

Article

Metal-Free Regiodivergent Addition of Carbon Nucleophiles to α,β -Unsaturated Electrophiles

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Abstract: A mild and metal-free regiodivergent addition of carbon nucleophiles to α,β -unsaturated electrophiles was developed. Total 1,2-regioselectivity was observed in the addition of nitrobenzyl chloride derivative **1** to α,β -unsaturated aldehydes **2** in the presence of TDAE. Moreover, the reaction between *p*-nitrobenzyl chloride **1a** and α,β -unsaturated iminium salts **4** led to the formation of the 1,4-adduct with total regioselectivity.

Keywords: metal-free; regiodivergent; α,β -unsaturated electrophiles

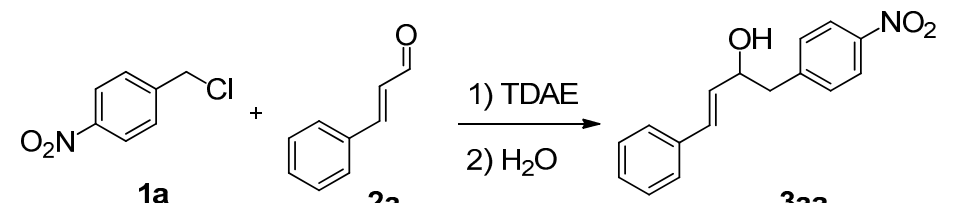
1. Introduction

The conjugate addition of carbanions to α,β -unsaturated carbonyl compounds is one of the most fundamental carbon–carbon bond-forming reactions in organic synthesis [1–6]. When a carbon nucleophile is added to α,β -unsaturated aldehydes, it can lead to 1,2-addition or 1,4-addition. This depends on several factors, such as the nature of both organometallic species and substrates. As a general rule, organolithiums are considered the best reagents to promote 1,2-addition, whereas organocuprates predominantly promote conjugate addition.

Tetrakis(dimethylamino)ethylene (TDAE) is an organic reducing agent that reacts with halogenated derivatives to generate a carbanion under mild conditions via a charge transfer complex [7–9]. In particular, we have shown that from *o*- and *p*-nitrobenzyl chlorides, tetrakis(dimethylamino)ethylene (TDAE) is able to generate a nitrobenzyl carbanion that can react with various electrophiles such as aromatic aldehydes, α -ketoester, ketomalonate, α -ketolactam, and imine derivatives [10–18]. More recently, we showed that using TDAE for the regioselective addition of *p*-nitrobenzyl chloride or 2,3-bis(bromomethyl)quinoxaline to α,β -unsaturated tosylimines allowed the synthesis of allylamines in good yields and with total 1,2-regioselectivity [19]. Here, our aim was to determine how the carbanion generated by our metal-free conditions would react in the presence of α,β -unsaturated aldehydes.

2. Results and Discussion

First, the reaction between *p*-nitrobenzyl chloride **1a** and *trans*-cinnamaldehyde **2a** in the presence of TDAE was selected as a model (Table 1). Using 1 equivalent of *p*-nitrobenzyl chloride **1a**, 1 equivalent of TDAE and 1.2 equivalent of *trans*-cinnamaldehyde **2a** in acetonitrile gave a low 33% yield of compound **3aa** (Entry 1). Interestingly, however, total 1,2-regioselectivity was observed. Using two equivalents of aldehyde allowed the synthesis of **3aa** in 48% yield (Entry 2). Using DMF instead of acetonitrile or changing the order of addition slightly decreased the reactivity (Entry 3 and 4). A better 53% yield was obtained using two equivalents of *p*-nitrobenzyl chloride **1a**, two equivalents of TDAE, and one equivalent of *trans*-cinnamaldehyde **2a** (Entry 5).

Table 1. Optimization of the 1,2-addition of *p*-nitrobenzyl chloride **1a** to *trans*-cinnamaldehyde **2a** in the presence of TDAE ^a.


