We wish to report that reaction of amines with silicon isocyanates of the above type results in cleavage of the isocyanate group from the silicon atom with formation of theoretical yields of the corresponding monosubstituted urea.

Silicon tetraisocyanate and isocyanates of empirical formula $R_xSi(NCO)_y$, where R is methyl or phenyl and x and y are 1, 2, or 3, were prepared by reaction of R_xSiCl_y with silver (iso)cyanate in anhydrous benzene.[2,3] Treatment of these isocyanates either alone or in anhydrous benzene with allylamine, diallylamine, aniline, benzylamine, *o*- or *p*-toluidine, produced theoretical yields of the corresponding urea. In every case the NCO: NH_2 ratio was 1:1. No evidence was obtained for the formation of ureidosilanes, and the fate of the silicon-containing moiety was not determined.[6]

EXPERIMENTAL

Allylurea from phenylsilicon triisocyanate. In a typical reaction, phenylsilicon triisocyanate (2.31 g., 0.01 mole) was added, dropwise, to a well-stirred mixture of allylamine (1.71 g., 0.03 mole) in anhydrous benzene (10 ml.). After the initial strongly exothermic reaction had moderated the mixture was heated on the steam bath for 2 hr., then allowed to cool. The white solid was washed thoroughly with benzene, yield 3.94 g. (98%). Recrystallization from isopropyl alcohol gave a white crystalline product of m.p. 85.0°. The mixed melting point of this product with authentic allylurea was undepressed.

Anal. Calcd. for $C_4H_8N_2O$: N, 28.0. Found: N, 27.9.

Similarly, allylurea was produced by reaction of allylamine with silicon tetraisocyanate, methylsilicon triisocyanate, dimethylsilicon diisocyanate, trimethylsilicon isocyanate, and diphenylsilicon diisocyanate.

Products of reaction with other amines. Reaction of aniline, benzylamine, diallylamine, *o*-, and *p*-toluidines with the above silicon isocyanates produced 95–100% yields of, respectively, phenylurea, benzylurea, *N,N*-diallylurea, *o*-, and *p*-tolylurea, which gave undepressed mixed melting points with the authentic ureas and analyzed correctly for nitrogen.

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(6) Further work is in progress to determine the nature of the silicon-containing fragment.

Disulfides

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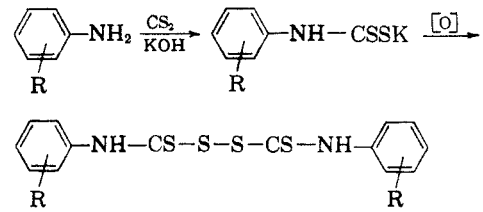
Chemotherapeutic activity can be conceived as due to the interference of the agent in the progression of the parasites metabolic reaction. This interference takes the form of inactivation or displacement of a metabolite essential to the parasite (*a*) by oxidizing a substance that requires to be reduced, (*b*) by molecular combination forming an inactive product, or (*c*) by competition with an enzyme associated with the essential metabolite.[1-3]

It was reported by Srinivasan[4] that paludrine can inhibit the oxygen uptake of the malarial parasite. He is of the opinion that the drug acts through inhibition of the activity of some —SH groups essential for the respiration of the parasite.

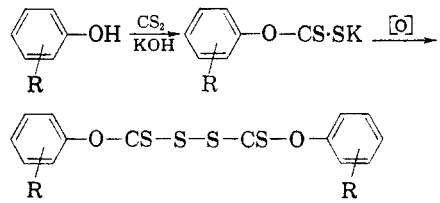
It was, therefore, decided to prepare some —S—S— compounds as potential antimalarials, since these compounds might be active by oxidizing some of the —SH groups essential to the parasite. The potency of thiuramdisulfides as bacterial poisons as well as the antimalarial activity exhibited by them in experimental malaria led us to prepare some analogous disulfides.

