Oxidative intramolecular cyclization reactions of cinnamyl ethers mediated by cerium(IV) ammonium nitrate (CAN): a stereoselective synthesis of 3,4-*trans*-disubstituted tetrahydrofuran derivatives

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Dedicated with best wishes to Professor Keiichiro Fukumoto on the occasion of his 70th birthday

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Abstract

Various alkoxy-cinnamyl cinnamyl ethers and an alkoxy-cinnamyl prenyl ether underwent stereoselective oxidative cyclizations on treatment with a methanolic solution of cerium(IV) ammonium nitrate to afford 3,4-*trans*- disubstituted tetrahydrofuran derivatives. Different products were obtained under aerobic and anaerobic conditions.

Keywords: Cerium(IV) ammonium nitrate, one-electron oxidation, radical cyclization, tetrahydrofurans, cinnamyl ethers

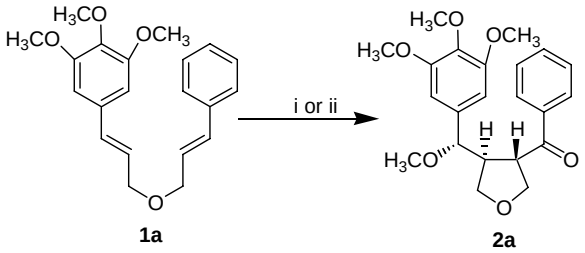
Introduction

Carbon–carbon bond formation is pivotal to organic synthesis and considerable efforts have been directed towards developing newer methods for the same. The various strategies for carbon–carbon bond formation can be broadly classified as involving polar, pericyclic, or radical reactions. The radical reactions have gained popularity only recently. This dramatic change may be attributed to the demonstration by Stork that the controlled generation and addition of vinyl radicals to olefins constitutes a powerful method for carbocyclic ring construction.[1] Today, the radical methodology assumes prime significance as evidenced by the multitude of syntheses based on a rational application of the method in their key steps.[2] In this context, the oxidative generation of radicals using single-electron-transfer reagents has received ample attention.[3] Among these, intramolecular reactions mediated by manganese(III) acetate have invoked much

interest.[4] In spite of the superiority of cerium(IV) ammonium nitrate (CAN) over manganese(III) acetate in several respects,[5] its potential in promoting oxidative intramolecular annulations has not been exploited successfully.[6] Our explorations of the intramolecular cyclization reactions of alkoxycinnamyl ethers mediated by CAN have afforded a simple route for the stereoselective construction of 3,4-*trans*- disubstituted tetrahydrofurans, and our preliminary results have been published.[7] The results of our expanded investigations on this topic are presented in this paper.

Results and Discussion

Our studies started with the reaction of the 3,4,5-trimethoxycinnamyl cinnamyl ether **1a** with a methanolic solution of CAN.* The reaction afforded the corresponding 3,4-*trans*- disubstituted tetrahydrofuran derivative, **2a,** in moderate yield. A useful increase in the overall yield was noticed when the reaction was done under an atmosphere of oxygen (Scheme 1).

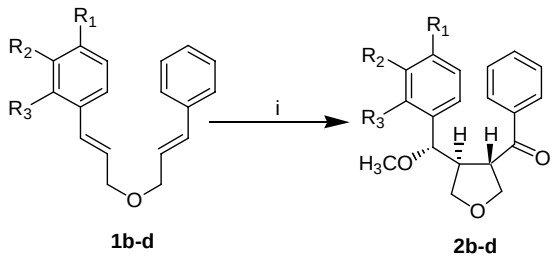


Scheme 1. (i) CAN, MeOH, 0 °C, Argon, 30 min, 47%. (ii) CAN, MeOH, 0 °C, 30 min, oxygen, 56%.

The IR spectrum of **2a** showed a strong absorption at 1664 cm^{-1} indicating the benzoyl group. In the ^{1}H-NMR spectrum, one of the β-protons on the tetrahydrofuran ring displayed a characteristic multiplet centered at δ 3.08. A singlet at δ 3.19 was attributed to the benzylic methoxy group. The aromatic methoxy protons afforded singlets at δ 3.77, 3.74 and 3.72. The multiplet centered at δ 3.82 was attributed to two of the four methylene protons on the tetrahydrofuran ring. The rest of the two α-methylene protons, the other β-methine proton and the benzylic proton together afforded another multiplet between δ 4.23–3.92. In the ^{13}C-NMR spectrum, a signal at δ 198.9 was typical of the benzoyl group. The characteristic β-carbons were discernible at δ 50.67 and 49.1, and the benzylic carbon resonance was observable at δ85.3. The compound also gave satisfactory microanalytical data. Final proof for the structure and stereochemistry of the product was obtained from single crystal X-ray analysis.[7]

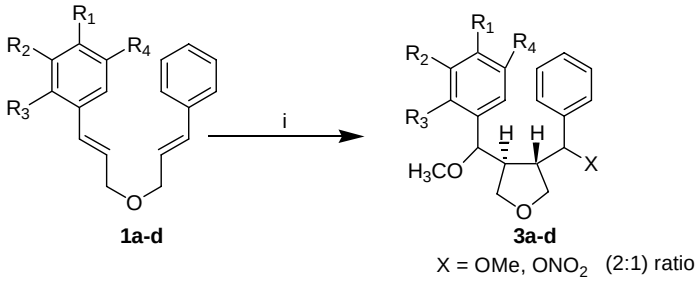
The reaction was found to be general and extendable to other similar substrates (Scheme 2).

* Cinnamyl is 3-phenyl- *E*-prop-2-enyl; the positions of the substituents are given for substitution in the phenyl ring.



