Mild and Chemoselective Synthesis and Deprotection of Geminal Diacetates Catalyzed by Titanium(IV) Halides

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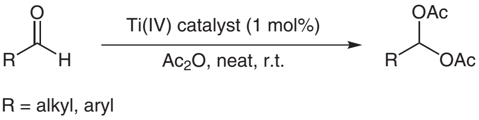
Abstract: A novel, mild, and chemoselective method was developed for the preparation of *gem*-diacetates from aldehydes and acetic anhydride in the presence of titanium(IV) fluoride (1–5 mol%) under solvent-free conditions at room temperature. The reaction showed a high chemoselectivity toward aldehydes in the presence of ketones. Moreover, titanium(IV) fluoride also catalyzed the deprotection of *gem*-diacetates to the corresponding aldehydes in water. This efficient and simple method has several benefits, including the use of an inexpensive catalyst, solvent-free conditions, mild reaction temperatures, and high yields, which make it both cost-effective and environmentally friendly.

Key words: aldehydes, protecting groups, chemoselectivity, deprotection, acylation

The chemoselective protection of an aldehyde group in the presence of a ketone group is a very important process in modern organic synthesis.[1] Although many carbonyl-protecting groups, including acetal and ketal groups, have been used, only a few chemoselective protection methods have been reported.[2] Therefore, the chemoselective protection of an aldehyde group in the presence of a ketone group remains a problem, and there is a need to develop an efficient method for chemoselective protection of aldehydes.

Because of its stability under basic and neutral conditions, the *gem*-diacetate (acylal) group is widely used as an alternative to acetal groups for the protection of carbonyl groups.[3] Furthermore, the *gem*-diacetate group is an important precursor for the preparation of 1-acetoxydienes,[4] vinyl acetates,[5] arylnitrile,[6] and dihydropyrimidinones.[7] This synthetically valuable protecting group is generally prepared from an aldehyde and acetic anhydride in the presence of a protic acid,[8] a Lewis acid,[9] or a heterogeneous inorganic catalyst.[10] However, some of these methods require expensive reagents (for example, triflate), hazardous solvents, strongly acidic conditions, high temperatures, or high catalyst loadings. Attempts have therefore been made to search for practical, milder, alternative protocols that use inexpensive and environmentally friendly reagents.

Titanium, the seventh-most abundant metal on Earth, is one of the cheapest transition metals. In contrast to highly toxic transition metals, such as mercury, lead, chromium, nickel, and manganese, many titanium compounds are nontoxic and environmentally friendly.[11] Titanium compounds are also mild and efficient Lewis acid catalysts, and they are therefore used extensively in organic transformations. Here, we report a chemoselective and mild method for the synthesis of *gem*-diacetates from aldehydes and acetic anhydride in the presence of a titanium(IV) catalyst under solvent-free conditions at room temperature (Scheme 1). Titanium(IV) compounds behave as efficient catalysts for both the protection of aldehydes and for the efficient deprotection of the resulting *gem*-diacetates.



Scheme 1 Titanium(IV)-catalyzed conversion of aldehydes into *gem*-diacetates

First, we tested the reaction of 3,4,5-trimethoxybenzaldehyde (**1a**) with acetic anhydride in the presence of various Ti(IV) catalysts (Table 1). Titanium tetraisopropoxide, dipotassium titanate (K_2TiO_3), dilithium titanate (Li_2TiO_3), calcium titanate ($CaTiO_3$), and titanium dioxide were insufficiently active to effect complete reaction under the standard conditions (1–10 mol% of titanium compound, room temperature, 24 hours). However, titanium halides such as titanium(IV) fluoride, titanium(IV) chloride, titanium(IV), or tri(isopropoxy)titanium chloride [ClTi(O-*i*-Pr)$_3$] gave the corresponding *gem*-diacetate **2a** within one hour at room temperature, even at 1 mol% of catalyst loading (Table 1, entries 8 and 11). The reaction of **1a** with titanium(IV) fluoride (1 mol%) was extremely rapid and the product was formed instantly on addition of all the reactants. The reactions with titanium halides worked well under solvent-free conditions, and the reaction mass solidified quickly. Because of the formation of solids during the reaction, we preferred to use an excess of liquid acetic anhydride (3 equiv). After completion of the reaction, the mixture was dissolved in dichloromethane and washed with 5% aqueous sodium bicarbonate. The aqueous layer was back-extracted with

