

coarse glass filter funnel into a vigorously stirred, cooled solution of 0.15 mol of  $\text{HBF}_4$  (54% in ether) in 500 ml of absolute ethanol. The fluoroborate 2 was precipitated by addition of dry ether, filtered off, washed with dry ether, and dried in vacuo. If necessary the product may be purified by dissolving it in a minimum amount of methanol, filtering, and reprecipitating with dry ether.

The fluoroborates were converted to the corresponding selones 3 by a procedure identical with that earlier reported for the perchlorates.<sup>1,3</sup> This step is facilitated by the fact that the fluoroborates are more readily soluble in methanol than are the perchlorates.

Melting points are uncorrected. Elemental analyses were performed by Mr. Preben Hansen, Department of General and Organic Chemistry.

### References and Notes

- (1) K. Bechgaard, D. O. Cowan, A. N. Bloch, and L. Henriksen, *J. Org. Chem.*, **40** 746 (1975).
- (2) E. M. Engler and V. V. Patel, *J. Am. Chem. Soc.*, **96** 7376 (1974).
- (3) K. Bechgaard, D. O. Cowan, A. N. Bloch, R. E. Pyle, and R. H. Banks, *J. Am. Chem. Soc.*, submitted for publication.
- (4) E. M. Engler and V. V. Patel, *J. Org. Chem.*, **40**, 387 (1975).
- (5) K. Bechgaard, D. O. Cowan, and A. N. Bloch, *J. Chem. Soc. Chem. Commun.*, 937 (1974).
- (6) A. N. Bloch, D. O. Cowan, K. Bechgaard, R. E. Pyle, R. H. Banks, and T. O. Poehler, *Phys. Rev. Lett.*, submitted for publication.
- (7) 1,3-Dithiolium perchlorate has been reported to detonate spontaneously; J. P. Ferraris and F. I. Mopsik, *Chem. Eng. News*, 3 (Sept 16, 1974). See also K. G. R. Sundelin, *ibid.*, 3 (Aug 5, 1974).
- (8) K. Bechgaard, unpublished results.

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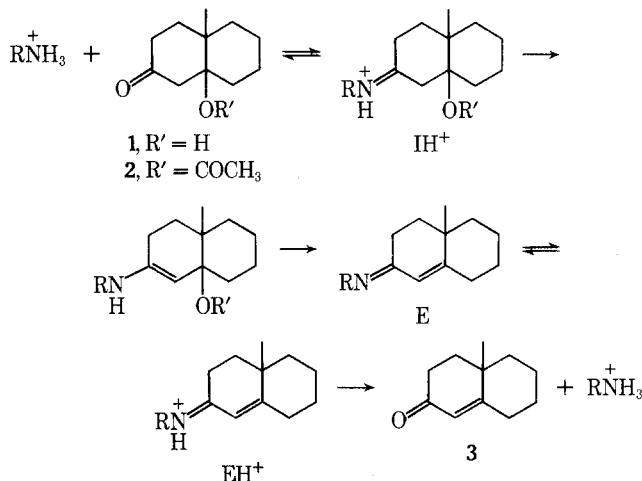
### Detection and Characterization of Eniminium Ion Intermediates in Nucleophilic Amine Catalyzed $\beta$ -Ketol Dehydration

**Summary:** Previously undetected chromophoric ( $\lambda_{\text{max}}^{\text{H}_2\text{O}}$   $\sim 270$  nm,  $\epsilon \sim 16,000$ ) intermediates in nucleophilic amine catalyzed dehydration of  $\beta$ -ketol 1 have been detected (when a large concentration of catalyst is used), isolated, and characterized as eniminium ions (e.g., 4).

**Sir:** Nucleophilic amine catalysis of the conversions of  $\beta$ -ketol 1 and  $\beta$ -acetoxy ketone 2 to enone 3 in aqueous solution has been reported by us<sup>1</sup> to proceed without appreciable accumulation of intermediate species according to the mechanism shown in Scheme I, with  $\alpha$ -deprotonation of iminium ion  $\text{IH}^+$  as the rate-limiting step. We have now found that under appropriate conditions eniminium ion  $\text{EH}^+$  is formed in significant concentrations. Since, as discussed below, this species is an intermediate in the sequence  $1 \rightarrow \text{EH}^+ \rightarrow 3$ , its detection constitutes important corroboration that catalysis is occurring via amine-carbonyl condensation.<sup>2</sup>

