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Efficient Synthesis of Spirobarbiturates and Spirothiobarbiturates Bearing Cyclopropane Rings by Rhodium(II)-Catalyzed Reactions of Cyclic Diazo Compounds

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Rhodium(II)-catalyzed reactions of cyclic diazo compounds derived from barbituric acid and thiobarbituric acid with a variety of styrene moieties were examined. These reactions provide rapid synthetic routes to the preparations of spirobarbiturates and spirothiobarbiturates bearing cyclopropane rings.

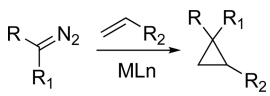
Key Words : Rhodium(II)-catalyzed reactions, Spirobarbiturates, Spirothiobarbiturates, Diazo compounds

Introduction

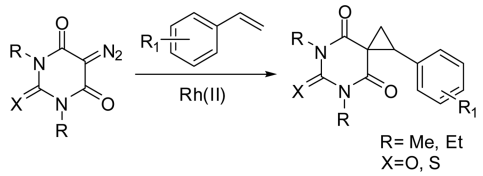
Cyclopropanes are widely found as a basic unit in a range of naturally occurring compounds and medicinal agents.[1,2] They have also been used as versatile and important intermediates during the syntheses of more functionalized cycloalkanes, acyclic compounds, and natural products.[3] Numerous methods have been reported for the preparation of cyclopropanes.[3] One of the most generally useful synthetic methods is based on the transition metal-catalyzed reactions of diazo compounds with olefins (Scheme 1).[4,5]

Barbiturates (barbituric acid derivatives) are a class of central nervous system depressants,[6] and are used as sedatives, hypnotics, anesthetics, anxiolytics, and anticonvulsants.[7] In addition, they have additional pharmacological activities as analeptics, immunomodulatory, *anti*-AIDA, and anticancer agents.[8] Spirobarbiturates are also a class of biologically important molecules with a variety of pharmacological and physiological activities,[9] which has stimulated interest in the synthesis of spirobarbiturates with cyclopropane rings. A number of synthetic approaches to barbiturates bearing cyclopropane rings have been reported.[10] These methods include reactions between *N*,*N*-dimethylbarbituric acid and dibromoethane in the presence of bases. However, these reactions have low yields and require phase transfer reaction conditions,[10a] and thus, there is a demand for more convenient and efficient synthetic methods that can efficiently provide a variety of spirobarbiturates with substituents on cyclopropane rings.

We have been interested in the rhodium(II)-catalyzed reactions between cyclic diazodicarbonyl compounds and different substrates,[11,12] and have developed a novel means for synthesizing a variety of heterocycles,[11] including dihydrofurans, dihydrooxepins, oxindoles, and oxazoles and versatile β-substituted α-haloenones from cyclic diazodicarbonyl compounds.[12] In addition, we have previously



Scheme 1. Transition metal catalyzed cyclopropanation.



Scheme 2

reported on the synthesis of cyclopropanes by the rhodium(II)-catalyzed reaction between diazo compounds derived from Meldrum's acid.[13] During our continuing studies on the development of a new methodology based on cyclic diazo compounds, we investigated the rhodium-catalyzed reactions of cyclic diazo compounds derived from barbituric acid and thiobarbituric acid with several styrenes. We report herein a simple and efficient synthesis of a variety of spirobarbiturates and spirothiobarbiturates with cyclopropane rings from cyclic diazo compounds derived from barbituric acid and thiobarbituric acid (Scheme 2).

Results and Discussion

Cyclic diazo compounds **1** and **2** were readily prepared by the diazotransfer reaction of *N*,*N*-dimethylbarbituric acid and 1,3-diethyl-2-thiobarbituric acid with mesyl azide in 85 and 80% yield, respectively (Figure 1).[14]

The reaction of **1** with styrene was first examined using several metal catalysts in flurobenzene (Table 1). Using $Cu(OAc)_2$ (10 mol %) or $Pd(OAc)_2$ (10 mol %) at 70 °C for 12 h in fluorobenzene, no products were produced. We then examined the catalytic activities of several rhodium complex in fluorobenzene. The electron-poor rhodium trifluoroacetate (2 mol %) at 50 °C for 10 h produced **3** in 25% yield, whereas rhodium acetate (2 mol %) at 50 °C for 10 h and

