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Synthesis of Phenol Derivatives from Cyclohex-2-enones Bearing an Alkyne through Lewis Acid-Catalyzed Enolization and Intramolecular Alder−Rickert Reaction

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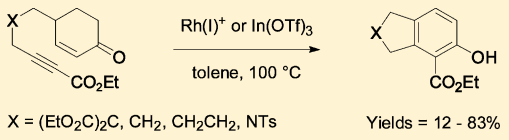
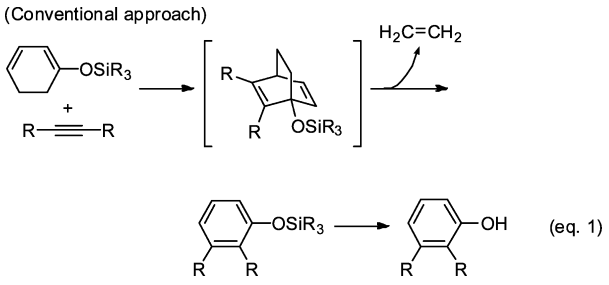
Supporting Information

ABSTRACT: A cationic rhodium(I) complex- or $In(OTf)_3$-catalyzed synthesis of phenol derivatives from cyclohex-2-enone having an ethoxycarbonyl-substituted alkyne has been achieved. This reaction proceeds via enolization and an intramolecular Alder−Rickert reaction.



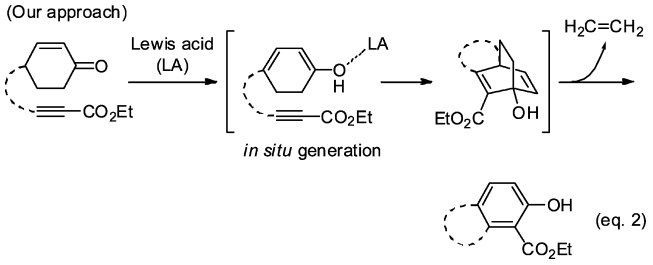
INTRODUCTION

The powerful synthetic method for generating highly substituted benzene derivatives by a cascade reaction comprising a Diels−Alder reaction of cyclohexa-1,3-dienes with alkynes and a retro Diels−Alder reaction accompanied by extrusion of ethylene gas is referred to as the Alder−Rickert reaction.[1] This method has also been applied to the synthesis of phenol derivatives, which are present in biologically active compounds,[2] natural products,[3] and chiral catalysts,[4] by utilizing siloxy-1,3-cyclohexadienes and related compounds as substrates (eq 1). While these starting materials could be



(eq. 1)

prepared from 1,3-cyclohexanedione in several steps, it is synthetically convenient and useful to generate hydroxy-1,3-cyclohexadienes from appropriate precursors in situ, which are then subjected to the Alder−Rickert reaction. This approach obviates the need to isolate the reactive dienes. To the best our knowledge, performing such a sequence in tandem has not been previously reported. In the course of our studies concerning Rh-catalyzed Pauson−Khand reactions, we chanced upon a remarkable observation in that a one-pot synthesis of phenol derivatives was achieved starting from cyclohex-2-enone having an activated alkyne. This reaction proceeded via in situ generation of a cyclohexa-1,3-dien-1-ol derivative by Lewis acid-mediated enolization followed by an intramolecular Alder−Rickert reaction (eq 2). We describe the experimental results in this paper.



(eq. 2)

RESULTS AND DISCUSSION

Preparation of requisite cyclohex-2-enone derivatives **6a−d** is shown in Scheme 1. Cyclohexenones **6a** and **6c** were prepared by a similar synthetic pathway from known alcohol **1**.[5] Alcohol **1** was converted to malonate derivative **4** via tosylate **2** and acetal **3**. Malonate derivative **4** was treated with 3-bromopropyne to give alkyne **5**. Cyclohexeone **6a** was obtained by ethoxycarbonylation of **5** and then removal of the acetal. Cyclohexeone **6c** was obtained by using 4-iodobut-1-yne (**10**)[6] in lieu of 3-bromopropyne of the above-mentioned pathway. Preparation of cyclohexeone **6b** was completed from known ketone **7**[7] in five steps via THP ether **8** and secondary alcohol **9**. Cyclohexeone **6d** was synthesized from tosylate **2** in six steps. Tosylate **11** was treated with 4-methyl-*N*-2-propyn-1-ylbenzenesulfonamide (**12**)[8] to give sulfonamide **13**. Sulfonamide **13** was converted to cyclohexeone **6d** via ester **14** and secondary alcohol **15** according to the above similar method.

We first expected that the Pauson−Khand reaction of enyne **6a** would proceed in the presence of Rh catalyst. However, treatment of **6a** with 5 mol % $[RhCl(CO)_2]_2$, 20 mol % $P(C_6F_5)_3$, and 40 mol % Ag(OTf) in toluene at 100 °C under CO atmosphere afforded only a trace amount of desired tricyclic product **16**, in addition to phenol derivative **17a** unexpectedly obtained in 56% yield (Scheme 2). A similar

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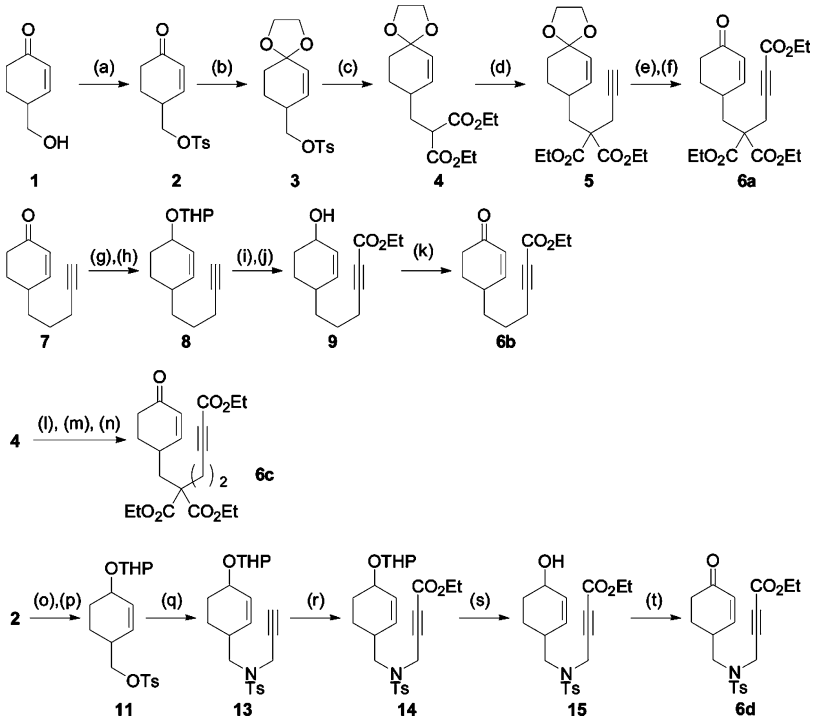
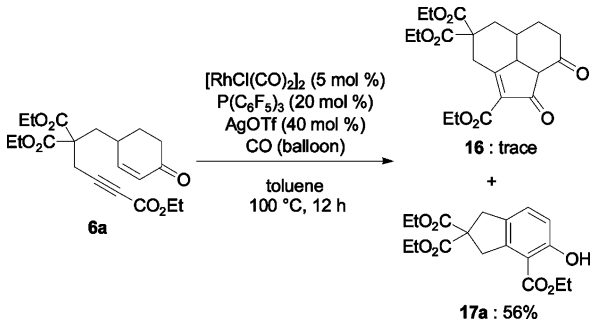
Scheme 1. Preparation of Cyclohex-2-enone Derivatives 6a–d[a]



