Acetonyltriphenylphosphonium Bromide (ATPB): A Versatile Reagent for the Acylation of Alcohols, Phenols, Thiols and Amines and for 1,1-Diacylation of Aldehydes under Solvent-Free Conditions

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Dedicated to Professor K. C. Majumdar[‡]

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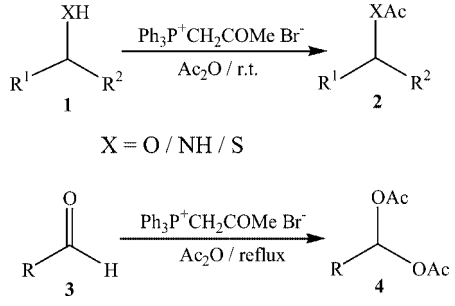
A wide variety of alcohols, phenols, amines and thiols may easily be converted into the corresponding acetate derivatives by treatment with acetic anhydride (1.5–2.0 equivalents) in the presence of acetonyltriphenylphosphonium bromide (ATPB; 5 mol %) in good yields at room temperature. With the same precatalyst, both aliphatic and aromatic aldehydes can also be transformed into the corresponding *gem*-diacetates under reflux conditions.

Introduction

The acylation of alcohols and phenols, amines and thiols is one of the most useful transformations in organic synthesis.[1] Of these, the conversion of a hydroxy group into the corresponding acetate is important due to its ease of introduction, stability under mild acidic reaction conditions and ease of removal by mild alkaline hydrolysis. The acylation of alcohols, phenols or amines is usually performed with acetic anhydride in the presence of amine bases such as triethylamine or pyridine, or pyridine together with 4-(dimethylamino)pyridine (DMAP), which acts as a cocatalyst, or 4-pyrrolidinopyridine (PPY).[2] It is also possible to use tributylphosphane (Bu_3P) as a less basic catalyst for acylation reactions, particularly for base-sensitive substrates.[3] Various metal salts such as $CoCl_2$,[4] $ZnCl_2$,[5] $RuCl_3$,[6] $TiCl_4$–$AgClO_4$,[7] $LiClO_4$,[8] $Mg(ClO_4)_2$,[9] $Zn(ClO_4)_2{\cdot}6H_2O$[10] and some triflates such as $Sc(OTf)_3$,[11] Me_3SiOTf,[12] $In(OTf)_3$,[13] $Cu(OTf)_2$,[14] $Ce(OTf)_3$[15] and $Bi(OTf)_3$[16] have also been employed for acylation reactions in recent years. Very recently, it was also shown that I_2 can be employed as a catalyst for the acetylation of alcohols under solvent-free conditions.[17] Though perchlorates[8–10] have been observed to be effective catalysts for this transformation, they have some serious drawbacks, such as some of them being highly explosive.[18] In addition, $Mg(ClO_4)_2$ has to be anhydrous in order to provide better yields.[9] Other methods based on triflates[11–16] or $RuCl_3$[6] also have some disadvantages: the reagents can be highly expensive or require longer reaction times and extremely dry reaction conditions. Although there are numerous known literature methods through which to obtain good yields of acetylated products, there is still a need for mild and effective catalysts applicable for acetylation reactions for a wide variety of substrates. As a part of our ongoing research project to develop newer synthetic methodologies, particularly in protection and deprotection chemistry,[19] we speculated that acetonyltriphenylphosphonium bromide (ATPB) might be a useful, effective and versatile precatalyst for acylation reactions. So far, acetonyltriphenylphosphonium bromide (ATPB) has been utilized mainly as a Wittig salt,[20a] for the tetrahydropyranylation/depyranylation of alcohols,[20b] and for the cyclotrimerization of aldehydes.[20c] Very recently, we have demonstrated the utility of ATPB for selective deprotection of *tert*-butyldimethylsilyl (TBS) ethers.[19c] Here we report the acetylation of alcohols, phenols, amines and thiols with acetic anhydride in the presence of catalytic amounts of acetonyltriphenylphosphonium bromide (ATPB) under solvent free-conditions, as shown in Scheme 1.



