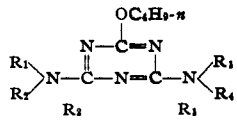
TABLE II

BUTYL ETHERS



R_1	R_2	R_3	R_4	M. p., °C.	Yield, %	Recrystallization solvent	Analyses,[a] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	A. H.[b] Value
H	H	H	H	174–175		Ref. 1					25
Methyl	H	H	H	173–175	88	Chloroform	48.71	48.76	7.67	7.81	6
Ethyl	H	H	H	116–118	86	Chloroform	51.16	50.91	8.11	7.99	12
n-Propyl	H	H	H	116–118	85	Isoöctane	53.31	53.54	8.50	8.48	25
n-Butyl	H	H	H	103–104	72	Isoöctane	55.20	55.36	8.85	8.63	..
n-Amyl	H	H	H	107–109	81	Isoöctane	56.89	[h]	9.15	9.17	12
n-Hexyl	H	H	H	119–121	99	Ethanol–water	58.41	58.76	9.43	9.52	12
Allyl	H	H	H	87–89	75	Dioxane–water	53.79	53.57	7.68	7.57	12
Methallyl	H	H	H	106–108	79	Isoöctane	55.67	55.77	8.07	8.13	>50
Cyclohexyl	H	H	H	141–143	96	Carbon tetrachloride	55.84	[h]	8.74	[h]	>50
Methyl	Methyl	H	H	103–104	88	Ethanol–water	51.16	50.98	8.11	7.97	12
Ethyl	Ethyl	H	H	73–75	51	Isoöctane	55.20	54.77	8.85	8.77	50
Allyl	Allyl	H	H	172–175/1[g]	65		59.29	59.64	8.04	7.93	>50
Methallyl	Methallyl	H	H	60–62	87	Isoöctane	61.82	61.56	8.65	8.66	>50
$HOCH_2CH_2$	Ethyl	H	H	123–125	64	Ethanol–water	51.74	51.47	8.29	8.24	>25
$HOCH_2CH_2$	Phenyl	H	H	157–159	61	Ethyl cellosolve–H_2O	59.38	59.44	6.98	7.18	>50
—C_5H_{10}—[d]		H	H	115–117	87	Ethanol–water	57.34	57.70	8.42	8.28	>50
—$C_2H_4OC_2H_4$—[e]		H	H	108–110	43	Ethanol–water	52.16	52.37	7.56	7.41	12
Methyl	H	Methyl	H	103–104	60	Propanol–water	51.16	51.36	8.11	8.09	12
Ethyl	H	Ethyl	H	50–52	85	Ethanol–water	55.20	55.58	8.85	9.05	25
Allyl	H	Allyl	H	185–190/1[g]	51		59.29	59.35	8.04	8.00	25
Methallyl	H	Methallyl	H	58–60	70	Methanol–water	61.82	61.72	8.65	8.55	..
Methyl	Methyl	Methyl	H[f]	129–131	87	Benzene	53.31	53.52	8.50	8.58	>25
Ethyl	Ethyl	Ethyl	H	80–82	96	Ethanol–water	58.40	58.19	9.43	9.49	>50
Methyl	Methyl	Methyl	Methyl	155–157/4[g]	69		55.20	55.51	8.85	8.79	>25
Ethyl	Ethyl	Ethyl	Ethyl	164–165/4[g]	84		60.98	60.97	9.89	9.64	>25
Allyl	Allyl	Allyl	Allyl	157–160/1[g]	93		66.41	66.92	8.51	8.53	>50
Methallyl	Methallyl	Methallyl	Methallyl	164–167/1[g]	82		69.14	69.31	9.34	9.28	>25
—C_5H_{10}—[d]		—C_5H_{10}—[d]		182–185/2[g]	71		63.91	63.98	9.15	9.09	>50
—$C_2H_4OC_2H_4$—[e]		—$C_2H_4OC_2H_4$—[e]		117–119	66	Isoöctane	55.71	55.90	7.79	7.90	>25

Footnotes the same as for Table I.

viously.[2] In order to limit the variables concerned, the methyl and *n*-butyl ethers of each triazine residue were prepared by the method reported previously.[1] The methyl ethers are reported in Table I and the butyl ethers in Table II.

