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NEW ROUTE TO NOVEL POLYSUBSTITUTED QUINOLINES STARTING WITH EUGENOL, THE MAIN CONSTITUENT OF *OCIMUM SANCTUM L.* OIL

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Abstract – An efficient and simple method has been reported for the synthesis of (6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q1**) starting with eugenol, the main constituent of *Ocimum sanctum L*. oil. The reaction pathway from a quinone-aci compound to the quinoline compound **Q1** was proposed on the basis of ^{1}H NMR method. **Q1** was used as a key compound for further transformation to 9 novel polysubstituted quinolines. The structure of the synthesized compounds was characterized by spectroscopic methods.

INTRODUCTION

Quinolines are an important class of heterocyclic compounds. The quinoline skeleton has been used as the basis for the design of many synthetic antimalarial,[1,2] antibacterial, antifungal,[3,4] anti-tuberculosis,[5-7] anticancer[8] compounds. Almost all these compound are polysubstituted quinolines, which have been synthesized starting from industrial petrochemical products. Moreover classical methods for quinoline synthesis often do not allow for adequate diversity and substitution on the quinoline ring system. Therefore, having new synthetic methods for preparing quinoline derivatives including a clean, efficient, large-scale and cheap technology is still needed to obtain useful poly-functionalized quinolines.

Some time ago, we had focused our attention to several main components of vegetable essential oils that, owing to their structure, could act as good substrate in order to prepare heterocyclic compounds. For example, some furoxans and metallacyclic complexes were prepared from safrole (in sassafras oil)[9,10] and from eugenol (in clove oil),[11,12] thiazolidinones and indoles were synthesized from anethole (in star anise

oil).[13]

In this context, now we present a novel route for synthesis of polysubstituted quinolines from eugenol (l-hydroxy-2-methoxy-4-allylbenzene), the main constituent of *Ocimum sanctum L.* oil (a cheap natural source for commercial extraction of eugenol).[14]

RESULTS AND DISCUSSION

The route for the preparation of the key compound to polysubstituted quinolines is described in Figure 1. Eugenoxyacetic acid, 2-methoxy-4-(2-propenyl)phenoxyacetic acid, is known to be a beneficial food additive. It is easily prepared by reaction of eugenol with monochloroacetic acid.[15] Treating with excess nitric acid in acetic acid eugenoxyacetic acid underwent an unexpected ether cleavage, a normal nitration, and then an unexpected electrophilic addition to the double bond of the side chain that led to the formation of a reactive quinone-aci compound **A**.[16] Reduction of the quinone-aci compound afforded (6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q1**).

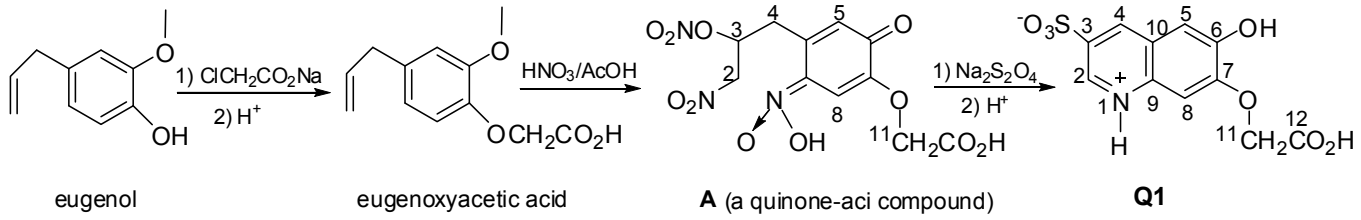


Figure 1. Synthesis the key compound (**Q1**) to polysubstituted quinolines

There are many methods of synthesis of quinoline ring. The classical syntheses such as Skraup, Doebner-von Miller, Friedländer, Pfitzinger, Conrad-Limpach, Combes are well-known. The new approaches diverse range of efficient quinoline synthesis were reviewed by V. V. Kouznetsov *et al.*,[17] however there is no similar to the method described in Figure 1. Therefore the accurately structural determination of the quinoline compound **Q1** is necessary.

