amine series where nonlinearity between rate and base concentration was observed.

A catalytic mechanism consistent with the experimental data discussed above involves a base-isocyanate complex formed by the direct attack of the isocyanate by the free base. The experimental data does not support a catalytic mechanism which involves the base-alcohol complex in the formation of the base-isocyanate complex.

The sensitivity of the catalytic activity to the steric requirements of the base does not support a mechanism involving activation through a base-alcohol interaction whereby the reacting species is an alkoxide anion. Such a mechanism would be insensitive to the steric requirements of the base because of the small spatial needs of the hydrogen entity. The independence of the basicity of an amine to the steric requirements of the base[15] supports this conclusion. Further, the mechanism can not account for the high catalytic activities of 1,4-diazabicyclo[2,2,2]octane, 1,2-dimethylimidazole and quinine. The very low activities of *N*,*N*,*N'*,*N'*-tetraethylmethane-diamine and dimorpholinomethane are also in conflict with the mechanism.

The large effect that the steric requirements of the base have on the catalytic activities is consistent with a catalytic mechanism involving direct attack of the isocyanate by the free base to form the reactive base-isocyanate complex. The dependence of the catalytic activity on the nucleophilicity of the base rather than base strength is consistent with such a catalytic mechanism.

Acknowledgment. The author wishes to express deep appreciation to Professor H. Kwart for many valuable discussions. The able technical assistance of John E. Wells is gratefully acknowledged.

WAYNE, N. J.

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[15] H. K. Hall, Jr., *J. Am. Chem. Soc.*, **60**, 63 (1956).

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, TOKYO INSTITUTE OF TECHNOLOGY]

Dehydration Reactions of Hydroxamic Acids. A New Method for the Preparation of Isocyanates

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Dehydration reactions of an aliphatic aldoxime and several hydroxamic acids with organic reagents have been studied. The reaction of hydroxamic acids with phenyl isocyanate in the presence of triethylamine led to the formation of ureas through the intermediate phenylcarbamyl hydroxamates. Isocyanates were not isolated in this process but they were successfully isolated from hydroxamic acids by use of ketene dimer. The pyrolysis at 350–400° of acetoacetyl hydroxamates, initially formed, gave the corresponding isocyanates in fairly good yields along with acetone and carbon dioxide.

Dehydration reactions of primary nitroparaffins into nitrile oxides by means of organic reagents such as phenyl isocyanate, carbodiimide, or acetylenic ether in the presence of a catalytic amount of an aliphatic tertiary amine have been described in preceding papers.[1,2] The reactions can be explained by assuming initial formation of addition compounds of *aci*-nitroalkanes and the above-mentioned reagents, which in turn decompose into nitrile oxides. Further study[2,3] on the dehydrations of aldoximes with carbodiimide, acetylenic ether, ketene acetal, vinyl ether, vinyl acetate, acrylonitrile, and benzil also suggests that the initially formed adducts are the necessary intermediates for the reaction.

In the present study, the dehydration of an aliphatic aldoxime with phenyl isocyanate was tried first. Benzaldoxime is known to react with phenyl isocyanate to form *O*-phenylcarbamylbenzaldoxime and this adduct decomposes[4] into nitrile, aniline, carbon dioxide, and sym-diphenyl urea by heating. It is now established that an aliphatic aldoxime, heptanaldoxime, also reacts with phenyl isocyanate in the presence of triethylamine to give *sym*-diphenylurea, carbon dioxide, and heptanenitrile in high yields.

$$C_6H_{13}CH{=}NOH + 2C_6H_5NCO \longrightarrow C_6H_{13}CN + CO_2 + CO(NHC_6H_5)_2$$

Analogous to the explanation used for nitroparaffins, the reaction is thought to produce the intermediate $C_6H_{13}CH{=}NOCONHC_6H_5$ (I), which is successively deprotonated by amine to yield the nitrile and phenylcarbamic acid (or aniline + carbon dioxide).

This type of reaction was next extended to hydroxamic acids, compounds which resemble *aci*-nitroalkanes and aldoximes in possessing the structural possibility of dehydration (Lossen re-

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[1] T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.*, **82**, 5339 (1960).

