TABLE I

ETHYL *t*-ALKYLCYANOACETATES, $RCH(CN)COOC_2H_5$

	t-Alkyl group, R	Halide used in preparation of Grignard reagent	Yield, %	B. p. °C.	B. p. mm.
	(A) From Ethyl 1-Methylethylidenecyanoacetate				
1	*t*-Butyl	Methyl iodide	75	88	5
2	1,1-Dimethylpentyl	*n*-Butyl bromide	42	109	2
3	1,1-Dimethyl-2-phenylethyl	Benzyl chloride	49	142–143	0.4
4	1,1-Dimethylbenzyl	Bromobenzene	60	155	0.5
	(B) From Ethyl 1-Methylpropylidenecyanoacetate				
5	1,1-Dimethylpropyl	Methyl iodide	41	75–76	0.9

		Molecular refraction			Carbon, %		Hydrogen	
$n^{20}D$	d^{20}_4	Calcd.	Found	Formula	Calcd.	Found	Calcd.	Found
		(A) From Ethyl 1-Methylethylidenecyanoacetate						
1.4278	0.9629	45.23	45.26	$C_9H_{15}O_2N$	63.88	64.17	8.94	9.07
1.4392	0.9430	59.08	59.07	$C_{12}H_{21}O_2N$	68.20	68.47	10.02	10.26
1.5032	1.0432	69.24	69.67	$C_{15}H_{19}O_2N$	73.44	73.57	7.81	8.08
1.5062	1.0570	64.72	65.15	$C_{14}H_{17}O_2N$	72.70	72.93	7.41	7.50
		(B) From Ethyl 1-Methylpropylidenecyanoacetate						
1.4369	0.9633	49.87	49.91	$C_{10}H_{17}O_2N$	65.55	65.39	9.34	9.42

atmosphere by a calcium chloride tube, was prepared a Grignard solution from 6.8 g. (0.28 mole) of magnesium, 39.9 g. (0.28 mole) of methyl iodide, and 60 ml. of ether. To this solution was then added 40.0 g. (0.234 mole) of ethyl isopropylidenecyanoacetate at such a rate that the reaction mixture refluxed gently. After addition was complete, the two-phase system was heated gently on the steam-bath, with stirring, for one hour. The complex was then cooled and poured onto a mixture of ice and 15% aqueous ammonium chloride solution. After separating the organic layer and extracting the aqueous layer with ether, the organic portion and the ether extracts were combined, washed with water, and dried over anhydrous magnesium sulfate. The excess ether was then removed *in vacuo* and the residue was distilled through an eight inch electrically heated column packed with glass helices.

Infrared analysis showed nitrile and ester-carbonyl groups, but there was no indication of carbon–carbon double bonds or hydroxyl groups.[4] The ester gave negative tests with sodium hypoiodite, acetyl chloride, 2,4-dinitrophenylhydrazine and ferric chloride. The odor of ammonia could be detected when it was heated with sodium hydroxide in diethylene glycol solution. Hydrogen bromide was evolved on treatment with bromine in carbon tetrachloride solution. Saponification gave *t*-butylmalonic acid, m. p. 149.5–151°[1] and conversion of the volatile portion of the saponification mixture to a 3,5-dinitrobenzoate gave a product which melted at 90° and showed no depression when admixed with ethyl 3,5-dinitrobenzoate.

(4) We are indebted to Dr. Foil A. Miller, Mrs. J. L. Johnson, and Miss Elizabeth Peterson for the determination and interpretation of these curves.

Summary

The conjugate addition of phenyl and primary Grignard reagents to ethyl 1-methylethylidenecyanoacetate constitutes a general method for the synthesis of several ethyl *t*-alkylcyanoacetates. The yields are 42–75%. An investigation of the scope and limitations of the reaction has been carried out.

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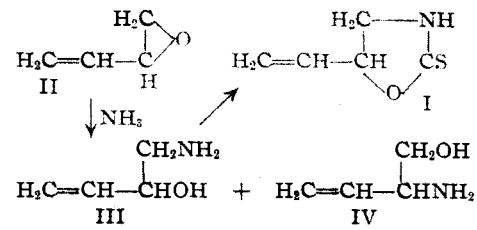
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthesis of the Natural Antithyroid Factor *l*-5-Vinyl-2-thioöxazolidone[1]

BY MARTIN G. ETTLINGER[2]

The antithyroid factor of turnip root and seeds of numerous *Brassicae*, including cabbage, turnip and rape, has been isolated and proved to be *l*-5-vinyl-2-thioöxazolidone (I).[3] Ingestion of the substance may cause simple goiter.[4,5] The present paper contains a description of synthesis of the naturally occurring form of I.