In the ^{1}H NMR of **Q1**, two doublets at 8.80 and 8.24 ppm (J = 2 Hz) are assigned to H2 and H4 respectively, two singlets at 7.28 and 7.25 ppm are assigned to H5 and H8, a singlet at 4.81 ppm (2H) is associated with methylene group (H11). In the ^{13}C NMR of **Q1** there are 9 signals associated with 9 aromatic carbon atoms (C2 – C10 in Figure 2), a signal of CH_2 group (C11, at 66.30 ppm), and a signal of C=O group (C12 at 171.42 ppm). HSQC spectrum of **Q1** allows to assign the signals of C2, C4 and C11. In HMBC spectrum of **Q1** two cross peaks of H11 showed signal of C7 at 152.16 ppm, signal of C12 at 171.41 ppm.

In Figure 2 the cross peak *a* of C7 indicates that singlet at 7.28 ppm belongs to H5, as a result singlet at 7.25 ppm belongs to H8. Two cross peaks *b* and *c* of H5 show signals of C9 and C4, two cross peaks *d*

and *e* of H8 show signals of C6 and C10, respectively. The cross peaks *h*, *i* and *k* show signals of C2, C9 and C5 respectively. The cross peaks *l*, *m* and *n* show signals of C9, C3 and C4 respectively.

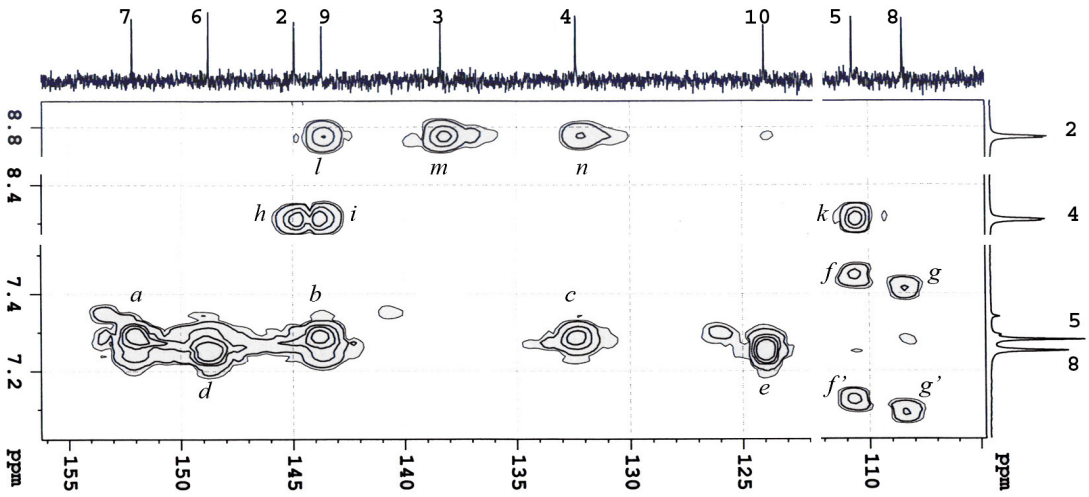


Figure 2. Partial HMBC spectrum of **Q1**

These NMR data are in good agreement with the quinoline structure of **Q1** but do not show the presence of SO_3^-, an unexpected group at 3-position of **Q1**. The mass spectra in the positive mode of **Q1** showed pseudomolecular ions $(M+H)^+$ as following, (au/%): 300/100, 301/12 (^{13}C), 302/5 (^{34}S), and negative mode mass spectra of **Q1** showed pseudomolecular ions $(M-H)^-$ as following, (au/%): 298/100, 299/12 (^{13}C), 300/5 (^{34}S). This is corresponding to molecular mass of **Q1** (299 au) which containing one S atom. In order to finally determine the structure of **Q1**, the single-crystal X-ray diffraction for it was analyzed. The results (Figure 3) show the presence of sulfonate at 3-position and **Q1** exists in a zwitterionic form (NH^+ and SO_3^-).

