Aminomethylation of Functionalized Organozinc Reagents and Grignard Reagents Using Immonium Trifluoroacetates

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Abstract: New immonium trifluoroacetates **1** and **2** react readily with functionalized organozinc or magnesium reagents leading to the corresponding aminomethylated products of type **5** and **7**. The resulting bis-allylamines were deallylated leading to primary amines.

Key words: organometallic reagents, zinc, magnesium, aminomethylation, primary amines, deprotection

Functionalized organozinc¹ reagents are available either by direct insertion of zinc powder,^{1,2} by the boron-zinc exchange reaction³ or by transmetallation of polyfunctional organolithiums⁴ at low temperature. In the presence of CuCN•2LiCl, they are converted in highly reactive zinccopper intermediates which react with organic electrophiles leading to highly functionalized products. Aminomethylation is an important transformation and has been performed with various immonium salts⁵⁻⁷ or iminium salts precursors.^{8,9} Since organozinc reagents themselves display a relatively low reactivity, highly reactive aminomethylation reagents are therefore necessary. In this work, we wish to report the direct reaction of organozinc reagents with immonium trifluoroacetates. We have prepared immonium trifluoroacetates⁷ 1 and 2 because the allyl or benzyl moieties could be removed to afford aminomethylated products. Their preparation is based on the work of Tietze.⁷ Thus heating an aqueous solution of formaldehyde with diallylamine and dibenzylamine results in the formation of the aminals 3 and 4, in 71% and 77% yield respectively. The treatment of 3 in CH₂Cl₂ (25 °C, 1 h) or 4 in diethyl ether (25 °C, 1 h) with trifluoroacetic anhydride provides solution of the immonium trifluorocetates 1 or 2 in essentially quantitative yields (Scheme 1).

The immonium salts 1 and 2 are readily soluble in CH_2Cl_2/THF and Et_2O/THF mixtures and rapidly react with various functionalized organozinc reagents (R^1ZnX or R^1_2Zn) providing the aminomethylated products **5a-n** (see Scheme 2 and Table 1).

Whereas arylzinc halides and benzylic zinc halides already undergo addition at -78 °C (see Entries 1, 2, 9 and 13 of Table 1), alkylzinc halides are best added at 25 °C. The reactions are always complete within 30 min. Various functional groups like an ester group (Entries 4, 7, 11 and 12), a cyano group (Entries 2, 3, 9, 10 and 13) or an imide function (Entry 8) are perfectly tolerated.







Scheme 2

Interestingly functionalized organomagnesium compounds prepared by iodine-magnesium exchange¹⁰ react at low temperature with the immonium salt **1** (see Scheme 3 and Table 2). While arylmagnesium bromides **6a–b** and **6e–f** smoothly undergo addition at $-60 \degree$ C or $-40 \degree$ C (see Entries 1, 2, 5 and 6 of Table 2), the functionalized magnesium carbenoids **6c–d** are best reacted at $-78 \degree$ C (Entries 3 and 4). This is essential in the case of the sensitive



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Table 1 Aminomethylated Products 5a-n Obtained by Reaction of Organozinc Halides or Diorganozincs with the Immonium Salts 1 or 2

Entry	Organozinc Reagent	Immonium Salts 1 or 2	Temp. (°C)	Product of Type 5	Yield (%) ^a
1	PhZnCl	1	-78	5a	85
2	NC	1	-78	5b	96
3	NC(CH ₂) ₃ ZnI	1	25	5c	68
4	EtO ₂ C(CH ₂) ₃ ZnI	1	25	5d	73
5	c-HexZnI	1	25	5e	83
6	Zn	1	25	5f	91
7	EtO ₂ C(CH ₂) ₅ ZnI	1	25	5g	75
8	N(CH ₂) ₃ Znl	1	25	5h	64
9	ZnBr	1	-78	5i	72
10	NC(CH ₂) ₃ ZnI	2	25	5j	77
11	EtO ₂ C(CH ₂) ₃ ZnI	2	25	5k	74
12	EtO ₂ C(CH ₂) ₅ ZnI	2	25	51	77
13	NCZnBr	2	-78	5m	92
14	Zn	2	25	5n	73

^a Isolated yields of analytically pure products.

carbenoids **6c-d** which already decompose at -70 °C.¹¹ The desired aminomethylated products **7a-f** are obtained in 70–81% yield.

The resulting bis-allylated amines can be deprotected according to the method of Guibé.¹² Thus, the reaction of diallylamines of type **7** with N,N'-dimethylbarbituric acid in presence of Pd(PPh₃)₄ (2 mol%) in CH₂Cl₂ at 35 °C produces within 1 to 3 h the primary amines **8a–j** in satisfactory yields (Scheme 4 and Table 3). Debenzylation of the amines **5j–n** was unsucessful under various hydrogenation conditions with Pearlman's catalyst and no other efficient deprotection has been found.¹³

In summary, functionalized primary amines were prepared in a two step sequence from organozinc and magnesium reagents using aminomethylation and selective deallylation reactions.



