yield was ~100%, mp 132-134°. Found: C 32.44; H 2.14; N 11.80; Cl 44.01%. $C_{13}H_{10}O_3N_4Cl_6$. Calculated: C 32.30; H 2.07; N 11.59; Cl 44.10%. Infrared spectrum (ν, cm^{-1}): 1730 (cyclic C=O), 1690 (noncyclic C=O), 1620 (C=N). NMR spectrum (δ, ppm): 2.60 s (Me_2N); 7.88-8.79 m (C_5H_4N).

Reaction of Trifluoroacetyl Isocyanate with Triethylamine. To a solution of 0.84 g of (III) in 30 ml of ether was added 0.61 g of triethylamine. A precipitate was obtained immediately, which was filtered and washed with ether. The yield of the adduct was 0.96 g (65.5%), mp 119-125° (decompn.). Found: C 45.48; H 6.13; N 11.06%. $C_9H_{15}O_2N_2F_3$. Calculated: C 45.00; H 6.25; N 11.67%. Infrared spectrum (ν, cm^{-1}): 1750 (C=O).

CONCLUSIONS

1. The dimethyl amides of the α-, β-, and γ-pyridinecarboxylic acids causes the dimerization of benzoyl isocyanate.

2. Trichloroacetyl isocyanate when reacted with N,N-dimethylisonicotinamide and N,N-dimethylpicolinamide gives saltlike adducts, and when reacted with N,N-dimethylnicotinamide it gives the cycloadduct with the intermediately formed acylamidine.

3. Trifluoroacetyl isocyanate reacts with N,N-dimethylpicolinamide to give the acylamidine, while with the β and γ isomers it gives a mixture of acylamidines and saltlike adducts.

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NEW DATA ON DAKIN – WEST REACTION WITH α-ALANINE AND ITS HOMOLOGS

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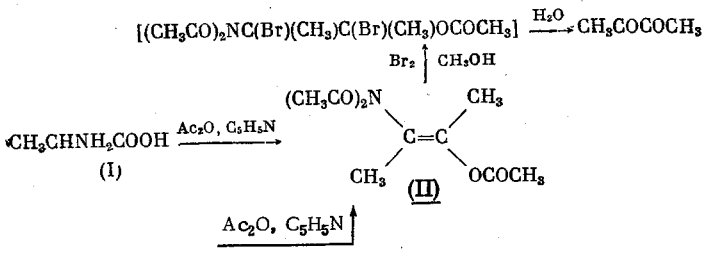
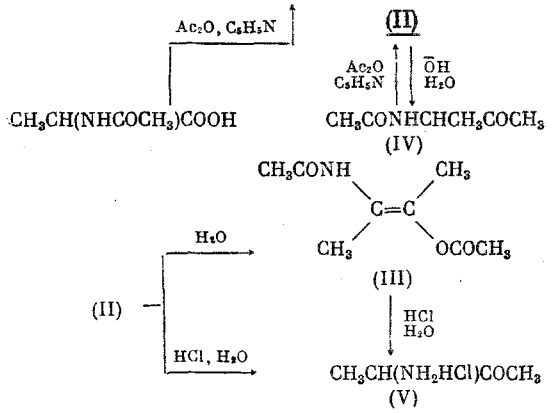
It is assumed that [1, 2] only N-acyl-α-amino ketones are formed in the Dakin–West reaction with α-alanine (I) and its homologs.

The error of this generally accepted concept was shown in the present paper and it was established that when (I) is heated with Ac_2O and pyridine at ~140°C the product obtained ~ 70% yield is 2-acetoxy-3-(N,N-diacetylamino)-2-butene (II), whose structure was proved by elemental analysis, and by the spectra and chemical transformations.



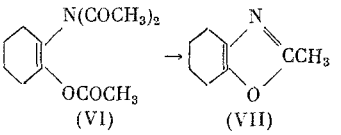
N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1, pp. 219-221, January, 1977. Original article submitted July 1, 1976.



