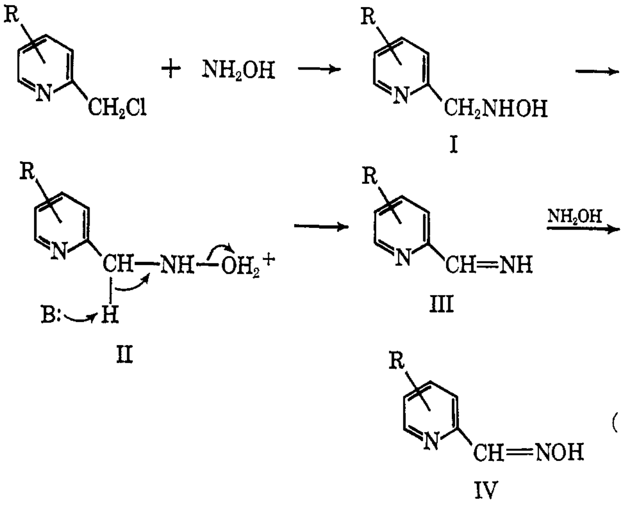
substituted 2-picoline N-oxides is 23–30%.[5] Recently Forman[6] has reported the direct high yield oximation of 2-picoline using sodium amide and n-butyl nitrite. The applicability of the procedure to substituted 2-picolines is not presently known.

We have found that the reaction of 2-chloromethyl pyridines with buffered solutions of aqueous hydroxylamine gives good yields of the corresponding 2-pyridine aldoximes. The procedure consists of heating the 2-chloromethylpyridine in an aqueous ethanolic solution of hydroxylamine hydrochloride buffered to pH 7–8 on a steam bath for 2 to 3 hr. Upon cooling the reaction to room temperature, the product usually crystallized from the solution.

The reaction is significant in view of the fact that treatment of p-chlorobenzyl chloride under identical conditions gave the dialkyl hydroxylamine as the only product. The acidity of the hydrogens α to the halo group seems to be important since 2-bromocyclohexanone on treatment with buffered hydroxylamine solution affords a 34% yield[7] of 1,2-cyclohexanedione dioxime.

In view of this acidity requirement, the mechanism shown (1) may be postulated: nucleophilic displacement of the chloro group yields the alkylhydroxylamine (I); subsequent protonation of the hydroxyl group of I followed by the elimination yields the aldimine III;[8] the aldimine in the presence of excess hydroxylamine yields the product oxime IV.



(1)

Experimental Section

Melting points were determined using a Thomas–Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind.

The 2-chloromethylpyridines were prepared by a modification and extension of previously reported procedures.[9,10] Substituted pyridine N-oxides were treated with a twofold excess of methanesulfonyl chloride or p-toluenesulfonyl chloride in refluxing dioxane for 6 to 12 hr. Best results were obtained with p-toluenesulfonyl chloride in the case of 6-methyl, 5-methyl, and 5-ethyl derivatives.

New 2-chloromethylpyridines prepared by this procedure were as follows: 4-chloro, 51%, bp 51° (0.9 mm), $n^{25}\text{D}$ 1.5225, picrate mp 123–125°; 4-carboethoxy, 62%, 75° (0.12 mm), $n^{25}\text{D}$ 1.5208, picrate mp 110–111°; 5-carboethoxy, 59%, 64° (0.05 mm), $n^{25}\text{D}$ 1.5252, picrate mp 123–125°; 5-chloro, 40%, 48° (0.5 mm), $n^{25}\text{D}$ 1.5293, picrate mp 96–98°. All compounds had acceptable elemental analyses in carbon, hydrogen, and nitrogen (chlorine).

The appropriate 2-chloromethyl pyridine (0.02 mole) was added to a solution of hydroxylamine hydrochloride (0.1 mole) in 40 ml of 50% aqueous ethanol (v/v) which had been buffered to pH 7 to 8 with 10 N sodium hydroxide solution. The solution was heated on a steam bath for 2 to 3 hr; ethanol was added from time to time so as to maintain a homogeneous solution. Upon cooling the solution, the product crystallized and was recrystallized from either benzene or aqueous ethanol. The data are summarized in Table I.

