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Organocatalytic Mannich-Type Reactions of Cyclic *N*-Sulfimines with Trimethylsiloxyfuran and Pyrazolin-5-one

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ABSTRACT. Mannich-type reactions of cyclic *N*-sulfimines with 2-trimethylsiloxyfuran and pyrazolin-5-one have been developed using phosphoric acid (**PA**) as an organocatalyst. 2-Trimethylsiloxyfuran underwent a vinylogous Mannich-type reaction with cyclic *N*-sulfimines in the presence of the **PA** catalyst to give sulfamidate γ-butenolides in good yields and with high diastereoselectivities (up to 90% yield and 7:1 dr). In addition, the reaction between pyrazolin-5-one and a diverse range of cyclic *N*-sulfimines provided access to sulfamidates in good to high yields (up to 94% yield).

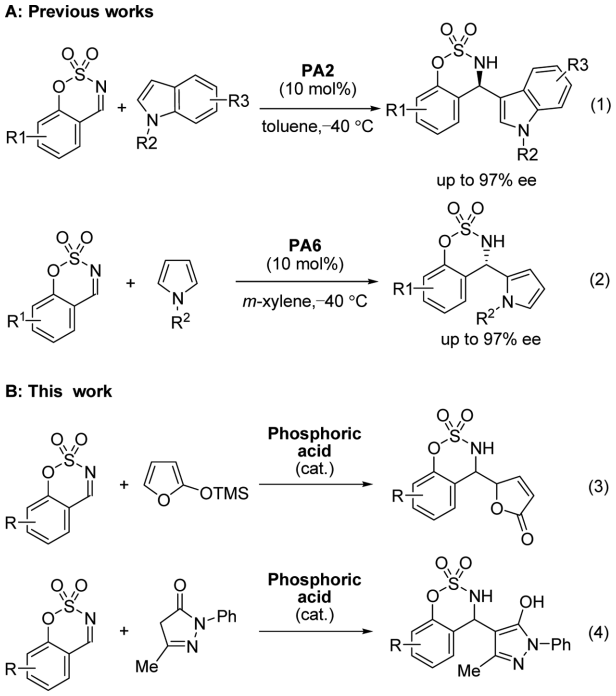
Key words: Mannich reaction, Sulfamidate, Trimethylsiloxyfuran, Pyrazolin-5-one, Phosphoric acid

INTRODUCTION

The butenolide ring is important molecular skeleton that is widespread in natural products and complex heterocyclic synthetic compounds.[1] Owing to its prevalence and significance, the butenolide scaffold has continuously attracted attention from a medicinal point of view. Therefore, the development of synthetic strategies for useful and more complex molecules containing the butenolide skeleton remains an active area of research in the field of the organic chemistry.[2]

The vinylogous Mannich-type reaction of imines with trimethylsiloxyfuran is a useful means of for the construction of alkylamine-substituted γ-butenolide derivatives.[3] A wide range of metal complex catalysts and organocatalysts has been developed for the catalytic Mannich-type reaction of trimethylsiloxyfuran with imines such as aldimines,[3a–c] ketimines,[3d,3f] and isatin-derived ketimines.[3e,3g]

Recently, we reported the organocatalytic asymmetric aza-Friedel–Crafts reaction of cyclic *N*-sulfimines with indoles and pyrroles using a chiral Brønsted acid as an organocatalyst.[4] Phosphoric acid (**PA**) has recently been recognized as a powerful chiral Brønsted acid catalyst for various asymmetric reactions.[5] The enantioselective aza-Friedel–Crafts reaction of cyclic *N*-sulfimines with indoles using **PA2** as a catalyst at −40 °C afforded chiral 3-indolyl sulfamidate derivatives in good yields and with high enantioselectivities (up to 97% ee; *Scheme* 1(1)). The enantioenriched 3-pyrrolyl sulfamate derivatives were also obtained in the aza-Friedel–Crafts reaction of cyclic *N*-sulfimines with pyrroles using **PA6** as a catalyst in *m*-xylene at −40 °C (*Scheme* 1(2)). We were interested in further expanding these addition reactions with cyclic *N*-sulfimines using chiral **PA** as the organocatalysts. Thus, we focused our attention on the application of chiral **PA** catalysts to the vinylogous Mannich-type reaction involving a trimethylsiloxyfuran (*Scheme* 1(3)). We also report the first direct Mannich-type reaction of cyclic *N*-sulfimines with pyrazolin-5-one using a **PA** catalyst to obtain pyrazole containing sulfamidates



***Scheme* 1.** Organocatalytic Mannich-type reaction of cyclic *N*-sulfimine.

(*Scheme* 1(4)).