Scheme 1.

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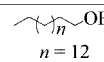
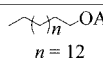
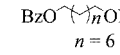
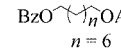
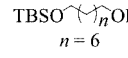
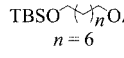
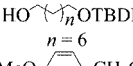
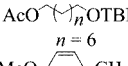
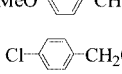
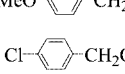
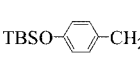
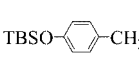
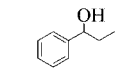
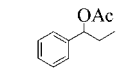
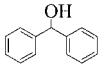
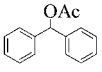
Results and Discussion

For this study we first prepared the reagent acetonyltriphenylphosphonium bromide by the literature procedure.[20a] We then attempted the acylation of cetyl alcohol (**1a**) with acetic anhydride in the presence of acetonyltriphenylphosphonium bromide (5 mol%) at room temperature (Table 1). The reaction was complete within 25 min, and the pure acetate derivative of cetyl alcohol (**2a**) was obtained in 96% yield after chromatographic separation. We next examined benzoyl-, *tert*-butyldimethylsilyl- and *tert*-butyldiphenylsilyl-protected alcohols **1b**–**d** and found that they were smoothly converted into the corresponding acetates **2b**–**d** in good yields under identical reaction conditions, without the protecting groups being affected. Likewise, various benzylic alcohols (**1e**–**g**), secondary alcohols (**1h**–**k**), allyl alcohol (**1l**) and butyne-1,4-diol (**1m**) were converted in similar manner into the corresponding acetate derivatives **2e**–**m** in very good yields. It is interesting to mention that neither alkyl bromide formation nor HBr addition at double bonds or even triple bonds took place under the experimental conditions. It had been observed that the TBS group was unlikely to survive acetylation with use of $Ce(OTf)_3$,[15] while our procedure offered the advantage that the TBS group was unaffected under the reaction conditions. It is also worthwhile to point out that our procedure is more efficient: the acetylation of cholesterol (entry **1k**), for example, was completed much more quickly than in the recently reported procedure.[15] Notably, chiral alcohols such as menthol (entry **1j**) were easily acetylated in high yields and with complete retention of optical activity. Remarkably, an isopropylidene-protected alcohol **1n** could also be acetylated under identical conditions without cleavage of the isopropylidene group. A tertiary alcohol (**1o**) and a sterically hindered tertiary alcohol, adamentanol (**1p**), were also smoothly converted into the corresponding acetate derivatives **2o** and **2p**, respectively, without any difficulty. We have noticed that this method is more efficient than the ruthenium(III) chloride method[6] in terms of reaction times, particularly for the preparation of **2p**.

We next investigated whether or not the same reagent can be employed for acetylation of phenolic compounds. By the same procedure, various phenolic compounds **1q**–**s** were easily transformed into the corresponding acetate derivatives **2q**–**s**. Again, we observed that 4-nitrophenol (entry **1r**) and 2-naphthol (entry **1s**) were converted into the corresponding acetate derivatives much more quickly than in the recently reported procedure.[6] We next turned our attention to whether or not our methodology could be extended further, for acetylation of carbohydrates and nucleosides. We found that various carbohydrate molecules such as **1t**–**v** and thymidine (**1w**) were converted into the corresponding acetate derivatives **2t**–**w** in good yields under similar reaction conditions. Importantly, a thio group and a methoxy group at the anomeric position were unaffected under the experimental conditions. The reaction times and yields of the products are summarized in Table 1. Interestingly, it is also possible for a primary OH group to be acetylated chemose-

Table 1. Acetylation of alcohols, phenols, amines and thiols at room temperature in the presence of acetonyltriphenylphosphonium bromide as precatalyst.