The starting material, butadiene-1,2-oxide[6] (II), furnished on ammonolysis 1-amino-3-buten-

(1) Preliminary communication: Astwood, Greer and Ettlinger, *Science*, **109**, 631 (1949).

(2) Member of the Society of Fellows, Harvard University.

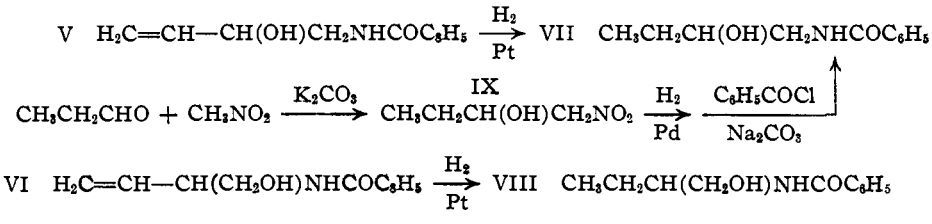
(3) Astwood, Greer and Ettlinger, *J. Biol. Chem.*, **181**, 121 (1949).

(4) Astwood, *Ann. Internal Med.*, **30**, 1087 (1949).

(5) Greer, Ettlinger and Astwood, *J. Clin. Endocrinol.*, **11**, 1069 (1949); *Trans. Am. Goiter Assoc.*, 55 (1949).

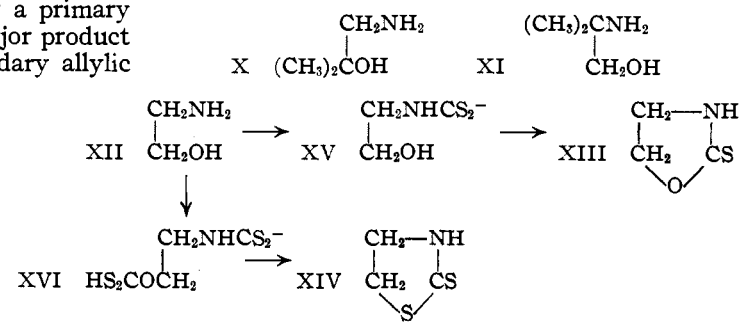
(6) Pariselle, *Ann. chim.*, [8] **24**, 315 (1911); Kadesch, THIS JOURNAL, **68**, 41 (1946).

2-ol (III) and 2-amino-3-buten-1-ol (IV), separated by crystallization of their acid oxalates. Previous experience with addition of nucleophilic reagents like ammonia to II has shown that methoxide ion,[7] sodium diethyl malonate,[8] lithium aluminum hydride[9] or, probably, cyanide ion[10] attack both carbons of the oxide ring, preponderantly at the 1-position. Only sodium allylate[11] has been alleged to give mainly a primary alcohol with II. As expected, the major product from II and ammonia was the secondary allylic alcohol III, isolated in 45% yield from the mixture as the acid oxalate, m. p. 132° (dec.), regenerated from the salt as a deliquescent solid, m. p. *ca.* 40°, and characterized as the benzamide (V), m. p. 72°. The minor component IV was separated to the extent of 7% as the dimorphous acid oxalate, m. p. 112.5° (dec.) or 126° (dec.), and characterized as the benzamide (VI), m. p. 64.5°. The preparation[12,13] of benzamides from amino alcohols by treatment with a molar equivalent of benzoyl chloride in excess sodium carbonate was convenient; the derivatives possessed amide absorption bands at 5.98–6.05 μ. The structures of the aminobutenols were proved by catalytic hydrogenation of V to 1-benzoylamino-2-butanol (VII), m. p. 113.5°, and VI to 2-benzoylamino-1-butanol (VIII), m. p. 100.5°.

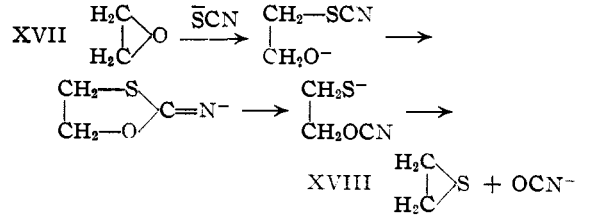


The reduction products were identical with unambiguously synthesized specimens, Authentic VII was obtained by condensation of propionaldehyde and nitromethane to 1-nitro-2-butanol[14] (IX), hydrogenation on palladium[12] to 1-amino-2-butanol and benzoylation.

