From organocatalysed desilylations to high-yielding benzylidenations of electron-deficient benzaldehydes

Qun Niu, Linlin Xing and Chunbao Li*

Department of Chemistry, School of Science, Tianjin University, 135 Yaguan Road, Jinnan District, Tianjin 300354, P.R. China

A new type of organoprecatalyst ($MeSCH_2Cl$/KI) for desilylation and benzylidenation reactions has been designed. Both reactions are user friendly and high yielding (71–>99%) and have fast reaction rates. The desilylation of iodo silyl ethers was achieved with no sequential etherification side reactions like those seen for reactions when using TBAF. In the application of the catalytic system to a 6-TBDMS ether of a glucoside, glucoside benzylidenations using electron-deficient benzaldehydes were achieved in 87% yield compared with the previously reported yields of 69–77%. Altogether, 14 benzylidenation reactions were realised using silyloxy alcohols and electron-deficient benzaldehydes instead of their activated acetal forms. In terms of reaction rates and yields, the order of the benzylidenations is *p*-fluorobenzaldehyde > benzaldehyde > *p*-anisaldehyde, and a possible mechanism is discussed. These experiments have preliminarily differentiated this cost-effective catalytic system from the classic Lewis acids.

Keywords: desilylation, electron-deficient benzaldehyde, benzylidenation

The silylation of hydroxyl groups and desilylation of silyl ethers are two of the most commonly employed protection and deprotection reactions in organic chemistry and medicinal chemistry. This is due to mild reaction conditions, high yields and the selectivity controlled by the nucleophilicity of the oxygen atom and the steric environments of the silyloxy and hydroxyl groups.[1] In the deprotection of silyl ethers, fluoride-based reagents such as TBAF, NH_4F and py/HF are often used.[2] Other reagents are proton acids such as *p*-TsOH[3] or AcOH,[4] Lewis acids such as ICl[5] or $ZrCl_4$,[6] or bases such as $CsCO_3$[7] or *i*-Bu_2AlH.[8] However, due to the basicity associated with TBAF, side product ethers from the Williamson reaction are formed in rather large amounts in the desilylation of halide-containing substrates.[2] Proton acid catalysts are incompatible with acid-labile compounds. Therefore, the development of new catalysts that overcome these problems is necessary. Herein, a desilylation procedure catalysed by chloromethyl methyl sulfide/KI is reported. This procedure was then applied to the synthesis of 19 benzylidene acetals from silyloxy alcohols and aromatic aldehydes. In previously reported reactions,[9–14] electron-rich benzaldehydes deliver much higher yields of benzylidene acetals than electron-deficient ones, and activated benzaldehyde acetals are often used to replace benzaldehydes. In our method, the reversed order of benzylidenations was observed: *p*-fluorobenzaldehyde > benzaldehyde > *p*-anisaldehyde.

Results and discussion

First, treatment of silyl ether **1a** (100 mg) with cyanuric chloride (TCT, 0.3 equiv.), DMSO (1.5 equiv.) and H_2O (2 equiv.) in dioxane (2 mL) at 50 °C for 8.7 h produced diosgenin (**1aa**) in 62% yield. Although the performance of the desilylation reaction was acceptable, the side products from TCT had to be removed by careful column chromatography.

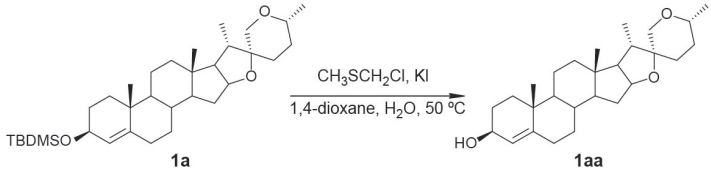
Previously our group has employed TCT/DMSO in several organic transformations, including selective chlorinations,[15] etherifications,[16] the methylene acetalation of alcohols[17] and the synthesis of methylenebisamides from amides.[18] Based on this research and other related reports,[19–21] it was speculated that the precatalyst here is chloromethyl methyl sulfide ($MeSCH_2Cl$). Therefore, chloromethyl methyl sulfide was prepared using TCT and DMSO,[22] and then used in the desilylation reactions. No desilylation reaction occurred for **1a** when chloromethyl methyl sulfide was used to replace TCT/DMSO (Table 1, entry 1). However, the reaction took place to yield diosgenin (**1aa**) quantitatively when 0.05 equiv. of KI was added (Table 1, entry 2). Changing the solvent from dioxane to EtOH or EtOAc gave 30 and 70% yields of **1aa** in 18 h, respectively (Table 1, entries 2–4). No desilylation reaction occurred in MeCN, CH_2Cl_2 and $CHCl_3$ (Table 1, entries 5–7). Therefore, dioxane was chosen as the solvent for the reaction. Next, the amounts of chloromethyl methyl sulfide (from 0.15 to 0.05 equiv.) and KI (from 0.05 to 0.01 equiv.) were optimised (Table 1, entries 2, 8 and 9). The reaction rate was faster when 0.1 equiv. of $MeSCH_2Cl$ and 0.03 equiv. of KI were used. Raising the reaction temperature to 35, 50 or 70 °C led to increased reaction rates of 13.0, 4.6 and 0.8 h, respectively (Table 1, entries 10–12). Since higher temperatures are more likely to cause side products, 50 °C was chosen as the optimal temperature. Various amounts of dioxane (2, 4 and 8 mL) were tested and the optimal amount was 4 mL (Table 1, entries 11, 13 and 14). The amount of water used in the reaction was varied between 7.5 and 60 equiv. and the fastest rate was achieved with 15 equiv. of water (Table 1, entries 11 and 15–17). In summary, the optimised conditions were $MeSCH_2Cl$ (0.1 equiv.), KI (0.03 equiv.), H_2O (15 equiv.), dioxane (4 mL) and 50 °C (Table 1, entry 16).

Following the optimised procedure, three steroidal silyl ethers were successfully desilylated in short reaction times (3.3–5.7 h; Scheme 1, **1aa**, **1bb** and **1cc**) with nearly quantitative yields. Carbonyl and olefinic groups were well tolerated by these reaction conditions. In particular, the acid labile tertiary hydroxyl group of 17-methyltestosterone remained intact (Scheme 1, **1dd**). In addition, methyl 6-*O*-(*t*-butyldimethylsilyl)-α-D-glucopyranoside (**1e**) and 5'-*O*-(*t*-butyldimethylsilyl)thymidine (**1f**) were desilylated in high yields (Scheme 1, **1ee** and **1ff**). The deprotection of iodides 1-*O*-(*t*-butyldimethylsilyl)-4-iodobutanol (**1g**) and 4'-iodobutyl 3β-(*t*-butyldimethylsilyloxy)urs-12-en-28-oate (**1h**) also yielded the corresponding iodo alcohols in excellent yields (Scheme 1, **1gg** and **1hh**). This kind of deprotection cannot be achieved using TBAF because of the sequential etherification.[2] Other methods using acids such as *p*-TsOH can also cause hydrolysis of the ester group.[3] To the best of our knowledge, this is the only method that is suitable for this type of deprotection. In addition, chloromethyl methyl sulfide is a low-boiling-point liquid, which can be prepared easily and inexpensively, and removed from reaction mixtures without contaminating the products.

