nitroketonate anion in equation 6. Under the basic conditions of the reactions formation of these anions results in more favorable free energy changes in the same sense that reaction of base with hydrogen chloride, acetic acid or nitrous acid with liberation of chloride, acetate or nitrite ion is more favorable than reaction of base with hydrogen cyanide with liberation of cyanide ions. The conjugate acid of the nitroketonate anion is undoubtedly a considerably stronger acid than hydrogen cyanide.

Experimental

The following experiments illustrate the procedures employed.

α-Nitropropiophenone. Reaction of Benzoyl Cyanide with Lithium Ethanenitronate in *t*-Butyl Alcohol.—Nitroethane (7.8 g., 0.1 mole) was added to a solution of lithium *t*-butoxide formed by treating lithium metal (0.69 g., 0.1 mole) with *t*-butyl alcohol (dried over calcium hydride, 300 ml.) in a 500-ml., 3-necked flask equipped with a stirrer, dropping funnel and reflux condenser protected with a sodium hydroxide drying tube. Benzoyl cyanide (13 g., 0.1 mole) was added in 0.5 hr. to the cooled suspension, and the mixture was stirred for 4 hr. Most of the solvent was removed under vacuum and a mixture of ether, 100 ml., water, 200 ml., acetic acid, 10 g., and urea, 10 g., was added. The aqueous layer was separated and extracted with four 50-ml. portions of ether. The combined ether extracts were washed with water, dried, and distilled. α-Nitropropiophenone, b.p. 124° (2 mm.), $n^{25}D$ 1.5434, 9.0 g. (50%), was isolated.

3-Nitro-2-butanone. Reaction of Acetyl Cyanide with Lithium Ethanenitronate in *t*-Butyl Alcohol.—Freshly distilled acetyl cyanide (17 g., 0.25 mole) was added in 2 hr. to a suspension of lithium ethanenitronate (20.2 g., 0.25 mole) in *t*-butyl alcohol (400 ml.) and the mixture was stirred for 4 hr. Most of the solvent was removed under water aspiration and a mixture of ether, 100 ml., water, 300 ml., acetic acid, 18 g., and urea, 10 g., was added. The aqueous layer was separated and extracted with four 50-ml. portions of ether. The combined ether layers were washed with water, dried and distilled. 3-Nitro-2-butanone, b.p. 58° (1 mm.), $n^{25}D$ 1.4362, 11.6 g. (30% theory), was isolated.

Attempted Acylation of Lithium 2-Propanenitronate with Benzoyl Cyanide in *t*-Butyl Alcohol.—Benzoyl cyanide (20 g., 0.15 mole) was added in 0.5 hr. to a solution of lithium 2-propanenitronate (19 g., 0.2 mole) in *t*-butyl alcohol, 400 ml., and the mixture was stirred for 5.5 hr. The reaction mixture was poured into ice-water, 1.5 l., and extracted with six 100-ml. portions of ether. The combined ether layers were washed with water, dried and distilled. There were obtained *t*-butyl benzoate, b.p. 59° (1 mm.), $n^{25}D$ 1.4658, 12.0 g. (44% theory); and acetone oxime benzoate, b.p. 124° (1 mm.), $n^{25}D$ 1.5184, 8 g. (17% theory).

Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.27; N, 8.06. Found: C, 67.62; H, 5.82; N, 8.16.

The oxime benzoate gave benzanilide, m.p. 161°, upon treatment with aniline. Its infrared spectrum showed carbonyl absorption at 5.82 μ and C=N absorption at 6.02 μ.

α-Nitrobutyrophenone. Reaction of Benzoyl Cyanide with Lithium 1-Propanenitronate in Tetrahydrofuran.—Benzoyl cyanide (10 g., 0.077 mole) was added in 0.5 hr. to a suspension of lithium 1-propanenitronate (9.5 g., 0.1 mole) in purified tetrahydrofuran, 200 ml., and the mixture was stirred for 8 hr. at room temperature and 1 hr. at 65°. The reaction mixture was worked up by following the procedure given for α-nitropropiophenone. α-Nitrobutyrophenone, b.p. 128° (1 mm.), $n^{25}D$ 1.5344, 9 g. (60% theory), was isolated.

Reaction of Benzoyl Chloride with Sodium 2-Propanenitronate.—Benzoyl chloride (15.6 g., 0.1 mole) was treated with sodium 2-propanenitronate (22.2 g., 0.2 mole) in ether, 200 ml. The reaction was relatively rapid and was complete in 2 hr. Benzoic acid, m.p. 120°, 11 g. (91% theory), was isolated.

Nitroacetophenone. Reaction of Benzoyl Cyanide with Nitromethane and Sodium Carbonate in Pyridine.—Benzoyl cyanide (13 g., 0.1 mole) was added in 0.5 hr. to a mixture of nitromethane (12 g., 0.2 mole) and sodium carbonate (21 g., anhydrous powder, 0.2 mole) in pyridine (dried over calcium hydride, 300 ml.) and the reaction mixture was stirred for 3.5 hr. The suspension was filtered and the precipitate was washed with dry ether (100 ml.). The solid was partially dissolved in water (400 ml.) and acidified with dilute hydrochloric acid (3 *N*, 200 ml.) at 0–5°. Nitroacetophenone, m.p. 105–106°, 12 g. (73% theory), was isolated by filtration, and recrystallized from petroleum ether (b.p. 65–67°)-ethyl ether mixture; literature[9] m.p. 106°.

LAFAYETTE, IND.

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, UNION CARBIDE CHEMICALS CO.]

