ACTION OF ACETIC ANHYDRIDE ON BENZO-1,5-DIAZEPINE DERIVATIVES

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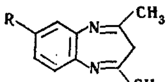
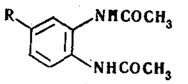
Under the action of acetic anhydride in benzene, 7-amino-2,4-dimethyl- and 2,4-dimethylbenzo-1,5-diazepine undergo cleavage at the $-C{=}N-$ bond with simultaneous acylation of the primary amino groups formed.

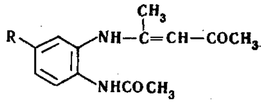
Continuing previous work [1], we have studied the action of acetic anhydride on benzo-1, 5-diazepine derivatives. The reaction of 7-amino-2,4-dimethylbenzo-1,5-diazepine (Ia) with an equimolar amount of acetic anhydride in benzene at 18–20°C gave 7-acetamido-2,4-dimethylbenzo-1,5-diazepine (Ib). The structure of Ib and its hydrochloride was confirmed by the presence in their IR spectra of the bands of an amide group (1680, 3200–3500 cm^{-1}). In the UV region, Ib has a maximum at 240 nm (log ε 4.06) and its hydrochloride a maximum at 500 nm (log ε 3.98), which is characteristic for benzo-1,5-diazepine salts. The action of 5 moles of acetic anhydride on Ia not only led to the acetylation of the amino group but also to the acetolysis of the $-C{=}N-$ bond and the formation of 1,2,4-triacetamidobenzene (IIa). The structure of IIa was confirmed by its independent synthesis from 1,2,4-triaminobenzene and acetic anhydride. When 1 mole of compound Ia was treated with 2 moles of acetic anhydride, a substance was formed which had no definite melting point and, on dissolution in dilute hydrochloric acid, did not give the dark violet coloration characteristic for the benzo-1,5-diazepinium cation. The IR spectrum of this compound had the absorption of an amide group (1670, 3200–3400 cm^{-1}) and of $-C{=}C-$ and $-C{=}N-$ bonds (1610–1650 cm^{-1}). From these facts it may be assumed that the substance isolated has the structure IIIa. Compound IIIa is apparently an intermediate in the synthesis of IIa and is formed from Ib by the cleavage of one $-C{=}N-$ bond and the acetylation of the amino group in position 1.



Ia-c



IIa,b



IIIa,b

I a $R = NH_2$, b $R = CH_3CONH$, c $R = H$; II a $R = CH_3CONH$, b $R = H$; III a $R = CH_3CONH$, b $R = H$

Similar transformations take place when acetic anhydride acts on 2,4-dimethylbenzo-1,5-diazepine (Ic). Thus, the treatment of Ic with an equimolar amount of acetic anhydride forms a mixture of N,N'-diacetyl-1,2-phenylenediamine (IIb) and compound IIIb, while the use of a fivefold excess of acetic anhydride gives only IIb. Compounds IIIa and IIIb have similar properties and identical IR spectra. The structure of IIIb was also confirmed by its PMR spectrum, which had the following signals: signals due to three different methoxyl groups (δ 1.76, 2.03, and 2.10 ppm), the signal of the proton of a CH group (δ 5.1 ppm), confirming the position of the double band in the side chain, and the signals of the ring protons forming a complex multiplet (δ 6.95–8.03 ppm).

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TABLE 1. Characteristics of the Compounds Obtained.

Compound	mp, °C	Empirical formula	Found, %			Calculated, %		
			C	H	N	C	H	N
I *	139—142	$C_{13}H_{15}N_3O \cdot H_2O$	63,2	6,9	—	63,2	6,9	—
IIIa	160—180	$C_{15}H_{19}N_3O_3$	62,8	6,0	15,5	62,3	6,6	15,5
IIa	233—235†	$C_{12}H_{15}N_3O_3$	—	—	—	—	—	—
IIb	185—186†	$C_{10}H_{12}N_2O_2$	—	—	—	—	—	—
IIIb	121—123	$C_{13}H_{16}N_2O_2$	66,8	6,9	12,4	67,1	6,9	12,1

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*The hydrochloride $C_{13}H_{15}N_3O \cdot HCl \cdot H_2O$, mp 226°C;

†A mixture with an authentic sample showed no depression of the melting point.