Scheme 2. (i) CAN, MeOH, oxygen, 0 °C, 30 min. (**b**), R_1, R_2 = H, R_3 = OCH_3; yield (**2b**), 42%. (**c**) R_1 = OCH_3, R_2 R_3 = H; yield (**2c**), 46%. (**d**) R_1, R_2 = OCH_3, R_3 = H; yield (**2d**), 36%.

It is obvious that oxygen plays a crucial role in these reactions and this aroused our curiosity to explore the outcome of the reaction in an oxygen-free atmosphere. The reaction of 2-methoxycinnamyl cinnamyl ether **1b** with CAN in methanol under scrupulously oxygen- free conditions furnished the corresponding tetrahydrofuran derivative **3b** as a 2:1 mixture of methoxy and nitrato derivatives in 80% overall yield. The reaction was found to be general, as is shown in Scheme 3.

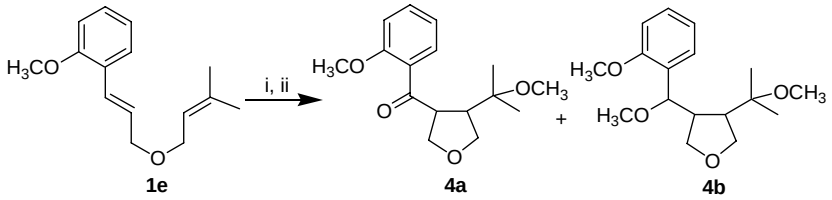


Scheme 3. (i) CAN, MeOH, argon, R.T., 90 min, 80%. (**a**) R_3 = H, R_1, R_2, R_4 = OCH_3; yield (**3a**), 87%. (**b**) R_1, R_2, R_4 = H, R_3 = OCH_3, yield (**3b**), 80%. (**c**) R_1 = OCH_3, R_2, R_3, R_4 = H, yield (**3c**), 78%. (**d**) R_1, R_2 = OCH_3, R_3, R_4 = H; yield (**3d**), 76%.

The ratio of products was determined from the ^{1}H NMR spectrum of the mixture, in which the benzylic proton adjacent to the methoxy and nitrato groups appeared at δ 4.23 and δ 5.43 respectively. In the carbon spectrum, the benzylic carbon adjacent to the methoxy group was discernible at δ 84.6 whereas the one adjacent to the nitrato moiety was visible at δ 89.1. Catalytic hydrogenation of the mixtures effected the selective conversion of the nitrato derivatives to the corresponding carbinols. These carbinols were methylated using methyl iodide to furnish the methoxy derivatives which were found to be analytically pure. The ring stereochemistry is assumed to be *trans*, by analogy to the earlier examples, whereas the relative disposition of the methoxy and nitrato/methoxy groups is unknown.

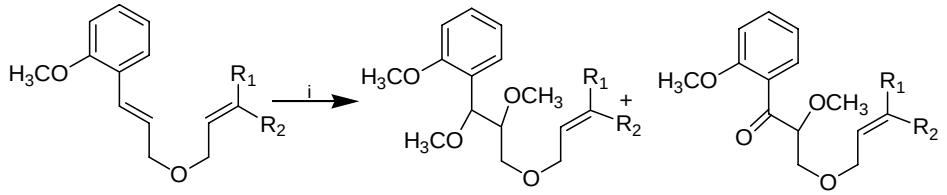
In the next phase of our study, we focused on the use of other alkenyl tethers in conjunction with the alkoxystyrene moiety, to identify the scope of the key reaction. In an initial experiment, the reaction of 2-methoxycinnamyl prenyl ether **1e** with a methanolic solution of CAN under an

oxygen atmosphere resulted in the formation of the tetrahydrofuran derivative **4a**, of unknown stereochemistry, in moderate yield. Under anaerobic conditions, the dimethoxy derivative, **4b**, of unknown stereochemistry was isolated in 71% yield (Scheme 4).



Scheme 4. (i) CAN, MeOH, oxygen, 0 °C, 30 min, yield of **4a**, 35%. (ii) CAN, MeOH, argon, RT, 30 min, yield of **4b**, 71%.

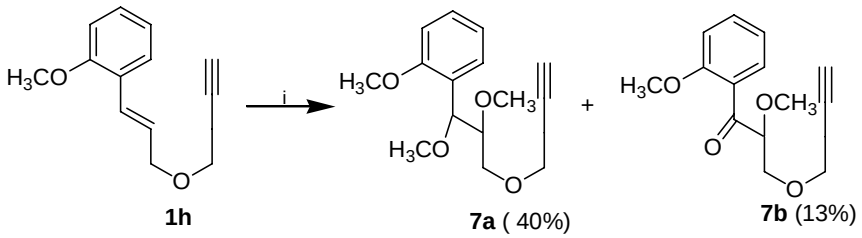
Attempts to extend the reaction to the corresponding crotyl- and allyl- tethered ethers were unsuccessful. In these cases, the expected intramolecular reaction did not occur. The results obtained are presented in Scheme 5. A plausible explanation for the difference in reactivity in these cases may be ascribed to the lesser stability of the secondary radicals formed after the initial cyclization.



1f, R_1 = H, R_2 = CH_3 **5a,** R_1 = H, R_2 = CH_3 (35%) **5b,** R_1 = H, R_2 = CH_3 (17%)
1g, R_1 = H, R_2 = H **6a,** R_1 = H, R_2 = H (46%) **6b,** R_1 = H, R_2 = H (11%)

Scheme 5. (i) CAN, MeOH, RT, 30 min.

In an analogous reaction, 2-methoxycinnamyl propargyl ether also afforded the uncyclized products **7a** and **7b** as shown in Scheme 6. The relative stereochemistries of compounds **5a**, **6a** and **7a** are unknown.



