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Synthesis and application of benzyl-TMS derivatives as bench stable benzyl anion equivalents

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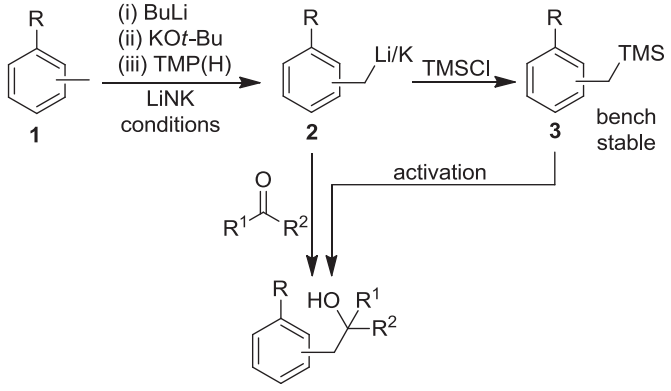
ABSTRACT

The regioselective benzylic metalation of toluenes using BuLi/KO^{t}Bu/TMP(H) (LiNK metalation conditions) and subsequent transmetalation to Si by reaction with TMSCl provides a general one-pot procedure for the synthesis of substituted benzyltrimethylsilanes. $ArCH_2Si(Me)_3$ derivatives are bench stable reagents yet can serve as benzyl anion equivalents under mild reaction conditions. Following activation with fluoride they can successfully participate in a wide range of additions to both non-enolizable and enolizable carbonyls. In addition, their use in the synthesis of isochromanones and trifluoromethylated amines is illustrated. The broad synthetic scope and mild practical conditions of use for $ArCH_2Si(Me)_3$ reagents demonstrate their general potential as benzyl anion equivalents.

1. Introduction

Organometallic addition to carbonyls form part of the fundamental bedrock of carbon–carbon bond forming transformations.[1] Specifically, nucleophilic addition of benzylic organometallics is an effective means of introducing the $ArCH_2$ group in a synthetic program. Typically these organometallics are accessible from their corresponding benzylhalides or benzylethers by reaction with a metal source, such as Li, Mg, Zn, Cd or Mn, though each of these methods are not without challenging practical problems.[2,27] We have recently contributed to this field with the development of a general method for direct benzylic metalation of substituted toluenes and xylenes via deprotonation.[3] Our approach used a mixed Li and K metal amide system generated in situ from BuLi, KO^{t}Bu, and TMP(H) (LiNK metalation conditions), which can provide the benzylic metal species **2** with excellent selectivity from substituted toluenes **1** (Scheme 1). Following this direct metalation, their addition to electrophiles, such as Bu_3SnCl and CO_2 proceeded in the expected fashion in good yields.[3a]

Notwithstanding their indispensable requirement for organic synthesis, a perceived barrier to the use of some organometallics exists due to their high reactivity and low stability. In general, organometallic reactivity/stability can be correlated to the anionic nature of the carbon metal bond, which for potassium and lithium is high.[4] This prompted us to explore the possibility of developing a nucleophilic benzylic reagent class, which would have the general synthetic attributes of organometallics, such as **2** but would be bench stable and practically facile to utilize.



Scheme 1. Bench stable benzyl anion equivalents.

To achieve this goal we chose to transmetalate from the K/Li organometallics **2** generated by LiNK metalation to Si, which would be readily achievable by reaction with trimethylsilylchloride (Scheme 1). We envisaged the low ionic character of the C–Si bond of the benzyltrimethylsilanes **3** would provide a new bench stable set of benzyl anion equivalent reagents (Scheme 1). As the percentage ionicity of the C–Si bond is only 12%, it would be necessary to use an activator of **3** for carbonyl addition reactions. A precedent for this type of activation was first reported by Hosomi and Sakurai in the fluoride promoted addition of allyltrimethylsilane to carbonyls, which has been extended to several other trimethylsilane derivatives.[5] Despite their synthetic potential, surprisingly, the addition reactions of benzyl silanes have concentrated on unsubstituted benzyl silane[6a–c] itself, *o*-nitro benzyl silanes[6d–f] and a few

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others.[6g,h] In this report we describe a general synthesis of substituted benzyl silanes, which have not been previously used in addition reactions, and identify mild conditions in which they can be in situ activated to act as benzyl anion equivalents.

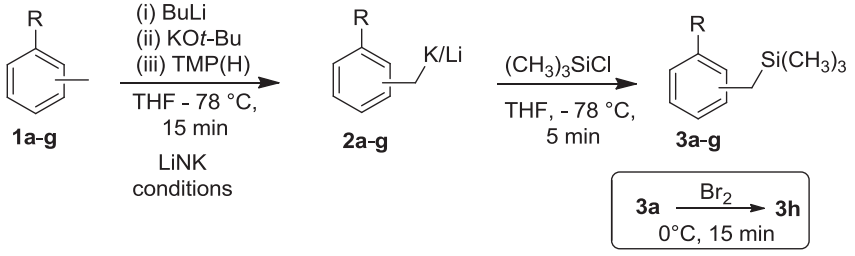
2. Results and discussion

Toluenes **1a**–**g** were selected as a representative set of diversely substituted derivatives containing carboxylic acid, ether, amino, and amido functional groups. LiNK metalation to **2a**–**g** and in situ reaction with trimethylsilylchloride gave the benzylsilane organometallics in good to excellent yields (Table 1, entries 1–7). While numerous functional groups tolerate organolithium metalation conditions, some halogens, such as bromine are problematic due to competing metal halogen exchange. An inherent advantage of selecting Si as the surrogate metal lies in the fact that further derivatization can be performed on a benzylsilane prior to its use as benzyl anion equivalent. For example, aryl bromination of **3a** was readily achieved by reaction with Br_2 providing the 4-bromobenzyltrimethylsilane **3h** in excellent yield (Table 1, entry 8).[7] The silanes **3a**–**h** were stored at rt without any special precautions for prolonged time periods with no observable decomposition.

Optimization of addition reaction conditions was carried out using 3-methoxybenzyltrimethylsilane **3e** and benzaldehyde. Testing of 1 equiv CsF in THF, acetonitrile, and DMF showed that DMF was the optimal solvent with 80% yield of addition product **4a** obtained following heating at 80 °C for 4 h (Table 2, entries 1–4). Reducing the quantity of CsF in DMF to 5 mol % maintained a good yield of 63%. Examination of two alternative fluoride sources, tetrabutylammonium fluoride (TBAF) and tetrabutylammonium triphenyldifluorosilicate (TBAT), at 5 mol % in THF under reflux showed that TBAT was marginally superior but also practically advantageous as it is non-hygroscopic (Table 2, entries 6 and 7).[8] Encouragingly, TBAT continued to perform well even at 1 mol % levels (Table 2, entry 8). Overall two sets of conditions CsF/DMF or TBAT/THF were identified for benzylsilane additions and we chose to proceed with the latter as it avoided use of the higher boiling point solvent DMF. As a comparative illustration, the low temperature addition of **2e** (generated via LiNK metalation) to benzaldehyde in THF also gave **4a** in a yield equivalent to **3e** (Table 2).

Using optimized conditions of 5 mol % TBAT/THF/reflux, the addition of **3a**–**h** to 11 different non-enolizable aromatic, heteroaromatic, α,β-unsaturated, and aliphatic aldehydes was successfully achieved in good to excellent yields (Table 3). The high functional group compatibility displayed by the results in Table 3 is very en-

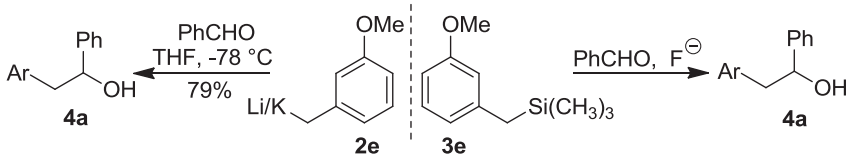
Table 1
LiNK metalation route to benzyl-TMS derivatives



Entry	Substrate	R	Product	Yield
1	**1a**	H	**3a**	83
2	**1b**	2-CO_2H[b]	**3b**	77
3	**1c**	2-OMe	**3c**	72
4	**1d**	2-$N(Me)_2$	**3d**	84
5	**1e**	3-OMe	**3e**	81
6	**1f**	4-CON^iPr_2	**3f**	89
7	**1g**	3,4,5-$(OMe)_3$	**3g**	79
8	**3a**	4-Br	**3h**	94[a]

[a] Br_2, CCl_4, 0 °C 15 min.
[b] BuLi (2.2 equiv) used.

Table 2
Optimization of reaction conditions



Entry	Fluoride	mol %	Solv.	Temp	Time h	% Yield
1	CsF	100	THF	rt	12	—
2	CsF	100	MeCN	rt	12	17
3	CsF	100	MeCN	Reflux	4	62
4	CsF	100	DMF	80	4	80
5	CsF	5	DMF	80	4	63
6	TBAF[a]	5	THF	Reflux	3	77
7	TBAT	5	THF	Reflux	3	82
8	TBAT	1	THF	Reflux	4	71

[a] Molecular sieves added.

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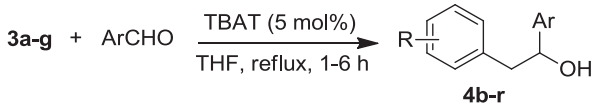
couraging for the general use of benzyltrimethylsilanes as benzyl anion equivalents.

Table 3
Addition to non-enolizable aldehydes



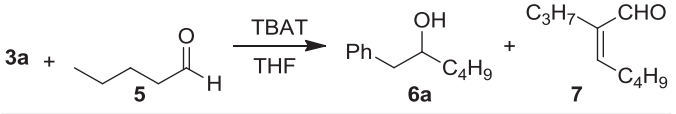
4b-r

Entry		R	Ar	Prod	% Yield
1	**3a**	H	4-$MeOC_6H_4$	**4b**	70
2	**3a**	H	4-FC_6H_4	**4c**	78
3	**3a**	H	*t*-Bu	**4d**	63
4	**3a**	H	4-C_5H_4N	**4e**	74
5	**3c**	2-OMe	4-ClC_6H_4	**4f**	60[a]
6	**3c**	2-OMe	3-MeC_6H_4	**4g**	61[a]
7	**3d**	2-N(Me)$_2$	4-BrC_6H_4	**4h**	84
8	**3d**	2-N(Me)$_2$	PhCH=CH	**4i**	80
9	**3e**	3-OMe	4-BrC_6H_4	**4j**	80
10	**3e**	3-OMe	4-C_5H_4N	**4k**	67
11	**3f**	4-CON^{i}Pr$_2$	4-C_5H_4N	**4l**	75
12	**3f**	4-CON^{i}Pr$_2$	4-BrC_6H_4	**4m**	81
13	**3g**	3,4,5-(OMe)$_3$	2-Naphthyl	**4n**	82
14	**3g**	3,4,5-(OMe)$_3$	4-$CF_3C_6H_4$	**4o**	70
15	**3h**	4-Br	4-$MeOC_6H_4$	**4p**	73
16	**3h**	4-Br	PhCH=CH	**4q**	71

[a] TBAT (10 mol %) used.

