ester in a similar manner failed. *Anal.* Calcd. for $C_{18}H_{14}O_2S$: C, 73.4; H, 4.8. Found: C, 73.6, 74.0; H, 5.0, 4.9.

Summary

The preparation of 4,5-dimethylphenanthrene from pyrene is described. The steps involved are: (1) ozonization to 5-formyl-4-phenanthrenecarboxylic acid, (2) esterification, (3) reduction to 4,5-phenanthrenedimethanol, (4) cyclization to the corresponding cyclic ether and (5) reduction to 4,5-dimethylphenanthrene.

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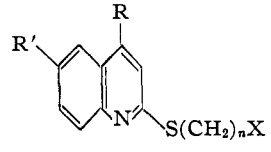
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

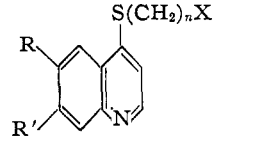
Some Dialkylaminoalkylmercaptoquinolines

BY HENRY GILMAN AND MARY ALYS PLUNKETT[1]

In connection with some studies on the pharmacological activity of certain mercapto quinolines, a series of dialkylaminoalkylmercaptoquinolines has been prepared. It seemed of interest to introduce into nuclei which have chemotherapeutic potentialities certain alkylamino groupings connected directly to the nuclei by a sulfur atom. The quinoline derivatives are of types I and II. Compounds of these types are reported by Bachman, *et al.*,[2] and by Clinton and Suter.[3]

(I) 

Where R is methyl, hydrogen or carboxy; R′ is methoxy or hydrogen; X is diethylamino, N-piperidyl or N-morpholyl; *n* is 2 or 3.

(II) 

Where R is methoxy or hydrogen; R′ is chloro or hydrogen; X is diethylamino, N-piperidyl or N-morpholyl; *n* is 2 or 3.

The compounds reported were prepared by condensation of the appropriate chloroquinoline with the sodium alkyl mercaptide or by condensation of the sodium quinolyl mercaptide with the appropriate alkyl chloride. In general, absolute ethanol was used as solvent for the condensations involving chloroquinolines. In the case of 2-chloro-4-methyl-6-methoxyquinoline it was found that the reflux temperature of methyl cellosolve was necessary for condensation. Reactions using the quinolyl mercaptides were carried out in a 1:1 mixture of ethylene glycol and methyl cellosolve.

In the preparation of 6-methoxy-2-(β-diethylaminoethylmercapto)-quinoline both the quinolyl and the alkyl mercaptides were used. Similar yields were obtained in the two cases. 6-Methoxy-4-methyl-2-(γ-diethylaminopropylmercapto)-quinoline was prepared by treating a mixture of γ-diethylaminopropylisothiouronium chloride hydrochloride and 2-chloro-4-methyl-6-methoxyquinoline in methyl cellosolve with excess sodium ethoxide. The same compound was obtained from the alkyl mercaptide and the chloroquinoline.

(1) Present address: Vassar College, Poughkeepsie, New York.

(2) Bachman, Welton, Jenkins and Christian, THIS JOURNAL, **69**, 366 (1947).

(3) Clinton and Suter, *ibid.*, **70**, 491 (1948).

In general, the mercaptoquinolines were isolated as the hydrochlorides in yields varying from 23–75%. The compounds prepared are listed in Table I. Details of the preparation of typical compounds are given in the experimental section. The sodium alkyl mercaptides were prepared in accordance with procedures described earlier from the corresponding alkyl chloride[4] or by the isothiouronium salt synthesis.[5]

Most of these compounds have been tested for their pharmacological activity toward malaria-causing plasmodia. Results of these tests will be reported elsewhere.

The authors are grateful to William Meikle for assistance and to Parke Davis and Co. for arranging for the tests.

Experimental

6-Methoxy-2-(β-diethylaminoethylmercapto)-quinoline.—A solution of 5 g. (0.04 mole) of β-diethylaminoethyl chloride and 0.02 mole of the sodium salt of 2-mercapto-6-methoxyquinoline in absolute ethanol was refluxed for four hours. After removal of the solvent the residue was dissolved in ether, dried over anhydrous sodium sulfate and treated with ethereal hydrogen chloride. Recrystallization of the dihydrochloride from absolute ethanol gave a product melting at 168–170° which was identical with that obtained from the reaction of sodium β-diethylaminoethyl mercaptide and 2-chloro-6-methoxyquinoline.[6]

4-Methyl-2-[β-(N-piperidyl)-ethylmercapto]-quinoline.—This compound was prepared by a method analogous to the above procedure from N-β-chloroethylpiperidine[7] and 2-mercapto-4-methylquinoline[8] using a 1:1 mixture of ethylene glycol and methyl cellosolve as solvent. The free base deposited from an ether solution as crystals melting at 75–76°.

The corresponding N-morpholyl compound, as well as the intermediates[9] for the reaction, were prepared in a similar manner.

2-Mercapto-6-methoxyquinoline.—This compound was prepared with some modification, according to the directions of John[10] for the preparation of 4-mercapto-6-methoxyquinoline.

(4) Gilman, Plunkett, Tolman, Fullhart and Broadbent, THIS JOURNAL, **67**, 1845 (1945); Gilman and Woods, *ibid.*, **67**, 1844 (1945).

