increased strength of the hydrogen bonding in the latter compounds.

Most peaks below 1180 cm.$^{-1}$ are produced by vibrations involving the basic ring skeleton and the attached hydrogen atoms. These frequencies appear to be primarily related to the substitution pattern and are less dependent on the type of substituents. This is shown in Table IV in which, for convenience, these substances are classified as substituted benzenes in terms of their substitution type.

EXPERIMENTAL

Spectra were obtained in potassium bromide disks because of the insolubility of most of the compounds in suitable solvents. The instrument used was a Perkin-Elmer 21 double-beam recording spectrometer with a rock-salt prism.

Compounds. Substituted isatin oximes were prepared from the corresponding isatins[6-8] in the usual way.

N-Methylindoxyl oxime. N-Methyl-O-acetylindoxyl was dissolved in excess hot 2*N* sodium hydroxide under nitrogen. Sufficient aqueous hydroxylamine hydrochloride was then added to neutralize the solution. The oxime, m.p. 208°, was collected and crystallized from aqueous ethanol.

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(6) P. W. Sadler, *J. Org. Chem.*, **21**, 169 (1956).

(7) P. W. Sadler and R. L. Warren, *J. Am. Chem. Soc.*, **78**, 1251 (1956).

(8) D. G. O'Sullivan and P. W. Sadler, *J. Chem. Soc.*, 2202 (1956).

[CONTRIBUTION FROM THE PHYSICAL RESEARCH LABORATORY AND THE SPECTROSCOPY LABORATORY, THE DOW CHEMICAL COMPANY]

Evidence for Esters of *Aci*-Nitrocyclohexane as Intermediates in Production of Cyclohexanone Oxime

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Processes yielding cyclohexanone oxime by reactions of *aci*-nitrocyclohexane salts with an alcohol and an acid and with an alkyl halide were recently disclosed. It is proposed that these reactions proceed *via* an unstable ester of *aci*-nitrocyclohexane. To test this hypothesis, salts of *aci*-nitrocyclohexane were treated with alkyl sulfates. As anticipated, cyclohexanone oxime was the principal product. Attempts to isolate the esters in these reactions have failed. Titrimetric data suggest that the reaction of *aci*-nitrocyclohexane with alcohols is esterification. Only three types of reagents are known to convert *aci*-nitrocyclohexane or its salts to cyclohexanone oxime; in each case an ester of *aci*-nitrocyclohexane is a logical intermediate.

Hamann and Bauer obtained cyclohexanone oxime and an aldehyde or ketone by reaction of nitrocyclohexane with a base and a primary or secondary alkyl halide.[1] Welz and Weise obtained oximes, especially cyclohexanone oxime, by gradual addition of salts of the corresponding nitroparaffins to acidified alcohols.[2]

It is proposed here that the path of reaction in the first case involves formation of a salt of *aci*-nitrocyclohexane, its conversion to an ester of *aci*-nitrocyclohexane by reaction with the alkyl halide, and the rapid decomposition of this unstable ester to give cyclohexanone oxime and a carbonyl compound. In the second case it is proposed that the path of reaction involves formation of the *aci*-nitro compound on addition of the salt to the acid medium, esterification of the *aci* form, and decomposition of the ester.[3] If these hypotheses are correct, it follows that reaction of salts of *aci*-nitrocyclohexane with alkyl sulfates, which should effect alkylation of the *aci* form, will also produce cyclohexanone oxime.

It was found, as predicted, that reaction of methyl or ethyl sulfate with the sodium, potassium, or calcium salt of *aci*-nitrocyclohexane yielded cyclohexanone oxime as the principal product. Yields as high as 76% were obtained by reaction of methyl sulfate with the sodium salt of *aci*-nitrocyclohexane in methanol.

