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Silylformylation – Fluoride-Assisted Aryl Migration of Acetylenic Derivatives in a Versatile Approach to the Synthesis of Polyfunctionalised Compounds

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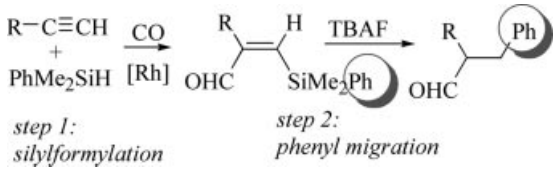
Polyfunctionalised aldehydes and dihydropyrans are prepared from easily available functionalised 1-alkynes through a two-step silylformylation/aryl migration sequence. The silylformylation process is performed under mild experimental conditions and affords the corresponding β-silylalkenals in high yields. The fluoride-promoted migration step occurs instantaneously with quantitative conversion. The chemo-, regio- and stereoselectivity can be modulated according to the nature and the position of the functional group on the acetylene precursors. When a good leaving group is present in the ω position of the aliphatic chain of the alkyne a cyclisation product is obtained, while α,β-unsaturated aldehydes are generated from propargylic tosylamides.

Introduction

Carbon–silicon bond-formation reactions are of great importance and are widely used in organic synthesis. Among a variety of methods developed for such transformations, transition metal-promoted silylations[1] provide useful routes to organosilicon compounds, currently subjects of much attention owing to their low cost, low toxicity, generality, selectivity and ease of handling. Rhodium-mediated silylformylation of acetylenic substrates, for instance, has been being intensively studied for over ten years,[2] since it generates β-silylalkenals, polyfunctionalised compounds that can be subjected to Peterson olefination,[3] Nazarov- and Trost-type annulations,[4] isomerization of the double bond, reduction and Wittig transformation of the carbonyl group.[5]

Recently, taking advantage of the high chemical affinity (BDE Si–F = 135 kcal) between silicon and fluorine,[6] we were able to convert 2-(dimethylphenylsilylmethylene)hexanal into the corresponding 2-benzylhexanal through aromatic ring migration from the dimethylphenylsilyl moiety to the adjacent carbon atom of the β-silylalkenal (Scheme 1, step 2).[7] The two-step silylformylation/phenyl migration sequence was successfully applied to several terminal acetylenes and arylsilanes to yield 2-(arylmethyl)alkanals, useful building blocks for organic chemistry[8] and important industrial products.[9] Here we report the extension of this tandem process to variously functionalised acetylenic substrates and the preparation of different classes of compounds (linear, cyclic, unsaturated) according to the nature and the position of the functional group on the aliphatic chain of the alkyne.



Scheme 1.

Results and Discussion

An important condition for the synthetic utility of a two-step approach based on such a Si–C migration is ready access to the requisite (*Z*)-β-silylalkenals. Silylformylations of terminal acetylenes can be easily performed at room temperature in a stainless steel autoclave. In a typical run, a toluene solution of equimolar amounts of silane and alkyne and a catalytic quantity of $Rh_4(CO)_{12}$ was introduced into the autoclave, the reactor was pressurized with carbon monoxide, and the mixture was stirred for the required time (Table 1, Table 2, step 1).

As would be expected, the reactions proceeded with complete regioselectivity, since the silicon is usually introduced onto the terminal position of the acetylene. The pressure of carbon monoxide was chosen according to the steric hindrance of both the unsaturated substrates and the silanes. The corresponding (*Z*)-β-silylalkenals were obtained in high yields regardless of the electronic and steric require-

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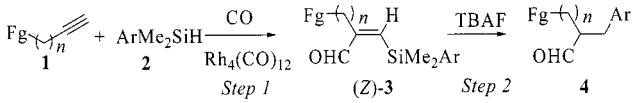
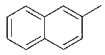
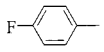
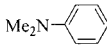
Table 1. Silylformylation/aryl migration reactions of terminal acetylenes and aryldimethylsilanes.



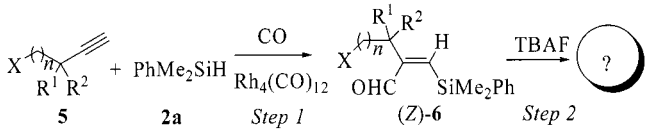
						step 1: silylformylation[a]			*step 2: aryl migration*[b]	
Entry	**1**	Fg	*n*	**2**	Ar	P_{CO} (atm)	(*Z*)-**3**	Yield (%)[c]	**4**	Yield (%)[c]
1	**a**	H	4	**b**		30	**ab**	99 (74)	**ab**	100 (52)
2	**a**	H	4	**c**		30	**ac**	98 (81)	**ac**	100 (50)
3	**a**	H	4	**d**		30	**ad**	94 (66.5)[d]	**ad**	100 (73)
4	**a**	H	4	**e**		30	**ae**	98 (63)	**ae**	100 (70)
5	**b**	C≡CH	4	**a**	Ph	40	**ba**	70 (28)[e]	**ba**	100 (78)
6	**c**	HC=CH_2	3	**a**	Ph	10	**ca**	100 (82)	**ca**	100 (67)
7	**d**	CN	3	**a**	Ph	10	**da**	99 (87)	**da**	100 (58)
8	**e**	OH	4	**a**	Ph	20	**ea**	74 (55)[f]	**ea**[g]	100 (53)

