Direct Addition of Functionalized Organozinc Reagents to Carbon Dioxide, Ketones, and Aldehydes in the Presence of $MgCl_2$

Sebastian Bernhardt, Albrecht Metzger, Paul Knochel*

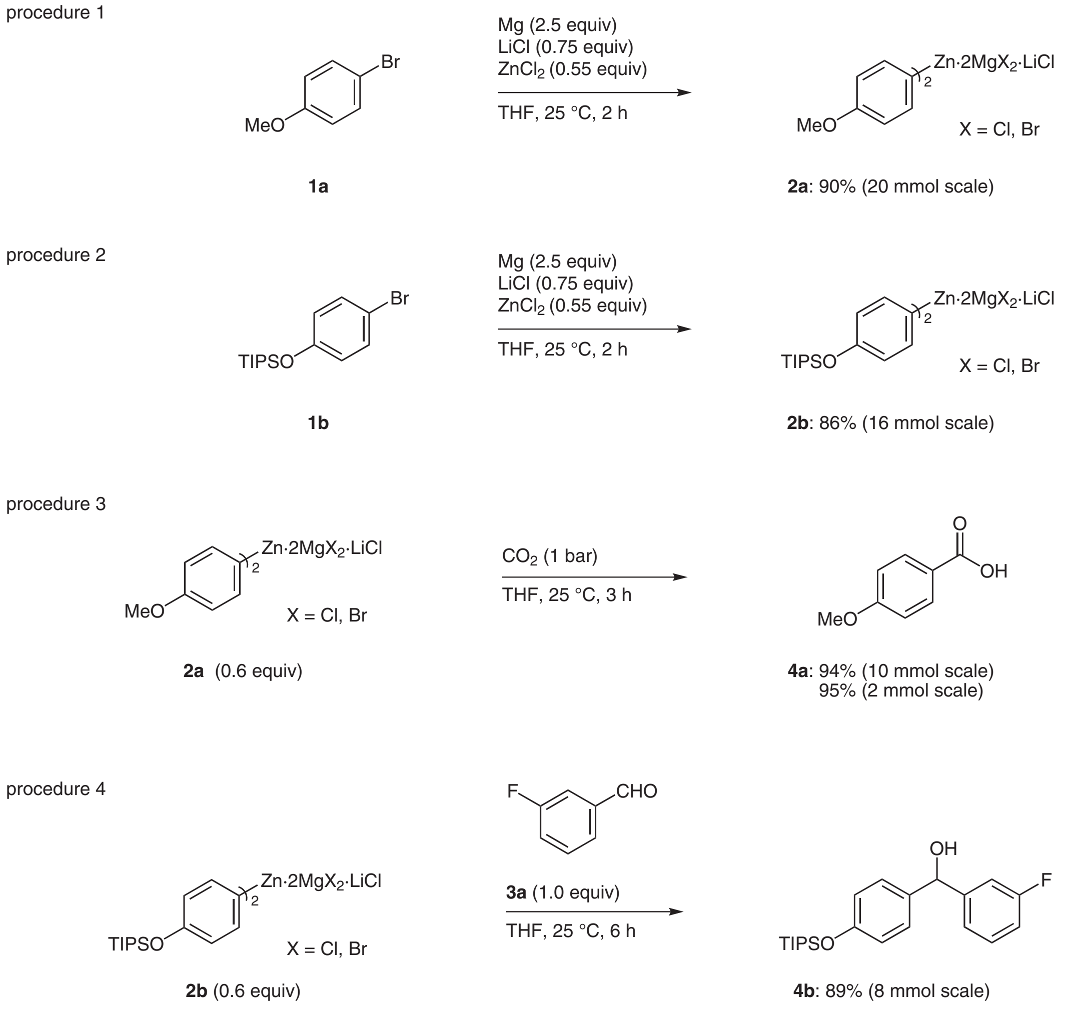
Ludwigs-Maximilians-Universität München, Department Chemie, Butenandtstraße 5-13, Haus F,
81377 München, Germany
Fax +49(89)218077680; E-mail: Paul.Knochel@cup.uni-muenchen.de

Received 22 September 2010; revised 6 October 2010

PSP No 196

Abstract: A variety of functionalized organozinc reagents undergo smooth addition reactions at ambient temperature to carbon dioxide, ketones, and aldehydes in the presence of stoichiometric amounts of $MgCl_2$. Several reactions were performed on a 20 mmol scale.

Key words: organozinc reagents, magnesium chloride, carbon dioxide, phenylacetic acid derivatives, addition reactions



Scheme 1 Typical procedures for the preparation of organozinc reagents by direct magnesium insertion into the corresponding organic halides in the presence of LiCl and $ZnCl_2$ (procedures 1 and 2) and their addition reactions to carbon dioxide (procedure 3) or aldehydes (procedure 4) at room temperature.

SYNTHESIS 2010, No. 22, pp 3802–3810
Advanced online publication: 22.10.2010
DOI: 10.1055/s-0030-1258314; Art ID: T19210SS

Introduction

The addition reactions of organometallic reagents to ketones, aldehydes, and carbon dioxide are essential transformations in organic synthesis as they provide a convenient access to various types of alcohols or carboxylic acids.[1] Among the different classes of organometallic reagents, organozincs display a high functional group tolerance.[2] Their moderate reactivity towards various electrophiles can be dramatically increased in the presence of catalytic amounts of transition metal salts.[3] Alternatively, it would be more economical to use inexpensive main-group metal centered Lewis acids for the activation of carbonyl functions towards the addition reaction of zinc reagents. Recently, we reported the preparation of functionalized aryl-,[4] benzyl-[5] and alkylzinc[6] reagents by the direct magnesium insertion into the corresponding halides in the presence of LiCl and $ZnCl_2$. Furthermore, we have shown that these zinc reagents undergo smooth addition reactions to various carbonyl derivatives and carbon dioxide at room temperatures without the use of polar cosolvents.[7] The increased reactivity of these organozincs can be assigned to the presence of stoichiometric amounts of the Lewis acid $MgCl_2$, which is usually formed during the preparation of the reagent.[4–6] Herein, we wish to report typical practical procedures illustrating these methods and their scale-up.