Organometallic addition to enolizable aldehydes and ketones presents the challenge of competing substrate deprotonation potentially leading to aldol products.[9] Addition of silane **3a** to pentanal was used as a test reaction to identify conditions that provided the desired product **6a** in favor of the α,β-unsaturated aldehyde **7** (Table 4). Attempts at rt reactions using 5 mol % TBAT gave low conversions to **6a**, but increasing the amount of TBAT to 50 mol % did give complete consumption of aldehyde with a ratio of **6a**/**7** of 4:1 (Table 4, entries 1, 2). To avoid using elevated amounts of TBAT, the reactions were repeated at reflux for 6 h using lower amounts of fluoride activator. Complete conversion of aldehyde was obtained with 5 mol % TBAT and, following chromatography, purified **6a** was obtained in a 73% yield (entry 3). The efficiency of TBAT to promote addition was evident as a 30% conversion was obtained in 6 h with a fluoride loading of only 1 mol % (entry 4).

Table 4
Optimization of addition to pentanal[a]



5 6a 7

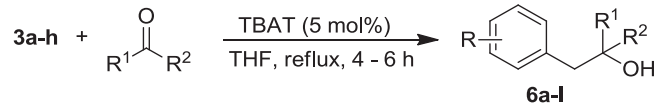
Entry	TBAT mol %	Temp/time	% Conversion	Ratio **6a**/**7**	% Yield **6a**
1	5	rt/12 h	10	—	—
2	50	rt/12 h	100	4:1	73
3	5	Reflux/6 h	100	4:1	73
4	1	Reflux/6 h	30	4:1	19

[a] 2:1 equiv ratio of **3a**/**5** used.

The tolerance of addition of benzyl silanes **3a**–**h** to pentanal and seven other enolizable substrates, such as 3-phenylpropionaldehyde, cyclohexanone, and substituted acetophenones, is illustrated in Table 5. The additions were all successful with products **6a**–**l** obtained in good to excellent yields.

The combination of addition reactions with further in situ transformations is a commonly used and effective synthetic strategy. The *o*-carboxylic acid substituent of ((trimethylsilyl)methyl)

Table 5
Reaction with enolizable carbonyls



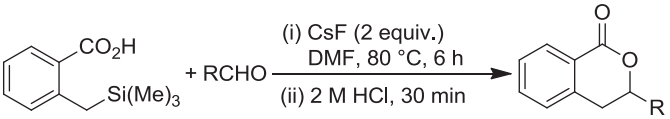
6a-l

Entry	Subst	R	R^1/R^2	Prod	% Yield
1	**3a**	H	Bu/H	**6a**	73
2	**3a**	H	Ph/CH_3	**6b**	93
3	**3a**	H	$-(CH_2)_5-$	**6c**	71[a]
4	**3c**	2-OMe	3-BrC_6H_4/CH_3	**6d**	56[b]
5	**3d**	2-N(Me)$_2$	Bu/H	**6e**	62
6	**3e**	3-OMe	Bu/H	**6f**	67
7	**3f**	4-CON^{i}Pr$_2$	Bu/H	**6g**	70
8	**3f**	4-CON^{i}Pr$_2$	2-BrC_6H_4/CH_3	**6h**	71
9	**3g**	3,4,5-(OMe)$_3$	4-FC_6H_4/CH_3	**6i**	78
10	**3g**	3,4,5-(OMe)$_3$	Ph/C_4H_9	**6j**	67
11	**3h**	4-Br	Ph/CH_3	**6k**	75
12	**3h**	4-Br	$PhCH_2CH_2$/H	**6l**	65

[a] Reaction at rt, 10 mol % TBAT used.
[b] TBAT (10 mol %) used.

benzoic acid **3b** offers the potential to achieve this as following carbanion carbonyl addition, lactonization can occur (Table 6). The alternative reaction conditions of 2 equiv of CsF in DMF at 80 °C were employed in this case as deprotonation of the carboxylic acid with CsF as base was first required. Under these conditions, reaction of **3b** with aromatic, heteroaromatic, and aliphatic aldehydes for 6 h, followed by acidic work up gave the 3-substituted isochroman-1-ones in yields up to 85% (Table 6).

Table 6
3-Substituted isochroman-1-ones



3b 8a-f

Entry	R	**8**	% Yield
1	Ph	**8a**	85
2	3,4-$(MeO)_2C_6H_3$	**8b**	77
3	5-Me–furan	**8c**	75
4	5-Me–thiophene	**8d**	72
5	Bu	**8e**	68
6	*t*-Bu	**8f**	45

Addition of **3a** and **3g** to inexpensive ethyl trifluoroacetate was examined as an illustrative example of how their addition reaction to esters could be used to introduce the trifluoromethyl group into biological active 1-arylpropan-2-amines **11** (Scheme 2).[10] Using catalytic TBAT in THF no reaction was observed but using CsF/DMF the trisubstituted *Z*-alkenes **9a**,**b** were isolated, as a result of formal olefination of the ester carbonyl, in good yields.[11] Hydrolysis of **9a**,**b** to their corresponding ketones and reaction with hydroxylamine gave the oximes **10a**,**b**. $LiAlH_4$ reduction gave the 1,1,1-trifluoro-3-arylpropan-2-amines **11a**,**b**.[12]

To gain insight into the mechanistic pathway, the course of the reaction of **3e** with benzaldehyde in THF was followed over a 3 h time period by ^{19}F NMR spectroscopy.[13] After 10 min, a broad TBAT signal (−97.0 ppm) and a smaller resonance for TMSF (−158.1 ppm) were observed. Over the course of 1 h the TMSF increased, but the TBAT was only partially consumed and its peak shape sharpened significantly. Between 1 and 2 h the TMSF signal decreased and a new signal at −111.3 ppm emerged, which corresponded to TBAF (Fig. 1).

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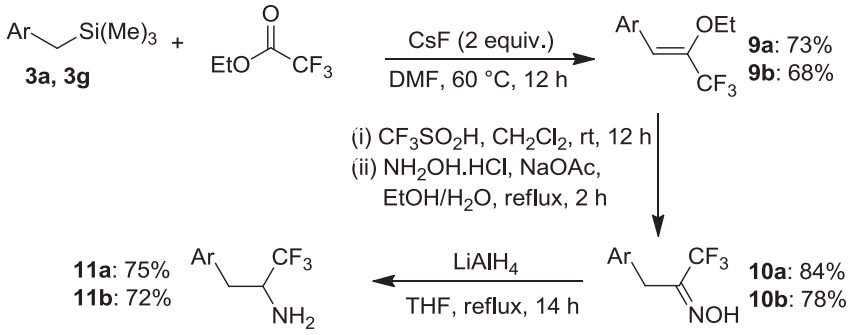


Scheme 2. 1,1,1-Trifluoro-3-arylpropan-2-amine synthesis.

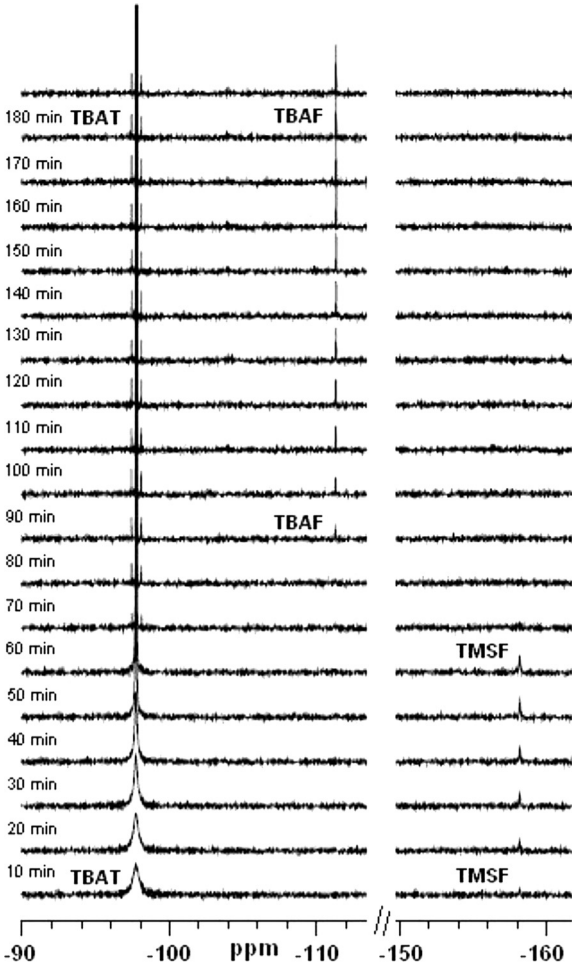


Fig. 1. ^{19}F NMR time course for the reaction of **3e** with benzaldehyde.

We interpret these results as a three stage mechanistic pathway involving a fluoride initiation (black), autocatalytic cycle (blue), and termination step (red) (Scheme 3). Overall, TBAT mediated fluoride initiation generates the hypervalent silicon intermediate **12**, which upon carbonyl addition provides the alkoxide **13** with formation of TMSF. The alkoxide **13** then enters into an autocatalytic cycle with starting material **3** to produce the secondary hypervalent silicon species **14**, which upon carbonyl addition generates silyl ether product **15** and completes the cycle. Upon consumption of the starting benzylsilane **3** the remaining alkoxide **13** then reacts with TMSF producing **15** and TBAF. Whether the carbonyl addition takes place from a hypervalent siliconate complex, such as **12** or a benzyl carbanion remains to be established.[14]

3. Conclusion

In summary, the synthesis and carbonyl addition chemistry of benzyltrimethylsilanes has been described. These bench stable organometallics offer a user-friendly alternative to other metal based nucleophiles. Further synthetic and mechanistic developments with LiNK metalation and silicon organometallics are under investigation and will be reported on in due course.

