P: ISSN No. 2231-0045 RNI No. UPBIL/2012/55438 VOL.-10, ISSUE-2 November -2021
E: ISSN No. 2349-9435 Periodic Research

The Facial Selectivity of 2-Acetoxy-2, 4 Dimethyl -3, 5-Cyclohexadienone During Diels-Alder Reaction

Paper Submission:10/11/2021, Date of Acceptance: 23/11/2021, Date of Publication: 24/11//2021

Mridula Verma
Associate Professor,
Dept. of Chemistry,
M.M.H. College,
Ghaziabad, U.P., India

Abstract

Diels-Alder Reaction between 2-Acetoxy-2,4-Dimethyl-3,5-cyclo hexadienone with maleic anhydride produced exclusively single product in which the anhydride ring was endo to the olefinic linkage of the bicyclic cage.

Key Words: Endo/Exo, Configuration, Cycloaddition

Introduction

Diels-Alder reaction is highly stereospecific since the bonds formed lie on the same face of the system undergoing the reaction and hence in the terminology of orbital symmetry classification, it is mentioned as a (π4s +2s) cycloaddition, an allowed process. The reaction between a cyclic diene and dienophile follows a concerted mechanism and may lead to two stereoisomers in which stereochemistry of both the reactants is retained in the cyclization process[1]. The facial selectivity in between 2,4-cyclohexadienone- 1 and acetylene dicarboxylate is a result of stereochemical control. Especially when the substituents on the dienophile are unsaturated groups such as carbonyl. The preference of this mode of addition which is often more stèrically crowded, is because of a combination of dipolar and van der Walls attractions as well as orbital interaction[2-] Chemical transformations have been widely applied in configurational assignment of Diels-Alder adducts. In this method the adduct in question is subjected to a series of chemical reactions of known mechanism, which may lead to either of the two different products or may proceed through different reaction paths depending on the exo and endo configurations. The chemical methods used for the configurational assignments through highly reliable, are quite laborious and in many cases it may be accompanied by many side reactions, e.g. rearrangements etc. Where the identification of the products becomes difficult. Under such circumstances, chemical methods may not yield fruitful results due to isomeric modifications.

The stereochemical assignment of complex organic molecules by NMR spectroscopy has been made with accuracy. The exploitation of restricted rotation about the Nsp2-Csp2 bond was made with relative ease. Besides the study of the geometry of organic molecules the role of substituents in controlling the conformation of phenyl ring and hence helping the configurational assignment of a bicyclic adduct has been studied with the help of ^{1}H NMR and ^{13}C NMR techniques[6]. Studies on several aspects of restricted rotations about a wide variety of single bonds are time dependent phenomenon. Dynamics of simple stereomutations about the Nsp2-Csp2 and Nsp2-Nsp2 bonds has been investigated through high resolution NMR spectroscopy. With increasing non-bonded compression between the ortho-substituent and cage, preference for the anti orientation has been observed[5].

The compound taken under study is a bicyclic adduct of a cyclic diene and a cyclic dienophile, both having strong electron withdrawing groups like acetoxy and carbonyls. Verma et al[7] reported the behavior of 6-acetoxy-6-methyl-2,4- cyclohexadienone as an efficient dienophile which undergoes Diels- Alder cycloaddition reaction with open chain dienes[8].

Theoretical study of cycloaddition reaction between ketenes and their derivatives have been studied thoroughly[9]. The multicomponent cycloaddition reactions with preferred orientation have also been reported[10],. Configurational assignments are invariably made by the application of physical techniques.

^{1}H NMR and ^{13}C NMR spectroscopy has been found of extensive application in the configurational assignments[11]. Experimentally this technique has certain advantages over other physical methods employed for configurational assignments. This technique is simple and straight forward and avoids skeletal rearrangements.

Formation of single exo adduct between 6-acetoxy -2,6-dimethyl -2 ,4-cyclohexadienone and maleic anhydride has been reported[12-14]. Auksi and Yates[13] studied the cycloaddition reaction between 6-Acetoxy-2,4- dimethyl and maleic anhydride and obtained a single product. Our experiments also gave a single product. The high stereoselectivity of these reactions is interpretable in terms of orbital overlap, closed-shell repulsion, steric and van der Walls-London effects.

This communication is about the configurational assignment of Diels-Alder Adduct of 2,4-Dimethyl-3,5- Cyclohexadienone 4 as cyclic diene and Maleic Anhydride as dienophile.