Scope and Limitations

The organozinc reagents were accessible under mild conditions starting from the corresponding aryl and alkyl bromides or benzyl chlorides. Thus, bis(4-methoxyphenyl)zinc·$2MgX_2$ (**2a**; X = Cl, Br) was prepared on a 20 mmol scale from 4-bromoanisole (**1a**) by oxidative addition of 2.5 equivalents of magnesium turnings in the presence of 0.5 equivalent of $ZnCl_2$ and 1.5 equivalents of LiCl in 90% yield (procedure 1 of Scheme 1). The reaction proceeds smoothly in two hours at room temperature. In an analogous manner bis(4-TIPSO-phenyl)zinc·$2MgX_2$ (**2b**) was prepared from (4-bromophenoxy)(triisopropyl)silane (**1b**) in 86% yield on a 16 mmol scale (procedure 2). Bis(4-methoxyphenyl)zinc·$2MgX_2$ (**2a**; X = Cl, Br) added to carbon dioxide at 25 °C in THF and the corresponding benzoic acid **4a** was obtained within three hours in 94% yield on a 10 mmol scale (procedure 3 of Scheme 1). Furthermore, the reaction of bis(4-TIPSO-phenyl)zinc·$2MgX_2$ (**2b**) with 3-fluorobenzaldehyde (**3a**) led to the secondary alcohol **4b** in 89% on a 8 mmol scale (procedure 4 of Scheme 1). Remarkably, both aryl groups were transferred in this addition reaction. Similarly, bis(4-methoxyphenyl)zinc·$2MgX_2$ (**2a**) added within one hour to 4-cyanoacetophenone (**3b**) and the desired alcohol **4c** was isolated in 62% yield (Table 1, entry 1). In an analogous manner, substituted diarylzinc reagents **2c** and **2d** reacted with functionalized benzaldehydes **3c**,**d** providing the corresponding alcohols **4d** and **4e** in 85–95% yield (entries 2 and 3). Furthermore, a direct addition of bis(4-chlorophenyl)zinc·$2MgX_2$ (**2d**) to 4-fluorobenzoyl chloride (**3e**) furnished the benzophenone derivative **4f** within 12 hours at 25 °C (81% yield; entry 4) without the need of using stoichiometric amounts of copper(I) salts. Moreover, heteroarylzinc reagents underwent addition reactions to benzaldehydes. Thus, the bis(5-pyrazolyl)zinc·$2MgX_2$ (**2e**) as well as the bis(1,2-oxazol-4-yl)zinc·$2MgX_2$ (**2f**) added to aldehydes **3f** and **3g** providing the secondary alcohols **4g** and **4h** in 76–80% yield (entries 5 and 6). Bis(hexylzinc)·$2MgX_2$ (**2g**) was successfully used for the addition to 3-chlorobenzaldehyde (**3f**) and the desired secondary alcohol **4i** was obtained after 14 hours in 87% yield (entry 7). Bis-benzylic zinc reagents of type **2** [$(ArCH_2)_2Zn{\cdot}2MgCl_2$] as well as benzylic zinc chlorides of type **5** ($ArCH_2ZnCl{\cdot}MgCl_2$) can also be used for efficient addition reactions. Thus, the electron-poor bis[3-(ethoxycarbonyl)benzyl]zinc·$2MgCl_2$ (**2h**) and the electron-rich bis(3-methoxybenzyl)zinc·$2MgCl_2$ (**2i**) were used for the addition reactions to various ketones **3h**,**i** and the desired alcohols **4j**,**k** were isolated in 68 and 84% yield, respectively (entries 8 and 9). Furthermore, 4-methoxybenzylzinc chloride·$MgCl_2$ (**5a**) added to 4-*N*,*N*-dimethylaminobenzaldehyde (**3j**) within one hour and the alcohol **4l** was obtained in 99% yield on a 10 mmol scale (entry 10). Moreover, the reaction of 4-fluorobenzylzinc chloride·$MgCl_2$ (**5b**) with the acetophenone **3b** and the benzophenone **3k** led to the tertiary alcohols **4m**,**n** in 80 and 78% yield, respectively (entries 11 and 12).

Remarkably, these new zinc reagents reacted with carbon dioxide without the need of a polar cosolvent and transition metal catalysis. Thus, bis(benzylzinc)·$2MgCl_2$ (**2j**) and bis[3-methoxybenzyl]zinc·$2MgCl_2$ (**2i**) were readily converted to the phenylacetic acids **4o** and **4p** at ambient temperature in 76 and 98% yield, respectively (Table 2, entries 1 and 2). Furthermore, the 2-chloro-substituted bis-benzylzinc reagent **2k** was treated with carbon dioxide and the functionalized phenylacetic acid derivative **4q** was obtained in 80% yield (entry 3) on a 10 mmol scale. Finally, bis(hexylzinc)·$2MgX_2$ (**2g**) smoothly led to heptanoic acid (**4r**) after reaction with CO_2 for 12 hours.

In summary, efficient addition reactions of functionalized organozinc reagents to various carbonyl derivatives in the presence of $MgCl_2$ were demonstrated. We have extended our previous work and have reported herein readily scalable experimental procedures (10–20 mmol scale). These reactions can be performed with standard laboratory glassware and do not require the use of expensive chemicals. Further studies are currently underway in our laboratories to extend this method.

Table 1 Addition Reactions of Functionalized Organozinc Reagents to Various Carbonyl Derivatives at 25 °C

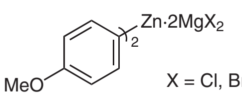
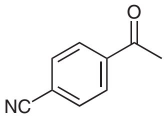
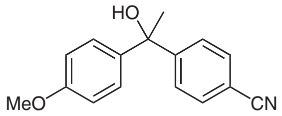
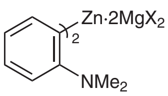
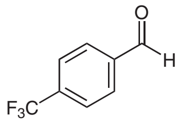
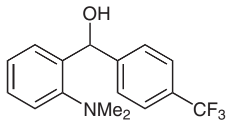
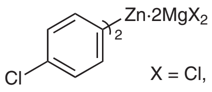
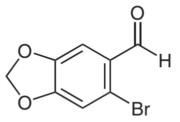
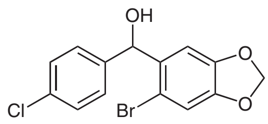
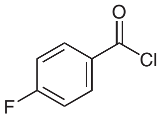
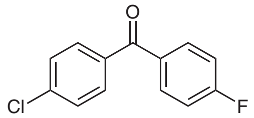
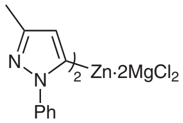
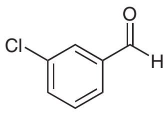
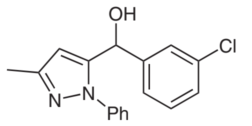
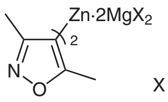
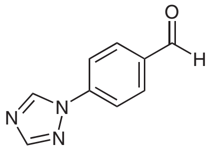
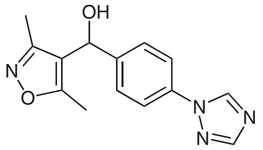
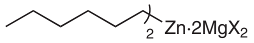
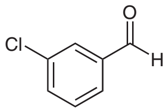
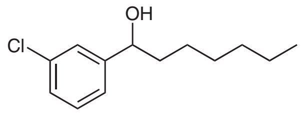
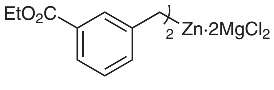
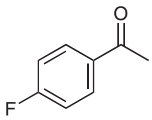
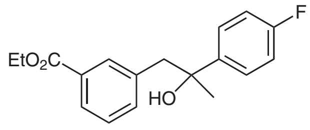
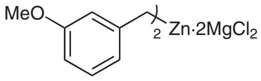
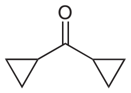
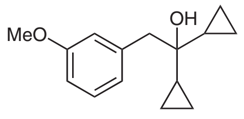
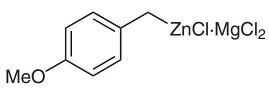
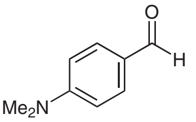
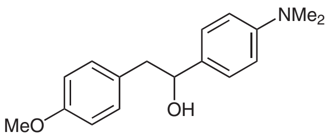
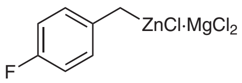
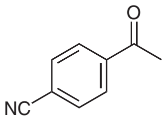
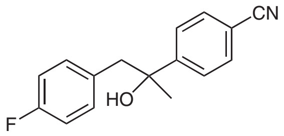
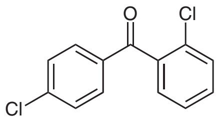
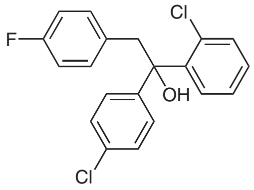
Entry	Zinc reagent[a]	Electrophile	Time (h)[b]	Product	Yield (%)[c]
1	 X = Cl, Br **2a** (0.6 equiv)	 **3b** (1.0 equiv)	1	 **4c**	62
2	 X = Cl, Br **2c** (0.6 equiv)	 **3c** (1.0 equiv)	3	 **4d**	93
3	 X = Cl, Br **2d** (0.6 equiv)	 **3d** (1.0 equiv)	10	 **4e**	95% (10 mmol scale) 85% (1.5 mmol scale)
4	**2d** (0.6 equiv)	 **3e** (1.0 equiv)	12	 **4f**	81
5	 **2e** (0.6 equiv)	 **3f** (1.0 equiv)	6	 **4g**	80
6	 X = Cl, Br **2f** (0.6 equiv)	 **3g** (1.0 equiv)	14	 **4h**	76
7	 X = Cl, Br **2g** (0.6 equiv)	 **3f** (1.0 equiv)	14	 **4i**	87
8	 **2h** (1.2 equiv)	 **3h** (1.0 equiv)	24	 **4j**	68[d]
9	 **2i** (0.6 equiv)	 **3i** (1.0 equiv)	1	 **4k**	84