Scheme 4

All reactions were carried out under argon. THF and ether were freshly distilled from sodium/benzophenone and CH_2Cl_2 from CaH₂. Reactions were monitored by GC analysis of worked up reaction aliquots. Zinc foil was activated with 1,2-dibromoethane and

Table 2	Aminomethylated Products 7a	-f Obtained by	the Reaction of Function	nalized Organomagn	nesium Reagents wit	h the Immonium Salt 1

Entry	Organomagnesium Reagent	Temp. (°C)	Product of Type 7	Yield (%) ^a
1	EtO ₂ C MgBr 6a	-60	EtO ₂ C	70
2	MgBr 6b	-60	7b	76
3	<i>t</i> -Bu O MgCl	-78	r-Bu O N	73
4	o MgCl 6d	-78	7d	81
5	MgCl CO ₂ Et	-40	Te	76
6	EtO ₂ C MgBr 6f	-40	EtO_2C	77

^a Isolated yields of analytically pure products.

TMSCl. Analytical TLC was performed using Merck silica gel (60 F-254) plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was carried out on silica gel 60 (70–230 mesh). NMR spectra were recorded on a 200 or 300 MHz NMR spectrometer. The ionization method used for mass spectrometry was electron impact (EI, 70 eV). In the case of **8e** Fast Atom Bombardment was used. Elemental analyses were performed by the Microanalytical Service Laboratory of Universität München.

N,N,N',N'-Tetraallylmethanediamine (3)

A 37% aq solution of formaldehyde (8.9 g, 0.11 mol) was added slowly at 0 °C to diallylamine (24.7 mL, 0.20 mol) placed in a twonecked flask equipped with a refluxing condenser and the mixture was refluxed for 2 h. After cooling to r.t. the upper layer was separated and dried (KOH pellets). The residue was distilled under reduced pressure (bp 95 °C/15 Torr) to afford the product (14.6 g, 71% yield) as a colorless liquid (Table 4).

N,N,N',N'-Tetrabenzylmethanediamine (4)

A 37% aq solution of formaldehyde (8.9 g, 0.11 mol) was added slowly at 0 °C to a two-necked flask equipped with a refluxing condenser and containing dibenzylamine (38 mL, 0.20 mol) and the

mixture was refluxed for 3.5 h. After cooling to r.t. the solid was crystallized from hexane (50 mL) to afford the product (31.3 g, 77% yield) as white crystals (Table 4).

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Immonium Trifluoroacetates 1 and 2

Trifluoroacetic anhydride (0.85 mL, 6.0 mmol) was added slowly at 0 °C to a solution of the aminal **3** (2.4 g, 6.0 mmol) in CH_2Cl_2 (12 mL). After stirring at r.t. for 1 h, the resulting orange solution was ready for use. The preparation of the aminal **2** was performed in ether following the same procedure to give a clear yellow solution.

Aminomethylation of Functionalized Organozinc Reagents Affording the Amines 5; General Procedure A

A solution of the functionalized organometallic reagent (1.3 to 1.5 equiv) in THF was added at the temperature indicated in Table 1 to a solution of immonium trifluoroacetate (1 equiv) in CH_2Cl_2 (salt 1) or Et₂O (salt 2). After stirring for 30 min, the reaction was quenched with sat. aq Na₂CO₃ (or NH₄Cl) and extracted with CH_2Cl_2 or Et₂O. The combined organic layers were washed with H₂O, brine and dried (MgSO₄). The products were isolated after evaporation of the solvents and purification by flash-chromatogra-

Table 3 Deallylation of Bis-allylamines **5** or **7** Using *N*,*N*'-Dimethylbarbituric Acid Leading to Primary Amines **8a**–j

Amine	Product of Type 8	Yield (%) ^a
5b	NC NH ₂	63
	8a ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
5c	NC(CH ₂) ₄ NH ₂ 8b	59
5d	Src NH	57
5f	NH ₂	74
5g	8d EtO ₂ C(CH ₂) ₆ NH ₂ 8e	71 ^b
5i	NC NH ₂	80
	8f	
7b	NH2 NH2	87
	8g	
7d	NH ₂	62
	8h	
7e	NH	50
	0 8i	
7f	EtO ₂ C S NH ₂ 8j	60

^a Isolated yields of analytically pure products.

^b Product isolated as its hydrochloride salts.

phy on silica gel. The NMR and mass spectral data of compounds **5a-n** are shown in Table 4.

N-Benzyl-N,N-diallylamine (5a)

The reaction was carried out according to General Procedure A using a solution of phenylzinc chloride (3.75 mmol), freshly prepared from a 1.7 M cyclohexane/Et₂O solution of PhLi (2.2 mL, 3.75 mmol) and ZnCl₂ (0.51 g, 3.75 mmol) in THF (5.5 mL), and a solution of **1** (2.5 mmol) in CH₂Cl₂ (5 mL) at -78 °C. After workup

the crude residue was purified by flash chromatography on silica gel ($CH_2Cl_2/MeOH$, 99:1) affording the product **5a** (400 mg, 85%).