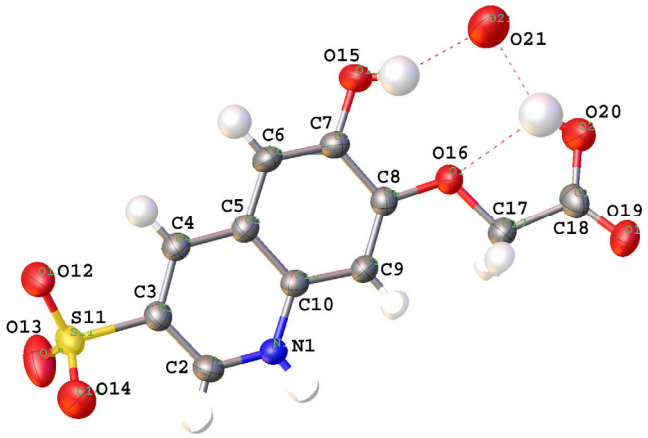
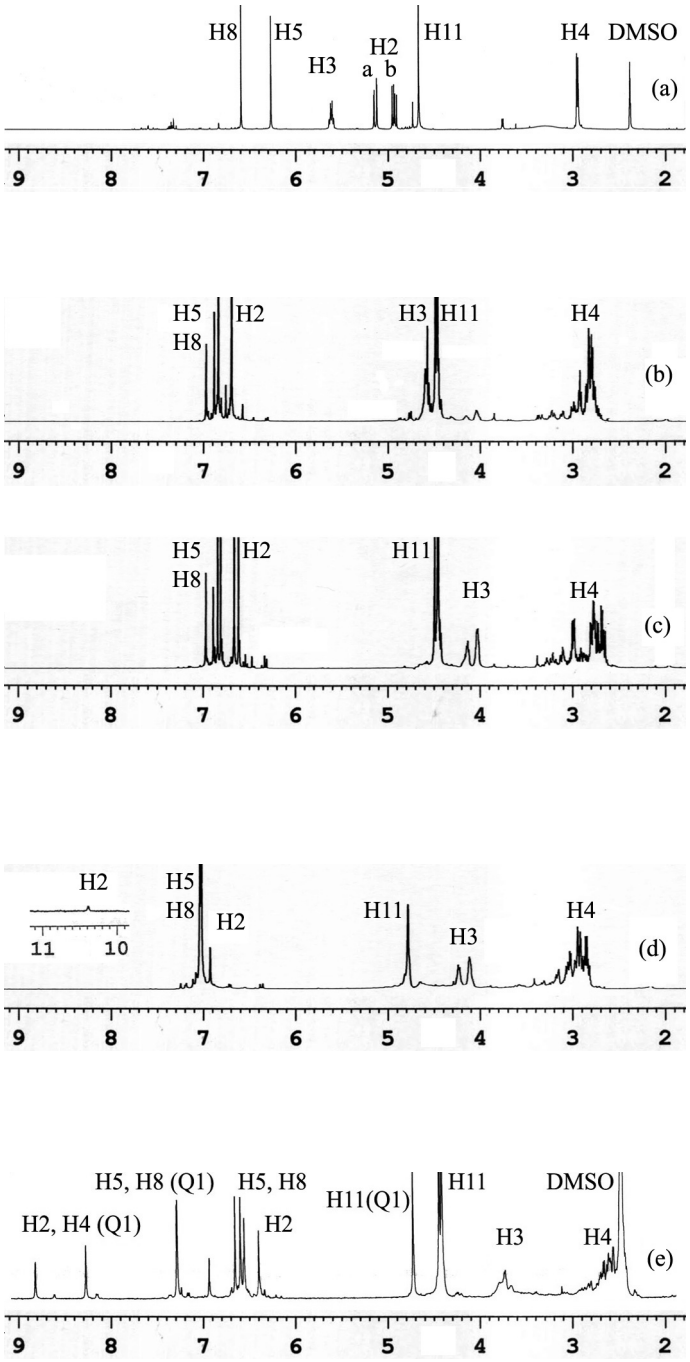


Figure 3. Atomic displacement plot of the molecular structure of **Q1**

This brings up the question: how was the quinone-aci compound **A** converted into the quinoline

compound **Q1**? In order to answer this question, reaction process of the conversion from **A** to **Q1** in sample tube was monitored with ^{1}H NMR. The representative spectra and the important remarks are presented in Figure 4.



a. Spectrum of **A**, a quinone-aci compound in d_6-DMSO (Formular in Figure 1). H8, H5: quinone protons; H2a, H2b: H_2C-NO_2; H3: HC-ONO_2; H4: H_2C-Ar.

b. Spectrum recorded immediately after dissolution of **A**, $Na_2S_2O_4$, NaOD and D_2O in a sample tube. H8, H5: aromatic protons; H2: HC=NOOH (aci form); H3: HC-OH; H4: H_2C-Ar. These signals associate with **A1** in Figure 5 and its nitro tautomer form.

