Tetrahedron 66 (2010) 2675–2682

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Highly diastereoselective synthesis of tetrahydrobenzofuran derivatives by palladium-catalyzed reaction of propargylic esters with substituted β-dicarbonyl compounds

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ARTICLE INFO

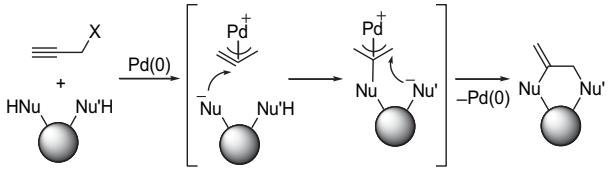
Article history:
Received 19 January 2010
Received in revised form 2 February 2010
Accepted 2 February 2010
Available online 10 February 2010

ABSTRACT

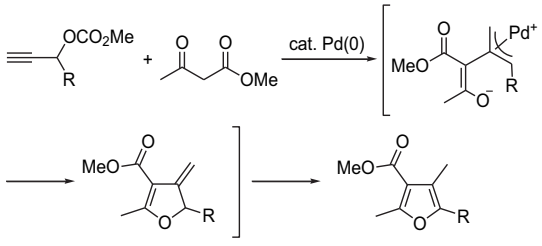
Reactions of propargylic esters with 2-substituted cyclohexane-1,3-diones and 2-oxocyclohexanecarboxylic esters in the presence of palladium catalyst are described. Substituted tetrahydrobenzofuran derivatives having a quaternary carbon stereocenter were synthesized in a highly diastereoselective manner.

1. Introduction

Palladium-catalyzed reactions of propargylic compounds have received considerable attention and have been extensively studied due to their versatile and specific reactivity.[1] The reaction of propargylic compounds with reactants having two nucleophilic moieties is one of the more successful chemical processes developed to date.[2] In this reaction, the initially formed π-propargylpalladium intermediate is subjected to successive nucleophilic attacks by the reactant to afford the cyclized product (Eq. 1). For example, Tsuji et al. reported that propargylic carbonates reacted with β-keto esters to produce substituted furans (Eq. 2).[2a] In this reaction, the propargylic carbonates react with β-keto esters using a palladium catalyst to generate the π-allylpalladium complex, which then causes the intramolecular nucleophilic attack of the resulting enolate oxygen to afford the cyclized product. This type of cyclization reaction is useful for the construction of various substituted heterocyclic compounds in one-step, but the stereochemistry of the cyclization step has not been well examined. During the course of our studies on the reaction of propargylic carbonates **1** in the presence of a palladium catalyst,[2g,3] we focused on the nucleophilic activity of the 2-substituted cyclohexane-1,3-diones **2** and the 2-oxocyclohexanecarboxylic ester **3**. By introducing a substituent on the α carbon of the β-dicarbonyl compounds, the corresponding cyclized products **4** and **5** having two asymmetric centers including a quaternary carbon could be obtained (Eq. 3).[4] Herein, we describe the palladium-catalyzed reaction of propargylic esters with 2-substituted cyclohexane-1,3-diones and a 2-oxocyclohexanecarboxylic ester, in which substituted



(1)



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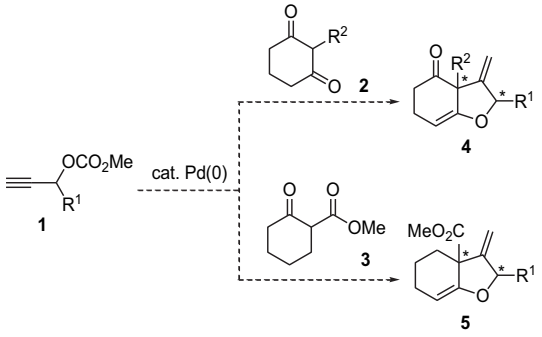

(3)

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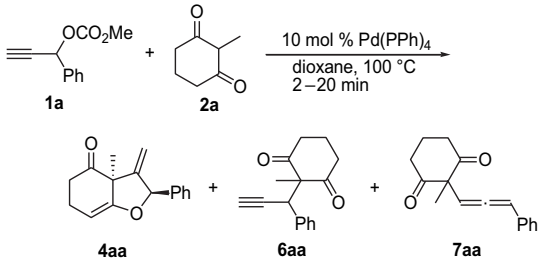
doi:10.1016/j.tet.2010.02.023

tetrahydrobenzofuran derivatives were produced with high diastereoselectivity.[5]

2. Results and discussion

The initial reactions were attempted using methyl 1-phenylprop-2-ynyl carbonate (**1a**) with 2-methylcyclohexane-1,3-dione (**2a**). When **1a** and **2a** were subjected to the reaction in the presence of 10 mol % $Pd(PPh_3)_4$ in dioxane at 100 °C for 5 min, tetrahydrobenzofuranone **4aa** was obtained in 37% yield as a single diastereomer together with the propargylic and allenic substituted compounds **6aa** and **7aa** in 5% and 10% yields, respectively (Table 1, entry 1). Examination under various reaction temperatures and solvents (entries 2–9) revealed that the yield of **4aa** was improved to 66% by carrying out the reaction in DMSO at 120 °C (entry 8).

Table 1
Initial attempts using propargylic carbonate **1a** and 2-methyl-1,3-cyclohexanedione (**2a**)

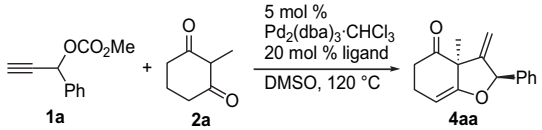


Entry	Solvent	Temp (°C)	Yield (%)		
			4aa	**6aa**	**7aa**
1	Dioxane	100	37	5	10
2	DMF	100	40	6	3
3	DMSO	100	51	4	4
4	NMP	100	51	2	1
5	Toluene	100	4	37	7
6	1,2-Dichloroethane	100	6	32	6
7	DMSO	80	39	8	3
8	DMSO	120	66	6	3
9	DMSO	140	55	5	4

The results of the attempted reactions using various bidentate phosphine ligands[6] are summarized in Table 2. All the reactions proceeded to afford the tetrahydrobenzofuranone **4aa** (entries 1–7), and the best result was obtained when dppf was used as the ligand (84% yield, entry 5).

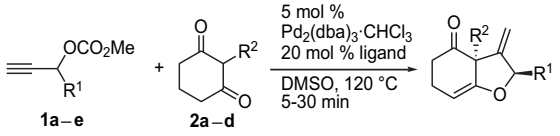
Having identified a useful set of reaction conditions, we next carried out a study on the substrate scope (Table 3). When 2-propylcyclohexane-1,3-dione (**2b**) was subjected to the reaction with **1a**, the propyl-substituted tetrahydrobenzofuranone **4ab** was obtained in 75% yield (entry 1). The benzyl- and 2-cyanoethyl-substituted substrates **2c** and **2d** uneventfully reacted with **1a** to deliver the corresponding products **4ac** and **4ad** in 76% and 82% yields, respectively (entries 2 and 3). The propargylic carbonates **1b** and **1c** having a 1- and 2-naphthyl group at the propargylic position, successfully reacted with **2a** to produce the tetrahydrobenzofuranones **4ba** and **4ca**, respectively, in high yields (entries 4 and 5). The structure of **4ca**, including the stereochemistry, was confirmed by X-ray crystallographic analysis (Fig. 1).[7] The reactions of the 3-furanyl- and pentyl-substituted substrates **1d** and **1e** also gave the corresponding products **4da** and **4ea** in moderate yields (entries 6 and 7). When the propargylic carbonate **1f** containing a 3,4-dimethoxyphenyl group was subjected to the reaction, decomposition of the substrate was observed (entry 8).