4. Experimental

4.1. General methods

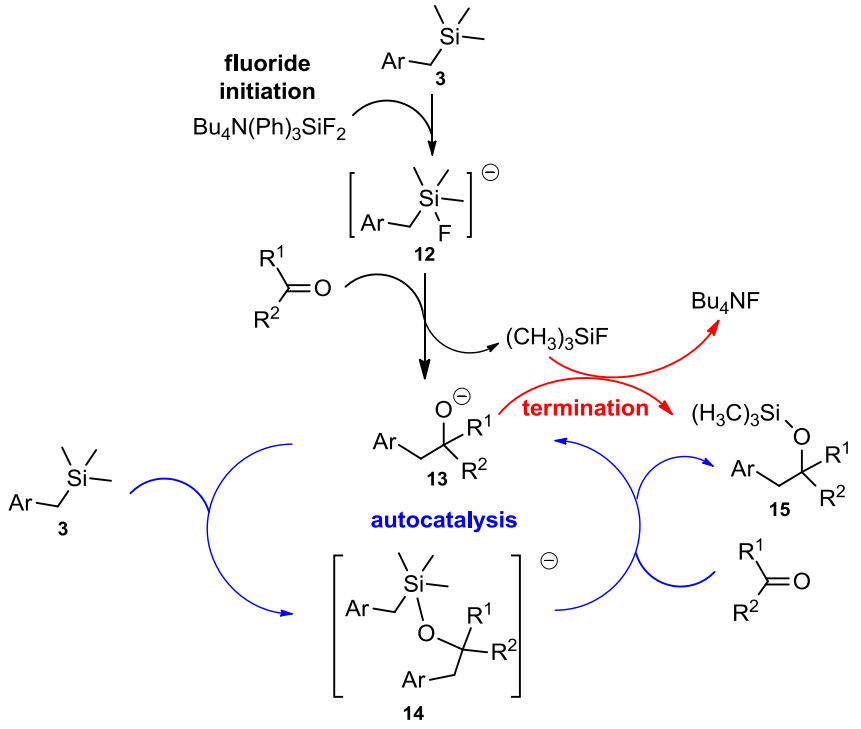
All commercially available reagents were used as supplied unless otherwise stated. All reactions were performed under nitrogen or argon atmosphere in oven dried or flame dried glassware. 2,2,6,6-Tetramethylpiperidine was distilled from CaH_2 and THF was distilled from a sodium/benzophenone prior to use. BuLi was purchased as a 2.5 M solution in hexanes. KO^{t}Bu was purchased as a 1 M solution in THF. The exact concentration of the butyllithium solution was determined by titration with diphenylacetic acid in THF prior to use.[15] Low temperatures were obtained with an acetone/solid CO_2 bath. Aldehydes and ketones were purified prior to use. Chromatography was performed on silica gel 60 PF254 or aluminum oxide 90. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz, 400 MHz or 500 MHz instrument.

4.2. Benzyltrimethylsilane, 3a[16]

A solution of toluene **1a** (184 mg, 2.0 mmol) in THF (25 mL) at −78 °C was treated dropwise with BuLi (2.45 M, 0.98 mL, 2.4 mmol) and stirred for 5 min. KO^{t}Bu (1.0 M in THF, 2.4 mL, 2.4 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.34 mL, 2.0 mmol). The reaction mixture was stirred for 15 min at −78 °C and chlorotrimethylsilane (0.76 mL, 6.0 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. Diethyl ether (30 mL) was added to the residue, washed with HCl (2 M, 3×10 mL), water (2×10 mL), and brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane yielded a colorless liquid (273 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.18 (m, 2H), 7.11–6.97 (m, 3H), 2.09 (s, 2H), 0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 128.3, 128.2, 124.0, 27.21, −1.7 ppm. IR (CH_2Cl_2): 2985, 1599, 1265 cm^{-1}. HRMS–EI $[M]^+$: 164.1026, $C_{10}H_{16}Si$ requires 164.1021.

4.3. 2-((Trimethylsilyl)methyl)benzoic acid, 3b[17]

A solution of *o*-toluic acid **1b** (200 mg, 1.47 mmol) in THF (18.4 mL) at −78 °C was treated dropwise with BuLi (2.31 M,



Scheme 3. Outline of mechanistic pathway.

1.40 mL, 3.325 mmol) and stirred for 5 min. KO^{t}Bu (1.0 M in THF, 1.765 mL, 1.765 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.248 mL, 1.47 mmol). The reaction mixture was stirred for 15 min at −78 °C and chloromethylsilane (0.56 mL, 4.41 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. Diethyl ether (30 mL) was added to the residue, washed with HCl (2 M, 3×10 mL), water (2×10 mL), and brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (98:2) yielded a colorless solid (236 mg, 77%); mp 97–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J=8.1 Hz, 1H), 7.40 (dd, J=8.1, 6.6 Hz, 1H), 7.07–7.19 (m, 2H), 2.75 (s, 2H), −0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 145.1, 132.7, 132.0, 131.0, 126.5, 124.1, 26.1, −1.35 ppm. IR (CH_2Cl_2): 3055, 1681, 1260 cm^{-1}. HRMS–ESI [M−H]$^-$: 207.0848, $C_{11}H_{15}O_2Si$ requires 207.0841.

4.4. (2-Methoxybenzyl)trimethylsilane, 3c[3a]

A solution of 1-methoxy-2-methylbenzene **1c** (610 mg, 5.0 mmol) in THF (62.5 mL) at −78 °C was treated dropwise with BuLi (2.35 M, 2.55 mL, 6.0 mmol) and stirred for 5 min. KO^{t}Bu (1.0 M in THF, 6.0 mL, 6.0 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.85 mL, 5.0 mmol). The reaction mixture was stirred for 15 min at −78 °C and chlorotrimethylsilane (1.9 mL, 15.0 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. HCl (2 M, 30 mL) was added to the residue, washed with diethyl ether (3×30 mL). The organic layer washed with brine (20 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane yielded a colorless oil (706 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09–7.04 (m, 1H), 6.98–6.95 (m, 1H), 6.86–6.78 (m, 2H), 3.78 (s, 3H), 2.09 (s, 2H), 0.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 129.6, 129.4, 125.1, 120.3, 110.0, 55.0, 20.6, −1.4 ppm. IR (CH_2Cl_2): 2954, 1598, 1242 cm^{-1}. HRMS–EI [M]$^+$: 194.1130, $C_{11}H_{18}OSi$ requires 194.1127.

4.5. *N,N*-Dimethyl-2-((trimethylsilyl)methyl)aniline, 3d[18]

A solution of *N,N*-dimethyl-*o*-toluidine **1d** (540 mg, 4.0 mmol) in THF (50 mL) at −78 °C was treated dropwise with BuLi (2.45 M, 1.96 mL, 4.8 mmol) and stirred for 5 min. KO^{t}Bu (1.0 M in THF, 4.8 mL, 4.8 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.68 mL, 4.0 mmol). The reaction mixture was stirred for 15 min at −78 °C and chlorotrimethylsilane (1.53 mL, 12.0 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. Diethyl ether (30 mL) was added to the residue, washed with pH 7 aqueous buffer (3×10 mL), water (10 mL), and brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by aluminum oxide chromatography eluting with cyclohexane yielded a colorless oil (703 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11–6.91 (m, 4H), 2.63 (s, 6H), 2.17 (s, 2H, CH_2), −0.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 136.4, 129.9, 125.0, 123.4, 119.7, 44.9, 22.2, −1.0 ppm. IR (CH_2Cl_2): 2953, 1594, 1246 cm^{-1}. HRMS–EI [M]$^+$: 207.1434, $C_{12}H_{21}NSi$ requires 207.1443.

4.6. (3-Methoxybenzyl)trimethylsilane, 3e[19]

A solution of 1-methoxy-3-methylbenzene **1e** (300 mg, 2.46 mmol) in THF (30.75 mL) at −78 °C was treated dropwise with BuLi (2.31 M, 1.28 mL, 2.95 mmol) and stirred for 5 min. KO^{t}Bu (1.0 M in THF, 2.95 mL, 2.95 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.415 mL, 2.46 mmol). The reaction mixture was stirred for 15 min at −78 °C and chlorotrimethylsilane (0.936 mL, 7.38 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. Diethyl ether (30 mL) was added to the residue, washed with HCl (2 M, 3×10 mL), water (2×10 mL), and brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane yielded a colorless oil (390 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10–7.15 (m, 1H), 6.65–6.55 (m, 3H), 3.78 (s, 3H), 2.07 (s, 2H), 0.0 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7,

142.3, 129.1, 120.8, 114.0, 109.3, 55.2, 27.4, −1.7 ppm. IR (CH_2Cl_2): 2955, 1600, 1260 cm^{-1}. HRMS–EI $[M]^+$: 194.1114, $C_{11}H_{18}OSi$ requires 194.1127.

4.7. *N,N*-Diisopropyl-4-((trimethylsilyl)methyl)benzamide, 3f

A solution of *N,N*-diisopropyl-4-methylbenzamide, **1f** (438 mg, 2.0 mmol) in THF (25 mL) at −78 °C was treated dropwise with BuLi (2.31 M, 1.04 mL, 2.4 mmol) and stirred for 5 min. KO^{t}Bu (1.0 M in THF, 2.4 mL, 2.4 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.34 mL, 2.0 mmol). The reaction mixture was stirred for 15 min at −78 °C and chloromethylsilane (0.76 mL, 6.0 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. Diethyl ether (30 mL) was added to the residue, washed with HCl (2 M, 3×10 mL), water (2×10 mL), and brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (98:2) yielded a colorless solid (518 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, J=8.0 Hz, 2H), 7.00 (d, J=8.0 Hz, 2H), 3.71 (br s, 2H), 2.09 (s, 2H), 1.33 (br s, 12H), 0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 141.6, 134.7, 128.0, 125.9, 27.3, 21.0, −1.8 ppm. IR (KBr disc): 2958, 1618, 1342 cm^{-1}. HRMS–ESI $[M+H]^+$: 292.2091, $C_{17}H_{30}NOSi$ requires 292.2097.

