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Electron transfer-induced four-membered cyclic intermediate formation: Olefin cross-coupling *vs*. olefin cross-metathesis

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1. Introduction

Since an effective catalyst for olefin cross-metathesis was first developed by Grubbs, this reaction has been employed extensively to construct a wide variety of carbogenic skeletons in synthetic chemistry [1–4]. The investigation and modification of novel catalysts for olefin cross-metatheses still remain important areas of inquiry [5–8]. However, the theoretical study of the exchange of substituents between different olefins involving a key intermediate consisting of a four-membered ring coordinated to a transition metal has also been of interest [9,10].

To date, electrochemical processes have proven to be practical methods for triggering reactions based on olefins—intra- and intermolecular—because of their ability to reverse the polarity of the olefins. Several radical ion-based olefin cross-couplings have also been reported [11–14]. Furthermore, the mechanistic details of olefin cross-couplings have been described [15–22]. In this context, we previously developed an electron transfer-induced, intermolecular, olefin cross-coupling reaction (Scheme 1) [23–27]. Enol ethers were anodically oxidized to generate the corresponding radical cations, which were trapped by the unactivated olefins to form cyclobutane ring frameworks. We also demonstrated that olefin cross-metathesis between enol ethers and unactivated olefins could be induced through an electrode process (Scheme 2) [28]. For a cross-coupling to occur, an intramolecular electron trans-

ABSTRACT

An electron transfer-induced four-membered cyclic intermediate, formed between a radical cation of an enol ether and an unactivated olefin, played a key role in the pathway toward either cross-coupling or cross-metathesis. The presence of an alkoxy group on the phenyl ring of the olefin entirely determined the synthetic outcome of the reaction, which mirrored the efficiency of the intramolecular electron transfer. © 2010 Elsevier Ltd. All rights reserved.

fer from the alkoxyphenyl group was essential for the formation of the cyclobutane ring. The alkoxyphenyl group functioned as an electron-donating group, and the cyclobutyl moiety tethered by a methylene unit acted as an electron-accepting group. Considering the olefin cross-metathesis, a lack of this alkoxy group was required.

Four-membered cyclic intermediates are thought to be involved in these reactions; however, the mechanistic details are ambiguous. In particular, the presence of radical cations, which would offer clear-cut evidence for the formation of the four-membered cyclic intermediate, has yet to be detected (Scheme 3). With these results and theories in hand, we sought to study the mechanistic aspects of electron transfer-induced four-membered cyclic intermediates.

2. Experimental

2.1. General information

¹H and ¹³C NMR spectra were recorded in CDCl₃ with TMS as the internal standard on JEOL alpha 600 (600 MHz). The following abbreviations were used to explain multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; and m, multiplet. TLC analysis was performed with Merk Silica Gel 60 F254 plates, and detection was achieved by UV absorption (254 nm) and by charring the plates after spraying them with 12 molybdo(VI) phosphoric acid *n*-hydrate in 95% ethanol. Column chromatography was performed with silica gel (0.04–0.063 mm). All reagents and solvents were purchased from Kanto Chemical, Tokyo Kasei Kogyo, Aldrich, and Wako and used as received. Redox

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Scheme 2. Electron transfer-induced olefin cross-metathesis.

potentials were measured by cyclic voltammetry using a glassy carbon-working electrode, Pt wire counter electrode, and Ag/AgCl reference electrode.

3. Spectra information

2.2. Olefin cross-coupling reactions

Olefins possessing an alkoxyphenyl group (4.0 mmol) and aliphatic enol ethers (0.20 mmol) were added to 1.0 M LiClO₄/CH₃NO₂ (20 mL). The reaction cells were capped with septa equipped with carbon felt anodes ($20 \text{ mm} \times 20 \text{ mm}$), carbon felt cathodes ($20 \text{ mm} \times 20 \text{ mm}$), and Ag/AgCl reference electrodes. Electrolysis was performed at 1.2 V (*vs.* Ag/AgCl). Once the reactions were complete, the reaction mixtures were poured into EtOAc, and the EtOAc solutions were successively washed with brine and dried over anhydrous MgSO₄. After filtration and evaporation under reduced pressure, the residues were purified by silica gel column chromatography using *n*-hexane and EtOAc (isocratic, 1–5% EtOAc in *n*-hexane) to give the cycloadducts. The product yields and diastereomer ratios were determined by NMR and GC–MS (JEOL JMS-K9).

2.3. Olefin cross-metathesis reactions

The olefins (4.0 mmol) and aliphatic enol ethers (0.20 mmol) were added to $1.0 \text{ M LiClO}_4/\text{CH}_3\text{NO}_2$ (20 mL). The reaction cells were capped with septa equipped with carbon felt anodes (20 mm × 20 mm), carbon felt cathodes (20 mm × 20 mm), and Ag/AgCl reference electrodes. Electrolysis was performed at 1.2 V (vs. Ag/AgCl). After the reactions were completed, the product yields were determined by GC–MS.