Entry	Substrate **1**	Time	Product[a] **2**	Yield[b] [%]
a	 $n = 12$	25 min	 $n = 12$	96
b	 $n = 6$	30 min	 $n = 6$	92
c	 $n = 6$	30 min	 $n = 6$	89
d	 $n = 6$	30 min	 $n = 6$	91
e		40 min		96[21]
f		40 min		90[22]
g		35 min		85
h		30 min		95
i		50 min		93
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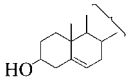
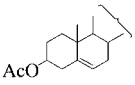
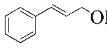
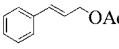
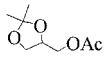
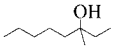
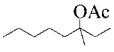
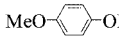
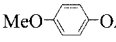
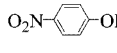
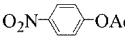
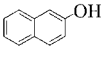
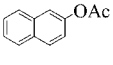
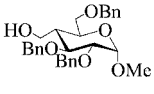
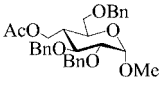
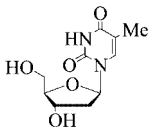
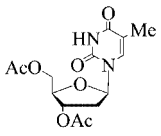
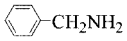
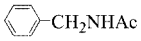
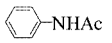
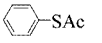
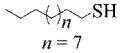
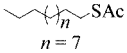
k		3.5 min		94[d][12]
l		40 min		92[c]
m		30 min		90[d]
n		30 min		75[10]
o		2.0 h		63
p		1.5 h		87[23]
q		55		94[24]
r		2 h		80[c]
s		3 h		72[c]
t		55 min		74
u		55 min		72
v		1.2 h		78

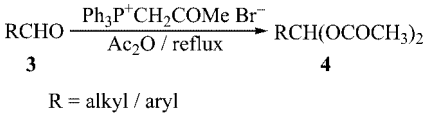
Table 1. *(Continued)*

Entry	Substrate 1	Time	Product[a] 2	Yield[b] [%]
w		3.5 h		77[d]
x		35 min		65[e]
y		35 min		86[c]
z		45 min		85[c]
a′		1 h		90[c]
b′		45 min		82

[a] All the acetylated compounds were characterized by IR, ^{1}H NMR and elemental analyses. [b] Isolated yield. [c] The data for the acetates were also compared with those for the authentic compounds. [d] Acetic anhydride (3–5 equivalents) was used instead of 1.5–2.0 equivalent. [e] Acetic anhydride (1 equivalent) was used.

lectively (entry **1x**) under similar reaction conditions. By our procedure, both aliphatic and aromatic amines (entry **1y**–**z**), as well as thiols (entry **1a**′ and **1b**′), were transformed into the corresponding acetate derivatives **2y**–**b**′ in good yields with the same precatalyst.

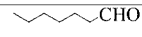
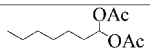
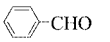
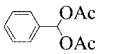
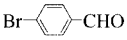
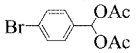
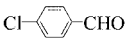
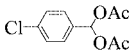
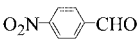
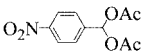
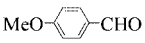
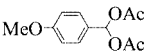
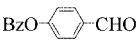
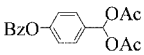
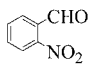
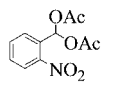
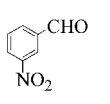
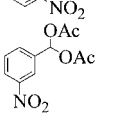
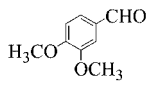
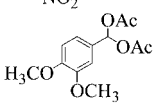
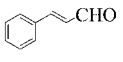
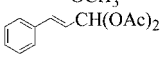
We next turned our attention to whether the same precatalyst would be useful for the 1,1-diacetylation of aldehydes. The formation of geminal diesters from the corresponding aldehyde compounds is an important organic transformation because they serve as building blocks for asymmetric allylic alkylation[25] and Diels–Alder reactions.[26] Moreover, acylals are commonly used as protecting groups for aldehydes because they are stable under neutral and basic conditions.[27] The formation of a 1,1-diacetate is usually achieved by treatment of an aldehyde compound with acetic anhydride in the presence of an acid or Lewis acid, acting as a catalyst. The literature includes several reported methods employing various reagents such as LiOTf,[28] ceric ammonium nitrate,[29] $InCl_3$,[30] H_2NSO_3H,[31] $LiBF_4$,[32] H_2SO_4,[33] PCl_3,[34] NBS,[35] I_2,[36] TMSCl·NaI,[37] $FeCl_3$,[38] and $Bi(NO_3)_3·5H_2O$ for similar transformations.[39] Some metal triflates (e.g., $Cu(OTf)_2$[40] and $Sc(OTf)_3$[41]) have also been utilized as catalysts for the preparation of 1,1-diacetate derivatives from the corresponding aldehydes. Some of these methods have certain drawbacks, such as requirements for longer reaction times or use of expensive reagents, and sometimes fail to provide acylals from aliphatic aldehydes or aromatic aldehydes possessing electron-donating groups in the aromatic ring,[39] so there would be scope for an alternative method. With our precatalyst, various aldehydes can be converted smoothly into the corresponding 1,1-diacetates, as shown in Scheme 2.