[a]Reagents and conditions: (a) TsCl, Et_3N, DMAP, CH_2Cl_2, rt, 68%; (b) 1,2-bis(trimethylsiloxy)ethane, TMSOTf, CH_2Cl_2, −70 °C, 96%; (c) diethyl malonate, NaH, NaI, DMF, 100 °C, 67%; (d) 3-bromopropyne, NaH, NaI, THF, rt, 99%; (e) LDA, $ClCO_2Et$, THF, −78 °C to rt; (f) *p*-TsOH·H_2O, H_2O, acetone, rt, 71% for two steps; (g) $NaBH_4$, $CeCl_3$·$7H_2O$, MeOH, rt; (h) DHP, PPTS, CH_2Cl_2, rt, 70% for two steps; (i) LDA, $ClCO_2Et$, THF, −78 °C to rt; (j) PPTS, EtOH, rt, 84% for two steps; (k) Dess–Martin periodinane, pyridine, CH_2Cl_2, rt, 99%; (l) 4-iodobut-1-yne (**10**), NaH, DMF, 50 °C; (m) LDA, $ClCO_2Et$, THF, −78 °C to rt; (n) *p*-TsOH·H_2O, H_2O, acetone, rt, 34% for three steps; (o) $NaBH_4$, $CeCl_3$·$7H_2O$, MeOH, rt; (p) DHP, PPTS, CH_2Cl_2, rt, 86% for two steps; (q) 4-methyl-*N*-2-propyn-1-ylbenzenesulfonamide (**12**), NaH, DMF, 50 °C, 60%; (r) *n*-BuLi, $ClCO_2Et$, THF, −78 to 40 °C, 62%; (s) PPTS, EtOH, rt, quant.; (t) Dess–Martin periodinane, pyridine, CH_2Cl_2, rt, 98%.

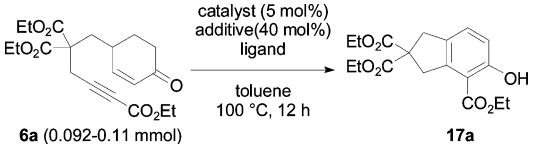
Scheme 2. Reaction of Enyne 6a in the Presence of Rh(I) Catalyst



reaction under an Ar atmosphere in lieu of CO gave **17a** in 62% yield. Because we took an interest in the one-pot synthesis of phenol derivative **17a** from **6a**, reaction conditions were then examined in an effort to improve the chemical yield of **17a**. The results are summarized in Table 1.

When the reaction was performed in the absence of AgOTf, the desired reaction did not proceed and 72% of starting material **6a** was recovered (entry 1). Furthermore, no reaction was observed when AgOTf was used in the absence of $[RhCl(CO)_2]_2$, which indicated that cationic Rh(I) is an essential catalyst. The reaction without $P(C_6F_5)_3$ ligand afforded product **17a** in 50% yield (entry 3). Investigation of monodentate phosphine ligands (entries 4–7) revealed that using P(2-furyl)$_3$ was optimal, giving **17a** in 81% yield (entry 4). Although several bidentate ligands were also examined, the chemical yields were not improved (entries 8–12).

Table 1. Examination of Catalysts and Screening of Phosphine Ligands for One-Pot Synthesis of Phenol Derivative 17a



entry[a]	catalyst	additive	ligand (mol %)	yield (%)[b]
1[c]	$[RhCl(CO)_2]_2$	no	no	0
2	no	AgOTf	no	0
3	$[RhCl(CO)_2]_2$	AgOTf	no	50
4	$[RhCl(CO)_2]_2$	AgOTf	P(2-furyl)$_3$ (20)	81
5	$[RhCl(CO)_2]_2$	AgOTf	P[O(2-MeC_6H_4)]$_3$ (20)	45
6	$[RhCl(CO)_2]_2$	AgOTf	PPh_3 (20)	37
7	$[RhCl(CO)_2]_2$	AgOTf	P(*o*-tolyl)$_3$ (20)	51
8	$[RhCl(CO)_2]_2$	AgOTf	dppe (10)	39
9	$[RhCl(CO)_2]_2$	AgOTf	dppp (10)	12
10	$[RhCl(CO)_2]_2$	AgOTf	dppb (10)	36
11	$[RhCl(CO)_2]_2$	AgOTf	(*rac*)-BINAP (10)	16
12	$[RhCl(CO)_2]_2$	AgOTf	$P(C_6F_5)_2C_2H_4P(C_6F_5)_2$ (10)	31

[a]All reactions were carried out under an Ar atmosphere. [b]Isolated yields. [c]72% of starting material **6a** was recovered.

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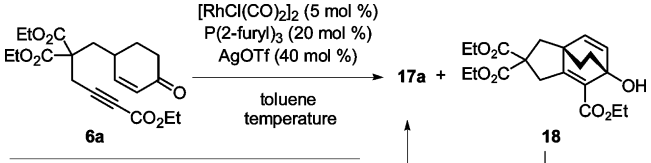
It was important to employ high temperature conditions in order for the present reactions to proceed smoothly. When the reaction was conducted by lowering the temperature from 100 to 80 °C, **17a** was formed in poor yield (37%) with diene **18** in 11% yield (Scheme 3). Reaction at 60 °C resulted in no

Scheme 3. Optimization of Reaction Temperature and Conversion of Intermediate 18 to 17a



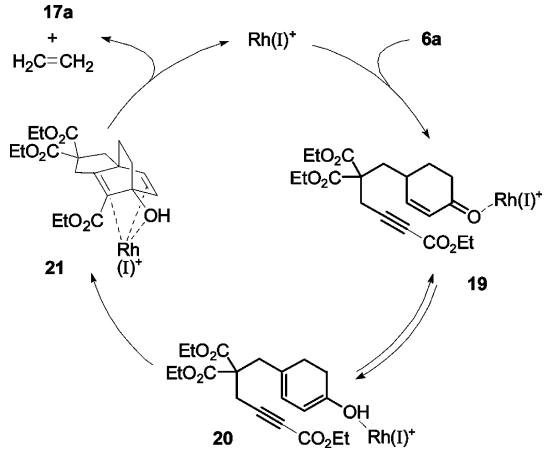
entry	temperature (°C)	time (h)	yield[a] 17a	18
1	80	12	37%	11%
2[b]	60	24	0%	11%

[a]Isolated yields. [b]31% of starting material **6a** was recovered.

formation of phenol **17a** and gave **18** in 11% yield, and 31% of starting material **6a** was recovered. The formation of diene **18** might be accounted for by an intramolecular Diels–Alder reaction of the diene generated from **6a**. Compound **18** was converted to **17a** by heating at 100 °C in toluene. The results suggested that diene **18** was an intermediate of the present reaction.