[2] T. Mukaiyama and T. Hata, submitted for publication to the *Bull. of Chem. Soc. of Japan.*

[3] T. Mukaiyama and T. Hata, submitted for publication to the *Bull. of Chem. Soc. of Japan.*

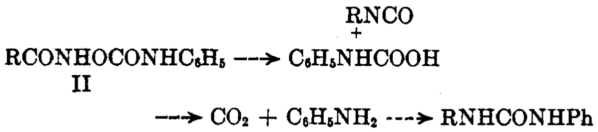
[4] H. Goldschmidt, *Ber.*, **22**, 3101 (1889); O. L. Brady and F. P. Dunn, *J. Chem. Soc.*, 672 (1916).

TABLE I

PHYSICAL PROPERTIES OF THE ACETOACETYL HYDROXAMATES

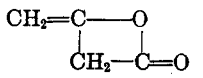
Hydroxamic Acids	Acetoacetyl Hydroxamates	Yield, %	M.P.	Dec. p.	Nitrogen, % Calcd.	Nitrogen, % Found
Hexane-	$C_{10}H_{17}NO_4$	85	69–70	140	6.65	6.51
Phenylaceto-	$C_{12}H_{13}NO_4$	81	115	135	5.96	6.03
p-Aniso-	$C_{12}H_{13}NO_5$	86	114–115	125	5.58	5.63
p-Toluo-	$C_{12}H_{13}NO_4$	78	99–100	115	5.96	6.02
p-Chlorobenzo	$C_{11}H_{10}ClNO_4$	80	93–94	130	5.49	5.48

arrangement).[5] In this connection, Hurd[6] reported addition of two moles of phenyl isocyanate to benzohydroxamic acid when no solvent was present. Later, Hurd and Bauer[7] reported reaction of one mole of phenyl isocyanate to benzohydroxamate anion by use of a suspension of the sodium salt in cold chloroform. This adduct, phenylcarbamyl benzohydroxamate, was rearranged to form *sym*-diphenylurea by heating above 180°. It is now found that phenylcarbamyl hydroxamates (II) may be obtained in high yield by addition of phenyl isocyanate to the hydroxamic acid (*p*-anisohydroxamic acid, phenylacetohydroxamic acid) in the presence of a catalytic amount of triethylamine at 50°. These adducts (II) decompose almost quantitatively in toluene at 90–100° into the ureas, RNH—CO—NHC_6H_5, and carbon dioxide if triethylamine is present, but the other isocyanate (RNCO) could not be isolated, even though it is regarded as an intermediate in the process.



$$\underset{\text{II}}{RCONHOCONHC_6H_5} \longrightarrow \overset{\displaystyle RNCO}{\overset{+}{C_6H_5NHCOOH}}$$
$$\longrightarrow CO_2 + C_6H_5NH_2 \longrightarrow RNHCONHPh$$

Finally a successful plan was discovered for the conversion of hydroxamic acids into isocyanates. This involved treatment with ketene dimer which gave adducts (III) in 78–86% yields with a variety of hydroxamic acids (Table I). Ketene dimer has

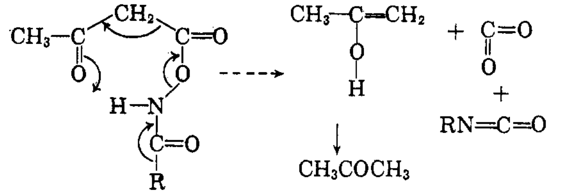
$RCONHOH +$ 

$$\longrightarrow \underset{\text{III}}{RCONHOCOCH_2COCH_3}$$

been proved to be a β-lactone[8] and is readily hydrated to give acetoacetic acid. As acetoacetic acid decomposes to give acetone and carbon dioxide which are unreactive with isocyanate, the isolation of isocyanate becomes feasible. The adducts (III) are acetoacetyl hydroxamates which are formed by opening the β-lactone ring of the dimer. These adducts are typical dihydroxamic acids, showing no color reaction with ferric chloride. They decompose at about 130° into acetone, carbon dioxide, and tarry products but no simple isocyanate. Isocyanates could be formed, however, in yields ranging from 36–71% (see Table II) along with acetone in nearly the same yields by carrying out the pyrolysis rapidly at 350–400° under reduced pressure:

$$\text{III} \longrightarrow RNCO + CH_3COCH_3 + CO_2$$

The decomposition is regarded as proceeding through a cyclic intermediate;