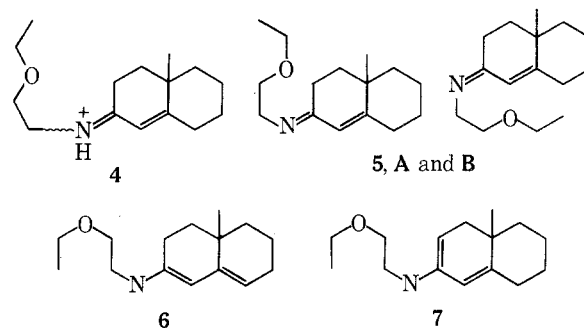
Intermediate  $\text{EH}^+$  is characterized by an ultraviolet absorption maximum at  $\sim 270$  nm. Our failure to detect this species earlier resulted from the use of conditions (low substrate and catalyst concentrations) which tend not to lead to appreciable accumulation of  $\text{EH}^+$ .<sup>3</sup> Absorption at  $\sim 270$  nm is readily detectable, however, when relatively high concentrations of reactant and catalyst (pseudo-zero-order conditions) are used at  $\text{pH} \leq \text{pK}_a$ . For example, an

### Scheme I



aqueous solution of 1 ( $5.85 \times 10^{-3}$  M) and ethoxyethylamine ( $\text{pK}_a = 9.44$ ; 0.52 M) at pH 8.65 develops absorption predominantly at 270 nm through approximately the first 10% of consumption of 1.

Identification of this chromophoric species as 4 was accomplished by extraction of the reaction mixture with deuteriochloroform and determination of the mass spectrum [ $m/e$  235.1938 (calcd for  $\text{C}_{15}\text{H}_{15}\text{NO}$  235.1936)] and the NMR spectrum of the extract. In addition to a peak at  $\delta$  5.70 in the latter due to the vinyl proton peak of 3, two peaks appeared at  $\delta$  5.92 and 6.09 (area ratio of  $\sim 2:1$ ) which can only reasonably be assigned to the vinyl protons of the geometrical isomers 5A and 5B of the neutral enimine derived from 4.<sup>4,5</sup>



If the extracted species were dienamine 6,<sup>6</sup> the olefinic protons should appear at  $\sim 5$  ppm,<sup>7,8</sup> and a mixture of 5 and 6 prepared by the method of Malhotra<sup>9</sup> did indeed show the expected additional resonances of equal intensity at  $\delta$  4.89 and 5.06.<sup>10</sup> If the species were dienamine 7, it should have an NMR peak at about  $\delta$  4.25.<sup>7</sup> The vinyl proton of 4 itself would be expected to appear well below 6 ppm,<sup>8,11</sup> and, when DCl was added to a  $\text{CD}_3\text{OD}$  solution of the synthesized mixture of 5 and 6, peaks at  $\delta$  5.85 and 6.18 were replaced by ones at  $\delta$  6.30 and 6.55. The ir spectrum of the extract showed  $\nu$  1630 and 1615  $\text{cm}^{-1}$ , consistent with the postulated imine structure.<sup>12</sup>

The fact that 4 is observed in reactions run at a pH near the  $\text{pK}_a$  of the catalyst means that this species must be at least comparable in basicity to ethoxyethylamine. This is not unreasonable. Although imines are generally believed to be  $\sim 10^3$  less basic than the corresponding amines,<sup>13-16</sup> the additional double bond in the enimine should help to stabilize its protonated form.<sup>17</sup> Unsaturated ketones are  $\sim 10^3$  more basic than saturated ketones.<sup>18</sup>

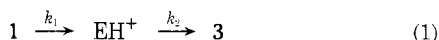
The pH-dependent equilibrium between 4 and neutral enimine can be easily demonstrated. A chloroform solution of 5, prepared in the manner described above, was extract-

ed with strongly acidic D<sub>2</sub>O, and the extract had  $\lambda_{\max}$  270 nm. When excess KOH solution was added, the peak at 270 nm was replaced by one of equal intensity at 245 nm.<sup>12,1</sup> Reacidification returned the peak to 270 nm, but with somewhat diminished intensity, presumably owing to partial hydrolysis to **3**.<sup>20</sup>

An extinction coefficient for **4** was determined in the following manner. As previously demonstrated,<sup>1</sup> dehydration of **1** occurs predominantly by a third-order process at pH's near the  $pK_a$  (rate proportional to  $[1][RNH_2][RNH_3^+]$ ). Dilution about thirtyfold of a reaction mixture displaying a peak at 270 nm slows the production of **4** sufficiently so that the hydrolysis of **4** to **3** ( $\epsilon_{247}^{H_2O}$  15,500) could readily be followed. An isosbestic point was observed, and a value for **4** of  $\epsilon_{\max}^{H_2O}$  16,000 was calculated.<sup>21</sup>

Other  $EH^+$  species analogous to **4** have been observed under appropriate conditions with the following catalysts for **1**  $\rightarrow$  **3**: pyrrolidine, proline, ethyl glycinate, methyl alanate, cyanomethylamine, histamine,<sup>22</sup> histidine,<sup>22</sup> and histidine methyl ester.<sup>22</sup> A value of  $\epsilon_{\max}^{H_2O}$  17,000 was obtained by the method described for  $EH^+$  incorporating histamine.

