

24. *The Decarboxylative Acylation of Succinic Acid Derivatives. Part II.** *o*-Hydroxyphenylsuccinic, Tricarballic, and Thiobenzamidosuccinic Acid.

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Preliminary benzoylation of α -amino-monocarboxylic acids, by providing a sufficiently strong electrophilic influence, allows decarboxylative acylation to proceed in the absence of a base catalyst. These reactions are however slow in comparison with those of benzamidossuccinic, *o*-hydroxyphenylsuccinic, tricarballic, and thiobenzamidossuccinic acid which react very readily and completely by virtue of the intermediate formation of the 4-carboxylic acids of the corresponding 1:3-oxazine (III), dihydrocoumarin (VII), tetrahydrodioxopyran (XIV), and the 1:3-thiazine (XVII) respectively. The course of the reactions of acetic anhydride with *o*-hydroxyphenylsuccinic and thiobenzamidossuccinic acids is described.

IN the Dakin and West reaction¹ amino-acids, when heated with aliphatic acid anhydrides under the catalytic influence of a base such as pyridine, undergo decarboxylative *C*-acylation with formation of the corresponding acylamino-ketones. The reaction is not confined to α -amino-acids. Dakin and West^{2a} observed evolution of carbon dioxide when various substituted acetic acids were heated with acetic anhydride, and acetic acids having aryl,^{2a} heterocyclic,³ and aryloxy-substituents⁴ are known to undergo such decarboxylative acylation.

It is generally agreed that the function of the base catalyst in these acylations is to promote carbanion formation in the acceptor molecule^{2a} and this effect must apparently be supplemented by the presence of an electrophilic group in the α -position to the original carboxylic acid group.

A number of acids are known however which, having a sufficiently electrophilic group in the α -position, undergo decarboxylative acylation in the absence of an added base catalyst. Ethyl hydrogen acetamidomalonate, for example, when warmed with acetic anhydride gives some ketonic product³ but this cannot be considered as a representative example since unlike the other substances under discussion it is decarboxylated under the same conditions in the absence of the anhydride to give *N*-acetyl glycine ethyl ester. More typical examples are α -phenylglycine^{2b} and *NN*-dimethylaminoacetic acid.^{2c} The authors reported^{2c} that under the same conditions (no addition of catalyst) *NN*-dimethyl- α -phenylglycine failed to react. This finding, rather remarkable in view of the behaviour of the two above-mentioned closely related substances, and the fact that the reaction proceeded quite well in the presence of pyridine, has not been confirmed by the author. It was found that with boiling acetic anhydride alone *NN*-dimethyl- α -phenylglycine

* Part I, *J.*, 1954, 3363.

¹ Dakin and West, *J. Biol. Chem.*, 1928, **78**, (a) 91, (b) 745.

² King and McMillan, *J. Amer. Chem. Soc.*, (a) 1951, **73**, 4911; (b) 1955, **77**, 2814; (c) 1951, **73**, 4451.

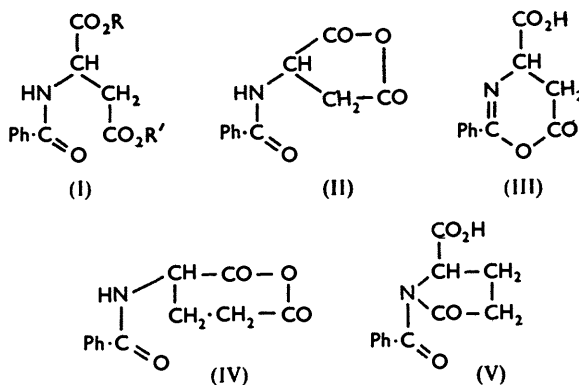
³ Burger and Walter, *ibid.*, 1950, **72**, 1988.

⁴ Smith, *ibid.*, 1953, **75**, 1134.

evolves carbon dioxide and hydrolysis of the appropriate fraction of the reaction products gives dimethylamine in accordance with the reaction mechanism put forward by the authors for the pyridine-catalysed reaction. In this case the electrophilic effect of the ammonium ion formed from the tertiary amino-group doubtless plays a part.