c. Spectrum recorded 6 hours after dissolution of **A**, $Na_2S_2O_4$, NaOD in D_2O. H8, H5: aromatic protons; H2: $HC=NOO^-$; H3: HC-OH; H4: H_2C-Ar. These signals associate with **A2** and **A1** in Figure 5.

d. Spectrum recorded after addition of CF_3COOH into the sample tube (after spectrum *c* has been recorded). H8, H5: aromatic protons; H3: HC-OH; H4: H_2C-Ar. The very weak singlets at 10.4 and 6.9 ppm possibly belong to H2 of CH=O and CH=N, respectively. These associate with **A3** and **A4.**

e. Spectrum recorded 72 hours after addition of CF_3COOH, and precipitated solid was dissolved by d_6-DMSO. H2, H4, H8, H5 of quinoline **Q1** give rise to 4 singlets at 7.3-8.9 ppm; H11 of **Q1** gives rise to the singlet at 4.75 ppm. Other signals associate with **A2**, **A3**, **A4** and **A5**.

Figure 4. Representative spectra recorded in reaction process from **A** to **Q1**

On the basis of data in Figure 4, we suggest a reaction pathway for the conversion from **A** to **Q1** as in Figure 5.

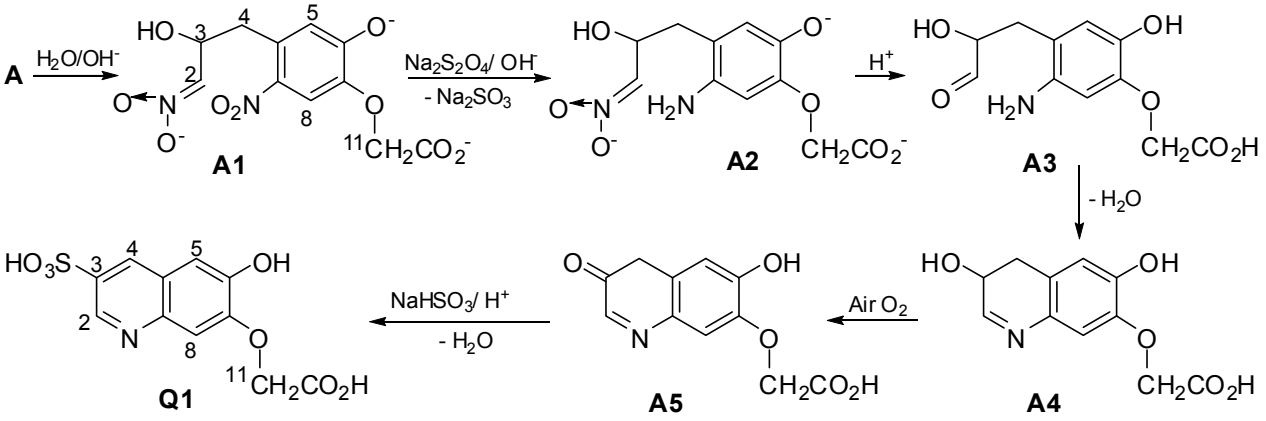


Figure 5. The reaction pathway from quinone-aci compound **A** to quinoline compound **Q1**

When treating with $Na_2S_2O_4/OH^-$ during 6 hours the phenol-nitro compoud **A1** (a tautomer of the quinone-aci compound **A**) was reduced into amino compound **A2** (Figure 5). After the addition of trifloroacetic acid into the reaction mixture the –CH=NOO$^-$ group of **A2** was transformed into –CH=O group to give **A3** (Nef reaction[18]). The condensation of –CH=O and H_2N- groups caused the cyclization to form **A4**, which was oxidized by air oxygen to **A5**. The addition of $NaHSO_3$ into carbonyl group of **A5** followed by the elimination of H_2O afforded the target compound **Q1**. In fact the stage from **A** to **A2** (alkaline stage) took place for 6 hours while the stage from **A2** to **Q1** (from the addition of trifloroacetic acid to the appearance of a significant amount of the precipitate, acidic stage) took place for more than 72 hours. The acidic stage can be accelerated by addition sulfuric acid and heating at 90 ^oC.

The other polysubstituted quinolines were prepared starting from **Q1** as shown below:

i) Esterification of **Q1** with acetic anhydride afforded (6-acetoxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q2**). In the NMR spectra of **Q2**, for $CH_3C=O$ group: proton signal appeared at 2.38 ppm, carbon signals appeared at 168.41 and 20.33 ppm. In the HMBC of **Q2** signal of proton H2 (9.32 d; J 1.5) has not cross peak with signal of the carbonyl carbon (168.41) indicating that the $CH_3C=O$ group does not attached to N of quinoline ring.

ii) Esterification of **Q1** with methanol gave methyl ester **Q3**, which was transformed into acylhydrazine **Q4** (Experimental and Table 1).