4.8. Trimethyl(3,4,5-trimethoxybenzyl)silane, 3g

A solution of 1,2,3-trimethoxy-5-methylbenzene **1g** (728 mg, 4.0 mmol) in THF (50 mL) at −78 °C was treated dropwise with BuLi (2.35 M, 2.04 mL, 4.8 mmol) and stirred for 5 min. KO^{t}Bu (1.0 M in THF, 4.8 mL, 4.8 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.68 mL, 4.0 mmol). The reaction mixture was stirred for 15 min at −78 °C and chlorotrimethylsilane (1.53 mL, 12.0 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. HCl (2 M, 30 mL) was added to the residue, washed with diethyl ether (3×30 mL). The organic layer washed with brine (20 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (810 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.2 (s, 2H), 3.82 (s, 6H), 3.81 (s, 3H), 2.02 (s, 2H), −0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 136.4, 134.9, 105.1, 61.0, 56.1, 27.5, −1.64 ppm. IR (CH_2Cl_2): 2954, 1586, 1240 cm^{-1}. HRMS–ESI $[M+H]^+$: 255.1411, $C_{13}H_{23}O_3Si$ requires 255.1416.

4.9. (4-Bromobenzyl)trimethylsilane, 3h[7]

A solution of benzyltrimethylsilane **3a** (1.0 g, 6.1 mmol) in CCl_4 at 0 °C was treated with solid I_2 (77.5 mg, 0.305 mmol) followed by bromine (0.32 mL, 6.1 mmol) dropwise under a N_2 atmosphere. The reaction mixture stirred for 15 min and then immediately quenched with 20% $Na_2S_2O_3$ solution. Diethyl ether (30 mL) was added to the residue, washed with water (10 mL) and brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane yielded a colorless oil (1.39 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, J=8.4 Hz, 2H), 6.87 (d, J=8.4 Hz, 2H), 2.04 (s, 2H), 0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.7, 131.3, 129.8, 117.5, 26.8, −1.85 ppm. IR (CH_2Cl_2): 2955, 1482, 1243 cm^{-1}. HRMS–EI $[M]^+$: 242.0125, $C_{10}H_{15}Si^{79}Br$ requires 242.0126.

4.10. 2-(3-Methoxyphenyl)-1-phenylethanol, 4a[20]

*4.10.1. Addition of **3e** to benzaldehyde using CsF in CH_3CN.* A solution of (3-methoxybenzyl)trimethylsilane, **3e** (58.2 mg, 0.30 mmol) and benzaldehyde (37 μL, 0.36 mmol) in anhydrous CH_3CN (1.2 mL) was treated with CsF (45.6 mg, 0.30 mmol) under N_2 and the resulting solution was stirred at reflux for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a yellow oil (42.5 mg, 62%).

*4.10.2. Addition of **3e** to benzaldehyde using CsF in DMF.* A solution of (3-methoxybenzyl)trimethylsilane, **3e** (97 mg, 0.50 mmol) and benzaldehyde (51 μL, 0.50 mmol) in anhydrous DMF (2.0 mL) was treated with CsF (4.0 mg, 0.025 mmol) under N_2 and the resulting solution was stirred at 80 °C for 4 h. The reaction mixture was cooled to rt, 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (2×10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (72.0 mg, 63%).

*4.10.3. Addition of **3e** to benzaldehyde using TBAF in THF.* A solution of (3-methoxybenzyl)trimethylsilane, **3e** (97 mg, 0.50 mmol), benzaldehyde (51 μL, 0.5 mmol), and 4 Å MS (100 mg) in anhydrous THF (2.0 mL) was treated with TBAF (25 μL, 1 M solution in THF, 0.025 mmol) under N_2 and the resulting solution was stirred at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded colorless oil (87.5 mg, 77%).

*4.10.4. Addition of **3e** to benzaldehyde using TBAT in THF.* A solution of (3-methoxybenzyl)trimethylsilane, **3e** (97 mg, 0.50 mmol) and benzaldehyde (51 μL, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution was stirred under N_2 at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded colorless oil (94.1 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.32 (m, 4H), 7.31–7.26 (m, 1H), 7.22 (t, J=7.9 Hz, 1H), 6.82–6.76 (m, 2H), 6.72 (s, 1H), 4.90 (dd, J=8.3, 4.8 Hz, 1H), 3.77 (s, 3H, OCH_3), 3.06–2.92 (m, 2H), 1.98 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 143.7, 139.5, 129.5, 128.4, 127.6, 125.9, 121.8, 115.0, 112.1, 75.2, 55.1, 46.2 ppm. HRMS–ESI $[M+Na]^+$: 251.1039, $C_{15}H_{16}O_2Na$ requires 251.1048.

*4.10.5. Addition of **2e** to benzaldehyde.* A solution of 1-methoxy-3-methylbenzene **1c** (122 mg, 1 mmol) in THF(12.5 mL) at −78 °C was treated dropwise with *n*-BuLi (2.35 M, 0.5 mL, 1.2 mmol) and stirred for 5 min. KO^{t}Bu(1.0 M in THF, 1.2 mL, 1.2 mmol) was added dropwise followed by 2,2,6,6-tetramethylpiperidine (0.17 mL, 1 mmol). The reaction mixture was stirred for 15 min at −78 °C and benzaldehyde (0.205 mL, 2 mmol) added. The reaction mixture was warmed to rt and the solvent removed under reduced pressure. Diethyl ether (20 mL) was added to the residue, washed with HCl (2 M, 3×10 mL), water (2×10 mL), and brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica

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gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (180 mg, 79%).

4.11. 1-(4-Methoxyphenyl)-2-phenylethanol, 4b[21]

A solution of benzyltrimethylsilane, **3a** (82 mg, 0.50 mmol) and *p*-anisaldehyde (73 μL, 0.6 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution was stirred under N_2 at reflux for 2 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 54–55 °C (79.8 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.16 (m, 7H), 6.87 (d, J=8.7 Hz, 2H), 4.85 (t, J=6.7 Hz, 1H), 3.80 (s, 3H), 3.05–2.95 (m, 2H), 1.89 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 138.1, 136.0, 129.5, 128.4, 127.1, 126.5, 113.8, 74.9, 55.3, 46.0 ppm. HRMS–ESI $[M+Na]^+$: 251.1053, $C_{15}H_{16}O_2Na$ requires 251.1048.

4.12. 1-(4-Fluorophenyl)-2-phenylethanol, 4c[22]

A solution of benzyltrimethylsilane, **3a** (82 mg, 0.50 mmol) and *p*-fluorobenzaldehyde (64 μL, 0.6 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution under N_2 was stirred at reflux for 1 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 46–48 °C (84.4 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.20 (m, 5H), 7.16 (d, J=6.9 Hz, 2H), 7.02 (t, J=8.7 Hz, 2H), 4.88 (t, J=6.6 Hz, 1H), 3.04–2.93 (m, 2H), 1.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2 (d, J=245.4 Hz), 139.5 (d, J=3.2 Hz), 137.7, 129.5, 128.5, 127.5 (d, J=8.1 Hz), 126.7, 115.2 (d, J=21.4 Hz), 74.7, 46.2 ppm. HRMS–ESI $[M+Na]^+$: 239.0848, $C_{14}H_{13}FONa$ requires 239.0849.

4.13. 3,3-Dimethyl-1-phenylbutan-2-ol, 4d[23]

A solution of benzyltrimethylsilane, **3a** (164 mg, 1.0 mmol) and pivalaldehyde (55 μL, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (270 mg, 0.5 mmol) and the resulting solution under N_2 was stirred at reflux for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (56.2 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.29 (m, 2H), 7.25–7.20 (m, 3H), 3.43 (dd, J=10.7, 1.6 Hz, 1H), 2.91 (dd, J=13.6, 1.6 Hz, 1H), 2.47 (dd, J=13.6, 10.7 Hz, 1H), 1.00 (s, 9H), OH not observed, ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 129.5, 128.7, 126.5, 80.7, 38.5, 35.0, 26.0 ppm.

4.14. 2-Phenyl-1-(pyridin-4-yl)ethanol, 4e[24]

A solution of benzyltrimethylsilane, **3a** (82 mg, 0.50 mmol) and 4-pyridinecarboxaldehyde (57 μL, 0.6 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution under N_2 was stirred at reflux for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (5 mL) was added. 2 M NaOH (8 mL) was added to make the solution basic. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by alumina gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 109–111 °C (74.5 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, J=6.0 Hz, 2H), 7.33–7.22 (m, 5H), 7.16 (d, J=6.0 Hz, 2H), 4.90 (dd, J=8.3, 4.9 Hz, 1H), 3.07–2.91 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 149.6, 137.0, 129.5, 128.6, 126.9, 120.9, 73.7, 45.7 ppm. HRMS–ESI $[M+H]^+$: 200.1069, $C_{13}H_{14}NO$ requires 200.1075. OH not observed.

4.15. 1-(4-Chlorophenyl)-2-(2-methoxyphenyl)ethanol, 4f

A solution of (2-methoxybenzyl)trimethylsilane, **3c** (97 mg, 0.50 mmol) and 4-chlorobenzaldehyde (70.25 mg, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (27.0 mg, 0.05 mmol) and the resulting solution was stirred under N_2 at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded colorless solid, mp 62–64 °C (78.9 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.30–7.20 (m, 5H), 7.04–7.00 (m, 1H), 6.91–6.85 (m, 2H), 4.96–4.90 (m, 1H), 3.84 (s, 3H), 3.12–3.05 (m, 1H), 2.97–2.89 (m, 1H), 2.60 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 143.1, 132.9, 131.7, 128.4, 128.3, 127.3, 126.2, 120.9, 110.6, 73.8, 55.5, 41.3 ppm. HRMS $[M+Na]^+$: 285.0660, $C_{15}H_{15}O_2ClNa$ requires 285.0658.

4.16. 2-(2-Methoxyphenyl)-1-*m*-tolylethanol, 4g

A solution of (2-methoxybenzyl)trimethylsilane, **3c** (97 mg, 0.50 mmol) and 3-methylbenzaldehyde (59 mg, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (27.0 mg, 0.05 mmol) and the resulting solution was stirred under N_2 at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded colorless solid, mp 51–53 °C (73.9 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.15 (m, 4H), 7.13–7.09 (m, 2H), 6.93–6.86 (m, 2H), 4.98–4.88 (m, 1H), 3.86 (s, 1H), 3.14–3.07 (m, 1H), 3.01–2.92 (m, 1H), 2.48 (s, 1H), 2.36 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 144.7, 138.0, 131.6, 128.3, 128.1, 126.9, 126.5, 123.0, 120.9, 110.6, 74.4, 55.5, 41.3, 21.6 ppm. HRMS–ESI $[M+Na]^+$: 265.1196, $C_{16}H_{18}O_2Na$ requires 265.1204.

