxide / CH_2Cl_2).

The same reaction carried out without alkyl bromide but with addition of KBr (240 mg, *ca.* 2 mM) led to 1-methylthiomethyl derivative **6e** (38%). Acidification of aqueous layer afforded *non*-alkylated 4(1*H*)-quinolinones **5a** (27%).

c) Hydrolysis of 3-alkanesulfonyl-4-alkylsulfanylquinolines **4** to 3-alkanesulfonyl-4(1*H*)-quinolinones **5**.

A mixture of 3-alkanesulfonyl-4-alkylsulfanylquinolines **4a** or **4b** (1.5 mM), 50% aqueous NaOH (2 mL), tetrabutylammonium bromide (50 mg), HMPT (0.2 mL) and benzene (1.5 mL) was refluxed with stirring for 3 h. The mixture was cooled down to rt. The precipitated solid was filtered off to give *ca.* 40% of *non*-converted substrate **4**. The filtrate was transfered into a separatory funnel, and the aqueous layer was separated. This solution was then acidified with 10% HCl aq. to precipitate 3-alkanesulfonyl-4(1*H*)-quinolinones (**5a**, 37%, or **5b**, 39%).

Alkylation of 3-alkanesulfonyl-4(1*H*)-quinolinones **5** to 3-alkanesulfonyl-1-alkyl-4(1*H*)-quinolinones **6**

3-Alkanesulfonyl-4(1*H*)-quinolinones **5a** or **5b** were subjected to alkylation under the PTC conditions mentioned above (procedure *a* for compounds **4)**. *N*-Alkyl derivative **6c** or **6g** was isolated as described above. For details, see Table – entry 9 and 10.

3-Methanesulfonyl-1-methyl-4(1*H*)-quinolinone (**6a**):

mp 215-216 °C. MS (EI, 70 eV): m/z (%) = 237 (M^+, 95), 173 (M-SO_2 100). ^{1}H NMR ($CDCl_3$), δ: 3.36 (s, 3H, $SO_2C\mathbf{H}_3$), 3.95 (s, 3H, $NC\mathbf{H}_3$), 7.51-7.56 (m, 2H, **H**6, **H**8), 7.79-7.81 (m, 1H, **H**7), 8.44 (s, 1H, **H**2), 8.49-8.52 (m, 1H, **H**5). *Anal*. Calcd for $C_{11}H_{11}NO_3S$: C 55.68, H 4.67, N 5.90, S 13.51. Found: C 55.80, H 4.41, N 6.02, S 13.87.

1-Ethyl-3-methanesulfonyl-4(1*H*)-quinolinone (**6b**):

mp 184-185 °C. MS (EI, 70 eV): m/z (%) = 251 (M^+, 100), 187 (M-SO_2, 77). ^{1}H NMR ($CDCl_3$), δ: 1.58 (t, *J*=7.2 Hz, 3H, $CH_2C\mathbf{H}_3$), 3.36 (s, 3H, $C\mathbf{H}_3$), 4.32 (q, *J*=7.2 Hz, 2H, $C\mathbf{H}_2CH_3$), 7.49–7.54 (m, 1H, **H**6), 7.51–7.56 (m, 1H, **H**8), 7.76–7.81 (m, 1H, **H**7), 8.46 (s, 1H, **H**2), 8.50–8.52 (m, 1H, **H**5). *Anal*. Calcd for $C_{12}H_{13}NO_3S$: C 57.35, H 5.21, N 5.57, S 12.76. Found: C 57.67, H 5.26, N 5.69, S 13.03.

3-Methanesulfonyl-1-propyl-4(1*H*)-quinolinone (**6c**):

mp 167-169 °C. MS (EI, 70 eV): m/z (%) = 265 (M^+, 100), 201 (M-SO_2, 59). ^{1}H NMR ($CDCl_3$), δ: 1.06 (t, *J*=7.2 Hz, 3H, $CH_2CH_2C\mathbf{H}_3$), 1.92–2.00 (m, 2H, $CH_2C\mathbf{H}_2CH_3$), 3.37 (s, 3H, $C\mathbf{H}_3$), 4.20 (t, *J*=7.2 Hz, 2H, $C\mathbf{H}_2CH_2CH_3$), 7.50–7.55 (m, 2H, **H**6, **H**8), 7.75-7.80 (m, 1H, **H**7), 8.42 (s, 1H, **H**2), 8.50–8.53 (m, 1H, **H**5). *Anal*. Calcd for $C_{13}H_{15}NO_3S$: C 58.85, H 5.70, N 5.28. Found: C 58.53, H 5.50, N 5.31.

