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CAMPHOROXALIC ACID DERIVATIVES. VI.

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INTRODUCTION.

IN the course of an investigation of the action of ethereal oxalates on aliphatic ketones,[1] it was found that the impure sodium camphor, obtained by the action of one atomic proportion of sodium on camphor, in boiling toluene solution, condenses with ethylic oxalate. The yield was extremely poor. At that time, the question of the presence in the camphor molecule of the group $—CH_2.CO—$ was an open one, and the first conclusive and direct proof of its occurrence was afforded by this work. Apart from the special interest which the subject thus acquired, it possessed other more general ones; hence, the investigation of the above condensation product, termed ethylic camphoroxalate, was continued at the Heriot-Watt College, Edinburgh.

The yield was improved materially and a number of derivatives prepared and studied. Pressure of other work caused the suspension of the research until 1897. During this interval, the point alluded to above, regarding the constitution of camphor, was generally recognized as settled, but other questions had arisen that appeared to make the extended investigation of camphoroxalic acid desirable. One of these concerned the true constitution of "diketones," of which ethylic camphoroxalate may be taken as an example: were they to be regarded as unsaturated

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[1] Inaugural Dissertation., Munich University, 1889, p. 34.

keto-alcohols or as true diketones? From the almost neutral character of the camphor nucleus, and its relatively large mass, camphoroxalic acid appeared to be peculiarly well fitted for the purpose of investigation in this direction. A further object was to accumulate data which might elucidate to some extent the mechanism of the Claisen condensation. The work was therefore resumed at the University of Chicago, and has since been continuously prosecuted, first at the University of Pennsylvania, and subsequently in this laboratory. The results as regards the constitution of camphoroxalic acid are apparently complete, and indicate that it is an unsaturated keto-alcohol. In addition to this, a new class of compounds has been discovered, formed by the condensation of the acid with amines. Most of the observations which have been made have been published at intervals as the work proceeded; in the present paper, these scattered communications[1] are briefly coordinated, corrected where necessary, and a description is given for the first time of a series of compounds obtained by the action of camphoroxalic acid and ethyl camphoroxalate on ammonia and certain aliphatic amines.

THEORETICAL.

A number of experiments were made in order to determine the most suitable conditions for the preparation of camphoroxalic acid and its ethyl salt; these may be thus summarized: (1) Sodium with ethyl oxalate and camphor in boiling toluene; (2) Dried sodium ethoxide suspended in boiling ether; (3) Sodium ethoxide in absolute alcoholic solution; (4) Sodium wire with the camphor and ethyl oxalate in absolute ethereal solution; (5) Sodium wire as in 4, in dried, light petroleum solution. The results are as follows:

Experiment.	Molecules camphor to 1 molecule ethyl oxalate.	Atoms sodium.	Crude ethyl salt and acid per cent. of theoretical.	Acid formed per cent. of theory.	Acid 1 part: of ethyl salt.
1	2	2	small	....	....
2	1	1	10	....	....
3	1	1	4.4	....	....
4	1⅓	1	58.0	4.9	0.07
5*a*	1⅓	1	63.5	Ethylic salt only	
5*b*	1⅓	1	92.4	17.0	0.2
5*c*	2	2	66.5	44.6	1.8

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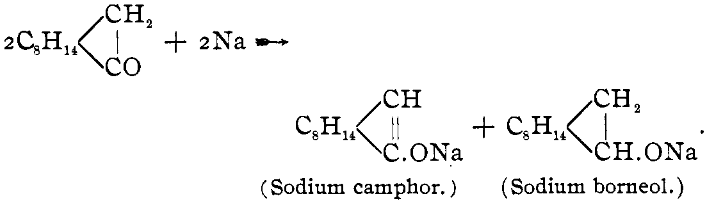
[1] Inaug. Diss., Munich, 1889, p. 34; *J. Chem. Soc.* (London), 1890, 652; *Am. Chem. J.*, **19.** 393 (1897); *Ibid.*, **20.** 318 (1898); *Ibid.*, **21.** 238 (1899); *Ibid.*, **23**, 214 (1900).

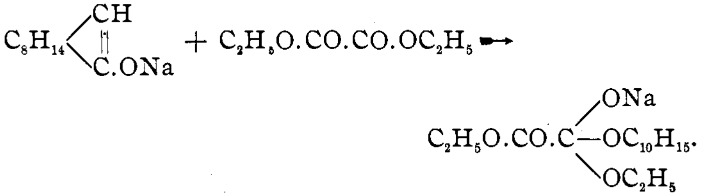
It is immediately evident that the first three methods are quite unsuited for the preparation of the acid on a large scale. Experiments 4 and 5 show that the use of light petroleum is more favorable to the yield than that of ether, probably because of its higher boiling-point (about 70°) ; its cheapness, and the ease with which it can be dehydrated are also incidental, but highly important advantages. The influence of the varying amount of sodium is illustrated in experiments 5*a*, *b*, and *c*, the total yield is improved by the use of 1 atom to 1½ molecules of camphor, but a larger proportion of the latter favors the formation of acid at the expense of ethylic salt.

Recent research appears to indicate that, except in the case of hydrocarbons of the acetylene type, or those containing the linkage *C:C.C.C:C.*,[1] none of the organo-metallic compounds have the metal directly linked with carbon ; accordingly, in formulating the above facts, Claisen's explanation of his condensation requires some modification. The figures in the above table show that the action of sodium on camphor is by no means complete, but it may be represented as follows :

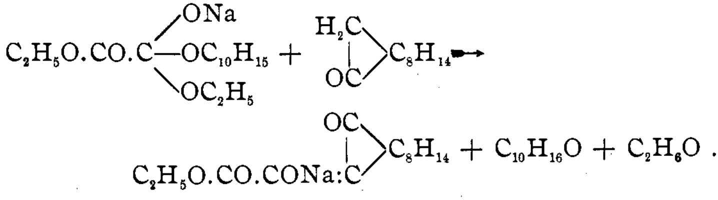
(1.)



(2.)



(3)



The sodium salt when acidified yields the ketone directly.

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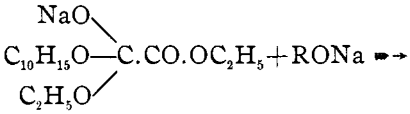
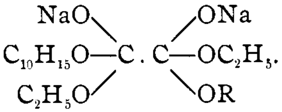
[1] J. Thiele : *Ber. d. chem. Ges.*, **34**, 69 (1901).

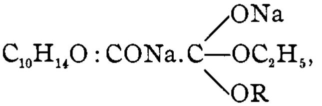
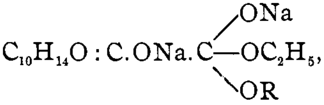
The large amount of acid produced and the conditions which have been shown to favor its formation, prove that this cannot be ascribed to hydrolysis of the ethyl salt, either while the borneol and excess of camphor are being extracted, or as the result of traces of moisture in the apparatus. The idea that the borneol and camphor mechanically retain ethyl salt sufficient to yield, by subsequent hydrolysis, the amount of acid actually obtained, is also not supported by the comparative experiments. With the modifications already suggested, Brömme & Claisen's explanation of the formation of acetophenone oxalic acid may be accepted.[1] According to this the compound formed, as represented in the second equation, combines either with a second molecule of sodium camphor, or with one of sodium ethoxide, this last being produced from the alcohol eliminated in the third phase of the reaction:

(4). 

$$\mathrm{C_{10}H_{15}O{-}\overset{NaO\diagdown}{\underset{C_2H_5O\diagup}{C}}.CO.OC_2H_5+RONa} \rightarrow$$



$$\mathrm{C_{10}H_{15}O{-}\overset{NaO\diagdown}{\underset{C_2H_5O\diagup}{C}}\,.\,\overset{\diagup ONa}{\underset{\diagdown OR}{C}}{-}OC_2H_5}.$$