4.17. 1-(4-Bromophenyl)-2-(2-(dimethylamino)phenyl)ethanol, 4h

A solution of *N*,*N*-dimethyl-2-((trimethylsilyl)methyl)aniline, **3d** (103.5 mg, 0.50 mmol) and *p*-bromobenzaldehyde (92.5 mg, 0.50 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution was stirred under N_2 at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and phosphate buffer solution (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by aluminum oxide chromatography eluting with

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cyclohexane/ethyl acetate (98:2) yielded a colorless oil (135.7 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J=7.2 Hz, 2H), 7.32 (s, 1H), 7.27–7.17 (m, 3H), 7.01–7.04 (m, 1H), 6.93 (d, J=7.5 Hz, 1H), 4.91 (dd, J=6.8, 3.1 Hz, 1H), 3.16–3.05 (m, 2H), 2.75 (s, 6H), 1.63 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 144.4, 134.5, 132.1, 131.1, 128.1, 127.41, 125.4, 120.5, 120.2, 75.1, 44.9, 43.8 ppm. HRMS–EI $[M]^+$: 319.0578, $C_{16}H_{18}NO^{79}Br$ requires 319.0572.

4.18. (*E*)-1-(2-(Dimethylamino)phenyl)-4-phenylbut-3-en-2-ol, 4i

A solution of *N*,*N*-dimethyl-2-((trimethylsilyl)methyl)aniline, **3d** (103.5 mg, 0.50 mmol) and *trans*-cinnamaldehyde (63 μL, 0.50 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution was stirred under N_2 at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and phosphate buffer solution (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by aluminum oxide chromatography eluting with cyclohexane/ethyl acetate (98:2) yielded a yellow oil (107.7 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.06 (m, 9H), 6.82 (br s, 1H, OH), 6.64 (d, J=15.8 Hz, 1H), 6.25 (dd, J=15.8, 4.6 Hz, 1H), 4.54–4.47 (m, 1H), 3.13–3.01 (m, 2H), 2.73 (d, J=1.3 Hz, 6H), ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 137.2, 134.8, 133.1, 132.0, 129.1, 128.4, 128.0, 127.2, 126.4, 125.4, 120.3, 74.0, 44.9, 41.7. HRMS–EI $[M]^+$: 267.1624, $C_{18}H_{21}NO$ requires 267.1623.

4.19. 1-(4-Bromophenyl)-2-(3-methoxyphenyl)ethanol, 4j

A solution of (3-methoxybenzyl)trimethylsilane, **3e** (97 mg, 0.50 mmol) and *p*-bromobenzaldehyde (110 mg, 0.6 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution was stirred under N_2 at reflux for 1.5 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a light yellow oil (123.7 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J=8.4 Hz, 2H), 7.27–7.19 (m, 3H), 6.81–6.74 (m, 2H), 6.71 (s, 1H), 4.90–4.82 (dd, J=8.4, 4.9 Hz, 1H), 3.77 (s, 3H), 3.02–2.87 (m, 2H), 1.97 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 142.7, 139.0, 131.4, 129.6, 127.6, 121.7, 121.3, 115.1, 112.2, 74.5, 55.1, 46.1 ppm. HRMS–ESI $[M-H]^-$: 305.0165, $C_{15}H_{14}O_2^{79}Br$ requires 305.0177.

4.20. 2-(3-Methoxyphenyl)-1-(pyridin-4-yl)ethanol, 4k

A solution of (3-methoxybenzyl)trimethylsilane, **3e** (97 mg, 0.50 mmol) and 4-pyridinecarboxaldehyde (57 μL, 0.6 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution was stirred under N_2 at reflux for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (5 mL) was added. 2 M NaOH (8 mL) was added to make the solution basic. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (76.6 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, J=6.0 Hz, 2H), 7.28 (d, J=6.0 Hz, 2H), 7.23 (t, J=7.9 Hz, 1H), 6.83–6.75 (m, 2H), 6.71 (s, 1H), 4.91 (dd, J=8.6, 4.6 Hz, 1H), 3.78 (s, 3H), 3.06–2.86 (m, 2H), OH not observed, ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 152.4, 149.7, 138.4, 129.7, 121.7, 120.8, 115.2, 112.4, 73.6, 55.2, 45.7 ppm. HRMS–ESI $[M+H]^+$: 230.1171, $C_{14}H_{16}NO_2$ requires 230.1181.

4.21. 4-(2-Hydroxy-2-(pyridin-4-yl)ethyl)-*N*,*N*-diisopropylbenzamide, 4l

A solution of *N*,*N*-diisopropyl-4-((trimethylsilyl)methyl)benzamide, **3f** (87.3 mg, 0.30 mmol) and 4-pyridinecarboxaldehyde (35 μL, 0.36 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (8.1 mg, 0.015 mmol) and the resulting solution under N_2 was stirred at reflux for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (5 mL) was added. 2 M NaOH (8 mL) was added to make the solution basic and the solution extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 161–163 °C (73.6 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (br s, 2H), 7.27–7.14 (m, 6H), 4.88 (dd, J=8.3, 4.8 Hz, 1H), 3.66 (br s, 2H), 3.06–2.91 (m, 2H), 1.87 (br s, 1H), 1.30 (br s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 152.6, 149.7, 137.8, 137.4, 129.6, 125.9, 120.9, 73.5, 45.4, 20.7 ppm. HRMS–ESI $[M+H]^+$: 327.2085, $C_{20}H_{27}O_2N_2$ requires 327.2073. ^{i}Pr carbon not observed.

4.22. 4-(2-(4-Bromophenyl)-2-hydroxyethyl)-*N*,*N*-diisopropylbenzamide, 4m

A solution of *N*,*N*-diisopropyl-4-((trimethylsilyl)methyl)benzamide, **3f** (87.3 mg, 0.30 mmol) and *p*-bromobenzaldehyde (66.6 mg, 0.36 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (8.1 mg, 0.015 mmol) and the resulting solution was stirred under N_2 at reflux for 1.5 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 145–147 °C (98.4 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J=8.4 Hz, 2H), 7.27–7.14 (m, 6H), 4.86 (t, J=6.6 Hz, 1H), 3.68 (br s, 2H), 3.04–2.93 (m, 2H), 1.75 (br s, 1H), 1.33 (br s, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 142.6, 138.15, 137.3, 131.4, 129.5, 127.6, 125.9, 121.4, 74.5, 45.8, 20.7 ppm (^{i}Pr carbon not observed). HRMS–ESI $[M+H]^+$: 404.1235, $C_{21}H_{27}O_2N^{79}Br$ requires 404.1225.

4.23. 1-(Naphthalen-2-yl)-2-(3,4,5-trimethoxyphenyl)ethanol, 4n[25]

A solution of (3,4,5-trimethoxybenzyl)trimethylsilane, **3g** (76.2 mg, 0.30 mmol) and 2-napthaldehyde (46.8 mg, 0.3 mmol) in anhydrous THF (1.2 mL) was treated with TBAT (8.1 mg, 0.015 mmol) and the resulting solution was stirred under N_2 at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a colorless solid, mp 60–62 °C (83.4 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.79 (m, 4H), 7.54–7.46 (m, 3H), 6.40 (s, 2H), 5.1–5.04 (m, 1H), 3.83 (s, 3H), 3.77 (s, 6H), 3.12–2.96 (m, 2H), 2.17 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 141.2, 136.9, 133.6, 133.4, 133.1, 128.3, 128.1, 127.8, 126.3, 126.0, 124.8, 124.2, 106.6, 75.4, 61.0, 56.2, 46.5 ppm. HRMS–ESI $[M+Na]^+$: 361.1399, $C_{21}H_{22}O_4Na$ requires 361.1416.

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4.24. 1-(4-(Trifluoromethyl)phenyl)-2-(3,4,5-trimethoxyphenyl) ethanol, 4o

A solution of (3,4,5-trimethoxybenzyl)trimethylsilane, **3g** (76.2 mg, 0.30 mmol) and 4-(trifluoromethyl)benzaldehyde (41 μL, 0.3 mmol) in anhydrous THF (1.2 mL) was treated with TBAT (8.1 mg, 0.015 mmol) and the resulting solution was stirred under N_2 at reflux for 3 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a colorless solid, mp 95–97 °C (74.7 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J*=8.0 Hz, 2H), 7.48 (d, *J*=8.0 Hz, 2H), 6.35 (s, 2H), 4.96 (dd, *J*=8.3, 4.6 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 6H), 2.99 (dd, *J*=13.6, 4.6 Hz, 1H), 2.89 (dd, *J*=13.6, 8.3 Hz, 1H), 2.12 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 147.7 (br s), 137.1, 132.9, 129.9 (q, *J*=32.3 Hz), 126.4, 125.5 (q, *J*=3.8 Hz), 124.3 (q, *J*=272 Hz), 106.5, 74.6, 61.0, 56.2, 46.7 ppm. HRMS–ESI $[M+Na]^+$: 379.1117, $C_{18}H_{19}O_4F_3Na$ requires 379.1133.

4.25. 2-(4-Bromophenyl)-1-(4-methoxyphenyl)ethanol, 4p

A solution of (4-bromobenzyl)trimethylsilane, **3h** (121.5 mg, 0.50 mmol) and *p*-anisaldehyde (61 μL, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) under N_2 and the resulting solution was stirred at reflux for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 76–78 °C (112.1 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J*=8.1 Hz, 2H), 7.23 (d, *J*=8.3 Hz, 2H), 7.02 (d, *J*=8.1 Hz, 2H), 6.87 (d, *J*=8.3 Hz, 2H), 4.81 (t, *J*=6.5 Hz, 1H), 3.81 (s, 3H), 3.03–2.89 (m, 2H), 1.86 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 137.1, 135.6, 131.4, 131.2, 127.1, 120.4, 113.8, 74.8, 55.3, 45.2 ppm. HRMS–ESI $[M-H]^-$: 305.0174, $C_{15}H_{14}O_2^{79}Br$ requires 305.0177.

4.26. (*E*)-1-(4-Bromophenyl)-4-phenylbut-3-en-2-ol, 4q

A solution of (4-bromobenzyl)trimethylsilane, **3h** (121.5 mg, 0.50 mmol) and *trans*-cinnamaldehyde (63 μL, 0.50 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (13.5 mg, 0.025 mmol) and the resulting solution under N_2 was stirred at reflux for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 80–82 °C (107.8 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J*=7.1 Hz, 2H), 7.39–7.21 (m, 5H), 7.13 (d, *J*=7.1 Hz, 2H), 6.57 (d, *J*=16.0 Hz, 1H), 6.24 (dd, *J*=16.0, 6.4 Hz, 1H), 4.54–4.45 (m, 1H), 2.95–2.80 (m, 2H), 1.71 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.7, 136.4, 131.5, 131.3, 131.1, 130.8, 128.6, 127.8, 126.5, 120.5, 73.3, 43.4 ppm. HRMS–ESI $[M-H]^-$: 301.0215, $C_{16}H_{14}O^{79}Br$ requires 301.0228.

