Synthesis of sulfoalkylated and sulfoarylated 2-pyrrolidinone, 6-hexanelactam and 1-phenyl-3-pyrazolidinone derivatives

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In phase transfer catalysis conditions and depending upon the ratio of reacting materials and the reaction conditions, 2-pyrrolidinone, 6-hexanelactam and 1-phenyl-3-pyrazolidinone with 1,3-propanesultone or 1,2-benzoxathiol-3-on-1,1-dioxide form N-mono- or N,C-disubstituted derivatives. In non-catalytic conditions, during the reaction of 2-pyrrolidinone or 1-phenyl-3-pyrazolidinone with sodium bromomethane sulfonate, in the presence of sodium hydroxide, substitution takes place at the nitrogen atom. In neutral conditions, 6-hexanelactam and 1-phenyl-3-pyrazolidinone react with 1,3-propanesultone, and O-sulfoalkylated products of the reaction are formed.

Key words: 2-pyrrolidinone, 6-hexanelactam, 1-phenyl-3-pyrazolidinone, 1,3-propanesultone, 1,2-benzoxathiol-3-on-1,1-dioxide, sodium bromomethanesulfonate

INTRODUCTION

Lactams are widely used in the production of polymers [1] as solvents for synthetic resins [2], *etc*. Phenyl-3-pyrazolidinone is useful as a photomaterial [3].

Three potentially nucleofilic atoms (N, O and α-C with respect to CO group) existing in the lactam cycle predetermine the multivariance of the course of the substitution reaction. According to the data [4, 5], the alkylation of lactams with alkyl halides in the presence of a strong base ($NaOC_2H_5$ or NaH) takes place at the nitrogen atom, while N-substituted lactams (with the presence of sodium amide) are alkylated at α-C atom with respect to CO group. In delicate conditions, alkylation of lactams nitrogen atom with alkyl halides takes place by phase transfer catalysis in a liquid/liquid [6] or liquid/solid body systems [7].

In the present work we explored the possibility to obtain sulfoalkylated or sulfoarylated derivatives of these important substances by using 1,3-propanesultone, 1,2-benzoxathiol-3-on-1,1-dioxide and sodium bromoalkane sulfonates as sulfoalkylating agents. The literature provides no description of the interaction between 1,3-propanesultone and lactams.

Even though 1,3-propanesultone has high reactivity, it is also sensitive to hydrolysis and to the influence of alcohol. Therefore, a water-free medium is essential for the synthesis of sulfonates, howerver, it makes the sulfoalkylation process more difficult and more expensive. The phase transfer (PT) catalysis method would allow to escape the usage of espensive absolute solvents and simplify the process of the experiment.

RESULTS AND DISCUSSION

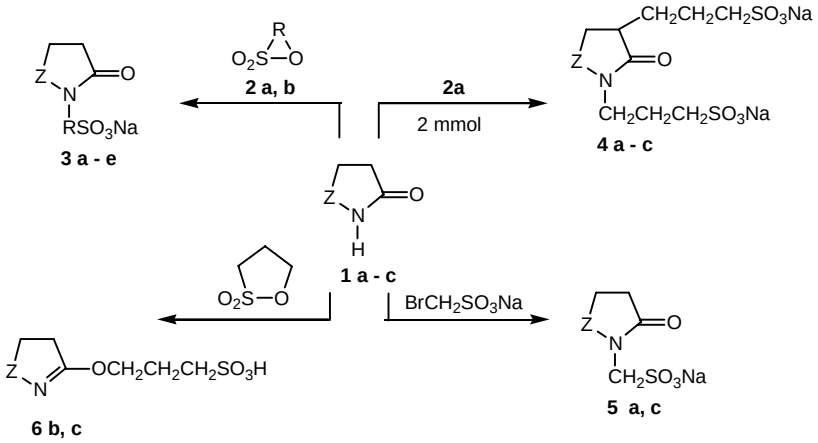
Similarly to the reaction of lactams with alkylhalides [6], the reaction of 2-pyrrolidinone (**1a**), 6-hexanelactam (**1b**) and 1-phenyl-3-pyrazolidinone (**1c**) with 1,3-propanesultone (**2a**) or 1,2-benzoxathiol-3-on-1,1-dioxide (**2b**) in a two-phase benzene/water system, in the presence of sodium hydroxide and the PT catalyst triethylbenzylammonium chloride $[(C_2H_5)_3N^+CH_2C_6H_5 \cdot Cl^-]$ (TEBA), N-substituted derivatives **3 a–e** were formed. Such a structure of the N-substituted derivatives **3 a–e** was confirmed by triplets at 2.21, 2.25, 2.28, 2.23 and 2.26 ppm present in their ^{1}H NMR spectra and characteristic of the chemical shifts of protons of CH_2CO group. Besides, triplets at 3.79, 3.61 and 3.72 ppm present in spectra of **3 a–c** compounds confirmed the formation of CH_2N group. In the IR spectra of **3 a–e**, one can see intensive absorbtion bands at 1011–1034 and 1191–1199 cm^{-1}, ascribed to *as* and *s* ν SO_2. The absence of a strong band in the zone characteristic of the frequency of valent fluctations of COOH group in IR spectra of **3d** and **3e** confirms that a