Table 2
Effect of the bidentate ligand



Entry	Ligand	Time (min)	Yield of **4aa** (%)
1	dppe	40	46
2	dppp	20	49
3	dppb	5	75
4	dpppentane	5	61
5	dppf	5	84
6	BINAP	10	57
7	Tol-BINAP	5	76

Table 3
Reactions using various substrates **1a–e** and **2a–d**



Entry	Substrates		Product	Yield (%)
	R^1	R^2		
1[a]	Ph (**1a**)	Pr (**2b**)	**4ab**	75
2[a]	Ph (**1a**)	Bn (**2c**)	**4ac**	76
3[d]	Ph (**1a**)	2-Cyanoethyl (**2d**)	**4ad**	82
4[a]	1-Naphthyl (**1b**)	Me (**2a**)	**4ba**	83
5[b]	2-Naphthyl (**1c**)	Me (**2a**)	**4ca**	81
6[c]	3-Furanyl (**1d**)	Me (**2a**)	**4da**	55
7[d]	Pentyl (**1e**)	Me (**2a**)	**4ea**	43
8[a]	3,4-Dimethoxyphenyl (**1f**)	Me (**2a**)	—	decomp.

[a] Dppf was used as a ligand.
[b] Dppp was used as a ligand.
[c] Dpppentane was used as a ligand.
[d] Dppb was used as a ligand.

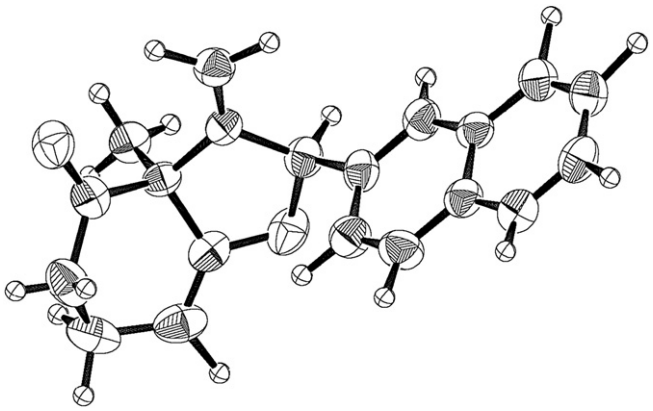
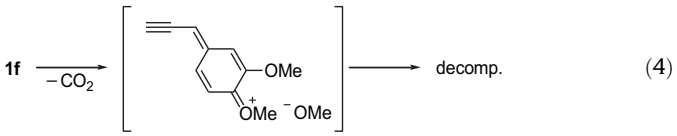


Figure 1. ORTEP drawing of **4ca**.

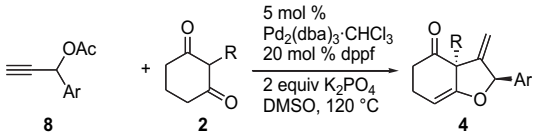
Consequently, it was thought that the electron-donating methoxy groups on the phenyl ring accelerated the elimination of the carbonate moiety producing an unstable intermediate (Eq. 4).



(4)

To overcome this problem, the propargylic acetate having a less reactive leaving group was examined (Table 4). When the palladium-catalyzed reaction of 3,4-dimethoxyphenyl-substituted propargylic acetate **8a** with **2a** in the presence of 2 equiv K_3PO_4 was carried out, the desired tetrahydrobenzofuranone **4ga** was obtained in 93% yield (entry 1). Similarly, substrate **8b** having a phenyl group successfully reacted with **2a** to afford the product **4aa** in 85% yield (entry 2). The reaction of **8a** with the cyanoethyl-substituted cyclohexane-1,3-dione **2d** also gave the corresponding product **4gd** in 67% yield (entry 3).

Table 4
Reactivity of the propargylic acetates **8**



Entry	Ar	R	Product	Yield (%)
1	3,4-Dimethoxy-phenyl (**8a**)	Me (**2a**)	**4ga**	93
2	Ph (**8b**)	Me (**2a**)	**4aa**	85
3	3,4-Dimethoxy-phenyl (**8a**)	Cyanoethyl (**2d**)	**4gd**	67

The resulting tetrahydrobenzofuranones **4**(**aa**–**gd**) were obtained as a single diastereomer in all cases, clearly demonstrating that this cyclization reaction proceeds in a highly diastereoselective manner. Since these compounds include a core structure of porosin, a neolignan from *Ocotea porosa* and *Urbanodendron verrucosum* (Fig. 2),[8] we expect that the product **4gd** might be a useful intermediate for the synthesis of porosin.

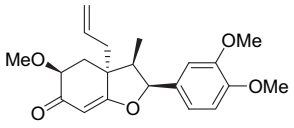
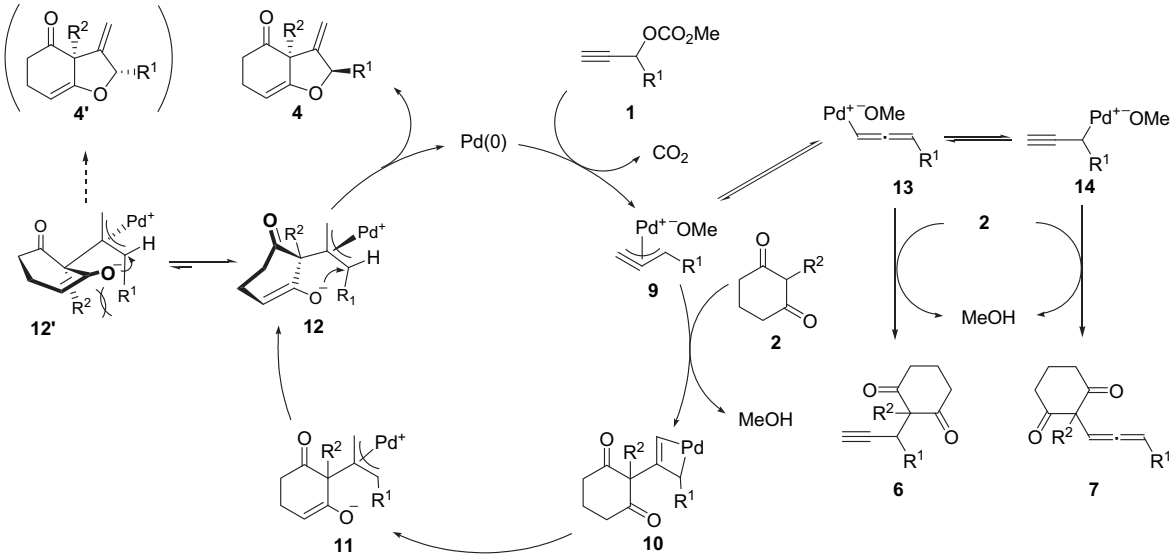


Figure 2. Structure of porosin.

