CXLVII.—*Ring-chain Tautomerism. Part XV. The Phenol-succineins and -glutareins.*

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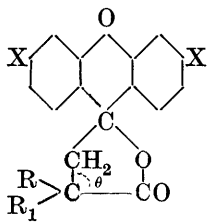
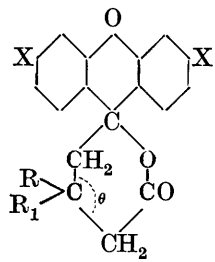
IN a previous paper (Dutt and Thorpe, J., 1924, **125**, 2524) it was shown that the effect of increasing complexity of the substituents R and R_1 in fluoresceins and rhodamines, derived from αα-disubstituted succinic and ββ-disubstituted glutaric acids, of the following constitutions



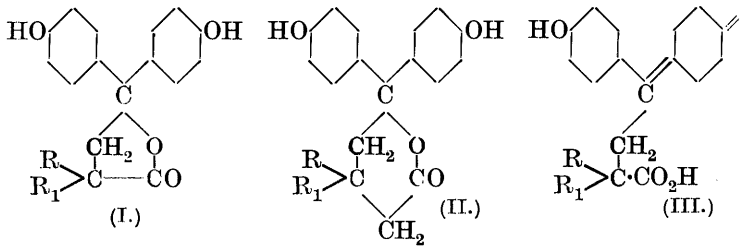
Succinylfluoresceins; X = OH.
Succinylrhodamines; X = NMe_2.



Glutarylfluoresceins; X = OH.
Glutarylrhodamines; X = NMe_2.

is to diminish the tetrahedral angle (θ) between the directions of the two remaining valencies of the substituted carbon atom; the stability of the lactone ring is thereby progressively increased, and consequently the amount of open-chain coloured quinonoid derivative produced by the action of alkalis and acids on these compounds progressively diminishes. The results of that research, which were based on spectroscopic data, were in complete accord with the results obtained by Thorpe and his collaborators, working on the same problem from other points of view.

The phenolsuccineins (I) and phenolglutareins (II),



where RR_1 represent HH, MeMe, MeEt, EtEt, and the *cyclo*hexane residue, have now been prepared and their absorption maxima determined. The results obtained are in complete agreement with those found in the cases of the corresponding fluoresceins and rhodamines (*loc. cit.*) and thus serve to confirm the generalisation stated above.

Like phenolphthalein, the phenol-succineins and -glutareins described in this paper are all colourless, crystalline substances which dissolve in alkalis with a bright pink colour, the mechanism of transformation from the colourless (I) to the coloured form (III) being the same as in the cases of the fluoresceins and rhodamines, *viz.*, fission of the lactone ring and formation of a quinonoid substance. The red quinonoid form is stable only in alkaline solution, the stability being due to salt formation at the carboxyl group, and on acidification reverts to the original colourless lactone form.

Green and Perkin have shown (J., 1904, **85**, 398) that the gradual disappearance of the deep pink colour produced by treating phenolphthalein with an excess of alkali is due to the formation of a carbinol salt, $(ONa{\cdot}C_6H_4)_2C(OH){\cdot}C_6H_4{\cdot}CO_2Na$, produced by hydration of the quinonoid form, $ONa{\cdot}C_6H_4{\cdot}C(:C_6H_4:O){\cdot}C_6H_4{\cdot}CO_2Na$. On acidifying the colourless solution of the carbinol salt, the free carbinol is obtained, which spontaneously loses water and is reconverted into the original lactone.

In presence of alkali, the phenolsuccineins and, very much more rapidly, the phenolglutareins undergo changes similar to the above, only a slight excess of alkali being necessary to produce them. In fact, the normal red quinonoid salts of the phenolglutareins are unstable in solution even in the absence of an excess of alkali. These salts, which have an alkaline reaction in solution, probably dissociate into the monoalkali salts and alkali hydroxide :

$$ONa{\cdot}C_6H_4{\cdot}C(:C_6H_4:O){\cdot}CH_2{\cdot}CRR_1{\cdot}CH_2{\cdot}CO_2Na \xrightarrow{H_2O} HO{\cdot}C_6H_4{\cdot}C(:C_6H_4:O){\cdot}CH_2{\cdot}CRR_1{\cdot}CH_2{\cdot}CO_2Na + NaOH.$$

The liberated alkali then brings about hydration at the quinonoid linking, the carbinol derivatives being formed. The red quinonoid forms, however, are more stable in very dilute solution.