2-Acetoxy-2,4-dimethyl-3,5-cyclohexadienone (I) is reacted with maleic anhydride and gave a single product (II), m.p. 163-64^{0}c. The product formed has been transformed into its hydroxy derivative(III) m.p. 160°c and analyzed.

Aim of the Study

To study the behaviour and facial selectivity of a substituted cyclic dienone as diene in cycloaddition reaction.

Preparation of Compounds

1. Compound 2 -Acetoxy-2,4-dimethyl-3,5-cyclohexadienone (I) was obtained by the oxidation 2,4-dimethyl phenol by Wessely oxidation method. For this reaction a solution of 2,4-dimethyl phenol in dry dichloromethane was added to a solution of lead tetra acetate in dry dichloromethane in dropwise manner over period of 1.5 hrs. at room temperature. The excess lead tetra acetate was destroyed by adding ethylene glycol, washed with 1% sodium carbonate solution and isolated as yellow plates (m.p. 69-70^{0}c). The product 2-Acetoxy-2,4-dimethyl-3,5-cyclohexadienone was refluxed with maleic anhydride in dry benzene for 30 hrs. to give adduct (II). The solution was treated with sodium hydroxide to give adduct (III). The compound was purified through fractional crystallization.
2. The aryl imides were prepared by condensing the hydroxy adduct (III) with ortho-toluidine, ortho-anisidine and α-Naphthyl amine in dry conditions to give compounds (1,2,3) respectively. The resultant aryl imides were purified with 1:1 mixture of benzene and petroleum ether.
3. The dibromide (4) was obtained by bromination of hydroxy adduct (III). For which a solution of bromine in dry dichloromethane was added in dropwise manner to a solution of adduct (III) in dry dichloromethane with constant stirring and maintaining anhydrous conditions. The dibromide of bicyclic adduct was obtained as white crystalline solid. The product was purified with 50% alcohol.

Results and Discussion

The elemental analysis of all the compounds supported the isolated products. The configurational assignment was made by applying the dynamic NMR spectroscopic technique. All the NMR spectra were taken in $CDCl_3$. The 500 MHz'HNMR spectrum of the compound (II) may be interpreted as follows:
δ1.33 (s, 3H, 6-CH_3), δ1.64 (1H, OH), δ1.94 (s, 3H, 7-CH_3), δ3.32 (d, 1H,2-H), δ3.5 (dd, 1H, 4-H), δ3.64 (dd, 1H, 1-H), δ3.96 (dd, 1H, 3-H) and δ5.89 (dd, 1H, 8-H).
The spectral pattern is evident for the formation of the bicyclic Diels-Alder adduct (III). Some aryl-imide derivatives (1-3) have been prepared to investigate the stereochemistry of the adduct through conformational analysis about N-C (phenyl) bond.
^{1}H NMR(90MHz) spectrum of N-(2'-methyl) aryl imide(1) displays a pair of singlets at δ2,0 (1.44 H) and δ2.06 (1.56 H) for 2'-methyl protons and

singlets at δ1.3(3H) and δ1.9(3H) for the methyl protons at 6-and7- positions and a multiplet at δ5.75(1H) for 8-H along with other resonances.
The duplexity in the methyl resonances suggests hindered rotation about the N-C (phenyl) bond and two non-planar ground state conformations syn (1a) and anti (1b). The shielding parameter of the 2'-methyl protons indicates that it is under the anisotropic interaction of an olefinic bond. Similar shielding in the 2'-CH, protons has been observed in N-aryl imide of cyclohexadiene maleic anhydride adduct[12] where, the anhydride ring is endo to the olefinic bridge. The observed duplexity of the 2'-methyl protons suggests the endo configuration (III B) of the adduct (III). Further, the intensity ratio of the two conformers shows that anti conformer (1a) is slightly more populated. Molecular model also supports the preference of an anti-orientation of the bulkier methyl group.

The ^{1}H NMR spectrum of the compound (2) also shows duplexity for the 2'-OCH_3 group and suggests the presence of two non-planar conformations. The spectral pattern supports the endo configuration of the adduct. The ^{1}H NMR spectrum of N-(α-naphthyl) imide (3) exhibits two multiplets at δ5.77 (0.5 H) and δ5.92 (0.5 H) for the 8-olefinic proton and a pair of singlets centered at δ1.92 for 7-CH_3, protons along with other proton resonances. The multiplicity of 8-oleifinic proton and 7-methyl proton resonances have been attributed to the interaction of the N-naphthyl moiety with the cage olefinic system and endo geometry of the succinimidyl ring to the 7, 8 olefinic linkage. The spectral pattern suggests the two non-eclipsed conformations syn(3a) and anti (3b) for the naphthyl moiety and the deshielded 7-methyl and 8-olefinic proton corresponds to the syn-conformation (3a).

