

Summary

1. The specific heats of twelve aromatic hydrocarbons have been measured over a wide range of temperatures. The heats of fusion of seven of these compounds have also been determined.

2. The entropies of the twelve hydrocarbons have been calculated from these heat capacity data. The results thus obtained have been found to agree in most cases with the values predicted by means of a simple, empirical equation.

3. The corresponding free energies have also been calculated and certain regularities noted. The free energy change in the hydrogenation of benzene to give cyclohexane has been derived in two different ways.

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THE ACTION OF DIAZOMETHANE ON BENZOIC AND SUCCINIC ANHYDRIDES, AND A REPLY TO MALKIN AND NIERENSTEIN

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The memoir by Malkin and Nierenstein¹ contains some statements requiring comment.

(1) **The Course of the Interaction of Diazomethane and Acid Chlorides.**—The implication of these authors that the merit of experiments on the interaction of benzoyl chloride and diazomethane is directly proportional to the yield of ω -chloro-acetophenone obtained is quite unwarranted. In our work, for example, we were not trying to obtain the chloro-ketone, but rather to isolate the first stage and product of the reaction, and, with this end in view, we operated at a low temperature and, for reasons that appear in the sequel, kept the diazomethane in excess.² Under these circumstances benzoyl chloride is rapidly and completely transformed into diazo-acetophenone, and evolution of nitrogen is evident.

Therefore, we have the reaction



The resulting hydrogen chloride, reacting with the diazomethane in excess, must then give methyl chloride and nitrogen



Thus when benzoyl chloride (1 mole) is added to a cold ethereal solution of diazomethane (2 moles), the reaction is undoubtedly represented by the equation



¹ Malkin and Nierenstein, *THIS JOURNAL*, **52**, 1504 (1930).

² Bradley and Robinson, *J. Chem. Soc.*, 1317 (1928).

We think this so obvious that experimental confirmation of the formation of methyl chloride is unnecessary; nevertheless, it is hoped to remedy the omission in the near future.

We must further point out that our view of the course of the reaction is based on this ready formation of an almost quantitative yield of diazo-acetophenone, and *not* on Experiment V of Bradley and Schwarzenbach,³ to which Malkin and Nierenstein attribute an importance not claimed in the original. This and analogous experiments must be carried out accurately under various conditions before the discussion can be profitably continued. Nevertheless, it should be stated at once that the volume of nitrogen at N. T. P. theoretically obtainable from the diazomethane used by Bradley and Schwarzenbach is 1355 cc. as originally computed, and not 1772 cc. as now corrected, albeit erroneously, by Malkin and Nierenstein.

Equations I and II are summarized in III, but, if the concentration and total quantity of diazomethane is diminished, then, clearly, the less reactive diazo-acetophenone may be decomposed by accumulated hydrogen chloride



Equations I and IV are summarized by the following



On the basis of this theory, it is easy to devise a process which will give the maximum yield of ω -chloro-acetophenone. In the first place, the total amount of diazomethane used should be restricted to the minimum requisite, and it should be slowly added to a solution of the acid chloride. In this way Reaction I should occur and II should be avoided, since diazomethane is not present in significant concentration. Time must be allowed for the occurrence of IV, after which more diazomethane may be introduced. It is not surprising that, under such conditions, the net result may be represented by V. An elevated temperature, by increasing the velocity of the reactions, will shorten the time expended and allow of a relatively more rapid introduction of the diazomethane. We cannot agree that the course of the reaction is fundamentally different at 0 and at 18°. Thus the experiments of Malkin and Nierenstein, in which these requirements are fulfilled, afford strong support to our view of the mechanism of the reaction.

The sole existing evidence opposed to our hypothesis, and favoring the view of Malkin and Nierenstein that an addition compound of acid chloride and diazomethane breaks down directly into chloro-ketone and nitrogen, is furnished by the formation of the diaryldihalogenodioxanes of Lewis, Nierenstein and Rich,⁴ which, however, we have not been able to obtain. Naturally, we agree that a loose additive complex must be formed in the first phase of the reaction even on our hypothesis, and this view we have

³ Bradley and Schwarzenbach, *J. Chem. Soc.*, 2904 (1928).

