[CONTRIBUTION FROM THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY, AND THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

A COMPARISON OF HETEROCYCLIC SYSTEMS WITH BENZENE. I. 6,7-INDAZOLEQUINONE-4-SULFONIC ACID

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The pronounced difference in the oxidizing power of the similarly constituted quinones of the benzene and the naphthalene series seems to be ascribable to the so-called aromatic nature of the benzenoid nucleus which the naphthoquinones contain. The reduction potential of α-naphthoquinone is 224 millivolts below that of *p*-benzoquinone; and β-naphthoquinone, while differing greatly in potential from the *para* isomer, has a reduction potential 220 mv. lower than that of *o*-benzoquinone.[1] The effect of attaching the phenylene group to either of the benzoquinones is not only a constant one but is very pronounced, being about twice as great as the effect produced by the substitution of two alkyl radicals or of a tetramethylene ring.[2] Consequently, this great lowering in potential can be attributed neither to the composition of the phenylene group nor to its cyclic character, but must be due to the peculiar nature of the benzenoid nucleus. The effect is adequately accounted for[3] by considering that one of the quinonoid ethylene linkages which in the benzoquinones contributes to the reactivity of the molecule is, in the naphthoquinones, incorporated in a benzenoid nucleus and thus rendered less reactive, the double bonds of benzene being relatively inert.

Since it is this very inertness of the double linkages, this apparently diminished degree of unsaturation which is in large part responsible for the distinctive properties of benzene, and since reduction-potential data give an exact, if relative, measure of this inertness, a very fundamental comparison of heterocyclic ring systems with the benzenoid system would be given by comparing the lowering in potential produced by the attachment of these various nuclei to quinone with the lowering produced by the phenylene group.

The problem presented by the heterocyclic compounds has formed the subject of illuminating researches by T. Zincke[4] and, in more recent years, by Fries,[5] both of these investigators employing purely chemical methods of comparison. Since the method here outlined is of an entirely different nature, it should furnish additional information on the same general problem.

[1] Conant and Fieser, THIS JOURNAL, **46**, 1858 (1924).

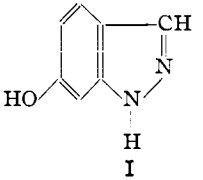
[2] The reduction potential of tetrahydro-α-naphthoquinone is 116 mv. below that of quinone. (Private communication from Dr. J. B. Conant.)

[3] Willstätter and Parnas, *Ber.*, **40**, 1406 (1907).

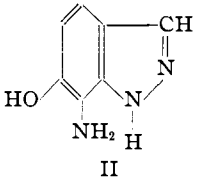
[4] T. Zincke and students, *Ann.*, **264**, 196 (1891); **290**, 321, 359 (1896); **311**, 277 (1900); **313**, 251 (1900); **370**, 297 (1909); *Ber.*, **21**, 2977 (1888).

[5] Fries and students, *Ann.*, (a) **389**, 305, (b) 318, (c) 345, (d) 367, (e) 384 (1912); (f) **404**, 50, (g) 53, (h) 81 (1914); (i) *Ber.*, **56**, 1630 (1923).

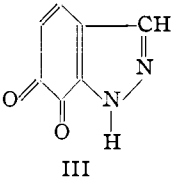
As a first step in what is hoped will be a comprehensive comparison of the several heterocyclic nuclei, the effect of the pyrazole ring has been examined. 6,7-Indazolequinone (III) was obtained by Fries and Roth,[5h] but these authors describe it as being unstable in the solid state, rapidly destroyed by acids or alkalies, and fairly readily decomposed by organic solvents. Such a compound would hardly be suitable for extensive electrochemical investigation. Since, however, the method employed in the preparation of the material, namely, through the nitro-chloro-keto-indazole, yields, when applied to the preparation of β-naphthoquinone, an abnormally unstable product,[6] it seemed possible that another method of preparation might yield a more suitable specimen of indazolequinone. 6-Hydroxy-indazole (I) readily couples with benzene diazonium chloride to give an azo compound, which was reduced to 6-hydroxy-7-amino indazole (II); this in turn yielded 6,7-indazolequinone (III) on oxidation. The



I



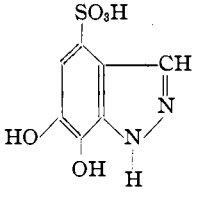
II



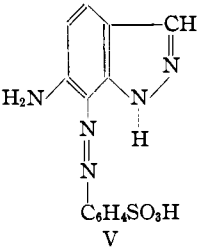
III

material so obtained corresponded in its properties in solution exactly with those given by Fries and Roth; in the solid state the substance was somewhat more stable than that obtained from the nitro-chloro-ketone, but in the course of a few months it had lost its bright red color and become dark red.

