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STUDY OF ACYLATION REACTION OF AMINES OF VARIOUS STRUCTURES WITH CHLOROANHYDRIDE OF HEXANE ACID

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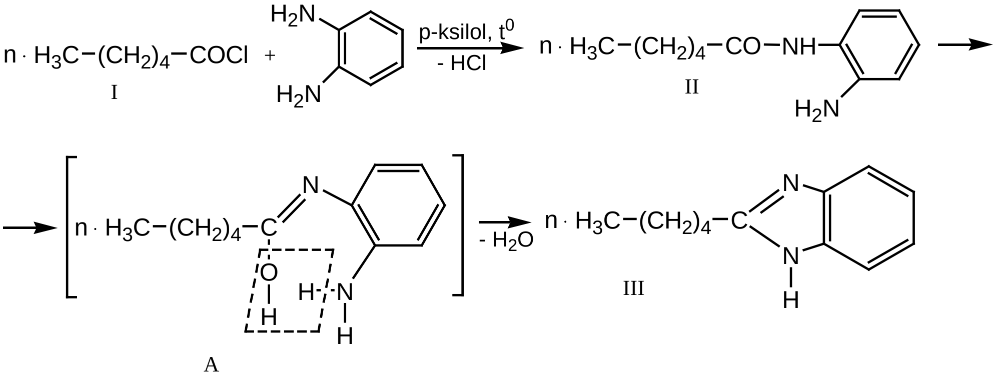
Research into the acylation *reaction of various amines by chloroanhydride hexane acid showed that the nature and conditions of functional groups in the molecule of amine compounds has a great influence on the reaction direction and reaction yield. Unlike para-phenylenediamine when acylating ortho-phenylenediamine, together with monocarboxyamide formation there is C-alkyl derivative of benzimidazole following the conversion of N-(2-aminophenyl)of pentancarboboxiamide into enolform and intermolecular cyclization.*

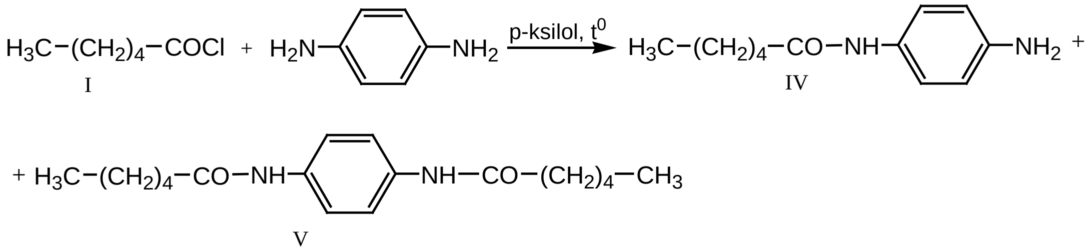
Keywords: *acylation reaction, chloroanhydride hexane acid, o-phenylenediaminein, p-phenylenediamine, monocarboxyamide, intermolecular cyclization*

In previous research works [1-5] the acylation reaction of various functionally substituted amines was studied with chloroanhydrides of alicycliccarboxylic acids. It found that in addition to carboxyamide compounds nitrogenous heterocyclic compounds, there are also obtained benzimidazole, benzoxazole, oxadiapezine derivatives. It went to show that synthesized carboxyamide compounds exhibit their inhibitor properties against corrosion [6, 7], stimulator property for plants [8, 9]. The nature and condition of functional groups in their molecules considerably effect on bioactivity properties of these substances. With that end in view, chloroanhydride of hexane acid was used as a reagent to synthesize new functionally substituted nitrogenous compounds for acylation of amines with varied structures. When acylating chloroanhydride (I) of hexane acid with aromatic ortho- and para-diamines, relevant carboxyamide compounds are obtained. Reaction goes by the following scheme:



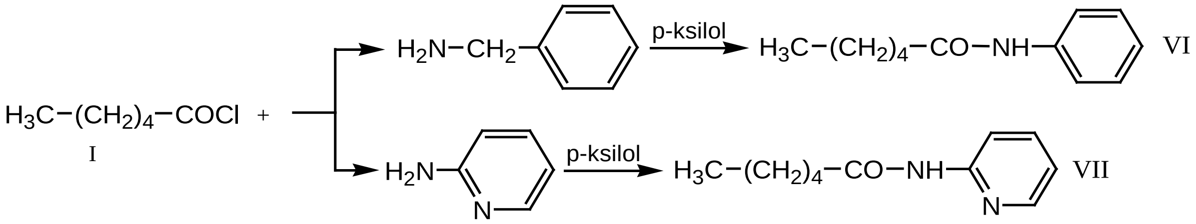
As seen from the scheme, due to the reaction of chloroanhydride (I) with ortho-phenylenediamine both carboxyamide, compounds (II) and C-alkyl derivative of benzimidazole (III) are obtained. Generation of the substance (III) is related to intermolecular cyclization of N-(2-aminephenyl)-pentancarboxyamide compound (II) by converting to enol form.

