SYNTHESIS OF HEXAMETHYLENEAMIDES OF ORGANIC ACIDS

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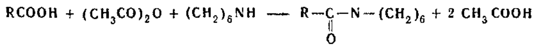
Twenty hexamethyleneamides of various organic acids have been synthesized by a direct transamidation reaction. The process consists in the previous mixing of hexamethyleneimine, acetic anhydride, and the corresponding acid, heating the resulting mixture to the boil, and distilling off the acetic acid formed through a fractionating column. The synthesis of amides by this method is characterized by high yields and comparatively short times.

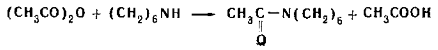
It is known that hexamethyleneamides of organic acids possess repellent properties with respect to various blood-sucking insects [1,2]. At present, a fairly active preparation of the hexamethyleneamide of benzoic acid is being produced on the industrial scale under the commercial name benzimin. The hexamethyleneamides of organic acids are obtained by the reaction of hexamethyleneimine with acid chlorides, the yields amounting to 18–61%.

This paper gives information on the synthesis of hexamethyleneamides of a number of organic acids by the transamidation reaction. The process consists in mixing hexamethyleneimine, acetic anhydride, and the corresponding acid, heating the resulting mixture to the boil, and distilling off the acetic acid formed in the reaction. The over-all process of the production of the hexamethyleneamides can be represented by the following equation



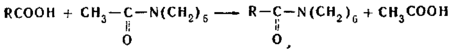
$$RCOOH + (CH_3CO)_2O + (CH_2)_6NH \longrightarrow R{-}\underset{\underset{O}{\Vert}}{C}{-}N{-}(CH_2)_6 + 2\ CH_3COOH$$

However, in actual fact the formation of the amides takes place as a result of the occurrence of two consecutive reactions. As is well known, the rate of the reaction of acetic anhydride with amines, including hexamethyleneimine is fairly high, even with cooling. In view of this, even when the reactants are mixed and on subsequent heating the hexamethyleneamide of acetic acid is first formed.



$$(CH_3CO)_2O + (CH_2)_6NH \longrightarrow CH_3\underset{\underset{O}{\Vert}}{C}{-}N(CH_2)_6 + CH_3COOH$$

The formation of the amide of the acid added to the mixture takes place by an exchange reaction between the acid and the acethexamethyleneamide, i. e., as the result of a transamidation reaction.



$$RCOOH + CH_3{-}\underset{\underset{O}{\Vert}}{C}{-}N(CH_2)_5 \longrightarrow R{-}\underset{\underset{O}{\Vert}}{C}{-}N(CH_2)_6 + CH_3COOH,$$

The transamidation reaction is an equilibrium one. Consequently, with the successful performance of the transamidation process the acetic acid formed must be separated continuously and effectively from the other components of the reaction mixture. The continuous and effective separation of the acetic acid was achieved by using a fractionating column to perform the transamidation process.

Parameters of the Transamidation Process and Characteristics of the Compounds Obtained