We propose a plausible mechanism of this reaction based on the aforementioned results (Scheme 4). Starting material **6a** is

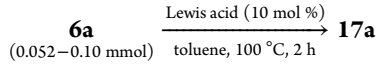
Scheme 4. Proposed Reaction Pathway



converted into dienol **20** via complex **19**, wherein cationic Rh(I) might act as Lewis acid to activate the ketone and promote enolization. The intramolecular Diels–Alder reaction of generated **20** then proceeds under thermal conditions to afford diene **21**, and subsequent retro-Diels–Alder reaction would give phenol derivative **17a** and ethylene gas. With respect to the transformation of **21** to **17a**, it is known that the retro Diels–Alder reaction is accelerated by the presence of alkoxide and trimethylsilyloxy substituents at the bridgehead of bicyclo[2.2.2]octa-2,5-diene.[9] The present one-pot synthesis of phenol derivative **17a** can be achieved via enolization of **6a** and subsequent Alder–Rickert reaction.

As shown in Scheme 4, it was assumed that the cationic rhodium(I) complex acts as a Lewis acid in this reaction. Therefore, we investigated other Lewis acid catalysts for the production of phenol derivative **17a** from **6a** (Table 2). The

Table 2. Screening of Lewis Acid Catalysts and the Control Experiment Using Triflic Acid



entry	Lewis acid	yield (%)[a]
1[b]	$BF_3{\cdot}OEt_2$	0
2	$SnCl_4$	0
3	$TiCl_4$	0
4	$AlCl_3$	0
5	$InCl_3$	0
6	$Al(OTf)_3$	12
7	$Cu(OTf)_2$	27
8[c]	$Yb(OTf)_3{\cdot}xH_2O$	0
9	$In(OTf)_3$	61
10	TfOH	16

[a]Isolated yields. [b]80% of starting material **6a** was recovered. [c]79% of starting material **6a** was recovered.

reaction of **6a** in toluene at 100 °C with 10 mol % Lewis acid, which is generally utilized for the Diels–Alder reaction, did not give desired product **17a** (entries 1–5). Interestingly, the use of $Al(OTf)_3$ and $Cu(OTf)_2$ produced desired product **17a** in 12% and 27% yields, respectively (entries 6 and 7), although use of $Yb(OTf)_3$ did not produce **17a** (entry 8). When $In(OTf)_3$ was used as the Lewis acid catalyst, the yield of **17a** was considerably improved to 61% (entry 9). Incidentally, although the use of triflic acid which is a known contaminant of the Lewis acid-bearing triflate as counterion produced **17a** in 16% yield, the yield was remarkably low in comparison with the reaction which used $In(OTf)_3$ (entry 10). Thus, cationic rhodium(I) complex and $In(OTf)_3$ were shown to be two effective Lewis acid catalysts in this reaction.

Having established two types of suitable conditions for the present reactions, the use of other cyclohex-2-enone derivatives as substrates was then investigated (Table 3). Upon treatment of **6b** with $[RhCl(CO)_2]_2$ (5 mol %), P(2-furyl)$_3$ (20 mol %), and Ag(OTf) (40 mol %) in toluene at 100 °C (method A), product **17b** was formed in good yield (83%) (entry 1, method A). However, the treatment of **6b** with $In(OTf)_3$ (10 mol %) in toluene at 100 °C (method B) gave **17b** in low yield (12%) (entry 1, method B). The reaction of **6c**, having a one-carbon elongated tether moiety compared to **6a**, under the conditions of method A gave **17c** in 12% yield (entry 2, method A), and in the case of method B, **17c** was not obtained (entry 2, method B). The reaction of **6d** bearing a tosyl amide under the conditions of method A gave **17d**, albeit with 24% yield (entry 3, method A). On the other hand, the reaction of **6d** under the conditions of method B led to improved chemical yields by up to 57% (entry 3, method B). Furthermore, also in the case of the reaction employing excess reaction substrate **6a** (1.2 mmol) under the conditions of methods A and B, **17a** was obtained in 82% yield and 65% yield, respectively, similar to chemical yields of the present reaction which employed **6a** on a small scale (entry 4).

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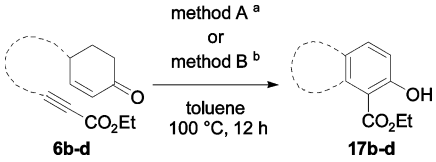
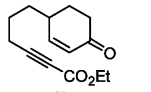
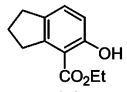
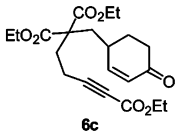
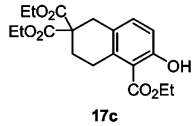
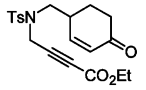
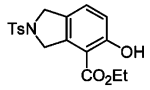
Table 3. Rhodium or In(OTf)$_3$-Catalyzed One-Pot Synthesis of phenol Derivatives 17b–d from Cyclohex-2-enones 6b–d



6b-d 17b-d

entry	substrate	product	method	yield (%) [c]
1[d]	 6b	 17b	A B	83 12
2[d]	 6c	 17c	A B	12 0
3[d]	 6d	 17d	A B	24 57
4	6a (1.2 mmol)	17a	A B	82 65

[a]In the presence of $[RhCl(CO)_2]_2$ (5 mol %), AgOTf (40 mol %), and P(2-furyl)$_3$ (20 mol %). [b]In the presence of In(OTf)$_3$ (10 mol %). [c]Isolated yields. [d]Reactions were carried out using 0.057–0.10 mmol of reaction substrates.

CONCLUSION

In summary, we have achieved the one-pot synthesis of phenol derivatives from compounds possessing cyclohex-2-enone and ethoxycarbonyl-substituted alkyne moieties. This cascade reaction proceeds via enolization and an intramolecular Alder–Rickert reaction. Furthermore, the cationic rhodium(I) complex and In(OTf)$_3$ were found to be two effective Lewis acid catalysts in this reaction. It is possible to synthesize phenol derivatives which have an indane unit, a 1,2,3,4-tetrahydronaphthalene unit, or an isoindoline unit from the corresponding substrates using this reaction.