The Reaction of Nitrosyl Chloride with Acetophenone in Ethanol–Pyridine Solution[1]

BY DAVID T. MANNING AND HARRY A. STANSBURY, JR.

RECEIVED NOVEMBER 26, 1958

The reaction between nitrosyl chloride and acetophenone at 25 to 60° in an ethanol medium containing pyridine was studied. Phenylglyoxal aldoxime and benzoic acid were obtained in low yields and the main reaction products were ethyl benzoate, ethyl phenylacetate, ethyl phenylglyoxylate and phenylglyoxal diethyl acetal. By treatment of phenylglyoxal aldoxime with nitrosyl chloride under the conditions of the acetophenone reaction, the oxime was shown to be the intermediate responsible for the formation of all of these products with the exception of ethyl phenylacetate. Simple acid-catalyzed solvolysis of the aldoxime under the mild conditions employed did not occur. Ethyl phenylglyoxylate and phenylglyoxal diethyl acetal were probably formed by reaction of phenylglyoxal aldoxime with nitrosyl chloride to give an intermediate which then decomposed by either of two pathways, one leading to phenylglyoxylyl chloride and the other to phenylglyoxal. Reaction of these with ethanol would yield the observed ester and acetal, respectively. Ethyl phenylacetate was probably formed from α-nitrosoacetophenone by reaction with nitric oxide to give diazoacetophenone which then underwent the Wolff rearrangement.

Introduction

The nitrosation of acetophenone to give phenylglyoxal aldoxime has been accomplished employing either basic or acidic conditions. When the nitrosation was performed with sodium ethoxide and a nitrite ester, a 50% yield of phenylglyoxal aldoxime was obtained,[2–5] whereas the use of nitrite ester and a mineral acid catalyst, in general, has led to inferior results.[5–7] Hartung[5] obtained

(1) D. T. Manning and H. A. Stansbury, Jr., Abstracts of Papers, 133rd Meeting, American Chemical Society, April 13 to 18, 1958, p. 93-N.

(2) L. Claisen, *Ber.*, **20**, 655 (1887).

(3) L. Claisen and O. Manasse, *ibid.*, **20**, 2194 (1887).

(4) L. Claisen, *ibid.*, **38**, 693 (1905).

(5) W. H. Hartung, J. C. Munch, W. A. Deckert and F. Crossley, THIS JOURNAL, **52**, 3317 (1930).

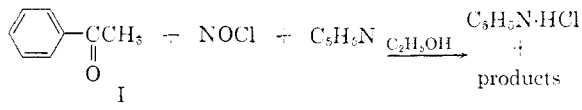
(6) L. Claisen and O. Manasse, *Ber.*, **22**, 526 (1889).

(7) W. K. Slater, *J. Chem. Soc.*, **117**, 587 (1920).

yields of only 6–12% of phenylglyoxal aldoxime upon nitrosation with methyl nitrite and dry hydrogen chloride, while Claisen and Manasse[6] observed an extensive reaction leading to the formation of chlorinated by-products. Unidentified by-products were also observed by Slater[7] who concluded that phenylglyoxal aldoxime and aldoximes of α-keto aldehydes, in general, are sensitive to the hydrogen chloride present in nitrosations catalyzed by this acid. In contrast to these results, the monoximes of α-diketones are relatively stable toward acidic nitrosation media and are often prepared in excellent yield by acid-catalyzed nitrosation of the corresponding methylene ketones.[5–7]

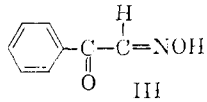
Results and Discussion

Acetophenone (I) was treated with a 63% molar excess of nitrosyl chloride in ethanol solution with added pyridine sufficient to combine with by-product hydrogen chloride. A smooth reaction



I

occurred at 60° and, after a reaction period of 3.5–4 hours, only 19.1% of the acetophenone remained unreacted. The reaction mixture was extracted with aqueous sodium bicarbonate and sodium carbonate to obtain benzoic acid (II) in 5.1% yield and the expected product, phenylglyoxal aldoxime (III), in 3.4% yield. The main



III

reaction product consisted of a mixture of neutral liquid compounds amounting to 97.9% of the original acetophenone by weight. Fractional distillation of this mixture at reduced pressure followed by infrared and mass spectrometric examination of the cuts and the preparation of derivatives enabled identification of five products, listed with their estimated yields and boiling points (10 mm.) in Table I.

TABLE I

No.	Product	B.p. at 10 mm.,[8] °C.	Estimated yield, %
I	Acetophenone (recovd.)	79	..
IV	Benzoyl cyanide	82	2.9
V	Ethyl benzoate	88	10.7
VI	Ethyl phenylacetate	112	8.4
VII	Ethyl phenylglyoxylate	129	18.1
VIII	Phenylglyoxal diethyl acetal	134	12.4

Estimation of the yields of ethyl benzoate and ethyl phenylglyoxylate depended largely upon their saponification to benzoic acid and phenylglyoxylic acid, respectively, while phenylglyoxal diethyl acetal was readily recovered in pure form following saponification of the high boiling fractions. Ethyl phenylacetate was identified by infrared and mass spectrometric study of the fractions and by ammonolysis to phenacetamide. However, since the conversion of ethyl phenylacetate to phenacetamide was low, estimation of the yield of phenylacetic ester was based upon mass spectrometric data. Mass spectrometric analysis of synthetic mixtures of the five products plus acetophenone showed this method to be fairly reliable for the estimation of all the constituents except for ethyl phenylglyoxylate and phenylglyoxal diethyl acetal. The yields of these, however, were readily determined by mild basic hydrolytic treatment of the high-boiling fractions. The yield of benzoyl cyanide was based entirely upon mass spectrometric analysis.

