phases of the study of the absorption spectrum of americium.

A Baird Eagle Mount Spectrograph, having 5.6 Å./mm. dispersion in the first order, was used for the solution work. A 1 cm. path length cell 2 mm. wide was mounted on the arm of a micro-manipulator. The cell was then placed as close to the slit as possible. The cell was of fused silica. For the wave lengths below 3500 Å. a water cooled hydrogen discharge lamp was used and above 3500 Å. a tungsten filament lamp.

The absorption spectrum of trivalent americium in perchloric acid solution has been measured in the wave length range 2200 to 10,000 Å., and the results appear in Table I. The spectrograms show a marked similarity to those of rare earth solutions, but the americium absorption is much more intense. The absorption in the 5000 Å. region is especially strong and was found to persist at very low concentrations.

TABLE I

Am^{+++} IN $HClO_4$ AT ROOM TEMPERATURE

λ, Å.	8133	5166	5104	5078	5030	4543	4287
λ, Å.	4198	4018	3784	3771	3756	3605	3391
λ, Å.	3353	3312	2893	2861	2847	2826	2754
λ, Å.	2705	2699	2651	2597	2537	2436	2433

The measurements were made using a solution 0.04 *M* in americium and 0.5 *M* in perchloric acid. However, to detect the four components of the 5000 Å. peak, it was necessary to reduce the americium concentration to about 10% of the above. With this solution none of the other lines were discernible.

This work was performed under the auspices of the U. S. Atomic Energy Commission.

DEPARTMENT OF CHEMISTRY AND RADIATION LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIF.

RECEIVED SEPTEMBER 11, 1950

Some Synthetic Esters of Germine

BY HOWARD L. WHITE

The hypotensive principles of *Veratrum viride*, germidine and germitrine, have been characterized as mixed di- and triesters, respectively, of the alkamine germine.[1] The constituting acids in germidine are acetic acid and *l*-α-methylbutyric acid, while germitrine contains in addition *d*-methylethylglycolic acid. Removal of the acyl groups by hydrolysis all but abolishes the hypotensive activity. Hence it was of interest to prepare simple synthetic esters of germine and to compare their hypotensive potency with that of the natural ester alkaloids.

Germine, $C_{27}H_{43}O_8N$, is an octahydric alcohol in which five hydroxyl groups are esterifiable.[2] Esterification with acyl chlorides in cold pyridine solution should therefore lead primarily to pentaesters. However, the crude products thus obtained invariably proved to be complex mixtures, much to the detriment of the yield of crystalline esters isolated. In the majority of cases no crystalline products were realizable even when resort was taken to chromatographic fractionation. The properties of the four new crystalline esters obtained are listed in Table I, together with those of germine and of germine pentaacetate.[1] As can be seen, acylation of all five reactive hydroxyl groups was attained in only two cases. It is evident that although esterification greatly potentiates the (weak) hypotensive effect of germine, the potency of the best compound of the series, the triisobutyrate, still falls short of that of the natural ester alkaloid, germitrine, by a factor of about 1:12.[3]

TABLE I

	M. p. °C.	[α]D, in pyridine	Minimum effective dose[a] μg./kg.
Germine	208 (dec.)	− 2.5	2000
pentaacetate	256–257	−85	300–400
tetrapropionate	216–217	−92.4	300–400
triisobutyrate	197–201	−65.8	6–8
pentacyclohexane-carboxylate	201–205	−60.4	32
tetrabenzoate	223–225	−68.1	300–400
Germitrine	216–219	−69	0.5

[a] By intravenous route in the anesthetized dog. The assays involved comparison of the hypotensive effect with that given by a standard preparation ("total amorphous bases"[1]) having one-fourth of the hypotensive potency of germitrine.

All the synthetic esters showed high specific rotation in pyridine, of the order of that of germitrine. In the natural triester this property is specifically associated with its acetoxy group, since it is no longer in evidence in the de-acetylated diester, germerine, formed from germitrine by methanolysis.[1] Hence it appears probable that the hydroxyl group which carries the acetyl group in germitrine is also esterified in all the synthetic esters.

Esterification of germine with *n*-valeric, isovaleric, diethylacetic, piperonylic and veratric acids failed to yield crystalline products even after chromatographic fractionation. The hypotensive potency of the main fractions, while invariably exceeding that of germine, was generally of too low an order to warrant further investigation.

