give 20 g of product, mp 160–162°, which had an infrared spectrum identical with that of **8e** described in part A.

1,3-Disubstituted 4-Imino-1,3-imidazolidine-2,5-dione. Procedure A (from Acetone Cyanohydrin) (10a, 10d, 10e, and 10f).—To a solution of acetone cyanohydrin (0.1 mole), an isocyanate (0.2 mole), and benzene (100 ml) was added triethylamine (0.5 ml). When an aryl isocyanate was used, an exothermic reaction began immediately after adding the catalyst, and the reaction was complete within 30 min. However, when alkyl isocyanates were used, heating at reflux temperature for 3–5 hr was required to complete the reaction. If the products did not crystallize out of the cooled reaction solution, they were isolated by evaporation of the solvent. The crude products were evaporated from benzene, ethanol, or hexane, or a combination of them.

Procedure B (from 1-Cyanocyclopentanol, 1a) (10c and 10f).—To a solution of **1a** (0.1 mole) and an isocyanate (0.2 mole) in benzene (50–100 ml) was added triethylamine (0.5–1 ml) to catalyze the reaction. If an exothermic reaction ensued, it was allowed to proceed without additional heat. Otherwise, the reaction solution was heated at reflux temperature for 3 hr. The products were isolated and purified by the same techniques used for the products formed from acetone cyanohydrin.

Procedure C (from Hydrogen Cyanide) (10a).—Benzene (100 ml) was cooled to 10° and hydrogen cyanide (generated from 0.5 mole of sodium cyanide) was bubbled into it. After the addition of triethylamine (0.5 ml) the solution was added dropwise to a solution of **2a** (15.3 g, 0.1 mole) in benzene (25 ml). The resulting solid product was collected by filtration. It weighed 8 g (48% yield) and melted at 200–201°. The infrared spectrum was identical with that of the product (**10e**) prepared by method A.

1,3-Disubstituted Parabanic Acids. Procedure A (11a, 11c, 11e, and 11f).—To a hot solution of 1,3-disubstituted 4-imino-1,3-imidazolidine-2,5-dione (**10a**, **10c**, **10e**, or **10f**, respectively) (0.002–0.04 mole) in ethyl alcohol (100–200 ml) was added concentrated hydrochloric acid (25–50 ml). After slowly cooling to room temperature, the colorless product crystallized from solution. It was collected, dried, and recrystallized from an appropriate solvent. The infrared spectra of the products showed the following carbonyl absorption peaks: **11a**, 5.77 μ; **11c**, 5.75 μ; **11e**, 5.58 and 5.78 μ; and **11f**, 5.65 and 5.80 μ.

Procedure B (11b and 11e).—The intermediate 1,3-disubstituted 4-imino-1,3-imidazolidine-2,5-dione was prepared by any one of the procedures described above. Then the crude product was dissolved in ethanol, hydrolyzed with hydrochloric acid, and purified by the method described in procedure A. The infrared spectrum of **11b** showed absorption at 5.76 μ (C=O).

Procedure C (11g).—The 1,3-disubstituted 4-substituted carbamoylimino-1,3-imidazolidine-2,5-dione (**12b**) was hydrolyzed by the same general method used in procedure A. The infrared spectrum showed absorption maxima at 5.68 and 5.85 μ.

1,3-Dialkyl-4-alkylcarbamoylimino-1,3-imidazolidine-2,5-dione. Procedure A (12a and 12b).—To a solution of an alkylisocyanate (0.2–0.3 mole) and the cyanohydrin (0.1 mole) of acetone, cyclopentanone, or cyclohexanone in benzene (100 ml) was added triethylamine (0.5–1 ml). The solution was heated at reflux temperature for 3–16 hr. Evaporation of the solvent left a residue from which pure product was obtained by recrystallization.

Procedure B (12a).—A solution of **10f** (14.1 g, 0.1 mole), methyl isocyanate (5.7 g, 0.1 mole), benzene (100 ml), acetone (25 ml), and triethylamine (1 ml) was heated at reflux temperature overnight. The product (2.5 g, 12.6% yield) separated from the cooled solution. It had an infrared spectrum which was identical with that of **12a** synthesized by procedure A.