Subsequently, benzoyl cyanide was found to be an artifact rather than a primary reaction product. This was established by an infrared scan of an undistilled reaction mixture prepared under identical conditions which showed benzoyl cyanide to be absent. Benzoyl cyanide results from thermal dehydration,[8] during distillation, of small amounts of phenylglyoxal aldoxime which remained in the neutral liquid fraction following the carbonate extraction procedure.

A brief study of the exit gases formed during the reaction revealed that nitrous oxide, nitric oxide and nitrogen were the only gaseous products.

The reaction was then repeated, employing a deficiency of nitrosyl chloride. In this case, the original molar proportions of reactants were approximately reversed with a 50% excess of acetophenone over nitrosyl chloride being used. Benzoic acid was again formed in low yield (3.5%), but the yield of phenylglyoxal aldoxime was increased to 20.9% and the neutral liquid reaction products were reduced in quantity.

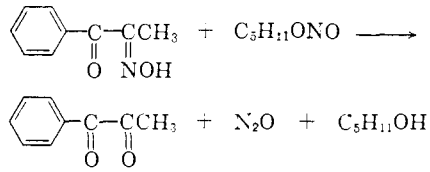
From these results it seemed likely that phenylglyoxal aldoxime, formed by acid-catalyzed nitrosation of acetophenone, gave rise to the high boiling liquid products by further reaction with excess nitrosating agent. To investigate this possibility, phenylglyoxal aldoxime was treated with a 50% excess of nitrosyl chloride in an ethanolic solution containing pyridine under conditions similar to the acetophenone reaction. At the end of the reaction period, 4.8% of unreacted phenylglyoxal aldoxime was recovered in addition to benzoic acid (4.9% yield) and a high boiling liquid fraction amounting to 77% of the original weight of oxime. This fraction consisted of ethyl benzoate (17.4% yield), ethyl phenylglyoxylate (24.1% yield) and phenylglyoxal diethyl acetal (16.7% yield). Both benzoyl cyanide and ethyl phenylacetate were absent as indicated by infrared and mass spectrometric studies. In this case also, the gaseous products consisted entirely of nitrous oxide, nitric oxide and nitrogen.

Some insight into the origins of these products may be gained by considering the reactions of oximes known to occur under acidic nitrosating conditions. One possibility considered was that some of the products obtained from the acid-catalyzed nitrosation of phenylglyoxal aldoxime might result from mere reaction of the oxime with ethanol in the presence of pyridine hydrochloride. To test this hypothesis, phenylglyoxal

(8) Estimated.

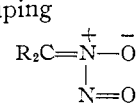
aldoxime was treated with a 50% excess of moist pyridine hydrochloride, containing an excess of hydrogen chloride, in ethanol solution under conditions simulating the nitrosation reaction. No significant reaction occurred as evidenced by recovery of 98% of the original phenylglyoxal aldoxime, although it must be emphasized that these conditions, in the absence of nitrosyl chloride, are not identical to those in the nitrosating medium. Benzoic acid is known to arise from phenylglyoxal aldoxime by treatment with heat and mineral acid,[2,3] but it is not always clear whether it is formed directly from the oxime by the abnormal Beckmann reaction[9] or by hydrolysis of benzoyl cyanide. Presumably, both benzoic acid and ethyl benzoate might be formed by direct reaction of water or ethanol, respectively, with phenylglyoxal aldoxime under acidic conditions. That this occurs in the present case, however, seems doubtful in view of the failure of the oxime to react with an acidic ethanol solution containing pyridine hydrochloride. A more reasonable possibility is that benzoic acid, as well as the other products, results from some specific action of a nitrosating agent on the oxime.

The reaction of oximes with nitrosating agents to produce the parent carbonyl compounds is, in fact, well known[6,10-19] and has been observed in the absence of donor solvents such as water and alcohols.[10] Thus, Manasse[10] treated α-oximinopropiophenone with amyl nitrite to produce the corresponding diketone and nitrous oxide as indicated

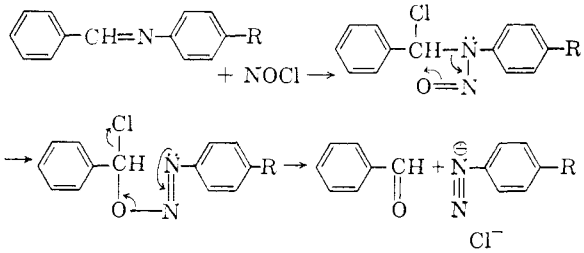


A vigorous reaction also occurred upon treatment of phenylglyoxal aldoxime with amyl nitrite, but phenylglyoxal was not obtained nor were the reaction products identified.[6] Later, Neuberg, Hofmann and Cusmano succeeded in deoximating phenylglyoxal aldoxime to phenylglyoxal by the action of aqueous nitrosylsulfuric acid[13,14] and by oxides of nitrogen in aqueous medium.[15] Neuberg and Hofmann also deoximated pyruvaldoxime to pyruvaldehyde by this method[16] and reported the formation of nitrous oxide as the by-product.