⁴ Lewis, Nierenstein and Rich, *THIS JOURNAL*, 47, 1728 (1925).

already embodied in a discussion of the reaction on an electronic basis, using Langmuir's translation of the Thiele formula.^{2,5}

(2) **The Constitution of Diazo-acetophenone.**—Our statement that diazo-acetophenone was decomposed by iodine in cold alcoholic solution was based on a test-tube experiment. If a few crystals of iodine are added to a cold, concentrated alcoholic solution of the diazo-ketone, there is an immediate evolution of nitrogen, accompanied by a rise of temperature. Heat could not be produced unless the reaction started in the cold, and, in any case, the experiment was sufficient for our purpose, which was to show the analogy of diazo-acetophenone with other diazo compounds. The reaction seems to go better in methyl than in ethyl alcohol, and proceeds slowly in cold, dilute, alcoholic, ethereal or chloroform solutions. Diazo-acetophenone is quickly decomposed by cold solutions of hydrogen chloride, and it is, therefore, very unlikely that it possesses a full diazo-anhydride structure, as suggested by Malkin and Nierenstein. True diazo-anhydrides have been considered to be represented by such substances as diazo-benzoylacetone and ethyl diazo-acetoacetate, and these are very much more stable than is diazo-acetophenone toward hydrochloric acid and iodine. For example, Wolff⁶ stated that diazobenzoylacetone was soluble in cold, concentrated hydrochloric acid and was recovered unchanged on the addition of water. Similarly, ethyl diazo-acetoacetate was not attacked by iodine in hot chloroform solution.

The stabilizing effect of the carbonyl group on the diazo center in diazo-acetophenone is but one manifestation of a very general phenomenon; another example is found in ethyl diazoacetate. The relative resistance to the action of cationoid reagents, such as acids and halogens, varies from case to case, and is entirely in agreement with the hypothesis that such resistance is increased by the proximity of electron-attracting (cationoid) groups in the molecule. Such centers, by virtue of the positive field which they produce, quite naturally hinder the attack of cations or electron-seeking agents generally. We consider it very probable that there is a weak but definite *electrovalency* established between the oxygen of the carbonyl and the diazo group, either directly or through the medium of polar centers in the surroundings. The value of the poles on this *betaine* theory will depend on the constitutive factors; the substances, in fact, are probably anhydronium bases (Armit and Robinson),⁷ intermediate in constitution between the keto-diazo and enol-diazonium-betaine forms, and even the reputed true diazo-anhydrides may be accommodated in this scheme.

⁵ The formulation suggested and preferred by W. A. Noyes affords an equally satisfactory basis of discussion and this is also true of the cyclic formula, recently revived by Sidgwick.

⁶ Wolff, *Ann.*, **325**, 129 (1902).

⁷ Armit and Robinson, *J. Chem. Soc.*, **127**, 1604 (1925).

On the basis of the above suggestions, it is possible to arrange the aliphatic diazo compounds in a predicted order of stability toward cationoid agents. Placing the more reactive substances first, this should be: 2-diazopropane, diazoethane, diazomethane, phenyldiazomethane, ethyl α -diazopropionate, ethyl diazoacetate, diazo-acetone (in derivatives, substitution by alkyl should increase reactivity, and by halogen decrease reactivity, subject to influences of a steric nature in highly substituted compounds), diazophenylacetone, diazo-acetophenone (alkylated, more reactive, halogenated, carbethoxylated, and especially nitro derivatives, less reactive), diazo derivatives of aliphatic β -ketonic esters, diazo derivatives of aromatic β -ketonic esters, diazo derivatives of diketones (aliphatic and alkylated, more reactive; aromatic and nitroxylated, less reactive).

(3) **The Practical Aspect.**—Clibbens and Nierenstein⁸ gave very sparse details of their experimental procedure, so that it was quite possible to repeat their experiments and obtain divergent results. Neither the temperature nor the scale of the operations was specified, and the rate of addition of the diazomethane, the most vital detail, was not mentioned. We agree, of course, that, when a temperature is not indicated, the ordinary temperature is implied, but, for our own part, cooling in ice water is also a normal procedure in manipulating solutions of diazomethane.

We have made no direct criticism of the memoir of Clibbens and Nierenstein, other than that involved in the contrast with our own results; this divergence has been satisfactorily explained by the disclosure of further details of the original preparations.