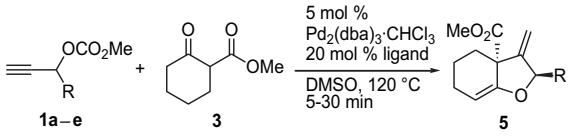
A plausible mechanism, which accounts for the observed highly diastereoselective nature of this process, is shown in Scheme 1. By reacting with the palladium catalyst, the propargylic carbonate **1** undergoes decarboxylation to give the π-propargylpalladium complex **9**, which further reacts with cyclohexane-1,3-dione **2** to lead to the π-allylpalladium intermediate **11** via the palladacyclobutene **10**.[9] The intermediate **11** undergoes intramolecular attack of the enolate oxygen to produce the tetrahydrobenzofuranone **4**. The observed high diastereoselectivity is likely the result of steric factors, which influence the relative energies of the competing transition states **12** and **12′**. It is expected that the transition state **12**, leading to the product **4**, has lower energy because of the absence of the steric repulsion between the R^1 and R^2 groups that are present in **12′**, which yields the diastereomer **4′**. The propargylic and allenic substitution byproducts **6** and **7** are produced via direct nucleophilic substitution from the allenylpalladium **13** and the propargylpalladium **14**, which are in equilibrium with the π-propargylpalladium **9**.[10]

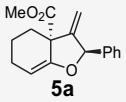
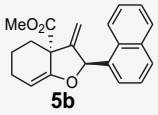
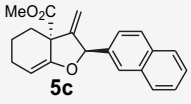
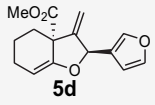
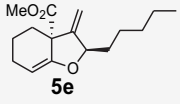
We next turned our attention to the reaction with the 2-oxocyclohexanecarboxylic ester. When methyl 2-oxocyclohexanecarboxylate (**3**) and propargylic carbonate **1a** were subjected to the reaction in the presence of 5 mol% $Pd_2(dba)_3{\cdot}CHCl_3$ and 20 mol% dppf in DMSO at 120 °C for 5 min, the tetrahydrobenzofuran **5a** was



Scheme 1. Proposed reaction mechanism for production of **4**, **6**, and **7**.

Table 5
Reactions of propargylic carbonates **1a–e** with ketoester **3**



Entry	R	Product	Yield (%)
1[a]	Ph (**1a**)	 **5a**	92
2[a]	1-Naphthyl (**1b**)	 **5b**	66
3[a]	2-Naphthyl (**1c**)	 **5c**	76
4[b]	3-Furanyl (**1d**)	 **5d**	51
5[c]	Pentyl (**1e**)	 **5e**	56

[a] Dppf was used as a ligand.
[b] Dpppentane was used as a ligand.
[c] Dppb was used as a ligand.

obtained in 92% yield as a single diastereomer (Table 5, entry 1). The reactions of the naphthyl-substituted substrates **1b** and **1c** with **3** successfully proceeded to produce the cyclized products **5b** and **5c** in 66% and 76% yields, respectively (entries 2 and 3). The structure of the resulting **5c**, including the stereochemistry, was confirmed by X-ray crystallographic analysis (Fig. 3).[11] The propargylic carbonates **1d** and **1e** containing a 3-furyl and a pentyl group also reacted with **3** to afford the corresponding products **5d** and **5e** in 51% and 56% yields, respectively (entries 4 and 5). Since the resulting tetrahydrobenzofurans **5**(**a–e**) had been obtained as a single diastereomer in all cases, it is clear that this reaction also proceeds in a highly diastereoselective manner.

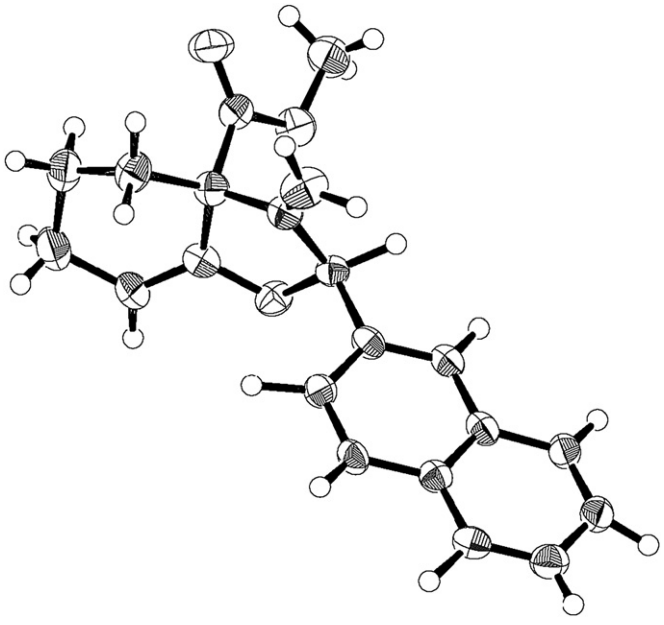
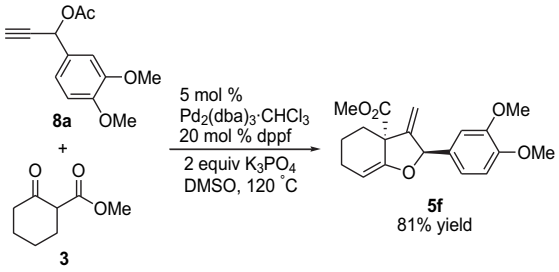


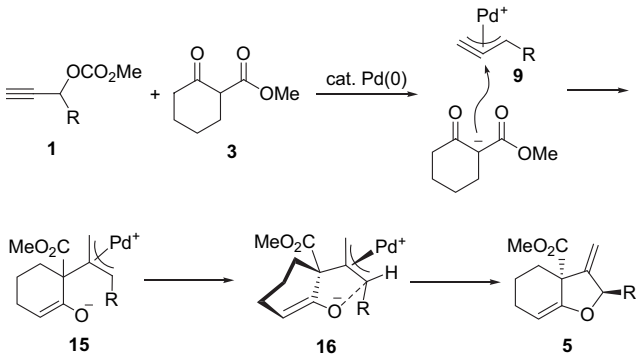
Figure 3. ORTEP drawing of **5c**.

The reaction of the 3,4-dimethoxyphenyl-substituted propargylic acetate **8a** with the 2-oxocyclohexanecarboxylic ester **3** was next examined. When the palladium-catalyzed reaction of **8a** with **3** in the presence of K_3PO_4 was carried out, the desired tetrahydrobenzofuran **5f** was selectively obtained in 81% yield (Eq. 5). We expect that the product **5f** would also be an attractive precursor toward the efficient synthesis of porosin.



(5)

A plausible mechanism for the production of **5** with high diastereoselectivity is shown in Scheme 2. The initially formed π-propargylpalladium complex **9** from the propargylic carbonate **1** reacts with the 2-oxocyclohexanecarboxylic ester **3** to lead to the π-allylpalladium intermediate **15**. The intermediate **15** is further subjected to intramolecular attack via the favorable transition state **16** to produce the tetrahydrobenzofuran **5**.



Scheme 2. Proposed reaction mechanism for production of **5**.