By the interaction of camphor as in equation 3, we get the salt  $\mathrm{C_{10}H_{14}O:CONa.\overset{\diagup ONa}{\underset{\diagdown OR}{C}}{-}OC_2H_5}$, which, with water, yields the compound $\mathrm{C_{10}H_{14}O : CONa.CO.ONa + C_2H_6O + ROH}$ ($\mathrm{R = C_2H_5}$ or $\mathrm{C_{10}H_{15}}$). It must be confessed that this explanation is not wholly satisfactory, as it affords no very obvious reason for the failure of the ortho carbon atom in the above compound.  $\mathrm{C_{10}H_{14}O:C.ONa.\overset{\diagup ONa}{\underset{\diagdown OR}{C}}{-}OC_2H_5}$, to react with camphor like the first one in equation 3, and yield, eventually, dicamphoroxalyl, $\mathrm{C_{10}H_{14}O : COH.COH : OC_{10}H_{14}}$. Hitherto, none of this substance has been found, although attempts have been made to prepare it; therefore, the inference is, either that it is hydrolyzed during the extraction of the acid, or that the experimental conditions are

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[1] *Ber. d. chem. Ges.*, 21, 1132.

unfavorable for its production. A similar lack of success was experienced in an attempt to obtain the corresponding acetone derivative from ethyl camphoroxalate and acetone in the presence of sodium. An attempt which was made to test the above theory was based upon the following considerations: The symmetry of ethyl oxalate precludes the formation of more than one camphoroxalic acid, apart from possible stereoisomers, but an unsymmetrical dibasic ester should yield two structurally different acids according to which of the original carbethoxyl groups reacted; this is illustrated by the following equations, in which the carbon atoms of the carbethoxyl groups are distinguished as 1 and 2; ($R = C_2H_5$ or $C_{10}H_{15}$; $R'' = C_8H_{14}:CO$).

The additive compound $NaO.\overset{1}{C}(OR)_2 \cdots \overset{2}{C}(OR)_2.ONa$ of equation 4 would become successively

(*a*) $NaO.\overset{1}{C}:CR'' \cdots \overset{2}{C}(OR)_2.ONa$ or $NaO.\overset{1}{C}(OR)_2 \cdots \overset{2}{C}.ONa:CR''$;

(*b*) $NaO.\overset{1}{C}:CR'' \cdots \overset{2}{C}:O.ONa$ or $NaO.\overset{1}{C}O \cdots \overset{2}{C}.ONa:CR''$;

(*c*) $HO.\overset{1}{C}:CR'' \cdots \overset{2}{C}O.OH$ or $HO.\overset{1}{C}O \cdots \overset{2}{C}.OH:CR''$.

Pyrotartaric acid, $HO.OC.CH(CH_3).CH_2.CO.OH$, is perhaps the simplest acid fulfilling the conditions necessary to test the above hypothesis, and experiments were made with it. *Diethyl pyrotartrate* is readily prepared by E. Fischer's method[1] and the yield is excellent. Sodium wire dissolves slowly in a light petroleum solution of camphor and ethyl pyrotartrate; the condensation product which was finally isolated, gave a red coloration with ferric chloride and alcohol, but no acid could be obtained from it by hydrolysis. The yield of condensation product was small, and was not improved by the varying conditions employed. In pursuit of the same object *ethyl oxalacetate* was employed instead of the ethyl pyrotartate. The product was a syrup having a yellowish brown color in ethereal solution; in aqueous solution, a blue-purple coloration is produced on the addition of a little mineral acid; with a larger excess, the color is discharged; alkalies change it to deep red. When hydrolyzed, the compound yields a liquid acid which readily liberates carbonic anhydride from carbonates; an attempt to induce it to crystallize, after purification by means of the barium salt, was unsuccessful. The compound is probably a condensation product of ethyl oxalacetate similar to those described by Claisen[1] alone, and in conjunction with Hare,[2] and by Ruhesmann and Hemmy.[3]

Camphoroxalic Acid is readily soluble in ether and benzene, moderately so in light petroleum, and sparingly in water ; it is preferably purified by recrystallization from light petroleum, being deposited in large, well-developed six-sided monoclinic plates, resembling those of quartz in appearance, and melting at 88°. When quickly distilled under the ordinary pressure some camphor is produced, but the greater portion of the acid passes over unchanged. Prolonged exposure to a temperature of 150° failed to yield any isomeric compound (cf. pp. 377). When heated with barium hydroxide, in a current of dry purified hydrogen, hydrolysis occurs at the position of the ethylene linkage, and camphor and barium oxalate are formed. No physiological action is produced on a dog by the intravenous injection of 0.241 gram of sodium camphoroxalate per kilo of body weight. The *copper*, *silver*, *calcium*, *lead*, *and barium salts* are sparingly soluble and amorphous ; the first is green, the second slightly yellow, and the remainder white. The *sodium salt*, which is very readily soluble, rapidly decolorizes potassium permanganate at the ordinary temperature. When reduced by means of sodium amalgam the acid yields a *lactone*,  $C_8H_{14}\left\langle\begin{array}{l} CH.CH.OH.CO \\ \mid \qquad\qquad\quad\ \mid \\ CH\text{————}O \end{array}\right.$, which is deposited from ether as an unctuous solid, melting at 75°–76°. The action of *bromine* on camphoroxalic acid was studied in the hope that it might yield evidence of the presence or otherwise of an ethylene linkage, and also because, by its means, it appeared possible that an isomeric acid might be produced. The substances react either in chloroform solution, or when bromine vapor is brought into contact with the dry acid ; hydrogen bromide is eliminated more quickly in the former than in the latter case, and the product is an oil which crystallizes with difficulty, cannot be completely purified, and contains bromine. It gives no coloration with ferric chloride and alcohol, and when reduced with magnesium amalgam yields an acid closely resembling camphoroxalic acid in general properties but differing from it in crystallographic form. These results may be explained in one of two

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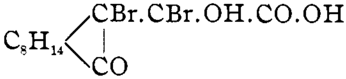
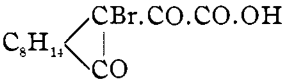
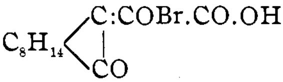
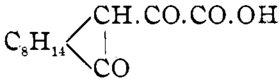
[1] *Ber. d. chem. Ges.*, **24**, 130.

[2] *Ibid.*, **24**, 120.

[3] *J. Chem. Soc.*, **71**, 334 (1897).

ways: If the ethylene linkage is attacked, the additive compound would be  $C_8H_{14}\left<\begin{matrix}CBr.CBr.OH.CO.OH\\ |\\ CO\end{matrix}\right.$; this should readily eliminate hydrogen bromide and yields either the compound  $C_8H_{14}\left<\begin{matrix}CBr.CO.CO.OH\\ |\\ CO\end{matrix}\right.$, or  $C_8H_{14}\left<\begin{matrix}C{:}COBr.CO.OH\\ |\\ CO\end{matrix}\right.$; on reduction the former would give the diketonic acid,

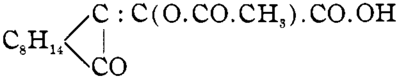


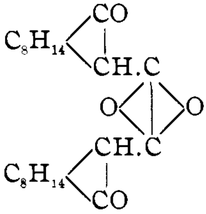
$$C_8H_{14}\left<\begin{matrix}CH.CO.CO.OH\\ |\\ CO\end{matrix}\right.,$$

and the latter camphoroxalic acid. On the other hand it is well-known that camphor itself very readily combines with bromine, forming the dibromide $C_{10}H_{16}Br_2O$, which easily eliminates hydrogen bromide and is converted into bromocamphor, $C_{10}H_{15}BrO$; if the nucleus of camphoroxalic acid acts in a similar manner, then, by the reduction of this bromo acid, an isomeric camphoroxalic acid should be formed which should not differ materially from the ordinary compound in properties, and should give a similar red coloration with ferric chloride, while the keto acid could not do so. This second view of the reaction appears at present to be the more probable.