Scheme 2.

When an aliphatic aldehyde was treated with acetic anhydride in the presence of ATPB (10 mol%) at room temperature, the reaction was very sluggish and the yield was low. On heating at reflux, however, the same reaction mixture provided the corresponding *gem*-diacetate derivative in good yield by our procedure, more activation energy for the formation of 1,1-diacetates having been provided. Various aliphatic and aromatic aldehydes were smoothly converted into the corresponding *gem*-diacetates in good yields in the presence of the same precatalyst under reflux conditions; the reaction times and yields of the 1,1-diacetates are listed in Table 2. The products were characterized by checking of their melting points and by their IR and ^{1}H NMR spectra, and elemental analyses, as well as by comparison of the compounds' data with the reported data. It is important to mention that neither α-bromination nor cyclotrimerization under the experimental conditions were noticed. This method is relatively harsher than previously reported meth-

Table 2. Formation of *gem*-diacetates from the corresponding aldehydes in the presence of ATPB (10 mol%) as precatalyst under solvent-free conditions.

Entry	Substrate 3	Time	Product[a] 4	Yield[b] [%]	m. p. [°C] (lit.)
a		9 h		88	–
b		5 h		85[35]	–
c		6 h		78	84
d		7 h		78[36]	80 (79–80)
e		11 h		75[36]	126 (125)
f		6 h		82[36]	68 (67–68)
g		10 h		72[28]	97–98
h		15 h		69	85–86
i		14 h		71[38]	62–64 (64–66)
j		5 h		79	63–64
k		5 h		90[38]	85–86 (84–85)

[a] All the products were characterized by melting point, IR, ^{1}H NMR and elemental analysis. [b] Isolated yield.

ods for the formation of *gem*-diacetates, but both aliphatic and aromatic aldehydes can nevertheless be converted into the corresponding diacetates in good yields. Like a previously reported method,[39] this procedure did not provide any 1,1-diacetates from ketones under identical reaction conditions: when acetophenone, for example, was treated with acetic anhydride in the presence of the same precatalyst under reflux conditions, it did not give the corresponding 1,1-diacetate derivative.

The formation of the product can be explained as follows. We believe that HBr is generated in the reaction medium from the reaction between acetonyltriphenylphosphonium bromide and alcohol, and that this catalyses the acetylation of the alcohols to provide the corresponding acetates. However, the corresponding reaction failed when carried out with benzyltriphenylphosphonium bromide instead of acetonyltriphenylphosphonium bromide, indicating that ATPB generates HBr much more easily than the other alkylphosphonium bromide.

Conclusions

In conclusion, we have demonstrated a new, efficient and chemoselective procedure for the acetylation of alcohols, phenols, amines and thiols by use of a catalytic amount of acetonyltriphenylphosphonium bromide as precatalyst at room temperature under very mild conditions. In addition, both aliphatic and aromatic aldehydes can be converted into *gem*-diacetates by employing the same catalyst under reflux conditions. The significant features of this method include its ease of operation, high efficiency, mild conditions and chemoselectivity, which may prove widely useful in organic synthesis. Moreover, a wide variety of other protecting groups, such as benzyl, benzoyl, TBS, TBDPS and isopropylidene, survived under the experimental conditions, as did methoxy and thio groups at anomeric positions.

