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N. P. ZAPEVALOVA, T. A. SOKOLOVA, N. M. BAZHENOV,

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Abstract

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N. P. ZAPEVALOVA, T. A. SOKOLOVA, N. M. BAZHENOV,
A. I. KOL' TSOV

METHOD FOR PREPARING N-SUBSTITUTED β-LACTAMS

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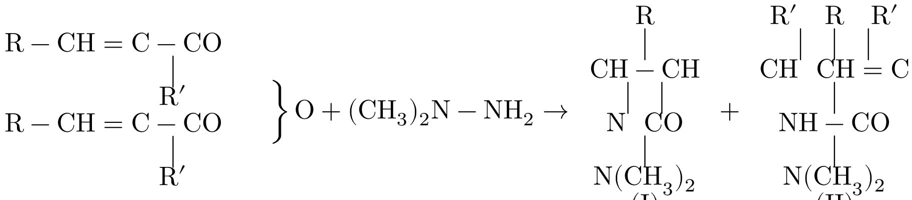
It was reported earlier (^{1}) that, in the interaction of methacrylic acid anhydride or acid chloride with unsymmetrical dimethylhydrazine, two isomeric compounds are formed: 1-dimethylamino-3-methylazetidinone-2 (Ib) and dimethylhydrazide of methacrylic acid (IIb). It was of interest to establish whether this reaction is general for the anhydrides and acid chlorides of α, β-unsaturated acids. As the experimental results have shown, this interaction is indeed a general reaction, expressed by the following scheme:



(I) (II)

where
a) $R = H; \quad R' = H;$
b) $R = CH_3; \quad R' = H;$
c) $R = H; \quad R' = CH_3$

In the interaction of crotonic acid anhydride with dimethylhydrazine, 1-dimethylamino-4-methylazetidinone-2 (Ib) and dimethylhydrazide of crotonic acid (IIb) are formed. Isolation of the reaction products in this case is complicated by the fact that the azetidinone gives a salt with the crotonic acid formed. The free base is isolated from the aqueous solution of the salt by passing it through a basic ion-exchange resin. The dimethylhydrazide of crotonic acid distills in vacuo, crystallizing in the receiver.

In the interaction of crotonic and acrylic acid chlorides with dimethylhydrazine, hydrochloride salts of 1-dimethylamino-4-methylazetidinone-2 (Ib) and 1-dimethylaminoazetidinone-2 (Ia), respectively, are obtained in yields

Fig. 1. NMR spectra of the compounds studied. The spectrum of compound Ib at a frequency of 12 MHz is shown on the same frequency scale as the spectra at 40 MHz.

Figure 1: Fig. 1. NMR spectra of the compounds studied. The spectrum of compound Ib at a frequency of 12 MHz is shown on the same frequency scale as the spectra at 40 MHz.

up to 90% of theory. The bases are isolated by passing solutions of the salts through anion exchangers. Dimethylhydrazides (IIa) and (IIb) are isolated by distillation in vacuo in very small yields and are purified by recrystallization from heptane. Azetidinones and dimethylhydrazides obtained from derivatives of acrylic, methacrylic, and crotonic acids are bases capable of giving salts with hydrochloric acid and with certain organic acids, and with methyl iodide —iodomethylates.

Thus, it has been shown that the interaction of dimethylhydrazine with anhydrides (acid chlorides) of α, β-unsaturated aliphatic acids is a general reaction leading to the formation of azetidinones-2 and of the isomeric dimethylhydrazides of the corresponding acids. The structure of compounds Ia, Ib, Iv and IIb and IIv has been definitively confirmed by proton spectra.

nuclear magnetic resonance (NMR), as follows from the interpretation of the spectra, the results of which are given in Fig. 1. In interpreting the NMR spectra of solutions of the compounds studied in deuterated methanol, data on the chemical shifts and spin-spin splittings of protons of organic compounds, contained in a number of works (2-6), were used.

Fig. 1. NMR spectra of the compounds studied. The spectrum of compound Ib at a frequency of 12 MHz is shown on the same frequency scale as the spectra at 40 MHz.