Pyrazoles and pyrazolones are important classes of five-membered aza-heterocycles that are found in natural products and pharmaceutically relevant molecules.[6] The pyrazolone moiety shows significant pharmacological activities in various synthetic compounds. Hence, much effort has been undertaken to develop synthetic methods toward new pyrazoles and pyrazolone-containing heterocyclic compounds.[7]

EXPERIMENTAL

General Procedures

Organic solvents were distilled prior to use. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63. Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Developed chromatograms were visualized by fluorescence quenching and with anisaldehyde stain. ^{1}H and ^{13}C NMR spectra were recorded (400 MHz for ^{1}H and 100 MHz for ^{13}C), and were internally referenced to residual protio solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration. Data for ^{13}C NMR are reported in terms of chemical shift. IR spectra were recorded on an FT-IR spectrometer and are reported in wave numbers. High-resolution mass spectroscopy (HRMS) was performed by electron impact (EI).

General Procedure for the Catalytic Vinylogous Mannich-Type Reaction of Cyclic *N*-Sulfimines with 2-Trimethylsiloxyfuran

To a solution of cyclic *N*-sulfimine **1** (0.1 mmol) in toluene (0.5 mL) was added catalyst **PA2** (0.01 mmol). The solution was stirred at room temperature for 10 min, and then 2-trimethylsiloyfuran **2** (0.2 mmol) was added in one portion. The reaction mixture was stirred at same temperature until cyclic *N*-sulfimine **1** was complete consumed, as determined by TLC. Then, the resulting mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude residue was purified by flash column chromatography with EtOAc/hexanes as eluent to afford desired product **3**.

4-(5-Oxo-2*H*-fur-2-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (3a). White solid; m.p. 157–160 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.84 (dd, *J* = 5.8, 1.5 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.43 (td, *J* = 8.0, 1.1 Hz, 1H), 7.28 (td, *J* = 7.7, 1.1 Hz, 1H), 7.08 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.32 (dd, *J* = 5.8, 2.0 Hz, 1H), 5.68 (dt, *J* = 7.8, 1.7 Hz, 1H), 4.78 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 173.03, 155.00, 151.29, 129.98, 128.16, 124.99, 122.27, 118.76, 118.33, 83.76, 58.13; IR (film) 3331, 3181, 2923, 2851, 1742, 1583, 1454, 1428, 1364, 1105, 1071, 1035 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{11}H_9NO_5S$: 267.0201 Found: 267.0231.

6-Methyl-4-(5-oxo-2*H*-fur-2-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (3b). White solid; m.p. 85–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 5.5 Hz, 1H), 7.30 (s, 1H), 7.18 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.24 (d, *J* = 4.7 Hz, 1H), 5.92 (d, *J* = 6.9 Hz, 1H), 5.54 (d, *J* = 7.1 Hz, 1H), 4.68 (t, *J* = 7.0 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.90, 154.58, 148.71, 135.90, 131.22, 128.09, 123.14, 118.80, 117.48, 83.91, 58.71, 20.88; IR (film) 3302, 3118, 1747, 1600, 1491, 1431, 1373, 1202, 1176, 1115, 1088, 1044 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{12}H_{11}NO_5S$: 281.0358 Found: 281.0351.

8-Methoxy-4-(5-oxo-2*H*-fur-2-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (3c). White solid; m.p. 84–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 5.7 Hz, 1H), 7.17 (t, *J* = 8.1 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.23 (d, *J* = 4.5 Hz, 1H), 6.00 (d, *J* = 7.1 Hz, 1H), 5.55 (d, *J* = 7.4 Hz, 1H), 4.74 (t, *J* = 7.2 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.78, 154.46, 148.80, 140.47, 125.58, 123.18, 118.91, 118.60, 112.85, 83.72, 58.78, 56.30; IR (film) 3215, 2921, 2852, 1789, 1746, 1582, 1479, 1435, 1374, 1317, 1273, 1180, 1156, 1082, 1043 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{12}H_{13}NO_6S$: 297.0307 Found: 297.0307.