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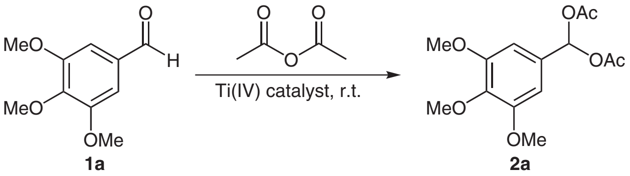
dichloromethane, and the combined organic layers were dried over anhydrous sodium sulfate, filtered, concentrated, and purified by column chromatography. In this procedure, dichloromethane can be replaced by ethyl acetate without decreasing the yield or purity of the product.

Table 1 Conversion of Aldehydes into *gem*-Diacetates with Various Titanium(IV) Catalysts



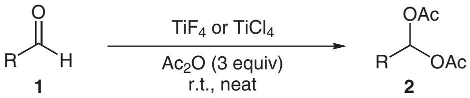
Entry[a]	Catalyst	Catalyst amount (mol%)	Time (h)	Yield (%)[b]
1	Ti(O-*i*-Pr)$_4$	10	24	0
2	K_2TiO_3	10	24	0
3	Li_2TiO_3	10	24	0
4	$CaTiO_3$	10	24	0
5	TiO_2	5	24	0
6	Ti[NMe$_2$]$_4$	5	24	0
7	ClTi(O-*i*-Pr)$_3$	5	24	97
8	TiF_4	1	0.01	99
9	TiF_4	5	0.17	96
10	TiF_4	10	0.17	85
11	$TiCl_4$	1	0.25	98
12	$TiCl_4$	5	0.33	99
13	$TiCl_4$	10	0.33	96
14	$TiBr_4$	1	1.5	97
15	$TiBr_4$	5	0.15	97
16	$TiBr_4$	10	0.15	95

[a] Conditions: aldehyde (2.00 mmol), Ti(IV) catalyst (1–10 mol%), Ac_2O (0.57 mL, 6.00 mmol), r.t.

[b] Isolated yield.

Next, we examined the reactions of various aldehydes in the presence of 1–5 mol% of titanium(IV) fluoride or 10 mol% of titanium(IV) chloride (Table 2). Generally, the former was more efficient as a catalyst than the latter, and a relatively high loading of titanium(IV) chloride (10 mol%) was required for the completion of some reactions. Some reactions proceeded to more than 80% completion within the initial several minutes and then the remaining substrate was consumed slowly over days (Table 2, entries 1, 4, 8, 9, and 13). The reactions are effective with both aliphatic and aromatic aldehydes, even when the aldehyde contains an electron-withdrawing substituent, such as a nitro group in the aromatic ring (entry 10). Aldehydes with various functional or protecting groups gave the corresponding *gem*-diacetates in good yields at room temperature. The reactions are compatible with acid-sensitive protecting groups, such as methylene acetal (entry 5) and *tert*-butyldimethylsilyl ether (entry 8) groups. The silyl protecting group is not affected by the fluoride of titanium(IV) fluoride, making this method practical for multistep syntheses. In case of benzaldehyde, the *gem*-diacetate **2h** was the sole product, and no side products could be observed by thin-layer chromatography or NMR spectroscopy of the crude mixture. However, the isolation of this volatile product by extraction and chromatography sometimes resulted in a decreased isolated yield (entry 7).

