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Highly Regioselective Construction of Spirocycles via Phosphine-Catalyzed [3 + 2]-Cycloaddition

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A direct entry to spirocycles with low to moderate regioselectivity was achieved by triphenylphosphine-catalyzed [3 + 2]-cycloaddition of active *exo*-methylenecycles (**1**) and ethyl 2,3-butadienoate (**2**). The regioselectivity of the reaction was greatly improved by using the bulky *tert*-butyl ester of the 2,3-butadienoate (**5**). The regioselectivity of the reaction was further enhanced by using the *tert*-butyl 2-butynoate as the substrate. This protocol provided an efficient entry to the skeleton of spirocarbocycles, especially spiro[4.*n*]alkanes.

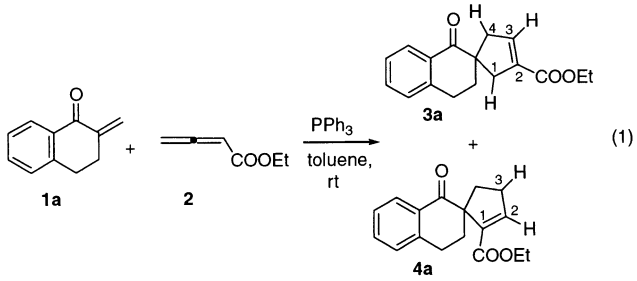
Introduction

Spirocyclic skeletons widely occur in a large number of natural products.[1] Among many approaches to make spirocycles, [3 + 2]-cycloaddition is one of the most efficient methods of synthesizing spiro[4.*n*]alkanes.[2] The common difficulty lies in the selective construction of the spirocycles and the control of their stereochemistry. It is still a challenge for synthetic chemists to develop a simple method to construct spirocarbocycles.

Recently, some important reactions were discovered in the phosphine-catalyzed reaction of 2,3-butadienoates or 2-butynoates,[3] such as isomerization,[4] α-addition,[5] γ-addition,[6] and [3 + 2]-cycloaddition.[7] We envisioned that an efficient entry to spirocarbocycles might be achieved by the application of our recently developed method of the phosphine-catalyzed [3 + 2]-cycloaddition reaction.[8] Herein, we wish to report an efficient and practical method of constructing spirocyclic skeletons with high regioselectivity.

Results and Discussion

To initiate our studies, a solution of 2-methylene-3,4-dihydro-2*H*-naphthalen-1-one (**1a**) (1.0 mmol) and ethyl 2,3-butadienoate (**2**) (1.2 mmol) in dry toluene (10 mL) was treated with Ph_3P (10 mol %) at room temperature for 11 h. Two regioisomers were obtained in total yield of 93% with moderate selectivity (**3a**:**4a** = 79:21) (eq 1).



Compounds **3a** and **4a** have been characterized by spectroscopic analysis (IR, ^{1}H NMR, ^{13}C NMR, ^{1}H −^{1}H

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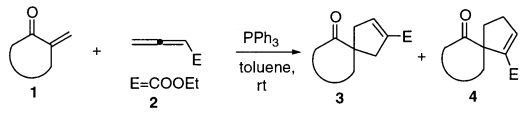
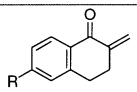
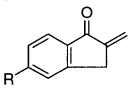
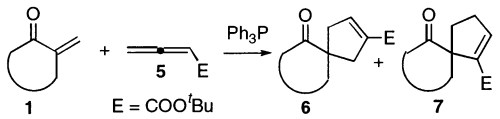
TABLE 1. . Triphenylphosphine-Catalyzed [3 + 2]-Cycloaddition of 1 and 2[a]



Substrate		Time, h	Yield / %[b] (Ratio: **3**:**4**)[c]
	R = H: **1a**	11	93 (79:21)
	R = OMe: **1b**	64	55 (83:17)
	R = H: **1c**	6	98 (84:16)
	R = Br: **1d**	4	98 (78:22)
	R = OMe: **1e**	12	92 (83:17)
	**1f**	-[d]	-[d]
	**1g**	13	73 (58:42)
	R = Boc: **1h**	120	33 (62:38)
	R = Ts: **1i**	13	94 (82:18)
	**1j**	23	96 (65:35)

[a] A solution of **1** (1.0 mmol), **2** (1.2 mmol), and PPh_3 (0.10 mmol) in dry toluene (10 mL) was stirred at room temperature. [b] Isolated yield. [c] Determined by ^1H NMR. [d] The reaction is sluggish.

