219. *Studies with Dithizone. Part IV.* The Dissociation Constant of Dithizone.*

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Measurements of the distribution coefficient of dithizone between a variety of organic solvents and aqueous buffers of known pH lead to the value $pK_{HDz} = 4{\cdot}5 \pm 0{\cdot}3$. A tapless apparatus has been devised for Golumbic and Weller's "interchange extraction" procedure, and a modification of this technique has been shown to be suitable for measuring very small partition coefficients.

IT has already been clearly established that the important analytical reagent diphenylthiocarbazone ("dithizone," HDz) behaves as a monobasic acid, at least up to pH 12 (Irving, Cooke, Woodger, and Williams, *J.*, 1949, 1847), but owing to its extremely low solubility in water (about 10^{-7}M) conventional methods cannot be used to measure the dissociation constant, $K_{HDz} = [H^+][Dz^-]/[HDz]$, and its value is still in doubt.

The value $pK_{HDz} = 5{\cdot}25$ was calculated (*loc. cit.*) from the known dissociation constants of methyl-red and bromothymol-blue in water and the values of the apparent dissociation constants of these indicators and of dithizone as determined spectrophotometrically in a homogeneous mixture of water, alcohol, and chloroform, on the assumption that change of solvent does not alter the relative order of magnitude of acid strengths—but this must be treated with some reserve (cf. Bayles, D.Phil. Thesis, Oxford, 1951).

An alternative method requires a knowledge of $p_o = [HDz]_w/[HDz]_o$, the partition coefficient of molecular dithizone between water and an immiscible organic phase, together with measurements at various pH's of p, the distribution ratio for this solute between aqueous buffers (in which it dissolves both as molecules, HDz, and as dithizonate ions, Dz^-) and an organic phase : it has been shown (*loc. cit.*) that K, p_o, and $pH_{\frac{1}{2}}$, the hydrogen-ion exponent for which p is unity, are related by the equation

$$pK = \log_{10}p_o + pH_{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The value of this method for determining the dissociation constants of sparingly soluble phenols has recently been demonstrated by Golumbic, Orchin, and Weller (*J. Amer. Chem. Soc.*, 1949, **71**, 2624), but its applicability to the case of dithizone depends upon the precision with which the component terms of equation (1) can be determined. So far as $pH_{\frac{1}{2}}$ is concerned there is very satisfactory agreement between the measurements of different observers (cf. Table 1), but values for the extremely small partition coefficient of undissociated dithizone are difficult to measure experimentally and the discrepancy between our value of $p_o = 6{\cdot}4 \times 10^{-4}$ for water/carbon tetrachloride and that of Sandell (*loc. cit.*), who recently reported $9{\cdot}1 \times 10^{-5}$, leads to the seriously discordant values for pK_{HDz} of 5·6 and 4·8, respectively.

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* Part III, *J.*, 1952, 356.

TABLE 1.

$pH_{\frac{1}{2}}$	Temp.	Ref.	Comments
8·72	31°	*a*	One measurement at pH 10
8·90	~ 20	*b*	Nine measurements from pH 7·85 to 10
8·85	25	*c*	Determinations at pH 8 and 9
8·80	—	*d*	Seven determinations from pH 7 to 9
8·80	~ 20	*e*	Five determinations between pH 8·2 and 9·1 with buffers of ionic strength 0·14

[a] Clifford and Wichmann, *J. Assoc. Offic. Agric. Chem.*, 1936, **19**, 130. [b] Irving *et al.*, *loc. cit.* [c] Sandell, *J. Amer. Chem. Soc.*, 1950, **72**, 4660. [d] Buch and Koroleff, *Finska Kem. Medd.*, 1945, **54**, 98, quoted in *Chem. Abstracts*, 1950, **44**, 8750[d]. [e] Present authors.