6-Fluoro-4-(5-oxo-2*H*-fur-2-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (3d). White solid; m.p. 161–164 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.18 (s, 1H), 7.81 (dd, *J* = 5.7, 1.4 Hz, 1H), 7.49 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.36 (dd, *J* = 8.0, 2.9 Hz, 1H), 7.30–7.24 (m, 1H), 6.44 (dd, *J* = 5.7, 1.9 Hz, 1H), 5.75 (d, *J* = 6.8 Hz, 1H), 5.09 (d, *J* = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.64, 158.83 (d, J^1 = 242.0 Hz), 155.41, 147.43, 123.07, 120.92 (d, J^3 = 8.9 Hz), 120.84 (d, J^3 = 8.5 Hz), 117.66 (d, J^2 = 23.8 Hz), 115.41 (d, J^2 = 25.7 Hz), 82.88, 57.02; IR (film) 3114, 2924, 2853, 1738, 1598, 1486, 1421, 1374, 1286, 1258, 1194, 1100, 1088, 1012 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{11}H_8FNO_5S$: 285.0107 Found: 285.0117.

6-Chloro-4-(5-oxo-2*H*-fur-2-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (3e). White solid; m.p. 172–

177 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.24 (s, 1H), 7.85 (d, J = 5.7 Hz, 1H), 7.69 (s, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.25 (d, J = 8.9 Hz, 1H), 6.44 (d, J = 5.2 Hz, 1H), 5.73 (d, J = 6.9 Hz, 1H), 5.07 (d, J = 7.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.60, 155.48, 150.06, 130.59, 129.54, 128.60, 123.09, 121.05, 120.90, 82.87, 57.00; IR (film) 3169, 2918, 2851, 1758, 1748, 1476, 1444, 1290, 1260, 1193, 1166, 1-45, 1024 cm^{-1}; HRMS (EI) m/z calcd for [M]$^+$ $C_{11}H_8ClNO_5S$: 299.0019 Found: 299.0014.

6-Bromo-4-(5-oxo-2*H*-fur-2-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (3f). White solid; m.p. 205–208 ºC; ^{1}H NMR (400 MHz, CD_3OD) δ 7.88 (dd, J = 5.8, 1.5 Hz, 1H), 7.80 (d, J = 1.7 Hz, 1H), 7.59 (dd, J = 8.8, 2.0 Hz, 1H), 7.04 (d, J = 8.8 Hz, 1H), 6.36 (dd, J = 5.8, 2.0 Hz, 1H), 5.67 (dt, J = 8.1, 1.8 Hz, 1H), 4.77 (d, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 172.81, 154.83, 150.47, 132.99, 131.03, 122.41, 120.93, 120.26, 117.34, 83.42, 57.84; IR (film) 3117, 2920, 2851, 1746, 1474, 1441, 1389, 1376, 1312, 1266, 1170, 1107, 1082, 1046, 1024 cm^{-1}; HRMS (EI) m/z calcd for [M]$^+$ $C_{11}H_8BrNO_5S$: 344.9307 Found: 344.9285.

6,8-Dibromo-4-(5-oxo-2*H*-fur-2-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (3g). White solid; m.p. 92–95 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 2.0 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H), 7.68 (d, J = 1.8 Hz, 1H), 6.32 (dd, J = 5.8, 1.8 Hz, 1H), 6.00 (s, 1H), 5.57 (d, J = 8.0 Hz, 1H), 4.66 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.38, 154.21, 147.03, 136.80, 130.06, 123.58, 121.30, 118.58, 113.72, 83.28, 58.86; IR (film) 3095, 2923, 2852, 1787, 1748, 1555, 1444, 1379, 1193, 1159, 1090, 1047, 1021 cm^{-1}; HRMS (EI) m/z calcd for [M]$^+$ $C_{11}H_7Br_2NO_5S$: 422.8412 Found: 422.8398.

