

The adduct of the Diels-Alder levoglucosenone and isoprenein approaches to iridoids

© Lilia Kh. Faizullina,¹⁺ Regina D. Karimova,² Alena S. Ryabova,³
Nailya F. Galimzyanova,³ and Farid A. Valeev^{1*}

¹ Ufa Institute of Chemistry of the Russian Academy of Sciences. October Ave., 71.
Ufa, 450054. Russia. Fax: +7 (3472) 35-60-66. E-mail: sinvmet@anrb.ru

² Bashkir State University. Zaki Validi St., 32. Ufa, 450074. Bashkortostan, Russia.
Phone: +7 (3472) 29-97-07. E-mail: chemistry@bsunet.ru

³ Ufa Institute of Biology of the Russian Academy of Sciences. October Ave., 71. Ufa, 450054. Russia.
Phone: +7 (3472) 35-57-04. E-mail: galnailya@yandex.ru

*Supervising author; ⁺Corresponding author

Keywords: iridoids, levoglucosenone, Diels-Alder adducts, aldol condensation.

Abstract

One of the most widely used ways of obtaining complex natural compounds is the use of optically active, but simpler, and therefore accessible compounds in chemical syntheses. Such a chiral source is levoglucosenone, which has a unique structure, high reactivity and, at the same time, sufficient stability; he found application in the synthesis of a number of natural compounds and continues to be studied in this regard. Due to the ability of levoglucosenone to interact with 1,3-dienes by the Diels-Alder reaction under stereocontrol conditions, dinitrocompounds by the Michael reaction open the possibility for obtaining chiral derivatives that are promising for use in the synthesis of a wide class of natural compounds, including terpenoids. In continuation of the work in the direction of iridoids, we developed a new approach based on the adduct of Diels-Alder of levoglucosenone and isoprene-4-methyl-10,12-dioxatricyclo [7.2.1.02,7] dodec-4-en-8-one (**1**). Thus, taking the fact that when the Diels-Alder adduct of levoglucosenone and isoprene **1** is boiled in benzene in the presence of *p*-TsOH, isomerization of the double bond occurs, we studied the possibilities of synthesizing iridoid using the isomerized adduct 4-methyl-10,12-dioxatricyclo [7.2.1.02,7] dodec-3-en-8-one (**2**).

Ozonolitic cleavage of the double bond and subsequent treatment of Me₂S ozonides in adduct **2** led to unstable aldehyde ketone **3** – (1*S*,2*S*,3*R*,5*R*)-4-oxo-3-(3-oxobutyl)-6,8-dioxabicyclo[3.2.1]octan-2-carbaldehyde. Oxidation of the obtained dicarbonyl compound of KMnO₄ proceeded with significant a resin is formed, while Jones oxidation smoothly led to acid. The attempt of chromatographic isolation of the acid was unsuccessful. Therefore, the unisolved acid was esterified with diazomethane, the resulting ester **4** – (1*S*,2*S*,3*R*,5*R*)-methyl-4-oxo-3-(3-oxobutyl)-6,8-dioxabicyclo[3.2.1]octan-2-carboxylate was identified.

Intramolecular aldol condensation in diketone **4** was carried out in benzene in the presence of a catalytic amount of DBU (1,8-diazobicyclo [5.4.0]-undec-7-ene). The structure of the compound – methyl(1*R*,9*S*)-2-hydroxy-4-oxo-11,12-dioxatricyclo [7.2.1.02,7] dodecane-8-carboxylate (**5**) was proved on the basis of ¹H and ¹³C NMR spectra. The fungicidal activity of the obtained target compound. Thus, compound **5** in a concentration of 0.5% in DMSO (dimethylsulfoxide) had a pronounced fungistatic effect on the development of *Rhizoctoniasolani*, retarding the growth of mycelium and the formation of chlamydospores.

References

- [1] M. Isobe, N. Fukami, N. Nishikava. Synthesis of chiral cyclohexanes from levoglucosenone and application to an to an indole alkaloid reserpine. *Heterocycles*. **1987**. Vol.25. P.521-532.
- [2] B.T. Sharipov, A.A. Pershin, F.A. Valeev. Synthesis of sarcodictyin A analogue containing 14-methyl group and C(12)=C(13) bond in ring A from levoglucosenone. *Mendeleev Communications*. **2017**. Vol.27. P.119-121. DOI: 10.1016/j.mencom.2017.03.003
- [3] I.P. Tsypysheva, E.V. Gorobets, L.Kh. Kalimullina, G.Sh. Singhizova, M.G. Safarov, F.A. Valeev. Beckmann rearrangement of oximes of left-glucosenone, its dihydro derivative, and proof of the stereochemical structure of the products obtained. *Chemistry of Natural Compounds*. **2003**. Vol.39. No.6. P.563-568. (russian)

- Full Paper** _____ L.Kh. Faizullina, R.D. Karimova, A.S. Ryabova, N.F. Galimzyanova, and F.A. Valeev
- [4] I.M. Biktagirov, L.Kh. Faizullina, Sh.M. Salihov, F.A. Valeev. Some transformation of adducts of levoglucosenone and 1,3-dienes in approaches to iridoides. *Butlerov Communications*. **2015**. Vol.42. No.4. P.41-47. ROI: jbc-02/15-42-4-41
- [5] M.M. Iskakova, I.M. Biktagirov, L.Kh. Faizullina, Sh.M. Salikhov, M.G. Safarov, F.A. Valeev. Regiocontrol of Dieckmann condensation of 3,4-bismethoxycarbonylmethyl derivative of levoglucosenone. *Russian Journal of Organic Chemistry*. **2014**. Vol.50. P.105-109. 10.1134/S1070428014010205.
- [6] I.M. Biktagirov, L.Kh. Faizullina, Sh.M. Salikhov, F.A. Valeev. Transformation of the cyclohexene fragment in the Diels–Alder adducts of levoglucosenone with 1,3-dienes into cyclopentane. *Russian Journal of Organic Chemistry*. **2015**. Vol.51. No10. P.1457-1463.
- [7] I.M. Biktagirov, L.Kh. Faizullina, Sh.M. Salikhov, F.A. Valeev. Contraction of the cyclohexene ring in the Diels–Alder adduct of levoglucosenone with piperylene. *Russ. J. Org. Chem.* **2016**. Vol.52. P.1468-1474. 10.1134/S107042801610016X
- [8] I.M. Biktagirov, L.Kh. Faizullina, Sh.M. Salikhov, F.Z. Galin and F.A. Valeev. Photochemical rearrangement of 5,6-epoxy derivatives of the Diels–Alder adduct of levoglucosenone and piperylene. *Mendeleev Commun.* **2017**. Vol.27. P.237-239. DOI:10.1016/j.mencom.2017.05.006
- [9] I.M. Biktagirov, L.Kh. Faizullina, Sh.M. Salihov, F.A. Valeev. Directed synthesis of glycosides of iridoid type on the basis of levoglucosenone. *Butlerov Communications*. **2017**. Vol.50. No.6. P.18-21. ROI: jbc-02/17-50-6-18
- [10] I.M. Biktagirov, L.Kh. Faizullina, Sh.M. Salikhov, M.G. Safarov, F.Z. Galin, F.A. Valeev. Oxidation with CrO₃·2Py of levoglucosenone and 1,3-dienes Diels-Alder adducts. *Russian Journal of Organic Chemistry*. **2016**. Vol.52. No.5. P.711-720. 10.1134/S107042801605016X.