The conversion of 1,2-amino alcohols to 2-thioöxazolidones requires introduction of the cyclic thioncarbamate group. A simple procedure used to prepare 5,5- and 4,4-dimethyl-2-thioöxazolidones[15] was to heat the amino alcohol (X or XI) with carbon disulfide and alcoholic alkali. However, ethanolamine (XII) treated similarly or with carbon disulfide alone gave not 2-thioöxazolidone (XIII) but 2-thiothiazolidone (XIV).[16] The anomalous loss of oxygen in the transformation of XII to XIV can be explained only by the argument that formation of a thioöxazolidone from X or XI proceeded through a dithiocarbamate like XV, but that in XII the unhindered primary hydroxyl reacted to give the xanthate XVI, which like a benzenesulfonate or sulfate



underwent internal displacement by the dithiocarbamate group. The best syntheses[17] of XIII began by combination of XII and carbon disulfide at low temperature to the amine salt of XV, followed by thermal decomposition of the lead salt (reported 79% yield of crude product) or a carbalkoxy derivative[18] of XV (yield[19] 48%). Thiocyanate ion and ethylene chlorohydrin afforded[20] a small proportion (2%) of XIII but reacted principally by alkylation of sulfur. Likewise, the addition[21] of thiocyanate to ethylene oxide (XVII) produced 2-thiocyanoethanol in acid, or in neutral medium, probably by the steps indicated, ethylene sulfide (XVIII).



In the present work, the smooth reaction of XII with equivalents of carbon disulfide and potas-

(7) Bartlett and Ross, THIS JOURNAL, **70**, 926 (1948).
(8) Russell and Vanderwerf, *ibid.*, **69**, 11 (1947).
(9) Trevoy and Brown, *ibid.*, **71**, 1675 (1949).
(10) Bissinger, *et al.*, *ibid.*, **69**, 2955 (1947).
(11) Swern, Billen and Knight, *ibid.*, **71**, 1152 (1949).
(12) Schmidt and Wilkendorf, *Ber.*, **52**, 389 (1919).
(13) Barrow and Ferguson, *J. Chem. Soc.*, 410 (1935).
(14) Henry, *Bull. Acad. roy. Belg.*, [3] **32**, 17 (1896); Montmollin and Achermann, *Helv. Chim. Acta*, **12**, 873 (1929).
(15) Bruson and Eastes, THIS JOURNAL, **59**, 2011 (1937); Hopkins, *Can. J. Research*, **B20**, 268 (1942).
(16) Maquenne and Roux, *Compt. rend.*, **134**, 1589 (1902); Knorr and Roessler, *Ber.*, **36**, 1278 (1903); Roux, *Ann. chim.*, [8] **1**, 72 (1904).
(17) Sergeev and Ivanova, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 1495 (1937); [*C. A.*, **32**, 2534 (1938)].
(18) Kaluza, *Monatsh.*, **33**, 363 (1912).
(19) Private communication from Dr. R. O. Roblin, Jr., American Cyanamid Company.
(20) Sergeev, Kolychev and Kondratiev, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 2600 (1937); [*Chem. Zentr.*, **109**, II, 2587 (1938)].
(21) Sergeev and Kolychev, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 1890 (1937); [*Chem. Zentr.*, **109**, I, 598 (1938)]; Meade and Woodward, *J. Chem. Soc.*, 1894 (1948); Wagner-Jauregg, *Ann.*, **561**, 87 (1949).

sium hydroxide in the solvent 45% dioxane, which unlike alcohol could not consume reagents by xanthate formation, furnished XV in double the amount possible without alkali. By analogy with a preparation of isothiocyanates,[22] the solution of XV was treated with molar equivalents of hydroxide and lead nitrate, and the basic lead salt decomposed in suspension at 60° with production in 33% yield of XIII. The absence of substituents in XV apparently impeded ring closure. Application of the procedure to III afforded in 70% yield *dl*-I, m. p. 65°, which in dilute chloroform solution had the identical infrared absorption spectrum as natural *l*-I.[3] The structure of the turnip antithyroid factor was thereby proved synthetically. Racemic I, which was also obtained by direct conversion of the raw mixture of III and IV to the thioöxazolidones, had the same antithyroid activity as the natural optical isomer.[5]