In a reinvestigation of the dissociation constant of dithizone, we have modified the method of " interchange extraction " recently proposed by Golumbic and Weller (*Analyt. Chem.*, 1950, **22**, 1418) for the determination of very large (or very small) partition coefficients so as to avoid the complete separation of phases after each equilibration—an operation which presents considerable experimental difficulties. The basic procedure was as follows: 45 ml. of 0·1M-hydrochloric acid were equilibrated with 5 ml. of a concentrated solution of dithizone in the organic solvent under investigation by 1½ hours' shaking in a stoppered Pyrex test-tube. After the phases had separated, exactly 40 ml. of the aqueous phase were transferred to a second Pyrex test-tube and, after the addition of 5 ml. of 0·1M-hydrochloric acid and 5 ml. of pure organic solvent, equilibration was carried out as before. Simultaneously, equilibration was effected in the first tube after the addition of 40 ml. of 0·1M-hydrochloric acid. This completed the first interchange, at which stage each tube contained 5 ml. of organic phase and 45 ml. of aqueous phase; 40 ml. of each aqueous phase were then interchanged, and the equilibrations repeated. This completed the second interchange, and further stages of interchange were carried out in the same way. By interchanging a (large) aliquot portion rather than the whole of each aqueous phase at each stage, disturbance of the water–organic phase boundary was minimised and gross errors caused by the inadvertent transfer of droplets of the organic phase could be completely avoided. The necessary modification in Golumbic's quantitative treatment of the equilibria (*loc. cit.*) is shown in Table 2, which portrays the position at the end of each successive stage when V ml. of organic phase are equilibrated with nV ml. of aqueous phase, $V' < nV$ ml. being transferred at each interchange. For convenience, we write $R = V'/nV$, $a = 1 + (1 - R)np_o$, $b = 1 + np_o$, and $c = nRp_o$. It is clear from Table 2 that the *total* amount of solute in either tube at the end of each stage is obtained by taking the sum of alternate terms in the expansion of $(a + c)^m/b^m$, terms with even powers of c appearing in the expression for the first tube, and those with odd powers of c in that for the second tube. The fraction of each successive total amount present in the organic phase after equilibration is obtained by dividing the successive entries of Table 2 by the quantity $b = 1 + np_o$. In our experiments $R = 0{\cdot}89$, and the partition coefficient of dithizone was given by

TABLE 2.

Number of interchange, *m*.	Fraction of the total solute in: first tube	second tube
0	1	0
1	a/b	c/b
2	$(a^2 + c^2)/b^2$	$2ac/b^2$
3	$(a^3 + 3ac^2)/b^3$	$(3a^2c + c^3)/b^3$
. . .	. . .	. . .
m	$[a^m + m(m - 1)a^{m-2}c^2/2!$ $+ m(m - 1)(m - 2)(m - 3)a^{m-4}c^4/4!$ $+ \ldots\ldots]/b^m$	$[ma^{m-1}c$ $+ m(m - 1)(m - 2)a^{m-3}c^3/3!$ $+ \ldots\ldots]/b^m$

$$\frac{\text{Dithizone concentration in the organic phase of the second tube after } m \text{ interchanges}}{\text{Dithizone concentration of the original organic phase in the first tube}}$$

$$= [ma^{m-1}c + m(m - 1)(m - 2)a^{m-3}a^3/3! + \ldots\ldots]/b^m \cong 8mp_o$$

The magnitude of the quantity, p_o, to be measured is effectively magnified 8-fold at each exchange, and theoretically there is no reason why the process should not be continued until the concentrations of the organic extracts in the two tubes approach equality. In practice, since each stage of equilibration took 1½ hours, the process was terminated after comparatively few stages in order to minimise errors due to the gradual decomposition of the dithizone and the introduction of adventitious metallic impurities.

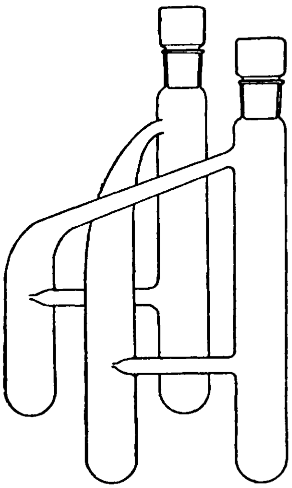
TABLE 3.