Table 1 Addition Reactions of Functionalized Organozinc Reagents to Various Carbonyl Derivatives at 25 °C (continued)

Entry	Zinc reagent[a]	Electrophile	Time (h)[b]	Product	Yield (%)[c]
10	 **5a** (1.2 equiv)	 **3j** (1.0 equiv)	1	 **4l**	99 (10 mmol scale)
11	 **5b** (1.2 equiv)	 **3b** (1.0 equiv)	15	 **4m**	80
12	**5b** (1.2 equiv)	 **3k** (1.0 equiv)	48	 **4n**	78

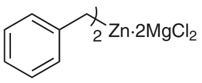
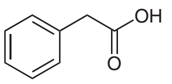
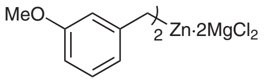
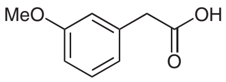
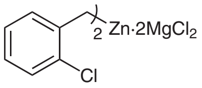
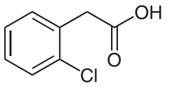
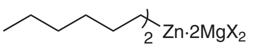
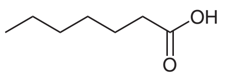
[a] Complexed LiCl is omitted for the sake of clarity.

[b] The reaction time for the addition reaction at 25 °C is given.

[c] Yield of isolated analytically pure product.

[d] The addition reaction was performed at 50 °C.

Table 2 Addition Reactions of Functionalized Organozinc Reagents to Carbon Dioxide at 25 °C

Entry	Zinc reagent[a]	Time (h)[b]	Product	Yield (%)[c]
1	 **2j**	2.5	 **4o**	76
2	 **2i**	25	 **4p**	98
3	 **2k**	12	 **4q**	80 (10 mmol scale)[d]
4	 X = Cl, Br **2g**	12	 **4r**	86[d]

[a] Complexed LiCl is omitted for the sake of clarity.

[b] The reaction time for the addition reaction to carbon dioxide at 25 °C is given.

[c] Yield of isolated analytically pure product.

[d] The addition reaction was performed at 50 °C.

All reactions were carried out under argon atmosphere in dried glassware. All starting materials were purchased from commercial suppliers and used without further purification unless otherwise stated. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under N_2. Yields refer to isolated compounds estimated to be >95% pure as determined by ^{1}H NMR spectroscopy and capillary GC analyses.

Mixed $ZnCl_2$/LiCl Solution

$ZnCl_2$/LiCl solution (1.1/1.5 M in THF) was prepared by drying $ZnCl_2$ (37.5 g, 275 mmol) and LiCl (15.9 g, 375 mmol) together in a Schlenk flask under high vacuum (1 mbar) at 150 °C for 5 h under vigorous stirring. After cooling to 25 °C, anhyd THF (250 mL) was added and stirring was continued until all salts were dissolved.

Bis(4-Methoxyphenyl)zinc (2a); Typical Procedure 1

A 50 mL Schlenk flask, equipped with a magnetic stirring bar and a septum, was flame-dried under high vacuum. Mg turnings (1.22 g, 50.0 mmol) were added followed by $ZnCl_2$/LiCl solution (10.0 mL, 11.0 mmol/15.0 mmol, 1.1/1.5 M in THF). Then, 4-bromoanisole (**1a**; 3.74 g, 20.0 mmol) was added dropwise as a solution in anhyd THF (13.0 mL) using a water bath to keep the temperature below 30 °C. The reaction mixture was stirred for 2 h (GC analysis of a reaction aliquot quenched with sat. aq NH_4Cl showed complete conversion). Then, the supernatant solution was carefully cannulated to a new dry and argon-flushed 50 mL Schlenk flask through a syringe filter. Iodometric titration of the zinc reagent **2a** indicated a concentration of 0.39 M, corresponding to a yield of 90%.[8]

Bis(4-TIPSO-phenyl)zinc (2b); Typical Procedure 2

A 50 mL Schlenk flask, equipped with a magnetic stirring bar and a septum, was flame-dried under high vacuum. Mg turnings (1.03 g, 42.5 mmol) were added followed by $ZnCl_2$/LiCl solution (7.9 mL, 8.7 mmol/11.9 mmol, 1.1/1.5 M in THF). Then, (4-bromophenoxy)(triisopropyl)silane (**1b**; 5.19 g, 15.8 mmol) was added dropwise as a solution in anhyd THF (23.0 mL) using a water bath to keep the temperature below 30 °C. The reaction mixture was stirred for 2 h (GC analysis of a reaction aliquot quenched with sat. aq NH_4Cl showed complete conversion). Then, the supernatant solution was carefully cannulated to a new dry and argon-flushed 50 mL Schlenk flask through a syringe filter. Iodometric titration of the zinc reagent **2b** indicated a concentration of 0.23 M, corresponding to a yield of 86%.[8]

4-Methoxybenzoic Acid (4a); Typical Procedure 3

A 50 mL Schlenk flask, equipped with a magnetic stirring bar and a septum, was flame-dried under high vacuum. After cooling to 25 °C, the flask was filled with gaseous CO_2 generated from dry ice and predried by streaming through a tube filled with solid $CaCl_2$. Then, bis(4-methoxyphenyl)zinc (**2a**; X = Cl, Br; 12.8 mL, 5.0 mmol, 0.39 M in THF) was added and dry CO_2 was bubbled through the reaction mixture for 5 min until a balloon attached to the reaction flask by a short length rubber tubing and a needle adapter was inflated. The reaction mixture was stirred for 3 h at 25 °C until the zinc reagent had been completely consumed (GC analysis of a reaction aliquot quenched with I_2 showed complete conversion). The reaction mixture was diluted with Et_2O (20 mL) and sat. aq $NaHCO_3$ (10 mL) was added. After filtration, the organic phase was separated and extracted with sat. aq $NaHCO_3$ (3 × 50 mL). The combined aqueous phases were carefully acidified with 5 M HCl until pH <5 and extracted with Et_2O (3 × 100 mL). The combined organic phases were dried (Na_2SO_4). Evaporation of the solvents in vacuo provided 4-methoxybenzoic acid (**4a**; 1.47 g, 94%) as a white solid; mp 185–186 °C.

IR (Diamond-ATR, neat): 2842 (w), 2542 (w), 1678 (vs), 1602 (s), 1426 (m), 1260 (vs), 1166 (s), 1024 (s), 924 (s), 844 (s), 772 (s), 614 cm^{-1} (s).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.59 (s, 1 H), 7.91–7.85 (m, 2 H), 7.03–6.96 (m, 2 H), 3.81 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.9, 162.8, 131.3, 122.9, 113.8, 55.4.

MS (EI, 70 eV): *m*/*z* (%) = 152 (M^+, 100), 135 (86), 107 (10), 92 (16), 77 (25), 63 (12).

HRMS: *m*/*z* calcd for $C_8H_8O_3$: 152.0473; found: 152.0468.