Table 2 Titanium(IV) Tetrahalide-Catalyzed Conversion of Aldehydes into *gem*-Diacetates



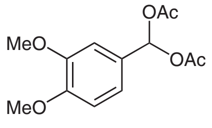
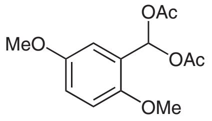
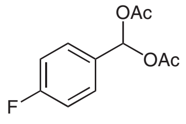
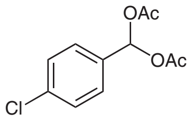
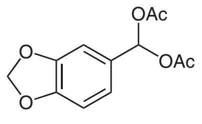
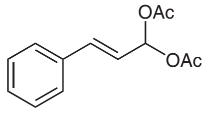
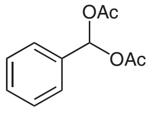
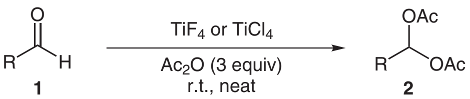
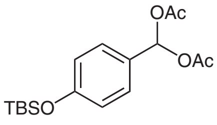
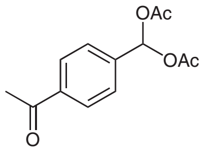
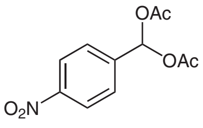
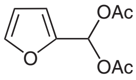
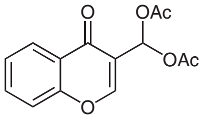
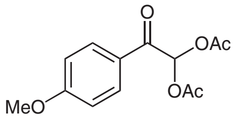
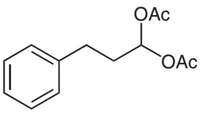
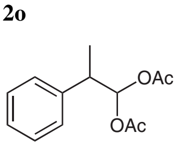
Entry[a]	Product	Catalyst (amount)	Time (h)	Yield (%)[b]
1	 **2b**	TiF_4 (1 mol%) $TiCl_4$ (10 mol%)	92 48	97 72
2	 **2c**	TiF_4 (1 mol%) $TiCl_4$ (10 mol%)	0.18 15	92 100
3	 **2d**	TiF_4 (1 mol%) $TiCl_4$ (10 mol%)	1 16	96 100
4	 **2e**	TiF_4 (1 mol%)	102	85
5	 **2f**	TiF_4 (1 mol%) $TiCl_4$ (10 mol%)	2 23	98 93
6	 **2g**	TiF_4 (1 mol%) $TiCl_4$ (1 mol%)	0.33 23	92 98
7	 **2h**	TiF_4 (1 mol%) $TiCl_4$ (1 mol%)	2 26	70 91

Table 2 Titanium(IV) Tetrahalide-Catalyzed Conversion of Aldehydes into *gem*-Diacetates (continued)