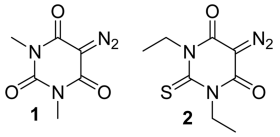
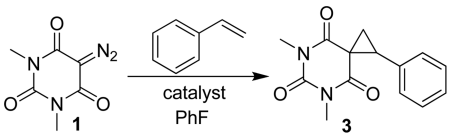


Figure 1

Table 1. Effect of metal catalysts in the reaction of **1** with styrene



Catalyst	Condition	Yield (%)
$Pd(OAc)_2$ (10 mol %)	70 °C, 12 h	0
$Pd(OAc)_2$ (10 mol %)	70 °C, 12 h	0
$Rh_2(OCOCF_3)_4$ (2 mol %)	50 °C, 10 h	25
$Rh_2(OAc)_4$ (2 mol %)	50 °C, 10 h	45
$Rh_2(OPiv)_4$ (2 mol %)	50 °C, 3 h	82

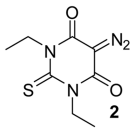
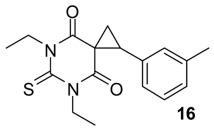
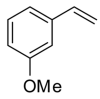
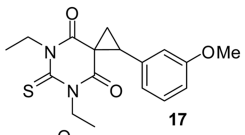
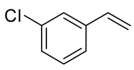
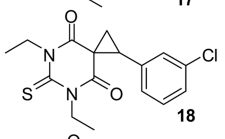
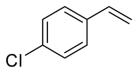
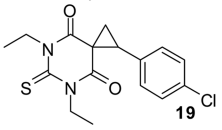
rhodium pivalate (2 mol %) at 50 °C for 3 h both afforded **3** in 45 and 82% yield, respectively. The ^{1}H NMR spectrum of **3** has a methine peak at δ = 3.51 ppm as a triplet (J = 9.3 Hz) and a proton of one methylene peak at 2.59 ppm as a double-doublet (J = 9.3, 4.1 Hz) and the other at 2.45 ppm as a double-doublet (J = 9.3, 4.1 Hz). The structure of **3** was further confirmed by ^{13}C NMR, which showed the expected two carbonyl peaks at 168.3 and 164.9 ppm due to the two amides and one carbonyl peak at 151.9 ppm due to the urea group.

To prepare cyclopropanobarbiturates with a variety of substituents on the benzene ring, **1** was reacted with a

Table 2. Rhodium(II)-catalyzed reactions of **1** and **2** with a variety of styrene moieties

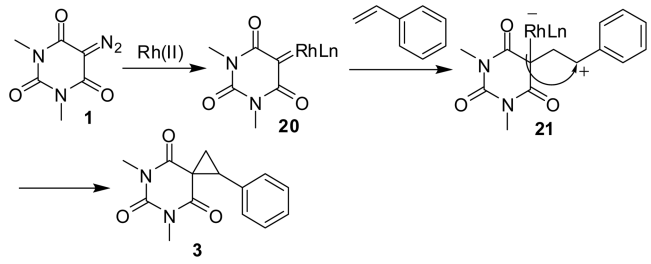
Entry	Diazo compound	Styrene	Condition	Product	Yield (%)
1			50 °C, 3 h	**4**	80
2			50 °C, 3 h	**5**	92
3			50 °C, 3 h	**6**	84
4		OMe	50 °C, 4 h	**7**	72
5	**1**	AcO	50 °C, 3 h	**8**	82
6		Cl	50 °C, 3 h	**9**	79
7		Cl	50 °C, 3 h	**10**	82
8		CHO	50 °C, 4 h	**11**	74
9			50 °C, 4 h	**12**	80
10			50 °C, 4 h	**13**	83
11			50 °C, 4 h	**14**	50
12			50 °C, 4 h	**15**	63

