neutralized with ammonium hydroxide and extracted with ether. After drying the ethereal extract, ethanolic hydrogen chloride was added until no further precipitation occurred. The mixture was cooled and filtered to give 14 g. of product melting at 206–211°. A recrystallization from about 100 cc. of 95% ethanol gave 10 g. (72%) of compound melting at 218–224°. Another crystallization from the same solvent gave 7.5 g. (54%) of light yellow needles melting at 220–224°.

Anal. Calcd. for $C_{24}H_{32}O_2N_2Cl_2S$: Cl, 14.69; S, 6.63; N, 5.80. Found: Cl, 14.92; S, 6.38; N, 5.79.

α-(3-Diethylaminopropylmercaptomethyl)-6-methoxy-2-phenyl-4-quinolinemethanol, Dihydrochloride.—The sodium mercaptide was prepared by adding 5.9 g. (0.04 mole) of γ-diethylaminopropylmercaptan to sodium ethoxide prepared from 0.69 g. (0.03 g. atom) of sodium in 150 cc. of absolute ethanol. After addition of 7.8 g. (0.022 mole) of the bromohydrin, the reddish solution was refluxed with stirring for one-half hour. The subsequent operations were those described above for the next lower homolog. It was found desirable to crystallize the yellow dihydrochloride, obtained subsequent to addition of ethanolic hydrogen chloride, from absolute ethanol. The first crystallization yielded a hygroscopic solid, but the product obtained after another crystallization was essentially non-hygroscopic. This yellow amorphous solid, after drying in a vacuum desiccator over phosphorus pentoxide, melted at 182–185° with preliminary softening. The yield was 8 g. (73%).

Anal. Calcd. for $C_{25}H_{34}O_2N_2Cl_2S$: Cl, 14.28; S, 6.45. Found: C, 13.95; S, 6.69.

CHEMICAL LABORATORY
IOWA STATE COLLEGE
AMES, IOWA

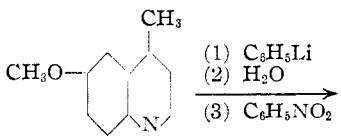
RECEIVED APRIL 5, 1946

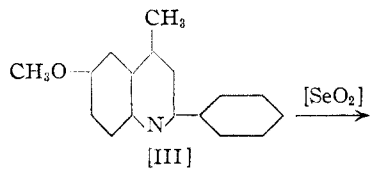
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

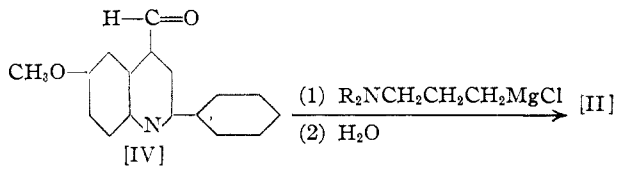
α-(3-Dialkylaminopropyl)-2-phenyl-6-methoxy-4-quinolinemethanols[1]

BY HENRY GILMAN, FREDERICK J. MARSHALL AND ROBERT A. BENKESER

Incidental to studies on experimental avian malaria, it was desirable to compare the effectiveness of α-(dialkylaminomethyl)-2-phenyl-6-methoxy-4-quinoline methanols [I][2] with homologs like α-(3-dialkylaminopropyl)-2-phenyl-6-methoxy-4-quinolinemethanols [II]. Several unsuccessful attempts[3a] were made to prepare compounds of type [II]. Finally, the compounds (where R = $-N(C_2H_5)_2$[3b] and $-N(C_4H_9\text{-}n)_2$) were synthesized by the sequence of reactions







In the conversion of the aldehyde [IV] to the 4-quinolinemethanol [II] it was necessary to use the activated copper–magnesium alloy[4,11] to form the Grignard reagent from γ-diethylaminopropyl chloride and γ-di-*n*-butylaminopropyl chloride.

The arylation of 6-methoxy-4-methylquinoline to give a 2-aryl type may be a procedure of choice in some cases. This general procedure was used recently[5a] for the preparation of some quinolines patterned as "open models" of atebrin. In the present study [III] was formed in satisfactory yields (73–87%) by the action of phenyllithium, followed by the use of nitrobenzene as an oxidizing agent to remove the two hydrogens in the precursory dihydro compound. The compound [III] was previously obtained in 9% yield by John and Noziczka[5b] from *p*-anisidine hydrochloride and benzalacetone.

Experimental

2-Phenyl-6-methoxy-4-methylquinoline.—To a stirred solution of 75 g. (0.435 mole) of 6-methoxy-4-methylquinoline, prepared both by the method of Ainley and King[6]

(1) Most of the work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Iowa State College.

(2) *Cf.* Lutz *et al.*, THIS JOURNAL, **68**, 1813 (1946).

(3) (a) Gilman and Tolman, *ibid.*, **68**, 1848 (1946). (b) The Survey Number, assigned to this drug by the Survey of Antimalarial Drugs is SN-12,858-4. The activities of these compounds will be tabulated in a forthcoming monograph.

(4) Gilman, Peterson, and Schulze, *Rec. trav. chim.*, **47**, 19 (1928).

(5) (a) Gilman and Spatz, THIS JOURNAL, **66**, 621 (1944); (b) John and Noziczka, *J. prakt. Chem.*, [2] **111**, 65 (1925).

(6) Ainley and King, *Proc. Roy. Soc.* (London), **125B**, 60 (1938). This procedure was found more adaptable to large runs.