Entry	1a (Equiv)	2a (Equiv)	TDAE (Equiv)	Solvent	Yield of 3aa (%) ^b
1	1	1.2	1	MeCN	33
2	1	2	1	MeCN	48
3	1	2	1	DMF	42
4	1	2	1	MeCN	37 ^c
5	2	1	2	MeCN	53
6	2	1	2	MeCN	55 ^d
7	3	1	3	MeCN	62 ^d
8	3	1	3	MeCN	67 ^{d,e}
9	3	1	3	MeCN	71 ^{d,f}

^a Reaction conditions (unless otherwise specified): under nitrogen atmosphere, to a solution of **2a** was added TDAE followed by addition of a solution of **1a**. Reactions were stirred at $-20\text{ }^{\circ}\text{C}$ for 1 h and then maintained at room temperature for 2 h; ^b Isolated yields; ^c To a solution of **2a** and **1a** was added TDAE; ^d Reactions were performed at room temperature for 2 h; ^e A first 1.5 equiv of TDAE followed by 1.5 equiv of **1a** were added to a solution of **2a**. 1 h later, another 1.5 equiv of TDAE followed by 1.5 equiv of **1a** were added; ^f Solution of **1a** was added over 30 min.

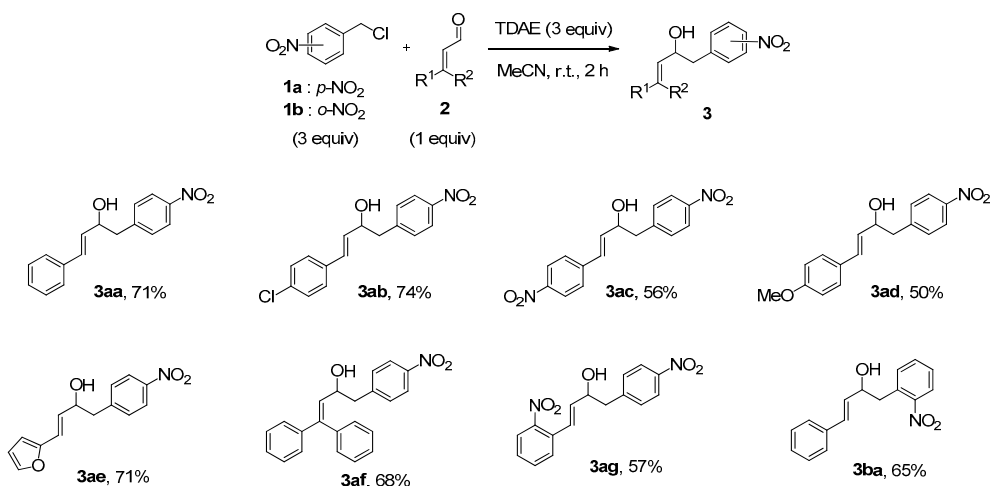
Interestingly, there is no need to decrease temperature to $-20\text{ }^{\circ}\text{C}$, as the yield was slightly better at room temperature (Entry 6). More equivalents of **1a** and TDAE were beneficial to the reaction (Entry 7). A sequential addition of both *p*-nitrobenzyl chloride **1a** and TDAE afforded alcohol **3aa** in a good 67% yield (Entry 8). So, the best reaction conditions were three equivalents of *p*-nitrobenzyl chloride **1a**, three equivalents of TDAE, and one equivalent of *trans*-cinnamaldehyde **2a** in acetonitrile at room temperature, with slow addition of **1a** over 30 min (Entry 9).

With the optimized conditions in hand, we next investigated the generality and scope of the reaction with a series of α,β -unsaturated aldehydes **2a–g** (Scheme 1). Both electron-poor (**3ab** and **3ac**) and electron-rich substituents (**3ad**) gave good yields and total 1,2-regioselectivities. Interestingly, the reaction conditions are tolerant towards the formation of alcohol **3ae** from heteroaromatic aldehyde **2e**.