TABLE I

CONVERSION OF MONOSUBSTITUTED (R) 2-CHLOROMETHYL PYRIDINES TO 2-PYRIDINE ALDOXIMES

R	Yield, %	Mp, °C
H	50	112–114[a]
4-Cl	18	151–153[b]
5-Cl	63	194–195[c]
4-$COOC_2H_5$	52	157–158[d]
5-$COOC_2H_5$	72	128–129[e]
5-C_2H_5	78	149–150[f]
6-CH_3	91	170–172[g]

[a] S. Ginsberg and I. Wilson [*J. Am. Chem. Soc.*, **79**, 481 (1957)] report mp 114°; mixture melting point with an authentic sample was undepressed. [b] S. Furukawa[5] reports 154–155°; mixture melting point with an authentic sample was undepressed. [c] Calcd for $C_6H_5ClN_2O$: C, 46.04; H, 3.22; N, 17.90. Found: C, 45.74; H, 3.40; N, 17.63. [d] Calcd for $C_9H_{10}N_2O_3$: C, 55.66; H, 5.19; N, 14.42. Found: C, 55.39; H, 5.29; N, 14.32. [e] Found: C, 55.86; H, 5.42; N, 14.07. [f] Calcd for $C_9H_{10}N_2O$: C, 64.00; H, 6.70; N, 18.65. Found: C, 64.17; H, 6.95; N, 18.53. [g] S. Ginsberg and I. Wilson [*J. Am. Chem. Soc.*, **79**, 481 (1957)] report mp 170–171°.

Acknowledgment.—This work was performed under U. S. Army Contract No. 18-035-AMC-374(A) for the U. S. Army Edgewood Arsenal, Edgewood Arsenal, Maryland.

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A New Self-Condensation Product of Biacetyl[1a]

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Received April 12, 1966

The self-condensation products of biacetyl have been of interest to organic chemists since 1889. Three dimers[2–4] and two trimers[5,6] have been isolated in crystalline form from reactions in which biacetyl was treated with either strongly alkaline or acidic catalysts. While studying the reaction of biacetyl with certain heterocyclic amines, we came upon considerable quan-

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(1) (a) This research has been supported by a grant, GM-11437-03, from the U. S. Public Health Service; (b) National Science Foundation Cooperative Fellow, 1964–1965, Allied Chemical Fellow, 1965–1966; (c) Participant, National Science Foundation summer undergraduate research program at New York University, 1965.

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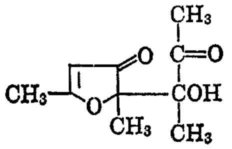
tities of a product which did not correspond in its properties to any of the known self-condensation products of biacetyl. It was neither a dimer nor a trimer, but analyzed as $C_{10}H_{14}O_4$. The structure of this product has been found to be 2-(1-hydroxy-1-methyl-2-oxopropyl)-2,5-dimethyl-3(2H)-furanone (1).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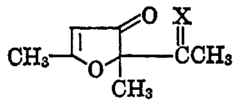
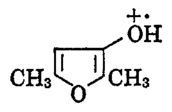

2a, X=O
b, X=NNHCONH$_2$

The nuclear magnetic resonance spectrum of 1 revealed the presence of one hydroxyl proton, one vinyl proton, and four methyl groups. Two of the methyl groups had chemical shifts that indicated that they were α to carbonyl or double bond, while the others were felt to be α to a hydroxyl or ether linkage. The ultraviolet maximum of 1 (265 mμ) was at longer wavelengths than the major absorption usually arising from a simple α,β-unsaturated ketone.[7] The infrared spectrum of 1 included a hydrogen-bonded hydroxyl peak at 2.93 μ, two carbonyl bands at 5.84 and 5.91 μ, and a strong carbon–carbon double bond absorption at 6.22 μ. The 3(2H)-furanone system has been reported[8,9] to have characteristic bands at about 5.87 and 6.23 μ. The mass spectrum of 1 did not show the expected molecular ion of m/e 198. It was concluded that this suffered ready decomposition into fragments observed at m/e 112 and 86.

