TABLE I

Alcohol	Yield of ketone, % Meth. A	Meth. B	Source of alcohol	Identification of ketone
Benzohydrol	33	33	[a]	[b]
Xanthhydrol	70	100	[a]	[b]
Furoin	88	66	[a]	[b]
Phenylmethylcarbinol	34		[a]	[c]
α-Naphthylmethylcarbinol	45		[d,g]	[e]
1,3-Diphenylpropanol-1	50		[e]	[b]
3-Furyl-1-(2-naphthyl)-propanol-1	59		[f]	[b]
1-Hydroxy-1,2,3,4-tetrahydrophenanthrene	50		[d,h]	[b,c]
1-Hydroxy-1,2,3,4,5,6,7,8-octahydrophenanthrene	50		[f]	[b,c,f]
1-Hydroxy-1,2,3,4,5,6,7,8-octahydroanthracene	50		[d,i]	[b,c,f]

[a] Commercial preparation (Distillation Products Inc.). [b] By melting point of mixture with authentic sample. [c] By conversion to semicarbazone and comparison with authentic sample. [d] By reduction of ketone with sodium borohydride in methanol. The alcohols were free of ketone as indicated by treatment with semicarbazide. [e] By reduction of benzalacetophenone using a method described in the Experimental section for a furfuryl ketone. [f] Preparation described in Experimental section. [g] M.p. 64–65°; reported m.p. 66° by Pickard and Kenyon, *J. Chem. Soc.*, **105**, 1126 (1914). [h] M.p. 100–101°; reported m.p. 100–101° by Cook, *Proc. Roy. Soc. (London)*, **B121**, 133 (1936). [i] M.p. 92–94°; reported m.p. 94–95° by Schroeter.[11]

has been used for the preparation of the corresponding 5,6,7,8-tetrahydro-2-naphthylbutyric acid. The product crystallized from cyclohexane, m.p. 95–97° (reported[9] 94–95°), yield 40%. The preliminary Huang-Minlon reduction facilitated the purification of the product.[8]

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.04; H, 8.31. Found: C, 77.11; H, 8.08.

1-Hydroxy-1,2,3,4,5,6,7,8-octahydrophenanthrene.—The preceding acid was cyclized by a standard method[10] to 1-keto-1,2,3,4,5,6,7,8-octahydrophenanthrene, m.p. 80–81° (reported[9] 80.5–81°).

Anal. Calcd. for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.06; H, 7.96.

The ketone (5 g.) was dissolved in 50 ml. of methanol, and treated with 1 g. of sodium borohydride. After standing overnight, the solution was diluted with water, the product was filtered and recrystallized from ether–pentane; yield 3.0 g., m.p. 104–105° (reported[11] 94°). It showed no reaction with semicarbazide, and formed a phenylurethan, m.p. 192–194° (reported[11] 194°).

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.04; H, 9.01.

1-Hydroxy-1,2,3,4,5,6,7,8-octahydroanthracene.—The cyclization of γ-(5,6,7,8-tetrahydro-2-naphthyl)-butyric acid was effected by the use of stannic chloride[10,12] on the acid chloride prepared with phosphorus pentachloride. The yield of crude product, b.p. 140–160° (4 mm.), was 95%. On crystallization from pentane, material of m.p. 47.5–48° was obtained in a yield of 65% (reported[13] m.p. 47°). This is the 1-keto-1,2,3,4,5,6,7,8-octahydroanthracene. The alternative cyclization product[11,12] may have been present in the mother liquor. The ketone was reduced to the alcohol with sodium borohydride. It had m.p. 92–93°; phenylurethan, m.p. 151–153° (reported[11] 94–95°, 153°). A sample of the alcohol was dehydrogenated with palladium to anthracene to make sure that it was indeed the linearly cyclized product.

3-Furyl-1-(2-naphthyl)-propanone-1.—This was prepared from furfurylidene-2-acetylnaphthalene by hydrogenation in methanol at 40° in the presence of palladium–strontium carbonate catalyst. Crystallized from methanol, it had m.p. 64–65°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.52; H, 5.70.