General Procedure for the Catalytic Mannich-Type Reaction of Cyclic *N*-Sulfimines with pyrazolin-5-one

To a solution of cyclic *N*-sulfimine **1** (0.1 mmol) in toluene (0.5 mL) was added catalyst **PA2** (0.01 mmol). The solution was stirred at room temperature for 10 min, and then 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one **4** (0.2 mmol) was added in one portion. The reaction mixture was stirred at same temperature until cyclic *N*-sulfimine **1** was complete consumed, as determined by TLC. Then, the resulting mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude residue was purified by flash column chromatography with EtOAc/hexanes as eluent to afford desired product **5**.

4-(3-Hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5a). White solid; m.p. 124–127 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.58 (d, J = 6.8 Hz, 1H), 7.76 (d, J = 7.8 Hz, 2H), 7.47 (t, J = 7.5 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.28–7.07 (m, 4H), 5.94 (s, 1H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.35, 148.46, 138.15, 129.81, 129.44, 128.27, 125.80, 125.72, 122.46, 120.55, 118.73, 100.27, 79.65, 51.66, 13.21; IR (film) 2955, 2924, 2854, 1726, 1594, 1575, 1497, 1482, 1451, 1409, 1371, 1273, 1247, 1191, 1072, 1021 cm^{-1}; HRMS (EI) m/z calcd for [M]$^+$ $C_{17}H_{15}N_3O_4S$: 357.0783 Found: 357.0786.

4-(3-Hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-6-methyl-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5b). White solid; m.p. 148–151 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.06 (m, 6H), 7.00 (d, J = 8.3 Hz, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.60 (s, 1H), 5.55 (s, 1H), 2.19 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.53, 148.99, 146.17, 135.19, 134.84, 130.34, 128.97, 127.08, 126.72, 120.95, 120.74, 118.27, 100.83, 52.63, 20.81, 10.77; IR (film) 2955, 2924, 2854, 1593, 1567, 1487, 1406, 1369, 1308, 1247, 1205, 1174, 1105, 1028 cm^{-1}; HRMS (EI) m/z calcd for [M]$^+$ $C_{18}H_{17}N_3O_4S$: 371.0940 Found: 371.0970.

4-(3-Hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-7-methyl-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5c). White solid; m.p. 127-131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.01 (m, 6H), 6.84 (d, J = 7.9 Hz, 1H), 6.73 (s, 1H), 6.66 (d, J = 7.9 Hz, 1H), 5.54 (s, 1H), 2.27 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.43, 150.89, 146.21, 140.24, 134.86, 129.00, 126.76, 126.18, 120.82, 119.14, 118.77, 118.22, 100.79, 52.45, 20.98, 10.75; IR (film) 2954, 2922, 2853, 1594, 1574, 1497, 1409, 1370, 1307, 1250, 1192, 1101, 1023 cm^{-1}; HRMS (EI) m/z calcd for [M]$^+$ $C_{18}H_{17}N_3O_4S$: 371.0940 Found: 371.0929.

4-(3-Hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-8-methoxy-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5d). White solid; m.p. 117–119 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.07 (m, 6H), 6.8 (d, J = 8.5 Hz, 1H), 6.75 (d, J = 7.5 Hz, 1H), 6.28 (s, 1H), 5.51 (s, 1H), 3.64 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.62, 156.58, 146.30, 144.90, 134.87, 129.07, 126.84, 122.37, 120.73, 119.44, 114.05, 112.54, 101.11, 55.74, 52.70, 10.78; IR (film) 2921, 2851, 1595, 1567, 1486, 1413, 1370, 1279, 1202, 1167, 1109, 1026 cm^{-1}; HRMS (EI) m/z calcd for [M]$^+$ $C_{18}H_{17}N_3O_5S$: 387.0889 Found: 387.0878.

6-Fluoro-4-(3-hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5e). White solid; m.p. 198–201 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.66 (s, 1H), 7.76 (d, J = 7.8 Hz, 2H), 7.63–7.12 (m, 5H), 6.95 (d, J = 7.7 Hz, 1H), 5.91 (s, 1H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.13 (d, J^1 =

242.2 Hz), 148.44, 147.48, 138.06, 129.43, 125.82, 124.52, 124.47, 121.28, 120.70 (d, J^3 = 8.3 Hz), 116.85 (d, J^2 = 23.8 Hz), 114.54 (d, J^2 = 24.9 Hz), 100.02, 51.68, 13.21; IR (film) 3314, 3077, 2920, 1622, 1594, 1584, 1501, 1488, 1423, 1403, 1370, 1278, 1255, 1210, 1164, 1104, 1034 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{17}H_{14}FN_3O_4S$: 375.0689 Found: 375.0691.

