Directed Zincation or Magnesiation of 2- and 4-Pyrones and Their Derivatives

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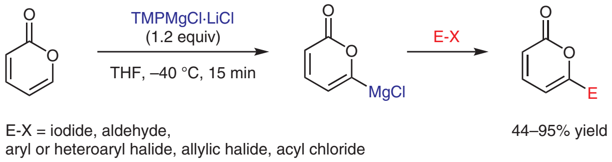
Dedicated to Professor Scott Denmark on the occasion of his 65th birthday



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Abstract A regioselective magnesiation of the 2-pyrone scaffold was developed. Magnesiation of this heterocycle by using TMPMgCl·LiCl (TMP = 2,2,6,6-tetramethylpiperidyl) followed by trapping reactions with electrophiles such as aldehydes, allylic bromides, acid chlorides, and aryl iodides provided functionalized 2-pyrones. Furthermore, methyl coumalate and 3,5-dibromo-2*H*-pyran-2-one were zincated by using TMPZnCl·LiCl to afford zincated heterocycles, which reacted with typical electrophiles. A second magnesiation at position C3 of the 2-pyrone scaffold was achieved by using TMPMgCl·LiCl. Also, the zincation of the 4-pyrone scaffold at position C2 is reported, leading to functionalized 4-pyrones.

Key words pyrone, metalation, magnesium, zinc, heterocycle functionalization

Pyrones are important scaffolds that are highly biologically active and widely distributed in biological processes of bacteria, microbes, plants, and animals, and are therefore interesting heterocycles in modern drug discovery.[1] Furthermore, the resulting functionalized pyrones can be used in a broad range of synthetic applications, in particular as dienes in Diels–Alder reactions[2] as well as precursors for the preparation of more complex heterocyclic systems in natural products.[3] Therefore, a number of methods have been developed to derivatize this core structure by transition-metal-catalyzed cross-couplings.[4] Despite the synthetic utility of pyrones, the preparation of substituted derivatives of this class of heterocycles can be accomplished only with difficulty, often requiring multistep syntheses.[5]

Recently, we have reported that a broad array of functionalized aromatic and heteroaromatic compounds can be metalated by using various TMP-derived Mg and Zn bases (TMP = 2,2,6,6-tetramethylpiperidyl).[6] Herein, we report the functionalization of 2- and 4-pyrones (**1** and **2**) and methyl coumalate (**3**) as well as the 3,5-dibrominated 2-pyrone **4** (Figure 1) using TMPMgCl·LiCl[7] (**5**), TMPZnCl·LiCl[8] (**6**), and $TMP_2Zn·2LiCl·2MgCl_2$[9] (**7**), followed by reactions with various electrophiles (E-X).

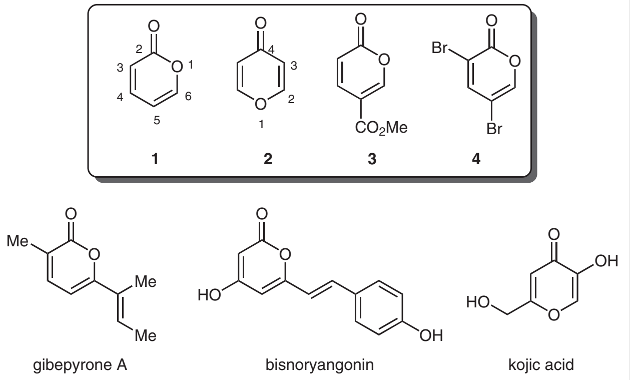
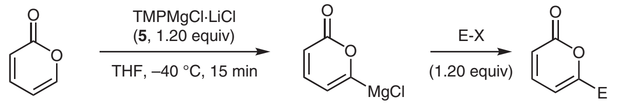


Figure 1 Structures of 2- and 4-pyrone and their derivatives

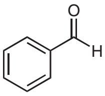
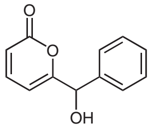
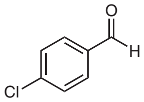
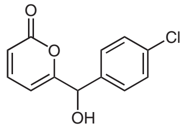
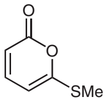
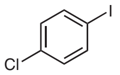
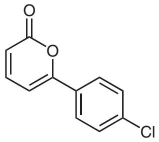
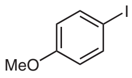
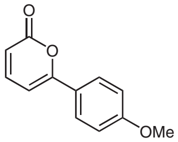
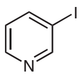
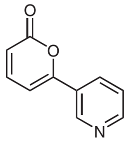
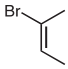
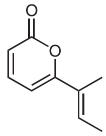
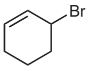
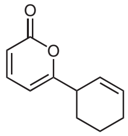
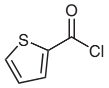
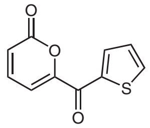
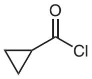
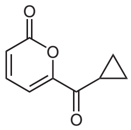
Thus, 2-pyrone (**1**) was treated with TMPMgCl·LiCl[7] (**5**, 1.20 equiv) for 15 minutes at –40 °C in THF, which results in the coordination of the TMP base to the oxygen atom O1, inducing a magnesiation at the C6 position (Table 1). This method led to a magnesium species of type **8**, which, after quenching with aldehydes, gave alcohols **9a** and **9b** in 72 and 60% yield (entries 1 and 2). Reaction of magnesium intermediate **8** with *S*-methyl methanethiosulfonate led to the thiolated 2-pyrone **9c** in 72% yield (entry 3). After transmetalation of the magnesium species to zinc using $ZnCl_2$, a Negishi cross-coupling[10] was performed with aryl iodides containing electron-withdrawing or -donating substituents in the presence of 4 mol% $Pd(dba)_2$ and 8 mol% tris(*o*-furyl)phosphine,[11] affording arylated 2-pyrones **9d** and **9e** in

75 and 90% yield (entries 4 and 5). Reaction of this zinc species in a Pd-catalyzed cross-coupling with 3-iodopyridine or (*E*)-2-bromobut-2-ene provided **9f** and **9g**, each in 95% yield (entries 6 and 7). After transmetalation to the corresponding copper species using CuCN·2LiCl[12] and subsequent reaction with 3-bromocyclohex-1-ene led to the allylated product **9h** in 50% yield (entry 8). Moreover, acylation reactions of the copper intermediates by using various acid chlorides afforded 6-acyl-2-pyrones **9i**,**j** in 44 and 60% yield (entries 9 and 10).

Table 1 Magnesiation of 2-Pyrone (**1**) Leading to Metalated Species **8** Followed by Reactions with Several Electrophiles



1 **8** **9a–j**

Entry	Electrophile	Product	9	Yield (%)[a]
1			**9a**	72
2			**9b**	60
3	MeSSO$_2$Me		**9c**	95
4			**9d**	75[b]
5			**9e**	90[b]
6			**9f**	95[b]
7			**9g**	99[b]
8			**9h**	50[c]
9			**9i**	44[c]
10			**9j**	60[c]

[a] Yields of isolated, analytically pure products.
[b] Obtained by Negishi cross-coupling[10] using 4 mol% Pd(dba)$_2$ and 8 mol% P(*o*-furyl)$_3$.[11]
[c] Obtained after transmetalation with CuCN·2LiCl[12] (1.20 equiv).

2-Pyrones bearing an ester functionality at the C5 position also underwent metalation when TMPZnCl·LiCl[8] (**6**, 1.20 equiv, –78 °C, 10 min) was used, allowing facile functionalization of the C6 position (Table 2). Pd-catalyzed Negishi cross-couplings[10] with aryl iodides led to cross-coupling products **11a**,**b** in 45 and 58% yield (entries 1 and 2). Transmetalation of **10** with CuCN·2LiCl[12] and subsequent reaction with an allyl bromide provided methyl coumalate **11c** in 70% yield (entry 3). The corresponding reaction with acyl chlorides afforded the expected ketones **11d–f** in 40–64% yield (entries 4–6).

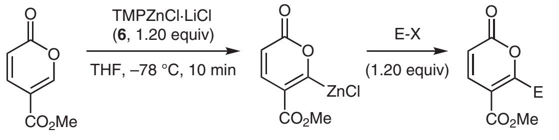
We further explored the scope of this zincation using the zinc base **6** on 3,5-dibrominated 2-pyrone **4**,[3] achieving a regioselective zincation of 3,5-dibromo-2*H*-pyran-2-one (**4**) at position C6 with the zinc base (**6**, 1.20 equiv, –10 °C, 1.5 h). The resulting zinc reagent **12** was readily functionalized by reaction with various electrophiles to furnish 6-substituted 3,5-dibromo-2*H*-pyran-2-ones **13** (Table 3). Similarly, iodolysis, Pd-catalyzed Negishi cross-coupling,[10] and Cu-mediated allylation or acylation provided the C6-substituted pyrones **13a–e** in 53–65% yield (entries 1–5).