3-[2-(N,N-diallylamino)ethyl]benzonitrile (5b)

The reaction was carried out according to General Procedure A using 3-cyanobenzylzinc bromide (11.3 mmol), freshly prepared from 3-bromomethylbenzonitrile (8.7 g, 44.0 mmol) and activated zinc foil (8.63 g, 0.13 mol) in THF (40 mL), and a solution of **1** (7.6 mmol) in CH₂Cl₂ (15 mL) at -78 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH 99:1) affording the product **5b** (1.6 g, 96%).

5-(N,N-Diallylamino)pentanenitrile (5c)

The reaction was carried out according to General Procedure A using a solution of 3-cyanopropylzinc iodide (3.75 mmol), freshly prepared from 3-iodopropionitrile (0.73 g, 3.75 mmol) and activated zinc foil (0.74 g, 11.25 mmol) in THF (2 mL), and a solution of 1 (2.75 mmol) in CH₂Cl₂ (4 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/ MeOH, 97:3) affording the product **5c** (330 mg, 68%).

Ethyl 5-(N,N-Diallylamino)pentanoate (5d)

The reaction was carried out according to General Procedure A using a solution of 4-carboethoxypropylzinc iodide (3.0 mmol), freshly prepared from ethyl 4-iodobutanoate (0.72 g, 3.0 mmol) and activated zinc foil (0.59 g, 9.0 mmol) in THF (2.3 mL), and a solution of **1** (2.0 mmol) in CH₂Cl₂ (4 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 98:2) affording the product **5d** (330 mg, 73%).

N-Cyclohexylmethyl-N,N-diallylamine (5e)

The reaction was carried out according to General Procedure A using cyclohexylzinc iodide (30.7 mmol), freshly prepared from iodocyclohexane (6.5 mL, 50.0 mmol) and activated zinc foil (10.1 g, 0.155 mol) in THF (48 mL), and a solution of **1** (20.0 mmol) in CH₂Cl₂ (42 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 98:2) affording the product **5e** (3.2 g, 83%).

N-Myrtanylmethyl-N,N-diallylamine (5f)

The reaction was carried out according to General Procedure A using dimyrtanylzinc (3.40 mmol), freshly prepared from (–)- β -Pinene (16 mL, 0.10 mol), BH₃,SMe₂ (3 mL, 0.03 mol) and Et₂Zn (12 mL, 0.12 mol) in THF (40 mL), and a solution of **1** (2.0 mmol) in CH₂Cl₂ (4 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 98:2) affording the product **5f** (450 mg, 91%).

Ethyl 7-(N,N-Diallylamino)heptanoate (5g)

The reaction was carried out according to General Procedure A using a solution of 6-ethoxycarbonylhexylzinc iodide (10 mmol), freshly prepared from ethyl 6-iodoheptanoate (2.7 g, 10 mmol) and activated zinc foil (2.0 g, 30 mmol) in THF (5 mL), and a solution of **1** (7 mmol) in CH₂Cl₂ (14 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 100:0 to 97:3) affording the product **5g** (1.33 g, 75%).

2-[4-(N,N-Diallylamino)butyl]isoindole-1,3-dione (5h)

The reaction was carried out according to General Procedure A using a solution of 3-phthalimidopropylzinc iodide (10 mmol), freshly prepared from *N*-(3-iodopropyl)phthalimide (3.1. g, 10 mmol) and activated zinc foil (1.96 g, 30 mmol) in THF (5 mL), and a solution of **1** (7 mmol) in CH₂Cl₂ (14 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 98:2 to 97:3) affording the product **5h** (1.33 g, 64%).

4-(N,N-Diallylaminomethyl)benzonitrile (5i)

The reaction was carried out according to General procedure A using 4-cyano-phenylzinc bromide (13.4 mmol), freshly prepared from 4-bromo-benzonitrile (2.4 g, 13.1 mmol), *n*-BuLi 15% hexane solution (9.0 mL, 14 mmol) and ZnBr_2 (3.15 g, 14 mmol) in THF (14 mL), and a solution of **1** (5.2 mmol) in CH₂Cl₂ (10 mL) at

