room temperature. After standing for 6 hr the mixture was diluted with ether, washed (H_2O), dried ($MgSO_4$), and evaporated to give a black oil, which when chromatographed on silica (300 g), eluting with ether:light petroleum (1:9), gave the alkene II[11] (0.46 g): mass spectrum (70 eV) *m/e* (rel intensity) 224 (100) M^+, 209 (47), 193 (64), 115 (100), 91 (54), and 77 (42); uv, ir, and nmr spectral values correspond with those reported in the literature.[12] Also isolated from the column were the same polymeric hydrocarbon as mentioned previously (0.80 g), *p*-toluenesulfonyl chloride (1.3 g), di-*p*-methoxybenzyl ether (0.74 g), dicinnamyl ether (0.60 g), *p*-methoxybenzyl cinnamyl ether (1.00 g), cinnamyl alcohol (0.66 g), and *p*-methoxybenzyl alcohol (0.50 g).

Registry No.—I, 26057-48-7; II, 35856-80-5; *trans*-cinnamyl *p*-toluenesulfonate, 37611-16-8; *p*-methoxybenzyl *p*-toluenesulfonate, 14670-03-2.

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Anhydrous Hydrofluoric Acid as a Cyclizing Agent in the Preparation of Several Substituted Oxazoles from *N*-Aroyl-α-amino Ketones[1a]

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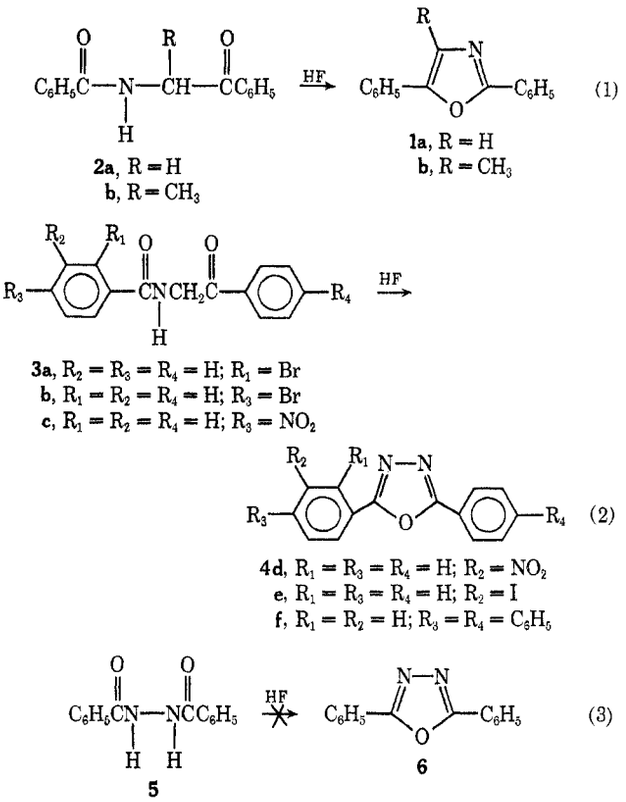
In the course of our studies of the photooxidation of 2,5-diphenyloxazole (PPO) (**1a**) it was necessary to prepare 4-methyl-2,5-diphenyloxazole (**1b**).[2] Attempts to cyclize α-benzamidopropiophenone (**2b**) to **1b** (Scheme I, eq 1) with concentrated sulfuric acid in accordance with the procedure given by Cleland and Nieman[3] gave a maximum yield of 12.5% of the desired product. Consequently, it was decided to try anhydrous hydrofluoric acid as a condensing agent in this reaction, and a 95% yield of the oxazole **1b** was isolated.

The customary condensing agents used by Hayes and coworkers[4] in the preparation of oxazoles from the corresponding *N*-aroyl-α-amino ketones were phosphorus oxychloride or concentrated sulfuric acid and the recorded yields generally ranged from 50 to 80%. In another paper[5] we reported yields of 39–62% of 2,5-diaryloxazoles when phosphorus oxychloride was used as a cyclizing agent. The nearly quantitative yield of 4-methyl-2,5-diphenyloxazole (**1b**) obtained when anhydrous hydrofluoric acid was used led to a study of the general efficiency of the acid in condensations of this type.