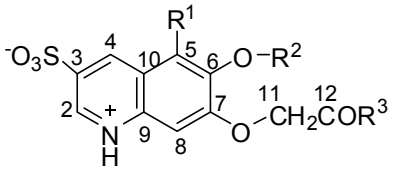
iii) Nitration of **Q1** leaded to (5-nitro-6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q5**), which was reduced into amino compound **Q6** (Experimental and Table 1). The HSQC and HMBC spectra of **Q5** and **Q6** show the nitro group and the amino group are attached to C5 of the quinoline ring.

iv) Chlorination of **Q1** afforded (5-chloro-6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q7**, Experimental and Table 1). The HMBC spectrum of **Q7** shows Cl is attached to C5 of the quinoline ring.

v) Bromination of **Q1** afforded (5-bromo-6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q8**), which was transformed into methyl ester **Q9** and then into acylhydrazine **Q10** (Experimental and Table 1). The HMBC spectra of **Q8** and **Q9** show Br is attached to C5 of the quinoline ring.

The structure of **Q1** - **Q10** was established by IR, NMR, and ESI MS methods. The assignment of ^{1}H NMR and ^{13}C NMR signals (Tables 1, 2) of the reported compounds was based on their chemical shift, spin-spin splitting patterns, and 2D NMR spectra.

Table 1. The ^{1}H signals of the reported compounds, δ (ppm), J (Hz)



	R^1	R^2	R^3	H2	H4	H5	H8	H11	Others
Q1*	H	H	ONa	8.77 d; J 1.5	8.31 d; J 1.5	7.25 s	7.28 s	4.81 s	-
Q1	H	H	OH	9.04 d; J 1	8.98 d; J 1	7.69 s	7.58 s	5.00 s	-
Q2	H	MeCO	OH	9.32 d; J 1.5	9.11 d; J 1.5	8.19 s	7.58 s	4.99 s	Me: 2.38 s
Q3	H	H	OMe	9.12 d; J 1.5	9.06 d; J 1.5	7.64 s	7.43 s	5.13 s	Me: 3.76 s
Q4	H	H	$NHNH_2$	8.79 d; J 1.5	8.23 d; J 1.5	7.39 s	7.29 s	4.72 s	$NHNH_2$:9.72; 4.42
Q5	NO_2	H	OH	9.08 s	8.27 s	-	7.62 s	5.12 s	-
Q6	NH_2	H	OH	8.72 d; J 1	8.48 d; J 1	-	6.87 s	4.22 s	NH_2: 5.14 s
Q7	Cl	H	OH	9.17 d; J 1	8.87 d; J 1	-	7.44 s	5.07 s	-
Q8	Br	H	OH	9.10 d; J 1	8.81 d; J 1	-	7.47 s	5.06 s	-
Q9	Br	H	OMe	9.07 s	8.77 s	-	7.45 s	5.17 s	Me: 3.75 s
Q10	Br	H	$NHNH_2$	8.80 d; J 1.5	8.44 d; J 1.5	-	7.43 s	4.77 s	$NHNH_2$: 4.24; br.

(*) Solvent: d_6-DMSO in presence of NaOD (in order to increase solubility); for the others: d_6-DMSO alone; br.: Broadened.

Table 2. The ^{13}C signals of the reported compounds: δ (ppm), the formulas: see Table 1

	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	Others
Q1*	144.94	138.37	132.37	110.70	148.77	152.16	108.47	143.70	124.00	66.30	171.42	-
Q2	143.87	139.65	140.29	122.00	142.08	154.57	103.90	139.18	123.27	65.79	168.74	MeCO: 20.33; 168.41
Q3	140.07	138.82	138.49	110.14	150.16	154.29	101.52	134.66	125.14	65.57	168.16	Me: 52.21
Q4	145.26	143.35	139.27	110.06	147.26	149.88	108.89	130.10	123.12	67.08	166.10	-
Q5	143.08	141.26	138.33	115.77	144.70	151.38	108.90	132.85	127.05	66.00	169.15	-
Q6	144.79	137.28	126.16	131.22	135.65	153.41	106.98	142.33	114.12	74.66	173.13	-
Q7	141.25	140.45	133.16	122.37	146.40	153.45	101.96	136.45	113.66	66.03	169.05	-
Q8	141.77	140.70	134.75	123.35	147.31	152.63	103.18	137.72	104.93	65.92	168.70	-
Q9	142.55	140.65	133.75	123.20	146.95	152.03	104.28	138.67	105.02	65.82	168.27	Me: 52.23
Q10	142.60	140.13	128.98	122.56	144.95	150.35	104.20	140.12	108.52	67.41	165.97	-