3-Methanesulfonyl-1-(2-propyl)-4(1*H*)-quinolinone (**6d**):

mp 198-199 °C. MS (EI, 70 eV): m/z (%) = 265 (M^+,100), 201 (M-SO_2, 48). ^{1}H NMR ($CDCl_3$), δ: 1.64 (d, *J*=6.4 Hz, 6H, $(C\mathbf{H}_3)_2$), 3.38 (s, 3H, $C\mathbf{H}_3$), 4.95–5.01 (m, 1H, $C\mathbf{H}(CH_3)_2$), 7.50–7.53 (m, 1H, **H**6), 7.66–7.68 (m, 1H, **H**8), 7.77–7.81 (m, 1H, **H**7), 8.53–8.56 (m, 1H, **H**5), 8.58 (s, 1H, **H**2). *Anal*. Calcd for $C_{13}H_{15}NO_3S$: C 58.85, H 5.70, N 5.28. Found: C 58.71, H 5.90, N 5.42.

3-Methanesulfonyl-1-methylthiomethyl-4(1*H*)-quinolinone (**6e**):

mp 223-224 °C. MS (EI, 70 eV): m/z (%) = 283 (M^+, 48), 236 (M-SO_2, 100). ^{1}H NMR ($CDCl_3$), δ: 2.23 (s, 3H, $SC\mathbf{H}_3$), 3.37 (s, 3H, $SO_2C\mathbf{H}_3$), 5.24 (s, 2H, $C\mathbf{H}_2SCH_3$), 7.53–7.57 (m, 1H, **H**6), 7.58–7.61 (m, 1H, **H**8), 7.78–7.82 (m, 1H, **H**7), 8.47 (s, 1H, **H**2), 8.50–8.52 (m, 1H, **H**5). *Anal*. Calcd for $C_{12}H_{13}NO_3S_2$: C 50.87, H 4.62, N 4.94, S 22.63. Found: C 51.03, H 4.40, N 4.80, S 22.03.

3-Ethanesulfonyl-1-methyl-4(1*H*)-quinolinone (**6f**):

mp 157-159 °C. MS (EI, 70 eV): m/z (%) = 251 (M^+, 17) 158 (M- $SO_2CH_2CH_3$, 100). ^{1}H NMR ($CDCl_3$) δ: 1.41 (t, *J*=7.3 Hz, 3H $CH_2C\mathbf{H}_3$), 3.65 (q, *J*=7.3 Hz, 2H, $C\mathbf{H}_2$ CH_3), 3.94 (s, 3H, $C\mathbf{H}_3$), 7.51-7.54 (m, 2H, **H**6, **H**8), 7.78-7.81 (m,1H, **H**7), 8.39 (s, 1H, **H**2), 8.46-8.47 (m, 1H, **H**5). *Anal*. Calcd for $C_{12}H_{13}NO_3S$: C 57.35, H 5.21, N 5.57, S 12.76. Found: C 57.16, H 5.10, N 5.65, S 12.97.

3-Ethanesulfonyl-1-ethyl-4(1*H*)-quinolinone (**6g**):

mp 116-118 °C. MS (CI, 70 eV): m/z (%) = 265 (M^+ +1, 100).^{1}H NMR ($CDCl_3$), δ: 1.29 (t, *J*= 7,4 Hz, 3H, $SO_2CH_2C\mathbf{H}_3$), 1.57 (t, *J*=7.3 Hz, 3H, $NCH_2C\mathbf{H}_3$), 3.58 (q, *J*= 7,4 Hz, 2H, $SO_2C\mathbf{H}_2CH_3$), 4.32 (q, *J*=7.3 Hz, 2H, $NC\mathbf{H}_2CH_3$), 7.49-7.55 (m, 2H, **H**6, **H**8), 7.77-7.80 (m,1H, **H**7), 8.42 (s, 1H, **H**2), 8.49-8.50 (m, 1H, **H**5). *Anal*. Calcd for $C_{13}H_{15}NO_3S$: C 58.85, H 5.70 ,N 5.28, S 12.08. Found: C 58.57, H 5.56, N 5.33, S 12.00.

