XCIX.—*Formation of Ethereal Salts of Polycarboxylic Acids.*

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AFTER it had been found by one of us that ethylic aconitrate is readily transformed into citrazinamide, and that, in like manner, ethylic glutaconate and its homologues condense with ammonia to form pyridine derivatives, the idea occurred to us to apply this reaction to ethereal salts of unsaturated acids, which stand in a close relation to glutaconic and aconitic acids, with the view of arriving at compounds belonging to the pyridine series. For the synthesis of such ethereal salts, a method was proposed by A. Michael (*J. pr. Chem.*, 1887, [ii], 35, 349), which has since been modified by Auwers and his pupils (*Ber.*, 1891, 24, 307, 2887).

Of these two methods, preference is to be given to that of Michael, a modification of which has been employed in this research, namely,

using sodium ethoxide dried in a vacuum at 180° , instead of granulated sodium; the details are given in the experimental section.

In the course of our experiments, we made the interesting observation that a very small quantity of sodium ethoxide is sufficient to effect the union of the ethereal salt of the above acids with that of the unsaturated acid, heat being developed in most cases.

The readiness with which the combination takes place depends, not only on the nature of the ethereal salt of the unsaturated acid, but also on that of the malonic acid (or its homologue), and seems in some measure to be determined by the negative character of both reacting ethereal salts; for as the negative character is diminished by the introduction of an alkyl into ethylic malonate, or into the ethylic salt of the unsaturated acid, so does the development of heat decrease.

Although this difference is very evident, we intend to determine the thermal variation in the heat evolution with the view of establishing fixed values for the influence which groups, entering into these ethereal salts, exert on the course of this reaction.

Some of the compounds described in this paper have been previously obtained by Michael and Auwers, but we thought it advisable to analyse them for the purpose of identification, as the boiling points, in most cases, had been determined at a pressure different from that which we used.

EXPERIMENTAL.

The formation of this ethereal salt takes place with the greatest ease.

A mixture of 8 grams of ethylic malonate (1 mol.) and 8.6 grams of ethylic fumarate (1 mol.), on the addition of 0.5 gram of sodium ethoxide, turns yellow and becomes exceedingly hot; the product when cold is acidified with dilute sulphuric acid, the oil extracted with ether, and after removal of the latter distilled under diminished pressure; more than 15 grams of ethylic propanetetra-carboxylate are thus obtained, boiling at 200° under a pressure of 14 mm.

The identity of this product with the compound obtained by Michael and Schulthess (*J. pr. Chem.*, 1891, [ii], 45, 56) is sufficiently established by the boiling point, which they gave as $202-203^{\circ}$ (pressure 16 mm.).

Action of Ammonia on Ethylic Propanetetra-carboxylate.—Concentrated aqueous ammonia acts but slowly on the ethylic salt, the oil not disappearing for a week, part of the product appearing as a crys

talline deposit on the sides of the vessel; this is somewhat soluble in cold water, readily so on boiling, and crystallises from the aqueous solution in colourless prisms which melt with decomposition at 237—238°.

The ammoniacal mother liquor, on concentration, gives a second crop of the same substance, but the whole amount which is formed corresponds with about half only of that required by theory, the remainder being converted into a very soluble ammonium salt.

The composition of the compound, as ascertained by analysis, corresponds with the formula for the diamido-imide of propanetetra-

0.2136 gave 0.3268 CO_2 and 0.0904 H_2O . C = 41.73; H = 4.70.

0.2192 „ 0.3370 CO_2 „ 0.0890 H_2O . C = 41.92; H = 4.61.

0.1800 „ 32 c.c. of nitrogen at 16° and 759 mm. N = 21.07.

$\text{C}_7\text{H}_9\text{N}_3\text{O}_4$ requires C = 42.21; H = 4.52; N = 21.11 per cent.

Action of Bromine on the Ethylic Salt.—Bromine acts on the ethereal salt with formation of a substitution product. Although a considerable amount of heat is developed on adding the halogen to the oil, yet the reaction is not complete, a small quantity of the reagents remaining unaltered. As the bromo-derivative suffers decomposition on distillation, we analysed it after it had been freed from the bromine and its hydride by heating at 100° under diminished pressure, and allowed to stand in a vacuum over potash and sulphuric acid until the weight was constant.

The following results were obtained with samples from different preparations.

0.3208 gave 0.1335 AgBr. Br = 17.70.