(5) Albertson and Clinton, THIS JOURNAL, **67**, 1222 (1945); L. Fullhart, unpublished studies, Iowa State College.

(6) Magidson and Rubtsov, *J. Gen. Chem. (U. S. S. R.)*, **7**, 1896 (1937) (*C. A.*, **32**, 564 (1938)).

(7) I. G. Farbenindustrie, French Patent 802,416 (1936) (*Chem. Zentr.*, **107**, II, 4255 (1936)).

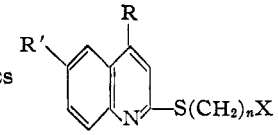
(8) Rosenhauer, *Ber.*, **62**, 2732 (1929).

(9) Mason and Block, THIS JOURNAL, **62**, 1443 (1940).

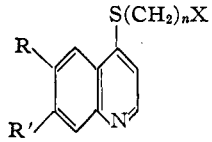
(10) John, *J. prakt. Chem.*, [2] **128**, 218 (1930).

TABLE I

DIALKYLAMINOALKYLMERCAPTOQUINOLINE HYDROCHLORIDES



Substituent groups				M. p.,	Yield,		Percentage composition					
							Nitrogen		Sulfur		Chlorine	
R	R′	n	x	°C.	%	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found
H	H	2	NEt_2	192–193[d]	64	$C_{15}H_{21}N_2ClS$	9.46	9.28	10.81	10.66	11.82	11.45
H	H	3	NEt_2	141–142	50	$C_{16}H_{23}N_2ClS$	9.03	9.10	...	...	11.29	11.34
CH_3	H	2	NEt_2	216–217	43	$C_{16}H_{24}N_2Cl_2S$	8.09	8.10	9.24	9.40	20.23	20.22
CH_3	H	3	NEt_2	199–200[d]	60	$C_{17}H_{26}N_2Cl_2S$	7.77	7.80	...	...	...	...
H	CH_3O	2	NEt_2	168–170	33	$C_{16}H_{24}ON_2Cl_2S$	7.73	7.94	8.84	8.78	19.33	19.00
CH_3	H	2	NC_5H_{10}[a]	75–76[b]	40	$C_{17}H_{22}N_2S$	9.79	9.74	11.18	11.03	...	...
CH_3	H	2	NC_4H_8O[a]	85–85.5[b]	40	$C_{16}H_{20}ON_2S$	9.72	9.79	11.11	11.00	...	...
CH_3	CH_3O	3	NEt_2	200–201	50	$C_{18}H_{27}ON_2ClS$	7.91	8.09	...	...	...	...
COOH[c]	H	2	NEt_2	240–242	70	$C_{16}H_{21}O_2N_2ClS$	8.23	8.25	...	...	...	...



CH_3O	H	2	NEt_2	219–220	23	$C_{16}H_{24}ON_2Cl_2S$	7.73	7.76	8.84	8.78	19.33	19.03
H	Cl	2	NEt_2	236–238[d]	75	$C_{15}H_{21}N_2Cl_3S$	7.65	8.00	8.74	8.50	19.12	18.99

[a] NC_5H_{10} refers to the N-piperidyl radical; NC_4H_8O refers to the N-morpholyl radical. [b] M. p. of free base. [c] Starting materials for this compound were made according to references 11–12. [d] Reported by Clinton and Suter.[2]

A mixture of 14 g. (0.08 mole) of 2-chloro-6-methoxyquinoline, 11 g. of potassium hydrosulfide and 56 ml. of absolute ethanol was heated at reflux temperature for fifteen hours. The solid material which formed was washed well with water and neutralized with acetic acid. After recrystallization from absolute ethanol 5 g. (33%) of product melting at 185–187° was obtained.

Anal. Calcd. for $C_{10}H_9ONS$: N, 7.33. Found: N, 7.40.

6-Methoxy-4-methyl-2-(γ-diethylaminopropylmercapto)-quinoline.—To a solution of 7.8 g. (0.03 mole) of γ-diethylaminopropylisothiouronium chloride hydrochloride[4] in 50 ml. of methyl cellosolve was added 6.2 g. (0.03 mole) of 2-chloro-4-methyl-6-methoxyquinoline[11] dissolved in a minimum of methyl cellosolve. The mixture was heated under reflux with stirring and treated with a solution of 3.2 g. (0.14 g. atom) of sodium in absolute ethanol, added in a thin stream over a period of one hour. The reaction mixture was refluxed for seven hours, filtered and freed from solvent by distillation under reduced pressure. The residue was dissolved in ether, washed with water and dried over anhydrous sodium sulfate. Treatment with ethereal hydrogen chloride gave 46% of product which, after recrystallization from absolute ethanol, melted at 200–201°.

This compound was also prepared in 50% yield according to the usual method using sodium γ-diethylaminopropyl mercaptide and 2-chloro-4-methyl-6-methoxyquinoline.[12,13]

(11) Kindly furnished by S. P. Massie.

Summary

The preparation of a series of dialkylaminoalkylmercapto quinolines is described. The compounds were isolated and identified as the hydrochlorides.

AMES, IOWA RECEIVED JANUARY 14, 1949

(12) Ainley and King, *Proc. Roy. Soc.* (*London*), **125B**, 69 (1938).

(13) Camp, *Arch. Pharm.*, **237**, 687 (1899).