Unlike ortho-phenylenediamine due to the reaction of chloroanhydride (I) with para-phenylenediamine, just mono- (IV) and dicarboxyamide (V) compounds are obtained.

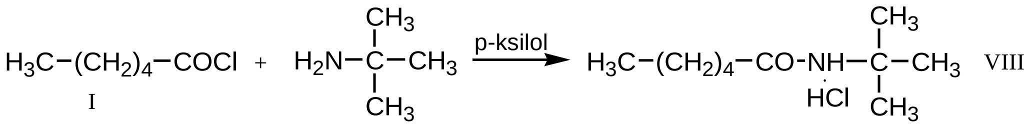


As a result of the reaction of chloroanhydride (I) para-phenylenedimine at 2:1 ratio, the yield of –N,N-(1,4-phenylene)dipentancarboxyamide (V) of dicarboxyamide compound rose up to 92.8%.

Relevant carboxyamide-N-(benzene)-pentancarboxyamide (VI) and N-(pyridin-2-yl)-pentancarboxyamide (VII) compounds were synthesized by the interaction of chloroanhydride with benzeneamine and ortho-aminepyridine.



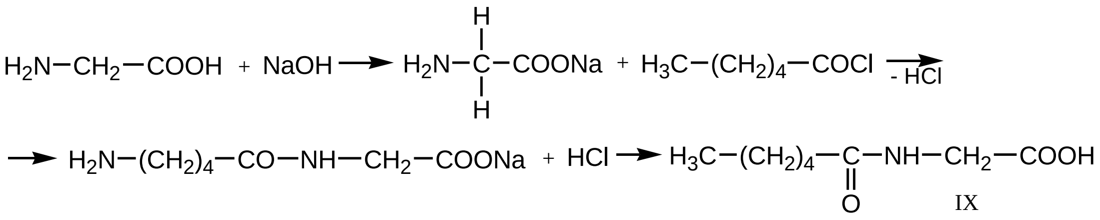
Depending on the nature of functional groups in the molecule of amine compounds, basicity of amine group changes sharply. Of great interest is the review of acylation reaction of amine compound with electrodonor group in the molecule. Acylation reaction of izobutylamine hexan acid with electrodonor group in the molecule as substrate with chloroanhydride was studied. The reaction goes as follows.



At p-xylene medium when adding chloroanhydride (I) drop by drop on amine compound the temperature of reaction mass roses. Reaction is performed at 55-60^{0}C by cooling. Unlike other amine compounds due to the acylation of isobutyl-amine ammonium salt of N-(izobutyl)-hexanecarboxyamide (VIII) is obtained. This causes the growth of basis property of amine group under the positive inductive (+J) effect of methyl groups in the amine molecule and integration of HCl gas emitted during the reaction into amide group.

To obtain acyl derivatives of bipolar amine compounds, we studied the acylation reaction of amine-acetate acid with chloroanhydride (I) of hexane acid.

Since the amine compound contains amine group (NH$_2$) and carboxyl (-COOH) group, the reaction is performed at basis medium, so we controlled the basicity of medium until the reaction was over. The reaction goes as follows.



$$H_2N-CH_2-COOH + NaOH \longrightarrow H_2N-\overset{H}{\underset{H}{C}}-COONa + H_3C-(CH_2)_4-COCl \xrightarrow[-HCl]{}$$

$$\longrightarrow H_2N-(CH_2)_4-CO-NH-CH_2-COONa + HCl \longrightarrow H_3C-(CH_2)_4-\underset{\underset{O}{\|}}{C}-NH-CH_2-COOH$$

IX

Bioactive property of synthesized 2-(pentancarboxyamide)-acetic acid (IX) and free carboxyl (-COOH) group in the molecule make it possible to use it as a synthon for synthesizing practically useful new class organic compounds. The composition and structure of synthesized substances and their physical-chemical constants were determined by IR and NMR spectroscopy analysis method.

