DEPENDENCE OF CLICK CHEMISTRY IN THE SYNTHESIS OF BIS-CARBAMATES OF THE MEE SERIES

Eldor Mashaev
Senior lecturer of the Tashkent Institute of Chemical Technology
Abduhamid Makhsumov
Professor of the Tashkent Institute of Chemical Technology
Obidjon Kodirov
Senior lecturer of the Tashkent Institute of Chemical Technology
Feruz Shapatov
Senior lecturer of the Alfraganus University

https://doi.org/10.5281/zenodo.10406358

Abstract. In this work, the synthesis of bis-carbamates was investigated for the suitability of the mechanism of nucleophilic addition to the requirements of "click chemistry" reactions. As a result, it was concluded that it is expedient to include the synthesis of bis-carbamates that meet all the criteria in "click chemistry" reactions.

Keywords: Bis-carbamate, click chemistry, synthesis, reactions, nucleophil, connect, molecules, structure, atoms, criteria.

ЗАВИСИМОСТЬ КЛИК-ХИМИИ ПРИ СИНТЕЗЕ БИС-КАРБАМАТОВ СЕРИИ МЭЭ

Аннотация. В данной работе синтез бис-карбаматов исследовался на предмет соответствия механизма нуклеофильного присоединения, требованиям реакций «клик-химии». В результате сделан вывод о целесообразности включения синтеза бис-карбаматов, отвечающих всем критериям, в реакции «клик-химии».

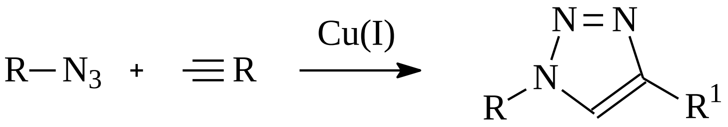
Ключевые слова: Бис-карбамат, клик-химия, синтез, реакции, нуклеофил, соединение, молекулы, строение, атомы, критерии.

INTRODUCTION

The term click chemistry was first introduced in the world in 2001 by the American scientist Barry Sharpless [1]. The essence of this concept is that it describes chemical reactions adapted for the rapid and reliable production of chemicals by connecting individual small elements together. Click chemistry is not only about one reaction, but also designed to imitate nature, in which compounds are created from modular elements. This concept has emerged in connection with the search for new approaches to the creation of drug candidate structures. But a few years later, the Nobel Prize for the development of click chemistry and bioorthogonal chemistry methods was awarded to the American scientists Caroline Bertozzi and Barry Sharpless, as well as the Danish scientist Dane Morten Meldahl.

"Click chemistry" is a branch of science that studies the methods of connecting different molecules into a whole (for different purposes). They "connect" to each other in the same way that we take our seats on an airplane and fasten our seat belts. However, the belt has a buckle—meaning that the attached molecules need some external element to interact with each other, forming a strong, stable chemical bond (Figure 1). At the current stage of technological development, the task may seem trivial, but there is another important aspect. This connection should be absolutely "neutral", that is, it should not have any effect on the chemical properties of the resulting compound. But this is a much more difficult matter.

Nobel laureates announced today managed to solve it using the carbon-nitrogen bond. Three successive chains of nitrogen atoms (azide) are "attached" to one of the molecules to be joined, and two carbon atoms (alkyne) to the other. In the presence of a catalyst (copper ions), the two parts of our "bonds" cross-link into a stable triazole ring, holding both parts together, from which this chemical structure is assembled Formula 1:



Valery Fokin, co-author of Barry Sharpless and 2013 Nobel Prize in Chemistry nominee, explains the concept of click chemistry in a 2002 article [2]:

.. the idea gives A + B = C and nothing else. It works all the time and under all circumstances. The basic idea of click chemistry is that if we imagine that we have two reactants, the reaction will always and everywhere happen. Accordingly, an irreversible bond appears - a fastener that allows you to connect two reactive blocks, two molecules into one thing.

Although the criteria for being a click reaction are relatively subjective, some reactions have been identified as being most suitable for this category: 3+2-cycloadditions, in particular azide-alkyne cycloadditions; thiol-ene addition; Diels-Alder reaction; 4+1-cycloaddition between isonitriles and tetrazines; nucleophilic substitution, especially in strained small rings; reactions of carbonyl compounds with nitrogen-containing nucleophiles and addition reactions to carbon-carbon double bonds, for example, dihydroxylation [3,4].

The authors of the article synthesized bis-carbamates and their derivatives, studied their physicochemical properties and applied them in several fields [5-8]. Thus, the authors of this article came up with the idea of comparing the click chemistry reaction and the synthesis of bis-carbamates of the MEE series. The purpose of this work is to identify the similarities of the synthesis and also to meet the criteria for a click chemistry reaction.

MATERIALS AND METHODS

Synthesis of N,N' – hexamethylene bis[(ortho-cresolyl)-carbamate] i.e. MEE-1: To 10 ml of triethylamine (TEA), 35 ml of dimethylformamide (DMF) are added to 10.8 g (0.1 mol) of ortho-cresol, mixed, dissolved in 20 ml of DMF at room temperature 8.4 g (0.05 mol) of hexamethylene diisocyanate (HMD) is added. After time, the reaction mixture is stirred at 35-45 ºC for 3.0-4.0 hours, the contents of the flask are transferred to a glass, and water is added. After drying, a white powder is obtained; the yield of the product is 18.74 g (97.6% of theory).

RESULTS AND DISCUSSIONS

Drawing of a strong and stable chemical bond by the scientist Bertolli Sharpless (Fig. 1).