Experimental

Germine Tetrabenzoate.—A solution prepared by adding at 0° freshly distilled benzoyl chloride (564 mg., 4.0 millimoles) in dry pyridine (4 cc.) to germine (250 mg., 0.5 millimole) dissolved in the same solvent (4 cc.) was allowed to stand at 0° for 19 hours. It was then worked up by pouring it into a saturated sodium bicarbonate solution containing excess chopped ice, and extracting after 30 minutes with four 50-cc. portions of chloroform. The brown oil (450 mg.) obtained by evaporation *in vacuo* of the dried extract was triturated for a short time with a 1:1 mixture of 5% acetic acid and 10% sodium chloride solution. The resulting microcrystalline hydrochloride was filtered off (m.p. of a dried sample 187–188°), decomposed with saturated sodium bicarbonate solution, and the basic ester recovered by chloroform extraction. The product crystallized in part when its solution in absolute ethanol was allowed to stand at 4°. After three recrystallizations from the same solvent the pure ester (50 mg.) melted at 223–

---

(1) J. Fried, H. L. White and O. Wintersteiner, THIS JOURNAL, **72**, 4621 (1950).

(2) W. Poethke, (a) *Arch. Pharm.*, **275**, 357 (1937); (b) *ibid.*, **275**, 571 (1937); (c) *ibid.*, **276**, 170 (1938).

(3) A preliminary clinical assay conducted on three hypertensive patients by Dr. E. D. Freis of the Veterans' Administration Hospital, Washington, D. C., showed the potency of the triisobutyrate to be about one-fortieth that of germitrine by the intravenous route.

225° (dec.); $[\alpha]^{25}\mathrm{D}$ −16.8° (*c*, 0.48 in ethanol–chloroform 1:1); −69° (*c*, 0.22 in pyridine); ϵ at 232 mμ 52,000; 3(β)-cholestanyl benzoate, ϵ at 232 mμ 12,000.

Anal. Calcd. for $C_{27}H_{38}O_8N(C_7H_5O)_5$: C, 72.31; H, 6.17; for $C_{27}H_{39}O_8N(C_7H_5O)_4$: C, 71.32; H, 6.42. Found: C, 71.28, 71.46; H, 6.41, 6.49.

Germine Tetrapropionate.—A solution of germine (250 mg., 0.5 millimole) in pyridine (4 cc.) was mixed at 0° with freshly distilled propionic anhydride (7.6 cc., 6.0 millimoles). After standing at room temperature for 19 hours, the solvents were removed *in vacuo*. The residue crystallized in part from dilute ethanol. After two recrystallizations from the same solvent needles (10.8 mg.) melting at 216–217° were obtained, $[\alpha]^{25}\mathrm{D}$ −92.4° (*c*, 0.24 in pyridine).

Anal. Calcd. for $C_{27}H_{39}O_8N(C_2H_5CO)_4$: C, 63.83; H, 8.10; $4C_2H_5CO$, 31.1. Found: C, 63.72; H, 8.31; C_2H_5CO, 31.0.[4]

Germine Triisobutyrate.—A solution of germine (923 mg., 1.81 millimoles) in dry pyridine (16 cc.) was mixed at −20° with freshly distilled isobutyryl chloride (1.58 g., 15.5 millimoles) in pyridine (8 cc.). The mixture was kept at −20° for a half-hour and then at 0° overnight. It was poured onto chopped ice and saturated sodium bicarbonate solution and, after some standing, exhaustively extracted with a total of 500 cc. of chloroform. The residue of the dried and evaporated extract was triturated with benzene, and the insoluble portion was removed by centrifugation. The residue obtained from the supernatant was throughly dried (970 mg.) and adsorbed in benzene solution on 20 g. of sulfuric acid-washed alumina.[1] Continued washing with benzene brought through only traces of material, but with benzene containing 2.5% methanol a substantial fraction (339 mg.) was eluted. This material was crystallized by dissolving it in the minimum amount of boiling hexane and allowing the solution to stand at 4° overnight (128 mg., m.p. 196–200°). The melting point remained virtually unchanged on 2 recrystallizations from the same solvent (197–201°); ($[\alpha]^{25}\mathrm{D}$ −65.8 (*c*, 0.76 in pyridine).

Anal. Calcd. for $C_{27}H_{39}O_8N(C_4H_7O)_4$: C, 65.36; H, 8.55; $4(CH_3)_2CHCO$, 36.0; for $C_{27}H_{40}O_8N(C_4H_7O)_3$: C, 65.07; H, 8.54; $3(CH_3)_2CHCO$, 29.6. Found: C, 65.24, 65.02; H, 8.61, 8.63; $(CH_3)_2CHCO$[4], 31.6, 29.3.

Further elution with more polar solvent mixtures yielded only small additional amounts of material which failed to crystallize either as such or after reacylation under the above conditions.