Infrared spectrum of acetate (II) (ν, cm^{-1}): 1750 (CH_3COO); 1712 $(CH_3CO)_2N$; 1690 (C=C); 1206 (C–O). NMR spectrum of (II) (δ, ppm): 1.70 s ($2CH_3$); 2.14 s (CH_3COO); 2.28 s $(CH_3CO)_2N$. The empirical formula $C_{10}H_{15}NO_4$ also corresponds to the structure of (II), which was derived from the elemental analysis and mass-spectral (M^+ 213) data.

The partial hydrolysis of (II) with boiling water gives 2-acetoxy-3-acetamido-2-butene (III). NMR spectrum of (III) (δ, ppm): 1.75 s ($2CH_3$); 2.00 s (CH_3CON); 2.17 s (CH_3COO); IR spectrum (ν, cm^{-1}): 3300 (NH); 1745 (CH_3COO); 1675 (C=C); 1645 (CH_3CON); 1230 (C–O). The alkaline hydrolysis of (II) leads to the normal Dakin–West reaction product, viz., 3-acetamido-2-butanone (IV), while the acid hydrolysis of (II) and (III) leads to 3-amino-2-butanone hydchloride (V). The bromination of (II) in CH_3OH and subsequent hydrolysis with water converts it to biacetyl, which was isolated as dimethylglyoxime and its Ni comples

Taking into consideration the ability of the cis-fixed enol acetate (VI) to undergo cyclization to the oxazole derivative (VII) under partial hydrolysis conditions [3], and the lack of this ability for enol acetate (II), the latter can be assigned the trans configuration.



The formation of (II) in the Dakin–West reaction with Ac_2O and pyridine must be considered to be a multistep process, which proceeds via the intermediate step of 3-acetamido-2-butanone (IV) and its subsequent N- and O-acetylation. In order to confirm this scheme it was shown by us that (IV) when heated with Ac_2O in pyridine is converted to (II) in 72% yield. The reaction of N-acetyl-α-alanine with Ac_2O and pyridine proceeds more smoothly, and here (II) is obtained in 90% yield.

The analogous enol acetates (VIII) and (IX), as mixtures with the corresponding N-acyl-α-amino ketones (X) and (XI), are also formed by the reaction of the (I) homologs, α-aminobutyric acid (XII) and leucine (XIII), with Ac_2O and pyridine (~150°).

$$\underset{\text{(XII), (XIII)}}{RCHNH_2COOH} \xrightarrow{Ac_2O,\ C_5H_5N} \underset{\text{(X), (XI)}}{RCH(NHCOCH_3)COCH_3} + \underset{\text{(VIII), (IX)}}{RC[N(COCH_3)_2]=C(OCOCH_3)CH_3}$$

R = C_2H_5 (VIII), (X), (XII); R = $(CH_3)_2CHCH_2$(IX), (XI), (XIII). At a lower temperature (~ 100°) the main products obtained from (I), (XII), and (XIII) are N-acyl-α-amino ketones (IX), (X), and (XI), which are contaminated with small amounts of enol acetates (II), (VIII), and (IX)

$$CH_3CONHCH_2COCH_3 \leftarrow\times\!- H_2NCH_2COOH \xrightarrow{Ac_2O,\ C_5H_5N} \underset{\text{(XIV)}}{(CH_3CO)_2NCH_2COCH_3}$$

N,N-Diacetylaminoacetone (XIV) is isolated when glycine is reacted with Ac_2O and pyridine [4], but in some popular handbooks [2, 5] this transformation product is erroneously assigned the structure of acetamidoacetone. The structure of (XIV) is in agreement with the NMR spectral data [4] and the results of acid hydrolysis, which leads to the formation of aminoacetone hydrochloride [6].

EXPERIMENTAL

The IR spectra were taken as KBr pellets on a UR-10 instrument, the NMR spectra were taken in CCl_4 solution on a DA-60-IL instrument (internal standard = TMS), while the mass spectra were taken on an MKh 13-03 instrument. The TLC was run on Silufol UV-254 using ethyl acetate as the solvent and detection of the spots with I_2 vapors.