(3-Fluorophenyl){4-[(triisopropylsilyl)oxy]phenyl}methanol (4b); Typical Procedure 4

A 50 mL Schlenk flask, equipped with a magnetic stirring bar and a septum, was flame-dried under high vacuum. After cooling to 25 °C, 3-fluorobenzaldehyde (**3a**; 1.05 g, 8.44 mmol) was added and dissolved in THF (5 mL). Bis{4-[(triisopropylsilyl)oxy]phenyl}zinc·2MgX_2 (**2b**; X = Cl, Br; 22.2 mL, 5.1 mmol, 0.23 M in THF) was added dropwise over a period of 5 min and the reaction mixture was stirred for 6 h at 25 °C (GC-analysis of a reaction aliquot quenched with sat. aq NH_4Cl showed complete conversion). Then, the reaction mixture was cooled to 0 °C and quenched with sat. aq NH_4Cl (30 mL) and extracted with EtOAc (3 × 60 mL). The combined organic phases were dried ($MgSO_4$). Evaporation of the solvents in vacuo and purification by flash chromatography (silica gel, isohexane–Et_2O, 5:1) afforded the alcohol **4b** (2.81 g, 89%) as a colorless oil.

IR (Diamond-ATR, neat): 3329 (w), 2866 (m), 1606 (m), 1507 (vs), 1263 (vs), 1011 (w), 911 (s), 881 (vs), 762 (s), 712 (m), 681 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.24 (m, 1 H), 7.19–7.16 (m, 2 H), 7.12–7.07 (m, 2 H), 6.96–6.90 (m, 1 H), 6.86–6.81 (m, 2 H), 5.75 (br s, 1 H), 2.19 (br s, 1 H), 1.29–1.16 (m, 3 H), 1.09 (d, *J* = 7.1 Hz, 18 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.9 (d, $^1J_{C,F}$ = 246.0 Hz), 155.8, 146.6 (d, $^3J_{C,F}$ = 6.7 Hz), 135.8, 129.8 (d, $^3J_{C,F}$ = 8.1 Hz), 127.9, 122.0 (d, $^4J_{C,F}$ = 3.1 Hz), 119.9, 114.1 (d, $^2J_{C,F}$ = 21.3 Hz), 113.3 (d, $^2J_{C,F}$ = 22.2 Hz) 75.3, 18.1, 15.2.

MS (EI, 70 eV): *m*/*z* (%) = 374 (M^+, 29), 331 (100), 303 (22), 275 (26), 207 (12), 183 (14), 151 (20), 137 (25), 125 (28), 123 (18), 97 (30), 77 (12), 59 (10).

HRMS: *m*/*z* calcd for $C_{22}H_{31}FO_2Si$: 374.2077; found: 374.2076.

Preparation of the Zinc Reagents of Type 2

Bis[2-(dimethylamino)phenyl]zinc (2c)

According to TP1/2, (2-bromophenyl)dimethylamine (2.00 g, 10.0 mmol) in THF (6.7 mL) was treated with Mg turnings (608 mg, 25.0 mmol) in a THF solution (5.0 mL) of $ZnCl_2$ (5.5 mmol) and LiCl (7.5 mmol) at 25 °C for 2 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2c** indicated a concentration of 0.29 M.

Bis(4-chlorophenyl)zinc (2d)

According to TP1/2, 1-bromo-4-chlorobenzene (3.83 g, 20.0 mmol) in THF (4.0 mL) was treated with Mg turnings (1.22 g, 50.0 mmol) in a THF solution (10 mL) of $ZnCl_2$ (11.0 mmol) and LiCl (15.0 mmol) at 25 °C for 1.5 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2d** indicated a concentration of 0.71 M.

Bis(3-ethyl-1-phenyl-1*H*-pyrazol-5-yl)zinc (2e)

According to TP1/2, 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole (2.70 g, 14.0 mmol) in THF (9.3 mL) was treated with Mg turnings (851 mg, 34.9 mmol) in a THF solution (7 mL) of $ZnCl_2$ (7.7 mmol) and LiCl (10.5 mmol) at 25 °C for 4 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2e** indicated a concentration of 0.34 M.

Bis(3,5-dimethylisoxazol-4-yl)zinc (2f)
According to TP1/2, 4-bromo-3,5-dimethylisoxazole (3.52 g, 20.0 mmol) in THF (10.0 mL) was treated with Mg turnings (1.22 mg, 50.0 mmol) in a THF solution (10 mL) of $ZnCl_2$ (11.0 mmol) and LiCl (15.0 mmol) at 25 °C for 1 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2f** indicated a concentration of 0.20 M.

Bis(hexyl)zinc (2g)
According to TP1/2, hexyl bromide (3.30 g, 20.0 mmol) in THF (10.0 mL) was treated with Mg turnings (1.22 mg, 50.0 mmol) in a THF solution (10.0 mL) of $ZnCl_2$ (11.0 mmol) and LiCl (15.0 mmol) at 25 °C for 2 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2g** indicated a concentration of 0.31 M.

Bis(3-ethoxycarbonyl)benzylzinc (2h)
According to TP1/2, 3-(ethoxycarbonyl)benzyl chloride (2.71 g, 13.6 mmol) in THF (12 mL) was treated with Mg turnings (826 mg, 34.0 mmol) in a THF solution (6.80 mL) of $ZnCl_2$ (7.45 mmol) and LiCl (10.2 mmol) at 25 °C for 1.5 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2h** [premix of an aliquot with excess $ZnCl_2$ solution (1.00 M in THF)] indicated a concentration of 0.33 M.

Bis(3-methoxybenzyl)zinc (2i)
According to TP1/2, 3-methoxybenzyl chloride (2.35 g, 15.0 mmol) in THF (8.0 mL) was treated with Mg turnings (608 mg, 25.0 mmol) in a THF solution (7.5 mL) of $ZnCl_2$ (8.25 mmol) and LiCl (11.3 mmol) at 25 °C for 2 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2i** [premix of an aliquot with excess $ZnCl_2$ solution (1.00 M in THF)] indicated a concentration of 0.31 M.

Bis(benzyl)zinc (2j)
According to TP1/2, benzyl chloride (1.27 g, 10.0 mmol) in THF (2.0 mL) was treated with Mg turnings (608 mg, 25.0 mmol) in a THF solution (5.0 mL) of $ZnCl_2$ (5.5 mmol) and LiCl (7.5 mmol) at 25 °C for 1 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2j** [premix of an aliquot with excess $ZnCl_2$ solution (1.00 M in THF)] indicated a concentration of 0.42 M.

Bis(2-chlorobenzyl)zinc (2k)
According to TP1/2, 2-chlorobenzyl chloride (3.22 g, 20.0 mmol) in THF (5.0 mL) was treated with Mg turnings (1.22 g, 50.0 mmol) and a THF solution (10 mL) of $ZnCl_2$ (11.0 mmol) and LiCl (15.0 mmol) at 25 °C for 1 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **2k** [premix of an aliquot with excess $ZnCl_2$ (1.00 M in THF)] indicated a concentration of 0.54 M.

4-Methoxybenzylzinc Chloride (5a)
According to TP1/2, 4-methoxybenzyl chloride (1.10 g, 7.00 mmol) in THF (1.0 mL) was treated with Mg powder (425 mg, 17.5 mmol) in a THF solution (7.0 mL) of $ZnCl_2$ (7.7 mmol) and LiCl (10.5 mmol) at 25 °C for 2 h. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **5a** indicated a concentration of 0.72 M.

