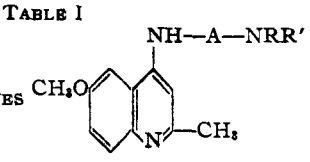
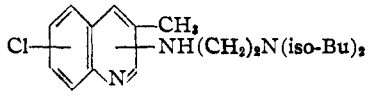
TABLE I

6-METHOXYQUINALDINES



SN[a]	-A-	R	R'	Yield, %	Formula	M. p., °C.	Analyses, %[b] Calcd. C	Calcd. H	Found C	Found H
..	$-(CH_2)_3-$	H	Iso-Pr	34	$C_{17}H_{25}ON_3 \cdot 2HCl \cdot 2H_2O$[c]	150–153	56.65	7.56	56.54	7.55
									56.62	7.59
5204	$-(CH_2)_3-$	H	Iso-Bu	32	$C_{18}H_{27}ON_3 \cdot 2HCl \cdot H_2O$[d]	283–284	57.75	7.81	57.83	7.75
..	$-(CH_2)_3-$	Iso-Bu	Iso-Bu	43.5	$C_{22}H_{35}ON_3$	159–160	73.90	9.87	73.85	9.72
6556	$-p-C_6H_4-$	Me	Me	45	$C_{19}H_{21}ON_3 \cdot 2HCl$	276–277	60.00	6.10	59.90	6.08
6557	$-HC(CH_2CH_2)_2CH-$	Me	Me	31	$C_{19}H_{27}ON_3 \cdot 2HCl$	295–297	59.05	7.57	59.70	7.67
6560	$-HC(CH_2CH_2)_2CH-$	Et	Et	32	$C_{21}H_{31}ON_3 \cdot 2HCl$	270–272	60.85	8.03	60.74	8.03

3-METHYLQUINOLINES



	Diamine position	Cl position							
9215	2	7	38	$C_{20}H_{30}N_3Cl \cdot 2HCl \cdot H_2O$[e]	203–206	57.10	7.67	57.16	7.62
6562	4	7	53	$C_{20}H_{30}N_3Cl \cdot 2HCl$	213–215	57.10	7.67	57.16	7.64
9216	4	5	29.5	$C_{20}H_{30}N_3Cl \cdot 2HCl$[f]	215–217	57.10	7.67	57.03	7.64

[a] The reference number of compounds listed in "A Survey of Antimalarial Drugs," ed. by Wiselogle, J. W. Edwards, Ann Arbor, Mich., 1946. [b] Analyses on the anhydrous material, in the case of the hydrates. [c] *Anal.* calcd. for dihydrate: Cl^-, 17.89. Found: Cl^-, 17.85. [d] Moisture loss at 125°: 4.82%; calcd. for monohydrate: 4.59%. Free base, 66.5% yield, b. p. (0.5 mm.) 200–215°. [e] Moisture loss at 125°: 4.07%; calcd. for monohydrate: 4.28%. [f] Free base had m. p. 129–131°.

Some Quinaldine and 3-Methylquinoline Derivatives

BY KEITH W. WHEELER, CHARLES H. TILFORD, M. G. VAN CAMPEN, JR., AND ROBERT S. SHELTON

Termination of our work on antimalarials left unfinished a proposed series of 4-substituted-6-methoxyquinaldines and a similar group of 3-methylquinoline derivatives. Since further work in this direction is not anticipated, it seems desirable to record the preparation and properties of those compounds we did obtain and which have not been previously described in the literature. None of these compounds was appreciably active against the malaria parasite, the activities ranging from $Q<0.03$ for SN9215 to $Q<1.0$ for SN5204, although serveral of them showed moderate activity against *T. equiperdum* in mice.[1]

The intermediates 4-chloro-6-methoxyquinaldine,[2] 4,5-dichloro-3-methylquinoline,[3] 4,7-dichloro-3-methylquinoline[3] and 2,7-dichloro-3-methylquinoline[4] were prepared by standard procedures. The required diamines were obtained from the catalytic hydrogenation of the β-(di)-alkylaminopropionitrile, or the commercially available *p*-aminodiethyl (or methyl) anilines, and from the phthalimide synthesis.

(1) We are indebted to Dr. Lloyd D. Seager, Woman's Medical College of Pennsylvania, for these tests.

(2) Conrad and Limpach, *Ber.*, **21**, 1650 (1888).

(3) Steck, Hallock and Holland, THIS JOURNAL, **68**, 380–383 (1946).

