N O T E S

Thermodynamics of Ionization of Substituted Benzoic Acids: 3, 4, 5-Trimethoxybenzoic Acid

By R. K. CHATURVEDI and Sarvagya S. KATIYAR

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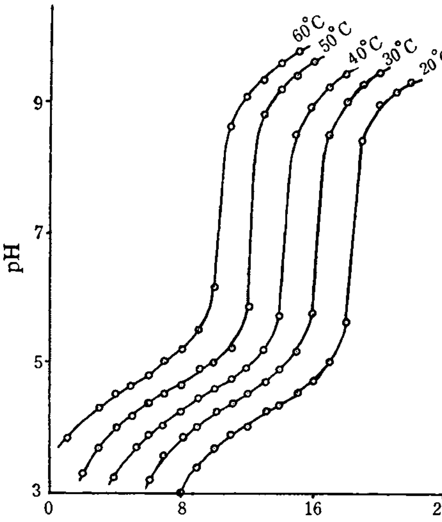
The studies on the dissociation of carboxylic acids at different temperatures were undertaken by us originally in connection with our studies on the interaction of these acids with the metal ions[1]. The knowledge of dissociation constant of these acids which we found essential to have, led to some interesting conclusions regarding the influence of the substituents on the dissociation of the acids. It was, therefore, considered of value to examine this latter aspect by studying a number of substituted benzoic acids. The present paper reports the pH metric determination of dissociation constant of 3, 4, 5-trimethoxybenzoic acid in the temperature range 20~60°C and the thermodynamic functions associated with the dissociation of this acid.

Experimental

3, 4, 5-Trimethoxybenzoic acid was synthesized by the method described in the literature[2]. Recrystallization from water gave a product of satisfactory purity with m. p. 169°C (reported 168°C[3]). Solutions of the acid prepared in double distilled water were titrated pH metrically against standard sodium hydroxide solution prepared from a Merck "Guaranteed" reagent. All the pH metric measurements were made with a Beckmann pH meter model G employing the extension electrode assembly. The arrangement for the temperature control was the same as described earlier[4].

Results and Discussion



Volume of NaOH added, ml.

Fig. 1

Figure 1 gives the typical set of results on the pH metric titration of the acid against standard sodium hydroxide solution. The curves refering to different temperatures (indicated in the body of the Fig. 1) show a marked inflexion characteristic of the carboxylic acids. The values of the classical dissociation constant of the acid at different temperatures were calculated from the data in Fig. 1 by the method discussed by Britton[5]; these values at various temperatures are returned in Table I, column 2. The values of the thermodynamic dissociation constants of the acid were obtained by using the modified Debye-Hückel equation[6] and with the values of the Debye-Hückel constant A due to Bates and coworkers[7]; these values are presented in column 3 of

TABLE I. DISSOCIATION CONSTANT OF 3, 4, 5-TRIMETHOXYBENZOIC ACID

Temperature °K	pk*	pK*
293	4.17	4.19
303	4.27	4.30
313	4.36	4.38
323	4.49	4.53
333	4.62	4.65

* Mean deviation of the order of ±0.05

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Table I. It may be seen from these data that increase in the temperature causes an increase in the pK of the acid; the values, for example, are 4.30±0.07 and 4.65±0.05 at 30 and 60°C respectively.

By applying the method of least squares the following equation,

$$-\ln K = \frac{7430.55}{T} - 44.24 - 9.725 \times 10^{-2}\, T \qquad (1)$$

was derived[8] which governed satisfactorily the variation of pK with T. From the values of the constant of Eq. 1 the thermodynamic functions such as change in free energy, entropy, enthalpy and heat capacity were computed from the well known thermodynamic relationships[8]; the values of these quantities at different temperatures are given in Table II.