Table 2. Continued

Entry	Diazo compound	Styrene	Condition	Product	Yield (%)
13			50 °C, 4 h		52
14			50 °C, 4 h		55
15			50 °C, 4 h		71
16			50 °C, 4 h		54

number of styrenes under optimized reaction conditions. To investigate the influence of substituents on reactivity, a variety of styrenes bearing electron-donating or -withdrawing groups on the benzene ring were examined. Results are summarized in Table 2. Reactions of several styrenes with an electron-donating group on the benzene ring were first attempted. Reaction of **1** with 3- and 4-methylstyrenes in the presence of 2 mol % of $Rh_2(OPiv)_4$ at 50 °C for 3 h in fluorobenzene produced compounds **4** (80%) and **5** (92%), respectively (entries 1-2). Using 2,4-dimethylstyrene, product **6** was produced in 84% yield (entry 3). Treatment with 3-vinylanisole at 50 °C for 4 h afforded adduct **7** in 72% yield (entry 4), whereas reaction with 4-acetoxystyrene at 50 °C for 3 h produced cyclopropane **8** in 82% yield (entry 5). Reactions with several styrenes possessing an electron-withdrawing group on the benzene ring were also successful. When **1** was treated with 3- and 4-chlorostyrenes in the presence of 2 mol % $Rh_2(OPiv)_4$ at 50 °C for 3 h in fluorobenzene, cyclopropanes **9** and **10** were produced at yields of 79 and 82%, respectively (entries 6-7). Using 3-vinylbenzaldehyde at 50 °C for 4 h, cyclopropane **11** was obtained in 74% yield (entry 8). In order to extend the utility of these reactions, further reactions with other compounds bearing a styrene moiety were examined. Treatment of **1** with 1-vinylnaphthalene, 2-vinylnaphthalene, and 9-vinylanthracene in the presence of 2 mol % of rhodium pivalate at 50 °C for 4 h gave **12**, **13**, and **14** in 80, 83, and 50% yield, respectively (entries 9-11).

To prepare cyclopropanothiobarbiturates, **2** was reacted with several styrenes in the presence of 2 mol % of $Rh_2(OPiv)_4$. Treatment of **2** with styrene at 50 °C for 4 h in fluorobenzene provided **15** in 63% yield (entry 12). Reactions between **2** and 3-methylstyrene or 3-vinylanisole provided **16-17** in 52 and 55% yield (entries 13-14), respectively, whereas those with 3-chlorostyrene or 4-chlorostyrene at 50 °C for 4 h in fluorobenzene afforded the desired products **18** and **19** in 71 and 54% yield (entries 15-16), respectively.



Scheme 3

The formation of product **3** may be explained as shown in Scheme 3. The diazo compound **1** first gives a carbenoid **21** (or carbene) by displacement of nitrogen by $Rh_2(Opiv)_4$.[15] The carbenoid **20** is trapped by the double bond of styrene to give intermediate **21**, which undergoes ring closure by elimination of $Rh_2(OPiv)_4$ to give the cyclopropane **3**.

In conclusion, rhodium(II)-catalyzed reactions of the cyclic diazo compounds **1** and **2** with a variety styrene moieties are described. These reactions provide a rapid means of synthesizing a variety of spirobarbiturates or spirothiobarbiturates bearing cyclopropane rings.

Experimental

All reactions were conducted under nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Model ARX (300 and 75 MHz, respectively) spectrometer in $CDCl_3$ or benzene-d_6. The IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. The HRMS spectra were carried out at the Korea Basic Science Institute.

General Procedure for the Synthesis of Spirobarbitu-

rates 3-15 and Spirothiobarbiturates 16-20. To a solution of diazo compound **1** or **2** (1.0 mmol) and styrenes (2 mmol) in fluorobenzene (2 mL) was added rhodium pivalate (0.02 mmol) at room temperature. The reaction mixture was stirred at 50 °C for 3-6 h. The solvent was evaporated under reduced pressure to give the residue. The residue was purified by flash column chromatography on silica gel to give the products.

5,7-Dimethyl-1-phenyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (3). Reaction of **1** (182 mg, 1.0 mmol) and styrene (208 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **3** (212 mg, 82 %) as a solid: mp 78-80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.25 (5H, m), 3.51 (1H, t, *J* = 9.3 Hz), 3.37 (3H, s), 3.11 (3H, s), 2.59 (1H, dd, *J* = 9.3, 4.1 Hz), 2.45 (1H, dd, *J* = 9.3, 4.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 164.9, 151.9, 132.5, 129.8, 128.2, 128.1, 46.3, 35.9, 28.9, 28.6, 24.7; IR (KBr) 3426, 1732, 1682, 1458, 1419, 1379, 1285, 1230, 1128, 1080, 1057, 814, 750, 692 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{14}H_{14}N_2O_3$: 258.1004. Found: 258.1006.