EXPERIMENTAL SECTION

General Information. All reagents were obtained from commercial sources and used as received unless stated otherwise. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts are given on the δ (ppm) scale using tetramethylsilane (TMS) as the internal standard (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). Coupling constants (J) are reported in hertz (Hz). Infrared spectra were recorded on a Fourier transform infrared (FTIR) spectrometer. Absorption band positions are reported in reciprocal centimeters (cm^{-1}). High resolution mass spectra were obtained on a time-of-flight (TOF) mass instrument equipped with electrospray ionization (ESI) interface. Melting points were determined on a melting point apparatus and are uncorrected. Flash column chromatography was performed using silica gel 60, 40–50 μm. Thin-layer chromatography analysis was performed on commercial silica gel 60 F254 glass-backed plates.

(4-Oxocyclohex-2-enyl)methyl 4-Methylbenzenesulfonate (2). To a solution of **1** (1.50 g, 11.9 mmol) in CH_2Cl_2 (60 mL) were added triethylamine (1.8 mL, 13.1 mmol), *p*-toluenesulfonyl chloride (2.50 g, 13.1 mmol), and DMAP (727 mg, 5.95 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 4 h. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ solution and stirred for 20 min. The mixture was extracted with AcOEt, and the organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 1:1) to give tosylate **2** (2.22 g, 68% yield) as a white solid. Tosylate **2** is unstable under air at room temperature. mp 63–64 °C; IR (KBr) 1680, 1597, 1493, 1451, 1356, 1172 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 7.80 (2H, d, J = 8.3 Hz), 7.37 (2H, d, J = 8.1 Hz), 6.74 (1H, ddd, J = 10.1, 2.5, 1.5 Hz), 6.04 (1H, dd, J = 10.1, 2.5 Hz), 4.00–4.07 (2H, m), 2.82 (1H, m), 2.48 (1H, m), 2.46 (3H, s), 2.37 (1H, m), 2.09 (1H, m), 1.78 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.2, 148.0, 145.2, 132.4, 131.0, 129.9, 129.9, 127.8, 127.8, 71.1, 36.1, 35.8, 25.1, 21.6; HRMS (ESI) m/z calcd for $C_{14}H_{17}O_4S$ $(M + H)^+$ 281.0848, found 281.0830; Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 59.72; H, 5.79.

1,4-Dioxaspiro[4.5]dec-6-en-8-ylmethyl 4-Methylbenzenesulfonate (3). To a solution of **2** (2.22 g, 7.93 mmol) in CH_2Cl_2 (60 mL) was added 1,2-bis(trimethylsilyloxy)ethane (9.0 mL, 36.7 mmol) at −78 °C under an Ar atmosphere. TMSOTf (0.29 mL, 1.59 mmol) was added dropwise to the mixture at the same temperature, and the mixture was stirred at −70 °C for 30 h. The reaction mixture was treated with addition of pyridine (1.0 mL). After concentration of solvent under reduced pressure, the residue was purified by a silica gel column chromatography (hexane/AcOEt = 1:1) to give acetal **3** (2.47 g, 96% yield) as a colorless oil. Acetal **3** is unstable under air at room temperature. IR (neat) 1598, 1495, 1452, 1361, 1177 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ ppm: 7.76 (2H, d, J = 8.0 Hz), 7.42 (2H, d, J = 8.0 Hz), 5.67 (1H, dd, J = 10.4, 1.5 Hz), 5.60 (1H, dd, J = 10.4, 1.5 Hz), 3.82–3.93 (6H, m), 2.43 (3H, s), 2.40 (1H, m), 1.73–1.81 (2H, m), 1.62 (1H, m), 1.44 (1H, m); ^{13}C NMR (100 MHz, CD_3OD) δ ppm: 146.6, 134.3, 131.8, 131.3, 131.1, 131.1, 129.0, 129.0, 106.2, 73.9, 65.6, 65.4, 36.6, 32.9, 24.4, 21.6; HRMS (ESI) m/z calcd for $C_{16}H_{21}O_5S$ $(M + H)^+$ 325.1110, found 325.1124.

Diethyl 2-(1,4-Dioxaspiro[4.5]dec-6-en-8-ylmethyl)malonate (4). To a solution of diethyl malonate (1.3 mL, 8.37 mmol) in DMF (15 mL) was added NaH (365 mg, 8.37 mmol) at 0 °C under an Ar atmosphere. After stirring at room temperature for 1 h, to the mixture were added a solution of **3** (2.47 g, 7.61 mmol) in DMF (10 mL) via a cannula and NaI (1.14 g, 7.61 mmol) at 0 °C. The mixture was stirred at 100 °C for 14 h. After cooling the reaction mixture to room temperature, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution, the mixture was extracted with AcOEt, and the organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 3:1) to give **4** (1.59 g, 67% yield) as a colorless oil: IR (neat) 1732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 5.81 (1H, dd, J = 10.1, 2.5 Hz), 5.60 (1H, dd, J = 10.1, 1.6 Hz), 4.17–4.23 (4H, m), 3.88–4.02 (4H, m), 3.45 (1H, t, J = 7.6 Hz), 1.99–2.13 (2H, m), 1.85–1.92 (3H, m), 1.72 (1H, m), 1.48 (1H, m), 1.26 (6H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 169.3, 169.2, 135.4, 128.0, 105.4, 64.6, 64.4, 61.4, 61.4, 49.6, 34.0, 33.2, 32.3, 26.6, 14.0, 14.0; HRMS (ESI) m/z calcd for $C_{16}H_{24}O_6Na$ $(M + Na)^+$ 335.1471, found 335.1486; Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74. Found: C, 61.75; H, 7.85.

Diethyl 2-(1,4-Dioxaspiro[4.5]dec-6-en-8-ylmethyl)-2-(prop-2-ynyl)malonate (5). To a solution of **4** (500 mg, 1.60 mmol) in DMF (8.0 mL) was added NaH (69.8 mg, 1.60 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 1 h. To the mixture were added 3-bromopropyne (0.15 mL, 1.92 mmol) and NaI (1.14 g, 7.61 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 3:1) to give **5** (553 mg, 99% yield) as a colorless oil: IR (neat) 3281, 2122, 1735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 5.76 (1H, dd, J = 10.1, 2.0 Hz), 5.55 (1H,

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d, J = 10.1 Hz), 4.15−4.25 (4H, m), 3.89−4.00 (4H, m), 2.88 (2H, t, J = 2.8 Hz), 2.08−2.27 (3H, m), 2.02 (1H, t, J = 2.8 Hz), 1.81−1.90 (2H, m), 1.70 (1H, m), 1.49 (1H, m), 1.25 (6H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 170.3, 170.1, 136.7, 127.3, 105.1, 78.6, 71.7, 64.5, 64.4, 61.6, 61.6, 56.0, 36.8, 32.4, 31.3, 27.9, 23.1, 13.9, 13.9; HRMS (ESI) m/z calcd for $C_{19}H_{27}O_6$ $(M + H)^+$ 351.1808, found 351.1805; Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 64.83; H, 7.54.