^{1}H NMR Spectral Data of Compounds

(**1**) δ1.3 (s, 3H, 6-CH_3), δ1.65 (bs, 1H, -OH), δ1.9 (s, 3H, 7-CH_3,), δ2.0 and δ2.06 (ds, 3H, 2'-CH_3), δ3.35-3.7 (Complex multiplet, 4H, 1,2,3 and 4-H), δ5.75 (m, 1H, 8H), δ6.8-7.1 (m, 4H, aromatic protons).

(**2**) δ1.33 (s, 3H, 6-CH_3), δ2.36 (bs, 1H, -OH), δ2.0 (s, 3H, 7-CH_3,), δ3.38-4.1 (Complex multiplet, 4H, 1,2,3 and 4-H), δ3.6 and δ3.62 (ds, 3H, 2-OCH_3), δ5.75 (m, 1H, 8-H), δ7.1-7.5 (m, 4H, aromatic protons).

(**3**) δ1.33 (s, 3H, 6-CH_3), δ1.9 (m, 4H, 7-CH_3, and -OH), δ3.3- 3.74 (bm, 4H, 1,2,3 and4-H), δ5.77 and δ5.92 (dm, 1:1, 8-H), δ7.0-7.8 (m, 7H, aromatic protons).

Mode of addition of bromine atoms to the olefinic bond and coupling constants were employed for determining the endo/exo-configuration of the Diels-Alder adducts . In the case of endo-adduct of cyclopentadiene and maleic anhydride, cis-addition of bromine from the same side of methylene bridge has been reported, where trans-addition has been observed in the case of exo-adduct[14] . Addition of bromine to olefinic bond is stereoselective and the attack of bromine atom from the less hindered side is preferred. The mode of addition of bromine atoms to an olefinic bonds of bicycloheptenes has been widely studied and has been successfully employed for the configurational assignment.

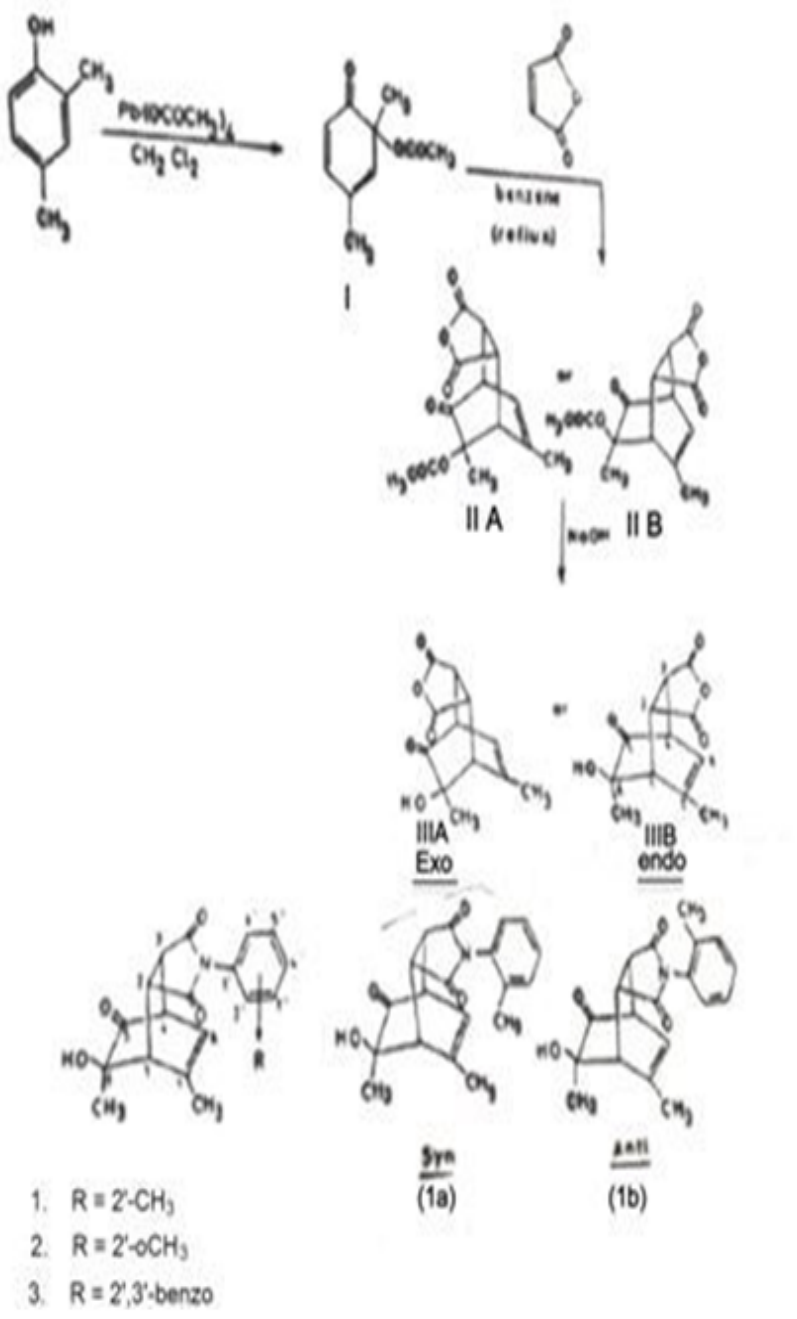
Bromination of the hydroxy adduct (III) in dry chloroform yields an addition product (4). The 500 MHz ^{1}H NMR spectral pattern has been interpreted as follows:

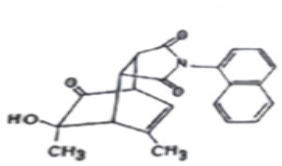
δ1.53 (s, 3H, 6-CH_3), δ1.79 (s, 3H, 7-CH_3),δ2.0 (bs, 1H, 6-OH), δ3.14 (d, 1H, 2-H), δ3.18 (d, 1H, 4-H), δ3.25 (d, 1H, 1-H),δ3.46 (d, 1H, 3-H) and δ5.1 (d, 1H, 8-H).

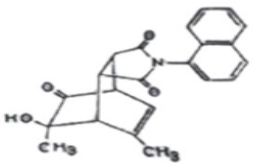
Appearance of -CHBr methine proton as a doublet (J=4 Hz) suggested a cis addition of bromine atoms across the olefinic bond. The cis addition of bromine atoms may be either from the oxo side (5) i.e. exo cis addition or from the anhydride (6) i.e. endo cis addition of the bicyclo [2.2.2] octane system. The spectral pattern and chemical shifts are quite similar to those observed for the endo adducts of cyclopentadiene and cycloheptatriene with

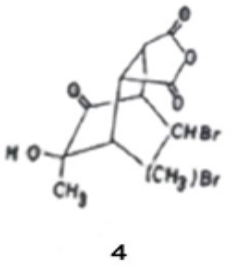
maleic anhydride[11]. The exo cis addition of bromine is further substantiated by the deshielding observed for the 6-CH_3, protons ($\Delta\delta$ = 0.2 ppm) in the brominated product and support the presence of 6-CH_3 group towards the olefinic bridge.

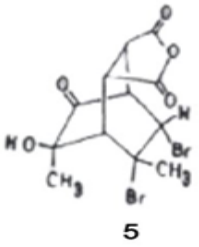
The observed exo cis mode of addition of bromine atoms to the olefinic bond confirms the endo configuration of the anhydride ring (towards the olefinic bridge) in the adduct. The stereoselective addition has been explained on steric grounds[13] and the more bulky substituent (-Br) remains away from the anhydride ring. The coupling constant (J=4 Hz) also supports the exo cis mode of addition to the olefinic linkage of cage.

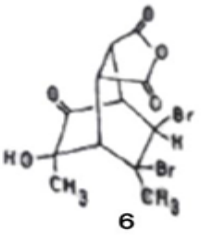












Conclusion

The cycloaddition reaction between 2-Acetoxy-2,4- dimethyl - 3,5 -Cyclohexadienone and Maleic Anhydride is an stereospecific reaction and exclusively gives an endo adduct. The sharp melting point and ^{1}H NMR spectral pattern confirmed the exclusive formation of a single product in which anhydride ring is endo to the olefinic linkage of the asymmetric cage. Mode of addition of bromine atoms further support the formation of endo adduct.

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