TABLE II

LIQUID PRODUCTS FROM BUTADIENE PYROLYSIS, RUN 2

Amount, g.	Description	B. p. °C.	Mm.	F. p., °C.	$n^{20}D$	Probable composition
2.5	Colorless liq.	39–42.5		−90	1.4388	Cyclopentadiene
1.7	Colorless liq.	*ca.* 70		−15	1.4807	
2.6	Colorless liq.	78		0.1	1.4967	Mostly benzene
27.6	Colorless liq.	79.5		3.5	1.5000	Benzene
2.8	Colorless liq.	41–42	60	−96	1.4951	Toluene
1.5	Sl. yellow	50–65	60	−70	1.5037	Ethylbenzene, xylenes and dimethylfulvene
1.0	Yellow	66.6	57	−60	1.5251	Dimethylfulvene
2.7	Sl. yellow	59–62	39	−45	1.5383	Styrene
0.7	Yellow	64–65	40	Glass −82	1.5240	
0.8	Colorless liq.	46.5	10	Glass −80	1.5268	
9.0	White solid			75		Naphthalene

the previously reported products, cyclopentadiene, styrene and dimethylfulvene, a yellow hydrocarbon, have been identified. The presence of two higher boiling yellow fractions is indicated, but they have not been identified.

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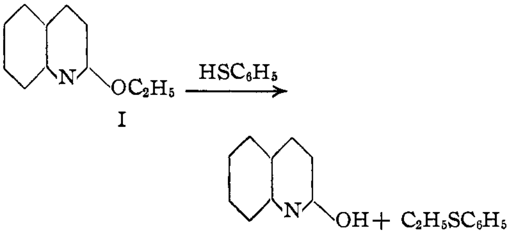
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Reactions of Thiols with Some Alkyl and Aryl Heterocyclic Ethers

BY GABRIELLO ILLUMINATI AND HENRY GILMAN

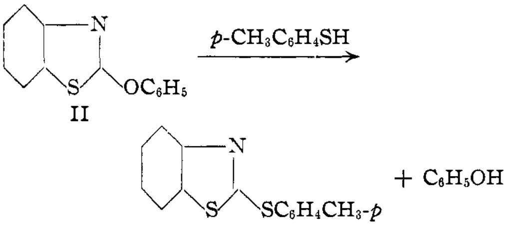
Recent work[1] on the action of organolithium compounds on some 2-substituted quinolines has emphasized the special character of the 2-position in quinoline. The present study describes the reactions of aryl thiols on some alkyl and aryl 2- and 4-quinolyl ethers and on corresponding derivatives of 2-benzothiazolyl and 2-benzoxazolyl ethers.

The 2-ethoxy compounds of quinoline (I), benzothiazole and benzoxazole are known to be cleaved by hydrogen chloride[2] to form ethyl chloride and the corresponding 2-hydroxy derivatives. We have now found that a similar cleavage occurs by the action of aryl thiols on these ethoxy compounds at 150–170°, in accordance with the following typical reaction.



(1)

This alkylating reaction appears to be general, for 2-benzyloxyquinoline behaves in an analogous manner. However, with aryloxy compounds, the following representative cleavage reaction takes place.



(2)

From the results given in Table I it appears that the ease of cleavage of the heterocyclic types varies as follows:

2-Quinolyl > 2-Benzothiazolyl > 2-Benzoxazolyl.—An alkylating reaction appears not to occur with 4-alkoxyquinolines, for 4-ethoxy-7-chloroquinoline (III) reacts in essential accordance with reaction (2).

These reactions generally take place in good yield (see Table I) when aryl thiols like thiophenol, *m*- and *p*-thiocresol and β-thionaphthol are used. An exception in the experiments carried out was *o*-thiocresol, which did not react appreciably with (I), possibly because of steric hindrance. Some reagents containing an acidic hydrogen, other than aryl thiols, have given corresponding exchange reactions with 2-alkoxyquinolines.[3] The fact that benzyl mercaptan cleaved (I) to a small extent (see Table I, Expt. 6) may be accounted for by the lower acidic character of the benzyl mercaptan as compared with that of the aryl thiols.