TABLE 2. Triphenylphosphine-Catalyzed [3 + 2]-Cycloaddition Reaction of 1 and 5[a]



entry	substrate	time, h	yield, %[b] (ratio **6**:**7**)[c]
1	**1a**	18	98 (91:9)
2	**1b**	50	95 (92:8)
3	**1c**	3	99 (95:5)
4	**1d**	2	98 (93:7)
5	**1e**	4	96 (92:8)
6[d]	**1f**	72	78 (80:20)
7[d]	**1g**	2	63 (78:22)
8	**1h**	96	92 (92:8)
9	**1i**	7	93 (91:9)
10	**1j**	12	90 (74:26)

[a] A solution of **1** (0.20 mmol), **5** (0.24 mmol), and PPh_3 (0.02 mmol, 10 mol %) in dry benzene (2 mL) was stirred at reflux. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Reaction was performed in toluene.

COSY, DEPT 135°, HMQC, and MS) and elemental analysis. The characteristic feature of the spectra of **3a** was that the olefinic hydrogen C_3−H, which appeared as a multiplet, showed two strong vicinal couplings with C_4−H and two weak allylic couplings with C_1−H in ^1H−^1H COSY experiments. The spectra of **4a** showed that the olefinic hydrogen C_2−H exhibited only one vicinal coupling with C_3−H as a triplet. Another important difference between **3a** and **4a** in the ^1H NMR spectra is that the chemical shift of the olefinic hydrogen of **3a** lies in a higher field than that of **4a** due to the effect of the carbonyl group.

SCHEME 1

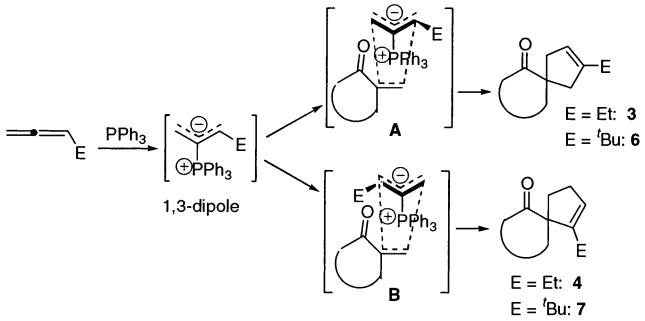
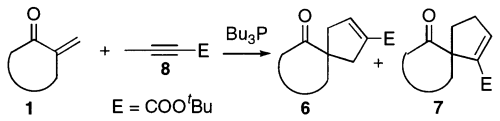


TABLE 3. Tributylphosphine-Catalyzed [3 + 2]-Cycloaddition Reaction of 1 and 8[a]



entry	substrate	time, h	yield, %[b] (ratio **6**:**7**)[c]
1	**1a**	-	-[d]
2	**1b**	40	96 (90:10)
3	**1c**	-	-[d]
4	**1d**	-	-[d]
5	**1e**	11	10[d] (>97:3)
6	**1f**	48	56 (92:8)
7	**1g**	4	19 (89:11)
8	**1h**	17	96 (>97:3)
9	**1i**	16	30[d] (>97:3)
10	**1j**	21	94 (>97:3)

[a] A solution of compound **1** (0.20 mmol), **8** (0.24 mmol), and PBu_3 (0.04 mmol, 20 mol %) in dry toluene (2 mL) was stirred at room temperature. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Precipitation of a white solid occurred.

Under similar conditions as shown in eq 1, other *exo*-methylenecycles underwent addition of ethyl 2,3-butadienoate to obtain regioisomeric spirocycles in total yields of 28−98% with low to moderate selectivity (**3**:**4** = 58:42 to 84:16) (Table 1).

The regioselectivity of the reaction was greatly improved by introducing a bulky group into the 2,3-butadienoate. When *tert*-butyl 2,3-butadienoate (**5**) was used as a three-carbon synthon instead of ethyl 2,3-butadienoate, the reaction proceeded smoothly to afford spirocycles **6** and **7** in high yields (63−99%) with moderate to high selectivities (**6**:**7** = 74:26 to 95:5) (Table 2).

The great enhancement of the regioselectivity by introducing a bulky group into the 2,3-butadienoate might be rationalized by comparing the transition states **A** and **B** of the reaction. The higher energy will occur in **B** due to the steric influence of the bulky group (E) with the skeleton of C2 components, making the product **3** or **6** more preferable (Scheme 1).