Scheme 6. (i) CAN, MeOH, RT, 30 min.

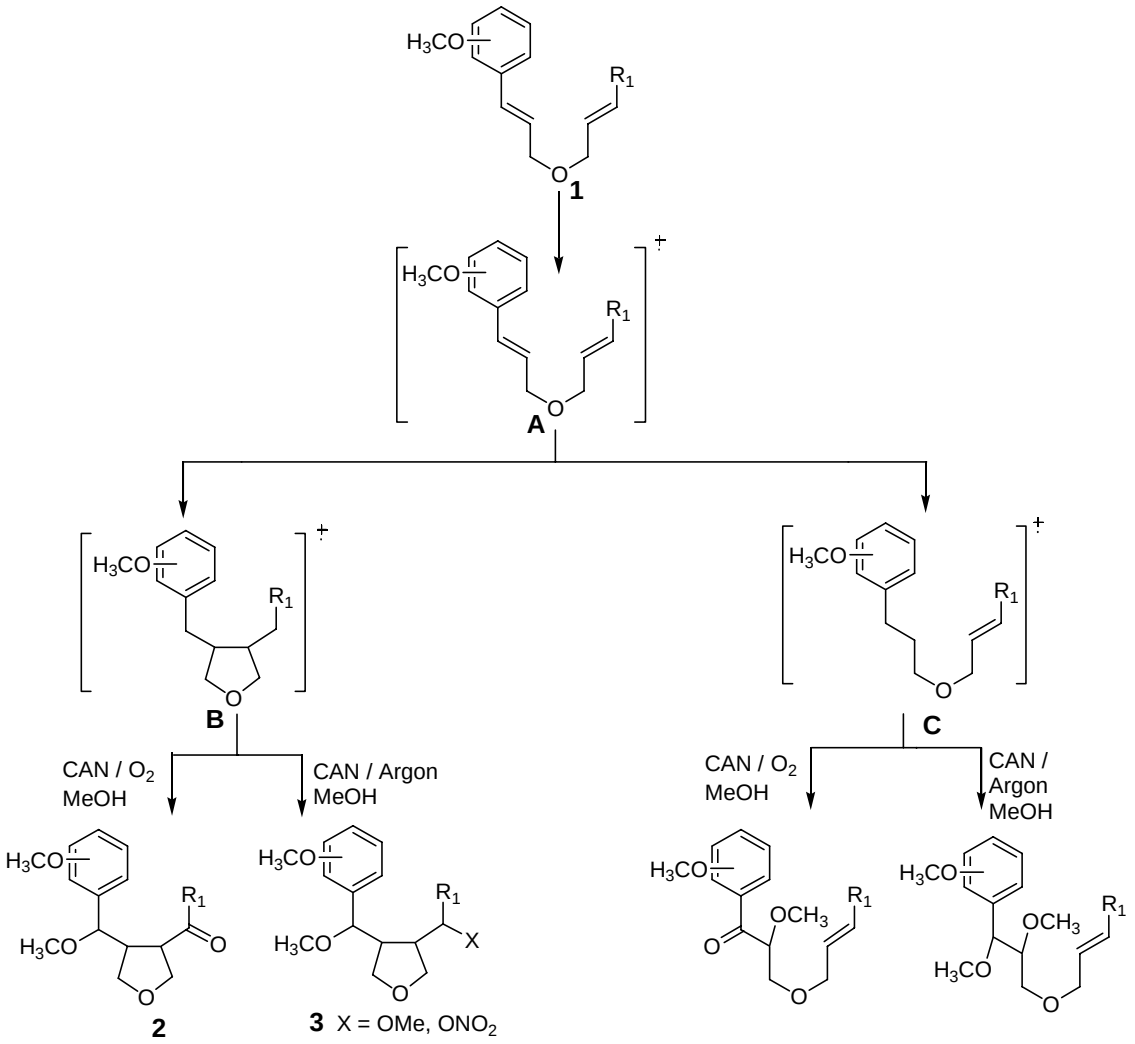
A mechanistic rationalization for the formation of the different products can be given as shown in Scheme 7. Conceivably, the initial event involves the oxidative generation of the radical cation **A** which can exist in equilibrium with the cyclic isomer **B**. In the case of cinnamyl and prenyl ethers, the formation of the stable secondary radical drives the equilibrium in favor of **B**. The cationic site is quenched by the addition of methanol whereas the radical center is prone to two transformations. Under an oxygen atmosphere, it is quenched by molecular oxygen affording the keto product. Such a transformation has precedent in our earlier work.[8] On the other hand, under argon, the radical may be oxidized by excess of CAN to the cation with subsequent addition of methanol, to afford the dimethoxy product. Alternatively, ligand-transfer from CAN will lead to the nitrato derivative.[9] In the case of crotyl, allyl and propargyl ethers, the formation of uncyclized products may be attributed to the formation of a less stable secondary radical after the initial cyclization.

Conclusions

The results of our investigations constitute a novel and efficient route for the construction of 3,4-*trans*-dibenzyltetrahydrofuran skeletons. Of particular appeal is the fact that substituted tetrahydrofurans are widely encountered in several natural products of biological interest including lignans and polyether antibiotics, and the methodologies uncovered might lead to facile syntheses of such compounds.