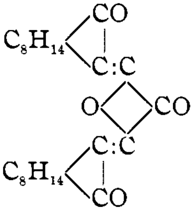
When heated with hydrochloric acid, or with dilute sulphuric acid (1 : 3), camphoroxalic acid yields a little oxalic acid, but by far the larger proportion of it is converted, by the addition of the elements of 2 mols. water, into an *acid* which crystallizes with some difficulty in granular nodules melting at 92°–93°. This compound, $C_{12}H_{20}O_6$, differs from the parent substance by its sparing solubility in light petroleum, the production of a deep blue coloration with ferric chloride and alcohol, and by its failure to give a precipitate with calcium chloride in ammoniacal solution.

The action of acetic anhydride on camphoroxalic acid is complex, and although much time and labor have been spent on its study, the results cannot be considered satisfactory. This arises from the fact that under the most favorable circumstances the yields are poor, and very slight alterations in the experimental conditions cause the acid to undergo complete decomposition. The purity of the anhydride employed is a most important factor. Three compounds have been isolated, the first is *acetylcamphor-*

oxalic acid,  $C_8H_{14}\left\langle\begin{array}{l}C:C(O.CO.CH_3).CO.OH\\ |\\ CO\end{array}\right.$, which is also formed by the interaction of the anhydride and ethyl camphoroxalate; it crystallizes from a mixture of benzene and light petroleum in reticulated stellate needles, melting at 133.5°–134.5°. The second compound is also formed by the action of benzoyl chloride on camphoroxalic acid; it gives no coloration with alcohol and ferric chloride, is insoluble in sodium hydroxide solution, and crystallizes in colorless slender needles melting at 192°–193°. Bromine and hydroxylamine are both without action on the compound to which the formula



is, at least provisionally, assigned. The third compound is formed with great difficulty, and all attempts to improve the yield were fruitless. It crystallizes in small, slender, colorless needles which darken at about 240°, and melt at 242°. It does not react with bromine in chloroform solution, while aqueous sodium hydroxide dissolves a portion and turns the remainder yellow. The formula



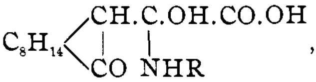
is in harmony with the little which is known of the substance.

Acetylcamphoroxalic acid readily reacts with bromine either in the form of vapor, or in chloroform solution; in both cases hydrogen bromide is copiously evolved, but no crystalline product could be isolated. The result confirms the explanation offered above of the action of bromine on camphoroxalic acid itself, and there appears little room for doubt that the haloid attacks the camphor nucleus of both compounds.

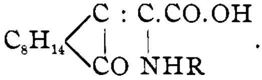
With benzoic anhydride, and camphoroxalic acid, no definite results could be obtained; at 110° benzoic acid sublimed, and at 150° carbonic anhydride was evolved.

Phenylhydrazine and camphoroxalic acid, in anhydrous ethereal solution, yield a salt which crystallizes in minute colorless needles, darkens at 205°, and melts and evolves gas at 214°-215°.

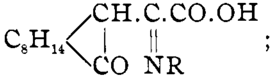
A somewhat extensive study has been made of the condensation compounds of camphoroxalic acid and amines, both of the aromatic and aliphatic series. The primary products in all cases are apparently simply additive substances of the type



but only one body of this formula has been isolated, that obtained from hydroxylamine: the remainder appear to be unstable, and eliminate the elements of water, giving rise to products of the general formula



Compounds of this nature have been prepared from ammonia, semicarbazine,[1] aniline, and α- and β-naphthylamine. These substances may then undergo further change; in the case of the aniline derivative carbonic anhydride is evolved; the hydroxylamine compound, mentioned above, loses the elements of two molecules of water and yields an isoxazole, while orthophenylenediamine condenses directly with the acid to form a quinoxaline derivative. The above series of compounds might be formulated in various other ways; perhaps one of the most plausible is



the three chief reasons for preferring the first formula are: (1) The stability of the compounds toward alkalies; (2) The fact that with all reagents that have been successfully tried, and which could afford crucial tests, both camphoroxalic acid, and ethyl camphoroxalate act as hydroxy-unsaturated compounds; hence, analogy is strongly in favor of adopting the same view in any

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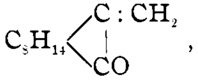
[1] It appears preferable to the writer to designate the compound $NH_2.CO.NH.NH_2$, *semicarbazine*, in analogy with phenylhydrazine.

doubtful cases; (3) There is some direct evidence of the existence, in the above compounds, of the imido group, and in the case of the ammonium derivative, of the amido radical. On the other hand, there has been complete failure to obtain similar derivatives of secondary amines, either aliphatic or aromatic, and, except on stereochemical grounds, this is not readily explicable by the first formula, but is easily understood from the second one. It is hoped that subsequently further light may be obtained on the subject.

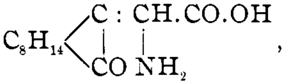
In naming the compounds the simplest and most advisable plan appeared to be to regard them as derived from the complex



$$C_8H_{14}\left\langle\begin{array}{l} C:CH_2 \\ \;| \\ CO \end{array}\right. ,$$

for which the term *camphoformene* suggests itself; it is self-explanatory and indicates the presence of the double linkage.

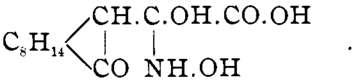
By the action of ammonia on sodium or potassium camphoroxalate, in alcoholic solution, at 100° under pressure, *sodium camphoformeneamine carboxylate* is obtained, from which the free *acid*,



$$C_8H_{14}\left\langle\begin{array}{ll} C & :CH.CO.OH \\ \;| & \;\;| \\ CO & \;NH_2 \end{array}\right. ,$$

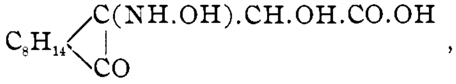
is readily liberated. It crystallizes in colorless plates, melts, and evolves gas at 178°, is not soluble in light petroleum, and gives no coloration with ferric chloride and alcohol. The acid dissolves readily in hot, but not in cold, sodium carbonate solution, and is reprecipitated on acidification; by means of the diazo reaction it regenerates camphoroxalic acid. An attempt to prepare camphoformeneamine by heating the acid was unsuccessful; absolute alcoholic ammonia and free camphoroxalic acid yield, as chief product, ammonium camphoroxalate, which is crystalline, and melts and evolves gas at about 212°.

Sodium camphoroxalate combines with hydroxylamine in concentrated aqueous-alcoholic solution, at the ordinary temperature, forming the compound



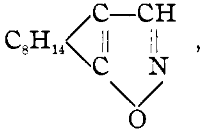
$$C_8H_{14}\left\langle\begin{array}{ll} CH & .C.OH.CO.OH \\ \;| & \;\;| \\ CO & \;NH.OH \end{array}\right. .$$

This crystallizes in bushy clusters of colorless, lustrous needles, which sometimes appear flattened into plates; it melts and evolves gas at 146.5°. No alkaline fumes are evolved when the compound is boiled with sodium hydroxide solution, and no coloration is produced with alcohol and ferric chloride. That this additive compound is represented by the above formula, and not by the possible alternative one,



$$C_8H_{14}\left\langle\begin{array}{l}C(NH.OH).CH.OH.CO.OH\\ |\\ CO\end{array}\right. ,$$

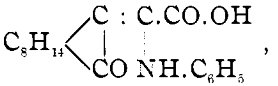
is proved by the production of *camphylisoxazole*,



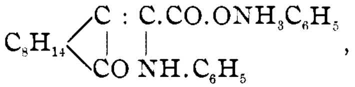
when the additive compound is treated with a mixture of glacial acetic acid and acetic anhydride. The isoxazole crystallizes in colorless, lustrous needles, which melt at 124°–125°. At about 70° it sublimes slowly, and forms very slender, silky, long needles; no coloration is produced with concentrated nitric acid.

