CXCVII.—*The Stability of Organic Molecular Compounds.*

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COMPARATIVELY few determinations of the relative stability of the compounds of picric acid with hydrocarbons and of nitro-compounds with amines are recorded in the literature and it appeared desirable to carry out a series of measurements under comparable conditions. The partition method of investigating such equilibria was chosen since it has the advantage over the cryoscopic method (Brown, J., 1925, **127**, 345) that both solvent and temperature can be varied, and over the solubility method (Behrend, *Z. physikal. Chem.*, 1894, **15**, 183; Kuriloff, *ibid.*, 1897, **23**, 90; Dimroth and Bamberger, *Annalen*, 1924, **438**, 94) that equilibrium between the two phases concerned is attained with greater ease and certainty. The present paper deals with the addition compounds of picric acid at 18°, and of aniline at 25°, in chloroform solution, and is intended as a survey of the possibilities of the method in these cases.

If an aqueous solution of picric acid is shaken with chloroform containing a hydrocarbon at a concentration $[Z]$ until equilibrium is reached, and we then determine the concentration of the picric acid $[X]$ in the aqueous phase, and the total concentration of picric acid $[Y]$ in the chloroform phase, we have $[Y] = [C] + [P]$, and $[Z] = [C] + [H]$, where $[C]$, $[P]$, and $[H]$ represent the concentrations of the addition compound, free picric acid, and the free hydrocarbon respectively in the chloroform phase, the hydrocarbon being assumed insoluble in water. If we have already determined the partition curve for picric acid between the two solvents, we can read off the value of $[P]$ corresponding to $[X]$. The equilibrium constant for the reaction : picric acid + hydrocarbon $\rightleftharpoons$ addition compound, can then be calculated as

$$K = ([Y] - [P])/[P]([Z] - [Y] + [P])$$

if it be assumed that one molecule of picric acid combines with one molecule of hydrocarbon.

A similar method and formula, in which aniline and a nitro-compound insoluble in water replace picric acid and the hydrocarbon, give the equilibrium constant for the reaction : aniline + nitro-compound $\rightleftharpoons$ addition compound.

By using the potassium iodide–potassium iodate method for estimating picric acid, and finishing the titration with $0{\cdot}01N$-thiosulphate after titrating nearly all the iodine by $0{\cdot}1N$-thiosulphate from a weight pipette, it was found possible to ensure an accuracy of 1 part in 400 parts over the whole range covered, and the estimation was found to be unaffected by the various " hydrocarbons " used in the equilibrium experiments. (The term " hydrocarbon " is here intended to include the halogen and nitro-substitution products used.) The partition curve was constructed from the following numbers, where, as throughout this paper, concentrations are in g.-mols. per litre.

Conc. of picric acid.			Conc. of picric acid.		
H_2O phase.	$CHCl_3$ phase.	$\frac{\text{Conc. in } CHCl_3}{\text{Conc. in } H_2O}$.	H_2O phase.	$CHCl_3$ phase.	$\frac{\text{Conc. in } CHCl_3}{\text{Conc. in } H_2O}$.
0·01629	0·01601	0·983	0·02390	0·03169	1·326
0·01915	0·02145	1·120	0·02584	0·03632	1·406
0·02070	0·02482	1·194	0·02682	0·03891	1·451
0·02153	0·02643	1·227	0·02912	0·04468	1·534
0·02267	0·02883	1·272			

For the partition in presence of a " hydrocarbon," water and a chloroform solution of picric acid were shaken together until they were approximately in equilibrium. The chloroform phase was used to make up a weighed quantity of the " hydrocarbon " to a suitable concentration in a standard flask, and this solution was then shaken with the aqueous phase to produce final equilibrium, after which the picric acid was estimated in each phase. Since the only concentration change taking place after addition of the " hydrocarbon " is a very small transfer of picric acid from water to chloroform, there was no danger of volume change which, if it occurred, would alter the concentration of the " hydrocarbon."