Triethyl 5-(4-Oxocyclohex-2-enyl)pent-1-yne-1,4,4-tricarboxylate (6a). To a solution of LDA, which was prepared in situ by mixing i-Pr_2NH (0.39 mL, 2.77 mmol) and n-BuLi (1.65 M hexane solution, 1.60 mL, 2.63 mmol) in THF (8.0 mL) at 0 °C for 30 min, was added a solution of **5** (462 mg, 1.32 mmol) in THF (5.0 mL) at −78 °C under an Ar atmosphere. The mixture was stirred at the same temperature for 1 h. To the mixture was added ethyl chloroformate (0.38 mL, 3.96 mmol) at −78 °C, and the mixture was stirred at room temperature for 12 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was used for the next reaction without further purification.

To a solution of the above crude product in acetone (13 mL) and H_2O (0.9 mL) was added p-TsOH·H_2O (25.0 mg, 0.132 mmol) at 0 °C, and the mixture was stirred at room temperature for 18 h. The reaction mixture was extracted with AcOEt, and the organic layer was washed with saturated aqueous $NaHCO_3$ solution, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 4:1) to give **6a** (355 mg, 71% yield, two steps) as a pale yellow solid: mp 49−50 °C; IR (KBr) 2244, 1753, 1730, 1674 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 6.77 (1H, dd, J = 10.1, 2.3 Hz), 5.96 (1H, dd, J = 10.1, 2.3 Hz), 4.18−4.29 (6H, m), 3.06 (2H, d, J = 3.5 Hz), 2.47−2.54 (2H, m), 2.31−2.39 (2H, m), 2.21 (1H, m), 2.10 (1H, m), 1.77 (1H, m), 1.26−1.31 (9H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.7, 169.5, 169.4, 153.7, 153.0, 129.3, 82.5, 76.2, 62.2, 62.2, 62.0, 55.8, 36.8, 36.5, 32.1, 29.7, 23.7, 13.9, 13.9, 13.9; HRMS (ESI) m/z calcd for $C_{20}H_{27}O_7$ $(M + H)^+$ 379.1757, found 379.1744; Anal. Calcd for $C_{20}H_{26}O_7$: C, 63.48; H, 6.98. Found: C, 63.50; H, 7.07.

2-(4-(Pent-4-ynyl)cyclohex-2-enyloxy)tetrahydro-2*H*-pyran (8). To a solution of **7** (390 mg, 2.40 mmol) in MeOH (24 mL) were added $CeCl_3$·$7H_2O$ (983 mg, 2.64 mmol) and $NaBH_4$ (100 mg, 2.64 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was used for the next reaction without further purification.

To a solution of the above crude product in CH_2Cl_2 (12 mL) were added 3,4-dihydro-2H-pyran (DHP) (0.65 mL, 7.20 mmol) and PPTS (302 mg, 1.20 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 18 h. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ solution, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 20:1) to give **8** (419 g, 70% yield, two steps) as a colorless oil: IR (neat) 3294, 2116 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 5.69−5.78 (2H, m), 4.74 (1H, m), 4.19 (1H, m), 3.93 (1H, m), 3.51 (1H, m), 1.16−2.21 (18H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 135.6, 135.2, 134.3, 134.1, 129.5, 128.2, 128.0, 126.8, 98.1, 97.9, 96.9, 96.6, 84.4, 84.4, 77.2, 72.1, 70.8, 69.8, 68.6, 68.3, 68.3, 62.8, 62.7, 62.5, 35.1, 35.0, 35.0, 34.6, 34.5, 31.3, 31.2, 31.2, 31.1, 30.0, 28.5, 27.9, 27.2, 26.8, 26.5, 26.1, 25.7, 25.7, 25.5, 24.6, 24.4, 19.9, 19.9, 19.8, 19.7, 18.6; HRMS (ESI) m/z calcd for $C_{16}H_{24}O_2Na$ $(M + Na)^+$ 271.1674, found 271.1689; Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.47; H, 9.83.

6-(4-Hydroxycyclohex-2-enyl)hex-2-ynoate (9). To a solution of LDA, which was prepared in situ by mixing i-Pr_2NH (0.50 mL, 3.55 mmol) and n-BuLi (2.69 M hexane solution, 1.26 mL, 3.38 mmol) in THF (10 mL) at 0 °C for 30 min under an Ar atmosphere, was added a solution of **8** (419 mg, 1.69 mmol) in THF (7.0 mL) at −78 °C, and the mixture was stirred at the same temperature for 1 h. To the mixture was added ethyl chloroformate (0.48 mL, 5.07 mmol) at −78 °C, and the mixture was stirred at room temperature for 21 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution, the mixture was extracted with AcOEt, and the organic layer was washed with saturated aqueous $NaHCO_3$ solution, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was used for the next reaction without further purification.

To a solution of the above crude product in EtOH (10 mL) was added PPTS (50.0 mg, 0.198 mmol) at 0 °C, and the mixture was stirred at room temperature for 18 h. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ solution, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 2:1) to give **9** (211 mg, 84% yield, two steps) as a colorless oil: IR (neat) 3393, 2235, 1713 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 5.64−5.81 (2H, m), 4.14−4.24 (3H, m), 2.32−2.36 (2H, m), 2.04−2.10 (2H, m), 1.19−1.88 (11H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 153.8, 135.2, 133.7, 130.7, 129.0, 88.9, 73.4, 66.9, 64.4, 61.8, 35.0, 34.9, 34.8, 34.7, 31.8, 30.3, 26.6, 25.0, 24.8, 23.8, 18.8, 14.0; HRMS (ESI) m/z calcd for $C_{14}H_{20}O_3Na$ $(M + Na)^+$ 259.1310, found 259.1310; Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 70.99; H, 8.44.

Ethyl 6-(4-Oxocyclohex-2-enyl)hex-2-ynoate (6b). To a solution of **9** (170 mg, 0.765 mmol) in CH_2Cl_2 (7.7 mL) were added Dess−Martin periodinane (389 mg, 0.918 mmol) and $NaHCO_3$ (321 mg, 3.83 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 18 h. The reaction mixture was quenched by addition of 1:1 mixture saturated aqueous $Na_2S_2O_3$ solution and saturated aqueous $NaHCO_3$ solution, and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 1:1) to give **6b** (166 mg, 99% yield) as a colorless oil: IR (neat) 2234, 1708, 1683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 6.83 (1H, ddd, J = 10.4, 2.5, 1.3 Hz), 5.99 (1H, dd, J = 10.4, 1.9 Hz), 4.22 (2H, q, J = 7.1 Hz), 2.32−2.54 (5H, m), 2.13 (1H, m), 1.50−1.75 (5H, m), 1.31 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 199.5, 154.1, 153.6, 129.3, 88.2, 73.7, 61.8, 36.8, 35.6, 33.6, 28.4, 24.9, 18.7, 14.0; HRMS (ESI) m/z calcd for $C_{14}H_{19}O_3$ $(M + H)^+$ 235.1334, found 235.1329; Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.55; H, 7.76.