Attempts to obtain an oxime or 2,4-dinitrophenylhydrazone of 1 led only to isolation of the corresponding derivatives of biacetyl. Reactions between 1 and bromine in carbon tetrachloride, neutral potassium permanganate, triethylamine in chloroform, and aqueous HCl were also noted, but no crystalline products could be isolated from the reaction mixtures. Compound 1 decomposed in strongly alkaline solutions, and this reaction was accompanied by a shift of the ultraviolet absorption maximum from 265 to 295 mμ over 15 min. After neutralization, biacetyl could be distilled from the solution, which contained a complex mixture of substances and gave a strong ferric chloride test.

Treatment of 1 with sodium metaperiodate solution smoothly converted it to a product to which we have assigned the structure 2-acetyl-2,5 dimethyl-3(2H)-furanone (2a). Its nmr spectrum indicated the presence of a vinyl hydrogen and three methyl groups, two of which were α to a carbonyl or double bond, and one which was α to a hydroxyl or ether linkage. This is consistent with the conversion of the $CH_3COCOH(CH_3)$ side chain of 1 to an acetyl group. The ultraviolet spectrum of 2a showed a peak at 263 mμ, indicating no substantial change from the chromophore of 1. The mass spectrum of 2a revealed a weak molecular ion at m/e 154 (0.2% of the intensity of the base peak). A prominent peak of m/e 112 was observed here, as in the case of 1. In alkali, 2a showed a behavior analogous to 1. Upon acidification a complex mixture, somewhat similar to that from 1, was revealed by thin layer chromatography. A crystalline monosemicarbazone (2b) could, however, be obtained from 2a. Its ultraviolet spectrum was similar to that of 2a, indicating that the acetyl group, rather than the conjugated carbonyl of the chromophore, was the site of reaction. The nuclear magnetic resonance and infrared spectra of 2b were consistent with this assumption.

The above data are best accommodated by the structures shown for 1, 2a, and b. An alternative series of structures, in which the methyl and hydrogen on the double bond are interchanged also fits the data, but is much less likely on mechanistic grounds. The peak at m/e 112 observed in the mass spectra of 1 and 2a is readily explained by fragmentation of the molecular ions through six-membered cyclic intermediates to give ion 3. The decomposition of 1 and 2a at high pH can be attributed to alkali-catalyzed cleavage of the biacetyl or acetyl side chains, giving the anion of 3-hydroxy-2,5-dimethylfuran (4). Hydroxyfurans are known to be quite unstable in alkaline solution, giving perioxides and other products.[10,11]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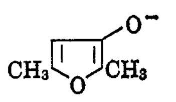
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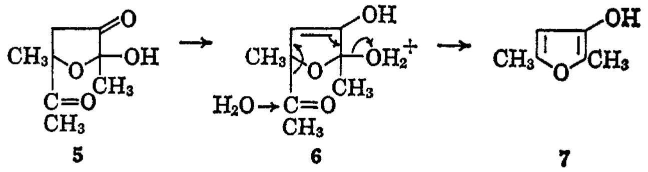
A number of possible mechanisms can be written to describe the formation of 1 from biacetyl. Only one of these, perhaps the simplest, will be given here. It assumes the initial formation of 5, a known dimer of biacetyl. Enolization and protonation of 5 would give intermediate 6. Hydrolytic cleavage of an acetyl group with simultaneous loss of water would then directly yield 3-hydroxy-2,5-dimethylfuran (7), which could react with an additional molecule of biacetyl in an aldol condensation to give 1.


5 6 7

Experimental Section

Melting points were determined on a Thomas–Hoover capillary apparatus and are uncorrected. Ultraviolet spectra were taken using a Perkin-Elmer 202 spectrophotometer. Infrared spectra were obtained with a Perkin-Elmer Infracord spectrophotometer. Nuclear magnetic resonance spectra were determined using a Varian A-60 spectrophotometer and are reported on the τ scale with tetramethylsilane (τ 10.00) as standard. Mass spectra were obtained from the Morgan Schaffer Corp., Montreal, Quebec. They used a Hitachi Perkin-Elmer RMU-6D instrument. Microanalyses and molecular weight determinations were performed by Mr. George I. Robertson, Florham Park, N. J. Thin layer chromatography was run on silica gel G (Merck). Ultraviolet absorbing materials were located with the aid of an ultraviolet lamp equipped with a short-wavelength filter.