The mechanism for this reaction probably involves the formation of methyl methylene sulfonium (I) from the reaction

* Correspondent. E-mail: lichunbao@tju.edu.cn

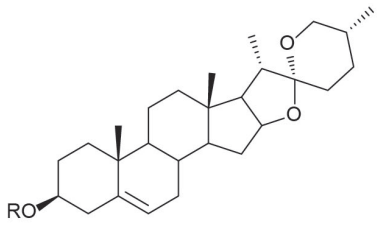
Table 1 Optimisation of the desilylation reaction using **1a**[a]



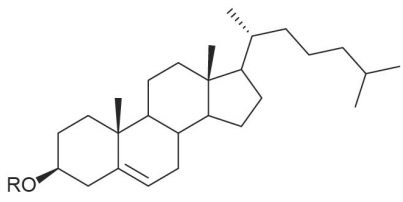
1a **1aa**

Entry	$MeSCH_2Cl$ (equiv.)	KI (equiv.)	Solvent (mL)	H_2O (equiv.)	Temperature (°C)	Time (h)	**1aa** yield (%)[b]
1	0.15	0	Dioxane (4.0)	30	r.t.	24.0	NR[c]
2	0.15	0.05	Dioxane (4.0)	30	r.t.	18.0	>99
3	0.15	0.05	EtOH(4.0)	30	r.t.	18.0	30
4	0.15	0.05	EtOAc(4.0)	30	r.t.	18.0	70
5	0.15	0.05	MeCN (4.0)	30	r.t.	18.0	NR
6	0.15	0.05	CH_2Cl_2 (4.0)	30	r.t.	18.0	NR
7	0.15	0.05	$CHCl_3$ (4.0)	30	r.t.	18.0	NR
8	0.05	0.01	Dioxane (4.0)	30	r.t.	36.0	>99
9	0.10	0.03	Dioxane (4.0)	30	r.t.	30.0	>99
10	0.10	0.03	Dioxane (4.0)	30	35	13.0	>99
11	0.10	0.03	Dioxane (4.0)	30	50	4.6	>99
12	0.10	0.03	Dioxane (4.0)	30	70	0.8	>99
13	0.10	0.03	Dioxane (2.0)	30	50	6.0	>99
14	0.10	0.03	Dioxane (8.0)	30	50	9.2	>99
15	0.10	0.03	Dioxane (4.0)	7.5	50	2.6	>99
16	0.10	0.03	Dioxane (4.0)	15	50	2.3	>99
17	0.10	0.03	Dioxane (4.0)	60	50	6.3	>99

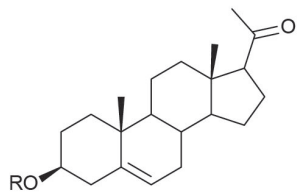
[a]Reaction conditions: 1a (200 mg, 1 equiv.), $MeSCH_2Cl$/KI, H_2O, solvent.
[b]Isolated yield.
[c]NR: no reaction.



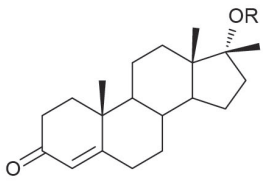
1a: R = TBDMS; **1aa**: 99%, 2.3 h, R = H



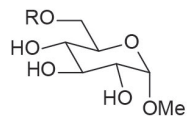
1b: R = TBDMS; **1bb**: 98%, 5.7 h, R = H



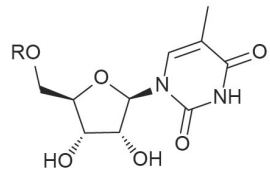
1c: R = TBDMS; **1cc**: 97%, 3.3 h, R = H



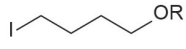
1d: R = TBDMS; **1dd**: 99%, 4.8 h, R = H



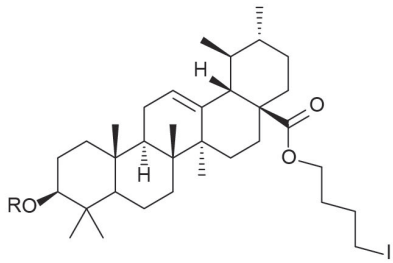
1e: R = TBDMS; **1ee**: 95%, 2.4 h, R = H



1f: R = TBDMS; **1ff**: 93%, 5.3 h, R = H



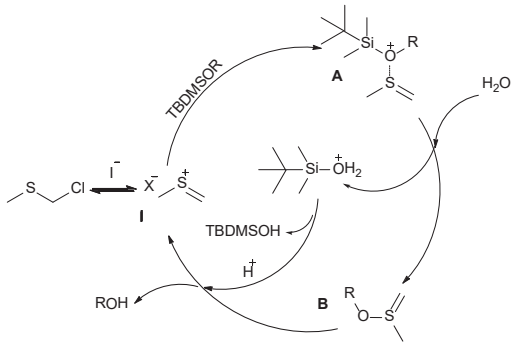
1g: R = TBDMS; **1gg**: 83%, 3.7 h, R = H



1h: R = TBDMS; **1hh**: 87%, 3.8 h, R = H

Reaction conditions: silyl ether (200 mg, 1 equiv.), chloromethyl methyl sulfide (0.1 equiv.), KI (0.03 equiv.), H_2O (15 equiv.) and dioxane (4 mL) at 50 °C; all yields are isolated yields

Scheme 1 Deprotection of silyl ether catalysed by $MeSCH_2Cl$/KI.



Scheme 2 Proposed mechanism of deprotection of silyl ether.

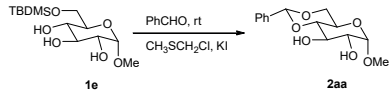
between chloromethyl methyl sulfide and iodide. The sulfonium, as a positively charged Lewis acid, activates the silyl ether (**A**), which is then attacked by water to release **B**. Protonation of **B** liberates an alcohol (Scheme 2).

The scope of this new organoprecatalyst for organic synthesis was then expanded by reacting methyl 6-*O*-(*t*-butyldimethylsilyl)-α-D-glucopyranoside (**1e**) and benzaldehyde. The acetal product was isolated in 82% yield from stirring a mixture of **1e** (200 mg), benzaldehyde (0.25 mL), $MeSCH_2Cl$ (0.2 equiv.) and KI (0.2 equiv.) at r.t. for 2.8 h (Table 2, entry 1). Increasing the amount of PhCHO to 0.5 mL increased the reaction rate to 2.3 h, but further increasing the amount of PhCHO to 1.0 mL, decreased the reaction rate to 3.0 h (Table 2, entries 2 and 3). When the amounts of PhCHO were increased even further to 1.5, 3.0, 5.0 or 7.0 mL, the reactions were incomplete or did not occur (Table 2, entries 4–7). The reason for these results may be that a certain amount of PhCHO is required to dissolve the substrate and precatalyst. However, if excessive PhCHO is used, it reduces concentrations of the catalyst and substrates, which lowers the reaction rate. Keeping the amount of PhCHO at 0.5 mL and raising the amount of KI to 0.03, 0.05 or 0.10 equiv. led to slightly decreased reaction rates (5.3, 5.0 and 3.5 h, respectively; Table 2, entries 8–10). Next the amount of $MeSCH_2Cl$ was reduced to 0.05, 0.10 or 0.15 equiv. while keeping the amount of PhCHO at 0.5 mL and KI at 0.03 equiv. This resulted in lower reaction rates of 10.4, 7.7 and 7.3 h (Table 2, entries 11–13). Based on these results, the optimised reaction conditions were benzaldehyde (0.5 mL), $MeSCH_2Cl$ (0.1 equiv.) and KI (0.03 equiv.) (Table 2, entry 12).