EXPERIMENTAL PART

Note that IR spectrum of synthesized substances taken in “Nicolet is 10” spectrometer in thin film or paraffinic oil in suspension form.

NMR spectrum is taken in “Bruker 300” spectrometer (operating frequency 300 MHz), internal standard – hexamethyldisiloxane, chemical displacement in scale δ.

Reaction of chloroanhydride (I) of hexane acid with o-phenylenediamine. 60 ml of p-xylene and 10.8 g (0.01 mol) of o-phenylenediamine mixture is placed into three-neck flask provided with a mechanical mixer, thermometer and reverse cooler and 13.45 g (0.01 mol) of chloroanhydride (I) are added to it drop by drop by mixing. When chloroanhydride is added the temperature of reaction mass increased up to 60^0C. Then the reaction mass is heated at $110\text{-}120^0C$ for 50-55 min. After cooling the resultant deposit is filtered and separated from liquid part. Crystalline substance is recrystallized in water-alcohol mixture. Two fractions are obtained: 1) 2.25 g (10.8%) N-(2-aminephenyl)-pentancarboxyamide (II), $T_{melt.}193\text{-}194^0C$ ($EtOH\text{-}H_2O$), in IR-spectrum (ν, sm^{-1}): 3280-2900 (NH_2, NH), 1740-1620 (CO-NH), 1540-1480 (C = C_{ar}), 720-690 (C = C_{ar}, 1.2-substituted). 2) 15.55 g (82.7%) 2-pentyl-1H-benzimidazole (III).$T_{melt.}90\text{-}91^0C$ ($EtOH\text{-}H_2O$). In IR spectrum (ν, sm^{-1}): 3250 (-NH, valence connected), 1660 (C = N -), 1580-1480 (C = $C_{ar.}$), 1090 (C – N -, valence vibrations), 730, 700 (C = $C_{ar.}$, 1.2-substituted), NMR 1H spectrum (δ, m.h.): 0.98 s (3H, CH_3), 1.32-2.46 m (8H, $4CH_2$), 5.2 s (1H, NH), 7.30 s (2H, Ar), 7.68 s (2H, Ar.).

Reaction of chloroanhydride (I) of hexane acid with p-phenylenediamine. Two substances were obtained from the reaction of 6.7 g (0.05 mol) of chloroanhydride (I) with 5.4 g (0.05 mol) of p-phenylenediamine at 60ml p-xylene medium: 1) 6.32 g (41.6%) N,N-(1,40phenylene-dipentacarboxyamide) (V). $T_{melt.}196\text{-}197^0C$ ($EtOH\text{-}H_2O$). IR spectrum (ν, sm^{-1}): 3330-3270 (N – H, trans), 3060-2860 (N – H, sis and trans), 1680, 1620 (- CO – NH, double amide), 1490, 1460 (C = $C_{ar.}$), 980-860 (C = $C_{ar.}$, 1,4 substituted). 2) 4.76 g (46.2%) N-(4-aminephenyl)-pentancarboxyamide (IV). $T_{melt.}171\text{-}172^0C$ ($EtOH\text{-}H_2O$). IR spectrum (ν, sm^{-1}): 3450 (NH_2, valence vibrations), 1640 (CO - NH), 1560, 1500 (C = $C_{ar.}$), 900, 860 (C = $C_{ar.}$, 1,4-substituted) absorption bands confirm its structure.

Reaction of chloroanhydride (I) of hexane acid with benzylamine.60 ml of p-xylene and 5.4 ml (0.05 mol) of benzylamine is placed into three-neck flask and mixed with 8 ml (0.05 mol) of chloroanhydride (I). When chloroanhydride is added the temperature of reaction mass rises from 18^0C to 30^0C. Then reaction mass is heated at $110\text{-}115^0C$ for 45-50 min. After cooling, the resultant white deposit is filtered and separated from liquid part. Obtained: 9.67 g (94.3%) N-(benzyl)-pentancarboxyamide. (VI) $T_{melt.}179\text{-}180^0C$ (benzene). IR spectrum (ν, sm^{-1}): 3330 (valence vibrations of N – H bond), 1690 (C = O), 1650 (CO – NH -), 1600, 1500 (C = $C_{ar.}$), 759, 700 (C = $C_{ar.}$, monosubstituted), NMR 1H spectrum (δ m.h.): 0.97 s (3H, CH_3), 1.32-2.45 m (8H, $4CH_2$), 7.85 (1H, NH), 7.20 s (1H, Pr-H), 8.05 (1H, Pr), 8.4-8.5 d (2H, Pr).