6-Chloro-4-(3-hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5f). White solid; m.p. 189–191 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (s, 1H), 7.74 (dd, J = 8.6, 1.0 Hz, 2H), 7.53–7.34 (m, 3H), 7.25 (dd, J = 15.9, 8.0 Hz, 2H), 7.13 (s, 1H), 5.91 (s, 1H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.53, 149.56, 147.77, 137.47, 129.21, 128.93, 128.85, 127.14, 125.24, 123.95, 120.22, 118.72, 100.80, 50.94, 13.14; IR (film) 3323, 1919, 1851, 1594, 1583, 1500, 1471, 1403, 1364, 1278, 1251, 1212, 1191, 1168, 1107, 1030 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{17}H_{14}ClN_3O_4S$: 391.0394 Found: 391.0406.

6-Bromo-4-(3-hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5g). White solid; m.p. 119–122 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (s, 1H),7.76 (d, J = 7.9 Hz, 2H), 7.58 (d, J = 8.1 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.25 (d, J = 9.8 Hz, 2H), 7.16 (d, J = 8.7 Hz, 1H), 5.94 (s, 1H), 1.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.66, 148.24, 138.07, 132.67, 130.60, 129.42, 125.83, 124.89, 121.10, 120.56, 117.42, 99.73, 79.64, 51.45, 12.90; IR (film) 2921, 2852, 1593, 1573, 1497, 1468, 1392, 1372, 1261, 1208, 1188, 1167, 1110, 1078, 1032 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{17}H_{14}BrN_3O_4S$: 434.9888 Found: 434.9893.

6,8-Dibromo-4-(3-hydroxy-5-methyl-2-phenyl-2*H*-pyrazol-4-yl)-3,4-dihydro-1,2λ^6,3-benzoxathiazine-2,2-dione (5g). White solid; m.p. 190–192 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (s, 1H), 7.98 (s, 1H), 7.73 (d, J = 7.9 Hz, 2H), 7.47 (t, J = 7.9 Hz, 2H), 7.26 (dd, J = 14.3, 6.6 Hz, 2H), 5.93 (s, 1H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.25, 147.55, 138.15, 135.17, 130.25, 129.44, 126.42, 125.84, 120.90, 120.41, 117.52, 113.03, 100.03, 51.81, 13.48; IR (film) 3256, 2920, 1597, 1572, 1502, 1441, 1411, 1375, 1312, 1252, 1196, 1152, 1109, 1028 cm^{-1}; HRMS (EI) m/z calcd for $[M]^+$ $C_{17}H_{13}Br_2N_3O_4S$: 512.8994 Found: 512.9003.

RESULTS AND DISCUSSION

Based on our previous asymmetric catalytic aza-Friedel–Crafts reaction of cyclic *N*-sulfimines,[4] we first evaluated a chiral **PA** (*Fig.* 1) as a catalyst for the asymmetric

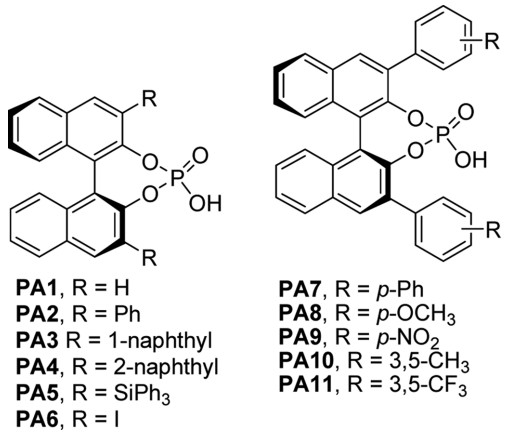
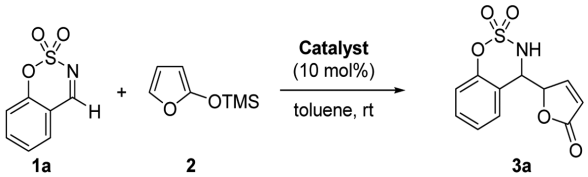