Experimental Section

Melting points were recorded on a Büchi B-545 melting point apparatus and were uncorrected. IR spectra were recorded in KBr or neat on a Nicolet Impact 410 spectrophotometer. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Jeol 400-MHz spectrometer in $CDCl_3$ with TMS as internal reference. Elemental analyses were carried out with a Perkin–Elmer 2400 automatic carbon, hydrogen, nitrogen and sulfur analyzer. Column chromatographic separations were carried out on SRL silica gel (60–120 mesh).

General Procedure for Acetylation of Alcohols or Phenols or Amines and Thiols: Acetonyltriphenylphosphonium bromide (0.05 mmol) was added to a mixture of the alcohol, or phenol, or amine or thiol (1 mmol) and acetic anhydride (1.5–2.0 mmol) and the mixture was stirred at room temperature for ca. 0.5–3.5 h. After complete disappearance of the starting material as monitored by TLC, the mixture was quenched with a saturated hydrogencarbonate solution (2 mL). Finally, the reaction mixture was extracted with ethyl acetate (20 mL × 3). The combined organic extract was washed with water and dried over anhydrous sodium sulfate. After removal of the organic solvent in a rotary evaporator, the crude residue was subjected to silica gel column to isolate the desired pure acetate.

General Procedure for 1,1-Diacetylation of Aldehydes: A mixture of aldehyde (1 mmol) and acetic anhydride (4 mmol) was placed in a 10 mL round-bottomed flask fitted with a reflux condenser. The acetonyltriphenylphosphonium bromide precatalyst (0.1 mmol) was then added and the mixture was stirred under reflux conditions. After completion of the reaction as monitored by TLC, it was quenched with a saturated solution of sodium hydrogencarbonate (2 mL) and the mixture was extracted with ethyl acetate (20 mL × 2). The combined organic layer was dried over anhydrous sodium sulfate and was concentrated in vacuo. Finally, the crude residue was passed through a silica gel column to provide the desired 1,1-diacetate derivatives.

Compound 2a: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, $-CH_3$), 1.22–1.36 (m, 26 H, $-CH_2$), 1.48–1.62 (m, 2 H, $-CH_2$), 2.04 (s, 3 H, $-COCH_3$), 4.04 (t, J = 7.2 Hz, 2 H, $-OCH_2$) ppm. IR (neat): $\tilde{\nu}$ = 2919, 2858, 1747 (CO), 1465, 1368, 1235, 1045 cm^{-1}. $C_{18}H_{36}O_2$ (284.48): calcd. C 76.00, H 12.75; found C 75.82, H 12.69%.

Compound 2b: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30–1.50 (m, 8 H, $-CH_2$), 1.60–1.70 (m, 2 H, $-CH_2$), 1.72–1.80 (q, 2 H, $-CH_2$), 2.04 (s, 3 H, $-COCH_3$), 4.05 (t, J = 7.2 Hz, 2 H, $-OCH_2$), 4.32 (t, J = 6.8 Hz, 2 H, $-OCH_2$), 7.44 (t, J = 8.0 Hz, 2 H, ArH), 7.55 (t, J = 8.0 Hz, 1 H, ArH), 8.04 (d, J = 7.6 Hz, 2 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3063, 2930, 2858, 1731 (CO), 1593, 1455, 1378, 1271, 1240, 1112, 1035 cm^{-1}. $C_{17}H_{24}O_4$ (292.37): calcd. C 69.84, H 8.27; found C 69.70, H 8.21%.