3. Conclusion

In conclusion, we have developed a palladium-catalyzed reaction of propargylic carbonates with 2-substituted cyclohexane-1,3-diones. The process yields tetrahydrobenzofuranones in a highly diastereoselective manner. Since natural products having a similar tetrahydrobenzofuranone structure have been reported,[8,12] our methodology would provide a new protocol for the synthesis of these compounds with high efficiency.

4. Experimental

4.1. General

All non-aqueous reactions were carried out under a positive atmosphere of argon in dried glassware unless otherwise indicated. Materials were obtained from commercial suppliers and used

without further purification except when otherwise noted. Solvents were dried and distilled according to the standard protocols. 2-Substituted cyclohexane-1,3-diones **2b**,[13] **2c**,[14] and **2d**[15] and 2-oxocyclohexanecarboxylic ester **3**[16] were prepared according to the procedures described in the literature. The phrase 'residue upon workup' refers to the residue obtained when the organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure.

4.2. General procedure for the synthesis of propargylic carbonates 1

Synthesis of **1a**: To a stirred solution of 1-phenylprop-2-yn-1-ol (1.5 g, 11.3 mmol) in CH_2Cl_2 (50 mL) were added methyl chloroformate (1.05 mL, 13.6 mmol), and pyridine (2.74 mL, 33.9 mmol) at 0 °C, and stirring was continued for 1 h at the same temperature. The reaction mixture was diluted with aqueous NH_4Cl and extracted with AcOEt. The combined extracts were washed with brine. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (8:2 v/v) as eluent to give propargylic carbonate **1a** (2.5 g, quant) as a pale yellow oil.

*4.2.1. Methyl 1-phenylprop-2-ynyl carbonate (**1a**).* Pale yellow oil; IR (neat) 3290, 2958, 1750, 1442, 1260, 931, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.72 (1H, d, J=2.4 Hz), 3.82 (3H, s), 6.29 (1H, d, J=2.4 Hz), 7.38–7.43 (3H, m), 7.54–7.57 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2 (CH_3), 69.3 (CH), 76.5 (CH), 79.6 (Cq), 127.6 (CH), 128.7 (CH), 129.3 (CH), 135.8 (Cq), 154.7 (Cq); HRMS (ESI) m/z calcd for $C_{11}H_{10}O_3Na$ $[M+Na]^+$ 213.0528, found 213.0529.

*4.2.2. Methyl 1-(naphthalen-1-yl)prop-2-ynyl carbonate (**1b**).* Colorless oil; IR (neat) 3286, 3052, 2956, 1751, 1599, 1512, 1441, 1263, 1095, 980, 647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.78 (1H, d, J=2.4 Hz), 3.83 (3H, s), 6.91 (1H, d, J=2.4 Hz), 7.47–7.61 (3H, m), 7.82 (1H, d, J=7.2 Hz), 7.90 (2H, d, J=8.0 Hz), 8.22 (1H, d, J=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2 (CH_3), 67.8 (CH), 77.0 (CH), 79.5 (Cq), 123.6 (CH), 125.1 (CH), 126.1 (CH), 126.7 (CH), 126.8 (CH), 126.8 (CH), 130.3 (CH), 130.3 (Cq), 131.0 (Cq), 133.9 (Cq), 154.8 (Cq); HRMS (ESI) m/z calcd for $C_{15}H_{12}O_3Na$ $[M+Na]^+$ 263.0684, found 263.0681.

*4.2.3. Methyl 1-(naphthalen-2-yl)prop-2-ynyl carbonate (**1c**).* Colorless crystals; mp 80.1–81.8 °C (recrystallized from benzene); IR (neat) 3257, 2958, 2125, 1732, 1442, 1267, 1016, 926, 823, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.78 (1H, d, J=2.4 Hz), 3.83 (3H, s), 6.46 (1H, d, J=2.4 Hz), 7.51–7.54 (2H, m), 7.64 (1H, dd, J=1.6 and 8.4 Hz), 7.84–7.90 (3H, m), 8.02 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0 (CH_3), 69.4 (CH), 76.7 (CH), 79.5 (Cq), 124.7 (CH), 126.4 (CH), 126.7 (CH), 127.2 (CH), 127.6 (CH), 128.2 (CH), 128.7 (CH), 132.8 (Cq), 133.0 (Cq), 133.5 (Cq), 154.7 (Cq); HRMS (ESI) m/z calcd for $C_{15}H_{12}O_3Na$ $[M+Na]^+$ 263.0684, found 263.0688.

*4.2.4. 1-(Furan-3-yl)prop-2-ynyl methyl carbonate (**1d**).* Colorless oil; IR (neat) 3281, 3063, 1638, 1454, 1385, 1360, 1218, 912, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.65 (1H, d, J=2.0 Hz), 3.83 (3H, s), 6.25 (1H, d, J=2.0 Hz), 6.54 (1H, d, J=1.6 Hz), 7.41 (1H, t, J=1.6 Hz), 7.62 (1H, d, J=1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.1 (CH_3), 61.9 (CH), 75.0 (CH), 78.8 (Cq), 109.4 (CH), 121.6 (Cq), 141.9 (CH), 143.7 (CH), 154.7 (Cq); HRMS (ESI) m/z calcd for $C_9H_8O_4Na$ $[M+Na]^+$ 203.0323, found 203.0320.

*4.2.5. Methyl oct-1-yn-3-yl carbonate (**1e**).* Pale yellow oil; IR (neat) 3292, 2957, 2862, 1752, 1443, 1267, 1119, 949, 791 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, t, J=6.8 Hz), 1.30–1.35 (4H, m), 1.44–1.53 (2H, m), 1.77–1.87 (2H, m), 2.51 (1H, d, J=2.0 Hz), 3.82 (3H, s), 5.20 (1H, dt, J=2.0 and 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3), 22.4 (CH_2), 24.4 (CH_2), 31.1 (CH_2), 34.5 (CH_2), 54.9 (CH_3), 67.8 (CH), 74.3 (CH), 80.5 (Cq), 154.9 (Cq); HRMS (ESI) m/z calcd for $C_{10}H_{16}O_3Na$ $[M+Na]^+$ 207.0997, found 207.0994.

4.3. General procedure for the synthesis of propargylic acetates 8

Synthesis of **8a**: To a stirred solution of 1-phenylprop-2-yn-1-ol (150 mg, 0.8 mmol) in CH_2Cl_2 (15 mL) were added acetic anhydride (0.11 mL, 1.2 mmol), pyridine (0.20 mL, 2.3 mmol), and DMAP (9.5 mg, 78 μmol) at 0 °C, and stirring was continued for 2 h at the same temperature. The reaction mixture was diluted with water and extracted with AcOEt. The combined extracts were washed with brine. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (8:2 v/v) as eluent to give propargylic acetate **8a** (136 mg, 91%) as a pale yellow oil.