A second metalation of 6-substituted 2-pyrone **9c** and **9e** occurred at position C3 or C5 when TMPMgCl·LiCl[7] (**5**) was used. Thus, 6-thiolated 2-pyrone **9c** was metalated at position C5 with **5** (1.20 equiv, –40 °C, 1.5 h), and this magnesiated species **14** was then iodinated to provide iodo derivative **15** in 43% yield (Scheme 1).

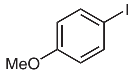
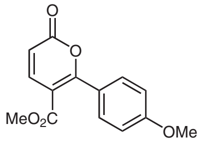
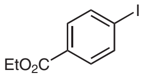
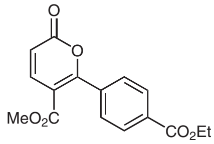
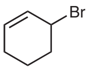
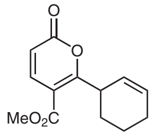
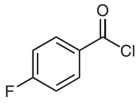
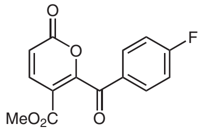
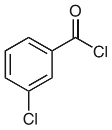
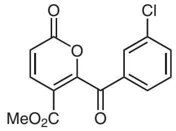
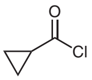
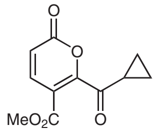
Furthermore, treatment of 6-arylated 2-pyrone **9e** with magnesium amide **5** (1.20 equiv, –40 °C, 1.5 h) led to the quantitative formation of 3-magnesiated pyrone **16** (Table 4). The magnesium reagent **16** reacted with iodine and benzaldehyde to provide 3,6-disubstituted 2-pyrones **17a** and **17b** in 95 and 45% yield, respectively (entries 1 and 2).

To extend the substrate scope, we prepared 2-zincated 4-pyrone **18**[13] by treating 4-pyrone (**2**) with $TMPZn_2·2LiCl·2MgCl_2$[10] (**7**) at –35 °C for 2 hours (Table 5). Zinc intermediate **18** reacted readily with aryl iodides in the presence of 4 mol% $Pd(dba)_2$ and 8 mol% $P(o\text{-furyl})_3$,[11] providing the corresponding arylated products **19a** and **19b** in 50 and 86% yield, respectively (entries 1 and 2). Copper-mediated acylation with thiophene-2-carbonyl chloride or cyclopropanecarbonyl chloride gave 4-pyrone ketones **19c** and **19d** in 71 and 50% yield, respectively (entries 3 and 4).

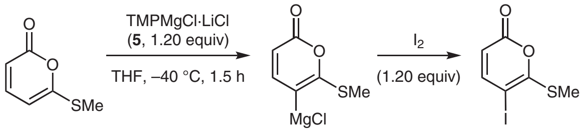
Table 2 Zincation of Methyl Coumalate (**3**) Leading to Metalated Species **10** Followed by Reactions with Several Electrophiles



3 **10** **11a–f**

Entry	Electrophile	Product	11	Yield (%)[a]
1			**11a**	45[b]
2			**11b**	58[b]
3			**11c**	70[c]
4			**11d**	55[c]
5			**11e**	64[c]
6			**11f**	40[c]

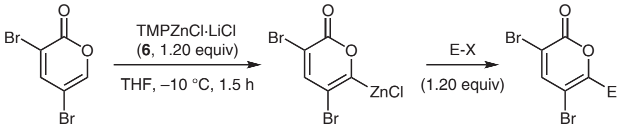
[a] Yields of isolated, analytically pure products.
[b] Obtained by Negishi cross-coupling[10] using 4 mol% $Pd(dba)_2$ and 8 mol% $P(o\text{-furyl})_3$.[11]
[c] Obtained after transmetalation with CuCN·2LiCl[12] (1.20 equiv).



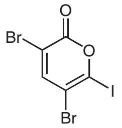
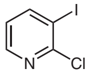
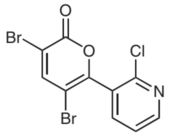
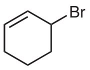
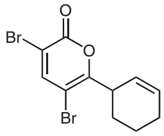
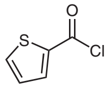
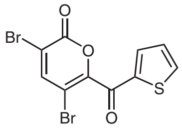
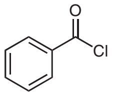
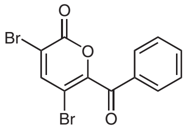
9c **14** **15** 43%

Scheme 1 Further functionalization of the 6-substituted 2-pyrone **9c**

Table 3 Zincation of 3,5-Dibromo-2*H*-pyran-2-one (**3**) Leading to Metalated Species **12** Followed by Reactions with Several Electrophiles



4 **12** **13a–e**

Entry	Electrophile	Product	13	Yield (%)[a]
1	I_2		**13a**	64
2			**13b**	60[b]
3			**13c**	60[c]
4			**13d**	55[c]
5			**13e**	53[c]

[a] Yields of isolated, analytically pure products.
[b] Obtained by Negishi cross-coupling[11] using 4% $Pd(dba)_2$ and 8% $P(o\text{-furyl})_3$.[12]
[c] Obtained after transmetalation with CuCN·2LiCl[13] (1.20 equiv).

In conclusion, we have developed a new general method for the regioselective metalation of 2-pyrone (**1**), 4-pyrone (**2**), and methyl coumalate (**3**), as well as 3,5-brominated 2-pyrone **4**, by using TMP bases, leading to a variety of new functionalized 2-pyrones and 4-pyrones. A second metalation of the 2-pyrone scaffold was achieved by using TMP-MgCl·LiCl.

All reactions were carried out under argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhyd solvents or reagents were purged with argon prior to use. Yields refer to isolated yields of compounds estimated to be >95% pure as determined by ^{1}H NMR (25 °C) and capillary GC analysis. Column chromatographic purification was performed by using silica gel (0.040–0.063 mm, 230–400 mesh ASTM) from Merck. NMR spectra were recorded on VARIAN Mercury 200, BRUKER AXR 300, VARIAN VXR 400 S, and BRUKER AMX 600 instruments. Chemical shifts are reported as δ values in ppm relative to the deuterated solvent peak: CDCl$_3$ (δH = 7.26; δC = 77.16) or acetone-d_6 (δH = 2.05; δC = 29.80). High resolution mass spectra by electron impact ionization (EI) and low resolution mass spectra were recorded on a FINNIGAN MAT 95Q instrument. EI was conducted with an electron energy of 70 eV. For the combination of gas chromatography with mass spectroscopic detection, a GC/MS from Hewlett-Packard HP 6890/MSD 5973 was used. IR spectra were recorded from 4500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument. For detection, a SMITHS DETECTION DuraSamplIR II Diamond ATR sensor was used. The absorption bands were reported in wavenumbers (cm^{-1}). Melting points (mp:) were determined on a BÜCHI B-540 apparatus and are uncorrected.

GC-spectra were recorded on Hewlett-Packard 6890 or 5890 Series II instruments (Hewlett Packard, 5 % phenylmethylpolysiloxane; length: 10 m, diameter: 0.25 mm; film thickness: 0.25 μμm). All reagents not listed in the Supporting Information were obtained from commercial sources. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen N$_2$ and stored over molecular sieves. Solvents for column chromatography were distilled on a rotary evaporator prior to use. The starting materials 2-pyrone (**1**) and 4-pyrone (**2**) were purchased from TCI. Methyl coumalate was purchased from Alfa Aesar. 3,5-Dibromo-2*H*-pyran-2-one was prepared by using known procedures.[2a]

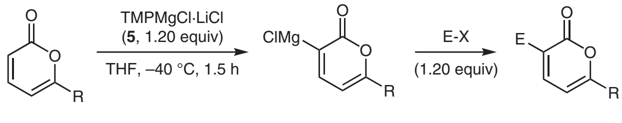
CuCN·2LiCl[12] Solution

A 250 mL Schlenk flask, equipped with a magnetic stirring bar and rubber septum, was charged with CuCN (80.0 mmol, 7.17 g) and LiCl (160 mmol, 6.77 g). The mixture was heated under vacuum at 140 °C for 5 h. After cooling of the mixture to 25 °C, anhyd THF (80 mL) was added and stirring was continued until the salts were dissolved, providing a 1.0 M solution.