0.5138 „ 0.2263 AgBr. Br = 18.74.

$\text{C}_{15}\text{H}_{23}\text{BrO}_8$ requires Br = 19.46 per cent.

The ethereal salt of the bromo-acid, on heating at 210—215°, loses hydrogen bromide, and the product, when distilled after an hour's exposure to that temperature, yields an oil which boils at 195—204° (pressure 16 mm.), but still contains a small quantity of bromine.

We have made several experiments with the object of obtaining the ethylic salt of propylenetetracarboxylic acid, which appears to be the product formed when the bromo-acid is heated. On redistilling the oil, the amount of bromine is diminished, but its entire removal cannot be accomplished by repeating the operation; it is, however, effected by digesting a solution of the oil in absolute alcohol with small quantities of sodium ethylate until the presence of the halogen can no longer be detected by Beilstein's test.

The compound obtained after this treatment boils at 198--199° (pressure 12 mm.).

The following analytical data indicate that it is almost pure ethylic propylenetetracarboxylate,

0.2348 gave 0.4675 CO₂ and 0.1515 H₂O. C = 54.30 ; H = 7.16.

C₁₅H₂₂O₈ requires C = 54.54 ; H = 6.67 per cent.

Further experiments with the view of supporting the formula of this product and of transforming it into a pyridine derivative are in progress.

Ethylic α-Methylpropanetetracarboxylate.

This ethereal salt has been obtained before by Auwers, Köbner, and v. Meyenburg (*Ber.*, 1891, 24, 2890) by digesting for some hours on the water bath equivalent quantities of ethylic methylmalonate, sodium, and ethylic fumarate in alcoholic solution. They find that the reaction is accompanied by a dark green coloration, and that the oil, which separates on adding water and dilute sulphuric acid, boils at 190—210° under a pressure of 20 mm.; the chief portion at 196—198°.

Using our modified method, the result obtained is as follows. The mixture of ethylic fumarate and ethylic methylmalonate, on the addition of 0.5 gram of sodium ethoxide, becomes yellow and evolves heat, which, however, is much less than in the case of ethylic malonate. The reaction is completed by 2—3 hours digestion on the water bath. The oil, after washing with dilute sulphuric acid, boils at 201° (pressure 12 mm.), only a very small quantity distilling below that temperature ; *d* 26°/26° = 1.1153.

The analytical numbers correspond with the formula for ethylic methylpropanetetracarboxylate,

0.2445 gave 0.4958 CO₂ and 0.1642 H₂O. C = 55.30 ; H = 7.46.

C₁₆H₂₆O₈ requires C = 55.49 ; H = 7.51 per cent.

Ethylic Ethylpropanetetracarboxylate.

The heat which is evolved on the addition of 0.5 gram of sodium ethoxide to the mixture of equivalent quantities of the ethereal salts of ethylmalonic and fumaric acids is very small, and the time of digestion required for the completion of the reaction much longer than in

the former cases. After 4 hours heating on the water bath, only partial combination has taken place, but the fraction of low-boiling point, containing the unaltered ethereal salts, on prolonged warming with a little sodium alcoholate, is also transformed into ethylic ethylpropanetetracarboxylate, which distils at 203—204° (pressure 11 mm.); $d_{23}^{23}/23^{\circ} = 1.1042$.

The result of the analysis agrees with the formula

0.2437 gave 0.5015 CO_2 and 0.1705 H_2O . $\text{C} = 56.12$; $\text{H} = 7.77$.

$\text{C}_{17}\text{H}_{28}\text{O}_8$ requires $\text{C} = 56.66$; $\text{H} = 7.77$ per cent.

Ethylic Isopropylpropanetetracarboxylate.

Auwers and his pupils (*loc. cit.*), who prepared this ethereal salt by the combination of the sodium derivative of ethylic isopropylmalonate and ethylic fumarate, give the boiling point as 205—206° (pressure 19 mm.). They did not, however, analyse the compound.

The union of the two salts takes place readily on treatment by our method, and is almost complete after 3—4 hours warming on the water bath.

The compound boils at 204—205° (pressure 12 mm.), and has the sp. gr. $d_{27}^{27} = 1.0964$.

The formula of the compound

is verified by the following analytical result.

0.2162 gave 0.4545 CO_2 and 0.1550 H_2O . $\text{C} = 57.33$; $\text{H} = 7.96$.