These optimised conditions were then applied to four substrates and benzylidenations were achieved in excellent yields with relatively short reaction times (Table 3, entries 1–4). One of the substrates was pentaerythritol silyl ether and the other three were carbohydrate derivatives. The benzylidenation of methyl 6-*O*-(*t*-butyldimethylsilyl)-α-D-glucopranoside (**1e**) was successfully enlarged to a 10 g scale in 91% yield. The 91% yield included 72% of the product isolated by crystallisation and 19% by chromatography of the mother liquor. In the case of **2aa**, the yield (87%) and reaction rate (7.7 h) are much better than those of classic methods catalysed by $ZnCl_2$ (52–72% yields, 3–36 h)[11,12,23,24] or TsOH (77% yield, 170 h).[25] There have been some improvements using various reagents such as TMSOTf,[26] $Sc(NTf_2)_3$,[27] $Bi(OTf)_3$[28] and NBS.[29] A recently reported method using vanadyl triflate and aldehydes can realise benzylidenation at r.t.[9] However, the catalyst is much more expensive (*ca.* $44,444 mol^{-1}) than ours (*ca.* $0.42 mol^{-1}). Even taking the silylation cost into account, our method still has the advantage in terms of reaction cost, as the silylation is a high-yielding reaction.

When benzaldehyde was replaced with 4-fluorobenzaldehyde, the benzylidenation rates were dramatically improved (Table 3,

Table 2 Optimisation of the benzylidenation using **1e** catalysed by CH_3SCH_2Cl/KI[a]



1e **2aa**

Entry	PhCHO (mL)	CH_3SCH_2Cl (equiv.)	KI (equiv.)	Time (h)	**2aa** yield (%)[b]
1	0.25	0.2	0.2	2.8	82
2	0.5	0.2	0.2	2.3	83
3	1.0	0.2	0.2	3.0	85
4	1.5	0.2	0.2	3.0	53
5	3.0	0.2	0.2	3.0	12
6	5.0	0.2	0.2	3.0	NR[c]
7	7.0	0.2	0.2	3.0	NR
8	0.5	0.2	0.03	5.3	84
9	0.5	0.2	0.05	5.0	85
10	0.5	0.2	0.1	3.5	89
11	0.5	0.05	0.03	10.4	41
12	0.5	0.1	0.03	7.7	87
13	0.5	0.15	0.03	7.3	85

[a]Reaction conditions: 1e (200 mg, 1 equiv.), PhCHO, $MeSCH_2Cl$, KI at r.t.

[b]Isolated yield.

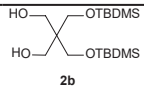
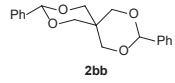
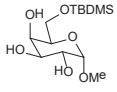
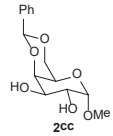
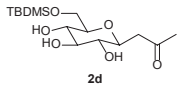
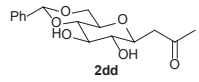
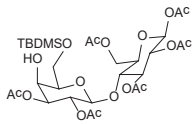
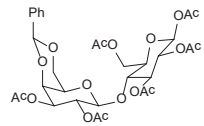
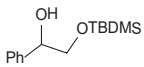
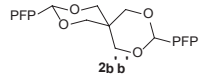
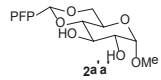
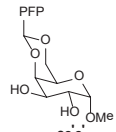
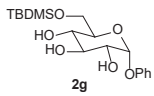
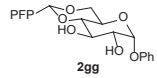
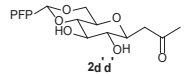
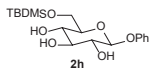
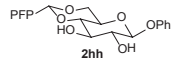
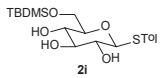
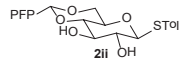
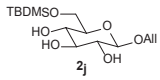
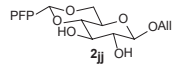
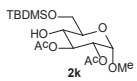
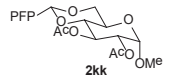
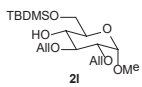
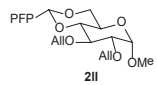
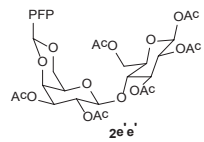
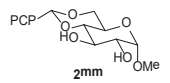
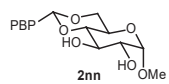
[c]NR: no reaction.

entry 1 versus 6, entry 2 versus 8 and entry 4 versus 16). The reaction times were in the range of 1.0–14.8 h, and most reactions were complete in 3 to 4 h. For all 12 examples, the yields were excellent (72–99%). The benzylidenation reactions occurred faster for substrates with more hydroxyl groups (**2j** versus **2e**). The hydroxyl group ratio between the two compounds is 6.41 (**2j**/**2e**). The ratio (w/w) between the substrate and 4-fluorobenzaldehyde is 1.0 to 2.8, and if the hydroxyl content of the substrate is high, then the polarity of the reaction mixture is increased, which increases the solubility of KI and stabilises the charged methyl methylene sulfonium species (Scheme 3, **I**). These results show that keto (Table 3, entries 3 and 10), hydroxyl (entries 1, 5 and 6), olefinic (entries 13 and 15), ester (entries 4, 14 and 16), glycosidic phenoxy (entries 9 and 11) and phenylthio groups (entry 12) all tolerate these reaction conditions. The carbohydrate substrates included D-glucose (Table 3, entries 7, 9 and 11–15), D-galactose (Table 3, entries 2 and 8), monosaccharide and disaccharide (Table 3, entries 4 and 16). Electron-deficient analogues of 4-fluorobenzaldehyde, such as 4-chloro and 4-bromobenzaldehyde, also performed very well in the benzylidenations of **1e** (Table 3, entries 18 and 19).

Most of the 4,6-*O*-benzylidenations employ α-dimethoxy-*p*-fluorotoluene under the catalysis of TsOH[30] or D-camphorsulfonic acid[31] in 69–77% yield, while the yield *via* our method is 87%. Therefore, our method is to record the highest-yielding direct carbohydrate benzylidenation of electron-deficient benzaldehydes. These types of carbohydrate benzylidene acetals are not only for diol protections, but also can be transformed into various substituted carbohydrates,[32,33] some of which are bioactive.[34]

To gain insights into the reaction mechanism, the following experiments were performed. A combination of (ethylthio) methanol (**3a**) and TBDMSCl or TMSCl was used to replace the chloromethyl methyl sulfide as the catalyst for the benzylidenation reactions (Table 4, entries 1–4). The reactions took place at roughly the same rate as those catalysed by chloromethyl methyl sulfide/KI. However, with (ethylthio) methanol (**3a**) alone, the reaction did not occur (Table 4, entry 5). To determine whether $EtSCH_2OTBDMS$ (**3b**) can generate