Compound 2c: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.01 [s, 3 H, $-Si(CH_3)_2$], 0.00 [s, 3 H, $-Si(CH_3)_2$], 0.85 [s, 9 H, $-SiC(CH_3)_3$], 1.26–1.40 (m, 8 H, $-CH_2$), 1.44–1.55 (m, 2 H, $-CH_2$), 1.57–1.61 (m, 2 H, $-CH_2$), 2.00 (s, 3 H, $-COCH_3$), 3.54 (t, J = 6.8 Hz, 2 H, $-OCH_2$), 4.00 (t, J = 6.8 Hz, 2 H, $-OCH_2$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.3, 0.0, 18.3, 21.0, 25.7, 25.8, 26.0 (3C), 29.2, 29.3, 32.3, 32.8, 63.2, 64.6, 171.2 ppm. IR (neat): $\tilde{\nu}$ = 3056, 2920, 2848, 1740 (CO), 1475, 1433, 1373, 1245, 1112, 1035 cm^{-1}. $C_{16}H_{34}O_3Si$ (302.53): calcd. C 63.52, H 11.33; found C 63.34, H 11.24%.

Compound 2d: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 [s, 9 H, $-SiC(CH_3)_3$], 1.20–1.40 (m, 8 H, $-CH_2$), 1.52–1.68 (m, 4 H, $-CH_2$), 2.01 (s, 3 H, $-COCH_3$), 3.65 (t, J = 6.4 Hz, 2 H, $-OCH_2$), 4.05 (t, J = 6.8 Hz, 2 H, $-OCH_2$), 7.36–7.42 (m, 6 H, ArH), 7.66–7.68 (dd, J = 1.6, J = 7.6 Hz, 4 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3058, 2925, 2848, 1742 (CO), 1475, 1434, 1373, 1245, 1112, 1035 cm^{-1}. $C_{26}H_{38}O_3Si$ (426.67): calcd. C 73.19, H 8.98; found C 73.01, H 8.91%.

Compound 2g: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.19 [s, 6 H, $Si(CH_3)_2$], 0.98 [s, 9 H, $-SiC(CH_3)_3$], 2.08 (s, 3 H, $-COCH_3$), 5.02 (s, 2 H, $-OCH_2$), 6.81 (d, J = 8.0 Hz, 2 H, ArH), 7.22 (d, J = 8.0 Hz, 2 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 2954, 2930, 2888, 2859, 1747 (CO), 1610, 1521, 1237, 1229, 913 cm^{-1}. $C_{15}H_{24}SiO_3$ (280.44): calcd. C 64.24, H 8.63; found C 64.59, H 8.55%.

Compound 2h: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 7.2 Hz, 3 H, $-CH_3$), 1.81–1.95 (m, 2 H, $-CH_2$), 2.07 (s, 3 H, $-COCH_3$), 5.66 (t, J = 7.2 Hz, 1 H, –CHOAc), 7.20–7.37 (m, 5 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3063, 3022, 2976, 2925, 2879, 1742 (CO), 1491, 1460, 1378, 1250, 1055 cm^{-1}. $C_{11}H_{14}O_2$ (178.23): calcd. C 74.13, H 7.92; found C 74.01, H 7.85%.

Compound 2i: Colourless gummy liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, $-COCH_3$), 6.88 (s, 1 H, –CHOAc), 7.32–7.34 (m, 10 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3073, 3037, 2935, 1747

(CO), 1598, 1496, 1445, 1373, 1235, 1020 cm^{-1}. $C_{15}H_{14}O_2$ (226.27): calcd. C 79.62, H 6.24; found C 79.41, H 6.18%.

Compound 2m: Colourless, low-melting solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 6 H, 2×–$COCH_3$), 4.71 (s, 4 H, 2×–OCH_2) ppm. IR (neat): $\tilde{\nu}$ = 2949, 1752 (CO), 1435, 1383, 1222, 1156, 1038 cm^{-1}. $C_8H_{10}O_4$ (170.16): calcd. C 56.47, H 5.92; found C 56.19, H 5.85%.