[a] Reaction conditions: 3 mmol of alkyne **1**, 3 mmol of silane **2**, 3 mL of toluene, 0.1 mmol% of $Rh_4(CO)_{12}$, room temperature, 24 h. [b] Reaction conditions: 2 mmol of aldehydes (*Z*)-**3** added to 5 mL of TBAF (1 M in THF) in 10 mL of THF and immediately hydrolysed. [c] Determined by GC analysis; the isolated yields are reported in parentheses (not optimised). [d] Reaction time: 41 h. [e] Reaction performed with alkyne/silane ratio = 2:1, 0.2 mol% of catalyst; 30% of doubly silylated by-products. [f] Diastereomers mixture: *Z*/*E* = 60:40; 26% of phenyldimethylsilyloxy aldehydes. [g] The mixture of *Z*/*E* diastereomers yielded **4ea** as sole product.[7a]

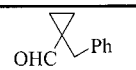
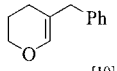
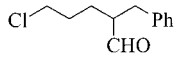
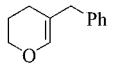
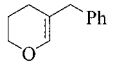
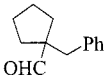
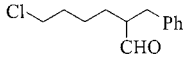
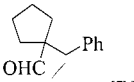
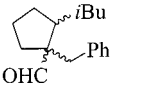
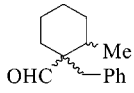
ments either of the alkynes or of the silanes (Table 1, Table 2, step 1), confirming the trend we had observed previously.[7b] It is well known that the silylformylation reaction can tolerate many functional groups on the alkynes; indeed, when α-, β- and ω-substituted acetylenes were treated with Me_2PhSiH, chosen as model reagent, the presence of double or triple bonds, nitrile, halogens, tosylate, hydroxy or amido groups did not markedly affect the reactions, which in most cases yielded the expected products quantitatively (Table 1, Table 2, Scheme 3, step 1). It is noteworthy that when an acetylene bearing a free amino group was treated with the silane it was not possible to isolate the β-silylalkenal, although complete conversion of the reagents was observed, with concomitant formation of some unidentified materials. Moreover, small amounts of by-products of double silylation were detected when 1,7-octadiyne was used even if the reaction was carried out in this case with excess alkyne and under high CO pressure (Table 1, entry 5).

With easy access to the (*Z*)-β-silylalkenals to hand, we turned to the TBAF-promoted migration step (Table 1, Table 2, step 2). The reactions were performed at room temperature, with addition of aldehyde (2 mmol) to TBAF (1 M in THF solution, 5 mL) and hydrolysis of the resulting solution with water immediately afterwards. The 1,2 rearrangement of the aromatic ring occurred smoothly with complete retention of the original configuration of the Ar group (Table 1, entries 1–4, step 2). In contrast, the chemical features of the functional group situated on the acetylenic substrate had a great influence on how the reactions proceeded. Unsaturated moieties (C=C, C≡C) or nitrile or hydroxy groups in the ω positions of the alkynes were not involved in the migration step but were directly transferred to the saturated aldehydic products (Table 1, entries 5–8, step 2). In contrast, the presence and the position of a leaving group on the aliphatic chain of the acetylene had a dramatic effect on the chemo- and regioselectivity of the process. When a halide or a tosyl substituent was positioned at the end of the hydrocarbon chain, *exo*-*tet* ring-closure reactions took place with the formation of three-, five- and six-membered ring products, all favoured according to Baldwin's rules (Table 2, step 2).[12] Cycloalkanecarbaldehydes **7**, **11**, **13** and **14** (Table 2, entries 1 and 5–8, step 2) and 5-benzyl-3,4-dihydro-2*H*-pyran (**8**, Table 2, entries 2–4, step 2) were obtained as major products. In particular, aldehydes **7**, **11**, **13** and **14** were generated by intramolecular *C*-alkylation of the carbanion **15** formed after the fluoride addition to the silicon atom and subsequent phenyl migration (Scheme 2). In the cases of α-branched acetylenes **5g**–**h** the cyclisation reactions took place with good diastereoselectivity, with (*Z*)-**13** and (*Z*)-**14** being formed as major isomers (Table 2, entries 7–8, step 2). The benzyldihydropyran **8** (Table 2, entries 2–4, step 2) was obtained by kinetically favoured intramolecular *O*-alkylation of the enolate form of **15** (Scheme 2). Complete chemoselectivity towards **8** was observed in the presence of an excellent leaving group such as tosylate (Table 2, entry 4, step 2), while the reactions of ω-chlorinated and ω-brominated β-silylalkenales (*Z*)-**6b** and

Table 2. Silylformylation/phenyl migration reactions of acetylenes characterised by the presence of a leaving group.