Table 3 Benzylidenations using benzaldehydes catalysed by CH_3SCH_2Cl/KI

Entry	Substrate	Aldehydes	Time (h)	Yield (%)[c]	Product[d]
1[a]	 **2b**	Benzaldehyde	11.0	91	 **2bb**
2[a]	 **2c**	Benzaldehyde	6.8	85	 **2cc**
3[a]	 **2d**	Benzaldehyde	4.0	82	 **2dd**
4[a]	 **2e**	Benzaldehyde	17.0	97	 **2ee**
5[a]	 **2f**	4-Fluorobenzaldehyde	2.3	72	 **2ff**
6[a]	**2b**	4-Fluorobenzaldehyde	5.1	>99	 **2b'b'**
7[a]	**1e**	4-Fluorobenzaldehyde	3.0	83	 **2a'a'**
8[a]	**2c**	4-Fluorobenzaldehyde	1.3	80	 **2c'c'**
9[a]	 **2g**	4-Fluorobenzaldehyde	4.3	74	 **2gg**
10[a]	**2d**	4-Fluorobenzaldehyde	3.7	93	 **2d'd'**
11[a]	 **2h**	4-Fluorobenzaldehyde	3.8	83	 **2hh**
12[a]	 **2i**	4-Fluorobenzaldehyde	3.5	84	 **2ii**
13[a]	 **2j**	4-Fluorobenzaldehyde	1.0	87	 **2jj**
14[a]	 **2k**	4-Fluorobenzaldehyde	1.8	81	 **2kk**
15[a]	 **2l**	4-Fluorobenzaldehyde	11.4	85	 **2ll**
16[a]	**2e**	4-Fluorobenzaldehyde	14.8	92	 **2e'e'**
17[b]	**1e**	4-Fluorobenzaldehyde	0.5	81	**2a'a'**
18[b]	**1e**	4-Chlorobenzaldehyde	1.4	78	 **2mm**
19[b]	**1e**	4-Bromobenzaldehyde	4.4	71	 **2nn**

[a]Reaction conditions: silyl ether (200 mg, 1 equiv.), aromatic aldehyde (0.5 mL), $MeSCH_2Cl$ (0.1 equiv.), KI (0.03 equiv.) at r.t. (entries 1–16).

[b]These reactions were carried out at 70 °C because 4-chloro- and 4-bromobenzaldehyde are solid at r.t. (entries 17–19).

[c]Isolated yield.

[d]PFP: *p*-fluorophenyl, PCP: *p*-chlorophenyl, PBP: *p*-bromophenyl.

Table 4 Mechanism exploration of benzylidenation

Entry	Substrate	Aromatic aldehydes	Catalyst	Product
1[a]	**1e**	Benzaldehyde	TBDMSCl/**3a**	**2aa**
2[a]	**1e**	Benzaldehyde	TBDMSCl/KI/**3a**	**2aa**
3[a]	**1e**	Benzaldehyde	TMSCl/**3a**	**2aa**
4[a]	**1e**	Benzaldehyde	TMSCl/KI/**3a**	**2aa**
5[a]	**1e**	Benzaldehyde	**3a**	Trace
6[a]	**1e**	Benzaldehyde	KI/**3b**	Trace
7[a]	**1e**	*p*-Anisaldehyde	$MeSCH_2Cl$/KI	Trace
8[a]	**1e**	4-Fluorobenzaldehyde	TsOH/**3b**	Trace
9[a]	**1ee**	4-Fluorobenzaldehyde	$MeSCH_2Cl$/KI	Trace
10[b]	**1ee**	4-Fluorobenzaldehyde	**3b**	Trace
11[b]	**1ee**	4-Fluorobenzaldehyde	$ZnCl_2$/**3b**	Trace
12[b]	**1ee**	4-Fluorobenzaldehyde	$BF_3{\cdot}Et_2O$/**3b**	Trace
13[c]	**1ee**	4-Fluorobenzaldehyde	TsOH/**3b**	Trace
14[c]	**1ee**	4-Fluorobenzaldehyde	$FeCl_3$/**3b**	Trace
15[c]	**1ee**	4-Fluorobenzaldehyde	$AlCl_3$/**3b**	Trace

[a]Reaction conditions: **1e** (200 mg, 1 equiv.), aromatic aldehydes (0.5 mL), catalyst (0.1 equiv. for each component), r.t.

[b]Reaction conditions: **1ee** (200 mg, 1 equiv.), 4-fluorobenzaldehyde (0.5 mL), catalyst (0.1 equiv. for each component), 4 h, 50 °C.

[c]Reaction conditions: **1ee** (200 mg, 1 equiv.), 4-fluorobenzaldehyde (0.5 mL), catalyst (0.1 equiv. for each component), 4 h, 80 °C.

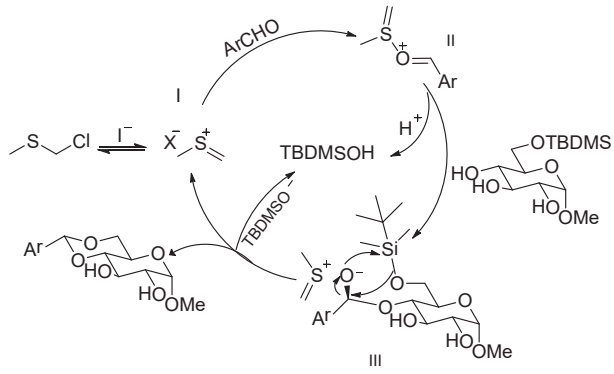
ethyl methylene sulfonium, it was used in the benzylidenation of methyl α-D-glucopyranoside (**1ee**) with 4-fluorobenzaldehyde, and no reaction took place (Table 4, entry 10). The addition of a Lewis acid or TsOH also did not produce any benzylidenation products (Table 4, entries 11–15). This suggests that **3b** is not the catalyst. The catalytically active species, ethyl methylene sulfonium, must be generated from the chloromethyl ethyl sulfide or (ethylthio)methanol (Scheme 3).

Based on these experiments, the following mechanism is proposed (Scheme 3). Chloromethyl methyl sulfide is in equilibrium with methyl methylene sulfonium iodide or chloride (**I**). The reaction between sulfonium **I** and benzaldehyde leads to **II**, which is then attacked by the hydroxyl group of the sugar to yield **III**. The acetal ring of the product is formed under the catalysis of sulfonium **I**.

This mechanism is in agreement with the following facts. Benzylidenation did not take place with *p*-anisaldehyde (Table 4, entry 7) and was faster with 4-fluorobenzaldehyde than with benzaldehyde (Table 3, entry 7 versus Table 2, entry 12). This is in contrast to previously reported results, where the order of benzylidenations catalysed by proton acids or Lewis acids is *p*-anisaldehyde[9,10] > benzaldehyde[11,12] > 4-nitrobenzaldehyde[13,14] both in terms of reaction rates and yields. Possibly, in these reactions, the formation of the benzylic carbocation *via* an S_N1 mechanism is the rate-determining step. In our case, the acetal ring closure *via* an S_N2 path is possible.[35] To our knowledge, this type of mechanism has never been reported.

Conclusion

In conclusion, a new method for the hydrolysis of silyl ethers has been developed. The reaction is mild and high yielding. Notably, the silyl ether substrates bearing an iodo group were desilylated without sequential etherification. In addition, a mild and high-yielding method for benzylidenation has been developed. We have achieved the highest yield to date for benzylidene acetals by directly using electron-deficient benzaldehydes. The reaction probably proceeds *via* an S_N2 substitution at the benzylic position instead of more common S_N1 reaction. This helps reveal the bulky nature of catalytically



Scheme 3 Proposed mechanism of benzylidenation reaction.

active sulfonium species generated from new organoprecatalyst system $MeSCH_2Cl$/KI, and its unique catalysis in organic reactions. There has been no report of catalysts with similar activities to $MeSCH_2Cl$/KI. Research on its further applications is underway in our group.