1,3-Disubstituted 4-Amino-2,5-imidazolidinedione (13a and 13b).—The imino compound **10a** or **10f**, respectively (0.01–0.03 mole), was dissolved in ethyl acetate (200 ml) and hydrogenated in the presence of 5% palladium on charcoal (0.5–1 g) in a Parr pressure reaction apparatus at 60 psig for 2 hr at room temperature. After removal of the catalyst and evaporation of the solvent, the residual product was recrystallized from a mixture of benzene and hexane. The infrared spectra of the products exhibited the following absorption maxima: **13a**, 2.92, 2.99, 5.64, and 5.81 μ; **13b**, 2.95, 3.01, 5.60, and 5.85 μ.

1,3-Dimethyl-4-arylureido-2,5-imidazolidinedione (14a, 14b, and 14c).—To a stirred solution of **13b** (0.02 mole) and an aryl isocyanate (0.02 mole) in benzene (50 ml) was added DABCO (0.1 g). An exothermic reaction began immediately. After stirring for 30 min, hexane was added, and the solution was cooled. The products (91–96% yield) were collected and recrystallized from a mixture of benzene and hexane. The infrared spectra of the products exhibited the following absorption maxima: **14a**, 2.96, 2.98, 5.62, and 5.95 μ; **14b**, 2.98, 3.02, 5.63, and 5.92 μ; **14c**, 2.92, 3.01, 5.66, 5.82, and 6.05 μ.

The Reaction of 3-Unsubstituted N-Arylisoxazolium Salts with Carboxylic Acid Anions

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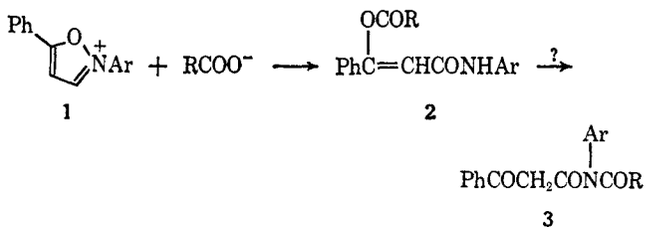
Examination of the reaction of the N,5-diphenylisoxazolium cation with triethylammonium acetate has revealed that 3-unsubstituted N-arylisoxazolium salts are not suitable for use in peptide synthesis, because of ready base-catalyzed rearrangement of the derived enol ester acylating agents.

As part of an investigation[2] of the isoxazolium salt method of peptide synthesis,[3-5] we have studied the use of N-arylisoxazolium salts (**1**) for converting carboxylic acids to reactive enol esters (**2**). Isoxazolium salts bearing an N-aryl substituent were of interest, because they were expected to give enol ester acylating agents **2** which would be resistant to a side reaction encountered with the N-alkyl compounds. In previous work it was shown[3] that N-methyl enol esters were subject to intramolecular rearrangement to ketoimides. It was hoped that the formation of ketoimides (**3**) from enol esters of the type **2** would be relatively slow as a result of the operation of steric and electronic factors, associated with the presence of the N-aryl substituent, which would bring about a diminution of the effective nucleophilicity of the nitrogen atom.



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The method for synthesis of N-arylisoxazolium salts, reported in an earlier communication,[6] involves con-

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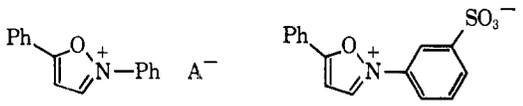
densation of a hydroxymethylene ketone with an N-arylhydroxylamine, followed by cyclization of the vinylogous hydroxamic acid (**4**) in concentrated sul-

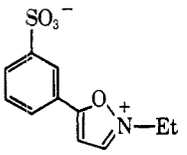
$$\mathrm{PhCOCH{=}CHOH + ArNHOH \longrightarrow PhCOCH{=}CHNAr \xrightarrow{H_2SO_4} 1}$$
(**4**: OH)

furic acid. The isoxazolium salts used in this study were the bisulfate (**5a**) and perchlorate (**5b**) salts of the N,5-diphenylisoxazolium cation and the zwitterion N,5-diphenylisoxazolium-3$^{N\text{-}ph}$-sulfonate (**6**).



5a, $A^- = HSO_4^-$
b, $A^- = ClO_4^-$

6



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The first synthetic test with the sulfonated reagent **6** revealed that the new compound was, surprisingly, not as efficient in peptide synthesis as the previously studied zwitterion, N-ethyl-5-phenylisoxazolium-3′-sulfonate (**7**). When **6** was used for the coupling of carbobenzoxyglycine with glycylglycine ethyl ester, only 75% yield of the desired carbobenzoxytriglycine ethyl ester was obtained. Under the same conditions the reagent **7** was reported[7] to give 91% of the pure tripeptide.