3.1. 1-Methoxy-4-((2-methoxy-3-octylcyclobutyl)methyl) benzene **3a (all trans, major)**

¹H NMR (CDCl₃, 600 MHz) δ: 7.07 (2H, d, *J*=8.1 Hz), 6.81 (2H, d, *J*=8.1 Hz), 3.78 (3H, s), 3.23 (3H, s), 3.15 (1H, t, *J*=6.6 Hz), 2.86 (1H, dd, *J*=13.9, 5.9 Hz), 2.57 (1H, dd, *J*=13.9, 8.8 Hz), 2.27–2.16 (1H, m), 1.99–1.89 (2H, m), 1.37–1.12 (14H, m), 0.88 (3H, t, *J*=6.6 Hz), 0.83–0.74 (1H, m); (¹³DCl₃, 150 MHz) δ: 157.7, 132.7, 129.4, 113.6, 85.9, 56.5, 55.2, 41.9, 40.6, 40.3, 35.2, 31.9, 29.7 29.6, 29.3, 27.3, 25.4, 22.7, 14.1; IR (NaCl, cm⁻¹): 2924, 2853, 1612, 1513, 1464, 1247, 1040, 821; MS (rel. int., *m/z*): 318(M⁺, 1), 178(68), 163(7), 148(100), 121(27), 71(33); HRMS (*m/z*) calc. for C₂₁H₃₄O₂: 318.2559 (M–CH₃O: 287.2445); found: 287.2438.

3.2. 1-Methoxy-4-(2-(2-methoxy-3-octylcyclobutyl)ethyl) benzene **21a (all trans, major)**

¹H NMR (CDCl₃, 600 MHz) δ : 7.09 (2H, d, *J*=8.1 Hz), 6.82 (2H, d, *J*=8.1 Hz), 3.79 (3H, s), 3.30 (3H, s), 3.10 (1H, t, *J*=7.3 Hz), 2.58–2.44 (2H, m), 2.02 (1H, quint, *J*=8.8 Hz), 1.99–1.92 (2H, m), 1.92–1.82 (1H, m), 1.65–1.55 (1H, m), 1.38–1.13 (14H, m), 0.88 (3H, t, *J*=7.3 Hz), 0.72 (1H, q, *J*=8.8 Hz); ¹³NMR (CDCl₃, 150 MHz) δ : 157.6, 134.6, 129.2, 113.7, 86.5, 56.4, 55.2, 40.6, 40.0, 37.4, 35.3, 32.8, 31.9, 29.7, 29.6, 29.3, 27.4, 25.4, 22.7, 14.1; IR (NaCl, cm⁻¹): 2925, 2852, 1613, 1513, 1463, 1246, 1039, 824; MS (rel. int., *m/z*): 332(M⁺, 1), 192(12), 162(10), 147(1), 121(100), 71(25); HRMS (*m/z*) calc. for C₂₂H₃₆O₂: 332.2715 (M–CH₃O: 301.2602); found: 301.2619.



Scheme 3. Possible reaction mechanism for the electron transfer-induced olefin cross-metathesis.



Scheme 4. Electron transfer-induced olefin cross-coupling between 4-allylanisole (2) and 1-methoxydec-1-ene (1a-b).



Scheme 5. Electron transfer-induced olefin cross-metathesis between allylbenzene (**4**) and 1-methoxydec-1-ene (**1a-b**).

3.3. 1-Methoxy-4-(3-(2-methoxy-3-octylcyclobutyl)propyl) benzene **23a (all trans, major)**

¹H NMR (CDCl₃, 600 MHz) δ : 7.08 (2H, d, *J*=8.1 Hz), 6.82 (2H, d, *J*=8.1 Hz), 3.79 (3H, s), 3.29 (3H, s), 3.05 (1H, t, *J*=6.6 Hz), 2.58–2.47 (2H, m), 2.00 (1H, quint, *J*=8.8 Hz), 1.98–1.88 (2H, m), 1.64–1.46 (4H, m), 1.39–1.14 (14H, m), 0.88 (3H, t, *J*=6.6 Hz), 0.67 (1H, q, *J*=9.5 Hz); (¹³Cl₃, 150 MHz) δ : 157.6, 134.8, 129.2, 113.6, 86.5, 56.4, 55.2, 40.6, 40.3, 35.2, 35.0, 34.7, 31.9, 29.7, 29.6, 29.5, 29.3, 27.4, 25.4, 22.7, 14.1; IR (NaCl, cm⁻¹): 2925, 2852, 1614, 1514, 1462, 1247, 1040, 827; MS (rel. int., *m/z*): 206(53), 174(56), 147(18), 134(100), 121(69), 71(68); HRMS (*m/z*) calc. for C₂₃H₃₈O₂: 346.2872 (M–CH₃O: 315.2758); found: 315.2756.

