Anal. Calcd. for $C_{18}H_{18}$: C, 92.28; H, 7.72. Found: C, 92.22, 92.10; H, 7.78, 7.71.

1,2-Diphenylcyclohexane.—A solution of 11.7 g. of the diphenylcyclohexene in 200 cc. of ethanol was shaken with hydrogen at two to three atmospheres pressure in the presence of 1 g. of 10% palladium–on–charcoal until absorption of hydrogen ceased. At this point approximately 1 mole equivalent of hydrogen had been absorbed. The catalyst was removed by filtration and the solution concentrated to 75 cc. on the steam-bath. Chilling produced 8.3 g. of colorless needles, m. p. 45–46°. Further concentration of the mother liquor gave an additional 2.1 g. of product, m. p. 42–46°. This represents a yield of 88%. An analytical sample, recrystallized three times from methanol, melted at 46–47°.

Anal. Calcd. for $C_{18}H_{20}$: C, 91.50; H, 8.50. Found: C, 91.50, 91.48; H, 8.50, 8.56.

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Alkoxy-*s*-triazines. II

BY WILLIAM M. PEARLMAN AND C. K. BANKS

In the first paper of this series[1] a group of 2-alkoxy-4,6-diamino-*s*-triazines having antihistaminic activity was reported. Most of these compounds contained no alkyl substituents on nitrogen. Since the tautomeric possibilities of the triazine nucleus (I–III) are limited by the number and arrangement of alkyl substituents on nitrogen, it was considered of interest to prepare a series of ethers in which one to four of the hydrogens on the two amine groups were replaced by alkyl groups. These compounds were prepared by the reaction of the chosen sodium alkoxide with an appropriate 2-chloro-4,6-di-(amino or substituted amino)-*s*-triazine. The necessary chlorodiaminotriazines have been reported pre-

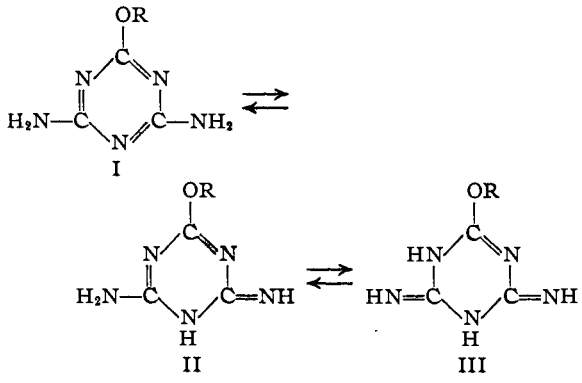
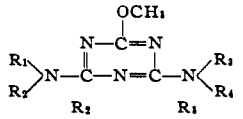


TABLE I

METHYL ETHERS



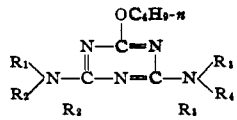
R_1	R_2	R_3	R_4	M. p., °C.	Yield, %	Recrystallization solvent	Analyses,[a] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	A. H.[b] Value
H	H	H	H	229–230	81	Ref. 1					50
Methyl	H	H	H	155–156	66	Benzene	38.70	38.97	5.85	5.81	50
Ethyl	H	H	H	168–170	24	Water	42.59	42.59	6.55	6.31	25
n-Propyl	H	H	H	148–150	81	Water	45.89	46.20	7.15	7.03	12
n-Butyl	H	H	H	125–127	89	Methanol–water	48.71	49.13	7.67	7.64	>50
n-Amyl	H	H	H	[c]	86	Benzene–isoöctane	51.38	51.19	8.13	8.23	12
n-Hexyl	H	H	H	104–106	92	Isoöctane	53.31	53.03	8.50	8.73	12
Allyl	H	H	H	148–150	89	Water	46.40	46.66	6.12	6.07	12
Methallyl	H	H	H	129–131	88	Methanol–water	49.22	49.30	6.71	6.66	>50
Cyclohexyl	H	H	H	170–172	99	Benzene	53.79	53.62	7.67	7.47	12
Methyl	Methyl	H	H	169–171	81	Water	42.59	42.62	6.55	6.31	25
Ethyl	Ethyl	H	H	113–115	73	Methanol–water	48.71	48.58	7.67	7.42	12
Allyl	Allyl	H	H	87–89	83	Methanol–water	54.31	54.12	6.83	6.59	>50
Methallyl	Methallyl	H	H	101–103	90	Methanol–water	57.80	57.84	7.68	7.65	50
$HOCH_2CH_2$	Ethyl	H	H	162–164	87	Methanol–water	45.06	45.02	7.09	7.04	>50
$HOCH_2CH_2$	Phenyl	H	H	224–226	91	Methylcellosolve–H_2O	55.12	55.47	5.78	5.74	50
—C_5H_{10}—[d]		H	H	137–139	95	Chloroform	51.66	51.59	7.23	7.42	6
—$C_2H_4OC_2H_4$—[e]		H	H	182–184	80	Methanol–water	45.49	45.65	6.20	6.07	50
Methyl	H	Methyl	H	184–186	76	Methanol–water	42.59	[h]	6.55	[h]	6
Ethyl	H	Ethyl	H	81–83	46	Ethanol–water	48.71	48.69	7.63	7.64	6
Allyl	H	Allyl	H	84–86	88	Methanol–water	54.28	54.28	6.83	6.92	25
Methallyl	H	Methallyl	H	112–114	93	Methanol–water	57.80	57.76	7.68	7.34	12
Methyl	Methyl	Methyl	H[f]	187–188	80	Methanol	45.89	45.64	7.15	7.00	25
Ethyl	Ethyl	Ethyl	H	107–109	99	Isoöctane	53.31	53.30	8.50	8.24	12
Methyl	Methyl	Methyl	Methyl	90–92	73	Methanol–water	48.71	48.75	7.66	7.48	25
Ethyl	Ethyl	Ethyl	Ethyl	146–149/1.5[g]	65		56.89	57.22	9.15	9.09	50
Allyl	Allyl	Allyl	Allyl	150–153/1[g]	93		63.76	64.07	7.69	7.88	>50
Methallyl	Methallyl	Methallyl	Methallyl	151–154/1.5[g]	71		67.19	66.83	8.74	8.44	>50
—C_5H_{10}—[d]		—C_5H_{10}—[d]		89–91	94	Isoöctane	60.62	60.60	8.36	7.93	>50
—$C_2H_4OC_2H_4$—[e]		—$C_2H_4OC_2H_4$—[e]		153–155	78	Methanol–water	51.23	51.38	6.81	6.86	12

[a] Analyses by Mr. A. W. Spang and Miss Patricia Keller. [b] Determined by Dr. Graham Chen and Mr. C. R. Ensor. Dose of compound in mg./kg. intraperitoneally allowing survival of 50% of histamine-shocked guinea pigs, see Ref. 1 for details. The comparable dose for Aminophylline is 50 and for Benadryl is 1.5. [c] Sinters 98–104°, plastic 104–108°, glass 108–122°. [d] Piperidino. [e] Morpholino. [f] Prepared by Mr. John Controulis. [g] Boiling point, not crystallized at −40°. [h] Concordant results not obtained on repeated assays. This may be due to solvation.

(1) Controulis and Banks, THIS JOURNAL, 67, 1946 (1945).

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).