4.27. 1-Phenylhexan-2-ol, 6a[26]

A solution of benzyltrimethylsilane, **3a** (164 mg, 1.0 mmol) and valeraldehyde (54 μL, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (27 mg, 0.05 mmol) and the resulting solution under N_2 was heated at 70 °C for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (65 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.28 (m, 2H), 7.26–7.19 (m, 3H), 3.86–3.76 (m, 1H), 2.86–2.60 (m, 2H), 1.91 (s, 1H), 1.59–1.44 (m, 4H), 1.40–1.29 (m, 2H), 0.91 (t, *J*=7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 129.4, 128.5, 126.4, 72.7, 44.1, 36.5, 27.9, 22.7, 14.0 ppm. HRMS–EI $[M]^+$: 178.1361, $C_{12}H_{18}O$ requires 178.1358.

4.28. 1,2-Diphenylpropan-2-ol, 6b[20]

A solution of benzyltrimethylsilane, **3a** (164 mg, 1.0 mmol) and acetophenone (59 μL, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (27 mg, 0.05 mmol) and the resulting solution under N_2 was heated at 70 °C for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (98.6 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.37 (m, 2H), 7.35–7.29 (m, 2H), 7.27–7.18 (m, 4H), 7.02–6.96 (m, 2H), 3.13 (d, *J*=13.2 Hz, 1H), 3.02 (d, *J*=13.2 Hz, 1H), 1.84 (s, 1H), 1.56 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 136.7, 130.3, 128.0, 126.6, 124.9, 74.4, 50.5, 29.4 ppm. HRMS–ESI $[M+Na]^+$: 235.1103, $C_{15}H_{16}ONa$ requires 235.1099.

4.29. 1-Benzylcyclohexanol, 6c[27]

A solution of benzyltrimethylsilane, **3a** (164 mg, 1.0 mmol) and cyclohexanone (52 μL, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (54 mg, 0.10 mmol) and the resulting solution was stirred under N_2 at rt for 12 h. The solvent was removed under reduced pressure, 2 M HCl (10 mL) was added, and the residue extracted with diethyl ether (10×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless solid, mp 41–43 °C (69 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.18 (m, 5H), 2.75 (s, 2H), 1.65–1.38 (m, 10H), 1.25 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 130.6, 128.1, 126.4, 71.1, 48.7, 37.3, 25.8, 22.1 ppm. HRMS–EI $[M]^+$: 190.1361, $C_{13}H_{18}O$ requires 190.1358.

4.30. 2-(3-Bromophenyl)-1-(2-methoxyphenyl)propan-2-ol, 6d

A solution of (2-methoxybenzyl)trimethylsilane, **3c** (194 mg, 1.0 mmol) and 3-bromoacetophenone (66 μL, 0.5 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (40.5 mg, 0.075 mmol) and the resulting solution was heated under N_2 at 70 °C for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (89.5 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.62 (m, 1H), 7.41–7.32 (m, 2H), 7.24–7.14 (m, 2H), 6.94–6.83 (m, 3H), 3.83 (s, 3H), 3.52 (br s, 1H), 3.17–3.06 (m, 2H), 1.50 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 151.2, 135.1, 132.8, 129.5, 128.5, 128.0,

125.4, 123.8, 122.3, 120.1, 110.7, 75.2, 55.6, 44.9, 29.5 ppm. HRMS–ESI $[M+Na]^+$: 343.0324, $C_{16}H_{17}O_2Na^{79}Br$ requires 343.0310.

4.31. 1-(2-(Dimethylamino)phenyl)hexan-2-ol, 6e

A solution of *N*,*N*-dimethyl-2-((trimethylsilyl)methyl)aniline, **3d** (124.2 mg, 0.6 mmol) and valeraldehyde (32 μL, 0.3 mmol) in anhydrous THF (1.2 mL) was treated with TBAT (16.2 mg, 0.03 mmol) and the resulting solution was heated under N_2 at 70 °C for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and phosphate buffer (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by alumina gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (41.3 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.18 (m, 2H), 7.14–7.04 (m, 2H), 6.42 (br s, 1H), 3.80–3.72 (m, 1H), 2.98–2.90 (m, 1H), 2.85–2.78 (m, 1H), 2.70 (s, 6H), 1.55–1.21 (m, 6H), 0.91 (t, *J*=6.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 135.8, 132.0, 127.8, 125.38, 120.3, 73.6, 45.0, 41.3, 38.0, 28.2, 23.0, 14.3 ppm. HRMS–ESI $[M+H]^+$: 222.1853, $C_{14}H_{24}NO$ requires 222.1858.

4.32. 1-(3-Methoxyphenyl)hexan-2-ol, 6f

A solution of (3-methoxybenzyl)trimethylsilane, **3e** (116.4 mg, 0.6 mmol) and valeraldehyde (32 μL, 0.3 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (16.2 mg, 0.03 mmol) and the resulting solution under N_2 was heated at 70 °C for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (98:2) yielded a colorless oil (42 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25–7.20 (m, 1H), 6.83–6.75 (m, 3H), 3.85–3.77 (m, 1H), 3.80 (s, 3H), 2.84–2.78 (m, 1H), 2.65–2.58 (m, 1H), 2.17 (s, 1H), 1.59–1.44 (m, 4H), 1.41–1.28 (m, 2H), 0.91 (t, *J*=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 140.2, 129.5, 121.7, 115.1, 111.8, 72.6, 55.1, 44.1, 36.5, 27.9, 22.7, 14.0 ppm. HRMS–EI $[M]^+$: 208.1459, $C_{13}H_{20}O_2$ requires 208.1463.

4.33. 4-(2-Hydroxyhexyl)-*N*,*N*-diisopropylbenzamide, 6g

A solution of *N*,*N*-diisopropyl-4-((trimethylsilyl)methyl)benzamide, **3f** (116.4 mg, 0.40 mmol) and valeraldehyde (21 μL, 0.20 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (10.8 mg, 0.02 mmol) and the resulting solution was heated under N_2 at 70 °C for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (98:2) yielded a colorless oil (43 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, *J*=8.1 Hz, 2H), 7.22 (d, *J*=8.1 Hz, 2H), 3.88–3.76 (m, 1H), 3.70 (br s, 2H), 2.86–2.79 (m, 1H), 2.71–2.62 (m, 1H), 2.16 (s, 1H), 1.75–1.05 (br m, 18H), 0.91 (t, *J*=7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 139.4, 137.0, 129.4, 125.9, 72.5, 43.8, 36.5, 27.9, 22.6, 20.7, 14.0 ppm. HRMS–ESI $[M+H]^+$: 306.2438, $C_{19}H_{32}O_2N$ requires 306.2433.

4.34. 4-(2-(2-Bromophenyl)-2-hydroxypropyl)-*N*,*N*-diisopropylbenzamide, 6h

A solution of *N*,*N*-diisopropyl-4-((trimethylsilyl)methyl)benzamide, **3f** (116.4 mg, 0.40 mmol) and 2′-bromoacetophenone (27 μL, 0.20 mmol) in anhydrous THF (2.0 mL) was treated with TBAT (10.8 mg, 0.02 mmol) and the resulting solution was heated under N_2 at 70 °C for 4 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (94:6) yielded a colorless solid, mp 98–100 °C (59.9 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J*=7.8 Hz, 1H), 7.46 (d, *J*=7.8 Hz, 1H), 7.17–7.19 (m, 1H), 7.13 (d, *J*=6.7 Hz, 2H), 7.06–7.09 (m, 1H), 7.02 (d, *J*=6.7 Hz, 2H), 3.63 (d, *J*=13.5 Hz, 1H), 3.61 (br s, 2H), 3.29 (d, *J*=13.5 Hz, 1H), 2.58 (s, 1H), 1.74 (s, 3H), 0.98–1.6 (br m, 12H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 144.7, 137.5, 137.1, 134.9, 130.5, 128.6, 128.5, 127.4, 125.4, 120.1, 75.5, 45.8, 27.3, 20.7 ppm. HRMS–ESI $[M+H]^+$: 418.1371, $C_{22}H_{29}O_2N^{79}Br$ requires 418.1382.

4.35. 2-(4-Fluorophenyl)-1-(3,4,5-trimethoxyphenyl)propan-2-ol, 6i

A solution of (3,4,5-trimethoxybenzyl)trimethylsilane, **3g** (152.4 mg, 0.60 mmol) and 4-fluoroacetophenone (37 μL, 0.3 mmol) in anhydrous THF (1.2 mL) was treated with TBAT (16.2 mg, 0.03 mmol) and the resulting solution was heated under N_2 at reflux for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a colorless oil (75 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.30 (m, 2H), 7.03–6.96 (m, 2H), 6.09 (s, 2H), 3.78 (s, 3H), 3.68 (s, 6H), 3.05 (d, *J*=13.3 Hz, 1H), 2.91 (d, *J*=13.3 Hz, 1H), 1.92 (br s, 1H), 1.58 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8 (d, *J*=245.0 Hz), 152.9, 143.4 (d, *J*=3.2 Hz), 137.0, 132.0, 127.0 (d, *J*=7.9 Hz), 114.8 (d, *J*=21.2 Hz), 107.6, 74.4, 61.0, 56.1, 51.1, 29.9, 27.1 ppm. HRMS–ESI $[M+Na]^+$: 343.1308, $C_{18}H_{21}O_4NaF$ requires 343.1322.

4.36. 2-Phenyl-1-(3,4,5-trimethoxyphenyl)hexan-2-ol, 6j

A solution of (3,4,5-trimethoxybenzyl)trimethylsilane, **3g** (152.4 mg, 0.60 mmol) and valerophenone (50 μL, 0.3 mmol) in anhydrous THF (1.2 mL) was treated with TBAT (16.2 mg, 0.03 mmol) and the resulting solution was heated under N_2 at reflux for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with ethyl acetate (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a colorless oil (69.1 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.29 (m, 4H), 7.25–7.19 (m, 1H), 6.03 (s, 2H), 3.78 (s, 3H), 3.63 (s, 6H), 3.14 (d, *J*=13.3 Hz, 1H), 2.94 (d, *J*=13.3 Hz, 1H), 2.05–1.80 (m, 2H), 1.60 (br s, 1H), 1.41–1.18 (m, 4H), 0.84 (t, *J*=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 146.0, 136.8, 131.8, 128.1, 126.5, 125.8, 107.6, 60.9, 56.0, 50.2, 42.3, 27.1, 25.9, 23.2, 14.2 ppm. MS–ESI $[M+Na]^+$: 367.1882, $C_{21}H_{28}O_4Na$ requires 367.1885.

