REACTION OF ARYL-SUBSTITUTED GLYCINEAMIDINES WITH OXALIC ACID DERIVATIVES

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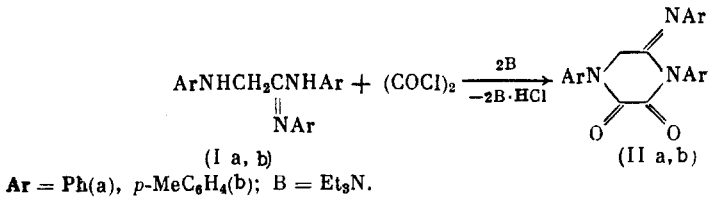
The reaction of N^1,N^2-diaryl-N-arylglycineamidines with oxalyl chloride and diethyl oxalate leads to 1,4-diaryl-5-aryliminopiperazine-2,3-diones and 1,3-diaryl-4-aryliminoimidazolidin-2-ones.

α-Aminoamidines (α-AA) are one of the least studied types of α-amino acid derivatives. N^1,N^2-diphenyl-N-phenylglycineamidine (Sabaneev's base) (Ia) reacts with benzoyl chloride [1] and acetic anhydride [2] to give acyclic products of the monoacylation, which predominantly involves the α-amino group. 4-Phenylamino-1,3-diphenylimidazolium chlorides were isolated in the reaction of acid chloride derivatives of the lower aliphatic carboxylic acids under analogous conditions [3]. A rather general method for the synthesis of aminopyrazines was developed on the basis of the reaction of unsubstituted or N-alkyl-substituted α-AA with α-dicarbonyl compounds [4]. Other reactions of α-AA with difunctional electrophiles have virtually not been studied.

We have shown that N^1,N^2-diaryl-N-arylglycineamidines (Ia) and (Ib) react readily with oxalyl chloride in the presence of Et_3N to give piperazines (IIa) and (IIb).

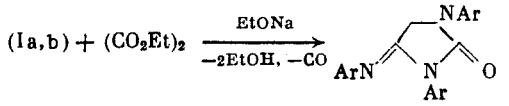


(I a, b) (II a, b)

Ar = Ph(a), p-MeC_6H_4(b); B = Et_3N.

Products (II) are high-melting, fine crystalline compounds with poor solubility in organic solvents and water, which complicates obtaining their PMR spectra. The structure of (II) was supported by IR and UV spectroscopy and mass spectrometry, while its composition was supported by elemental analysis.

By analogy with glycineamide [5], we might have expected that the reaction of (I) with diethyl oxalate would proceed readily to the same piperazinediones (II). However, the presence of aryl substituents at the nitrogen atoms in (I) apparently hinders this reaction, which proceeds efficiently only at 130-140°C in the presence of EtONa. Under these conditions, CO is eliminated and five-membered 4-arylimino-1,3-diarylimidazolidin-2-ones (III) are formed.



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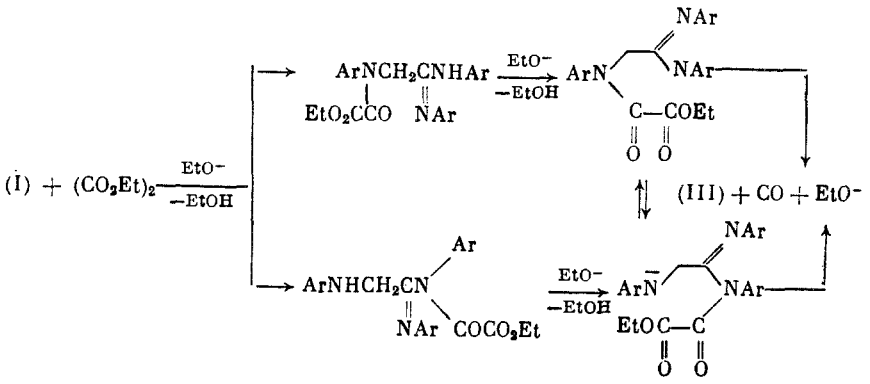
α-AA (I) react with diethyl oxalate at 170-180°C also in the absence of alcoholate but heavy tar formation does not permit isolation of more than 5% (III). Piperazine-2,3-diones (II) are stable under the conditions for the formation of (III) and, thus, they are not precursors of (III). The loss of a CO molecule probably occurs as follows:



