be involved in reactions analogous to those which characterize the parent substance of the group.

ANN ARBOR, MICHIGAN.

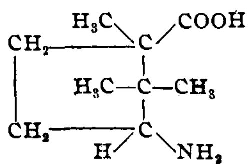
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS.]

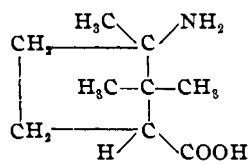
MOLECULAR REARRANGEMENTS IN THE CAMPHOR SERIES. XI. DERIVATIVES OF ISOCAMPHORIC ACID; ISOAMINOCAMPHONANIC ACID AND ITS DECOMPOSITION PRODUCTS.[1]

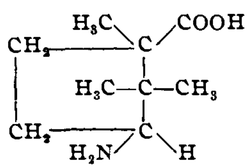
BY WILLIAM A. NOYES AND LEONIDAS R. LITTLETON.

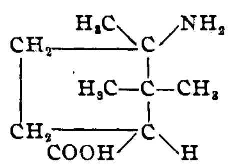
Received November 20, 1912.

There are four acids derived from camphor that have the general formula $C_8H_{14}\langle^{COOH}_{NH_2}$. Two of these, aminocamphonanic acid[2] and aminodihydrocampholytic acid,[3] are derived from *d*-camphoric acid, and the other two, isoaminocamphonanic acid[4] and isoaminodihydrocampholytic acid,[5] are derivatives of isocamphoric acid. The first two have the carboxyl groups in the tertiary position while the other two are secondary acids. These four amino acids have the following structures:


Aminocamphonanic acid.


Aminodihydrocampholytic acid.


Isoaminocamphonanic acid.


Isoaminodihydrocampholytic acid.

On treatment with nitrous acid aminocamphonanic acid[6] is decomposed into lauronolic acid, $C_8H_{13}COOH$, hydroxylauronic acid, laurolene, C_8H_{14},

[1] Abstract of a thesis presented by Leonidas R. Littleton in partial fulfilment of the requirement for the degree of Doctor of Philosophy at the University of Illinois.

[2] For the nomenclature used in this paper see THIS JOURNAL, **34**, 1067 (1912); *Am. Chem. J.*, **16**, 506 (1894); *Ber.*, **33**, 2963 (1900).

[3] *Am. Chem. J.*, **16**, 310, 503 (1894); *Ibid.*, **24**, 290 (1900).

[4] This paper.

[5] THIS JOURNAL, **32**, 1672 (1900).

[6] *Am. Chem. J.*, **16**, 508 (1894); THIS JOURNAL, **31**, 279 (1909); *Ber.*, **33**, 294 (1900).

and isocampholactone, C_8H_{13}  . The nitrosoderivative[1] is decomposed by sodium hydroxide into these same compounds together with *cis*-camphononolactone, C_8H_{14}  , and an unnamed acid of the same empirical formula as lauronolic acid. In the formation of laurolene and lauronolic acid a methyl group has wandered from the β- to the γ-position, while the *cis*-camphononolactone is formed without any rearrangement. The structures of the other decomposition products are still unknown.

Aminodihydrocampholytic acid[2] has been decomposed into campholytolactone, C_8H_{14}  , *trans*-hydroxydihydrocampholytic acid, C_8H_{14}  , campholytic acid $C_8H_{13}COOH$, and isolaurolene, C_8H_{14}. While campholytolactone is formed directly, *trans*-hydroxydihydrocampholytic acid is formed by a Walden inversion,[3] which makes it a derivative of *d*-isocamphoric acid instead of *d*-camphoric acid. So far as is known, this is the only instance in this series in which the rearrangement takes place on the tertiary carbon.

Isoaminocamphonanic acid[4] is decomposed into *cis*-camphononolactone, C_8H_{13}  , an unsaturated acid, and probably a hydroxy acid. In the formation of this lactone a rearrangement takes place on the secondary carbon which again gives a derivative of *d*-camphoric acid.

Isoaminodihydrocampholytic acid[5] gives *d*-campholytic acid, $C_8H_{13}COOH$, *l*-hydroxydihydrocampholytic acid, C_8H_{14}  , a lactone, and a hydrocarbon. It was at first thought that this hydroxy acid was formed by a rearrangement, but it was subsequently shown by Noyes and Potter that such is not the case.[6]

It was the purpose of this investigation to prepare isoaminocamphonanic acid and to study its decomposition products with nitrous acid. We

[1] *Am. Chem. J.*, 32, 288 (1904); *Ibid.*, 35, 379 (1906); THIS JOURNAL, 31, 671 (1909); *Ber.*, 35, 1291 (1902).