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Preparation of 2-(1-Hydroxy-1-methyl-2-oxopropyl)-2,5-dimethyl-3(2H)-furanone (1).—To a solution of 51 ml of biacetyl (Fisher Scientific Co., reagent grade) in 500 ml of water was added 1 ml of acetic acid, and the reaction was heated at 70° for 13 days. The dark orange reaction mixture was evaporated under vacuum and the residual oil was extracted with petroleum ether. The extract was discarded and the remaining residue was crystallized from carbon tetrachloride in several crops, melting between 91 and 96°. The yield was 12.54 g (36% from biacetyl, assuming the conversion of 3 moles of biacetyl to 1 mole of 1; 25% from biacetyl by weight). An analytical sample, mp 95–96°, was prepared by recrystallization from carbon tetrachloride: infrared absorption (KBr) at 2.93, 3.33, 3.41, 5.84, 5.91, 6.22, 6.83, 6.91, 7.04, 7.28, 7.38, 7.48, 8.02, 8.39, 8.70, 8.87, 9.25, 9.50, 9.95, 10.38, 10.70, 11.10, 12.38 μ; ultraviolet maximum (H_2O) at 265 mμ (ϵ 10,600); nmr spectrum ($CDCl_3$), singlets at τ 4.53, 5.90, 7.78, 8.52, and 8.55 with peak area ratio 1:1:6:3:3; nmr spectrum (D_2O), singlets at τ 4.45, 7.79, 7.82, 8.64, 8.67 with peak area ratio 1:3:3:3:3; mass spectrum (peaks with 10% or more of the intensity of the base peak are listed), *m/e* 112, 86, 68, 43 (base peak), 40, 39, and 15; the ratio of the intensities of the peaks of *m/e* 112, 113, and 114 was 100:7.2:0.8 (expected[12] for $C_6H_8O_2$, 100:6.7:0.6); thin layer chromatography (95% benzene, 5% methanol), R_f 0.44.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12; CH_3, 30.2. Found: C, 60.64; H, 7.20; CH_3, 27.0; mol wt (vapor pressure), 169.

3-Acetyl-2,5-dimethyl-3(2H)-furanone (2a) and Its Derivatives.—Compound 1 (1 g) was dissolved in 50 ml of saturated sodium metaperiodate solution and allowed to stand at room temperature overnight. The solution was extracted several times with ether, and the ether solution was washed with water until the washings gave a negative starch iodide test. The ether solution was dried (Na_2SO_4) and evaporated. The resulting oil crystallized on standing to give 408 mg (56%) of **2a**, mp 49–50°. An analytical sample, mp 51–52°, was prepared by recrystallizing from petroleum ether (bp 30–60°) and drying in air: infrared absorption (KBr) at 3.32, 3.38, 5.76, 5.89, 6.22, 7.00, 7.20, 7.37, 7.50, 8.15, 8.37, 8.64, 8.72, 9.07, 9.65, 9.88, 10.38, 10.58, 11.17, 11.71, 12.32, and 13.57 μ; ultraviolet maximum (H_2O) at 263 mμ; nmr spectrum ($CDCl_3$), singlets at τ 4.43, 7.60, 7.88, and 8.47 with peak area ratio 1:3:3:3; mass spectrum, molecular ion at *m/e* 154 (0.2% of base peak), peaks with 10% or more of the intensity of the base peak occurred at *m/e* 112, 97, 43, 40, 30, and 15; the ratio of the intensities of the peaks of *m/e* 112, 113, and 114 was 100:7.1:0.7 (expected[12] for $C_6H_8O_2$, 100:6.7:0.6); thin layer chromatography (95% benzene, 5% methanol), R_f 0.74.

Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.81; H, 6.61.

When **2a** was dissolved in water and treated with a solution of semicarbazide hydrochloride was sodium acetate, a crystalline **semicarbazone** (**2b**) quickly separated. It was filtered and an analytical sample, mp 219–220° dec, was prepared by recrystallization from ethanol–water: infrared absorption (KBr) at 2.87, 3.15, 5.87, 6.23, 6.27 (shoulder), 6.77, 6.97, 7.26, 7.49, 7.69, 8.27, 8.54, 8.94 (shoulder), 9.10, 9.37, 10.46, 11.20, 12.00, 13.03, and 13.42 μ; ultraviolet maximum (H_2O) at 230 and 265 mμ; nmr spectrum (CD_3SOCD_3 with added D_2O), singlets at τ 4.25, 7.59, 8.24, and 8.39 with peak area ratio 1:3:3:3; thin layer chromatography (95% benzene, 5% methanol), R_f 0.04.

