

ELECTROPHYLIC REACTIONS OF CHLOROCARBOXYLIC ANHYDRIDE OF 1-METHYL-CYCLOHEX-3-ENE WITH 3-OXINDOLE AND N-PHENYLACETIC ACID

M.A.Rustamov, Sh.M.Eyvazova, N.A.Veysova, G.A.Mirzayeva

Azerbaijan Technical University

*Email: rustamov.mahmud353@gmail.com, shukufa.eyvazova@aztu.edu.az,
naileveysova@gmail.com, mirzayeva70@mail.ru*

Keywords: *carboxylic acid,
chloroanhydride,
carboxamide, oxindole*

Abstract. The properties of various functionally substituted nitrogen-organic compounds depend on their structure, the state and nature of the functional group in their molecule. Functionally substituted proteins obtained on the basis of the peptide bond of substituted heterocyclic compounds from various amino acids perform a physiological function that is widespread in nature and is important for the vital activity of the body. The direct acidification reaction of aromatic amines with aromatic carboxylic acids takes place under severe conditions at temperatures above 280°C, the product is obtained with low yield, and at the same time additional products are formed.

Among carbonaceous compounds, chloranhydrides of carbonic acids have the strongest electrophilic properties. The reaction of acylation with chloranhydrides proceeds in mild conditions and the reaction product is obtained with a high yield.

Relevant carboxamide compounds have been obtained by acidification of N-phenylacetic acid and 3-oxindole with chlorocarboxylic anhydride of 1-methyl-cyclohex-3-ene. It has been found that the carboxamide compound obtained on the basis of N-phenylacetic acid forms carboxamide compound of 3-oxindole in the basic medium cycling intramolecularly.

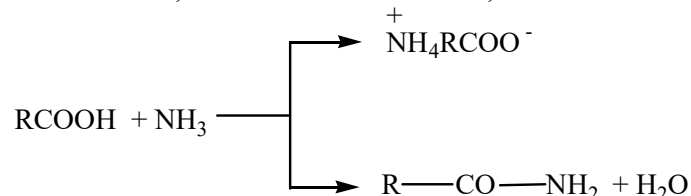
Introduction

Amide compounds are of special scientific and practical importance among the derivatives of carboxylic acids. Organic compounds containing amide groups in the molecule have a wide range of applications.

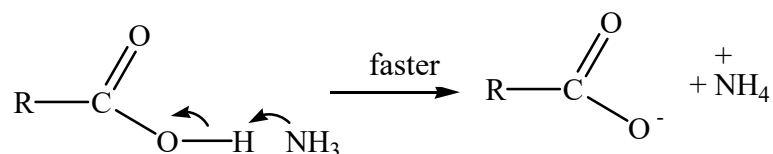
Amide compounds are widely used in medicine as medicine preparates [1; p. 185-187], in agriculture as bio stimulant for plants [2, 3], in technology as inhibitor [4] for protection of metals from corrosion.

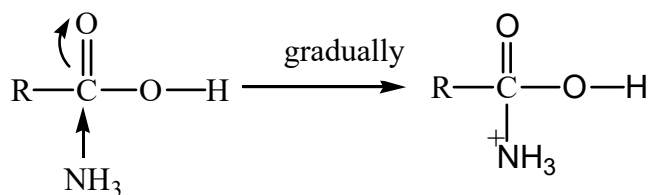
In this article, the reaction of acylation of 3-hydroxyindole and N-phenylacetic acid with 1-methylcyclohex-3-enecarboxylic acid chloride (II) (1) was studied.

At first glance, it seems that amide compounds can be obtained in a very simple way by acidifying amines with carboxylic acids. However, as a result of this reaction, first no amide but salt is obtained:



The reason why the amide compound cannot be obtained directly in this reaction is that the carbonyl group of the acid (RCOOH) moves to the base (NH₃) faster than to the electrophilic group of ammonia.