Reaction of chloroanhydride (I) of hexane acid with 2-aminepyridine. The mixture of 9.40 g (0.1 mol) of 2-aminepyridine and 70 ml p-xylene is mixed with 13.45 g (0.1 mol) of chloroanhydride (I) of hexane acid. When chloroanhydride is added, the temperature of reaction mass rises up to 40^0C. Then reaction mass is heated at 110^0C for 45 min. After cooling, the resultant white crystal substance is filtered and separated from liquid part. Obtained: 14.47 g (81.75%) N-(pyridin -2-yl)pentan-carboxyamide (VIII). After recrystallization, it made up (EtOH-H_2O) $T_{melt.}$97-98^0C. In IR spectrum (v, sm^{-1}): 3270 (N – H, valence vibrations), 1710 (Co – NH -), 770, 690 (C = C_{ar}, monosubstituted) absorption bands confirm its structure.

Reaction of chloroanhdyride (I) of hexane acid with iso-butylamine. Using the same method, we obtained HCl salt of 15.15 g (88.6%) of N-(isobutyl)-hexanecarboxyamide (VIII) through the reaction of 13.45 g (0.1mol) of chloroanhydride of hexane acid and 7.3 g (0.1mol) of isobutylamine with 60ml p-xylene. $T_{melt.}$$293^0$C (it is decomposed). In IR spectrum (v, sm^{-1}): 3397-3233 (sis-, trans-, linked NH group), 2717-2245 (valence vibrations of ion (NH_2), 1712 (C = O), 1625, 1618 (- CO – NH -) absorption bands confirm its composition and structure.

Reaction of chloroanhydride (I) of hexane acid with amineacetic acid. Using the above mentioned method, we obtained 14.16 g (93.8%) of white crystal N-(pentancarboxyamide) of acetic acid (IX) by the reaction of 13.45 g (0.1 mol) of chloroanhydride (I) of hexane acid and 7.5 g (0.1 molamineacetic acid) with 5.2 g (0.13 mol) of NaOH alkali. $T_{melt.}$110-111^0C EtOH-H_2O.In IR spectrum (v, sm^{-1}): 2980 (- OH), 1710 (C = O), 1650 (- CO – NH -) absorption bands confirm its structure.

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MÜXTƏLİF QURULUŞLU AMİNLƏRİN HEKSAN TURŞUSUNUN XLORANHİDRİDİ İLƏ ASİLLƏŞMƏ REAKSİYASININ TƏDQİQİ

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Funksionaləvəzli mono- və aromatik diaminlərin heksan turşusunun xloranhidridi ilə asilləşdirməklə müvafiq karboksiamid birləşmələri sintez edilmişdir. Tədqiqat nəticəsində müəyyən edilmişdir ki, amin birləşmələrin molekulunda olan funksional qrupların təbiəti və vəziyyəti reaksiyanın getmə istiqamətinə əsaslı təsir göstərir. Para-fenilendiamindən fərqli olaraq orto-fenilendiamini asilləşdirdikdə monokarboksiamid birləşməsi ilə yanaşı, onun enol- formaya keçməsi və molekuldaxili tsiklləşməsi nəticəsində benzimidazolun C-alkil törəməsi də alınır.

Açar sözlər: *asilləşdirmə reaksiyası, heksan turşusunun xloranhidridi, p-fenilendiamin, o-fenilendiamin, monokarboksiamid, molekuldaxili tsiklləşmə*

ИССЛЕДОВАНИЕ РЕАКЦИИ АЦИЛИРОВАНИЯ АМИНОВ РАЗЛИЧНОГО СТРОЕНИЯ ХЛОРАНГИДРИДАМИ ГЕКСАНОВОЙ КИСЛОТЫ

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В результате исследования реакции ацилирования различных аминов хлорангидридом гексановой кислоты установлено, что на направление реакции и выход продуктов реакции большое влияние оказывает положение и природа функциональных групп, имеющихся в молекуле аминов. В отличие от пара-фенилендиамина, при ацилировании орто-фенилендиамина наряду с образованием орто-фенилендиамина образуется и С-алкил производное бензимидазола в результате перехода N-(2-аминофенил)-пентанкарбоксиамида в енольную форму и внутримолекулярной циклизации.

Ключевые слова: *реакция ацилирования, хлорангидрид гексановой кислоты, орто-фенилендиамин, пара-фенилендиамин, бензимидазол, внутримолекулярная циклизация*