The *carbinol* derivative of phenolglutarein,

$$(HO\cdot C_6H_4)_2C(OH)\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2H,$$

has been isolated as a colourless, crystalline substance. It is stable under ordinary conditions, but is converted into the lactone by the action of heat or dehydrating agents, such as concentrated hydrochloric or sulphuric acid, anhydrous zinc or aluminium chloride, and stannic chloride. The *carbinol* derivative of phenol-β-methylglutarein is very unstable and, although capable of isolation, passes into the lactone in the course of a few minutes. No carbinol derivative could be isolated from any of the remaining phenol-succineins or -glutareins.

The rate of hydration of the phenolglutareins under the influence of alkali, the end-point being where the red solution became colourless, was, under exactly similar conditions, slowest in the case of phenolglutarein, and progressively increased with the complexity of the substituents in the glutaric acid residue.

From the table (p. 1139) showing the relative rates of hydration of the various phenolglutareins in different concentrations of alkali, it will be seen that in dilute solution the rate is almost unaffected by the concentration of the alkali, thus proving that the change is a unimolecular one. The hydration of the phenolsuccineins was so slow and irregular that trustworthy measurements could not be made.

Stannic chloride is the only agent that has been found to bring about the condensation of phenol with succinic and glutaric acids and their substituted derivatives in the desired direction and in a satisfactory manner; with fused zinc chloride and with hydrogen chloride, the yields obtained are practically valueless. Strong sulphuric acid and phosphorus oxychloride produce the diphenyl esters of these acids, and anhydrous aluminium chloride produces complex pyrone derivatives which are probably similar in constitution to *o*-phenolphthalein anhydride.

EXPERIMENTAL.

Phenolsuccinein.—The preparation of this compound is attended with difficulty on account of the ease with which it becomes hydrated to the carbinol derivative and subsequently further decomposed into simpler substances. Dilute alkalis effect this change very quickly; even long contact with water, dilute alcohol, or dilute acids brings about the same transformation. The effect is quickened

by heating. But once the compound has been isolated and dried, the rate of hydration becomes very much slower. After a trial of various methods the following was adopted for the preparation of this compound :

A mixture of 12 g. of succinic acid, 25 g. of phenol, and 13 c.c. of stannic chloride was heated on the steam-bath for 4 hours, the melt treated with pure dry ether, and the insoluble salmon-coloured crystalline compound filtered off and washed with absolute alcohol–ligroin (1 : 3 by vol.). The almost colourless residue, containing tin salts, was dissolved in cold absolute alcohol, dry hydrogen sulphide passed through the solution, the excess of the gas removed by carbon dioxide, and the filtered solution concentrated in a vacuum at the ordinary temperature; addition of light petroleum then precipitated *phenolsuccinein* in colourless needles. This compound and the succeeding ones are described in the tables.

Phenol-as-*dimethylsuccinein.*—A mixture of *as*-dimethylsuccinic acid (1 mol.), phenol (2 mols. plus 20% excess), and stannic chloride (1 mol. plus 20% excess) was heated on the steam-bath for 4 hours, the melt poured into water, and the excess of phenol distilled in steam; the condensation product solidified, on cooling, to a mass of crystals in a matrix of brittle, dark brown, resinous matter. The latter was removed by washing the finely-powdered product with absolute alcohol–ligroin (b. p. 70—80°); the almost colourless crystalline residue recrystallised from alcohol (animal charcoal) in long, colourless, silky needles.

Phenolsuccineins were obtained from *as*-methylethyl-, *as*-diethyl-, and *as-cyclo*hexane-succinic acids by exactly similar methods.

Phenolglutarein.—The rapid hydration of this compound and subsequent decomposition into simpler substances make its preparation exceedingly difficult.

The *lactone form* was obtained from a mixture of glutaric acid (13 g.), phenol (25 g.), and stannic chloride (13 c.c.) by the method for preparing phenolsuccinein. It crystallised from absolute alcohol–ligroin in colourless, silky needles.