4. Results and discussion

The present work began with the preparation of 1-methoxydec-1-ene (1a-b) [28]. The radical cation of 1a-b was effectively trapped by an excess of 4-allylanisole (2) to afford the corresponding [2+2] cycloadduct **3a-c** in good yield as a diastereomeric mixture (Scheme 4). In contrast, when an excess of allylbenzene (4) was used, **1a-b** was anodically oxidized to give dec-1-ene (**5**), an olefin cross-metathesis product, in moderate yield (several other unidentifiable products were also formed; Scheme 5). The oxidation potential of **1a-b** ($E_p^{ox} = 1.33 \text{ V}$ vs. Ag/AgCl) was lower than **2** ($E_p^{\text{ox}} = 1.51 \text{ V vs. Ag/AgCl}$) and **4** ($E_p^{\text{ox}} = 2.19 \text{ V vs. Ag/AgCl}$), enabling the selective anodic oxidation of **1a-b** in the presence of excess 2 or 4. In the reaction with 2, the presence of the electron-donating alkoxy on the phenyl group provided a thermodynamic effect by increasing the electron donor character of 2 and rendering an effective intramolecular electron transfer. For 4, the phenyl group's electron donor ability was hindered and led to a complicated reaction. The olefin cross-metathesis became the dominant process when an anodic oxidation of 1a-b was attempted in the presence of excess allylcyclohexane (6), which is incapable of forming a phenyl radical cation; 5 was obtained in a good yield with high chemoselectivity (Scheme 6). The use of excess non-1-ene (7) instead of 6 also gave 5 in good yield, suggesting steric hindrance is not a concern when a terminal olefin is used (Scheme 7). On the other hand, the yields of the olefin cross-metatheses with varying internal olefins were significantly lower (Table 1). These results suggest that the substitutions on the olefins disfavor the formation of four-membered cyclic inter-



Scheme 6. Electron transfer-induced olefin cross-metathesis between allylcyclohexane (**6**) and 1-methoxydec-1-ene (**1a-b**).

mediates and the formation of subsequent olefin cross-metathesis products.

Next, we became interested in investigating the role of the phenyl ring in this system. The radical cation of **1a-b** was anodically generated in the presence of an excess amount of 4-phenyl-1-butene (**16**), where the phenyl group was expanded one alkyl group from the four-membered cyclic intermediate compared to **4** and gave **5** in good yield (Scheme 8). Notably, the presumed thermodynamic effect of the phenyl group was completely quenched when the tether to the olefin was only two methylenes long.

A four-membered cyclic intermediate is thought to play a role in olefin cross-metathesis; however, little evidence for the formation of a counterpart radical cation **17**^{*+} has been detected (Scheme 9). We, thus, turned our attention to the mechanistic aspects of electron transfer-induced olefin cross-metatheses. For this purpose, (4-methoxybut-3-en-1-yl)benzene (**17a-b**), which was expected to form from a one-electron reduction of **17**^{*+}, was prepared to compare with the products from the oxidation of **1a-b** [28]. With **17a-b** independently synthesized, we found the anodic oxidation of **1a-b** in the presence of excess **16** gave **5** in good yield, while also forming **17a-b**. This result clearly suggests that a four-membered cyclic intermediate plays a key role in the reaction. However, it should be noted that **17**^{*+} with some degree of decomposition during the reaction.

In the absence of an olefin nucleophile, the oxidative cleavage of **17a-b** resulted in the formation of 3-phenylpropanal (**18**)



Scheme 7. Electron transfer-induced olefin cross-metathesis between non-1-ene (**7**) and 1-methoxydec-1-ene (**1a-b**).



Scheme 8. Electron transfer-induced olefin cross-metathesis between 4-phenyl-1butene (16) and 1-methoxydec-1-ene (1a-b).

Table 1

Electron transfer-induced olefin cross-metathesis between olefins **8–12** and 1-methoxydec-1-ene (**1a-b**). R¹ 1.2 V (vs. Ag/AgCl) R² \mathbb{R}^3 1.1 F/mol 8-12 1.0 M LPC/NM 1a-b 5, 13 (+)CF-CF(-) 20 mol equiv. Producta Entry Olefin Ì C₈H₁₇ 1 8 (R¹=H, R²=C₄H₉, R³=H) 5 (76%) C8H17 2 13 (47%) 9 (R¹=H, R², R³=C₂H₅, *cis*) C_8H_{17} 3 10 (R¹=H, R², R³=C₂H₅, *trans*) 13 (30%) C₈H C₈H₁₇ 4 5 (17%) 11 (R¹, R²=C₂H₅, R³=H) 14 (0%) C₈H₁₇ C_8H_{17} 5 13 (3%) **12** (\mathbb{R}^1 , \mathbb{R}^2 =CH₃, \mathbb{R}^3 =C₂H₅) 15 (0%)

^a Determined by GC-MS.



