logical Coördination Center of the National Research Council. Preparation was accomplished by heating 5 g. of either the corresponding ethyl 2-pyridylaminomethylenemalonate (I)[2] or the 3-carbethoxy-2H-pyrido-1,2-a-pyrimidine-4-one (II)[2] with 250 ml. of 1% aqueous sodium hydroxide solution at 90° for five minutes with II or thirty minutes with I. The solution was filtered hot and made acid to congo red with dilute hydrochloric acid while still hot. The precipitated acid was twice recrystallized from pyridine.

3-(4-Methyl-2-pyridylamino)-acrylic Acid.—M. p. 238° with decarboxylation; yield from I 43%, from II 61%.

Anal. Calcd. for $C_9H_{10}O_2N_2$; N, 15.72; neut. equiv., 178. Found: N, 15.65[3]; neut. equiv., 176.

3-(5-Methyl-2-pyridylamino)-acrylic Acid.—M. p. 258° with decarboxylation; yield from I 36%, from II 67%.

Anal. Calcd. for $C_9H_{10}O_2N_2$: N, 15.72; neut. equiv., 178. Found: N, 15.74[3]; neut. equiv., 180.

(2) G. R. Lappin, THIS JOURNAL, **70**, 3348 (1948).

(3) Microanalysis by the Clark Microanalytical Laboratory, Urbana, Ill.

CHEMICAL LABORATORY
ANTIOCH COLLEGE
YELLOW SPRINGS, OHIO GERALD R. LAPPIN

RECEIVED MAY 16, 1949

Some Quaternary Salts of Carbamates of Amino Alcohols[1]

A series of compounds of the general formula $[R_3'N—A—OCONR_2]^+I^-$ has been prepared (Table I). The unsubstituted carbamates (both R = H) were prepared by method 1, the N-methylcarbamates (R = CH_3, and R = H) by method 2, and the N,N-dimethylcarbamates (both R = CH_3) by method 3.

(1) Reaction of a dialkylamino alcohol with phosgene gave the dialkylaminoalkyl chloroformate, which reacted with ammonia to give the urethan. Condensation with an alkyl iodide gave the quaternary salt.[2]

$$R_2N(CH_2)_nOH \xrightarrow{COCl_2} R_2N(CH_2)_nOCOCl \xrightarrow{NH_3} R_2N(CH_2)_nOCONH_2 \xrightarrow{RI} [R_3N(CH_2)_nOCONH_2]^+I^-$$

(2) Reaction of a dialkylamino alcohol with methyl isocyanate gave a carbamate, which reacted with an alkyl iodide to give the quaternary salt.

$$R_2N(CH_2)_nOH \xrightarrow{CH_3NCO} R_2N(CH_2)_nOCONHCH_3 \xrightarrow{RI} [R_3N(CH_2)_nOCONHCH_3]^+I^-$$

(3) Reaction of a chloro alcohol and phosgene gave the chloroalkyl chloroformate, which was converted to the iodoalkyl carbamate by reaction first with dimethylamine and then with sodium iodide in acetone. Condensation of the iodoalkyl carbamate with a tertiary amine gave the quaternary salt.[3]

$$Cl(CH_2)_nOH \xrightarrow{COCl_2} Cl(CH_2)_nOCOCl \xrightarrow{(CH_3)_2NH} Cl(CH_2)_nOCON(CH_3)_2 \xrightarrow{NaI} I(CH_2)_nOCON(CH_3)_2 \xrightarrow{R_3N} [R_3N(CH_2)_nOCON(CH_3)_2]^+I^-$$

(3) Sprinson, THIS JOURNAL, **63**, 2249 (1941).