Triethyl 6-(4-Oxocyclohex-2-enyl)hex-1-yne-1,5,5-tricarboxylate (6c). To a solution of **4** (300 mg, 0.960 mmol) in DMF (6.0 mL) was added NaH (50.2 mg, 1.15 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 1 h. To the mixture was added a solution of 4-iodo-1-butyne (**10**) (931 mg, 4.80 mmol) in DMF (3.6 mL) via a cannula at 0 °C, and the mixture was stirred at 50 °C for 15 h. After cooling to room temperature, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 2:1) to give unseparable mixture (288 mg) of the desired product and unidentified byproduct.

To a solution of LDA, which was prepared in situ by mixing i-Pr_2NH (0.30 mL, 2.09 mmol) and n-BuLi (1.65 M hexane solution, 1.2 mL, 2.02 mmol) in THF (4.7 mL) at 0 °C for 30 min under an Ar atmosphere, was added a solution of the aforementioned mixture in THF (2.0 mL) at −78 °C, and the mixture was stirred at the same temperature for 1 h. To the mixture was added ethyl chloroformate (0.26 mL, 2.69 mmol) at −78 °C, and the mixture was stirred at room temperature for 14 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution, and the mixture was extracted

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with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was used for the next reaction without further purification.

To a solution of the above crude product in acetone (6.7 mL) and H_2O (0.5 mL) was added *p*-TsOH·H_2O (12.8 mg, 0.0673 mmol) at 0 °C, and the mixture was stirred at room temperature for 4 h. The reaction mixture was extracted with AcOEt, and the organic layer was washed with saturated aqueous $NaHCO_3$ solution, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 5:1) to give **6c** (127 mg, 34% yield, three steps) as a white solid: mp 62−63 °C; IR (KBr) 2237, 1721, 1708, 1681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 6.74 (1H, dd, J = 10.1, 2.0 Hz), 5.96 (1H, dd, J = 10.1, 2.0 Hz), 4.19−4.24 (6H, m), 2.45−2.52 (2H, m), 2.04−2.39 (8H, m), 1.72 (1H, m), 1.25−1.32 (9H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.5, 170.6, 170.5, 153.6, 153.4, 129.3, 87.1, 73.9, 61.8, 61.8, 61.8, 56.4, 37.9, 36.5, 32.3, 31.7, 29.9, 14.5, 14.0, 14.0, 14.0; HRMS (ESI) m/z calcd for $C_{21}H_{29}O_7$ $(M + H)^+$ 393.1913, found 393.1911.

(4-(Tetrahydro-2*H*-pyran-2-yloxy)cyclohex-2-enyl)methyl 4-Methylbenzenesulfonate (11). To a solution of **2** (500 mg, 1.78 mmol) in MeOH (18.0 mL) were added $CeCl_3·7H_2O$ (730 mg, 1.96 mmol) and $NaBH_4$ (74.2 mg, 1.96 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was used for the next reaction without further purification.

To a solution of the above crude product in CH_2Cl_2 (9.0 mL) were added DHP (0.48 mL, 5.34 mmol) and PPTS (224 mg, 0.890 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 60 h. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ solution, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 3:1) to give **11** (564 mg, 86% yield, two steps) as a colorless oil: IR (neat) 1598, 1496, 1450, 1361, 1177 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.77−7.79 (2H, m), 7.33−7.35 (2H, m), 5.85 (1H, m), 5.61 (1H, m), 4.70 (1H, m), 4.16 (1H, m), 3.81−3.92 (3H, m), 3.49 (1H, m), 2.39−2.52 (4H, m), 1.23−2.06 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 144.7, 144.7, 133.0, 132.6, 131.4, 131.2, 130.2, 129.8, 129.0, 128.6, 128.2, 127.9, 127.8, 98.1, 97.9, 97.0, 96.8, 77.2, 73.0, 72.9, 72.6, 72.5, 71.1, 70.0, 69.4, 68.3, 62.8, 62.7, 62.6, 62.5, 35.2, 35.2, 35.1, 35.1, 31.1, 31.1, 31.0, 31.0, 30.6, 28.7, 27.5, 26.7, 25.6, 25.4, 25.4, 23.4, 22.9, 21.6, 21.2, 20.9, 19.8, 19.7, 19.6; HRMS (ESI) m/z calcd for $C_{19}H_{26}O_5NaS$ $(M + Na)^+$ 389.1399, found 389.1384; Anal. Calcd for $C_{19}H_{26}O_5S$: C, 62.27; H, 7.15. Found: C, 62.27; H, 7.20.

4-Methyl-*N*-(prop-2-ynyl)-*N*-((4-(tetrahydro-2*H*-pyran-2-yloxy)cyclohex-2-enyl)methyl)benzenesulfonamide (13). To a solution of amide **12** (314 mg, 1.50 mmol) in DMF (3.0 mL) was added NaH (65.5 mg, 1.50 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 1 h. To the mixture was added a solution of **11** (500 mg, 1.36 mmol) in DMF (3.8 mL) via a cannula at 0 °C, and the mixture was stirred at 50 °C for 18 h. After cooling to room temperature, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution at 0 °C, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 3:1) to give **13** (331 mg, 60% yield) as a colorless oil: IR (neat) 3276, 2118, 1598, 1495, 1452, 1349, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.70−7.79 (2H, m), 7.27−7.35 (2H, m), 5.68−5.90 (2H, m), 4.74 (1H, m), 4.06−4.28 (3H, m), 3.88 (1H, m), 3.51 (1H, m), 3.01−3.21 (2H, m), 2.37−2.50 (4H, m), 2.00−2.13 (2H, m), 1.47−1.91 (8H, m), 1.31 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 143.5, 143.4, 135.8, 135.7, 131.4, 131.2, 130.8, 130.5, 130.4, 130.2, 130.1, 129.8, 129.4, 129.4, 127.8, 127.7, 98.0, 96.9, 77.2, 76.4, 76.3, 74.0, 73.9, 71.5, 70.4, 69.7, 68.7, 62.7, 62.6, 50.8, 50.6, 50.2, 50.2, 37.0, 36.8, 33.6, 33.6, 33.5, 33.5, 31.1, 31.1, 29.1, 27.8, 27.1, 25.7, 25.5, 25.4, 24.7, 24.1, 22.0, 21.5, 19.8, 19.7, 19.7; HRMS (ESI) m/z calcd for $C_{22}H_{29}NO_4NaS$ $(M + Na)^+$ 426.1715, found 426.1686.

