LXXXIV.—*Anhydro-derivatives of Citric and Aconitic Acids.*

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Introduction.

PILZ (*Jahresbericht*, 1861, 368), Perkin (*Annalen*, Suppl., 5, 287), and Anschütz (*Ber.*, 14, 2791) have shown that by the long continued action of acetyl chloride on certain hydroxy bibasic acids of the aliphatic series acetyl anhydrides may be obtained. These derivatives have been but little investigated, though it can scarcely be doubted that they are likely to afford interesting derivatives. Bearing in mind the ease with which the ethereal salts of citric acid are converted into pyridine derivatives, it appeared of interest to attempt the preparation of an acetyl anhydro-citric acid by the above method; it was found that it could be readily obtained in almost quantitative yield, and our expectations as to its chemical activity were completely realised. Thus it combines with water to form acetylcitric acid, and by its action on ammonia forms citrazinic acid, whilst with aniline it yields citrodianilic acid. Boiling alcoholic potash eliminates acetic acid, and a very satisfactory yield of aconitic acid is obtained. If the anhydride is distilled, it loses carbon dioxide and acetic acid, and, according as the distillation is performed, under ordinary pressure or in a vacuum, citraconic or itaconic anhydride is produced.

The preparation of the hitherto undescribed anhydride of aconitic acid was undertaken as an almost necessary supplement to the above work. Full details of the experimental work appear in the following pages.

Acetanhydrocitric Acid.

If anhydrous citric acid is digested upon the water-bath for a couple of hours with a slight excess of acetyl chloride (calculated for 4 mols.), in a flask provided with a reflux condenser, complete dissolution takes place, and the contents of the flask, on cooling, set to a mass of crystals. If these are drained by the aid of the filter-pump, washed with a small quantity of acetyl chloride, and dried in a vacuum over sulphuric acid and solid potash, a snow-white substance is obtained. On analysis it gave numbers which agree with the formula $C_8H_8O_7$.

I. 0.1692 gram of substance gave 0.0574 gram H_2O and 0.2744 gram CO_2 .

1004 EASTERFIELD AND SELL: ANHYDRO-DERIVATIVES

II. 0.1360 gram of substance gave 0.0455 gram H_2O and 0.2210 gram CO_2 .

III. 0.2045 gram of substance gave 0.0682 gram H_2O and 0.3340 gram CO_2 .

		Found.		
		I.	II.	III.
Calculated for $\text{O}_5\text{H}_8\text{O}_7$.				
C	44.44	44.20	44.31	44.54
H	3.70	3.76	3.71	3.70

The three analyses were performed on different preparations; III had been recrystallised from ether.

The method of formation and reactions of the new compound show it to be acetanhydrocitric acid,

the former formula being the more probable. If boiled with excess of dilute potash, the substance behaved as a quadribasic acid.

0.3195 gram neutralised 5.9 c.c. normal KOH ; calculated = 5.8 c.c.

After treatment with potash and careful neutralisation with nitric acid, a silver salt was precipitated; it contained 63.49 per cent. of silver. Silver citrate contains 63.15 per cent.

Acetanhydrocitric acid melts sharply at 115° (uncorr.), and is sparingly soluble in benzene, but very readily in ether, and on allowing the ethereal solution to evaporate spontaneously, it is deposited in groups of short prisms. The yield is very satisfactory, 153 grams of citric acid giving 149 grams of anhydride, and a further quantity can be obtained from the mother liquor.

Action of Heat.

Anschütz (*loc. cit.*) has shown that acetomalic anhydride distils unchanged in a vacuum, but that under ordinary pressure complete decomposition into acetic acid and maleic anhydride takes place. Acetanhydrocitric acid might similarly be expected to furnish acetic and anhydroaconitic acids. As a matter of fact, however, we were unable to prepare the last named compound in this way, though it was easily obtained by the action of acetyl chloride on aconitic acid (see below).

As already mentioned, the acetanhydrocitric acid melts at 115° to a colourless liquid, at 150° decomposition takes place with evolution of

acetic acid and carbon dioxide, whilst at 200° the decomposition is very rapid indeed, but ceases after a time, leaving a residue consisting of a brown oil. This distilled uniformly between 210° and 212°, and came over as a pale-yellow liquid having the characteristic odour of citraconic anhydride. A small quantity was warmed with water, and the solution allowed to cool, when crystalline plates of citraconic acid were deposited.

Analysis:—

0.099 gram of substance gave 0.0395 gram H₂O and 0.1665 gram CO₂.

	Calculated for C ₅ H ₆ O ₄ .	Found.
C	46.15	45.85
H	4.61	4.43

The decomposition had evidently taken place according to the equation

The acetic acid produced in one operation was collected and weighed: 7.5 grams of the anhydride gave 2 grams of acetic acid, boiling at 110—120°. Theoretical yield = 2.08 grams.