That  $EH^+ (\rightleftharpoons E)$  is an intermediate in the formation of **3** from **1** is supported by the following facts: (1) when  $EH^+$  appears it appears before **3** and (2) only **3** is present at the end of reaction, despite typical catalyst/substrate ratios of  $\sim 100$ .<sup>23</sup> In addition, the rate data for appearance and disappearance of  $EH^+$  can be fitted successfully to a nonlinear least-squares consecutive first-order kinetics program.<sup>24</sup> For the reaction of  $2.97 \times 10^{-3} M$  **1** with  $0.40 M$  ethoxyethylamine buffer at pH 9.16, this program yielded the following values for the pseudo-first-order rate constants in eq 1:  $k_1 = 7.14 \times 10^{-5} \text{ sec}^{-1}$  and  $k_2 = 6.26 \times 10^{-4} \text{ sec}^{-1}$



( $k_2/k_1 = 9$ ). With  $0.40 M$  cyanomethylamine buffer at pH 5.47, the values were  $k_1 = 9.92 \times 10^{-5} \text{ sec}^{-1}$  and  $k_2 = 1.92 \times 10^{-3} \text{ sec}^{-1}$  ( $k_2/k_1 = 19$ ). The third-order rate constants for the conversion of **1** to  $EH^+$  calculated from these values of  $k_1$  are in good agreement with the rate constants ( $k_{AB}$ 's) previously determined<sup>1b</sup> for nucleophilic amine catalyzed dehydration of **1**.

The detection of these chromophoric eniminium ion intermediates in amine catalyzed  $\beta$ -ketol dehydration suggests that a search for analogous species in other model, as well as enzymic,<sup>25</sup> reactions would be worthwhile, and we are exploring some of these possibilities.