In an attempt to obtain further evidence that the esters of *aci*-nitrocyclohexane are intermediates in the production of cyclohexanone oxime, this reaction and those of the prior authors[1,2] were repeated at 0° and at dry-ice temperature. It was hoped to retard decomposition of the ester sufficiently to permit its detection, but this was not realized.[7]

Dilute solutions of *aci*-nitrocyclohexane salts in

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(1) Hamann and Bauer, German Patent 825,547 (1951).

(2) Welz and Weise, German Patent 837,692 (1952).

(3) The suggested path of reaction is similar to that observed with certain nitro compounds[4-6] in which the C=N bond of the *aci* form is conjugated with at least one benzene ring or multiple bond. In these cases both the *aci* form and the ester are generally sufficiently stable that their identification is relatively simple, in distinct contrast to the corresponding derivatives of nitrocyclohexane.

(4) Bamberger, *Ber.*, **34**, 589 (1901).

(5) Nenitzescu and Isacescu, *Ber.*, **63**, 284 (1930); *Bull. Chem. Soc. Rom.*, **14**, 53 (1932).

(6) Arndt and Rose, *J. Chem. Soc.*, 1, (1935).

(7) This failure may have been due to lack of analytical equipment designed for operation below room temperature. The samples could be kept cold only until the analytical instruments were loaded.

methanol and ethanol were acidified with hydrochloric acid and titrated immediately with base on a *p*H recorder. A large portion of the theoretical amount of *aci*-nitrocyclohexane did not appear in the titration but disappeared irreversibly.[8] The titration curves are strikingly similar to those of mixtures of hydrochloric and acetic acid in the alcohols. Although this suggests that the disappearance of *aci*-nitrocyclohexane, like that of acetic acid, results from esterification, the ester could not be identified in these solutions. The mass spectra (obtained at an inlet temperature of 100° C.) revealed the presence of cyclohexanone oxime.

So far as the authors are now aware, no organic compound other than an alcohol, an alkyl halide, or an alkyl sulfate has been reported to convert nitrocyclohexane to cyclohexanone oxime, and these reagents must act on the *aci* form or its salt to accomplish this result.[9] In all of these reactions, therefore, it is reasonable to assume as common intermediates the esters of *aci*-nitrocyclohexane.[10]

EXPERIMENTAL

Materials. Nitrocyclohexane obtained from the Union Oil Co. of California had been steam distilled by the supplier. Infrared and mass spectra indicated good purity, and a pale yellow color was not objectionable; it was used without further treatment. Nitrocyclohexane from Du Pont was from pilot plant production. Analyses indicated purity similar to that of the other material, but upon standing several months a deep color developed. Therefore most of this sample was subsequently repurified by distillation. A colorless product boiling at 100.5° at 25 mm. was obtained. Aside from intensity of colors no significant differences in behavior of the various nitrocyclohexane samples were observed. Standard reagent grade chemicals, solvents purified by distillation, and de-ionized water were used throughout these investigations.

Reaction of dialkyl sulfates with salts of nitroparaffins. In one of the best experiments 0.1 mole sodium salt of nitrocyclohexane was prepared in 100 ml. methanol. This mixture was heated to reflux, and a mixture of 10 ml. dimethyl sulfate and 40 ml. methanol was added dropwise. Two hours later a little concentrated ammonia was added to destroy any excess methyl sulfate. The yield of cyclohexanone oxime, determined from mass spectrometer analysis of the solution, was about 76 per cent.

For purposes of determining the effect of different variables on the yield, the solutions produced in a large number of experiments were analyzed by mass spectrometry and the calculated yields were compared. (The identification of the compounds from their mass spectra is explained at the end of the Experimental section.) Yields calculated from mass spectra in this series of experiments exceeded those obtained by isolation in a few trials by about 10–15%. This is considered a measure of the loss in isolating the product from the complex reaction mixture, and the mass spectrometer data are believed to give a more reliable measure of the oxime produced.

