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

MOLECULAR REARRANGEMENTS IN THE CAMPHOR SERIES. VI. ISOCAMPHOLACTONE.[1]

BY WILLIAM A. NOYES AND A. W. HOMBERGER.

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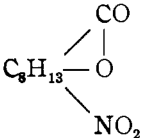
In a previous paper[2] we gave a brief report of a compound which we then considered to be a dilactone and to which we assigned the formula $C_8H_{13}O_4$. The compound is formed when isocampholactone is heated for some time with nitric acid and this led us to examine the substance qualitatively for nitrogen. For some reason, probably because the compound does not respond very readily to the usual test with metallic sodium, the result was negative, but after pursuing the study of the compound for some time further it was discovered that it has the composition of a nitrolactone,  $C_8H_{13}\begin{array}{l} \diagup CO \\ -O \\ \diagdown NO_2 \end{array}$ This has a molecular weight of 199 and does not agree with the determinations of the molecular weight reported in our first paper. The determinations by Victor Meyer's method were not, however, concordant and the low values found may have been due to partial decomposition.

The *isocampholactone* required for our experiment was prepared by decomposing the nitroso derivative of the anhydride of aminelauronic acid by boiling with a 10 per cent. solution of sodium hydroxide.[3] The specific rotation was determined in an 8.8 per cent. solution in alcohol, and gave $(\alpha)_D = -63.1^\circ$ at 28°. Taveau[4] gives the rotation in a 5 per cent. solution in alcohol as —60.7°.

Action of Ammonium Hydroxide on Isocampholactone.—Five tenths of a gram of isocampholactone were heated in a sealed tube in a water bath for 18 hours, till the lactone had passed into solution. The solution was evaporated in a vacuum desiccator and the residue purified by solution in absolute alcohol and precipitation with ligroin. It then melted at 137° and the analysis showed that it was the *ammonium* salt of the hydroxy acid corresponding to the lactone.

Calculated for $C_8H_{14}(OH)CO_2NH_4$:	C, 57.14;	H, 10.05;	N. 7.4.
Found:	C, 57.20;	H, 10.2 ;	N, 7.26.

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[1] Abstract of a thesis presented by Mr. Homberger to the Graduate School of the University of Illinois in partial fulfilment of the requirement for the degree of Doctor of Philosophy.

[2] THIS JOURNAL, **31**, 281.

[3] Noyes and Taveau, *Am. Chem. J.*, **32**, 285; **35**, 379.

[4] *Am. Chem. J.*, **32**, 290.

On standing in the air or on heating the salt passes back to isocampholactone.

Oxidation of Isocampholactone.—When isocampholactone is heated for 48 to 72 hours with nitric acid of sp. gr. 1.27 in a flask sealed to an upright condenser it is chiefly converted into the *nitroisocampholactone* which was described in our first paper as a lactone. If this is removed by dilution and filtration, the acid mother liquors leave on evaporation a viscous residue which crystallizes on standing.

Acid, $C_9H_{12}O_4$, melting at 138°.—After spreading the residue on porous porcelain to remove oily impurities it was crystallized from benzene. The analyses agree with the formula $C_9H_{12}O_4$.

Calculated for $C_9H_{12}O_4$ C, 58.67; H, 6.57.
Found: C, 59.09, 59.3, 59.0; H, 7.2, 7.02, 7.2.

The titration with standard alkali gave results corresponding to the molecular weights 186.0 and 186.9, for a monobasic acid. Calculated 184. The rotation of the acid in a 6 per cent. solution in alcohol was $(\alpha)_D = -42.05°$.

The Barium Salt, $(C_9H_{11}O_4)_2Ba$, was prepared by warming the acid with barium carbonate and water. It is easily soluble and separates without water of hydration.

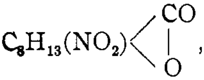
Found: Ba, 27.04. Calculated for $(C_9H_{11}O_4)_2Ba$, 27.29 per cent.

The *amide*, $C_8H_{11}O_2CONH_2$, was prepared by warming 0.5 gram of the acid with an excess of phosphorus pentachloride over a free flame in a test tube closed with a "Wallach's Aufsatz" until the mixture became liquid and pouring the cooled product into ammonium hydroxide. The amide which separated melts at 164°.

Calculated for $C_9H_{13}O_3N$: N, 7.65. Found: 7.84 per cent.