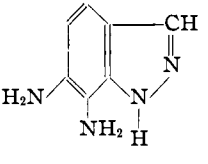
Since the great reactivity of indazole quinone is no doubt due to the presence of a free 4 position, it was decided to block this position with a sulfonic acid group, which would at the same time facilitate electrochemical measurement in aqueous solution. The quinone was found to add sodium bisulfite just as readily as does β-naphthoquinone[7] giving sodium 6,7-indazolehydroquinone-4-sulfonate, which was readily isolated in the form of the free acid (IV), no doubt existing in the form of an inner salt



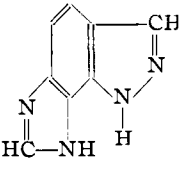
IV



V



VI



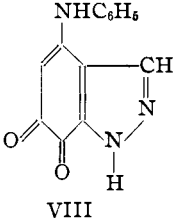
VII

[6] Fries, Ref. 5 a, p. 315.

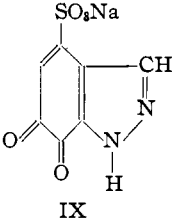
[7] Ger. pat. 70,867 (1892).

On oxidation, best with sodium nitrite in dilute alcoholic solution, this readily passed into the sodium salt of the corresponding quinone (IX). As will be shown, this compound was well suited to the purpose at hand.

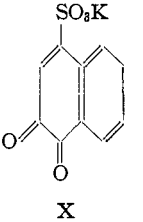
The structures of indazolequinone and of the other compounds described may be deduced from evidence independent of that of Fries and Roth. Since this appears to be the first case in which the coupling or nitroso reactions have been applied to 6-hydroxy- or 6-amino-indazole, and since indazole itself is converted into a nitrosamine by nitrous acid,[8] it was important to establish the position at which coupling to these derivatives occurs. 6-Amino-indazole was coupled with diazotized sulfanilic acid and the resulting azo compound (V) reduced to a diamine (VI). This compound proved to be an *ortho* diamine, for it condensed with phenanthrenequinone to give an azine, and an imidazole ring was closed on reaction with formic acid (Formula VII). Therefore, the *p*-sulfobenzene-azo group must have entered either the 5 or the 7 position and, since the same position must be attacked in the coupling of the hydroxy compound, the indazolequinone obtained must have been either the 5,6- or the 6,7-derivative. A distinction between the two possibilities is furnished by the reaction of the quinone with sodium bisulfite, giving rise to a substituted hydroquinone. Since in this distinctive quinone reaction the substituting group always enters a position at the end of a system conjugated with one of the quinone carbonyl groups, and since no such position is available in the 5,6-derivative, the quinone in question could only be 6,7-indazolequinone. That the



VIII



IX



X

sulfonic acid group enters the 4 position was further shown by the ready replacement of this group in the indazolequinone-sulfonate by aniline giving 4-anilino-6,7-indazolequinone (VIII), a reaction characteristic of β-naphthoquinone-4-sulfonate, and not even shared by α-naphthoquinone-2-sulfonate.[9]

The above reactions indicate a striking similarity between the derivatives of indazole and naphthalene; Fries and Roth, from their study of the action of chlorine and of nitric acid on chloro-hydroxy-indazole, concluded that indazole occupies a position intermediate between benzene and naphthalene.

Measurements of the oxidation-reduction potential of the system formed

[8] E. Fischer and Tafel, *Ann.*, **227**, 310 (1885).