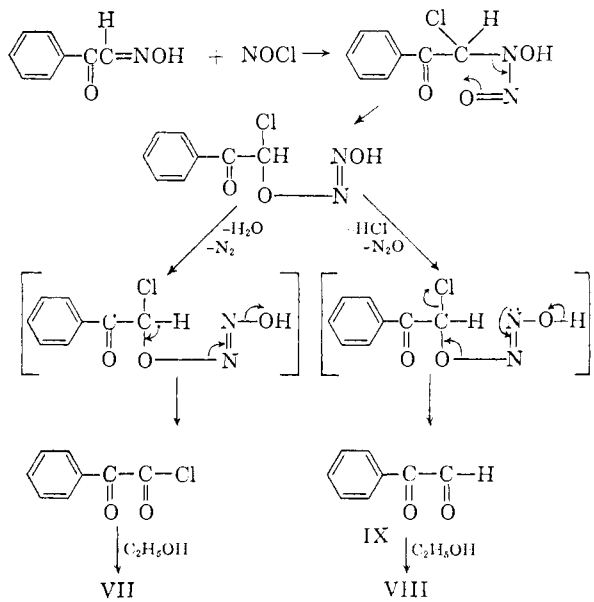
The frequent appearance of nitrous oxide[10-14,16-20] as a by-product of nitrosative deoximation suggests the occurrence of an initial attack of a nitrosating entity, such as nitrosonium ion, upon the oximino nitrogen. Such a mechanism is further suggested by the many instances[17-22] in which pernitroso derivatives, having the general structure $R_2C{=}N_2O_2$, have been isolated following the treatment of oximes with nitrosating agents. Schenck[17-19] prepared several of these derivatives from ketoximes of bile acids and noted that derivatives containing the pernitroso grouping in the 12-position were readily decomposed to give nitrous oxide and the corresponding ketone. Of the many structures which have been suggested for the pernitroso grouping



is favored by Fusco and Trisoglio[22] and Schenck.[18-19] On the other hand, some oximes are decomposed by nitrosation to give the parent ketone and nitrogen, instead of nitrous oxide.[17-19] The intermediate formation of an unstable diazo nitrate appears to be involved in these cases.[17-19,23] A reaction similar to nitrosative deoximation has been reported[24] to occur between NOCl and Schiff bases in anhydrous ether solution at 0°.



This reaction pictured above shares many features in common with the mechanism recently suggested by White[25] for the rearrangement of N-alkyl-N-nitrosoamides to diazo esters prior to nitrogen elimination. Formation of phenylglyoxal as its

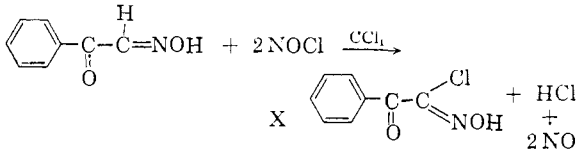


(9) O. Diels and M. Stern, *Ber.*, **40**, 1629 (1907).
(10) O. Manasse, *ibid*, **21**, 2176 (1888).
(11) L. Claisen and O. Manasse, *ibid.*, **22**, 530 (1889).
(12) Harries, *ibid.*, **34**, 1494 (1901).
(13) C. Neuberg and E. Hofmann, *Biochem. Z.*, **229**, 443 (1930).
(14) C. Neuberg and E. Hofmann, *ibid.*, **239**, 495 (1931).
(15) S. Cusmano, *Gazz. chim. ital.*, **68**, 129 (1938).
(16) E. Hofmann and C. Neuberg, *Biochem. Z.*, **226**, 489 (1930).
(17) M. Schenck, *Ber.*, **75**, 198 (1942).
(18) M. Schenck, *ibid.*, **76**, 874 (1943).
(19) M. Schenck, *ibid.*, **77B**, 29 (1944).
(20) A. Angeli and E. Rimini, *ibid.*, **28**, 1077 (1895).
(21) A. Hantzsch and F. E. Dollfus, *ibid.*, **35**, 260 (1902).
(22) R. Fusco and G. Trisoglio, *Atti accad. Italia, Rend. classe sci. fis., mat. nat.*, [7] **2**, 618, 751 (1941).
(23) J. F. Brown, Jr., Abstracts of Papers, 126th Meeting, American Chemical Society, September 12-17, 1954, p. 43-O.
(24) J. Turcan, *Bull. soc. chim. France*, [5] **2**, 627 (1935).
(25) E. H. White, THIS JOURNAL, **76**, 4497 (1954).

diethyl acetal VIII as well as ethyl phenylglyoxylate (VII) may be visualized in an analogous manner as already shown.

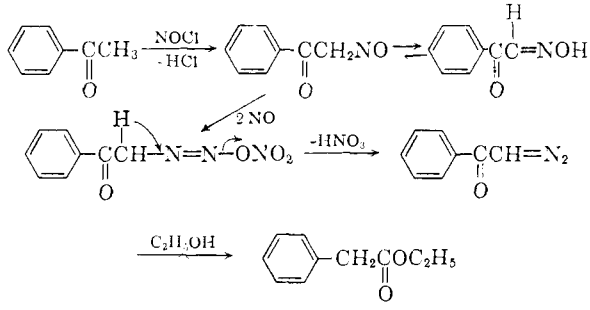
The last step in the formation of the acetal VIII was shown to be possible by treating phenylglyoxal (IX) with a reaction mixture prepared from ethanol, nitrosyl chloride and pyridine under the conditions of the acetophenone reaction. Phenylglyoxal diethyl acetal was formed in 60% yield.

Originally, the formation of ethyl phenylglyoxylate was thought to occur by another mechanism. Nitrosyl chloride is known to react with phenylglyoxal aldoxime in carbon tetrachloride solution to produce benzoylformohydroxamyl chloride (X).[26] The presence of nitric oxide in the exit



gas suggested that the hydroxamic acid chloride (X) might be formed and then serve as a source of ethyl phenylglyoxylate either by solvolysis or by some nitrosation reaction. That this does not occur, however, was shown by the failure of the hydroxamic acid chloride to form ethyl phenylglyoxylate when treated with ethanolic pyridine hydrochloride at 60° either with or without added nitrosyl chloride.