It is true that, for all the primary amino-acids, decarboxylative acylations proceed more readily if the *N*-benzoyl derivatives are used instead of the free amino-acids. Thus it has been found that decarboxylative acetylation proceeds in the absence of a base catalyst with all the α -benzamido-acids that have been tried. In the case of benzoylalanine (reported by King and McMillan,^{2b} not to react in the absence of a base) carbon dioxide is given off very slowly (23% of the theoretical amount in 3 hr.), and the 1-benzamidoethyl methyl ketone formed can be identified as its dinitrophenylhydrazone. In the presence of dimethyl formamide as solvent the reaction proceeds more satisfactorily and sufficient of the amino-ketone is obtained after hydrolysis to allow of the isolation of 2-mercapto-4:5-dimethylglyoxaline on treatment with thiocyanate. α -Benzamido-butyric, -*n*-valeric and -octanoic acid also react slowly with boiling acetic anhydride, to give the corresponding benzamido-ketones which have in the first two cases been hydrolysed and treated with thiocyanate to give the appropriate 4:5-disubstituted 2-mercaptoglyoxalines. The promoting effect of the phenyl group in these examples is due no doubt to its ability to favour the production of the anionic acceptor.

Derivatives of succinic acid also readily undergo uncatalysed decarboxylative acylation; indeed smoother reaction is obtained with compounds (I; R = R' = H) and (II) in the absence of a catalyst.⁶ The mechanism is not apparently the same as in the decarboxylation of quinaldonic acid⁷ since no reaction is obtained on heating the amide (II) with benzaldehyde. Reaction through an intermediate oxazolone is unlikely since the ester (I; R = H, R' = Me) reacts slowly, like the benzamidomonocarboxylic acids; the isomeric ester (I; R = Me, R' = H) is inert. Direct acylation of the anhydride (II)⁸ is improbable, for α -benzamidoglutamic acid (cf. IV) reacts only in the presence of a base, although the pyrrolidone (V) could be formed.⁹ A 1:3-oxazine is the intermediate of choice for benzamidosuccinic acid, since *o*-hydroxyphenylsuccinic acid (VI) also reacts



smoothly without a catalyst. This acid like (I; R = R' = H) can form a six-membered oxygen-ring compound (VII). It seems likely that the pyrone is indeed the reacting intermediate in this case, because the dehydration product, obtained by heating the acid at 150° *in vacuo*, and thought by Bredt and Kallen¹⁰ to be the anhydride, is actually, as is

⁵ Wiley and Borum, *J. Amer. Chem. Soc.*, 1950, **72**, 1626.

⁶ Lawson, *J.*, 1953, 1046.

⁷ Dyson and Hammick, *J.*, 1937, 1724.

⁸ Cf. Baker, Ollis, and Poole, *J.*, 1950, 1542.

⁹ Bullerwell, Lawson, and Morley, *J.*, 1954, 3288.

¹⁰ Bredt and Kallen, *Annalen*, 1896, **293**, 368.

shown below, the corresponding α -pyrone derivative (VII). This substance when decarboxylatively acetylated in the presence of a base gives the same product as does *o*-hydroxyphenylsuccinic acid in the absence of a base, though the reaction of last-named substance in the presence of a base takes a different course. Moreover *p*-hydroxyphenylsuccinic acid does not undergo uncatalysed decarboxylative acylation nor does phenylsuccinic acid, though both are capable of intramolecular anhydride formation. *o*-Hydroxyphenylacetic acid, capable of forming the corresponding furan derivative, also fails to react.

A third succinic acid derivative conforming to this pattern, *i.e.*, being capable of forming a six-membered oxygen-ring with a carboxylic acid group at position 4, is tricarballylic acid (XIII). This substance was shown by Fittig¹¹ to undergo *C*-acylation, to give the dilactones (XV; R = C_nH_{2n+1} or Ph) when its sodium salt was heated with acid anhydrides. The free acid itself, however, undergoes decarboxylative acylation no less readily than the salt, and the yields obtained are greater than those recorded by Fittig.

