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Highly atom economical uncatalysed and I_2-catalysed silylation of phenols, alcohols and carbohydrates, using HMDS under solvent-free reaction conditions (SFRC)

Marjan Jereb *

Faculty of Chemistry and Chemical Technology, Aškerčeva 5, 1000 Ljubljana, Slovenia

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ABSTRACT

An uncatalysed silylation of phenols, regardless on the aggregate state and nature of the substituents with 0.55 equiv of HMDS under solvent-free reaction conditions (SFRC) at room temperature is reported. Sterically hindered phenols, carbohydrates and most of the alcohols additionally required a catalytic amount (up to 2 mol %) of iodine. The reaction protocol is very simple; obtaining a pure product, particularly of uncatalysed reactions, was frequently a completely solvent-free process.

1. Introduction

Clean and environmentally friendly synthesis is an increasingly important hot topic in chemistry.[1] Sustainable development has become one of the central demands in both academic and industrial research.[2] Consideration of environmental impact is important both for the final product and, increasingly, its means of production. Solvent-free reaction conditions[3] (SFRC) represent one of the most efficient contributions to the minimization of waste; further advantages include reduction of health hazards, improved cost efficiency and operational simplicity. Highly atom economical processes are also a noteworthy part of the overall process efficiency.[4] A generally desirable process is the uncatalysed transformation of neat reactants under mild reaction conditions due to their simplicity and cost efficiency. Reactions with product isolation and purification without any solvent deserve a special mention.

Iodine is an extremely versatile catalyst[5] and reagent[6] in organic chemistry; it is mild, air and moisture tolerant, compatible with a broad range of functional groups, and (in numerous cases) it is an effective substitute for expensive and sensitive metallic Lewis acid catalysts. It was demonstrated to be efficient in a solution, under highly concentrated reaction conditions and also under SFRC.[5d]

Trimethylsilyloxy moiety is very attractive in the chemistry of the protecting groups, due to its selective introduction and mild and selective removal. TMS derivatisation of polar and non-volatile molecules enhances their volatility, making them suitable for the GC and MS analysis. This is particularly important for the analysis of different natural products. HMDS is a very popular transfer agent of the TMS group into organic molecules; however, it often needs activation. Thus, the introduction of the TMS group is usually accomplished using TMSCl and HMDS in the presence of different catalysts, i.e., Aliquat 336,[7] $MgBr_2 \cdot Et_2O$,[8] NH_4SCN,[9] $LiClO_4$,[10] $LaCl_3$,[11] $Mg(HSO_4)_2$,[12] trichloroisocyanuric acid,[13] $ZrCl_4$,[14] ZnO,[15] $Fe(ClO_4)_3 \cdot 6H_2O$,[16] tungstophosphoric acid,[17] zirconium sulfophenyl phosphonate,[18] poly(4-vinylpyridinium tribromide),[19] cerium-containing polyoxometalate,[20] H-β zeolite,[21] zirconyl triflate,[22] montmorillonite K-10,[23] superparamagnetic iron oxide,[24] a porous nanocomposite Nafion SAC-13,[25] a solid supported sulfate,[26] $FeCl_3$[27] and $ZnCl_2$,[28] sulfonic acid-functionalised silica,[29] Bu_4NBr[30] in combination with $TMSN_3$ and 1,3-dibromo-5,5-dimethylhydantoin[31] and others. The main drawbacks of the known methods are metal-based catalysts, the use of organic solvents and the presence of different bases for neutralisation of HCl, elevated temperature, long reaction times, tedious workup and considerable excess of the silylating agent.

A recent report showed uncatalysed protection of phenols and alcohols; however, the reaction took place in nitromethane using 50 mol % excess of HMDS.[32] Iodine was also showed to be an

* Tel.: +386 1 241 9248; fax: +386 1 241 9220; e-mail address: marjan.jereb@fkkt.uni-lj.si.

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effective catalyst for trimethylsilylation of phenols and alcohol; nevertheless, the reaction proceeded in halogenated solvents and with a considerable excess of HMDS[33] and TMSCl.[34] Our goal was the protection of hydroxyl derivatives using an as-low-as-possible excess of HMDS in the absence of solvent. We report on uncatalysed and iodine-catalysed trimethylsilylation of phenols, alcohols and carbohydrates under SFRC.