Experimental

^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded with a Bruker AM400, 400 MHz spectrometer using TMS as an internal standard and CF_3COOH as an external standard for ^{19}F NMR. Multiplicities are reported as follows: singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q), multiplet (m) and dd (doublet of doublets). High-resolution mass spectra (HRMS) were recorded on a QTOF mass analyser using electrospray ionisation (ESI). Melting points were recorded with a micro melting point apparatus. Aromatic benzaldehydes were freshly distilled or recrystallised before use. The synthetic procedures for compounds **1e**, **1f**, **2b**, **2c** and **2f–j** were essentially identical to the ones reported.[36] Compounds **1a–d**,[37] **1g**,[38] **1h**,[39,40] **2d**,[36,41] **2e**,[36,42] **2k**[36,43] and **2l**[36,44] were synthesised according to the literature.

Deprotection of silyl ethers; the desilylation of **1a**

Protected diosgenin **1a** (200 mg, 1 equiv.), chloromethyl methyl sulfide (4 mg, 0.1 equiv.), KI (2 mg, 0.03 equiv.), dioxane (4.0 mL) and water (102 mg, 15 equiv.) were added to a 25 mL round-bottom flask. The mixture was then stirred at 50 °C for 2.3 h. The solvent was then removed under reduced pressure for silica gel chromatography to furnish diosgenin **1aa** as: White solid; yield 152 mg (>99%).

Benzylidenations; general procedures A–C

Procedure A: Silyl ether (200 mg, 1 equiv.), aromatic benzaldehyde (0.5 mL, 10–20 equiv.), chloromethyl methyl sulfide (0.1 equiv.) and KI (0.03 equiv.) were added to a 25 mL round-bottom flask. The mixture was stirred at r.t. until completion of the substrate as assessed by TLC (**2mm** and **2nn** at 70 °C).

Procedure B (on the basis of Procedure A): The crude reaction mixture was Kugelrohr distilled under reduced pressure for silica gel chromatography (eluents containing 1% of Et_3N) to furnish the desired product (**2aa**, **2bb**, **2cc**, **2ff**, **2a'a'**, **2b'b'**and **2c'c'**).

Procedure C (on the basis of Procedure A): The crude reaction mixture was treated with petroleum ether (3 × 5 mL), filtered to remove excess aldehyde and purified by silica gel chromatography (eluents containing 1% of Et_3N) to furnish the desired product (**2dd**, **2ee**, **2d'd'**, **2e'e'**, **2gg**, **2hh**, **2ii**, **2jj**, **2kk**, **2ll**, **2mm** and **2nn**).

Products **1aa**,[45] **1bb**,[46] **1cc**,[47] **1dd**,[48] **1ee**,[49] **1ff**,[50] **1gg**,[51] **2aa**,[9] **2bb**,[9] **2cc**,[9] **2dd**,[52] **2ee**,[42] **2ff**,[53] **2b'b'**,[54] **2jj**,[30] **2mm**[55] and **2nn**[55] are known. Products **1hh**, **2a'a'**, **2c'c'**, **2d'd'**, **2e'e'**, **2gg**, **2hh**, **2ii**, **2kk** and **2ll** are new compounds.

Diosgenin (**1aa**): White solid; m.p. 203–204 °C (lit.[45] 204–207 °C); yield 152 mg (>99%).

Cholesterol (**1bb**): White solid; m.p. 148–149 °C (lit.[46] 150–151 °C); yield 151 mg (98%).

3β-Hydroxypregn-5-en-20-one (**1cc**): White solid; m.p. 190–192 °C (lit.[47] 189–191 °C); yield 142 mg (97%).

17β-Hydroxy-17-methylandrost-4-en-3-one (**1dd**): Light yellow solid; m.p. 160–162 °C; yield 144 mg (>99%).

Methyl α-D-glucopyranoside (**1ee**): White solid; m.p. 162–164 °C (lit.[49] 165–166 °C); yield 120 mg (95%).

5-Methyluridine (**1ff**)*:* White solid; m.p. 182–184 °C (lit.[50] 181–182 °C); yield 129 mg (93%).

4-Iodo-butanol (**1gg**): Yellow oil; yield 106 mg (83%).

4-Iodobutyl (3β)-3-hydroxyurs-12-en-28-oate (**1hh**): Colourless syrup; yield 148 mg (87%); IR (KBr) (ν_{max} cm^{-1}): 3449, 2926, 2870, 1721, 1455, 1382, 1228; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.25 (t, *J* = 3.2 Hz, 1H), 4.08–3.95 (m, 2H), 3.26–3.17 (m, 3H), 2.22 (d, *J* = 11.3 Hz, 1H), 2.02–1.87 (m, 5H), 1.75–1.46 (m, 14H), 1.37–1.25 (m, 9H), 1.08 (s, 3H), 0.99 (s, 3H), 0.95–0.90 (m, 6H), 0.86 (d, *J* = 6.4 Hz, 3H), 0.78 (s, 3H), 0.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.5, 138.2, 125.6, 78.9, 63.0, 55.2, 52.8, 48.1, 47.5, 42.0, 39.5, 39.1, 38.9, 38.7, 38.6, 37.0, 36.8, 33.0, 30.7, 30.3, 29.7, 29.6, 28.2, 28.0, 27.2, 24.2, 23.6, 23.3, 21.2, 18.3, 17.2, 17.1, 15.7, 15.5, 6.0. HRMS (ESI) found: *m/z* 661.3087 $[M + Na]^+$; calcd for $C_{34}H_{55}IO_3Na^+$: 661.3088.

*Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside* (**2aa**): White solid; m.p. 163–165 °C (lit.[9] 168–169 °C); yield 159 mg (87%).

3,9-Diphenyl-2,4,8,10-tetraoxaspiro[5,5]undecane (**2bb**): White solid; m.p. 161–163 °C (lit.[9] 160–162 °C); yield 156 mg (91%).

*Methyl 4,6-*O*-benzylidene-α-D-galactopyranoside* (**2cc**): White solid; m.p. 169–170 °C (lit.[9] 202–204 °C); yield 156 mg (95%).

*1-(4,6-*O*-Benzylidene-β-D-glucopyranosyl)-2-propanone* (**2dd**): White solid; m.p. 150–151 °C (lit.[52] 152–154 °C); yield 151 mg (82%).

*1,2,3,6,2',3'-Hexa-*O*-acetyl-4',6'-benzylidene-β-D-lactose* (**2ee**): White solid, m.p. 212–215 °C; yield 187 mg (97%).

2-(4-Flurophenyl)-4-phenyl-1,3-dioxolane (**2ff**): Colourless oil; yield 139 mg (72%), a mixture of two diastereomers.

3,9-Di(4-fluorophenyl)-2,4,8,10-tetraoxaspiro[5,5]undecane (**2b'b'**): White solid; m.p. 162–164 °C; yield 195 mg (>99%).

*Methyl 4,6-*O*-(4-fluorobenzylidene)-α-D-glucopyranoside* (**2a'a'**): White solid; m.p. 184–185 °C; yield 162 mg (83%); IR (KBr) (ν_{max} cm^{-1}): 3400, 3005 2938, 2882, 1609, 1515, 1460, 1379, 1128, 1072, 839; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.06 (t, *J* = 8.7 Hz, 2H), 5.51 (s, 1H), 4.78 (d, *J* = 3.9 Hz, 1H), 4.29 (dd, *J* = 9.4, 4.0 Hz, 1H), 3.91 (t, *J* = 9.3 Hz, 1H), 3.83–3.70 (m, 2H), 3.61 (dd, *J* = 9.1, 3.9 Hz, 1 H), 3.51–3.44 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.4–161.9 (d, J_{CF} = 247.4 Hz), 133.14–133.11 (d, J_{CF} = 3.1 Hz), 128.33–128.25 (d, J_{CF} = 8.4 Hz), 115.3–115.1 (d, J_{CF} = 21.6 Hz), 101.2, 99.9, 80.9, 72.8, 71.3, 68.9, 62.3, 55.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ –112.4. HRMS (ESI) found: *m/z* 323.0916 $[M + Na]^+$; calcd for $C_{14}H_{17}FO_6Na^+$: 323.0907.