Semicarbazine combines with camphoroxalic acid under the same conditions as hydroxylamine, and also in alcoholic solution, under pressure, at 100°. The product consists of two compounds which are separated by means of ether. The more soluble one crystallizes from acetone in small white needles, melting and decomposing at 218°. The second compound is insoluble in all ordinary neutral organic media ; it is purified by means of glacial acetic acid and alcohol, and is deposited in microscopic needles—aggregated into cubical clusters ; these melt and decompose at 209°–210°. Both compounds dissolve in sodium carbonate solution with equal readiness; the first is reprecipitated in a gelatinous condition. but after drying, its melting-point is unchanged. The solution of the second compound is also precipitated by acids, but the precipitate shows the same melting-point as the "soluble" body. Identical results are obtained by the elementary analysis of the two substances. It would be easy to suggest possible explanations of the above phenomena, but it appears better to abstain from doing so until more experimental information is forthcoming.

Aniline and camphoroxalic acid yield three compounds, one of these, *phenylcamphoformeneamine carboxylic acid*,

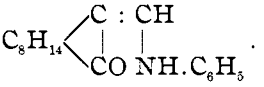


corresponds with the ammonia derivative of camphoroxalic acid, and is formed by boiling aniline with sodium camphoroxalate in aqueous alcoholic solution; it crystallizes in bright yellow needles, and melts and decomposes at 174°. The second compound,



is the *aniline salt* of the preceding acid, and is formed by warming for a few moments on the water-bath, a mixture of aniline and camphoroxalic acid in concentrated benzene solution. It crystallizes from benzene on the addition of light petroleum, in small, colorless needles which melt and decompose at 158°. The salt is stable at the ordinary temperature in the absence of moisture and acid vapors; when cautiously heated below its melting-point, it is resolved into aniline and phenylcamphoformeneamine carboxylic acid, and the same change is produced immediately by dilute sulphuric acid, hydrochloric acid, alkalies, and more slowly, by water. Rapid heating above its melting-point results in the production of aniline, carbonic anhydride, and phenylcamphoformeneamine (see below). Prolonged boiling with concentrated alkali, aqueous or alcoholic, converts the carboxylic acid, and therefore, of course, the aniline salt, into aniline and the alkali salt of camphoroxalic acid.

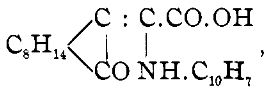
The third compound from aniline and camphoroxalic acid is formed by heating either of the preceding substances above their melting-points, and also by the direct action of the constituents at 130°. Its preparation and reactions characterize it as *phenylcamphoformeneamine*,



It crystallizes in colorless, rhombic plates, and occasionally in characteristic slender hair-like needles, upwards of an inch in length. With bromine, it forms a *hydrobromide*, while hydroaurochloric acid and hydroplatinochloric acid yield *salts*, of which the former is very unstable. Prolonged boiling with concentrated alkali is without effect on the compound. With acetic anhydride an unstable crystalline derivative is obtained which melts at 134°.

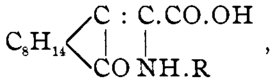
Benzoyl chloride reacts with the amine, yielding crystals resembling those of potassium nitrate in shape, and melting at 160–161°. The derivative formed by the action of phenylsulphonic chloride is crystalline, melts at 133°, and does not dissolve in sodium hydroxide solution. With methyl iodide, the amine apparently does not react.

α-Naphthylamine reacts with sodium camphoroxalate under somewhat similar conditions to aniline and forms *α-naphthylcamphoformeneamine carboxylic acid*,



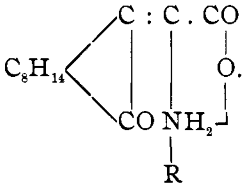
$$C_8H_{14}\left\langle\begin{matrix} C & : & C.CO.OH \\ | & & | \\ CO & & NH.C_{10}H_7 \end{matrix}\right. ,$$

which crystallizes with $\frac{1}{2}$ mol. C_6H_6 in well developed, transparent, amber-colored prisms, melting at 170°. At a little above 100°, the crystals lose their benzene and change to a brown powder which also melts at 170°. The corresponding *derivative* of *β-naphthylamine* is deposited from benzene or toluene in bright yellow needles which melt and decompose at 173°. From neither of these compounds has it hitherto been possible to obtain a naphthyl camphoformeneamine, corresponding with the phenyl-derivative. The pronounced color—bright yellow to brown,—of these three carboxylic acids suggests the possibility, that instead of being represented by the formula



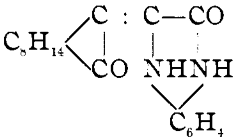
$$C_8H_{14}\left\langle\begin{matrix} C & : & C.CO.OH \\ | & & | \\ CO & & NH.R \end{matrix}\right. ,$$

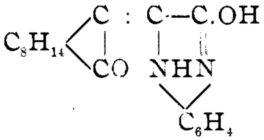
they, in reality, possess a "betaine" structure,

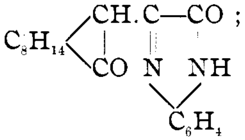


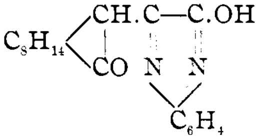
$$C_8H_{14}\left\langle\begin{matrix} C & : & C & . & CO \\ | & & | & & | \\ | & & | & & O. \\ | & & | & & | \\ CO & & NH_2 & - & \lrcorner \\ & & | & & \\ & & R & & \end{matrix}\right.$$

The interaction of orthophenylenediamine and camphoroxalic acid, carried out under similar conditions to those employed for the preparation of the preceding carboxylic acids, results in the production of *camphoquinoxaline*, $C_{18}H_{20}N_2O_2$; it crystallizes in bright yellow needles, melts at 246°, and dissolves in concentrated sulphuric acid, giving a color resembling that produced by potassium chromate in the same circumstances. Under conditions which preclude the idea of hydrolysis, ethylic camphoroxalate and orthophenylenediamine yield a substance identical with that from the acid. The compound may be represented by one or other of the formulae:

(1)  ;

(2)  ;

(3)  ;

(4)  .

The relationship of formulae 1 and 2 to 3 and 4 respectively, is that of a lactam to the corresponding lactim; excluding this aspect of the question as involving the broader one of the constitution of the quinoxalines, sodium camphoroxalate should give the compound having the second formulae, while ethylic camphoroxalate should yield that represented by the first one. Hence it must be concluded, either that the first compound is unstable and changes spontaneously into the second, or that the sodium salt of the second, after acidification, changes to the first; at present, this latter suggestion appears to be the more probable, unless, of course, the case is one of tautomerism in the strict sense of the term.

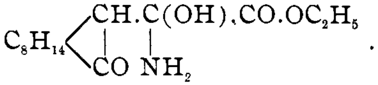
ETHYL CAMPHOROXALATE.

The crude condensation product of ethyl oxalate and camphor always contains ethyl oxalate, and although this is of little consequence for some purposes, a supply of pure substance is, of course, highly desirable and occasionally absolutely necessary. The crude ethyl salt does not react with copper acetate either in neutral, or ammoniacal solutions, irrespective of whether the ester is dissolved in water, ether, or light petroleum. The compound thus exhibits a striking contrast to formylcamphor, which is a strong acid. When boiled, a portion suffers decomposition and part is volatilized unchanged. An attempt to separate the mixed ethyl salts by systematic treatment with sodium hydroxide, sodium carbonate, and sodium hydrogen carbonate solutions, resulted only in the hydrolysis of the compounds. It was ultimately found to be most convenient to hydrolyze the crude ester, and then esterify the purified camphoroxalic acid by a modification of E. Fischer's method. The compound is deposited from light petroleum in fern-like aggregates, consisting of long needles, melting at 40.5°. It is miscible with ether in all proportions, and is extremely readily soluble in ordinary media, with the exception of light petroleum. With alcohol and ferric chloride solution a deep red coloration is obtained. Fractional esterification failed to show any lack of homogeneity in camphoroxalic acid (cf. pp. 368).

Bromine and ethylic camphoroxalate readily react, hydrogen bromide being evolved; when the two are heated in chloroform solution oxalic acid is formed, but at the ordinary temperature the product was an oil which refused to crystallize.