5 2a

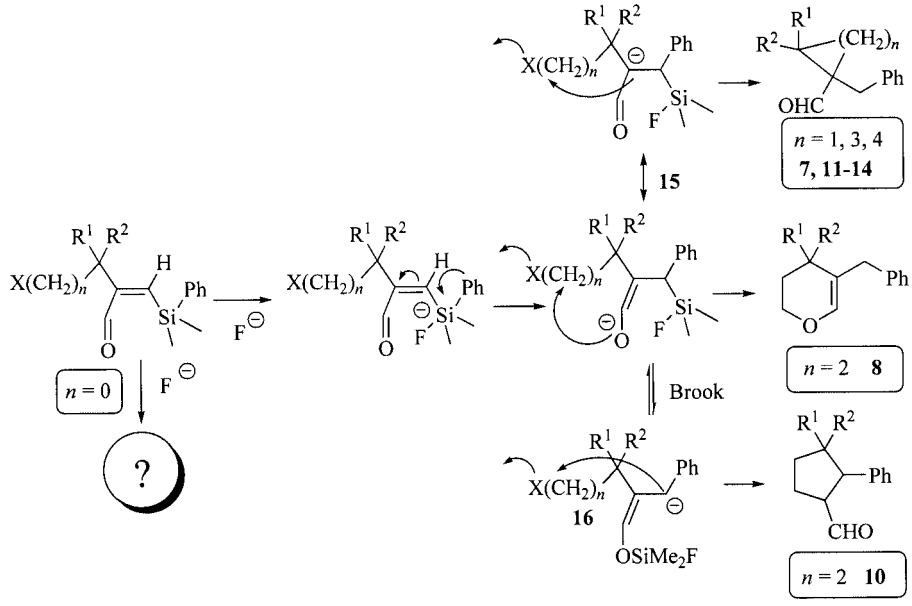
Entry	5	X	R^1, R^2	n	Step 1: silylformylation[a] P_{CO} (atm)	(Z)-6	Yield (%)[c]	Step 2: phenyl migration[b] Products, yield (%)[c]
1[7b]	a	Br	H, H	1	35	a	100 (62)	 **7**, 100 (90)[7b]
2	b	Cl	H, H	2	20	b	99 (69)	 **8**, 60 (52)[10]  **9**, 40 (25)
3	c	Br	H, H	2	30	c	100 (82)	 **8**, 75 (43)[10]  **10**, 25 (9.5, *E*/*Z* = 90/10)[11]
4	d	OTs	H, H	2	40	d	95	 **8**, 100 (75)[10]
5	e	Cl	H, H	3	30	e	99 (77)	 **11**, 73 (58)[7b]  **12**, 27 (13.5)
6[7b]	f	Br	H, H	3	10	f	100 (87)	 **11**, 100 (82)[7b]
7	g	I	H, *i*Bu	3	50	g	99 (55)	 **13**, 100 (49, *Z*/*E* = 70/30)
8	h	Br	H, Me	4	40	h	99 (60)	 **14**, 100 (41, *Z*/*E* = 70/30)

[a] Reaction conditions: 3 mmol of alkyne **1**, 3 mmol of silane **2**, 3 mL of toluene, 0.1 mmol% of $Rh_4(CO)_{12}$, room temperature, 24 h. [b] Reaction conditions: 2 mmol of aldehydes (*Z*)-**3** added to 5 mL of TBAF (1 M in THF) in 10 mL of THF and immediately hydrolysed. [c] Determined by GC analysis; the isolated yields are reported in parentheses (not optimised). [d] Crude product (diastereomers mixture: *Z*/*E* = 80:20).

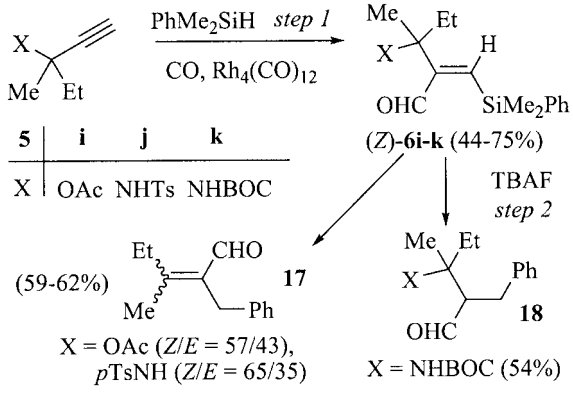
(*Z*)-**6c** involved the formation of relevant amounts of by-products (Table 2, entries 2, 3, step 2). In the case of aldehyde (*Z*)-**6b** the TBAF-mediated reactions yielded the linear 1-benzylaldehyde **9** together with the cyclisation products **8**, probably due to the poor leaving group properties of chlorine (Table 2, entry 2, step 2). Analogously, when (*Z*)-**6e** was treated with TBAF the formation of the chloroaldehyde **12** was detected (Table 2, entry 5, step 2). The presence of bromine in the ω position induced the formation of carbacyclic aldehyde **10**, which can be ascribed to the carbanion **16**, generated by Brook rearrangement[13] of **15** (Scheme 2).