Solvent	$p_o \times 10^5$	pH½	p*K*	Method
*cyclo*Hexane	43	7·44	4·1	*a*
*cyclo*Hexane	52	7·44	4·2	*b*
Carbon tetrachloride	9·1	8·85	4·8	*c*
Carbon tetrachloride	6·6	8·8	4·6	*b*
Benzene	1·3	9·09	4·2	*a*
Chloroform	1·3	10·58	5·7	*b*

[a] Approaching equilibrium from a supersaturated aqueous phase. [b] Interchange method. [c] Average value from Sandell (*loc. cit.*).

Since the solubility of dithizone in *cyclo*hexane (14 mg./l.) is much lower than in most other organic solvents (Irving and Tilley, to be published shortly), the partition coefficient should be proportionately increased and thus be more suitable for accurate measurements. Values of p_o were therefore obtained by the interchange method using the solvents *cyclo*hexane, carbon tetrachloride, and chloroform, and, as a further check, measurements of p_o were made with the solvents *cyclo*hexane and benzene, by the technique described by Sandell (*loc. cit.*) in which equilibrium is approached from a supersaturated aqueous phase. Of the results shown in Table 3, together with measured values of pH½ and calculated values of p*K*, that for chloroform is clearly anomalous. The agreement between the values for *cyclo*hexane obtained by the two procedures confirms the reliability of the interchange technique, and the agreement between the value for carbon tetrachloride obtained by this method and the value reported by Sandell (*loc. cit.*) is not unsatisfactory, the discrepancy appearing almost entirely in the measured values of p_o. There can be little doubt that the value $p_o = 6{\cdot}4 \times 10^{-4}$ for carbon tetrachloride previously reported (Irving *et al.*, *loc. cit.*) was seriously in error owing to failure to reach equilibrium under the conditions employed when starting with a dilute organic solution of dithizone, and the value of p*K* reported in that paper should be discarded. However, it must be recognised that in these measurements we are in fact not measuring the dissociation constant of dithizone in water, but rather in a series of aqueous phases saturated with different organic solvents. Even so, the discrepancies between the values of p*K* derived from measurements with different water–solvent systems are disturbingly large, and at present it does not seem possible to give a more precise value for the dissociation constant of dithizone than $\mathrm{p}K_{\mathrm{HDz}} = 4{\cdot}5 \pm 0{\cdot}3$. It is, however, worth commenting on the fact that the biggest discrepancy occurs with chloroform, which is the most polar and the most water-soluble of the solvents studied.

Apparatus for interchange equilibration.



The apparatus shown (not to scale) in the figure was constructed to permit the processes of equilibration and phase-interchange incident to Golumbic and Weller's interchange extraction procedure to be carried out automatically and under conditions such that oxidation and the introduction of adventitious impurities could be avoided. It is an adaptation of the all-glass unit devised by Craig (*Analyt. Chem.*, 1950, **22**, 1346) for use in counter-current extraction work (cf. Irving, " Solvent Extraction and its Application to

Inorganic Analysis," *Quart. Reviews*, 1951, **5**, 200). The appropriate volumes of liquids are introduced and the stoppers replaced. The apparatus is then turned 90° clockwise and equilibration is effected by shaking horizontally or by rocking about a small angle. After the phases have separated at rest, phase-interchange is brought about by slowly turning the apparatus anti-clockwise to restore it to the vertical position shown in the figure and then returning it as before to the horizontal or shaking position. Although extensive tests showed that this apparatus could not be relied upon implicitly for the procedure described in the present paper, it has a number of useful applications in procedures requiring systematic back-extractions, etc., where the use of taps is undesirable.

