Investigation of the Pathway for Intramolecular Electron Transfer in Anodic [2 + 2] Cycloaddition Reactions

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ABSTRACT

Intramolecular electron transfer is expected to play a key role in anodic [2 + 2] cycloaddition reactions. We synthesized 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene as an olefin nucleophile to study the [2 + 2] reaction, leading to the finding that the intramolecular electron transfer that completes the formation of cyclobutane rings occurs mainly through space rather than through bonds.

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1. Introduction

Cycloaddition reactions offer a reliable means in organic synthesis to construct complicated ring systems in one step. While both synthetic applications and their theoretical counterparts have been studied extensively, the mechanism of ring formations remains controversial. In particular, the “concerted versus stepwise” question has been addressed frequently. Diels-Alder reactions are representative examples of [4 + 2] cycloadditions, which are considered to take place in a concerted manner. On the other hand, electron-transfer-induced cycloaddition reactions generally proceed in a stepwise fashion, including the initial electron transfer processes. [2 + 2] variants can be triggered by photochemical approaches and one-electron chemical redox agents. Additionally, several mechanistic studies have provided further insights into the ring closures of such [2 + 2] cycloaddition reactions and have discussed the motion of electrons in detail.

In this context, we have been developing anodic [2 + 2] cycloaddition reactions, which are induced through electrochemical processes. The anodic oxidation of electron-rich olefins produces the corresponding radical cations, which were then trapped by olefin nucleophiles to construct cyclobutane rings. For example, 3,4-dihydro-2H-pyran (1) was oxidized at the anode and followed by the resulting radical cation reacted with 4-allylanisole (2) to give the corresponding cycloadduct (3) (Scheme 1). When allylbenzene (4) was used instead of 4-allylanisole (2), the cycloadduct (5) was not obtained even in combination with anisole (6). Therefore, we concluded that the methoxyphenyl ring served as a “redox tag” that was oxidized to form the cyclobutane ring and was then reduced to complete the overall reaction (Scheme 2). Moreover, 1-methoxy-4-(pent-4-en-1-yl)benzene (7) could also trap the radicalcation of 3,4-dihydro-2H-pyran (1) to afford the desired cycloadduct (8) (Scheme 3). These results suggested that the intramolecular electron transfer from the methoxyphenyl ring to the cyclobutyl radical cation took place effectively even though the reactive groups were separated by three methylenes. However, it remained unclear whether this electron transfer occurred through space or through bonds. Described herein is an investigation into the pathway of intramolecular electron transfer in anodic [2 + 2] cycloaddition reactions.

2. Experimental

All reagents and solvents were purchased from Kanto Chemical, Tokyo Chemical Industry, Sigma-Aldrich, and Wako Pure Chemical Industries and were used without further purification. 1H and 13C NMR spectra were taken on a 600 MHz JNM-ECA spectrophotometer. High resolution mass spectrometry was performed on AccuTOF time-of-flight mass spectrometer.

2.1 Anodic [2 + 2] cycloaddition reaction

Olefins (4.0 mmol) and enol ether (0.20 mmol) were added to 1.0 M LiClO4/MeNO2 (20 mL). The undivided reaction cell was capped with a septum equipped with the carbon felt anode (20 mm × 20 mm), carbon felt cathode (20 mm × 20 mm), and the Ag/AgCl reference electrode. The electrolysis was then performed at 1.2 V vs. Ag/AgCl. After the reaction was completed, the reaction mixture was poured into EtOAc, and the EtOAc solution was successively washed with brine. The organic layer was dried over anhydrous MgSO4. After filtration and evaporation under reduced pressure, the residue was purified by silica gel column chromatography using n-hexane-EtOAc to give cycloadduct.

2.2 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9)

1H NMR (CDCl3, 600 MHz) δ 6.95 (1H, d, J = 8.3 Hz), 6.66 (1H, dd, J = 8.3, 2.1 Hz), 6.60 (1H, m), 5.89–5.80 (1H, m), 5.08–5.01 (2H, m), 3.74 (3H, s), 2.82–2.71 (3H, m), 2.34 (1H, dd, J = 15.6, 10.3 Hz), 2.11 (2H, t, J = 7.2 Hz), 1.95–1.88 (1H, m), 1.81–

1.72 (1H, m), 1.43–1.32 (1H, m) \(^{13}\)C NMR (CDCl\(_3\), 150 MHz) \(\delta\) 157.6, 137.9, 137.2, 130.0, 128.9, 116.0, 113.5, 111.9, 55.3, 40.9, 35.1, 34.5, 29.5, 29.1 HRMS [M + H]\(^{+}\) calcd. for C\(_{19}\)H\(_{26}\)O\(_2\) 203.1436; found 203.1442.