sulfogroup has been formed during the reaction of lactams and **2b**. A high water solubility of the obtained compounds is another proof that sulfonates were formed indeed.

When the quantity of sodium hydroxide and **2a** was increased twice and when toluene was used instead of benzene, sulfoalkylation took place not only at the nitrogen atom of the lactam cycle, but also at the α-carbon atom with respect to carbonyl group, and the N,C-disubstituted derivatives **4 a–c** were formed. Multiplets at 2.34, 2.30 and 2.28 ppm present in spectra ^{1}H NMR of **4 a–c** ompounds and those conformed to chemical shifts of protons of CHCO groups confirmed that the sulfoalkylation also took place at α-carbon atom with respect to CO group.

When the quantity of **2a** and sodium hydroxide was increased three times, no di-C-substituted derivatives of 2-pyrrolidinone were obtained, *viz*. according to the data of ^{1}H NMR spectrum the mixture of sulfoalkylated compounds was formed, which could not be separated.

The reaction of **1a** and **1c** with sodium bromoalkanesulfonates proceeds in a more cîmpliceted way. In non-catalytic conditions, in the aqueous solution of sodium hydroxide **1a** and **1c** with sodium 2-bromomethanesulfonate N-sulfoalkylated derivatives **5a** and **5c** were also formed. The ^{1}H NMR spectra confirmed that the reaction of **1a** and **1c** with sodium 2-bromoethanesulfonate yielded a mixture of the sulfonates, which could not be separated.



1 a Z = -CH_2-, **b** Z = -$(CH_2)_3$-, **c** Z = -NC_6H_5, **2 a** R = -$(CH_2)_3$-, **b** R = -2-COC_6H_4-,
3 a Z = -CH_2-, R = -$(CH_2)_3$-, **b** Z = -$(CH_2)_3$-, R = -$(CH_2)_3$-, **c** Z = -NC_6H_5,
R = -$(CH_2)_3$-, **d** Z = -CH_2-, R = -2-COC_6H_4-, **e** Z = -NC_6H_5, R = -2-COC_6H_4-,
4 a Z = -CH_2-, **b** Z = -$(CH_2)_3$-, **c** Z = -NC_6H_5,
5 a Z = -CH_2-, **c** Z = -NC_6H_5, **6 b** Z = -$(CH_2)_3$-, **c** Z = -NC_6H_5.

The reaction of **1b** and **1c** with **2a** in neutral conditions in dioxane at a temperature of 40–45 °C resulted in O-sulfoalkylated products **6b** and **6c**. Such a structure of **6b** and **6c** was confirmed by triplets at 4.22 and 4.40 ppm present in their ^{1}H NMR spectra, which were in conformity with the chemical shifts of protons of CH_2O group, and also by the absence of strong bands in their IR spectra in the zone characteristic of the frequency of valency fluctuations of CO group.