[9] Seidel, *Ber.*, **25**, 427 (1892).

by sodium 6,7-indazolequinone-4-sulfonate and its hydroquinone were carried out by the titration method. The normal reduction potential of the quinone was found to be constant over a fairly extended range of hydrogen-ion concentration (to P_H 5), which indicates that dissociation of the various acidic and basic groups common to the quinone and hydroquinone is either complete or inappreciable in this range of acidity, or that there is no change in the degree of dissociation of such groups on converting the quinone into the hydroquinone. Consequently, the normal reduction potential may be taken as a reliable constant of the system, involving no secondary dissociation phenomena. The value found for the normal reduction potential at 25° was 0.620 v. For potassium β-naphthoquinone-sulfonate, which was reinvestigated,[10] the figure found was 0.630 v. That these two compounds (IX and X) should be so close together on the potential scale is remarkable. Considering that the average effect of the phenylene group is 0.222 v., it may be concluded that the effect on the potential of a quinone of attaching a pyrazole ring in a similar manner is the same within about 5%. One is tempted to consider this evidence as indicating that the ethylene linkage of pyrazole is equivalent to a benzenoid double bond, but there is some uncertainty in such a conclusion due to the fact that the composition of the two systems compared is not the same. Perhaps the nitrogen atoms in the pyrazole ring exert an influence of their own, similar to the influence of substituted amino or hydroxy groups, and independent of the stability of the ring system. Since this question can probably be answered experimentally, further discussion can best await an extension of this work.

Experimental Part

6-Amino-indazole.—6-Nitro-indazole was prepared by boiling a solution in dil. acetic acid of diazotized *p*-nitro-*o*-toluidine.[11] Reduction of the amine was best effected by means of stannous chloride, a reagent which has hitherto been avoided because reduction of 4-nitro-indazole by this method yields a chlorinated product.[12]

Sixteen g. of nitro-indazole was added to a warmed solution of 100 g. (4 molecular equivalents) of stannous chloride in 100 cc. of concd. hydrochloric acid. The stannochloride separating from the well-cooled reaction mixture was dissolved in sufficient hot water and the solution poured into a solution of 50 g. of sodium hydroxide in 1 liter of hot water. After digestion on the water-bath the amine, separated from the cooled solution, was dissolved in dil. hydrochloric acid, the solution boiled with animal charcoal, and the last traces of tin removed with hydrogen sulfide. The 6-amino-indazole which separated from the filtered solution on neutralization with ammonia in the form of fine, white plates, on drying at 100°, melted at 203° and proved to be identical with

[10] A few measurements with this compound have already been recorded (Ref. 1). The average of four determinations in strongly acidic solution was 0.628 v.

[11] Noelting, *Ber.*, **37**, 2578 (1904).

[12] Witt, Noelting and Grandmougin, *Ber.*, **23**, 3642 (1890).

a sample prepared by reduction with alcoholic ammonium sulfide; yield, 11.1 g., or 83.6%.

6-Hydroxy-indazole.[12]—Fries and Roth[5h] obtained this substance with an average yield of 54% by boiling a solution of diazotized amino-indazole in rather concentrated sulfuric acid for one and a half hours. The yield may be increased to 74% and the time required for complete evolution of nitrogen shortened to 15 minutes by adding 1.5 molecular equivalents of boric acid to the reaction mixture before boiling.

A solution of 50 g. of 6-amino-indazole in a mixture of 50 cc. of concd. sulfuric acid and 330 cc. of water was diazotized at 0° with a solution of 28 g. of sodium nitrite in 80 cc. of water. After the addition of 35 g. of boric acid and 50 cc. of sulfuric acid, the solution was boiled for 15 minutes, cooled, neutralized with ammonia and the precipitate extracted with boiling water, yielding 25.6 g. of pure hydroxy-indazole. By extraction with ether, 2.1 g. of material was obtained from the mother liquor, giving a total yield of 74%.

6-Hydroxy-7-benzene-azo-indazole.—To a solution of 13.4 g. of hydroxy-indazole in 250 cc. of water containing 20 g. (5 molecular equivalents) of sodium hydroxide was added a solution of benzenediazonium chloride prepared from 9.3 g. of aniline, 50 cc. of concd. hydrochloric acid, 50 cc. of water and 50 cc. of 2 *N* sodium nitrite solution. At the end of the reaction the separation of the brick-red dye was completed by adding a little acid. The material, dried on a porous plate, was quite pure and weighed 22.0 g. (92%). It is very sparingly soluble in hot water or dil. acids, readily soluble in alkali, soluble in alcohol, benzene, or toluene, very readily soluble in glacial acetic acid. A sample for analysis was recrystallized to a constant melting point from dil. acetic acid with the use of animal charcoal. It forms very long, bright-red needles melting at 238°.