2.3 [2 + 2] Cycloadduct (13), mixture of diastereomers (1:1)

\(^{1}\)H NMR (CDCl\(_3\), 600 MHz) \(\delta\) 6.98–6.93 (1H, m), 6.68–6.64 (1H, m), 6.60 (1H, s), 3.76–3.74 (1H, m), 3.74–3.72 (4H, m), 2.72 (4H, m), 2.40–2.28 (2H, m), 2.00–1.83 (2H, m), 1.83–1.67 (2H, m), 1.63–1.23 (TH, m) \(^{13}\)C NMR (CDCl\(_3\), 150 MHz) \(\delta\) 157.7, 138.0, 138.0, 130.0, 129.0, 131.4, 113.4, 111.9, 111.9, 75.7, 75.7, 63.0, 63.0, 55.3, 41.2, 41.1, 36.0, 36.0, 35.6, 35.5, 33.3, 33.2, 30.8, 29.8, 29.6, 29.6, 29.5, 27.9, 27.7, 26.1, 26.1, 23.5 HRMS [M + H]\(^{+}\) calcd. for C\(_{19}\)H\(_{26}\)O\(_2\) 287.2011; found 287.2011.

3. Results and Discussion

The present work began with the synthesis of 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9) (Scheme 4). While the olefin moiety was separated from the methoxyphenyl ring by three methylenes, analogous with 1-methoxy-4-(pent-4-en-1-yl)benzene (7), an additional ring structure was introduced to restrict the motion of the molecule. Initially, 6-methoxy-3,4-dihydropyran-1(2H)-one (10) was allylated to give the corresponding olefin (11) in 54\% yield. The carbonyl group was then reduced to a hydroxyl group to afford the corresponding alcohol (12) quantitatively. Finally, the hydroxyl group was eliminated to construct 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9) in 97\% yield.

Both oxidation potentials and \(^{1}\)H NMR chemical shifts of 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9) were measured to compare the values to 1-methoxy-4-(pent-4-en-1-yl)benzene (7), indicating that the electron densities of their aromatic rings and the electron distribution of their olefin moieties were similar (Scheme 5). These results suggested that 3,4-dihydro-2H-pyran (1) could be oxidized preferentially even in the presence of 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9) and that there was little difference between the nucleophilicity of olefin moieties in 1-methoxy-4-(pent-4-en-1-yl)benzene (7) and 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9).

When 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9) was used for the anodic [2 + 2] cycloaddition reaction instead of 1-methoxy-4-(pent-4-en-1-yl)benzene (7), however, the corresponding cycloadduct (13) was obtained only in 2\% yield (Scheme 6). Based on the \(^{1}\)H NMR chemical shifts of the olefin moiety, 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9) was expected to react with the radical cation of 3,4-dihydro-2H-pyran (1) and the oxidation potential indicated that its aromatic ring would serve as a “redox tag”. Therefore, it is perhaps fair to say that there was a major difference between the rates of intramolecular electron transfer to complete the formation of cyclobutane rings (Scheme 7). This significant difference could be explained by the rigidity of the reagents and conditions: LiClO\(_4\), MeNO\(_2\), carbon felt electrodes, 1.2 V vs. Ag/AgCl.

Scheme 4. Synthesis of 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9).

Scheme 5. Oxidation potentials and \(^{1}\)H NMR chemical shifts of olefin nucleophiles.

Scheme 6. Anodic [2 + 2] cycloaddition reaction using 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9).
molecules. When 1-methoxy-4-(pent-4-en-1-yl)benzene (7) was used as an olefin nucleophile for the anodic \([2 + 2]\) cycloaddition reaction, the three methylenes that tethered the aromatic ring and the cyclobutyl radical cation were flexible. Thus, the aromatic ring and cyclobutyl radical cation were able to come close each other, while this was not the case when 2-allyl-6-methoxy-1,2,3,4-tetrahydro-naphthalene (9) was used. With these results in hand, we concluded that the intramolecular electron transfer from the aromatic ring to the cyclobutyl radical cation took place through space rather than through bonds.

4. Conclusion

In conclusion, the synthesis of 2-allyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (9) led to the finding that the intramolecular electron transfer that completes the formation of cyclobutane rings in anodic \([2 + 2]\) cycloaddition reactions occurs mainly through space rather than through bonds. The rigidity of the molecule affects the rate of intramolecular electron transfer significantly. The results described herein would be a great aid for further design of such anodic \([2 + 2]\) cycloaddition reactions.

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References


Scheme 7. Intramolecular electron transfer over three methylenes.