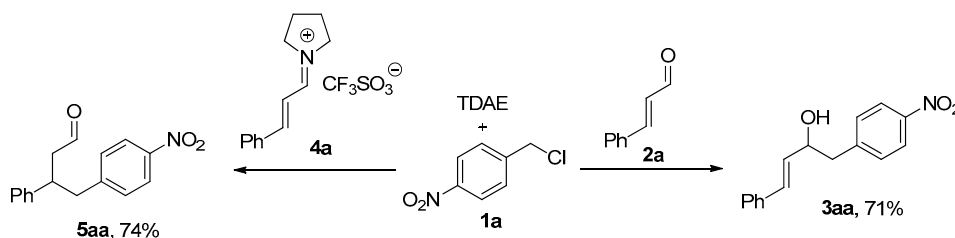
Moreover, the more bulky β -disubstituted aldehyde **2f** gave only the product of 1,2-addition **3af** in 68% yield. Ortho substituents on the aldehyde (**3ag**) and on the benzyl chloride derivative (**3ba**) were both well tolerated.

Thus, in all cases, the carbanion generated by our metal-free conditions gave only the 1,2-regioisomer when reacting with α,β -unsaturated aldehydes. Could the reactivity be changed from 1,2 to 1,4-addition? As organocuprates predominantly promote conjugate addition, we tested different conditions using copper salts but no reaction occurred, probably due to problems of compatibility between TDAE and copper derivatives.

To our satisfaction, however, using α,β -unsaturated iminium salts instead of aldehydes completely changed the regioselectivity of the addition. Indeed, the reaction between *p*-nitrobenzyl chloride **1a** and (*E*)-1-(3-phenylallylidene)pyrrolidin-1-ium **4a** in the presence of TDAE led to the formation of the 1,4-adduct **5aa** alone, in a very good 74% yield (Scheme 2).



Scheme 1. Regioselective 1,2-addition of nitrobenzyl chloride derivative **1** to various cinnamaldehyde **2** in the presence of TDAE.

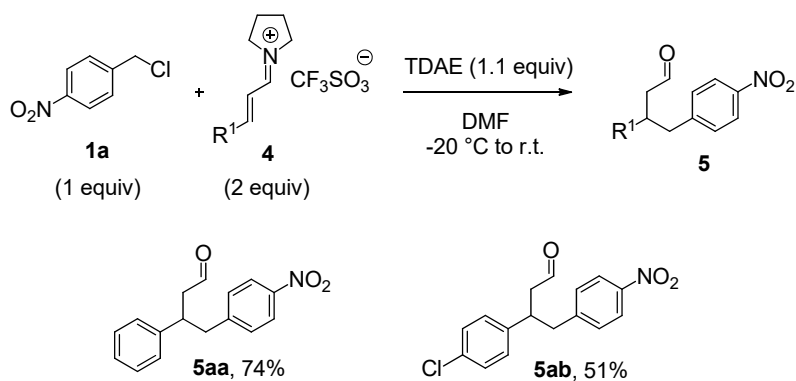


Scheme 2. Regiodivergent addition of *p*-nitrobenzyl chloride **1a** to α,β -unsaturated electrophiles.

A general feature that emerges from the ^{13}C -NMR studies of unsaturated imines is the observed downfield shift (ca. 5–10 ppm) at C^3 in iminium salts compared to the parent unsaturated aldehydes. This feature might reflect the increased electrophilicity of the iminium cation at C^3 compared to the parent aldehyde [20].

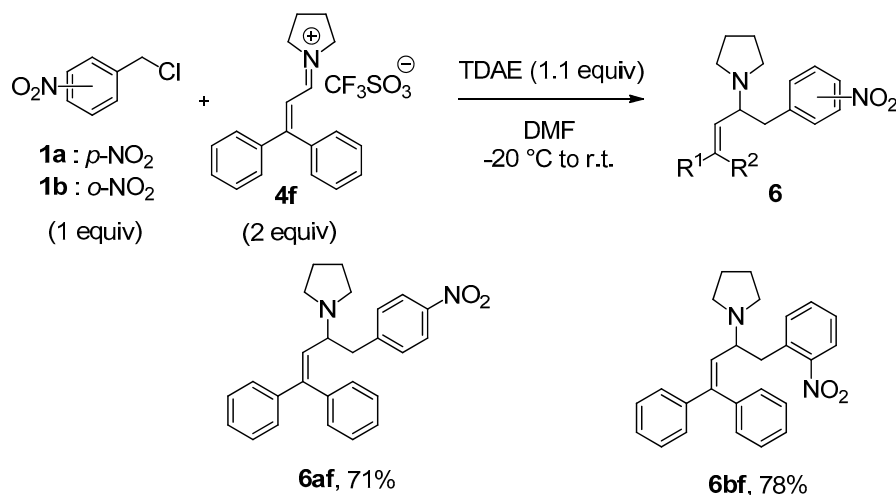
This metal-free controlled regiodivergence is of great interest, because the same *p*-nitrobenzyl chloride **1a** can lead to the formation of both 1,2 and 1,4-adduct without requiring metallic species like organolithiums for 1,2-addition or organocuprates for 1,4-addition.