Analysis of the silver salt of the acid gave 64.63 per cent. Ag. Calculated = 64.67.

The yield of re-distilled citraconic anhydride was 20 per cent. of the theoretical.

If the acid is distilled in a vacuum (30 mm.), the only difference in the result obtained is that itaconic anhydride is produced instead of citraconic; the itaconic anhydride was recrystallised from chloroform, and showed the m. p. 68—70°. Upon analysis:—

I. 0.1159 gram of substance gave 0.2260 gram CO₂ and 0.0372 gram H₂O.

II. 0.1378 gram of substance gave 0.2633 gram CO₂ and 0.0430 gram H₂O.

	Calculated for C ₅ H ₄ O ₃ .	Found.	
		I.	II.
C	53.57	53.18	53.10
H	3.57	3.56	3.47

Acetocitric Acid.

This is easily obtained by dissolving the anhydride in lukewarm water and evaporating the filtered solution in a vacuum over sulphuric acid; a colourless syrup remains which soon deposits the acid in

1006 EASTERFIELD AND SELL: ANHYDRO-DERIVATIVES

hard, shining crystals; these melted at 138—140°, were very soluble in water, and gave the following results upon analysis:—

0.1713 gram of substance gave 0.0661 gram H_2O and 0.2564 gram CO_2 .

	Calculated for $\text{C}_8\text{H}_{10}\text{O}_8$	Found.
C	41.02	40.82
H	4.27	4.29

We were unable to obtain any characteristic salts of the acid. The silver salt blackened rapidly, even when precipitated from faintly acid solutions.

Action of Aniline on Acetanhydrotartronic Acid.

If a solution of the acid in anhydrous ether is added drop by drop to a solution of aniline ($2\frac{1}{2}$ mols.) also in dry ether, an amorphous, deliquescent mass separates; this may possibly be regarded as an aniline salt of acetocitrannilic acid. The crude product, when dried in a vacuum over sulphuric acid, was a brittle, pumice-like mass, and gave the following numbers on analysis:—

	Calculated for $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_7$	Found.
C	59.7	59.2
H	5.2	5.7
N	6.9	6.0

The substance is insoluble in ether, but dissolves readily in water, alcohol, and ethereal solution of aniline. The aqueous solution deposits crystals after a few days, and the ethereal aniline solution deposits a large quantity of crystalline matter if kept for a short time at the temperature of boiling ether. The crystals from both sources, when recrystallised from alcohol, showed the m. p. 180—182°, and on analysis were found to be citrodianilic acid.

- I. (From ether-aniline.) 0.1150 gram of substance gave 0.0556 gram H_2O and 0.2655 gram CO_2 .
- II. (From ether-aniline.) 0.1267 gram of substance gave 9.25 c.c. N at 20° and 757 mm.
- III. (From water.) 0.1629 gram of substance gave 11.75 c.c. N at 19° and 760 mm.

	Calculated for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_5$	Found.		
		I.	II.	III.
C	63.18	62.94	—	—
H	5.26	5.35	—	—
N	8.12	—	8.36	8.15

The melting point of citrodianilic acid is, however, usually stated to be about 153° (Pebal, *Annalen*, **82**, 87). Recognising the possibility of at least two isomeric dianilic acids of the above formula, we prepared citrodianilic acid according to Pebal's directions; it was in appearance just like that which we obtained from the acetyl anhydride, and melted at 183° , so that the two substances must be considered as identical. Possibly 153° is a misprint for 183° .

Conversion of the Anhydro-acid into Aconitic Acid.

The ease with which acetic acid is removed from the acetyl anhydrides by the action of heat, suggested that alkalis might decompose these anhydrides in a similar manner with formation of unsaturated derivatives. In the case of the acetanhydrocitric acid, the reaction gives excellent results, and we propose to apply it to other acetyl derivatives in order to ascertain whether it is to be regarded as a general method for the production of unsaturated compounds.

10 grams of the acetyl derivative were dissolved in a small quantity of 96 per cent. alcohol, and allowed to fall drop by drop into a boiling solution of 20 grams of potash in 100 c.c. of alcohol. After all the acetyl derivative had been added, the solution was boiled for a few minutes and then allowed to cool; a slight yellow precipitate separated, but this was neglected. The liquid was now strongly acidified with hydrochloric acid, allowed to stand for a short time, and filtered from the precipitate of sodium chloride. Water was then added, the excess of alcohol removed by distillation, and the aqueous solution evaporated to dryness and extracted with ether.

After removing the ether by distillation, and recrystallising the residue from hot water, with addition of pure animal charcoal, a colourless product was obtained, crystallising in minute needles.