The values of K, which were constant within analytical error, are given on p. 1451. As an example, the details for picric acid and naphthalene are quoted below.

$[P]$.	$[Y]$.	$[Z]$.	$[C]$.	K.
0·0225	0·0298	0·1577	0·0073	2·15
0·0263	0·0349	0·1577	0·0086	2·20
0·0297	0·0374	0·1278	0·0077	2·16
0·0312	0·0412	0·1577	0·0100	2·18
0·0325	0·0408	0·1278	0·0083	2·14
0·0333	0·0486	0·2267	0·0153	2·18
0·0358	0·0521	0·2267	0·0163	2·16
0·0398	0·0548	0·1876	0·0150	2·18
0·0410	0·0565	0·1876	0·0155	2·20

Aniline was estimated by bromination in acid solution with a solution of bromide and bromate. With the following procedure the error did not exceed 1 part in 300 parts and was usually much less. To the aniline solution in a stoppered bottle, 20 c.c. of 18% hydrochloric acid were added, and the bromide–bromate solution was run in slowly with shaking. When the colour showed that there was excess of bromine, potassium iodide was added, and the iodine titrated with $0{\cdot}01N$-thiosulphate. In the analysis of the chloroform phase it was necessary to shake the mixture for ½ hour to get complete bromination of the aniline. In all cases a parallel experiment with hydrochloric acid and potassium iodide was carried out, and the thiosulphate equivalent of any iodine liberated subtracted from the titre in the actual estimation. The partition curve for aniline was plotted from the following numbers.

Conc. of aniline.			Conc. of aniline.		
H_2O phase.	$CHCl_3$ phase.	$\frac{\text{Conc. in } CHCl_3}{\text{Conc. in } H_2O}$.	H_2O phase.	$CHCl_3$ phase.	$\frac{\text{Conc. in } CHCl_3}{\text{Conc. in } H_2O}$.
0·01244	0·2957	23·8	0·01725	0·4125	23·9
0·01336	0·3178	23·8	0·01749	0·4180	23·9
0·01414	0·3370	23·8	0·01862	0·4465	24·0
0·01552	0·3693	23·8			

For the partition of aniline in presence of nitro-compounds the procedure was similar to that described on p. 1448. The precaution of allowing the two phases to approach equilibrium before addition of the nitro-compound is here very important, since appreciable changes in volume accompany the passage of aniline from one phase to the other. The values of K were constant within experimental error and are given on p. 1451. The details for aniline and *m*-dinitrobenzene are given below, the concentrations of free and total aniline in the chloroform phase being represented by $[A]$ and $[Y]$, and the total concentration of the nitro-compound by $[N]$.

$[A]$.	$[Y]$.	$[N]$.	$[C]$.	K.
0·3330	0·3464	0·2559	0·0134	0·17
0·3352	0·3494	0·2736	0·0142	0·16
0·3699	0·3909	0·3612	0·0210	0·17
0·3877	0·4061	0·3038	0·0184	0·17
0·4585	0·4765	0·2496	0·0180	0·17