We next investigated the possibility of using another α,β -unsaturated iminium salt **4b** (Scheme 3). Here, too, total 1,4-regioselectivity was observed and allowed the synthesis of the aldehyde **5ab** in 51% yield.



Scheme 3. Regioselective 1,4-addition of *p*-nitrobenzyl chloride **1a** to α,β -unsaturated iminium salt **4** in the presence of TDAE.

By contrast with the previous examples, the reaction between *p*-nitrobenzyl chloride **1a** and the more bulky β -disubstituted iminium salt **4f** gave only the 1,2-adduct **6af**, probably due to steric hindrance at the β -position (Scheme 4). We next turned our attention to the use of *o*-nitrobenzyl chloride **1b** instead of *p*-nitrobenzyl chloride **1a**. As expected, the reaction between *o*-nitrobenzyl chloride **1b** and the bulky β -disubstituted iminium salt **4f** also gave only the 1,2-adduct **6bf** with a very good 78% yield.



Scheme 4. Regioselective 1,2-addition of nitrobenzyl chloride derivative **1** to bulky α,β -unsaturated iminium salt **4f** in the presence of TDAE.

3. Experimental Section

3.1. General

Melting points were determined on a Büchi melting point B-540 apparatus (BÜCHI Labortechnik AG, Flawil, Switzerland) and are uncorrected. Element analyses were performed on a Thermo Finnigan EA1112 (San Jose, CA, USA) at the spectropole of Aix-Marseille University. Both ¹H- and ¹³C-NMR spectra were determined on a Bruker AC 250 spectrometer (Wissembourg, France) at the Service de RMN de la Faculté de Pharmacie de Marseille of the Aix-Marseille University. The ¹H and the ¹³C chemical shifts are reported from CDCl₃ peaks: ¹H (7.26 ppm) and ¹³C (77.16 ppm). Multiplicities are represented by the following notations: s, singlet; d, doublet; t, triplet; q, quartet; m, a more complex multiplet or overlapping multiplets. The following adsorbents were used for column chromatography: Silica gel 60 (Merck, Darmstadt, Germany, particle size 0.063–0.200 mm, 70–230 mesh ASTM). TLC was performed on 5 × 10 cm aluminum plates coated with silica gel 60 F₂₅₄ (Merck, Darmstadt, Germany) in an appropriate solvent.

3.2. General Procedure for the Synthesis of Alcohols **3**

Under nitrogen atmosphere at room temperature, to a stirred solution of α,β -unsaturated aldehydes **2** (0.2 mmol) in MeCN (1 mL) was added TDAE (140 μ L, 0.6 mmol) followed by addition of a solution of the nitrobenzyl chloride derivative **1** (103 mg, 0.6 mmol) in MeCN (1 mL) over 30 min. Reactions were stirred at RT for 2 h. Water (10 mL) was added and the aqueous solution was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layer was washed with brine (20 mL) and dried over MgSO₄. Evaporation of the solvent furnished the crude product. Purification by silica gel chromatography (PE/EtOAc: From 9/1 to 6/4 depending on the polarity of substrates) afforded pure alcohol products **3**.