Scheme 9. Possible reaction mechanism of the electron transfer-induced olefin cross-metathesis between 4-phenyl-1-butene (16) and 1-methoxydec-1-ene (1a-b).



Scheme 10. Oxidative cleavage of (4-methoxybut-3-en-1-yl)benzene (17a-b).

through electrolysis (Scheme 10). A possible reaction mechanism for the formation of **18** is depicted below (Scheme 11) [29,30]. Also of note, a small amount of nonanal (**19**), the oxidative cleavage product of **1a-b**, was detected in the product mixtures of all electron transfer-induced olefin cross-metatheses (Scheme 12). When monitoring the application of electricity, the yields of **5**, **17a-b**, **18**, and **19** were clearly detected for each stage (Fig. 1). Based on these results, there looked to be two pathways for **17**^{*+}, gener-



Scheme 11. Possible reaction mechanism for the oxidative cleavage of (4-methoxybut-3-en-1-yl)benzene (17a-b).



Scheme 12. Oxidative cleavage of 1-methoxydec-1-ene (1a-b).

ated from the four-membered cyclic intermediate: one-electron reduction to **17a-b** and oxidative cleavage to **18**. The oxidation potential of **17a-b** ($E_p^{\text{ox}} = 1.39 \text{ V}$ vs. Ag/AgCl) is significantly higher than **1a-b** ($E_p^{\text{ox}} = 1.33 \text{ V}$ vs. Ag/AgCl), rendering the oxidative cleavage of **1a-b** to be slightly faster than **17a-b**. The overall reaction (Scheme 13) and possible reaction mechanism (Scheme 14) of the electron transfer-induced olefin cross-metathesis are depicted below.

Finally, the anodic oxidation of **1a-b** in the presence of excess 4-(but-3-enyl)anisole (**20**), a *para*-alkoxy substituted version of **16**, was performed to confirm the formation of a four-membered cyclic intermediate. This reaction led to a [2+2] cycloadduct **21a-c** product in good yield as a diastereomeric mixture and produced a small amount of the olefin cross-metathesis product **5** (Scheme 15). Comparatively, when **2** was employed in place of **20**, no olefin cross-metathesis occurred (Scheme 4). These observations suggest that the alkoxyphenyl group functioned as an electron-donating group



Fig. 1. Electron transfer-induced olefin cross-metathesis monitoring between 4-phenyl-1-butene (16) and 1-methoxydec-1-ene (1a-b).

to complete the olefin cross-coupling reaction effectively, which supported the formation of a four-membered cyclic intermediate. However, due to the extended distance between the alkoxyphenyl group and the cyclobutyl moiety, an olefin cross-metathesis was also possible. To enhance this effect, the distance between the



Scheme 13. Overall electron transfer-induced olefin cross-metathesis between 4-phenyl-1-butene (16) and 1-methoxydec-1-ene (1a-b).



Scheme 14. Possible overall reaction mechanism for the electron transfer-induced olefin cross-metathesis between 4-phenyl-1-butene (16) and 1-methoxydec-1-ene (1a-b).



Scheme 15. Anodic oxidation of 1-methoxydec-1-ene (1a-b) with 4-(but-3-enyl)anisole (20).



Scheme 16. Anodic oxidation of 1-methoxydec-1-ene (1a-b) with 4-(pent-4-envl)anisole (22).

alkoxyphenyl group and the cyclobutyl moiety was increased further. Alkene 4-(pent-4-enyl)anisole (22) was used in place of 20, affording the corresponding [2+2] cycloadduct 23a-c in good yield as a diastereomeric mixture and produced an increased amount of 5 (Scheme 16). This result was likely due to the slowed intramolecular electron transfer from the alkoxyphenyl group to the cyclobutyl moiety through the extra distance, which gave heed to the olefin cross-metathesis reaction.

5. Conclusion

In this study, we demonstrated the formation of an electron transfer-induced four-membered cyclic intermediate between a radical cation of an enol ether and an unactivated olefin, leading toward either a cross-coupling or a cross-metathesis. The synthetic outcomes of the four-membered cyclic intermediates mirrored the efficiencies of the intramolecular electron transfer, which was influenced by the alkoxy group on the phenyl ring.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.electacta.2010.10.042.

General information, experimental details, characterization data, and copies of ¹H NMR and ¹³C NMR spectra of new compound are presented here.

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