In the foregoing, it has been assumed (*a*) that the compounds are formed from one molecule of each constituent, (*b*) that the "hydrocarbons" in the picric acid series and the nitro-compound in the aniline series have no effect on the partition except in so far as they form compounds, (*c*) that no association of picric acid or of aniline occurs in chloroform, and (*d*) that neither picric acid nor aniline combines with chloroform. Assumption (*a*) is justified, since recalculation of the numbers for a 2 : 1 or 3 : 2 combination gives values of K much less constant than those quoted. As regards (*b*), it is known that in aqueous solution considerable effects on the solubility or partition coefficient of a substance may be produced by small addition of a second, these effects corresponding to Rothmund's theoretical equation $\log (C_0/C) = kC_a$, where, for partition experiments, C_0 and C represent the concentrations of the first substance in the pure solvent and in a solution containing C_a of the second substance, the two solutions being such as exist in equilibrium with the same aqueous solution of the first substance (Rothmund, *Z. physikal. Chem.*, 1909, **69**, 523; Dawson, J., 1901, **79**, 493, 1069; Debye and McAulay, *Physikal. Z.*, 1925, **26**, 22). It was necessary, therefore to see whether the magnitude of such "solvent" effects with un-ionised substances in organic solvents was such as to affect our results. The measurements were carried out as described on p. 1449, but, instead of the "hydrocarbon" or nitro-compound, substances not expected to combine with picric acid and aniline were used. Solubility depressions were found and "depression constants" were calculated as $K_d = (C_0 - C)/CC_a$, a form of Rothmund's equation applicable to the dilute solutions used. It is to be noticed that when the concentration change caused by an added substance is small compared with the original concentration, the expression for K (p. 1447) becomes identical with that for K_d except for the sign of the numerator, which represents an increase in the concentration in the case of K, but a decrease for K_d. It is thus impossible to say whether a small value for K corresponds to the formation of a small amount of compound, or whether it represents a small solubility exaltation. The values of K_d are collected on p. 1451; the details for picric acid and *cyclo*hexane are given below.

C_a.	C_0.	C.	K_d.	C_a.	C_0.	C.	K_d.
0·301	0·0311	0·0271	0·49	0·447	0·0415	0·0341	0·49
0·379	0·0297	0·0252	0·47	0·454	0·0249	0·0206	0·46
0·447	0·0336	0·0277	0·48	0·454	0·0360	0·0296	0·48

As regards assumption (*c*), the molecular weights of picric acid and aniline in chloroform have not been determined, but our partition results can be used to show whether there is appreciable polymerisation in chloroform, if we know the proportion of un-ionised solute in the aqueous phase. Von Halban and Ebert (*Z. physikal. Chem.*, 1924, **112**, 359), on the basis of Bjerrum's relation between activity and ionic strength, have arrived at values of the dissociation of picric acid which give a satisfactory interpretation of solubility and freezing-point data. Using their values in conjunction with the numbers on p. 1448, we find that the ratio of the concentration of picric acid in the chloroform phase to that of undissociated picric acid in the aqueous phase increases steadily with concentration from 21·70 to 22·86. Thus picric acid is either slightly associated in chloroform or its activity coefficient decreases with concentration even in such dilute solutions (0·016—0·045*N*) as we used. If it is assumed that this effect is due wholly to association, the association constant, *i.e.*,

$$(\text{conc. of bimolecular form})/(\text{conc. of unimolecular form})^2,$$

is found to be unity and constant within 10%. The effect of this amount of association on the equilibrium constants would not be more than 4%, and is negligible.

In the case of aniline the dissociation in the aqueous phase is negligible, and although the variation of the partition coefficient is slightly beyond the error of experiment, it is evident that such association as occurs in chloroform cannot affect our numbers.

As regards assumption (*d*), although combination of solute with solvent would have a great effect on the actual values of the constants, it would not alter their relative order.

Picric acid.

" Hydrocarbon."	*K*.	*K* (corr.).
Benzene	0·08	0·09
Toluene	0·09	0·12
o-Xylene	0·12	0·16
m- „	0·10	0·14
p- „	0·12	0·16
Mesitylene	0·12	0·18
Naphthalene	2·17	
α-Methylnaphthalene	2·76	
β- „	3·44	
Tetrahydronaphthalene	0·20	0·26
Nitrobenzene	0·56	
m-Dinitrobenzene	1·03	
o-Nitrotoluene	0·41	
p- „	0·57	
2 : 4-Dinitrotoluene	0·67	
2 : 4 : 6-Trinitrotoluene	1·02	
α-Nitronaphthalene	1·02	
Bromobenzene	0·06	0·09
o-Dichlorobenzene	0·07	0·10
p- „	0·00	0·03
α-Bromonaphthalene	0·17	0·23
	K_d.	
Hexane	0·54	
*cyclo*Hexane	0·48	
Hexachlorobenzene	0·38	
Carbon tetrachloride	0·27	

Aniline.