2. Results and discussion

Initially, 4-bromophenol **1a** was functionalised with 0.8 equiv of HMDS under SFRC, and full conversion to **2a** was noted in 10 min. A decrease in the amount of HMDS to 0.6 equiv resulted in the full conversion of **1a** into **2a** within 15 min. Full conversion could also be achieved with 0.55 and 0.53 equiv of HMDS only. Unfortunately, the latter threshold amount appears not to be general; for convenience, 0.55 equiv of HMDS was used. The evaluation of the potential new method was performed on a series of structurally different phenols; the results are summarised in Table 1. Phenol **1b** was fully transformed to **2b**, using 0.55 equiv of HMDS (entry 2); 4-chlorophenol **1c** exhibited similar reactivity to **1a**. Electron deficient phenols **1d**–**g** were effectively transformed into their TMS derivatives **2d**–**g** (entries 4–7), even though the opposite might have been be expected, since 4-nitrophenol **1d** failed to react in an uncatalysed reaction in nitromethane. Moreover, the reactivity of **1d**–**g** was surprisingly high. Naphthols **1h** and **1i** produced derivatives **2h** and **2i** in high yields (entries 8 and 9).

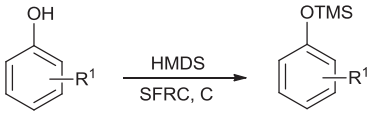
Indane and tetraline derivatives **1j**–**l** efficiently provided their TMS analogues **2j**–**l** (entries 10–12), though phenol **1l** required iodine (2 mol %) as a catalyst. 3- and 4-Alkylphenols could be successfully derivatised with HMDS, without a catalyst (entries 13–15), while the uncatalysed protection of 2-alkylphenols took a longer time and was not complete. The functionalisation of **1p**–**r** in the presence of iodine effectively furnished derivatives **2p**–**r** (entries 16–18). Electron-rich phenols **1s**–**u** were transformed to the corresponding TMS derivatives **2s**–**u** (entries 19–21) without a catalyst. Trisubstituted phenols **1v** and **1w** were efficiently protected in the presence of iodine under SFRC (entries 22 and 23). Sterically hindered phenols **1x**–**z** required iodine for successful transformation (entries 24–26). Functionalisation of 4-methylcatechol **1aa** and pyrogallol **1bb** proceeded effectively in the presence of iodine under SFRC giving **2aa** and **2bb** in good yields (entries 27 and 28). 4-Hydroxybenzyl alcohol **1cc** was converted to its **2cc** analogue, showing that alcohols and phenols could be protected under SFRC (entry 29). Oestrone **1dd** was transformed to its TMS derivative **2dd**; no difficulties due to the heterogeneous reaction mixture were noted (entry 30). Phenolphthalein **1ee** was converted into its di-OTMS ether **2ee** in an iodine-catalysed reaction using 10 mol % excess of HMDS (entry 31). A highly viscous reaction mixture was obtained after approximately 30 min of stirring, and a stronger stirring bar was needed for effective stirring.

An interesting feature of the transformation is the unexpected reactivity of activated and deactivated phenols with HMDS without a catalyst; known methods usually work either with one or the other type of phenol.[23] 4-Nitrophenol was much more reactive than 4-methoxyphenol, indicating the proton transfer as the key step in the reaction.

Scale-up of the uncatalysed protection of phenols with HMDS was exemplified on solid 4-nitrophenol **1d**. 50 mmol of **1d** and 0.55 equiv of HMDS were stirred at room temperature for 170 min, and pure product **2d** was obtained in high yield after distillation of the crude reaction mixture in a completely solvent-free process.

Next, we examined the reactivity of different alcohols; the results are presented in Table 2. Benzyl alcohol **3a** was smoothly derivatised with HMDS in an uncatalyzed reaction under SFRC