5,7-Dimethyl-1-*m*-tolyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (4). Reaction of **1** (182 mg, 1.0 mmol) and 3-methylstyrene (236 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **4** (218 mg, 80%) as a solid: mp 112-113 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21-7.16 (1H, m), 7.09-7.03 (3H, m), 3.48 (1H, t, *J* = 9.3 Hz), 3.36 (3H, s), 3.12 (3H, s), 2.58 (1H, dd, *J* = 9.2, 4.0 Hz), 2.42 (1H, dd, *J* = 9.4, 4.0 Hz), 2.31 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 164.9, 151.9, 137.7, 132.4, 130.5, 129.0, 127.9, 126.7, 46.4, 35.8, 28.8, 28.5, 24.7, 21.3; IR (KBr) 3416, 2920, 1738, 1674, 1467, 1417, 1385, 1292, 1130, 1103, 1065, 820, 756, 704 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{15}H_{16}N_2O_3$: 272.1161. Found: 272.1161.

5,7-Dimethyl-1-*p*-tolyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (5). Reaction of **1** (182 mg, 1.0 mmol) and 4-methylstyrene (236 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **5** (251 mg, 92 %) as a solid: mp 119-120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16-7.08 (4H, m), 3.48 (1H, t, *J* = 9.3 Hz), 3.36 (3H, s), 3.11 (3H, s), 2.57 (1H, dd, *J* = 9.2, 4.0 Hz), 2.43 (1H, dd, *J* = 9.4, 4.0 Hz), 2.31 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 164.9, 152.0, 138.1, 129.6, 129.3, 128.9, 46.6, 36.0, 28.8, 28.6, 24.7, 21.2; IR (KBr) 3449, 2924, 1736, 1672, 1466, 1419, 1379, 1290, 1092, 1069, 818, 752 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{15}H_{16}N_2O_3$: 272.1161. Found: 272.1162.

1-(2,4-Dimethylphenyl)-5,7-dimethyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (6). Reaction of **1** (182 mg, 1.0 mmol) and 2,4-dimethylstyrene (264 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **6** (241 mg, 84%) as a solid: mp 94-95 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (1H, d, *J* = 7.8 Hz), 7.00 (1H, d, *J* =7.8 Hz), 6.93 (1H, s), 3.38 (3H, s), 3.35 (1H, t, *J* = 9.3 Hz), 3.12 (3H, s), 2.58 (1H, dd, *J* = 9.3, 3.9 Hz), 2.45 (1H, dd, *J* = 9.2, 3.9 Hz), 2.28 (3H, s), 2.05 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 164.8, 151.9, 138.1, 137.3, 130.6, 129.5, 128.4, 126.4, 45.3, 35.3, 28.8, 28.5, 25.4, 21.1, 19.2; IR (KBr) 3420, 2916, 1736, 1688, 1454, 1416, 1375, 1287, 1130, 1074, 833, 821, 758 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{16}H_{18}N_2O_3$: 286.1317. Found: 286.1316.

1-(3-Methoxyphenyl)-5,7-dimethyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (7). Reaction of **1** (182 mg, 1.0 mmol) and 3-vinylanisole (268 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **7** (208 mg, 72%) as a solid: mp 102-103 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (1H, d, *J* = 7.9 Hz), 6.85-6.78 (3H, m), 3.79 (3H, s), 3.47 (1H, t, *J* = 9.3 Hz), 3.36 (3H, s), 3.13 (3H, s), 2.55 (1H, dd, *J* = 9.2, 4.0 Hz), 2.42 (1H, dd, *J* = 9.4, 4.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 164.8, 159.2, 151.9, 134.1, 129.0, 122.0, 115.6, 113.4, 55.1, 46.1, 35.8, 28.8, 28.6, 24.8; IR (KBr) 2959, 1738, 1674, 1462, 1421, 1385, 1292, 1261, 1165, 821, 756 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{15}H_{16}N_2O_4$: 288.1110. Found: 288.1112.