It was also shown in Table 2 that the regioselectivities of α-methylenecycloalkanones **1f,g** (entries 6 and 7) and compound **1j** (entry 10) were still not good enough. According to our previous study, nucleophilic addition of phosphines to 2-butynoates can form the similar 1,3-dipole intermediates as those derived from 2,3-butadienoates with phosphines,[3,7a] and the regioselectivities of 2-butynoate were generally better than that of 2,3-butadienoate in the [3 + 2]-cycloaddition.[7a]

When *tert*-butyl 2-butynoate (**8**) was used instead of *tert*-butyl 2,3-butadienoate (**5**) in the tributylphosphine-catalyzed [3 + 2]-cycloaddition reaction, the regioselectivity was further improved in some cases (>97:3). Especially, improved high regioselectivities were observed for the simple α-methylenecycloalkanones (entries 6 and 7, **6**:**7** = 89:11 to 92:8), which were of considerable interest as a synthetic route to naturally occurring spiro[4.5]decane sesquiterpenes and spiro[4.4]nonanes (Table 3).

Conclusion

An efficient approach with high regioselectivity to prepare spiro[4.*n*]alkanes, especially the skeleton of spiro[4.5]decanes, via phosphine-catalyzed [3 + 2]-cycloaddition reaction was developed, which features a rapid and efficient construction of the spirocarbocyclic skeleton.

Experimental Section

General. For ^{13}C NMR, chemical shifts were reported relative to $CHCl_3$ (77.00 ppm for ^{13}C NMR) as an internal reference. 2-Methylene-3,4-dihydro-2*H*-naphthalen-1-one (**1a**),[9] 2-methylenecyclohexanone (**1f**),[10] 2-methylenecyclopentanone (**1g**),[10] 1,3-bibenzyl-5-methylenehydantoin (**1j**),[11] ethyl 2,3-butadienoate (**2**),[12] *tert*-butyl 2,3-butadienoate (**5**),[12] and *tert*-butyl 2-butynoate (**8**)[13] were prepared by the reported methods.

Synthesis of α-Methylenecycloalkanones or -cycloalkanamides (1). Compounds **1b**,[9] **1c**,[9] **1d**,[14] and **1e**[14] were synthesized by a method similar to that of the literature. Compounds **1h** and **1i** were prepared from the 3-methylenepyrrolidin-2-one by the usual methods.[15]

2-Methylene-3,4-dihydro-2*H*-naphthalen-1-one (1a):[9] white solid; mp 46−47 °C (ethyl acetate−hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.8, 1.0 Hz, 1 H), 7.38 (td, J = 7.5, 1.4 Hz, 2H), 7.24 (bt, J = 7.9 Hz, 1H), 7.15 (dd, J = 7.5, 0.5 Hz, 1H), 6.14 (br s, 1H), 5.35 (q, J = 1.6 Hz, 1H), 2.90 (t, J = 6.0 Hz, 2H), 2.76 (br t, J = 6.0 Hz, 2H).

6-Methoxy-2-methylene-3,4-dihydro-2*H*-naphthalen-1-one (1b):[16] white solid; mp 44−45.5 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1664, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 8.7 Hz, 1 H), 6.76 (dd, J = 8.7, 2.4 Hz, 1H), 6.61 (d, J = 2.1 Hz, 1H), 6.10 (br s, 1H), 5.31 (br s, 1H), 3.76 (s, 3H), 2.87 (t, J = 5.9 Hz, 2H), 2.74 (m, 2H); MS (*m*/*z*) 188 (M^+, 100), 160, 148, 145, 120, 115, 91. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.38; H, 6.39.

2-Methyleneindan-1-one (1c):[17] oil;^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.7 Hz, 1 H), 7.65 (td, J = 7.7, 1.0 Hz, 1H), 7.53 (d, J = 7.7 Hz, 1H), 7.45 (t, J = 7.7 Hz, 1H), 6.41 (s, 1H), 5.68 (s, 1H), 5.07 (s, 2H).

5-Bromo-2-methyleneindan-1-one (1d): white solid; mp 95−97 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1697, 1642 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 8.2 Hz, 1H), 7.68 (s, 1H), 7.55 (d, J = 8.2 Hz, 1H), 6.39 (br s, 1H), 5.67 (br s, 1H), 3.75 (br s, 2H); MS (*m*/*z*) 222 (M^+, ^{79}Br). Anal. Calcd for $C_{10}H_7BrO$: C, 53.84; H, 3.16. Found: C, 53.81; H, 3.19.

5-Methoxy-2-methyleneindan-1-one (1e): white solid; mp 83−85 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1691, 1647 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 1H), 6.94 (d, J = 8.2 Hz, 1H), 6.92 (s, 1H), 6.30 (m, 1H), 5.57 (m, 1H), 3.90 (s, 3H), 3.71(s, 2H); MS (*m*/*z*) 175 (M^+ + 1), 174 (M^+, 100), 146, 131, 115, 103, 102, 77. Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.99; H, 5.84.

2-Methylenecyclohexanone (1f):[10] ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (m, 1H), 5.14 (m, 1H), 2.61−2.56 (m, 2H), 2.47−2.43 (m, 2H), 1.92−1.88 (m, 2H), 1.79−1.75 (m, 2H).

