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Ene reaction of Diels–Alder adducts of levoglucosenone and 1,3-dienes with acetaldehyde

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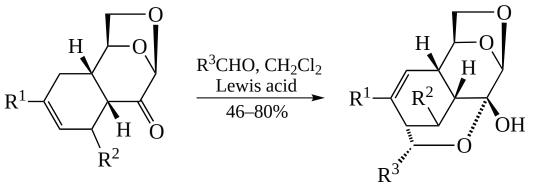
Diels–Alder adducts of levoglucosenone with isoprene, butadiene and piperylene in the presence of $AlCl_3$ smoothly react with acetaldehyde or benzaldehyde to give products of the ene reaction, the hydroxy group of the primary intermediates participating in the formation of semiketal moiety. The yields of the reaction products depend both on the Lewis acid used ($AlCl_3$, $BF_3{\cdot}Et_2O$, $ZnBr_2$, $SnCl_4$ or $EtAlCl_2$) and on the nature of the substrate.

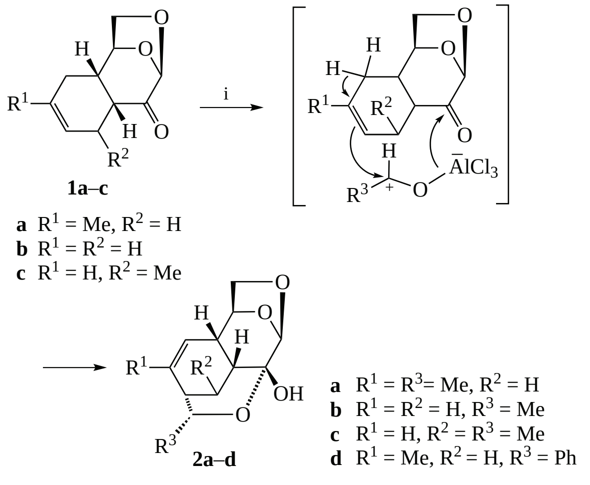


R^1, R^2 = H, Me; R^3 = Me, Ph

Keywords: levoglucosenone, acetaldehyde, Diels–Alder adduct, ene reaction, Lewis acids, ketals, oxetanes.

Levoglucosenone, a carbohydrate enone, smoothly enters Michael and cycloaddition reactions proceeding under strict stereochemical control from the carbohydrate residue, which, in turn, allows subsequent transformations characteristic of 1,6-anhydro sugars in the direction of the target products. On the basis of Michael adducts of levoglucosenone and cycloalkanones, syntheses of lactones of various size have been developed.[1] The Diels–Alder adducts of levoglucosenone and 1,3-dienes were used in syntheses of natural compounds such as tetrodotoxin,[2] eleutheside analogues,[3] prostanoids[4] and steroids.[5] The syntheses can be based on differences in the chemical behaviour of keto groups[6] as well as on the transformations of the carbohydrate fragment.

Previously,[7] we reported on the reaction of acetaldehyde with Diels–Alder adducts of levoglucosenone and 1,3-dienes under the McMurry reaction conditions when acetaldehyde was added to the acetal center. Besides, another product of the ene reaction was also formed in the case of the Diels–Alder adduct of levoglucosenone and isoprene.[7] In this work we studied whether similar reactions were possible with other adducts of levoglucosenone with 1,3-dienes in the presence of Lewis acids that are traditional for the ene reaction. We found herein that the reaction of cycloadduct **1a** with MeCHO and PhCHO in the presence of $AlCl_3$ gave the products of the ene–oxacyclization reaction sequence, **2a** and **2d**, in 65 and 80% yields, respectively (Scheme 1, *cf.* ref. 8). Under these conditions, in contrast to those used elsewhere,[5] the addition of acetaldehyde to the Diels–Alder adducts of levoglucosenone with butadiene **1b** and piperylene **1c** was also accompanied by isomerization of the double bond followed by intramolecular etherification of the keto group into analogous semiketals **2b**,**c**. It should be noted that, like in many reactions of Diels–Alder adducts of levoglucosenone and 1,3-dienes, the process occurs under strict stereochemical control from the 1,6-anhydro bridge.