Since I was prepared from III in neutral or alkaline solution, fission between the oxygen and asymmetric carbon did not occur and optical activity could remain intact. The notable prior example of resolution of an aliphatic amino alcohol was that of valinol[13] by means of *d*-tartaric acid. The amino alcohol III formed a crystalline neutral *d*-tartrate, but the molecular rotation of the salt, +61°, showed[23] that the substance was a derivative of *dl*-III. However, the *d*-camphor-10-sulfonate of III and the *d*-α-bromocamphor-π-sulfonate, prepared by displacement from the ammonium salt, were separable mixtures of diastereoisomers, of which the salts of the *l*-amine were the less soluble. The resolution with *d*-α-bromocamphor-π-sulfonic acid was particularly facile because that acid formed only one solid salt, a monohydrate derived from *l*-III, which was pure after one recrystallization. The *d*-amine in the mother liquor was isolated as the *l*-camphor-10-sulfonate. From the molecular rotations of *d*-III *l*-camphor-10-sulfonate, −43° in water, −22° in excess alkali, and *l*-III *d*-α-bromocamphor-π-sulfonate, +264° in water, +241° in alkali, with the known rotations of the anions, respectively −50°[24] and +270°,[25] it follows that $[M]_D = \pm 7°$ for the pure optically active cations of III, $[M]_D = \pm 28°$ for the free amines. Since the acids used for resolution did not react with carbon disulfide or form water insoluble lead salts, the salts of the *d* and *l*-amines were converted directly with two equivalents of base to the dithiocarbamates and thence respectively to *d* and *l*-I, m. p. 51°, $[\alpha]_D \pm 70°$. The synthetic *l*-isomer was identical with the natural product.

Experimental

Ammonolysis of Butadiene-1,2-oxide.[26]—To 3 l. of 28% aqueous ammonia stirred at 5° was added during two hours 70 g. of butadiene-1,2-oxide.[27] The cloudy solution, after standing overnight in the refrigerator and twenty-four hours at room temperature, was boiled gently under the hood to expel ammonia and concentrated through a 40-cm. Vigreux column at 20 mm. on a water-bath at 50°. The residue (68.5 g.), fractionated in vacuum, afforded 53.7 g. (62%) of colorless, viscous raw aminobutenol, b. p. 79–79.3° at 12 mm., $n^{22}D$ 1.474.

Separation of Aminobutenols.—A hot solution of 38.8 g. of crude aminobutenol and 60 g. of oxalic acid dihydrate in 1.5 l. of absolute ethanol was cooled overnight and filtered. There was obtained 40.85 g. of crystals, m. p. 127–129° (dec.); the mother liquor, concentrated to 200 cc., chilled and scratched, gave 18.4 g. of gelatinous solid, m. p. 98–102° (dec.). The first crop, combined with 2.5 g. of high-melting material from the second and twice crystallized fractionally from alcohol, furnished altogether 35.95 g. (45%) of cottony balls of **1-amino-3-buten-2-ol acid oxalate**, m. p. 129.5–131.5° (dec.). The analytical sample formed rosettes of needles, m. p. 130.5–132° (dec.).

Anal. Calcd. for $C_6H_{11}O_5N$: C, 40.68; H, 6.26; N, 7.91. Found: C, 40.82; H, 6.37; N, 8.07.

The low-melting crop of aminobutenol oxalate was crystallized successively from 125 cc. and 50 cc. of alcohol. The residual solid (3.35 g.) was principally salt of the 1-amine; the mother liquors, concentrated and chilled, furnished 10.4 g. of more soluble substance, m. p. 100–107° (dec.). This material, which formed more massive crystals than the contaminant 1-amine oxalate and hence redissolved less rapidly when heated, was fractionally crystallized three times from alcohol and afforded 5.45 g. (7%) of **2-amino-3-buten-1-ol acid oxalate**. The substance is dimorphous and crystallizes as slender prisms, m. p. 111.5–112.5° (dec.), from an undisturbed solution or if seeded and scratched as hexagonal blocks, m. p. 124.5–126° (dec.).

Anal. Calcd. for $C_6H_{11}O_5N$: N, 7.91. Found: N, 7.99 (prisms), 8.05 (blocks).

1-Amino-3-buten-2-ol.—A solution of 35.9 g. of 1-amino-3-buten-2-ol acid oxalate in 150 cc. of water was added dropwise to a hot, stirred solution of 67 g. of barium hydroxide octahydrate in 250 cc. of water, the thick mixture centrifuged, and the barium oxalate washed with 400 cc. of water. The solution was concentrated at the water pump on a bath at 50°, and the residue was dissolved in 25 cc. of alcohol, filtered, and distilled in vacuum. The product, 13.87 g. (79%) of **1-amino-3-buten-2-ol**, b. p. 72° at 8 mm., solidified as white, deliquescent plates, m. p. 33–37°. A sample in a dark, sealed tube became yellow and liquefied after several months.