The obtained results prompted us to extend our investigation to the reactivity of propargyl derivatives (Scheme 2, *n* = 0) characterised by a good leaving group such as acetate or tosylamide in the α position with respect to the triple bond. As shown in Scheme 3, while treatment of propargylamine **5k** protected as NHBOC exclusively yielded the "normal" rearrangement product **18**, TBAF treatment of the β-silylalkenals derived from alkynes **5i** and **5j** resulted in the formation of α,β-unsaturated aldehydes **17**.

The observed behaviour is consistent with the mechanism depicted in Scheme 4 and can be easily explained by

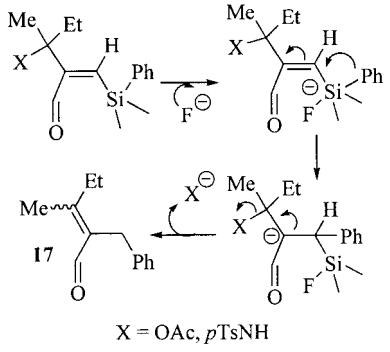


Scheme 2.



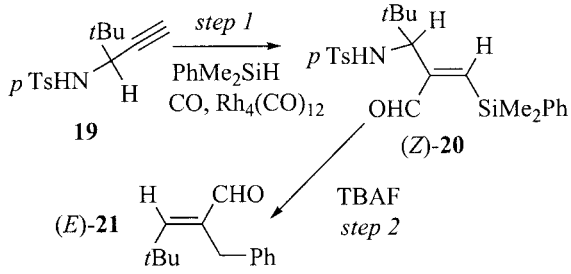
Scheme 3.

considering that in this case the carbanion generated after the phenyl migration induces the elimination of OAc and *p*TsNH and consequent double bond formation (Scheme 4). 2-Benzyl-3-methylpentenal (**17**) was obtained in good yields (59–62%, pure product) but with poor stereoselectivity, as might be expected in view of the very similar steric requirements of the methyl and ethyl substituents. In contrast, the



Scheme 4.

β-silylalkenal **20** derived from propargylamide **19** exclusively afforded the stereoisomer **21** characterised by the bulky *tert*-butyl substituent *trans* to the carbonyl moiety (Scheme 5).



Scheme 5.

Conclusions

In conclusion, the chemo-, regio- and stereoselectivity of the desilylation reaction in the tandem silylformylation/fluoride-promoted Si→C rearrangement process turned out to be strongly dependent on the nature and the position of the functional group present on the silylformylation product. The ready access to functionalised β-silylalkenals through silylformylation reactions enhances the versatility of the procedure, which can be successfully employed in the preparation of polyfunctionalised aldehydes and pyrans, useful building blocks for organic chemistry.

Experimental Section

General Procedure for the Rhodium-Catalyzed Silylformylation of 1-Alkynes with Aryldimethylsilanes: Carbonylation reactions were run in a 25 mL stainless steel autoclave fitted with a Teflon inner crucible and a stirring bar. In a typical run, the silane (3 mmol), the

required 1-alkyne (3 mmol), toluene (3 mL) and $Rh_4(CO)_{12}$ (0.1 mol%) were placed under CO in a Pyrex Schlenk tube. This solution was introduced into the previously evacuated (0.1 Torr) autoclave through a steel siphon. The reactor was pressurized with carbon monoxide and the mixture was stirred at room temperature for 24 h, unless otherwise specified. After removal of excess CO (fume hood), the reaction mixture was diluted with *n*-hexane, filtered through Celite and concentrated under vacuum. The residue was purified by column chromatography on silica gel with an appropriate solvent mixture as eluent.

General Procedure for the Fluoride-Promoted Migration Reaction: In a typical run, the substrate (2 mmol), dissolved in anhydrous THF (10 mL), was added slowly at room temperature to TBAF (1 M in THF, 5 mL). Immediately after the addition, the reaction mixture was hydrolysed with water and extracted three times with ether, and the organic layers were dried with Na_2SO_4. After concentration under vacuum, the crude product was purified by column chromatography on silica gel with an appropriate solvent mixture as eluent.