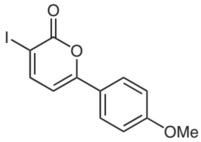
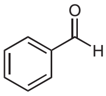
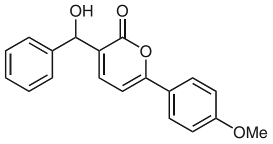
ZnCl$_2$ Solution

A 250 mL Schlenk flask, equipped with a magnetic stirring bar and rubber septum, was charged with ZnCl$_2$ (136 g, 100 mmol). The mixture was heated under vacuum at 140 °C for 5 h. After cooling of the mixture to 25 °C, anhyd THF (100 mL) was added and stirring was continued until the salt was dissolved, providing a 1.0 M solution.

Table 4 A Second Metalation of the 6-Substituted 2-Pyrone **9e**

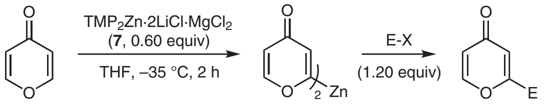


9e R = 4-anisyl **16** **17a,b**

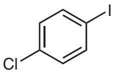
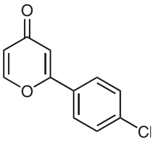
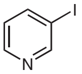
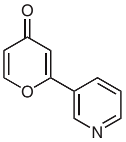
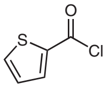
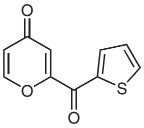
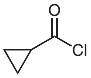
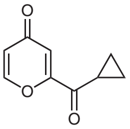
Entry	Electrophile	Product	17	Yield (%)[a]
1	I$_2$		**17a**	99
2			**17b**	45

[a] Yields of isolated, analytically pure products.

Table 5 Zincation of 4-Pyrone (**4**) Leading to Metalated Species **18** Followed by Reactions with Several Electrophiles



2 **18** **19a–e**

Entry	Electrophile	Product	19	Yield (%)[a]
1			**19a**	50[b]
2			**19b**	86[b]
3			**19c**	71[c]
4			**19d**	50[c]

[a] Yields of isolated, analytically pure products.
[b] Obtained by Negishi cross-coupling[10] using 4 mol% Pd(dba)$_2$ and 8 mol% P(*o*-furyl)$_3$.[11]
[c] Obtained after transmetalation with CuCN·2LiCl[12] (1.20 equiv).

TMPMgCl·LiCl (5)[7]

A dry and argon-flushed 500 mL Schlenk flask, equipped with a magnetic stirring bar and a rubber septum, was charged with *i*-PrMgCl·LiCl (1.31 M in THF, 229 mL, 300 mmol). Then, TMPH (52.0 mL, 306 mmol, 1.02 equiv) was added and the mixture was stirred until gas evolution ceased (48 h). The freshly prepared TMPMgCl·LiCl (**5**) solution was titrated prior to use at 0 °C with benzoic acid and by using 4-(phenylazo)diphenylamine as indicator.

TMPZnCl·LiCl[8]

A dry and argon-flushed 500 mL Schlenk flask, equipped with a magnetic stirring bar and a rubber septum, was charged with freshly distilled TMPH (10.2 mL, 60.0 mmol, 1.00 equiv) dissolved in THF (60.0 mL). This solution was cooled to –40 °C and *n*-BuLi (2.40 M in hexane, 25.0 mL, 60.0 mmol) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm slowly to –10 °C for 1 h. $ZnCl_2$ (1.00 M in THF, 66.0 mL, 66.0 mmol) was added dropwise and the resulting solution was stirred for 30 min at –10 °C and then for 30 min at 25 °C. The solvents were then removed under vacuum affording a yellowish solid. Freshly distilled THF was then slowly added under vigorous stirring until the salts were completely dissolved. The freshly prepared TMPZnCl·LiCl (**6**) solution was titrated prior to use at 0 °C with benzoic acid and by using 4-(phenylazo)diphenylamine as indicator.

$TMP_2Zn·2MgCl_2·2LiCl$[9]

A flame-dried and argon-flushed 500 mL Schlenk flask, equipped with a magnetic stirring bar and rubber septum, was charged with a solution of TMPMgCl·LiCl (**8**, 1.20 M, 50.0 mL, 60.0 mmol) and cooled to 0 °C. Then, $ZnCl_2$ (1.00 M in THF, 30.0 mL, 30.0 mmol, 0.50 equiv) was added over a period of 15 min. After stirring of this mixture for 12 h at 25 °C, $TMP_2Zn·2MgCl_2·2LiCl$ (**10**) was titrated prior to use at 0 °C with benzoic acid and by using 4-(phenylazo)diphenylamine as indicator.

Magnesation of 2-Pyrone (1) Using TMPMgCl·LiCl (5); Typical Procedure TP1

In a dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, 2-pyrone (**1**, 1.00 equiv) was dissolved in anhyd THF (0.50 M solution). After the solution had been cooled to –40 °C, TMPMgCl·LiCl (**5**, 1.20 equiv) was added and the mixture was stirred at the same temperature. The completion of the metalation was achieved after 15 min, shown by TLC analysis of reaction aliquots quenched with a solution of I_2 in anhyd THF. Subsequent reactions with electrophiles were carried out under the indicated conditions. After complete conversion, the mixture was quenched with sat. aq NaCl (10 mL) and extracted with Et_2O (3 × 20 mL) if not noted differently. The combined organic extracts were dried over anhyd Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography.

Zincation of Methyl Coumalate (3) Using TMPZnCl·LiCl (6); Typical Procedure TP2

In a dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, methyl coumalate (**3**, 1.00 equiv) was dissolved in anhyd THF (0.50 M solution). After the solution had been cooled to −78 °C, TMPZnCl·LiCl (**6**, 1.20 equiv) was added and the mixture was stirred at the same temperature. The completion of the metalation was achieved after 15 min, shown by TLC analysis of reaction aliquots quenched with a solution of I_2 in anhyd THF. After complete conversion, the mixture was quenched with sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL) if not specifically indicated. The combined organic extracts were dried over anhyd Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography.

Zincation of 3,5-Dibromo-2*H*-pyran-2-one (4) Using TMPZnCl·LiCl (6); Typical Procedure TP3

In a dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, 3,5-dibromo-2*H*-pyran-2-one (**4**, 1.00 equiv) was dissolved in anhyd THF (0.50 M solution). After the solution had been cooled to −10 °C, TMPZnCl·LiCl (**6**, 1.20 equiv) was added and the mixture was stirred at the same temperature. The completion of the metalation was achieved after 15 min, shown by TLC analysis of reaction aliquots quenched with a solution of I_2 in anhyd THF. After complete conversion, the mixture was quenched with sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL) if not specifically indicated. The combined organic extracts were dried over anhyd Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography.

Magnesiation of 6-Substituted 2-Pyrone (9) using TMPMgCl·LiCl (5); Typical Procedure TP4

In a dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, the 6-substituted 2-pyrone (**9**, 1.00 equiv) was dissolved in anhyd THF (0.50 M solution). After the solution had been cooled to −40 °C, TMPMgCl·LiCl (**5**, 1.20 equiv) was added and the mixture was stirred at the same temperature. The completion of the metalation was achieved after 1 h, shown by TLC analysis of reaction aliquots quenched with a solution of I_2 in anhyd THF. After complete conversion, the mixture was quenched with sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL) if not specifically indicated. The combined organic extracts were dried over anhyd Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography.

Zincation of 4-Pyrone (2) Using $TMP_2Zn·2MgCl_2·2LiCl$ (7); Typical Procedure TP5

In a dry and argon-flushed Schlenk flask, equipped with a magnetic stirring bar and a septum, 4-pyrone (**2**, 1.00 equiv) was dissolved in anhyd THF (0.50 M solution). After the solution had been cooled to −35 °C, $TMP_2Zn·2MgCl_2·2LiCl$ (**7**, 1.20 equiv) was added and the mixture was stirred at the same temperature. The completion of the metalation was achieved after 2 h, shown by TLC analysis of reaction aliquots quenched with a solution of I_2 in anhyd THF. After complete conversion, the mixture was quenched with sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL) if not specifically indicated. The combined organic extracts were dried over anhyd Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography.

Reactions of Magnesiated 2-Pyrone (1) with Electrophiles

6-[Hydroxy(phenyl)methyl]-2*H*-pyran-2-one (9a)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at –40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). Benzaldehyde (60.0 μL, 0.60 mmol, 1.20 equiv) was then added dropwise at –40 °C. The reaction mixture was warmed to 25 °C and was stirred until completion of the reaction. The crude product was purified by column chromatography (silica gel, *i*-hexane/Et_2O, 5:5) furnishing **9a**.

Yield: 73.0 mg (72%); yellow solid; mp 107–108 °C.

