EXPERIMENTAL METHOD

The PMR spectra of 25% solutions of the compounds in CCl_4 were recorded with an RYa-2305 spectrometer (60 MHz). The IR spectra of 2-5-nm-thick layers of the compounds were obtained with UR-20 and IKS-29 spectrometers.

Analysis by GLC was carried out with a Khrom-3 chromatograph with a flame-ionization detector and a 1.2-m-long column filled with 5% lucoprene G 1000 impregnated with porovina (Czechoslovakian SSR) at 190°. The molecular weights were determined cryoscopically in benzene.

2-Hydroxyethylhydrazones (Ia-f). 2-Hydroxyethylhydrazine (1 mole) was added dropwise in the course of 1.5 h at 15° with stirring to 1 mole of the ketone or aldehyde, after which the mixture was stirred for another h. It was than allowed to stand over potassium carbonate for 12 h, after which it was vacuum distilled in a stream of nitrogen.

Alkylidene(arylidene)aminooxazoles (IIa-f). The 2-hydroxyethylhydrazone (1 mole) was added dropwise in the course of 20 min to a stirred mixture of 30 g (1 mole) of paraformaldehyde and 50 ml of benzene, after which the mixture was stirred at 80° for 1.5 h. It was then cooled and allowed to stand over potassium carbonate for 12 h, after which it was vacuum fractionated in a stream of nitrogen with a rectification column with a glass packing and an efficiency of 25 theoretical plates.

LITERATURE CITED

1. G. Yu. Gadzhiev, K. V. Veiisov, and Sh. T. Akhmedov, Zh. Organ. Khim., 11, 655 (1975).
2. B. V. Ioffe and V. S. Stopskii, Dokl. Akad. Nauk SSSR, 1064 (1967).
3. V. S. Stopskii and N. V. Burmanova, Khim. Geterotsikl. Soedin., No. 8, 1066 (1969).
4. L. Knorr and H. Mattes, 34, 3484 (1901).
5. A. A. Potekhin, Zh. Organ. Khim., 7, 16 (1971).

PECULIARITIES OF THE REACTIVITIES OF 3-CARBOXYALKYLSYDNONES

I. S. Slyusarenko, V. V. Ogorodnikova, and V. G. Yashunskii

UDC 547.793.1:543.422.25.4

In contrast to the 3-alkyl analogs, the heteroring in 3-carboxyalkylsydnones is cleaved by the action of hydrogen chloride in alcohols. The kinetics of the previously known alkaline cleavage of the ring in 3-carboxyalkylsydnones and sydnoneimines were studied by a spectrophotometric method.

We have previously shown [1] that the carboxyl group and the heteroring in 3-carboxyalkylsydnones (I) have a mutual effect on one another. The peculiarities of the reactivities of these groups in the indicated compounds are set forth in the present paper.

In contrast to sydnone-4-carboxylic acids [2], which are smoothly converted successively to acid chlorides and ester, 3-carboxymethylsydnone (Ia) does not react with thionyl chloride. Under the combined action of thionyl chloride and methanol (the Brenner method) this sydnone undergoes cleavage to give methyl hydrazinoacetate hydrochloride (IIa).

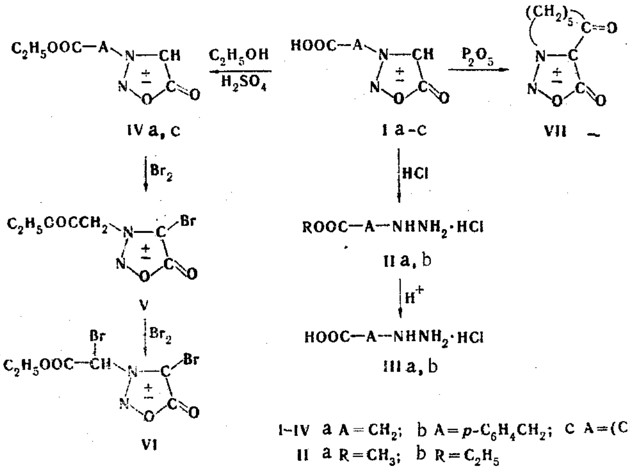
It was shown in [2] that cleavage of 3-alkylsydnones by the action of hydrogen chloride does not take place in anhydrous media. Ring opening also was not observed when hydrogen chloride was bubbled briefly through

---

Institute of Biophysics, Ministry of Public Health of the USSR, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 450-453, April, 1976. Original article submitted February 24, 1975.

alcohol solutions of sydnones Ia, b. However, prolonged treatment of these compounds with an alcohol solution of hydrogen chloride gave esters II, which were readily converted to the corresponding hydrazinecarboxylic acids (III).