Unfortunately, we cannot attempt to confirm later experiments of Nierenstein,⁹ the results of which are not in harmony with our views, because the preparation of the starting point—namely, 3,4,2',4',6'-pentamethoxydiphenylacetic acid—could not be repeated by one of us (R. R.), despite several attempts at intervals. The great importance of the reaction in synthetic work makes it desirable to add that, if a chloro-ketone is the object aimed at, then diazomethane should be led into a solution of the acid chloride until the former is present in excess after a short interval; any diazo-ketone should then be decomposed by the introduction of hydrogen chloride. In all other cases it is best to proceed through the diazo-ketone, and the acid chloride is then added to two or more molecular proportions of diazomethane.

(4) **The Historical Aspect.**—Nierenstein and his collaborators, working with acid chlorides and diazomethane over a long period, never observed the formation of the diazo-ketones, although the chlornitraldin of Dale and Nierenstein¹⁰ may have been ω -dialzo-*o*-nitro-acetophenone. The recogni-

⁸ Clibbens and Nierenstein, *J. Chem. Soc.*, 107, 1491 (1915).

⁹ Nierenstein, *ibid.*, 117, 1153 (1920).

¹⁰ Dale and Nierenstein, *Ber.*, 60, 1026 (1927).

tion that the product of the action of diazomethane on *o*-nitrobenzoyl chloride has this constitution is due to Arndt, Eistert and Partale.¹¹

This single instance escaped the attention of the present authors, who encountered another case in connection with work on the synthesis of malvidin. Memoirs on the interaction of benzoyl chloride and diazomethane were then published simultaneously by Arndt and Amende, and by the present authors. We have already taken an opportunity to admit the priority of Arndt, established by the diazo-*o*-nitro-acetophenone case, but the fact that we made the discovery of the formation of the diazo-ketones independently could not be gathered from a perusal of the references given by Malkin and Nierenstein.

(5) A short experimental section is appended, in which it is shown that diazomethane reacts with benzoic anhydride, forming methyl benzoate and diazo-acetophenone.



Using succinic anhydride and normally dried reagents, we could isolate nothing but methyl succinate. With exceptional precautions for the exclusion of water and alcohols, the products were methyl succinate, a diazo derivative and other unidentified compounds. The formation of methyl succinate was not found to depend on the preliminary hydrolysis to succinic acid, and evidently succinic anhydride and diazomethane give a complex which is quite abnormally reactive toward water or one of the simple alcohols.

Related observations have already been recorded. Herzig and Tichatshek¹² noticed that *m*-acetoxybenzoic acid gave with diazomethane in not quite anhydrous neutral media an 88% yield of *m*-methoxybenzoic acid (after hydrolysis of the ester) in forty-eight hours. It is difficult to believe that this is the result of consecutive hydrolysis and methylation, although this is the view put forward by Herzig and Tichatshek.

Again, Meerwein and Burneleit¹³ found that diazomethane does not react with cold acetone and only slowly with water and the simple alcohols. Nevertheless, a vigorous evolution of nitrogen occurs when the gas is led into acetone containing 10–15% of water. The main product is then asymmetric-dimethylethylene oxide, but isobutyraldehyde and methyl ethyl ketone are also formed. Arndt and collaborators have observed and discussed other cases of a similar kind.

Experimental

Benzoic Anhydride and Diazomethane.—Benzoic anhydride (1 mol., 4.5 g.), dissolved in ether (20 cc.) cooled to 0°, was added in one portion to ethereal diazomethane

¹¹ Arndt, Eistert and Partale, *Ber.*, **60**, 1364 (1927).

¹² Herzig and Tichatshek, *ibid.*, **39**, 1558 (1906).

¹³ Meerwein and Burneleit, *ibid.*, **61**, 1841 (1928).

(from 10.5 cc. of nitrosomethylurethan, 2.5 mols of CH_2N_2) at -5° . There was no immediate evolution of nitrogen, and none was observed on occasional inspection during three days, on the first two of which the solution was cooled in ice water. During the third day, the flask was allowed to reach the room temperature and the product was isolated by removal of the solvent in a current of dry air. The residual yellow oil was taken up in light petroleum and, on cooling in ice, pale yellow crystals (1.25 g., m. p. $42-44^\circ$) separated. The substance had all the properties of diazo-acetophenone (m. p. $48-48.5^\circ$), and, on recrystallization, separated as flat, pale yellow needles, m. p. $47-48^\circ$. Nitrogen was estimated by decomposition with 20% hydrochloric acid. (Found: diazo nitrogen, 19.0, 19.0. Calcd. for $\text{C}_8\text{H}_8\text{ON}_2$: N, 19.2.) Further crops of less pure material separated on evaporation of the mother liquor and, after complete removal of the solvent, the oil was distilled. The boiling point rose quickly to 195° and 1.4 g. of colorless methyl benzoate (b. p., 198°) was collected at $195-197^\circ$. There was only a small, dark brown residue in the flask.