Reaction of α-Alanine (I) with Ac_2O and Pyridine. A mixture of 5 g of (I), 32 ml of Ac_2O, and 23 ml of pyridine was heated for 6 h at 100° (bath temperature here and subsequently), after which another 16 ml of Ac_2O and 12 ml of pyridine were added, the mixture was heated for 4 h at 135-140°, the Ac_2O and pyridine were vacuum distilled, and the residue was distilled. We obtained 9 g (75%) of (II), bp 92-94° (3 mm), mp 84-85° (after low-temperature recrystallization from ether), R_f 0.65. Found: C 56.25; H 7.14; N 6.24%. $C_{10}H_{15}NO_4$. Calculated: C 56.34; H 7.04; N 6.56%.

Reaction of N-Acetyl-α-alanine with Ac_2O and Pyridine. A mixture of 10 g of N-acetyl-α-alanine, 64 ml of Ac_2O, and 43 ml of pyridine was heated for 7 h at 140° and (II) was isolated as described above. The yield of (II) was 14.7 g (90%).

Partial Hydrolysis of (II). A mixture of 2 g of (II) and 25 ml of water was refluxed for 10 h, after which it was evaporated in vacuo and the residue was recrystallized from ether at −70°. We obtained 1.4 g (86%) of (III), mp 94-95°, R_f 0.27. Found: C 55.77; H 7.75; N 8.47%. $C_8H_{13}NO_3$. Calculated: C 56.12; H 7.65; N 8.19%

Conversion of 3-Acetamido-2-butanone (IV) to (II). A mixture of 2.5 g of (IV) [7], 11 ml of Ac_2O, and 9 ml of pyridine was heated for 6 h at 140°. Then the excess Ac_2O and pyridine were moved and the residue was vacuum distilled to give 2.9 g (72%) of (II).

Alkaline Hydrolysis of (II). A mixture of 2.5 g of (II) and a solution of 1.45 g of KOH in 30 ml of alcohol was kept for 4 h at ~20°, after which it was evaporated in vacuo, the residue was treated with water, and extraction with ethyl acetate gave 0.92 g (61%) of (IV) with bp 108-110° (3 mm): n_D^{19} 1.4564. R_f 0.18. Infrared spectrum (ν, cm^{-1}): 3290 (NH), 1724 (C=O), 1660 (CH_3CON). NMR spectrum (δ, ppm): 1.25 d (CH_3); 1.92 s (CH_3CON); 2.14 s (CH_3CO); 4.37 g (CH); 7.33 d (NH).

Acid Hydrolysis of (II). A mixture of 0.5 g of (II) and 10 ml of dilute HCl solution was refluxed for 10 h, cooled to 20°, filtered, the filtrate was evaporated in vacuo to dryness, and the residue was washed with acetone. We obtained 0.26 g (90%) of (V), mp 107-109° [8].

The hydrolysis of (III) under analogous conditions gave (V) in 85% yield.

Bromination of (II). With stirring, 0.32 ml of Br_2 was added to a solution of 1 g of (II) in 15 ml of MeOH. After decolorization (in ~40 min) 8 ml of water was added, the mixture was kept at 20° for 12 h, heated at 90-100° for 1.5 h, NH_2OH solution (from 3.2 g of the hydrochloride and 2.6 g of KOH in 5 ml of water) was added, the mixture was heated at 100-110° for 1.5 h, cooled to 20°, and excess $Ni(OAc)_2$ solution was added. The obtained precipitate was filtered and dried in the air. We obtained 0.58 g (85%) of the Ni complex of dimethylglyoxime. Infrared spectrum (ν, cm^{-1}): 1573, 1430, 1386, 1372, 1262, 1103, 990.

A mixture of 0.3 g of the Ni complex and 3 ml of dilute HCl solution (1:3) was stirred at 20° for 5 min, and the precipitate was filtered and dried in the air. We obtained 0.21 g (88%) of dimethylglyoxime with mp 237-240°.