EXPERIMENTAL

Materials. Hydroxamic acids were prepared from carboxylic ethyl esters, hydroxylamine hydrochloride, and potassium hydroxide according to the method of Renfrow and Hauser.[9] Phenyl isocyanate and ketene dimer were obtained from a commercial source and purified by distillation.

Reaction of heptanaldoxime with phenyl isocyanate. To a solution of heptanaldoxime (6.5 g., 0.05 mole) and 5 drops of triethylamine in 30 ml. of dry benzene placed in a 100-ml. three necked flask equipped with dropping funnel and reflux condenser, at the top of which was connected a gas-outlet leading into aqueous barium hydroxide, was added phenyl isocyanate (11.9 g., 0.1 mole) of 10 ml. of dry benzene. After the mixture was refluxed for 2 hr., it was cooled and *sym*-diphenylurea was collected. It was recrystallized from ethanol and weighed 9.9 g. (93%), m.p. 237–238°. A fractional distillation of the filtrate *in vacuo* gave 4.9 g. (89%) of heptanenitrile, 67–67.5°/13 mm. The amount of carbon dioxide was 1.8 g. (82%), calculated from barium carbonate obtained.

Reaction of p-anisohydroxamic acid with phenyl isocyanate. To a solution of phenyl isocyanate (1.2 g., 0.01 mole) and *p*-anisohydroxamic acid (1.7 g., 0.01 mole) in 15 ml. of dry ethyl acetate was added 3 drops of triethylamine. The reaction started soon with liberation of heat. The reaction mixture was shaken for 30 min. at 50° and cooled. The precipitate of phenylcarbamyl *p*-anisohydroxamate (IIa. R = *p*-$CH_3OC_6H_4$—) was separated and washed with ethyl acetate. It weighed 2.7 g. (94%), and recrystallized from 95% ethanol.

Anal. Calcd. for $C_{15}H_{14}N_2O_4$: N, 9.79. Found: N, 9.79.

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(5) H. L. Yale, *Chem. Rev.*, **33**, 209 (1943).

(6) C. D. Hurd, *J. Am. Chem. Soc.*, **45**, 1478 (1923).

(7) C. D. Hurd and L. Bauer, *J. Am. Chem. Soc.*, **76**, 2791 (1954).

(8) C. D. Hurd and C. Blanchard, *J. Am. Chem. Soc.*, **72**, 1461 (1950).

(9) W. B. Renfrow, Jr., and C. R. Hauser, *J. Am. Chem. Soc.*, **59**, 2312 (1937); *Org. Syntheses*, Coll. Vol. II, 67 (1943).

TABLE II

PYROLYSIS OF ACETOACETYL HYDROXAMATES

Acetoacetyl Hydroxamates	Amount Pyrolyzed, G.	Pyrolysis conditions Temp.	Pyrolysis conditions Pressure, mm.	Product Acetone Yield, %	Product Isocyanate Yield, %	Product Isocyanate B.P. (mm.)
Hexano-	5.0	400	15	45	36	48–50/14
Phenoaceto-	5.0	350	15–20	68	63	88–90/10
Benzo-	5.0	400	1	84	67	62–64/20
p-Aniso-	2.0	370–380	3	78	71	116–118/37
p-Toluo-	2.0	350	15	74	54	71–72/13
p-Chlorobenzo-	2.0	370–380	3	61	48	107–108/41

It decomposed at 149–150° with evolution of gas and gave 1-phenyl-3-*p*-methoxyphenylurea which melted at 180–185°.

Similarly, phenylcarbamyl phenylacetohydroxamate (IIb. R = $C_6H_5CH_2$—) was obtained from phenyl isocyanate and phenylacetohydroxamic acid in 82% yield, 124° dec. (recrystallized from 95% ethanol).