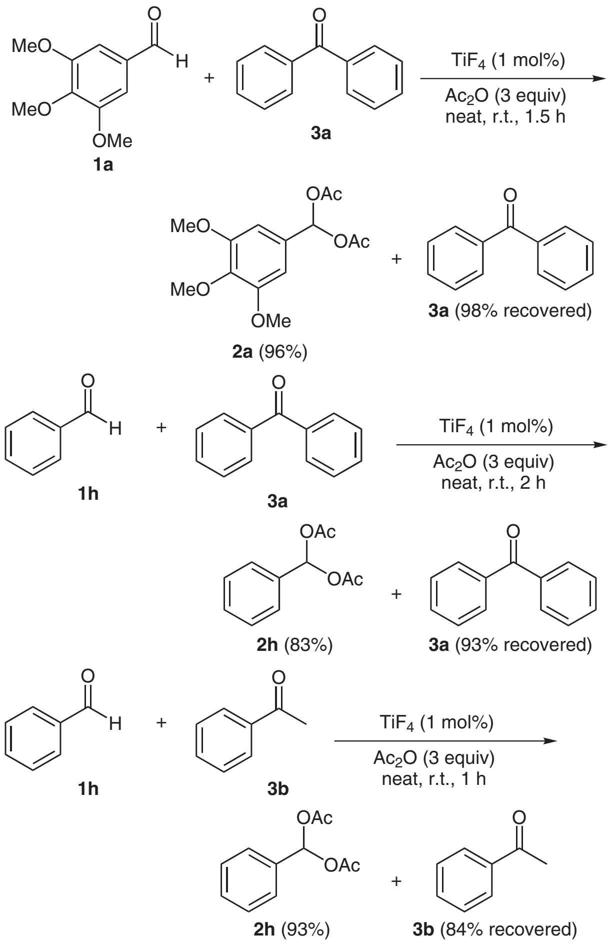


Entry[a]	Product	Catalyst (amount)	Time (h)	Yield (%)[b]
8	 **2i**	TiF_4 (1 mol%) $TiCl_4$ (10 mol%)	48 96	83 92
9	 **2j**	TiF_4 (1 mol%)	48	71
10	 **2k**	TiF_4 (1 mol%) $TiCl_4$ (10 mol%)	0.17 2.66	88 53
11	 **2l**	TiF_4 (1 mol%) $TiCl_4$ (10 mol%)	2 0.83	64 75
12	 **2m**	TiF_4 (5 mol%)	0.3	90
13	 **2n**	TiF_4 (5 mol%)	97	64
14	 **2o**	TiF_4 (5 mol%)	0.7	84
15	 **2p**	TiF_4 (5 mol%)	2.5	83

[a] Conditions: aldehyde (2.00 mmol), Ti(IV) catalyst (1–10 mol%), Ac_2O (0.57 mL, 6.00 mmol), neat, r.t.

[b] Isolated yield.

The clean formation of *gem*-diacetates from various aldehydes prompted us to test the selective protection of aldehyde groups in the presence of ketone groups. When substrates bearing both aldehyde and ketone groups were subjected to the standard catalytic reaction conditions, we found that the aldehyde groups were selectively protected without formation of the *gem*-diacetate from the ketone (entries 9, 12, and 13). The difference in reactivity between aldehyde and ketone groups for the formation of *gem*-diacetates was also confirmed by means of intermolecular competition reactions (Scheme 2). In the competition reactions, almost all the original benzophenone (**3a**) and acetophenone (**3b**) were recovered, and no *gem*-diacetates of these ketones were obtained.



Scheme 2 Competitive formation of *gem*-diacetates in the presence of titanium(IV) fluoride

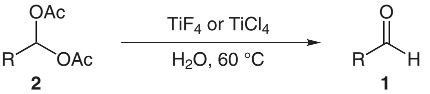
A number of reagents, including sulfuric acid,[12] hydrochloric acid,[13] montmorillonite clay,[14] boron triiodide *N*,*N*-diethylaniline complex,[15] graphite,[16] cerium(IV) ammonium nitrate on silica,[17] neutral alumina,[18] phenoxides,[19] boron trichloride,[20] carbon tetrabromide,[21] or cerium(III) chloride heptahydrate/sodium iodide,[22] can convert *gem*-diacetates into the corresponding aldehydes. However, some of these reactions require high temperatures, long reaction times, or harmful solvents or reagents. Only cerium(IV) ammonium nitrite,[23] zirconium(IV) chloride,[9k] zeolite Y,[24] zirconium sulfophenyl phosphonate,[25] a heteropolymolybdate ($H_3PMo_{12}O_{40}$),[26] silica/sulfuric acid,[27] or a heteropolytungstate ($H_3PW_{12}O_{40}$)[28] can be used in protecting aldehydes and deprotecting *gem*-diacetates. During our study on titanium(IV)-catalyzed formation of *gem*-diacetates, we found that titanium(IV) halides also regenerated the aldehydes from *gem*-diacetates in water. In comparison with conventional conditions for deprotection of *gem*-diacetates, the use of titanium(IV) halides is more environmentally friendly, as it does not require toxic reagents or organic solvents. Deprotection was most effective for *gem*-diacetates bearing electron-donating substituents (Table 3, entries 1–3). The electron-rich *gem*-diacetates gave the corresponding aldehydes almost quantitatively within several hours. Moreover, the protocol also worked with *gem*-diacetates containing an α,β-unsaturated group (entry 7) or an acid-sensitive group (entries 6 and 9). In contrast, deprotection was sluggish for *gem*-diacetates bearing a 4-nitrophenyl group (entry 11). In the case of low-molecular weight aldehydes, despite their clean conversion, as judged by thin-layer chromatography and NMR spectroscopy of the crude mixture, the aldehydes were obtained in low isolated yields, presumably because of their volatility (entries 4, 5, and 8).