These compounds were made by first treating various amines with carbon disulfide in presence of aqueous potassium hydroxide and then oxidizing the thiocarbamido derivative with sodium nitrite, methyl alcohol, and hydrochloric acid.



o-, *m*-, *and p*-Aminobenzoic acids and the three aminobenzene sulfonic acids were thus treated to give the corresponding bisaryl thiuram disulfides.

The dixanthogens are a class of compounds closely related in structure and hence it was decided to prepare some derivatives of this type to study their effect in experimental malaria. The preparation of these compounds follows a similar route, different phenol carboxylic and phenol sulfonic acids being used instead.



These compounds were quite active in inhibiting the respiration of *Plasmodium gallinaceum in vitreo*, using the Warburg technique. However, only diphenylxanthogen-*p,p'*-disulfonic acid and *N,N'*-diphenylthiuram disulfide-*p,p'*-disulfonic acid were active *in vivo* against *P. gallinaceum* in chicks. Detailed pharmacological data will be published elsewhere.

(1) D. D. Woods, *Brit. J. Exp. Pathol.*, **21**, 274, (1940).
(2) P. Fildes, *Lancet*, **1**, 955, (1940).
(3) E. M. Lourie, *Ann. Rev. Microbiol.*, **1**, 237, (1947).
(4) V. R. Srinivasan, a thesis submitted for the Ph.D., Madras University.

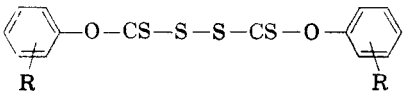
EXPERIMENTAL

Bis(o-carboxyphenyl)xanthogen. Seven grams of salicylic acid, 4 g. of carbon disulfide, 6 g. of potassium hydroxide, and 250 ml. of water were heated on the water bath for six hours. To the yellow solution was added a solution of 3 g. sodium nitrite, 3 ml. methyl alcohol, and under good cooling and stirring 10 ml. of concentrated hydrochloric acid. The precipitated product was collected and crystallized from water.

The procedure was essentially the same for the preparation of the rest of the compounds listed in the tables.

TABLE I

DISULFIDES

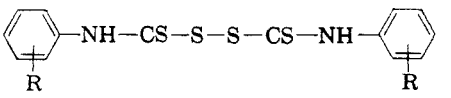


R	M.P., °C.	Yield, %	Formula	S Found	S Required
H[a]	182–183	60	$C_{14}H_{10}O_2S_4$	38.02	37.90
2—COOH	154–155	66	$C_{16}H_{10}O_6S_4$	30.14	30.01
3—COOH	198–200	70	$C_{16}H_{10}O_6S_4$	30.21	30.01
4—COOH	339–340	60	$C_{16}H_{10}O_6S_4$	30.18	30.01
2—SO_3H	360–dec.	48	$C_{14}H_{10}O_8S_6$	42.51	42.70
3—SO_3H	360–dec.	56	$C_{14}H_{10}O_8S_6$	42.34	42.70
4—SO_3H	360–dec.	40	$C_{14}H_{10}O_8S_6$	42.50	42.70
4—Cl[a]	128	70	$C_{14}H_8Cl_2O_2S_4$	30.54	30.70

[a] Crystallized from alcohol.

TABLE II

DISULFIDES



R	M.P., °C.	Yield, %	Formula	N Found	N Required
H[a]	183	66	$C_{14}H_{12}N_2S_4$	8.39	8.42
2—COOH	236–238	75	$C_{16}H_{12}N_2O_4S_4$	6.51	6.60
3—COOH	224.5	57	$C_{16}H_{12}N_2O_4S_4$	6.80	6.60
4—COOH	238–240	57	$CL_6H_{12}N_2O_4S_4$	6.39	6.60
2—SO_3H	360–dec.	53	$C_{14}H_{12}N_2O_6S_6$	5.39	5.36
3—SO_3H	360–dec.	49	$C_{14}H_{12}N_2O_6S_6$	5.42	5.36
4—So_3H	360–dec.	65	$C_{14}H_{12}N_2O_6S_6$	5.51	5.36
4—Cl[a]	100	70	$C_{14}H_{10}Cl_2N_2S_4$	6.58	6.90

[a] Crystallized from alcohol.

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