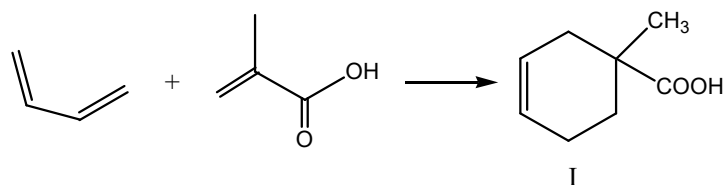




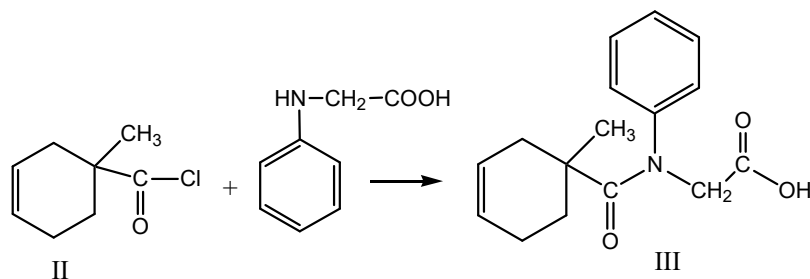
The direct acylation reaction of aromatic carboxylic acids and aromatic amines proceeds under harsh conditions at temperatures above 280°C, the product is obtained in low yield, and by-products are also formed.

It is known that chlorocarboxylic anhydrides have the strongest electrophilic properties among carbonyl compounds. The acidification reaction with chlorocarboxylic anhydrides occurs under soft condition and the reaction product is obtained with high yield.

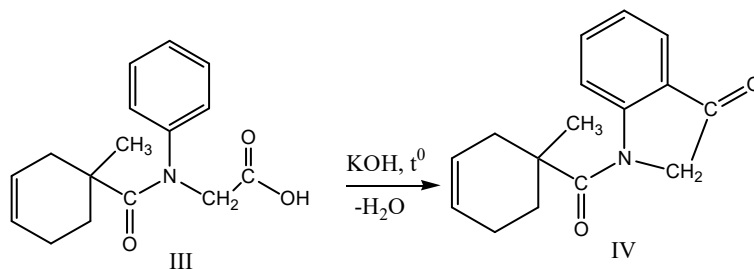
1-methyl-cyclohex-3-enecarboxylic acid (I) has been obtained by condensation of divinyl with methacrylic acid according to the Diels-Alder reaction [5].



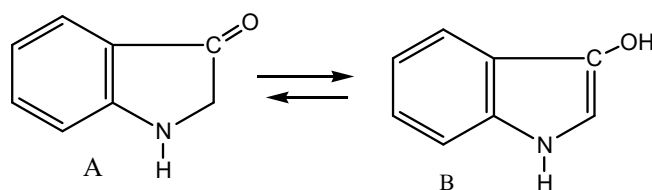
Chlorocarboxylic anhydride (II) of 1-methyl-cyclohex-3-ene (I) has been synthesized by the affection of trichlorophosphorus (PCl₃) in benzene medium according to the method of [6; p.358-359]. The reaction of chlorocarboxylic anhydride (II) with N-phenylacetic acid occurs by the following scheme:



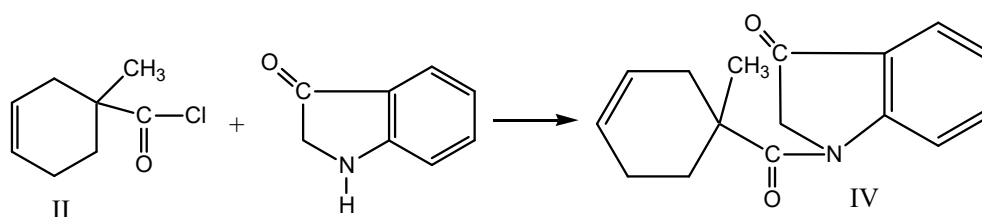
1-(1-methyl-cyclohex-3-enecarbonyl)-3-oxindole (IV) – derivative of 3-oxindole (IV) has been obtained as a result of intramolecular cyclization when heating [(1-methyl-cyclohex-3-enecarbonyl)-phenyl-amino]acetic acid (III) obtained as a result of the reaction in the basic medium.



This substance (IV) has been obtained by acidification of 3-oxindole with chlorocarboxylic anhydride (II) of 1-methyl-cyclohex-3-ene on the basis of cross-synthesis. It is known from the literature that 3-oxindole is found in two keto (A) and enol (B) forms of tautomer.