By analogy with benzoylaspartic acid, it was to be expected that thiobenzoylaspartic acid (XVI) would also undergo uncatalysed decarboxylative acylation and this proved to be so. On the basis of the arguments advanced above it would appear that the 1 : 3-thiazine structure (XVII) is the reacting form here. This being so it can be said that compounds which can give rise to the 4-carboxylic acids of the systems 5 : 6-dihydro-6-oxo-2-phenyl-1 : 3-oxazine (III), 5 : 6-dihydro-6-oxo-2-phenyl-1 : 3-thiazine (XVII), 3 : 4-dihydrocoumarin-4-carboxylic acid (VII), and 2 : 3 : 5 : 6-tetrahydro-2 : 6-dioxopyran are unique in being so readily capable of undergoing decarboxylative acylation in the absence of an added base catalyst.

Bredt and Kallen¹⁰ by heating *o*-hydroxyphenylsuccinic acid at 150° under reduced pressure obtained a dehydration product which on the basis of its reaction with acetyl chloride to give an acetyl derivative was designated *o*-hydroxyphenylsuccinic anhydride. This product, however, dissolves in sodium hydrogen carbonate and is recovered unchanged on acidification. Moreover, with diazomethane it gives a neutral monomethyl derivative which on hydrolysis with 3*N*-sodium hydroxide at 50°, *i.e.*, under conditions which would not be expected to hydrolyse a phenol ether, is converted into the original *o*-hydroxyphenylsuccinic acid. These reactions are best explained on the basis that the dehydration product is 3 : 4-dihydrocoumarin-4-carboxylic acid (VII). In any case the reaction with acetyl chloride is not a simple one as is shown by the fact that after several hours' heating the bulk of the material is recovered unchanged.

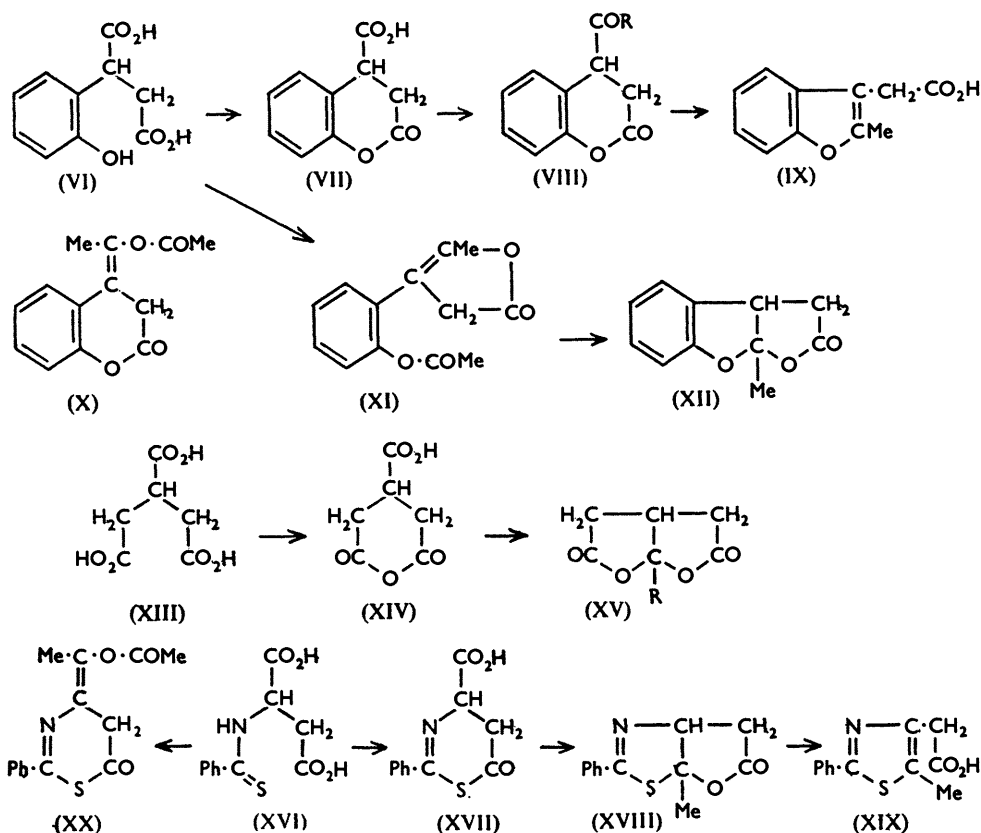
When *o*-hydroxyphenylsuccinic acid is heated with boiling acetic anhydride carbon dioxide is rapidly evolved and the neutral non-phenolic ketonic product C₁₁H₁₀O₃ has been designated as 4-acetyl-3 : 4-dihydrocoumarin (VIII; R = Me). Hydrolysis with dilute hydrochloric acid yields an isomeric acid having no ketonic properties. There seems little doubt that the coumarin ring has been opened and a new ring formed through the enolised ketone and the phenolic group to give the benzofuran derivative (IX). This is supported by the absorption spectrum which like that of benzofuran itself has maxima in the 2490 and the 2750 Å region. Analogous acylcoumarins have been prepared by using propionic and butyric anhydride.