Table 1
Protection of phenols with HMDS under SFRC



1 2

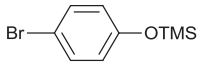
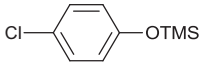
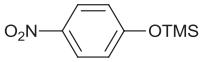
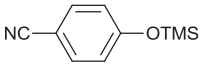
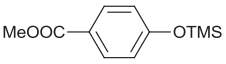
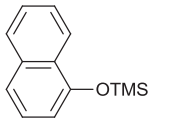
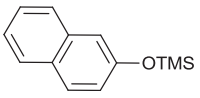
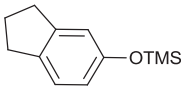
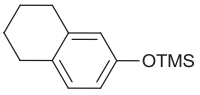
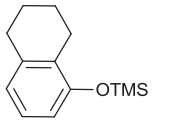
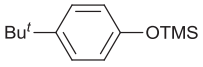
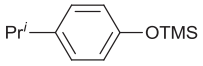
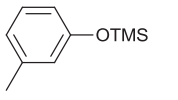
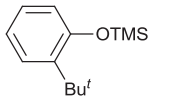
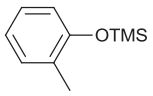
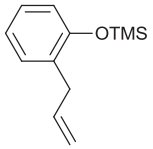
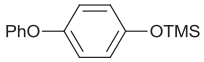
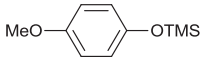
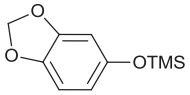
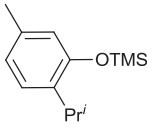
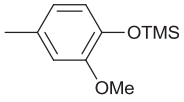
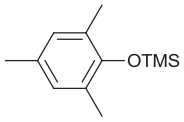
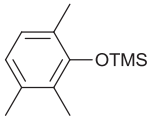
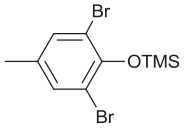
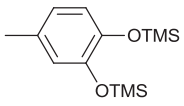
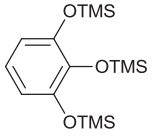
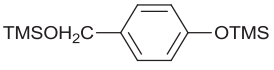
	C	2		t (h)	Yield[a] (%)
1	A		**2a**	0.25	91
2	A	PhOTMS	**2b**	4	77
3	A		**2c**	0.25	85
4	A		**2d**	1.5	92
5	A		**2e**	1	87
6	A		**2f**	1	93
7	A		**2g**	9	90
8	A		**2h**	4	89
9	A		**2i**	3	91
10	A		**2j**	1.5	90
11	A		**2k**	4	88
12	B		**2l**	2.5	86
13	A		**2m**	12	90
14	A		**2n**	2.5	85
15	A		**2o**	2	85
16	B		**2p**	4	86

Table 1 (*continued*)

	C	2		*t* (h)	Yield[a] (%)
17	B		**2q**	3.5	78
18	B		**2r**	10	83
19	A		**2s**	1.5	96
20	A		**2t**	22	88
21	A		**2u**	2.2	95
22	B		**2v**	10	90
23	B		**2w**	0.5	86
24	B		**2x**	0.5	85
25	B		**2y**	4	86
26	B		**2z**	0.4	87
27	B		**2aa**	12	83[b]
28	B		**2bb**	15	81[c]
29	B		**2cc**	1.2	48[b]
30	B	TMSO-oestrone	**2dd**	3.5	72[d]
31	B	Di-OTMS-phenolphthalein	**2ee**	0.8	88[e]

Reaction conditions C: A: 1 mmol **1** and 0.55 mmol HMDS stirred at room temperature. B: 1 mmol **1**, 0.55 mmol HMDS and 0.02 mmol I_2 stirred at room temperature.

[a] Isolated yield.

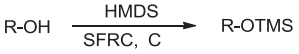
[b] 1 mmol **1aa**, 1.1 mmol HMDS and 0.04 mmol I_2.

[c] 1 mmol **1bb**, 1.65 mmol HMDS and 0.039 mmol I_2.

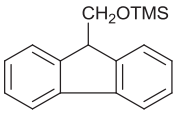
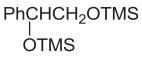
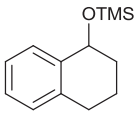
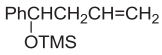
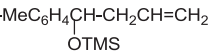
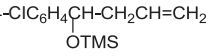
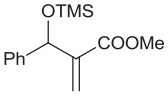
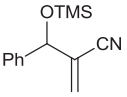
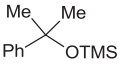
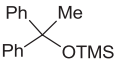
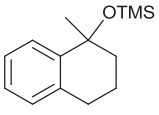
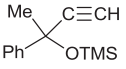
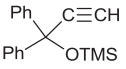
[d] 0.2 mmol **1dd**, 0.24 mmol HMDS and 0.004 mmol I_2.

[e] 0.3 mmol **1ee**, 0.33 mmol HMDS and 0.012 mmol I_2.