[2] *Am. Chem. J.*, 16, 505 (1894); *Ibid.*, 17, 422 (1895); *Ber.*, 33, 2936 (1900); *Ann.*, 314, 392 (1901); *Bull. soc. chim.*, [3] 25, 81 (1901).

[3] THIS JOURNAL, 34, 1069 (1912).

[4] This paper.

[5] THIS JOURNAL, 32, 1672 (1910).

[6] *Loc. cit.*

were especially desirous to learn whether the iso-series acts similarly to the camphoric series.

Experimental

Preparation of Isocamphoric Acid.

The isocamphoric acid was prepared by the methods of Aschan as modified by Noyes and Knight[1] with a few further modifications. The furnace was loaded with eight tubes, each containing 75 grams of *d*-camphoric acid, 38 cc. of glacial acetic acid, and 5 cc. of concentrated hydrochloric acid. They were then heated for 10 hours at 175–185°. After cooling, the viscous contents of the tubes were poured into a large evaporating dish and the tubes were washed out with water, this wash water being added to the other material. On standing a few hours, the mass crystallized. The liquid was sucked off with a filter pump, and the filtrate was evaporated on the water bath. The residue was dried in a separate dish. After having been thoroughly dried, the two portions were mixed, powdered, and treated with one-fourth of their weight of acetyl chloride. This converted any unchanged camphoric acid into its anhydride, while the isocamphoric acid was unchanged. After having stood in a flask for a little over an hour with frequent shaking, the mixture was treated with water and acid sodium carbonate. The camphoric anhydride was filtered off as quickly as possible so as not to convert it back to camphoric acid. The isocamphoric acid was precipitated from the filtrate by hydrochloric acid. It was purified by dissolving it in a small quantity of strong alcohol, pouring it into three or four volumes of hot water, and letting the alcohol evaporate on exposure to air. As the solubility of camphoric acid at 20° is 6.96 grams per 100 grams of water, while that of isocamphoric acid is only 0.337,[2] this is an easy way to separate the isocamphoric acid from the last traces of camphoric acid. The rotation of a few selected crystals in 10% solution in absolute alcohol is $[\alpha]_D = -47.6°$, while Aschan and Knight found $[\alpha]_D = -47.1°$.

Dimethyl Ester of Isocamphoric Acid, $C_8H_{14}(COOCH_3)_2$.—Two hundred grams of isocamphoric acid, 800 cc. of methyl alcohol, and 80 cc. of concentrated sulfuric acid were boiled with a return condenser for 48 hours. The methyl alcohol was distilled off, first at atmospheric, and then under diminished pressure. The mixed esters were then precipitated with water, and shaken with a strong solution of sodium carbonate, which dissolved any acid ester. The neutral ester was taken up in ether, and the ether, after drying, was distilled off under diminished pressure. The neutral ester was then distilled under diminished pressure. It is a colorless oil, which boils at 146° (27 mm.), and has a rotation in 10% solution in absolute alcohol of $[\alpha]_D = -63.6°$.[3]

[1] THIS JOURNAL, 32, 1670 (1910).

[2] *Ber.*, 27, 1700 (1896).

[3] THIS JOURNAL, 32, 1671 (1910).

Secondary[1] *Monomethyl Ester of Isocamphoric Acid*, $C_8H_{14}\begin{matrix}COCOH_3\\COOH\end{matrix}$.—The secondary monomethyl ester was precipitated from the sodium carbonate solution with hydrochloric acid, and crystallized from boiling ligroin, and recrystallized from methyl alcohol. It melts at 89.5–90°, and has a rotation in 10% solution in absolute alcohol of $[\alpha]_D = -58.4°$. Noyes and Knight found the melting point to be 88°, and the rotation $[\alpha]_D = -57.9°$.[2]

Tertiary[1] *Monomethyl Ester of Isocamphoric Acid*, $C_8H_{14}\begin{matrix}COOH\\COOCH_3\end{matrix}$.—Fifty grams of the neutral ester were dissolved in 25 cc. of methyl alcohol and 27 cc. (4% in excess of one molecule) of sodium hydroxide (3 cc. = 1 gram) were added, and the mixture was boiled for 40 minutes with a return condenser. After boiling off the methyl alcohol, the neutral ester was taken up in ether, and the acid ester precipitated with hydrochloric acid. The yield was about 38 grams. The neutral ester was recovered and used again. The acid ester was obtained as a very viscous oil. It was even kept at —20° for a few hours without crystallizing, but it hardened at this temperature. It has a rotation in 10% solution in absolute alcohol of $[\alpha]_D = -53.1°$.