TABLE II. THERMODYNAMIC FUNCTIONS OF DISSOCIATION OF 3, 4, 5-TRIMETHOXYBENZOIC ACID

Temperature °K	ΔF kcal./mol.	ΔH kcal./mol.	ΔS cal./mol. deg.	ΔC_p cal./mol. deg.
293	5.59	−1.83	−25.33	−113.24
303	5.87	−2.98	−29.19	−117.10
313	6.18	−4.17	−33.06	−120.96
323	6.53	−5.39	−36.93	−124.83
333	6.92	−6.66	−40.79	−128.69

For a number of substituted benzoic acids it was shown by Shorter and Stubbs[9] that the total effect of the substituents in different positions on ionization of the parent acid is roughly the sum of the individual contributions of the substituents; this is especially true in case the substituent occupies meta or para positions. These observations indicating the additivity of pK have been theoretically well discussed by a number of workers[10]. It is of interest to examine the applicability of the additivity principle to the data on pK of the 3, 4, 5-trimethoxybenzoic acid. From the data in column 3 of Table III, it may be seen that the substitution of a methoxy group in meta position lowers the pK of benzoic acid by 0.12 unit while that in the para position enhances the same by 0.26 unit. These consideration suggest, by the application of the above principle, a value of 4.23 at 25°C for pK of the acid under investigation is good agreement with our values in this temperature range.

TABLE III. OBSERVED AND CALCULATED VALUES OF pK AND ΔF

Acid	pK	Contribution to pK	ΔF kcal./mol.	Contribution to ΔF
Benzoic	4.21	—	5.74	—
m-Methoxybenzoic	4.09	−0.12	5.58	−0.16
p-Methoxybenzoic	4.47	+0.26	6.09	+0.35
3, 4, 5-Trimethoxybenzoic	4.23	+0.02	5.77	+0.03

Further, the change in free energy of ionization obeys additivity principle in cases in which steric effects are not significant. Even in certain cases when steric effects are considerable the additivity of ΔF is maintained presumably because of the compensation of the steric effects on ΔH and $T\Delta S$[11]. Besides steric effects, the solvent effects are also known to influence the additivity of ΔF. But the large size of –COO group and the fact that the charge is carried by both the oxygen atoms because of resonance, minimizes the possibility of a significant solvent effect in case of benzoic acids[12,13]. The data in column 4 of Table III gives the ΔF values for benzoic and methoxybenzoic acids. From the contribution to ΔF of methoxy group in *p*- and *m*-positions we get a value of 5.77 kcal./mol. at 25°C in good agreement with our value in the same temperature range. The application of the additivity principle to ΔF values might lead to the view that purely polar effects arising out of inductive influences are operative. But the consideration of the ΔS value clearly shows that this is not the case. It is known that purely polar effects hardly cause any change in ΔS. Thus for example ΔS for *m*-methoxybenzoic acid (−18.5) and *p*-methoxybenzoic acid (−18.5) are hardly different from the value of −18.9 for benzoic acid whereas the value of ΔS for 3, 4, 5-trimethoxybenzoic acid is significantly different from that of benzoic acid.

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Chemistry Department
Indian Institute of Technology
Kanpur, India (*S. S. K.*)

Harcourt Butler Technology Institute
Kanpur, India (*R. K. C.*)

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Preparation of 2-Bromo-2-nitro-pentylamine

By Mitsuo Masaki and Masaki Ohta

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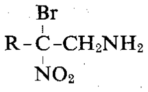
Only a few β-halogeno-β-nitro amines are known to be the products of the addition of ammonia or amines to α-halogeno-α-nitro-olefines. The reaction of β-bromo-β-nitrostyrene with ammonia gives 2-bromo-2-nitro-1-phenylethylamine[1], and the reaction of 1-bromo-1-nitrobutene with ammonia or amines gives unstable adducts[2], but in most cases the products have not been characterized.

We wish to report the preparation of 2-bromo-2-nitro-pentylamine (I, $R=C_3H_7$) required for other work by a new method, which involves the reaction of 1,2-dibromo-2-nitropentane with potassium phthalimide.



$$R-\underset{NO_2}{\overset{Br}{C}}-CH_2NH_2$$

(I)

2-Nitropentene-1[3] (b. p. 73~74°C/45 mmHg), which was prepared in a good yield by the direct dehydration of 2-nitropentanol using the technique of Buckley and Scaife[4], was converted, by the addition of bromine in chloroform, into 1,2-dibromo-2-nitropentane (II), a colorless oil with a b. p. of 99~100.5°C/7.5 mmHg. (Found: N, 4.93; C, 21.87; H, 3.48. Calcd. for $C_5H_9O_2 \cdot NBr_2$: N, 5.09; C, 21.82; H, 3.27%).