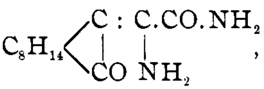
With acetic anhydride the ester yields acetylcamphoroxalic acid, as already described (cf. p. 369). No derivative could be obtained by the action of either benzoyl chloride or benzoic anhydride, in spite of considerable variation of the experimental conditions. The greater relative stability of the ethylic salt, as compared with camphoroxalic acid, towards these reagents, is interesting, and supports the view that the acid, under their influence, undergoes deep-seated changes involving the carboxyl group.

Carefully dried ammonia produces a white precipitate when passed into a well cooled absolute alcoholic solution of ethylic camphoroxalate; the substance is unstable, and is resolved spontaneously into its constituents. It is doubtless an additive compound with the formula



$$C_8H_{14}\left\langle\begin{array}{l}\mathrm{CH.C(OH).CO.OC_2H_5}\\ \ \mid\qquad\mid\\ \mathrm{CO\ \ NH_2}\end{array}\right. .$$

When heated at 100°, with alcoholic ammonia in excess, it is converted into *camphoformeneaminecarboxylamide*,



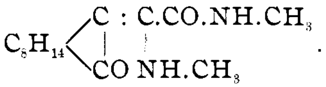
$$C_8H_{14}\left\langle\begin{array}{l}\mathrm{C : C.CO.NH_2}\\ \ \mid\qquad\mid\\ \mathrm{CO\ \ NH_2}\end{array}\right. ,$$

which is also formed directly by the interaction of ammonium chloride, potassium hydroxide, and ethylic camphoroxalate under the same conditions. It crystallizes in colorless microscopic needles, melting at 227°-228°. Boiling with sodium hydroxide solution causes the regeneration of ammonia and camphoroxalic acid.

A compound which melted at 225°, and was previously[1] obtained by the action of dry ammonia on ethyl camphoroxalate in absolute ethereal solution, was prepared from the crude ethylic salt, containing, therefore, ethyl oxalate, and was almost certainly oxamide.

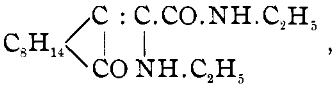
In the first paper on this subject,[2] a substance was described which was produced by the interaction of crude ethyl camphoroxalate and hydroxylamine; it crystallized in silky needles, and melted at 193°. From its melting-point and general properties, the compound is probably oxalenediamidoxime $OH.N:C(NH_2).C(NH_2):N.OH$; in any case it is not a derivative of ethyl camphoroxalate, as all attempts to obtain it from the pure compound were fruitless. Experiments with the ethyl salt and hydroxylamine at 100° led to no definite results, but at the ordinary temperature a product is formed which crystallizes in colorless, slender needles, melting at 120°–121°. Its nature has not yet been investigated.

Methylamine and ethyl camphoroxalate readily condense at 100°, under conditions similar to those employed in the case of ammonia. The product is deposited in small, white needles which melt at 130° ; it is not very stable, and spontaneously evolves methylamine, but there is no doubt that it is *methyl camphoformeneaminecarboxylmethylamide*,



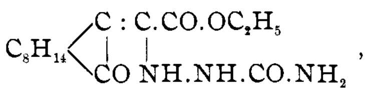
$$C_8H_{14}\left<\begin{array}{l} C : C.CO.NH.CH_3 \\ | \quad\quad | \\ CO\ NH.CH_3 \end{array}\right. .$$

Ethyl camphoformeneaminecarboxylethylamide,



$$C_8H_{14}\left<\begin{array}{l} C : C.CO.NH.C_2H_5 \\ | \quad\quad | \\ CO\ NH.C_2H_5 \end{array}\right. ,$$

is formed from ethylamine in a similar manner to the preceding compound, which it resembles in general properties; it crystallizes in colorless needles, melts at 148°, and very slowly evolves ethylamine. Semicarbazine condenses with ethyl camphoroxalate, either at the ordinary temperature, or at 100°, forming *ethyl semicarbazylcamphoformeneaminecarboxylate*,



$$C_8H_{14}\left<\begin{array}{l} C : C.CO.OC_2H_5 \\ | \quad\quad | \\ CO\ NH.NH.CO.NH_2 \end{array}\right. ,$$

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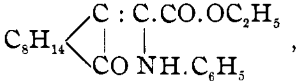
[1] *Am. Chem. J.*, **20**, 332 (1898).

[2] *J. Chem. Soc.* (London), **57**, 655 (1890).

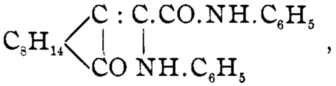
which crystallizes in colorless needles, melting at 202°. Molecular weight determinations agree with the formula given. Accompanying this compound a second was sometimes obtained in small quantity which also crystallized in colorless needles, melted at 225°, and may possibly be semicarbazine sulphate.

Ethyl camphoroxalate forms two compounds with aniline. The one, *ethyl phenylcamphoformenecarboxylate*,



$$C_8H_{14}\left\langle\begin{array}{l} C : C.CO.OC_2H_5 \\ |\qquad | \\ CO\ NH.C_6H_5 \end{array}\right. ,$$

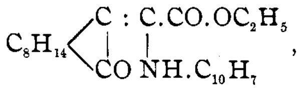
is prepared from its constituents, at 100°, and is deposited in almost white, microscopic, needle-shaped crystals, melting and decomposing at 158°–160°. When hydrolyzed by means of alkalies it yields the corresponding *acid*, m. p. 174, the preparation of which from aniline and sodium camphoroxalate has been already described (cf. p. 374). The second condensation product of aniline and ethyl camphoroxalate is obtained by heating these substances together at 130°; it consists of *phenylcamphoformeneaminecarboxylicanilide*,



$$C_8H_{14}\left\langle\begin{array}{l} C : C.CO.NH.C_6H_5 \\ |\qquad | \\ CO\ NH.C_6H_5 \end{array}\right. ,$$

which crystallizes in small, colorless needles, melting at 193°. The compound is not changed by admixture with bromine in chloroform solution, nor by prolonged boiling with aqueous or alcoholic sodium hydroxide. Treatment with sulphuric acid readily gives rise to resinous products. An unstable *platinochloride* appears to be formed, but hydroaurochloric acid quickly undergoes reduction when mixed with the anilide. In the first paper on this subject it was stated that aniline and ethyl camphoroxalate yield oxanilide; this is incorrect as the foregoing account shows. At the time that the statement was made pure ethyl camphoroxalate had not been prepared, and the mistake arose from the use of crude material containing ethyl oxalate. Unfortunately the error has been copied into Morley & Muir's edition of "Watts' Dictionary of Chemistry."

β-Naphthylamine and ethyl camphoroxalate yield, at 100°, *ethyl β-naphthylcamphoformeneaminecarboxylate*,

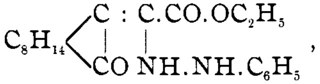


$$C_8H_{14}\left\langle\begin{array}{l} C : C.CO.OC_2H_5 \\ |\qquad | \\ CO\ NH.C_{10}H_7 \end{array}\right. ,$$

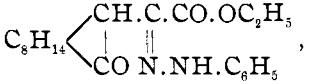
which closely resembles the corresponding phenyl derivative in appearance, and crystallizes in colorless, microscopic needles, softening at about 160°, and melting and decomposing at 174°. The exact melting-point is largely dependent on the rapidity with which the bath is heated. Hitherto, no naphthalide has been obtained corresponding to the "anilide" described above.

The condensation of orthophenylenediamine and ethyl camphoroxalate, leading to the production of camphoquinoxaline, has been described in connection with camphoroxalic acid (p. 375).