Nitro-compound.	*K*.	*K* (corr.).
2 : 4 : 6-Trinitrotoluene	0·56	
1 : 5-Dinitronaphthalene	0·57	
p-Dinitrobenzene	0·18	
m- „	0·17	
2 : 4-Dinitrotoluene	0·10	0·15
m-Bromonitrobenzene	0·02	0·06
p-Chloronitrobenzene	0·01	0·03
α-Nitronaphthalene	(see K_d)	0·02
Nitrobenzene	(see K_d)	0·01

Added substance.	K_d.	K_d (corr.).
α-Nitronaphthalene	0·04	[see *K* (corr.)]
Nitrobenzene	0·01	[see *K* (corr.)]
o-Nitrotoluene	0·05	0·01
p- „	0·06	0·02
p-Xylene	0·19	0·15
α-Methylnaphthalene	0·15	0·09
β- „	0·15	0·09
Toluene	0·15	0·12
α-Bromonaphthalene	0·12	0·06
Carbon tetrachloride	0·12	0·10
Naphthalene	0·11	0·07
p-Dichlorobenzene	0·09	0·06
o- „	0·09	0·06
Bromobenzene	0·08	0·05

A correction should be applied to all the constants on account of the difference between the molecular volumes of chloroform and of the " hydrocarbons " and nitro-compounds. In the presence of the latter, which all have greater molecular volume than chloroform, a smaller concentration of picric acid or aniline is required to produce a given molecular fraction than is necessary in chloroform alone, so that for equilibrium with a given aqueous solution, a smaller concentration of the solute is required in the mixed solvent than in chloroform alone, quite apart from any other physical or chemical effect of the " hydrocarbon " or nitro-compound on the solute. In dilute solution this effect would give a depression constant equal to $(V_a - V)/1000$, where V_a and V are the molecular volumes of the added substance and of chloroform respectively. Thus, to get the specific effect of the added substance the depression constants must be diminished, and the equilibrium constants increased, by this quantity. The correction varies from 0·02 to 0·06 and is of importance only where very small constants are found. In particular, the depression constants found for nitrobenzene and α-nitronaphthalene with aniline become small equilibrium constants, since in these cases the depression of the aniline concentration found is less than that due to the molecular-volume effect. All the constants are collected in the table, K (corr.) and K_d (corr.) denoting values corrected for the molecular-volume effect.

Discussion.

No simple explanation of the depression constants is possible. The degree of polymerisation of picric acid and of aniline in chloroform has been shown to be small, and is insufficient to account for the solubility depression as due to depolymerisation caused by the added substance. If the cause were dissociation of a compound between solute and chloroform, the maximum possible effect (*i.e.*, when the solute is almost completely combined with chloroform and the added substance does not combine with the solute at all) would produce a depression constant equal to $V_a/1000$, *e.g.*, 0·13 in the case of hexane, whereas the actual value of K_d (corr.) for picric acid and hexane is 0·48. Although in the aniline series the constants are of the order required by this explanation, practically complete combination of aniline with chloroform is incompatible with the vapour-pressure measurements of Weissenberger, Schuster, and Lielacher (*Monatsh.*, 1925, **46**, 303).

Further, an additive solubility effect would also produce a maximum K_d of $V_a/1000$, and so is excluded for picric acid though not for aniline. Other possible causes for the depression effect are variation in the mutual solubility of water and chloroform in the presence of solutes, and departure from ideality in the mixtures of chloroform, picric acid or aniline, and added substance. As regards the former, it is known that such variations can have considerable effect (compare Beilstein's Handbuch, Vol. VI, 267; Kendall, *Proc. Roy. Soc.*, *A*, 1911, 204); and as regards the latter, the vapour-pressure curves for mixtures of chloroform with some of the addenda are known and show departures from ideality which are not likely to be diminished by the presence of a third substance.