4.37. 1-(4-Bromophenyl)-2-phenylpropan-2-ol, 6k

A solution of (4-bromobenzyl)trimethylsilane, **3h** (145.8 mg, 0.60 mmol) and acetophenone (36 μL, 0.3 mmol) in anhydrous THF (1.2 mL) was treated with TBAT (32.4 mg, 0.06 mmol) under N_2 and the resulting solution was stirred at reflux for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with

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diethyl ether (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (96:4) yielded a colorless oil (65.6 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.29 (m, 6H), 7.28–7.23 (m, 1H), 6.84 (d, J=8.4 Hz, 2H), 3.07 (d, J=13.4 Hz, 1H), 2.98 (d, J=13.4 Hz, 1H), 1.69 (br s, 1H), 1.57 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 136.0, 132.4, 131.2, 128.3, 127.0, 125.1, 120.8, 74.6, 50.0, 29.5 ppm. HRMS–ESI $[M-OH]^+$: 273.0278, $C_{15}H_{14}^{79}Br$ requires 273.0279.

4.38. 1-(4-Bromophenyl)-4-phenylbutan-2-ol, 6l

A solution of (4-bromobenzyl)trimethylsilane, **3h** (145.8 mg, 0.60 mmol) and 3-phenylpropionaldehyde (40 μL, 0.3 mmol) in anhydrous THF (1.2 mL) was treated with TBAT (32.4 mg, 0.06 mmol) and the resulting solution was stirred under N_2 at reflux for 6 h. The reaction mixture was cooled to rt, solvent removed under reduced pressure, and 2 M HCl (10 mL) was added. The residue was extracted with diethyl ether (10×3 mL), the organic layer washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (98:2) yielded a colorless solid, mp 67–69 °C (59.6 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J=8.3 Hz, 2H), 7.30–7.23 (m, 2H), 7.21–7.14 (m, 3H), 7.06 (d, J=8.3 Hz, 2H), 3.84–3.75 (m, 1H), 2.87–2.60 (m, 4H), 1.89–1.73 (m, 2H), 1.50 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 137.5, 131.7, 131.3, 128.6, 128.6, 126.1, 120.5, 71.9, 43.6, 38.6, 32.2 ppm. HRMS–ESI $[M+Na]^+$: 327.0367, $C_{16}H_{17}ONa^{79}Br$ requires 327.0360.

4.39. 3-Phenylisochroman-1-one, 8a[28]

A solution of 2-((trimethylsilyl)methyl)benzoic acid, **3b** (41.6 mg, 0.20 mmol) and benzaldehyde (25 μL, 0.24 mmol), and 4 Å MS (50 mg) in anhydrous DMF (0.8 mL) was treated with CsF (58.4 mg, 0.40 mmol) under N_2 and the resulting solution was stirred at 80 °C for 6 h. The reaction mixture was cooled to rt, 2 M HCl (10 mL) was added and stirred for another 30 min. The residue was extracted with ethyl acetate (10×3 mL), the organic layer washed with water (2×10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a colorless solid, mp 58–60 °C (38.1 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J=7.5 Hz, 1H), 7.57 (td, J=7.5, 1.3 Hz, 1H), 7.51–7.34 (m, 6H), 7.29 (d, J=7.5 Hz, 1H), 5.57 (dd, J=12.0, 3.1 Hz, 1H), 3.35 (dd, J=16.4, 12.0 Hz, 1H), 3.14 (dd, J=16.4, 3.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 139.1, 138.7, 134.0, 130.6, 128.9, 128.8, 128.0, 127.5, 126.3, 125.3, 80.1, 35.8 ppm. HRMS–ESI $[M+H]^+$: 225.0918, $C_{15}H_{13}O_2$ requires 225.0916.

4.40. 3-(3,4-Dimethoxyphenyl)isochroman-1-one, 8b[29]

A solution of 2-((trimethylsilyl)methyl)benzoic acid, **3b** (104 mg, 0.50 mmol) and 3,4-trimethoxybenzaldehyde (99.6 mg, 0.60 mmol), and 4 Å MS (100 mg) in anhydrous DMF (2.0 mL) was treated with CsF (152.0 mg, 1.0 mmol) under N_2 and the resulting solution was stirred at 80 °C for 6 h. The reaction mixture was cooled to rt, 2 M HCl (20 mL) was added and stirred for another 30 min. The residue was extracted with ethyl acetate (20×3 mL), the organic layer washed with water (2×10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (80:20) yielded a colorless solid, mp 68–70 °C (109.4 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, J=7.5 Hz, 1H), 7.57 (td, J=7.5, 1.3 Hz, 1H), 7.43 (t, J=7.5 Hz, 1H), 7.29 (d, J=7.5 Hz, 1H), 7.04 (d, J=1.9 Hz, 1H), 6.98 (dd, J=8.2, 1.9 Hz, 1H), 6.88 (d, J=8.2 Hz, 1H), 5.51 (dd, J=12.0, 3.1 Hz, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.36 (dd, J=16.4, 12.0 Hz, 1H), 3.11 (dd, J=16.4, 3.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 149.5, 149.4, 139.2, 134.0, 131.3, 130.6, 128.0, 127.5, 125.3, 118.9, 111.2, 109.6, 80.1, 56.2, 56.1, 35.8 ppm. HRMS–ESI $[M+H]^+$: 285.1125, $C_{17}H_{17}O_4$ requires 285.1127.

4.41. 3-(5-Methylfuran-2-yl)isochroman-1-one, 8c

A solution of 2-((trimethylsilyl)methyl)benzoic acid, **3b** (104 mg, 0.50 mmol), 5-methylfurfural (60 μL, 0.60 mmol), and 4 Å MS (100 mg) in anhydrous DMF (2.0 mL) was treated with CsF (152.0 mg, 1.0 mmol) under N_2 and the resulting solution was stirred at 80 °C for 6 h. The reaction mixture was cooled to rt, 2 M HCl (20 mL) was added and stirred for another 1 h. The residue was extracted with ethyl acetate (20×3 mL), the organic layer washed with water (2×10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a brown crystalline solid, mp 73–75 °C (85.5 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J=7.5 Hz, 1H), 7.57 (td, J=7.5, 1.2 Hz, 1H), 7.42 (t, J=7.5 Hz, 1H), 7.30 (d, J=7.5 Hz, 1H), 6.28 (d, J=3.1 Hz, 1H), 5.95 (d, J=3.1 Hz, 1H), 5.53 (dd, J=11.2, 3.4 Hz, 1H), 3.57 (dd, J=16.4, 11.2 Hz, 1H), 3.18 (dd, J=16.4, 3.4 Hz, 1H), 2.30 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 153.3, 149.0, 138.8, 134.0, 130.6, 128.0, 127.6, 125.1, 110.1, 106.6, 73.3, 31.6, 13.7 ppm. HRMS–ESI $[M+Na]^+$: 251.0683, $C_{14}H_{12}O_3Na$ requires 251.0684.

4.42. 3-(5-Methylthiophen-2-yl)isochroman-1-one, 8d

A solution of 2-((trimethylsilyl)methyl)benzoic acid, **3b** (104 mg, 0.50 mmol), 5-methylthiophene-2-carbaldehyde (65 μL, 0.60 mmol), and 4 Å MS (100 mg) in anhydrous DMF (2.0 mL) was treated with CsF (152.0 mg, 1.0 mmol) under N_2 and the resulting solution was stirred at 80 °C for 6 h. The reaction mixture was cooled to rt, 2 M HCl (20 mL) was added and stirred for another 1 h. The residue was extracted with ethyl acetate (20×3 mL), the organic layer was washed with water (2×10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (98:2) yielded a yellow oil (87.9 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J=7.6 Hz, 1H), 7.57 (td, J=7.6, 1.3 Hz, 1H), 7.42 (t, J=7.6 Hz, 1H), 7.29 (d, J=7.6 Hz, 1H), 6.92 (d, J=3.4 Hz, 1H), 6.64 (d, J=3.4 Hz, 1H), 5.72 (dd, J=10.6, 3.6 Hz, 1H), 3.43 (dd, J=16.3, 10.6 Hz, 1H), 3.28 (dd, J=16.3, 3.6 Hz, 1H), 2.47 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 141.1, 138.7, 138.6, 134.0, 130.6, 128.1, 127.6, 126.4, 124.9, 75.9, 35.2, 15.5 ppm. HRMS–ESI $[M+Na]^+$: 267.0448, $C_{14}H_{12}O_2NaS$ requires 267.0456.

4.43. 3-Butylisochroman-1-one, 8e[30]

A solution of 2-((trimethylsilyl)methyl)benzoic acid, **3b** (104 mg, 0.50 mmol), valeraldehyde (27 μL, 0.25 mmol), and 4 Å MS (100 mg) in anhydrous DMF (2.0 mL) was treated with CsF (152.0 mg, 1.0 mmol) under N_2 and the resulting solution was stirred at 80 °C for 6 h. The reaction mixture was cooled to rt, 2 M HCl (20 mL) was added and stirred for another 1 h. The residue was extracted with ethyl acetate (20×3 mL). Organic layer was washed with water (2×10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a colorless oil (34.7 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J=7.6 Hz, 1H), 7.52 (td, J=7.6, 1.2 Hz, 1H), 7.37 (t, J=7.6 Hz, 1H), 7.23 (d, J=7.6 Hz, 1H), 4.56–4.47 (m, 1H), 3.02–2.86 (m, 2H), 1.94–1.83 (m, 1H), 1.77–1.67 (m, 1H), 1.63–1.31 (m, 4H), 0.93 (t, J=7.2 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 139.4, 133.7, 130.4, 127.7, 127.5,

125.4, 78.9, 34.8, 33.4, 27.2, 22.6, 14.1 ppm. HRMS–ESI $[M+H]^+$: 205.1224, $C_{13}H_{17}O_2$ requires 205.1229.