(*RS*)-2-[(1-Naphthyl)methyl]hexanal (4ab): Isolated yield (*n*-hexane/ethyl ether, 95:5): 0.25 g, 52%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.87 (t, J = 7.0 Hz, 3 H), 1.23–1.78 (m, 6 H), 2.72–2.87 (m, 1 H), 3.11 (dd, J = 7.0, 14.4 Hz, 1 H), 3.46 (dd, J = 7.3, 14.4 Hz, 1 H), 7.29–7.56 (m, 4 H), 7.71–8.00 (m, 3 H), 9.70 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.8, 22.7, 29.0, 29.1, 32.3, 52.3, 123.3, 125.3, 125.6, 126.1, 127.1, 127.3, 128.9, 131.7, 134.0, 134.9, 204.5 ppm. IR (neat): $\tilde{\nu}$ = 2725 (CHO), 1722 (C=O) cm^{-1}. GC-MS (int. rel.%): m/z = 280 $[M]^+$ (15), 165 (15), 141 (100), 128 (15), 115 (22), 41 (19). $C_{17}H_{20}O$ (240.15): calcd. C 84.96, H 8.39; found C 84.88, H 8.40.

(*RS*)-2-[(2-Naphthyl)methyl]hexanal (4ac): Isolated yield (*n*-hexane/ethyl ether, 90:10) 0.24 g, 50%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.84 (t, J = 7.0 Hz, 3 H), 1.19–1.62 (m, 6 H), 2.56–2.71 (m, 1 H), 2.83 (dd, J = 7.0, 13.9 Hz, 1 H), 3.11 (dd, J = 7.3, 13.9 Hz, 1 H), 7.24 (dd, J = 8.7, 1.6 Hz, 1 H), 7.34–7.45 (m, 2 H), 7.55 (t, J = 1.6 Hz, 1 H), 7.70–7.77 (m, 3 H), 9.63 (d, J = 2.6 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.7, 22.6, 28.2, 29.0, 35.0, 53.1, 125.3, 125.9, 127.1, 127.2, 127.3, 127.5, 128.0, 132.1, 133.4, 136.4, 204.4 ppm. IR: $\tilde{\nu}$ = 2722 (CHO), 1722 (C=O) cm^{-1}. GC-MS (int. rel.%): 240 $[M]^+$ (16), 165 (10), 155 (11), 141 (100), 128 (16), 115 (28), 41 (26). $C_{17}H_{20}O$ (240.15): calcd. C 84.96, H 8.39; found C 85.00, H 8.37.

(*RS*)-2-(4-Fluorobenzyl)hexanal (4ad): Isolated yield (*n*-hexane/ethyl ether, 80:20) 0.30 g, 73%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.86 (t, J = 5.9 Hz, 3 H), 1.19–1.65 (m, 6 H), 2.48–2.66 (m, 1 H), 2.67 (dd, J = 6.6, 13.8 Hz, 1 H), 2.94 (dd, J = 7.1, 13.8 Hz, 1 H), 6.90–6.99 (m, 2 H), 7.06–7.14 (m, 2 H), 9.63 (d, J = 2.6 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.7, 22.6, 28.1, 28.9, 34.0, 53.4, 115.1 (d, J = 20.9 Hz), 130.2 (d, J = 7.6 Hz), 134.5 (d, J = 3.4 Hz), 161.4 (d, J = 244.2 Hz), 204.2 ppm. IR (neat): $\tilde{\nu}$ = 2714 (CHO), 1724 (C=O) cm^{-1}. GC-MS (int. rel.%): m/z = 208 $[M]^+$ (7), 166 (19), 151 (45), 109 (100), 83 (12), 41 (7). $C_{13}H_{17}FO$ (208.13): calcd. C 74.97, H 8.23, F 9.12; found C 75.15, H 8.20, F 9.09.

(*RS*)-2-[4-(Dimethylamino)benzyl]hexanal (4ae): Isolated yield (*n*-hexane/ethyl ether, 90:10): 0.32 g, 70%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.88 (J = 6.2 Hz, 3 H), 1.22–1.72 (m, 6 H), 2.47–2.60 (m, 1 H), 2.63 (dd, J = 7.0, 20.2 Hz, 1 H), 2.90 (dd, J = 7.0, 20.2 Hz, 1 H), 2.91 (s, 6 H), 6.67 (d, J = 8.8 Hz, 2 H), 7.03 (d, J = 8.8 Hz, 2 H), 9.64 (J = 2.6 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.7, 22.6, 28.2, 29.1, 35.0, 40.6, 53.6, 112.7, 126.5, 129.5, 149.2, 205.1 ppm. GC-MS (int. rel.%): m/z = 233 $[M]^+$ (7), 134 (100), 118 (8), 91 (5), 41 (12). IR (neat): $\tilde{\nu}$ = 2704 (CHO), 1720 (C=O) cm^{-1}. $C_{15}H_{23}NO$ (233.18): calcd. C 77.21, H 9.93, N 6.00; found C 77.35, H 9.90, N 5.98.