2-Methylene-cyclopentanone (1 g).[10] ^1H NMR (300 MHz, $CDCl_3$) δ 5.98 (m, 1H), 5.32 (m, 1H), 2.72−2.65 (m, 2H), 2.35 (t, J = 8.2 Hz, 2H), 1.99−1.92 (m, 2H).

1-*tert*-Butoxycarbonyl-3-methylenepyrrolidin-2-one (1h): white solid; mp 73−75 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1778, 1742, 1716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.11 (t, J = 2.8 Hz, 1H), 5.40 (t, J = 2.5 Hz, 1H), 3.66 (t, J = 7.0 Hz, 2H), 2.67 (m, 2H), 1.49 (s, 9H); MS (*m*/*z*) 198 (M^+ + 1), 197 (M^+), 142, 124, 98, 96, 57 (100), 56, 43, 41. Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.90; H, 7.67; N, 7.10. Found: C, 60.54; H, 7.63; N, 7.47.

3-Methylene-1-tosylpyrrolidin-2-one (1i): white solid; mp 104−106 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1718, 1660, 1596 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.97 (dd, J = 7.6, 0.5 Hz, 2 H), 7.35 (dd, J = 7.6, 0.5 Hz, 2 H), 6.11 (t, J = 2.8 Hz, 1H), 5.47 (t, J = 2.5 Hz, 1H), 3.89 (t, J = 6.9 Hz, 2H), 2.85−2.78 (m, 2H), 2.44 (s, 3H); MS (*m*/*z*) 252 (M^+ + 1), 187 (100), 186, 119, 91, 89, 68, 65. Anal. Calcd for $C_{12}H_{13}NO_3S$: C, 57.35; H, 5.21; N, 5.57. Found: C, 57.21; H, 5.41; N, 5.50.

1,3-Bibenzyl-5-methylenehydantoin (1j):[11] white solid; mp 84−85 °C (ethyl acetate−petroleum ether); ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (m, 10H), 6.30 (d, J = 2 Hz, 1H), 4.72 (s, 4H), 4.63 (d, J = 2 Hz, 1H).

Triphenylphosphine-Catalyzed [3 + 2]-Cycloaddition of 1 with Ethyl 2,3-Butadienoate (2) (Table 1). A solution of **1** (1.0 mmol), ethyl 2,3-butadienoate (**2**) (1.2 mmol), and PPh_3 (0.10 mmol) in dry toluene (10 mL) was stirred at room temperature. The mixture was then stirred for the indicated time at room temperature. The reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (petroleum ether−ethyl acetate) to give **3** and **4**.

Ethyl 1′-oxo-3′,4′-dihydrospiro[cyclopent-3-ene-1,2′-naphthalene]-3-carboxylate (3a): oil; IR (neat) ν 1713, 1683, 1639 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 7.9 Hz, 1H), 7.40 (td, J = 7.5, 1.2 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 6.64 (m, 1H), 4.11 (q, J = 7.2 Hz, 2H), 3.09 (ddd, J = 18.7, 4.5, 2.2 Hz, 1H), 3.04−2.87 (m, 3H), 2.63 (br d, J = 15.3 Hz, 1H), 2.39 (ddd, J = 18.6, 4.4, 1.9 Hz, 1H), 2.12 (t, J = 6.9 Hz, 2H) 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.1, 164.8, 143.3, 140.9, 133.6, 133.4, 131.2, 128.8, 128.4, 126.9, 60.4, 52.1, 42.2, 40.2, 34.7, 25.9, 14.4; MS (*m*/*z*) 270 (M^+). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.50; H, 6.94.

Ethyl 1′-oxo-3′,4′-dihydrospiro[cyclopent-2-ene-1,2′-naphthalene]-2-carboxylate (4a): white solid; mp 52−54 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1710, 1677, 1625 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, J = 7.7, 1.3 Hz, 1H), 7.39 (td, J = 7.5, 1.4 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 6.94 (t, J = 2.6 Hz, 1H), 4.05 (q, J = 7.1 Hz, 2H), 3.05 (ddd, J = 16.7, 13.2, 4.5 Hz, 1H), 2.86 (ddd, J = 16.7, 4.5, 2.9 Hz, 1H), 2.70 (tdd, J = 13.2, 4.5, 0.5 Hz, 1 H), 2.51 (td, J = 7.6, 2.5 Hz, 2H), 2.17 (dt, J = 13.1, 6.5 Hz, 1H), 2.04 (dtd, J = 13.1, 7.6, 0.6 Hz, 1H) 1.86 (ddd, J = 13.1, 4.5, 2.8 Hz, 1 H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.8, 164.0, 145.8, 143.5, 140.2, 133.3, 131.9, 128.5, 128.2, 126.8, 60.3, 59.5, 33.5, 32.0, 30.9, 26.4, 14.2; MS (*m*/*z*) 270 (M^+). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.34; H, 6.60.