When **1a** reacted with **2a** under such conditions, according to ^{1}H NMR spectral data a mixture of N- and O-substituted compounds was formed. After comparison of the integral intensities of CH_2O and CH_2S groups (in the ^{1}H NMR spectrum of the obtained product) the ratio of these compounds was found to be ~1 : 1. The obtained mixture could not be separated.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75 IR spectrometer with pressed KBr pellets. ^{1}H NMR spectra were recorded on a TESLA BS-567 A (80 MHz) instrument in D_2O and are reported as chemical shifts (δ) relative to DSS in ppm. Sodium bromomethanesulfonate was synthesised [8].

General procedure for synthesis of N-substituted 1-pyrrolidinone, 6-hexanelactam and 1-phenyl-3-pyrazolidinone (3 a–e). A mixture composed of 20 mmol of 2-pyrrolidinone **(1a),** 6-hexanelactam **(1b)** or 1-phenyl-3-pyrazolidinone **(1c),** 0.8 g (20 mmol) of NaOH dissolved in 40 ml of H_2O, 20 mmol of 1,3-propanesultone **(2a)** or 1,2-benzoxathiol-3-on-1,1-dioxide **(2b)** dissolved in 30 ml of benzene and 0.2 g of TEBA was heated under reflux for 1 h and filtered off. The layers of the filtrate were separated, the aqueous layer was evaporated until the first crystals appeared. 30 ml of 2-propanol and propanone as well as 40 ml of diethyl ether were added to the residue. The formed crystals were filtered off, washed with ethanenitrile and recrystallised from 2-propanol-water (1:1). The constants and the data of ^{1}H NMR spectrum of **3 a–e** are listed in Table.

General procedure for synthesis of N,C-disubstituted 2-pyrrolidinone, 6-hexanelactam and 1-phenyl-3-pyrazolidinone (4 a–c). A mixture composed of 20 mmol of 2-pyrrolidinone (**1a**), 6-hexanelactam (**1b**) or 1-phenyl-3-pyrazolidinone (**1c),** 1.6 g (40 mmol) of NaOH dissolved in 50 ml of H_2O, 4.48 g (40 mmol) of 1,3-propanesultone (**2a**) dissolved in 40 ml of toluene and 0.2 g of TEBA was heated for 4 h while stirring. Upon cooling it to room temperature the layers were separated, the aqueous layer was evaporated until the first crystals appeared. Propanone and 2-propanol (30 ml each) were added to the residue.

Constans, ^{1}H NMR spectra data and elemental analysis of synthesised compounds **3 a–e, 4 a–c, 5 a, b**