IR (diamond-ATR, neat): 3072, 1716, 1535, 148, 1398, 1090, 1074, 845, 801 cm^{-1}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 7.53–7.46 (m, 3 H), 7.40–7.29 (m, 3 H), 6.50 (dt, *J* = 6.6, 1.0 Hz, 1 H), 6.13–6.09 (m, 1 H), 5.52 (d, *J* = 3.8 Hz, 1 H), 5.42 (d, *J* = 4.4 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 167.7, 161.8, 144.9, 141.7, 129.2, 128.9, 127.8, 114.4, 101.9, 73.1.

MS (EI, 70 eV): *m*/*z* (%) = 202 (48), 198 (46), 186 (100), 173 (14), 128 (16), 107 (52), 95 (100).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}O_3$: 202.0630; found: 202.0622.

6-[(4-Chlorophenyl)(hydroxy)methyl]-2*H*-pyran-2-one (9b)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at −40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). 4-Chlorobenzaldehyde (60.0 μL, 0.60 mmol, 1.20 equiv) was then added dropwise at −40 °C. The reaction mixture was warmed to 25 °C and was stirred until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et$_2$O, 4:6) furnishing **9b**.

Yield: 71.0 mg (60%); yellow oil.

IR (diamond-ATR, neat): 3072, 1716, 1535, 1488, 1398, 1090, 1074, 845, 801 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 7.54–7.47 (m, 3 H), 7.43–7.38 (m, 2 H), 6.50 (dt, *J* = 6.6, 0.9 Hz, 1 H), 6.12 (dd, *J* = 9.4, 1.2 Hz, 1 H), 5.53 (d, *J* = 12.5 Hz, 2 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 167.0, 161.6, 144.9, 140.7, 134.2, 129.5, 129.3, 114.7, 102.1, 72.4.

MS (EI, 70 eV): *m*/*z* (%) = 236 (20), 234 (10), 220 (11), 143 (34), 142 (10), 138 (100), 113 (25), 111 (45), 97 (56), 96 (28), 77 (79), 75 (33), 51 (19), 50 (15).

HRMS (EI): *m*/*z* calcd for $C_{12}H_9ClO_3$: 236.0240; found: 236.0243.

6-(Methylthio)-2*H*-pyran-2-one (9c)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at −40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). Methyl methanethiosulfonate (60.0 μL, 0.60 mmol, 1.20 equiv) was then added dropwise at −40 °C. The reaction mixture was warmed to 25 °C and was stirred until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et$_2$O, 4:6) furnishing **9c**.

Yield: 67.0 mg (95%); orange oil.

IR (diamond-ATR, neat): 2928, 1724, 1606, 1513, 1435, 1173, 1080, 780 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 7.42 (dd, *J* = 9.3, 7.0 Hz, 1 H), 6.22 (dd, *J* = 7.0, 0.8 Hz, 1 H), 5.99 (dd, *J* = 9.3, 0.8 Hz, 1 H), 2.54 (s, 3 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 165.7, 161.7, 145.0, 110.1, 102.4, 13.8.

MS (EI, 70 eV): *m*/*z* (%) = 142 (42), 114 (12), 95 (100), 43 (13), 39 (37), 28 (22), 18 (20).

HRMS (EI): *m*/*z* calcd for $C_6H_6O_2S$: 142.0089; found: 142.0076.

6-(4-Chlorophenyl)-2*H*-pyran-2-one (9d)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at −40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was transmetalated to zinc in the presence of ZnCl$_2$ (0.75 mL, 1.00 M in THF, 0.75 mmol, 1.50 equiv) and stirring for 30 min at −40 °C. The zinc reagent underwent a Negishi cross-coupling reaction in the presence of Pd(dba)$_2$ (11.0 mg, 8 mol%), P(2-furyl)$_3$ (9.00 mg, 15 mol%) and 1-chloro-4-iodobenzene (143 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et$_2$O, 5:5) furnishing **9d**.

Yield: 78.0 mg (75%); yellowish solid; mp 100–101 °C.

IR (diamond-ATR, neat): 3072, 1716, 1535, 1488, 1398, 1090, 1074, 845, 801 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 7.87–7.83 (m, 2 H), 7.58 (dd, *J* = 9.3, 6.8, 1 H), 7.53–7.48 (m, 2 H), 6.92 (dd, *J* = 6.8, 0.8 Hz, 1 H), 6.25 (dd, *J* = 9.3, 0.8 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 161.3, 160.2, 144.9, 137.0, 131.3, 130.0, 127.9, 115.0, 102.4.

MS (EI, 70 eV): *m*/*z* (%) = 206 (53), 180 (31), 179 (11), 178 (100), 149 (16), 139 (10), 115 (30), 111 (14).

HRMS (EI): *m*/*z* calcd for $C_{11}H_7ClO_2$: 206.0135; found: 206.0110.

6-(4-Methoxyphenyl)-2*H*-pyran-2-one (9e)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.5 M in THF, 0.50 mmol) was completely metalated within 15 min at −40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was transmetalated to zinc in the presence of ZnCl$_2$ (0.75 mL, 1.00 M in THF, 0.75 mmol, 1.50 equiv) and stirring for 30 min at −40 °C. The zinc reagent underwent a Negishi cross-coupling reaction in the presence of Pd(dba)$_2$ (11.0 mg, 8 mol%), P(2-furyl)$_3$ (9.00 mg, 15 mol%) and 1-iodo-4-methoxybenzene (140 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et$_2$O, 6:4) furnishing **9e**.

Yield: 91.0 mg (90%); yellowish solid; mp 137–139 °C.

IR (diamond-ATR, neat): 3007, 1719, 1606, 1505, 1415, 1235, 1178, 1021, 835, 787 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 7.85–7.80 (m, 2 H), 7.55 (dd, *J* = 9.3, 6.9 Hz, 1 H), 7.08–7.03 (m, 2 H), 6.79 (dd, *J* = 6.9, 0.8 Hz, 1 H), 6.16 (dd, *J* = 9.3, 0.8 Hz, 1 H), 3.87 (s, 3 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 162.8, 161.8, 161.8, 145.3, 128.0, 125.0, 115.3, 113.2, 100.5, 55.9.

MS (EI, 70 eV): *m*/*z* (%) = 202 (44), 174 (100), 131 (40), 103 (16).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}O_3$: 202.0630; found: 202.0622.

6-(Pyridin-3-yl)-2*H*-pyran-2-one (9f)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at −40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was transmetalated to zinc in the presence of ZnCl$_2$ (0.75 mL, 1.00 M in THF, 0.75 mmol, 1.50 equiv) and stirring for 30 min at −40 °C. The zinc reagent underwent a Negishi cross-coupling reaction in the presence of Pd(dba)$_2$ (11.0 mg, 8 mol%), P(2-furyl)$_3$ (9.00 mg, 15 mol%) and 3-iodopyridine (60.0 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et$_2$O, 4:6) furnishing **9f**.

Yield: 83.0 mg (95%); yellowish solid; mp 96–98 °C.

IR (diamond-ATR, neat): 2917, 2849, 1726, 1628, 1540, 1476, 1266, 1108, 1069, 841, 793, 695 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 9.07 (d, *J* = 0.8 Hz, 1 H), 8.68 (dd, *J* = 4.8, 1.6 Hz, 1 H), 8.22 (ddd, *J* = 8.1, 2.4, 1.6 Hz, 1 H), 7.65 (dd, *J* = 9.4, 6.8 Hz, 1 H), 7.55–7.50 (m, 1 H), 7.05 (dd, *J* = 6.8, 0.8 Hz, 1 H), 6.32 (dd, *J* = 9.4, 0.8 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 161.3, 159.2, 152.2, 147.6, 144.9, 133.5, 124.6, 115.6, 103.1.

MS (EI, 70 eV): *m*/*z* (%) = 173 (45), 145 (100), 117 (11), 95 (17), 78 (16), 57 (12), 55 (10), 50 (12), 43 (13), 43 (16).

HRMS (EI): *m*/*z* calcd for $C_{10}H_7NO_2$: 173.0477; found: 173.0472.

(*E*)-6-(But-2-en-2-yl)-2*H*-pyran-2-one (9g)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at –40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was transmetalated to zinc in the presence of $ZnCl_2$ (0.75 mL, 1.00 M in THF, 0.75 mmol, 1.50 equiv) and stirring for 30 min at –40 °C. The zinc reagent underwent a Negishi cross-coupling reaction in the presence of PEPPSI-^{iPr} (11.8 mg, 8 mol%) and (*E*)-2-bromobut-2-ene (60.0 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et_2O, 4:6) furnishing **9g**.

Yield: 75.0 mg (99%); yellowish solid; mp 63–66 °C.