(*RS*)-2-Benzyloct-7-ynal (4ba): Isolated yield (*n*-hexane/ethyl ether, 80:20): 0.33 g, 78%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.26–1.57 (m, 6 H), 1.83 (t, J = 2.5 Hz, 1 H), 2.01–2.09 (m, 2 H), 2.47–2.60 (m, 1 H), 2.61 (dd, J = 7.0, 13.5 Hz, 1 H), 2.88 (dd, J = 6.9, 13.5 Hz, 1 H), 7.03–7.18 (m, 5 H), 9.55 (d, J = 2.6 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 18.0, 25.8, 27.8, 28.2, 34.8, 53.1, 68.4, 83.9, 126.2, 128.4, 128.8, 138.6, 204.2 ppm. IR (neat): $\tilde{\nu}$ = 3293 (≡C–H), 2713 (CHO), 1723 (C=O) cm^{-1}. GC-MS (int. rel.%): m/z = 214 $[M]^+$, 133 (26), 105 (12), 91 (100), 65 (14). $C_{15}H_{18}O$ (214.14): calcd. C 84.07, H 8.47; found C 84.24, H 8.50.

(*RS*)-2-Benzylhept-6-enal (4ca): Isolated yield (*n*-hexane/ethyl ether, 90:10): 0.27 g, 67%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.23–1.68 (m, 4 H), 1.94 (m, 2 H), 2.45–2.60 (m, 1 H), 2.62 (dd, J = 6.8, 13.4 Hz, 1 H), 2.90 (dd, J = 7.3, 13.4 Hz, 1 H), 4.82–4.95 (m, 2 H), 5.66 (ddt J = 6.6, 10.3, 16.9 Hz, 1 H), 7.04–7.23 (m, 5 H), 9.56 (d, J = 2.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 26.1, 27.9, 33.5, 34.9, 53.2, 114.8, 126.3, 128.4, 128.9, 137.9, 138.8, 204.3 ppm. IR (neat): $\tilde{\nu}$ = 3062 (=C–H), 2708 (CHO), 1723 (C=O), 1638 (C=C) cm^{-1}. GC-MS (int. rel.%): m/z = 202 $[M]^+$ (3), 133 (16), 117 (11), 91 (100), 78 (8), 65 (12), 41 (15). $C_{14}H_{18}O$ (202.14): calcd. C 83.12, H 8.97; found C 82.91, H 8.93.

(*RS*)-2-Benzyl-6-cyanopentanal (4da): Isolated yield (*n*-hexane/ethyl acetate 50:50): 0.23 g, 58%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.50–1.88 (m, 4 H), 2.32 (t, J = 6.7 Hz, 2 H), 2.59–2.74 (m, 1 H), 2.73 (dd, J = 7.2, 13.4 Hz, 1 H), 3.05 (dd, J = 6.4, 13.4 Hz, 1 H), 7.16–7.33 (m, 5 H), 9.69 (d, J = 2.2 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 17.0, 22.7, 27.1, 34.9, 2.4, 119.0, 126.5, 128.5, 128.7, 137.8, 203.3 ppm. IR: $\tilde{\nu}$ = 2716 (CHO), 2247 (C≡N), 1722 (C=O) cm^{-1}. GC-MS (int. rel.%): m/z = 183 $[M - 18]^+$ (4), 172 (39), 144 (21), 133 (32), 105 (13), 91 (100), 65 (13), 51 (19), 41 (31). $C_{13}H_{15}NO$ (201.11): calcd. C 77.58, H 7.51, N 6.96; found C 77.72, H 7.48, N 6.99.

(*RS*)-2-Benzyl-6-hydroxyhexanal (4ea): Isolated yield (dichloromethane/acetone 80:20): 0.22 g, 53%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.26–1.74 (m, 6 H), 2.54–2.70 (m, 1 H), 2.73 (dd, J = 6.8, 13.0 Hz, 1 H), 2.99 (dd, J = 7.2, 13.0 Hz, 1 H), 3.22 (s, 1 H), 3.56 (t, J = 6.1 Hz, 2 H), 7.14–7.33 (m, 5 H), 9.64 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.9, 28.0, 32.2, 34.7, 53.1, 61.8, 126.1, 128.2, 128.6, 138.5, 204.6 ppm. IR (neat): $\tilde{\nu}$ = 3384 (O–H), 2720 (CHO), 1721 (C=O) cm^{-1}. GC-MS (int. rel.%): m/z = 206 $[M]^+$ (3), 188 (35), 170 (8), 144 (13), 133 (20), 117 (23), 104 (15), 91 (100), 77 (12), 65 (27), 39 (18). $C_{13}H_{18}O_2$ (206.13): calcd. C 75.69, H 8.80; found C 75.78, H 8.77.