(4) This compound, m. p. 125–127°, was obtained along with the known 4,7-dichloro isomer from the action of phosphoryl chloride on 7-chloro-3-methylquinoline N-oxide. Although no analytical data are available, it is assumed to be the 2,7-isomer.

Procedure.—A mixture of 0.1 mole of the chloroquinoline and 0.2 mole of the diamine was heated for eight to fifteen hours at 175–200° or for twenty-four to thirty-six hours at 145–150°. Water and ether were added to the mixture, the layers were separated, and the ether layer was washed with 10% hydrochloric acid. The aqueous layer and acidic extracts were combined and made strongly basic. The liberated oil was taken up in ether, dried, and distilled under reduced pressure in some cases, while in other cases only the more volatile material was distilled, leaving the crude free base as a residue. The hydrochloride salts were prepared in the usual manner and recrystallized from mixtures of ethanol and butanone or from aqueous ethanol.

The yields, properties, and analyses of the new compounds prepared are recorded in Table I. The yields reported here do not take into account the quinoline bases recovered in some instances.

Acknowledgment.—We wish to express our appreciation to Mr. Wm. J. Corbett for technical assistance.

THE DEPARTMENT OF ORGANIC CHEMISTRY
RESEARCH LABORATORIES
THE WM. S. MERRELL CO.
CINCINNATI 15, OHIO

RECEIVED NOVEMBER 22, 1948

Optically Active 2-Methylbutyl 3,5-Dinitrobenzoate

BY JONATHAN W. WHITE, JR., AND W. P. RATCHFORD

A lack of agreement in the literature concerning the melting point of optically active 2-

methylbutyl 3,5-dinitrobenzoate was encountered during a study of the volatile constituents of apple juice. The melting point of 2-methylbutyl 3,5-dinitrobenzoate is reported as 62°,[1] 70°[2] (both presumably from *d,l* alcohol), and 83–84°[3] (from alcohol of $[\alpha]$ +5.21°). The last value is the only one for a preparation obtained from an active alcohol of a given specific rotation. The stereoisomer available from fusel oil is *d*-2-methylbutanol, $[\alpha]^{20}D$ −5.90.[4] No data were found on the optical activity of the derivative.

An alcohol was obtained from apple juice which gave a dinitrobenzoate with a melting point of 81.5° (all melting points given here are uncorrected); its analysis was that of an amyl derivative. Mixed melting points with all inactive and racemic amyl derivatives were depressed below the melting point of either component except that with *dl*-2-methylbutyl dinitrobenzoate (m. p. 66.5°). The compound was optically active, $[\alpha]^{25}D$ +4.4°.

To determine which isomer had been obtained from apples, refined fusel oil was fractionally distilled. A fraction with $[\alpha]^{25}D$ −5.67° was obtained, equivalent to a purity of 96%. From this was prepared a 3,5-dinitrobenzoate, which melted at 83–84° and had $[\alpha]^{25}D$ +4.9°. This identified the alcohol from apples as *d*-2-methylbutanol, *i. e.*, the same as present in fusel oil.

Experimental

Dinitrobenzoate from Apple Fraction.—A distillate fraction (the full procedure appears elsewhere,[5] 0.98 g. b. p. (150 mm.) 90–100°, $n^{20}D$ 1.4104, yielded a chromatographically[6] homogeneous 3,5-dinitrobenzoate on treatment with dinitrobenzoyl chloride in the presence of pyridine. It had a m. p. of 81.5–82.5°, analyzed as an amyl derivative, and failed to depress the m. p. of only the *dl*-2-methylbutyl derivative (m. p. 66.5°), in which case the melting range was 67–79°. It was then found to have $[\alpha]^{25}D$ +4.4° (4.8% in acetone). *Anal.* Calcd. for $C_{12}H_{14}O_6N_2$: C, 51.10, H, 4.96, N, 9.93. Found: C, 51.09; H, 5.04; N, 9.99.[7]

Distillation of *d*-2-Methylbutanol from Fusel Oil.—One gallon (3.78 l.) of "isoamyl alcohol"[8] was fractionated at atmospheric pressure in a Podbielniak column operated with intermittent take-off; it yielded 200 ml. of crude *d*-2-methylbutanol, b. p. 128–129°, estimated to be 53% pure. When redistilled, this fraction yielded 65 ml. of the alcohol, 93% pure. This material, redistilled in turn, yielded a fraction, b. p. 128.5°, $n^{20}D$ 1.4105, $[\alpha]^{25}D$ −5.67°, which is 96.1% of the accepted value.[4] The 3,5-dinitrobenzoate of this fraction melted at 83–84°, and had $[\alpha]^{25}D$ +4.9° (6.4% in acetone). *Anal.* Calcd. for $C_{12}H_{14}O_6N_2$: C, 51.10; H, 4.96. Found: C, 51.00; H, 5.00. A mixed melting point with the product from apple juice was 82–84°; therefore the alcohol from apples was *-d* 2-methylbutanol.