Table 2
Protection of alcohols with HMDS under SFRC

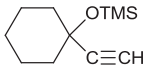
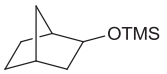


3 **4**

	C	4		*t* (h)	Yield[a] (%)
1	A	$PhCH_2OTMS$	**4a**	12	73
2	A	$4\text{-}MeOC_6H_4CH_2OTMS$	**4b**	20	84
3	A	$2,4\text{-}diMeOC_6H_3CH_2OTMS$	**4c**	20	83[b]
4	B	$4\text{-}NO_2C_6H_4CH_2OTMS$	**4d**	0.17	78[c]
5	A	$PhCH{=}CHCH_2OTMS$	**4e**	16	80
6	A	$PhC{\equiv}CCH_2OTMS$	**4f**	6	86
7	A		**4g**	0.7	79
8	B	$n\text{-}C_{16}H_{23}OTMS$	**4h**	0.17	77
9	B	$c\text{-}C_{12}H_{23}OTMS$	**4i**	0.33	84
10	B		**4j**	0.33	87
11	B		**4k**	0.25	76[d]
12	B		**4l**	0.17	78
13	B	(+)-Menthol-OTMS	**4m**	0.17	83
14	B	(−)-Menthol-OTMS	**4n**	0.17	92
15	B		**4o**	0.25	76
16	B		**4p**	0.25	75
17	B		**4q**	0.25	72
18	B		**4r**	0.5	74[e]
19	B		**4s**	0.5	78[e]
20	B		**4t**	0.17	79
21	B		**4u**	0.42	83
22	B	$PhCH_2CH_2C(Me)_2OTMS$	**4v**	0.17	88
23	B		**4w**	0.17	72
24	B		**4x**	0.17	79
25	B		**4y**	0.17	82

(*continued on next page*)

Table 2 (*continued*)

	C	4		*t* (h)	Yield[a] (%)
26	B		**4z**	0.17	54
27	B		**4aa**	0.17	67
28	B	1-Adamantyl-OTMS	**4bb**	0.7	82
29	B	TMSO-cholesteryl	**4cc**	3.33	93[f]

Reaction conditions C: A: 1 mmol **1** and 0.55 mmol HMDS stirred at room temperature. B: 1 mmol **1**, 0.55 mmol HMDS and 0.02 mmol I_2 stirred at room temperature.

[a] Isolated yield.
[b] 1 mmol **1** and 0.67 mmol HMDS.
[c] 1 mmol **1**, 0.65 mmol HMDS and 0.02 mmol I_2.
[d] 1 mmol **1**, 1.1 mmol HMDS and 0.04 mmol I_2.
[e] 1 mmol **1**, 083 mmol HMDS and 0.026 mmol I_2.
[f] 5 mmol **1cc**, 3.90 mmol HMDS and 0.1 mmol I_2.

(Table 2, entry 1). Similarly, activated benzylic alcohols **3b** and **3c** yielded products **4b** and **4c** (entries 2 and 3) in good yield. In contrast, 4-nitrobenzyl alcohol **3d** required iodine as catalyst; the reaction was completed in 10 min (entry 4).

Unsaturated alcohols **3e** and **3f** were converted into products **4e** and **4f** and isolated in good yields (entries 5 and 6). 9-Fluorenylmethanol **3g** formed a highly viscous reaction mixture with HMDS, and furnished derivative **4g** without iodine (entry 7). 1-Hexadecanol **3h** and cyclododecanol **3i** were fully converted into silyl ethers **4h** and **4i** in the presence of iodine (entries 8 and 9). Alcohols **1j**–**l** were silylated under SFRC by means of iodine in a short reaction time (entries 10–12). (+)-Menthol **3m** and (−)-menthol **3n** were functionalised without the loss of stereochemical integrity, furnishing analogues **4m** and **4n** (entries 13 and 14). Homoallylic alcohols **3o**–**q** smoothly yielded the corresponding derivatives **4o**–**q** (entries 15–17). Baylis–Hillman adducts **3r** and **3s** gave the related silyl ethers **4r** and **4s**, though 0.75 equiv of HMDS was used for effective transformation (entries 18 and 19). Sterically hindered tertiary alcohols **3t**–**w** could be easily silylated in the presence of iodine as catalyst giving products **4t**–**w** in good yields (entries 20–23). Tertiary propargyl alcohols **3x**–**z** also furnished the desired products **4x**–**z** in a short reaction time and good yields (entries 24–26). *exo*-Norborneol **3aa** smoothly gave non-rearranged product **4aa**, thus indicating that carbocationic intermediates were not intermediates of the prime importance in this transformation (entry 27). Sterically more hindered 1-adamantanol **3bb** effectively produced its silylated derivative **4bb** in good yield (entry 28).