That the acid contains a lactone group was demonstrated by heating a portion of it for 12 hours on a water bath in a closed tube with somewhat more than two molecules of sodium hydroxide. Under these conditions 0.0569 gram neutralized 6.37 cc. of 0.1 *N* sodium hydroxide. Calculated for a bibasic acid, 6.18 cc.

It seems probable that this acid is formed by the oxidation of one of the methyl groups of isocampholactone.

Nitroisocampholactone,  $C_8H_{13}(NO_2)\left\langle \begin{matrix} CO \\ | \\ O \end{matrix} \right.$, is the principal product formed by the action of nitric acid (sp. gr. 1.27) on isocampholactone. It crystallizes from ligroin in needles. It is moderately soluble in ether and benzene. It melts at 122° and boils without apparent decomposition at 272°. The analyses were not altogether satisfactory, but leave no reasonable doubt as to the composition.[1]

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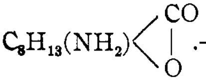
[1] Schryver's analyses of nitrocampholactone (*J. Chem. Soc.*, **73**, 562) were also unsatisfactory and somewhat similar to ours.

Calculated for $C_9H_{13}O_4N$: C, 54.29, ; H, 6.53, ; N, 7.04.
Found: C, 56.09; 55.89; H, 7.10, 7.25; N, 7.1.
54.85, 54.80; H, 7.12, 7.24; N, 7.2.
54.81, 54.90; H, 7.12, 6.95.
54.90

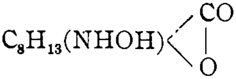
The specific rotation of a 5.5 per cent. solution in alcohol is $(\alpha)_D = -85.4°$.

Aminoisocampholactone,  $C_8H_{13}(NH_2)<\begin{matrix}CO\\|\\O\end{matrix}$.—One gram of nitroisocampholactone was suspended in 4 cc. of concentrated hydrochloric acid, the mixture cooled with ice water and granulated tin, and, later, 2 or 3 cc. of hydrochloric acid added till all of the nitro compound passed into solution. Sodium hydroxide was then added in slight excess and the amino compound was extracted with ether. A large excess of sodium hydroxide seems to cause the decomposition of the product. The yield was about 0.35 gram. The aminolactone crystallizes in small, indefinit crystals, which melt at 84°.

Calculated for $C_9H_{15}O_2N$: C, 63.90; H, 8.87; N, 8.28.
Found: C, 63.22; 63.10; H, 9.54; N, 8.10.

A solution of the aminolactone in absolute ether gave a precipitate of the chloride with dry hydrochloric acid. The aqueous solution of the chloride gave a yellow crystallin precipitate on standing for some time with chloroplatinic acid.

When the solution containing the amino compound was treated with a large excess of sodium hydroxide the amino compound was, apparently, decomposed and a relatively small amount of a compound melting at 152° was obtained. Owing to the small amount, this was not examined further.

Hydroxylaminoisocampholactone,  $C_8H_{13}(NHOH)<\begin{matrix}CO\\|\\O\end{matrix}$—One gram of the nitroisocampholactone was dissolved in 8 cc. of glacial acetic acid and zinc dust added in small quantities, great care being taken to keep the solution cold. Zinc dust was added till the further addition caused no appreciable rise in temperature. The solution was then filtered from the excess of zinc dust and zinc acetate and the precipitate washed with a very little water. The solution was then made alkaline with sodium hydroxide, the temperature being kept low by cooling with ice. Care must be taken to avoid the use of too large an excess of sodium hydroxide. The best results were obtained by adding about 5 per cent. more than was required to neutralize the acid solution. The alkaline, turbid solution was then extracted with ether and the ethereal solution dried with sodium sulphate. The residue left on evaporating the ether was recrystallized from dry ether. It crystallizes in small, star shaped crystals, which melt at 144°.

Calculated for $C_9H_{15}NO_3$: N, 7.56. Found: N, 7.62.

Hydroxylaminoisocampholactone is slightly basic. It reduces Fehling's solution readily.

Decomposition of Nitroisocampholactone by Ammonium Hydroxide and by Sodium Hydroxide.—When nitroisocampholactone is treated with ammonium hydroxide or sodium hydroxide it is decomposed with the formation of compounds containing six atoms of carbon in the molecule. Carbon dioxide is also found but we have been unable to discover what becomes of the other two carbon atoms or to interpret the action which takes place.