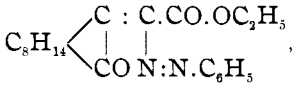
Phenylhydrazine and ethyl camphoroxalate, in equimolecular proportion, readily react when boiled in anhydrous ethereal, or light petroleum solution. The product is sparingly soluble, and comparatively stable towards aqueous sodium hydroxide at the ordinary temperature, but gives a deep blue-purple coloration with concentrated nitric acid. It crystallizes in slender, small, white needles, which melt sharply at 212°. A trace of impurity depresses this value very considerably; hence the incorrect melting-point (187°-188°) given in the first paper. The proof that this compound is a *phenylhydrazide*,



and not a *phenylhydrazone*,

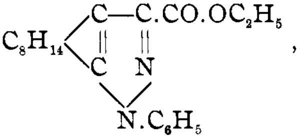


is afforded by its oxidation to *ethyl camphoroxalateazobenzene*,

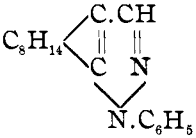


which crystallizes in red needles, melts at 210°, and is much more readily soluble in ether than the phenylhydrazide. The oxidation may be accomplished by means of mercuric oxide in the presence of absolute alcohol, but is preferably carried out by the help of hydrogen peroxide at the ordinary temperature in ethereal solution. The proof of the constitution of this compound affords a strong argument, by analogy, in favor of that assigned to the other condensation compounds described in the preceding pages.

Ethyl camphylphenylpyrazolcarboxylate,

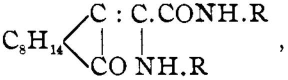


is formed by heating the phenylhydrazide at 200°, or by treating it with acetic anhydride, glacial acetic acid, or hydrogen chloride. It crystallizes in bunches of white needles, melts at 114°, and gives a pale yellow-colored solution with concentrated nitric acid. The free *acid*, prepared by hydrolyzing the preceding compound, crystallizes in lustrous needles, which melt at 192°; these appear to contain benzene of crystallization, as they slowly lose their luster, even at the ordinary temperature, and then melt at 197°. The compound, in the form of *sodium salt*, is without marked physiological action. When the *barium salt* is distilled with excess of barium oxide, care being taken to avoid the presence of moisture, an oily compound is formed which gives a reddish purple coloration with concentrated nitric acid, and also Knorr's pyrazoline reaction; it therefore, presumably, contains *camphylphenylpyrazole*,



The study of the preceding condensation compounds shows that their stability increases as the mass of the radical in the amine becomes greater, at least as regards the aliphatic derivatives; in the case of ammonia the symmetry of the molecule probably accounts for the high melting-point of the product. The question as to the formation of compounds of the type,

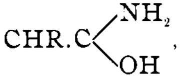
or



,

appears to depend upon the basicity of the amine, and the temperature at which the reaction proceeds; thus at 100°, when $R = H$, CH_3, or C_2H_5, compounds of the second type are obtained, but when $R = NH.NH.CO.NH_2, C_6H_5, NH, C_6H_5$, or $C_{10}H_7$, the products belong to the first type. At higher temperatures, with $R = C_6H_5$, a compound of the second type is produced, but under similar conditions, when $R = C_{10}H_7$, this was not found to be the case. The substances of the first type are strict analogues of the primary condensation products of camphoroxalic acid and amines.

It is worthy of note, that in spite of many attempts to prepare them, no compounds could be isolated in which the carbonyl group of the camphor nucleus had primarily reacted with an amine ; that it had remained intact was proved by the subsequent formation, from the actual condensation-products of pyrazole, and isoxazole derivatives. It is now generally recognized that many α-β, α-γ, and α-Δ-diketones are capable of existing or reacting in two or more forms, the change may be expressed by the equation : $CHR.CO \rightleftarrows CR:C.OH$. Analogy leads to the conclusion that all compounds of these classes are capable, under suitable conditions of undergoing the change. It is customary to assume that the ordinary "ketonic reagents" react primarily with the carbonyl group, giving compounds of the type of aldehyde ammmonia



$$CHR.C\begin{matrix} \diagup NH_2 \\ \diagdown OH \end{matrix},$$

which are generally unstable and change spontaneously into $CHR.C:NH(R)+H_2O$ (formation of oximes, hydrazones, etc.). This idea of the carbonyl group, *always* being the point of attack, does not appear to have any very definite foundation. The above results show that "ketonic reagents," in the presence of a compound containing both carbonyl and the group $R_2C:C.OHR$, react preferably with the latter, and not at all with the former under any conditions hitherto devised, and that, in the case of hydroxylamine, the compound formed by its addition to the double carbon linkage is quite stable. Similar results were subsequently obtained with mesityl oxide and phorone by Harries and his coworkers.[1] The relative stability of such additive compounds would naturally be expected to vary between limits at least as wide as those limiting the existence of the ketonic and enolic forms of the parent substances. Moreover, the stability might be greatly dependent on the reagents with which the compounds are brought into contact. In cases where the group in question could occur twice or thrice, as in triketones, such as

$$R.CO.CH_2.CO.CH_2.CO.R',$$

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[1] Ber. d. chem. Ges., **30**, 231, 2726 (1897).

the forms,

$$R.COH{:}CH.CO.CH_2.CO.R'$$

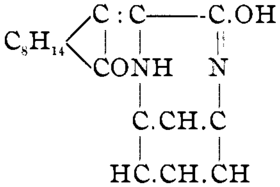
and

$$R.COH{:}CH.COH{:}CH.CO.R,$$

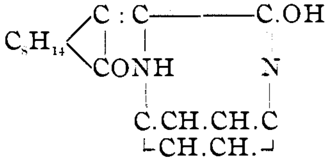
might be produced successively as any given reaction proceeded, the end products being, of course, direct derivatives of these forms and not the free enolic bodies themselves. On the other hand, the production of the enolic form might, at any given stage of the reaction, be entirely inhibited by the chemical or stereometrical influence of the new groups which become linked to the original molecule. In the preceding sentences, the ketonic and enolic forms of ketones have been referred to, for the sake of simplicity, as if they were fixed quantities ; in reality we should doubtless regard them as extreme phases of reversible systems, tending, with very varying velocities, towards more or less widely separated states of equilibrium. The question naturally arises whether the above considerations are not also applicable to monoketones; in this connection, Freer's very interesting researches on acetone may be mentioned; they show that under certain conditions it forms derivatives of the compound $CH_3.COH{:}CH_2$. An attempt has been made to discover whether any simple relationship exists which would explain the production of highly colored ferric compounds by the enolic forms of diketones and of phenols, but so far, unsuccessfully.

Whatever may be the fate of these suggestions, some explanation must ultimately be given of the following facts : (1) The great reactivity of the "carbonyl" group in camphor with a number of reagents which are generally regarded as tests for the presence of this radical ; (2) of the complete quiescence of this group in camphoroxalic acid towards the same reagents ; (3) of the great reactivity of the second "carbonyl" in that acid ; (4) of the fact that this last group certainly reacts as an unsaturated hydroxyl complex towards some of the reagents, and possibly does so with them all.

Condensation products could not be obtained from ethyl camphoroxalate or sodium camphoroxalate, with the amines enumerated below, under the conditions employed in the preparation of the compounds described in the preceding pages. For convenience both classes of failures are discussed together. *Urea*, *para-* and *meta-phenylenediamine*, *ethylaniline*, and *dimethylaniline* failed to react with either ethyl or sodium camphoroxalate; *α-naphthylamine* reacted with the latter but not with the former; *dimethylamine* was only tried with the ethyl salt, with which it did not combine. The failure in the case of urea is probably due to its comparatively feeble basicity, while that with meta- and para-phenylenediamine is ascribable to the difficulty of producing rings of seven and eight members, such as



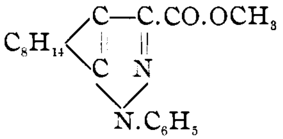
and



The behavior of secondary amines (ethylaniline and dimethylamine) has already been discussed (cf. p. 372), and dimethylaniline, being a tertiary base, would not be expected to react. For the failure of α-naphthylamine to condense with ethyl camphoroxalate, while it interacts so readily with sodium camphoroxalate, no very plausible reason can, at present, be suggested.

Ethyl camphoroxalate readily combines with methyl iodide, in the presence of silver oxide, forming *ethyl methylcamphoroxalate* which appears to be an oil; the corresponding *acid* crystallizes in six-sided prisms and plates, and melts at 95°–96°. Like the ethyl salt it gives no coloration with ferric chloride and alcohol.