1-Amino-3-buten-2-ol neutral oxalate crystallized from alcohol (250 cc./g.) as shimmering leaflets, m. p. 177–179° (darkening).

Anal. Calcd. for $C_{10}H_{20}O_6N_2$: N, 10.60. Found: N, 10.32.

The amine did not form a solid *l*-malate or acid *d*-tartrate. ***dl*-1-Amino-3-buten-2-ol neutral *d*-tartrate** crystallized from alcohol (15 cc./g.) as rosettes of prisms, m. p. 146–147.5° (darkening), $[\alpha]_D$ +18.8° in 2% sodium hydroxide (100.0 mg./2.51 cc., 1 dm., +0.75°).

Anal. Calcd. for $C_{12}H_{24}O_8N_2$: N, 8.64. Found: N, 8.72.

The amine also formed an acid dibenzoyl-*d*-tartrate,[28] prisms from absolute ethanol, m. p. 167.5–168.5° (dec.), $[\alpha]_D$ −91° in alcohol, and a neutral dibenzoyl-*d*-tartrate, prisms from absolute ethanol, m. p. 162.5–164° (dec.), $[\alpha]_D$ −91° in water.

A solution of 1 g. of 1-amino-3-buten-2-ol acid oxalate in 20 cc. of 10% sodium carbonate was shaken five minutes

(22) Delépine, *Bull. soc. chim.*, [4] **3**, 641 (1908).

(23) Landolt, *Ber.*, **6**, 1073 (1873).

(24) Pope and Gibson, *J. Chem. Soc.*, **97**, 2211 (1910).

(25) Walden, *Z. physik. Chem.*, **15**, 196 (1894).

(26) Dr. Franklin Strain, Pittsburgh Plate Glass Company, graciously communicated preliminary information.

(27) Generously supplied by Dr. P. D. Bartlett. The substance rapidly solidifies ground joints.

(28) Preparation of dibenzoyl-*d*-tartaric acid: Butler and Cretcher, THIS JOURNAL, **55**, 2605 (1933). The crude dibenzoyl-*d*-tartaric anhydride melted at 195–199°, 25° higher than previously reported.

with 0.8 g. of benzoyl chloride, diluted with 20 cc. of water and extracted thoroughly with ether, which was dried and evaporated. The residue on crystallization from 10 cc. of benzene furnished 0.85 g. (79%) of **1-benzoylamino-3-buten-2-ol**, m. p. 72–74°. Benzoylation of the raw aminobutenol mixture gave the same substance in 30% yield. The analytical sample formed rhombic plates, m. p. 70.5–72°.

Anal. Calcd. for $C_{11}H_{13}O_2N$: N, 7.33. Found: N, 7.31.

Derivatives of 2-Amino-3-buten-1-ol.—The amine, liberated from 0.5 g. of 2-amino-3-buten-1-ol acid oxalate by 0.92 g. of barium hydroxide octahydrate in aqueous solution, was separated from barium oxalate and treated with 0.18 g. of oxalic acid dihydrate. The solution was evaporated in vacuum; the residue, crystallized from 20 cc. of alcohol, afforded 0.33 g. (88%) of **2-amino-3-buten-1-ol neutral oxalate**, m. p. 164.5–166.5°. A mixture with 1-amino-3-buten-2-ol neutral oxalate melted at 144–159°. The analytical sample formed irregular clusters of plates, m. p. 163–165.5° (dec., rapidly heated).

Anal. Calcd. for $C_{10}H_{20}O_6N_2$: C, 45.44; H, 7.63; N, 10.60. Found: C, 45.22; H, 7.58; N, 10.48.

The benzoyl derivative was prepared from the acid oxalate and crystallized from chloroform–carbon tetrachloride and from ether–petroleum ether. **2-Benzoylamino-3-buten-1-ol** formed slender prisms, m. p. 62.5–64.5°. A mixture with 1-benzoylamino-3-buten-2-ol melted at 45–66°.

Anal. Calcd. for $C_{11}H_{13}O_2N$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.10; H, 6.51; N, 7.34.