4-(5,7-Dimethyl-4,6,8-trioxo-5,7-diazaspiro[2.5]octan-1-yl)phenyl acetate (8). Reaction of **1** (182 mg, 1.0 mmol) and 4-acetoxystyrene (324 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **8** (259 mg, 82%) as a solid: mp 156-158 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (2H, d, *J* = 8.6 Hz), 7.03 (2H, d, *J* = 8.6 Hz), 3.47 (1H, t, *J* = 9.3 Hz), 3.36 (3H, s), 3.12 (3H, s), 2.56 (1H, dd, *J* = 9.2, 4.1 Hz), 2.45 (1H, dd, *J* = 9.4, 4.1 Hz), 2.27 (3H, s), 1.57 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 168.1, 164.8, 151.8, 150.4, 130.8, 129.9, 121.2, 45.5, 35.9, 28.8, 28.6, 24.8, 21.1; IR (KBr) 3425, 1759, 1672, 1512, 1462, 1421, 1383, 1196, 1169, 1092, 1017, 853, 756 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{16}H_{16}N_2O_5$: 316.1059. Found: 316.1060.

1-(3-Chlorophenyl)-5,7-dimethyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (9). Reaction of **1** (182 mg, 1.0 mmol) and 3-chlorostyrene (276 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **9** (231 mg, 79%) as a solid: mp 114-115 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25-7.23 (3H, m), 7.16-7.11 (1H, m), 3.46 (1H, t, *J* = 9.3 Hz), 3.36 (3H, s), 3.14 (3H, s), 2.53 (1H, dd, *J* = 9.1, 4.1 Hz), 2.43 (1H, dd, *J* = 9.4, 4.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 164.8, 151.8, 134.6, 134.0, 130.0, 129.3, 128.4, 127.9, 44.8, 35.6, 28.9, 28.6, 24.9; IR (KBr) 3425, 2961, 1740, 1676, 1462, 1421, 1385, 1294, 1236, 1130, 1068, 816, 756 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{14}H_{13}Cl\,N_2O_3$: 292.0615. Found: 296.0611.

1-(4-Chlorophenyl)-5,7-dimethyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (10). Reaction of **1** (182 mg, 1.0 mmol) and 4-chlorostyrene (276 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **10** (240 mg, 82%) as a solid: mp 157-159 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* = 8.6 Hz), 7.19 (2H, d, *J* = 8.6 Hz), 3.45 (1H, t, *J* = 9.3 Hz), 3.36 (3H, s), 3.13 (3H, s), 2.53 (1H, dd, *J* = 9.2, 4.1 Hz), 2.44 (1H, dd, *J* = 9.4, 4.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 164.8, 151.8, 134.1, 131.1, 131.0, 129.3, 128.3, 45.1, 35.8, 28.9, 28.6, 24.8; IR (KBr) 3418, 2966, 1740, 1680, 1462, 1416, 1385, 1294, 1253, 1132, 1087, 1010, 824, 756 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{14}H_{13}Cl\,N_2O_3$: 292.0615. Found: 296.0616.

3-(5,7-Dimethyl-4,6,8-trioxo-5,7-diazaspiro[2.5]octan-1-yl)benzaldehyde (11). Reaction of **1** (182 mg, 1.0 mmol) and 3-vinylbenzaldehyde (264 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **11** (212 mg, 74%) as a solid: mp 120-122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.99 (1H, s),

7.80-7.78 (2H, m), 7.59-7.46 (2H, m), 3.56 (1H, t, J = 9.3 Hz), 3.36 (3H, s), 3.11 (3H, s), 2.61 (1H, dd, J = 9.1, 4.1 Hz), 2.48 (1H, dd, J = 9.4, 4.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.9, 168.0, 164.9, 151.7, 136.2, 135.6, 133.9, 130.7, 129.8, 128.8, 45.5, 35.5, 28.9, 28.6, 25.1; IR (KBr) 1736, 1687, 1462, 1421, 1385, 1292, 1236, 1132, 1069, 756 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{15}H_{14}N_2O_4$: 286.0954. Found: 286.0956.

5,7-Dimethyl-1-(naphthalen-1-yl)-5,7-diazaspiro[2.5]octane-4,6,8-trione (12). Reaction of **1** (182 mg, 1.0 mmol) and 1-vinylnaphthalene (308 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **12** (247 mg, 80%) as a solid: mp 168-169 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86-7.80 (2H, m), 7.61-7.57 (1H, m), 7.51-7.43 (4H, m), 3.81 (1H, t, J = 9.0 Hz), 3.48 (3H, s), 2.85 (3H, s), 2.71 (1H, dd, J = 9.0, 3.9 Hz), 2.60 (1H, dd, J = 9.2, 3.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 164.6, 151.8, 133.3, 132.4, 129.2, 129.1, 128.0, 126.7, 125.8, 125.1, 121.9, 43.8, 35.5, 29.0, 28.3, 25.0; IR (KBr) 3422, 3061, 2957, 1736, 1674, 1462, 1420, 1379, 1292, 1113, 1064, 777 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{18}H_{16}N_2O_3$: 308.1161. Found: 308.1158.