Methyl oxalate condenses with camphor, in presence of sodium methoxide, but the time of heating requires to be prolonged owing to the sparing solubility of the resulting sodium salt in light petroleum. It is, therefore, more readily prepared by esterifying the acid. The *compound* crystallizes from light petroleum in arborescent needles, belonging to the orthorhombic system, which melt at 74.5°–75°. With phenylhydrazine, methyl camphoroxalate yields a *phenylhydrazide*, which is deposited from methyl alcohol in slender, white needles, melting at 204°–205°. *Methyl camphylphenylpyrazolecarboxylate*,



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is formed by the interaction of the phenylhydrazide and glacial acetic acid. It crystallizes in colorless needles, melts at 80.5°–81.5°, and when hydrolyzed yields the acid (m. p. 193°–194°) described above (p. 381).

The preparation of *isoamyl camphoroxalate* was necessarily preceded by that of isoamyl oxalate. The only method described in Beilstein's "Handbuch" is due to Friedel and Crafts, and consists in heating ethyl oxalate with isoamyl alcohol at 220°–250°. No difficulty was experienced in obtaining the compound, in any desired quantity, by the action of isoamyl alcohol on dehydrated oxalic acid at 100°. The preparation of *isoamyl camphoroxalate* was carried out in a similar manner to that of the ethyl salt. The sodium dissolves easily, and the resulting compound is readily soluble in light petroleum. The isoamyl salt itself is sparingly soluble in ether, and crystallizes in colorless triclinic needles, melting at 98.5°–99.5°. The chief object in view in preparing this compound was to ascertain the influence, if any, of the increase of the mass of the carbalkyloxy group on the course of the condensation. The results show that it proceeds more readily with the higher than with the lower homologues ; the solubility in ether or light petroleum of ethereal sodium salts also increases as the mass of the alkyl becomes greater, and it is highly probable that this is the chief reason, if not practically the only one, for the improved yield, as the sodium is more readily dissolved. On the other hand the solubility of the free ethereal salts in ether and light petroleum is least in the case of isoamyl, greatest in that of ethyl, while methyl occupies the intermediate position. As regards melting-points the compounds resemble the corresponding ethereal salts of oxalic acid since the ethyl derivative melts at a lower temperature than the methyl salt.

Isoamylic camphoroxalate phenylhydrazide, prepared in a similar manner to the lower homologues, is very sparingly soluble in ordinary media, with the exception of isoamyl alcohol, at the boiling-point of which it slowly suffers decomposition.

Condensation takes place tolerably readily between camphor and ethyl pyruvate ; the product is difficult to purify and has, therefore, hitherto not been investigated.

EXPERIMENTAL.

Camphoroxalic Acid.

The best method of preparing this compound in quantity has been previously described.[1]

Ammonia and Camphoroxalic Acid.

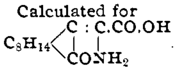
The acid (4.4 grams = 1 mol.) was mixed in a bottle of about 150 cc. capacity, with ammonium chloride (3.2 grams = 3 mol.), potassium hydroxide (4.5 grams = 4 mol.) and alcohol (95 per cent., 50 cc.); the bottle was provided with a well fitting glass stopper which was suitably clamped, and the contents heated at 100° in a water-bath during four hours. When cold, the alcohol was removed by evaporation, and the residue treated with water, acidified with dilute sulphuric acid, and extracted three times with ether. The solid residue from the dried ethereal solution was then recrystallized several times from benzene, and finally from a mixture of acetone and light petroleum. The compound, which is *camphorformeneamine carboxylic acid*, is deposited in colorless plates melting at 178° with evolution of gas; it is readily soluble in benzene, acetone, and ethyl acetate, insoluble in light petroleum. It does not dissolve in sodium carbonate solution at the ordinary temperature, but does so readily when heated, and is reprecipitated on acidification. With alcohol and ferric chloride no coloration is produced, but a deep red one is obtained if the compound is previously treated with hydrochloric acid and potassium nitrite. Sodium hydroxide may be employed for the preparation of the compound instead of potassium hydroxide.

Analysis:

I. 0.2485 gram substance gave 0.5850 gram carbon dioxide and 0.1720 gram water.

II. 0.1946 gram substance gave 10 cc. nitrogen at 13° and 755 mm.

III. 0.1207 gram substance gave 6.8 cc. nitrogen at 28.5° and 741.5 mm.

	Calculated for  $C_8H_{14}<\begin{matrix}C : C.CO.OH\\ \vert \quad \vert \\ CONH_2\end{matrix}$	Found.		
		I.	II.	III.
Carbon	64.57	64.20	....	....
Hydrogen	7.62	7.69	....	....
Nitrogen	6.28	....	6.04	6.01

When heated at 170°–180°, the compound evolves gas; the resinous residue dissolves in alcohol, and also in hydrochloric

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[1] *Am. Chem. J.*, 19, 399 (1897); 21, 247 (1899).

acid; from this latter solution sodium hydroxide precipitates an amorphous substance, while platinic chloride gives crystals of ammonium platinichloride, which were identified by analysis and comparison with a pure preparation of that salt. It is thus evident that the attempt to eliminate the carboxyl group in this simple manner from the original compound was unsuccessful.

By the action of free camphoroxalic acid on absolute alcoholic ammonia, in excess, at 100°, under pressure, a crystalline compound is formed which melts and evolves gas at about 212°, but when very slowly heated it melts at about 100°. Ammonia is evolved when the compound is boiled with aqueous sodium hydroxide, and the solution, after acidification, gives a deep red coloration with ferric chloride and alcohol. The compound is presumably *ammonium camphoroxalate.*

ETHYL CAMPHOROXALATE DERIVATIVES.

Ammonia and Ethyl Camphoroxalate.—The ester (5 grams = 1 mol.) was mixed with ammonium chloride (3.2 grams = 3 mol.), potassium hydroxide (3.1 grams = less than 3 mol.), and alcohol of 95 per cent. (50 cc.). The mixture was then heated in a closed bottle, at 100°, during four hours. The alcohol was removed on the water-bath, the residue washed with water and dried. The yield is practically quantitative. The compound is sparingly soluble in chloroform, acetic acid, alcohol, and benzene, but readily in xylene; it was crystallized from this three times, and after being washed with benzene formed colorless, microscopic needles melting at 227°-228°.

Analysis:

I. 0.2158 gram substance gave 0.5086 gram carbon dioxide.

II. 0.2135 gram substance gave 0.5040 gram carbon dioxide and 0.1560 water

III. 0.1274 gram substance gave 14.0 cc. nitrogen at 18.5° and 743 mm.

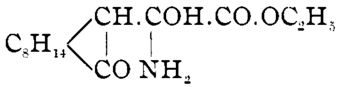
IV. 0.1323 gram substance gave 15.4 cc. nitrogen at 19.5° and 747 mm.

V. 0.2061 gram substance gave 23.4 cc. nitrogen at 17.5° and 750 mm.

	Calculated for  $C_8H_{14}<\begin{matrix}C : C.CONH_2\\ CONH_2\end{matrix}$	Found.				
		I.	II.	III.	IV.	V.
Carbon	64.86	64.28	64.38	....	....	....
Hydrogen	8.10	....	8.11	....	....	....
Nitrogen	12.61	....	....	12.31	13.11	12.97

Camphoformeneaminecarboxylamide gives no coloration with ferric chloride and alcohol; when boiled with aqueous sodium hydroxide, ammonia is evolved, and the residue, after acidifying, gives, on the addition of ferric chloride and alcohol, the deep red coloration characteristic of camphoroxalic acid. The amide is also produced by heating ethyl camphoroxalate, or the ammonia additive compound of this mentioned below, with alcoholic ammonia at 100° in a sealed tube ; the yield is excellent, but the method is not so convenient as the one given above. With alcoholic hydroplatinichloric acid the amide yields a sparingly soluble *platinichloride* which crystallizes in hexagonal, orange-colored plates.