SCHEME I



Anhydrous hydrofluoric acid was used for the cyclization of α-benzamidoacetophenone (**2a**), α-(2-bromobenzamido)acetophenone (**3a**), α-(4-bromobenzamido)-acetophenone (**3b**), α-(4-nitrobenzamido)acetophenone (**3c**), α-(3-nitrobenzamido)acetophenone (**3d**), α-(3-iodobenzamido)acetophenone (**3e**), and 2-aza-1,4-di-(4-biphenylyl)-1,4-butanedione (**3f**) to the corresponding oxazoles, **1a** and **4a–f** (Scheme I, Table I).

TABLE I
CYCLIZATION OF *N*-AROYL-α-AMINO KETONES TO OXAZOLES

Substrate	Product	Yield,[a] %
α-Benzamidopropiophenone (**2b**)	4-Methyl-2,5-diphenyloxazole (**1b**)	95
α-Benzamidoacetophenone (**2a**)	2,5-diphenyloxazole (**1a**)	91[b]
α-(2-Bromobenzamido)-acetophenone (**3a**)	2-(2-Bromophenyl)-5-phenyloxazole (**4a**)	61[c]
α-(4-Bromobenzamido)-acetophenone (**3b**)	2-(4-Bromophenyl)-5-phenyloxazole (**4b**)	62
α-(4-Nitrobenzamido)-acetophenone (**3c**)	2-(4-Nitrophenyl)-5-phenyloxazole (**4c**)	Trace
α-(3-Nitrobenzamido)-acetophenone (**3d**)	2-(3-Nitrophenyl)-5-phenyloxazole (**4d**)	64
α-(3-Iodobenzamido)-acetophenone (**3e**)	2-(3-Iodophenyl)-5-phenyloxazole (**4e**)	79
2-Aza-1,4-di(4-biphenylyl)-1,4-butanedione (**3f**)	2,5-Di(4-biphenylyl) oxazole (**4f**)	96[d]
1,2-Dibenzoylhydrazine (**5**)	2,5-Diphenyloxadiazole (**6**)	0[e]

[a] In all cases the yield reported is of crystallized product (or crude product) having a melting point corresponding to that of pure material reported in the literature. [b] Using sulfuric acid yields of 53–81% are obtained. [c] Treated with two portions of HF. [d] Using phosphorus oxychloride the yield was 51%. [e] Using phosphorus oxychloride the yield was 55%.

(1) (a) From the Ph.D. dissertation of Margaret E. Ackerman (1971). This investigation was supported in part by a research grant from the Division of Biology and Medicine of the U. S. Atomic Energy Commission, Contract No. AT (29-2) 915. (b) Work performed under the auspices of the U. S. Atomic Energy Commission.
(2) We are indebted to Arapahoe Chemicals, Inc., for their generous gift of 100 g of the α-benzamidopropiophenone for use in this synthesis.
(3) G. H. Cleland and C. Niemann, *J. Amer. Chem. Soc.*, **71**, 841 (1949).
(4) F. N. Hayes, B. S. Rogers, and D. G. Ott, *ibid.*, **77**, 1850 (1955).
(5) M. D. Barnett, G. H. Daub, F. N. Hayes, and D. G. Ott, *ibid.*, **82**, 2282 (1960).

Yields of 2,5-diphenyloxazole (**1a**) and 2,5-di(4-biphenylyl)oxazole (**4f**) greater than 90% were obtained from compounds **2a** and **3f**, respectively. The other amido ketones gave yields of the oxazoles ranging from 61 to 79% with the exception of **3c**, which gave only a trace of product.

An attempt to condense 1,2-dibenzoylhydrazine (**5**) to 2,5-diphenyloxadiazole (**6**) with anhydrous hydrofluoric acid failed (Scheme I, eq 3). In initial experiments only benzoic acid was isolated. The experiment was repeated with the exclusion of moisture following the addition of the hydrofluoric acid; this precaution did prevent cleavage to benzoic acid but only the starting material **5** was recovered. The use of phosphorus oxychloride gave a 55% yield of **6** from **5**.

Experimental Section[6]

General Procedure.—The *N*-aroyl-α-amino ketone was dissolved in anhydrous hydrofluoric acid (10 ml of acid/1 g of ketone) in a polyethylene beaker, and the resulting solution was allowed to evaporate to dryness. The dry, crystalline material obtained was slurried in saturated aqueous sodium bicarbonate to destroy any hydrogen fluoride salts which may have formed. The product was then extracted into benzene; this benzene extract was washed with water, dried (Na_2SO_4), and chromatographed on neutral Woelm alumina. The solvent was removed *in vacuo* from the eluate and the crude product obtained was crystallized from cyclohexane or benzene–cyclohexane except for **4f**, which was recrystallized from dimethylformamide.