Derivatives of 1-Amino-2-butanol.—The condensation[14] of propionaldehyde and nitromethane by potassium carbonate furnished 1-nitro-2-butanol, b. p. 102–103° at 16 mm., which could not be reduced on platinum. A solution of 10 g. of 1-nitro-2-butanol and 5.3 g. of oxalic acid dihydrate in 125 cc. of alcohol and 50 cc. of water was shaken for an hour and a half with 1 g. of 10% palladium charcoal and 15–30 lb. of hydrogen, filtered, the precipitated oxalate dissolved from the catalyst by water, and the filtrate evaporated in vacuum. The residue (9.3 g., 83%), crystallized from 175 cc. of 80% alcohol, afforded 8.45 g. of square plates of 1-amino-2-butanol neutral oxalate, m. p. 196–200° (dec., bath preheated to 180°) (lit.[29] 193°). The same substance, which did not depress the melting point, was obtained by hydrogenation in 70% alcohol on platinum oxide (Adams) of 1-amino-3-buten-2-ol neutral oxalate.

1-Benzoylamino-2-butanol, prepared from the amine neutral oxalate and crystallized from benzene, formed rhomboid plates, m. p. 112–113.5°. The same substance was obtained by hydrogenation in alcohol on platinum of 1-benzoylamino-3-buten-2-ol.

Anal. Calcd. for $C_{11}H_{15}O_2N$: N, 7.25. Found: N, 7.34.

Derivatives of 2-Amino-1-butanol.—Equivalent quantities of 2-amino-1-butanol[30] and oxalic acid combined to 2-amino-1-butanol neutral oxalate, fine needles from alcohol, m. p. 173–178° (dec., bath preheated to 160°) (lit.[31] 176°). Benzoylation of the free amine in 10% sodium carbonate furnished **2-benzoylamino-1-butanol**, fine needles from benzene, m. p. 99.5–100.5°. The same substance, undepressed in melting point by an authentic sample, was obtained by hydrogenation of 2-benzoylamino-3-buten-1-ol. A mixture with 1-benzoylamino-2-butanol melted at 83–104°.

Anal. Calcd. for $C_{11}H_{15}O_2N$: N, 7.25. Found: N, 7.37.

Resolution of 1-Amino-3-buten-2-ol.—A solution of 0.5 g. of 1-amino-3-buten-2-ol and 1.8 g. of ammonium *d*-α-bromocamphor-π-sulfonate (British Drug Houses) in 25 cc. of hot methanol was stripped of ammonia and solvent in vacuum. The glassy residue was dissolved in 10 cc. of hot ethyl acetate and the solution treated with 0.2 cc. of water, chilled and filtered. The salt (1.14 g., m. p. 102–105°, $[\alpha]_D$ +59.8° in alkali) was crystallized from 0.4 cc. of water and 20 cc. of ethyl acetate to afford 1.03 g. (86%) of *l*-**1-amino-3-buten-2-ol** *d*-α-**bromocamphor-π-sulfonate monohydrate**, m. p. 100–108°, $[\alpha]_D$ +57.8° in alkali. The analytical sample, air-dried three hours, formed long, flat bars, m. p. 103–107.5°, $[\alpha]^{25}_D$ +63.4° in water (52.3 mg./2.51 cc., 1 dm., +1.32°), $[\alpha]^{23}_D$ +57.8° in 0.5% sodium hydroxide (52.1 mg./2.51 cc., 1 dm., +1.20°). The substance lost one molecule of water when dried fifteen hours at room temperature and 0.6 mm. The dehydrated crystals retained their original form and luster but sintered to a glass at 55–65°.

Anal. Calcd. for $C_{14}H_{24}O_5NSBr \cdot H_2O$: C, 40.38; H, 6.30; H_2O, 4.33. Found: C, 40.58; H, 6.15; H_2O, 4.3.

A solution of 0.5 g. of 1-amino-3-buten-2-ol and 1.2 g. of *d*-camphor-10-sulfonic acid in 2 cc. of alcohol and 10 cc. of ethyl acetate, cooled and filtered, gave 0.5 g. of salt, m. p. 145–148°. The mother liquor, evaporated, taken up in 5 cc. of ethyl acetate and chilled, deposited 0.62 g. of solid, m. p. 95–120°. The first crop, crystallized from 1 cc. of alcohol and 8 cc. of ethyl acetate, yielded 0.38 g. (41%) of fine needles of *l*-**1-amino-3-buten-2-ol** *d*-**camphor-10-sulfonate**, m. p. 148.5–150°, $[\alpha]_D$ +14° in water, +8.4° in 1% sodium hydroxide.