Among the products of the acetophenone reaction, ethyl phenylacetate is unique in having a carbonyl group separated from the benzene ring by a methylene group. It seems likely that a carbon skeleton rearrangement of the Wolff[27] type is involved. Ethyl phenylacetate was not formed from the nitrosation of phenylglyoxal aldoxime, but probably arises from α-nitrosoacetophenone, its tautomeric precursor, as



In support of this hypothesis is the well known reaction of nitroso compounds with nitric oxide to form the corresponding diazo nitrate[23] with subsequent elimination[28] of a proton and anion to produce the diazo compound. These steps are also probably involved in the reported conversion of dibenzoylmethane to dibenzoyldiazomethane by treatment with oxides of nitrogen.[29]

(26) H. Reinboldt and O. Schmitz-Dumont, *Ann.*, **444**, 113 (1925).

(27) W. E. Bachmann and W. S. Struve, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 38.

(28) C. D. Gutsche and H. E. Johnson, THIS JOURNAL, **77**, 109 (1955).

(29) H. Wieland and S. Bloch, *Ber.*, **37**, 2524 (1904).

Experimental

Materials and Reference Samples.—Nitrosyl chloride, purchased from The Matheson Co., was distilled and the fraction boiling at −6° collected for use in the nitrosation experiments. Phenylglyoxal diethyl acetal was prepared by refluxing a solution of phenylglyoxal[30] in ethanol containing a small amount of sulfuric acid for a 30-hour period. The acetal, recovered by steam distillation and purified by fractionation at reduced pressure, had the b.p. 134–134.5° (10 mm.), $n^{20}D$ 1.4998. Benzoyl cyanide,[31] phenylglyoxylic acid[32] and ethyl phenylglyoxylate 2,4-dinitrophenylhydrazone[33] were prepared according to standard procedures. Phenylglyoxal 2,4-dinitrophenylosazone was synthesized as follows: To a solution of 3.65 g. (0.024 mole) of phenylglyoxal hydrate in 500 ml. of ethanol was added 75 ml. of a 0.25 *M* solution[34] of 2,4-dinitrophenylhydrazine in phosphoric acid while stirring the mixture. An orange precipitate formed which was collected and washed with benzene to give 2.1 g. of a yellow solid. This was recrystallized twice from ethanol–benzene to give lemon-yellow needles, m.p. 205–207°. The yellow compound appears to be the previously unreported 2,4-dinitrophenylhydrazone of phenylglyoxal.

Anal. Calcd. for $C_{14}H_{10}O_5N_4$: C, 53.51; H, 3.21. Found: C, 53.69; H, 3.44.

A 1.0-g. sample of the yellow crystalline material was heated under reflux for 50 hours with a mixture of 50 ml. of ethanol and 35 ml. of 0.25 *M* 2,4-dinitrophenylhydrazine. Upon cooling, 1.0 g. of an orange solid, m.p. 292.5–293°, was recovered by filtration. Recrystallization from boiling glacial acetic acid gave fine vermillion crystals of phenylglyoxal 2,4-dinitrophenylosazone, m.p. 295–296° (reported[35] red powder, m.p. 297–300°).

Anal. Calcd. for $C_{20}H_{14}O_8N_8$: C, 48.59; H, 2.85; N, 22.67. Found: C, 48.00; H, 2.47; N, 22.88.

Reaction of Acetophenone with Nitrosyl Chloride in Ethanol Solution in the Presence of Pyridine.—To a stirred solution of 120 g. (1.0 mole) of acetophenone and 120 g. (1.517 moles) of pyridine in 1500 ml. of absolute ethanol was added 75 ml. (1.63 moles at −30°) of nitrosyl chloride over a period of 21 minutes during which time the temperature rose from 24 to 28°. Heat was then applied and the temperature increased to 58–63° over an interval of 21 minutes where it was held, with stirring, for a period of 3.5 hours. During the reaction, the initial greenish color changed to yellow and the reflux of ethyl nitrite, which had commenced with the increase in temperature, subsided and finally ceased approximately one hour after reaching 60°. Finally, ethanol was removed from the reaction mixture by vacuum (water aspirator) evaporation on the steam-bath to a maximum internal temperature of 60°.

The residue remaining after removal of ethanol was repeatedly extracted with ethyl ether to recover all soluble organic materials, essentially free of pyridine hydrochloride. The ether solution was then adjusted to about 300 ml. in volume by evaporation, cooled to 0–5°, and extracted with four 150-ml. portions of cold 10% sodium bicarbonate solution. The bicarbonate extract was acidified and extracted with ethyl ether to give 2.7 g. of crude benzoic acid which was recrystallized from water to give white crystals, m.p. 121–123°, undepressed by admixture with an authentic sample.

The ether solution of the main organic phase was again chilled to 0–5° and extracted with six 150-ml. portions of cold 10% sodium carbonate. The combined carbonate extracts were acidified to *p*H 5 with 6 *N* hydrochloric acid and extracted with ethyl ether to give, upon evaporation, 5.1 g. of crude phenylglyoxal aldoxime, containing benzoic acid as an impurity. The material was recrystallized once from water, powdered, and benzoic acid removed by agitation with cold 10% sodium bicarbonate. The recovered oxime was again recrystallized from water and finally from

(30) H. A. Riley and A. R. Gray, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 509.

(31) T. S. Oakwood and C. A. Weisgerber, *ibid.*, Coll. Vol. III, 1955, p. 112.