Table 4	NMR and	Mass Spectral	Data of Com	pounds 3, 4	and 5a–n
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Product	¹ H NMR (CDCl ₃ , 300 MHz) δ, <i>J</i> (Hz)	13 C NMR (CDCl ₃ , 75 MHz) δ	MS ^a <i>m</i> / <i>z</i> (%)
3	5.81–5.62 (2 H, m), 5.00 (2 H, d, <i>J</i> = 12.2), 4.93 (2 H, d, <i>J</i> = 6.0), 3.02 (4 H, d, <i>J</i> = 6.4), 2.98 (1 H, s)	150.5, 128.7, 124.9, 59.6	205, 110
4	7.29–7.19 (10 H, m), 3.61 (4 H, s), 3.10 (1 H, s)	140.2, 129.4, 128.6, 127.2, 72.8, 56.6	406, 314, 210, 106, 91
5a	7.27–7.15 (5 H, m), 5.84 (2 H, ddt, $J = 16.6$, 10.2, 6.4), 5.12 (2 H, d, $J = 16.6$, 5.07 (2 H, d, $J = 10.2$), 3.51 (2 H, s), 3.01 (4 H, d, $J = 6.4$)	139.5, 135.7, 129.0, 128.2, 126.9, 117.5, 57.6, 56.4	187, 160, 110, 96, 91
5b	7.41–7.28 (4 H, m), 5.78–5.67 (2 H, m), 5.13–5.05 (4 H, m), 3.07 (4 H, d, <i>J</i> = 6.4), 2.70 (2 H, t, <i>J</i> = 6.5), 2.61 (2 H, t, <i>J</i> = 6.5)	142.5, 135.8, 133.8, 132.7, 130.1, 129.4, 119.4, 118.0, 112.6, 57.3, 54.7, 33.4	226, 199, 110, 41
5c	5.76-5.65 (2 H, m), 5.07 (2 H, d, $J = 15.0$), $5.02(2 H, d, J = 9.0), 2.95 (4 H, d, J = 6.0), 2.34 (2 H, t, J = 6.0), 2.26 (2 H, t, J = 6.0), 1.58-1.49 (4 H, m)$	136.0, 120.2, 118.0, 57.3, 52.3, 26.4, 23.8, 17.5	178, 151, 110
5d	5.70 (2 H, m), 5.06 (2 H, d, $J = 15.0$), 5.01 (2 H, d, $J = 6.0$), 4.03 (2 H, q, $J = 6.0$), 2.97 (4 H, d, $J = 9.0$), 2.32 (2 H, t, $J = 6.0$), 2.20 (2 H, t, $J = 6.0$), 1.56–1.35 (4 H, m), 1.14 (3 H, t, $J = 6.0$)	174.1, 136.2, 117.8, 60.7, 57.3, 53.2, 34.7, 26.9, 23.4, 14.7	225, 184, 110
5e	5.84–5.71 (2 H, m), 5.12–5.02 (4 H, m), 2.98 (4 H, d, <i>J</i> = 6.3), 2.12 (2 H, d, <i>J</i> = 7.0), 1.72–0.74 (11 H, m)	135.2, 115.9, 59.5, 56.4, 34.9, 30.8, 25.2	193, 110, 73
5f	2.63 (4 H, m), 2.37–0.80 (19 H, m)	131.5, 117.6, 67.1, 45.5, 40.5, 40.0, 39.6, 37.8, 37.7, 32.7, 29.4, 27.2, 23.4, 22.9	246, 135, 107, 82
5g	$\begin{array}{l} 5.95-5.75\ (2\mathrm{H},\mathrm{m}), 5.16\ (2\mathrm{H},\mathrm{d},J=17.1), 5.11\ (2\mathrm{H},\mathrm{d},J=7.2), 4.12\ (2\mathrm{H},\mathrm{q},J=7.2), 3.9\ (4\mathrm{H},\mathrm{d},J=6.3),\\ 2.41\ (2\mathrm{H},\mathrm{t},J=7.2), 2.28\ (2\mathrm{H},\mathrm{t},J=7.5), 1.70-1.58\\ (2\mathrm{H},\mathrm{m}), 1.54-1.42\ (2\mathrm{H},\mathrm{m}), 1.33-1.29\ (4\mathrm{H},\mathrm{m}),\\ 1.25\ (3\mathrm{H},\mathrm{t},J=7.2) \end{array}$	174.1, 135.9, 117.8, 60.5, 57.2, 53.6, 34.7, 28.7, 27.5, 27.2, 25.3, 14.6	253, 212, 208, 110
5h	7.83 (2 H, m), 7.75 (2 H, m), 5.83 (2 H, m), 5.15 (2 H, d, $J = 18.0$), 5.10 (2 H, q, $J = 9.0$), 3.69 (2 H, t, $J = 9.0$), 3.06 (4 H, d, $J = 6.0$), 2.45 (2 H, t, $J = 6.0$), 1.71–1.64 (2 H, m), 1.52–1.47 (2 H, m)	168.8, 136.1, 134.2, 132.5, 123.5, 117.7, 57.2, 53.0, 38.3, 26.9, 24.8	298, 257, 160, 110
5i	5.79–5.68 (2 H, m), 5.12–5.03 (4 H, m), 3.51 (2 H, s), 2.97 (4 H, d, <i>J</i> = 6.3)	146.1, 135.7, 132.4, 129.2, 119.4, 118.1, 111.0, 57.5, 57.0	212, 185, 116, 89
5j	7.34–7.22 (10 H, m), 3.52 (4 H, s), 2.41 (2 H, t, <i>J</i> = 6.3), 2.10 (2 H, t, <i>J</i> = 6.9), 1.64–1.60 (4 H, m)	140.0, 129.5, 128.8, 127.4, 120.2, 58.9, 52.1, 26.3, 23.3, 16.9	278, 210, 91
5k	7.37–7.20 (10 H, m), 4.10 (2 H, q, J = 7.2), 3.53 (4 H, s), 2.39 (2 H, t, J = 7.5), 2.39 (2 H, t, J = 7.5), 1.56–1.45 (4 H, m), 1.24 (7 H, t, J = 6.0)	174.3, 140.5, 129.2, 128.6, 127.2, 60.6, 58.8, 53.7, 34.8, 29.4, 27.3, 25.4, 14.7	353, 308, 262, 210, 91
51	7.37–7.20 (10 H, m), 4.09 (2 H, q, J = 6.9), 3.53 (4 H, s), 2.41 (2 H, t, J = 6.9), 2.18 (2 H, t, J = 6.9), 1.62–1.54 (4 H, m), 1.22 (3 H, t, J = 6.9)	174.1, 140.3, 129.3, 128.6, 127.2, 60.5, 58.7, 53.2, 34.5, 26.9, 23.0, 14.7	325, 210, 91
5m	7.38–7.13 (14 H, m), 3.52 (4 H, s), 2.69 (2 H, t, <i>J</i> = 6.9), 2.61 (2 H, t, <i>J</i> = 6.9)	141, 138.2, 126–132, 118.0, 111.1, 57.4, 53.1, 32.1	324, 233, 210, 91
5n	7.24–7.08 (10 H, m), 3.44 (4 H, s), 2.31 (4 H, t, <i>J</i> = 7.5), 2.15–0.69 (15 H, m)	140.5, 129.3, 128.6, 127.2, 58.8, 52.4, 46.8, 42.0, 41.5, 39.5, 35.3, 34.1, 28.7, 27.1, 23.8, 23.0	324, 233, 210, 91, 65