$\text{C}_{18}\text{H}_{30}\text{O}_8$ requires $\text{C} = 57.75$; $\text{H} = 8.02$ per cent.

Ethylic β -Methylpropanetetracarboxylate.

The experiments described above show the influence which the introduction of hydrocarbon groups into the molecule of ethylic malonate has on the interaction of the resulting ethereal salts and ethylic fumarate, and an analogous difference is found when using the ethylic salt of a homologue instead of ethylic fumarate. As ethylic mesaconate was not at our disposal, we took ethylic citraconate. The mixture of the ethylic salts of citraconic and malonic acids, on adding sodium ethoxide, becomes only slightly warm, and several hours digestion on the water bath is necessary to effect their union.

The chief portion of the oily product boils at 200—201° (pressure 12 mm.) and has the density $d_{25^\circ/25^\circ} = 1.1055$.

The result of the analysis is in accordance with the formula for ethylic β -methylpropanetetracarboxylate.

0.2368 gave 0.4805 CO_2 and 0.1580 H_2O . $\text{C} = 55.34$; $\text{H} = 7.41$.

$\text{C}_{16}\text{H}_{26}\text{O}_8$ requires $\text{C} = 55.49$; $\text{H} = 7.51$ per cent.

This ethereal salt also had been prepared before by Michael and Schulthess (*loc. cit.*) and by Auwers (*Ber.*, 1891, 24, 2894) by heating on the water bath a mixture of ethylic malonate and ethylic citraconate with an alcoholic solution of sodium ethoxide.

Ethylic Cyanotricarballylate.

Ethylic cyanacetate (4.3 grams) reacts with ethylic fumarate (4.8 grams) in the presence of sodium ethoxide (0.5 gram) with great evolution of heat; after one hour's subsequent digestion on the water bath, the union is complete. The product, on treatment with dilute sulphuric acid, extraction with ether, &c., and two rectifications, yields a pale yellow oil (about 6 grams) which boils at 197—199° (pressure 11 mm.); $d_{26^\circ/26^\circ} = 1.1257$.

On analysis, the following numbers were obtained, which correspond with the formula

0.2588 gave 0.5205 CO_2 and 0.1605 H_2O . $\text{C} = 54.85$; $\text{H} = 6.88$.

$\text{C}_{13}\text{H}_{19}\text{NO}_6$ requires $\text{C} = 54.73$; $\text{H} = 6.67$ per cent.

Müller (*Compt. rend.*, 1892, 114, 1204), who obtained this ethereal salt by heating a mixture of ethylic cyanacetate and ethylic fumarate with an alcoholic solution of sodium ethoxide, found that it boiled at 180—190° under a pressure of 15—20 mm.

Ethylic iso-Amylidenemalonate.

The action of ethylic malonate on ethylic iso-amylidenemalonate in the presence of sodium ethoxide is quite in accordance with the view expressed before as to the influence which the negative character of the ethereal salts has on their power of combining.

Ethylic isoamylidenemalonate was prepared by the method Komnenos (*Annalen*, 218, 107) used for obtaining ethylic ethylidenemalonate, namely, by heating a mixture of ethylic malonate

(32 grams), acetic anhydride (32 grams), and valeraldehyde (25 grams) at 100° in a soda-water bottle for 3—4 days. The liquid is then distilled, at the ordinary pressure, to remove unaltered aldehyde and acetic anhydride, and the oily residue fractionated under diminished pressure. After repeated rectifications, the ethereal salt is obtained as a colourless oil which has an odour of valeraldehyde, and boils at 133—135° (11 mm.).

The following analytical results correspond with the formula

0.2168 gave 0.5034 CO_2 and 0.1718 H_2O . $\text{C} = 63.32$; $\text{H} = 8.80$.

$\text{C}_{12}\text{H}_{20}\text{O}_4$ requires $\text{C} = 63.15$; $\text{H} = 8.77$ per cent.

The yield is unsatisfactory, as from the above quantities only 13.5 grams of the ethereal salt were obtained, a large portion of the reagents remaining unaltered, even on heating the mixture at 150° for 8—10 hours.

On the addition of 0.5 gram of sodium ethoxide to the mixture of 8 grams of ethylic iso-amylidenemalonate and 5.7 grams of ethylic malonate, a strong development of heat takes place; after being allowed to stand for an hour, the compound is isolated as in the former cases. The pale yellow oil obtained after two rectifications amounts to about 9 grams, and boils at 208—209° (at 12 mm.); $d_{27^\circ/27^\circ} = 1.0645$.