The data in tables 1 and 2 are good agreement with the structure of the reported compounds. The molecular weights of **Q1** - **Q10** determined from ESI MS (see Experimental) correspond with their molecular formula.

In conclusion, a new route for synthesis of polysubstituted quinolines from eugenol, a natural arylolefin, was firstly reported. The reaction pathway from the quinone-aci compound to the quinoline compound was proposed on the basis of ^{1}H NMR method.

EXPERIMENTAL

General

IR spectra were recorded on an IMPACK-410 NICOLET spectrometer in KBr discs at 400–4000 cm^{-1}. ESI mass spectra were recorded using Agilent LC-MSD-Trap-SL series 1100 spectrometer. NMR spectra were recorded on a Bruker AVANCE 500 MHz spectrometer, in d_6-DMSO with TMS as the internal standard, at 298–300 K. C, H, and N were analyzed in Analytical Laboratory – Institute of Chemistry of Natural Compounds (in Hanoi). Single-crystal X-ray diffraction is recorded on a Bruker SMART6000 diffractometer (fine-focus sealed tube, CuKα radiation, crossed Göbel mirrors) at 100K. The intensity data were corrected for Lorentz and polarization effects, and for absorption (SADABS).[19] The structure was solved by direct methods (SHELXS-97)[20] and refined by full-matrix least-squares based on F^2 using SHELXL-97.[21] Hydrogen atoms were located in the calculated positions.

Preparation

(6-Hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q1**). 10.92 g (0.04 mol) of the quinon-aci compound **A** (previously prepared in reference[16]) was added to a solution of 41.76 g (0.24 mol) $Na_2S_2O_4$, 40 mL concentrated ammonia and 80 mL H_2O during 30 min. The resulting solution was stirred at room temperature for 6 h. and then acetic acid was added (until pH 2). The reaction mixture was kept openly at air at room temperature for 72 h. The crystalline compound obtained was isolated by filtration and washed with water. The crude product was recrystallized from EtOH/water 2:1 by volume to afford the product as light yellow crystals, decomposed at above 250 ^oC. The yield was 8.13 g (68%). IR (cm^{-1}): 3470, 3234 (OH); 3075, 2930 (C-H); 1680, 1632 (C=O); 1610, 1503 (ring). ^{1}H NMR and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): +MS, 300/100 ($M+H^+$), -MS: 298/100 ($M-H^+$). *Anal.* Calcd. for $C_{11}H_9NO_7S$ (M 299.26): C, 44.15; H, 3.03; N, 4.68. Found: C, 44.46; H, 3.26; N, 4.42. For single-crystal X-ray diffraction **Q1** was recrystallized from a solution of 1M HCl.

(6-Acetoxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q2**). 299 mg (1 mmol) **Q1** was added to a solution of 0.4 mL H_2SO_4 in 6 mL Ac_2O. The reaction mixture was stirred at 40-50 ^oC for 2 h. The solid obtained was isolated by filtration and washed with water, EtOH and recrystallized from water. The yield was 188

mg (55%), light yellow crystals, decomposed above 260 °C. IR (cm^{-1}): 3512, 3480 (OH); 3082, 3046, 2931, 2852 (C-H); 1758, 1645 (C=O); 1601, 1503 (ring). ^1H NMR and ^{13}C NMR see Tables 1 and 2. *Anal.* Calcd. for $C_{13}H_{11}NO_8S$ (M 341.29): C, 45.75; H, 3.25; N, 4.10. Found: C, 45.48; H, 3.16; N, 4.32.