^a Mass spectra were measured using electron impact ionization (EI).

-78 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH $_2$ Cl $_2$ /MeOH, 99:1) affording the product 5i (800 mg, 72%).

5-(N,N-Dibenzylamino)pentanenitrile (5j)

The reaction was carried out according to General Procedure A using a solution of 3-cyanopropylzinc iodide (9 mmol), freshly pre-

Table 5 NMR and Mass Spectral Data of Compounds 7a-f and 8a-j

Product	¹ H NMR (CDCl ₃ , 300 MHz) δ, <i>J</i> (Hz)	13 C NMR (CDCl ₃ , 75 MHz) δ	$\frac{\text{MS}^{\text{a}}}{m/z} (\%)$
7a	7.91 (2 H, d, <i>J</i> = 8.2), 7.33 (2 H, d, <i>J</i> = 8.2), 5.91–5.67 (2 H, m), 5.20–4.99 (4 H, m), 4.29 (2 H, q, <i>J</i> = 7.0), 3.53 (2 H, s), 2.99 (4 H, d, <i>J</i> = 6.5), 1.31 (3 H, t, <i>J</i> = 7.0)	167.0, 145.5, 136.0, 129.9, 129.5, 129.0, 118.0, 61.2, 57.7, 57.0, 14.7	259, 232, 163, 110, 96
7b	7.43–7.21 (4 H, m), 5.86–5.73 (2 H, m), 5.15–5.02 (4 H, m), 3.62–3.56 (2 H, m), 3.50 (2 H, s), 3.27–3.12 (2 H, m), 3.00 (2 H, d, <i>J</i> = 6.3), 1.60–1.29 (6 H, m)	170.4, 141.1, 135.7, 135.1, 128.8, 126.9, 117.5, 57.2, 56.5, 48.8, 43.2, 26.5, 24.7	298, 271, 202, 174, 110, 96, 69
7c	5.83–5.70 (2 H, m), 5.15–5.04 (4 H, m), 4.06 (2 H, t, <i>J</i> = 6.0), 3.07 (4 H, d, <i>J</i> = 6.3), 2.64 (2 H, t, <i>J</i> = 6.0), 1.13 (9 H, s)	178.6, 135.8, 117.5, 62.8, 57.4, 51.5, 38.8, 27.3	184, 129, 110, 57
7d	5.83-5.69 (2 H, m), $5.14-5.04$ (4 H, m), 4.06 (2 H, t, $J = 6.2$), 3.07 (4 H, d, $J = 6.3$), 2.63 (2 H, t, $J = 6.2$), 2.22 (1 H, m), $1.84-1.16$ (10 H, m)	176.3, 136.0, 117.8, 62.6, 57.7, 51.8, 43.5, 29.4, 26.1, 25.8	210, 122, 110, 83, 81
7e	7.72 (2 H, dd, $J = 10.8$, 1.5), 7.60 (1 H, dd, $J = 10.8$, 1.5), 7.41 (1 H, t, $J = 10.8$), 7.26 (1 H, t, $J = 10.8$), 5.89–5.80 (2 H, m), 5.18 (2 H, d, $J = 17.1$), 5.10 (2 H, d, $J = 10.2$), 4.33 (2 H, q, $J = 7.2$), 3.88 (2 H, s), 3.07 (4 H, dt, $J = 6.3$, 1.2), 1.38 (3 H, t, $J = 7.2$)	168.7, 141.4, 136.1, 131.8, 131.5, 130.0, 126.9, 117.5, 61.2, 56.8, 56.0, 14.7	258, 218, 173, 172, 110
8a	7.54–7.39 (4 H, m), 3.01 (2 H, t, <i>J</i> = 6.5), 2.80 (2 H, t, <i>J</i> = 6.5), 1.47 (2 H, br s)	140.4, 132.4, 131.3, 129.0, 128.2, 117.9 , 111.4, 41.7, 38.5	145, 128, 117, 89, 75, 63
8b	2.27 (2 H, t, <i>J</i> = 6.6), 2.39 (2 H, t, <i>J</i> = 6.6), 1.79–1.57 (4 H, m)	127.3, 48.8, 40.1, 30.5, 24.7	98
8c	6.79 (1 H, br s), 3.25 (2 H, m), 2.29 (2 H, t, <i>J</i> = 6.0), 1.78–1.69 (4 H, m)	171.6, 41.2, 30.5, 21.3, 19.9	99
8d	2.63 (m, 4 H), 2.37–0.80 (13 H, m)	131.5, 117.6, 67.1, 45.5, 40.5, 40.0, 39.6, 37.8, 37.7, 32.7, 29.4, 27.2, 23.4, 22.9	246, 135, 107, 82
8e	4.15 (2 H, q, J = 7.1), 2.98 (6 H, t, J = 7.5), 2.37 (3 H, t, J = 7.1), 2.35 (3 H, t, J = 7.2), 1.28 (3 H, t, J = 7.1) ^b	$176.1, 60.0, 39.3, 33.3, 26.9, 25.7, 24.3, 22.1, \\13.2^{b}$	174, 146°