Succinic Anhydride and Diazomethane.—The succinic anhydride employed was crystallized from ethyl acetate, and had m. p. $118-119^\circ$ (literature, 118°).

EXPERIMENT I.—Diazomethane (2.5 mols) from 50 cc. of nitrosomethylurethan was distilled into finely powdered succinic anhydride (9.0 g.) suspended in a little dry ether and cooled to -10° . There was no visible evolution of nitrogen but, despite the extremely sparing solubility of the anhydride in cold ether, the whole of the material passed into solution within three days, during the first two of which the reaction mixture was kept in ice, and, later, at the room temperature. The solution was evaporated in a current of dry air and the bright yellow oil which remained was dissolved in dry ether (25–30 cc.) and filtered from a small, insoluble residue (0.6 g.). When cooled in an ice-salt freezing mixture during thirty minutes, only a very small amount of a flocculent substance separated from the filtrate; the absence of unchanged succinic anhydride was thus assured.

For purposes of calculation, the filtrate was diluted to 90 cc. with dry ether, and portions of the solution ($Y-10$ cc. corresponded to 1 g. of succinic anhydride) were examined as follows.

(a) Ten cc. of Y was evaporated as completely as possible in a current of dry air. The residue weighed 1.2104 g. (X). This product gave very readily all the common reactions of diazo compounds. It was a bright yellow, mobile oil, from which nitrogen was evolved on heating or keeping. The same decomposition was effected by iodine, mineral acids and glacial acetic acid; the product reduced Fehling's solution. The alcoholic solution gave with a drop of aqueous sodium hydroxide a yellow color; this became red immediately on warming. Quantitatively, however, the matter assumed a different aspect (found in X : diazo nitrogen, 0.6%).

A specimen (Z), prepared and isolated in a similar manner, but kept in a vacuum over sulfuric acid, decreased continuously in weight during two weeks. In the meantime the color changed from pale yellow to light orange. (Found in Z : diazo nitrogen, 0.37%, and N by Dumas, N, 1.85%.)

(b) Seventy cc. of the ethereal solution (Y) was evaporated on the water-bath and the residual oil distilled from a glycerol bath in a current of dry carbon dioxide. The oil passed over almost completely at $90-92^\circ$ (14 mm.), leaving only a small brown residue; it was colorless (yield, 7.43 g.) and had a slight basic odor. Redistilled, the oil boiled constantly at $91-92^\circ$ (14 mm.), and solidified in contact with ice within a few minutes to a crystalline mass of stout prisms, m. p. $18-19^\circ$. On heating with hydriodic acid under Zeisel conditions, methyl iodide was formed at below 60° . (Found: CH_3O , 42.0, 42.0. Calcd. for $\text{C}_4\text{H}_4\text{O}_2(\text{OCH}_3)_2$, CH_3O , 42.5%.) Dimethyl succinate has m. p. 19° (18.5°); b. p. 80° (10–11 mm.) and 195.3° (corr.). Calculated for the original

g. of succinic anhydride, the yield of dimethyl succinate is 9.55 g., or 72.7% of the theoretical.

EXPERIMENT II.—Experiment I was repeated with the following modifications. Succinic anhydride (4.5 g.) and nitrosomethylurethan (25 cc.) were used. The methyl alcoholic potassium hydroxide was replaced by absolute *n*-butyl alcoholic potassium hydroxide. The access of moisture was completely prevented. The amount of diazomethane consumed was estimated.

Ether, already dried by phosphoric anhydride, was treated with sodium wire during three days and then redistilled over phosphoric anhydride. Toward the end of the diazomethane preparation, it was necessary to raise the temperature of the generating flask to 50–60°, in order to prevent the separation of solid matter which interfered with the diffusion of the alcoholic potash.

When the distillation was complete, about 15 cc. of the ethereal distillate, after being well mixed and allowed to settle, was decanted into a small, dry flask, and this was kept under the same conditions as the main portion (135 cc.), which contained finely powdered succinic anhydride (4.5 g.) in suspension. Contact of the solution with the atmosphere was reduced to a minimum by sealing the flasks with wax and inserting a capillary mercury seal between the flask and the usual calcium chloride tube. The reactants were kept at 0° during one day, and subsequently at the room temperature.