*Methyl 4,6-*O*-(4-fluorobenzylidene)-α-D-galactopyranoside* (**2c'c'**): White solid; m.p. 161–162 °C; yield 156 mg (80%); IR (KBr) (ν_{max} cm^{-1}): 3441, 2913, 2859, 1609, 1514, 1453, 1398, 1089, 1043, 832; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.46 (m, 2H), 7.05 (t, *J* = 8.7 Hz, 2H), 5.53 (s, 1H), 4.92 (d, *J* = 2.7 Hz, 1H), 4.71 (bs, 1H), 4.30–4.24 (m, 2H), 4.07 (dd, *J* = 12.6, 1.6 Hz, 1H), 3.93–3.86 (m, 2H), 3.70 (bs, 1H), 3.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.4–161.9 (d, J_{CF} = 247.5 Hz), 133.66–133.63 (d, J_{CF} = 3.1 Hz), 128.3–128.2 (d, J_{CF} = 8.4 Hz), 115.2–115.0 (d, J_{CF} = 21.6 Hz), 100.5, 100.2, 76.0, 69.5, 69.4, 69.3, 62.7, 55.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ –112.4. HRMS (ESI) found: *m/z* 323.0906 $[M + Na]^+$; calcd for $C_{14}H_{17}FO_6Na^+$: 323.0907.

*Phenyl 4,6-*O*-(4-fluorobenzylidene)-α-D-glucopyranoside* (**2gg**): White solid; m.p. 217–218 °C; yield 145 mg (74%); IR (KBr) (ν_{max} cm^{-1}): 3381, 2931, 2871, 1602, 1508, 1227, 1082, 1030, 835; ^{1}H NMR (400 MHz, DMSO): δ 7.53–7.47 (m, 2H), 7.36–7.30 (m, 2H), 7.21 (t, *J* = 8.9 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.03 (t, *J* = 7.3 Hz, 1H), 5.62 (s, 1H), 5.55 (d, *J* = 3.7 Hz, 1H), 4.09–4.01 (m, 1H), 3.82 (t, *J* = 9.3 Hz, 1H), 3.76–3.68 (m, 2H), 3.56–3.47 (m, 2H); ^{13}C NMR (101 MHz, DMSO): δ 164.0–161.5 (d, J_{CF} = 244.7 Hz), 157.2, 134.59–134.57 (d, J_{CF} = 2.9 Hz), 130.0, 129.1–129.0 (d, J_{CF} = 8.5 Hz), 122.6, 117.3, 115.5–115.3 (d, J_{CF} = 21.5 Hz), 100.6, 98.4, 81.5, 72.5, 70.2, 68.5, 63.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ –112.3. HRMS (ESI) found: *m/z* 385.1062 $[M + Na]^+$; calcd for $C_{19}H_{19}FO_6Na^+$: 385.1063.

*1-(4,6-*O*-(4-Fluorobenzylidene)-β-D-glucopyranosyl)-2-propanone* (**2d'd'**): White solid; m.p. 187–188 °C; yield 181 mg (93%); IR (KBr) (ν_{max} cm^{-1}): 3501, 2984, 2906, 2831, 1710, 1607, 1512, 1376, 1082, 1020, 829; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.43 (m, 2H), 7.07 (t, *J* = 8.5 Hz, 2H), 5.50 (s, 1H), 4.30 (d, *J* = 10.3 Hz, 1H), 3.93–3.82 (m, 1H), 3.80–3.70 (m, 1H), 3.65 (t, *J* = 8.0 Hz, 1H), 3.53–3.32 (m, 3H), 3.10 (bs, 2H), 2.91 (d, *J* = 16.3 Hz, 1H), 2.68 (dd, *J* = 16.1, 7.2 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, DMSO): δ 207.0, 163.9–161.5 (d, J_{CF} = 244.7 Hz), 134.70–134.67 (d, J_{CF} = 3.0 Hz), 129.0–128.9 (d, J_{CF} = 8.4 Hz), 115.4–115.2 (d, J_{CF} = 21.5 Hz), 100.4, 81.5, 77.1, 74.7, 74.4, 70.5, 68.4, 46.7, 30.7; ^{19}F NMR (376 MHz, DMSO): δ –113.1. HRMS (ESI) found: *m/z* 349.1060 $[M + Na]^+$; calcd for $C_{16}H_{19}FO_6Na^+$: 349.1063.

*Phenyl 4,6-*O*-(4-fluorobenzylidene)-β-D-glucopyranoside* (**2hh**): White solid; m.p. 155–157 °C; yield 162 mg (83%); IR (KBr) (ν_{max} cm^{-1}): 3559, 3388, 2883, 1602, 1502, 1230, 1087, 1019, 830; ^{1}H NMR (400 MHz, DMSO): δ 7.51 (dd, *J* = 8.6, 5.7 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.22 (t, *J* = 8.9 Hz, 2H), 7.10–6.98 (m, 3H), 5.63 (s, 1H), 5.62 (s, 1H), 5.47 (d, *J* = 5.1 Hz, 1H), 5.12 (d, *J* = 7.7 Hz, 1H), 4.22 (dd, *J* = 9.4, 4.2 Hz, 1H), 3.74–3.53 (m, 3H), 3.47 (t, *J* = 9.0 Hz, 1H), 3.41–3.34 (m, 1H); ^{13}C NMR (101 MHz, DMSO): δ 164.0–161.5 (d, J_{CF} = 244.7 Hz), 157.6, 134.63–134.60 (d, J_{CF} = 2.9 Hz), 129.9, 129.1–129.0 (d, J_{CF} = 8.5 Hz), 122.6, 116.8, 115.5–115.3 (d, J_{CF} = 21.5 Hz), 101.0, 100.4, 80.8, 74.6, 73.3, 68.3, 66.2; ^{19}F NMR (376 MHz, DMSO): δ –113.0. HRMS (ESI) found: *m/z* 385.1061 $[M + Na]^+$; calcd for $C_{19}H_{19}FO_6Na^+$: 385.1063.

*4-Methylphenyl 4,6-*O*-(4-fluorobenzylidene)-1-thio-β-D-glucopyranoside* (**2ii**): White solid; m.p. 150–151 °C; yield 164 mg (84%); IR (KBr) (ν_{max} cm^{-1}): 3442, 2973, 2870, 1607, 1511, 1459, 1377, 1104, 1006, 830, 807; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.39 (m, 4H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.04 (t, *J* = 8.7 Hz, 2H), 5.50 (s, 1H), 4.74 (bs, 2H), 4.56 (d, *J* = 9.7 Hz, 1H), 4.36 (dd, *J* = 10.5, 4.2 Hz, 1H), 3.86–3.71 (m, 2H), 3.52–3.38 (m, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.4–162.0 (d, J_{CF} = 247.6 Hz), 138.8, 133.6, 132.96–132.93 (d, J_{CF} = 3.2 Hz), 129.9, 128.3–128.2 (d, J_{CF} = 8.4 Hz), 127.4, 115.4–115.2 (d, J_{CF} = 21.7 Hz), 101.2, 88.8, 80.2, 74.4, 72.6, 70.4, 68.6, 21.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ –112.3. HRMS (ESI) found: *m/z* 415.0985 $[M + Na]^+$; calcd for $C_{20}H_{21}FO_5SNa^+$: 415.0991.