The dimethyl acetal group is the most widely used protecting group for carbonyl groups in multistep organic synthesis. We were therefore interested in examining the direct conversion of dimethyl acetals into *gem*-diacetates (Table 4). The conversion of dimethyl acetals to *gem*-diacetates was performed under solvent-free conditions at room temperature. In the presence of 5 mol% of titanium(IV) fluoride, the reaction proceeded smoothly to give the corresponding *gem*-diacetates, together with small amounts of the corresponding aldehyde.

We also investigated the selective conversion into a *gem*-diacetate of a dimethyl acetal in a mixture with a dimethyl ketal (Scheme 3). The mixture of the dimethyl acetal **4h** and dimethyl ketal **5a** was treated with 10 mol% of titanium(IV) fluoride and excess acetic anhydride at room temperature under solvent-free conditions. After 49 hours, dimethyl acetal **4h** was converted into the corresponding *gem*-diacetate **2h** in 88% yield. In addition, the reaction gave the complete conversion of the dimethyl ketal **5a** into the ketone **3a**. Not surprisingly, ketone **3a** was not converted into the corresponding *gem*-diacetate, and remained nearly unaffected.

In conclusion, we have developed a mild method for the synthesis and deprotection of *gem*-diacetates using relatively nontoxic and cheap titanium(IV) catalysts. The synthesis of *gem*-diacetates from aldehydes is highly selective in the presence of 1–5 mol% titanium(IV) fluoride under solvent-free conditions. Deprotection involves the use of titanium(IV) fluoride in water. No organic solvent is necessary in either the protection or deprotection reaction. Few catalysts that mediate both the protection and deprotection reaction were previously known. The mild reaction temperature, high yields, inexpensive catalyst, low catalyst loadings, solvent-free conditions in the protection reaction, and the use of water instead of organic solvent in the deprotection reaction render this protocol both cost-effective and environmentally friendly.

Table 3 Titanium(IV) Halide-Catalyzed Deprotection of *gem*-Diacetates



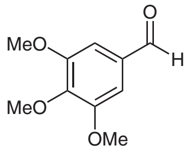
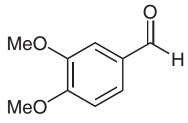
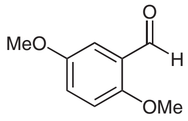
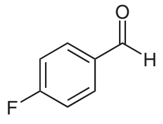
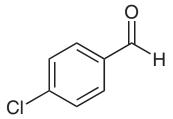
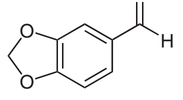
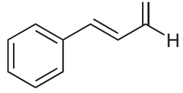
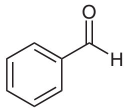
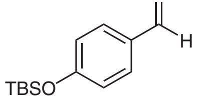
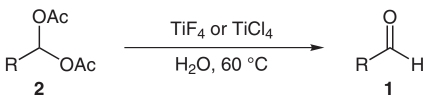
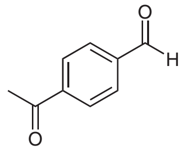
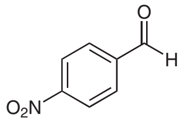
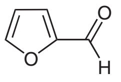
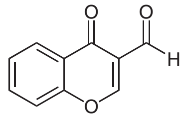
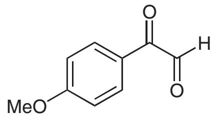
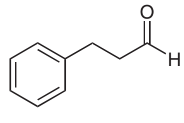
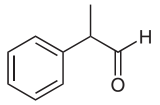
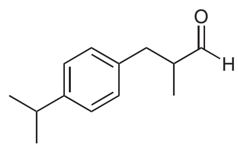
Entry[a]	Product	Catalyst (amount)	Time (h)	Yield (%)[b]
1	 **1a**	TiF_4 (10 mol%)	24	92
2	 **1b**	TiF_4 (10 mol%)	1.3	100
3	 **1c**	TiF_4 (10 mol%)	5	99
4	 **1d**	TiF_4 (10 mol%)	18	54
5	 **1e**	TiF_4 (10 mol%)	68	30
6	 **1f**	TiF_4 (10 mol%)	4	92
7	 **1g**	TiF_4 (10 mol%)	19	83
8	 **1h**	TiF_4 (10 mol%)	6	49
9	 **1i**	$TiCl_4$ (10 mol%)	17	66