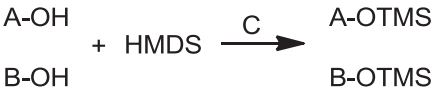
Cholesterol **3cc** was taken to demonstrate the feasibility of scaling up the present iodine-catalysed SFRC method in the case of solid substrates. Numerous solid substrates dissolved during the reaction, while **3cc** remained solid and, in this sense, it can be regarded as 'tough' substrate. Nevertheless, the transformation of 5 mmol of **3cc** using 0.78 equiv of HMDS and 2 mol % of I_2 was completed in 200 min, and the pure product **4cc** was obtained in excellent yield by crystallisation.

Scale-up of uncatalysed silylation of alcohols was performed on liquid 4-methoxybenzyl alcohol **3b**. 20 mmol of **3b** and 0.6 equiv of HMDS were stirred for 22 h at room temperature, and an almost pure product **4b** was obtained in an excellent yield only with the distillation of excess of HMDS. Distillation of the crude **4b** only slightly improved its purity.

Scale-up of the I_2-catalysed silylation under SFRC was manifested on (−)-menthol **3n**. 25 mmol of **3n**, 2 mol % of I_2 and 0.55 equiv of HMDS were stirred at room temperature for 15 min; the crude reaction mixture was diluted with small amount of TBME, and after quenching of iodine and filtration of solids, the distillation afforded pure **4n** in an excellent yield.

The heterogeneous reaction mixtures were dealt with to a great extent in this study. Consequently, the role of iodine was examined in a competitive silylation of the selected couples; the results are summarised in Table 3. Benzyl alcohol exhibited higher reactivity than 1-hexadecanol in an uncatalyzed reaction, while in the presence of I_2 the situation was reversed (entries 1 and 2). A primary alcohol was much more reactive than a secondary one (entry 3), and the situation changed in the presence of I_2 (entry 4).

Table 3
Competitive silylation with HMDS with and without I_2 under SFRC

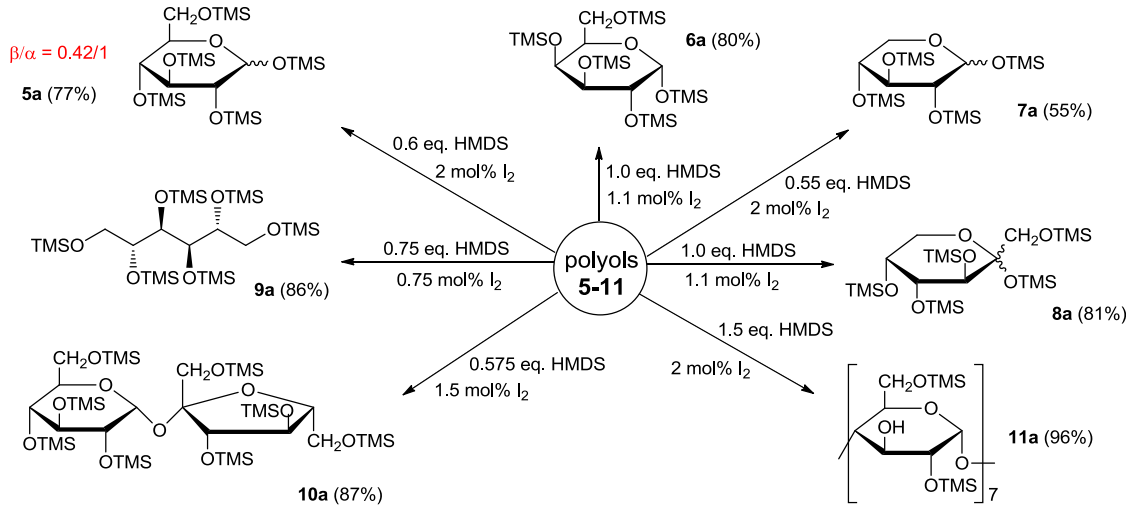


	Couple[a] A-OH/B-OH	C	Relative ratio[b] A-OTMS/B-OTMS
1	$PhCH_2OH/C_{16}H_{33}OH$	/	65/33
2		I_2	47/51
3	$PhCH_2OH/Ph_2CH(OH)$	/	100/0
4		I_2	50/50
5	$PhCH_2OH/Ph_2C(OH)Me$	/	100/0
6		I_2	100/0
7	$Ph_2CH(OH)/Ph_2C(OH)Me$	/	100/0
8		I_2	100/0
9	$PhCH_2OH/PhOH$	/	65/35
10		I_2	65/35
11	$PhOH/Ph_2CH(OH)$	/	81/21
12		I_2	50/50
13	$PhOH/Ph_2C(OH)Me$	/	100/0
14		I_2	100/0

Reaction conditions, C.
[a] 0.3 mmol A-OH, 0.3 mmol B-OH and 0.165 mmol HMDS stirred 14 h at room temperature with and without 0.006 mmol I_2.
[b] Relative distribution of products determined from ^1H NMR spectra.