*4.3.1. 1-(3,4-Dimethoxyphenyl)prop-2-ynyl acetate (**8a**).* Pale yellow oil; IR (neat) 3279, 2839, 2123, 1740, 1596, 1517, 1384, 1220, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.11 (3H, s), 2.66 (1H, d, J=2.0 Hz), 3.89 (3H, s), 3.91 (3H, s), 6.41 (1H, d, J=2.0 Hz), 6.86 (1H, d, J=8.4 Hz), 7.06 (1H, d, J=2.0 Hz), 7.11 (1H, dd, J=2.0 and 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0 (CH_3), 55.9 ($CH_3\times2$), 65.2 (CH), 75.2 (CH), 80.4 (Cq), 110.9 (CH), 110.9 (CH), 120.6 (CH), 128.9 (Cq), 149.0 (Cq), 149.7 (Cq), 169.6 (Cq); HRMS (ESI) m/z calcd for $C_{13}H_{14}O_4Na$ $[M+Na]^+$ 257.0790, found 257.0783.

*4.3.2. 1-Phenylprop-2-ynyl acetate (**8b**).* Pale yellow oil; IR (neat) 3289, 3035, 2125, 1743, 1495, 1455, 1370, 1226, 1017, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.13 (3H, s), 2.65 (1H, d, J=2.0 Hz), 6.45 (1H, d, J=2.0 Hz), 7.36–7.42 (3H, m), 7.52–7.55 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9 (CH_3), 65.2 (CH), 75.3 (CH), 80.2 (Cq), 127.6 (CH), 128.7 (CH), 129.0 (CH), 136.4 (Cq), 169.6 (Cq); HRMS (ESI) m/z calcd for $C_{11}H_{10}O_2Na$ $[M+Na]^+$ 197.0578, found 197.0575.

4.4. General procedure for the reaction of propargylic carbonate 1 with 2-substituted cyclohexane-1,3-dione 2 using palladium catalyst

Reaction of **1a** with **2a** (Table 2, entry 5): To a stirred solution of **1a** (30.0 mg, 158 μmol) in DMSO (2.0 mL) were added 2-methylcyclohexane-1,3-dione (**2a**) (26.3 mg, 189 μmol), $Pd_2(dba)_3\cdot CHCl_3$ (8.2 mg, 7.9 μmol), and dppf (17.5 mg, 31.6 μmol) at rt, and stirring was continued for 20 min at the same temperature under argon atmosphere. The reaction mixture was allowed to heat to 120 °C, and stirred for 5 min at the same temperature. After filtration of the reaction mixture using small amount of silica gel followed by concentration, the residue was chromatographed on silica gel with AcOEt–hexane (9:1 v/v) as eluent to give the tetrahydrobenzofuranone **4aa** (32.0 mg, 133 μmol, 84%) as colorless needles.

4.4.1. (2R,3aS*)-3a-Methyl-3-methylene-2-phenyl-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4aa**).* Colorless needles; mp 53.7–55.6 °C (recrystallized from hexane); IR (neat) 2926, 1715, 1695, 1661, 1454, 1342, 1160, 1090, 978, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.53 (3H, s), 2.33–2.42 (2H, m), 2.48–2.56 (1H, m), 2.61–2.68 (1H, m), 4.71 (1H, d, J=2.4 Hz), 5.19–5.21 (1H, m), 5.67 (1H, d, J=2.4 Hz), 5.73 (1H, t, J=2.4 Hz), 7.22–7.27 (2H, m), 7.31–7.37 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5 (CH_2), 25.4 (CH_3), 37.7 (CH_2), 53.2 (Cq), 83.6 (CH), 92.6 (CH), 110.3 (CH_2), 127.3 (CH×2), 128.4 (CH), 128.5 (CH×2), 140.1 (Cq), 149.3 (Cq), 158.9 (Cq), 210.4 (Cq); HRMS (ESI) m/z calcd for $C_{16}H_{16}O_2Na$ $[M+Na]^+$ 263.1048, found 263.1041.

*4.4.2. 2-Methyl-2-(1-phenylprop-2-ynyl)cyclohexane-1,3-dione (**6aa**).* Pale yellow oil; IR (neat) 3282, 2695, 1695, 1454, 1025, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (3H, s), 1.66–1.75 (2H,

m), 2.42–2.43 (1H, d, J=2.4 Hz), 2.48–2.64 (4H, m), 4.43 (1H, d, J=2.4 Hz), 7.23–7.26 (2H, m), 7.27–7.30 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9 (CH_2), 18.9 (CH_3), 39.2 (CH_2), 39.4 (CH_2), 44.0 (CH), 67.7 (Cq), 74.1 (CH), 81.6 (Cq), 128.0 (CH), 128.3 (CH), 129.1 (CH), 135.8 (Cq), 208.6 (Cq), 208.8 (Cq); HRMS (ESI) m/z calcd for $C_{16}H_{16}O_2Na$ $[M+Na]^+$ 263.1048, found 263.1053.

*4.4.3. 2-Methyl-2-(3-phenylpropa-1,2-dienyl)cyclohexane-1,3-dione (**7aa**).* Pale yellow oil; IR (neat) 2933, 2924, 1948, 1697, 1384 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (3H, s), 1.74–1.86 (1H, m), 2.08–2.17 (1H, m), 2.55–2.65 (2H, m), 2.80–2.93 (2H, m), 5.65 (1H, d, J=6.4 Hz), 6.39 (1H, d, J=6.4 Hz), 7.22–7.27 (2H, m), 7.31–7.37 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.7 (CH_3 and CH_2), 37.9 (CH_2), 38.0 (CH_2), 66.5 (Cq), 97.4 (CH), 98.9 (CH), 127.0 ($CH_2\times2$), 127.9 (CH), 128.9 ($CH_2\times2$), 132.6 (Cq), 204.8 (Cq), 206.8 (Cq), 206.9 (Cq); HRMS (ESI) m/z calcd for $C_{16}H_{16}O_2Na$ $[M+Na]^+$ 263.1048, found 263.1051.

4.4.4. (2R,3aS*)-3-Methylene-2-phenyl-3a-propyl-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4ab**).* White solid; mp 67.8–69.4 °C (recrystallized from hexane); IR (neat) 2958, 1713, 1455, 1343, 1153, 1107, 964, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (3H, t, J=7.2 Hz), 1.39–1.46 (2H, m), 1.69–1.77 (1H, m), 1.89–1.96 (1H, m), 2.31–2.40 (2H, m), 2.48–2.62 (2H, m), 4.75 (1H, d, J=1.6 Hz), 5.25–527 (1H, m), 5.63 (2H, s), 7.22–7.24 (2H, m), 7.27–7.36 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1(CH_3), 18.2 (CH_2), 19.7 (CH_2), 37.6 (CH_2), 41.0 (CH_2), 58.1 (Cq), 84.1 (CH), 93.7 (CH), 110.9 (CH_2), 127.3 (CH), 128.3 (CH), 128.5 (CH), 140.5 (Cq), 148.0 (Cq), 158.0 (Cq), 210.0 (Cq); HRMS (ESI) m/z calcd for $C_{18}H_{20}O_2Na$ $[M+Na]^+$ 291.1361, found 291.1367.