Table 3 Titanium(IV) Halide-Catalyzed Deprotection of *gem*-Diacetates (continued)



Entry[a]	Product	Catalyst (amount)	Time (h)	Yield (%)[b]
10	 **1j**	TiF_4 (10 mol%)	66	85
11	 **1k**	TiF_4 (10 mol%)	24	10[c]
12	 **1l**	TiF_4 (10 mol%)	2	77
13	 **1m**	TiF_4 (10 mol%)	99	69
14	 **1n**	TiF_4 (10 mol%)	97	42
15	 **1o**	TiF_4 (20 mol%)	99	40
16	 **1p**	$TiCl_4$ (10 mol%)	97	32
17	 **1q**	TiF_4 (20 mol%)	69	40[d]

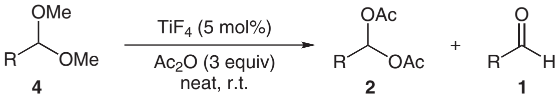
[a] Conditions: *gem*-diacetate (1.0 mmol), Ti(IV) catalyst (10–20 mol%), H_2O (2.0 mL), 60 °C.

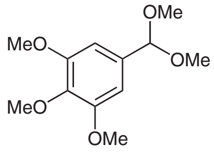
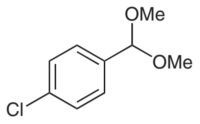
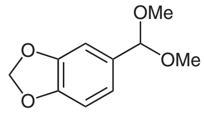
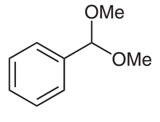
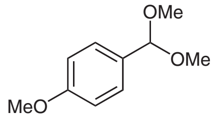
[b] Isolated yield.

[c] 83% of the starting material was recovered.

[d] 80 °C.

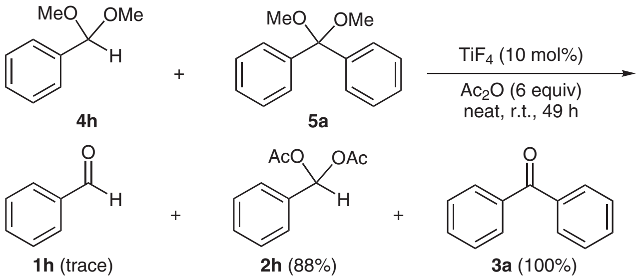
Table 4 Titanium(IV)-Catalyzed Conversion of Dimethyl Acetals into *gem*-Diacetates



Entry[a]	Substrate	Time (h)	Yield (%)[b]	
			2	**1**
1	 **4a**	9	85	2.6
2	 **4e**	24	82	7.7
3	 **4f**	57	70	3.1
4	 **4h**	18	92	7.5
5	 **4q**	65	77	16

[a] Conditions: *gem*-dimethyl acetal (2.0 mmol), TiF_4 (12.4 mg, 5 mol%), Ac_2O (0.57 mL, 6.00 mmol), r.t.

[b] Isolated yield.



