

ПЕРСПЕКТИВЫ ПРИМЕНЕНИЯ КЛИК-РЕАКЦИИ АЗИД-АЛКИНОВОГО ЦИКЛОПРИСОЕДИНЕНИЯ В ФАРМАЦЕВТИЧЕСКОЙ ПРОМЫШЛЕННОСТИ

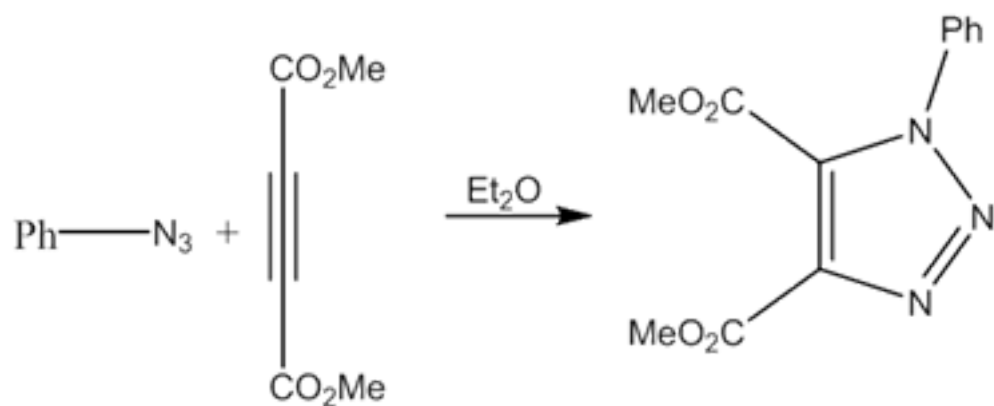
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Губкина, РФ, г. Оренбург

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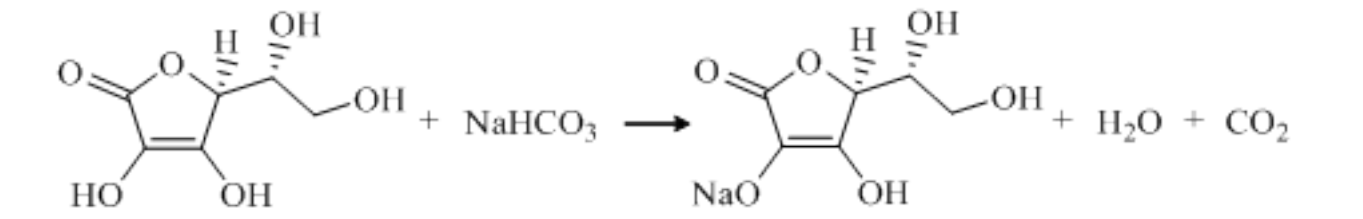
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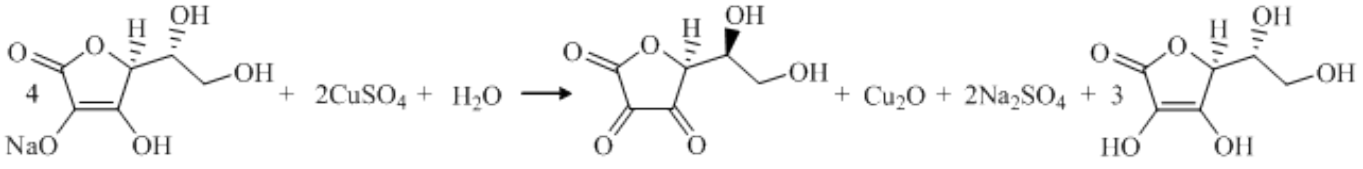
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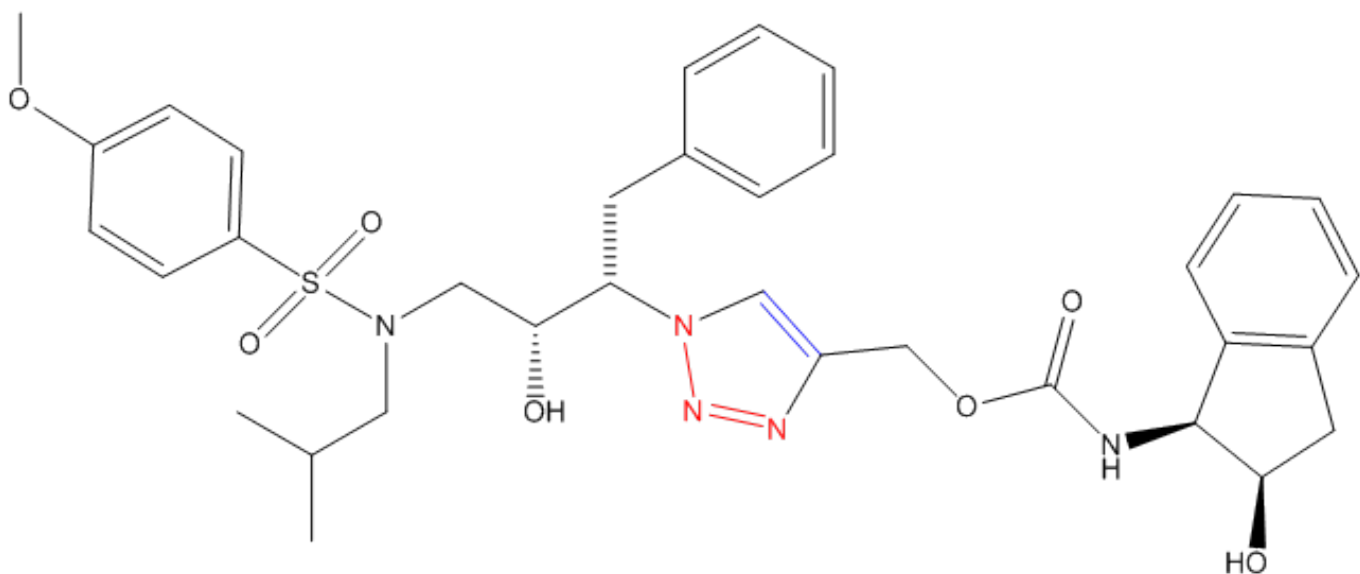
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 ???-1 [15]:



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 N-[(1S,2R)-2-?????-1-??]?????????

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Список литературы:

1. Agard N.J., Prescher J.A., Bertozzi C.R. A Strain-Promoted [3 + 2] Azide-Alkyne Cycloaddition for Covalent Modification of Biomolecules in Living Systems. *J. Am. Chem. Soc.*, 2004, v. 126, — p. 15046-15047.
2. Cho J.H., et al. Synthesis of Cyclopentenyl Carbocyclic Nucleosides as Potential Antiviral Agents Against Orthopoxviruses and SARS. *J. Med. Chem.*, 2006, v. 49, — p. 1140—1148.
3. Drews J. Strategic trends in the drug industry. *Drug Discov. Today*, 2003, v. 8, — p. 411—420.
4. Dijk, van M., Rijkers D.T., Liskamp R.M., Nostrum van C. F., Hennink W.E. Synthesis and Applications of Biomedical and Pharmaceutical Polymers via Click Chemistry Methodologies. *Bioconjugate Chem.*, 2009, v. 20, — p. 2001—2016.
5. Frantz S., Smith A. New drug approvals for 2002. *Nature Rev. Drug Discov. Today*, 2003, v. 2, — p. 95—96.
6. Huisgen R. Kinetics and Mechanism of 1,3-Dipolar Cycloadditions. *Angew. Chem. Int. Ed.*, 1963, v. 2, — p. 633—645.
7. Kolb H.C., Finn M.G., Sharpless K.B. Click Chemistry: Diverse Chemical Function from a Few Good Reactions. *Angew. Chem. Int. Ed.*, 2001, v. 40, — p. 2004—2021.
8. Li W., et al. Bitriazolyl acyclonucleosides with antiviral activity against tobacco mosaic virus. *Tetr. Letters*, 2008, v. 49, — p. 2804—2809.
9. McNulty J., Keskar K., Vemula R. The First Well-Defined Silver(I)-Complex-Catalyzed Cycloaddition of Azides onto Terminal Alkynes at Room Temperature. *Chem. Eur. J.*, 2011, v. 17, — p. 14727—14730.
10. Michael A. Ueber die Einwirkung von Diazobenzolimid auf Acetylendicarbonsäuremethylester. *J. Prakt. Chem*, 1893, v. 48, — p. 94—95
11. Perez-Castro I., et al. Synthesis of 4-substituted-1,2,3-triazole carbanucleoside analogues of ribavirin via click chemistry. *Org. Biomol. Chem.*, 2007, v. 5, — p. 3805—3813.
12. Rodionov V.O., Fokin V.V., Finn M.G. [Mechanism of the Ligand-Free CuI-Catalyzed Azide-Alkyne Cycloaddition Reaction](#). *Angew. Chem.*, 2005, v. 44, — p. 2210—2215.
13. Rostovtsev V.V., Green L.G., Fokin V.V., Sharpless K.B. A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective “Ligation” of Azides and Terminal Alkynes. *Angew. Chem. Int. Ed.*, 2002, v. 41, — p. 2596—2599.
14. Spilker B. The seven(teen) deadly sins in pharmaceutical companies. *Drug. News Perspect*, 1997, v. 10, — p. 203—207
15. Whiting M., Muldoon J., Lin Y.C., Silverman S.M., Lindstrom W., Olson A.J., Kolb H.C., Finn M.G., Sharpless K.B., Elder J.H., Fokin V.V. Inhibitors of HIV-1 protease by using in situ click chemistry. *Angew. Chem. Int. Ed.*, 2006, v. 45, — p. 1435—1439.
16. Wojtczak B. A., et al. “Chemical Ligation”: A Versatile Method for Nucleoside Modification with Boron Clusters. *Chem. Eur. J.*, 2008, v. 14, — p. 10675—10682.
17. Wu P., Fokin V.V. Catalytic Azide-Alkyne Cycloaddition: Reactivity and Application. *Aldrichimica Acta*, 2007, v. 40, — p. 7—17.
18. Xia Y., et al. Synthesis of bitriazolyl nucleosides and unexpectedly different reactivity of azidotriazole nucleoside isomers in the Huisgen reaction. *Org. Biomol. Chem.*, 2007, v. 5, — p. 1695—1701.
19. Zhang L, Chen X., Xue P., Sun H.H.Y., Williams I.D., Sharpless K.B., Fokin V.V., Jia G.

Ruthenium-Catalyzed Cycloaddition of Alkynes and Organic Azides. *J. Am. Chem. Soc.*, 2005, v. 127, — p. 15998—15999.