(32) *Ibid.*, p. 114.

(33) S. D. Brewer and R. M. Herbst, *J. Org. Chem.*, **6**, 867 (1941).

(34) G. D. Johnson, THIS JOURNAL, **73**, 5888 (1951).

(35) T. L. Jacobs and W. R. Scott, Jr., *ibid.*, **75**, 3500 (1953).

chloroform to give nearly pure phenylglyoxal aldoxime as pale brownish colored prisms, m.p. 127–128° (reported[3] 126–128°), undepressed by admixture with an authentic sample. The oxime-free carbonate extract was further acidified to *p*H 0.5–1.0 to give, upon ether extraction, an additional 3.5 g. of crude benzoic acid.

The ether solution containing the bulk of the reaction products was evaporated on the steam-bath to remove ether and flash distilled *in vacuo* through a short column. The distillate weighed 117.4 g. and boiled at 67.5–134° (3.5–5 mm.). A dark residue (9.6 g.), was discarded. An attempted fractional distillation of the flashed material at reduced pressure (10 mm.) produced a series of imperfectly resolved cuts whose compositions were estimated by mass spectrometric and infrared analyses (see Table I). The identification of these substances was then confirmed by further studies including the preparation of derivatives.

The evolution of gaseous products during the reaction was measured by a wet-test meter connected to the exit of the Dry Ice–acetone reflux condenser. Samples of gas, taken during the reaction, were analyzed by the mass spectrometer and found to consist of nitrous oxide, nitric oxide, nitrogen and traces of ethanol. The gas-yielding reaction became prominent at 56° and proceeded rapidly at 60° for approximately one hour before slackening. Approximately one-half of the total gas evolution occurred during the first 15 minutes of the gas-producing reaction. Approximately 0.64 mole of gas was evolved in the one-hour period and the estimated approximate molar composition was nitrous oxide (41%), nitrogen (31%) and nitric oxide (28%).

Identification of the Constituents of the Distillation Fractions.—The reliability of the mass spectrometric method which was employed to a certain extent in estimating the yields of the products was established by analysis of synthetic mixtures of authentic samples of the reaction products.

Acetophenone (I).—Some unreacted acetophenone was present in the ethanol stripped from the reaction mixture and was determined[36] by reaction with hydroxylamine hydrochloride in the presence of triethanolamine followed by titration of the liberated hydrochloric acid with standard base. By this procedure, the ethanol solution was found to contain 12.4 g. of acetophenone. Acetophenone present in distillation fractions 1 and 2 was estimated by mass spectrometric analysis.

Benzoyl Cyanide (IV).—The presence of benzoyl cyanide in fractions 1–9 was indicated by a single sharp band at 4.5 μ corresponding to C≡N stretching and in fractions 1–10 by mass spectrometric analysis which revealed the characteristic parent-molecule ion of mass 131.

Infrared examination of an undistilled reaction mixture resulting from a repetition of the acetophenone–nitrosyl chloride reaction under the conditions described above showed none of the absorption at 4.5 μ characteristic of benzoyl cyanide.

Ethyl Benzoate (V).—Ethyl benzoate occurred to some extent in all the fractions and chiefly in fractions 1–5. Its presence was indicated by mass spectrometric detection of a highly characteristic fragment of mass 122. This is formed by the shift of a proton to the carboxyl moiety of the benzoate fragment and was not due to benzoic acid, a fact indicated by absence of this peak in the spectrograms of synthetic mixtures containing benzoic acid. Infrared evidence of ethyl benzoate consisted of bands at 5.84 μ (C=O stretching) and 9.00 μ. At 9.00 μ there was a regular decrease in absorption with increasing fraction number with concomitant shift in the 5.84 μ band to shorter wave lengths indicative of replacement of benzoate ester by the higher-boiling ethyl phenylacetate (C=O stretching, 5.82 μ).

Chemical evidence of ethyl benzoate in fractions 1 and 2 was afforded by saponification of samples of the cuts and identification of the resulting benzoic acid. Samples of fraction 1 (8.0 g.) and fraction 2 (6.7 g.) were combined and saponified by refluxing with 10% sodium hydroxide to give, upon acidification, 6.3 g. of benzoic acid.

Ethyl Phenylacetate (VI).—The presence of ethyl phenylacetate in all of the fractions was indicated by mass spectrometric analysis which revealed the highly characteristic positive ion of mass 91. Further evidence was afforded by infrared examination which yielded strong bands at 5.82 μ (C=O stretching), and 6.7 μ (monosubstituted aromatic ring.). In fractions 3–6, the shift of the 5.84 μ band, characteristic of conjugated aromatic ester carbonyl (ethyl benzoate), to the shorter wave length was clearly evident. While the 6.7 μ band is present in the spectrum of benzoyl cyanide as well as that of ethyl phenylacetate, it is a relatively weak band in the case of the former, amounting to less than one-half of the absorption of the characteristic C≡N stretching band (4.5 μ) of benzoyl cyanide. In all of the fractions exhibiting bands at 4.5 and 6.7 μ, however, the 6.7 μ band was considerably stronger and actually amounted to 2–8 times the absorption of the 4.5 μ band in fractions 3–9, clearly indicating the presence of the phenylacetic ester. None of the other constituents in the reaction mixture possess infrared absorption bands in the 6.7 μ region.

Confirmation of the presence of ethyl phenylacetate in fractions 3–9 was obtained by ammonolysis to phenacetamide which was isolated and identified. The combined fractions were dissolved in ethanol, the solution chilled to 0–5° and saturated with anhydrous ammonia. After standing several days at room temperature, the reaction mixture was worked up to give a low yield of phenacetamide which was recrystallized from benzene to give white plates, m.p. 157–157.5° (reported[37] 155–156°). Mixed melting point and infrared comparison confirmed the identification.