*Allyl 4,6-*O*-(4-fluorobenzylidene)-β-D-glucopyranoside* (**2jj**): White solid; m.p. 155–157 °C; yield 170 mg (87%).

*Methyl 2,3-di-*O*-acetyl-4,6-*O*-(4-fluorobenzylidene)-α-D-gluco-pyraniside* (**2kk**): White solid; m.p. 107–109 °C; yield 158 mg (81%); IR (KBr) (ν_{max} cm^{-1}): 3476, 3070, 2932, 2859, 1749, 1610, 1514, 1433, 1374, 1234, 1055, 994, 836; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.39 (m, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 5.57 (t, *J* = 9.7 Hz, 1H), 5.48 (s, 1H), 4.96–4.88 (m, 2H), 4.29 (dd, *J* = 10.3, 4.8 Hz, 1H), 3.95–3.87 (m, 1H), 3.76 (t, *J* = 10.3 Hz, 1H), 3.64 (t, *J* = 9.6 Hz, 1H), 3.41 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.4, 169.8, 164.3–161.9 (d, J_{CF} = 247.4 Hz), 132.98–132.94 (d, J_{CF} = 3.1 Hz), 128.14–128.05 (d, J_{CF} = 8.4 Hz), 115.2–115.0 (d, J_{CF} = 21.6 Hz), 100.9, 97.6, 79.2, 71.6, 69.0, 68.8, 62.3, 55.4, 20.8, 20.7; ^{19}F NMR (376 MHz, $CDCl_3$): δ –112.7. HRMS (ESI) found: *m/z* 407.1121 $[M + Na]^+$; calcd for $C_{18}H_{21}FO_8Na^+$: 407.1118.

*Methyl 2,3-di-*O*-allyl-4,6-*O*-(4-fluorobenzylidene)-α-D-gluco-pyraniside* (**2ll**): White solid; m.p. 83–85 °C; yield 166 mg (85%); IR (KBr) (ν_{max} cm^{-1}): 3425, 3080, 2919, 2865, 1607, 1511, 1461, 1374, 1153, 1003, 827; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.43 (m, 2H), 7.08–7.02 (m, 2H), 5.99–5.88 (m, 2H), 5.51 (s, 1H), 5.33–5.29 (m, 1H), 5.29–5.25 (m, 1H), 5.23–5.18 (m, 1H), 5.17–5.12 (m, 1H), 4.77 (d, *J* = 3.7 Hz, 1H), 4.37–4.31 (m, 1H), 4.31–4.23 (m, 3H), 4.21–4.15 (m, 1H), 3.88–3.76 (m, 2H), 3.74–3.68 (m, 1H), 3.53 (t, *J* = 9.3 Hz, 1H), 3.48–3.41 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.3–161.8 (d, J_{CF} = 247.0 Hz), 135.2, 134.8, 133.46–133.43 (d, J_{CF} = 3.0 Hz), 128.0–127.9 (d, J_{CF} = 8.4 Hz), 117.7, 116.7, 115.2–115.0 (d, J_{CF} = 21.6 Hz), 100.7, 99.3, 82.0, 79.1, 77.9, 74.0, 73.1, 69.1, 62.3, 55.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ –113.0. HRMS (ESI) found: *m/z* 403.1530 $[M + Na]^+$; calcd for $C_{20}H_{25}FO_6Na^+$: 403.1533.

*1,2,3,6,2',3'-Hexa-*O*-acetyl-4',6'-(4-fluorobenzylidene)-β-D-lactose* (**2e'e'**): Colourless syrup; yield 182 mg (92%); IR (KBr) (ν_{max} cm^{-1}):

3065, 2925, 2861, 1749, 1610, 1514, 1436, 1373, 1221, 1154, 1053, 835; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.41 (m, 2H), 7.10–7.04 (m, 2H), 5.68 (d, *J* = 8.3 Hz, 1H), 5.45 (s, 1H), 5.30–5.21 (m, 2H), 5.07 (dd, *J* = 9.7, 8.3 Hz, 1H), 4.87 (dd, *J* = 10.3, 3.6 Hz, 1H), 4.50–4.44 (m, 2H), 4.34–4.25 (m, 2H), 4.14 (dd, *J* = 12.2, 4.7 Hz, 1H), 4.03 (dd, *J* = 12.5, 1.4 Hz, 1H), 3.84–3.80 (m, 1H), 3.78–3.72 (m, 1H), 3.48–3.43 (m, 1H), 2.11 (s, 3H), 2.10 (s, 3H), 2.06–2.01 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 170.3, 170.0, 169.5, 168.9, 168.8, 164.4–161.9 (d, J_{CF} = 247.3 Hz), 133.53–133.50 (d, J_{CF} = 3.0 Hz), 128.4–128.3 (d, J_{CF} = 8.4 Hz), 115.2–115.0 (d, J_{CF} = 21.6 Hz), 100.9, 100.5, 91.7, 75.4, 73.6, 73.1, 72.3, 71.9, 70.4, 68.9, 68.3, 66.3, 61.7, 20.8, 20.7, 20.6, 20.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ −112.4; HRMS (ESI) found: *m/z* 723.1914 [M + Na]$^+$; calcd for $C_{31}H_{37}FO_{17}Na^+$: 723.1912.

Methyl 4,6-O-*(4-chlorobenzylidene)*-α-D-*glucopyranoside* (**2mm**): White solid; m.p. 167–168 °C; yield 159 mg (78%).

Methyl 4,6-O-*(4-bromobenzylidene)*-α-D-*glucopyranoside* (**2nn**): White solid; m.p. 208–209 °C; yield 166 mg (71%).

Electronic Supplementary Information

The ^{1}H, ^{13}C and ^{19}F NMR spectra of the compounds are available through: stl.publisher.ingentaconnect.com/content/stl/jcr/supp-data/content-jcr1704641_esi

Received 11 March 2017; accepted 16 May 2017
Paper 1704641
https://doi.org/10.3184/174751917X14955339414758
Published online: 26 May 2017