Aryl thiols can also effect a related reaction with the chlorine atom in the activated positions of quinoline and benzothiazole. For example,

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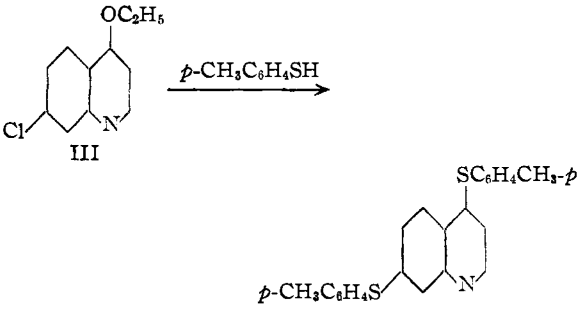
(1) Gilman and Beel, unpublished results.

(2) Friedlaender and Ostermaier, *Ber.*, **15**, 335 (1882); Jacobson, *ibid.*, **19**, 1077 (1886); Sandmeyer, *ibid.*, **19**, 2655 (1886); MacCoy, *Am. Chem. J.*, **21**, 122 (1899).

(3) Unpublished studies; see, also, ref. 2.

2-chloroquinoline was converted by thiophenol to phenyl 2-quinolyl sulfide in 79% yield. Surprisingly, this type of reaction was also observed in (III), in which the supposedly stable 7-chlorine in the benzenoid ring was replaced by a *p*-thiocresoxy group to form 4,7-di-(*p*-thiocresoxy)-quinoline.



III

Compound (III) was obtained quantitatively from 4,7-dichloroquinoline and sodium ethoxide, even when the latter reagent was used in excess.[3a]

A discussion of the course of cleavage of the ethers examined warrants a consideration of an intermediate addition product to the azomethine linkage, in view of the tendency of the ring system of quinoline to form isolable 1,2-dihydro-2-substituted derivatives with some organometallic reagents.[4] However, in our work, no experimental evidence has been found to support such an hypothesis. Also, the conditions in which reactions with organometallic reagents are carried out are different from those used in our experiments, in which we used higher temperatures and no solvent. We have observed that a mixture of thiophenol and 2-ethoxyquinoline, stirred for three days at room temperature, underwent no reaction and no change in color; the starting materials were recovered at low temperature by high vacuum distillation.

Because of a possible relationship between extent of cleavage of the ether and acidity of reagent used and by comparison with other related observations, it appears rather likely that thiols act as nucleophilic cleavage reagents on ethers containing an especially weakened carbon–oxygen bond. Thus ethyl benzyl ether was cleaved to an extent of 2.5% by *p*-thiocresol to give benzyl *p*-tolyl sulfide. This reaction was promoted, as expected, by either sulfuric acid or anhydrous aluminum chloride to give 50 and 75% yields, respectively, of the same sulfide. In an analogous manner thiols react with compounds like ethylene oxide[5] to yield sulfides of the type $HOCH_2CH_2SR$. In addition, ether linkages are cleaved in lignin by mercaptoacetic acid, in presence of hydrogen chloride, to form sulfides of the type $RSCH_2COOH$.[6]

Depending on the firmness of attachment of the groups to the oxygen of the ether, the bond may be cleaved on either side, as we have observed with the alkyl and aryl ethers reported in Table I. It is interesting to note that ethyl β-naphthyl ether, unlike 2-ethoxyquinoline, does not react with thiophenol, even after prolonged treatment. From this point of view the weakening effect of the aromatic ring nitrogen on the carbon–oxygen bond resembles that of the nitro groups in polynitro aromatic ethers.[7] However, a weak ether bond has also been found in piperidinomethyl ethyl ether,[8] in which the tertiary nitrogen bears no double bond.

Experimental

Cleavage by Thiols.—A mixture of the compound to be cleaved and the thiol, in a molar ratio 1:2 to 1:3, was stirred for twenty-four to forty-eight hours, at 150–170°, in a dry nitrogen atmosphere. In the experiments 1 to 9 (see Table I), the 2-hydroxy derivative crystallized at the end of the reaction after cooling and was isolated by filtration. The crystals were washed with a little diethyl ether or petroleum ether (b. p. 32–35°) to give a practically pure compound.

The reaction mixture, or the filtrate, was diluted with diethyl ether or petroleum ether (b. p. 32–35°) and extracted with a 5% sodium hydroxide solution. This alkaline extract contained the unreacted thiol and, for the experiments 10 and 11, the phenol formed as one of the cleavage products. In some cases, as, for instance, in the experiments 1 to 6, it was possible to extract completely the unreacted heterocyclic compounds with hydrochloric acid, so the ether-soluble fraction consisted of cleavage products only (sulfides). Usually, however, the ether-soluble fraction contained more or less large amounts of the disulfide corresponding to the thiol used.