(*RS*)-2-Benzyl-5-chloropentanal (9): Isolated yield (*n*-hexane/ethyl ether, 90:10): 0.10 g, 25% ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.58–1.87 (m, 4 H), 2.57–2.71 (m, 1 H), 2.72 (dd, J = 6.7, 14.0 Hz, 1 H), 3.01 (dd, J = 7.0, 14.0 Hz, 1 H), 3.48 (t, J = 6.0 Hz, 2 H), 7.14–7.33 (m, 5 H), 9.65 (d, J = 2.2 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 25.5, 29.6, 34.9, 44.4, 52.4, 126.4, 128.4, 128.7, 138.2, 203.7 ppm. IR (neat): $\tilde{\nu}$ = 2719 (CHO), 1724 (C=O) cm^{-1}. $C_{12}H_{15}ClO$ (210.08): calcd. C 68.40, H 7.18, Cl 16.83; found C 68.63, H 7.20, Cl 16.78.

(*RS*)-2-Benzyl-6-chlorohexanal (12): Isolated yield (*n*-hexane/ethyl ether, 90:10): 0.06 g, 13.5%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.42–1.77 (m, 6 H), 2.54–2.70 (m, 1 H), 2.72 (dd, J = 6.8, 14.0 Hz, 1 H), 3.00 (dd, J = 6.8, 14.0 Hz, 1 H), 3.48 (t, J = 6.6 Hz, 2 H), 7.13–7.30 (m, 5 H), 9.66 (d, J = 2.2 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.1, 27.6, 32.3, 34.9, 44.5, 53.1, 126.4,

128.5, 128.8, 138.5, 204.1 ppm. IR (neat): $\tilde{\nu}$ = 2720 (CHO), 1724 (C=O) cm^{-1}. $C_{13}H_{17}ClO$ (224.09): calcd. C 69.48, H 7.62, Cl 15.78; found C 69.29, H 7.60, Cl 15.83.

1-Benzyl-2-isobutylcyclopentanecarbaldehyde (Diastereomeric Mixture, *Z*/*E* = 70:30) (13): Isolated yield (*n*-hexane/ethyl ether, 90:10): 0.24 g, 49%. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.00 (d, J = 6.2 Hz, 6 H), 1.05 (d, J = 6.2 Hz, 6 H), 1.32–2.09 (m, 20 H), 2.44 (d, J = 13.9 Hz, 0.6 H), 2.85 (d, J = 13.7 Hz, 1.4 H), 3.28 (d, J = 13.7 Hz, 1.4 H), 3.39 (d, J = 13.9 Hz, 0.6 H), 7.21–7.37 (m, 10 H), 9.51 (s, 0.6 H), 9.87 (s, 1.4 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.9 and 21.5, 22.2 and 22.3, 24.1 and 23.8, 26.8 and 26.3, 30.8 and 29.8, 31.0 and 31.1, 37.9 and 32.8, 39.0 and 39.2, 46.8 and 43.1, 59.9 and 60.9, 126.1 and 125.9, 127.9, 130.0 and 130.1, 137.7 and 138.6, 206.4 and 205.0 ppm. IR (neat): $\tilde{\nu}$ = 2710 (CHO), 1691 (C=O) cm^{-1}. GC-MS (int. rel.%) (minor diastereomer): m/z = 245 $[M + 1]^+$ (62), 227 (22), 188 (100), 171 (12), 158 (15), 120 (17). GC-MS (int. rel.%) (major diastereomer): m/z = 245 $[M + 1]^+$ (75), 188 (100), 171 (25), 120 (22).

1-Benzyl-2-methylcyclohexanecarbaldehyde (Diastereomeric Mixture, *Z*/*E* = 70:30) (14): Isolated yield (*n*-hexane/ethyl ether, 90:10): 0.18 g, 41%. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.98 (d, J = 7.0 Hz, 4.2 H), 1.17 (d, J = 7.0 Hz, 1.8 H), 1.26–2.02 (m, 18 H), 2.65 (d, J = 13.8 Hz, 1.4 H), 2.78 (d, J = 13.7 Hz, 0.6 H), 3.03 (d, J = 13.7 Hz, 0.6 H), 3.08 (d, J = 13.8 Hz, 1.4 H), 7.15–7.35 (m, 10 H), 9.56 (s, 1.4 H), 9.92 (s, 0.6 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.4 and 16.3, 21.1 and 22.3, 23.6 and 24.7, 27.5 and 29.7, 30.1 and 31.4, 33.3 and 34.7, 36.7 and 40.3, 53.4 and 52.4, 126.1 and 126.4, 128.0, 130.3 and 130.4, 137.4 and 136.7, 207.2 and 207.4 ppm. IR (neat): $\tilde{\nu}$ = 2699 (CHO), 1721 (C=O) cm^{-1}.