Ethyl Phenylglyoxylate (VII).—The bulk of the ethyl phenylglyoxalate occurred in fractions 10 and 11, but first appeared in fraction 8 as indicated by a strong sharp band in the infrared at 8.31 μ (C–O stretching mode) and by mass spectrometric detection of the parent-molecule ion of mass 178.

Mass spectrometric analysis, however, did not prove satisfactory in providing reliable estimations of the concentrations of the phenylglyoxylic ester or of phenylglyoxal diethyl acetal in fractions 8–11, and was considered as offering only slightly more than qualitative evidence of their presence. This difficulty apparently arises from the low volatility of these constituents at the operating temperature and pressure of the mass spectrometer which results in low intensity fragmentation patterns.

Chemical evidence of ethyl phenylglyoxylate in fractions 10 and 11 was provided by saponification to phenylglyoxylic acid. The bulk of fractions 10 and 11 (58.7 g.) were combined and saponified with 300 ml. of 2 *N* sodium hydroxide according to the method of Baer and Kates.[38] Upon completion of the saponification and cooling, phenylglyoxal diethyl acetal remained as an oily upper layer and was removed by ethyl ether extraction.

The clear aqueous phase was acidified to *p*H 4 with 6 *N* hydrochloric acid and extracted with six 100-ml. portions of ethyl ether which were combined and dried over anhydrous sodium sulfate. Removal of the ether by evaporation left 2.9 g. of crude benzoic acid containing small amounts of phenylacetic and phenylglyoxylic acid. The benzoic acid arises from ethyl benzoate, present in fractions 10 and 11 and may occur to a certain extent in these fractions as the free acid if it is not completely removed by bicarbonate extraction prior to distillation.

After removing benzoic acid from the aqueous hydrolysate, phenylglyoxylic acid was liberated as a light yellow oil by further acidification with 6 *N* hydrochloric acid to *p*H 0.5. The crude acid was recovered by ether extraction and stored in a vacuum dessicator for three days whereupon it crystallized. The phenylglyoxylic acid thus obtained weighed 26.1 g., m.p. 57.5–63°, and had a neutralization equivalent of 150.0 (calcd. for $C_8H_6O_3$: 150.1). Recrystallization from carbon tetrachloride raised the melting point to 64–66° (reported[32] 64–66°). The identity was confirmed by mixed melting point and comparison of the infrared spectrum with that of an authentic sample.

Further evidence of ethyl phenylglyoxylate was afforded by conversion to the 2,4-dinitrophenylhydrazone, m.p. 156–157° (reported[33] m.p. 156°). The mixed melting point with an authentic sample was undepressed.

Phenylglyoxal Diethyl Acetal (VIII).—The presence of phenylglyoxal diethyl acetal in fractions 9–11 was indicated by strong bands in the infrared at 3.5 μ (C–H stretching), 8.92 and 9.40 μ (C–O stretching), and by mass spectrometric detection of a 47^+ ion (typical of acetals) and an ion of

(36) An unpublished method of the Union Carbide Chemicals Co.

(37) A. Bernthsen, *Ann.*, **184**, 318 (1877).

(38) E. Baer and M. Kates, THIS JOURNAL, **67**, 1482 (1945).

mass 103. Mass spectrometric analysis, however, was unable to offer much more than a qualitative estimation of the acetal in the fractions.

Direct isolation of the acetal was achieved from fractions 10 and 11 following saponification of the esters. The ether extract of the basic hydrolysate was distilled to give 22.0 g. of colorless phenylglyoxal diethyl acetal, b.p. 131–134° (10 mm.), $n^{20}D$ 1.4995. The material possessed an infrared spectrum identical to that of an authentic sample.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 68.60; H, 8.00.

Phenylglyoxal diethyl acetal was converted to phenylglyoxal-2,4-dinitrophenylosazone by heating the acetal (5.0 g.) with an excess of 2,4-dinitrophenylhydrazine reagent[34] in ethanol solution. The crude product (2.0 g.) was recrystallized from glacial acetic acid to give scarlet crystals, m.p. 295–296° (reported[35] 297–300°). The mixed m.p. with an authentic sample was undepressed.

Reaction of Acetophenone with a Deficiency of Nitrosyl Chloride in Ethanol Solution in the Presence of Pyridine.—To a stirred solution of 180 g. (1.5 moles) of acetophenone and 82 g. (1.04 moles) of pyridine in 1500 ml. of ethanol was added 71.1 g. (1.09 moles) of nitrosyl chloride as described above in this section. After a period of 2 hours at 60° the reaction mixture was worked up in the usual manner to give 31.1 g. (20.9% yield) of phenylglyoxal aldoxime, 4.3 g. (3.5% yield) of benzoic acid and a volatile material. The latter was distilled at reduced pressure to give 92.0 g. of unreacted acetophenone, b.p. 76–80° (10 mm.), and a 28.0-g. fraction, the bulk of which boiled above acetophenone. The high-boiling fraction was treated with excess 2 *N* sodium hydroxide[36] after which an additional 5.2 g. of acetophenone and 8.1 g. (3.9%) of phenylglyoxal diethyl acetal were recovered by vacuum distillation.