Formation of the Amide, $C_5H_8NO_2CONH_2$.—This amide is formed when nitroisocampholactone is warmed with alcoholic ammonia or when it is allowed to stand, with frequent shaking, with cold concentrated aqueous ammonium hydroxide. The product was obtained by evaporation at ordinary temperatures in a strong current of air. The residue was recrystallized from benzene with the addition of a little petroleum ether. It melts at 96–97°.

Calculated for $C_8H_{10}O_3N_2$:	C, 45.57,	H, 6.3	; N, 17.71.
Found:	C, 45.7, 45.6;	H, 7.0, 7.06;	N, 17.6, 17.6
	45.8, ;	N, 7.14	; N, 16.6.

Saponification of the Amide.—One-tenth of a gram of the amide was heated for 12 hours with 10 cc. of 0.5 *N* sodium hydroxide. The solution was then acidified and extracted with ether and the residue from the ethereal solution converted into the barium salt by warming with barium carbonate and water. Two samples of the salt prepared in this way lost on drying, 9.62 and 9.83 per cent. water. Calculated for $(C_6H_8NO_4)_2Ba$ $2^1/_2$ H_2O, 9.03 per cent. The anhydrous salt gave 30.34 and 30.40 per cent. Ba. Calculated 30.30 per cent. The acid recovered from the barium salt melted at 73° and was identical with the acid formed by the decomposition of nitroisocampholactone with sodium or barium hydroxide.

Acid, $C_5H_8O_2N.CO_2H$.—One gram of nitroisocampholactone was put in a test tube with 30 cc. of 0.5 *N* sodium hydroxide and allowed to stand with occasional shaking till all had dissolved. The solution was acidified with hydrochloric acid and extracted with ether. The ethereal solution was dried with sodium sulphate and the ether distilled. From the residue the barium salt of the acid was prepared by treatment with water and barium carbonate. After filtering from the excess of carbonate the solution was concentrated in a vacuum desiccator. The barium salt crystallizes well in needles which are moderately soluble in water. From the pure barium salt the acid was recovered by acidifying its solution with hydrochloric acid and extracting with ether. The acid is easily soluble in ether and in benzene, almost insoluble in ligroin. It melts at 73–74°. The acid appears to decompose and become semisolid on standing. Perhaps for this reason the analyses, especially the nitrogen determinations are not very satisfactory, but when these are taken with the titration values and the composition of the barium salt the formula assigned to the acid seems to be established.

Calculated for $C_6H_9O_4N$: C, 45.2 ; H, 5.66 ; N, 8.80.
Found: C, 45.6, 45.8, 45.8; H, 5.9, 6.35, 6.4; N, 7.8, 7.5.

Titration with 0.1 *N* sodium hydroxide gave a molecular weight of 162.9 and 163.0; with barium hydroxide 166. Theory 159.

The Barium Salt, $(C_6H_8NO_4)_3Ba.\ 2^1/_2\ H_2O$ was analyzed completely because of the apparent instability of the acid. For the carbon determinations it was mixed with potassium dichromate to expel the carbon dioxide from the barium carbonate.

Calculated for $(C_8H_9NO_4)_2Ba.2\ 1/2\ H_2O$: C, 28.9 ; H, 4.2.
Found: C, 29.2, 29.0; H, 4.8, 44.7.
The anhydrous salt gave 6.38 per cent. N; calculated 6.14.

The salt lost 9.73 per cent. water at 80°. Calculated for 2 1/2 H_2O, 9.04 per cent. The anhydrous salt gave 30.34 and 30.27 per cent. Ba; calculated 30.30.

From lack of time and the difficulty of preparing the material we have been unable to undertake experiments which might throw light on the structure of the acid.

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

MOLECULAR REARRANGEMENTS IN THE CAMPHOR SERIES. VII. DERIVATIVES OF ISOCAMPHORIC ACID; *l*-DIHYDROHYDROXYCAMPHOLYTIC ACID.

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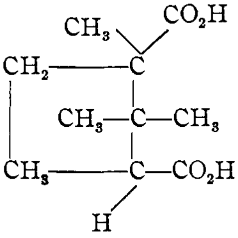
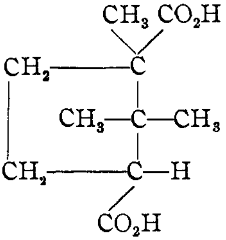
It is generally assumed that *d*-camphoric acid and *l*-isocamphoric acid, which, as Aschan has shown, are each convertible into the other, are stereomers and differ only in that one is a *cis* and the other a *trans* form. This may be expressed by the following formulas:


d-Camphoric acid.


l-Isocamphoric acid.