Anal. Calcd. for $C_{13}H_{10}ON_4$: C, 65.5; H, 4.2; N, 23.5. Found: C, 65.8; H, 4.4; N, 23.2.

Since benzene-azo-β-naphthol is insoluble in alkali, the acidity of the above substance is probably a property of the heterocyclic ring, indazoles having unsaturated substituents such as the nitro group being regularly soluble in alkali.

6-Hydroxy-7-amino-indazole (II).—The reduction of the azo dye was conveniently carried out in alkaline solution by means of sodium hyposulfite ($Na_2S_2O_4$). To a hot solution of 23.8 g. of dye in 700 cc. of water containing 30 g. of sodium hydroxide, solid sodium hyposulfite was added until the red solution became pale yellow and then remained unaltered in color. About 80 g. of hyposulfite was required. After the solution had been boiled with animal charcoal for 5 minutes, it was filtered by suction while hot, quickly cooled and acidified with glacial acetic acid. The aminophenol which separated was slightly yellow. It was dissolved in a small quantity of hot water containing 8.5 cc. of concd. hydrochloric acid, the solution boiled with animal charcoal, and the product isolated either as the monohydrochloride by allowing the solution to crystallize or, by adding concd. hydrochloric acid, as the dihydrochloride. The dihydrochloride so obtained consisted of colorless, microscopic needles and weighed 15.0 g. (68%). For analysis a sample was dissolved in an aqueous solution of sulfur dioxide, precipitated with hydrochloric acid, and dried over sulfuric acid in a vacuum.

Anal. Calcd. for $C_7H_9ON_3Cl_2$: Cl, 32.0. Found: 31.8.

The monohydrochloride, prepared as above, or by crystallization of the dihydrochloride from aqueous sulfur dioxide, forms pale yellow needles containing one molecule of water of crystallization which is retained when the substance is dried in a vacuum at room temperature.

Anal. Calcd. for $C_7H_8ON_3Cl$, H_2O: Cl, 17.4. Found: 17.4.

When the material is dried at 100° the water of crystallization is given up but the compound suffers some decomposition, becoming slightly violet in color. The same is true of the dihydrochloride, though both compounds keep indefinitely when dried in a desiccator. The solution of either substance in water rapidly becomes brown as the result of oxidation; the presence of a little sulfur dioxide effectively arrests the process.

To obtain the free base, the dihydrochloride was dissolved in aqueous sulfur dioxide and an excess of sodium acetate solution added. On cooling, the solution deposited hydroxy-amino-indazole in the form of long, colorless, feathery needles which were dried at 120°. The substance has no melting point but darkens at about 190° and is completely decomposed at about 260°.

Anal. Calcd. for $C_7H_7ON_3$: C, 56.3; H, 4.7; N, 28.2. Found: C, 56.2; H, 4.8; N, 28.4.

6-Hydroxy-7-aminoindazole is readily soluble in water or alcohol, difficultly soluble in benzene, and its solutions are rapidly oxidized by the air. It is converted by oxidizing agents into *6,7-indazolequinone*.[5h] For the preparation of this compound, 2.2 g. of hydroxy-amino-indazole dihydrochloride was dissolved in 20 cc. of water containing a little sulfur dioxide, and the cooled solution stirred into a solution of 1.5 g. of sodium dichromate in 5 cc. of 5 *N* sulfuric acid containing a few ice particles. The quinone, which separated in the form of fine, bright-red crystals, was collected after the mixture had been stirred for half an hour. The yield was 0.9 g. (61%) and the product was pure enough for further use though it contained a little ash. In its reactions it corresponded to the compound described by Fries and Roth,[5h] although it proved to be more preservable. In the course of a few months, however, it had become dark red.

6,7-Indazolehydroquinone-4-sulfonic Acid (IV).—One and one-half g. of indazolequinone was dissolved in a concentrated solution of 2 g. of sodium bisulfite, the solution filtered and allowed to stand for 5 hours at room temperature, when a paste of fine white crystals had formed, probably consisting of the sodium salt of the sulfonated hydroquinone. Since this salt is extremely soluble in water and readily oxidized by the air, the compound is best isolated as the free acid, which forms a much less soluble and a more stable inner salt. Thus, on warming this reaction mixture until the crystals were dissolved and then acidifying the solution, indazole-hydroquinone sulfonic acid separated as the liquid cooled in the form of long, almost colorless needles; yield, 1.5 g., or 65%. Recrystallized from aqueous sulfur dioxide and dried at 120°, it was obtained colorless.