The amine in old mother liquors from isolation of the *l*-form was recovered by treatment with excess aqueous barium hydroxide, evaporation in vacuum, and extraction with absolute ethanol. A sample of a solution of 1.75 g. of crude *d*-amine ($[\alpha]_D$ +17° in water) and 4.25 g. of *l*-camphor-10-sulfonic acid (British Drug Houses) in 5 cc. of alcohol and 35 cc. of ethyl acetate was evaporated and induced to crystallize with the *l*-amine *d*-sulfonate, and the main portion seeded and chilled. The salt (1.62 g., m. p. 150–153°) after one recrystallization furnished 1.38 g. of *d*-**1-amino-3-buten-2-ol** *l*-**camphor-10-sulfonate**, m. p. 149.5–151.5°. A mixture with the antipodal salt melted at 118–132°. The analytical sample formed fine needles, m. p. 149–150.5°, $[\alpha]^{21}_D$ −13.5° in water (98.4 mg./2.51 cc., 1 dm., −0.53°), $[\alpha]^{22}_D$ −7.0° in 1% sodium hydroxide (99.9 mg./2.51 cc., 1 dm., −0.28°).

Anal. Calcd. for $C_{14}H_{25}O_5NS$: C, 52.64; H, 7.89. Found: C, 52.24; H, 7.56.

Thioöxazolidones.—A cold solution of 5 g. of ethanolamine and 5.5 g. of 85% potassium hydroxide pellets in 50 cc. of water was shaken vigorously with 6.5 g. of carbon disulfide in 40 cc. of dioxane for five minutes, during which the mixture warmed to room temperature and became orange and homogeneous. After 5.5 g. of potassium hydroxide in 100 cc. of water, a solution of 27.5 g. of lead nitrate in 150 cc. of water was added and the resulting orange slurry mixed violently for a minute. The suspension was digested at 60° for half an hour, while the precipitate darkened and settled, the supernatant was decanted, and the lead sulfide was filtered and washed with 150 cc. of hot water. After evaporation of the aqueous solution in vacuum, the powdered residue was extracted with 350 cc. of boiling benzene and the potassium nitrate discarded. The benzene solution, concentrated to 150 cc., transferred to a clean flask and cooled, furnished 3.65 g. of crude product, m. p. 90–94°. The material, recrystallized three times from benzene (25 cc./g.) with care to remove a less soluble gum, afforded 2.75 g. (33%) of long, flat prisms of 2-thioöxazolidone, m. p. 98–99° (lit.[17] 96–97°). The ultraviolet[3] and infrared[32] absorption spectra of the substance have been published.

dl-**5-Vinyl-2-thioöxazolidone**, prepared from *dl*-1-amino-3-buten-2-ol in 70% yield (1.55 from 1.5 g.), crystallized from ether as slender prisms, m. p. 64–65°.

Anal. Calcd. for C_5H_7ONS: N, 10.84. Found: N, 10.45.

A solution of 1.16 g. of *d*-1-amino-3-buten-2-ol *l*-camphor-10-sulfonate and 0.48 g. of potassium hydroxide in

(29) Tordoir, *Bull. classe sci. Acad. roy. Belg.*, 695 (1901).

(30) Kindly donated by the Commercial Solvents Corporation.

(31) Stiénon, *Bull. classe sci. Acad. roy. Belg.*, 703 (1901).

(32) Ettlinger, THIS JOURNAL, **72**, 4699 (1950).

10 cc. of water was shaken with 0.30 g. of carbon disulfide in 8 cc. of dioxane, treated successively with 0.24 g. of potassium hydroxide and 1.20 g. of lead nitrate dissolved in a total of 20 cc. of water, and warmed to 60° for fifteen minutes. The lead sulfide was centrifuged, the supernatant evaporated in vacuum, and the residue dissolved with 3 g. of sodium chloride in 15 cc. of water and extracted with 75 cc. of ethyl acetate. The ethyl acetate, washed, dried and evaporated, left 0.38 g. of oil which slowly solidified and was crystallized from ether. There was obtained 0.31 g. (66%) of *d*-**5-vinyl-2-thioöxazolidone**, m. p. 50–51°, $[\alpha]^{20}D$ +70.5° in methanol (47.0 mg./2.51 cc., 1 dm., +1.32°). A mixture with the *l*-isomer melted at 50.5–52°, solidified instantly when seeded with the racemic compound and melted at 64–66°. A solution of equal parts of the synthetic *d* and natural *l*-compound in methanol, evaporated on a watch glass and scratched, crystallized as *dl*-5-vinyl-2-thioöxazolidone, m. p. 63.5–64.5°, undepressed by an authentic sample.