4-Fluorobenzylzinc Chloride (5b)
According to TP1/2, 4-fluorobenzyl chloride (2.17 g, 15.0 mmol) in THF (7.5 mL) was treated with Mg turnings (911 mg, 37.5 mmol) in a THF solution (15 mL) of $ZnCl_2$ (16.5 mmol) and LiCl (22.5 mmol) at 25 °C for 45 min. After subsequent cannulation to another argon-flushed Schlenk flask, iodometric titration of the zinc reagent **5b** indicated a concentration of 0.39 M.

Preparation of the Title Compounds of Type 4

4-[1-Hydroxy-1-(4-methoxyphenyl)ethyl]benzonitrile (4c)
According to TP4, bis(4-methoxyphenyl)zinc·$2MgX_2$ (**2a**; X = Cl, Br; 2.31 mL, 0.90 mmol, 0.39 M in THF) was added to 4-acetylbenzonitrile (**3b**; 218 mg, 1.50 mmol) in THF (0.5 mL) and the reaction mixture was stirred for 1 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et_2O, 9:1 + 1 vol% Et_3N) afforded the alcohol **4c** (236 mg, 62%) as a white solid; mp 77–79 °C.

IR (Diamond-ATR, neat): 3494 (m), 2231 (m), 1504 (s), 1448 (m), 1403 (m), 1245 (vs), 1194 (m), 1178 (s), 1028 (vs), 840 (s), 816 cm^{-1} (s).

^1H NMR (400 MHz, C_6D_6): δ = 7.13–7.07 (m, 4 H), 7.05–7.00 (m, 2 H), 6.76–6.70 (m, 2 H), 3.30 (s, 3 H), 1.70 (br s, 1 H), 1.50 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 159.3, 153.7, 139.5, 131.8, 127.4, 126.6, 118.9, 113.8, 111.0, 75.2, 54.8, 30.5.

MS (EI, 70 eV): m/z (%) = 253 (M^+, 12), 235 (100), 220 (27), 190 (9), 151 (8), 130 (21), 43 (5).

HRMS: m/z calcd for $C_{16}H_{15}NO_2$: 253.1103; found: 253.1094.

[2-(Dimethylamino)phenyl][4-(trifluoromethyl)phenyl]methanol (4d)
According to TP4, bis[2-(dimethylamino)phenyl]zinc·$2MgX_2$ (**2c**; X = Cl, Br; 3.00 mL, 0.90 mmol, 0.30 M in THF) was added to 4-(trifluoromethyl)benzaldehyde (**3c**; 261 mg, 1.5 mmol). The reaction mixture was stirred for 3 h at 25 °C. Purification by flash chromatography (silica gel, pentane–EtOAc, 8:1 + 1 vol% Et_3N) afforded the alcohol **4d** (413 mg, 93%) as a yellow oil.

IR (Diamond-ATR, neat): 2945 (w), 2833 (w), 1618 (w), 1489 (m), 1322 (vs), 1160 (s), 1110 (s), 1065 (s), 1016 (s), 936 (m), 859 (m), 768 cm^{-1} (m).

^1H NMR (400 MHz, DMSO-d_6): δ = 7.63 (d, J = 8.2 Hz, 2 H), 7.52 (d, J = 8.4 Hz, 2 H), 7.32–7.26 (m, 1 H), 7.24–7.18 (m, 2 H), 7.09–7.02 (m, 1 H), 6.27 (d, J = 4.3 Hz, 1 H), 6.01 (d, J = 4.9 Hz, 1 H), 2.61 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.6, 150.7 (q, $^4J_{C,F}$ = 1.5 Hz), 139.7, 128.0, 128.0, 127.0 (q, $^2J_{C,F}$ = 31.9 Hz), 126.8, 124.8 (q, $^3J_{C,F}$ = 3.8 Hz), 124.4 (q, $^1J_{C,F}$ = 271.7 Hz), 124.1, 120.3, 68.3, 45.4.

MS (EI, 70 eV): m/z (%) = 295 (M^+, 94), 280 (100), 276 (20), 262 (65), 242 (69), 173 (16), 145 (12), 106 (9), 91 (10), 77 (11).

HRMS: m/z calcd for $C_{16}H_{16}F_3NO$: 295.1184; found: 295.1178.

(6-Bromo-1,3-benzodioxol-5-yl)(4-chlorophenyl)methanol (4e)
According to TP4, bis(4-chlorophenyl)zinc·$2MgX_2$ (**2d**; X = Cl, Br; 6.00 mL, 0.90 mmol, 0.15 M in THF) was added to 6-bromo-1,3-benzodioxole-5-carbaldehyde (**3d**; 344 mg, 1.50 mmol) in THF (1.0 mL). The reaction mixture was stirred for 10 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et_2O, 6:1 + 1 vol% Et_3N) afforded the alcohol **4e** (438 mg, 85%) as pale yellow oil.

IR (Diamond-ATR, neat): 3316 (w), 2896 (w), 1471 (vs), 1407 (m), 1388 (m), 1231 (s), 1103 (m), 1035 (vs), 1013 (s), 931 (s), 845 (s), 780 cm^{-1} (m).

^1H NMR (400 MHz, acetone-d_6): δ = 7.44–7.38 (m, 2 H), 7.35–7.30 (m, 2 H), 7.12 (s, 1 H), 7.02 (s, 1 H), 6.07 (s, 1 H), 6.05 (d, J = 1.0 Hz, 1 H), 6.01 (d, J = 1.0 Hz, 1 H), 2.83 (br s, 1 H).

^{13}C NMR (100 MHz, acetone-d_6): δ = 148.8, 148.7, 143.7, 138.0, 133.2, 129.3, 129.0, 112.9, 112.7, 108.8, 103.0, 73.6.

MS (EI, 70 eV): m/z (%) = 342 (100), 340 (M^+, 76), 229 (48), 209 (13), 201 (10), 149 (14), 139 (50), 122 (35), 110 (10), 77 (18), 63 (8).

HRMS: m/z calcd for $C_{14}H_{10}BrClO_3$: 339.9502; found: 339.9504.

(4-Chlorophenyl)(4-fluorophenyl)methanone (4f)

According to TP4, bis(4-chlorophenyl)zinc·2MgX$_2$ (**2d**; X = Cl, Br; 2.90 mL, 0.90 mmol, 0.31 M in THF) was added to 4-fluorobenzoylchloride (**3e**; 238 mg, 1.5 mmol) and the reaction mixture was stirred for 12 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et$_2$O, 8:1) afforded the benzophenone **4f** (286 mg, 81%) as a colorless solid mp 118–119 °C.

IR (Diamond-ATR, neat): 1648 (s), 1591 (s), 1504 (m), 1400 (m), 1271 (s), 1227 (s), 1155 (s), 1145 (s), 1085 (s), 853 (vs), 838 (s), 757 (vs), 672 cm^{-1} (s).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.84–7.79 (m, 2 H), 7.75–7.72 (m, 2 H), 7.63–7.60 (m, 2 H), 7.41–7.35 (m, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 193.7, 164.8 (d, $^1J_{C,F}$ = 251.8 Hz), 137.6, 135.6, 133.2 (d, $^4J_{C,F}$ = 3.1 Hz), 132.6 (d, $^3J_{C,F}$ = 9.6 Hz), 131.4, 128.7, 115.7 (d, $^2J_{C,F}$ = 22.9 Hz).

MS (EI, 70 eV): *m*/*z* (%) = 234 (M$^+$, 44), 199 (15), 141 (20), 138 (59), 123 (100), 111 (21), 95 (28), 75 (19).

HRMS: *m*/*z* calcd for $C_{13}H_8ClFO$: 234.0248; found: 234.0246.