The existence of the depression effect makes it impossible to lay any stress on small variations in our constants. Nevertheless, certain regularities appear from which it seems likely that less confusion is caused than might be expected. In the aniline series, excluding compounds containing more than one nitro-group, the constants for aromatic substances can be calculated with an average error of less than 0·01 from the values found for toluene and naphthalene, by assigning specific values to the substituent groups irrespective of their positions, *viz.* :

NO_2, + 0·10; Br, + 0·04; Cl, + 0·03; and CH_3, − 0·03.

[*E.g.*, K (corr.) for naphthalene = − K_d (corr.) = − 0·07; then K (corr.) for nitronaphthalene = 0·10 − 0·07 = 0·03. Found, 0·02. For α-methylnaphthalene K (corr.) = − 0·03 − 0·07 = − 0·10, then K_d (corr.) = 0·10. Found, 0·09.] Moreover, it is to be noticed that these values are in practically the same order as the dipole moments produced by the groups when attached to a benzene nucleus, *viz.*, − 3·8, − 1·4, − 1·5, and + 0·4. With two or more nitro-groups the calculated constants are much smaller than those found.

Although the evidence is not sufficient to establish the additive relation with certainty, it does indicate that the same mechanism is operative in producing both small increases and small decreases of the aniline concentration. Since the latter must be due to physical causes, it appears that small values of K in the aniline series are probably measures of solubility exaltation, rather than of chemical combination.

The results are best interpreted by the view that groups with a negative charge substituted in benzene or naphthalene, cause an increase in the solubility of aniline by their attraction for its positively charged hydrogen atoms, while substitution of a methyl group, by increasing the number of positively charged hydrogen atoms in the hydrocarbon, has an opposite effect. With two or more nitro-groups a new influence appears—presumably combination. The production of colour by mononitro-compounds and aniline, *e.g.*, nitrobenzene and aniline (Ostromisslensky, *Ber.*, 1911, **44**, 268), may be quoted against a purely physical interpretation of the constants for such cases; but it is now generally recognised that chemical action is not the sole cause of colour change (see also p. 1455).

In the picric acid–" hydrocarbon " series no additive relation appears. The methyl group, except in nitro-compounds, causes an increase in the constant—very small in benzene derivatives but large in derivatives of naphthalene. Halogens, up to two atoms, have little effect in benzene derivatives, but six atoms (hexachlorobenzene) change the positive constant for benzene into a large depression constant, while one halogen atom in naphthalene diminishes the constant greatly. The constants for benzene and its methyl and mono- and di-halogen derivatives may, of course, be due to solubility exaltation, but there is no evidence for this view, such as there was in the aniline series. The nitro-group has a large effect in increasing the constants for benzene derivatives, but an opposite effect in naphthalene, and among nitro-compounds, an ortho-methyl group causes a diminution in the constant but a para-methyl group has little effect. The comparatively large changes in the constant for derivatives of naphthalene are noteworthy, and indicate that any extension of this work should be with derivatives of naphthalene and other polynuclear hydrocarbons.

The effect of the nitro-group is anomalous in that it produces in all benzene derivatives a change opposite in sign to that produced by halogens and of the same sign as that produced by methyl. Further, although colour appears in solutions where certainly very little compound can be present, *e.g.*, picric acid with benzene, the solutions of picric acid with nitro-compounds give practically no colour, though the constants found are comparatively large. On making up chloroform solutions of picric acid with *m*-dinitrobenzene, α-nitronaphthalene, and naphthalene in such concentrations that, according to our constants, equal amounts of compound were produced, a barely perceptible tint was produced with the first, a faint colour by the second, and an intense colour by the last. Another difference is that, whereas solid compounds of picric acid with numerous benzenoid hydrocarbons have been isolated, where the amount of combination in solution is certainly small, we have been able to find in the literature no examples of compounds of picric acid with nitro-compounds. Our attempts to make them have failed except in the case of α-nitronaphthalene, where the *compound* can be made in the usual way and consists of pale yellow needles, m. p. 71° [Found : $C_6H_3O_7N_3$, 56·5. $C_{10}H_7{\cdot}NO_2,C_6H_2(NO_2)_3{\cdot}OH$ requires $C_6H_3O_7N_3$, 56·9%]. It is noteworthy that *m*-dinitrobenzene and 2 : 4 : 6-trinitrotoluene, which do not form such compounds, have practically the same values of *K* as α-nitronaphthalene.