Experimental Section

General Procedures. All reactions were in oven-dried glassware with magnetic stirring unless otherwise noted. Solvents were dried or distilled before use as specified. NMR spectra were recorded at 300 MHz (^{1}H) and 75 MHz (^{13}C), respectively, on a Bruker Avance DPX-300 MHz FT-NMR spectrometer for samples dissolved in $CDCl_3$–CCl_4 mixtures (7/3, v/v). Chemical shifts were reported in δ (ppm) relative to TMS (^{1}H NMR) or $CDCl_3$ (^{13}C NMR) as internal standards. IR spectra were recorded in Bomem MB Series FT-IR spectrophotometer. High-resolution mass spectra were obtained using an Auto Spec. M mass spectrometer. Elemental analyses were performed on a Perkin Elmer-2400 Elemental Analyzer. Melting points were recorded on Mel-Temp-II Laboratory Devices, USA, and are uncorrected. All reactions were monitored by thin layer chromatography (TLC) on silica, with visualization by UV and/or by exposure to iodine vapor. Chromatography refers to open-column chromatography on silica gel (100–200 mesh).



Scheme 7

Preparation of cinnamyl alcohols

4-Methoxycinnamyl alcohol, 3,4-dimethoxycinnamyl alcohol, 3,4,5-trimethoxycinnamyl alcohol and 4-chlorocinnamyl alcohol were prepared by lithium aluminum hydride–aluminum chloride reduction of the corresponding α,β-unsaturated esters according to a reported procedure.[10] 2-Methoxycinnamyl alcohol was prepared by sodium borohydride reduction of 2-methoxycinnamaldehyde at 5 °C.

Preparation of alkoxycinnamyl alkenyl ethers

Alkoxycinnamyl alkenyl ethers were prepared according to a reported procedure.[10] To a solution of alkoxycinnamyl alcohol (1 mmol) and the alkenyl bromide (1.5 mmol) in 20 mL dichloromethane was added tetra-n-butyl ammonium bromide (TBAB) (100 mg) followed by 5 mL of 50% aqueous sodium hydroxide. The reaction mixture was stirred at room temperature until complete consumption of cinnamyl alcohol was indicated by TLC. The organic layer was separated by repeated extraction with dichloromethane (3x15 mL), and washed with water, then

brine, and dried over anhydrous sodium sulfate. After filtration, and removal of volatile materials, the residue was purified by silica gel column chromatography using appropriate hexane–ethyl acetate solvent mixtures to afford the pure product.

General procedure for CAN-mediated oxidative cyclization of cinnamyl ethers

A solution of CAN (2.3 mmol) in methanol (15 mL) was added dropwise to a solution of alkoxycinnamyl alkenyl ether (1 mmol) in methanol (10 mL) stirred at room temperature, then left until complete consumption of the starting material was confirmed by TLC. It was then diluted with water (50 mL) and extracted with dichloromethane (3x15 mL). The combined organic extract was washed with water, brine and dried over anhydrous sodium sulfate. After the removal of solvent on a rotary evaporator, the residue was subjected to column chromatography on silica gel. Elution with petroleum–ethyl acetate furnished the pure products.

General procedure for CAN-mediated oxidative cyclization of cinnamyl ethers under an oxygen atmosphere

A solution of CAN (2.3 mmol) in methanol (15 mL), saturated with oxygen, was added dropwise to an oxygenated solution of alkoxycinnamyl ether (1 mmol) in methanol (10 mL) stirred at 5 °C. Oxygen was continuously passed through the reaction mixture. On completion of the reaction, the mixture was processed by the general procedure. The residue was purified by silica gel column chromatography with hexane–ethyl acetate mixtures to afford the pure products.

General procedure for CAN-mediated oxidative cyclization of cinnamyl ethers under an argon atmosphere

A deoxygenated solution of CAN (2.3 mmol) in methanol (15 mL) was added dropwise to a deoxygenated solution of alkoxycinnamyl ether (1 mmol) in methanol (10 mL) stirred at ambient temperature. Argon, thoroughly deoxygenated by passing through Fieser's solution, was continuously bubbled through the reaction mixture. On completion of the reaction, the mixture was processed as described above, and the residue purified by silica gel column chromatography with hexane–ethyl acetate mixtures.

(3,4,5-Trimethoxycinnamyl) cinnamyl ether (1a). Prepared according to the general procedure. Colorless viscous liquid; yield 96%. IR/cm^{-1} (thin film): 3009, 2942, 2840, 1580, 1506, 1479, 1425, 1344, 1249, 1135, 1007. ^{1}H NMR: 7.39–7.20 (m, 5H), 6.65–6.47 (m, 4H), 6.35–6.17 (m, 2H), 4.19–4.18 (m, 4H), 3.85 (s, 6H), 3.83 (s, 3H). ^{13}C NMR: 153.2, 136.6, 132.4, 128.5, 127.6, 126.4, 125.4, 103.6, 70.7, 70.5, 60.7, 55.9.

3-Benzoyl-4-[(methoxy)(3,4,5-trimethoxyphenyl)]methyltetrahydrofuran (2a). Colorless crystalline solid, m.p. 115–117 °C (from dichloromethane–hexane). IR/cm^{-1} (KBr): 2940, 2845, 1720, 1664, 1589, 1496, 1458, 1328, 1234, 1128, 1085, 1004, 917. ^{1}H NMR: 7.54–7.46 (m, 3H), 7.35–7.30 (m, 2H), 6.42 (s, 2H), 4.23–3.92 (m, 4H), 3.86–3.79 (m, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.19 (s, 3H), 3.10–3.06 (m, 1H). ^{13}C NMR: 198.9, 153.2, 136.4, 135.2, 133.0, 128.3, 127.9,

104.3, 85.3, 71.3, 71.2, 60.5, 56.7, 55.9, 50.6, 49.1. Analysis; Calcd for $C_{22}H_{26}O_6$ C, 68.38; H, 6.78. Found: C, 68.00; H, 6.75%.