During the preparation of the necessary chlorotriazines it was noted that the degree of substitution markedly influenced the physical properties of the resulting compounds. Thus, compounds having the structure of 2-chloro-4,6-diamino-*s*-triazine wherein one, any two, or three of the amino hydrogens were replaced by methyl groups were all high melting solids while the corresponding tetramethyl compound was very low melting. Similarly, the mono-, di- and triethyl, -allyl and -methylallyl derivatives were solids while the tetrasubstituted compounds were oils which failed to solidify at −40°. A similar relationship was expected with the ethers. While the tetraalkyldiamino ethers were all liquids except for one low melting solid, the melting points of the mono-, di- and tri-substituted ethers did not follow regular progression noted for the chloro compounds.

The compounds were tested for antihistamine activity in guinea pigs using the histamine–aerosol technique of E. R. Loew.[3] In the previous series of unsubstituted aminotriazine ethers, a regular variation in activity dependent on the length of the alkoxy chain was observed. No orderly variation in activity was noted with variation in the alkyl chain on nitrogen or with multiple substitution on the amine groups.

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(2) Pearlman and Banks, THIS JOURNAL, **70**, 3726 (1948).

(3) Loew, *et al.*, *J. Pharmacol.*, **83**, 120 (1945).

The Resolution of Chloroquine, SN 7618[1]

BY BYRON RIEGEL AND L. T. SHERWOOD, JR.

Since 4-(4-diethylamino-1-methylbutylamino)-7-chloroquinoline (chloroquine) proved to be one of the most effective suppressive drugs for malaria developed during the war, its resolution was undertaken in the hope that the toxicity or activity of one of the forms might be favorably different. The salts of *l*-malic, *d*-camphorsulfonic, *l*-menthoxyacetic, *d*-tartaric and *dl*-mandelic were all unsuitable as resolving agents but an adaptation of the work of Chelintsev and Osetrova[2] on the resolution of atabrine with *d*-bromocamphorsulfonic acid proved fairly satisfactory.

(1) This work was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Northwestern University.

(2) G. V. Chelintsev and E. D. Osetrova, *J. Gen. Chem.* (*U. S. S. R.*), **10**, 1978 (1940).

The salts obtained by the addition of two moles of *d*-bromocamphorsulfonic acid to one of chloroquine were low melting, hygroscopic, finely divided, and somewhat unstable crystals. This made handling difficult and some mechanical loss unavoidable. The quality of the *d*-bromocamphorsulfonic acid was also of great importance and the poor results of some runs was supposed due to slight decomposition during preparation of the free acid. The enantimorphs of the drug are much more soluble than the racemic mixture.

Neither of the optically active forms submitted to the Survey Office showed any significant differences[3] in antimalarial activity in birds and for toxicity in dogs from the racemate.

Experimental

Starting Materials.—Chloroquine diphosphate was kindly furnished by Dr. R. C. Elderfield of Columbia University. The free base was liberated from an aqueous solution of the salt with ammonia and was recrystallized from benzene and hexane. We are indebted to Dr. H. R. Snyder of the University of Illinois for the ammonium salt of *d*-bromocamphorsulfonic acid. The free acid was liberated from the salt by the method of Pope and Peachey.[4]

A solution was made of 21 g. of chloroquine and 45 g. of *d*-bromocamphorsulfonic acid in 300 ml. of hot absolute ethanol. The solution was filtered to remove any insoluble material and then allowed to crystallize in a cold room. The crystals were separated rapidly by filtration and recrystallized from about 150 ml. of absolute ethanol to a constant rotation of $[\alpha]^{27}D + 62°$ (0.200 g. was made up to 10 ml. with water). The base was obtained by dissolving the salt in water, adding an excess of ammonia, and extracting with benzene. The benzene solution was filtered and mixed with an equal volume of petroleum ether (b.p. 80–100°). The solution was concentrated until crystallization took place upon standing in the cold room. The crystals (9.7 g.) melted at 84–86°; $[\alpha]^{25}D + 12.3°$ (0.200 g. was made up to 10 ml. with 95% ethanol).