(3-Chlorophenyl)(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)methanol (4g)

According to TP4, 3-chlorobenzaldehyde (**3f**; 211 mg, 1.50 mmol) was added to bis(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)zinc·2MgCl$_2$ (**2e**; 2.65 mL, 0.90 mmol, 0.34 M in THF). The reaction mixture was stirred for 6 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et$_2$O, 1:1 + 1 vol% Et$_3$N) afforded the alcohol **4g** (358 mg, 80%) as a white solid; mp 100–102 °C.

IR (Diamond-ATR, neat): 1504 (m), 1437 (m), 1370 (m), 1194 (m), 1146 (w), 1130 (w), 1050 (m), 1032 (s), 797 (vs), 772 (vs), 726 (s), 697 cm^{-1} (vs).

^{1}H NMR (400 MHz, C$_6$D$_6$): δ = 7.53–7.47 (m, 2 H), 7.28–7.25 (m, 1 H), 7.07–6.94 (m, 4 H), 6.87–6.83 (m, 1 H), 6.74 (t, *J* = 7.7 Hz, 1 H), 5.78 (s, 1 H), 5.45 (s, 1 H), 2.92 (s, 1 H), 2.16 (s, 3 H).

^{13}C NMR (100 MHz, C$_6$D$_6$): δ = 149.0, 145.8, 144.9, 140.3, 134.4, 129.6, 129.1, 127.8, 127.7, 126.9, 125.5, 124.8, 107.3, 67.3, 13.5.

MS (EI, 70 eV): *m*/*z* (%) = 298 (M$^+$, 100), 221 (5), 204 (7), 185 (12), 159 (48), 139 (9), 116 (4), 77 (11).

HRMS: *m*/*z* calcd for $C_{17}H_{15}ClN_2O$: 298.0873; found: 298.0869.

(3,5-Dimethylisoxazol-4-yl)[4-(1*H*-1,2,4-triazol-1-yl)phenyl]methanol (4h)

According to TP4, bis(3,5-dimethylisoxazol-4-yl)zinc·2MgX$_2$ (**2f**; X = Cl, Br; 3.64 mL, 1.20 mmol, 0.33 M in THF) was added to 4-(1*H*-1,2,4-triazol-1-yl)benzaldehyde (**3g**; 346 mg, 2.00 mmol) in THF (1.0 mL). The reaction mixture was stirred for 14 h at 25 °C. Purification by flash chromatography (silica gel, EtOAc + 1 vol% Et$_3$N) afforded the alcohol **4h** (413 mg, 76%) as a white solid; mp 129–130 °C.

IR (Diamond-ATR, neat): 3328 (m), 1608 (m), 1522 (vs), 1424 (s), 1274 (s), 1154 (s), 1032 (s), 982 (s), 958 (m), 862 (s), 792 (vs), 674 cm^{-1} (vs).

^{1}H NMR (400 MHz, acetone-d_6): δ = 9.01 (s, 1 H), 8.08 (s, 1 H), 7.89–7.81 (m, 2 H), 7.62–7.55 (m, 2 H), 5.93 (s, 1 H), 2.91 (br s, 1 H), 2.36 (s, 3 H), 2.03 (s, 3 H).

^{13}C NMR (100 MHz, acetone-d_6): δ = 166.4, 159.4, 153.2, 144.0, 142.4, 137.1, 128.0, 120.2, 117.7, 66.2, 11.3, 10.8.

MS (EI, 70 eV): *m*/*z* (%) = 270 (M$^+$, 29), 253 (8), 211 (7), 172 (9), 146 (100), 124 (13), 82 (7), 43 (9).

HRMS: *m*/*z* calcd for $C_{14}H_{14}N_4O_4$: 270.1117; found: 270.1115.

1-(3-Chlorophenyl)heptan-1-ol (4i)

According to TP4, bis(hexyl)zinc·2MgX$_2$ (**2g**; X = Cl, Br; 2.90 mL, 0.90 mmol, 0.31 M in THF) was added to 3-chlorobenzaldehyde (**3f**; 211 mg, 1.5 mmol) and the reaction mixture was stirred for 14 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et$_2$O, 3:1) afforded the alcohol **4i** (295 mg, 87%) as a colorless oil.

IR (Diamond-ATR, neat): 3334 (w), 2927 (s), 1574 (w), 1432 (m), 1198 (m), 1044 (m), 882 (m), 783 (vs), 696 cm^{-1} (s).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.35–7.34 (m, 1 H), 7.32–7.30 (m, 1 H), 7.26–7.23 (m, 2 H), 5.25 (d, *J* = 4.7 Hz, 1 H), 4.52–4.48 (m, 1 H), 1.61–1.48 (m, 2 H), 1.34–1.16 (m, 8 H), 0.84–0.81 (m, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.2, 132.7, 129.8, 126.4, 125.6, 124.5, 71.6, 39.2, 31.3, 28.6, 25.1, 22.1, 13.9.

MS (EI, 70 eV): *m*/*z* (%) = 226 (M$^+$, 4), 143 (37), 141 (100), 113 (22), 77 (29).

HRMS: *m*/*z* calcd for $C_{13}H_{19}ClO$: 226.1124; found: 226.1119.

Ethyl 3-[2-(4-Fluorophenyl)-2-hydroxypropyl]benzoate (4j)

According to TP4, 1-(4-fluorophenyl)ethanone (**3h**; 276 mg, 2.0 mmol) was added to bis(3-(ethoxycarbonyl)benzyl)zinc·2MgCl$_2$ (**2h**; 6.67 mL, 2.2 mmol, 0.33 M in THF). The reaction mixture was stirred for 24 h at 50 °C. Purification by flash chromatography (silica gel, pentane–EtOAc, 4:1 + 1 vol% Et$_3$N) afforded the alcohol **4j** (444 mg, 68%) as a pale yellow oil.

IR (Diamond-ATR, neat): 3480 (w), 1699 (s), 1603 (m), 1508 (s), 1277 (vs), 1223 (s), 1199 (s), 1160 (m), 1106 (s), 1088 (s), 836 (s), 755 (s), 720 cm^{-1} (s).

^{1}H NMR (400 MHz, C$_6$D$_6$): δ = 8.07–8.01 (m, 1 H), 7.95–7.92 (m, 1 H), 7.02–6.95 (m, 3 H), 6.95–6.91 (m, 1 H), 6.82–6.74 (m, 2 H), 4.17–4.08 (m, 2 H), 2.76 (d, *J* = 13.3 Hz, 1 H), 2.69 (d, *J* = 13.3 Hz, 1 H), 1.23 (s, 1 H), 1.16 (s, 3 H), 1.03 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, C$_6$D$_6$): δ = 166.4, 162.0 (d, $^1J_{C,F}$ = 244.4 Hz), 143.6 (d, $^4J_{C,F}$ = 3.1 Hz), 137.8, 135.1, 132.2, 130.8, 128.0, 128.0, 127.1 (d, $^3J_{C,F}$ = 8.0 Hz), 114.8 (d, $^2J_{C,F}$ = 21.0 Hz), 73.9, 60.8, 50.5, 29.2, 14.2.

MS (EI, 70 eV): *m*/*z* (%) = 302 (M$^+$, <1), 184 (15), 257 (23), 211 (13), 196 (11), 164 (100), 139 (88), 136 (42), 118 (11), 91 (18), 43 (36).

HRMS: *m*/*z* calcd for $C_{18}H_{19}FO_3$: 302.1318; found: 302.1306.

1,1-Dicyclopropyl-2-(3-methoxyphenyl)ethanol (4k)

According to TP4, dicyclopropylmethanone (**3i**; 156 mg, 1.50 mmol) was added to bis(4-methoxybenzyl)zinc·2MgCl$_2$ (**2i**; 2.90 mL, 0.90 mmol, 0.31 M in THF). The reaction mixture was stirred for 1 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et$_2$O, 9:1 + 1 vol% Et$_3$N) afforded the alcohol **4k** (292 mg, 84%) as a colorless oil.