In the presence of pyridine, *o*-hydroxyphenylsuccinic acid reacts with acetic anhydride at a lower temperature to give a neutral substance C₁₃H₁₂O₄ having neither phenolic nor ketonic properties. In this case it seems likely that the phenolic group has been acetylated and the carboxylic and the ketonic group mutually blocked by lactone formation to give the ester-lactone (XI). Confirmatory evidence of such a reaction course is provided by the fact that the dehydration product of *o*-hydroxyphenylsuccinic acid, 3 : 4-dihydrocoumarin-4-carboxylic acid (VII), under the same rather mild conditions, in the presence of pyridine is decarboxylatively acetylated to give 4-acetyl-3 : 4-dihydrocoumarin (VIII; R = Me). A possible alternative for C₁₃H₁₂O₄ would be the acetyl derivative of the enolised 4-acetylcoumarin (X), but this is excluded by the fact that, although such acetyl

¹¹ Fittig, *Annalen.*, 1901, 314, 1.

groups are usually readily hydrolysed, hydrolysis of the compound with dilute hydrochloric acid takes a different course from that of the acetylcoumarin; the $C_{13}H_{13}O_4$ compound gives acetic acid together with a neutral substance $C_{11}H_{10}O_3$. The latter has been designated as the lactone (XII) corresponding to the removal of the acetyl group followed by migration of the phenolic hydrogen atom to the double bond of the lactone group with consequent ring formation.

Thiobenzoylaspatic acid evolves carbon dioxide very readily with boiling acetic anhydride, to give a neutral non-ketonic product $C_{13}H_{11}O_3NS$ having no thiobenzamido-group as shown by its failure to react with ethanolic silver nitrate (cf. Jepson, Lawson,



and Lawton¹²). This substance has been designated as the lactone (XVIII). Its close relation to a thiazole is shown by its hydrolysis with hydrochloric acid to the thiazole-4-acetic acid (XIX), isolated as its sparingly soluble hydrochloride from which the free acid and a picrate have been prepared. In the presence of picoline the decarboxylative acetylation takes a different course. The neutral product $C_{14}H_{13}O_3NS$, showing no ketonic properties and having no free thiobenzamido-group, appears to have arisen through acetylation of the enol form of the initially produced ketone (a reaction occurring frequently with base-catalysed acylative decarboxylations) followed by ring closure between the benzamido- and the ω -carboxylic acid group. The substance has been designated as 4-1'-acetoxyethylidene-4:5-dihydro-6-oxo-2-phenyl-1:3-thiazine (XX). Such a formulation seems a reasonable alternative to a thiazoline structure in view of the deep-seated decomposition which occurs on hydrolysis, reminiscent of the behaviour of the corresponding lactone obtained from benzamidossuccinic acid by a similar method.

¹² Jepson, Lawson, and Lawton, *J.*, 1955, 1791.