Hexamethyleneamide of	Reaction time, hr-min	Initial and final reaction temperatures, °C	Bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Empirical formula	N, % found	N, % calculated	Yield, %
Butyric acid	4—45	163—254	133—134 (11)	0.9800	1.4849	49.40	49.80	$C_{10}H_{19}NO$	7.95	8.30	63.2
Isobutyric acid	4—15	156—255	106—107 (6)	0.9907	1.4801	49.60	49.87	$C_{10}H_{19}NO$	8.17	8.30	91.0
Valeric acid	3—15	175—265	141—142 (7)	0.9645	1.4821	54.10	54.45	$C_{11}H_{21}NO$	7.38	7.70	84.0
Isovaleric acid	3—15	186—265	104—106 (2)	0.9761	1.4819	54.10	54.42	$C_{11}H_{21}NO$	7.45	7.70	88.2
Caproic acid	3—00	148—280	138—139 (6)	0.9543	1.4810	58.70	59.03	$C_{12}H_{23}NO$	7.00	7.10	76.5
C_7–C_9 fatty acid fraction	2—15	100—270	180—210 (22)	0.9485	1.4811	—	—		—	—	71.0
Enanthic acid	3—00	174—234	174—175 (10)	0.9460	1.4800	63.50	63.55	$C_{13}H_{25}NO$	6.41	6.64	92.9
Caprylic acid	2—45	132—256	199—200 (22)	0.9401	1.4789	68.30	68.17	$C_{14}H_{27}NO$	6.13	6.23	75.0
Capric acid	3—15	140—321	181—183 (6)	0.9289	1.4781	77.40	77.51	$C_{16}H_{31}NO$	5.61	5.54	81.0
Lauric acid	2—30	144—320	204—205 (7)	0.9194	1.4780	87.01	86.75	$C_{18}H_{35}NO$	5.14	5.00	83.5
Undecylenic acid	3—45	183—325	204—205 (6)	0.9378	1.4870	79.60	79.46	$C_{17}H_{31}NO$	5.48	5.29	74.0
Oleic acid	1—45	175—364	218—220 (3)	0.9125	1.4851	114.85	114.59	$C_{24}H_{45}NO$	4.01	3.90	75.3
Benzoic acid	2—45	190—311	200—201 (14) mp. 37°	—	—	—	—	$C_{13}H_{17}NO$	6.87	6.90	88.0
o-Chlorobenzoic acid	2—45	186—298	199—200 (6) mp. 47°	—	—	—	—	$C_{13}H_{16}ClNO$	5.92	5.91	73.4
Salicylic acid	0—30	198—246	118—119 (3)	1.0293	1.5083	62.40	62.08	$C_{13}H_{17}NO_2$	6.34	6.40	81.5
m-Toluic acid	1—15	165—312	153—155 (2)	1.0681	1.5520	65.30	65.79	$C_{14}H_{19}NO$	6.78	6.45	70.5
Phenylacetic acid	1—55	172—280	182—183 (5)	1.0689	1.5511	64.70	64.96	$C_{14}H_{19}NO$	6.38	6.39	81.6
Phenoxyacetic acid	1—45	184—305	178—179 (3)	1.1147	1.5503	66.60	66.49	$C_{14}H_{19}NO_2$	5.99	6.00	83.0
Adipic acid	1—30	164—315	214—244 (1)	0.9921	1.5149	93.10	93.51	$C_{18}H_{32}N_2O_2$	8.92	9.12	79.5
Maleic acid	0—30 (vacuum 100 mm)	120—190	105—106 (2)	1.0105	1.4899	79.60	79.00	$C_{16}H_{26}N_2O_2$	4.71	5.03	83.5

It must be mentioned that the transamidation process performed by the variant with the simultaneous elimination by distillation of acetic acid can be used for the synthesis of amides of only those acids that have higher boiling points than acetic.

EXPERIMENTAL

The experiments on the synthesis of the hexamethyleneamides of organic acids were carried out as follows. The flask of a standard packed fractionating column of the Klin factory 400 mm high was charged with 0.25 mole of the appropriate acid with a 30% excess of acetic anhydride and hexamethyleneimine. The flask was attached to the column, the heating was switched on, and the reaction mixture was heated to the boil. After the temperature in the column had reached boiling point of acetic acid and the working conditions of the column had become stable, the withdrawal of acetic acid was begun. The first portion of acid, obtained as a result of the reaction of the acetic anhydride and the hexamethyleneimine generally distilled over in 15–30 min. The acid liberated in the transamidation process took a longer time to pass over, in the majority of cases.

It must be emphasized that as the low-boiling component was removed from the reaction zone, the temperature in the flask gradually rose. Consequently, to maintain the mixture at the boil it was necessary gradually to increase the heating of the flask. After the end of the process, which could be judged from the cessation of the distillation of acetic acid, the contents of the flask were cooled, diluted with an equal volume of benzene, and washed successively with water, 5% alkali solution, and water again to neutrality. The washed product was distilled. The solvent was first taken off at atmospheric pressure and then the desired product was obtained by vacuum distillation.

Twenty hexamethyleneamides of saturated and unsaturated monobasic and dibasic aliphatic and aromatic acids have been synthesized by the above-described method. Some parameters of the transamidation process and characteristics of the compounds obtained are given in the table. As can be seen from this table, for all the acids studied the transamidation process is characterized by fairly high yields of the desired products with comparatively short reaction times. The yields of the hexamethyleneamides of various acids, with a few exceptions, amount to 70–93%.

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