For the purpose of elucidating the nature of the difficulties with the new reagent **6**, the model reaction of the unsulfonated N-arylisoxazolium perchlorate **5a** with acetate ion was investigated. It was found that the desired enol ester, β-acetoxycinnamanilide (**8**), could be prepared in 85% yield from **5a** and triethylammonium acetate in dichloromethane, if excess acetic acid was present and the base was added slowly to the

$$\mathbf{5a} + Et_3N + MeCO_2H \longrightarrow \underset{\mathbf{8}}{PhC(OCOMe){=}CHCONHPh}$$

stirred reaction mixture. Pure crystals of the enol ester **8**, stored in the cold with protection from atmospheric moisture, appeared to be stable, and a dilute solution of **8** in dichloromethane was unchanged after 2 days at room temperature. However, addition of bases to organic solutions of **8** caused the ester to decompose. One equivalent of triethylamine added to a 0.1 *M* solution of **8** in dichloromethane brought about the immediate disappearance of the enol ester carbonyl absorption in the infrared spectrum of the solution. Similar addition of 0.1 equiv of triethylammonium acetate resulted in rapid reduction of the enol ester band.

The product of the decomposition reaction, an isomer of **8** isolated in 90% yield, has the nmr and infrared spectral properties expected for the ketoimide, N-acetylbenzoylacetanilide (**9**). That the acetyl group had actually migrated onto nitrogen was confirmed by treating the decomposition product with benzylamine. The nmr spectrum of the product mixture was consistent with that to be expected of an equimolar mixture of the four cleavage products, N-benzylacetamide (**10**), benzoylacetanilide (**11**), acetanilide (**12**), and N-benzylbenzoylacetamide (**13**). The identification of the first three compounds was supported by nmr and thin layer chromatographic comparisons with authentic samples of **10**, **11**, and **12**.

$$\mathbf{8} \xrightarrow{\text{base}} \underset{\mathbf{9}}{PhCOCH_2CON(Ph)COMe}$$

$$\mathbf{9} \xrightarrow{PhCH_2NH_2} \underset{\mathbf{10}}{MeCONHCH_2Ph} + \underset{\mathbf{11}}{PhCOCH_2CONHPh} + \underset{\mathbf{12}}{MeCONHPh} + \underset{\mathbf{13}}{PhCOCH_2CONHCH_2Ph}$$

Although rearrangement to ketoimides (**3**) may be relatively slow as predicted for neutral enol ester molecules of type **2**, the base catalysis of the conversion of **8** to **9** suggests that a process involving the conjugate base of the enol ester is a very ready one in these cases. Spectral tests with enol esters from N-alkylisoxazolium salts revealed no comparable degree of base sensitivity. Apparently, then, the N-aryl substituent stabilizes the enol ester anion to the extent that it is readily accessible, even with a weak base such as acetate ion; yet the degree of stabilization of the anion is not sufficient to make it unreactive in the O→N rearrangement of the acyl group.

Enol ester rearrangement is the probable explanation for the poor yield in the model peptide synthesis with **6**, since in that test much of the initially formed enol ester might have been converted to ketoimide by the action of unconsumed triethylammonium carboxylate in the reaction mixture. This explanation was supported by the finding that the infrared absorption associated with the carbonyl group of the enol ester was much stronger in reaction mixtures obtained when the carboxylate ion concentration during reaction was minimized by slowly adding the triethylamine to a suspension of **6** in a solution of acetic acid, than was the case when the normal procedure of adding the solid **6** to a triethylammonium acetate solution was followed.

Rearrangement might also have taken place in the synthetic test as a side reaction during the subsequent reaction of the enol ester with the basic amine component. A test reaction of **8** with benzylamine, for example, gave not only **10** and **11**, the expected cleavage products from **8**, but also **12** and **13**. Assuming that **12** and **13**, along with equimolar amounts of **10** and **11**, were formed by cleavage of **9**, the relative amounts of the four products (assayed by nmr spectroscopy) indicated that rearrangement of **8** to **9** was favored over direct cleavage by a factor of 2 in the reaction with benzylamine.

$$\mathbf{10} + \mathbf{11} \xleftarrow{PhCH_2NH_2} \mathbf{8} \xrightarrow{PhCH_2NH_2} \mathbf{9} \xrightarrow{PhCH_2NH_2} \mathbf{10} + \mathbf{11} + \mathbf{12} + \mathbf{13}$$

While it might be possible to minimize rearrangement during the formation and cleavage of enol esters by maintaining relatively acidic conditions, the lability

(7) R. A. Olofson, Ph.D. Thesis, Harvard University, 1961.

of the model compound **8** shows that the simple N-arylisoxazolium salts fail to provide that advantage of stability of the derived enol ester acylating agents which is desirable for the purposes of peptide synthesis.