The rate of dissolution of the anhydride was markedly less rapid than under the conditions of Experiment I, and this was probably not the result of difference in the state of subdivision of the finely powdered anhydride. After three days the diazomethane content of the 15-cc. ethereal solution was determined, and after six days that of the main 135-cc. portion. In each estimation ethereal diazomethane solution was added to excess of benzoic acid dissolved in ether, and the excess estimated by titration with 0.1 *N* sodium hydroxide after dilution with much aqueous alcohol. The 15-cc. solution contained 0.0250 g. of $\text{CH}_2\text{N}_2/\text{cc.}$, and the 135-cc. solution contained 0.00645 g. of $\text{CH}_2\text{N}_2/\text{cc.}$

After six days a considerable amount of solid remained undissolved; this was collected and dried (1.72 g., m. p. 115–118°—a trace persists to 122°). It was, presumably, unchanged anhydride (m. p., 117–118°). The filtrate was evaporated in a current of dry air, and the diazo nitrogen content of the residue—a deep yellow oil, which lost nitrogen on keeping during a few hours—determined. (Found: diazo nitrogen, 2.4%.)

The remainder of the oil was distilled from a glycerine-bath in a current of carbon dioxide. Unlike the product of Experiment I, it was far from homogeneous; a colorless oil passed over at 87–103° (17 mm.), and a dark brown, oily residue remained which did not distil below 150° (17 mm.). The residue formed about one-half of the product. The distillate solidified to a colorless, well crystallized mass when cooled in ice. This had m. p. 19° and was found to consist of methyl succinate by comparison with an authentic sample.

The amount of diazomethane which reacts with a given weight of the anhydride is not precisely known, since decomposition of the diazomethane is proceeding simultaneously with the fall in concentration due to reaction with the anhydride, and the rate of decomposition is probably itself a function of the concentration. If, however, the concentration after three days is a fair average, then the data show that the molecular reacting ratio, diazomethane/anhydride, is approximately 2 (actually, 2.15).

Summary

1. Since diazomethane and benzoyl chloride react at 0° with great facility to yield diazo-acetophenone, this substance is regarded as the pri-

mary product of the reaction. The validity of the categorical summary of Malkin and Nierenstein's paper is questioned.

2. It is suggested that the formation of ω -chloro-acetophenone is a secondary process and the result of the action of hydrogen chloride on diazo-acetophenone. The special conditions prescribed by Malkin and Nierenstein are such as to favor this secondary process.

3. The interaction of benzoic and succinic anhydrides with diazomethane has been studied. The formation of methyl succinate in the latter case occurs in the presence of water (or methyl alcohol), but, in all probability, succinic acid (or methyl hydrogen succinate) is not an intermediate in the process.

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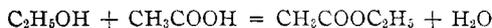
VAPOR PHASE ESTERIFICATION OF ACETIC ACID BY ETHYL ALCOHOL

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The object of this work was to determine the equilibrium concentration of ethyl acetate in the vapor phase esterification of ethyl alcohol by acetic acid according to the reaction



Of the various esterification reactions this is the one which has been most frequently studied in the vapor phase, but there does not appear to be any consistency in the values of the equilibrium constant reported in the literature. From experiments with zirconium oxide as the catalyst Mailhe and de Godon¹ concluded that the equilibrium constant was about 6.0 in the temperature range of 280–290°. Mulliken, Chappell and Reid,² in studying the formation of ethyl acetate in the presence of silica gel, obtained results which gave an equilibrium constant of 79.3 at 150°, although they believed the actual value to be considerably higher. These experimenters also observed a considerable variation in the equilibrium constant with temperature. By determining the composition of the vapor above a liquid equilibrium mixture of alcohol, acid, ester and water, Edgar and Schuyler³ obtained values of the equilibrium constant varying between 347 and 559 for the vapor phase in a temperature range of 72.6 to 77.6°, admitting the possibility of a considerable error. Recently

¹ Mailhe and de Godon, *Bull. soc. chim.*, **29**, 101 (1921).

² Mulliken, Chappell and Reid, *J. Phys. Chem.*, **28**, 872 (1924).

³ Edgar and Schuyler, *THIS JOURNAL*, **46**, 64 (1924).