EXPERIMENTAL

Reaction of Acetic Anhydride with NN-Dimethyl- α -phenylglycine.—*NN*-Dimethyl- α -phenylglycine (2 g.), prepared by the method of King and McMillan^{2c} from α -chloro- α -phenylacetyl chloride, was heated under reflux with freshly distilled acetic anhydride (10 ml.) for 5 hr. during which carbon dioxide was slowly evolved. The solution was then distilled at 100° under reduced pressure (13 mm.) and the distillate boiled with concentrated hydrochloric acid (30 ml.) for 3 hr. After evaporation to dryness the crystalline residue was recrystallised from ethanol to give dimethylamine hydrochloride (0.35 g.).

Reaction of Acetic Anhydride with Benzoyl- α -alanine.—*DL*-Benzoylalanine (2.0 g.) was boiled under reflux with acetic anhydride (10 ml.) for 3 hr. during which 0.105 g. of carbon dioxide (23%) was evolved. A small portion of the residue left after removal of the acetic anhydride by distillation under reduced pressure gave, on treatment with ethanolic dinitrophenylhydrazine containing a drop of concentrated sulphuric acid, *DL*- α -benzamidoethyl methyl ketone 2:4-dinitrophenylhydrazone, m. p. 192° (from toluene) (Found: C, 54.8; H, 4.9. Calc. for C₁₇H₁₇O₅N₅: C, 55.0; H, 4.6%). The remainder of the residue above was boiled under reflux for a further 7 hr. with acetic anhydride (10 ml.) and dimethylformamide (10 ml.). After evaporation under reduced pressure at 100°, the residual oil was hydrolysed with 20% hydrochloric acid for 1 hr. and the benzoic acid removed by filtration of the cooled solution. Distillation of the filtrate to dryness and treatment of the residue with potassium thiocyanate (0.5 g.) at 100° gave 2-mercapto-4:5-dimethylglyoxaline m. p. >300° (62 mg.) (Found: C, 47.1; H, 6.5. Calc. for C₈H₈N₂S: C, 46.9; H, 6.3%).

Reaction of Acetic Anhydride with α -Benzamido-acids.—When *DL*- α -benzamido-*n*-butyric acid (2.0 g.) was heated for 3 hr. with acetic anhydride as in the case of benzoylalanine (above), 0.079 g. of carbon dioxide (18.5%) was evolved. Further heating with acetic anhydride and dimethylformamide and treatment as in the previous case gave 4(5)-ethyl-2-mercapto-5(4)-methylglyoxaline (36 mg.) m. p. >300° (Found: C, 50.5; H, 7.1. Calc. for C₈H₁₀N₂S: C, 50.7; H, 7.0%). *DL*-Benzoylnorvaline and *DL*-2-benzamido-octanoic acid, boiled under reflux with acetic anhydride for 5 hr., gave, after treatment as for benzoylalanine (above), *DL*-1-benzamido-butyl methyl ketone dinitrophenylhydrazone, m. p. 185° (from ethanol-toluene) (Found: C, 56.8; H, 5.5. C₁₉H₂₁O₆N₅ requires C, 57.2; H, 5.3%), and 2-mercapto-4(5)-methyl-5(4)-*n*-propylglyoxaline (identified by comparison with an authentic sample) (0.13 g.), m. p. 254° (decomp.), in the case of benzoylnorvaline, and *DL*-1-benzamidoheptyl methyl ketone dinitrophenylhydrazone, m. p. 174° (from ethanol-toluene) (Found: C, 59.5; H, 6.2. C₂₂H₂₇O₆N₅ requires C, 59.8; H, 6.1%), in the case of benzamido-octanoic acid.