2-Benzyloxyquinoline.—To a solution of 0.16 mole of sodium benzyloxide in benzyl alcohol, 24.4 g. (0.15 mole) of 2-chloroquinoline was added, and the mixture was stirred at 120° overnight. After cooling, the reaction product was diluted with ether and washed with water. After removal of the ether, the excess benzyl alcohol was removed by distillation at reduced pressure. The residue was distilled at 170° at 0.8 mm. to give 28 g. (80%) of a solid melting at 46–48°, which was purified by crystallization from ethanol to form white crystals (m. p. 48.5–49.5°).[9]

Anal. Calcd. for $C_{16}H_{13}ON$: N, 5.95. Found: N, 5.87.

2-Phenoxybenzothiazole.—To a solution of 0.3 mole of sodium phenoxide in hot phenol, 33.8 g. (0.2 mole) of 2-chlorobenzothiazole was added, and the mixture was stirred at 120° overnight. After cooling, the reaction product was taken up in ether and the excess phenol was extracted with 5% sodium hydroxide solution. The residue obtained from the ether layer was distilled at 147° at 1 mm. to give 42 g. (94.6%) of a solid (m. p. 51–52.5°), which was purified by crystallization from ethanol as white crystals (m. p. 51.5–52.5°).

[3a] However, see Bradford, Elliott and Rowe, *J. Chem. Soc.*, 437 (1947), for a reaction at elevated temperature in a sealed tube in which a 7-halogen is replaced by a dimethylamino and a methoxy group, respectively.

[4] See, for example, Ziegler and Zeiser, *Ber.*, **63B**, 1847 (1930); *Ann.*, **485**, 174 (1931); Gilman and Gainer, THIS JOURNAL, **69**, 1946 (1947).

[5] Nenitzescu and Scârlătescu, *Ber.*, **68B**, 587 (1935).

[6] Richtzenhain, *ibid.*, **72B**, 2152 (1939).

[7] See, for example, Le Fèvre, *et al.*, *J. Chem. Soc.*, 1168 (1927). For a comparison of the structural effects of ring nitrogen and nitro groups, see, for example, Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 243.

[8] Yang, *J. Org. Chem.*, **10**, 67 (1945).

[9] This compound has just been reported by Lott and Shaw, THIS JOURNAL, **71**, 73 (1949). The m. p. reported by them is 46–47°.

TABLE I

REACTIONS WITH THIOLS

Expt.	Compound examined	Thiol	Time, hr.[a]	Products (yield, %)[b]	
1	2-Ethoxyquinoline (I)	Thiophenol	22, 44	2-Hydroxyquinoline (62–67)	Ethyl phenyl sulfide (51)
2	2-Ethoxyquinoline (I)	*o*-Thiocresol	48	No reaction	
3	2-Ethoxyquinoline (I)	*m*-Thiocresol	44	2-Hydroxyquinoline (55)	Ethyl *m*-tolyl sulfide (40)[c]
4	2-Ethoxyquinoline (I)	*p*-Thiocresol	48	2-Hydroxyquinoline (71)	Ethyl *p*-tolyl sulfide (60)
5	2-Ethoxyquinoline (I)	*β*-Thionaphthol	48	2-Hydroxyquinoline (92)	Ethyl *β*-naphthyl sulfide (71)
6	2-Ethoxyquinoline (I)	Benzyl mercaptan	12–48	2-Hydroxyquinoline (6–7)	...
7	2-Benzyloxyquinoline	Thiophenol	52	2-Hydroxyquinoline (96)	Benzyl phenyl sulfide (75)
8	2-Ethoxybenzothiazole	Thiophenol	48	2-Hydroxybenzothiazole (74)	Ethyl phenyl sulfide (50)
9	2-Ethoxybenzoxazole	Thiophenol	48	2-Hydroxybenzoxazole (87)	Ethyl phenyl sulfide (67)
10	2-Phenoxyquinoline	Thiophenol	48	Phenol	Phenyl 2-quinolyl sulfide (21)[d]
11	2-Phenoxybenzothiazole (II)	*p*-Thiocresol	26	Phenol	*p*-Tolyl 2-benzothiazolyl sulfide (21)[d]
12	2-Chloroquinoline	Thiophenol	53	...	Phenyl 2-quinolyl sulfide (79)[d]
13	4,7-Dichloroquinoline	*p*-Thiocresol	24	...	4,7-Di-(*p*-thiocresoxy)-quinoline (87)[e]
14	4-Ethoxy-7-chloroquinoline (III)	*p*-Thiocresol	24	...	4,7-Di-(*p*-thiocresoxy)-quinoline (34)[e]
15	Ethyl *β*-naphthyl ether	Thiophenol	48	No reaction	
16	Ethyl benzyl ether	*p*-Thiocresol	48	...	Benzyl *p*-tolyl sulfide (2.5)
17	Ethyl benzoate	Thiophenol	22	No reaction	
18	Benzyl benzoate	Thiophenol	48	No reaction	