(2-Methoxycinnamyl) cinnamyl ether (1b). Prepared according to the general procedure. Yield: 99%. Colorless viscous liquid. IR/cm^{-1} (thin film): 3024, 2943, 2837, 1595, 1489, 1457, 1351, 1295, 1295, 1114. ^{1}H NMR: 7.44–7.19 (m, 7H), 6.95–6.81 (m, 3H), 6.58 (d, J = 15 Hz, 1H), 6.33–6.27 (m, 2H), 4.20–4.17 (m, 4H), 3.82 (s, 3H). ^{13}C NMR: 156.6, 136.7, 132.3, 128.5, 128.4, 127.6, 127.4, 126.9, 126.5, 126.4, 126.1, 125.7, 120.5, 110.6, 71.1, 70.4, 55.2.

3-Benzoyl-4-[(methoxy)(2-methoxyphenyl)]methyltetrahydrofuran (2b). Colorless viscous liquid. IR/cm^{-1} (thin film): 3068, 2943, 2881, 2843, 1682, 1595, 1489, 1357, 1283, 1239, 1108, 1083, 1026, 884. ^{1}H NMR: 7.58–7.44 (m, 3H), 7.27 (t, J = 8.1 Hz, 3H), 7.17–7.11 (m, 1H), 6.91 (t, J = 7.3 Hz, 1H), 6.67 (d, J = 8.1 Hz, 1H), 4.66 (d, J = 8.0 Hz, 1H), 4.16–3.81 (m, 5H), 3.69 (s, 3H), 3.18 (s, 3H), 3.09 (bs, 1H). ^{13}C NMR: 199.1, 157.1, 136.6, 132.7, 128.6, 128.4, 128.2, 128.0, 127.3, 120.9, 110.2, 77.2, 71.7, 70.8, 56.7, 55.0, 49.8, 48.6.

(4-Methoxycinnamyl) cinnamyl ether (1c). Prepared by the general procedure. Yield: 86%. Colorless viscous liquid. IR/cm^{-1} (thin film): 3022, 2921, 2847, 1721, 1674, 1607, 1506, 1458, 1256, 1175, 1040. ^{1}H NMR: 7.38–7.18 (m, 7H), 6.82 (d, J = 8.6 Hz, 2H), 6.61 (d, J = 16.7 Hz, 1H), 6.55 (d, J = 16.6 Hz, 1H), 6.34–6.11 (m, 2H), 4.18–4.15 (m, 4H), 3.78 (s, 3H). ^{13}C NMR: 159.2, 136.6, 132.3, 132.2, 129.3, 128.4, 127.5, 126.0, 123.6, 70.8, 70.4, 55.0.

3-Benzoyl-4-[(methoxy)(4-methoxyphenyl)]methyltetrahydrofuran (2c). Colorless viscous liquid. IR (thin film): 3063, 2928, 2854, 1681, 1600, 1512, 1458, 1182, 1081cm^{-1}. ^{1}H NMR: 7.52–7.43 (m, 3H), 7.32–7.27 (uneven triplet, J_1 = 7.2 Hz, J_2 = 7.0 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 6.74 (d, J = 7.8 Hz, 2H), 4.16–3.76 (m, 6H), 3.72 (s, 3H), 3.15 (s, 3H), 3.05 (m, 1H). ^{13}C NMR: 199.0, 159.4, 136.4, 132.8, 128.5, 128.2, 128.0, 113.8, 84.3, 71.12, 56.4, 54.9, 50.5, 49.1. HRMS Calcd. for $C_{20}H_{22}O_4$; 326.15181: Found; 326.15183.

(3,4-Dimethoxycinnamyl) cinnamyl ether (1d). Prepared by the general procedure. Yield: 51%. Colorless viscous liquid. IR (thin film): 3022, 3002, 2935, 2840, 1681, 1600, 1505, 1465, 1265, 1134, 1006cm^{-1}. ^{1}H NMR: 7.38–7.21 (m, 6H), 6.93–6.76 (m, 2H), 6.62 (d, J = 16.1 Hz, 1H), 6.55 (d, J = 16.8 Hz, 1H), 6.34–6.12 (m, 2H). 4.17 (s, 4H), 3.86 (s, 6H). ^{13}C NMR: 148.9, 136.6, 132.4, 129.7, 128.5, 127.6, 126.4, 126.0, 123.9, 119.7, 111.1, 108.9, 70.8, 70.6, 55.7, 55.7.

3-Benzoyl-4-[(methoxy)(3,4-dimethoxyphenyl)]methyltetrahydrofuran (2d). Colorless viscous liquid. IR (thin film): 3198, 2935, 2867, 1681, 1607, 1519, 1452, 1283, 1034. ^{1}H NMR: 7.49–7.44 (m, 3H), 7.32–7.27 (m, 2H), 6.78–6.64 (m, 3H), 4.23–3.93 (m, 4H), 3.79 (s, 3H), 3.75 (s, 3H), 3.72–3.67 (m, 2H), 3.16 (s, 3H), 3.10–3.05 (m, 1H) ^{13}C NMR: 199.1, 149.4, 148.9, 142.0, 132.8, 128.4, 128.2, 128.0, 120.3, 110.5, 109.7, 84.9, 71.3, 71.1, 56.5, 55.6, 50.6, 49.2.