Experimental Section

Melting points were taken on a Kofler hot-stage microscope, calibrated with melting point standards from Arthur H. Thomas Co. Ultraviolet spectra were run on a Cary 14 spectrophotometer, infrared spectra on a Perkin-Elmer Infracord spectrophotometer, and nmr spectra on a Varian A-60 spectrometer. Unless otherwise specified, nmr data were determined in deuteriochloroform solutions, and chemical shifts are reported in τ values relative to tetramethylsilane as an internal standard (τ = 10.00 ppm). Analyses were performed by Scandinavian Microanalytical Laboratories and Dr. C. Daesslé of Montreal.

3-(N-Hydroxyanilino)acrylophenone (14).—A solution of 16.4 g (0.15 mole) of phenylhydroxylamine[8] in 900 ml of water was mixed with a freshly prepared solution of 25.6 g (0.15 mole) of hydroxymethyleneacetophenone, sodium salt,[7] in 250 ml of water. The resulting solution was stirred vigorously while 170 ml (0.17 mole) of 1 *N* hydrochloric acid was added at a rapid drop rate. Stirring was continued for 15 min after the addition was complete, and the orange-yellow precipitate was then filtered, washed with water, and pressed dry overnight with a rubber dam. Recrystallization of the crude product (31 g or 84%) from ethanol gave pure, orange crystals, mp 156–156.5° dec (lit.[9,10] mp 158°, 156.5°). The ultraviolet spectrum showed λ_{max}^{EtOH} 243–257 mμ (ϵ 11,500–13,600) and 377 mμ (ϵ 31,300). A model compound for the chromophore, 3-anilinoacrylophenone,[11-15] has a nearly identical spectrum, λ_{max}^{EtOH} 242–253 mμ (ϵ 11,500–13,600) and 375 mμ (ϵ 30,900). The long-wavelength absorption of **14** shifts to 429 mμ on addition of 1 drop of 0.1 *N* NaOH to the cell. The infrared spectrum in KBr contains a band at 6.18 μ, which may be assigned to the carbonyl group of the vinylogous hydroxamic acid system. The nmr spectrum (dimethyl sulfoxide) consists of signals at 241 (doublet, J = 11 cps, 1.0 H), 275–335 (multiplet, 10.0 H), 353 (doublet, J = 11 cps, 1.1 H), and 508 cps (singlet, 1.0 H) downfield from the solvent signal, in accord with the proposed structure.

Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85; O, 13.37. Found: C, 75.43; H, 5.46; N, 5.80; O, 13.36.

Sodium 3-(N-Hydroxyanilino)acrylophenone-3$^{N\text{-}ph}$-sulfonate (15).—A solution of 21.1 g (0.094 mole) of sodium *m*-nitrobenzenesulfonate and 22.5 g (0.375 mole) of glacial acetic acid in 500 ml of water was stirred vigorously in an ice bath (starting temperature 20°) while 13.3 g (0.188 g-atom) of zinc dust (assayed 92.6% zinc by volume of hydrogen evolved with acid, 12.3 g actual zinc used) was added rapidly. The temperature rose to 40°, as the solution turned green and then yellow. Stirring was continued for 3 min after the temperature had returned to 20°. Goldschmidt and Sunde[16] reported that similar conditions gave an 80% yield of the hydroxylamine.