The result of the analysis agrees with the formula for ethylic iso-amylidenedimalonate,

0.2482 gave 0.5375 CO_2 and 0.1840 H_2O . $\text{C} = 59.0$; $\text{H} = 8.23$.

$\text{C}_{19}\text{H}_{32}\text{O}_8$ requires $\text{C} = 58.76$; $\text{H} = 8.22$ per cent.

Ethylic Propanepentacarboxylate.

Bishop and Perkin (Proc. Chem. Soc., 1891, 41) some years ago, by the interaction of ethylic dichloracetate and ethylic monosodiummalonate, obtained the ethereal salts of ethylenetricarboxylic acid, $(\text{COOC}_2\text{H}_5)_2\text{C}\cdot\text{CH}\cdot\text{COOC}_2\text{H}_5$, and of propanepentacarboxylic acid, $(\text{COOC}_2\text{H}_5)_2\text{CH}\cdot\text{CH}(\text{COOC}_2\text{H}_5)\cdot\text{CH}(\text{COOC}_2\text{H}_5)_2$.

We have repeated their experiment with the object of ascertaining whether the ethylic salt of the unsaturated acid, in the presence of sodium ethoxide, condenses with ethylic malonate to form ethylic propanepentacarboxylate.

The action of ethylic dichloracetate on ethylic malonate and sodium

ethoxide in alcoholic solution takes place very slowly, and is not complete, even on heating the mixture at 100°. The product, after removal of the alcohol, is mixed with water, extracted with ether, &c., and fractionally distilled several times before fractions can be obtained of constant boiling point. One of these, ethylic ethylenetricarboxylate, is a colourless oil which distils at 158° (pressure 12 mm.), and has the density $d_{27^\circ/27^\circ} = 1.0888$. Bishop and Perkin found that it boiled at 203—205° (pressure 100 mm.).

The analytical results correspond with the formula given above.

0.2187 gave 0.4315 CO₂ and 0.1360 H₂O. C = 53.81; H = 6.90.

C₁₁H₁₆O₆ requires C = 54.09; H = 6.56 per cent.

The fraction of higher boiling point obtained in the above reaction, after repeated fractionations, yields a viscid oil which distils at 223—225° under a pressure of 10 mm.; $d_{27^\circ/27^\circ} = 1.1418$. (Bishop and Perkin observed the boiling point to be 265° at a pressure of 80 mm.)

The following analytical data correspond with the formula for ethylic propanepentacarboxylate.

0.2258 gave 0.4445 CO₂ and 0.1450 H₂O. C = 53.68; H = 7.13.

C₁₈H₂₈O₁₀ requires C = 53.46; H = 6.93 per cent.

This ethereal salt can also be obtained from ethylic ethylenetricarboxylate by mixing the latter with the equivalent quantity of ethylic malonate and a little sodium ethoxide, the reaction being accompanied by a marked evolution of heat. The identity of the compound thus formed and ethylic propanepentacarboxylate was proved by its boiling point.

Ethylic Propanehexacarboxylate.

A further support for the view as to the influence of the negative character of the ethereal salts on the course of the reaction is afforded by the behaviour of ethylic malonate towards ethylic ethylenetetracarboxylate (ethylic dicarbintetracarboxylate) in the presence of sodium ethoxide. The mixture becomes very hot, and the action is complete after 1 hour's digestion on the water bath, ethylic propanehexacarboxylate being formed.

The compound distils at 246° under a pressure of 15 mm., and is a very viscous, yellow oil.

On analysis, the following numbers were obtained.

0.2410 gave 0.4675 CO_2 and 0.1480 H_2O . $\text{C} = 52.90$; $\text{H} = 6.82$.

$\text{C}_{21}\text{H}_{32}\text{O}_{12}$ requires $\text{C} = 52.94$; $\text{H} = 6.72$ per cent.

Ethylic Butanepentacarboxylate.