IR (Diamond-ATR, neat): 1601 (m), 1488 (s), 1453 (m), 1437 (m), 1312 (m), 1260 (vs), 1167 (s), 1153 (s), 1043 (s), 1022 (s), 994 (s), 778 (s), 703 cm^{-1} (s).

^{1}H NMR (300 MHz, C$_6$D$_6$): δ = 7.16–7.08 (m, 1 H), 7.02–6.98 (m, 1 H), 6.94–6.88 (m, 1 H), 6.78–6.71 (m, 1 H), 3.39 (s, 3 H), 2.80 (s, 2 H), 0.67–0.55 (m, 3 H, incl. OH), 0.44–0.32 (m, 4 H), 0.27–0.06 (m, 4 H).

^{13}C NMR (75 MHz, C$_6$D$_6$): δ = 159.9, 139.7, 129.0, 123.5, 117.2, 111.8, 70.6, 54.7, 49.4, 19.0, 1.3, –0.2.

MS (EI, 70 eV): *m*/*z* (%) = 232 (M$^+$, <1), 214 (11), 185 (10), 122 (40), 111 (100), 91 (18), 77 (13), 69 (77), 57 (11), 41 (26).

HRMS: *m*/*z* calcd for $C_{15}H_{20}O_2$: 232.1463; found: 232.1453.

1-[4-(Dimethylamino)phenyl]-2-(4-methoxyphenyl)ethanol (4l)

According to TP4, 4-methoxybenzylzinc chloride·$MgCl_2$ (**5a**; 36.1 mL, 13.0 mmol, 0.36 M in THF) was added to 4-(dimethylamino)benzaldehyde (**3j**; 1.49 g, 10.0 mmol) in THF (5 mL) and the reaction mixture was stirred for 1 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et_2O, 2:5) afforded the alcohol **4l** (2.68g, 99%) as a yellow solid; mp 113–115 °C.

IR (Diamond-ATR, neat): 1614 (m), 1522 (s), 1508 (s), 1440 (m), 1354 (m), 1243 (s), 1204 (m), 1184 (m), 1175 (m), 1156 (m), 1106 (m), 1045 (m), 1027 cm^{-1} (s).

^{1}H NMR (400 MHz, C_6D_6): δ = 7.27–7.22 (m, 2 H), 7.04–6.99 (m, 2 H), 6.76–6.71 (m, 2 H), 6.63–6.58 (m, 2 H), 4.75–4.70 (m, 1 H), 3.30 (s, 3 H), 3.06 (dd, J = 13.5, 7.4 Hz, 1 H), 2.98 (dd, J = 13.5, 5.7 Hz, 1 H), 2.53 (s, 6 H), 1.66 (s, 1 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 158.7, 150.4, 133.0, 131.0, 130.9, 127.3, 114.0, 112.7, 75.6, 54.7, 45.7, 40.3.

MS (EI, 70 eV): m/z (%) = 271 (M$^+$, 2), 253 (58), 238 (27), 165 (6), 150 (100), 122 (7), 120 (6).

HRMS: m/z calcd for $C_{17}H_{21}NO$: 271.1572; found: 271.1570.

4-[2-(4-Fluorophenyl)-1-hydroxy-1-methylethyl]benzonitrile (4m)

According to TP4, 4-fluorobenzylzinc chloride·$MgCl_2$ (**5b**; 4.62 mL, 1.80 mmol, 0.39 M in THF) was added to 4-acetylbenzonitrile (**3b**; 218 mg, 1.50 mmol) in THF (0.5 mL) and the reaction mixture was stirred for 15 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et_2O, 1:1 + 1 vol% Et_3N) afforded the alcohol **4m** (305 mg, 80%) as yellowish solid; mp 93–95 °C.

IR (Diamond-ATR, neat): 3468 (m), 2234 (m), 1606 (m), 1404 (m), 1220 (s), 1144 (m), 1098 (m), 1075 (m), 1018 (m), 933 (m), 836 (vs), 821 (s), 770 (m), 709 cm^{-1} (m).

^{1}H NMR (300 MHz, C_6D_6): δ = 7.07–7.01 (m, 2 H), 6.91–6.85 (m, 2 H), 6.73–6.64 (m, 2 H), 6.61–6.53 (m, 2 H), 2.54 (d, J = 13.6 Hz, 1 H), 2.49 (d, J = 13.6 Hz, 1 H), 1.22 (br s, 1 H), 1.05 (s, 3 H).

^{13}C NMR (75 MHz, C_6D_6): δ = 162 (d, $^1J_{C,F}$ = 244.8 Hz), 152.5, 132.2 (d, $^3J_{C,F}$ = 7.9 Hz), 132.2 (d, $^4J_{C,F}$ = 3.1 Hz), 131.7, 125.9, 118.9, 115.0 (d, $^2J_{C,F}$ = 21.0 Hz), 111.0, 73.9 (d, $^5J_{C,F}$ = 1.4 Hz), 49.3, 28.8.

HRMS (ESI): m/z calcd for $C_{16}H_{14}FNO$: 273.1403 ([M + NH_4]$^+$); found: 273.1397 ([M + NH_4]$^+$).

1-(2-Chlorophenyl)-1-(4-chlorophenyl)-2-(4-fluorophenyl)ethanol (4n)

According to TP4, 4-fluorobenzylzinc chloride·$MgCl_2$ (**5b**; 4.62 mL, 1.80 mmol, 0.39 M in THF) was added to (2-chlorophenyl)(4-chlorophenyl)methanone (**3k**; 377 mg, 1.50 mmol) in THF (0.5 mL) and the reaction mixture was stirred for 48 h at 25 °C. Purification by flash chromatography (silica gel, pentane–Et_2O–CH_2Cl_2, 18:1:1) afforded the alcohol **4n** (422 mg, 78%) as yellow solid; mp 90–92 °C.

IR (Diamond-ATR, neat): 1510 (s), 1488 (m), 1433 (m), 1224 (s), 1159 (m), 1092 (m), 1035 (m), 1014 (m), 1002 (m), 822 (vs), 756 (vs), 748 cm^{-1} (s).

^{1}H NMR (400 MHz, C_6D_6): δ = 7.39 (dd, J = 7.8, 1.8 Hz, 1 H), 7.07–7.00 (m, 3 H), 6.88–6.63 (m, 8 H), 3.70 (d, J = 13.1 Hz, 1 H), 3.04 (d, J = 13.1 Hz, 1 H), 2.31 (br s, 1 H).

^{13}C NMR (100 MHz, C_6D_6): δ = 161.8 (d, $^1J_{C,F}$ = 244.2 Hz), 144.3, 142.2, 132.9, 132.2 (d, $^3J_{C,F}$ = 7.8 Hz), 132.0, 132.0 (d, $^4J_{C,F}$ = 3.3 Hz), 130.8, 128.6, 128.5, 128.0, 127.9, 126.1, 114.1 (d, $^2J_{C,F}$ = 21.0 Hz), 77.3 (d, $^1J_{C,F}$ = 1.4 Hz), 43.7.

HRMS (ESI): m/z calcd $C_{20}H_{15}Cl_3FO$: 405.0466 ([M + HCO_2]$^+$); found: 405.0462 ([M + HCO_2]$^+$).

Phenylacetic Acid (4o)

According to TP3, bis(benzyl)zinc·2$MgCl_2$ (**2j**; 2.38 mL, 1.00 mmol, 0.42 M in THF) was treated with dry gaseous CO_2 at 25 °C for 2.5 h. After purification, phenylacetic acid (**4o**; 208 mg, 76%) was obtained as a white solid; mp 80–82 °C.