Anal. Calcd. for $C_7H_6O_5N_2S$: C, 36.5; H, 2.6; N, 12.2. Found: C, 36.2; H, 2.7; N, 12.3.

The compound is readily soluble in hot water and in alcohol, and insoluble in benzene. It may be kept indefinitely without change. The substance turns black at 250° and is not completely decomposed at 200°. The alkaline solution is at first green; in the presence of air the color soon changes to brown, then to a clear red, and the addition of acid then gives a clear yellow solution. This probably indicates conversion to an hydroxy-quinone.

SODIUM 6,7-INDAZOLEQUINONE-4-SULFONATE (IX).—The preparation of this very readily soluble compound was best accomplished by oxidation of the hydroquinone in the form of the free acid by means of sodium nitrite. To a boiling solution of 2.3 g. of indazole-hydroquinone-sulfonic acid in the least possible quantity of 75% alcohol was added a solution of 2 g. of sodium nitrite in 10 cc. of 50% alcohol. The solution became yellow and, when cooled in a salt-ice mixture, deposited fine, orange-yellow needles of the indazolequinone-sulfonate. When washed with 50% alcohol and dried at 120° it seemed to be directly pure.

Anal. Calcd. for $C_7H_3O_5N_2SNa$: Na, 9.2. Found: 8.9.

The salt dissolves with difficulty in 95% alcohol, readily in 80% alcohol, very readily in water. It dissolves in alkali and the clear yellow color of the solution changes on heating to a clear red. The potassium salt is likewise very readily soluble in water. The tertiary nitrogen atom, which in the hydroquinone is sufficiently basic to allow the formation of an inner salt, appears to have lost this property on oxidation to the quinone, for the latter substance gives no precipitation on acidification of the aqueous solution of its salt; the presence of acids only brings about a slow decomposition. The neutral aqueous solution also decomposes, but at a somewhat slower rate. The quinone is readily reduced by sulfur dioxide.

Potassium indazolequinone sulfonate was also obtained from hydroxy-indazole by conversion into the 7-nitroso derivative, treatment of this substance with sodium bisulfite and hydrochloric acid to give a hydroxy-amino-indazolesulfonic acid, and oxidation of the latter substance with 25% nitric acid to the quinone, which was precipitated by the addition of potassium chloride. The hydroxy-nitroso-indazole, however, separated in a highly hydrated form and set to a gel when attempts were made to crystallize it from a variety of solvents. It was not obtained in pure condition.

4-Anilino-6,7-indazolequinone (VIII).—Upon addition of an excess of aniline to a boiling dil. alcoholic solution of sodium indazolequinone-sulfonate, the aniline derivative separated at once in the form of small, glistening, bright red plates. The product, which was quite pure, is very slightly soluble even in xylene or nitrobenzene and melts with decomposition at 360°. It is readily soluble in alkali, insoluble in dilute acids and soluble with some decomposition in concd. hydrochloric acid. It is readily reduced by stannous chloride or sodium hyposulfite to a hydroquinone very sensitive to air oxidation.

Anal. Calcd. for $C_{13}H_9O_2N_3$: C, 65.2; H, 3.8; N, 17.6. Found: C, 65.1; H, 4.1; N, 17.4.

6-Amino-7-(*p*-sulfobenzenazo)-indazole (V).—A suspension of diazotized sulfanilic acid prepared from 20.9 g. of sulfanilic acid, 70 cc. of concd. sulfuric acid, 200 cc. of water, and 50 cc. of 2 *N* sodium nitrite solution, was poured into a cold suspension of 13.3 g. of 6-amino-indazole in 700 cc. of water containing 68 g. of crystalline sodium acetate. After the mixture had been digested on the water-bath, the bright red precipitate was filtered and dried; yield, 31.3 g., or 98%. The compound is very slightly soluble in hot water. A sample for analysis was purified by solution in dil. alkali and precipitation with an excess of acetic acid. The material separated in an amorphous form but, on digestion on the water-bath for five to six hours, it passed over into fine, bright-red, lustrous crystals.