5,7-Dimethyl-1-(naphthalen-2-yl)-5,7-diazaspiro[2.5]octane-4,6,8-trione (13). Reaction of **1** (182 mg, 1.0 mmol) and 2-vinylnaphthalene (308 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **13** (256 mg, 83%) as a solid: mp 123-124 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.74 (4H, m), 7.47-7.44 (2H, m), 7.36-7.30 (1H, m), 3.65 (1H, t, J = 9.3 Hz), 3.39 (3H, s), 3.07 (3H, s), 2.72 (1H, dd, J = 9.2, 4.0 Hz), 2.53 (1H, dd, J = 9.3, 4.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 164.9, 151.8, 133.0, 132.9, 129.9, 129.3, 127.9, 127.7, 127.6, 127.1, 126.3, 126.2, 46.6, 36.1, 28.9, 28.6, 24.9; IR (KBr) 3424, 2959, 1738, 1674, 1460, 1420, 1381, 1290, 1124, 1065, 820, 752 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{18}H_{16}N_2O_3$: 308.1161. Found: 308.1165.

1-(Anthracen-9-yl)-5,7-dimethyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (14). Reaction of **1** (179 mg, 1.0 mmol) and 9-vinylanthracene (408 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **14** (143 mg, 50%) as a solid: mp 115-116 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (1H, d, J = 9.0 Hz), 8.41 (1H, s), 7.98 (2H, dd, J = 9.0, 7.5 Hz), 7.70 (1H, d, J = 9.0 Hz), 7.56-7.51 (1H, m), 7.46 (1H, d, J = 7.5 Hz), 7.43-7.35 (2H, m), 4.00 (1H, t, J = 9.3 Hz), 3.54 (3H, s), 3.05 (1H, dd, J = 9.3, 3.9 Hz), 2.70 (3H, s), 2.68 (1H, dd, J = 9.3, 3.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 165.0 151.8, 131.7, 131.5, 131.0, 130.7, 129.6, 129.4, 128.3, 126.2, 126.1, 125.8, 125.0, 124.7, 124.5, 122.2, 40.9, 36.1, 29.6, 29.1, 28.2; IR (KBr) 3457, 2968, 1672, 1435, 1378, 1283, 1053, 817, 740 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{22}H_{18}N_2O_3$: 358.1317. Found: 358.1314.

5,7-Diethyl-1-phenyl-6-thioxo-5,7-diazaspiro[2.5]octane-4,8-dione (15). Reaction of **2** (226 mg, 1.0 mmol) and styrene (208 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **15** (191 mg, 63%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.22 (5H, m), 4.55-4.44 (2H, m), 4.31-4.23 (1H, m), 4.22-4.11 (1H, m), 3.53 (1H, t, J = 9.2 Hz), 2.65 (1H, dd, J = 9.2, 4.1 Hz), 2.53 (1H, dd, J = 9.2, 4.1 Hz), 1.28 (3H, t, J = 7.0 Hz), 0.95 (3H, t, J = 7.0 Hz);^{13}C NMR (75 MHz, $CDCl_3$) δ 179.5, 166.4, 162.9, 132.2, 129.7, 128.3, 128.1, 48.4, 43.6, 43.4, 37.5, 24.5, 12.3, 12.0; IR (neat) 3441, 2982, 1690, 1435, 1392, 1273, 1251, 1113, 1074, 700 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{16}H_{18}N_2O_2S$: 302.1089. Found: 302.1090.