3-[(Methoxy)(3,4,5-trimethoxyphenyl)]methyl-4-[(methoxy)(phenyl)]methyltetrahydrofuran (3a); 3-[(Methoxy)(3,4,5-trimethoxyphenyl)]methyl-4-[(nitrato)(phenyl)]methyltetrahydrofuran (3a'). Yield: 87%. Colorless viscous liquid. IR (thin film): 3062, 2943, 2850, 1633, 1594, 1494, 1421, 1405, 1232, 1119, 1032. ^{1}H NMR: 7.28–6.92 (m, 7H), 5.30 (d, J = 9.5 Hz, 0.33H), 4.54 (d, J = 9.3 Hz, 0.66H), 4.33 (uneven triplet, J_1 = 7.6 Hz, J_2 = 7.2 Hz, 1H), 4.02–3.72 (m, 12H), 3.62 (uneven triplet, J_1 = 9.7 Hz, J_2 = 7.8 Hz, 1H), 3.58 (s, 1H), 3.51 (s, 2H), 2.98 (s, 2H), 2.26–2.14

(m, 2H). ^{13}C NMR: 152.6, 151.6, 147.7, 134.6, 128.5, 128.3, 128.2, 127.0, 126.6, 125.9, 125.6, 104.3, 103.3, 85.8, 81.8, 71.9, 71.5, 69.9, 69.9, 60.6, 60.1, 59.0, 57.4, 56.8, 55.9, 55.8, 55.7, 50.2, 46.6, 46.5, 46.3, 46.1.

3-[(Methoxy)(2-methoxyphenyl)]methyl-4[(methoxy)(phenyl)]methyltetrahydrofuran (3b); 3-[(methoxy)(2-methoxyphenyl)]methyl-4[(nitrato)(phenyl)]methyltetrahydrofuran (3b'). Colorless viscous liquid. IR (thin film): 2975, 2935, 2867, 2813, 2362, 1634, 1600, 1458, 1357, 1276, 1027. ^{1}H NMR: 7.31–6.79 (m, 9H), 5.43 (d, *J* = 9.3 Hz, 0.33 H), 4.23 (d, *J* = 6.8 Hz, 0.66H), 4.15 (d, *J* = 6.0 Hz, 0.33H), 3.93–3.63 (m, 7.66H), 3.07 (s, 3H), 3.06 (s, 2H), 2.64 (bs, 0.66H), 2.36–2.28 (m, 1.33H). ^{13}C NMR: 156.9, 156.6, 140.3, 136.3, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.2, 126.9, 126.9, 126.6, 126.2, 120.6, 120.6, 109.9, 109.8, 86.1, 84.6, 77.3, 76.7, 70.2, 70.0, 69.4, 56.6, 56.5, 56.4, 54.7, 54.7, 47.9, 46.9, 46.6, 44.9. Analysis; Calcd for $C_{21}H_{26}O_4$ C, 73.66; H, 7.65. Found: C, 73.39; H, 7.71%.

3-[(Methoxy)(4-methoxyphenyl)]methyl-4-[(methoxy)(phenyl)]methyltetrahydrofuran (3c); 3-[(Methoxy)(4-methoxyphenyl)]methyl-4-[(nitrato)(phenyl)]methyltetrahydrofuran (3c'). Colorless viscous liquid. IR (thin film): 2980, 2937, 2868, 1635, 1610, 1510, 1454, 1244, 1076, 1032. ^{1}H NMR: 7.29–6.72 (m, 9H), 5.30 (d, *J* = 9.3 Hz, 0.33H), 3.93–3.77 (m, 6.66H), 3.65–3.50 (m, 2H), 3.06 (s, 2H), 3.03 (s, 3H), 2.41–2.38 (m, 0.66H), 2.16–2.15 (m, 1.33H). ^{13}C NMR: 159.1, 158.9, 140.2, 136.3, 132.1, 131.3, 128.9, 128.7, 128.1, 127.9, 127.6, 127.4, 126.8, 126.7, 113.8, 113.5, 85.8, 84.5, 84.3, 83.5, 70.2, 69.9, 69.8, 69.7, 56.6, 56.4, 56.3, 56.2, 54.9, 48.6, 48.5, 48.3, 48.2. HRMS: calcd. for $C_{21}H_{26}O_4$ (**3c**): 342.1831, Found: 342.1839.

3-[(Methoxy)(3,4-dimethoxyphenyl)]methyl-4-[(methoxy)(phenyl)]methyltetrahydrofuran (3d); 3-[(Methoxy)(3,4-dimethoxyphenyl)]methyl-4-[(nitrato)(phenyl)]methyltetrahydrofuran (3d'). Colorless viscous liquid. IR (thin film): 2982, 2935, 2861, 2827, 1638, 1600, 1512, 1458, 1263, 1088, 1034. ^{1}H NMR: 7.31–6.33 (m, 8H), 5.31 (d, *J* = 9.7 Hz, 0.33H), 3.92–3.53 (m, 11.66H), 3.05 (s, 3H), 3.04 (s, 2H), 2.16–2.09 (m, 2H). ^{13}C NMR: 149.1, 148.5, 140.0, 132.7, 128.7, 128.6, 128.4, 128.0, 127.7, 127.0, 126.9, 126.8, 119.8, 119.6, 110.7, 110.3, 108.7, 108.4, 85.9, 84.8, 84.7, 70.3, 70.2, 69.8, 69.6, 56.6, 56,5, 55.7, 55.3, 48.8, 48.6, 48.5, 48.4. HRMS Calcd. for $C_{22}H_{28}O_5$ (**3d**): 372.1936, Found: 372.1946.

2-Methoxycinnamyl prenyl ether (1e). Prepared according to the general procedure. Yield: 78%. Colorless viscous liquid. IR (thin film): 2969, 2928, 2847, 1600, 1506, 1472, 1384, 1256, 1135, 1067. ^{1}H NMR: 7.42 (d, *J* = 7.41 Hz, 1H), 7.21–7.16 (m, 1H), 6.92–6.82 (m, 3H), 6.31–6.26 (m, 1H), 5.39–5.35 (m, 1H), 4.12 (d, *J* = 6.13 Hz, 2H), 3.99 (d, *J* = 6.7 Hz, 2H), 3.83 (s, 3H), 1.75 (s, 3H), 1.68 (s, 3H). ^{13}C NMR: 156.4, 136.4, 128.3, 127.2, 126.6, 125.5, 121.1, 120.4, 110.5, 70.8, 66.1, 55.0, 25.6, 17.8.