EXPERIMENTAL

The IR spectra (ν, cm^{-1}) were taken in vaseline mull on a UR-20 spectrometer. The UV spectra (λ_{max}, nm (log ε)) were taken in acetonitrile on a Specord M-40 spectrophotometer. The PMR spectra (δ, ppm) were taken in $CDCl_3$ on a Varian T-60 spectrometer with TMS as the internal standard. The electron impact mass spectra (m/z, intensity in %) were obtained on an MKh-1310 mass spectrometer with direct sample inlet into the ion source. The ionizing potential was 70 V. The relative error in determination of the ion mass $\Delta M/M \leq 1 \cdot 10^{-5}$. Samples of α-AA (Ia) and (Ib) were obtained according to Ruggli and Marszak [1].

1,4-Diphenyl-5-phenyliminopiperazine-2,3-dione (IIa). A solution of 2.0 g (0.016 mole) oxalyl chloride in 10 ml $CHCl_3$ was added to a mixture of 4.3 g (0.014 mole) α-AA (Ia) and 4.35 g (0.043 mole) Et_3N in 90 ml abs. $CHCl_3$ at from −25 to −30°C. The mixture was stirred for 4 h at ~20°C and poured into ice water. The organic layer was separated. The aqueous layer was extracted with two 50-ml portions of chloroform and dried over $MgSO_4$. The solvent was evaporated in vacuum and the precipitate was thoroughly washed with ether to give 3.1 g (61.5%) (IIa), mp >320°C (from 2:1 ethanol-dioxane). IR spectrum (ν, cm^{-1}): 1677 (C=N), 1736, 1757 (C=O). UV spectrum: 314 (3.97). Mass spectrum: $[M]^{+\cdot}$ 355 (66), $[C_{14}C_{11}N_2]$ 207 (17), $[C_7N_5NO]$ 119 (11), $[C_8H_7N]$ 117 (10), $[C_7H_7N]$ 105 (24), $[C_7H_6N]$ 104 (100), $[C_6H_7N]$ 93 (20), $[C_6H_5N]$ 91 (8), $[C_6H_5]$ 77 (72). Found: C, 74.19; H, 4.58; N, 11.47%. Calculated for $C_{22}H_{17}N_3O_2$: C, 74.37; H, 4.79; N, 11.73%. A total of 0.6 g unreacted (Ia) was recovered from the reaction mixture.

Analogously, 3.1 g (0.009 mole) (Ib), 1.32 g (0.0104 mole) oxalyl chloride, and 3.65 g (0.036 mole) Et_3N gave 2.10 g (58%) piperazine-2.3-dione (IIb), mp 309-310°C (from 3:1 ethanol-dioxane). IR spectrum: (ν, cm^{-1}): 1668 (C=N), 1728, 1755 (C=O). UV spectrum: 314 (3.59). Mass spectrum: $[M]^{+\cdot}$ 397 (65), $[C_{16}H_{15}N_2]$ 235 (6.5), $[C_{15}H_{13}N_2]$ 221 (6.5), $[C_8H_8N]$ 118 (100), $[C_7H_7]$ 91 (55). Found: C, 75.93; H, 5.58; N, 10.46%. Calculated for $C_{25}H_{23}N_3O_2$: C, 75.57; H, 5.79; N, 10.58%.

1,3-Diphenyl-4-phenyliminoimidazolidin-2-one (IIIa). A sample of 10.0 g (0.0332 mole) α-AA (Ia) was added to a suspension of EtONa obtained from 2.0 g (0.087 mole) metallic sodium and 6.0 g abs. ethanol in 50 ml abs. xylene at 60°C. After 5 min, 5.85 g (0.040 mole) diethyl oxalate was added. The mixture was heated at reflux for 5 h, diluted with 100 ml benzene, and washed with water. The organic phase was centrifuged for 15 min at 3000 rpm. Recrystallization of the precipitate from ethanol gave 2.8 g unreacted (Ia). The organic layer decanted to remove the precipitate was evaporated in vacuum to give 3.8 g (49%) (IIIa), mp 161-163°C (benzene). IR spectrum (ν, cm^{-1}): 1672 (C=N), 1736 (C=O). UV spectrum: 250 (4.34). PMR spectrum 4.33 s (2H, CH_2), 6.67-7.67 m (15H, 3Ph). Mass spectrum: $[M]^{+\cdot}$ 327 (75), $[C_{14}H_{11}N_2]$ 207 (15), $[C_{13}H_{11}N_2]$ 195 (11), $[C_7H_7N]$ 105 (100), $[C_6H_7N]$ 93 (15), $[C_6H_5]$ 77 (40). Found: C, 77.31; H, 5.37; N, 12.75%. Calculated for $C_{21}H_{17}N_3O$: C, 77.06; H, 5.20; N, 12.84%.