Quinonoid form. The ethereal filtrate in the preceding preparation was shaken with concentrated hydrochloric acid to remove tin salts, the ether distilled off, and the residue, after addition of an equal volume of 50% sulphuric acid, distilled in steam until phenol ceased to pass over. The red, sticky substance in the distilling flask was extracted with ether, the ethereal solution dried, diluted with ligroin, and allowed to evaporate at the ordinary temperature. After a month, the gummy residue had partly solidified, with separation of small crystals. These were spread

on a porous plate, washed free from the sticky mother-liquor with absolute alcohol–ligroin (1 : 4 by vol.), and recrystallised from ether; glistening, red prisms were thus obtained which, on heating, decomposed without melting. The substance changed into the colourless lactone form after contact with concentrated hydrochloric acid for several days or when its solution in concentrated sulphuric acid was poured into ice-cold water (Found: C, 71·5; H, 5·8. $C_{17}H_{16}O_4$ requires C, 71·3; H, 5·7%).

Carbinol form. The sticky mother-liquor was extracted from the porous plate by sodium carbonate solution, in which it dissolved with a bluish-red colour, but the solution soon became colourless. On acidification, a colourless solid was precipitated which crystallised from dilute alcohol in glistening, white needles, m. p. 220° (Found: C, 67·3; H, 5·8. $C_{17}H_{18}O_5$ requires C, 67·5; H, 5·9%).

The carbinol can also be prepared by dissolving the quinonoid or the lactone form in aqueous sodium carbonate or hydroxide and, after the dark red colour has disappeared, acidifying the solution with hydrochloric acid. An alkaline solution of the carbinol quickly decomposes in contact with air; from the products of decomposition phenol and *p*-hydroxybenzoic acid have been isolated.

Phenol-β-methylglutarein.—Only the *lactone* form of this compound was obtained by the method for preparing phenolglutarein. The *carbinol* derivative was obtained by keeping a solution of the lactone in dilute aqueous sodium hydroxide until the pink colour had disappeared, and then acidifying with dilute hydrochloric acid, filtering off the precipitated lactone, and extracting the filtrate with ether; on rapidly evaporating the ether in a current of air, the carbinol was obtained as a colourless, crystalline substance which in the course of about 15 minutes changed completely into the lactone. Immediately after isolation, it dissolves in aqueous sodium hydroxide, forming a colourless solution, but in a few minutes this begins to exhibit the red colour of the quinonoid form. Under no conditions could the carbinol be obtained in a stable form.

Phenol-ββ-dimethylglutarein.—A mixture of 16 g. of ββ-dimethylglutaric acid, 25 g. of phenol, and 13 c.c. of stannic chloride was heated on the steam-bath for about 4 hours; after cooling, the dark red melt was dissolved in moist ether. The ethereal solution was thoroughly washed with ice-cold dilute hydrochloric acid, water, and sodium bicarbonate solution, and then shaken with a saturated solution of sodium carbonate for 3 hours. The aqueous layer was separated, acidified with hydrochloric acid, and distilled in steam

to remove phenol. The yellow, sticky residue was extracted with ether, the ether evaporated, and the residue thus obtained was acetylated by boiling with twice its volume of acetic anhydride and a few drops of pyridine. The excess of anhydride was decomposed with water, and the viscous acetyl derivative dissolved in ether. The ethereal solution was repeatedly extracted with a 5% solution of sodium hydroxide until the extract was no longer pink. The ether was then evaporated, and the residual acetyl derivative hydrolysed by dissolving it in concentrated sulphuric acid and pouring the solution on to ice. The lactone was precipitated in pinkish-white flocks, which were filtered off, washed with water, dissolved in ether, the ethereal solution shaken with sodium bicarbonate solution, decolorised with animal charcoal, dried, and then allowed to evaporate at the ordinary temperature. Large, white, cubical crystals were obtained which were freed from the adhering sticky matter by washing with absolute alcohol–ligroin and then recrystallised from ether or dilute alcohol; large, transparent, silky prisms were thus obtained (yield about 1·3 g.).

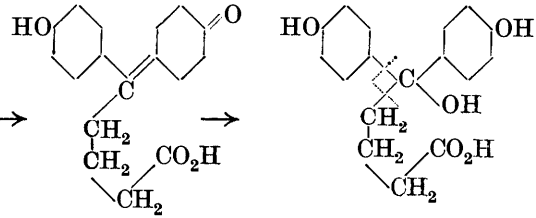
Phenolglutareins were obtained from ββ-methylethyl-, ββ-diethyl-, and β-*cyclo*hexane-glutaric acids in similar ways to the above.

Decomposition of Phenolglutarein by Alkali.—Phenolglutarein (5 g.) was dissolved in 200 c.c. of 10% sodium hydroxide solution, and the mixture heated under reflux for about 3 hours. The solution was diluted with water, acidified with hydrochloric acid, and distilled in steam until phenol ceased to pass over. The residual liquid, after cooling, was extracted with ether, and from the ethereal extract 0·7 g. of *p*-hydroxybenzoic acid, m. p. 213°, was obtained.