***Figure* 1.** Chiral BINOL-phosphoric acid.

Mannich-type reaction of benzoxathiazine 2,2-dioxide **1a** with 2-trimethyloxyfuran **2**. This Mannich-type reaction was conducted in toluene at room temperature in the presence of 10 mol% **PA1**. The reaction proceeded smoothly to give desired product **3a** in 55% yield and with 5:1 dr and 53:47 er (*Table* 1, entry 1). Encouraged by this result, we continued to test various BINOL-derived **PA**s (*Table* 1, entries 2–11). However, despite of the application of var-

***Table* 1.** Screen of chiral phosphoric acid catalysts for the asymmetric Mannich reaction of cyclic *N*-sulfimine **1a** with 2-trimethyloxyfuran **2**.[a]



1a **2** **3a**

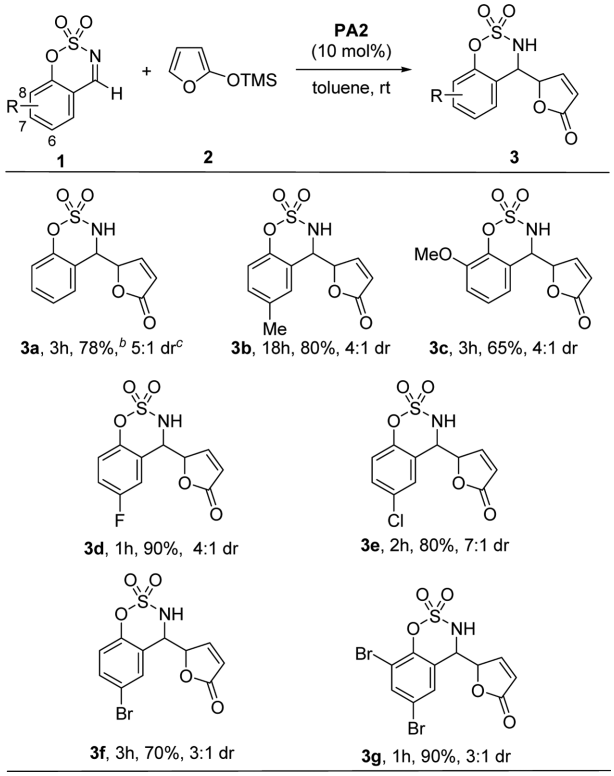
Entry	Catalyst	Time (h)	Yield (%)[b]	dr[c]	er[d]
1	**PA1**	3	55	5:1	53:47
2	**PA2**	3	78	5:1	53:47
3	**PA3**	3	51	5:1	58:42
4	**PA4**	3	78	5:1	50:50
5	**PA5**	4	66	5:1	51:49
6	**PA6**	2	91	2:1	50:50
7	**PA7**	3	77	5:1	50:50
8	**PA8**	6	49	3:1	51:49
9	**PA9**	3	64	4:1	50:50
10	**PA10**	4	62	5:1	50:50
11	**PA11**	3	69	3:1	51:49

[a]All of the reactions were carried out in toluene (0.2 M) with **1a** (0.10 mmol) and **2** (0.20 mmol) in the presence of 10 mol% catalyst catalyst at room temperature.
[b]Isolated yield after chromatographic purification.
[c]Determined by ^{1}H NMR analysis.
[d]Determined by chiral-phase HPLC analysis.

ious **PA** catalysts, asymmetric catalytic reaction did not give satisfactory results. The highest enantioselectivity with 58:42 er was obtained when using **PA3** (*Table* 1, entry 3). However, the Mannich-type reaction of **1a** with **2** provided the desired sulfamidate γ-butenolide **3a** in good yields and high diastereoselectivities under these reaction conditions. Therefore, we focused on substrate generality with respect to the cyclic *N*-sulfimine component in this Mannich-type reaction by considering only yields and diastereoselectivities. **PA2** was chosen as the catalyst from the viewpoints of reactivity and stereoselectivity.