Reactions involving click chemistry must meet the following requirements, and we have compared our mechanism for obtaining bis-carbamates to these requirements:

1. Being modular - our reaction proceeds with A_N joining of 3 molecules;
2. Having a wide scope of application - because our product is biologically active, it can be used in agriculture, pharmaceutical and chemical industries;
3. High yield - product yield in the reaction is not less than 90%.
4. Giving safe by-products - no additional intermediate products are formed in the reaction and it is environmentally friendly.

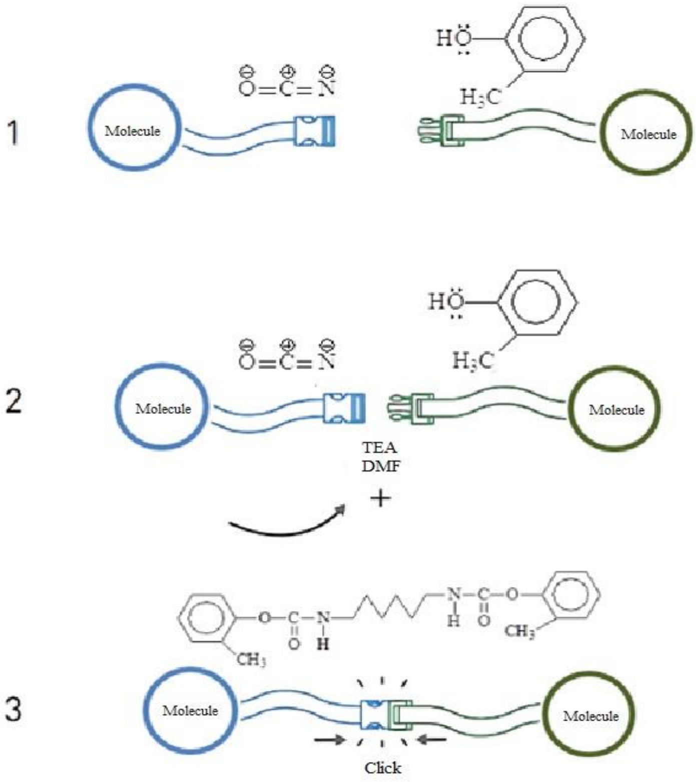


Fig. 1. Illustration of bis-carbamate MEE-1 theory of click chemistry

5. Being stereospecific - molecules of the same type in the product have the same location in space.

6. Proceeding in physiological conditions - the process proceeds at atmospheric pressure and room temperature.

7. Being thermodynamically very favorable (> 84 kJ/mol) for the formation of a single product - thermodynamically favorable for the formation of a single product.

8. Having a high economy of atoms - the number of atoms of the single product is 68, and the number of bonds is 69, which is much more economical than other organic substances.

9. Use of safe solvents - our reaction is carried out in non-gaseous solvents such as dimethylformamide (DMF) and dimethylsulfoxide (DMS).

10. Having normal reaction conditions - our reaction is environmentally friendly, at atmospheric pressure, at room temperature without external influences, energy efficient, lasts for 3-4 hours and produces high yield without intermediate products.

CONCLUSION

In conclusion, it would be appropriate to add our nucleophilic mechanism for obtaining bis-carbamates to the type of reactions associated with "click chemistry" because it meets all the above requirements.

References

1. Kolb H. C., Finn M. G., Sharpless K. B. Click Chemistry: Diverse Chemical Function from a Few Good Reactions (англ.) // Angew. Chem. Int. Ed. — 2001. –Vol. 40, no. 11. – P. 2004–2021. – doi:10.1002/1521-3773(20010601)40:11<2004:
2. The Nobel Prize in Chemistry 2022 (English). NobelPrize.org. Application Date: October 7, 2022. Archived 5 October 2022.

3. Spiteri C., Moses J.E. Copper-Catalyzed Azide–Alkyne Cycloaddition: Regioselective Synthesis of 1,4,5-Trisubstituted 1,2,3-Triazoles (англ.) // Angew. Chem. Int. Ed. — 2010. — Vol. 49, no. 1. — P. 31–33.
4. Jewett J. C., Sletten E. M., Bertozzi C. R. Rapid Cu-Free Click Chemistry with Readily Synthesized Biarylazacyclooctynones (англ.) // J. Am. Chem. Soc. — 2010. — Vol. 132, no. 11. — P. 3688–3690.
5. Махсумов Абдухамид Гафурович, Абдукаримова Саида Абдужалиловна, Машаев Элдор Эргашвой Угли, and Азаматов Уткирбек Рашидович. "Синтез и свойства производного - N,N' quote -гексаметилен бис- [(орто-крезолило) -карбамата] и его применение" Universum: химия и биология, no. 10-2 (76), 2020, pp. 33-40.
6. Махсумов А.Г., Жагфаров Ф.Г., Арипджанов О.Ю., Машаев Э.Э., Азаматов У.Р. "Синтез и свойства производных мета-крезолило-карбаматов, их биологическая активность" НефтеГазоХимия, №3, 2022, 52-59 с. doi:10.24412/2310-8266-2022-3-52-59
7. Махсумов Абдухамид Гафурович, Машаев Элдор Эргашвой Угли, Холбоев Юсубжон Хакимович, Уразов Фируз Бахтиярович, and Зохиджонов Сирожиддин Аскаржон Угли. "N,N’–гексаметилен бис [(м-крезолило) -карбамат] и его физико-химические свойства" Life Sciences and Agriculture, no. 1 (9), 2022, pp. 7-11.
8. Eldor Mashaev, Bakhodir Mukhiddinov, Tursinay Kongratbaeva, and Nargiza Jovlieva, “Application of BIS-Carbamates of the MEE Series as Corrosion Inhibitors of Metal Equipment of Oil Refineries”, AJEMA, vol. 1, no. 10, pp. 57–59, Dec. 2023.