Esterification of the carboxyl group in sydnones I in the presence of hydrogen chloride probably proceeds slowly, and a considerable excess of hydrogen chloride and an increase in the temperature are necessary for the realization of this process. Water is liberated as a result of esterification, and it promotes the acid cleavage of sydnones in nonaqueous media [2].



I-IV a $A = CH_2$; b $A = p\text{-}C_6H_4CH_2$; c $A = (CH_2)_5$, II a $R = CH_3$; b $R = C_2H_5$

It was found to be possible to esterify 3-carboxyalkylsydnones (Ia, c) in the presence of sulfuric acid. The use of KU-2-8 cation-exchange resin in the H^+ form in place of sulfuric acid did not lead to an increase in the yield of the ester.

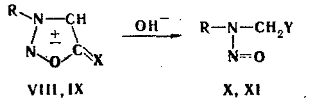
Electrophilic substitution reactions at the quaternary ring carbon atom, particularly bromination and acylation, are most characteristic for sydnones.

It was not possible to introduce bromine in Ia by bromination in acetic acid in the presence of sodium acetate. In contrast to the acid, ester IVa forms 4-bromo-3-carbethoxymethylsydnones (V) under the indicated conditions. When excess bromine is used, in addition to replacement of the hydrogen attached to the ring C_4 atom, the hydrogen atom of the α-methylene group of the substituents is replaced to give dibromo derivative VI.

The presence of a carboxyamyl chain in acid Ic made it possible to carry out intramolecular acylation at the ring C_4 atom. Brief heating of Ic in benzene with phosphorus pentoxide gave a high-melting crystalline substance, the elementary composition of which corresponded to sydno[3,4-a]-cyclooctazolone (VII).

A considerable bathochromic shift of the absorption maximum (343 nm) as compared with the starting sydnone (292 nm) was observed in the UV spectrum of VII. A similar longwave shift of the absorption maximum was observed on passing from o-nitrophenylsydnone to sydno[3,4-a]quinoxalines [3]. The absorption band of stretching vibrations of a C_4-H bond is absent in the IR spectrum of the product at 3100-3200 cm^{-1}, and absorption bands at 1780 and 1660 cm^{-1} appeared in place of the two absorption bands at 1732 and 1710 cm^{-1} corresponding to the stretching vibrations of the ring carbonyl group and the carboxyl group. In analogy with sydnone-4-carboxylic acids [4], the higher-frequency band can be assigned to the $\nu_{C=O}$ band of the sydnone ring, and the second band is found in the same region as the $\nu_{C=O}$ band of the acylcarbonyl group in 4-acylsydnones [5].

Using a spectrophotometric method (the method previously used for the study of the alkaline cleavage of 3-isopropylsydnones [2]) we studied the effect of the carboxyl group on the rage of alkaline ring opening in 3-carboxypolymethylenesydnones (VIII) and 3-carboxypolymethylenesydnoneimine hydrochlorides (IX), which are converted under these conditions to N-nitro acids (X) and N-nitrosoaminoacetonitriles (IX), respectively.