From *l*-1-amino-3-buten-2-ol *d*-α-bromocamphor-π-sulfonate (monohydrate, 5.08 g.) there was synthesized *l*-5-vinyl-2-thioöxazolidone (0.85 g., 54%), m. p. 50.5–51°, $[\alpha]^{30}D$ −72.8° in methanol (51.6 mg./2.51 cc., 1 dm., −1.45°), identical with the natural product[3] (m. p. 50–50.5°, $[\alpha]^{31}D$ −70.5°).

Acknowledgments.—The author is deeply indebted to Dr. E. B. Astwood for generous collaboration and Dr. R. B. Woodward for useful discussion.

Summary

The natural antithyroid factor *l*-5-vinyl-2-thioöxazolidone has been synthesized from butadiene-1,2-oxide through 1-amino-3-buten-2-ol.

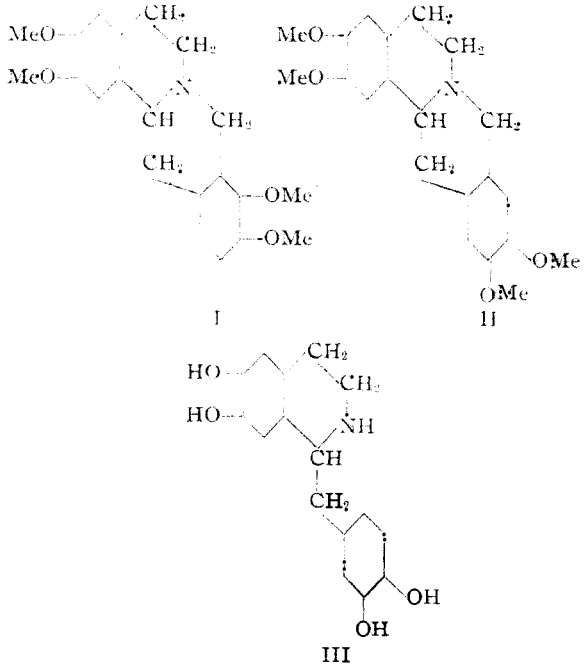
CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 31, 1950

[CONTRIBUTION FROM THE RESEARCH LABORATORY, DOMINION RUBBER CO., LTD.]

The Alkaloids of Fumariaceous Plants. XLV. Coreximine, a Naturally Occurring Coralydine

BY RICHARD H. F. MANSKE

The author has recorded the presence of an alkaloid, F29 ($C_{19}H_{21}O_4N$)[1] now termed *coreximine* which has two methoxyls and two phenolic hydroxyls. With diazomethane it yields a dimethyl ether, $C_{21}H_{25}O_4N$, m. p. 177°,[2] and with diazoethane it yields a diethyl ether, $C_{23}H_{29}O_4N$. The former is isomeric but not identical with tetrahydropalmatine (I) and like it is slowly oxidized by air to a quaternary base, a behavior which is characteristic of the tetrahydroprotoberberines. The conclusion, therefore, seemed to be inescapable that coreximine dimethyl ether is a tetramethoxytetrahydroprotoberberine and two formulas seemed *a priori* probable—the most likely of which (II) was already known as norcoralydine.[3] The latter is only known in the racemic form, whereas the dimethyl ether of natural origin is optically active. Racemization of bases of this type, however, is easily achieved by oxidation to the quaternary compound analogous to palmatine and subsequent reduction. When the dimethyl ether was thus racemized it melted at 157° and in admixture with a synthetic specimen of norcoralydine the mixture melted at the same temperature. Späth and Kruta[4] recorded the melting point of synthetic norcoralydine as 152° whereas Pictet and Chou[2] give 157–158°. The writer has obtained the synthetic base in these two forms, presumably isomorphic, but the lower melting form when very slowly heated resolidifies at 151–153° after partial melting and remelts completely at 157°. The picrates prepared from both sources were identical. Coreximine dimethyl ether, therefore, has formula



I II III

II and coreximine is one of the four possible bisdesmethyl derivatives of it.

In a paper dealing with the structure of cularine the writer[5] has called attention to the fact that ring closure of the isoquinoline nucleus in natural alkaloids can proceed in two ways. When the benzylisoquinoline first forms there is the possibility of yielding either a 6,7 or a 7,8-dihydroxy compound. The latter can then undergo oxidative ring closure to yield cularine. The former (III) can also undergo oxidative ring closure, but

(1) Manske, *Can. J. Research*, **B16**, 81 (1938)
(2) All melting points are corrected.
(3) Pictet and Chou, *Ber.*, **49**, 370 (1916).
(4) Späth and Kruta, *Monatsh.*, **50**, 341 (1928)
(5) Manske, THIS JOURNAL, **72**, 55 (1950).