Reaction of α-Aminobutyric Acid (XII) with Ac_2O and Pyridine. A mixture of 5 g of (XII), 28 ml of Ac_2O, and 20 ml of pyridine was heated for 6 h at 100°, after which another 14 ml of Ac_2O and 10 ml of pyridine were added, and the mixture was heated for 4 h at 140° and then vacuum-distilled. We obtained 8.2 g of a mixture of (VIII) and (X) in a 1:1 ratio (NMR spectral data). Compounds (VIII): R_f 0.72; IR spectrum (ν, cm^{-1}): 1755 (CH_3COO); 1710 ($(CH_3CO)_2N$), 1675 (C=C); 1205 (C−O). NMR spectrum (δ, ppm): 1.73 s ($CH_2C=C$); 2.22 s (CH_3COO); 2.32 s ($(CH_3CO)_2N$). (X) [8]: R_f 0.28; IR spectrum (ν, cm^{-1}): 3290 (NH); 1720 (CH_3CO); 1660 (CH_3CON). NMR spectrum (δ, ppm): 0.86 t (CH_3CH_2); 1.48 m (CH_2); 1.95 s (CH_3CON); 2.13 s (CH_3CO); 4.38 m (CH); 7.22 d (NH).

Reaction of Leucine (XIII) with Ac_2O and Pyridine. A mixture of 5 g of (XIII), 22 ml of Ac_2O, and 15 ml of pyridine was heated at 100° for 4 h, after which another 11 ml of Ac_2O and 8 ml of pyridine were added and the mixture was heated at 150-155° for 6 h. Vacuum-distillation gave 6.5 g of a mixture of (IX) and (XI) in a 1:1 ratio (NMR spectral data). Compound (IX): R_f 0.70; IR spectrum (ν, cm^{-1}): 1760 (CH_3COO); 1715 ($(CH_3CO)_2N$); 1685 (C=), 1202 (C−O). NMR spectrum (δ, ppm): 1.75 s ($CH_3C=C$); 2.20 s (CH_3COO); 2.30 s ($(CH_3CO)_2N$). Compound (XI) [9]: R_f 0.35; IR spectrum (ν, cm^{-1}): 3300 (NH); 1722 (CH_3CO); 1661 (CH_3CON).

NMR spectrum (δ, ppm): 0.92 d $(CH_3)_2CH$; 1.47 m (CH, CH_2); 1,93 s (CH_3CON); 2.12 s (CH_3CO); 4.25 s (CH); 7.22 d (NH).

CONCLUSIONS

The enol acetates of N,N-diacetyl-α-amino ketones are formed when α-alanine and its homologs are heated with acetic anhydride and pyridine.

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REACTION OF PHOSPHORUS- AND NITROGEN-CONTAINING HETEROCYCLES WITH AMINE HYDROCHLORIDES

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The catalytic effect of amine hydrochlorides (ARC) and other acid impurities in the reactions of acyclic amidophosphites and amidophosphonites is known [1]. We observed the AHC to exert an analogous effect in the reaction of oxazaphospholanes with aromatic [2] and aliphatic [3] aldehydes, cyclic ketones [4], and other carbonyl compounds. The reaction of the AHC with cyclic phosphorus- and nitrogen-containing compounds, the so-called oxaza- and diazaphospholanes, was studied in the present paper. Previously we had shown that the reactions of amidophosphites with AHC and certain other reagents are reversible, and when the amine is removed the equilibrium is shifted toward the formation of the chlorophosphite [5]. In this connection it was postulated [6] that the role of the third reagent introduced into the reaction consists in shifting this equilibrium to the right by binding one of the components.

The 2-alkoxy-3-methyl(phenyl)-1,3,2-oxazaphospholanes react with AHC at elevated temperatures. Here the amine is liberated from the salt, while the starting heterocycle remains unchanged, which is recorded via the ^{31}P NMR spectrum. The yield of the amine drops when certain dioxaphospholanes, devoid of nitrogen, are used as the phosphorus components. For example, in the case of 2-n-butoxy-1,3,2-dioxaphospholane the yield of diethylamine does not exceed 3% (Table 1). Here, according to the GLC data, diethylamine and n-butanol are formed in an ~1 : 1 ratio. The liberation of the alcohol can be explained by initial protonation at both the phosphorus atom and the oxygen atom of the alkoxy group [7]. The first direction includes the step of anionic exchange of the alkoxyl group by chlorine anion, with subsequent deprotonation and the formation of the end products, the same as in the case of carboxylic acids [8].

The formation of a positively charged ammonium center at the phosphorus should facilitate nucleophilic attack by chlorine anion on P(III) with subsequent opening of the ring:

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