No of comp.	Yield, %	M.p., °C	Molecular formula	Found, % / Calculated, %			^{1}H NMR spectra, δ, ppm., multiplicity
				C	H	S	
3a	64.2	>350	$C_7H_{12}NNaO_4S$	36.67	5.27	13.98	1.95 (t, 2H, CCH_2C), 2.15 (m, 2H, CCH_2C), 2.21 (t, 2H, CH_2CO) 2.91 (t,
				37.77	5.36	13.91	2H, CH_2 S), 3.28 (t, 2H, CH_2N-ring), 3.79 (t, 2H, CH_2N)
3b	67.6	229–230	$C_9H_{16}NNaO_4S$	39.18	6.58	13.07	1.81–2.14 (m, 8H, CCH_2C), 2.25 (t, 2H, CH_2CO), 2.94 (t, 2H, CH_2S), 3.05 (t,
				39.31	6.65	13.12	2H, CH_2N-ring), 3.76 (t, 2H, CH_2N)
3c	61,8	>350	$C_{12}H_{15}N_2NaO_4S$	47.05	4.93	10.46	2.07 (m, 2H, CCH_2C), 2.28 (t, 2H, CH_2CO), 3.01 (t, 2H, CH_2S), 3.63 (t, 2H,
				47.07	5.09	10.37	CH_2N-ring), 3.71 (t, 4H, CH_2N)
3d	74.9	225–226*	$C_{11}H_{10}NNaO_5S$	45.36	3.46	11.00	1.81 (m, 2H, CCH_2C), 2.23 (t, 2H, CH_2CO), 2.92 (t, 2H, CH_2N), 7.49–7.75 (m,
				45.29	3.55	11.14	4H, $CH_{arom.}$)
3e	44.2	>350	$C_{16}H_{13}N_2NaO_5S$	52.17	3.56	8.70	2.26 (t, 2H, CH_2CO), 3.89 (t, 2H, CH_2N), 7.75–8.04 (m, 10H, $CH_{arom.}$)
				52.11	3.61	8.84	
4a	67.6	>350	$C_{10}H_{17}NNa_2O_7S_2$	32.17	4.59	17.17	1.88–2.18 (m, 8H, CCH_2C), 2.34 (m, 1H, CHCO), 2.52 (t, 2H, CH_2S), 2.92 (t,
				32.25	4.48	17.21	4H, CH_2N), 3.61 (t, 2H, CH_2N)
4b	68.7	215–216*	$C_{12}H_{21}NNa_2O_7S_2$	35.90	5.27	15.97	1.71–2.12 (m, 12H, CCH_2C), 2.30 (m, 1H, CHCO), 2.95 (t, 4H, CH_2S), 3.27
				36.03	5.18	16.09	and 3.71 (t, 2H, CH_2N)
4c	60,1	191–192*	$C_{15}H_{20}N_2Na_2O_7S_2$	39.99	4.47	14.23	1.91-2.18 (m, 6H, CCH_2C), 2.28 (m, 1H, CHCO), 2,91 (t, 4H, CH_2S), 3.04 and
				40.08	4.36	14.26	3.72 (t, 2H, CH_2N), 7.61–7.72 (m, 5H, CH_{arom})
5a	57.1	232–233*	$C_5H_8NNaO_4S$	29.85	4.00	15.93	2.02 (m, 2H, CCH_2C), 2,35 (t, 1H, CH_2CO), 3.14 (t 2H, CH_2N), 4.61 (s, 2H,
				29.71	3.88	15.86	NCH_2S)
5b	64.3	>350	$C_{10}H_{11}N_2NaO_4S$	43.16	3.98	11.52	2.62 (t, 2H, CH_2CO), 3.02 (t, 2H, CH_2N), 4.96 (s, 2H, NCH_2S), 7.75–8.04 (m,
				43.18	4.02	11.43	5H, CH_{arom})

* With decomposition.

The formed crystals were filtered off, washed 3 times with ethanenitrile and recrystallised from water-2-propanol (2:1). The constants and the data of ^{1}H NMR spectrum of **4 a–c** are listed in Table.

General procedure for synthesis of N-sulfomethylated 2-pyrrolidinone and 1-phenyl-3-pyrazolidinone (5a, 5c). To a solution of 0.8 g (20 mmol) of NaOH in 50 ml of H_2O, 20 mmol of 2-pyrrolidinone **(1a)** or 1-phenyl-3-pyrazolidinone **(1c)** was added, and 3.34 g (20 mmol) of sodium bromomethanesulfonate was added to the obtained solution. The solution was heated for 5 h, filtered off, and the water was evaporated. 20 ml of ethanol and propanone was added to the remainder. The formed crystals were filtered off and recrystallised from 2-propanol-water (1:1). The constants and the data of ^{1}H NMR spectrum of **5a, 5c** are presented in Table.

3-(3,4,5,6-Tetrahydro-2H-7-azepinyloxy)-1-propanesulfonic acid (6b). 3.39 g (30 mmol) of 6-hexanelactam **(1b)** was dissolved in 50 ml of dioxane and 3.66 g (30 mmol) of 1,3-propanesultone **(2a)** was added to the mixture. The mixture was kept at a temperature of 40–45 °C for approximately 0.5 h (until on oil-like layer formed). Dioxane was removed in vacuum, and 50 ml of ethanenitrile and 30 ml of diethyl ether were added to the viscous remainder. The formed crystals were filtered off, washed with ethanol and diethyl ether, and recrystallised from 80% 2-propanol. Yield: 4.43 g (62.8 %) of **6b**, m. p. 197–198 °C. Found, %: C 45.83, H 7.41, S 13.49. $C_9H_{17}NO_4S$. Calculated, %: C 45.94, H 7.28, S 13.62. ^{1}H NMR spectrum (D_2O), δ, ppm.: 1.72–1.86 and 2.09 (m, 8H, CCH_2C), 2.43 (t, 2H, CH_2C=), 3.01 (t, 2H, CH_2S), 3.69 (t, 2H, CH_2N), 4.22 (t, 2H, CH_2O).