Reaction of Benzoylaspartic Acid β -Methyl Ester with Acetic Anhydride.— β -Methyl hydrogen benzoyl-*DL*-aspartate, prepared by Pauly and Weir's method,¹³ was heated on the steam-bath with acetic anhydride till a clear solution was obtained. The acetic anhydride was then removed by repeated distillation under reduced pressure after the addition of xylene, and the oily residue containing 4-methoxycarbonylmethyl-2-phenyloxazolone was warmed with aniline to give *DL*- α -benzamido- β -methoxycarbonylpropionanilide, m. p. 185° (needles from ethanol) (Found: C, 66.7; H, 5.4. C₁₈H₁₈O₄N₂ requires C, 66.4; H, 5.5%). When the original methyl ester was boiled for 3 hr. under reflux with acetic anhydride in the usual manner, the oil left after evaporation of the acetic anhydride gave, after treatment with the requisite reagent, methyl *DL*- β -benzamido- γ -oxovalerate 2:4-dinitrophenylhydrazone, m. p. 204° (from ethanol) (Found: C, 53.4; H, 4.5. C₁₉H₁₉O₇N₅ requires C, 53.1; H, 4.4%), and oxime, m. p. 158° (from ethanol) (Found: C, 58.6; H, 6.1. C₁₃H₁₆O₄N₂ requires C, 59.0; H, 6.1%). The oil (above) was hydrolysed with 20% hydrochloric acid and after evaporation of the solution the residue was heated with aqueous potassium thiocyanate, giving 2-mercapto-4(5)-methyl-5(4)-glyoxalinylic acid, m. p. >300° (from water-ethanol) (yield 5%) (Found: C, 42.1; H, 4.7. Calc. for C₆H₈O₂N₂S: C, 41.8; H, 4.7%).

3:4-Dihydrocoumarin-4-carboxylic Acid (VII).—Hydroxyphenylsuccinic acid was heated at 150°/2 mm. for 30 min., according to the method of Bredt and Kallen,¹⁰ or heated in boiling xylene containing phosphoric oxide, the product being crystallised from ethyl acetate-light petroleum (b. p. 40–60°) (yield 83%; m. p. 135°) (Found: C, 62.4; H, 4.1. Calc. for C₁₀H₈O₄: C, 62.5; H, 4.2%). The substance dissolved in aqueous sodium hydrogen carbonate and was precipitated unchanged on the addition of acid. It reacted with diazomethane in chloroform

¹³ Pauly and Weir, *Ber.*, 1910, **43**, 669.

solution to give *methyl 3 : 4-dihydrocoumarin-4-carboxylate*, m. p. 89° (prisms from ethyl acetate-ether) (Found : C, 64.2; H, 4.9. $C_{11}H_{10}O_4$ requires C, 64.1; H, 4.9%). Hydrolysis of this ester with 3*N*-sodium hydroxide at 50° for 30 min. gave *o*-hydroxyphenylsuccinic acid, m. p. 156° (decomp.). β -*Methoxycarbonyl- α -o-hydroxyphenylpropionanilide*, precipitated when a benzene solution of the dihydrocoumarincarboxylic acid was warmed with aniline for a few minutes, had m. p. 162° (prismatic needles from ethanol). It gave a green colour with ferric chloride (Found : C, 67.2; H, 5.3. $C_{16}H_{15}O_4N$ requires C, 67.4; H, 5.3%).

4-Acetyl-3 : 4-dihydrocoumarin (VIII; R = Me).—*Method A.* *o*-Hydroxyphenylsuccinic acid (1 g.) was boiled under reflux with acetic anhydride (10 ml.) for 1 hr., whereafter carbon dioxide evolution ceased. The *product* (1 g.), after removal of the acetic anhydride *in vacuo*, crystallised from aqueous ethanol as needles, m. p. 122° (Found : C, 69.2; H, 5.1. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%). The *oxime*, prisms from ethanol, had m. p. 158° (Found : C, 64.0; H, 5.5. $C_{11}H_{11}O_3N$ requires C, 64.3; H, 5.4%). The *2 : 4-dinitrophenylhydrazone* (prepared at room temperature), needles from ethanol-benzene, had m. p. 173° (Found : C, 55.1; H, 3.8. $C_{17}H_{14}O_6N_4$ requires C, 55.2; H, 3.8%).