The tetrasodium salt of ethylenediaminetetraacetic acid (86 g, 0.225 mole) was dissolved in the above hydroxylamine solution, which was then filtered by gravity through a fluted paper. A freshly prepared solution of 12.8 g (0.075 mole) of hydroxymethyleneacetophenone, sodium salt, in 150 ml of water and a solution of 4.5 g (0.075 mole) of acetic acid in 150 ml of water were added simultaneously at equal, rapid drop rates to the stirred hydroxylamine solution. Stirring was continued for 5 min after the additions were complete, and then 400 g of sodium chloride was added to the clear, orange reaction mixture. After the mixture was stirred vigorously for 15 min, the excess salt was allowed to settle. The suspended orange precipitate was decanted from the salt, filtered, washed with three portions of saturated sodium chloride solution, and air dried overnight in the funnel. This gave 26.0 g (theory 25.6 g) of crude material, contaminated with salt. The sodium chloride content was reduced by dissolving the crude product in 200 ml of methanol, filtering, and precipitating with 2 l. of acetone. The precipitate was filtered and pressed dry with a rubber dam, providing 9 g (35%) of amorphous solid. When heated rapidly, the product slowly darkened, with gradual melting to an orange oil between 220 and 290°. The crude material was used for cyclization with no further purification. The ultraviolet spectrum showed λ_{max}^{EtOH} 245–255 and 375 mμ. The long-wavelength absorption shifted to 434 mμ on addition of 1 drop of 0.1 *N* NaOH to the cell.

N,5-Diphenylisoxazolium Bisulfate (5a) and Perchlorate (5b).—The unsulfonated isoxazolium salts were prepared from **14** as described previously.[6]

N,5-Diphenylisoxazolium-3$^{N\text{-}ph}$-sulfonate (6).—Five grams (14.7 mmoles) of **15** was added in small portions to 20 ml of ice-cold, concentrated sulfuric acid. During the addition the mixture was swirled in an ice bath in the hood (HCl evolved from residual salt in the crude **15**). When the addition was complete, swirling was continued until no more bubbles formed and the dark solution was clear. Then the mixture was again swirled in an ice bath as 20 g of ice was added. Addition of 100 ml of acetone caused precipitation of the inorganic salt, which was removed by filtration and washed with an additional 200 ml of acetone. The combined filtrate and washings were further diluted with 40 ml of water, 500 ml of acetone, and, finally, 200 ml of ether. The resulting solution was stirred in an ice bath, and crystallization was induced by scratching (or seeding). Stirring in the ice bath was continued for 0.5 hr after the precipitation appeared complete. The finely divided, off-white solid was filtered, washed with water, washed with acetone, and air dried in the funnel. The crude product (2.2 g) slowly darkened above 100°, with decomposition to an orange tar near 170°. Precipitation from 11 ml of concentrated hydrochloric acid with 44 ml of water gave 2.1 g (50%) of **6** as off-white, microscopic needles, mp 170° dec. The light-sensitive compound was stored in the dark. The ultraviolet spectrum exhibited $\lambda_{max}^{0.1\ N\ HCl}$ 323 mμ (ϵ 24,800).

Anal. Calcd for $C_{15}H_{11}NO_4S$: C, 59.79; H, 3.68; N, 4.65; S, 10.64. Found: C, 59.46; H, 4.00; N, 4.36; S, 10.50.

Test Preparation of Carbobenzoxytriglycine Ethyl Ester Using 6.—A solution of 0.314 g (1.50 mmoles) of carbobenzoxyglycine and 0.152 g (1.50 mmoles) of triethylamine in 2 ml of acetonitrile was added to 0.380 g (1.50 mmoles) of **6**, suspended in 2 ml of acetonitrile, along with three 1-ml portions of the solvent used for rinsing. The mixture was stirred in an ice bath until the solution was clear. Then 0.295 g (1.50 mmoles) of glycylglycine ethyl ester hydrochloride was added, followed by 0.152 g (1.50 mmoles) of triethylamine and 2 ml more of solvent. After the mixture was stirred overnight, the solvent was removed under reduced pressure. Adding 15 ml of water, triturating and dissolving almost all the material on the steam bath, cooling in the refrigerator for 4 hr, filtering, washing with three 1-ml portions of water, and air drying in the funnel gave 0.395 g (75%) of the colorless, nearly pure tripeptide, mp 167–168° with some premelting (lit.[6] mp 167–168°).