8f	7.55–7.36 (4 H, m), 3.88 (2 H, s), 2.21 (2 H, br s),	147.3, 130.9, 126.7, 117.9, 109.6, 44.9	132, 104, 77
8g	7.25 (4 H, s), 3.77 (2 H, s), 3.65–3.40 (2 H, m), 3.40– 3.10 (2 H, m), 2.13 (2 H, s), 1.70–1.30 (6 H, m)	170.5, 144.5, 135.2, 127.3, 49.0, 46.2, 43.4, 26.7, 26.0, 24.8	217, 134, 105, 89
8h	3.75–3.50 (2 H, m), 3.50–3.25 (2 H, m), 2.20–2.00 (1 H, m), 1.95–1.00 (10 H, m)	178.0, 62.2, 45.8. 42.6, 45.8, 30.0, 26.1	171, 153, 141, 128, 111, 83
8i	8.25 (1 H, br s), 7.80 (1 H, m), 7.51–7.37 (3 H, m), 4.40 (2 H, s)	171.4, 142.7, 131.3, 130.7, 126.9, 122.6, 122.2, 44.8	133, 132, 105, 104, 77
8j	7.46 (1 H, d, <i>J</i> = 3.7), 6.83 (1 H, d, <i>J</i> = 3.7), 4.26 (2 H, q, <i>J</i> = 7.2), 4.00 (2 H, s), 1.31 (3 H, t, <i>J</i> = 10.9)	161.3, 154.0, 133.9, 131.3, 129.2, 60.0, 14.7	184, 155, 140, 112, 78

^a Mass spectra were measured using electron impact ionization (EI).

^b ¹H and ¹³C NMR spectra were recorded in CD₃OD.

^c Mass spectrum was measured using Fast Atom Bombardment desorption (FAB).

pared from 3-iodopropionitrile (1.75 g, 9 mmol) and activated zinc foil (1.76 g, 27 mmol) in THF (4 mL), and a solution of **2** (6 mmol) in Et₂O (12 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 100:0) affording the product **5j** (1.28 g, 77%).

Ethyl 5-(N,N-Dibenzylamino)pentanoate (5k)

The reaction was carried out according to General Procedure A using a solution of 4-carboethoxypropylzinc iodide (9 mmol), freshly prepared from ethyl 4-iodobutanoate (2.18 g, 9 mmol) and activated zinc foil (1.76 g, 27 mmol) in THF (4 mL), and a solution of **2** (6 mmol) in Et₂O (4 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 100:0 to 95:5) affording the product **5k** (1.46 g, 74%).

Ethyl 7-(N,N-Dibenzylamino)heptanoate (5l)

The reaction was carried out according to General Procedure A using a solution of 6-carboethoxyhexylzinc iodide (10 mmol), freshly prepared from ethyl 6-iodoheptanoate (2.70 g, 10 mmol) and activated zinc foil (2.0 g, 30 mmol) in THF (5 mL), and a solution of **2**

(7 mmol) in Et₂O (14 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 100:0 to 96:4) affording the product **5l** (1.90 g, 77%).

3-[2-(N,N-Dibenzylamino)ethyl]benzonitrile (5m)

The reaction was carried out according to General Procedure A using 3-cyanobenzylzinc bromide (11.7 mmol), freshly prepared from 3-bromomethylbenzonitrile (8.7 g, 40 mmol) and activated zinc foil (8.6 g, 130 mmol) in THF (40 mL), and a solution of **2** (10.0 mmol) in Et₂O (20 mL) at -78 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 100:0) affording the product **5m** (3.0 g, 92%).