The general procedure was followed with **2a** (26 mg) and **1a** (130 mg). (*E*)-1-(4-nitrophenyl)-4-phenylbut-3-en-2-ol (**3aa**). 71% yield; yellow solid; m.p. 94–96 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.16 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.35–7.26 (m, 5H), 6.58 (d, *J* = 15.9 Hz, 1H), 6.24 (dd, *J* = 15.9, 6.6 Hz, 1H), 4.61–4.53 (m, 1H), 3.03 (d, *J* = 5.5 Hz, 2H), 1.93 (s, 1H). ¹³C-NMR (63 MHz, CDCl₃) δ 146.8, 145.9, 136.2, 131.4, 130.8, 130.6, 128.8, 128.1, 126.6, 123.7, 73.3, 43.7; HRMS (ESI): *m/z* [M + Na]⁺ calcd. for [C₁₆H₁₅NO₃Na]⁺: 292.0944; found: 292.0945.

The general procedure was followed with **2b** (33 mg) and **1a** (130 mg). (*E*)-4-(4-chlorophenyl)-1-(4-nitrophenyl)but-3-en-2-ol (**3ab**). 74% yield; yellow solid; m.p. 112–114 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.17 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.28–7.24 (m, 4H), 6.53 (d, *J* = 15.9 Hz, 1H), 6.22 (dd, *J* = 15.9, 6.5 Hz, 1H), 4.60–4.53 (m, 1H), 3.04–3.01 (m, 2H), 1.78 (s, 1H). ¹³C-NMR (63 MHz, CDCl₃) δ 146.9, 145.8, 134.8, 133.8, 131.4, 130.6, 130.1, 129.0, 127.8, 123.7, 73.2, 43.7; HRMS (ESI): *m/z* [M + Na]⁺ calcd. for [C₁₆H₁₄NO₃ClNa]⁺: 326.0554; found: 326.0555.

The general procedure was followed with **2c** (35 mg) and **1a** (130 mg). (*E*)-1,4-bis(4-nitrophenyl)but-3-en-2-ol (**3ac**). 56% yield; yellow solid; m.p. 111–113 °C; ¹H-NMR (250 MHz, DMSO) δ 8.19–8.13 (m, 4H), 7.68 (d, *J* = 8.9 Hz, 2H), 7.54 (d, *J* = 8.7 Hz, 2H), 6.66 (s, 2H), 5.36 (s, 1H), 4.49 (s, 1H), 3.03 (dd, *J* = 13.4, 5.1 Hz, 1H), 2.90 (dd, *J* = 13.4, 7.7 Hz, 1H). ¹³C-NMR (63 MHz, DMSO) δ 147.3, 146.2, 146.0, 143.6, 138.7, 130.9, 127.2, 126.8, 124.0, 123.1, 71.1, 42.9; HRMS (ESI): *m/z* [M + Na]⁺ calcd. for [C₁₆H₁₄N₂O₅Na]⁺: 337.0795; found: 337.0797.

The general procedure was followed with **2d** (32 mg) and **1a** (130 mg). (*E*)-4-(4-methoxyphenyl)-1-(4-nitrophenyl)but-3-en-2-ol (**3ad**). 50% yield; yellow solid; m.p. 115–117 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.17 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.09 (dd, *J* = 15.9, 6.9 Hz, 1H), 4.58–4.51 (m, 1H), 3.81 (s, 3H), 3.03 (d, *J* = 5.7 Hz, 2H), 1.68 (s, 1H). ¹³C-NMR (63 MHz, CDCl₃) δ 159.7, 146.9, 146.1, 131.1, 130.6, 128.9, 128.5, 127.9, 123.7, 114.2, 73.6, 55.5, 43.8; HRMS (ESI): *m/z* [M + Na]⁺ calcd. for [C₁₇H₁₇NO₄Na]⁺: 322.1050; found: 322.1050.

The general procedure was followed with **2e** (24 mg) and **1a** (130 mg). (*E*)-4-(furan-2-yl)-1-(4-nitrophenyl)but-3-en-2-ol (**3ae**). 71% yield; yellow solid; m.p. 67–69 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.17 (d, *J* = 8.2 Hz, 2H), 7.44–7.36 (m, 3H), 6.44–6.38 (m, 2H), 6.25–6.14 (m, 2H), 4.55–4.50 (m, 1H), 3.08–2.99 (m, 2H), 1.72 (s, 1H). ¹³C-NMR (63 MHz, CDCl₃) δ 151.9, 146.9, 145.8, 142.5, 130.6, 129.2, 123.7, 119.6, 111.5, 108.9, 72.9, 43.7; HRMS (ESI): *m/z* [M + Na]⁺ calcd. for [C₁₄H₁₃NO₄Na]⁺: 282.0737; found: 282.0738.