The position of the line of the —NH—group in compounds IIb and IIv, which is prone to the formation of hydrogen bonds and to proton exchange, depends on the solvent, the concentration of the solution, and also on the temperature. In addition, in the medium of deuterated methyl alcohol, isotopic exchange H—D of the protons of the —NH—group is possible, which will lead to the disappearance of its line in the NMR spectrum. For these reasons, in the spectra of IIb and IIv the line of the —NH—group was not observed. Some lines of the spectra owe their appearance to impurities. The most intense of them is the line at 5.00-5.10 τ, belonging to water, to the OH groups of the alcohol and, possibly, to protons of other functional groups capable of rapid exchange.

The line of the $-N(CH_3)_2$ group in the spectrum of sample Ib is split into two components of equal intensity. The magnitude of the splitting proved to depend on the strength of the magnetic field and on the operating frequency. In the spectrum recorded at a frequency of 12 MHz, the distance between the components of this doublet is approximately three times smaller than in the spectrum at a frequency of 40 MHz. It follows from this that the splitting is caused by a chemical shift, and not by spin–spin interaction of protons. It is natural to assume in this case the existence, in approximately equal amounts, of two spatial isomers of the molecule Ib with different chemical shifts of the $-N(CH_3)_2$ group.

In conclusion, it should be noted that there is a substantial difference (~0.5 τ) between the chemical shifts of the $-N(CH_3)_2$ groups in molecules containing a four-membered ring and in molecules with the group $> C = C <$.

Experimental Part

Interaction of acid chlorides of α,β-unsaturated acids with dimethylhydrazine (DMH). To 0.2 gram-mole of the acid chloride of an α,β-unsaturated acid (acrylic or crotonic) in a round-bottom flask, with stirring and external cooling,

With cooling by melting ice, 0.2 gram-mole of DMH was added, after which the mixture was stirred for another $1\frac{1}{2}$ hours. After the precipitate had been washed with ether, it was treated with hot dimethylformamide (DMFA). On cooling, colorless crystals of the hydrochloride salts of 1-dimethylaminoazetidin-2-one (1a) (from acrylic acid chloride) and 1-dimethylamino-4-methylazetidin-2-one (1b) (from crotonic acid chloride) separated from the solution in yields of about 40% of theory.

When the reaction was carried out in water, the yields of crude product increased to 70–90%. The azetidinone bases (1a) and (1b) were isolated from the hydrochloride salts by passing their aqueous solutions through the basic ion-exchange resin "Amberlite." The properties of the compounds obtained and the analytical results are presented in the table.

Reaction of crotonic anhydride with dimethylhydrazine (DMH). To 0.2 gram-mole of crotonic anhydride in a round-bottomed flask, with stirring and cooling with melting ice, an equimolecular amount of DMH was added. The mixture was stirred for another 3 hours and left overnight. The syrup obtained

Table 1

Physical properties of the compounds obtained

No.	Substance	M.p., °C	Solubility	Gross formula	C, % calc.	C, % found	H, % calc.	H, % found	N, % calc.	N, % found	Halogen, % calc.	Halogen, % found
1	1-Dimethylaminoazetidin-2-one	91.5–92	In water, alcohol, hot acetone	$C_5H_{10}N_2O$	52.63	52.76 53.24	8.77	8.95 8.92	24.56	24.56 24.23	–	–
2	Hydrochloride salt of 1	198–200	In water, alcohol, hot dimethylformamide	$C_5H_{11}N_2OCl$	39.87	40.15 40.31	7.39	7.54 7.71	18.60	18.72 18.35	23.52	23.32 23.39
3	Iodomethylate of 1	184.5–185.5	In water, alcohol	$C_6H_{13}N_2OJ$	28.13	28.19 28.03	5.08	5.12 5.41	10.94	10.61 11.06	49.61	49.35 49.13
4	1-Dimethylamino-4-methylazetidin-2-one	238–239	In water, alcohol; extremely hygroscopic	$C_6H_{12}N_2O$	56.25	56.27 56.21	9.38	9.38 9.32	21.88	21.84 21.45	–	–