IR (diamond-ATR, neat): 3075, 2924, 1704, 1638, 1540, 1445, 1093, 1018, 832, 796, 784, 705 cm^{-1}.^{1}H NMR (400 MHz, acetone-*d*$_6$): δ = 7.48 (dd, *J* = 9.3, 6.9 Hz, 1 H), 6.56 (qd, *J* = 7.1, 1.2 Hz, 1 H), 6.32 (d, *J* = 6.9 Hz, 1 H), 6.12 (d, *J* = 9.3 Hz, 1 H), 1.88 (p, *J* = 1.0 Hz, 3 H), 1.86–1.82 (m, 3 H).

^{13}C NMR (101 MHz, acetone-*d*$_6$): δ = 162.6, 161.6, 145.1, 129.4, 128.4, 114.0, 101.3, 14.2, 12.1.

MS (EI, 70 eV): *m*/*z* (%) = 151 (10), 150 (94), 122 (100), 121 (13), 107 (71), 93 (18), 91 (13), 79 (49), 77 (21), 55 (28), 53 (17), 43 (25), 41 (11).

HRMS (EI): *m*/*z* calcd for $C_9H_{10}O_2$: 150.0681; found: 150.0671.

6-(Cyclohex-2-en-1-yl)-2*H*-pyran-2-one (9h)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at –40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −40 °C. A subsequent allylation reaction was performed in the presence of 3-bromocyclohex-1-ene (193 mg, 0.60 mmol, 1.20 equiv) at −40 °C. The reaction mixture was stirred at 25 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et_2O, 4:6) furnishing **9h**.

Yield: 44.0 mg (50%); yellow oil.

IR (diamond-ATR, neat): 2933, 1732, 1630, 1556, 1448, 1295, 1088, 801 cm^{-1}.^{1}H NMR (400 MHz, acetone-*d*$_6$): δ = 7.44 (dd, *J* = 9.3, 6.7 Hz, 1 H), 6.12–6.08 (m, 2 H), 5.93 (dtd, *J* = 9.9, 3.7, 2.3 Hz, 1 H), 5.67 (dq, *J* = 10.1, 2.3 Hz, 1 H), 3.27 (ddt, *J* = 9.2, 5.8, 2.7 Hz, 1 H), 1.97 (dddd, *J* = 13.4, 8.5, 5.8, 3.1 Hz, 2 H), 1.82–1.55 (m, 4 H).

^{13}C NMR (101 MHz, acetone-*d*$_6$): δ = 169.3, 162.4, 144.9, 131.2, 125.8, 113.8, 102.9, 40.3, 27.9, 25.4, 20.8.

MS (EI, 70 eV): *m*/*z* (%) = 176 (100), 169 (11), 167 (11), 162 (31), 149 (12), 148 (40), 147 (17).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{12}O_2$: 176.0837; found: 176.0830.

6-(Thiophene-2-carbonyl)-2*H*-pyran-2-one (9i)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at –40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −40 °C. Acylation was achieved with thiophene-2-carbonyl chloride (64.0 µL, 0.60 mmol, 1.20 equiv) at −40 °C and warming to −15 °C. The reaction mixture was stirred at −15 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et_2O, 5:5) furnishing **9i**.

Yield: 45.0 mg (44%); yellow solid; mp 143–146 °C.

IR (diamond-ATR, neat): 3090, 1726, 1636, 1604, 1509, 1410, 1358, 1289, 1077, 858, 811, 734 cm^{-1}.^{1}H NMR (400 MHz, acetone-*d*$_6$): δ = 8.33 (dd, *J* = 3.9, 1.1 Hz, 1 H), 8.10 (dd, *J* = 5.0, 1.1 Hz, 1 H), 7.74 (dd, *J* = 9.4, 6.6 Hz, 1 H), 7.35 (dd, *J* = 5.0, 3.9 Hz, 1 H), 7.20 (dd, *J* = 6.6, 0.9 Hz, 1 H), 6.63 (dd, *J* = 9.4, 0.9 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-*d*$_6$): δ = 176.9, 159.9, 156.6, 144.0, 141.5, 137.5, 137.0, 129.8, 121.1, 109.8.

MS (EI, 70 eV): *m*/*z* (%) = 247 (2), 244 (1), 208 (3), 207 (5), 206 (39), 205 (3), 178 (3), 155 (2), 149 (1), 128 (5), 126 (1).

HRMS (EI): *m*/*z* calcd for $C_{10}H_6O_3S$: 206.0038; found: 206.0045.

6-(Cyclopropanecarbonyl)-2*H*-pyran-2-one (9j)

According to TP1, 2-pyrone (**1**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 15 min at –40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −40 °C. Acylation was achieved with cyclopropanecarbonyl chloride (54.0 µL, 0.60 mmol, 1.20 equiv) at −40 °C and warming to −15 °C. The reaction mixture was stirred at −15 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/Et_2O, 5:5) furnishing **9j**.

Yield: 49.0 mg (60%); yellow solid; mp 84–85 °C.

IR (diamond-ATR, neat): 3058, 1718, 1672, 1406, 1244, 1060, 1018, 960, 816 cm^{-1}.^{1}H NMR (400 MHz, acetone-*d*$_6$): δ = 7.68 (dd, *J* = 9.4, 6.6 Hz, 1 H), 7.09 (dd, *J* = 6.6, 1.0 Hz, 1 H), 6.59 (dd, *J* = 9.4, 0.9 hz, 1 H), 2.84–2.78 (m, 1 H), 1.17–1.07 (m, 4 H).

^{13}C NMR (101 MHz, acetone-*d*$_6$): δ = 193.7, 160.2, 156.0, 143.8, 121.3, 107.6, 16.7, 12.9.

MS (EI, 70 eV): *m*/*z* (%) = 165 (5), 164 (42), 149 (2), 129 (2), 126 (2), 125 (3), 123 (2), 111 (3), 109 (3), 97 (4), 96 (8).

HRMS (EI): *m*/*z* calcd for $C_9H_8O_3$: 164.0473; found: 164.0472.

Reactions of Zincated Methyl Coumalate (3) with Electrophiles

Methyl 6-(4-Methoxyphenyl)-2-oxo-2*H*-pyran-5-carboxylate (11a)

According to TP2, methyl coumalate (**3**, 72.0 mg, 0.50 mmol) was completely metalated within 15 min at –78 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent underwent a Negishi cross-coupling reaction in the presence of $Pd(dba)_2$ (11.0 mg, 8 mol%), P(2-furyl)$_3$ (9.00 mg, 15 mol%) and 1-iodo-4-methoxybenzene (140 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **11a**.

Yield: 59.0 mg (45%); orange solid; mp 127–129 °C.

IR (diamond-ATR, neat): 2954, 1723, 1606, 1505, 1436, 1331, 1256, 1178, 1071, 857, 781 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 9.7 Hz, 1 H), 7.57–7.50 (m, 2 H), 6.97–6.91 (m, 2 H), 6.24 (d, *J* = 9.7 Hz, 1 H), 3.86 (s, 3 H), 3.72 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.2, 165.5, 162.3, 160.6, 144.6, 131.1, 124.3, 113.7, 112.4, 108.6, 55.5, 52.4.

MS (EI, 70 eV): *m*/*z* (%) = 260 (40), 232 (76), 201 (26), 135 (100), 77 (16).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}O_5$: 260.0685; found: 260.0681.

Methyl 6-[4-(Ethoxycarbonyl)phenyl]-2-oxo-2*H*-pyran-5-carboxylate (11b)

According to TP2, methyl coumalate (**3**, 72.0 mg, 0.50 mmol) was completely metalated within 15 min at –78 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent underwent a Negishi cross-coupling reaction in the presence of $Pd(dba)_2$ (11.0 mg, 8 mol%), $P(2\text{-furyl})_3$ (9.00 mg, 15 mol%) and ethyl 4-iodobenzoate (0.10 mL, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **11b**.

Yield: 87.0 mg (58%); yellowish liquid.

IR (diamond-ATR, neat): 2983, 1752, 1709, 1547, 1269, 1100, 1071, 997, 870, 769, 702 cm^{-1}.^1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.3 Hz, 2 H), 7.84 (d, *J* = 9.7 Hz, 1 H), 7.60 (d, *J* = 8.3 Hz, 2 H), 6.35 (d, *J* = 9.7 Hz, 1 H), 4.40 (q, *J* = 7.1 Hz, 2 H), 3.68 (s, 3 H), 1.40 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.1, 165.6, 164.5, 159.7, 143.9, 136.0, 132.7, 129.2, 129.0, 114.0, 110.0, 61.4, 52.4, 14.3.

MS (EI, 70 eV): *m*/*z* (%) = 302 (75), 274 (60), 257 (31), 246 (18), 243 (16), 229 (39), 197 (20), 178 (13), 177 (100), 149 (26), 121 (11), 76 (12), 71 (11), 65 (11), 43 (57).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}O_6$: 302.0790; found: 302.0785.