Compound 2o: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, J = 8.0 Hz, 3 H, –CH_3), 0.89 (t, J = 7.2 Hz, 3 H, –CH_3), 1.24–1.34 (m, 6 H, –CH_2), 1.37 (s, 3 H, –CH_3), 1.62–1.90 (m, 4 H, –CH_2), 1.97 (s, 3 H, –$COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.13, 14.17, 22.48, 22.72, 23.37 (2C), 30.91, 32.25, 37.81, 85.13, 170.18 ppm. IR (neat): $\tilde{\nu}$ = 2935, 2873, 1737 (CO), 1465, 1373, 1250, 1143, 1025 cm^{-1}. $C_{11}H_{22}O_2$ (186.29): calcd. C 70.92, H 11.90; found C 70.76, H 11.85%.

Compound 2t: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.94 (s, 3 H, –$COCH_3$), 2.07 (m, 1 H, 4-H), 3.39 (s, 3 H, –OCH_3), 3.59–3.63 (m, 3 H), 3.82–3.88 (m, 1 H, 5-H), 3.90 (t, J = 9.2 Hz, 1 H, 3-H), 4.01 (dd, J = 2.4, J = 11.4 Hz, 1 H, 6-H), 4.32 (dd, J = 2.8 Hz, 1 H, 6′-H), 4.47 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.58 (d, J = 10.8 Hz, 1 H, –OCHPh), 4.60 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.66 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.69 (d, J = 3.6 Hz, 1 H, 1-H), 4.78 (d, J = 12.0 Hz, 1 H, –OCHPh), 4.96 (d, J = 10.8 Hz, 1 H, –OCHPh), 7.22–7.40 (m, 15 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3032, 2899, 1742 (CO), 1455, 1363, 1240, 1091, 1055 cm^{-1}. $C_{31}H_{36}O_7$ (520.62): calcd. C 71.52, H 6.97; found C 71.25, H 6.90%.

Compound 2u: Solid, m.p.: 63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.6 Hz, 3 H, –SCH_2CH_3), 2.03 (s, 3 H, –$COCH_3$), 2.64–2.80 (m, 2 H, –SCH_2CH_3), 3.44 (t, J = 9.2 Hz, 1 H), 3.50–3.52 (m, 1 H, 5-H), 3.54 (t, J = 9.6 Hz, 1 H), 3.71 (t, J = 8.8 Hz, 1 H), 4.19 (dd, J = 4.4, J = 11.6 Hz, 1 H, H- 6), 4.33 (dd, J = 1.6, J = 12.0 Hz, 1 H, 6′-H), 4.47 (d, J = 9.6 Hz, 1 H, 1-H), 4.57 (d, J = 11.2 Hz, 1 H, –OCHPh), 4.74 (d, J = 10.4 Hz, 1 H, –OCHPh), 4.85 (d, J = 10.8 Hz, 1 H, –OCHPh), 4.86 (d, J = 10.8 Hz, 1 H, –OCHPh), 4.92 (d, J = 10.4 Hz, 1 H, –OCHPh), 4.95 (d, J = 10.8 Hz, 1 H, –OCHPh), 7.26–7.36 (m, 15 H, ArH) ppm. IR (KBr): $\tilde{\nu}$ = 3063, 3027, 2925, 2868, 1737 (CO), 1455, 1363, 1235, 1071 cm^{-1}. $C_{31}H_{36}O_6S$ (536.68): calcd. C 69.38, H 6.76, S 5.97; found C 69.23, H 6.70, S 5.70%.

Compound 2v: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.83 (s, 3 H, –$COCH_3$), 3.40–3.44 (m, 2 H), 3.59 (dd, 1 H), 3.83–3.87 (m, 1 H), 3.97 (t, 1 H), 4.46–4.56 (m, 4 H), 4.62–4.71 (m, 3 H), 4.82 (d, J = 3.6 Hz, 1 H, 1-H), 4.90 (d, J = 12.0 Hz, 1 H), 5.04 (t, J = 8.0 Hz, 1 H), 7.25–7.40 (m, 20 H, ArH) ppm. IR (neat): $\tilde{\nu}$ = 3065, 3030, 2918, 2867, 1748, 1503, 1457, 1376, 1234, 1101, 1045 cm^{-1}. $C_{36}H_{38}O_7$ (582.69): calcd. C 74.20, H 6.57; found C 74.01, H 6.60%.