Reaction of Phenylglyoxal Aldoxime with Nitrosyl Chloride in Ethanol Solution in the Presence of Pyridine.—To a stirred solution of phenylglyoxal aldoxime (25 g., 0.168 mole) and pyridine (19.9 g., 0.252 mole) in 500 ml. of absolute ethanol was added 16.5 g. (11.6 ml. at −30°, 0.252 mole) of nitrosyl chloride over a period of 13 minutes while the temperature was allowed to rise from 24 to 29°. The reaction mixture was then warmed to 55–60° over a one-hour period and held at 60° for 3.5 hours. Following completion of the reaction, ethanol was removed by evaporation *in vacuo* and the residue extracted with ethyl ether to separate soluble organic products from the pyridine hydrochloride. The ether layer was extracted with three 100-ml. portions of 10% sodium carbonate and the carbonate extracts combined, acidified to *p*H 7, and ether extracted to recover unreacted phenylglyoxal aldoxime (1.2 g.), m.p. 117–121°. Recrystallization from chloroform gave pure material, m.p. and mixed m.p. 126–127°. The aqueous layer from the carbonate extraction was then adjusted to *p*H 4 and extracted with ether to recover benzoic acid (1.0 g.) which was recrystallized from water to give white crystals, m.p. and mixed m.p. 121–122°.

The neutral organic layer was washed with water, dried and vacuum distilled through a short-path system giving 19.2 g. of distillate, b.p. 87–133° (1.5–2.5 mm.), and 6.5 g. of a dark, viscous residue. The distillate was then redistilled at reduced pressure to give a series of poorly resolved cuts containing ethyl benzoate, ethyl phenylglyoxylate, and phenylglyoxal diethyl acetal.

Except for the possible presence of trace quantities, benzoyl cyanide and ethyl phenylacetate were absent from the fractions as indicated by mass spectrometric and infrared analysis. The relative intensities of the infrared bands associated with ethyl benzoate (V), ethyl phenylglyoxylate (VII) and phenylglyoxal diethyl acetal (VIII), were in accord with the compositions of the fractions as estimated by mass spectrometric analysis.

The compositions of the fractions were confirmed by saponification of the contained esters followed by separation of phenylglyoxal diethyl acetal from the resulting benzoic and phenylglyoxylic acids. The acids as well as the acetal were identified as described previously in this section. Throughout the reaction, effluent gases were measured as in the acetophenone reaction. The evolution of gas was very rapid, one-half of the total estimated molar amount (0.095 mole) appearing during the first nine minutes of the gas-producing reaction. The gaseous mixture consisted of nitrous oxide, nitric oxide and nitrogen in the approximate molar percentages of 44, 41 and 15%, respectively.

Attempted Reaction of Phenylglyoxal Aldoxime with Ethanol in the Presence of Pyridine Hydrochloride.—A solution of 10.0 g. (0.067 mole) of phenylglyoxal aldoxime and 11.7 g. (0.101 mole) of pyridine hydrochloride in 100 ml. of ethanol containing a trace of water was warmed at 60° with stirring for a period of 5 hours. Ethanol was then removed by evaporation *in vacuo*, leaving a yellow solid residue. The latter was extracted repeatedly with ether and the combined ether extracts dried and evaporated to give 9.2 g. of unreacted phenylglyoxal aldoxime, m.p. 122–125°, mixed m.p. with an authentic sample, 124–125°. An additional 0.6 g. of oxime was recovered by dissolving the pyridine hydrochloride residue in water and extracting with ether.

Attempted Reaction of Benzoylformohydroxamyl Chloride with Ethanol in the Presence of Pyridine Hydrochloride.—A solution of 5.0 g. (0.0272 mole) of benzoylformohydroxamyl chloride[26] and 3.2 g. (0.0277 mole) of pyridine hydrochloride in 333 ml. of ethanol was warmed and stirred at 60° for a 3.5-hour period. The ethanol was then removed *in vacuo* on the steam-bath and the residue extracted with ethyl ether. Evaporation of the ether extract left 4.7 g. of yellowish starting material, m.p. 97–117°. Recrystallization from carbon tetrachloride–benzene raised the m.p. to 128–129° (reported[26] m.p. 132–133°). The mixed m.p. with benzoyl formohydroxamyl chloride was 128–130°.

Reaction of Benzoylformohydroxamyl Chloride with Nitrosyl Chloride in Ethanol Solution in the Presence of Pyridine.—To a solution of 3.62 g. (0.0457 mole) of pyridine in 200 ml. of ethanol was added 2.1 ml. (0.0457 mole at −30°) of nitrosyl chloride while stirring and maintaining a temperature of −30 to −40° with Dry Ice–acetone cooling. To this was added, in one portion, 5.6 g. (0.0305 mole) of benzoylformohydroxamyl chloride and the mixture warmed to 60° where it was held, with stirring, for a 5-hour period. During the course of the reaction, gas evolution was measured by a wet-test meter. Unlike the reactions of nitrosyl chloride with acetophenone and with phenylglyoxal aldoxime, the evolution of gas was very slow, approximately one hour being required for the evolution of one-half of the total (0.81 liter) volume of gas.

The reaction mixture was evaporated at 60° under reduced pressure (20 mm.) to obtain an orange-yellow sirup. This was diluted with diethyl ether and extracted first with water and then with cold 5% sodium carbonate to form an emulsion. Upon filtering and allowing to stand, two liquid layers were formed. Evaporation of ether from the organic layer left 2.3 g. of a viscous orange oil. When distillation through a short-path system was attempted, only a few drops of volatile material, b.p. 82–88° (6 mm.), were obtained. Infrared analysis showed strong absorption in the 8.8–9.35 μ region, but only weak bands in the carbonyl region. The strong sharp band at 8.31 μ, characteristic of ethyl phenylglyoxalate, was not present.

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