β-Acetoxycinnamanilide (8).—A solution of 0.60 g (10 mmoles) of acetic acid in 50 ml of dichloromethane was added to 3.22 g (10 mmoles) of **5b**. The suspension was stirred while a solution of 1.01 g (10 mmoles) of triethylamine and 0.60 g (10 mmoles) of acetic acid in 20 ml of the solvent was added dropwise in the course of 30 min. The resulting yellow solution was washed three times with water, dried over calcium chloride, and filtered. In a preliminary run solvent removal and scratching of the residual oil gave seed crystals. In the yield-determining experiment the organic solution was concentrated to about 12 ml and petroleum ether (bp 30–60°, about 12 ml) was added to the saturation point. Seeding and chilling in the deep freeze overnight gave 2.4 g (85%) of yellow crystals, mp 105–108°. Repeated recrystallization from 1:1 dichloromethane–petroleum ether increased the melting point to 112–113°. The ultraviolet spectrum showed $\lambda_{max}^{CH_2Cl_2}$ 286 mμ (ϵ 21,500). A model for the chromophore of **8**, β-methylcinnamanilide, has its absorption maximum at 288 mμ (ϵ 18,000).[17] The infrared spectrum in dichloromethane contains a band at 5.65 μ, as expected for the enol ester absorption of **8**. In accord with the structure **8**, the nmr spectrum consists

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of signals at τ 7.63 (singlet, 2.9 H), 3.61 (singlet, 0.9 H), 3.25–2.25 (multiplet, 10.3 H), and 1.65 (broad, 0.9 H).

Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.59; H, 5.38; N, 4.98. Found: C, 72.41; H, 5.38; N, 5.07.

Tests of the Stability of 8.—At room temperature without protection from atmospheric moisture, crystals of **8** slowly melted (odor of acetophenone) on prolonged standing. However, after storage for several months in a tightly stoppered vial in the deep freeze, crystals of **8** had not changed. The infrared spectrum of a 0.1 *M* solution of **8** in dichloromethane showed no change after 2 days at room temperature. Addition of 1 equiv of triethylamine to a 0.1 *M* solution of **8** in dichloromethane caused the immediate disappearance of the enol ester absorption in the infrared spectrum. Addition of a dichloromethane solution containing 0.1 equiv each of triethylamine and acetic acid to a solution of **8** caused an immediate decrease in the enol ester absorption at 5.65 μ. Within 5 min after addition of the triethylammonium acetate solution, the band at 5.65 μ was reduced to a shoulder. At the same time as the enol ester absorption decreased in the tests with added bases, the intensity of absorption between 5.8 and 5.9 μ increased.

N-Acetylbenzoylacetanilide (9).—Two drops of triethylamine was added to a solution of 2.2 g (7.8 mmoles) of **8** in 10 ml of dichloromethane. After 12 hr petroleum ether (about 40 ml) was added to the cloud point, and the solution was chilled in the deep freeze until crystallization was complete. Filtration gave 1.7 g of crude product. A second crop of 0.3 g of crystals was obtained by resaturating the mother liquor with about 60 ml more of petroleum ether and chilling again. The total yield was 2.0 g or 90%. Recrystallization by dissolving the crude product in the minimum amount (about 22 ml/g) of ether at room temperature and chilling in the deep freeze gave pure silky fibers, mp 79–80°, with partial solidification and complete melting at 86.5–87.5°. The infrared spectrum contains no NH absorption and has intense carbonyl absorption, centered at 5.83 μ (dichloromethane solution), comparable with that of N-acetyl-N-methylbenzoylacetamide.[7] The nmr spectrum is consistent with a mixture of 57–65% of the keto tautomer and 35–43% of the enol form of **9**. The nmr signals appear at τ 8.00 (singlet, 2.0 H), 7.60 (singlet, 1.1 H), 5.42 (singlet, 1.1 H), 3.80 (singlet, 0.4 H), 3.33–1.83 (multiplet, 9.9 H), and −4.37 (singlet, 0.4 H).

Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.59; H, 5.38; N, 4.98. found: C, 72.48; H, 5.52; N, 4.98.

Reaction of 9 with Benzylamine.—A dichloromethane solution containing 0.0536 g (0.500 mmole) of benzylamine was added to a 5-ml volumetric flask containing 0.141 g (0.500 mmole) of **6**, dissolved in dichloromethane. The solution was made up to the mark and shaken. Samples were removed periodically for infrared spectra, and, after 30 hr, no further change was observed in the spectrum of the reaction mixture. The solvent then was removed under reduced pressure, and the nmr spectrum of the residue was recorded.

The presence of two methyl signals (CH_3CO, τ 8.03 and 8.12, integral ratio 1:1) indicated that two modes of cleavage had occurred. The spectrum was that expected for an equimolar mixture of N-benzylacetamide (**10**), benzoylacetanilide (**11**), acetanilide (**12**), and N-benzylbenzoylacetamide (**13**). The assignments of the characteristic peaks (Table I) was based on comparisons with the nmr spectra of authentic samples of the first three compounds. The spectrum also contained weak peaks owing to NH and enolic protons and complex aromatic signals.