3-(1-Phenyl-4,5-dihydro-3-pyrazolyloxy)-1-propanesulfonic acid (6c). Similarly to the procedure for **6b** from 4.87 g (30 mmol) of 1-phenyl-3-pyrazolidinone **(1c),** 3.66 g (30 mmol) of 1,3-propanesultone **(2a)** and 50 ml dioxane gave 5.11 g (60.0%) **6c**, m. p. 206–207 °C. Found, %: C 50.63, H 5.79, S 11.29. $C_{12}H_{16}N_2O_4S$. Calculated, %: C 50.69, H 5.63, S 11.28. ^{1}H NMR spectrum (D_2O), δ, ppm: 1.92 (m, 2H, CCH_2C), 2.59 (t, 2H, CH_2C=), 3.10 (t, 2H, CH_2S), 3.52 (t, 2H, CH_2N), 4.40 (t, 2H, CH_2O).

CONCLUSIONS

1. Under phase transfer catalysis conditions and depending upon the ratio of the reacting materials, 2-pyrrolidinone, 6-hexanelactam and 1-phenyl-3-pyrazolidinone with 1,3-propanesultone or 1,2-benzoxathiol-3-on-1,1-dioxide afforded N-mono- or N,C-disubstituted derivatives.

2. Under non-catalytic conditions, 2-pyrrolidinone and 1-phenyl-3-pyrazolidinone with sodium bromomethanesulfonate and in the presence of sodium hydroxide result in N-sulfomethylated derivatives.

3. Under neutral conditions, 6-hexanelactam and 1-phenyl-3-pyrazolidinone react with 1,3-propanesultone, and O-sulfoalkylated derivatives are formed.

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SULFOALKILINTŲ IR SULFOARILINTŲ 2-PIROLIDINONO, 6-HEKSANLAKTAMO IR 1-FENIL-3-PIRAZOLIDINONO DARINIŲ SINTEZĖ

S a n t r a u k a

2-Pirolidinonas, 6-heksanlaktamas ir 1-fenil-3-pirazolidinonas su 1,3-propansultonu arba su 1,2-benzoksatiol-3-on-1,1-dioksidu tarpfazinės katalizės sąlygomis priklausomai nuo reaguojančių medžiagų santykio sudaro N-sulfoalkilintus, N-sulfoarilintus arba N,C-disulfoalkilintus darinius. Esant natrio hidroksidui, 2-pirolidinonas arba 1-fenil-3-pirazolidinonas su natrio brommetansulfonatu reaguoja, susidarant N-sulfoalkilintiems produktams. Neutraliomis sąlygomis 6-heksanlaktamas ir 1-fenil-3-pirazolidinonas su 1,3-propansultonu sudaro O-pakeistas sulforūgštis.

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СИНТЕЗ СУЛЬФОАЛКИЛИРОВАННЫХ И СУЛЬФОАРИЛИРОВАННЫХ ПРОИЗВОДНЫХ 2-ПИРРОЛИДИНОНА, 6-ГЕКСАНЛАКТАМА И 1-ФЕНИЛ-3-ПИРАЗОЛИДИНОНА

Р е з ю м е

При взаимодействии 2-пирролидинона, 6-гексанлактама и 1-фенил-3-пиразолидинона с 1,3-пропансультоном или с 1,2-бензоксатиол-3-он-1,1-диоксидом в условиях межфазного катализа в зависимости от соотношения реагирующих веществ образуются N-сульфоалкил-, N-сульфоарил- или N,C-дисульфоалкилпроизводные. В некаталитических условиях, в присутствии едкого натрия, 2-пирролидинон или 1-фенил-3-пиразолидинон с бромметансульфонатом натрия образуют N-сульфометилированные соединения. В отсутствии гидроксида натрия 6-гексанлактам и 1-фенил-3-пиразолидинон с 1,3-пропансультоном дают О-замещенные пропансульфонаты.