The *l*-form of the drug was liberated by evaporating the mother-liquor from the crystalline salt almost to dryness, dissolving in water, and treating as above. The concentration of the benzene and petroleum ether solution was adjusted so as to precipitate about one gram of solid in the cold. This material, almost inactive, was discarded and the solution was concentrated further. On cooling, 4.3 g., m.p. 84–87°, of the *l*-form separated; $[\alpha]^{27}D -13.2°$ (0.200 g. made up to 10 ml. with 95% ethanol).

(3) F. Y. Wiselogle, "A Survey of Antimalarial Drugs," J. W. Edwards, Ann Arbor, Michigan, 1946, p. 388.

(4) W. J. Pope and S. J. Peachey, *J. Chem. Soc.*, **73**, 893 (1898).

DEPARTMENT OF CHEMISTRY
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EVANSTON, ILLINOIS RECEIVED OCTOBER 29, 1948

An Improved Laboratory Preparation of Copper–Chromium Oxide Catalyst

BY THOMAS W. RIENER[1]

During the course of an investigation[2] of copper chromium oxides as a catalyst for hydrogenation of fatty esters to alcohols, a very satisfactory laboratory procedure for the decomposition of the copper ammonium chromate was developed. A catalyst of high activity and long life was obtained by this improved technique.

The method described here is similar to that previously reported[3] except that the decomposition of the copper ammonium chromate is carried out under carefully controlled conditions. If excessive temperatures are reached during the decomposition of the copper ammonium chromate, the activity of the catalyst is seriously affected.

A batch of copper ammonium chromate was prepared in the usual manner[3] and divided into several portions. A portion (I) was placed in a muffle furnace at 320° and in a short time the temperature inside the mixture reached 635°. Another portion (II) was fired as described below at 400°. A third portion (III) was similarly fired at 350°.

The catalysts obtained in each experiment were used in the hydrogenation of the lauryl ester of coconut oil fatty acids. The reductions were carried out in a 480-cc. Parr Instrument shaking bomb using 2 g. catalyst and 80 g. ester and run for two hours at 275°/3000 lb. H_2: (I) gave 30.5% hydrogenation; (II) gave 88.3% hydrogenation; (III) gave 92.1% hydrogenation.

Experimental

A solution of 260 g. of copper nitrate ($Cu(NO_3)_2 \cdot 3H_2O$) in 900 cc. of tap water at 80° was added while stirring to a solution of 178 g. of sodium dichromate ($Na_2Cr_2O_7 \cdot 2H_2O$) and 225 cc. of 28% ammonium hydroxide made up to 900 cc. at 25°. The precipitate was collected on a Buchner funnel and washed by slurrying in water three times. The copper ammonium chromate was dried at 75–80° overnight.

The copper ammonium chromate was powdered and added in small portions to a one-liter three-neck flask equipped with a stainless steel stirrer of the crescent type which scraped close to the bottom of the flask. The flask was partially immersed in a Woods metal-bath heated at 350°. The time of addition was fifteen minutes. The mixture was heated and stirred at 350° for fifteen minutes after all of the complex had been added. It was then passed through a 200-mesh screen with the aid of a camel's hair brush.

(3) Connor, Folkers and Adkins, THIS JOURNAL, **54**, 1138 (1932).

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PHILADELPHIA, PENNSYLVANIA RECEIVED JANUARY 25, 1949

The Effect of Heat and Sodium Sand upon Sodium Polybutadiene[1]

BY ROBERT M. ROSS

The percentage of external double bonds in sodium-polymerized polybutadiene has been shown to be dependent upon the temperature of polymerization.[2,3] Polybutadiene, polymerized with sodium at 30°, contains 65–75% external

(1) Present address: Industrial Rayon Corporation, Cleveland, Ohio.

(2) Work done at Rohm & Haas Company.

(1) The work described in this manuscript was done under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program. The author is deeply indebted to Dr. C. S. Marvel for initiating this investigation, as well as for his advice during the course of the work.

(2) Ziegler, Grimm and Willer, *Ann.*, **542**, 90 (1939).

(3) Kolthoff, Lee and Mairs, *J. Polymer Sci.*, **2**, 220 (1947).