3-(2-Methoxybenzoyl)-4-[(1-methoxy-1-methyl)]ethyltetrahydrofuran (4a). Colorless viscous liquid. IR (thin film): 2979, 2939, 2866, 2844, 1675, 1591, 1484, 1462, 1282, 1243, 1018. ^{1}H NMR: 7.59–7.56 (m, 1H), 7.46–7.41 (m, 1H), 7.01–6.93 (m, 2H) 4.15–3.95 (m, 4H), 3.90 (s, 3H), 3.82–3.75 (m, 1H), 3.12 (s, 3H), 3.09–3.07 (m, 1H), 1.09 (s, 6H). ^{13}C NMR: 202.9, 157.9, 133.5, 133.2, 130.4, 120.9, 111.3, 74.7, 72.6, 70.1, 55.4, 53.1, 51.5, 49.0, 23.3, 22.7. HRMS: Calcd. for $C_{16}H_{22}O_4$: 278.1518; Found: 278.1516.

3-[(Methoxy)(2-methoxyphenyl)methyl-4-[(1-methoxy-1-methyl)]ethyltetrahydrofuran (4b). Colorless viscous liquid. IR (thin film): 2975, 2935, 2874, 2834, 1607, 1499, 1479, 1243, 1101. ^{1}H NMR: 7.34–6.94 (m, 3H), 6.84 (d, J = 8.1 Hz, 1H), 4.61 (d, J = 5.6 Hz, 1H), 3.82–3.79 (m, 2H), 3.78 (s, 3H), 3.56–3.48 (m, 1H), 3.25–3.23 (m, 1H), 3.22 (s, 3H), 3.07 (s, 3H), 2.39–2.30 (m, 2H), 1.01 (s, 3H), 0.94 (s, 3H). ^{13}C NMR: 156.8, 128.1, 127.9, 126.5, 120.4, 109.9, 78.37, 75.6, 69.4, 69.3, 56.9, 54.8, 49.7, 48.6, 46.6, 22.3, 21.4.

2-Methoxycinnamyl crotyl ether (2-Methoxycinnamyl 3-methylbut-2-enyl ether) (1f). Prepared by the general procedure. Yield: 84%. Colorless viscous liquid. IR (thin film): 3016, 2948, 2840, 1607, 1506, 1458, 1290, 1249, 1108, 1047. ^{1}H NMR: 7.43–7.41 (m, 1H), 7.25–7.16 (m, 1H), 6.91–6.82 (m, 3H), 6.32–6.23 (m, 1H), 5.78–5.55 (m, 2H), 4.15–4.07 (m, 2H), 3.94 (d, J = 5.9 Hz, 2H), 3.83 (s, 3H), 1.73–1.66 (m, 3H). ^{13}C NMR: 156.6, 129.3, 128.5, 127.6, 127.4, 127.0, 126.9, 126.6, 120.6, 110.6, 70.9, 70.6, 17.7.

3-(2-Methoxyphenyl)-2,3-dimethoxy-1-[but-2-enyl-1-oxy]propane (5a). Colorless viscous liquid. IR (thin film): 2928, 2827 1600, 1492, 1465, 1357, 1283, 1243, 1094, 1027. ^{1}H NMR: 7.40–7.38 (m, 1H), 7.27–7.21 (m, 1H), 6.96 (t, J = 7.4 Hz, 1H), 6.84 (d, J = 8.1 Hz, 1H), 5.68–5.47 (m, 2H), 4.69 (d, J = 3.9 Hz, 1H), 3.86 (d, J = 3.3 Hz, 2H), 3.82 (s, 3H), 3.57–3.43 (m, 3H), 3.26 (s, 3H), 3.25 (s, 3H), 1.69 (d, J = 5.1 Hz, 3H). ^{13}C NMR: 157.0, 128.7,128.2, 128.1, 127.7, 120.4, 109.9, 82.5, 77.5, 71.7, 69.9, 59.6, 57.2, 55.1, 17.6.

2-(2-Methoxybenzoyl)-2-methoxy-1-(but-2-enyl-1-oxy)ethane (5b). Colorless viscous liquid. IR (thin film): 2943, 2856, 1682, 1595, 1482, 1463, 1245, 1108, 964. ^{1}H NMR: 7.64 (d, J = 6.6 Hz, 1H), 7.45 (t, J = 7.0 Hz, 1H), 7.02–6.94 (m, 2H), 5.65–5.43 (m, 2H), 4.89–4.87 (m, 1H), 3.91 (bs, 5H), 3.69 (d, J = 10.4 Hz, 1H), 3.55 (dd, J_1 = 6.1 Hz, J_2 = 10.2 Hz, 1H), 3.47 (s, 3H), 1.65 (d, J = 5.5 Hz, 3H). ^{13}C NMR: 199.8, 157.9, 133.5, 130.5, 129.2, 127.3, 120.9, 111.2, 86.2, 71.9, 70.1, 66.6, 58.2, 55.4, 17.6.