Methyl 6-(Cyclohex-2-en-1-yl)-2-oxo-2*H*-pyran-5-carboxylate (11c)

According to TP2, methyl coumalate (**3**, 72.0 mg, 0.50 mmol) was completely metalated within 15 min at –78 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The magnesium reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −78 °C. A subsequent allylation reaction was performed in the presence of 3-bromocyclohex-1-ene (70 μL, 0.60 mmol, 1.20 equiv) at −78 °C. The reaction mixture was stirred at 25 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **11c**.

Yield: 82.0 mg (70%); white solid; mp 90–92 °C.

IR (diamond-ATR, neat): 2947, 1742, 1716, 1622, 1549, 1437, 1290, 1258, 1071, 909, 847, 786 cm^{-1}.^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 9.8 Hz, 1 H), 6.17 (d, *J* = 9.8 Hz, 1 H), 5.93 (ddt, *J* = 9.7, 4.6, 2.7 Hz, 1 H), 5.56 (d, *J* = 12.4 Hz, 1 H), 4.53 (ddt, *J* = 8.8, 5.9, 2.9 Hz, 1 H), 3.87 (s, 3 H), 2.21–1.78 (m, 6 H), 1.73–1.62 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.6, 164.5, 160.7, 144.1, 130.2, 124.8, 112.5, 108.4, 52.5, 39.0, 27.4, 24.5, 21.5.

MS (EI, 70 eV): *m*/*z* (%) = 234 (94), 230 (62), 225 (40), 217 (4), 215 (100), 209 (24), 202 (100), 174 (72), 108 (52), 79 (76).

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}O_4$: 234.0892; found: 234.0885.

Methyl 6-(4-Fluorobenzoyl)-2-oxo-2*H*-pyran-5-carboxylate (11d)

According to TP2, methyl coumalate (**3**, 72.0 mg, 0.50 mmol) was completely metalated within 15 min at –78 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −78 °C. Acylation was achieved with 4-fluorobenzoyl chloride (54.0 mL, 0.60 mmol, 1.20 equiv) at −78 °C and warming to −15 °C. The reaction mixture was stirred at 0 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **11d**.

Yield: 77.0 mg (55%); yellow oil.

IR (diamond-ATR, neat): 2954, 1764, 1723, 1683, 1596, 1437, 1298, 1240, 1156, 1088, 924, 833, 802, 783 cm^{-1}.^1H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.83 (m, 3 H), 7.19 (t, *J* = 8.4 Hz, 2 H), 6.42 (d, *J* = 10.2 Hz, 1 H), 3.69–3.66 (m, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 184.6, 166.8 (d, *J* = 258.3 Hz), 163.6, 162.8, 158.2, 142.3, 132.3 (d, *J* = 9.8 Hz), 130.4, 116.6 (d, *J* = 22.4 Hz), 115.7, 109.5, 52.8.

MS (EI, 70 eV): *m*/*z* (%) = 245 (20), 232 (34), 217 (100), 203 (16), 189 (16), 175 (24), 153 (16), 123 (100), 85 (10).

HRMS (EI): *m*/*z* [M + H⁺] calcd for $C_{14}H_{10}FO_5$: 277.0507; found: 277.0504.

Methyl 6-(3-Chlorobenzoyl)-2-oxo-2*H*-pyran-5-carboxylate (11e)

According to TP2, methyl coumalate (**3**, 72.0 mg, 0.50 mmol) was completely metalated within 15 min at –78 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −78 °C. Acylation was achieved with 3-chlorobenzoyl chloride (80 μL, 0.60 mmol, 1.20 equiv) at −78 °C and warming to −15 °C. The reaction mixture was stirred at 0 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **11e**.

Yield: 93.0 mg (64%); yellow oil.

IR (diamond-ATR, neat): 2954, 1756, 1720, 1586, 1434, 1409, 1290, 1232, 1086, 1048, 916, 832, 784, 768, 740 cm^{-1}.^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.81 (d, *J* = 9.8 Hz, 1 H), 7.53 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1 H), 7.48–7.39 (m, 2 H), 6.41 (d, *J* = 9.8 Hz, 1 H), 3.69 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 184.6, 163.3, 163.1, 158.3, 142.7, 134.9, 134.3, 132.9, 132.4, 131.5, 127.4, 115.8, 109.7, 52.9.

MS (EI, 70 eV): *m*/*z* (%) = 292 (8), 250 (10), 203 (40), 153 (33), 140 (27), 139 (100), 111 (25), 85 (17), 75 (17).

HRMS (EI): *m*/*z* calcd for $C_{14}H_9ClO_5$: 292.0139; found: 292.0132.

Methyl 6-(Cyclopropanecarbonyl)-2-oxo-2*H*-pyran-5-carboxylate (11f)

According to TP2, methyl coumalate (**3**, 72.0 mg, 0.50 mmol) was completely metalated within 15 min at –78 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −78 °C. Acylation was achieved with cyclopropanecarbonyl chloride (50 μL, 0.60 mmol, 1.20 equiv) at −78 °C and warming to −15 °C. The reaction mixture was stirred at 0 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **11f**.

Yield: 44.0 mg (40%); yellow oil.

IR (diamond-ATR, neat): 2957, 1758, 1727, 1697, 1629, 1440, 1385, 1317, 1199, 1090, 977, 770 cm^{-1}.^1H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 9.8 Hz, 1 H), 6.43 (d, *J* = 9.7 Hz, 1 H), 3.83 (s, 3 H), 2.45 (tt, *J* = 8.3, 4.5 Hz, 1 H), 1.32 (p, *J* = 4.0 Hz, 2 H), 1.19 (dq, *J* = 7.8, 3.8 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.1, 164.0, 160.5, 158.5, 142.4, 117.2, 110.3, 53.1, 19.8, 13.9.

MS (EI, 70 eV): *m*/*z* (%) = 222 (2), 163 (6), 153 (100), 123 (10), 85 (68), 69 (98).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}O_5$: 222.0528; found: 222.0521.

Reactions of Zincated 3,5-Dibromo-2*H*-pyran-2-one (4) with Electrophiles

3,5-Dibromo-6-iodo-2*H*-pyran-2-one (13a)

According to TP2, 3,5-dibromo-2*H*-pyran-2-one (**4**, 126 mg, 0.50 mmol) was completely metalated within 1.5 h at −10 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). I_2 (153 mg, 0.60 mmol, 1.20 equiv) was then added at −10 °C. The reaction mixture was warmed to 25 °C and was stirred until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 9:1) furnishing **13a**.

Yield: 120 mg (64%); yellow-brown solid; mp 97–99 °C.

IR (diamond-ATR, neat): 2921, 2853, 1715, 1574, 1486, 1207, 1055, 983, 902, 885, 733 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.03 (s, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 157.1, 146.7, 118.1, 111.6, 111.1.

MS (EI, 70 eV): *m*/*z* (%) = 379 (45), 338 (24), 255 (47), 253 (100), 251 (51), 227 (25), 224 (49), 223 (26), 199 (26), 127 (12), 118 (20), 116 (21), 53 (6).

HRMS (EI): *m*/*z* calcd for $C_5HBr_2IO_2$: 377.7388; found: 377.7382.

3,5-Dibromo-6-(2-chloropyridin-3-yl)-2*H*-pyran-2-one (13b)

According to TP2, 3,5-dibromo-2*H*-pyran-2-one (**4**, 126 mg, 0.50 mmol) was completely metalated within 1.5 h at −10 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent reacted in a Negishi cross-coupling reaction in the presence of $Pd(dba)_2$ (11.0 mg, 8 mol%), $P(2\text{-furyl})_3$ (9.00 mg, 15 mol%) and 2-chloro-3-iodopyridine (143 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **13b**.

Yield: 100 mg (60%); yellow oil.

IR (diamond-ATR, neat): 2922, 2853, 1737, 1716, 1602, 1492, 1409, 1248, 1177, 1055, 1026, 913, 902, 845, 741, 733 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.62 (dd, *J* = 4.8, 1.9 Hz, 1 H), 8.26 (s, 1 H), 8.16 (dd, *J* = 7.6, 1.9 Hz, 1 H), 7.65 (dd, *J* = 7.6, 4.8 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 157.2, 154.9, 153.0, 149.9, 148.4, 141.6, 128.7, 124.0, 113.1, 101.6.

MS (EI, 70 eV): *m*/*z* (%) = 365 (100), 363 (38), 339 (42), 337 (75), 335 (28), 286 (20), 232 (14), 229 (78), 228 (58), 197 (13), 149 (14), 142 (17), 140 (60), 114 (17), 112 (40), 76 (21), 50 (11), 44 (18), 43 (11).