Tertiary alcohol exhibited the lowest reactivity among alcohols; primary and secondary ones were more reactive (entries 5–8). Reaction of benzyl alcohol and phenol with HMDS obviously took place uncatalyzed, and the former showed higher reactivity (entries 9 and 10). Phenol was more reactive than secondary and tertiary benzylic alcohols (entries 11–14), thus revealing that importance of sterical hindrance and acidity on the reactivity. Iodine had a substantial impact on the reactivity of the secondary alcohol and no impact on the reactivity of the tertiary alcohol in the combination with phenol (entries 11–14). It can be concluded that seemingly simple systems are rather complex, mainly because of the heterogeneity.

Carbohydrates and polyols possess several hydroxy groups that often need to be protected in a simple way during the multistep transformation. Derivatisation of polyols into fully silylated analogues is of practical value in analytical chemistry. The reactivity of some of the polyols with HMDS and catalytic amount of iodine under SFRC was examined, and the results are presented in Scheme 1. A variable excess of HMDS was needed in these examples; no general threshold was noted, and low amount of iodine was required. D-Glucose **5** was transformed into derivative **5a**, consisting of a mixture of α- and β-anomer in a relative ratio of 1:0.42. D-Galactose **6** was fully converted into α-anomeric analogue **6a**; no β-anomer was detected. Xylose **7** gave fully silylated product **7a**, consisting of almost an equimolar mixture of α- and β-anomer. D-Fructose **8** furnished its fully protected derivative **8a** as a mixture of stereoisomeric furanoses and pyranoses.



Scheme 1. Protection of carbohydrate derivatives with HMDS/I_2 under SFRC.

D-Mannitol **9** was fully protected, giving derivative **9a**. Saccharose **10** was successfully protected, i.e., all eight hydroxy groups were silylated, and product **10a** was isolated in high yield. β-Cyclodextrin **11** and its derivatives are gaining importance in the chemical, pharmaceutical, agricultural and food industries. Due to its very high polarity and sparing solubility, **10** was anticipated to be a difficult substrate for protection with HMDS/I_2 under SFRC. Although a considerable excess of HMDS was needed, the reaction took place surprisingly well, and the partly protected derivative **11a** was isolated in an excellent yield. The reaction exhibited excellent selectivity and furnished a product with two-thirds of the hydroxy groups protected.

3. Conclusions

In this paper, we describe environmentally friendly synthesis of trimethylsilyl ethers from phenols, alcohols and carbohydrates using a small excess of HMDS, thus contributing to a high atom economy and a reduced amount of waste. The procedure is very simple, performed in the presence of air with untreated substrates and HMDS at room temperature. Numerous substrates, mainly phenols, required no catalyst, while, sterically hindered phenols, carbohydrates and most of the alcohols required a catalytic amount of iodine. A noteworthy feature of the method is the reactivity of activated and deactivated phenols, and benzylic alcohols. Reactions were performed strictly without solvent, also in the case of highly polar and insoluble substrates. The crude products exhibited high purity, and could be directly used further. Isolation and purification in numerous cases were completely solvent-free. We have demonstrated the feasibility of the scale-up regardless on the aggregate state of the substrate and presence of the catalyst.

4. Experimental

4.1. Representative procedure of the non-catalysed reaction of phenols and alcohols with HMDS under SFRC (small scale)

To phenol **1a** (0.173 g, 1 mmol) or alcohol **3a** (0.108 g, 1 mmol) HMDS (0.089 g, 0.55 mmol) was added, and the mixture was stirred at room temperature until the complete consumption of the starting material (TLC check). The excess of HMDS was distilled off under reduced pressure and nearly pure products were obtained. Products can be purified with column chromatography and/or distillation.