Methyl (6-hydroxy-3-sulfoquinolin-7-yloxy)acetate (**Q3**). 150 mg (0.5 mmol) **Q1** and 0.01 mL H_2SO_4 were added to a solution of 2 mL DMSO in 5 mL MeOH. The reaction mixture was refluxed for 12 h. The crystalline compound obtained was isolated by filtration and washed with EtOH, and then EtOAc. The yield was 102 mg (65%), light yellow crystals, decomposed above 265 °C. IR (cm^{-1}): 3449, 3234 (OH); 3060, 2969 (C-H); 1784 (C=O); 1608, 1521 (ring). ^1H NMR and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): +MS, 314/4 ($M+H^+$), -MS: 312/100 ($M-H^+$). *Anal.* Calcd. for $C_{12}H_{11}NO_7S$ (M 313.28): C, 46.01; H, 3.54; N, 4.47. Found: C, 46.37; H, 3.28; N, 4.19.

[(6-Hydroxy-3-sulfoquinolin-7-yloxy)acetyl]hydrazine (**Q4**). 154 mg (0.5 mmol) **Q3** and 0.5 mL solution of $N_2H_4.H_2O$ 80% were added to 15 mL EtOH. The reaction mixture was refluxed for 10 h. and then was evaporated to volume 5 mL. The resulting solution was cooled to 5 °C. The crystalline compound obtained was isolated by filtration and recrystallized from EtOH/water 3:1 by volume. The yield was 97 mg (62%), light yellow crystals, decomposed above 270 °C. IR (cm^{-1}): 3506, 3334, 3227 (OH, NH); 3048, 2933 (C-H); 1690 (C=O); 1508, 1490 (ring). ^1H NMR and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): +MS, 314/100 ($M+H^+$), -MS: 312/100 ($M-H^+$). *Anal.* Calcd. for $C_{12}H_{11}NO_7S$ (M 313.28): C, 46.01; H, 3.54; N, 4.47. Found: C, 46.38; H, 3.44; N, 4.21.

(6-Hydroxy-5-nitro-3-sulfoquinolin-7-yloxy)acetic acid (**Q5**). To a stirring solution of 299 mg (1 mmol) **Q1** and 1 mL H_2SO_4 in 10 mL AcOH was slowly added 1 mL HNO_3 and stirred at room temperature for 2 h. The reaction mixture was kept at room temperature for 12 h. The crystalline compound obtained was isolated by filtration and washed with water and EtOH. The crude product was recrystallized from EtOH/water 3:1 by volume to afford the product as yellow crystals, decomposed above 250 °C. The yield was 190 mg (55%). IR (cm^{-1}): 3592, 3513 (OH); 3094, 2950 (C-H); 1730 (C=O); 1629, 1503, 1434 (ring). ^1H NMR and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): +MS, 345/2 ($M+H^+$), -MS: 343/100 ($M-H^+$). *Anal.* Calcd. for $C_{11}H_8N_2O_9S$ (M 344.25): C, 38.38; H, 2.34; N, 8.14. Found: C, 38.61; H, 2.12; N, 7.89.

(5-Amino-6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q6**). To 6 mL of solution 1M NaOH were added 1.1 g (6 mmol) $Na_2S_2O_4$ and then 344 mg (1 mmol) **Q5.** The reaction mixture was heated at 90 °C for 5 h. The solid obtained was isolated by filtration, washed with water and recrystallized from MeCN/water 2:1 by volume to afford the product as yellow crystals, decomposed above 250 °C. The yield was 160 mg (51%). IR (cm^{-1}): 3430, 3388, 3288 (OH, NH); 3089, 2960, 2932 (C-H); 1666 (C=O); 1628, 1510, 1480 (ring). ^1H NMR and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): -MS, 313/38 ($M-H^+$). *Anal.* Calcd. for $C_{11}H_{10}N_2O_7S$ (M 314.27): C, 42.04; H, 3.21; N, 8.91. Found:

C, 39.86; H, 3.43; N, 9.18.

(5-Chloro-6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q7**). 299 mg (1 mmol) **Q1** was dissolved in 10 mL solution of concentrated HCl/water 1:1. To the resulting solution 60 mg $KClO_3$ was added at 40 ^oC for 30 min. The solid obtained was isolated by filtration, washed with water and recrystallized from water to afford the product as light yellow crystals, decomposed above 280 ^oC. The yield was 227 mg (62%). IR (cm^{-1}): 3490 (OH); 3089, 2925 (C-H); 1740, 1643 (C=O); 1620, 1592, 1503 (ring). ^1H NMR and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): +MS, 334/100 (^{35}Cl), 335/12 (^{13}C), 336/29 (^{37}Cl + ^{34}S), 337/6 (^{13}C), 338/2 (^{34}S), ($M+H^+$); -MS: 332/100 (^{35}Cl), 333/16 (^{13}C), 334/32 (^{37}Cl + ^{34}S), 335/5 (^{13}C), 336/2 (^{34}S), ($M-H^+$). *Anal.* Calcd. for $C_{11}H_8ClNO_7S$ (M 333.70): C, 39.59; H, 2.42; N, 4.20. Found: C, 39.30; H, 2.55; N, 4.47.