Ethyl 4-(4-Methyl-*N*-((4-(tetrahydro-2*H*-pyran-2-yloxy)-cyclohex-2-enyl)methyl)phenylsulfonamido)but-2-ynoate (14). To a solution of **13** (235 mg, 0.582 mmol) in THF (5.8 mL) was added *n*-BuLi (1.69 M hexane solution, 0.41 mL, 0.698 mmol) at −78 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. To the mixture was added ethyl chloroformate (0.11 mL, 01.16 mmol) at −78 °C, and the mixture was stirred at room temperature for 1 h and stirred at 40 °C for 15 h. After cooling to room temperature, the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution at 0 °C, and the mixture was extracted with AcOEt. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 5:1) to give **14** (172 mg, 62% yield) as a colorless oil: IR (neat) 2240, 1713, 1598, 1495, 1448, 1351, 1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.70−7.72 (2H, m), 7.29−7.31 (2H, m), 5.67−5.91 (2H, m), 4.73 (1H, m), 4.12−4.34 (5H, m), 3.91 (1H, m), 3.51 (1H, m), 3.00−3.20 (2H, m), 2.34−2.41 (4H, m), 2.09 (1H, m), 1.47−1.92 (8H, m), 1.25−1.42 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 152.4, 152.4, 143.8, 143.8, 135.2, 135.2, 131.7, 130.9, 130.7, 130.5, 130.4, 130.1, 129.9, 129.7, 129.4, 127.7, 127.6, 98.0, 97.9, 96.9, 79.9, 79.8, 77.4, 77.2, 71.4, 70.3, 69.6, 68.6, 62.7, 62.6, 62.0, 51.3, 51.1, 50.8, 50.8, 37.1, 36.9, 33.7, 33.6, 33.6, 31.1, 31.1, 29.1, 27.8, 27.0, 25.7, 25.4, 24.7, 24.1, 22.3, 22.0, 21.5, 19.8, 19.7, 19.7, 13.9; HRMS (ESI) m/z calcd for $C_{25}H_{33}NO_6NaS$ $(M + Na)^+$ 498.1926, found 498.1924.

Ethyl 4-(*N*-((4-Hydroxycyclohex-2-enyl)methyl)-4-methylphenylsulfonamido)but-2-ynoate (15). To a solution of **14** (142 mg, 0.299 mmol) in EtOH (3.0 mL) was added PPTS (15.0 mg, 0.0598 mmol) at 0 °C, and the mixture was stirred at room temperature for 42 h. The reaction mixture was extracted with AcOEt, and the organic layer was washed with saturated aqueous $NaHCO_3$ solution, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 1:1) to give **15** (117 mg, quant.) as a colorless oil: IR (neat) 3530, 3403, 2239, 1711, 1598, 1495, 1450, 1353, 1161 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.71−7.74 (2H, m), 7.30−7.32 (2H, m), 5.68−5.84 (2H, m), 4.13−4.31 (5H, m), 3.06−3.14 (2H, m), 2.42−2.46 (4H, m), 2.11 (1H, m), 1.91 (1H, m), 1.35−1.54 (3H, m), 1.26−1.29 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 152.4, 143.9, 135.2, 132.6, 129.8, 129.7, 127.7, 127.6, 79.8, 77.5, 77.2, 66.4, 62.0, 51.1, 51.0, 37.0, 33.6, 30.9, 24.1, 21.8, 21.5, 14.0; HRMS (ESI) m/z calcd for $C_{20}H_{25}NO_5NaS$ $(M + Na)^+$ 414.1351, found 414.1350.

Ethyl 4-(4-Methyl-*N*-((4-oxocyclohex-2-enyl)methyl)-phenylsulfonamido)but-2-ynoate (6d). To a solution of **15** (78.0 mg, 0.199 mmol) in CH_2Cl_2 (4.0 mL) were added Dess−Martin periodinane (118 mg, 0.279 mmol) and $NaHCO_3$ (83.6 mg, 0.995 mmol) at 0 °C under an Ar atmosphere, and the mixture was stirred at room temperature for 12 h. The reaction mixture was quenched by addition of 1:1 mixture saturated aqueous $Na_2S_2O_3$ solution and saturated aqueous $NaHCO_3$ solution, and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (hexane/AcOEt = 1:1) to give **6d** (75.9 mg, 98% yield) as a white solid: mp 98−99 °C; IR (neat) 2238, 1718, 1681, 1596, 1496, 1450, 1350, 1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.73 (2H, d, J = 8.3 Hz), 7.34 (2H, d, J = 8.3 Hz), 6.92 (1H, ddd, J = 10.4, 2.5, 1.3 Hz), 6.08 (1H, dd, J = 10.4, 2.5 Hz), 4.22−4.34 (2H, m), 4.17 (2H, q, J = 7.1 Hz), 3.16−3.28 (2H, m), 2.78 (1H, m), 2.57 (1H, dt, J = 16.9, 4.8 Hz), 2.35−2.43 (4H, m), 2.17 (1H, m), 1.80 (1H, m), 1.28 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 198.8, 152.3, 149.7, 144.3, 134.8, 130.5, 129.9, 129.9, 127.7, 127.7, 79.4, 77.8, 62.2, 50.3,

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37.4, 36.3, 34.6, 26.4, 21.5, 14.0; HRMS (ESI) m/z calcd for $C_{20}H_{23}NO_5NaS$ $(M + Na)^+$ 412.1195, found 412.1187; Anal. Calcd for $C_{20}H_{23}NO_5S$: C, 61.68; H, 5.95; N, 3.60. Found: C, 61.47; H, 5.94; N, 3.65.

Typical Procedure for Rhodium(I)-Catalyzed Synthesis of Triethyl 5-Hydroxy-1*H*-indene-2,2,4(3*H*)-tricarboxylate (17a) (Table 1, entry 4). A solution of $[RhCl(CO)_2]_2$ (1.8 mg, 0.00463 mmol) and P(2-furyl)$_3$ (4.3 mg, 0.0185 mmol) in anhydrous toluene (0.4 mL) was stirred at room temperature for 20 min under an Ar atmosphere. To the solution was added AgOTf (9.5 mg, 0.0370 mmol) at room temperature, and the mixture was stirred at the same temperature for 30 min. To the suspension was added a solution of **6a** (35.0 mg, 0.0926 mmol) in anhydrous toluene (0.8 mL) via a cannula at room temperature, and the mixture was stirred at 100 °C for 12 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3:1) to give **17a** (26.2 mg, 81% yield) as a white solid. mp 76−77 °C; IR (KBr) 1731, 1667, 1604, 1468 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 11.1 (1H, s), 7.24 (1H, d, J = 8.3 Hz), 6.82 (1H, d, J = 8.3 Hz), 4.43 (2H, q, J = 7.1 Hz), 4.21 (4H, q, J = 7.1 Hz), 3.86 (2H, s), 3.49 (2H, s), 1.43 (3H, t, J = 7.1 Hz), 1.26 (6H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 171.7, 171.7, 170.7, 161.8, 141.9, 131.4, 130.6, 116.7, 109.7, 61.7, 61.7, 61.6, 60.0, 42.9, 39.4, 14.3, 14.0, 14.0; HRMS (ESI) m/z calcd for $C_{18}H_{22}O_7Na$ $(M + Na)^+$ 373.1263, found 373.1260; Anal. Calcd for $C_{18}H_{22}O_7$: C, 61.71; H, 6.33. Found: C, 61.95: H, 6.42.