Method B. **3 : 4-Dihydrocoumarin-4-carboxylic acid** (0.5 g.) was warmed on the steam-bath with acetic anhydride (3 ml.) and 3-picoline (3 ml.) for 30 min., at which time the carbon dioxide evolution had ceased. After evaporation at 100° *in vacuo*, the residue of 4-acetyl-3 : 4-dihydrocoumarin was crystallised from ethanol (charcoal).

2-Methylbenzofuran-3-ylacetic Acid (IX).—4-Acetyl-3 : 4-dihydrocoumarin was heated under reflux with 3*N*-hydrochloric acid for 1 hr. After cooling, the *acid* was filtered off and crystallised from benzene-light petroleum (b. p. 40–60°); it had m. p. 98° (Found : C, 69.6; H, 5.1. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%). Light absorption: λ_{max} . 2490 and 2750 Å (ϵ 11,820 and 3250 in EtOH).

3-*o*-Acetoxyphenyl-4-hydroxypent-3-enoic Lactone (XI).—*o*-Hydroxyphenylsuccinic acid (2 g.) was warmed with acetic anhydride (10 ml.) and pyridine (10 ml.) at 50° for 12 hr. After evaporation under reduced pressure the residue of *lactone* (XI) crystallised from ethanol in prisms, m. p. 116° (0.55 g.) (Found : C, 67.2; H, 5.2. $C_{13}H_{12}O_4$ requires C, 67.2; H, 5.2%). This was boiled with 2*N*-hydrochloric acid for 1 hr., the clear solution evaporated under reduced pressure, and the residue crystallised from ethanol and then from benzene, to give *2-hydroxy-2-methylcoumaran-3-ylacetic lactone* (XII), m. p. 95° (Found : C, 69.6; H, 5.1. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%). Light absorption: λ_{max} . 2710 and 3100 Å (ϵ 10,100 and 5800 in EtOH).

Reaction of o-Hydroxyphenylsuccinic Acid with Propionic Anhydride.—*o*-Hydroxyphenylsuccinic acid (2 g.) was heated under reflux with propionic anhydride (15 ml.) and xylene (15 ml.) till carbon dioxide evolution had ceased (1 hr.). The residue left after evaporation under reduced pressure gave **3 : 4-dihydro-4-propionylcoumarin** (VIII; R = Et) (1.4 g.), needles (from ethanol), m. p. 120° (Found : C, 70.4; H, 5.8. $C_{13}H_{12}O_3$ requires C, 70.6; H, 5.9%). The *oxime*, needles from ethanol, had m. p. 170° (Found : C, 65.6; H, 6.1. $C_{12}H_{13}O_3N$ requires C, 65.7; H, 5.9%). The *semicarbazone*, leaflets from ethanol, had m. p. 198° (Found : C, 59.8; H, 5.8. $C_{13}H_{15}O_3N_3$ requires C, 59.8; H, 5.7%).

Reaction of o-Hydroxyphenylsuccinic Acid with n-Butyric Anhydride.—The reaction between this acid (2 g.) and *n*-butyric anhydride was carried out as above. **4-n-Butyryl-3 : 4-dihydrocoumarin** (VIII; R = Prⁿ) (1.4 g.), needles from ethanol, had m. p. 96° (Found : C, 71.9; H, 6.8. $C_{13}H_{14}O_3$ requires C, 71.6; H, 6.5%). The *oxime*, needles from ethanol, had m. p. 138° (Found : C, 66.6; H, 6.5. $C_{13}H_{15}O_3N$ requires C, 66.9; H, 6.4%).

β -(α -Dihydroxyethyl)glutaric Dilactone (XV; R = Me).—Tricarballic acid (2 g.) was heated under reflux with boiling acetic anhydride (20 ml.) for 2 hr., at which time the carbon dioxide evolution had ceased. The residue, left on evaporation of the acetic anhydride under reduced pressure, was crystallised from ethyl acetate-light petroleum, to give the dilactone, m. p. 99° (1.5 g.) (Found : C, 53.9; H, 5.1. Calc. for $C_7H_8O_4$: C, 53.8; H, 5.1%).