Auwers (*Ber.*, 1893, **26**, 364), on examining the product formed by digesting a mixture of ethylic malonate and the ethereal salt of an unsaturated acid with sodium ethoxide dissolved in alcohol, was led to the conclusion that, on using the ethylic salts of unsaturated dicarboxylic acids, the reaction proceeded in one direction only, but that it was complicated when salts of unsaturated tricarboxylic acids were used. He studied especially the interaction of ethylic sodiomalonate and ethylic aconitate, and from the product of their condensation succeeded in isolating three acids, one of which was butanetetra-carboxylic acid, $\text{CH}_2(\text{COOH})\cdot\text{CH}(\text{COOH})\cdot\text{CH}(\text{COOH})\cdot\text{CH}_2\cdot\text{COOH}$. That other acids are produced besides this is undoubtedly due to the fact that ethylic aconitate itself is readily acted on by sodium alcoholate; indeed, on adding a trace of sodium alcoholate in the dry state or in alcoholic solution to the ethereal salt, a deep red coloration is produced, and on treating this red liquid with an acid, the colour disappears and an oil is obtained which decomposes on distillation under diminished pressure; the results of the investigation of this reaction will be published at some future date. This serves to explain Auwers' observation.

On applying our method, however, we find that the interaction of ethylic aconitate and ethylic malonate takes place with the formation of one product only, namely, ethylic butanepentacarboxylate; the mixture becomes warm and acquires a yellow colour; after standing at the temperature of the room for $1\frac{1}{2}$ hours, about half the quantity of the ethereal salts has entered into combination. The yield of ethylic butanepentacarboxylate is very satisfactory (more than 80 per cent. of the theoretical) if the mixture is heated on the water bath for a few hours. The product is a slightly yellowish oil which boils without decomposition at $232-233^\circ$ (pressure 12 mm.); $d_{21^\circ/21^\circ} = 1.0660$.

The analytical values correspond with the formula given above.

0.2685 gave 0.5362 CO_2 and 0.1730 H_2O . $\text{C} = 54.46$; $\text{H} = 7.16$.

$\text{C}_{19}\text{H}_{30}\text{O}_{10}$ requires $\text{C} = 54.54$; $\text{H} = 7.17$ per cent.

Ethylic Phenylpropanetricarboxylate.

The sodium derivative of this ethereal salt is the product which is formed by the union of ethylic sodiomalonate and ethylic cinnamate.

According to Michael's "positive-negative" theory of addition, this

combination takes place in the manner indicated by the following equation,

The combination, as Michael (*J. pr. Chem.*, 1887, [ii], 35, 351) found, is effected on keeping the mixture of the two compounds, in absolute alcohol, for several days.

The action of sodium ethoxide (0.5 gram) on a mixture of the ethylic salts of malonic and cinnamic acids, we find, differs most markedly from the action which takes place in the cases recorded above, as no evolution of heat is noticeable.

Combination takes place very slowly, even at 100°, with formation of ethylic phenylpropanetricarboxylate, which is characterised as such by the boiling point, which was observed to be 216° (pressure 14 mm.), whilst Michael gives it as 213—215° (pressure 15 mm.).

Ethylic Phenylpropylenetricarboxylate.

Ethylic sodiomalonate, as shown by Michael (*J. pr. Chem.*, 1894, [ii], 49, 20) combines with the ethereal salts of acids belonging to the acetylene series, and this reaction gives rise to ethereal salts of unsaturated polycarboxylic acids.

On using, for instance, ethylic phenylpropiolate, ethylic phenylpropylenetricarboxylate is formed, according to the equation,

The combination of these ethereal salts, in working according to Michael's directions, takes place rather slowly, whilst we find that it is readily effected by the addition of a small quantity of sodium ethoxide. The reaction, which is accompanied by evolution of heat, is aided by subsequent warming on the water bath for 3—4 hours. The dark red oil, thus obtained, is mixed with dilute sulphuric acid, extracted with ether, &c., and distilled under diminished pressure. The distillation is accompanied by partial decomposition, as was observed by Michael, but the yellow oil which passes over between 215° and 220°, at a pressure of about 11 mm., $d_{27^\circ/27^\circ} = 1.1232$, is sufficiently pure, as indicated by the following analysis.

0.2145 gave 0.5100 CO_2 and 0.1295 H_2O . C = 64.89 ; H = 6.70.

$\text{C}_{18}\text{H}_{22}\text{O}_6$ requires C = 64.67 ; H = 6.58 per cent.

The ethereal salts of unsaturated acids, which are thus formed, will be isomeric with those which result from the removal of hydrogen

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bromide from the bromo-substitution products of the corresponding salts of the saturated series of acids.

Their further study, with the object of transforming them into pyridine derivatives, will form the subject of a future communication.

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