Methyl Ester of Secondary[3] *Isocamphoramidic Acid*, $C_8H_{14}\begin{matrix}CONH_2\\COOCH_3\end{matrix}$.—To 40 grams of the secondary monomethyl ester in a flask, 45 grams of well powdered phosphorus pentachloride were gradually added, keeping the flask in a freezing mixture. The products of the reaction were poured off from the excess of phosphorus pentachloride into a distilling bulb. The hydrochloric acid was driven off under the diminished pressure obtained with the water pump, and afterwards, the phosphorus oxychloride was distilled off at 60° and 4 mm. The acid chloride was slowly poured, with constant shaking, into a slight excess of ammonia (0.90), keeping the mixture below —12°. It was found that the reaction went best when the temperature was kept low, and the flask was well shaken after each addition of the chloride. The precipitated amido ester was filtered off and taken up in alcohol to separate it from any ammonium chloride. It crystallizes in rectangular plates. It melts at 126–127°. In 10% solution in methyl alcohol it has a rotation of $[\alpha]_D = -54.1°$.

Calculated for $C_{11}H_{19}NO_3$: N, 6.57; C, 61.94; H, 8.99.
Found: N, 6.36; C, 62.11; H, 8.55.

[1] Secondary and tertiary refer to the carboxyl containing the methyl group.
[2] *Loc. cit.*
[3] Secondary refers to the CO_2CH_3 group.

Methyl Ester of Isoaminocamphonanic Acid, $C_8H_{14}\begin{cases}NH_2\alpha \\ COOCH_3\beta\end{cases}$.—It was thought that the Hofmann reaction[1] would not go smoothly, so a modification of the method was tried.[2] To 2.13 grams (0.01 mol) of the methyl ester of secondary isocamphoramidic acid in 8 cc. (3 parts) of methyl alcohol, was added 0.46 gram (0.01 mol) of sodium in 14.4 cc. (25 parts) of methyl alcohol. To this was added 0.50 cc. (0.01 mol) of bromine. This was warmed on the water bath for ten minutes, acidified with acetic acid, and evaporated. A little water was added, and the solution was extracted with ether, from which 2.2 grams of a yellow oil was obtained. One gram of this oil was warmed for 22 hours on the water bath with 3 mols of sodium hydroxide. The ether extract gave an oil which crystallized on standing. The remainder of the first oil, 1.2 grams, was warmed on the water bath for the same length of time with an excess of hydrochloric acid. The ether extract of this also crystallized on standing. As these substances were very difficult to purify and the yields were small, this method of procedure was discontinued.

To 125 cc. of a solution of sodium hypobromite prepared by aspirating the vapor of 25.5 grams of bromine through 700 cc. of a 10% solution of cold hydroxide,[3] were added 11.5 grams of the methyl ester of secondary isocamphoramidic acid, and the mixture was warmed on the water bath for fifty minutes. A yellow oil separated out on top, and the lower layer became clear. From the ethereal solution, some white crystals, which were insoluble in ether separated out on standing. This was shown to be the unchanged amide. The oil, which is the methyl ester of isoaminocamphonanic acid, has a fishy odor. It was not purified, but the hydrochloride was prepared immediately from this.

Hydrochloride.—To 3 grams of the amine ester were added 3.55 cc. of 5.017 *N* hydrochloric acid (10% excess), and on standing a few moments the hydrochloride crystallized out. It was filtered off with the pump, and recrystallized from water in a sulfuric acid desiccator. It crystallized in almost perfect rectangular plates. When placed in a bath at 115° it melted, but on cooling resolidified, and then did not melt until 177° was reached. On heating gradually, no change was noticed until the temperature was 177°, when it melted. Some of the hydrochloride was placed in a bath at 150° for a few moments. It boiled and then resolidified. A few drops of water condensed near the top of the tube. It was then dissolved in water and dried over sulfuric acid in a vacuum desiccator. It melted at the same two points as the original hydrochloride, showing that water had been driven off. Analysis gave

[1] *Ann.*, 74, 117 (1850); *Ber.*, 15, 762 (1882).
[2] *Am. Chem. J.*, 15, 215, 504 (1893); *Ibid.*, 16, 370 (1894); *Ber.*, 30, 898 (1897).
[3] *Ibid.*, 16, 503 (1894).

Calculated for $C_8H_{14}\begin{cases}NH_2.HCl.H_2O\\COOCH_3\end{cases}$: Cl, 14.80. Found: Cl, 14.84, 14.77.

It has a rotation in a 10% solution in water of $[\alpha]_D = -32.03°$; in a 10% solution in absolute alcohol of $[\alpha]_D = -42.03°$.