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Ethyl 6′-Methoxy-1′-oxo-3′,4′-dihydrospiro[cyclopent-3-ene-1,2′-naphthalene]-3-carboxylate (3b): oil; IR (neat) ν 1712, 1673, 1638 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 8.8 Hz, 1H), 6.74 (dd, J = 8.8, 2.5 Hz, 1H), 6.62 (m, 1H), 6.59 (d, J = 2.5 Hz, 1H), 4.09 (q, J = 7.1 Hz, 2H), 3.76 (s, 3H), 3.09−2.82 (m, 4H), 2.59 (br d, J = 18.3 Hz, 1H), 2.36 (br d, J = 18.5 Hz, 1H), 2.07 (t, J = 5.9 Hz, 2H) 1.19 (t, J = 7.1 Hz, 3H); MS (m/z) 300 (M$^+$); EI-HRMS calcd for $C_{18}H_{20}O_4$ 300.1361, found 300.1330.

Ethyl 6′-Methoxy-1′-oxo-3′,4′-dihydrospiro[cyclopent-2-ene-1,2′-naphthalene]-2-carboxylate (4b): oil; IR (neat) ν 1708, 1666 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 8.7 Hz, 1H), 7.00 (t, J = 2.5 Hz, 1H), 6.84 (dd, J = 8.7, 2.5 Hz, 1H), 6.69 (br d, J = 2.2 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.11−3.05 (m, 1H), 2.90−2.75 (m, 2H), 2.58 (m, 2H), 2.25−2.07 (m, 2H), 1.93−1.86 (m, 1H) 1.20 (t, J = 7.1 Hz, 3H); MS (m/z) 300 (M$^+$). Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.90; H, 6.72.

Ethyl 1′,3′-Dihydro-1′-oxospiro[cyclopent-3-ene-1,2′-indane]-3-carboxylate (3c): oil; IR (neat) ν 1712, 1636, 1608 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, J = 7.6, 0.4 Hz, 1H), 7.62 (td, J = 7.3, 1.1 Hz, 1H), 7.47−7.40 (m, 2H), 6.77 (m, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.22−3.03 (m, 4H), 2.64−2.47 (m, 2H), 1.30 (t, J = 7.1 Hz, 3H); MS (m/z) 256 (M$^+$). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.02; H, 6.41.

Ethyl 1′,3′-Dihydro-1′-oxospiro[cyclopent-2-ene-1,2′-indane]-2-carboxylate (4c): oil; IR (neat) ν 1712, 1629, 1609 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 7.6 Hz, 1H), 7.60 (td, J = 7.6, 1.2 Hz, 1H), 7.43 (dt, J = 7.7, 0.8 Hz, 1H), 7.36 (td, J = 7.7, 0.8 Hz, 1H), 7.08 (t, J = 2.6 Hz, 1H), 4.01 (q, J = 7.1 Hz, 2H), 3.44 (d, J = 17.1 Hz, 1H), 3.15 (d, J = 17.1 Hz, 1H), 2.74−2.64 (m, 2H), 2.48−2.38 (m, 1H), 2.03−1.95 (m, 1H), 1.01 (t, J = 7.1 Hz, 3H); MS (m/z) 256 (M$^+$). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.73; H, 6.43.

Ethyl 5′-bromo-1′,3′-dihydro-1′-oxospiro[cyclopent-3-ene-1,2′-indane]carboxylate and ethyl 5′-bromo-1′,3′-dihydro-1′-oxo-spiro[cyclopent-2-ene-1,2′-indane]-2-carboxylate (3d and 4d): oil; IR (neat) ν 1716, 1635 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66−7.54 (m, 3H), 7.07 (br s, 0.22H), 6.74 (br s, 0.78H), 4.25−4.02 (m, 2H), 3.36−3.03 (m, 4H), 2.70−2.45 (m, 2H), 1.32−1.00 (m, 3H); MS (m/z) 334 (M$^+$, ^{79}Br). Anal. Calcd for $C_{16}H_{15}BrO_3$: C, 57.33; H, 4.51. Found: C, 57.32; H, 4.66.