VIII X=O; IX X=NH; X Y=COOH; XI Y=CN

TABLE 1. Alkaline Cleavage Rate Constants (K) for 3-Carboxypolymethylenesydnones and Sydnoneimines and Equilibrium Constants (K_{eq}) of 3-Carboxypolymethylenesydnoneimines

R	X	$K \cdot 10^3$, min^{-1}	X · HCl	$K \cdot 10^2$, min^{-1}	$K_{eq} \cdot 10^{-2}$, min^{-1}
$HOOC(CH_2)$	O	1,71	NH	2,10	1,40
$HOOC(CH_2)_2$	O	1,96	NH	1,21	0,52
$HOOC(CH_2)_3$	O	1,95	NH	—	—
$HOOC(CH_2)_4$	O	2,10	NH	1,05	—
$HOOC(CH_2)_5$	O	3,10	NH	1,02	0,56
$HOOC(CH_2)_6$	O	3,60	NH	1,36	—
CH_3	O	4,35	NH	2,90	1,95

It follows from Table 1, in which the rate constant for cleavage of 3-methylsydnone is presented for comparison, that as the carboxyl group becomes more remote from the heteroring, the stability of the latter decreases somewhat but, nevertheless, remains higher than that of the 3-methyl analog.

As in the case of sydnones, the presence of a carboxyl group attached to the substituent in the ring 3 position promotes a certain increase in the stability of the sydnoneimine ring as compared with the 3-methyl derivative, but the difference in the constants is not so clearly expressed here.

EXPERIMENTAL METHOD

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer. The UV spectra of alcohol solutions of the compounds were recorded with a Shimadzu MPS-50L spectrophotometer in thermostatted 1-cm-thick quartz cuvettes. The kinetics of cleavage of the sydnone ring were studied in a 3.5 M aqueous NaOH solution. The 3-carboxypolymethylenesydnoneimine hydrochlorides were cleaved in alkaline media considerably more readily than the sydnones at pH 8.48 and 30°. The starting concentration of the sydnones was $1.2 \cdot 10^{-4}$ mole/liter, and the starting concentration of the sydnoneimines was $1 \cdot 10^{-4}$ mole/liter. The equilibrium constants (K_{eq}) were obtained at 5° and pH 8. The pseudomonomolecular rate constants were calculated from the optical densities at the absorption maxima (295-305 nm) from the formula $K = 2.303 (\log D_1^0 - \log D^1)/(t^1 - t_1^0)$, where $D_1^0 - D^1$ is the difference in the initial and final optical densities of the investigated solutions at the selected wavelengths after time $t^1 - t_1^0$.

Methyl Hydrazinoacetate Hydrochloride (IIa). Dry HCl was bubbled for 1 h through a solution of 1.3 g (9 mmole) of 3-carboxymethylsydnone Ia in 30 ml of methanol, during which the reaction mixture warmed up markedly. The mixture was then cooled, and the resulting precipitate was removed by filtration and purified by reprecipitation from methanol with ether to give 1.15 g (93%) of a product with mp 132°. Found: C 25.8; H 6.65; Cl 25.4; N 20.0%. $C_3H_8N_2O_2 \cdot HCl$. Calculated: C 25.6; H 6.6; Cl 25.2; N 19.9%.

Hydrazinoacetic Acid Hydrochloride (IIIa). A solution of 1.15 g of ester hydrochloride IIa in 10 ml of 10% hydrochloric acid was allowed to stand overnight, after which the solvent was removed by distillation to give 0.96 g (96%) of salt IIIa with mp 155-155.5° (mp 156° [6]).

Ethyl p-Hydrazinomethylbenzoate Hydrochloride (IIb). This compound, with mp 160.5-161.5° was obtained in 94% yield from p-carboxybenzylsydnone Ib by the method used to synthesize IIa. Found: C 51.9; H 6.6; Cl 15.5; N 12.0%. $C_{10}H_{14}N_2O_2 \cdot HCl$. Calculated: C 52.1; H 6.5; Cl 15.4; N 12.1%.

p-Hydrazinomethylbenzoic Acid Hydrochloride (IIIb). This compound, with mp 189-192°, was obtained in 92% yield from ester IIb by the method used to synthesize acid IIIa. Found: C 47.3; H 5.3; Cl 17.4; N 13.6%. $C_8H_{10}N_2O_2 \cdot HCl$. Calculated: C 47.4; H 5.5; Cl 17.5; N 13.8%.