N- and O-acidification products, even in N,O-acidification products are obtained, when acidified with acetic anhydride. This is due to the fact that acetic anhydride has weak electrophilic properties and the reaction is carried out under severe conditions. It is known from the literature that among the carbonyl compounds, anhydrides of carboxylic acids have the weakest, and halogen anhydrides have the strongest electrophilic properties. Therefore, when chlorocarboxylic anhydride of 1-methyl-cyclohex-3-ene (II) is acidified with 3-oxindole, the reaction proceeds to the direction of the obtaining the N-acyl compound, and only the N-acyl compound (IV) is obtained. The reaction takes place according to the following scheme:



The composition and structure of the synthesized substances have been confirmed by chemical reaction, cross-synthesis, IR and NMR spectroscopy.

Experimental part

The IR spectra of the synthesized substances have been recorded on a “Nicolet is 10” spectrophotometer in the suspension state in a thin layer or in Vaseline oil.

NMR spectrum has been recorded on “Bruker 300” spectrophotometer (operating frequency is 300 MHz); internal standard-HMDS, chemical shift δ scale.

TLC analysis has been performed on silica gel in the system of petroleum ether–diethyl ether–acetic acid (90:10:4.5).

1-Methyl-cyclohex-3-ene-carboxylic acid (I).

260 g (3 mol) of methacrylic acid and a mixture of 165 g (3 mol) of butadiene and 200 ml of toluene is heated in a rotating autoclave at 180-200°C for 2 hours in the presence of 2 g of hydroquinone. 350 g (85%) of adduct has been obtained after processing the reaction mixture by classic way. Melting point 78°C (EtOH-H₂O). This is same with the information of [5] literature: 77,5-78°C.

Chlorocarboxylic anhydride of 1-methyl-cyclohex-3-ene (II).

Mixture of 140 g (1.0 mol) of 1-methyl-cyclohex-3-ene-carboxylic acid (1) and 80 ml of benzene is placed in a three-neck flask equipped with a reverse refrigerator, stirrer, drip funnel and thermometer and 91.60 g (0.6 mol) of phosphorus chloride is added drop by drop with stirring. After the addition of phosphorus chloride, the reaction mass is heated up to 75-80°C. The yellow viscous liquid formed during the reaction precipitates at the bottom of the flask. The clear liquid phase is separated by decantation way and distilled under normal condition. 150.57 g (95%) of chlorocarboxylic anhydride of 1-methyl-cyclohex-3-ene (II) is obtained as a result of the reaction. T_{boiling} 185-187°C/760 mm.of mercury, n_D^{20} 1.4830, d_4^{20} 1.0925. This is same with the information of literature.

[(1-Methyl-cyclohex-3-ene-carbonyl)-phenyl-amino]acetic acid (III).

The mixture of 7.58 g (0.05 mol) of N-phenyl acetic acid and 70 ml of p-xylene is placed in a three-neck flask equipped with a mechanical stirrer, reverse refrigerator and thermometer and 7.93 g

(0.05 mol) of chlorocarboxylic anhydride of 1-methyl-cyclohex-3-ene (II) is added drop by drop with stirring. The temperature of the reaction mass increased up to 45⁰C when chlorocarbon anhydride (II) was added. After complete addition of chloroanhydride (II), the reaction mass was heated to 120-125⁰C for 2 h. and left overnight. The precipitated crystalline substance is washed with water and then recrystallized in a water-alcohol mixture. Obtained: 12,53g (91,80%), $t_{\text{melt}}=178-179^{\circ}\text{C}$ (EtOH-H₂O). R_f 0,36. IR spectrum, ν , cm⁻¹: 3340 (-OH), 1715 ($\overset{\text{O}}{\parallel}\text{C}-\text{N}^{\leftarrow}$), 1710 (C=O), 1640 (C=C_{in cycle}), 1580, 1510, 1480 (C=C_{ar.}), 760, 735, 720 (C=C_{ar.} mono-substituted). NMR spectrum ¹H δ , MHz: 1.32s (3H, CH₃), 1.90-2.20m (6H, 3CH₂), 5.52s (2H, CH=CH), 7.0-7.26m (5H, Ar), 10.8s (1H, -OH). R_f 0,35.