Ethyl 5′-methoxy-1′,3′-dihydro-1′-oxo-spiro[cyclopent-3-ene-1,2′-indane]-3-carboxylate and ethyl 5′-methoxy-1′,3′-dihydro-1′-oxo-spiro[cyclopent-2-ene-1,2′-indane]-2-carboxylate (3e and 4e): oil; IR (neat) ν 1702, 1634 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.5 Hz, 1H), 7.06 (m, 0.18H), 6.59 (br d, J = 8.5 Hz, 1H), 6.87 (br s, 1H), 6.75 (m, 0.82H), 4.20 (q, J = 7.1 Hz, 1.64H), 4.03 (q, J = 7.1 Hz, 0.36H), 3.88 (s, 3H), 3.40 (d, J = 17.2 Hz, 0.18H), 3.18−3.01 (m, 3.82H), 2.61−2.41 (m, 2H), 1.28 (t, J = 7.1 Hz, 2.46H), 1.05 (t, J = 7.1 Hz, 0.54H); MS (m/z) 286 (M$^+$); EI-HRMS calcd for $C_{17}H_{18}O_4$ 286.1205, found 286.1177.

Ethyl 6-oxospiro[4.4]non-2-ene-2-carboxylate and ethyl 6-oxospiro[4.4]non-1-ene-1-carboxylate (3g and 4g): oil; IR (neat) ν 1739, 1710, 1625 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94 (t, J = 2.5 Hz, 0.42H), 6.65 (m, 0.58H), 4.2−4.1 (m, 2H), 2.86−2.81 (m, 1.16H), 2.60−1.70 (m, 8.84H), 1.3−1.1 (m, 3H); MS (m/z) 208 (M$^+$). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 68.85; H, 7.94.

Ethyl 2-(*tert*-butoxycarbonyl)-1-oxo-2-azaspiro[4.4]-non-7-ene-7-carboxylate (3h): oil; IR (neat) ν 1785, 1751, 1716, 1638 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.67 (m, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.70 (td, J = 6.8, 0.7 Hz, 2H), 3.11−3.02 (m, 2H), 2.64−2.43 (m, 2H), 2.07−1.95 (m, 2H), 1.54 (s, 9H), 1.29 (t, J = 7.1 Hz, 3H); MS (m/z) 236 (M$^+$ − O^{t}Bu). Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 62.53; H, 7.76; N, 4.33.

Ethyl 2-(*tert*-butoxycarbonyl)-1-oxo-2-azaspiro[4.4]-non-6-ene-6-carboxylate (4h): white solid; mp 107−110.5 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1784, 1752, 1718, 1628 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (t, J = 2.5 Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 3.91 (m, 1H), 3.63 (m, 1H), 2.67−2.36 (m, 4H), 2.03−1.9 (m, 2H), 1.54 (s, 9H), 1.26 (t, J = 7.2 Hz, 3H); MS (m/z) 236 (M$^+$ − O^{t}Bu). Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 62.28; H, 7.53; N, 4.48.

Ethyl 2-tosyl-1-oxo-2-azaspiro[4.4]non-7-ene-7-carboxylate and ethyl 2-tosyl-1-oxo-2-azaspiro[4.4]non-6-ene-6-carboxylate (3i and 4i): oil; IR (neat) ν 1731, 1712 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 8.3 Hz, 2 H), 7.34 (dd, J = 8.5, 0.5 Hz, 2 H), 6.91 (t, J = 2.5 Hz, 0.18H), 6.57 (m, 0.82H), 4.16 (q, J = 7.1 Hz, 1.64H), 4.01(q, J = 7.1 Hz, 0.36H), 3.89−3.75 (m, 2H), 2.91−2.74 (m, 2H), 2.52−2.35 (m, 2H), 2.45 (s, 3H), 2.10−2.01 (m, 2H), 1.26 (t, J = 7.1 Hz, 2.46H), 1.13 (t, J = 7.1 Hz, 0.54H); MS (m/z) 363 (M$^+$); EI-HRMS calcd for $C_{18}H_{21}NO_5S$ 363.1140, found 363.1143.

Ethyl 1,3-dibenzyl-2,4-dioxo-1,3-diazaspiro[4.4]non-7-ene-7-carboxylate and ethyl 1,3-dibenzyl-2,4-dioxo-1,3-diazaspiro[4.4]non-6-ene-6-carboxylate (3j and 4j): oil; IR (neat) ν 1771, 1712, 1637, 1606 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.23 (m, 10H), 7.14 (m, 0.35H), 6.61 (m, 0.65H), 4.74 (d, J = 5.0 Hz, 2H), 4.56−4.15 (m, 3.30H), 3.89−3.86 (m, 0.35H), 3.72 (m, 0.35H), 3.03−2.99 (m, 1.30H), 2.57−2.41 (m, 2.35H), 2.0−1.85 (m, 0.35H), 1.26 (t, J = 7.2 Hz, 1.95H) 0.99 (t, J = 7.1 Hz, 1.05H); MS (m/z) 404 (M$^+$); EI-HRMS calcd for $C_{24}H_{24}N_2O_4$ 404.1736, found 404.1711.