4.4.5. (2R,3aS*)-3a-Benzyl-3-methylene-2-phenyl-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4ac**).* Pale yellow oil; IR (neat) 3029, 1709, 1494, 1454, 1384, 1137, 767, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49–1.59 (1H, m), 2.02–2.09 (1H, m), 2.21–2.30 (1H, m), 2.34–2.40 (1H, m), 2.94 (1H, d, J=12.8 Hz), 3.32 (1H, d, J=12.8 Hz), 4.73 (1H, d, J=2.4 Hz), 5.27–5.30 (2H, m), 5.68 (1H, d, J=2.8 Hz), 7.17–7.23 (4H, m), 7.27–7.34 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8 (CH_2), 38.7 (CH_2), 45.0 (CH_2), 59.6 (Cq), 83.7 (CH), 95.9 (CH), 110.7 (CH_2), 127.2 (CH), 127.2 (CH), 128.1(CH), 128.3 (CH), 128.4 (CH), 130.3 (CH), 135.7 (Cq), 140.4 (Cq), 148.3 (Cq), 156.4 (Cq), 210.7 (Cq); HRMS (ESI) m/z calcd for $C_{22}H_{21}O_2$ $[M+H]^+$ 317.1542, found 317.1544.

4.4.6. (2R,3aS*)-3a-(2-cyanoethyl)-3-methylene-2-phenyl-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4ad**).* Colorless plates; mp 102.8–103.4 °C (recrystallized from benzene); IR (neat) 3398, 2243, 1707, 1693, 1600, 1494, 1452, 1149, 1009, 928 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08–2.15 (1H, m), 2.22–2.30 (1H, m), 2.37–2.51 (5H, m), 2.61–2.66 (1H, m), 4.87 (1H, d, J=2.0 Hz), 5.36–5.38 (1H, dd, J=2.8 and 7.6 Hz), 5.65–5.67 (2H, m), 7.21–7.22 (2H, m), 7.33–7.37 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0 (CH_2), 19.4 (CH_2), 32.0 (CH_2), 37.8 (CH_2), 56.0 (Cq), 83.8 (CH), 95.5 (CH), 112.9 (CH_2), 118.7 (Cq), 127.1 (CH), 128.6 ($CH\times2$), 139.7 (Cq), 145.8 (Cq), 156.4 (Cq), 208.5 (Cq); HRMS (ESI) m/z calcd for $C_{18}H_{17}NO_2Na$ $[M+Na]^+$ 302.1157, found 302.1158.

4.4.7. (2S,3aS*)-3a-Methyl-3-methylene-2-(naphthalen-1-yl)-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4ba**).* Colorless crystals; mp 129.3–132.6 °C (recrystallized from benzene); IR (neat) 2927, 1709, 1385, 1341, 1157, 1092, 1038, 786 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (3H, s), 2.36–2.47 (2H, m), 2.50–2.59 (1H, m), 2.61–2.70 (1H, m), 4.74 (1H, d, J=2.8 Hz), 5.23–5.25 (1H, m), 5.66 (1H, d, J=2.8 Hz), 6.49 (1H, s), 7.41–7.46 (2H, m), 7.47–7.51 (2H, m), 7.81–7.84 (1H, m), 7.84–7.88 (1H, m), 7.92–7.95 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6 (CH_2), 25.5 (CH_3), 37.8 (CH_2), 53.6 (Cq), 81.7 (CH), 93.3 (CH), 110.2 (CH_2), 124.0 (CH), 125.2 (CH), 125.7 (CH), 125.7 (CH), 126.2 (CH), 128.8 (CH), 129.1 (CH), 131.1 (Cq), 134.0 (Cq), 135.1 (Cq), 148.2 (Cq), 158.8 (Cq), 210.4 (Cq); HRMS (ESI) m/z calcd for $C_{20}H_{18}O_2Na$ $[M+Na]^+$ 313.1204, found 313.1195.

4.4.8. (2R,3aS*)-3a-Methyl-3-methylene-2-(naphthalen-2-yl)-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4ca**).* Colorless needles; mp 86.3–87.9 °C (recrystallized from benzene); IR (neat) 2970, 1709, 1342, 1090, 1038, 912, 872, 795 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (3H, s), 2.38–2.44 (2H, m), 2.52–2.55 (1H, m), 2.64–2.69 (1H, m), 4.72 (1H, d, J=2.0 Hz), 5.24 (1H, dd, J=2.4 and 7.6 Hz), 5.70 (1H, d, J=2.0 Hz), 5.90 (1H, t, J=2.0 Hz), 7.29 (1H, dd, J=2.0 and 8.8 Hz), 7.47–7.51 (2H, m), 7.74 (1H, s), 7.80–7.85 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6 (CH_2), 25.5 (CH_3), 37.8 (CH_2), 53.3 (Cq), 83.9 (CH), 92.8 (CH), 110.6 (CH_2), 124.7 (CH), 126.3 ($CH\times2$), 126.9 (CH), 127.7 (CH), 128.0 (CH), 128.6 (CH), 133.0 (Cq), 133.3 (Cq), 137.3 (Cq), 149.2 (Cq), 159.0 (Cq), 210.5 (Cq); HRMS (ESI) m/z calcd for $C_{20}H_{18}O_2Na$ $[M+Na^+]^+$ 313.1204, found 313.1198.

4.5. X-ray crystallograohic analysis of compound 4ca[7]

A colorless platelet crystal of $C_{20}H_{18}O_2$ having approximate dimensions of 0.80×0.80×0.30 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo Kα radiation. The structure was solved by direct methods (SIR97) and expanded using Fourier techniques (DIRDIF99). The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement on F was based on 7617 observed reflections ($I>0.00\sigma(I)$) and 218 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of R=0.054 and R_w=0.158. Crystal data for **4ca**: $C_{20}H_{18}O_2$, M=290.36, orthorhombic, space group $P2_12_12_1$, a=9.086(5) Å, b=9.040(5) Å, c=18.67(1) Å, V=1533(1) Å^3, Z=4, D_c=1.257 g/cm^3, $F(000)$=616.00, μ(Mo Kα)=0.80 cm^{-3}.

4.5.1. (2S,3aS*)-2-(Furan-3-yl)-3a-methyl-3-methylene-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4da**).* Pale yellow oil; IR (neat) 2927, 1718, 1501, 1157, 784, 608 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (3H, s), 2.29–2.34 (2H, m), 2.45–2.54 (1H, m), 2.56–2.66 (1H, m), 4.94 (1H, d, J=2.4 Hz), 5.13–5.16 (1H, m), 5.69 (1H, d, J=2.4 Hz), 5.77 (1H, t, J=2.4 Hz), 6.27 (1H, s), 7.38 (1H, s), 7.44 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5 (CH_3), 25.3 (CH), 37.4 (CH_2), 53.1 (Cq), 76.2 (CH), 93.2 (Cq), 109.0 (CH), 110.0 (CH_2), 124.2 (Cq), 141.4 (CH), 143.8 (CH), 147.8 (Cq), 158.2 (Cq), 210.3 (Cq); HRMS (ESI) m/z calcd for $C_{14}H_{15}O_3$ $[M+H]^+$ 231.1021, found 231.1017.