EXPERIMENTAL

7-Amino-2,4-dimethylbenzo-1,5-diazepine (Ia). A solution of 5 g (0.0274 mole) of 2,4-dinitroaniline in 100 ml of absolute ethanol was treated with 0.5 g of freshly prepared Raney nickel catalyst and the resulting mixture was shaken in an atmosphere of hydrogen at room temperature for 4 hr 30 min. After this time, the theoretical amount of hydrogen (3.7 liters) had been absorbed and the solution had become decolorized. The catalyst was filtered off and 60 ml of the ethanol was distilled off in vacuum. To the residue were added 2.74 g (0.0274 mole) of acetylacetone and 3 ml of glacial acetic acid. The resulting solution was shaken at room temperature for 10 min, diluted with 20 ml of water, and, with vigorous stirring, added to 30 ml of a 10% solution of NaOH cooled to 1-2°C, the temperature of the reaction mixture not being allowed to rise above 5°C. The light yellow precipitate that deposited was filtered off, washed with ice water, dried, and recrystallized. Yield 3.89 g (76%), mp 179-180°C (from benzene). Found, %: C 70.3; H 6.9; N 22.4. Calculated for $C_{11}H_{13}N_3$, %: C 70.0; H 7.0; N 22.4. IR spectrum, cm^{-1}: 1615-1635 (C=N bond), 3200, 3340, 3435 (NH_2, ν), 1630 (NH_2, δ). UV spectrum: λ_{max} 240 nm (log ε 3.79).

Hydrochloride. Dark violet crystals with mp 210-213°C. Found, %: C 58.6; H 6.7; Cl 15.5; N 18.7. Calculated for $C_{11}H_{13}N_3 \cdot HCl$, %: C 59.1; H 6.3; Cl 15.9; N 18.8. IR spectrum, cm^{-1}: 1600-1615 (C=N bond), 1635-1645 (benzene ring), group of bands at 3200-3500 (NH, ν), broadened band at 3000-3200 (NH^+, ν). UV spectrum: λ_{max} 560 nm (log ε 2.75).

Action of Acetic Anhydride. A. On 7-Amino-2,4-dimethylbenzo-1,5-diazepine (Ia). Solutions of 1.87 g (0.01 mole) of Ia in 200 ml of absolute benzene were treated with acetic anhydride in the following amounts: a) 1.02 g (0.01 mole), b) 2.04 g (0.02 mole), and c) 5.1 g (0.05 mole). In case (a), the reaction mixture was stirred for 1 hr and then petroleum ether was added until the separation of the precipitate was complete. This was filtered off, reprecipitated from an aqueous bicarbonate solution, and recrystallized from a mixture of ethanol and benzene giving 0.74 g (30%) of the monohydrate of Ib and its hydrochloride. In case (b), after 36 hr the mixture obtained deposited a precipitate, which was filtered off and reprecipitated from ethanolic solution with ether. This gave 0.5 g of IIIa. In case (c), the reaction mixture was stirred for 1 hr and allowed to stand at room temperature for 24 hr. The precipitate that deposited was filtered off and recrystallized from ethanol, giving 0.4 g (16%) of IIa.

B. On 2,4-Dimethylbenzo-1,5-diazepine (Ic). Solutions of 1.72 g (0.01 mole) of Ic [2] in 100 ml of anhydrous benzene were treated with the following amounts of acetic anhydride: a) 1.02 g (0.01 mole), b) 5.1 g (0.05 mole). In case (a), after 5 hr, crystals separated out which were filtered off and recrystallized from a mixture of ethanol and benzene (1 : 5), giving 0.2 g (10.4%) of IIb. The addition of petroleum ether to the benzene mother solution led to a precipitate which was recrystallized from benzene, giving 0.72 g (31.4%) of IIIb. In case (b), the reaction mixture was stirred for 5 hr, and the benzene was evaporated off in vacuum. The residue was recrystallized from ethanol giving 0.7 g (40%) of IIb. A mixture of samples of substance IIb obtained at the molar ratios of the reactants (a) and (b) showed no depression. The melting points and analyses of the substances obtained are given in Table 1.

The IR spectra were taken on a UR-10 spectrophotometer in paraffin oil, the UV spectra in ethanol solution on an EPS-3 recording spectrophotometer, and the PMR spectra on a JNM-4 H-100 instrument with TMS as internal standard and $CDCl_3$ as solvent.

LITERATURE CITED

1. K. V. Levshina, L. P. Glazyrina, and T. S. Safonova, KhGS [Chemistry of Heterocyclic Compounds], 6, 1133 (1970).
2. J. Thiele and G. Steimmig, Ber., 40, 955 (1907).