2-Methoxycinnamyl allyl ether (1g). Prepared by the general procedure. Yield: 79%. Colorless viscous liquid. IR (thin film): 3076, 3022, 2948, 2847, 1600, 1499, 1458, 1249, 1115. ^{1}H NMR: 7.42 (d, J = 7.3 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 6.92–6.82 (m, 3H), 6.33–6.23 (m, 1H), 5.95 (ddd, J_1 = 5.4 Hz, J_2 = 10.7 Hz, J_3 = 16.2 Hz, 1H), 5.30 (d, J = 17.2 Hz, 1H), 5.19 (d, J = 10.2 Hz, 1H), 4.16 (d, J = 5.9 Hz, 2H), 4.03 (d, J = 5.25 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR: 156.6, 134.8, 128.5, 127.4, 126.8, 126.4, 125.6, 120.5, 116.7, 110.6, 71.1, 70.7, 55.1.

3-(2-Methoxyphenyl)-2,3-dimethoxy-1-(prop-2-enyl-1-oxy)propane (6a). Colorless viscous liquid. IR (thin film): 3076, 2928, 2827, 1640, 1600, 1492, 1465, 1243, 1081, 1027. ^{1}H NMR: 7.49 (d, J = 7.3 Hz, 1H), 7.23 (t, J = 7.5 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 5.85 (ddd, J_1 = 5.4 Hz, J_2 = 10.4 Hz, J_3 = 15.9 Hz, 1H), 5.22 (d, J = 17.0 Hz, 1H), 5.11 (d, J = 10.8 Hz, 1H), 4.71 (bs, 1H), 3.93–3.86 (m, 2H), 3.81 (s, 3H), 3.55–3.47 (m, 3H), 3.27 (s, 3H), 3.24 (s, 3H). ^{13}C NMR: 157.1, 134.9, 128.3, 128.1, 127.3, 120.5, 116.3, 110.0, 82.6, 77.5, 72.1, 70.3, 59.6, 57.2, 55.1.

2-(2-Methoxybenzoyl)-2-methoxy-1-(prop-2-enyl-1-oxy)ethane (6b). Colorless viscous liquid. IR (thin film): 2928, 2834, 1811, 1640, 1600, 1499, 1465, 1283, 1243, 1121. ^{1}H NMR: 7.65 (d, J = 7.3 Hz, 1H), 7.45 (t, J = 7.2 Hz, 1H), 7.01 (t, J = 7.4 Hz, 1H), 6.94 (d, J = 7.4 Hz, 1H), 5.85

(ddd, J_1 = 5.4 Hz, J_2 = 10.6 Hz, J_3 = 16.1 Hz 1H), 5.19 (d, J = 17.3 Hz, 1H), 5.11 (d, J = 10.3 Hz, 1H), 4.88 (d, J = 5.6 Hz, 1H), 3.97 (d, J = 5.2 Hz, 1H), 3.90, (s, 3H), 3.73 (d, J = 10.6 Hz, 2H), 3.60 (dd, J_1 = 6.1 Hz, J_2 = 10.4 Hz, 1H), 3.47(s, 3H). ^{13}C NMR: 199.8, 158.0, 134.5, 133.5, 130.6, 127.2, 121.0, 117.0, 111.2, 86.3, 72.4, 70.3, 58.4, 55.4.

2-Methoxycinnamyl propargyl ether (1h). Prepared by the general procedure. Yield: 85%. Colorless viscous liquid. IR (thin film): 3306, 3002, 2948, 2854, 1600, 1499, 1458, 1364, 1249, 1081, 1027. ^{1}H NMR: 7.40 (d, J = 8.5 Hz, 1H), 7.19 (t, J = 8.1 Hz, 1H), 7.02–6.84 (m, 3H), 6.30–6.21 (m, 1H), 4.22 (d, J = 7.1 Hz, 2H), 4.17 (d, J = 2.3 Hz, 2H), 3.83 (s, 3H), 2.42 (s, 1H). ^{13}C NMR: 156.6, 128.6, 128.3, 126.8, 125.4, 125.3, 120.4, 110.6, 79.7, 74.2, 70.5, 56.6, 55.1.

3-(2-Methoxyphenyl)-2,3-dimethoxy-1-(prop-2-ynyl-1-oxy)propane (7a). Colorless viscous liquid. IR (thin film): 3292, 2935, 2834, 1640, 1364, 1600, 1492, 1465, 1283, 1243, 1034. ^{1}H NMR: 7.40 (d, J = 7.41 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 6.99 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 4.70 (bs, 1H), 4.13–4.07 (m, 2H), 3.83 (s, 3H), 3.64–3.53 (m, 3H), 3.26 (s, 3H), 3.25 (s, 3H), 2.36 (s, 1H). ^{13}C NMR: 157.0, 128.3, 128.0, 120.5, 110.0, 82.3, 79.6, 77.4, 74.2, 59.6, 58.3, 57.2, 55.1.

2-(2-Methoxybenzoyl)-2-methoxy-1-(prop-2-ynyl-1-oxy)ethane (7b). Colorless viscous liquid. IR (thin film): 3292, 2942, 2840, 1688, 1640, 1600, 1485, 1438, 1276, 1249, 1162, 1094. ^{1}H NMR: 7.43 (d, J = 7.6 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 8.3 Hz, 1H) 4.91 (dd, J_1 = 2.4 Hz, J_2 = 6.2 Hz, 1H), 4.22 (dd, J_1 = 2.3 Hz, J_2 = 15.9 Hz, 1H), 4.12 (dd, J_1 = 2.3 Hz, J_2 = 15.9 Hz, 1H), 3.93 (s, 3H), 3.88 (dd, J_1 = 2.4 Hz, J_2 = 10.6 Hz, 1H), 3.66 (dd, J_1 = 6.2 Hz, J_2 = 10.6 Hz, 1H), 3.47 (s, 3H), 2.32 (t, J = 2.3 Hz, 1H). ^{13}C NMR: 199.1, 158.1, 133.7, 130.7, 126.9, 121.0, 111.2, 86.1, 79.4, 74.5, 69.8, 58.5, 58.3, 55.5.

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