Anal. Calcd. for $C_{13}H_{11}O_3N_5S$: C, 49.2; H, 3.5; N, 22.1 Found: C, 49.0; H, 3.7; N, 22.1.

6,7-Diamino-indazole Hydrochloride (VI).—Ten g. of the azo compound described above, finely powdered and suspended in 70 cc. of water, was reduced with a solution of 20 g. of stannous chloride in 20 cc. of concd. hydrochloric acid. The precipitate which separated on cooling was dissolved in water and freed from tin with hydrogen sulfide. On concentrating and cooling the solution, the sulfanilic acid largely separated and, on saturating the filtered solution with hydrogen chloride, diamino-indazole separated in the form of long, buff-colored needles, probably consisting of the di- or trihydrochloride. It was purified by re-precipitation with hydrogen chloride followed by crystallization from water, when it formed small, rose-colored, cluster-forming needles which proved to be the monohydrochloride; yield, pure, 3 g., or 51%.

Anal. Calcd. for $C_7H_9N_4Cl$: N, 30.4; Cl, 19.2. Found: N, 30.5; Cl, 19.2.

The free base is very soluble in water and the solution is readily oxidized by the

air. With an excess of dichromate mixture it is converted in the cold to a black, very difficultly soluble product, and this when warmed passes into a brown product, also exceedingly sparingly soluble.

6,7-Imidazo-indazole (1,2,6,8-Imidazo-indazole) (VIII).—A mixture of 1 g. of diamino-indazole hydrochloride and 0.5 g. of fused sodium acetate was covered with a little anhydrous formic acid and boiled for 1 hour. After most of the excess of formic acid had been boiled off, the residue was dissolved in hot water and the solution neutralized with ammonia and cooled. The reaction product was boiled in dilute acid solution for an hour in order to hydrolyze any formulated material which might be present, precipitated with ammonia, and crystallized from water. It forms very light, lustrous, colorless needles melting at 293°. The substance is readily soluble in hot water, practically insoluble in cold water, very readily soluble in alcohol or glacial acetic acid, very slightly soluble in benzene and soluble in both alkalies and acids.

Anal. Calcd. for $C_8H_6N_4$: C, 60.8; H, 3.8. Found: C, 61.0; H, 4.1.

6,7-Phenanthrazino-indazole (1,2,3,12-Indazo-phenanthrazine).—An alcoholic solution of 0.2 g. of diamino-indazole hydrochloride was neutralized with sodium acetate and added to a boiling solution of 0.2 g. of phenanthrenequinone. The bulky, yellow precipitate which formed was dried and extracted in the Soxhlet apparatus with xylene, in which it is very sparingly soluble. It was thus obtained in the form of fine, lemon-yellow needles melting at 364°, soluble in concd. sulfuric acid forming a carmine-red solution, insoluble in dilute acids, and very slightly soluble in the usual solvents.

Anal. Calcd. for $C_{21}H_{12}N_4$: C, 78.7; H, 3.8. Found: C, 78.5; H, 3.8.

E.m.f. Measurements

Owing to the extreme solubility of the salts of indazolequinone-sulfonic acid, and the slow decomposition of its aqueous solution, it is difficult to obtain a specimen of the material in a state of assured purity without great losses. Consequently, the hydroquinone, a substance readily obtainable in pure condition, was employed in most of the determinations to be recorded, though no essential difference in the results was observed in a few experiments with the quinone.

Potassium β-naphthoquinone-4-sulfonate[13] was obtained from a pure-white sample of aminonaphthol-sulfonic acid, through the ammonium salt, and recrystallized from water. It consisted of long, golden-yellow needles. From this the hydroquinone[13] was prepared by reduction with sodium hyposulfite in the presence of a little sodium carbonate and precipitation with potassium chloride. The potassium salt was crystallized from water until it formed long, feathery, colorless needles.

Electromotive-force measurements were carried out with a potentiometer accurate to 0.5 mv., in general according to the methods described elsewhere.[1] Hydrogen-electrode potentials were determined by reference to a saturated calomel electrode which was standardized against a carefully prepared 0.1 *N* calomel electrode. The potential of the oxidation-reduction half-cell was determined by measuring the potential difference between this half-cell and a hydrogen electrode containing the same buffer solution.

[13] Böniger, *Ber.*, **27**, 23 (1894).

Platinized, gold-plated and bright, platinum electrodes were employed in the oxidation-reduction half-cell.