The steam distillate, which had an acid reaction, was neutralised with sodium carbonate and extracted with ether. After the evaporation of the ether, a small quantity of a liquid smelling strongly of phenol was obtained which gave all the reactions of this substance. The aqueous mother-liquor, on evaporation to dryness, yielded about 1 g. of a solid which was qualitatively shown to be a mixture of sodium butyrate with smaller quantities of sodium acetate and succinate.

Phenolsuccinein, on treatment with sodium hydroxide, behaved in an exactly similar manner. Substituted phenol-succineins and -glutareins do not yield *p*-hydroxybenzoic acid on treatment with alkali but decompose into phenol and aliphatic acids in the manner described in J., 1924, **125**, 2529, for the corresponding resorcinol derivatives.

The decomposition of phenolglutarein by alkali may be represented as follows:

(II; RR_1=HH) →  → $C_6H_5\cdot OH + (p)OH\cdot C_6H_4\cdot CO_2H + CH_3\cdot CH_2\cdot CH_2\cdot CO_2H$.

The succineins and glutareins are fairly easily soluble in alcohol, acetone, acetic acid, or benzene and insoluble in water or ligroin. *a* is the absorption maximum (wave-lengths) for dilute aqueous solutions.

Phenolsuccineins.

	Appearance.	M. p.	Colour in alkali.	*a* (2 mols. KOH).	*a* (20 mols. KOH).	Analysis (calc. % in brackets).
Phenol-	Colourless prisms.	252°	Deep bluish-pink.	5350	5450	C, 71·3 (71·1); H, 5·5 (5·2).
Phenoldimethyl-	,,	225	Light pink.	5220	5280	C, 72·2 (72·5); H, 6·3 (6·0).
Phenolmethylethyl-	Colourless silky needles.	192	,,	5210	5280	C, 73·4 (73·1); H, 6·5 (6·4).
Phenoldiethyl-	,,	260	,,	5170	5200	C, 73·3 (73·6); H, 6·9 (6·7).
Phenol*cyclo*hexane-	Colourless glistening leaflets.	257	,,	5070	5100	C, 74·1 (74·3); H, 6·9 (6·8).

Phenolglutareins.

Phenol-	Colourless needles.	145—147	Deep bluish-pink.	5510	5540	C, 71·5 (71·8); H, 5·9 (5·6).
Phenolmethyl-	,,	249	,,	5470	5490	C, 72·2 (72·5); H, 6·3 (6·0).
Phenoldimethyl-	,,	185	Reddish-pink.	5420	5450	C, 72·8 (73·1); H, 6·7 (6·4).
Phenolmethylethyl-	,,	164—165	,,	5420	5450	C, 73·5 (73·6); H, 6·6 (6·7).
Phenoldiethyl-	,,	181	,,	5380	5410	C, 74·4 (74·1); H, 7·3 (7·0).
Phenol*cyclo*hexane-	,,	135	,,	5210	5310	C, 74·6 (74·8); H, 7·3 (7·1).

Rate of Transformation of the Lactonoid Phenolglutareins into the corresponding Carbinol Derivatives by the Action of Alkali.—1 C.c. of an *N*/100-alcoholic solution of the phenolglutarein was added to 10 c.c. of aqueous potassium hydroxide of definite strength, and the time (seconds) required for the disappearance of the red colour thus produced was noted. The experiments were conducted at about 22° under even conditions of illumination. The results were as follows :

	Strength of potassium hydroxide solution.								
Glutarein.	2*N*.	*N*.	*N*/2.	*N*/10.	*N*/50.	*N*/100.	*N*/200.	*N*/500.	*N*/1000.
Phenol-	485	423	422	422	422	422	422	Long time.	Very long time.
Phenol-methyl-	465	412	409	409	409	405	405	,,	,,
Phenoldi-methyl-	440	405	405	405	405	405	405	,,	,,
Phenol-methyl-ethyl-	430	405	401	400	400	400	400	,,	,,
Phenol-diethyl-	235	168	132	188	105	105	134	192	Long time
Phenol*cyclo*-hexane-	70	67	57	49	39	48	59	235	,,

My best thanks are due to Professor J. F. Thorpe for the kind interest he has taken in this work and to the Chemical Society for a grant which has defrayed a part of the expense.

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SOUTH KENSINGTON. [*Received, October 30th*, 1925.]