3-Furyl-1-(2-naphthyl)-propanol-1.—The preceding ketone was hydrogenated in acetone and hydrochloric acid, in the presence of palladium chloride-on-carbon (Wilkens-Anderson Co., 5% palladium), following a procedure developed for a different purpose by Londergan, Hause and Schmitz.[14] The resulting alcohol was crystallized from ether–pentane, and melted at 65°. Unlike the ketone, it was very soluble in methanol. A mixture with the ketone melted at 41–46°. It was purified before oxidation by treatment with Girard reagent.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.83, 80.88; H, 6.25, 6.26.

Acknowledgment.—This was part of a project aided by a grant, No. C-1585, from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service. I am grateful to Mr. Samuel Mason for technical assistance.

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Oxidation of Semicarbazide

BY PAUL F. WILEY

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Linch[1] has reported that oxidation of semicarbazide with sodium hypobromite forms tetrahydro-3,6-*sym*-tetrazinedione (I).[2] Stollé[3] in a short article containing no experimental results stated that the reaction product was biurea (II) rather than I.

$$O{=}C(NHNH)_2C{=}O \;\longleftarrow\; NH_2CONHNH_2 \longrightarrow \quad NH_2CONHNHCONH_2$$

I II

The latter interpretation seems more likely in view of D'Arcangelo's[4] oxidation of semicarbazide to biurea using iodine and cyanogen iodide. These oxidations are similar to the one using hypobromite in that the oxidizing agent is also positive halogen. Biurea was obtained in 66% yield using the procedure of Linch[1] which involves the use of 1.5 moles of bromine per mole of semicarbazide hydrochloride. The biurea was identified by comparison of physical properties with those of an authentic sample and by analysis. When equimolecular amounts of bromine and semicarbazide hydrochloride were used in the reaction, the yield of biurea was 91%. The probable sequence of reactions involved is

$$NH_2CONHNH_2 \xrightarrow{NaOBr} NH_2CONHNHBr \xrightarrow{NaOH} NH_2CONHN{=}NNHCONH_2 \longrightarrow II + N_2$$

Acknowledgment.—I wish to thank Mr. W. J. Schenck for the microanalyses.

(1) F. W. Linch, *J. Chem. Soc.*, **101**, 1755 (1912).
(2) Linch referred to I as *p*-urazine. However, it has been shown that *p*-urazine is 4-amino-1,2,4,1H-triazole-3,5-(2H,4H)dione [R. Stollé, *J. prakt. Chem.*, **75**, 416 (1907)].
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(4) A. T. D'Arcangelo, *Rev. facultad cienc. quim.*, **18**, 81 (1943); *C. A.*, **41**, 948 (1947).

Experimental[5]

Oxidation by Linch's[1] Procedure.—This experiment was run using the procedure and quantities reported by Linch.[1] There was obtained 3.5 g. of biurea, m.p. 248° dec. The yield was 66%. Three recrystallizations from water gave a product melting at 257° dec. which did not depress the melting point of a sample of authentic biurea melting with decomposition at 257°. The two materials were also shown to be identical by X-ray diffraction diagrams.

Anal. Calcd. for $C_2H_6N_4O_2$: N, 47.47. Calcd. for $C_2H_4N_4O_2$: N, 48.27. Found: N, 47.47.

Oxidation Using Equimolecular Amounts of Bromine and Semicarbazide.—A solution of sodium hypobromite was prepared by adding 5.1 ml. (16 g., 0.1 mole) of bromine to a solution of 12 g. (0.3 mole) of sodium hydroxide in 100 ml. of water. This solution was cooled to 5° and added dropwise with stirring to a solution of 11.5 g. (0.1 mole) of semicarbazide hydrochloride in 60 ml. of water while keeping the reaction mixture at 5–15°. During the reaction there was a vigorous evolution of a neutral gas, presumably nitrogen. The reaction mixture was cooled in an ice-bath and stirred for one hour longer. Filtration and drying of the product gave 5.4 g. (91%) of biurea, m.p. 257° dec. This product did not depress the melting point of an authentic sample of biurea, m.p. 257° dec.

(5) Melting points are uncorrected.