Scheme 3 Titanium(IV) fluoride-catalyzed competitive conversion of a dimethyl acetal and a dimethyl ketal

The reagents were obtained from Aldrich Chemical (www.sigma-aldrich.com) or Alfa Aesar (www.alfa.com), and were used without further purification. TLC was performed on 0.25 mm E. Merck silica gel 60 F_{254} plates which were visualized under UV light (254 nm) or by staining with $KMnO_4$ or cerium ammonium molybdate. Flash chromatography was performed on E. Merck 230–400 mesh silica gel 60. NMR spectra were recorded on Varian Unity 400 instruments at 24 °C. Chemical shifts are expressed in ppm relative to

TMS (^{1}H, 0 ppm), $CDCl_3$ (^{13}C, 77.0 ppm), or DMSO-d_6 (^{1}H, 2.50 ppm; ^{13}C, 39.51 ppm); coupling constants are expressed in Hz. Mass spectra were recorded on a VG Trio-2 GC/MS instrument. High-resolution mass spectra were recorded on a JEOL JMS-AX 505WA instrument.

(3,4-Dimethoxyphenyl)methylene Diacetate (2b); Typical Procedure

Aldehyde **1b** (332 mg, 2.00 mmol) and TiF_4 (2.5 mg, 0.02 mmol) were added to a screw-capped vial under argon. Ac_2O (0.57 mL, 6.00 mmol) was added, and the mixture was stirred at r.t. As the reaction proceeded, the mixture gradually solidified. When the reaction was complete, the solid mixture was dissolved in CH_2Cl_2 (40 mL), and the soln was washed with 5% aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3×40 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography [silica gel, hexane–EtOAc (8:1)] to give a white solid; yield: 520 mg (97%). (Pentene–Et_2O was used for column chromatography of volatile products.)

TLC: R_f = 0.20 (hexane–EtOAc, 6:1); mp 74–76 °C (Lit.[30] 70–72 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (s, 1 H), 7.40 (d, *J* = 2.0 Hz, 1 H), 7.11 (dd, *J* = 8.0, 2.0 Hz, 1 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 3.92 (s, 3 H), 3.89 (s, 3 H), 2.12 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 150.4, 149.3, 128.2, 119.8, 111.0, 109.8, 90.1, 56.2 (2C), 21.1.

MS (FAB): *m/z* (%): 209 (46) [M – OAc]$^+$, 268 (61) [M]$^+$, 291 (10) [M + Na]$^+$.

(3,4,5-Trimethoxyphenyl)methylene Diacetate (2a)

TLC: R_f = 0.30 (hexane–EtOAc, 3:1); mp 115–117 °C (Lit.[29] 114–116 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (s, 1 H), 6.76 (s, 2 H), 3.89 (s, 6 H), 3.85 (s, 3 H), 2.14 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 153.6, 139.3, 131.1, 104.1, 90.0, 61.0, 59.4, 21.1.

MS (FAB): *m/z* (%): 239 (51) [M – OAc]$^+$, 298 (72) [M]$^+$, 321 (6) [M + Na]$^+$.

(2,5-Dimethoxyphenyl)methylene Diacetate (2c)

TLC: R_f = 0.30 (hexane–EtOAc, 3:1); mp 112–114 °C (Lit.[30] 107–108 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (s, 1 H), 7.05 (d, *J* = 2.8 Hz, 1 H), 6.90 (dd, *J* = 9.2, 3.2 Hz, 1 H), 6.85 (d, *J* = 9.2 Hz, 1 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 2.12 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 153.8, 151.5, 125.0, 115.6, 113.3, 112.6, 85.7, 56.6, 56.0, 21.1.

MS (FAB): *m/z* (%): 209 (40) [M – OAc]$^+$, 268 (75) [M]$^+$, 291 (20) [M + Na]$^+$.

HRMS: *m/z* calcd for $C_{13}H_{16}O_6$: 268.0947; found: 268.0943.