Analogously, 6.8 g (0.0198 mole) α-AA (Ib), 3.5 g (0.024 mole) diethyl oxalate, and 3.55 g (0.0522 mole) EtONa gave 4.3 g (59%) imidazolidin-2-one (IIIb), mp 157-158°C (from 1:2 benzene-hexane). IR spectrum (ν, cm^{-1}): 1680 (C=N), 1742 (C=O). UV spectrum: 255

(4.38), 280 sh (4.22). PMR spectrum: 2.21 s (6H, $2CH_3$), 2.27 s (3H, CH_3), 4.18 s (2H, CH_2), 6.35-7.24 m (12H, $3C_6H_4$), Mass spectrum: $[M]^{+\cdot}$ 369 (100), $[C_{16}H_{15}N_2]$ 235 (10), $[C_8H_7NO]$ 133 (6), $[C_8H_9N]$ 119 (95), $[C_7H_7]$ 91 (32). Found: C, 78.16; H, 6.49; N, 11.30%. Calculated for $C_{24}H_{23}N_3O$: C, 78.05; H, 6.23; N, 11.38%.

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REACTIONS OF 2-[N,N-BIS(TRIMETHYLSILYL)]AMINO-4,5-BENZO-1,3,2-DIOXAPHOSPHOLANE WITH CARBOXYLIC AND PHOSPHOROUS ACIDS AND ACETIC ANHYDRIDE

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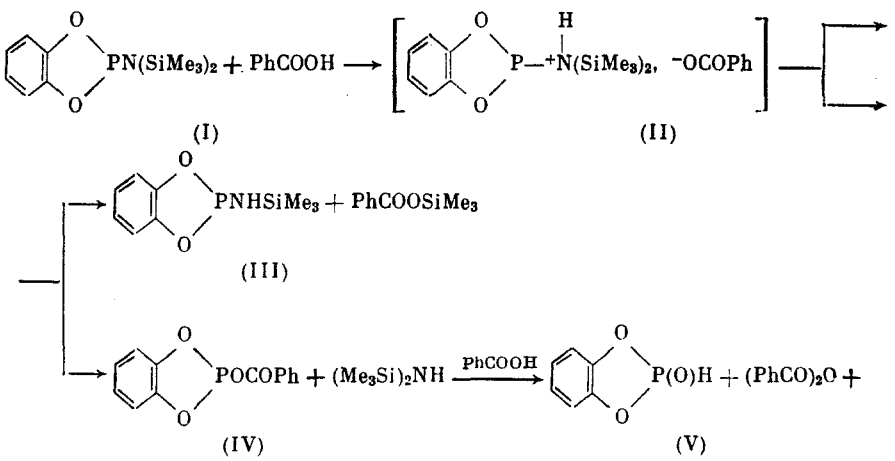
The reactions of 2-(N,N-bis(trimethylsilyl)]amino-4,5-benzo-1,3,2-dioxaphospholane with acetic acid, benzoic acid, and acetic anhydride yield 2-trimethylsiloxy-4,5-benzo-1,3,2-dioxaphospholane. Upon reaction with dialkyl phosphites, the silylamidophosphite acts as a silylating agent.

The reaction of 2-[N,N-bis(trimethylsilyl)]amino-4,5-benzo-1,3,2-dioxaphospholane (I) with benzoic acid leads to the formation of 2-trimethylsiloxy-4,5-benzo-1,3,2-dioxa- phospholane (VI) (δP 124 ppm) as the major product and a slight amount of 2-trimethylsilylamino-4,5-benzo-1,3,2-dioxaphospholane (III) (δP 150 ppm) (Scheme 1).

As in the case of the acidolysis of amidophosphites [1], the major pathway apparently involves protonation of the nitrogen atom with subsequent nucleophilic attack of the benzoyloxy anion at the electrophilic trivalent phosphorus atom of protonated form (II) to give 2-benzoyloxy-4,5-benzo-1,3,2-dioxaphospholane (IV) and hexamethyldisilazane.

Scheme 1



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