Anal. Calcd. for $C_{15}H_{14}N_2O_3$: C, 66.65; H, 5.22; N, 10.37. Found: C, 66.33; H, 5.15; N, 10.21.

Decomposition of IIa *in the presence of triethylamine.* A solution of 1.2 g. of IIa and 3 drops of triethylamine in 10 ml. of dry toluene was refluxed for 20 min. After cooling, the precipitate (1.0 g., 98%) of 1-phenyl-3-*p*-methoxyphenylurea was collected, m.p. 189–190°; it was recrystallized from 95% ethanol.

In a similar fashion IIb was converted into 1-phenyl-3-benzylurea in 95% yield, m.p. 169–170°; it was recrystallized from 95% ethanol.

Preparation of acetoacetyl benzohydroxamate. A solution of ketene dimer (15.0 g., 0.185 mole) in 10 ml. of ethyl acetate was added dropwise over a period of 20 min. to a suspension of benzohydroxamic acid (20.0 g., 0.165 mole) in 20 ml. of ethyl acetate at room temperature. After addition was completed, the mixture was stirred at 50° for 30 min. The solvent was subsequently removed under reduced pressure and the residual acetoacetyl benzohydroxamate was recrystallized from ethyl acetate, weighed 29.0 g. (88%). The white crystal melted at 83–84° and decomposed at 130–135°.

Anal. Calcd. for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.55; H, 5.13; N, 6.33.

Similarly, acetoacetyl phenylaceto-, *p*-toluo-, *p*-aniso-, and hexanohydroxamates were prepared from ketene dimer and corresponding hydroxamic acids. Their properties are listed in Table I.

The *p*-chlorobenzohydroxamate was prepared analogously except for the use of refluxing absolute ether (10 hr.) instead of the ethyl acetate.

Pyrolysis of acetoacetyl hydroxamates. The apparatus used for all pyrolyses consisted essentially of a vertical pyrex tube, 12 mm. or 18 mm. in diameter and 60 cm. long, equipped with standard taper joint and a side-inlet tube near the top for the exchange of air with nitrogen. This tube was packed with Pyrex chips and externally heated with electric furnace. The temperature was determined with a thermocouple located between the Pyrex tube and furnace. Before each pyrolysis the whole system was flushed for 10 min. with dry nitrogen. Pyrolysis was conducted under reduced pressure and 2.0 g. or 5.0 g. of acetoacetyl hydroxamate was dropped into the column at a rate of 0.2 g. per min. The pyrolysate was collected directly in a Claisen flask cooled in a Dry Ice acetone bath, and fractionated by distillation (Table II).

Acknowledgment. The authors wish to express their hearty thanks to Prof. Toshio Hoshino for his encouragement and to Mr. Makoto Tokizawa, Mr. Kazuyoshi Tonooka, and Mr. Mochihiro Iijima for their help during the course of this experiment. Thanks are also due to Mr. Asaji Kondo for the microanalyses.

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[CONTRIBUTION FROM THE SHELL DEVELOPMENT COMPANY]

Some Observations on the Pechmann Reaction[1]

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α-Resorcylic acid and 3-dimethylamino-5-pentylphenol do not undergo the Pechmann reaction with ethyl 5-methylcyclohexanone-2-carboxylate under conditions normally used. Separation of the carboxyl groups from the ring by one methylene group permits the reaction to proceed easily. An unusual ring closure between a 5-alkyl resorcinol and the above β-ketonic ester has been observed.

In the course of work on the condensation of ethyl 5-methylcyclohexanone-2-carboxylate with certain phenol and resorcinol derivatives, it was observed that α-resorcylic acid (3,5-dihydroxybenzoic acid) and 3-dimethylamino-5-pentylphenol would not undergo the Pechmann condensation with the above β-ketonic ester to give, respectively, the expected compounds I and II.

A number of references to the condensation of β- and γ-resorcylic acids or esters (2,4- and 2,6-dihydroxybenzoic acids, respectively) with β-ketonic

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[1] This paper reports work done under contract with the Chemical Corps, U. S. Army, Washington, D. C.