DEPARTMENT OF CHEMISTRY
STANFORD UNIVERSITY L. KAPLAN
STANFORD, CALIF. C. R. NOLLER

RECEIVED APRIL 27, 1949

TABLE I

QUATERNARY SALTS OF CARBAMATES OF AMINO ALCOHOLS

Compound	M. p., °C.	Formula	Iodide analyses, % Calcd.	Found
2-Di-*n*-butylaminoethyl carbamate butiodide	99–100	$C_{15}H_{33}IN_2O_2$	31.70	31.47
3-Di-*n*-butylaminopropyl carbamate butiodide	122–123	$C_{16}H_{35}IN_2O_2$	30.62	30.64
3-Di-*n*-amylaminopropyl carbamate amyl iodide	108–110	$C_{19}H_{41}IN_2O_2$	27.80	27.40
2-Diethylaminoethyl N-methylcarbamate ethiodide	90–92	$C_{10}H_{23}IN_2O_2$	38.42	38.52
2-Di-*n*-butylaminoethyl N-methylcarbamate butiodide	100–101.5	$C_{16}H_{35}IN_2O_2$	30.62	30.43
2-Pentamethyleneaminoethyl N-methylcarbamate methiodide	103–105	$C_{10}H_{21}IN_2O_2$	38.66	38.99
3-Di-*n*-butylaminopropyl N-methylcarbamate butiodide	110.5–112	$C_{17}H_{37}IN_2O_2$	29.62	29.36
3-Di-*n*-amylaminopropyl N-methylcarbamate amyliodide	78–83	$C_{20}H_{43}IN_2O_2$	26.97	27.05
1-(3,4-Methylenedioxybenzyl)-2-[(3,4-methylenedioxybenzyl)-methylamino]-ethyl N-methylcarbamate methiodide	155–157	$C_{22}H_{27}IN_2O_6$	23.40	23.30
3-Dimethylamino-*d*-bornyl N-methylcarbamate methiodide	187–189	$C_{15}H_{29}IN_2O_2$	32.02	31.91
2-Diethylaminoethyl N,N-dimethylcarbamate ethiodide	106–107	$C_{11}H_{25}IN_2O_2$	36.86	37.08
Octahydro-N-[2-(dimethylcarbamyloxy)-ethyl]-2-methyl-pyrrocolinium iodide	150–151.5	$C_{14}H_{27}IN_2O_2$	33.19	33.23

(1) These compounds were prepared for the Office of Scientific Research and Development under Contract OEMsr-136 with Stanford University.

(2) Dalmer and Diehl, U. S. Patent 1,894,162; *C. A.*, **27**, 2533 (1933).

Stilbestrol Esters

Since a new series of testosterone esters[1] was found to have greater androgenic activity than testosterone propionate, similar stilbestrol esters have been prepared to determine whether these esters have any advantage over stilbestrol dipropionate. Two representative esters have been prepared.

Diethylstilbestrol Di-ethoxyacetate.—A solution of 1 g. of diethylstilbestrol (1 mole) in 15 cc. of dry ether and 6 cc. of dry pyridine was prepared. To this was added 2 cc. of ethoxyacetyl chloride (5 mole) in 10 cc. of dry ether. The reaction mixture was refluxed for one hour and 100 cc. more ether was added. This was poured into water and the ether layer separated, washed with dilute sulfuric acid, dilute sodium carbonate solution and water. Evaporation of the ether left 1.40 g. of reddish white powder, m. p. 129–136°. The product was taken up in a large amount of ether and filtered through activated alumina (Aluminum Ore Co. mm. 80 mesh). The red color was adsorbed on the alumina. Evaporation of the ether left a residue which was twice crystallized from 95% ethanol giving a product (1.05 g.) melting at 136.5–137.5°.

Anal. Calcd. for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32. Found: C, 71.16; H, 7.57.

(1) Mooradian and Lawson, in press.

Diethylstilbestrol Di-ethylmercaptoacetate.—This ester was prepared just as was the preceding ester. The purification was carried out by evaporating the ether extract to dryness and taking the residue up in 10 cc. of ether and 40 cc. of Skellysolve A. This solution was passed through activated alumina and the alumina was then extracted with 1:4 ether–Skellysolve A. The extract was evaporated and the absorption-elution process carried out twice more. Finally the crude product (1.05 g.) was crystallized once from Skellysolve B and twice from 95% ethanol giving a yellowish product 0.30 g., m. p. 99–101°.

Anal. Calcd. for $C_{26}H_{32}O_4S_2$: C, 66.04; H, 6.83; S, 13.57. Found: C, 66.01; H, 6.73; S, 13.83.