The general procedure was followed with **2f** (42 mg) and **1a** (130 mg). 1-(4-nitrophenyl)-4,4-diphenylbut-3-en-2-ol (**3af**). 68% yield; yellow solid; m.p. 93–95 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.11 (d, *J* = 8.6 Hz, 2H), 7.35–7.17 (m, 10H), 7.01–6.98 (m, 2H), 6.08 (d, *J* = 9.2 Hz, 1H), 4.50–4.41 (m, 1H), 3.07–2.98 (m, 2H), 1.70 (s, 1H). ¹³C-NMR (63 MHz, CDCl₃) δ 146.8, 145.9, 144.6, 141.2, 139.0, 130.6, 129.44, 129.41, 128.5, 128.4, 128.1, 127.8, 127.5, 123.6, 70.3, 43.8; HRMS (ESI): *m/z* [M + Na]⁺ calcd. for [C₂₂H₁₉NO₃Na]⁺: 368.1257; found: 368.1255.

The general procedure was followed with **2g** (35 mg) and **1a** (130 mg). (*E*)-4-(2-nitrophenyl)-1-(4-nitrophenyl)but-3-en-2-ol (**3ag**). 57% yield; yellow solid; m.p. 118–120 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.17 (d, *J* = 8.7 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.61–7.50 (m, 2H), 7.46–7.38 (m, 3H), 7.05 (d, *J* = 15.7 Hz, 1H), 6.19 (dd, *J* = 15.7, 6.4 Hz, 1H), 4.68–4.60 (m, 1H), 3.07–3.04 (m, 2H), 1.97 (s, 1H). ¹³C-NMR (63 MHz, CDCl₃) δ 148.0, 147.0, 145.5, 136.2, 133.4, 132.3, 130.6, 128.9, 128.6, 126.8, 124.8, 123.8, 72.8, 43.4; HRMS (ESI): *m/z* [M + Na]⁺ calcd. for [C₁₆H₁₄N₂O₅Na]⁺: 337.0795; found: 337.0794.

The general procedure was followed with **2a** (26 mg) and **1b** (130 mg). (*E*)-1-(2-nitrophenyl)-4-phenylbut-3-en-2-ol (**3ba**). 65% yield; yellow solid; m.p. 69–70 °C; ¹H-NMR (250 MHz, CDCl₃) δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.48–7.16 (m, 8H), 6.50 (d, *J* = 15.8 Hz, 1H), 6.20 (dd, *J* = 15.9, 6.4 Hz, 1H), 4.56–4.49 (m, 1H), 3.23 (dd, *J* = 13.6, 4.4 Hz, 1H), 3.06 (dd, *J* = 13.6, 8.2 Hz, 1H), 1.94 (s, 1H). ¹³C-NMR

(63 MHz, CDCl₃) δ 150.0, 136.5, 133.6, 133.2, 132.9, 131.2, 130.9, 128.7, 128.0, 127.8, 126.7, 124.9, 73.0, 40.8; HRMS (ESI): m/z [M + Na]⁺ calcd. for [C₁₆H₁₅NO₃Na]⁺: 292.0944; found: 292.0945.

3.3. General Procedure for the Synthesis of Iminium Salts 4

Compound **4a** was synthesized according to a previously described procedure and experimental data are in accordance with the literature [21].

An aqueous solution of CF₃SO₃H (4.00 g in 20 mL of water, 27.0 mmol) was added to a solution of α,β -unsaturated aldehyde **2** (27.0 mmol) and pyrrolidine (2.25 mL, 27.0 mmol) in diethyl ether (25 mL). After 1 h, the organic phase was separated. The aqueous phase was extracted with CH₂Cl₂ (15 mL). The organic layers were combined, washed with brine, and dried (MgSO₄). After evaporation of the solvent under vacuum, the residue was mixed with Et₂O. The solvent was removed under vacuum, and then the residue was remixed with Et₂O. This cycle was repeated several times until iminium salt **4** was obtained as a solid.