In titrating the hydroquinones with oxidizing agents, the solid material was introduced to the oxygen-free buffer, the solution swept out for 20 minutes, and the titration commenced. In employing the methods of mixtures,[14] a concentrated solution of equimolecular quantities of the quinone and hydroquinone in oxygen-free water was prepared and 1 cc. of this solution added to 200 cc. of the oxygen-free buffer solution. The exact composition of the mixture was determined by comparing the potential in a certain buffer solution with the titration curve of the substance in that buffer. It was thus found that [Oxid.]/[Red.] = 1. The change in hydrogen-ion concentration due to dilution was assumed to be negligible. Titration of the quinones with sodium hyposulfite in neutral or alkaline solution was usually unsatisfactory because electrode equilibrium was established so slowly that the hyposulfite solution changed in strength during the titration. In such cases, the method of mixtures is to be preferred,

TABLE I

ELECTROMOTIVE FORCE MEASUREMENTS AT 25°

Sörensen value P_H	Hydrogen electrode Π_h, v.	Oxidation-reduction electrode Π_n, v.	$\Pi_n - \Pi_h$, v.	Nature of buffer soln.	Titrating reagent or method employed
6,7-INDAZOLEQUINONE-4-SULFONIC ACID					
1.25	−0.074	0.545	0.619	HCl	$TiCl_3$
1.25	.074	.545	.619	HCl	$K_2Cr_2O_7$
2.45	.144	.476	.620	KH Phthalate, HCl, KCl	$K_2Cr_2O_7$
3.23	.191	.429	.620	KH Phthalate, HCl, KCl	$K_2Cr_2O_7$
3.79	.224	.396	.620	KH Phthalate, HCl, KCl	$K_2Cr_2O_7$
4.97	.294	.329	.623	KAc, HAc, KCl	$K_2Cr_2O_7$
6.46	.382	.243	.625	KH_2PO_4, Na_2HPO_4, KCl	$K_2Cr_2O_7$
7.39	.437	.188	.625	KH_2PO_4, Na_2HPO_4, KCl	$K_2Cr_2O_7$
8.81	.521	.109	.630	$Na_2B_4O_7$, H_3BO_3, KCl	$K_3Fe(CN)_6$
9.53	.564	.071	.635	H_3BO_3, KOH, KCl	$K_3Fe(CN)_6$
10.01	.592	.046	.638	H_3BO_3, KOH, KCl	$K_3Fe(CN)_6$
Normal reduction potential (Av.) = 0.620					
1,2-NAPHTHOQUINONE-4-SULFONIC ACID					
0.49	−0.029	0.600	0.629	HCl	$TiCl_3$
1.25	.074	.556	.630	HCl	Mixtures
2.45	.144	.487	.631	KH Phthalate, HCl, KCl	Mixtures
3.23	.191	.440	.631	KH Phthalate, HCl, KCl	$K_2Cr_2O_7$
3.79	.224	.406	.630	KH Phthalate, HCl, KCl	$K_2Cr_2O_7$
4.97	.294	.336	.630	KAc, HAc, KCl	$K_2Cr_2O_7$
6.46	.382	.253	.635	KH_2PO_4, Na_2HPO_4, KCl	$K_2Cr_2O_7$
7.39	.437	.201	.638	KH_2PO_4, Na_2HPO_4, KCl	$K_2Cr_2O_7$
7.39	.437	.203	.640	KH_2PO_4, Na_2HPO_4, KCl	Mixtures
Normal reduction potential (Av.) = 0.630					

[14] Essentially according to the technique of Clark and Cohen, *Pub. Health Repts.*, **38**, 933 (1923).

though titration of the hydroquinone is equally accurate and furnishes some additional information. In all cases the total concentration of the organic substances was approximately 0.001 *M*.

The results obtained are recorded in Table I. The voltages given are single electrode potentials referred to the hydrogen scale; the values in Col. 4 also represent the electromotive forces of the cell: H_2, Pt | Buffer solution | Oxid.-Red. mixture, Buffer solution | Pt, when [Oxid.] = [Red.]. In Col. 3 are to be found values for the potential of the oxidation-reduction electrode when [Oxid.] = [Red.], on the hydrogen scale. The buffer mixtures were approximately 0.2 *M* in total salt content. In the last column, the method of measurement is indicated by stating what titrating reagent was employed or by indicating that a mixture of the pure components was used.