Ethyl 5-Hydroxy-2,3-dihydro-1*H*-indene-4-carboxylate (17b). White solid; mp 47−48 °C; IR (KBr) 1657, 1604, 1466 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 11.1 (1H, s), 7.27 (1H, d, J = 8.4 Hz), 6.79 (1H, d, J = 8.4 Hz), 4.36 (2H, q, J = 7.1 Hz), 3.21 (2H, t, J = 7.6 Hz), 2.83 (2H, t, J = 7.6 Hz), 2.06 (2H, quintet, J = 7.6 Hz), 1.43 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 171.3, 161.1, 146.5, 135.6, 130.7, 115.5, 110.0, 61.3, 35.6, 31.9, 25.1, 14.2; HRMS (ESI) m/z calcd for $C_{12}H_{15}O_3$ $(M + H)^+$ 207.1021, found 207.1015.

Triethyl 2-Hydroxy-7,8-dihydronaphthalene-1,6,6(5*H*)-tricarboxylate (17c). White solid; mp 104−105 °C; IR (KBr) 1735, 1659, 1592, 1466 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 11.0 (1H, s), 7.16 (1H, d, J = 8.6 Hz), 6.81 (1H, d, J = 8.6 Hz), 4.43 (2H, q, J = 7.1 Hz), 4.19 (4H, q, J = 7.1 Hz), 3.20 (2H, s), 3.13 (2H, t, J = 6.7 Hz), 2.27 (2H, t, J = 6.7 Hz), 1.42 (3H, t, J = 7.1 Hz), 1.23 (6H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 171.4, 171.3, 171.3, 161.3, 137.3, 135.6, 125.5, 116.9, 112.1, 61.6, 61.4, 61.4, 52.9, 35.1, 28.4, 26.4, 14.2, 14.0, 14.0; HRMS (ESI) m/z calcd for $C_{19}H_{24}O_7$ $(M + H)^+$ 365.1600, found 365.1588.

Ethyl 5-Hydroxy-2-tosylisoindoline-4-carboxylate (17d). White solid; mp 204−205 °C; IR (KBr) 1657, 1604, 1466 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 11.1 (1H, s), 7.76 (2H, d, J = 8.1 Hz), 7.32 (2H, d, J = 8.1 Hz), 7.20 (1H, d, J = 8.3 Hz), 6.88 (1H, d, J = 8.3 Hz), 4.83 (2H, s), 4.53 (2H, s), 4.44 (2H, q, J = 7.1 Hz), 2.40 (3H, s), 1.44 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 169.7, 162.2, 143.7, 143.7, 137.9, 134.0, 129.8, 129.8, 129.0, 127.5, 127.5, 117.8, 108.4, 62.0, 55.8, 52.9, 21.5, 14.3; HRMS (ESI) m/z calcd for $C_{18}H_{20}NO_5S$ $(M + H)^+$ 362.1062, found 362.1074.

Typical Procedure for In(OTf)$_3$-Catalyzed Synthesis of Triethyl 5-Hydroxy-1*H*-indene-2,2,4(3*H*)-tricarboxylate (17a) (Table 2, entry 9). To a solution of **6a** (19.6 mg, 0.0518 mmol) in anhydrous toluene (0.7 mL) was added In(OTf)$_3$ (2.9 mg, 0.00518 mmol) at room temperature under an Ar atmosphere, and the mixture was stirred at 100 °C for 12 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3:1) to give **17a** (11.0 mg, 61% yield).

Synthesis of Triethyl 6-Hydroxy-3a,6-ethanoindene-2,2,7-(1*H*,3*H*,6*H*)-tricarboxylate (18) (Scheme 3, entry 1). A solution of $[RhCl(CO)_2]_2$ (2.0 mg, 0.00514 mmol) and P(2-furyl)$_3$ (4.8 mg, 0.0206 mmol) in anhydrous toluene (0.4 mL) was stirred at room temperature for 20 min under an Ar atmosphere. To the solution was added AgOTf (10.6 mg, 0.0411 mmol) at room temperature, and the mixture was stirred at the same temperature for 30 min. To the suspension was added a solution of **6a** (38.9 mg, 0.103 mmol) in anhydrous toluene (0.9 mL) via a cannula at room temperature, and the mixture was stirred at 80 °C for 12 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3:1) to give **17a** (13.4 mg, 37% yield) and **18** (4.3 mg, 11% yield) as a colorless oil. **18**: IR (neat) 3429, 1732, 1681, 1645 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 6.33 (1H, d, J = 7.6 Hz), 6.32 (1H, s), 5.98 (1H, d, J = 7.6 Hz), 4.16−4.29 (6H, m), 3.43 (1H, d, J = 19.2 Hz), 3.30 (1H, d, J = 19.2 Hz), 2.90 (1H, d, J = 13.9 Hz), 2.59 (1H, d, J = 13.9 Hz), 1.45−1.61 (4H, m), 1.20−1.35 (9H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 171.4, 171.1, 166.6, 164.2, 140.2, 133.1, 126.2, 79.6, 62.0, 61.9, 61.9, 60.7, 53.4, 41.2, 38.5, 36.1, 31.7, 14.3, 14.0, 14.0; HRMS (ESI) m/z calcd for $C_{20}H_{27}O_7$ $(M + H)^+$ 379.1757, found 379.1747; Anal. Calcd for $C_{20}H_{26}O_7$: C, 63.48; H, 6.93. Found: C, 63.50: H, 6.97.

Conversion of Triethyl 6-Hydroxy-3a,6-ethanoindene-2,2,7-(1*H*,3*H*,6*H*)-tricarboxylate (18) to Triethyl 5-Hydroxy-1*H*-indene-2,2,4(3*H*)-tricarboxylate (17a) (Scheme 3). A solution of **18** (1.2 mg, 0.00317 mmol) in anhydrous toluene (0.5 mL) was stirred at 100 °C for 2 h under an Ar atmosphere. After cooling to room temperature, the solution was concentrated under reduced pressure. The residue was purified by preparative TLC (hexane/EtOAc = 2:1) to give **17a** (1.0 mg, 90% yield).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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