The general procedure was followed with **2b** (4.5 g). (*E*)-1-(3-(4-chlorophenyl)allylidene)pyrrolidin-1-ium trifluoromethanesulfonate (**4b**). 38% yield; white solid; m.p. 106–108 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.82 (d, J = 10.5 Hz, 1H), 7.86 (d, J = 15.3 Hz, 1H), 7.63 (d, J = 8.6 Hz, 2H), 7.35 (d, J = 8.6 Hz, 2H), 7.08 (dd, J = 15.3, 10.5 Hz, 1H), 4.15–4.01 (m, 4H), 2.21–2.06 (m, 4H). ¹³C-NMR (63 MHz, CDCl₃) δ 166.6, 159.4, 139.9, 132.0, 131.7, 129.8, 120.8 ($J_{C,F}$ = 321 Hz), 117.9, 57.4, 52.1, 24.7, 24.5; HRMS (ESI): m/z [M]⁺ calcd. for [C₁₃H₁₅ClN]⁺: 220.0888; found: 220.0892.

The general procedure was followed with **2f** (5.6 g). 1-(3,3-diphenylallylidene)pyrrolidin-1-ium trifluoromethanesulfonate (**4f**). 65% yield; light-blue solid; m.p. 136–138 °C; ¹H-NMR (250 MHz, CDCl₃) δ 8.01 (d, J = 10.8 Hz, 1H), 7.58–7.35 (m, 10H), 6.90 (d, J = 10.8 Hz, 1H), 4.18–4.07 (m, 4H), 2.28–2.13 (m, 4H). ¹³C-NMR (63 MHz, CDCl₃) δ 171.6, 162.5, 139.1, 136.0, 132.8, 131.64, 131.60, 130.6, 129.12, 129.10, 116.4, 57.9, 52.3, 24.7, 24.5 (CF₃ not visible under these conditions); HRMS (ESI): m/z [M]⁺ calcd. for [C₁₉H₂₀N]⁺: 262.1590; found: 262.1588.

3.4. General Procedure for the Synthesis of Aldehydes 5 and Allylic Amines 6

Under nitrogen atmosphere, TDAE (102 μ L, 0.44 mmol) was slowly added, with a syringe, at –20 °C to a vigorously stirred solution of iminium salt **4** (0.80 mmol) with the appropriate nitrobenzyl chloride derivative **1** (69 mg, 0.40 mmol) in 3 mL of DMF. The mixture was then stirred at –20 °C for 45 min and warmed to room temperature for 1 h. Then 10 mL of water was added to quench the reaction. The solution was extracted with dichloromethane (3 \times 30 mL), the combined organic layers were washed with brine (3 \times 40 mL), and dried over MgSO₄. The crude product was then obtained after evaporation of the solvent under reduced pressure. Purification by alumina gel chromatography (PE/DCM: From 10/0 to 0/10 depending on the polarity of substrates) afforded the corresponding products **5** or **6**.

The general procedure was followed with **4a** (268 mg) and **1a** (69 mg). 4-(4-nitrophenyl)-3-phenylbutanal (**5aa**). 74% yield; yellow oil; ¹H-NMR (250 MHz, CDCl₃) δ 9.70 (s, 1H), 8.04 (d, J = 8.6 Hz, 2H), 7.29–7.05 (m, 7H), 3.56–3.45 (m, 1H), 3.10 (dd, J = 13.3, 5.9 Hz, 1H), 2.95 (dd, J = 13.3, 9.2 Hz, 1H), 2.86–2.82 (m, 2H). ¹³C-NMR (63 MHz, CDCl₃) δ 200.8, 147.3, 146.8, 142.1, 130.1, 128.9, 127.6, 127.3, 123.6, 49.5, 42.9, 41.6; HRMS (ESI): m/z [M + Na]⁺ calcd. for [C₁₆H₁₅NO₃Na]⁺: 292.0944; found: 292.0953.