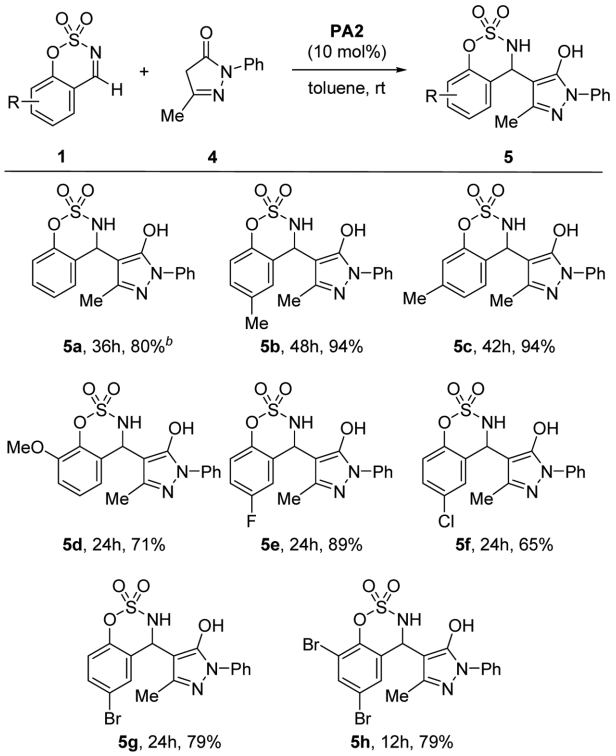
The influence of the electronic and steric properties of the substituents on the phenyl ring of the *N*-sulfimines were exploited (*Scheme* 2). Although sulfamidate γ-butenolide products were obtained in good yields, the reaction efficiency and diastereoselectivity were somewhat influenced by the electronic nature, bulkiness, and position of the substituent on the phenyl ring of the *N*-sulfimines. Cyclic *N*-sulfimines bearing electron-withdrawing groups were more reactive than those bearing electron-donating groups (*Scheme* 2, **3b** vs. **3d**–**3f**). Cyclic *N*-sulfimines bearing an electron-donating group at the 6-position exhibited lower reactivity but higher reaction yield than those bearing electron-donating groups at the 8-position (*Scheme* 2, **3b** vs. **3c**). In particular, the cyclic *N*-sulfimine with a bromine group at the 6-position showed the highest diastereoselectivity (7:1 dr). The presence of an additional halogen group in the phenyl ring led to slightly better reactivity and reaction yield, but did not affect the diastereoselectivity (*Scheme* 2, **3f** vs. **3g**).

Next, the Mannich-type reaction of cyclic *N*-sulfimines with pyrazolin-5-one was attempted. We investigated the scope of the Mannich-type reaction of 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one **4** with various cyclic *N*-sulfimines **1** in the presence of 10 mol% **PA2** in toluene at room temperature. The results are summarized in *Scheme* 3. Cyclic *N*-sulfimines bearing a diverse range of electron-donating and electron-withdrawing substituents on the phenyl ring provided the desired sulfamidate products in good to high yields (65–94%). The presence of an additional halogen substituent in the phenyl ring slightly increased the reactivity in this reaction (*Scheme* 3, **5g** vs. **5h**).



[a] All of the reactions were carried out in toluene (0.2M) with **1** (0.1 mmol) and **2** (0.20 mmol) in the presence of 10 mol% **PA2** at room temperature.
[b] Isolated yield after chromatographic purification.
[c] Determined by ^{1}H NMR analysis.

***Scheme* 2.** Variation of cyclic *N*-sulfimines in Mannich-type reaction of trimethyloxyfuran **2**.[a]



[a] All of the reactions were carried out in toluene (0.2M) with **1** (0.1 mmol) and **4** (0.20 mmol) in the presence of 10 mol% **PA2** at room temperature.
[b] Isolated yield after chromatographic purification.

***Scheme* 3.** Variation of cyclic *N*-sulfimines in Mannich-type reaction of pyrazolin-5-one **3**.[a]

CONCLUSION

In summary, we have developed a highly efficient Mannich-type reaction of 2-trimethylsiloxyfuran and pyrazolin-5-one with cyclic *N*-sulfimines using **PA** as an organocatalyst. The desired sulfamidate γ-butenolide derivatives were obtained in good yields and high diastereoselectivities (up to 90% yield and 7:1 dr). The Mannich-type reaction of pyrazolin-5-one with cyclic *N*-sulfimine provided access to sulfamidate derivatives in good to high yields (up to 94% yield). Current work is still focused on the asymmetric version of these Mannich-type reaction.

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