(5-Bromo-6-hydroxy-3-sulfoquinolin-7-yloxy)acetic acid (**Q8**). To a solution of 299 mg (1 mmol) **Q1** in 3 mL DMSO was added 0.2 mL Br_2 and stirred for 5 h. The reaction mixture poured into 5 mL water. After 5 h. the solid obtained was isolated by filtration, washed with water and recrystallized from water to afford the product as light yellow crystals, decomposed above 240 ^oC. The yield was 265 mg (70%). IR (cm^{-1}): 3363 (OH); 3048, 2933, 2855 (C-H); 1726, 1654 (C=O); 1592, 1503 (ring). ^1H NMR and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): +MS, 378/78 (^{79}Br), 379/11 (^{13}C), 380/73 (^{81}Br), 381/12 (^{13}C), 382/5 (^{34}S), ($M+H^+$); -MS, 376/100 (^{79}Br), 377/10 (^{13}C), 378/95 (^{81}Br), 379/13 (^{13}C), 380/4 (^{34}S), ($M-H^+$). *Anal.* Calcd. for $C_{11}H_8BrNO_7S$ (M 378.15): C, 34.94; H, 2.13; N, 3.70. Found: C, 35.21; H, 2.28; N, 3.38.

Methyl (5-bromo-6-hydroxy-3-sulfoquinolin-7-yloxy)acetate (**Q9**). A solution of 378 mg (1 mmol) **Q8**, 2 mL DMSO and 0.1 mL H_2SO_4 in 5 mL MeOH was refluxed for 6 h. The reaction mixture was cooled to room temperature. The solid obtained was isolated by filtration, washed with EtOH and recrystallized from EtOH/water 1:1 by volume to afford the product as needle yellow crystals, decomposed above 234 ^oC. The yield was 255 mg (65%). IR (cm^{-1}): 3420 (OH); 3081, 3024, 2940 (C-H); 1769 (C=O); 1620, 1550, 1493 (ring). ^1H- and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): -MS, 390/100 (^{79}Br), 391/16 (^{13}C), 392/94 (^{81}Br + ^{34}S), 393/14 (^{13}C), 394/6 (^{34}S). *Anal.* Calcd. for $C_{12}H_{10}BrNO_7S$ (M 392.18): C, 36.75; H, 2.57; N, 3.57. Found: C, 36.47; H, 2.78; N, 3.52.

[(5-Bromo-6-hydroxy-3-sulfoquinolin-7-yloxy)acetyl]hydrazine (**Q10**). A solution of 196 mg (0.5 mmol) **Q9**, 2 mL DMSO and 1 mL solution of $N_2H_4.H_2O$ 80% in 5 mL EtOH was refluxed for 8 h. The reaction mixture was cooled to room temperature. The solid obtained was isolated by filtration, washed with EtOH and recrystallized from EtOH/water 1:1 by volume to afford the product as light yellow crystals, decomposed above 235 ^oC. The yield was 135 mg (72%). IR (cm^{-1}): 3322, 3221 (OH, NH); 3080, 2922, 2851 (C-H); 1659 (C=O); 1628, 1543, 1457 (ring). ^1H- and ^{13}C NMR see Tables 1 and 2. ESI MS, m/z (au)/relative intensity (%): +MS, 392/100 (^{79}Br), 393/16 (^{13}C), 394/95 (^{81}Br + ^{34}S), 395/8 (^{13}C), 396/3

(^{34}S); -MS, 390/95 (^{79}Br), 391/15 (^{13}C), 392/100 (^{81}Br + ^{34}S), 393/13 (^{13}C), 394/5 (^{34}S). *Anal.* Calcd. for $C_{11}H_{10}BrN_3O_6S$ (M 392.18): C, 33.69; H, 2.57; N, 10.71. Found: C, 33.96; H, 2.36; N, 10.45.

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