Isoaminocamphonanic Acid, $C_8H_{14}\begin{cases}NH_2\alpha\\COOH\beta\end{cases}$.—The above hydrochloride was warmed for 37 hours on the water bath with a 10% solution of sodium hydroxide (10% over two mols), and a little methyl alcohol. The amine ester was extracted with ether, and the water portion was acidified with hydrochloric acid and evaporated on the water bath. From this the hydrochloride was taken up in alcohol. On crystallizing, it was washed with ether and recrystallized from water, in which it is very soluble. It melts at 320° (cor.). For this temperature a bath of 280 grams of concentrated sulfuric acid and 120 grams of potassium sulfate was used.

The ethereal solution of the amine ester was evaporated under diminished pressure, and the ester was distilled at atmospheric pressure. It is a colorless oil, and boils at 239° (cor.). On cooling, it partly crystallized. It was moistened with ether and dried on a porous plate for several days. The white crystals began to melt with decomposition at 230°.

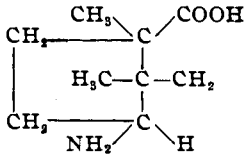
Decomposition of Isoaminocamphonanic Acid.—A solution of the hydrochloride of isoaminocamphonanic acid was treated with the calculated amount of a 20% solution of sodium nitrite. When the reaction was nearly completed, a little more hydrochloric acid was added, and the solution set aside until the evolution of nitrogen had ceased. The products were then taken up in ether. After the ether was distilled off under diminished pressure, the substances were subjected to steam distillation, when it was supposed that the hydrocarbon, lactone, and unsaturated acid would distil over, while any hydroxy acid would remain behind. The distillate, after being made alkalin with sodium carbonate and a little sodium hydroxide, was extracted with ether. From the ethereal extract white needles crystallized which melted at 160–162°. When these needles were mixed with some impure *cis*-camphonololactone (m. p. 157°), the melting point was unchanged. The rotation in 5.4% solution in absolute alcohol is $[\alpha]_D = -16.10°$. Noyes and Taveau[1] found for *cis*-camphonololactone a rotation of $[\alpha]_D = +13.87°$, while Noyes and Potter[2] found $[\alpha]_D^{28°} = -22.3$. The latter also found the melting point as 165–167°.[3] While the formation of *cis*-camphonololactone was not

[1] *Am. Chem. J.*, **35**, 385 (1906).

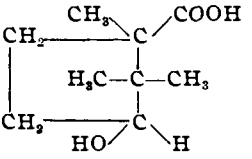
[2] THIS JOURNAL, **34**, 66 (1912).

[3] While these values are probably more accurate, it is well to note that Professor Bredt found for this lactone, which he prepared by reducing camphononic acid, in a 5% solution in alcohol $[\alpha]_D = -16.18°$, and it melted at 161°. See *Ann.*, **366**, 1 (1909).

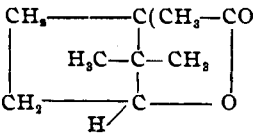
expected, still, the probability of a rearrangement was not overlooked. *Cis*-camphonololactone can be formed from isoaminocamphonanic acid by a rearrangement on the secondary carbon atom thus:



Isoaminocamphanic acid.



(Intermediate hydroxy acid.)



Cis-camphonololactone.

The alkalin portion was acidified with hydrochloric acid, and extracted with ether. From this a few drops of a light yellow oil was obtained. It was shown to be an unsaturated acid by its solubility in a solution of sodium carbonate, and by this solution instantly turning brown a solution of potassium permanganate. The acid was distilled at 150° and 60 mm., but with considerable decomposition.

The portion which contained the substances that are not distilled over with steam, presumably the hydroxy acid, was extracted with ether. From this a small amount of a dark colored oil was obtained, which did not crystallize, but became very viscous on standing. A boiling point could not be obtained, as it decomposed at 160° with considerable charring. It was shown to be a saturated acid by its conduct towards sodium carbonate and potassium permanganate.

URBANA, ILL.

THE PYROSULFATES OF SODIUM AND POTASSIUM AS CONDENSING AGENTS.

BY ALLAN F. ODELL AND CLEVE W. HINES.

Received November 18, 1912.

The availability of the pyrosulfates of sodium and potassium as condensing agents seems never to have been taken advantage of except in the preparation of acrolein from glycerol, and in the preparation of certain alkyl esters of aliphatic and aromatic acids.[1] The ready conversion of these salts into the bisulfates by the addition of water should be the means for their effective application as mediums to abstract water in organic syntheses.

Attention was drawn to this probability when an attempt was made in this laboratory to find a better method for the sulfonation of the mixed alkyl aryl ketones—acetophenone in particular. This ketone could not be sulfonated satisfactorily by the use of these salts in combination with sulfuric acid. At temperatures up to that of the water bath, acetophenone yielded triphenylbenzene in varying quantities. The greater part of the acetophenone was recovered, most of the time, unchanged.

[1] Bogojawlenski, *Ber.*, **38**, 3344 (1905).