2-Benzyl-3-methylpent-2-enal (Diastereomeric Mixture, *Z*/*E* = 57:43) (17): Isolated yield (*n*-hexane/ethyl ether, 80:20): 0.23 g, 62%. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.08 (t, J = 7.8 Hz, 2.58 H), 1.26 (t, J = 7.6 Hz, 3.42 H), 2.07 (s, 3.42 H), 2.31 (s, 2.58 H), 2.41 (q, J = 7.8 Hz, 1.72 H), 2.74 (q, J = 7.6 Hz, 2.28 H), 3.73 (s, 2.28 H), 3.75 (s, 1.72 H), 7.19–7.35 (m, 10 H), 10.28 (s, 1.14 H), 10.31 (s, 0.86 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.2 and 11.6, 21.5 and 16.7, 26.2 and 30.1, 30.7 and 30.7, 125.7 (2C), 128.0 (2C), 128.2 (2C), 135.3 and 135.0, 139.9 and 140.3, 162.6 and 161.5, 190.2 and 191.3 ppm. IR (neat): $\tilde{\nu}$ = 3021 (C=C–H), 2756 (CHO), 1660 (C=O), 1616 (C=C) cm^{-1}. GC-MS (int. rel.%) (major diastereomer): m/z = 188 $[M]^+$ (48), 159 (74), 141 (13), 131 (42), 129 (26), 117 (26), 115 (31), 105 (17), 91 (89), 77 (19), 65 (27), 53 (25), 51 (44), 46 (45), 41 (40), 39 (100). GC-MS (int. rel.%) (minor diastereomer): m/z = 188 $[M]^+$ (43), 173 (5), 159 (77), 141 (13), 131 (42), 129 (28), 115 (33), 105 (18), 91 (91), 77 (19), 65 (27), 51 (44), 43 (44), 41 (88), 39 (100).

2-Benzyl-3-(*tert*-butoxycarbonylamino)-3-methylpentanal (18): Isolated yield (CH_2Cl_2): 0.33 g, 54%. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.99 (t, J = 7.4 Hz, 3 H), 1.00 (t, J = 7.4 Hz, 3 H), 1.27 (s, 3 H), 1.40 (s, 3 H), 1.53 (m, 11 H), 1.55 (m, 11 H), 2.83 (t, J = 12.6 Hz, 1 H), 2.85 (t, J = 12.6 Hz, 1 H), 3.12 (t, J = 12.6 Hz, 1 H), 3.14 (t, J = 12.6 Hz, 1 H), 3.73 (m, 1 H), 3.76 (m, 1 H), 4.74 (s, 1 H), 4.84 (s, 1 H), 7.22–7.36 (m, 10 H), 9.84 (d, J = 2.4 Hz, 1 H), 9.87 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 7.6 and 7.3, 1.2 and 21.9, 28.3 and 29.5, 30.7 and 30.4, 51.1 and 53.3, 57.2 and 57.0, 60.3 and 59.6 79.2 (2C), 125.9 and 126.0, 128.3 (2C), 128.9 (2C), 139.8 and 139.7, 154.1 and 154.3, 203.9 and 204 ppm. IR (neat): $\tilde{\nu}$ = 3021 (N–H), 2732 (CHO), 1713 (C=O) cm^{-1}. GC-MS (int. rel.%): m/z = 134 (37), 116 (62), 92 (48), 91 (100), 72 (46), 57 (79), 42 (40), 41 (47), 39 (33). $C_{18}H_{27}NO_3$ (305.20): calcd. C 70.79, H 8.91, N 4.59; found 70.91, H 8.93, N 4.61.

(*E*)-2-Benzyl-4,4-dimethylpent-2-enal (21): Isolated yield (CH_2Cl_2): 0.12 g, 31%. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.20 (s, 9 H), 3.80 (s, 2 H), 6.58 (s, 1 H), 7.10–7.35 (m, 5 H), 9.41 (s, 1 H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 26.4, 29.5, 30.1, 125.9, 127.9, 128.3, 139.2, 139.3, 166.0, 196.4 ppm. IR (neat): $\tilde{\nu}$ = 3025 (C=C–H), 2708 (CHO), 1685 (C=O), 1632 (C=C) cm^{-1}. GC-MS (int. rel.%): m/z = 202 $[M]^+$ (36), 159 (40), 145 (32), 131 (53), 115 (37), 91 (85), 77 (8), 55 (23), 43 (40), 41 (100), 39 (89). $C_{14}H_{18}O$ (202.29): calcd. C 83.12, H 8.97; found C 83.38, H 8.92.

Supporting Information (for details see the footnote on the first page of this article): Procedures and spectroscopic data for the silylformylation products (*Z*)-**3ab** to (*Z*)-**3ea** and (*Z*)-**6c** to (*Z*)-**20**.

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