5,7-Diethyl-6-thioxo-1-*m*-tolyl-5,7-diazaspiro[2.5]octane-4,8-dione (16). Reaction of **2** (226 mg, 1.0 mmol) and 3-methylstyrene (236 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **16** (165 mg, 52%) as a solid: mp 89-90 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21-7.16 (1H, m), 7.09-7.03 (3H, m), 4.58-4.44 (2H, m), 4.33-4.17 (2H, m), 3.50 (1H, t, J = 9.3 Hz), 2.62 (1H, dd, J = 9.2, 4.0 Hz), 2.50 (1H, dd, J = 9.3, 4.0 Hz), 2.30 (3H, s), 1.28 (3H, t, J = 7.0 Hz), 0.97 (3H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.7, 166.6, 163.0, 137.8, 132.3, 130.6, 129.2, 128.0, 126.8, 48.6, 43.7, 43.4, 37.5, 24.7, 21.3, 12.3, 12.0; IR (KBr) 3441, 2986, 1709, 1682, 1435, 1400, 1271, 1250, 1105, 1068, 1018, 804, 708 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{17}H_{20}N_2O_2S$: 316.1245. Found: 316.1241.

5,7-Diethyl-1-(3-methoxyphenyl)-6-thioxo-5,7-diazaspiro[2.5]octane-4,8-dione (17). Reaction of **2** (226 mg, 1.0 mmol) and 3-vinylanisole (268 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **17** (183 mg, 55%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (1H, d, J = 7.9 Hz), 6.83-6.79 (2H, m), 6.76-6.75(1H, m), 4.58-4.44 (2H, m), 4.36-4.25 (1H, m), 4.23-4.16 (1H, m), 3.77 (3H, s), 3.49 (1H, t, J = 9.3 Hz), 2.61 (1H, dd, J = 9.2, 4.1 Hz), 2.50 (1H, dd, J = 9.3, 4.0 Hz), 1.27 (3H, t, J = 7.0 Hz), 0.96 (3H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, benzene-d_6) δ 179.8, 166.2, 162.5, 159.8, 134.3, 129.2, 122.6, 115.9, 113.8, 54.6, 48.0, 43.7, 43.3, 37.6, 23.8, 12.4, 12.2; IR (KBr) 2980, 1691, 1586, 1435, 1393, 1273, 1165, 785, 706 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{17}H_{20}N_2O_3S$: 332.1195. Found: 332.1197.

1-(3-Chlorophenyl)-5,7-diethyl-6-thioxo-5,7-diazaspiro[2.5]octane-4,8-dione (18). Reaction of **2** (226 mg, 1.0 mmol) and 3-chlorostyrene (277 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **18** (239 mg, 71%) as a solid: mp 74-75 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25-7.20 (3H, m), 7.15-7.12 (1H, m), 4.57-4.43 (2H, m), 4.36-4.15 (2H, m), 3.47 (1H, t, J = 9.2 Hz), 2.58 (1H, dd, J = 9.1, 4.1 Hz), 2.50 (1H, dd, J = 9.3, 4.1 Hz), 1.28 (3H, t, J = 7.0 Hz), 1.00 (3H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.5, 166.2, 162.9, 134.6, 134.1, 130.0, 129.4, 128.5, 127.8, 46.7, 43.8, 43.5, 37.1, 25.0, 12.3, 12.1; IR (KBr) 3443, 2976, 1713, 1690, 1435, 1393, 1271, 1248, 1109, 1069, 808, 789 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{16}H_{17}ClN_2O_2S$: 336.0699. Found: 336.0695.

1-(4-Chlorophenyl)-5,7-diethyl-6-thioxo-5,7-diazaspiro[2.5]octane-4,8-dione (19). Reaction of **2** (226 mg, 1.0 mmol) and 4-chlorostyrene (277 mg, 2.0 mmol) under $Rh_2(OPiv)_4$ (12 mg, 0.02 mmol) afforded **19** (182 mg, 54%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (2H, d, J = 8.5 Hz), 7.18 (2H, d, J = 8.3 Hz), 4.57-4.26 (2H, m), 4.36-4.24 (1H, m), 4.24-4.15 (1H, m), 3.48 (1H, t, J = 9.1 Hz), 2.59 (1H, dd, J = 9.2, 4.1 Hz), 2.51 (1H, dd, J = 9.3, 4.1 Hz), 1.28 (3H, t, J = 7.0 Hz), 0.99 (3H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 166.2, 162.9, 134.2, 131.1, 130.8, 128.3, 47.0, 43.7, 43.4, 37.4, 24.8, 12.2, 12.0; IR (KBr) 3430, 2980, 1692,

1499, 1439, 1395, 1316, 1273, 1248, 1113, 828 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{16}H_{17}ClN_2O_2S$: 336.0699. Found: 336.0699.

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