STERLING-WINTHROP RESEARCH INSTITUTE
RENSSELAER, N. Y.
ARAM MOORADIAN
E. J. LAWSON

RECEIVED MARCH 16, 1949

COMMUNICATIONS TO THE EDITOR

THE USE OF CADMIUM IODIDE IN STARCH-IODINE COLORIMETRIC PROCEDURES

Sir:

In the course of an investigation[1] on methods of analysis for trace amounts of selenium in water, it was found that cadmium iodide and starch form a stable solution which may be used as a colorimetric reagent for a number of oxidizing substances. The reduction potential of the iodide in such a solution is a function of the *p*H. By proper adjustment of the *p*H, the iodide may be "exposed" to oxidation by oxidizing agents for controlled periods of time and in this way it was found possible to determine one oxidizing agent in the presence of others.

Cadmium iodide crystals may have a brownish discoloration which is shown by reaction with starch to be free iodine. However, after an aqueous solution of cadmium iodide is boiled for ten or fifteen minutes, a colorless solution is obtained. This solution may be added to a solution of starch to give a mixture that is apparently stable indefinitely to atmospheric oxygen and diffused sunlight.

In neutral solution, only the very strongest oxidizing agents, such as chlorine or hypochlorite, are capable of oxidizing the iodide to iodine and producing the blue starch–iodine color. At lower *p*H values, weaker oxidizing agents are able to oxidize the iodide; *e. g.*, nitrous acid is capable of oxidizing the iodide if the *p*H is below about 4.0 but the *p*H must be in the neighborhood of 1.0 or lower before selenious acid is able to react. Dissolved oxygen attacks the cadmium iodide reagent only in the most highly acid solutions, and very slowly even then.

The linear starch "A-fraction" isolated by Schoch[2] gives the best results although commercial soluble starches can be used. The color of the A-fraction starch–iodine complex produced by selenious acid in concentrations from 0.1 to 2.0 p. p. m., as selenium, follows Beer's law quite closely. The absorption band is broad with maximum absorption occurring at about 615 mμ.

Cadmium iodide in aqueous solution has been shown to form one or more auto-complexes, the nature of which has been the subject of several investigations. The complex anion may be CdI_3^-, $CdI_4^=$ or $CdI_5^{\equiv}$, with the cation Cd^{++} or CdI^+.

This reagent is undergoing further investigation in connection with the development of colorimetric methods of determining traces of substances having oxidizing properties, particularly selenium as selenious acid.

We wish to thank T. J. Schoch of the Corn Products Refining Company for providing generous samples of the linear starch A-fraction.

DEPARTMENT OF CHEMISTRY
OKLAHOMA A. & M. COLLEGE
STILLWATER, OKLAHOMA
PAUL ARTHUR
T. E. MOORE
JACK LAMBERT

RECEIVED JULY 11, 1949

(1) This investigation is supported by a research grant from the National Institutes of Health.

(2) Schoch, THIS JOURNAL, **64**, 2957–2961 (1942); "Advances in Carbohydrate Chemistry," Vol. I, ed. by Pigman and Wolfrom, Academic Press Inc., New York, N. Y., 1945, pp. 247–277.

GERMIDINE AND GERMITRINE, TWO NEW ESTER ALKALOIDS FROM *VERATRUM VIRIDE*

Sir:

Recent evidence[1,2] indicates that powdered roots and rhizomes of *Veratrum viride* may produce marked reductions of arterial pressure in patients with essential hypertension. We have isolated from this material two new, highly active ester alkaloids derived from the alkamine germine, which we have named germidine and germitrine.[3]

(1) E. D. Freis and J. R. Stanton, *Am. Heart J.*, **36**, 723 (1948).

(2) E. D. Freis, *et al.*, *J. Clin. Investigation*, **28**, 353 (1949).

(3) Drs. E. D. Freis, J. A. Stanton and F. C. Moister of the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine, have evaluated more than 100 of our individual alkaloidal fractions in patients with essential hypertension. Their results will be published elsewhere.