1-(1-methyl-cyclohex-3-enecarbonyl)-2,2-dihydro-indole-3-on (IV).

A mixture of 13.65 g of carboxamide (III), 2.8 g of KOH and 70 ml of ethyl alcohol is placed in a three-neck flask equipped with a mechanical stirrer, a thermometer and reserve refrigerator with a water trap and heated to 65-70⁰C with stirring for 5 hours. After overnight, the precipitated substance is separated by filtration and washed several times with water. Obtained: 11.03g (86.5%) (IV) compound. $T_{\text{melt.}}=132-133^{\circ}\text{C}$ (EtOH-H₂O). R_f 0.52. IR spektr, ν , cm⁻¹: 1720 (C=O), 1715 ($\overset{\text{O}}{\parallel}\text{C}-\text{N}^{\leftarrow}$), 1650 (C=C_{in cycle}), 1600, 1560, 1480 (C=C_{ar.}), 760, 740 (C=C_{ar.} 1,2-substituted). NMR spectrum ¹H δ , MHz: 1.30s (3H, CH₃), 1.92-2.23m (6H, 3CH₂), 4.56 (2H, >CH₂), 5.54s (2H, HC=CH_{in cycle}), 7.20-7.85m (4H, C₆H₄). R_f 0.56.

Acidification reaction of chlorocarboxylic anhydride of 1-methyl-cyclohex-3-ene (II) with 3-oxindole (cross-synthesis).

Using the above method, 6.65 g (0.05 mol) of 3-oxindole and 80 ml of p-xylene have been placed in a three-neck flask equipped with a mechanical stirrer, reserve refrigerator, drip funnel and thermometer and 7.93 g (0.05 mol) of chlorocarboxylic anhydride (II) is added drop by drop by mixing. When chlorocarboxylic anhydride was added, the temperature of the reaction mass increased up to 50⁰C. The reaction mass is heated to 115-120⁰C stirring for 1.5 hours after complete addition of chlorohydride (II). After overnight, the crystalline substance is separated by filtration and recrystallized in a water-alcohol mixture. Obtained: 11.76 g (92.3%) of 1-(1-methyl-cyclohex-3-enecarbonyl)-2,2-dihydro-indole-3-on (IV) substance. The physical parameters, IR and NMR spectra of the substance (IV) obtained by both methods are the same.

Conclusion

In this article, the reaction of acylation of 3-oxindole and N-phenylacetic acid with 1-methyl-cyclohex-3-encarboxylic acid chlorohydride was studied for the first time. When the resulting substance is acylated with 3-hydroxyindole chlorohydride of 1-methylcyclohex-3-encarboxylic acid on the basis of mutual synthesis, the reaction proceeds in the direction of obtaining an N-acyl compound, and as a result of the reaction, only the N-acyl compound 1-(1-methylcyclohex-3-encarbonyl)-2,2-dihydro-indole-3 is obtained- him.

The obtained substances can be used in medicine as medicines, in agriculture as stimulants for plants, in engineering as inhibitors to protect metals from corrosion.

REFERENCES

1. Машковский М.Д. Лекарственные средства. Харьков, Торсинг, 1997, 2, 353 с.
2. Rüstəmov M.Ə., Veysova N.Ə., Eyvazova Ş.M., Zamanov P.B., İsmayılova S.H. 2-(tsikloheks-3-enkarboksiamido) sirkə turşusunun kalium duzu dənli və paxlalı bitkilərin boy stimulyatoru kimi. Patent-İXTİRA İ20160051, 2016.
3. Rüstəmov M.Ə., Eyvazova Ş.M., Əfkaribachebac A.Ş. (İR), Zamanov P.B., İsmayılova S.H., Qəmbərova R.F. Günəbaxanın boy stimulyatoru. Patent-İXTİRA. İ20160049, 2016.
4. Rüstəmov M.Ə., Veysova N.Ə., Eyvazova Ş.M., Bayramov M.R., Ağayeva M.A. N-(1,4-dimetil-tsikloheks-3-enkarbonil)benzamid poladın korroziya ingibitoru kimi. Patent-İXTİRA. İ20190030, 2019.