EXPERIMENTAL

Interchange Experiments.—Equilibration was carried out at 20° by shaking the appropriate mixtures mechanically in large stoppered Pyrex test-tubes; and centrifugation was employed to assist phase separation when necessary. Interchange of the appropriate 40-ml. aliquot of the aqueous phases (see above) was effected by means of calibrated pipettes. Both water and organic phases were pre-saturated with the second phase and the customary precautions necessary when working with dithizone were rigidly observed (cf. Irving, Andrew, and Risdon, *J.*, 1949, 539). The concentration of dithizone was determined absorptiometrically at 620 mμ in all cases, a Beckman Model DU Spectrophotometer with 1-cm. cells being used. An aliquot portion of the initial concentrated organic phase was suitably diluted before measurement (100-fold for carbon tetrachloride, 2-fold for *cyclo*hexane), but the absorbancy of the dilute organic extract in the second tube could be measured directly.

Carbon tetrachloride.

Absorbancy of initial solution ($\times 10^{-2}$)	0·557	0·581	0·501	0·501	0·501
Absorbancy of extract	0·117	0·157	0·106	0·109	0·098
Number of interchanges	3	4	3	3	3
$p_o \times 10^5$ (calc.)	6·6	6·75	6·6	6·8	6·1

cyclo*Hexane.*

Absorbancy of initial solution ($\times 0{\cdot}5$)	0·600	0·600	0·600	0·638	0·638	0·638
Absorbancy of extract	0·018	0·020	0·018	0·033	0·029	0·035
Number of interchanges	3	3	3	5	5	5
$p_o \times 10^4$	4·8	5·3	4·8	5·5	4·9	5·9

The Approach to Equilibrium from a Supersaturated Aqueous Phase.—5 ml. of a solution of dithizone in *cyclo*hexane were shaken in a large separating funnel with 500 ml. of water at 18° containing a few drops of concentrated ammonia solution. Dithizone was thus extracted into the aqueous phase as the yellow dithizonate ion, whence it was precipitated by the addition of 5 ml. of concentrated hydrochloric acid. After 15 minutes' shaking partition equilibrium had been established (this was confirmed by control experiments) and the greater part of the dithizone passed back into the organic solvent. After separation of the two phases (phase ratio 505/5) the concentration of dithizone in the organic layer was measured in terms of its absorbancy after suitable dilution, and that in the aqueous phase (approx. 0·1M-HCl) was obtained by equilibration with 5 ml. of fresh (pre-saturated) organic solvent and measuring the absorbancy of this extract.

cyclo*Hexane.*

Absorbancy of initial solution ($\times 0{\cdot}2$)	0·330	0·267	0·280	0·275	0·290
Absorbancy of organic extract	0·058	0·052	0·067	0·066	0·065
$p_o \times 10^4$	3·5	3·86	4·88	4·74	4·4

Benzene.

Absorbancy of initial solution ($\times 10^{-2}$)	0·147	0·147	0·143	0·595	0·575
Absorbancy of organic extract	0·022	0·017	0·016	0·096	0·068
$p_o \times 10^5$	1·47	1·14	1·11	1·63	1·17

The Distribution of Dithizone between Aqueous Buffers and Organic Solvents.—Distribution experiments were carried out as previously described (Irving *et al.*, *loc. cit.*) save that separating-funnels were replaced by stoppered Pyrex tubes wherever possible. Sodium hydroxide–boric acid buffers were employed in the case of benzene and carbon tetrachloride, potassium hydroxide–potassium hydrogen phosphate buffers were used with *cyclo*hexane : sodium nitrate was present in each case to maintain a constant ionic strength of 0·14.

Benzene.

pH	8·58	8·80	8·93	9·10	9·42
Percentage extracted	20·2	32·1	40·4	50·6	69·8

Carbon tetrachloride.

pH	8·20	8·46	8·74	8·94	9·10
Percentage extracted	16·0	32·2	46·8	57·0	66·5

cyclo*Hexane.*

pH	6·28	7·00	7·23	7·51	7·80	7·96
Percentage extracted	10·2	27·6	39·5	52·6	68·1	76·2

We are indebted to Mr. C. G. Tilley for making the measurements with the first two solvents. From plots of pH against $\log_{10}$ (percentage extracted) the values of $\text{pH}_{\frac{1}{2}}$ given in Table 3 were obtained by interpolation.

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