N-Myrtanylmethyl-N,N-dibenzylamine (5n)

The reaction was carried out according to General Procedure A using dimyrtanylzinc (4.0 mmol), freshly prepared from (-)- β -pinene (16 mL, 0.10 mol), BH₃,SMe₂ (3 mL, 0.03 mol) and Et₂Zn (12 mL, 0.12 mol) in THF (40 mL), and a solution of **2** (3.6 mmol) in Et₂O (10 mL) at 25 °C. After workup the crude residue was purified by flash chromatography on silica gel (pentane/Et₂O, 98:2) affording the product **5n** (910 mg, 73%).

Aminomethylation of Functionalized Magnesium Reagents Affording the Amines (7); General Procedure B

A solution of immonium trifluoroacetate (lequiv) in CH_2Cl_2 was added at the temperature indicated in the Table 2 to a solution of the functionalized organomagnesium reagent (1.25 equiv) in THF. After stirring for 30 min, the reaction was quenched with sat. aq Na_2CO_3 (or NH_4Cl) and extracted with CH_2Cl_2 or Et_2O . The combined organic layers were washed with H_2O , brine and dried (MgSO₄). The products were isolated after evaporation of the solvents and purification by flash-chromatography on silica gel. The NMR and mass spectral data of compounds **7a-f** are shown in Table 5.

Ethyl 4-(N,N-Diallylaminomethyl)benzoate (7a)

The reaction was carried out according to General Procedure B using a solution of **6a** (3.0 mmol), freshly prepared from ethyl 4-iodobenzoate (0.83 g, 3.0 mmol) and *i*-PrMgBr (3.3 mmol) in THF/NBP (*N*-butylpyrrolidinone) (5:1 mixture, 6 mL), and a solution of **1** (2.4 mmol) in CH₂Cl₂ (5 mL) at -60 °C. After workup the crude residue was purified by flash chromatography on silica gel (pentane/Et₂O, 9:1) affording the product **7a** (470 mg, 70%).

Piperidino 4-(N,N-Diallylaminomethyl)benzoate (7b)

The reaction was carried out according to General Procedure B using a solution of **6b** (3.0 mmol), freshly prepared from piperidino-4-iodobenzoate (0.95 g, 3.0 mmol) and *i*-PrMgBr (3.3 mmol) in THF/NBP (5:1 mixture, 6 mL), and a solution of **1** (2.4 mmol) in CH₂Cl₂ (5 mL) at -60 °C. After workup the crude residue was purified by flash chromatography on silica gel (pentane/Et₂O, 8:2) affording the product **7b** (580 mg, 81%).

2-(N,N-Diallylamino)ethyl Pivalate (7c)

The reaction was carried out according to General Procedure B using a solution of **6c** (3.0 mmol), freshly prepared from 2-iodomethylpivalate (0.72 g, 3.0 mmol) and *i*-PrMgBr (3.3 mmol) in THF/ NBP (5:1 mixture, 6 mL), and a solution of **1** (2.4 mmol) in CH₂Cl₂ (5 mL) at -78 °C. After workup the crude residue was purified by flash chromatography on silica gel (pentane/Et₂O, 9:1) affording the product **7c** (380 mg, 74%).

2-(N,N-Diallylamino)ethylcyclohexancarboxylate (7d)

The reaction was carried out according to General Procedure B using a solution of **6d** (3.0 mmol), freshly prepared from 2-iodoethyl-1-cyclohexane carboxylate (0.85 g, 3.0 mmol) and *i*-PrMgBr (3.3 mmol) in THF/NBP (5:1 mixture, 6 mL), and a solution of **1** (2.4 mmol) in CH₂Cl₂ (5 mL) at -78 °C. After workup the crude residue was purified by flash chromatography on silica gel (pentane/Et₂O, 7:3) affording the product **7d** (500 mg, 82%).

Ethyl 2-(N,N-Diallylaminomethyl)benzoate (7e)

The reaction was carried out according to General Procedure B using a solution of **6e** (10.0 mmol), freshly prepared from ethyl 2-io-dobenzoate (2.76 g, 10.0 mmol) and *i*-PrMgCl 0.8 M THF solution (13 mL, 10.5 mmol) in THF (20 mL), and a solution of **1** (7.0 mmol) in CH₂Cl₂ (14 mL) at -40 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 99:1) affording the product **7e** (1.37 g, 76%).

Ethyl 5-(N,N-Diallylaminomethyl)-2-thiophencarboxylate (7f)

The reaction was carried out according to General Procedure B using **6f** (7.7 mmol), freshly prepared from (1.8 g, 7.7 mmol) and *i*-PrMgBr (0.8 M THF solution, 11 mL, 8.8 mmol) in THF (12 mL), and a solution of **1** (4.9 mmol) in CH₂Cl₂ (10 mL) at -40 °C. After workup the crude residue was purified by flash chromatography on silica gel (CH₂Cl₂/MeOH, 100:0) affording the product **7f** (1.0 g, 77%).