Germine Pentacyclohexanecarboxylate.—A solution of germine (250 mg., 0.5 millimole) in dry pyridine (4 cc.) was cooled to −20° and a solution of 0.7 cc. cyclohexanecarboxylic acid chloride (770 mg., 5.25 millimoles, freshly prepared from the acid with thionyl chloride and distilled *in vacuo*) in dry pyridine (4 cc.) was added. The reaction mixture was kept at −20° for two hours, and then overnight at 4°. Treatment with ice-cold bicarbonate solution yielded a precipitate (600 mg.), which was extracted with boiling acetone. After removal of undissolved material by centrifugation the solution was concentrated to a small volume. The crystalline product which deposited on standing yielded on 2 recrystallizations from acetone prisms (21 mg.) melting at 202–205°; $[\alpha]^{25}\mathrm{D}$ −60.4° (*c*, 0.5 in pyridine).

Anal. Calcd. for $C_{27}H_{38}O_8N(C_6H_{11}CO)_5$: C, 70.26; H, 8.84. Found: C, 70.56; H, 9.19.

The non-crystallizable esters mentioned in the general part were prepared from germine and the appropriate acyl chlorides under conditions similar to those specified for the isobutyrate. The crude products were chromatographed as described in that section. Attempts to crystallize the early benzene–2.5% methanol eluates (which were assumed to contain the most highly esterified products) were uniformly unsuccessful.

Acknowledgments.—The author is indebted to Drs. O. Wintersteiner and Josef Fried for many helpful suggestions, to Mr. Norman Salzman for able technical assistance and to Mr. Joseph F. Alicino and his associates for the microanalyses. The assays for hypotensive activity were performed by Mr. Irving Miller, Division of Pharmacology, Squibb Institute.

SQUIBB INSTITUTE FOR MEDICAL RESEARCH
NEW BRUNSWICK, NEW JERSEY RECEIVED JULY 17, 1950

[4] Pregl-Roth, "Die quantitative organische Microanalyse," Julius Springer, Berlin, 1935, p. 235.

The Preparation and Some Properties of Curium Metal

BY J. C. WALLMANN, W. W. T. CRANE AND
B. B. CUNNINGHAM

Curium metal has been prepared on the microgram scale by reduction of curium trifluoride with barium metal vapor at 1275°, using a vacuum furnace and double crucible system similar to that described by Fried and Davidson.[1]

Six successful reductions, which yielded bright metallic globules of metal ranging in mass from about 0.01 to 4 μg. have been made. The metal is silvery in appearance and about as malleable as plutonium prepared under the same conditions. The metal retained its bright appearance in the dry atmosphere of a nitrogen "dry box" for some hours but gradually tarnished, and on standing for about 24 hours was rather badly corroded. Under the same conditions, samples of other actinide metals, such as americium or plutonium, have shown less evidence of reaction. The greater reactivity of curium probably is to be attributed to the radioactivity of the isotope[2] Cm^{242} (equivalent to a power output of 1.2×10^{-4} watts/μg.), which, under some conditions, is sufficient to maintain the temperature of the sample substantially above that of its environment.

The trifluoride used for the reductions was prepared by precipitating Cm(III) in dilute nitric acid in a fluorothene microcone with an excess of hydrofluoric acid, washing the precipitate with dilute hydrofluoric acid, and drying the CmF_3 in platinum under a heat lamp. Pieces of the dry fluoride were then transferred to the inner crucible for reduction. When the quantities of curium were relatively large (*ca.* 10 μg.), the trifluoride was compacted in the bottom of the crucible by tamping with a quartz rod.

The conditions for reduction to usable metal were rather critical. Reduction at 1380° left the metal as a thin film adhering to the wall of the crucible. Reduction at about 1250° resulted in the formation of a cokey residue, indicating poor agglomeration of the metal. Reduction with barium vapor at 1275° for 45 seconds, followed by additional heating at 1100° for 45 seconds and a final heating at 960° for 20 seconds produced optimum results. In one such run on 12 μg. of CmF_3, reduction yielded a single 4 μg. spheroidal piece of metal. This piece was separated from the crucible, intact and free of slag or other residues.

The volume of the piece was estimated by measurement with a filar micrometer under about 200× magnification. The mass of the sample was

---

[1] S. Fried and N. R. Davidson, THIS JOURNAL, **70**, 3539 (1948).

[2] The isotope used for this work was the 162-day Cm^{242}. The preparation and isolation of microgram quantities of Cm^{242} has been described by L. B. Werner and I. Perlman, National Nuclear Energy Series, Plutonium Project Record, Vol. 14B, "The Transuranium Elements: Research Papers," Paper No. 22.5 (McGraw-Hill Book Co., Inc., New York, N. Y., 1949).