- Петров А.А., Сопов Н.П. О конденсации диеновых углеводородов с метакриловой кислотой и метилметакрилатом. Ж.Общ.химии, 1948, т.18, №10, с.1781-1788.
- Вейганд-Хильегат. Методы эксперимента в Органической химии. Изд. Химия, 1969, с.231.

1-METİL-TSİKLOHEKS-3-ENKARBON TURŞUSU XLORANHİDRİDİNİN 3-OKSİİNDOL VƏ N-FENİLSİRKƏ TURŞUSU İLƏ ELEKTROFİL REAKSİYALARI

M.Ə.Rüstəmov, Ş.M.Eyvazova, N.Ə.Veysova, G.Ə.Mirzəyeva
Azərbaycan Texniki Universiteti

Xülasə. Müxtəlif funksional əvəzli azotüzvi birləşmələrin xassələri onların quruluşundan, molekulundakı funksional qrupun vəziyyətindən və təbiətindən asılıdır. Funksionaləvəzli heterotsiklik birləşmələrin müxtəlif aminturşulardan peptid rabitəsi əsasında alınan zülallar təbiətdə geniş yayılmış və orqanizmin həyat fəaliyyəti üçün mühüm əhəmiyyət kəsb edən fizioloji funksiyaları yerinə yetirir. Aromatik karbon turşuları ilə aromatik aminlərin birbaşa asilləşmə reaksiyası sərt şəraitdə 280°C temperaturdan yüksək temperaturda gedir, məhsul az çıxımla alınır, eyni zamanda əlavə məhsullar da əmələ gəlir.

Karbonilli birləşmələr sırasında karbon turşularının xloranhidridləri ən güclü elektrofil xassəyə malikdir. Xloranhidridlərlə asilləşmə reaksiyası yumşaq şəraitdə gedir və reaksiya məhsulu yüksək çıxımla alınır.

Tədqiqat işində N-fenilsirkə turşusu və 3-oksiindolu 1-metil-tsikloheks-3-enkarbon turşusunun xloranhidridi ilə asilləşdirməklə müvafiq karboksiamid birləşmələri alınmışdır. Müəyyən edilmişdir ki, N-fenilsirkə turşusu əsasında alınan karboksiamid birləşməsi əsasi mühitdə molekul daxili tsiklləşərək 3-oksiindolun karboksiamid birləşməsinə əmələ gətirir.

Açar sözlər: karbon turşusu, xloranhidrid, karboksiamid, oksiiindol.

ЭЛЕКТРОФИЛЬНЫЕ РЕАКЦИИ ХЛОРАНГИДРИДА 1-МЕТИЛЦИКЛОГЕКС-3-ЭНКАРБОНОВОЙ КИСЛОТЫ С 3-ОКСИИНДОЛОМ И N-ФЕНИЛУКСУСНОЙ КИСЛОТОЙ

M.A.Рустамов, Ш.М.Эйвазова, Н.А.Вейсова, Г.А.Мирзоева
Азербайджанский технический университет

Резюме. Свойства различных функционально замещенных азотсодержащих соединений зависят от их структуры, состояния и природы функциональной группы в их молекуле. Функционально замещенные белки, полученные на основе пептидной связи замещенных гетероциклических соединений из различных аминокислот, выполняют физиологическую функцию, широко распространенную в природе и имеющую важное значение для жизнедеятельности организма. Реакция прямого ацилирования ароматических карбоновых кислот и ароматических аминов протекает в жестких условиях при температуре выше 280°C, продукт получается с низким выходом, и в то же время - также образуются дополнительные продукты.

Среди карбонильных соединений наиболее сильными электрофильными свойствами обладают хлорангидриды углеродных кислот. Реакция ацилирования хлорангидрида протекает в мягких условиях и продукт реакции получается с высоким выходом.

В ходе исследования были получены соответствующие карбоксиамидные соединения путем ацилирования N-фенилуксусной кислоты и 3-оксииндола хлорангидридом 1-метилциклогекс-3-энкарбонической кислоты. Установлено, что карбоксиамидное соединение, полученное на основе N-фенилуксусной кислоты, в кислой среде внутримолекулярно циклизуется с образованием карбоксиамидного соединения 3-оксииндола.

Ключевые слова: углеводная кислота, хлорангидрид, карбоксиамид, оксииндол.

Daxil olub: 13.02.2023