HRMS (EI): *m*/*z* calcd for $C_{10}H_4Br_2ClNO_2$: 362.8297; found: 362.8296.

3,5-Dibromo-6-(cyclohex-2-en-1-yl)-2*H*-pyran-2-one (13c)

According to TP2, 3,5-dibromo-2*H*-pyran-2-one (**4**, 126 mg, 0.50 mmol) was completely metalated within 1.5 h at −10 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −40 °C. A subsequent allylation reaction was performed in the presence of 3-bromocyclohex-1-ene (70 μL, 0.60 mmol, 1.20 equiv) at −40 °C. The reaction mixture was stirred at 25 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **13c**.

Yield: 100 mg (60%); yellow oil.

IR (diamond-ATR, neat): 2927, 2834, 1719, 1608, 1532, 1287, 1134, 1033, 986, 959, 902, 867, 740, 716 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.02 (s, 1 H), 6.00–5.86 (m, 1 H), 5.65–5.56 (m, 1 H), 3.78 (ddp, *J* = 8.5, 5.7, 2.6 Hz, 1 H), 2.09 (ddd, *J* = 11.4, 5.7, 2.8 Hz, 2 H), 1.99 (dtd, *J* = 11.3, 5.7, 2.7 Hz, 1 H), 1.90 (dtt, *J* = 12.1, 5.5, 2.2 Hz, 1 H), 1.82–1.72 (m, 1 H), 1.71–1.58 (m, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 164.8, 157.9, 148.8, 131.0, 125.0, 109.9, 97.9, 40.5, 26.8, 25.0, 21.8.

MS (EI, 70 eV): *m*/*z* (%) = 334 (38), 332 (20), 305 (12), 280 (16), 255 (11), 254 (57), 253 (57), 251 (12), 224 (13), 197 (14), 146 (25), 117 (10), 81 (100), 80 (15), 79 (33), 77 (17), 53 (22), 51 (10), 41 (21).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}Br_2O_2$: 331.9048; found: 331.9033.

3,5-Dibromo-6-(thiophene-2-carbonyl)-2*H*-pyran-2-one (13d)

According to TP2, 3,5-dibromo-2*H*-pyran-2-one (**4**, 126 mg, 0.50 mmol) was completely metalated within 1.5 h at −10 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −40 °C. Acylation was achieved with thiophene-2-carbonyl chloride (60 μL, 0.60 mmol, 1.20 equiv) at −40 °C and warming to −10 °C. The reaction mixture was stirred at −15 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **13d**.

Yield: 100 mg (55%); yellow oil.

IR (diamond-ATR, neat): 2922, 2858, 1731, 1638, 1510, 1409, 1354, 1289, 1240, 1062, 1028, 933, 902, 823, 735 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.25 (d, *J* = 1.0 Hz, 1 H), 8.20–8.15 (m, 2 H), 7.34 (ddd, *J* = 4.9, 3.9, 1.0 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 177.6, 155.8, 152.2, 148.9, 141.5, 138.7, 138.3, 130.0, 116.0, 100.7.

MS (EI, 70 eV): *m*/*z* (%) = 364 (12), 285 (5), 283 (4), 112 (6), 111 (100), 83 (5).

HRMS (EI): *m*/*z* calcd for $C_9H_8O_3$: 361.8248; found: 361.8240.

6-Benzoyl-3,5-dibromo-2H-pyran-2-one (13e)

According to TP2, 3,5-dibromo-2*H*-pyran-2-one (**4**, 126 mg, 0.50 mmol) was completely metalated within 15 min at −10 °C, using TMPZnCl·LiCl (**6**, 0.63 mL, 0.95 M in THF, 0.60 mmol, 1.20 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −40 °C. Acylation was achieved with benzoyl chloride (70 μL, 0.60 mmol, 1.20 equiv) at −40 °C and warming to −10 °C. The reaction mixture was stirred at −10 °C until completion of the reaction. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **13e**.

Yield: 94.0 mg (53%); yellow oil.

IR (diamond-ATR, neat): 2923, 1741, 1668, 1594, 1448, 1272, 1226, 1040, 949, 798, 725, 681 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.23 (s, 1 H), 8.10–8.04 (m, 2 H), 7.80–7.74 (m, 1 H), 7.65–7.59 (m, 2 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 186.5, 156.0, 153.0, 148.4, 135.8, 135.0, 130.9, 130.0, 115.5, 100.1.

MS (EI, 70 eV): *m*/*z* (%) = 360 (5), 359 (9), 355 (5), 106 (6), 105 (100), 77 (28), 50 (2).

HRMS (EI): *m*/*z* calcd for $C_{12}H_6Br_2O_3$: 355.8684; found: 355.8678.

Further Functionalization of the 6-Substituted 2-Pyrones

5-Iodo-6-(methylthio)-2*H*-pyran-2-one (15)

According to TP4, 6-(methylthio)-2*H*-pyran-2-one (**9c**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 1 h at –40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). I_2 (152 mg, 0.60 mmol, 1.20 equiv) was then added at –40 °C. The reaction mixture was warmed to 25 °C and was stirred until completion of the reaction. The crude product was purified by column chromatography (silica gel, *i*-hexane/Et_2O, 4:6) furnishing **15**.

Yield: 58.0 mg (43%); yellow oil.

IR (diamond-ATR, neat): 2927, 2868, 1708, 1590, 1492, 1325, 1237, 1107, 967, 744 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.01 (d, *J* = 7.4 Hz, 1 H), 6.11 (d, *J* = 7.4 Hz, 1 H), 2.56 (s, 3 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 166.7, 158.9, 153.6, 104.3, 77.5, 14.0.

MS (EI, 70 eV): *m*/*z* (%) = 267 (64), 39 (13), 220 (100), 192 (17), 85 (13), 55 (10), 44 (11), 43 (10).

HRMS (EI): *m*/*z* calcd for $C_6H_5IO_2S$: 267.9055; found: 267.9063.

3-Iodo-6-(4-methoxyphenyl)-2*H*-pyran-2-one (17a)

According to TP4, 2-pyrone **9e** (1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 1 h at –40 °C, using TMPMgCl·LiCl (**5**, 0.54 mL, 1.10 M in THF, 0.60 mmol, 1.20 equiv). I_2 (152 mg, 0.60 mmol, 1.20 equiv) was then added at –40 °C. The reaction mixture was warmed to 25 °C and was stirred until completion of the reaction. The crude product was purified by column chromatography (silica gel, *i*-hexane/Et_2O, 4:6) furnishing **17a**.

Yield: 162 mg (99%); yellow-orange oil.

IR (diamond-ATR, neat): 2924, 1708, 1598, 1504, 1458, 1257, 1176, 1107, 1024, 837 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.19 (d, *J* = 7.4 Hz, 1 H), 7.89–7.84 (m, 2 H), 7.10–7.05 (m, 2 H), 6.68 (d, *J* = 7.4 Hz, 1 H), 3.89 (s, 3 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 163.2, 162.4, 159.0, 154.3, 128.2, 124.3, 115.4, 102.2, 81.4, 55.9.

MS (EI, 70 eV): *m*/*z* (%) = 327 (61), 299 (21), 201 (10), 146 (11), 145 (100), 135 (19), 130 (10), 102 (23), 92 (10), 77 (11), 76 (8), 63 (9).

HRMS (EI): *m*/*z* calcd for $C_{12}H_9IO_3$: 327.9600; found: 327.9585.

3-[Hydroxy(phenyl)methyl]-6-(4-methoxyphenyl)-2*H*-pyran-2-one (17b)

According to TP4, 2-pyrone **9e** (1.00 mL, 0.25 M in THF, 0.25 mmol) was completely metalated within 1 h at –40 °C, using TMPMgCl·LiCl (**5**, 0.27 mL, 1.10 M in THF, 0.30 mmol, 1.20 equiv). Benzaldehyde (30 μL, 0.30 mmol, 1.20 equiv) was then added at –40 °C. The reaction mixture was warmed to 25 °C and was stirred until completion of the reaction. The crude product was purified by column chromatography (silica gel, *i*-hexane/EtOAc, 8:2) furnishing **17b**.

Yield: 69.0 mg (45%); yellow oil.

IR (diamond-ATR, neat): 2838, 1697, 1694, 1605, 1554, 1510, 1257, 1175, 1026, 806, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.64 (m, 2 H), 7.39 (d, *J* = 7.3 Hz, 2 H), 7.34–7.29 (m, 2 H), 7.25 (dd, *J* = 8.3, 6.1 Hz, 1 H), 7.20–7.14 (m, 1 H), 6.88 (d, *J* = 9.0 Hz, 2 H), 6.47 (d, *J* = 7.1 Hz, 1 H), 5.74 (s, 1 H), 3.79 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.6, 161.9, 160.1, 140.8, 140.0, 128.7, 128.2, 127.4, 127.4, 126.8, 123.7, 114.5, 100.0, 72.1, 55.6.