The analytical results showed it to be aconitic acid; the yield was 80–85 per cent. of the theoretical.

0.1719 gram of substance gave 0.0555 gram H_2O and 0.2587 gram CO_2 .

	Calculated for $C_6H_6O_6$.	Found.
C	41.37	41.04
H	3.45	3.58

The melting point was found to be 190° (uncorr.), which is higher than that given in the text-books; it agreed, however, with that which we found for a recrystallised specimen of Kahlbaum's aconitic acid. Claisen and Höri (*Ber.*, **24**, 126) give the melting point of synthetical aconitic acid as 191° .

This is probably the most satisfactory method at present known

1008 EASTERFIELD AND SELL: ANHYDRO-DERIVATIVES

for the preparation of aconitic acid; it is unnecessary to purify the acetanhydrocitric acid before treatment with potash, the original syrup obtained by the action of acetyl chloride on citric acid being sufficiently pure for the purpose.

Citrazinic Acid.

When an excess of strong ammonia (sp. gr. 0.880) is added to acetanhydrocitric acid, a slight rise of temperature takes place, and a clear solution is obtained; but no condensation occurs even if the solution is kept in sealed tubes for several weeks. If, however, the solution is heated at 120—130° for a couple of hours, the liquid assumes a reddish tint and becomes fluorescent; on boiling off the excess of ammonia and acidifying with hydrochloric acid, a light yellow precipitate is formed, which, after being redissolved in ammonia, filtered, and reprecipitated by acid, gave numbers which agree well with those required for citrazinic acid, $C_6H_5NO_4$.

0.1771 gram of substance gave 0.0520 gram H_2O and 0.3010 gram CO_2 .

0.2280 gram of substance gave 18.4 c.c. N at 18° and 760 mm.

	Calculated for $C_6H_5NO_4$.	Found.	
		I.	II.
C.....	46.45	46.35	—
H.....	3.23	3.25	—
N.....	9.03	—	9.32

The sparing solubility of the substance in water, insolubility in alcohol, and the ready solubility in alkaline liquids, the intense blue fluorescence which such solutions show, and finally the brilliant blue coloration which the substance gives with a warm dilute solution of potassium nitrite, show the identity of the compound with the citrazinic acid of Behrmann and Hoffman. The yield is 35—40 per cent. of the anhydro-acid taken.

Attempts to effect a similar condensation by means of a concentrated solution of ethylamine were unsuccessful even when temperatures above 200° were employed. The solutions gave no precipitate with hydrochloric acid, but after removal of excess of ethylamine by a current of steam, and adding silver nitrate, a precipitate was obtained which contained a considerable percentage of nitrogen, showing the probable presence of an ethyl amic acid; as, however, the silver salts obtained were not constant in composition, the investigation was not followed up (compare Ruhemann, Trans., 1887, 51, 408).

The fact that the anhydro-acid when heated with ammonia yielded citrazinic acid, but does not do so in the cold, suggests that an amic acid is first formed, which subsequently undergoes condensation. In order to satisfy ourselves as to whether citramic derivatives would condense under similar circumstances, we heated (α) citramide and (β) the mixture of citramic acids which is left as mother liquor in the preparation of citramide, each with ammonia of 0·880 at 120—130°. In each case, a good yield of citrazinic acid was obtained; the absence of citrazinamide, which might have been expected to be produced, is indicated by the analyses:—

(α .)	0·1146	gram of substance	gave	9·6	c.c. N	at	759	mm.	and	21°.
(β .)	0·1611	„	„	12·7	„	759	„	19·5°.		

	Calculated for	Found.	
	$C_6H_5NO_4$.	(α .)	(β .)
N	9·03	9·5	9·08

Similarly, methyl citrate was found to yield citrazinic acid when heated with ammonia in a sealed tube; the yield was 33 per cent. of the citric salt taken.

Reduction of Acetocitric Acid.

Regarding acetocitric acid as an ethereal salt, it appeared possible that by the action of reducing agents it might be directly converted into tricarballic acid. Hitherto, however, we have been unable to effect this reduction, for, though a solution of acetocitric acid readily unites with hydrogen when acted on with sodium amalgam, the chief product of the reduction appears to be an uncrystallisable syrup easily soluble in water and alcohol, comparatively sparingly soluble in ether. We hope to return to this question in a subsequent communication.

The Anhydride of Aconitic Acid.