Triphenylphosphine-Catalyzed Cycloaddition of 1 with *tert*-Butyl 2,3-Butadienoate (5). General Procedure for the Preparation of Spirocycles 6 and 7 (Table 2). A solution of **1** (0.20 mmol), **5** (0.24 mmol), and PPh_3 (0.02 mmol, 10 mol %) in dry benzene (2 mL) was stirred at reflux. After the reaction was completed, the reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (petroleum ether−ethyl acetate) to give **6** and **7**.

Tributylphosphine-Catalyzed Cycloaddition of 1 with *tert*-Butyl 2-Butynoate (8). General Procedure for the Preparation of Spirocycles 6 and 7 (Table 3). A solution of compound **1** (0.20 mmol), **8** (0.24 mmol), and PBu_3 (0.04 mmol, 20 mol %) in dry toluene (2 mL) was stirred at room temperature. After the reaction was completed, the reaction mixture was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (petroleum ether−ethyl acetate) to give **6** and **7**.

***tert*-Butyl 1′-oxo-3′,4′-dihydrospiro[cyclopent-3-ene-1,2′-naphthalene]-3-carboxylate (6a)**: oil; IR (neat) ν 1705, 1684, 1636 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.8, 1.3 Hz, 1H), 7.47 (td, J = 7.5, 1.5 Hz, 1H), 7.31 (br t, J = 7.8 Hz, 1H), 7.23 (br d, J = 7.7 Hz, 1H), 6.60 (m, 1H), 3.17−2.94 (m, 4H), 2.65 (ddt, J = 18.5, 2.9, 1.8 Hz, 1H), 2.42 (ddt, J = 18.5, 2.9, 1.8 Hz, 1H), 2.18 (t, J = 5.8 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) 200.1, 164.0, 143.2, 139.6, 134.9, 133.2, 128.6, 128.2, 126.7, 80.2, 51.8, 42.0, 40.1, 34.6, 28.0 (2C), 25.7; MS (m/z) 399 (M$^+$ + 1), 243, 224 (100), 197, 196, 118, 57, 41. Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.10; H, 7.43.

***tert*-Butyl 6′-methoxy-1′-oxo-3′,4′-dihydrospiro[cyclopent-3-ene-1,2′-naphthalene]-3-carboxylate (6b)**: oil; IR (neat) ν 1699, 1688, 1638 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 8.8 Hz, 1H), 6.84 (dd, J = 8.8, 2.5 Hz, 1H), 6.68 (d, J = 2.5 Hz, 1H), 6.60 (m, 1H), 3.86 (s, 3H), 3.18−2.94 (m, 4H), 2.63 (br d, J = 16.6 Hz, 1H), 2.41 (br d, J = 16.6 Hz, 1H), 2.15 (m, 2H), 1.47 (s, 9H); MS (m/z) 329 (M$^+$ + 1), 273, 272, 254, 227, 226 (100), 198. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 73.01; H, 7.42.

***tert*-Butyl 1′,3′-dihydro-1′-oxospiro[cyclopent-3-ene-1,2′-indane]-3-carboxylate (6c):** oil; IR (neat) ν 1710, 1635 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 7.6 Hz, 1H), 7.63 (td, J = 7.5, 1.2 Hz, 1H), 7.44 (dt, J = 7.6, 0.8 Hz, 1H), 7.40 (td, J = 7.6, 1.2 Hz, 1H), 6.65 (m, 1H), 3.25 (d, J = 17.1 Hz, 1H), 3.17 (d, J = 17.1 Hz, 1H), 3.11−3.00 (m, 2H), 2.64−

2.40 (m, 2H), 1.49 (s, 9H); MS (*m*/*z*) 228, 211, 210 (100), 183, 182, 181, 165, 57. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.73; H, 7.25.

***tert*-Butyl 5′-bromo-1′,3′-dihydro-1′-oxospiro[cyclopent-3-ene-1,2′-indane]-3-carboxylate (6d):** white solid; mp 146.5−147.5 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1703, 1638 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 8.1 Hz, 1H), 7.63 (s, 1H), 7.54 (d, J = 8.1 Hz, 1H), 6.63 (m, 1H), 3.18 (d, J = 8.5 Hz, 2H), 3.09−2.99 (m, 2H), 2.58−2.42 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) 207.9, 163.8, 154.0, 139.5, 136.1, 134.6, 131.3, 130.4, 129.7, 125.5, 80.6, 55.5, 45.1, 44.7, 44.1, 28.1; MS (*m*/*z*) 308, 306, 290, 288 (100), 262, 261, 260, 182, 181, 57. Anal. Calcd for $C_{18}H_{19}BrO_3$: C, 59.52; H, 5.27. Found: C, 59.38; H, 5.43.