The dibromide II was heated under reflux with potassium phthalimide in acetone for 30 hr., cooled to room temperature, and filtered to remove the potassium bromide. After the bulk of acetone had been removed by distillation, the resultant syrup was crystallized by the addition of ethanol and then recrystallized from ethanol, giving colorless prisms of 1-phthalimide-2-bromo-2-nitropentane (III). M. p. 90~92°C (yield 70%). (Found: N, 8.35; C, 45.68; H, 3.99. Calcd. for $C_{13}H_{13}O_4N_2Br$: N, 8.22; C, 45.75; H, 3.81%).

The reaction of III with hydrazine hydrate in ethanol gave I ($R=C_3H_7$), which was isolated as its stable hydrochloride IV; the latter was then recrystallized from ethylacetate or ethanol-ether to give colorless needles with a m. p. of 126~127°C (yield 63%). (Found: N, 11.35; C, 23.84; H, 5.31. Calcd. for $C_5H_{11}O_2N_2Br \cdot HCl$: N, 11.31; C, 24.24; H, 4.85%). The infrared absorption band in IV at 1440 cm^{-1}, which has disappeared in I ($R=C_3H_7$), is ascribed to $-CH_2\overset{+}{N}H_3$; therefore, I ($R=C_3H_7$) is not the alternative nitro-amine, 1-bromo-2-amino-2-nitropentane.

This nitro-amine (I, $R=C_3H_7$) was also characterized by its conversion into the picrate (m. p. 156~157°C. Found: N, 15.64. Calcd. for $C_{11}H_{14}O_9N_5Br$: N, 15.86%), its reduction on Raney nickel to the corresponding diamine[5] (picrate m. p., 224~227°C. Found: N, 19.79; C, 36.79; H, 3.80. Calcd. for $C_{17}H_{20}N_8O_{14}$: N, 20.00; C, 36.43; H, 3.57%), its benzoylation to give the *N*-benzoyl compound of I ($R=C_3H_7$) (m. p. 90~91°C. Found: N, 8.63. Calcd. for $C_{12}H_{15}O_3N_2Br$: N, 8.89%), and its reaction with phenyl isocyanate to give the corresponding derivative of urea (m. p. 103~104°C. Found: N, 12.36. Calcd. for $C_{12}H_{16}O_3N_3Br$: N, 12.73%).

The applicability of this method in the preparation of other β-bromo-β-nitro-alkylamines (I) is now under study in this laboratory.

We are indebted to Mr. Keiji Naruse for performing the microanalyses.

Laboratory of Organic Chemistry
Tokyo Institute of Technology
Meguro-ku, Tokyo

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Decomposition of the Sydnone Ring

By Hiroshi Kato and Masaki Ohta

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In Part VII of the authors' report on mesoionic compounds[1], it was reported that 3-phenyl-4-iodosydnone (I, X=I) gives the corresponding 4-nitro derivative (I, $X=NO_2$) on treatment with fuming nitric acid, while decomposition of sydnone ring takes place when 3-phenyl-4-chlorosydnone (I, X=Cl) is treated by the same method. The decomposition product has now been proven to be *p*-nitrooxanilic acid (II). When the corresponding 4-bromo derivative (I, X=Br) was treated with

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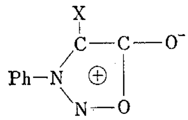
[1] M. Ohta and H. Kato, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **78**, 1653 (1957).

fuming nitric acid by the same procedure, an oily substance was formed which could not be identified. In connection with these reactions, the action of fuming nitric acid on 3-phenylsydnone (I, X=H) was studied, and the reaction product was found to be 2,4-dinitrophenol. It is remarkable that so many types of reaction are observed, depending on the nature of the substituents in the 4 position of the sydnone ring.