The value for the normal reduction potential was found in each case by averaging all values for the term ($\Pi n - \Pi h$) up to P_H 5, since up to this point the Πn:P_H curve is a straight line. Beyond P_H 5 there is a definite upward curvature, about parallel in the two cases. Unfortunately, in spite of several attempts, I was unable to obtain reliable results for either compound throughout the entire range of alkalinity. This was not due, as might at first be supposed, to the decomposition of the sulfonated quinones in alkaline solution, for the e.m.f.'s observed with the indazole derivative in 0.2 *M* potassium hydroxide solution were perfectly constant; with the naphthoquinone, the fall in potential was slow enough to permit approximate values being obtained. In the latter case, the final decomposition product was identified as 2-hydroxy-1,4-naphthoquinone by potentiometric analysis of a solution of β-naphthoquinone sulfonate in 0.2 *M* potassium hydroxide solution after heating at 90° for 10 minutes. The reduction potential of this compound is so low that the presence of a small amount of the material would have little influence on the result of a titration of β-naphthohydroquinone sulfonate. Indeed results which were fairly consistent and reproducible were obtained for both quinones in the range P_H 12 to 13.

It was in the intermediate regions of alkalinity that difficulties were encountered. In titrating indazolehydroquinone-sulfonic acid with potassium ferricyanide in both borate and phosphate buffer solutions of Sörensen value from P_H 10.2 to 11.5, the potentials were constant, the titration curves conformed closely to the theoretical form, but the values for Πn varied in duplicate determinations by as much as 6 mv. and fell irregularly as much as 20 mv. above the Πn:P_H curve formed by the other (reliable) points. With β-naphthoquinone sulfonic acid similar, but greater, discrepancies were observed in the range P_H 8.8 to 12.0. Here titration of the quinone was out of the question because electrode equilibrium was reached extremely slowly. Results obtained by the other two methods varied by as much as 10 mv. and the values for Πn again fell

above what seemed to be the true $\Pi n : P_H$ curve. The solutions, at the midpoint of reduction, were dark brown in color, that is, deeper in color than the quinone solution itself.

While no satisfactory account of these peculiarities suggests itself, it is of interest that Sullivan, Cohen and Clark[15] encountered entirely analogous discrepancies in this same region of alkalinity in their investigation of the electrode potentials of indigo sulfonates. While these authors considered the effect specific to borate buffers, though indeed certain divergences with alkaline phosphate buffers were recorded, no differentiation between borate and phosphate buffers was apparent in the present case. It seems likely that some phenomenon not yet understood is in operation at the particular alkalinity at which few but borate buffers are available. Thus glycine buffers are out of the question because the sulfonated quinones react with glycine.

Only those results about which there is no cause for uncertainty have been included in the table. Fortunately, these results furnish the comparison desired.

In conclusion I wish to express my gratitude to Professor William Henry Perkin, Jr., for his many kindnesses during a portion of this work.

Summary

Sodium 6,7-indazole-4-sulfonate has been prepared and characterized and compared with potassium β-naphthoquinone-4-sulfonate. The normal reduction potentials of the two substances at 25° are 0.620 v. and 0.630 v., respectively, which indicates a close relationship between the pyrazole and the benzene systems.

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[CONTRIBUTION FROM THE POLARIMETRY SECTION OF THE BUREAU OF STANDARDS, UNITED STATES DEPARTMENT OF COMMERCE][1]

THE IDENTITY OF ISOMALTOSE WITH GENTIOBIOSE

BY HENRY BERLIN[2]

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Introduction

The literature on isomaltose is quite extensive[3] yet the constitution of this sugar is still the subject of controversy and uncertainty, and some

[15] Sullivan, Cohen and Clark, *Pub. Health Repts.*, **38**, 1669 (1923).

[1] Published by permission of the Director of the Bureau of Standards, United States Department of Commerce.

[2] Research Associate at the Bureau of Standards, representing the Corn Products Refining Company.

[3] E. O. v. Lippmann, "Die Chemie der Zuckerarten," Vieweg, Braunschweig, **1904**, Vol. II, pp. 1504–1520. E. Abderhalden, "Biochemisches Handlexikon," Springer, Berlin, **1923**, Vol. X, pp. 608–609.