Registry No.—**1a**, 92-71-7; **1b**, 2549-31-7; **2a**, 4190-14-1; **2b**, 16735-29-8; **3a**, 37611-22-6; **3b**, 37611-23-7; **3d**, 37611-24-8; **3e**, 37611-25-9; **3f**, 37061-76-0; **4a**, 37611-27-1; **4b**, 14492-02-5; **4d**, 22397-43-9; **4e**, 37610-63-2; **4f**, 2083-09-2; hydrofluoric acid, 7664-39-3.

(6) All melting points were taken in Pyrex capillary tubes in a Hoover-Thomas melting point bath and in all cases were identical with those reported in the literature.

Hydrogen–Deuterium Exchange of *N*-Methylpyridinium Ion in Methanol Containing Amines. Identity of the Catalyzing Base

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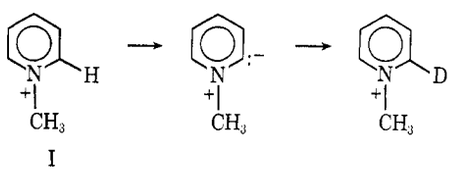
An attractive and useful solvent–base mixture for the study of hydrogen exchange reactions of weak carbon acids is found in alcohol–amines. Although a number of deprotonation studies have been carried out using such nonaqueous mixtures, the identity of the catalyzing base or bases has seldom been established.[1-4] Not only may the more abundant amine base catalyze the deprotonation reaction, but also the less abundant and more reactive alkoxide ion may serve as a catalyst. This ion is formed by the solvolysis reaction given in eq 1 where Am represents an amine. Without knowing

$$\mathrm{Am} + \mathrm{CH_3OD} \underset{}{\overset{K_b}{\rightleftharpoons}} \mathrm{AmD^+} + \mathrm{CH_3O^-} \qquad (1)$$

the identity of the catalyst(s), the significance of comparisons involving the reactivities of various carbon acids in such mixtures is obscured.

We here provide clear and unambiguous evidence concerning the identity of the base catalyst in the H–D exchange reaction of *N*-methylpyridinium ion (I) at the 2,6-positions in methanol-*O*-*d* containing amines. Considerable evidence is available to establish that the mechanism of hydrogen exchange of this substrate involves base-catalyzed deprotonation to give an ylide which then captures a deuteron from the solvent to give product, eq 2.[5,6] Exchange at only the 2 position is shown although the equivalent 6 position reacts as well.



I (2)

Results and Discussion

Two amine bases in CH_3OD were used to catalyze H–D exchange of I at 75.0°. They are morpholine (pK_a[7] in H_2O at 25° is 8.3) and 1,4-diazabicyclo[2.2.2]-octane (DABCO) (pK_a[8] in H_2O at 25° is 8.8). In both cases the rate of H–D exchange increased with increasing amine concentration and the more basic amine, DABCO, was the more effective. However, a tenfold change in the concentration of morpholine resulted in only a 3.1-fold change in the value of the pseudo-first-order rate constant, k_ψ. Similarly, a sevenfold change in DABCO concentration gave rise to a 3.0-fold change in k_ψ. If the amine were the sole catalyst, then the magnitude of the change in k_ψ would be the same as the magnitude of the change in the amine concentration, *i.e.*, the reaction rate would be first order in amine. This clearly is not the case. Methoxide ion resulting from the solvolysis reaction involving the amine (eq 1) must be acting as a catalyst.

Consider now the rate expression for H–D exchange given by eq 3 which includes terms for catalysis by both

$$k_\psi[\mathrm{CH}] = k_{\mathrm{MeO}}[\mathrm{CH}][\mathrm{CH_3O^-}] + k_{\mathrm{Am}}[\mathrm{CH}][\mathrm{Am}] \qquad (3)$$

methoxide ion and amine. In this equation k_{MeO} and k_{Am} are second-order rate constants for methoxide ion and amine catalysts and [CH] is the concentration of H at positions 2 and 6 as indicated by nmr. If the reaction mixture contains substrate and amine as in the experi-

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(2) For an authentic example of an amine-catalyzed deprotonation of a carbon acid in methanol, see F. G. Bordwell and M. W. Carlson, *ibid.*, **92**, 3370 (1970).

(3) It has been established that ethoxide ion is the catalyst for H–D exchange at position 2 of a thiazolium ion in ethanol containing an acetic acid–acetate ion buffer.[4]

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