The reaction mechanism might be suggested as follows: in the case of the reaction with the 4-iodo derivative, the iodine atom of the sydnone, which readily splits off as a cation[1,2], is replaced by a nitronium cation to give 3-phenyl-4-nitrosydnone. With the 4-chloro derivative, the 4 position is first oxidized by fuming nitric acid; the ring is then decomposed further to give *p*-nitroöxanilic acid. The first step of the reaction of 3-phenylsydnone with fuming nitric acid would not be the nitration of the sydnone ring, as it has been found[3] that concentrated nitric acid does not nitrate the sydnone ring in either acetic acid or acetic anhydride and that 3-phenyl-4-nitrosydnone is unaffected in fuming nitric acid. 3-Phenylsydnone is either directly oxidized[4] and nitrated or is first hydrolyzed to phenylhydrazine[5], which is later oxidized and nitrated to give 2,4-dinitrophenol.

A sample of 3-phenyl-4-iodosydnone was unchanged after being kept for three years in a dark place, but 3-phenyl-4-chloro- and -4-bromosydnone were nearly completely decomposed to the corresponding hydrogen halide salts of phenylhydrazine under the same conditions.



I

p-NO_2-C_6H_4-NHCOCOOH

II

Experimental

Reaction of 3-Phenyl-4-chlorosydnone with Fuming Nitric Acid.—To fuming nitric acid (100 ml., sp. gr., 1.52), was added 3-phenyl-4-chlorosydnone (10 g.) portionwise with stirring, while the solution was cooled by ice. After an hour, the solution was diluted with ice-water, and the pale yellow precipitate which separated out was collected (8 g., m. p. 204°C (decomp.)). Recrystallization from water gave analytically pure *p*-nitroöxanilic acid as white silky needles, m. p. 210°C (decomp.). It was identical in melting point and mixed melting point with *p*-nitroöxanilic acid.

Found: C, 46.02; H, 3.13; N, 13.44. Calcd. for $C_8H_6N_2O_5$: C, 45.72; H, 2.83; N, 13.33%.

Reaction of 3-Phenylsydnone with Fuming Nitric Acid.—One gram of 3-phenylsydnone was added in small portions to fuming nitric acid (10 ml., sp. gr., 1.52) with stirring and cooling. After an hour, the mixture was diluted by the addition of water. Concentration of the solution in vacuo afforded slight brown prisms (0.1 g., m. p. 109°C). Recrystallization from ethanol gave white prisms, m. p. 113°C, undepressed on admixture with an authentic specimen of 2,4-dinitrophenol.

Found: N, 15.07. Calcd. for $C_6H_4N_2O_5$: N, 15.22%.

Reaction of 3-Phenyl-4-bromosydnone with Fuming Nitric Acid. — When 3-phenyl-4-bromosydnone was treated with fuming nitric acid under a variety of conditions, the reaction product was a brown oily substance. A violent explosion took place during the concentration, so further investigation of this substance was abandoned.

Self-decomposition of 3-Phenyl-4-halogenosydnone.—A sample of 3-phenyl-4-chlorosydnone which had been kept for three years in a dark place at room temperature was recrystallized from ethanol to give phenylhydrazine hydrochloride as white leaflets, m. p. 222°C (decomp.).

Found: N, 19.35. Calcd. for $C_6H_9N_2Cl$: N, 19.38%.

Dibenzoyl derivative: white needles, m. p. 177°C, undepressed on admixture with an authentic specimen of *N,N'*-dibenzoylphenylhydrazine.

Similarly, from a sample of 3-phenyl-4-bromosydnone which had been kept under the same conditions, phenylhydrazine salt (presumably the hydrobromide) was obtained. Its dibenzoyl derivative was identical in melting point and mixed melting point with *N,N'*-dibenzoylphenylhydrazine.

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Laboratory of Organic Chemistry
Tokyo Institute of Technology
Meguro-ku, Tokyo

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