4.44. 3-*tert*-Butylisochroman-1-one, 8f[31]

A solution of 2-((trimethylsilyl)methyl)benzoic acid, **3b** (104 mg, 0.50 mmol), pivalaldehyde (28 μL, 0.25 mmol), and 4 Å MS (100 mg) in anhydrous DMF (2.0 mL) was treated with CsF (152.0 mg, 1.0 mmol) under N_2 and the resulting solution was stirred at 80 °C for 6 h. The reaction mixture was cooled to rt, 2 M HCl (20 mL) was added and stirred for another 1 h. The residue was extracted with ethyl acetate (20×3 mL), the organic layer washed with water (2×10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a colorless oil (23.5 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J*=7.5 Hz, 1H), 7.52 (t, *J*=7.5 Hz, 1H), 7.37 (t, *J*=7.5 Hz, 1H), 7.25 (d, *J*=7.5 Hz, 1H), 4.19–4.13 (m, 1H), 3.06–2.97 (m, 1H), 2.87–2.80 (m, 1H), 1.08 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 139.9, 133.7, 130.3, 127.6, 125.4, 86.3, 34.2, 28.6, 25.8 ppm. HRMS–ESI $[M+H]^+$: 205.1232, $C_{13}H_{17}O_2$ requires 205.1229.

4.45. (*Z*)-(2-Ethoxy-3,3,3-trifluoroprop-1-enyl)benzene, 9a[32]

A solution of benzyltrimethylsilane, **3a** (328 mg, 2.0 mmol) and ethyl trifluoroacetate (0.72 mL, 6.0 mmol), and powder 4 Å MS (200 mg) in anhydrous DMF (4 mL) was treated with CsF (608 mg, 4.0 mmol) under N_2 and the resulting solution was stirred at 60 °C for 12 h. The reaction mixture was cooled to rt, 0.5 M HCl (20 mL) and diethyl ether (30 mL) was added. Organic layer was separated and washed with water (2×15 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with pentane yielded a colorless oil (315 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J*=7.5 Hz, 2H), 7.44–7.30 (m, 3H), 6.45 (s, 1H), 3.99 (q, *J*=7.1 Hz, 2H), 1.37 (t, *J*=7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7 (q, *J*=31.9 Hz), 132.6, 129.6, 128.8, 128.7, 121.40 (q, *J*=276 Hz), 117.3 (q, *J*=4.2 Hz), 68.9, 15.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −69.09.

4.46. (*Z*)-5-(2-Ethoxy-3,3,3-trifluoroprop-1-enyl)-1,2,3-trimethoxybenzene, 9b

A solution of (3,4,5-trimethoxybenzyl)trimethylsilane, **3g** (508 mg, 2.0 mmol) and ethyl trifluoroacetate (0.72 mL, 6.0 mmol), and powder 4 Å MS (200 mg) in anhydrous DMF (4 mL) was treated with CsF (608 mg, 4.0 mmol) under N_2 and the resulting solution was stirred at 60 °C for 12 h. The reaction mixture was cooled to rt, 0.5 M HCl (20 mL) and diethyl ether (30 mL) was added. Organic layer was separated and washed with water (2×15 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with heptane/isopropanol (99.5:0.5) yielded a colorless oil (420 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (s, 2H), 6.35 (s, 1H), 4.00 (q, *J*=7.1 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 6H), 1.38 (t, *J*=7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 142.0 (q, *J*=31.7 Hz), 138.7, 128.0, 121.3 (q, *J*=276 Hz), 117.3 (q, *J*=4.2 Hz), 106.7, 68.7, 61.1, 56.2, 15.7 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −68.87. HRMS $[M+Na]^+$: 329.0992, $C_{14}H_{17}O_4NaF_3$ requires 329.0977.

4.47. 1,1,1-Trifluoro-3-phenylpropan-2-one oxime, 10a[12c]

A solution of (2-ethoxy-3,3,3-trifluoroprop-1-enyl)benzene, **9a** (324 mg, 1.5 mmol) in DCM (3 mL) was treated with triflic acid (664 μL, 7.5 mmol) at 0 °C for 10 min and the resulting solution was stirred at rt for 12 h. The reaction mixture was quenched with 20% $NaHCO_3$ solution until no effervescence of CO_2 evolved and water (10 mL) was added. The residue was extracted with DCM (3×15 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. A solution of this crude reaction mass and hydroxylamine hydrochloride (834 mg, 12 mmol) in EtOH/H_2O (1:1, 4 mL) was treated with sodium acetate (984 mg, 12 mmol) and the resulting solution was stirred at reflux for 2 h. The reaction mixture was cooled to rt and water (10 mL) was added. The residue was extracted with diethyl ether (3×15 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (95:5) yielded a yellow oil (256 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (br s, 1H), 7.34–7.21 (m, 5H), 3.86 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3 (q *J*=32.2 Hz), 134.15, 129.0, 128.8, 127.2, 120.9 (q, *J*=274.6 Hz), 30.0 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −68.60 ppm. HRMS $[M-H]^-$: 202.0479, $C_9H_7NOF_3$ requires 202.0480.

4.48. 1,1,1-Trifluoro-3-(3,4,5-trimethoxyphenyl)propan-2-one oxime, 10b

A solution of 5-(2-ethoxy-3,3,3-trifluoroprop-1-enyl)-1,2,3-trimethoxybenzene, **9b** (459 mg, 1.5 mmol) in DCM (3 mL) was treated with triflic acid (664 μL, 7.5 mmol) at 0 °C for 10 min and the resulting solution was stirred at rt for 12 h. The reaction mixture was quenched with 20% $NaHCO_3$ solution until no effervescence of CO_2 evolved and water (10 mL) was added. The residue was extracted with DCM (15×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. A solution of this crude reaction mass and hydroxylamine hydrochloride (834 mg, 12 mmol) in EtOH/H_2O (1:1, 4 mL) was treated with sodium acetate (984 mg, 12 mmol) and the resulting solution was stirred at reflux for 2 h. The reaction mixture was cooled to rt and water (10 mL) was added. The residue was extracted with diethyl ether (15×3 mL). Organic layer was washed with water (10 mL), brine (10 mL), dried over sodium sulfate, and concentrated to dryness. Purification by silica gel chromatography eluting with cyclohexane/ethyl acetate (90:10) yielded a yellow oil (343 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.30 (br s, 1H), 6.49 (s, 2H), 3.83 (s, 9H), 3.80 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 148.8 (q, *J*=31.8 Hz), 137.1, 130.0, 121.0 (q, *J*=274.6 Hz), 106.3, 61.0, 56.2, 30.1 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −68.4 ppm. HRMS $[M+H]^+$: 294.0964, $C_{12}H_{15}NO_4F_3$ requires 294.0953.

4.49. 1,1,1-Trifluoro-3-phenylpropan-2-amine, 11a[12c]

A solution of 1,1,1-trifluoro-3-phenylpropan-2-one oxime, **10a** (203 mg, 1.0 mmol) in THF (2 mL) was added dropwise to a mixture of $LiAlH_4$ (76 mg, 2.0 mmol) in THF (2 mL) at 0 °C. The resulting solution was warmed to rt and then it was heated at reflux for 14 h. The reaction mixture was cooled in an ice bath, 1 M NaOH solution was added dropwise until no H_2 evolution was observed and the solution was stirred for 30 min. The mixture was filtered through Celite and rinsed with ethyl acetate (4×15 mL). The organic layer was separated, dried over anhydrous sodium sulfate and the solvents removed under reduced pressure. Purification by alumina gel chromatography eluting with cyclohexane/ethyl acetate (95:5) yielded the product as a yellow oil (142 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.20 (m, 5H), 3.49–3.39 (m, 1H), 3.11 (dd, *J*=13.9, 3.4 Hz, 1H), 2.60 (dd, *J*=13.9, 10.4 Hz, 1H), 1.28 (br s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 129.4, 128.9, 127.2, 126.6 (q, *J*=281.3 Hz), 55.3 (q, *J*=28.6 Hz), 36.5 (q, *J*=2.0 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −78.45 (d, *J*=7.3 Hz) ppm.

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4.50. 1,1,1-Trifluoro-3-(3,4,5-trimethoxyphenyl)propan-2-amine, 11b[33]

A solution of 1,1,1-trifluoro-3-(3,4,5-trimethoxyphenyl)propan-2-one oxime, **10b** (249 mg, 0.85 mmol) in THF (2 mL) was added dropwise to a mixture of $LiAlH_4$ (64.6 mg, 1.7 mmol) in THF (2 mL) at 0 °C. The reaction mixture was warmed to rt and then it was heated at reflux for 14 h. The reaction mixture was cooled in an ice bath, 1 M NaOH solution was added dropwise until no H_2 evolution was observed and the solution was stirred for 30 min. The mixture was filtered through Celite, and the Celite pad was rinsed with ethyl acetate (4×15 mL). The rinses and filtrate were combined, organic layer separated, dried over anhydrous sodium sulfate and the solvents removed under reduced pressure. Purification by alumina gel chromatography eluting with cyclohexane/ethyl acetate (95:5) yielded a yellow oil (171 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.45 (s, 2H), 3.86 (s, 6H), 3.83 (s, 3H), 3.52–3.42 (m, 1H), 3.06 (dd, J=13.9, 3.3 Hz, 1H), 2.54 (dd, J=13.9, 10.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 137.2, 132.3, 126.3 (q, J=281 Hz), 106.3, 61.0, 56.3, 55.2 (q, J=28.5 Hz), 36.8–36.7 (m) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −78.40 (d, J=7.0 Hz) ppm. HRMS $[M+H]^+$: 280.1173, $C_{12}H_{17}NO_3F_3$ requires 280.1161.

4.51. ^{19}F NMR reaction times course of 3e with benzaldehyde

In an NMR tube, a solution of (3-methoxybenzyl)trimethylsilane, **3e** (0.15 mmol) and benzaldehyde (0.15 mmol) in anhydrous THF (0.5 mL) was treated with TBAT (0.015 mmol in 0.1 mL anhydrous THF) and placed in the NMR probe at 25 °C. ^{19}F NMR spectra were run every 10 min for 3 h. Chemical shifts observed were for TBAT at −97.0 ppm; for TMSF at −158.1 ppm, and TBAF at −111.3 ppm. Upon completion of the reaction an authentic sample of TBAF was added to confirm its peak assignment.

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11. (a) The mechanistic pathway for this transformation is currently under investigation. (b) The synthesis of **9a** via Wittig reaction has been previously reported Bégué, J.-P.; Bonnet-Delpon, D.; Mesureur, D.; Née, G.; Wu, S.-W. *J. Org. Chem.* **1992**, *57*, 3807.
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