4.2. Representative procedure of I_2-catalysed reaction of phenols, alcohols and carbohydrates with HMDS under SFRC (small scale)

Iodine (5.1 mg, 0.02 mmol) was added to phenol **1l** (0.148 g, 1 mmol) or alcohol **3h** (0.242 g, 1 mmol), followed by addition of HMDS (0.089 g, 0.55 mmol); the mixture was stirred at room temperature until the complete consumption of the starting material (TLC check). The crude reaction mixture was dissolved in 4 mL of hexane/TBME and stirred with the finely powdered $Na_2S_2O_3$ until the disappearance of iodine. From this point on, two different scenarios are possible:

a) The solids were filtered off and the solvent evaporated under the reduced pressure, yielding the crude product. In numerous cases, such products were practically pure; column chromatography and/or distillation improved their quality only slightly.
b) A solution of a product in hexane/TBME mixture could be directly subjected to the column chromatography, without filtration of the solids.

Caution: Although we experienced no problems when performing these reactions, care should taken due to the potential formation of NI_3.

4.3. Representative procedure of the non-catalysed reaction of the solid phenols and alcohols with HMDS under SFRC (scale-up)

To 4-nitrophenol **1d** (6.95 g, 50 mmol), HMDS (4.43 g, 27.5 mmol) was added; the mixture was stirred at room temperature for 170 min (full conversion). A slight evolution of ammonia accompanied the transformation. Solid phenol began dissolving during stirring and a homogenous, oily reaction mixture was finally obtained. The excess of HMDS was distilled off and 10.4 g of the crude product (light brown) was obtained; no impurities were observed in the ^{1}H NMR spectrum. Distillation of the crude product yielded yellow oily product **2d** (8.84 g, 84%).

4.4. Representative procedure of the non-catalysed reaction of the liquid phenols and alcohols with HMDS under SFRC (scale-up)

To 4-methoxybenzyl alcohol **3b** (2.76 g, 20 mmol), HMDS (1.94 g, 12 mmol) was added; the mixture was stirred at room temperature for 22 h (full conversion). At the beginning, two separate phases slowly turned into one homogenous oily phase, an oily reaction mixture was obtained. The excess of HMDS was distilled off and 4.06 g of the crude product (transparent) was obtained; in the ^{1}H NMR spectrum, no impurities were observed. Distillation of the crude product yielded transparent oily product **4b** (3.92 g, 93%).

4.5. Representative procedure of I_2-catalysed reaction of the solid phenols and alcohols with HMDS under SFRC (scale-up)

To (−)-menthol **3n** (3.9 g, 25 mmol) iodine (127 mg, 0.5 mmol) was added, followed by the dropwise addition of HMDS (2.22 g, 13.75 mmol); the mixture was stirred at room temperature for 15 min (full conversion). A vigorous evolution of ammonia began approx. 1 min after beginning of the stirring, and it almost completely ceased in a few minutes. After completion, the reaction mixture was dissolved in 7 mL of TBME, and stirred in the presence of a finely powdered $Na_2S_2O_3$ until the disappearance of iodine. The solids were filtered off, the solvent was distilled off and 5.61 g of crude product (yellow) was obtained. As can be judged from the ^{1}H NMR spectrum, the crude product was almost pure. Distillation of the crude product yielded slightly yellow, oily product **4n** (5.22 g, 92%).

4.6. Representative procedure of I_2-catalysed reaction of the solid phenols and alcohols with HMDS under SFRC (scale-up)

To cholesterol **3cc** (1.93 g, 5 mmol) iodine (25 mg, 0.1 mmol) was added, followed by the dropwise addition of HMDS (0.63 g, 3.90 mmol); the mixture was stirred at room temperature for 200 min (full conversion). No visible evolution of ammonia was noted. In spite of a heterogeneous reaction mixture (solid always present), the reaction progress took place smoothly. After completion, the crude reaction mixture was dissolved in approx. 85 mL of boiling acetone and cooled. Pure product **4cc** (2.13 g, 93%) as white crystals was obtained.

4.7. Spectral data for new products

(5,6,7,8-Tetrahydronaphthen-1-yloxy)trimethylsilane (**2l**). Colourless liquid; column chromatography R_f (20% Et_2O/hexane) 0.71; IR (neat): 2930, 1459, 1266, 1250, 1075, 1037, 975, 924, 838, 770 cm^{-1}; ^{1}H NMR: δ 0.27 (s, 9H), 1.73–1.81 (m, 4H), 2.57–2.65 (m, 2H), 2.71–2.79 (m, 2H), 6.58 (d, J=8.1 Hz, 1H), 6.68 (d, J=8.1 Hz, 1H), 6.94 (dd, J=8.1, 8.1 Hz, 1H); ^{13}C NMR: δ 0.5, 23.0, 23.8, 29.6, 115.5, 122.0, 125.4, 128.5, 138.9, 153.3; HRMS: (CI) calcd for $C_{13}H_{21}OSi$ 221.1362, found 221.1359 (M+1).