4.5.2. (2R,3aS*)-3a-Methyl-3-methylene-2-pentyl-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4ea**).* Pale yellow oil; IR (neat) 3458, 2930, 1717, 1384, 1089 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, J=7.6 Hz), 1.26–1.32 (5H, m), 1.41 (3H, s), 1.43–1.50 (2H, m), 1.67–1.69 (1H, m), 2.24–2.34 (2H, m), 2.42–2.51 (1H, m), 2.54–2.60 (1H, m), 4.79–4.83 (1H, m), 4.98 (1H, d, J=2.4 Hz), 5.07–5.10 (1H, m), 5.57 (1H, d, J=2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (CH_3), 19.5 (CH_2), 22.5 (CH_2), 25.7 (CH_3), 31.7 (CH_2), 34.8 (CH_2), 37.5 (CH_2), 53.4 (Cq), 81.7 (CH), 92.4 (CH), 107.3 (CH_2), 149.1 (Cq), 158.6 (Cq), 210.8 (Cq); HRMS (ESI) m/z calcd for $C_{15}H_{23}O_2$ $[M+H]^+$ 235.1698, found 235.1698.

4.5.3. (2R,3aS*)-2-(3,4-Dimethoxyphenyl)-3a-methyl-3-methylene-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4ga**).* Pale yellow oil; IR (neat) 2936, 1714, 1594, 1517, 1463, 1261, 1164, 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (3H, s), 2.32–2.41 (2H, m), 2.48–2.57 (1H, m), 2.60–2.69 (1H, m), 3.85 (3H, s), 3.87 (3H, s), 4.76 (1H, d, J=1.6 Hz), 5.17–5.19 (1H, m), 5.69–5.71 (2H, m), 6.73 (1H, s), 6.83 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5 (CH_2), 25.3 (CH_3), 37.6 (CH_2), 53.3 (Cq), 55.8 (CH_3), 55.8 (CH_3), 83.7 (CH), 92.5 (CH), 110.3 (CH_2), 110.4 (CH), 110.8 (CH), 120.3 (CH), 132.2 (Cq), 149.0 (Cq), 149.1

(Cq), 149.2 (Cq), 158.7 (Cq), 210.4 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{18}H_{21}O_4$ $[M+H]^+$ 301.1440, found 301.1446.

4.5.4. (2R,3aS*)-2-(3,4-Dimethoxyphenyl)-3a-(2-cyanoethyl)-3-methylene-3,3a,5,6-tetrahydrobenzofuran-4(2H)-one (**4gd**).* Pale yellow oil; IR (neat) 2937, 2248, 1714, 1594, 1518, 1261, 1141, 1027, 1027, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.11–2.15 (1H, m), 2.21–2.26 (1H, m), 2.36–2.50 (5H, m), 2.62–2.66 (1H, m), 3.85 (3H, s), 3.87 (3H, s), 4.93 (1H, d, *J*=2.4 Hz), 5.39 (1H, dd, *J*=2.4 and 7.2 Hz), 5.63 (1H, t, *J*=2.4 Hz), 5.69 (1H, d, *J*=2.4 Hz), 6.71 (1H, d, *J*=2.0 Hz), 6.80 (1H, dd, *J*=2.0 and 8.0 Hz), 6.84 (1H, d, *J*=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0 (CH_2), 19.4 (CH_2), 31.9 (CH_2), 37.7 (CH_2), 55.8 (CH_3), 55.9 (CH_3), 56.2 (Cq), 83.9 (CH), 95.4 (CH), 110.4 (CH), 111.0 (CH), 113.0 (CH_2), 118.7 (Cq), 120.2 (CH), 131.8 (Cq), 145.6 (Cq), 149.1 (Cq), 149.4 (Cq), 156.3 (Cq), 208.4 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{20}H_{21}NO_4Na$ $[M+Na]^+$ 362.1368, found 362.1374.

4.6. General procedure for the reaction of propargylic esters 1 with β-keto esters 3 using palladium catalyst

Reaction of **1a** with **3** (Table 5, entry 1): To a stirred solution of propargylic carbonate **1a** (25.0 mg, 131 μmol) in DMSO (2.0 mL) were added methyl-2-oxo-cyclohexane carboxylate **3** (40.9 mg, 262 μmol), $Pd_2(dba)_3 \cdot CHCl_3$ (6.8 mg, 6.6 μmol), and dppf (14.5 mg, 26.2 μmol) at rt, and stirring was continued for 30 min at the same temperature under argon atmosphere. The reaction mixture was then allowed to heat to 120 °C, and stirred for 5 min. After filtration of the reaction mixture using small amount of silica gel followed by concentration, the residue was chromatographed on silica gel with hexane–AcOEt (9:1 v/v) as eluent to give tetrahydrobenzofuranone **5a** (32.7 mg, 92%) as a pale yellow oil.

4.6.1. (2S,3aR*)-Methyl 3-methylene-2-phenyl-2,3,3a,4,5,6-hexahydrobenzofuran-3a-carboxylate (**5a**).* Colorless oil; IR (neat): 2950, 1731, 1495, 1454, 1334, 1000, 795 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.37–1.44 (1H, ddd, *J*=2.8, 12.4, and 14.0 Hz), 1.50–1.61 (1H, m), 1.84–1.90 (1H, m), 2.14–2.20 (2H, m), 2.69 (1H, td, *J*=3.2 and 12.4 Hz), 3.79 (3H, s), 4.71 (1H, d, *J*=2.4 Hz), 5.06 (1H, t, *J*=3.2 Hz), 5.24 (1H, d, *J*=2.4 Hz), 5.70 (1H, t, *J*=2.4 Hz), 7.25–7.29 (2H, m), 7.30–7.38 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2 (CH_2), 22.5 (CH_3), 30.0 (CH_2), 52.8 (CH_3), 54.5 (Cq), 83.3 (CH), 95.9 (CH), 110.4 (CH_2), 127.3 (CH), 128. 2 (CH), 128.4 (CH), 140.2 (Cq), 151.9 (Cq), 154.0 (Cq), 172.3 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{17}H_{18}O_3Na$ $[M+Na]^+$ 293.1154, found 293.1166.

4.6.2. (2S,3aR*)-Methyl 3-methylene-2-(naphthalen-1-yl)-2,3,3a,4,5,6-hexahydrobenzofuran-3a-carboxylate (**5b**).* Pale yellow oil; IR (neat) 2932, 1732, 1228, 1143, 991, 796 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.46–1.66 (2H, m), 1.89–1.95 (1H, m), 2.23–2.27 (2H, m), 2.73 (1H, td, *J*=3.2 and 12.4 Hz), 3.85 (3H, s), 4.68 (1H, d, *J*=2.8 Hz), 5.14 (1H, t, *J*=3.2 Hz), 5.19 (1H, t, *J*=2.8 Hz), 6.41 (1H, t, *J*=2.8 Hz), 7.44–7.53 (4H, m), 7.82–7.90 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2 (CH_2), 22.6 (CH_2), 29.9 (CH_2), 53.0 (CH_3), 54.8 (Cq), 81.7 (CH), 96.5 (CH), 110.1 (CH_2), 124.4 (CH), 125.3 (CH), 125.6 (CH), 125.8 (CH), 126.0 (CH), 128.8 (CH), 129.0 (CH), 131.0 (Cq), 134.1 (Cq), 135.4 (Cq), 150.6 (Cq), 153.9 (Cq), 172.4 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{20}O_3Na$ $[M+Na]^+$ 343.1310, found 343.1314.