β -(α -Dihydroxybenzyl)glutaric Dilactone (XV; R = Ph).—Tricarballic acid (2 g.) and benzoic anhydride (8 g.) were heated in boiling xylene for 9 hr. after which time carbon dioxide evolution had ceased. On evaporation of the xylene, benzene was added and the solution was left overnight at 0°. The crystals of the dilactone were removed and a further quantity was obtained by concentrating the benzene solution after extraction with sodium hydrogen carbonate. The total yield, after recrystallisation from benzene, was 0.33 g. (m. p. 122°; Fittig¹¹ gives 137°) (Found : C, 66.3; H, 4.5. Calc. for $C_{12}H_{10}O_4$: C, 66.1; H, 4.6%). β -Benzoylglutaric acid was obtained from the dilactone by dissolving it in 1.5*N*-sodium hydroxide,

acidifying the solution with dilute hydrochloric acid, and extracting it with ether. Evaporation of the ether gave the acid, recrystallised from ethyl acetate–light petroleum (b. p. 40–60°), m. p. 116° (Fittig¹¹ gave 122°) (Found : C, 60.9; H, 5.1. Calc. for $C_{12}H_{11}O_2$: C, 61.0; H, 5.1%).

5-Hydroxy-5-methyl-2-phenyl-2-thiazolin-4-ylacetic Lactone (XVIII).—Thiobenzoylaspartic acid (3 g.) was heated under reflux with acetic anhydride (20 ml.) till the carbon dioxide evolution had ceased (30 min.). The residue left on evaporation under reduced pressure was crystallised from ethyl acetate–light petroleum (b. p. 40–60°), to give the *lactone*, prisms, m. p. 107° (1.1 g.) (Found : C, 61.9; H, 4.8; N, 6.0. $C_{12}H_{11}O_2NS$ requires C, 61.8; H, 4.7; N, 6.0%).

5-Methyl-2-phenyl-4-thiazolylacetic Acid (XIX).—The above lactone slowly dissolved on boiling with 20% hydrochloric acid for 1 hr. The *acid hydrochloride* which crystallised on cooling was recrystallised from aqueous ethanol and had m. p. 203° (felted needles) (Found : C, 52.2; H, 4.7; N, 5.0. $C_{12}H_{11}O_2NS.HCl$ requires C, 52.0; H, 4.5; N, 5.2%). Light absorption: λ_{max} 3000 Å (ϵ 15,880 in EtOH). The free *acid*, obtained by neutralising the hydrochloride with sodium hydrogen carbonate, crystallised from ethanol, m. p. 133° (Found : C, 61.8; H, 4.7; N, 5.9. $C_{12}H_{11}O_2NS$ requires C, 61.8; H, 4.7; N, 6.0%). A somewhat unstable *picrate*, prisms from aqueous ethanol, had m. p. 162° (Found : C, 45.7; H, 3.2. $C_{18}H_{14}O_9N_4S$ requires C, 45.0; H, 2.9%).

4-1'-Acetoxyethylidene-4 : 5-dihydro-6-oxo-2-phenyl-1 : 3-thiazine (XX).—Thiobenzoylaspartic acid (2 g.) was heated for 3 hr. on the steam-bath in a solution of acetic anhydride (15 ml.) and 3-picoline (10 ml.), carbon dioxide being evolved. The solution was distilled under reduced pressure and a benzene solution of the residue was extracted with dilute hydrochloric acid and then with saturated aqueous sodium hydrogen carbonate. After removal of the benzene the residue was extracted several times with boiling light petroleum (b. p. 60–80°) which on cooling deposited the *thiazine* (0.6 g.) as yellow prisms, m. p. 87° (Found : C, 60.9; H, 4.8; N, 5.0. $C_{14}H_{13}O_3NS$ requires C, 61.1; H, 4.7; N, 5.1%). Hydrolysis with 20% hydrochloric acid gave acetic acid, benzoic acid, hydrogen sulphide, ammonium chloride, and a steam-volatile ketone which was not identified.

I thank Mr. J. O. Stevens for technical assistance.

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[Received, July 6th, 1956.]