Most variations in the preparative procedure given above resulted in lower yields of oxime; a few had no significant effect. Use of the calcium salt of nitrocyclohexane, which is largely insoluble in methanol, gave the same yield within the experimental error as the moderately soluble sodium salt. Substitution of the soluble potassium salt (the only salt tried which dissolves completely under the conditions of the experiment) resulted in yields only about two thirds as great. Diethyl sulfate appears to give slightly lower yields than dimethyl sulfate, but the difference may be within the experimental error. Diethyl sulfate does not react as rapidly as dimethyl sulfate. At room temperature or even at 0°, addition of dimethyl sulfate produces vigorous reaction with immediate evolution of heat; a slight delay in evolution of heat is observed on adding diethyl sulfate. Diethyl ether, ethylene glycol, and mixtures of these with methanol as solvents resulted in lower yields than those obtained in pure methanol; in water the yield was very low. Yields were not greatly changed by variation of the reaction temperature from 20° to the reflux temperature of the methanolic solution, but were considerably reduced at 0° and at 100°. Addition of the *aci*-nitro salt to the dialkyl sulfate gives lower yields than the reverse procedure. No increase in yield of the desired product was obtained by using other than stoichiometric amounts of reagents. An excess of alkyl sulfate results in formation of a significant amount of the corresponding alkyl ether of cyclohexanone oxime, rather than an increase in yield of oxime.

Other alkylations. The procedure used in reaction of salts of *aci*-nitrocyclohexane with alcohols and acid is similar to that of Welz and Weise,[2] but the ammonium salt was omitted

TABLE I

m/e	Cyclohexanone	Nitrocyclohexane (in Methanol)	Cyclohexanone Oxime (in Methanol)
129		0.	
114			8.6
113			100.-[a]
112			5.1
99	8.8	1.0	1.8
98	100.-[a]	0.8	27.
96	0.5		17.
85	0.3	0.4	19.
84	2.3	7.1	15.
83	20.	100.-[a]	2.7
82		10.	4.2
81	2.3	12.	28.
80	12.	0.6	6.4
79	1.9	3.6	10.
72	0.3	0.7	48.
70	52.	0.6	6.8
69	71.	1.5	17.
68	2.8	1.3	29.
67	1.0	15.	29.
59		1.7	54.
55	211.	128.	49.
54	15.	12.	28.
42	122.	5.9	28.
41	54.	77.	58.
39	32.	39.	30.
Sensitivity[b]	2.98	1.77	2.49

[a] Indicates the peak used as the basis for quantitative calculation of mixtures. [b] This value indicates the ratio of the *m/e* 92 peak of toluene to the base peak of the particular component on the weight basis; for example, 2.98 milligrams of cyclohexanone would give a *m/e* 98 peak of the same height as the *m/e* 92 peak of 1.00 milligram of toluene.

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(8) The salt of *aci*-nitrocyclohexane could be detected by titrating back with acid, while nitrocyclohexane could be reconverted to the salt by stirring at high pH.

(9) Diazomethane or other alkylating agents might also be successful.

(10) An exhaustive search of the literature and considerable unpublished effort in the laboratory have failed to provide any evidence for other reaction paths involving organic reducing agents.

and the temperature was lowered in an attempt to detect the ester rather than the oxime. In reaction of alkyl halides with salts of nitrocyclohexane the procedure employed differs from the reference,[1] in that the salt was first prepared by shaking an equivalent amount of base with a methanolic solution of the nitroparaffin until reaction was complete. The alkyl halide was then added in stoichiometric quantity and the mixture was stirred for several hours while controlling the temperature with a bath of ice, Dry Ice, or other coolant around the vessel.

Titrations. The titrimetric experiments employed about 0.01 mole of nitrocyclohexane or its salt, dissolved or suspended in 50 ml. or more of solvent (methanol or ethanol; a few runs were also tried in water). 1 *N* HCl and NaOH were used as titrating reagents. A Leeds and Northrup electronic *p*H recording titrator was used.

