The Synthesis of Substituted Quinolinols. II.

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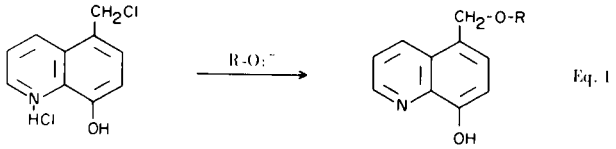
The author wishes to report the synthesis of several new organic compounds as a result of a study in this Laboratory of 5-substituted-8-quinolinols as corrosion inhibitors. The previous series (1) of 8-quinolinols was prepared by alkylation of alkoxides and amines with 5-chloromethyl-8-quinolinol hydrochloride (I) Eq. 1.

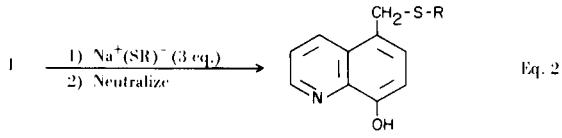


Eq. 1

I

The amines in this series showed inhibitory and bactericidal activity (2). A logical extension of this work was the alkylation of carbanions and mercaptides. The sulfides were of particular interest because of the large number of electrons on sulfur.

Four sulfides were prepared in good yield by the alkylation of the sodium mercaptide, generated *in situ*, with 5-chloromethyl-8-quinolinol hydrochloride (Eq. 2).



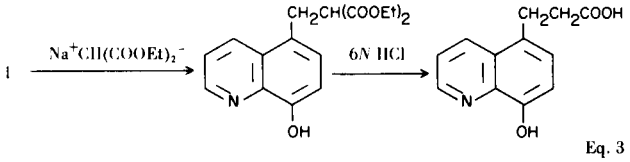
Eq. 2

II, R = $(CH_2)_2COOH$, 62.7%
III, R = CH_2COOH, 51.2%
IV, R = $CH_2COOCH_2CH_3$, 52.5%
V, R = $(CH_2)_2N(CH_2CH_3)_2$, 60%

As indicated, three quivalents of mercaptide were found to give the highest yields of sulfide. To further characterize II, the ester, VI, was prepared by Fischer esterification. The NMR spectra and combustion analyses confirmed the structures of the products. In VI, R = $CH_2CH_2CO_2CH_2CH_3$

Preliminary tests for inhibitory activity were performed in a highly caustic cleaner. Since compounds IV and VI contain esters, they were not tested in this medium. Compounds II, III and V were active corrosion inhibitors but lacked a reuse capability in this highly caustic cleaner. Compound V was the most effective inhibitor. A recent report (3) on metal-mercaptoethylamine complexes lends support to further investigation of V and similar compounds.

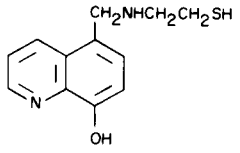
In order to determine the importance of the sulfur atom in compounds II and III, compound VIII was prepared by acidic decarbethoxylation of VII. Compound VII was obtained in fair yield from a malonic ester synthesis (Eq. 3). Compound VIII had little activity as a corrosion inhibitor, but the shorter chain length might be used as an explanation for the lack of activity. A synthetic program has been initiated to obtain compounds with longer chains to compare with II and III.



Eq. 3

VII, 62.5% VIII, 63%

Since compound V showed the greatest activity as an inhibitor, compounds of this type will be investigated further. From a recent report (3) on metal-mercaptoethylamine complexes, compounds similar to IX will be synthesized and tested.



IX

EXPERIMENTAL (4)

5-Chloromethyl-8-quinolinol (I).

Compound I was prepared by the method described by Kolobielski (1).

5-(4-Carboxy-2-thiabutyl)-8-quinolinol (II).

A sodium ethoxide solution was prepared by dissolving 6.9 g. (0.3 mole) of sodium metal in 250 ml. of dry ethanol. To this solution was added 13.1 ml. (0.15 mole) of 3-thiopropanoic acid and 11.5 g. (0.05 mole) of 5-chloromethyl-8-quinolinol hydrochloride. The reaction was stirred and refluxed for 5 hours. The inorganic salts were precipitated with ether and collected by filtration. The ether-washed salts were dissolved in 100 ml. of 30% acetic acid and this solution poured into 100 ml. of 30% sodium acetate solution. A yellow solid crystallized from solution upon standing and was collected by filtration. Recrystallization from hot methanol gave 7.4 g. (62.7%) of yellow needles, m.p. 143-144°.

Anal. Calcd. for $C_{13}H_{13}NO_3S$: C, 59.30; H, 4.98; N, 5.32. S, 12.18. Found: C, 59.30; H, 5.09; N, 5.28; S, 12.31.

5-(3-Carboxy-2-thiapropyl)-8-quinolinol (III).

Compound III was prepared in the same manner as II using 10.5 ml. of thioglycolic acid. Recrystallization from hot methanol yielded 6.4 g. (51.5%) of yellow solid, m.p. 194-197°.