Integration of the spectrum was in accord with the above assignment: peaks 1 + 2, 2.7 H (theory 3 H); peaks 3 + 4 + enolic, 2.1 H (theory 2 H), peaks 5 + 6 + 7, 2.0 H (theory 2 H), aryl + NH peaks, 17.2 H (theory 17 H).

TABLE I

ASSIGNMENTS OF CHARACTERISTIC NMR PEAKS

Peak, cps	Description, τ	Assignment
1, 113	Singlet, 8.12	$CH_3CONHCH_2C_6H_5$ (**10**)
2, 118	Singlet, 8.03	$CH_3CONHC_6H_5$ (**12**)
3, 234	Singlet, 6.10	$C_6H_5COCH_2CONHCH_2C_6H_5$ (**13**)
4, 240	Singlet, 6.00	$C_6H_5COCH_2CONHC_6H_5$ (**11**)
5, 255 6, 261 7, 267	Apparent triplet centered at τ 5.65 with J = 6 cps	Overlapping doublets, each with J = 6 cps, centered at τ 5.70 and 5.60: $CH_3CONHCH_2C_6H_5$ (**10**) and $C_6H_5COCH_2CONHCH_2C_6H_5$ (**13**)

Thin layer chromatography of the product mixture (10 cm, on silica gel plates, eluted with 9:1 chloroform–ether, developed with iodine vapor) gave four spots at R_f 0.10 (faint), 0.15 (faint), 0.25 (intense), and 0.43 (intense). Identical side-by-side and superimposed chromatograms with the known compounds showed that three of the components were N-benzylacetamide (**10**), 0.10; acetanilide (**12**), 0.15; and benzoylacetanilide (**11**), 0.43. The fourth spot, 0.25, was presumed to be N-benzylbenzoylacetamide (**13**).

Spectral Tests of Base Sensitivity of N-Alkyl Enol Esters.—Exactly 0.253 g (1.00 mmole) of N-ethyl-5-phenylisoxazolium-3′-sulfonate (**7**) was stirred in 10 ml of nitromethane containing 0.060 g (1.00 mmole) of acetic acid and 0.101 g (1.00 mmole) of triethylamine. The infrared spectrum of the product solution contained the characteristic enol ester carbonyl absorption between 5.6 and 5.7 μ. Approximately 0.101 g (1 mmole) more of triethylamine was added, and the infrared spectrum was again recorded. Even 6 min after the addition of base, there was no significant change in the infrared spectrum of the solution of the enol ester.

The experiment was repeated with 0.261 g (1.00 mmole) of N-ethyl-5-phenylisoxazolium fluoroborate in acetonitrile. No change was observed in the infrared spectrum 10 min after the excess base was added.

Spectral Tests of Enol Ester Formation with the Zwitterion 6.—A solution of 0.0603 g (1.00 mmole) of acetic acid and 0.1012 g (1.00 mmole) of triethylamine in 10 ml of nitromethane was added to 0.3013 g (1 mmole) of **6**, and the mixture was stirred in an ice bath until the reagent had all dissolved (5 min). The infrared spectrum contained an enol ester band at 5.65 μ, together with absorption of equal intensity between 5.8 and 5.9 μ, assignable to the ketoimide decomposition product.

The experiment was repeated, but the triethylamine was added as a dilute solution (total volume 4 ml) during 90 min at a constant rate with a motor-driven syringe control to the acetic acid and isoxazolium salt in 6 ml of the ice-cold solvent. This time the infrared spectrum of the product solution contained an enol ester band of increased intensity, and no peak was detected between 5.8 and 5.9 μ.

Cleavage of β-Acetoxycinnamanilide (8) with Benzylamine.—The enol ester **8** (0.281 g, 1 mmole) was added to a solution of 0.107 g (1.00 mmole) of benzylamine in 5 ml of dichloromethane. The solution was mixed and the infrared spectrum was taken at intervals. The enol ester carbonyl peak (5.65 μ) disappeared within 10 min, at which time the characteristic absorption of the rearrangement product **9** at 5.83 μ was intense. The 5.83-μ absorption decreased slowly, with complete disappearance within a few hours. The product nmr spectrum was taken as in the earlier experiment. Integration revealed approximately a 2:1 ratio of **10** and **11** to **12** and **13**.