4.6.3. (2S,3aR*)-Methyl 3-methylene-2-(naphthalen-2-yl)-2,3,3a,4,5,6-hexahydrobenzofuran-3a-carboxylate (**5c**).* Colorless crystals; mp 106.8–108.3 °C (recrystallized from hexane–benzene); IR (KBr) 2949, 1735, 1432, 1262, 1142, 996, 903, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (1H, ddd, *J*=2.8, 12.4, and 14.8 Hz), 1.52–1.64 (1H, m), 1.86–1.92 (1H, m), 2.16–2.25 (2H, m), 2.72 (1H, td, *J*=3.6 and 12.4 Hz), 3.81 (3H, s), 4.70 (1H, d, *J*=2.8 Hz), 5.11 (1H, t, *J*=3.6 Hz), 5.26 (1H, d, *J*=2.8 Hz), 5.87 (1H, t, *J*=2.8 Hz), 7.31 (1H, dd, *J*=1.6 and 22.4 Hz) 7.46–7.51 (2H, m), 7.76 (1H, m), 7.81–7.51 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2 (CH_2), 22.5 (CH_2), 29.9 (CH_2), 52.9 (CH_3), 54.5 (Cq), 83.5 (CH), 96.1 (CH), 110.6 (CH_2), 124.7 (CH), 126.2 (CH), 126.2 (CH), 126.8 (CH), 127.7 (CH), 127.9 (CH), 128.5 (CH), 133.0 (Cq), 133.3 (Cq), 137.5 (Cq), 151.8 (Cq), 154.1 (Cq), 172.3 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{20}O_3Na$ $[M+Na]^+$ 343.1310, found 343.1307.

4.7. X-ray crystallograohic analysis of compound 5c[11]

A colorless platelet crystal of $C_{21}H_{20}O_3$ having approximate dimensions of 0.50×0.50×0.10 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo Kα radiation. The structure was solved by direct methods (SIR97) and expanded using Fourier techniques (DIRDIF99). The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement on *F* was based on 7266 observed reflections ($I>0.00\sigma(I)$) and 474 variable parameters and converged (largest parameter shift was 1.13 times its esd) with unweighted and weighted agreement factors of R=0.110 and R_w=0.338. Crystal data for **5c**: $C_{20}H_{18}O_2$, M=320.39, monoclinic, space group $P2_1$, a=12.765(1) Å, b=7.2963(9) Å, c=18.400(3) Å, β=103.473(4)°, V=1666.5(4) $Å^3$, Z=4, D_c=1.277 g/cm^3, $F(000)$=680.00, μ(Mo Kα)=0.84 cm^{-3}.

4.7.1. (2S,3aR*)-Methyl 2-(furan-3-yl)-3-methylene-2,3,3a,4,5,6-hexahydrobenzofuran-3a-carboxylate (**5d**).* Pale yellow oil; IR (neat) 2951, 1733, 1447, 1334, 1228, 1142, 874, 799, 602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.39 (1H, ddd, *J*=2.8, 12.0, and 14.8 Hz), 1.49–1.60 (1H, m), 1.82–1.88 (1H, m), 2.10–2.17 (2H, m), 2.69 (1H, td, *J*=3.6 and 12.0 Hz), 3.76 (3H, s), 4.93 (1H, d, *J*=2.4 Hz), 5.00 (1H, t, *J*=3.6 Hz), 5.28 (1H, d, *J*=2.4 Hz), 5.75 (1H, t, *J*=2.4 Hz), 6.27–6.28 (1H, m), 7.39–7.42 (1H, m), 7.49 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2 (CH_2), 22.4 (CH_2), 29.9 (CH_2), 52.9 (CH_3), 54.2 (Cq), 75.7 (CH), 96.3 (CH), 109.0 (CH), 110.0 (CH_2), 124.0 (Cq), 141.4 (CH), 143.7 (CH), 150.3 (Cq), 153.2 (Cq), 172.3 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{15}H_{16}O_4Na$ $[M+Na]^+$ 283.0946, found 283.0944.

4.7.2. (2S,3aR*)-Methyl 3-methylene-2-pentyl-2,3,3a,4,5,6-hexahydrobenzofuran-3a-carboxylate (**5e**).* Pale yellow oil; IR (neat) 2935, 1735, 1699, 1263, 1227, 1151, 902, 794 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, *J*=6.8 Hz), 1.25–1.33 (5H, m), 1.39–1.59 (4H, m), 1.69–1.75 (1H, m), 1.79–1.82 (1H, m), 2.01–2.17 (2H, m), 2.62 (1H, td, *J*=3.6 and 12.4 Hz), 3.71 (3H, s), 4.76–4.79 (1H, m), 4.91 (1H, t, *J*=3.6 Hz), 5.01 (1H, d, *J*=2.4 Hz), 5.18 (1H, d, *J*=2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (CH_3), 19.2 (CH_2), 22.4 (CH_2), 22.5 (CH_2), 24.9 (CH_2), 29.9 (CH_2), 31.7 (CH_2), 34.1 (CH_2), 52.7 (CH_3), 54.4 (Cq), 80.9 (CH), 95.7 (CH), 107.1 (CH_2), 151.0 (Cq), 153.3 (Cq), 172.6 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{16}H_{25}O_3$ $[M+H]^+$ 265.1804, found 265.1808.

4.7.3. (2S,3aR*)-Methyl 2-(3,4-dimethoxyphenyl)-3-methylene-2,3,3a,4,5,6-hexahydrobenzofuran-3a-carboxylate (**5f**).* Pale yellow oil; IR (neat) 2938, 1732, 1518, 1464, 1263, 1207, 798, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.41 (1H, ddd, *J*=3.2, 12.0, and 14.8 Hz), 1.50–1.59 (1H, m), 1.86–1.89 (1H, m), 2.15–2.19 (2H, m), 2.69 (1H, td, *J*=3.2 and 12.0 Hz), 3.78 (3H, s), 3.86 (3H, s), 3.88 (3H, s), 4.75 (1H, d, *J*=2.4 Hz), 5.04 (1H, t, *J*=3.2 Hz), 5.26 (1H, d, *J*=2.4 Hz), 5.66 (1H, t, *J*=2.4 Hz), 6.75 (1H, s), 6.87 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0 (CH_2), 22.3 (CH_2), 29.8 (CH_2), 52.7 (CH_3), 54.4 (Cq), 55.7 (CH_3), 55.7 (CH_3), 83.2 (CH), 95.6 (CH), 110.2 (CH_2), 110.2 (CH), 110.7 (CH), 120.0 (CH), 132.3 (Cq), 148.8 (Cq), 149.0 (Cq), 151.6 (Cq), 153.7 (Cq), 172.1

(Cq); HRMS (ESI) m/z calcd for $C_{19}H_{23}O_5$ $[M+H]^+$ 331.1545, found 331.1542.

Acknowledgements

This study was supported in part by a Grant-in-Aid for the Encouragement of Young Scientists (B) from the Japan Society for the Promotion of Science (JSPS), Takeda Science Foundation, Uehara Memorial Foundation and the Program for Promotion of Basic and Applied Researches for Innovations in Bio-oriented Industry (BRAIN).

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5. One part of the results on our preliminary studies has been published: Yoshida, M.; Higuchi, M.; Shishido, K. *Tetrahedron Lett.* **2008**, *49*, 1678.
6. From previous studies, it is known that bidentate ligands are suitable for the palladium-catalyzed reactions of propargylic compounds with soft nucleophiles, see Refs. 2 and 3.
7. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 665659. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
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