The general procedure was followed with **4b** (296 mg) and **1a** (69 mg). 3-(4-chlorophenyl)-4-(4-nitrophenyl)butanal (**5ab**). 51% yield; orange oil; ¹H-NMR (250 MHz, CDCl₃) δ 9.71 (s, 1H), 8.07 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 7.15 (d, J = 8.5 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 3.56–3.45 (m, 1H), 3.08 (dd, J = 16.3, 6.0 Hz, 1H), 2.95–2.84 (m, 3H). ¹³C-NMR (63 MHz, CDCl₃) δ 200.1, 146.7, 146.6, 140.4, 132.8, 129.9, 128.9, 128.8, 123.6, 49.3, 42.6, 40.8; HRMS (ESI): m/z [M + Na]⁺ calcd. for [C₁₆H₁₄NO₃ClNa]⁺: 326.0560; found: 326.0562.

The general procedure was followed with **4f** (329 mg) and **1a** (69 mg). 1-(1-(4-nitrophenyl)-4,4-diphenylbut-3-en-2-yl)pyrrolidine (**6af**). 71% yield; orange oil; $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ 8.06 (d, $J = 8.7$ Hz, 2H), 7.25–7.10 (m, 10H), 6.48 (d, $J = 7.8$ Hz, 2H), 6.10 (d, $J = 10.0$ Hz, 1H), 3.31–3.19 (m, 2H), 2.89 (dd, $J = 13.0, 9.9$ Hz, 1H), 2.77–2.69 (m, 4H), 1.86–1.78 (m, 4H). $^{13}\text{C-NMR}$ (63 MHz, CDCl_3) δ 146.8, 146.6, 144.8, 141.5, 139.2, 130.9, 129.4, 128.4, 128.1, 127.8, 127.6, 127.2, 123.4, 64.2, 51.6, 41.3, 23.4 (1 carbon missing due to overlap); HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd. for $[\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}_2]^+$: 399.2067; found: 399.2070.

The general procedure was followed with **4f** (329 mg) and **1b** (69 mg). 1-(1-(2-nitrophenyl)-4,4-diphenylbut-3-en-2-yl)pyrrolidine (**6bf**). 78% yield; orange oil; $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ 7.90 (d, $J = 8.0$ Hz, 1H), 7.48–7.07 (m, 11H), 6.31 (d, $J = 7.9$ Hz, 2H), 6.17 (d, $J = 10.1$ Hz, 1H), 3.70 (dd, $J = 12.5, 3.5$ Hz, 1H), 3.32 (td, $J = 10.3, 3.5$ Hz, 1H), 3.00 (dd, $J = 12.4, 10.6$ Hz, 1H), 2.84–2.74 (m, 4H), 1.87–1.78 (m, 4H). $^{13}\text{C-NMR}$ (63 MHz, CDCl_3) δ 149.7, 144.4, 141.4, 139.1, 134.6, 134.0, 132.8, 129.2, 128.6, 128.3, 128.1, 127.59, 127.57, 127.11, 127.07, 125.0, 63.4, 51.9, 38.2, 23.3; HRMS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd. for $[\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}_2]^+$: 399.2067; found: 399.2069.

4. Conclusions

In conclusion, regiodivergent addition of nitrobenzyl chloride derivative **1** to α,β -unsaturated electrophiles led to 1,2-addition with α,β -unsaturated aldehydes **2** and 1,4-addition with α,β -unsaturated iminium salts **4**. The mild conditions and the tolerance of nitro groups on the nucleophiles suggest that this method is a good alternative to the use of organometallic reagents to achieve regiodivergent additions on α,β -unsaturated aldehydes. Further research is in progress to extend the scope to a catalytic and asymmetric version using enantiopure organocatalysts.

Supplementary Materials: Supplementary Material are available online, Figures S1–S28: ^1H - and ^{13}C -NMR of all compounds **3aa–3ag**, **3ba**, **4b**, **4f**, **5aa**, **5ab**, **6af** and **6bf**.

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Conflicts of Interest: The authors declare no conflict of interest.

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Sample Availability: Samples of the compounds **3aa–3ag**, **3ba**, **4b**, **4f**, **5aa**, **5ab**, **6af** and **6bf** are available from the authors.



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