Nitrocyclohexane does not interfere with titration. In methanolic media it does not react at an appreciable rate with base until the *p*H reading exceeds 11. Since hydrochloric acid makes little contribution to the titration curve above *p*H 3 in either water or methanol the bulk of the measured *p*H range is free of obstacles to titrating *aci*-nitrocyclohexane or its salt. The curves obtained in methanol are displaced toward higher *p*H than in water. Neither are symmetric because of the disappearance of the free *aci* form. Therefore the exact strength of *aci*-nitrocyclohexane is not readily determined from the titration curves. *Aci*-nitrocyclohexane appears to be comparable in strength to acetic acid—perhaps slightly stronger. This is similar to the reported ionization of *aci*-nitroethane.[11]

Mass spectrometer analysis. The mass spectrum of cyclohexanone dimethyl acetal, a frequent component of the reaction mixtures in this work, is presented elsewhere.[12] The mass spectra of the other important compounds involved in these reactions are shown in Table I. Peaks below *m/e* 35 were not used for analytical purposes and have been omitted here.

All analyses were performed on a modified 90° sector type mass spectrometer.[13] The sample inlet system temperature was 100° and the ion source temperature was 160°.

Calculation of the mass spectra of the samples was done by the usual stepwise subtraction of component spectra[14] in the conventional manner and needs no further explanation here.

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[11] Maron and Shedlovsky, *J. Am. Chem. Soc.*, **61**, 753 (1939).

[12] McCoy, Baker, and Gohlke, to be published.

[13] The instrument has been described by Caldecourt, ASTM Committee E-14 Mass Spectrometer Conference, New Orleans, May 1954.

[14] Washburn, Wiley, and Rock, *Ind. Eng. Chem., Anal. Ed.*, **15**, 541 (1943).

[CONTRIBUTION FROM THE INSTITUTE FOR CHEMICAL RESEARCH, KYOTO UNIVERSITY]

Nitration of Desoxybenzoin

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The action of nitric acid (*d* 1.30) on desoxybenzoin-carbonyl-C^{14} has been investigated. The reaction routes have been elucidated from radio assay of the reaction products and their fission products.

In the nitration of desoxybenzoin to nitrobenzil reported by Zinin,[1] it is not possible to decide which benzene nucleus of desoxybenzoin is nitrated. The nitration of the benzyl nucleus seems to be more probable, since Ney[2] found that desoxybenzoin gave *p*-nitrodesoxybenzoin by treating with fuming nitric acid at low temperatures. A decision as to the reaction route, however, is possible by using desoxybenzoin labeled in the carbonyl with isotopic carbon, since the different routes of reactions will lead to isotopically distinguishable products.

The syntheses and the reaction routes are shown in Fig. 1. The measured specific activities of the products at each step are also shown under the formulas. For the determination of specific radioactivity, the labeled compounds were burned in a wet combustion apparatus described by Claycomb *et al.*,[3] and converted to barium carbonate. The activity was counted at infinite thickness with a Geiger-Müller counter tube and compared with the count of a standard barium carbonate.

By the nitration of desoxybenzoin-carbonyl-C^{14} (I), prepared from phenylacetic acid-carboxyl-C^{14}, there were obtained benzoic acid-carboxyl-C^{14} (VI), inactive *p*-nitrobenzoic acid (V) and a mixture of *p*-nitrobenzil-carbonyl-C^{14} (II) and benzil-carbonyl-C^{14} (III). As the nitrating agent more concentrated nitric acid (*d* 1.30) than Zinin's nitric acid (*d* 1.20) was used, because the former gave better yield of pure II. The crude mixture of the two benzils was purified by means of chromatography

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[1] N. Zinin, *Ann.*, Supplementbandes **3**, 154 (1864). The position of nitro group of nitrobenzil obtained by him was obscure and he reported that when nitrobenzil was treated with alcoholic potassium hydroxide, he obtained oxybenzoic acid and azobenzoic acid.

[2] E. Ney, *Ber.*, **21**, 2448 (1888).

[3] C. K. Claycomb, T. T. Hutchens, and J. T. Van Bruggen, *Nucleonics*, **7**, No. 3, 38 (1950).