These facts lead to the view that combination of picric acid with nitro-compounds is in general of a type different from that between picric acid and hydrocarbons (referred to later as " nuclear " combination). Since dipole association must occur to some extent in solutions of nitro-compounds, and does not necessarily produce colour [*e.g.*, solutions of picric acid in several solvents are colourless (Beilstein's Handbuch, Vol. VI, p. 268), and many polynitro-compounds are colourless (Hantzsch, *Ber.*, 1906, **39**, 1096)], it seems probable that our constants represent the dipole association between a nitro-group of the picric acid and a nitro-group of the added substance. A consistent view of our results is obtained by the assumption of two modes of combination of picric acid: (1) " nuclear " combination, resulting in colour and leading generally to the isolation of solid compounds, and (2) dipole association, having neither of these effects. The nitro-group in the " hydrocarbon," being strongly negative, acts like the halogens to diminish the nuclear combination and so hinders the development of colour, but increases K on account of dipole association. A methyl group para to a nitro-group should have little effect, but what there is should be in the same direction as for a methyl group in a hydrocarbon; but a methyl group ortho to a nitro-group should have a considerable diminishing effect on dipole association, since the two groups would weaken each other's fields (compare *o*-nitrotoluene, 2 : 4 : 6-trinitrotoluene). Naphthalene, having a large power of nuclear combination, would not lose it all on the substitution of one nitro-group, so that the production of some colour and the isolation of a solid compound in the case of α-nitronaphthalene are to be expected. In this case it appears from the K values that the diminution of nuclear combination more than compensates for the dipole association.

The fact that the association constant we find for picric acid in chloroform (p. 1450) is of the same order as the values of K found for picric acid and polynitro-compounds, is in agreement with this view. Further, Jones and Bury (J., 1925, **127**, 1950) state that their cryoscopic results for picric acid, 2 : 4 : 6-trinitrotoluene, and α-nitronaphthalene indicate slight association in benzene but none in nitrobenzene. This also is possible on our view, since very little combination would occur between these substances and benzene, whereas in nitrobenzene, greater combination with solvent would occur, which, though small, could mask the slight association.

The results with picric acid have some bearing on discussions of the compounds formed by polynitro-compounds and bases, for they show that compounds of the nuclear type, involving an interaction between a nitro-group and an aromatic nucleus, are intensely coloured—colour being perceptible in solutions where, according to our experiments, the concentration of the compound may be as low as $N/1000$. So that, in the case of nitro-compounds and bases, where more than one mode of action is possible, colour may be due to the existence of a small amount of nuclear combination, even if the greater part of the interaction is of another kind. On this account, Pfeiffer's conclusion (*Annalen*, 1916, **412**, 253), that compounds of nitro-compounds with bases are of the nuclear type, which depends wholly on arguments from colour, is open to some doubt. This objection does not apply to the evidence from colour quoted by Bennett and Willis (J., 1929, 258, 259) in connexion with compounds formed by saturated bases, where nuclear combination is excluded.

As regards the detailed formulation of the union between a nitro-group and an aromatic nucleus, the only deduction we can make is that the latter appears to act as donor, for the directions of the effects of methyl and of halogens in the picric acid–" hydrocarbon " series are such as would be expected on this view. The formulation proposed by Bennett and Willis is, to this extent, supported by our results. It seems possible that further work in the naphthalene series, where the larger constants diminish the uncertainty due to the solvent effect, and the constitutional effects are greatest, might throw light on this problem.

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