This compound is readily prepared by boiling aconitic acid with excess of acetyl chloride until complete dissolution is effected. On evaporating the filtered solution in a vacuum over solid potash, the anhydride gradually separates in colourless octahedra. The anhydride thus prepared is a hygroscopic substance melting at 95°; it is easily soluble in ether, alcohol, and hot benzene, from which it separates, on cooling, in modified cubes. On analysis:—

0·1745	gram of substance	gave	0·0405	gram H_2O	and	0·2904	gram CO_2 .
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1010 EASTERFIELD AND SELL: ANHYDRO-DERIVATIVES

	Calculated for C ₆ H ₄ O ₅ .	Found.
C.....	45.56	45.43
H.....	2.53	2.57

There are three possible formulæ, any one of which might represent the constitution of this anhydride:—

Of these, formula I is improbable, since anhydrides approaching this type are almost unknown; at the same time, the easy conversion of the anhydride into citrazinic acid, a pyridine derivative, might, perhaps, be taken as an argument in favour of this formula. Formula III would seem more probable than formula II, for III would represent the compound as a derivative of maleïc anhydride, II as a derivative of succinic anhydride. Substituted maleïc anhydrides are, as a rule, more easily formed than the corresponding succinic derivatives (compare especially diethylsuccinic and diethylmaleïc acids).

If, then, we regard the anhydride as a maleïc derivative, we must regard the acid which is formed by the action of water also as a maleïc derivative, that is, of quasi plane-symmetrical structure,

The anhydride readily unites with water, and passes thereby into ordinary aconitic acid (melting at 190°), which is therefore to be regarded as "maleoïd" aconitic.* We have attempted, but hitherto without success, to prepare the isomeric "fumaroid" modification. Possibly the maleoïd form is so much more stable than the fumaroid that the latter cannot be isolated. We hope to follow this interesting line of inquiry to a more definite conclusion.

Action of Ammonia on Aconitic Anhydride.

When dry gaseous ammonia is passed into a solution of the anhydride in dry ether, an amorphous, hygroscopic precipitate is formed which appears to be the ammonium salt of aconitodiamic acid.

* Michael (*Ber.*, 19, 1382) has come to practically the same conclusion from the reactions of the acid with aniline.

0.2428 gram of substance gave 46.15 c.c. N at 20° and 763 mm.

	Calculated for $C_6H_{11}N_3O_4$.	Found.
N	22.2	21.80

When this substance, which is deliquescent, is dissolved in ammonia of 0.880, or, indeed, if aconitic anhydride itself is dissolved in the same liquid, a solution is obtained which becomes fluorescent after a time, showing that condensation is slowly taking place. If the liquid is heated in a sealed tube for a couple of hours at 120°, the reaction takes place more rapidly, and, on acidifying the contents of the tube after the excess of ammonia has been removed, a precipitate of citrazinic acid is formed.

1.5 grams of the anhydride thus gave 0.23 gram of citrazinic acid, that is, 20 per cent. of the theoretical yield.

0.851 gram of substance gave 7.6 c.c. N at 20° and 765 mm.

	Calculated for $C_6H_5NO_4$.	Found.
	9.03	9.10

The acid showed the characteristic blue fluorescence in alkaline solution, and deep blue coloration with a warm dilute solution of potassic nitrite.

The anhydride of tricarballic acid has recently been prepared by Emery (*Ber.*, **24**, 596), who has, moreover, shown that, by the action of gaseous ammonia on an ethereal solution of the anhydride, the ammonium salt of tricarballic acid is formed. It appeared possible that by the action of strong aqueous ammonia on this anhydride, a condensation might be effected as in the case of aconitic anhydride. We were, however, unable to effect such a condensation. The anhydride was heated at 140° and afterwards at 180° for several hours with an excess of concentrated ammonia, but no darkening of the solution occurred, and nothing was precipitated from the liquid on acidifying it with hydrochloric acid. On evaporating the ammoniacal solution upon the water-bath, an uncrystallisable syrup remained; this was dissolved in water and silver nitrate added, when a flocculent precipitate containing nitrogen was thrown down. Its composition was not constant, and it is probably a mixture of the salts of tricarballic and tricarballic acids.

This difference between the reactions of the anhydrides of acids so nearly related as aconitic and tricarballic is interesting, and seems to point to the fact that the formation of citrazinic acid from ethereal salts of citric acid is largely dependent on the easy formation of an "ethylene" linking.

1012 DIXON: DI-SUBSTITUTED SEMITHIOCARBAZIDES.

Several points in connection with the anhydrides which we have dealt with in this paper have still to be worked out. Notably the action of ammonia and the effect of heat on these compounds require more careful study than we have hitherto had time to give to them. Phenylhydrazine, too, acts readily on the substances in question, producing crystalline derivatives, which we have not yet investigated. We hope, in a subsequent paper, to deal with these and some other points of interest which have arisen during the course of this investigation.

We desire, in conclusion, to express our thanks to Mr. T. T. Knowles and Mr. P. Hudson for the willing assistance they have afforded us in connection with the above work.

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