Anal. Calcd. for $C_{12}H_{11}NO_3S$: C, 57.82; H, 4.45; N, 5.62; S, 12.86. Found: C, 57.97; H, 4.63; N, 5.65; S, 12.93.

5-(3-Carbethoxy-2-thiapropyl)-8-quinolinol (IV).

Sodium metal (3.45 g., 0.15 mole) was dissolved in 150 ml. of absolute ethanol. After adding 16.4 ml. (0.15 mole) of ethyl mercaptoacetate, 11.5 g. (0.05 mole) of 5-chloromethyl-8-quinolinol hydrochloride was added portionwise. After refluxing 5 hours, the reaction mixture was neutralized with ethanolic hydrogen chloride. The solid precipitate (sodium chloride) was removed by filtration and the ethanol evaporated. The solid residue was dissolved in hot ether containing a small amount of ethanol. Upon cooling, 7.25 g. (52.5%) of product was collected, m.p. 99-100°.

Anal. Calcd. for $C_{14}H_{15}NO_3S$: C, 60.63; H, 5.45; N, 5.05; S, 11.56. Found: C, 60.59; H, 5.36; N, 5.10; S, 11.46.

5-(4-Diethylamino-2-thiabutyl)-8-quinolinol (V).

To sodium ethoxide (0.3 mole) in 200 ml. of ethanol was added 25.45 g. (0.15 mole) of diethylaminoethanethiol hydrochloride followed by 11.5 g. (0.05 mole) of 5-chloromethyl-8-quinolinol hydrochloride. After refluxing 2 hours, the reaction mixture was neutralized to *p*H 8 and the ethanol evaporated. The residue was partitioned between ether and water at *p*H 8. After drying and evaporating the ether, the solid residue was crystallized from ether containing a small amount of methanol; yielding 8.7 g. (60%) of V, m.p. 76-77°.

Anal. Calcd. for $C_{16}H_{22}N_2OS$: C, 66.17; H, 7.64; N, 9.65; S, 11.04. Found: C, 66.23; H, 7.74; N, 9.80; S, 11.08.

5-(4-Carbethoxy-2-thiabutyl)-8-quinolinol (VI).

Hydrogen chloride was bubbled into a suspension of 2.63 g. (0.011 mole) of II in 50 ml. of ethanol until the solution was saturated at 0-5°. The solution was protected from moisture and allowed to warm to room temperature. After standing overnight, the reaction mixture was heated at reflux for 4 hours and the solvent removed *in vacuo*. The residue was dissolved in 30% sodium acetate (100 ml.) and extracted with ethyl acetate. After drying and evaporating the solvent, the residue was dissolved in hot ether. Upon cooling white needles of VI crystallized from solution in 78% yield (2.5 g.), m.p. 83-84°.

Anal. Calcd. for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81; S, 11.00. Found: C, 61.79; H, 5.93; N, 4.80; S, 10.95.

5-(2,2-Dicarbethoxyethyl)-8-quinolinol (VII).

A sodium ethoxide solution was prepared from 6.9 g. (0.3 mole) of sodium and 200 ml. of absolute ethanol. Diethyl malonate (60 ml.) was added slowly to the ethoxide solution. After adding 23.0 g. (0.10 mole) of 5-chloromethyl-8-quinolinol hydrochloride, the reaction mixture was stirred for ½ hour and then refluxed for 1 hour. After standing overnight, the solution was neutralized with ethanolic hydrogen chloride. The precipitate of sodium chloride was collected and excess hydrogen chloride was added to precipitate the crude salt. The salt was collected, and washed with ether; yielding 22 g. (62.5%).

The crude hydrochloride was converted to the free base for analysis by neutralization and extraction into ethyl acetate. Crystallization from ether-hexane gave a solid with m.p. 80-81°.

Anal. Calcd. for $C_{17}H_{19}NO_5$: C, 64.33; H, 6.04; N, 4.42. Found: C, 64.53; H, 6.03; N, 4.42.

5-(2-Carboxyethyl)-8-quinolinol (VIII).

Curde 5-(2,2-dicarbethoxyethyl)-8-quinolinol hydrochloride (10.6 g., 0.03 mole) was suspended in 30 ml. of 6*N* hydrochloric acid and heated at reflux temperature for 3 hours. The hydrochloric acid was evaporated *in vacuo* and the residue dissolved in water. After pouring into 100 ml. of 30% sodium acetate, an orange solid precipitated and was collected by filtration. Crystallization from 2-propanol yielded 4.1 g. (63%) of solid product, m.p. 216-217°.

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.11; N, 6.45. Found: C, 66.54; H, 5.14; N, 6.46.

REFERENCES

(1) M. Kolobielski, *J. Heterocyclic Chem.*, 3, 275 (1966).

(2) Unpublished results of screening tests.

(3) R. T. Wragg, *J. Chem. Soc.* (C), 2087 (1969).

(4) Melting points are uncorrected. Combustion analyses were performed by Micro-tech Laboratories, Inc. Skokie, Ill.