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Pantothenic Acid Salts

BY EVELYN H. WILSON, JOHN WEIJLARD AND MAX TISHLER

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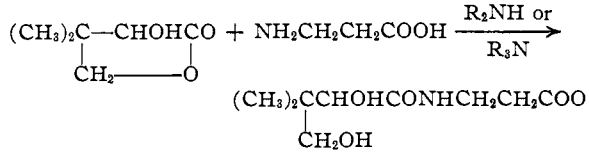
The reaction of an alkaline or alkaline earth salt of β-alanine with *d*(−)α-hydroxy-β,β-dimethyl-γ-butyrolactone, *d*(−)-pantolactone in an anhydrous alcoholic medium is considered the method of choice for the preparation of salts of *d*(+)-pantothenic acid.[1]

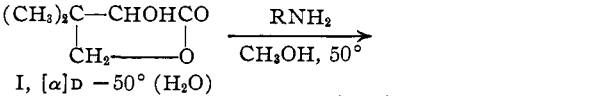
The direct combination of this *d*(−)-pantolactone with β-alanine has been accomplished only by the fusion of the two components; this method usually gives *d*(+)-pantothenic acid in poor yields.[2]

A new and practical method of synthesizing salts of pantothenic acid has been devised which does not require metal salts of β-alanine. When equimolar quantities of the pantolactone, β-alanine and a secondary or tertiary amine are heated in an anhydrous alcoholic medium, a homogeneous solution results from which calcium *d*(+)-pantothenate can be obtained in high yield upon the addition of calcium oxide. Sodium *d*(+)-pantothenate is similarly obtained, if, instead of calcium oxide, sodium ethoxide is used.

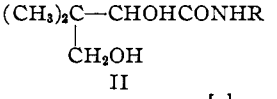


Some observations pertinent to an understanding of the condensation reaction were made. (1) β-Alanine does not react with the amine to a measurable extent under the conditions used for the condensation. The amino acid remains undissolved during protracted heating with the amine in alcohol and is recovered completely by filtration of such a mixture.

(2) Prolonged heating of a solution of the lactone and the amine in ethanol does not produce a change in optical rotation. Accordingly, amide or ester formation does not occur during the condensation since in all recorded cases a pantolactone derivative containing the lactone ring opened has a rotation opposite in direction from that of the parent lactone. The rotations of some amides II of pantolactone[3] illustrate this point.



I, $[\alpha]_D$ −50° (H_2O)



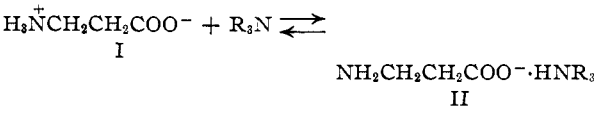
R– (II)	$[\alpha]_D$ (H_2O)	R– (II)	$[\alpha]_D$ (H_2O)
$-CH_2CH_2CH_2OH$	+29.7°	$-CH_2CH_2OH$	+31.5°
$-CH(CH_3)CH_2CH_2OH$	+16.1°	–H	+30.9°

(3) When β-alanine is added to the alcoholic solution of the amine and *d*(−)α-hydroxy-β,β-dimethyl-γ-butyrolactone, the β-alanine dissolves rapidly, and the levorotatory solution becomes dextrorotatory, indicating the lactone ring has opened. The combination of the lactone with β-alanine occurs prior to the addition of the inorganic salt-forming agent.

No reaction occurs in the absence of the amine. The effect of the amine, however, is not catalytic, since at least equimolar amounts of the amine, lactone and β-alanine are required for complete reaction.

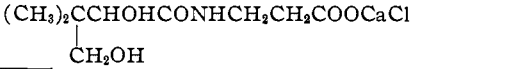
The efficacy of amines in this reaction does vary. Secondary amines are more effective (88% yield) than tertiary amines (46% yield), while primary amines have a negligible effect. The failure of primary amines in this reaction is probably attributable to their preferential formation of an amide (I → II) of the lactone.[3]

Notwithstanding the apparent lack of reactivity between the β-alanine and secondary and tertiary amines, it is likely that an equilibrium exists between the zwitterion I and the amine salt II, however small the concentration of the latter, which is responsible for the condensation reaction.



This system would permit β-alanine in its highly enhanced donor form II to react with the lactone producing an amine salt of pantothenic acid.

In the course of this work we have prepared the calcium chloride salt of *d*(+)-pantothenic acid



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