Compound 2x: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.71 (br. s, 1 H, OH, D_2O exchangeable), 2.12 (s, 3 H, –$COCH_3$), 3.60–3.64 (m, 2 H, –OCH_2), 4.07–4.09 (m, 1 H, –OCH), 4.21(d, J = 5.2 Hz, 2 H, –CH_2Cl) ppm. IR (neat): $\tilde{\nu}$ = 3437 (OH), 2960,1737 (CO),1424, 1240, 1045, 933 cm^{-1}. $C_5H_9ClO_3$ (152.62): calcd. C 39.35, H 5.94; found C 39.10, H 5.86%.

Compound 2b′: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, –CH_3), 1.20–1.40 (m, 18 H, –CH_2), 1.45–1.60 (m, 2 H, –CH_2), 2.32 (s, 3 H, –$COCH_3$), 2.86 (t, J = 7.6 Hz, 2 H, –SCH_2) ppm. IR (neat): $\tilde{\nu}$ = 2940, 2853, 1692 (CO), 1460, 1342, 1132, 948 cm^{-1}. $C_{14}H_{28}SO$ (244.44): calcd. C 68.79, H 11.55, S 13.12; found C 68.49, H 11.49, S 12.97%.

Compound 4a: Colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, J = 6.8 Hz, 3 H, CH_3), 1.22–1.40 (m, 8 H, –CH_2), 1.66–1.80 (m, 2 H, –CH_2), 2.07 (s, 6 H, 2×$COCH_3$), 6.77 [t, 1 H, CH(OAc)$_2$] ppm. IR (neat): $\tilde{\nu}$ = 2930, 2863, 1762, 1465, 1378, 1250, 1214, 1112, 1015, 968 cm^{-1}. $C_{11}H_{20}O_4$ (216.28): calcd. C 61.09, H 9.32; found C 60.89, H 9.27.

Compound 4c: Solid, m.p. 84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 6 H, 2×$COCH_3$), 7.39 (d, J = 8.4 Hz, 2 H, ArH), 7.53 (d, J = 8.8 Hz, 2 H, ArH), 7.61 [s, 1 H, CH(OAc)$_2$] ppm. IR (KBr): $\tilde{\nu}$ = 3063, 2986, 2930, 1762, 1593, 1486, 1378, 1245, 1214, 1076, 1015, 968 cm^{-1}. $C_{11}H_{11}BrO_4$ (287.10): calcd. C 46.02, H 3.86; found C 46.21, H 3.80.

Compound 4h: Solid, m.p. 85–86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 6 H, 2×$COCH_3$), 7.57–7.61 (m, 1 H, ArH), 7.67–7.74 (m, 2 H, ArH) 8.05 (dd, J = 0.8, J = 7.6 Hz, 1 H, ArH), 8.20 [s, 1 H, CH(OAc)$_2$] ppm. IR (KBr): $\tilde{\nu}$ = 1771, 1587, 1525, 1454, 1377, 1351, 1244, 1208, 1105, 1075, 1025 cm^{-1}. $C_{11}H_{11}NO_6$ (253.21): calcd. C 52.18, H 4.38, N 5.53; found C 51.93, H 4.30, N 5.38.

Compound 4j: Solid, m.p. 63–64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (s, 6 H, 2×$COCH_3$), 3.88 (s, 3 H), 3.92 (s, 3 H), 6.88 (d, J = 8.0 Hz, 1 H, ArH), 7.05 (s, 1 H, ArH), 7.11 (d, J = 8.0 Hz, 1 H, ArH), 7.62 [s, 1 H, CH(OAc)$_2$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (2C), 55.9 (2C), 89.8, 109.6, 111.5, 119.5, 128.0, 149.1, 150.1, 168.7 (2C) ppm. IR (KBr): $\tilde{\nu}$ = 2965, 2847, 1751, 1602, 1525, 1464, 1387, 1346, 1254, 1208, 1152, 1064, 998 cm^{-1}. $C_{13}H_{16}O_6$ (268.26): calcd. C 58.21, H 6.01; found C 57.95, H 5.96.

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