Deprotection of Functionalized Diallylamines 8; General Procedure C

A solution of diallylamine **5** or **7** (1 equiv) in CH₂Cl₂ (2.5 mL/ equiv) was added to *N*,*N*'-dimethylbarbituric acid (6 equiv) and Pd(PPh₃)₄ (0.02 equiv). The mixture was stirred at 35 °C for 1 to 3 h. After cooling to r.t., the solvents were evaporated and the residue dissolved with a 1:1 mixture of Et₂O and 1 N HCl. The aqueous layer was extracted three times with Et₂O and basified with a sat. aq solution of Na₂CO₃. The amine was extracted 6 to 9 times with CH₂Cl₂. The product was isolated after drying (MgSO₄), filtration and evaporation of the solvents. In the case of **8e**, Guibé's workup¹² was used to isolate the product. The NMR and mass spectral data of compounds **8a–j** are given in Table 5.

3-(2-Aminoethyl)benzonitrile (8a)

The reaction was carried out according to General Procedure C using **5b** (0.45 g, 2.0 mmol) in CH_2Cl_2 (5 mL) containing *N*,*N*'-dimethylbarbituric acid (1.86 g, 11.9 mmol) and Pd(PPh₃)₄ (69 mg, 0.06 mmol). The product was isolated as an oil (182 mg, 63%).

5-Aminopentanenitrile (8b)

The reaction was carried out according to General Procedure C using **5c** (0.18 g, 1.0 mmol) in CH₂Cl₂ (2.5 mL) containing *N*,*N*'-dimethylbarbituric acid (0.94 g, 6.0 mmol) and Pd(PPh₃)₄ (23 mg, 0.02 mmol). The product was isolated as an oil (58 mg, 59%).

2-Piperidinone (8c)

The reaction was carried out according to General Procedure C using **5d** (0.31 g, 1.4 mmol) in CH₂Cl₂ (3.5 mL) containing *N*,*N*'-dimethylbarbituric acid (1.32 g, 8.4 mmol) and Pd(PPh₃)₄ (32 mg, 0.03 mmol). The product was isolated as an oil (79 mg, 57%).

Myrtanylmethylamine (8d)

The reaction was carried out according to General Procedure C using **5f** (0.40 g, 1.6 mmol) in CH₂Cl₂ (3 mL), *N*,*N*'-dimethylbarbituric acid (1.58 g, 10.0 mmol) and Pd(PPh₃)₄ (50 mg, 0.04 mmol). The product was isolated as an oil (200 mg, 74%).

Ethyl 7-Aminoheptanoate (8e)

The reaction was carried out according to General Procedure C using **5g** (0.17 g, 1.0 mmol) in CH₂Cl₂ (3 mL), *N*,*N*'-dimethylbarbituric acid (0.94 g, 6.0 mmol) and Pd(PPh₃)₄ (23 mg, 0.02 mmol). Using Guibé's workup,¹² the product was isolated as a solid (143 mg, 71%).

4-Aminomethylbenzonitrile (8f)

The reaction was carried out according to General Procedure C using **5i** (0.40 g, 1.9 mmol) in CH_2Cl_2 (5 mL), *N*,*N*'-dimethylbarbituric acid (1.86 g, 11.9 mmol) and Pd(PPh₃)₄ (46 mg, 0.04 mmol). The product was isolated as an oil (200 mg, 80%).

Piperidino 4-Aminomethylbenzoate (8g)

The reaction was carried out according to General Procedure C using **7b** (0.60 g, 2 mmol) in CH_2Cl_2 (5 mL), *N*,*N*'-dimethylbarbituric

acid (1.88 g, 12.0 mmol) and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol). The product was isolated as an oil (380 mg, 87%).

2-Aminoethylcyclohexancarboxylate (8h)

The reaction was carried out according to General Procedure C using **7d** (0.30 g, 1.2 mmol) in CH₂Cl₂ (3 mL), *N*,*N*'-dimethylbarbituric acid (1.12 g, 7.2 mmol) and Pd(PPh₃)₄ (28 mg, 0.02 mmol). The product was isolated as an oil (119 mg, 62%).

Isoindolin-1-one (8i)

The reaction was carried out according to General Procedure C using **7e** (0.50 g, 1.9 mmol) in CH₂Cl₂ (5 mL), *N*,*N*'-dimethylbarbituric acid (1.80 g, 11.6 mmol) and Pd(PPh₃)₄ (45 mg, 0.04 mmol). The product was isolated as an oil (125 mg, 50%).

Ethyl 5-Aminomethyl-2-thiophencarboxylate (8j)

The reaction was carried out according to General Procedure C using **7f** (0.29 g, 1.1 mmol) in CH₂Cl₂ (3 mL), *N*,*N*'-dimethylbarbituric acid (1.06 g, 6.8 mmol) and Pd(PPh₃)₄ (30 mg, 0.03 mmol). The product was isolated as a solid (122 mg, 60%).

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