No.	Substance	M.p., °C	Solubility	Gross formula	C, % calc.	C, % found	H, % calc.	H, % found	N, % calc.	N, % found	Halogen, % calc.	Halogen, % found
5	Hydrochloride salt of 4	244–244.5	In water, hot dimethylformamide	$C_6H_{13}N_2OCl$	43.76	44.16 44.20	7.91	7.92 8.03	17.02	17.16 16.95	21.58	21.55 22.03
6	Crotonic acid salt of 4	98–99	In water, acetone, methanol, DMFA, hot benzene	$C_{10}H_{18}N_2O_3$	56.08	56.51 56.58	8.41	8.48 8.76	13.08	13.14 13.55	–	–
7	Iodomethylate of 4	224–224.5	In water, alcohol	$C_7H_{15}N_2OJ$	31.10	31.14 31.36	5.59	5.73 6.18	10.37	–	47.04	46.64 46.51
8	Dimethylhydrazide of crotonic acid	72–72.5	In water, alcohol, benzene, ether, DMFA, acetone	$C_6H_{12}N_2O$	56.25	56.40 56.52	9.38	9.38 9.43	21.88	21.29 21.54	–	–
9	Hydrochloride salt of 8	199–200	In water, hot DMFA	$C_6H_{13}N_2OCl$	43.76	44.08 44.10	7.91	8.23 8.38	17.02	17.54 17.59	21.58	21.92 21.97

No.	Substance	M.p., °C	Solubility	Gross formula	C, % calc.	C, % found	H, % calc.	H, % found	N, % calc.	N, % found	Halogen, % calc.	Halogen, % found
10	Iodomethylate of 8	182–184	In water, alcohol, hot chloroform	$C_7H_{15}N_2OJ$	31.10	31.59 31.76	5.56	5.83 5.91	10.37	10.23 10.07	47.04	47.08 47.08

was poured into absolute ether. The white powder that did not dissolve in ether was the salt of 1-dimethylamino-4-methylazetidinone-2 (Ib) and crotonic acid (yield 27%). Ib was liberated from the salt by passing its aqueous solution through a basic ion-exchange resin. For Ib, the methiodide and the hydrochloride salt were obtained; these did not depress the melting point with the sample obtained by the reaction of HCC with DMH.

The ether solution contained a mixture of crotonic acid dimethylhydrazide (IIb) and crotonic acid. Their separation is complicated by the fact that they form a eutectic mixture, liquid at room temperature and difficult to separate by distillation and recrystallization. Final purification of IIb from the admixture of crotonic acid was achieved on a basic ion-exchange resin. For IIb, the hydrochloride salt and the methiodide were obtained (Table 1).

Preparation of hydrochloride salts. The hydrochloride salts of Ia and Ib were obtained by treating them with an excess of hydrochloric acid, evaporating the resulting solutions, and recrystallizing from methylformamide.

The hydrochloride salt of IIb was obtained by passing a stream of dry hydrogen chloride through its ether solution.

Preparation of methiodides. The methiodides of Ia and Ib were obtained by treating the azetidinones with an excess of methyl iodide in an absolute alcohol solution and recrystallizing from the same solvent. The methiodide of IIb was obtained by standing a solution of IIb in an excess of methyl iodide and recrystallizing from chloroform.

Procedure for obtaining the NMR spectra. Samples of the compounds studied were dissolved in deuterated methanol, CD_3OD. The weight concentration of the solutions was 30%. High-resolution NMR spectra were obtained on a TNM-3 spectrometer. The internal standard was tetramethylsilane (TMS). The spectra of all samples were recorded at room temperature at a frequency of 40

MHz. In addition, the spectrum of a sample of Ib was obtained at a frequency of 12 MHz. The chemical shifts of the NMR lines were measured in τ units (^{4}).

Institute of High-Molecular-Weight Compounds
Academy of Sciences of the USSR

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CITED LITERATURE

1. T. A. Sokolova, P. A. Ovsyannikova, DAN, **143**, No. 1, 140 (1962).
2. N. F. Chembérlen, *Usp. khim.*, **28**, 1353 (1959).
3. J. Pople, W. Schneider, G. Bernstein, *High-Resolution Nuclear Magnetic Resonance Spectra*, IL, 1962.
4. L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, London—Oxford—N. Y.—Paris, 1959.
5. C. Franconi, *Zs. Electrochem.*, **65**, 7-8, 645 (1961).
6. M. V. Vol' kenshtein, A. I. Kol' tsov, Zh. Marshal, *Vysokomolek. soed.*, **4**, 6, 944 (1962).

Note: Figure translations are in progress. See original paper for figures.

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