EASTERN REGIONAL RESEARCH LABORATORY[9]
PHILADELPHIA 18, PENNSYLVANIA

RECEIVED AUGUST 27, 1948

(1) Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, New York, N. Y., 1948, p. 226.

(2) Reichstein, *Helv. Chim. Acta*, **9**, 799 (1926).

(3) Gordon, *J. Am. Pharm. Assoc.*, **16**, 419 (1927).

(4) W. Markwald and A. McKenzie, *Ber.*, **34**, 485 (1901).

(5) White, THIS JOURNAL, in press.

(6) Chromatography was on silicic acid-rhodamine 6G by the method of White and Dryden, *Anal. Chem.*, **20**, 853 (1948).

(7) The authors are indebted to C. L. Ogg for the microanalyses.

(8) This alcohol, $[\alpha]^{25}D$ −1.06°, was kindly donated by Publicker Industries, Inc.

(9) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration.

2,2-Disubstituted-thiazolidine-4-carboxylic Acids

BY RICHARD H. WILEY AND J. F. JEFFRIES

The present report describes the application of the method of Woodward and Schroeder,[1] first used to prepare thiazolidine carboxylic acids from cysteine and acetone, to cysteine and three other ketones to form the corresponding substituted thiazolidine carboxylic acids.

2-Methyl-2-ethylthiazolidine-4-carboxylic acid.—One gram of cysteine[2] was refluxed with 200 ml. of methyl ethyl ketone, b. p. 79–80°, in a 300-ml. flask attached by ground glass connection to a reflux condenser. After three hours the cysteine had nearly all dissolved. The solution was filtered, evaporated to 15 ml., and cooled to deposit crystals which were recrystallized from methyl ethyl ketone; yie d, 1.0 g., 70% of the theoretical amount, m. p. 131°. No reaction took place when rubber stoppered equipment was used.

Anal. Calcd. for $C_7H_{13}NO_2S$: C, 48.00; H, 7.42; N, 7.98; S, 18.28. Found: C, 47.75; H, 7.19; N, 8.02; S, 18.38.

2-Methyl-2-isopropylthiazolidine-4-carboxylic acid was prepared from methyl isopropyl ketone as in the preceding example; yield, 0.69 g. from 1 g. of cysteine, 44% of the theoretical amount, m. p. 154° recrystallized from methyl isopropyl ketone.

Anal. Calcd. for $C_8H_{15}NO_2S$: C, 50.8; H, 7.92; N, 7.40; S, 16.90. Found: C, 50.9; H, 7.94; N, 7.51; S, 17.20.

2,2-Tetramethylenethiazolidine-4-carboxylic acid was prepared from cysteine and cyclopentanone; yield 0.86 g. from 1 g. of cysteine, 56% of the theoretical amount, m. p. 138°, recrystallized from cyclopentanone.

Anal. Calcd. for $C_8H_{13}NO_2S$: C, 51.2; H, 6.94; N, 7.48; S, 17.10. Found: C, 50.8; H, 6.92; N, 7.34; S, 16.90.

(1) Woodward and Schroeder, THIS JOURNAL, **59**, 1690 (1937).

(2) Toennies and Bennett, *J. Biol. Chem.*, **121**, 323 (1937).

CONTRIBUTION FROM THE
VENABLE CHEMICAL LABORATORY
UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, N. C.

RECEIVED NOVEMBER 6, 1948

NEW COMPOUNDS

Esters of Mono-, Di- and Tri-chloro-acetic Acids[1]

The new esters of mono-, di-, and tri-chloro-acetic acids, listed in Table I, have been synthesized by refluxing the alcohol with a slight molar excess of the acid in the presence of benzene. A Dean–Stark moisture trap was included in the apparatus to collect the water produced during the reaction. Refluxing was continued until the theo-

(1) Work done at the American Home Products Corp. Development Laboratory, New York, N. Y.