References

1 P.G.M. Wuts and T.W. Greene, Protection for the hydroxyl group, including 1,2- and 1,3-diols. In: *Greene's protective groups in organic synthesis*, 4th edn. John Wiley & Sons, New Jersey, 2007, pp. 165–221.
2 J.H. Clark, *Chem. Rev.*, 1980, **80**, 429.
3 T. Taniguchi, G. Tanabe, O. Muraoka and H. Ishibashi, *Org. Lett.*, 2008, **10**, 197.
4 C.J. Moody, P. Shah and P. Knowles, *J. Chem. Soc. Perkin Trans. 1*, 1988, 3249.
5 N.D. Kjeldsen, E.D. Funder and K.V. Gothelf, *Org. Biomol. Chem.*, 2014, **12**, 3679.
6 G.V.M. Sharma, B. Srinivas and P.R. Krishna, *Lett. Org. Chem.*, 2005, **2**, 57.
7 Z.-Y. Jiang and Y.-G. Wang, *Tetrahedron Lett.*, 2003, **44**, 3859.
8 E.J. Corey and G.B. Jones, *J. Org. Chem.*, 1992, **57**, 1028.
9 C.-T. Chen, S.-S. Weng, J.-Q. Kao, C.-C. Lin and M.-D. Jan, *Org. Lett.*, 2005, **7**, 3343.
10 S. Traboni, E. Bedini, M. Giordano and A. Iadonisi, *Adv. Synth. Catal.*, 2015, **357**, 3562.
11 M.A. Brown, P.J. Cox, R.A. Howie, O.A. Melvin, O.J. Taylor and J.L. Wardell, *J. Organomet. Chem.*, 1995, **498**, 275.
12 V.P. Miller, D.-Y. Yang, T.M. Weigel, O. Han and H.-W. Liu, *J. Org. Chem.*, 1989, **54**, 4175.
13 O. Gronwald and S. Shinkai, *J. Chem. Soc. Perkin Trans. 2*, 2001, 1933.
14 F. Huber and S.F. Kirsch, *Chem. Eur. J.*, 2016, **22**, 5914.
15 L. Sun, G. Peng, H. Niu, Q. Wang and C. Li, *Synthesis*, 2008, **24**, 3919.
16 C. Li, L. Sun, Y. Guo and G. Peng *Synthesis*, 2008, **21**, 3487.
17 Z. Shi, L. Sun and C. Li, *J. Agric. Food Chem.*, 2014, **62**, 3287.
18 Q. Wang, L. Sun, Y. Jiang and C. Li, *Beilstein J. Org. Chem.*, 2008, **4**, 51.
19 R. Knorr, *Eur. J. Org. Chem.*, 2011, **2011**, 6335.
20 M. Cocivera, V. Malatesta, K.W. Woo and A. Effio, *J. Org. Chem.*, 1978, **43**, 1140.
21 K. Omura and D. Swern, *Tetrahedron*, 1978, **34**, 1651.
22 E.H. Amonoo-Neizer, S.K. Ray, R.A. Shaw and B.C. Smith, *J. Chem. Soc.,* 1965, 6250.
23 A. Banerjee, S. Senthilkumar and S. Baskaran, *Chem. Eur. J.*, 2016, **22**, 902.
24 V.H.F. Retief, V. Robert, H.R. Marthinus, L.R. Alec, M. Vinesh, W.R. Resmond, WO Patent: 98/46243, issued 22 October 1998.
25 G. Capozzi, C. Ciampi, G. Delogu, S. Menichetti and C. Nativi, *J. Org. Chem.*, 2001, **66**, 8787.
26 T. Tsunoda, M. Suzuki and R. Noyori, *Tetrahedron Lett.*, 1980, **21**, 71.
27 K. Ishihara, Y. Karumi, M. Kubota and H. Yamamoto, *Synlett*, 1996, 839.
28 N.M. Leonard, M.C. Oswald, D.A. Freiberg, B.A. Nattier, R.C. Smith and R.S. Mohan, *J. Org. Chem.*, 2002, **67**, 5202.
29 B. Karimi, G.R. Ebrahimian and H. Seradj, *Org. Lett.*, 1999, **1**, 1737
30 M. Mogemark, M. Elofsson and J. Kihlberg, *J. Org. Chem.*, 2003, **68**, 7281.
31 E.C. Boettger, A. Vasella and D. Perez Fernandez, WO Patent: 2008/092690 A1, issued 7 August 2008.
32 D. Crich, Q. Yao and A.A. Bowers, *Carbohydr. Res.*, 2006, **341**, 1748.
33 Y.-J. Zhang, W. Dayoub, G.-R. Chen and M. Lemaire, *Eur. J. Org. Chem.*, 2012, **2012**, 1960.
34 A.B. Reitz, M.G. Goodman, B.L. Pope, D.C. Argentieri, S.C. Bell, L.E. Burr, E. Chourmouzis, J. Come and J.H. Goodman, *J. Med. Chem.*, 1994, **37**, 3561.
35 F.A. Carey and R.J. Sundberg, Nucleophilic substitution. In: *Advanced organic chemistry, part A: structure and mechanism*, 4th edn. Kluwer Academic/Plenum Publishers, New York, 2000, pp. 276–290.
36 T. Halmos, R. Montserret, J. Filippi and K. Antonakis, *Carbohydr. Res.*, 1987, **170**, 57.
37 Q.-C. Xu, Y. Liu, J. Liu, C.-X. He, M.-C. Yan and M.-S. Cheng, *Chem. Lett.*, 2008, **37**, 780.
38 S. Sommer, M. Kühn and H. Waldmann, *Adv. Synth. Catal.*, 2008, **350**, 1736.
39 L. Liu, S. Feng and C. Li, *ACS Sustainable Chem. Eng.*, 2016, **4**, 6754.
40 E.J. Corey, H. Cho, C. Rücker and D.H. Hua, *Tetrahedron Lett.*, 1981, **22**, 3455.
41 J. Wang, Q. Li, Z. Ge and R. Li, *Tetrahedron*, 2012, **68**, 1315.
42 G. Tamerlani, I. Lombardi, D. Bartalucci, A. Danesi, L. Salsini, M. Manoni and G. Cipolletti, US Patent: 2012/0071441 A1, 22 March 2012.
43 K. Yamamoto, N. Watanabe, H. Matsuda, K. Oohara, T. Araya, M. Hashimoto, K. Miyairi, I. Okazaki, M. Saito, T. Shimizu, H. Kato and T. Okuno, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 4932.
44 S.E. House, K.W.C. Poon, H. Lam and G.B. Dudley, *J. Org. Chem.*, 2006, **71**, 420.
45 S.U. Rahman, M. Ismail, M.R. Shah, A. Adhikari, I. Anis, M.S. Ahmad and M. Khurram, *Steroids*, 2015, **104**, 270.
46 S. Yu, X. Ye, L. Chen, X.-Y. Lian and Z. Zhang, *Steroids*, 2014, **88**, 19.
47 Z. Szendi, P. Forgó, G. Tasi, Z. Böcskei, L. Nyerges and F. Sweet, *Steroids*, 2002, **67**, 31.
48 M.L.S. Almeida, P. Kočovský and J.E. Bäckvall, *J. Org. Chem.*, 1996, **61**, 6587.
49 M.F. Abreu, V.T. Salvador, L. Vitorazi, C.E.N. Gatts, D.R. dos Santos, R. Giacomini, S.L. Cardoso and P.C.M.L. Miranda, *Carbohydr. Res.*, 2012, **353**, 69.
50 H. Hayakawa, H. Tanaka and T. Miyasaka, *Tetrahedron*, 1985, **41**, 1675.
51 M. Bergdahl, M. Eriksson, M. Nilsson and T. Olsson, *J. Org. Chem.*, 1993, **58**, 7238.
52 V. Aucagne, D. Gueyrard, A. Tatibouët, A. Quinsac and P. Rollin, *Tetrahedron*, 2000, **56**, 2647.
53 P. Sebej, T. Solomek, L. Hroudna, P. Brancova and P. Klan, *J. Org. Chem.*, 2009, **74**, 8647.
54 B. Karimi, H. Hazarkhani and J. Maleki, *Synthesis*, 2005, **2**, 279.
55 F. Ono, O. Hirata, K. Ichimaru, K. Saruhashi, H. Watanabe and S. Shinkai, *Eur. J. Org. Chem.*, 2015, **2015**, 6439.