[a] The times selected for many of these reactions were arbitrary. [b] The solid cleavage products were identified by the method of mixed m. p.; the liquids by determining the b. p., density and refractive index. The compounds without corresponding yields were only identified qualitatively. [c] Not reported in literature; b. p. 216–219° (735 mm.); d^{25} 0.9947; $n^{15}\text{D}$ 1.5610. *Anal.* Calcd. for $C_9H_{12}S$: S, 21.05. Found: S, 20.63. [d] The authentic specimen was prepared according to the directions given in the Experimental. [e] Not reported in literature; b. p. 250° (0.5 mm.); m. p. 101–101.5°. *Anal.* Calcd. for $C_{23}H_{19}S_2N$: S, 17.17; N, 3.75. Found: S, 17.14; N, 3.77.

Anal. Calcd. for $C_{13}H_9ONS$: S, 14.08. Found: S, 13.95.

4-Ethoxy-7-chloroquinoline.—To a solution of 0.22 mole of sodium ethoxide in hot ethanol, an alcoholic solution of 39.8 g. (0.20 mole) of 4,7-dichloroquinoline was added and the mixture was refluxed and stirred for four hours. After cooling, the reaction product was diluted with ether and washed with a large volume of water. The residue from the ether layer was a white solid melting at 100–102° (95%) which by recrystallization from petroleum ether (b. p. 65–67°) gave bright colorless prisms (m. p. 103°). The same results were obtained when 0.22 mole of sodium ethoxide was allowed to react with 0.10 mole of the dichloro compound over a period of twenty-four hours.

Anal. Calcd. for $C_{17}H_{10}ONCl$: Cl, 17.07. Found: Cl, 16.91.

Phenyl 2-Quinolyl Sulfide.—This compound was prepared from 8.1 g. (0.050 mole) of 2-chloroquinoline and 0.055 mole of sodium thiophenoxide in ethanol solution by refluxing and stirring the mixture for four hours. The crude product was obtained in 80% yield by vacuum distillation (b. p. 164–166° at 0.6 mm.). Recrystallization from ethanol gave colorless crystals melting at 48–49°.

Anal. Calcd. for $C_{15}H_{11}NS$: S, 13.49. Found: S, 13.28.

***p*-Tolyl 2-Benzothiazolyl Sulfide.**—To a solution of 0.22 mole of sodium *p*-thiocresoxide in ethanol, 32.8 g. (0.20 mole) of 2-chlorobenzothiazole was added, and the mixture was refluxed and stirred for four hours; 48.4 g. (94%) of crude product (m. p. 69–71°) was obtained. The pure compound crystallizes from ethanol and melts at 71–72°.

Anal. Calcd. for $C_{14}H_{11}NS_2$: S, 24.94. Found: S, 24.71.

Summary

Some alkyl and aryl 2-quinolyl, 2-benzothiazolyl and 2-(benzoxazolyl) ethers are cleaved extensively by aryl thiols. The alkyl ethers have an alkylating action; for example, 2-ethoxyquinoline and thiophenol give ethyl phenyl sulfide and 2-hydroxyquinoline. The aryl ethers yield heterocyclic aryl sulfides.

Aryl thiols react with the 2-chloro compounds to form the aryl heterocyclic sulfides.

Both 4,7-dichloroquinoline and 4-ethoxy-7-chloroquinoline react with *p*-thiocresol to give 4,7-di-(*p*-thiocresoxy)-quinoline.

An interpretation of the course of some of these reactions has been considered.

AMES, IOWA RECEIVED MARCH 28, 1949