A second compound of ammonia and ethylic camphoroxalate is obtained by saturating a concentrated, well cooled solution of the latter, in absolute alcohol or ether, with the anhydrous gas. A white precipitate is formed, which, when removed, and drained on a porous plate, is gradually resolved into its constitutents. The substance could not be analyzed, but is almost certainly the simple additive *compound*



$$C_8H_{14}\left\langle\begin{array}{l}CH.COH.CO.OC_2H_5\\ \;\;|\quad\;\;|\\ CO\;\;NH_2\end{array}\right.$$

When heated with alcoholic ammonia in a sealed tube at 100°, camphoformeneaminecarboxylamide is obtained as described above. A third *compound*, which has been previously described, was obtained by the action of dried ammonia on *crude* ethylic camphoroxalate in anhydrous ethereal solution; it darkens at about 200°, melts at 225°, and is possibly impure oxamide, as subsequent experiments with the purified ester failed to yield it.

Hydroxylamine and Ethyl Camphoroxalate.

The ester (1 mol.) is dissolved in alcohol and mixed with a concentrated, aqueous solution of hydroxylamine hydrochloride (3.5 mol.); more alcohol is added if necessary to obtain a clear solution, and then solid sodium hydrogen carbonate until the liquid is slightly alkaline. The mixture is allowed to remain at the ordinary temperature during six days, in the course of which a white granular precipitate gradually forms. The liquid is then poured into water, acidified with dilute sulphuric acid, and extracted three times with ether. The ethereal solution is dried and distilled, and the residue crystallized twice from a mixture of toluene and light petroleum ; it is deposited in colorless, slender needles melting at 120°–121°. The *compound* is readily soluble in aqueous sodium hydroxide, more slowly in sodium carbonate solution; it dissolves in dilute sulphuric acid when heated, but crystallizes out on cooling. It does not appear to be soluble in water to any great extent, but when heated it melts and floats on the surface. An attempt to obtain the compound by the interaction of its constituents at 100°, under pressure, in the manner described in the preparation of camphoformeneaminecarboxylamide was not successful, neither did the ester react at all with hydroxylamine in absolute alcoholic solution, under pressure, at 100°. The constitution of this substance will be further investigated subsequently.

In the first paper on this subject (*loc. cit.*) brief mention was made of a *compound* obtained from *crude* ethylic camphoroxalate and hydroxylamine, as the latter was employed in the form of hydrochloride, and a large excess of potassium hydroxide added; it follows that the substance should be a derivative of a camphoroxalic acid and not of the ethyl salt. The body has now been further investigated, and it appears to be a *potassium salt* of an oxalic acid derivative; this is readily understood when it is remembered that the only specimens of ethyl camphoroxalate at that time procurable necessarily contained ethyl oxalate in varying proportion. The compound crystallizes in colorless, silky needles, melts at 193° with sudden decomposition, is readily soluble in water and sodium hydroxide solution, more sparingly in dilute alcohol, and is practically insoluble in absolute alcohol. It gives a red coloration with alcohol and ferric chloride after being boiled with hydrochloric acid, but oxalic acid could not be detected in the solution. The readiness with which it explodes, on heating, rendered the analysis so difficult that, after several unsuccessful attempts, further effort was abandoned.

Methylamine and Ethyl Camphoroxalate.—The ester (5 grams = 1 mol.) was mixed with methylamine hydrochloride (4 grams = 3 mol.), potassium hydroxide (3 grams = less than 3 mol.) and alcohol (95 per cent., 50 cc.) and heated under pressure, at 100°, during four hours. The alcohol was removed on the water-bath, the residue treated with water, and extracted with ether. The ethereal solution, after drying, was distilled. The crystalline residue consisted of *methyl camphoformeneaminecarboxylmethylamide*; it was purified by repeated crystallization from benzene, with the addition of light petroleum, and was deposited in small, white needles, melting at 130°. The compound is less readily soluble in benzene than the ethyl derivative described below, and is somewhat unstable; on this account, and from the difficulty of completely freeing it from ash, which contained iron, its analysis was abandoned after several unsuccessful attempts had been made.

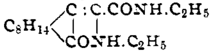
The aqueous liquid remaining after the removal of the amine was acidified with dilute sulphuric acid, and extracted with ether; this, after drying and distillation, gave only a small residue consisting, apparently, of impure camphoroxalic acid.

Ethylamine and Ethyl Camphoroxalate.—The experiments with ethylamine were carried out exactly as in the case of methylamine, the quantities of materials employed being ester (5 grams = 1 mol.), ethylamine hydrochloride (3.2 grams = 2 mol.), potassium hydroxide (2 grams = less than 2 mol.), and 95 per cent. alcohol, (50 cc.). The product, *ethyl camphoformeneaminecarboxylethylamide*, readily dissolves in ethyl acetate and benzene, but is insoluble in light petroleum. It gives no coloration with alcohol and ferric chloride solution, but even when purified, slowly evolves ethylamine. It is deposited from benzene, after two crystallizations, in colorless needles melting at 148°. The yield is good. The compound is also formed by the action of free ethylamine on the ester, in absolute alcoholic solution at 100°, under pressure.

Analysis:

I. 0.2606 gram substance gave 0.6558 gram carbon dioxide and 0.2262 gram water.

II. 0.1326 gram substance gave 11.8 cc. nitrogen at 18.5° and 739 mm.

	Calculated for  $C_8H_{14}\langle{}^{C:C.CONH.C_2H_5}_{CONH.C_2H_5}$	Found.	
		I.	II.
Carbon	69.06	68.63	..
Hydrogen	9.35	9.64	..
Nitrogen	10.07	..	9.96

Ethyl Camphoroxalate and Methyl Iodide.—The ethyl salt (2.5 grams) was mixed with dried silver oxide (3.5 grams),[1] and methyl iodide (3 grams), and heated in a sealed tube, at 100°, during four hours. The product was filtered, the silver compounds repeatedly washed with ether, and the combined filtrate and washings allowed to evaporate. The residue did not crystallize. It consisted of *ethyl methylcamphoroxalate* as it gave

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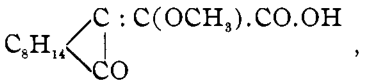
[1] Cf. Lauder: *J. Chem. Soc.* (London), 77, 729 (1900).

no coloration with alcohol and ferric chloride. The corresponding *acid*,



$$C_8H_{14}\left\langle\begin{array}{l}C:C(OCH_3).CO.OH\\ \quad|\\ CO\end{array}\right. ,$$

was obtained by hydrolyzing the preceding compound with dilute aqueous-alcoholic sodium hydroxide at 100°. It readily crystallizes from light petroleum in large hexagonal-shaped prisms and plates, and melts at 95°–96°. It gives no coloration with alcohol and ferric chloride, but with ammonium hydroxide and calcium chloride it gives a white precipitate soluble in acetic acid, thus resembling camphoroxalic acid. It is apparently gradually converted into this acid on exposure to the air.

Ethyl Camphoroxalate and Acetone.—These two compounds do not appear to react when mixed and treated with sodium in equimolecular proportion, in the presence of light petroleum. Some of the metal immediately dissolves, but the remainder is not attacked after boiling during two hours. Sufficient absolute alcohol was added to combine with the sodium, but the only product which could be eventually isolated was camphoroxalic acid. The similar negative result was obtained with *ethyl camphoroxalate and camphor*, the experiments being carried out under similar conditions to those just described.

Ethyl Pyruvate.—This compound can be readily prepared by the method of esterfication previously described (*loc. cit.*). Pyruvic acid (50 grams) is mixed with 95 per cent. alcohol (500 cc.), and conc. sulphuric acid (80 cc.) and boiled during seven hours. The excess of alcohol is removed on the water-bath, the acid being simultaneously neutralized with sodium hydrogen carbonate, the product poured into water, extracted with ether, and the ethereal solution washed, if needful, with sodium hydrogen carbonate solution.

Ethyl Pyruvate and Camphor.—When treated with camphor, (1 mol.) and sodium wire (1.5 atoms), in light petroleum solution, condensation apparently takes place. The product has hitherto proved difficult to purify; it gives a deep red coloration with ferric chloride and alcohol.

The work will be continued and extended in various directions as time permits.

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