3-Ethoxycarbonylmethylsydnone (IVa). A 5.4-g (35 mmole) sample of sydnone Ia was added to a solution of 5 ml of concentrated H_2SO_4 in 150 ml of absolute ethanol, and the mixture was allowed to stand for 48 h. Water (50 ml) was added, and the alcohol was removed in vacuo at 30°. The aqueous solution was neutralized to pH 7 with sodium bicarbonate, and the liberated oil was extracted with ether. The ether extract was dried with anhydrous sodium sulfate, the ether was evaporated in vacuo almost to dryness, and the residue was removed by filtration, washed with cold ether, and vacuum dried to give 4.3 g (67%) of a product with mp 60.5-61.5°. Found: C 41.8; H 4.7; N 16.2%. $C_6H_3N_2O_4$. Calculated: C 41.7; H 4.7; N 16.3%.

3-(5-Ethoxycarbonylamyl)sydnone (IVc). This compound, with bp 193-194° (0.4 mm) and $n_D^{22.5}$ 1.4900 was obtained in 50% yield by the method used to synthesize ester IVa. Found: C 52.8; H 7.2; N 12.0%. $C_{10}H_{16}N_2O_4$. Calculated: C 52.6; H 7.1; N 12.3%.

3-Ethoxycarbonylmethyl-4-bromosydnone (V). A 1.6-g (10 mmole) sample of bromine was added in the course of 30 min to a solution of 1.72 g (10 mmole) of sydnone IVa and 1.64 g (20 mmole) of anhydrous sodium acetate in 50 ml of glacial acetic acid, and the mixture was stirred at room temperature for 3 h, after which it was allowed to stand for 2 days. The solid material was removed from the mixture by filtration, the filtrate was vacuum evaporated, and 25 ml of water was added to the residue. The resulting precipitate was removed by filtration and washed with water to give 1.5 g (60%) of a product with mp 111-112° (from alcohol). Found: C 28.7; H 2.8; Br 31.7; N 10.8%. $C_6H_7BrN_2O_4$. Calculated: C 28.7; H 2.8; Br 31.8; N 11.1%.

3-Ethoxycarbonylbromomethyl-4-bromosydnone (VI). A 1.86-g (11.6 mmole) sample of bromine was added in the course of an hour at 12-15° to a solution of 1 g (5.8 mmole) of sydnone IVa and 0.95 g of anhydrous sodium acetate in 30 ml of glacial acetic acid, after which the mixture was stirred for 6 h and allowed to stand overnight. The solution was evaporated, 30 ml of water was added to the residue, and the liberated oil was extracted with ethyl acetate. The extract was dried with anhydrous sodium sulfate, the solvent was evaporated, and the residue was reprecipitated from ethyl acetate by the addition of hexane to give 1.68 g (88%) of a product with mp 77.5-79.5°. Found: C 22.0; H 2.0; Br 48.8; N 8.6%. $C_6H_6Br_2N_2O_4$. Calculated: C 21.8; H 1.8; Br 49.1; N 8.5%.

Sydno[3,4-a]cyclooctazol-3-one (VII). A mixture of 3 g (15 mmole) of acid IC, 6.2 g of phosphorus pentoxide, and 20 ml of absolute benzene was refluxed for 5 h, after which the solvent was removed by vacuum distillation, 50 ml of water was added to the residue, and the resulting precipitate was removed by filtration and washed thoroughly and successively with water and acetone. It was then dried over phosphorus pentoxide to give 2.63 g (96%) of VII with mp 350° (dec.). Found: C 52.5; H 5.7; N 15.4%. $C_8H_{10}N_2O_3$. Calculated: C 52.7; H 5.7; N 15.4%.

LITERATURE CITED

1. I. S. Slyusarenko, V. V. Ogorodnikova, N. G. Klyushina, and V. G. Yashunskii, Khim. Geterotsikl. Soedin., No. 4, 479 (1973).
2. S. A. Zotova and V. G. Yashunskii, Zh. Organ. Khim., 3, 942 (1967).
3. R. A. Coburn and J. P. O'Donnell, J. Org. Chem., 37, 1707 (1972).
4. S. A. Zotova and V. G. Yashunskii, Zh. Organ. Khim., 2, 1877 (1966).
5. V. G. Yashunskii and V. F. Vasil'eva, Dokl. Akad. Nauk SSSR, 130, 350 (1960).
6. A. Darapsky and M. Phabhakar, Ber., 45, 1162 (1912).