MS (EI, 70 eV): *m*/*z* (%) = 308 (100), 292 (15), 291 (11), 279 (18), 264 (15), 263 (39), 262 (24), 231 (30), 204 (10), 203 (71), 202 (11), 145 (13), 135 (66), 107 (10), 105 (30), 79 (14).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{16}O_4$: 308.1049; found: 308.1043.

Reaction of Zincated 4-Pyrone (2) with Electrophiles

2-(4-Chlorophenyl)-4*H*-pyran-4-one (19a)

According to TP5, 4*H*-pyran-4-one (**2**, 1.00 mL, 0.5 M in THF, 0.50 mmol) was completely metalated within 2 h at −35 °C, using $TMP_2Zn·2MgCl_2·2LiCl$ (**7**, 0.55 mL, 0.55 M in THF, 0.30 mmol, 0.60 equiv). The zinc reagent reacted in a Negishi cross-coupling reaction in the presence of $Pd(dba)_2$ (11.0 mg, 8 mol%), $P(2\text{-furyl})_3$ (9.00 mg, 15 mol%), and 1-chloro-4-iodobenzene (114 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **19a**.

Yield: 52.0 mg (50%); yellow solid; mp 124–126 °C.

IR (diamond-ATR, neat): 2914, 1649, 1539, 1424, 1363, 1201, 1092, 1055, 1029, 836, 798, 720 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 8.11 (d, *J* = 6.1 Hz, 1 H), 7.96–7.88 (m, 2 H), 7.61–7.54 (m, 2 H), 6.81 (d, *J* = 2.4 Hz, 1 H), 6.29 (dd, *J* = 5.9, 2.4 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 178.4, 163.0, 156.4, 137.6, 131.2, 130.1, 128.3, 117.5, 113.1.

MS (EI, 70 eV): *m*/*z* (%) = 206 (97), 205 (68), 138 (33), 101 (14), 89 (8).

HRMS (EI): *m*/*z* calcd for $C_{11}H_7ClO_2$: 206.0135; found: 206.0123.

2-(Pyridin-3-yl)-4*H*-pyran-4-one (19b)

According to TP5, 4*H*-pyran-4-one (**2**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 2 h at −35 °C, using $TMP_2Zn·2MgCl_2·2LiCl$ (**7**, 0.55 mL, 0.55 M in THF, 0.30 mmol, 0.60 equiv). The zinc reagent underwent a Negishi cross-coupling reaction in the presence of $Pd(dba)_2$ (11.0 mg, 8 mol%), $P(2\text{-furyl})_3$ (9.00 mg, 15 mol%) and 3-iodopyridine (60.0 mg, 0.60 mmol, 1.20 equiv) at 25 °C for 12 h. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **19c**.

Yield: 74 mg (86%); brown solid; mp 115–116 °C.

IR (diamond-ATR, neat): 2924, 1647, 1425, 1368, 1251, 1200, 1125, 1058, 1012, 932, 831, 703 cm^{-1}.^{1}H NMR (400 MHz, acetone-d_6): δ = 9.09 (dd, *J* = 2.4, 0.9 Hz, 1 H), 8.74 (dd, *J* = 4.8, 1.6 Hz, 1 H), 8.26 (ddd, *J* = 8.1, 2.4, 1.6 Hz, 1 H), 8.15 (dd, *J* = 5.9, 0.3 Hz, 1 H), 7.56 (ddd, *J* = 8.1, 4.8, 0.9 Hz, 1 H), 6.89 (d, *J* = 2.5 Hz, 1 H), 6.32 (dd, *J* = 5.9, 2.4 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 178.3, 162.2, 156.6, 152.8, 147.9, 134.0, 128.4, 124.6, 117.7, 113.8.

MS (EI, 70 eV): *m*/*z* (%) = 173 (100), 174 (12), 145 (59), 116 (10), 106 (14), 103 (35), 78 (11), 76 (15), 51 (7), 50 (11).

HRMS (EI): *m*/*z* calcd for $C_{10}H_7NO_2$: 173.0477; found: 173.0476.

2-(Thiophene-2-carbonyl)-4*H*-pyran-4-one (19c)

According to TP5, 4*H*-pyran-4-one (**2**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 2 h at −35 °C, using $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**7**, 0.55 mL, 0.55 M in THF, 0.30 mmol, 0.60 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −35 °C. Acylation was achieved with thiophene-2-carbonyl chloride (60 μL, 0.60 mmol, 1.20 equiv) at −35 °C and warming to −5 °C. The reaction mixture was stirred at −5 °C until completion of the reaction. The crude product was purified by flash column chromatography. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **19c**.

Yield: 73.0 mg (71%); yellow-orange solid; mp 128–131 °C.

IR (diamond-ATR, neat): 3077, 1634, 1409, 1376, 1352, 1279, 1201, 1109, 1057, 940, 833, 798, 720 cm^{-1}.^1H NMR (400 MHz, acetone-d_6): δ = 8.28 (dd, *J* = 3.9, 1.1 Hz, 1 H), 8.24 (dd, *J* = 5.9, 0.3 Hz, 1 H), 8.14 (dd, *J* = 5.0, 1.1 Hz, 1 H), 7.34 (dd, *J* = 5.0, 3.9 Hz, 1 H), 6.89 (dd, *J* = 2.6, 0.3 Hz, 1 H), 6.46 (dd, *J* = 5.9, 2.6 Hz, 1 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 178.2, 178.2, 159.7, 156.5, 141.2, 138.1, 137.4, 129.9, 119.0, 118.7.

MS (EI, 70 eV): *m*/*z* (%) = 206 (31), 178 (22), 110 (100), 82 (7).

HRMS (EI): *m*/*z* calcd for $C_{10}H_6O_3S$: 206.0038; found: 206.0037.

2-(Cyclopropanecarbonyl)-4*H*-pyran-4-one (19d)

According to TP5, 4*H*-pyran-4-one (**2**, 1.00 mL, 0.50 M in THF, 0.50 mmol) was completely metalated within 2 h at −35 °C, using $TMP_2Zn{\cdot}2MgCl_2{\cdot}2LiCl$ (**7**, 0.54 mL, 0.55 M in THF, 0.30 mmol, 0.60 equiv). The zinc reagent was treated with CuCN·2LiCl (0.60 mL, 1.00 M in THF, 0.60 mmol, 1.20 equiv) for 30 min at −35 °C. Acylation was achieved with cyclopropanecarbonyl chloride (50 μL, 0.60 mmol, 1.20 equiv) at −35 °C and warming to −5 °C. The reaction mixture was stirred at −5 °C until completion of the reaction. The crude product was purified by flash column chromatography. The crude product was purified by flash column chromatography (silica gel, *i*-hexane/EtOAc, 7:3) furnishing **19d**.

Yield: 41.0 mg (50%); yellow-brown solid; mp 75–77 °C.

IR (diamond-ATR, neat): 3078, 1648, 1410, 1367, 1244, 1197, 1178, 1103, 1056, 997, 834, 720 cm^{-1}.^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 5.8 Hz, 1 H), 6.98 (d, *J* = 2.6 Hz, 1 H), 6.44 (dd, *J* = 5.8, 2.6 Hz, 1 H), 2.66 (ddd, *J* = 12.4, 7.8, 4.5 Hz, 1 H), 1.32–1.26 (m, 2 H), 1.16 (dq, *J* = 7.6, 4.2, 3.7 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.1, 179.0, 157.9, 154.9, 118.8, 116.8, 17.0, 13.8.

MS (EI, 70 eV): *m*/*z* (%) = 164 (53), 123 (8), 69 (100), 41 (27).

HRMS (EI): *m*/*z* calcd for $C_9H_8O_3$: 164.0473; found: 164.0465.

Single-Crystal X-ray Diffraction Studies

Single crystals of compound **9a** and **13a**, suitable for X-ray diffraction, were obtained by slow evaporation of dichloromethane solutions. The crystals were introduced into perfluorinated oil and a suitable single crystal was carefully mounted on the top of a thin glass wire. Data collection was performed with an Oxford Xcalibur 3 diffractometer equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector, operating with Mo-Kα radiation (λ = 0.71071 Å). Data collection was performed with the CrysAlis CCD software;[14a] CrysAlis RED software[14b] was used for data reduction. Absorption correction using the SCALE3 ABSPACK multiscan method[14c] was applied. The structures were solved with SHELXS-97,[14d] refined with SHELXL-97,[14e] and finally checked using PLATON.[14f] CCDC-1847973 and CCDC-1851127 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

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Supporting Information

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