1a–c

a R^1 = Me, R^2 = H
b R^1 = R^2 = H
c R^1 = H, R^2 = Me

2a–d

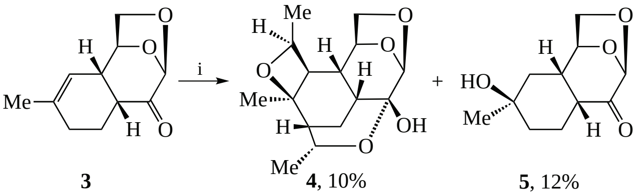
a R^1 = R^3= Me, R^2 = H
b R^1 = R^2 = H, R^3 = Me
c R^1 = H, R^2 = R^3 = Me
d R^1 = Me, R^2 = H, R^3 = Ph

Yields (%):
2a 65 ($AlCl_3$), 98 ($BF_3{\cdot}Et_2O$, $ZnBr_2$ or $SnCl_4$), 37 ($EtAlCl_2$)
2b 74 ($AlCl_3$), 45 ($ZnBr_2$), tar ($BF_3{\cdot}Et_2O$ or $SnCl_4$)
2c 51 ($AlCl_3$), 31 ($BF_3{\cdot}Et_2O$), 79 ($ZnBr_2$), 32 ($SnCl_4$)
2d 80 ($AlCl_3$)

Scheme 1 *Reagents and conditions*: i, R^3CHO (R^3 = Me or Ph), Lewis acid ($AlCl_3$, $BF_3{\cdot}Et_2O$, $ZnBr_2$, $SnCl_4$ or $EtAlCl_2$), 0 °C.

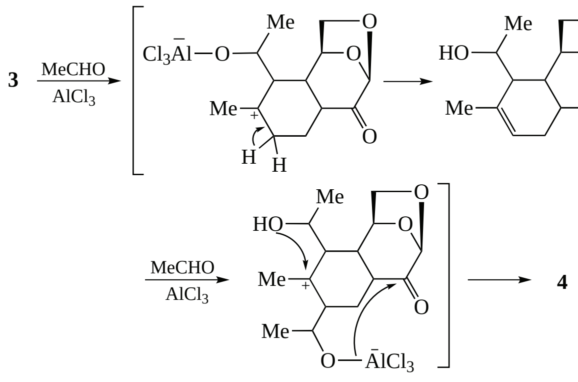
We also tested other Lewis acids[9] ($EtAlCl_2$, $BF_3{\cdot}Et_2O$, $SnCl_4$, $ZnBr_2$) for the reaction of MeCHO with substrates **1a–c**. The reaction with cycloadduct **1a** occurred efficiently in the presence of either $BF_3{\cdot}Et_2O$, $SnCl_4$ or $ZnBr_2$ and gave product **2a** in 98% yield while $EtAlCl_2$ exhibited low activity. Aluminium chloride was found to be the most efficient for substrate **1b** (yield of **2b** 74%) whereas for substrate **1c** the best catalyst was $ZnBr_2$ (yield of **2c** 79%).

The reaction of ‘isomerized’ cycloadduct **3**[10] with acetaldehyde resulted in two compounds (**4** and **5**) in low yields (Scheme 2).



3 **4**, 10% **5**, 12%

Scheme 2 *Reagents and conditions*: i, MeCHO, CH_2Cl_2, 0 °C.



Scheme 3

Most likely, the formation of oxetane **4** is preceded by a carbonyl-ene reaction accompanied by a double bond shift, a second ene reaction, and neutralization of the resulting carbocation by closure to give a four-membered heterocycle; the formation of the semiketal completes the reaction (Scheme 3). The fact that oxetane **4** is formed reveals the potential capabilities of the ene reaction that is realized with assistance of the neighbouring groups and is analogous to the Paternò–Büchi reaction.[11] The formation of alcohol **5** was proved by an additional experiment when substrate **3** was treated with $AlCl_3$ in the absence of acetaldehyde followed by hydrolysis thus affording alcohol **5** in 27% yield.

The reactions of the ‘cyclopentadiene’ and ‘cyclohexadiene’ adducts with acetaldehyde under similar conditions resulted in degradation of the adducts, like in the cases studied previously.[7]

In summary, the addition of acetaldehyde to the Diels–Alder adducts of levoglucosenone and 1,3-dienes under the ene reaction conditions depends on the nature of the adduct, occurs stereospecifically, and gives products of the carbonyl ene reaction followed by their intramolecular oxacyclization. Aluninium chloride is a reliable reagent in this reaction for all the adducts.

This work was carried out under subjects of government assignments (nos. 122031400259-1 and 122031400282-9). NMR spectra were recorded using the equipment of the Center for Collective Use of Scientific Equipment ‘Chemistry’ and the Regional Center for Collective Use ‘Agidel’ of the Ufa Institute of Chemistry of the Russian Academy of Sciences.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2023.01.002.

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