(4-Phenoxyphenoxy)trimethylsilane (**2s**). Colourless liquid; column chromatography R_f (20% Et_2O/hexane) 0.64; IR (neat): 1499, 1227, 920, 756, 679 cm^{-1}; ^{1}H NMR: δ 0.28 (s, 9H), 6.74–6.82 (m, 2H), 6.86–6.97 (m, 4H), 6.98–7.06 (m, 1H), 7.24–7.32 (m, 2H); ^{13}C NMR: δ 0.2, 117.8, 120.5, 120.9, 122.5, 129.6, 150.8, 151.2, 158.2; HRMS: (CI) calcd for $C_{15}H_{19}O_2Si$ 259.1154, found 259.1150 (M+1). Anal. Calcd for $C_{15}H_{18}O_2Si$: C, 69.72; H, 7.02. Found: C, 69.78; H, 7.14.

(3,4-Methylenedioxyphenoxy)trimethylsilane (**2u**). Colourless liquid; column chromatography R_f (17% Et_2O/hexane) 0.60; IR (neat): 2961, 1483, 1250, 1181, 1130, 1038, 957, 877, 800 cm^{-1}; ^{1}H NMR: δ 0.24 (s, 9H), 5.90 (s, 2H), 6.22 (dd, J=8.4, 2.4 Hz, 1H), 6.34 (d, J=2.4 Hz, 1H), 6.60 (d, J=8.4 Hz, 1H); ^{13}C NMR: δ 0.1, 101.1, 102.5, 107.9, 111.6, 142.0, 147.9, 149.9; HRMS: (CI) calcd for $C_{10}H_{15}O_3Si$ 211.0790, found 211.0789 (M+1). Anal. Calcd for $C_{10}H_{14}O_3Si$: C, 57.11; H, 6.71. Found: C, 56.98; H, 7.14.

3,3-Bis(4-trimethylsilyloxyphenyl)-1(3*H*)-isobenzofuranone (**2ee**). Colourless, highly viscous liquid; column chromatography R_f (25% Et_2O/hexane) 0.30; (0.3 mmol of phenolphthalein, 0.33 mmol of HMDS (0.55 equiv), 0.012 mmol of I_2 (2 mol %)): IR (neat) 2958, 1770, 1607, 1506, 1260, 1240, 1171, 906, 846, 709 cm^{-1}; ^{1}H NMR: δ 0.25 (s, 18H), 6.77 (d, J=8.7 Hz, 4H), 7.18 (d, J=8.7 Hz, 4H), 7.48–7.58 (m, 2H), 7.62–7.72 (m, 1H), 7.88–7.96 (m, 1H); ^{13}C NMR: δ 0.2, 91.7, 119.7, 124.1, 125.6, 125.9, 128.5, 129.1, 133.7, 134.0, 152.7, 155.4, 169.9; Anal. Calcd for $C_{26}H_{30}O_4Si_2$: C, 67.49; H, 6.54. Found: C, 67.64; H, 6.40.

2-Cyano-1-phenyl-1-trimethylsilyloxypropene (**4s**). Colourless liquid; column chromatography R_f (20% Et_2O/hexane) 0.48; (1 mmol of alcohol, 0.83 mmol of HMDS (0.83 equiv), 0.026 mmol of I_2 (2.6 mol %)): IR (neat): 2958, 2227, 1253, 1090, 1071, 876, 837, 760, 700 cm^{-1}; ^{1}H NMR: δ 0.11 (s, 9H), 5.18–5.22 (m, 1H), 5.91–5.94 (m, 1H), 5.96–6.00 (m, 1H), 7.28–7.40 (m, 5H); ^{13}C NMR: δ −0.2, 74.6, 117.1, 126.5, 127.6, 128.4, 128.5, 128.6, 139.8. Anal. Calcd for $C_{13}H_{17}NOSi$: C, 67.49; H, 7.41; N, 6.05. Found: C, 67.51; H, 7.52; N, 6.02.

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Supplementary data

Compound characterization and copies of ^{1}H NMR and ^{13}C NMR spectra of new products and products derived from polyols **5a**–**11a**.

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2012.03.040. These data include MOL files and InChiKeys of the most important compounds described in this article.

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