IR (Diamond-ATR, neat): 2921 (w), 1692 (s), 1407 (m), 1336 (m), 1228 (m), 1186 (m), 892 (m), 839 (m), 751 (m), 699 (vs), 676 cm^{-1} (s).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.29 (br s, 1 H), 7.33–7.28 (m, 2 H), 7.27–7.20 (m, 3 H), 3.56 (s, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 172.7, 135.0, 129.3, 128.2, 126.5, 40.7.

MS (EI, 70 eV): m/z (%) = 136 (M$^+$, 72), 91 (100), 65 (12), 44 (5).

HRMS: m/z calcd for $C_8H_8O_2$: 136.0524; found: 136.0509.

(3-Methoxyphenyl)acetic Acid (4p)

According to TP3, bis(3-methoxybenzyl)zinc·2$MgCl_2$ (**2i**; 3.13 mL, 1.0 mmol, 0.32 M in THF) was treated with dry gaseous CO_2 at 25 °C for 2 h. After purification, (3-methoxyphenyl)acetic acid (**4p**) (326 mg, 98%) was obtained as a slightly red solid; mp 67–68 °C.

IR (Diamond-ATR, neat): 2920 (m), 1692 (s), 1492 (m), 1258 (s), 1212 (s), 1167 (s), 1035 (s), 996 (m), 893 (m), 792 (s), 756 cm^{-1} (vs).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.21 (t, J = 8.0 Hz, 1 H), 6.83–6.79 (m, 3 H), 3.72 (s, 3 H), 3.52 (s, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 172.6, 159.2, 136.5, 129.3, 121.6, 115.1, 112.0, 55.0, 40.7.

MS (EI, 70 eV): m/z (%) = 166.1 (M$^+$, 100), 121.1 (87), 91.1 (21).

HRMS: m/z calcd for $C_9H_{10}O_3$: 166.0630; found: 166.0630 (M$^+$).

(2-Chlorophenyl)acetic Acid (4q)

According to TP3, bis(2-chlorobenzyl)zinc·2$MgCl_2$ (**2k**; 1.85 mL, 1.0 mmol, 0.52 M in THF) was treated with dry gaseous CO_2 at 50 °C for 12 h. After purification, (2-chlorophenyl)acetic acid (**4q**) (272 mg, 80%) was obtained as a white solid; mp 92–93 °C.

IR (Diamond-ATR, neat): 2916 (w), 1699 (s), 1402 (m), 1238 (s), 1055 (m), 926 (m), 761 (vs), 733 (s), 687 cm^{-1} (s).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.45–7.36 (m, 2 H), 7.30–7.26 (m, 2 H), 3.70 (s, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 171.5, 133.7, 133.3, 132.2, 129.0, 128.8, 127.1, 38.7.

MS (EI, 70 eV): m/z (%) = 170 (M$^+$, 40), 135 (76), 125 (100), 91 (50), 63 (10).

HRMS: m/z calcd for $C_8H_7ClO_2$: 170.0135; found: 170.0133 (M$^+$).

Heptanoic Acid (4r)

According to TP3, bis(hexyl)zinc·2MgX_2 (**2g**; X = Cl, Br; 3.22 mL, 1.00 mmol, 0.31 M in THF) was treated with dry gaseous CO_2 at 50 °C for 12 h. After purification, heptanoic acid (**4r**) (223 mg, 86%) was obtained as a colorless oil.

IR (Diamond-ATR, neat): 2928 (m), 1704 (vs), 1412 (m), 1283 (m), 1237 (m), 1206 (w), 1106 (w), 934 cm^{-1} (w).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.95 (s, 1 H), 2.17 (t, J = 7.4 Hz, 2 H), 1.50–1.43 (m, 2 H), 1.30–1.19 (m, 6 H), 0.86–0.83 (m, 3 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 174.5, 33.7, 31.0, 28.2, 24.5, 22.0, 13.9.

MS (EI, 70 eV): m/z (%) = 130 (M$^+$, 1), 101 (10), 87 (30), 73 (60), 60 (100), 55 (16), 43 (16), 41 (23).

HRMS: m/z calcd for $C_7H_{14}O_2$: 130.0994; found: 130.0987 (M$^+$).

Acknowledgment

We thank the DFG and the European Research Council (ERC) for financial support. We also thank Chemetall GmbH (Frankfurt) and BASF SE (Ludwigshafen) for the generous gift of chemicals.

References

(1) (a) *The Chemistry of Organolithium Compounds*; Rappoport, Z.; Marek, I., Eds.; Wiley: Chichester, **2004**. (b) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: New York, **1974**. (c) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49. (d) Tomioka, K.; Inoue, I.; Shindo, M.; Koga, K. *Tetrahedron Lett.* **1990**, *31*, 6681. (e) *The Chemistry of Organomagnesium Compounds*; Rappoport, Z.; Marek, I., Eds.; Wiley: Chichester, **2008**. (f) Luderer, M. R.; Bailey, W. F.; Luderer, M. R.; Fair, J. D.; Dancer, R. J.; Sommer, M. B. *Tetrahedron: Asymmetry* **2009**, *20*, 981.

(2) (a) Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117. (b) Knochel, P.; Millot, N.; Rodriguez, A.; Tucker, C. E. *Org. React.* **2001**, *58*, 417. (c) *Organozinc Reagents*; Knochel, P.; Jones, P., Eds.; Oxford University Press: New York, **1999**. (d) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 6040. (e) Metzger, A.; Schade, M. A.; Knochel, P. *Org. Lett.* **2008**, *10*, 1107. (f) Metzger, A.; Argyo, C.; Knochel, P. *Synthesis* **2010**, 882.

(3) For selected examples, see: (a) Shi, J.; Zeng, X.; Negishi, E. *Org. Lett.* **2003**, *5*, 1825. (b) Gavryushin, A.; Kofink, C.; Manolikakes, G.; Knochel, P. *Org. Lett.* **2005**, *7*, 4871. (c) Yeh, M. C. P.; Knochel, P.; Santa, L. E. *Tetrahedron Lett.* **1988**, *29*, 3887. (d) Reddy, C. K.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1700. (e) Kazmierski, I.; Bastienne, M.; Gosmini, C.; Paris, J.-M.; Périchon, J. *J. Org. Chem.* **2004**, *69*, 936. (f) Dong, Z.; Manolikakes, G.; Li, J.; Knochel, P. *Synthesis* **2009**, 681. (g) Monzon, G.; Knochel, P. *Synlett* **2010**, 304. (h) Tamaru, Y.; Nakamura, T.; Sakaguchi, M.; Ochiai, H.; Yoshida, Z. *J. Chem. Soc., Chem. Commun.* **1988**, 610. (i) Metzger, A.; Gavryushin, A.; Knochel, P. *Synlett* **2009**, 1433. (j) Seebach, D.; Beck, A. K.; Schmidt, B.; Wang, Y. M. *Tetrahedron* **1994**, *50*, 4363.

(4) (a) Piller, F. M.; Appukkuttan, P.; Gavryushin, A.; Helm, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 6802. (b) Piller, F. M.; Metzger, A.; Schade, M. A.; Haag, B. H.; Gavryushin, A.; Knochel, P. *Chem. Eur. J.* **2009**, *15*, 7192.

(5) Metzger, A.; Piller, F. M.; Knochel, P. *Chem. Commun.* **2008**, 5824.

(6) Blümke, T. D.; Piller, F. M.; Knochel, P. *Chem. Commun.* **2010**, *46*, 4082.

(7) Metzger, A.; Bernhardt, S.; Manolikakes, G.; Knochel, P. *Angew. Chem. Int. Ed.* **2010**, *49*, 4665.

(8) Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 890.