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### References and Notes

- (1) (a) D. J. Hupe, M. C. R. Kendall, and T. A. Spencer, *J. Am. Chem. Soc.*, **94**, 1254 (1972); (b) *ibid.*, **95**, 2271 (1973).
- (2) After completion of this manuscript, two reports have appeared describing analogous intermediates in amine catalyzed isomerization of  $\beta,\gamma$ -unsaturated ketones to their  $\alpha,\beta$ -unsaturated isomers: (a) R. H. Kayser and R. M. Pollack, *J. Am. Chem. Soc.*, **97**, 952 (1975); (b) W. F. Benisek and A. Jacobson, *Bioorg. Chem.*, **4**, 41 (1975).
- (3) Some of the rate constants for nucleophilic amine catalysis ( $k_{AB}$  and  $k_A$  terms) in ref 1a and 1b were calculated from kinetic data on reactions which showed, or would have shown if closely scrutinized, a brief induction period when monitored at 247 nm, the  $\epsilon_{\max}^{H_2O}$  of **3** (see A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", Second ed, Wiley, New York, N.Y., pp 166–169, for a discussion of "series reactions"). However the published values of  $k_{AB}$  and  $k_A$  were usually obtained over several half-times of reaction and are essentially correct (vide infra).
- (4) The methoxime formed from **3** shows analogous peaks at  $\delta$  5.80 and 6.40: C. W. Leong, unpublished work in these laboratories.
- (5) Interconversion of **5A** and **5B** would be very slow at room temperature; see, e.g., W. B. Jennings and D. R. Boyd, *J. Am. Chem. Soc.*, **94**, 7187 (1972).
- (6) *N,N*-Dialkylidenamines show  $\lambda_{\max}^{H_2O}$  275–280 nm: J. L. Johnson, M. E. Herr, J. C. Babcock, A. E. Fonken, J. E. Strafford, and F. W. Heyl, *J. Am. Chem. Soc.*, **78**, 430 (1956); S. K. Malhotra, in "Enamines: Synthesis, Structure, and Reactions", A. G. Cook, Ed., Marcel Dekker, New York, N.Y., 1969, Chapter 1.
- (7) H. O. House, B. M. Trost, R. W. Magin, R. G. Carlson, R. W. Franck, and G. H. Rasmussen, *J. Org. Chem.*, **30**, 2513 (1965).
- (8) M. J. M. Pollmann, U. K. Pandit, and H. O. Huisman, *Recl. Trav. Chim. Pays-Bas*, **89**, 941 (1970).
- (9) S. K. Malhotra, J. J. Hostynek, and A. F. Lundin, *J. Am. Chem. Soc.*, **90**, 6565 (1968).
- (10) On standing, the extracted **5** developed these peaks indicating presence of **6**. As further confirmation, 8,8,10-trimethyl- $\Delta^{1,9}$ -octalone-2 [W. G. Dauben and A. C. Ashcraft, *J. Am. Chem. Soc.*, **85**, 3673 (1963); we are very grateful to M. A. Tius for a generous sample of this substance], which has  $\delta$  (CDCl<sub>3</sub>) 5.95 and which cannot form a dienamine analogous to **6**, was treated with methoxyethylamine as in ref 9 to afford a product with  $\delta$  6.16 and 6.38.
- (11) R. W. Kelly, I. McClenaghan, and P. J. Sykes, *J. Chem. Soc. C*, 2375 (1967).
- (12) K. Irmischer, *Chem. Ber.*, **95**, 907 (1962), reports  $\nu$  1630 and 1620  $\text{cm}^{-1}$  and  $\lambda_{\max}^{EtOH}$  241 nm for hydroxyethylenimines of  $\Delta^4$ -3-keto steroids.
- (13) J. Hine, B. C. Menon, J. H. Jensen, and J. Mulders, *J. Am. Chem. Soc.*, **88**, 3367 (1966).
- (14) M. L. Bender and A. Williams, *J. Am. Chem. Soc.*, **88**, 2502 (1966).
- (15) F. H. Westheimer, Proceedings of the Robert A. Welch Foundation Conferences on Chemical Research, "XV. Bio-Organic Chemistry and Mechanisms", Houston, Texas, Nov 1–3, 1971, p 31.
- (16) However, B. Brezina and P. Zuman, *Chem. Listy*, **47**, 975 (1953), report several imine  $pK_a$ 's which are considerably closer to the  $pK_a$ 's of the corresponding amines.
- (17) E. M. Kosower and T. S. Sorensen, *J. Org. Chem.*, **28**, 692 (1963), report that the *n*-butylenimine from crotonaldehyde has a  $pK_a$  two units below the  $pK_a$  of *n*-butylamine. However, this system has two fewer alkyl substituents on the conjugated system than does  $EH^+$ .
- (18) G. C. Levy, J. D. Cargioli, and W. Racela, *J. Am. Chem. Soc.*, **92**, 6238 (1970).
- (19) It should be noted that in our monitoring of reactions of **1** and **2** at 247 nm we may have been registering absorption caused by species E as well as by **3** during the early part of some reactions. The  $\epsilon$  of E at 247 nm, based on  $\epsilon_{\max}^5 \geq \epsilon_{\max}^4 = \epsilon_{\max}^3 + 500$  (vide infra), is not very different from  $\epsilon_{\max}^3$ .
- (20) At pH < 3, **4** appears to be stable indefinitely, but conversion to **3** is rapid at pH  $\geq pK_a$  of **4**. See P. Bolla and M. Legrand, *Bull. Soc. Chim. Fr.*, 2143 (1973), for a study of dienamine hydrolysis in which eniminium ions figure prominently and for pertinent references.
- (21) H. H. Jaffe and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy", Wiley, New York, N.Y., 1962, p 557.
- (22) A study of intramolecular bifunctional nucleophilic amine catalysis using this compound will be the subject of a subsequent publication.
- (23) The absence of E is easily demonstrated by addition of acid, which does not affect the uv spectrum.
- (24) We thank Professor M. V. Olson for lending us this program and we thank him and Professor R. Ditchfield for generous assistance in using it.
- (25) (a) K. W. Rabinowitz, R. A. Niederman, and W. A. Wood, *J. Biol. Chem.*, **248**, 8207 (1973), report an eniminium ion intermediate ( $\epsilon_{\max}$  455) from  $\alpha$ -aminocrotonic acid and pyridoxal phosphate in the enzymic dehydration of threonine. (b) J. R. Butler, W. L. Alworth, and M. J. Nugent, *J. Am. Chem. Soc.*, **96**, 1617 (1974), propose such an intermediate in dehydroquinase catalyzed dehydration. (c) D. Portsmouth, A. C. Stoolmiller, and R. H. Abeles, *J. Biol. Chem.*, **242**, 2751 (1967), propose such an intermediate in the enzymic conversion of 2-keto-3-deoxy-L-arabonate to  $\alpha$ -ketoglutarate semialdehyde.

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### Reductive Deamination of Primary Amines. Sodium Borohydride Reduction of *N,N*-Disulfonimides in Hexamethylphosphoramide

**Summary:** Sodium borohydride in hexamethylphosphoramide provides a convenient and efficient reagent system for the reductive deamination of unhindered primary amines via initial conversion to *N,N*-disulfonimides and reduction at 150–175°.

**Sir:** Although procedures for the activation of hydroxyl groups for displacement or elimination are numerous and