3-(1-Propanesulfonyl)-1-methyl-4(1*H*)-quinolinone (**6h**):

mp 141-142 °C. MS (EI, 70 eV): m/z (%) = 265 (M^+, 1.2), 159 (M- $SO_2CH_2CH_2CH_3$, 100). ^{1}H NMR ($CDCl_3$), δ: 1.01 (t, *J*=7,4 Hz, 3H, $CH_2CH_2C\mathbf{H}_3$), 1.71-1.79 (m, 2H, $CH_2C\mathbf{H}_2CH_3$), 3.48-3.51 (m, 2H,

C**H**$_2$CH$_2$CH$_3$), 3.93 (s, 3H, C**H**$_3$), 7.48-7.51 (m, 2H, **H**6, **H**8), 7.76-7.79 (m, 1H, **H**7), 8.39 (s, 1H, **H**2), 8.41-8.43 (m, 1H, **H**5). *Anal*. Calcd for $C_{13}H_{15}NO_3S$: C 58.85, H 5.70, N 5.28. Found: C 58.63, H 5.40, N 5.29.

1-Ethyl-3-(1-propanesulfonyl)-4(1*H*)-quinolinone (**6i**):

mp 66–69 °C. MS (CI, 70 eV): m/z (%) = 279 (M^++1, 100). ^{1}H NMR ($CDCl_3$) δ: 1.04 (t, *J*=7.4 Hz, 3H, CH$_2$CH$_2$C**H**$_3$), 1.57 (t, *J*=7,3 Hz, 3H$_2$, 3H, CH$_2$-C**H**$_3$), 1.75-1.81 (m, 2H, CH$_2$C**H**$_2$CH$_3$), 3 52-3.55 (m, 2H, C**H**$_2$CH$_2$CH$_3$), 4 31 (t, *J*=7.3 Hz, 2H, C**H**$_2$CH$_3$), 7.50-7.55 (m, 2H, **H**6, **H**8), 7.77-7.80 (m,1H, **H**7), 8.42 (s, 1H, **H**2), 8.49-8.51 (m, 1H, **H**5). *Anal*. Calcd for $C_{14}H_{17}NO_3S$: C 60.19, H 6.13, N 5.01. Found: C 60.33, H 6.29, N 4.88.

1-Hexyl-3-methanesulfonyl-4(1*H*)-quinolinone (**6j**):

mp 83-84 °C. MS (EI, 70 eV): m/z (%) = 307 (M^+, 100). ^{1}H NMR ($CDCl_3$), δ: 0.82 (t, *J*=7.6 Hz, 3H, C**H**$_3$), 1.25-1.47 (m, 8H, (C**H**$_2$)$_4$), 3.34 (s, 3H, SO$_2$C**H**$_3$), 4.02 (t, *J*=7.6 Hz, 2H, NC**H**$_2$), 7.47-7.52 (m, 2H, **H**6, **H**8), 7.74-7.78 (m, 1H, **H**7), 8.40 (s, 1H, **H**2), 8.47-8.50 (m, 1H, **H**5). *Anal*. Calcd for $C_{16}H_{21}NO_3S$: C 62.52, H 6.89, N 4.56. Found: C 62.70, H 7.11, N 4.60.

X-Ray structure analysis

The diffraction data were collected with a KappaApexII diffractometer using graphite monochromated Mo Kα radiation. The structure was solved and refined using the programs SHELXS[14] and SHELXL[15] respectively. Crystals of 1,4-dihydro-4-oxo-3-(1-propanesulfonyl)quinoline (**5c**) were obtained by slow evaporation of aqueous ethanol solution at room temperature. Crystal data for **5c**: $C_{12}H_{13}NO_3S$, M = 251.29, crystal size 0.50 x 0.35 x 0.10 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 12.0856(7), b = 7.6792(5), c = 12.4887(5) Å, β = 98.846(4)°, V = 1145.3(1) Å^3, Z = 4, D_c = 1.457 g/cm^3, F_{000} = 528, Mo$K\alpha$ radiation, λ= 0.71073 Å, T = 100(2)K, $2\theta_{max}$ = 55.0º, 8985 reflections collected, 2548 unique (R_{int} = 0.034). Final *GooF* = 1.12, R = 0.067, wR = 0.1367, R indices based on 2027 reflections with $I > 2\sigma(I)$ (refinement on F^2), 159 parameters, 0 restraints. Lp and absorption corrections applied, μ = 0.278 mm^{-1}.

Crystallographic data for compound **5c** have been deposited with Cambridge Crystallographic Data Centre (CCDC deposition number 805112). Copies of the data can be obtained upon request from CCDC, 12 Union road, Cambridge CB2 1EZ, UK).

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