Anal. Calcd for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found: C, 50.99; H, 6.20; N, 19.40.

Treatment of **2a** with a solution of sodium acetate and hydroxylamine hydrochloride led to the precipitation of an **oxime**. After recrystallization from ethanol–water, white crystals, mp 131–132°, were obtained: infrared spectrum (KBr) contained bands at 3.10, 5.99, and 6.31 μ; ultraviolet maximum (H_2O) at 264 mμ; thin layer chromatography (95% benzene, 5% methanol), R_f 0.44.

Reaction of 1 and 2a with Sodium Hydroxide. Compound 1 (50 mg) was dissolved in 20 ml of NaOH solution, pH 13.5. During the next 20 min, the absorption maximum at 265 mμ in the ultraviolet was seen to disappear, and a new well-defined peak appeared at 295 mμ, with an absorption about 25% greater than the original solution. A portion of the solution was allowed to remain at pH 13.5 for several hours and the absorption at 295 mμ gradually disappeared. The remainder of the solution had been neutralized with HCl after 20 min. Only a weak absorption maximum in the ultraviolet, at 265 mμ, remained. A portion of this solution was distilled. The aqueous distillate was treated with 2,4-dinitrophenylhydrazine reagent and a yellow compound, mp 313–315°, precipitated. It was identical with the 2,4-dinitrophenylhydrazone of biacetyl, mp 314°. The remainder of the neutralized solution gave a strong positive ferric chloride test. Thin layer chromatography (95% benzene, 5% methanol) revealed ultraviolet-absorbing spots of R_f 0.06, 0.15, 0.27, 0.44, 0.67, and 0.90.

When dissolved in NaOH solution of pH 13.5, **2a** also showed a shift of the ultraviolet maximum, from 263 to 295 mμ, over 15 min. A portion of the solvent, kept at pH 13.5 for several hours, gradually lost the absorption at 295 mμ. Another portion was neutralized after 15 min and then showed only weak absorption at 265 mμ in the ultraviolet. The solution was concentrated and revealed on thin layer chromatography (95% benzene, 5% methanol) ultraviolet-absorbing spots of R_f 0.04, 0.25, and 0.40.

Acknowledgments.—We wish to thank Mr. Frank Litterio for the infrared spectra, Mr. Leonard Glass for the nmr spectra, and Miss Gisela Witz for a suggestion concerning the mechanism.

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On the Mechanism of Cinnamic Acid Decarboxylation in an Acid Medium

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Received March 7, 1966

Johnson and Heinz[1] had demonstrated that the decarboxylation of β-phenylcinnamic acid (I) and β-methylcinnamic acid (II) to *unsym*-diphenylethylene and α-methylstyrene, respectively, is acid catalyzed but the first-order rate constants are not a linear function of the hydrobromic acid concentration. In 1961, Noyce, King, and Woo[2] reported that β-*p*-methoxylphenyl-β-hydroxypropionic acid undergoes a decarboxyative dehydration reaction in which the decarboxylation reaction was nearly independent of acid concentration while the dehydration reaction closely paralleled the acidity function. This suggested the intermediacy of a β-hydroxy propionic acid in the decarboxylation of cinnamic acids. Having previously ascertained the validity of the acidity function, H_0, for the hydrogen bromide–acetic acid–water system,[3] we undertook an investigation aimed at elucidation of the mechanism of the acid-catalyzed decarboxylation of cinnamic acids. At the outset of this work however, Noyce, Brauman, and Kirby[4] published a detailed account of the decarboxylation mechanism showing the decarboxylation is the result of hydration of the olefinic function to the β-hydroxy acid followed by a synchronous decarboxylation and dehydration reaction of the hydroxy acid. Their data predict that in the H_0 range from -0.8 to -2.4 (regardless of the mineral acid used) a plot of log *k vs.* H_0 should be linear with a slope of 1.0 and at higher acidities the slope of the line should

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