***tert*-Butyl 5′-methoxy-1′,3′-dihydro-1′-oxospiro[cyclopent-3-ene-1,2′-indane]-3-carboxylate (6e)**: oil; IR (neat) ν 1702, 1633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.5 Hz, 1H), 6.93 (d, J = 8.5 Hz, 1H), 6.87 (s, 1H), 6.30 (br s, 1H), 3.89 (s, 3H), 3.16−3.00 (m, 4H), 2.56−2.41 (m, 2H), 1.49 (s, 9H); MS (*m*/*z*) 315 (M^+ + 1), 259, 258, 241, 240, 213, 212, 211. Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.26; H, 7.04.

tert-Butyl 6-oxospiro[4.5]dec-2-ene-2-carboxylate (6f): oil; IR (neat) ν 1708, 1637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.50 (m, 1H), 3.16 (d, J = 16.7 Hz, 2 H), 2.93 (br d, J = 16.7 Hz, 2 H), 2.55−2.25 (m, 3H), 2.21 (d, J = 12.0 Hz, 2H), 2.05−1.25 (m, 15H); MS (*m*/*z*) 177 ($M^+ - O^tBu$), 176 (100), 150, 149, 148, 124, 57, 41. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.32; H, 9.07.

***tert*-Butyl 6-oxospiro[4.4]non-2-ene-2-carboxylate and *tert*-butyl 6-oxospiro[4.4]non-1-ene-1-carboxylate (6g and 7g)**: oil; IR (neat) ν 1739, 1706, 1637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.85 (t, J = 2.5 Hz, 0.11H), 6.53 (m, 0.89H), 2.81−2.75 (m, 1.78H), 2.50−1.80 (m, 8.22H), 1.45 (s, 9H); MS (*m*/*z*) 237 (M^+ + 1), 181, 180, 163, 162 (100), 135, 134, 124, 57. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 70.99; H, 8.50.

***tert*-Butyl 2-(*tert*-butoxycarbonyl)-1-oxo-2-azaspiro-[4.4]non-7-ene-7-carboxylate (6h):** white solid; mp 56−57.5 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1787, 1753, 1710, 1637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.56 (m, 1H), 3.69 (deformed t, J = 6.8 Hz, 2H), 3.07−2.99 (m, 2H), 2.57−2.40 (m, 2H), 2.04−1.94 (m, 2H), 1.54 (s, 9H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.5, 163.7, 150.3, 139.0, 135.4, 81.0, 80.5, 51.6, 43.3, 43.2, 42.1, 33.8, 28.0; MS (*m*/*z*) 282, 264 ($M^+ - O^tBu$), 226, 225, 181, 180, 163, 57, 41. Anal. Calcd for $C_{18}H_{27}NO_5$: C, 64.07; H, 8.07; N, 4.15. Found: C, 64.08; H, 7.94; N, 3.81.

***tert*-Butyl 2-tosyl-1-oxo-2-azaspiro[4.4]non-7-ene-7-carboxylate (6i):** white solid; mp 95−97 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1724, 1714, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 8.3 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 6.48 (m, 1H), 3.87−3.78 (m, 2H), 2.89−2.72 (m, 2H), 2.48−2.33 (m, 5H), 2.11−2.02 (m, 2H), 1.46(s, 9H); MS (*m*/*z*) 335, 317, 290, 162 (100), 91, 65, 57. Anal. Calcd for $C_{20}H_{25}NO_5S$: C, 61.36; H, 6.44; N, 3.58. Found: C, 61.11; H, 6.53; N, 3.44.

***tert*-Butyl 1,3-dibenzyl-2,4-dioxo-1,3-diazaspiro[4.4]-non-7-ene-7-carboxylate (6j):** white solid; mp 91−93 °C (ethyl acetate−petroleum ether); IR (KBr) ν 1770, 1712, 1637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.23 (m, 10H), 6.53 (m, 1H), 4.74 (s, 2H), 4.54 (d, J = 15.5 Hz, 1H), 4.32 (d, J = 15.6 Hz, 1H), 3.02 (br d, J = 15.6 Hz, 2H), 2.52−2.45 (m, 2H), 1.46 (s, 9H); MS (*m*/*z*) 432 (M^+), 376, 358, 331, 330, 91 (100), 84, 57. Anal. Calcd for $C_{26}H_{28}N_2O_4$: C, 72.20; H, 6.53; N, 6.48. Found: C, 72.17; H, 6.87; N, 6.34.

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Supporting Information Available: $^1H-^1H$ COSY data of **3a** and **4a**,^1H NMR spectra of compounds **3b**, **3e**, **4e**, **3i**, **4i**, **3j**, and **4j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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