(4-Fluorophenyl)methylene Diacetate (2d)

TLC: R_f = 0.30 (hexane–EtOAc, 9:1); mp 49–51 °C (Lit.[31] 51–52 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (s, 1 H), 7.51 (m, 2 H), 7.09 (m, 2 H), 2.12 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 163.6 (d, J_{CF} = 246.9 Hz), 131.7, 129.0 (d, J_{CF} = 9.1 Hz), 115.8 (d, J_{CF} = 22.1 Hz), 89.4, 21.2.

MS (FAB): *m/z* (%): 167 (13) [M – OAc]$^+$, 226 (1.5) [M]$^+$, 249 (6) [M + Na]$^+$.

(4-Chlorophenyl)methylene Diacetate (2e)

TLC: R_f = 0.30 (hexane–EtOAc, 9:1); mp 82–84 °C (Lit.[32] 84–85 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (s, 1 H), 7.45 (m, 2 H), 7.38 (m, 2 H), 2.12 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 136.0, 134.2, 129.1, 128.4, 89.3, 21.0.

MS (FAB): *m/z* (%): 183 (67) [M – OAc]$^+$, 242 (4) [M]$^+$, 265 (20) [M + Na]$^+$.

1,3-Benzodioxol-5-ylmethylene Diacetate (2f)

TLC: R_f = 0.30 (hexane–EtOAc, 6:1); mp 78–80 °C (Lit.[33] 78–79 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (s, 1 H), 7.01 (m, 2 H), 6.81 (dd, *J* = 6.8, 2.4 Hz, 1 H), 5.99 (s, 2 H), 2.11 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 128.9, 148.1, 129.6, 121.2, 108.4, 107.2, 101.6, 89.9, 21.1.

MS (FAB): *m/z* (%): 193 (68) [M – OAc]$^+$, 252 (65) [M]$^+$, 275 (12) [M + Na]$^+$.

(1*E*)-1-Phenylprop-1-ene-3,3-diyl Diacetate (2g)

TLC: R_f = 0.30 (hexane–EtOAc, 8:1); mp 83–85 °C (Lit.[34] 83–85 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (m, 2 H), 7.32 (m, 3 H), 6.87 (d, *J* = 15.6 Hz, 1 H), 6.22 (dd, *J* = 16.0, 6.4 Hz, 1 H), 2.12 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 135.8, 135.4, 129.0, 128.9, 127.2, 121.9, 90.0, 21.1.

MS (FAB): *m/z* (%): 175 (68) [M – OAc]$^+$, 234 (12) [M]$^+$, 257 (13) [M + Na]$^+$.

Phenylmethylene Diacetate (2h)

TLC: R_f = 0.30 (hexane–EtOAc, 6:1); mp 44–46 °C (Lit.[30] 44–46 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (s, 1 H), 7.52 (m, 2 H), 7.41 (m, 3 H), 2.13 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 135.7, 130.0, 128.8, 126.9, 89.9, 21.1.

MS (FAB): *m/z* (%): 149 (100) [M – OAc]$^+$, 209 (3) [M + H]$^+$, 231 (10) [M + Na]$^+$.

(4-{[*tert*-Butyl(dimethyl)silyl]oxy}phenyl)methylene Diacetate (2i)

TLC: R_f = 0.30 (hexane–EtOAc, 8:1); mp 55–57 °C (Lit.[29] 57–59 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (s, 1 H), 7.38 (m, 2 H), 6.85 (dd, *J* = 6.4, 2.0 Hz, 2 H), 2.11 (s, 6 H), 0.98 (s, 9 H), 0.02 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 157.1, 128.5, 128.3, 120.3, 89.9, 25.8, 21.1, 18.4, –4.2.

MS (FAB): *m/z* (%): 279 (21) [M – OAc]$^+$, 338 (13) [M]$^+$, 361 (3) [M + Na]$^+$.

(4-Acetylphenyl)methylene Diacetate (2j)

TLC: R_f = 0.30 (hexane–EtOAc, 4:1); mp 62–64 °C (Lit.[35] 56–59 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (m, 2 H), 7.71 (s, 1 H), 7.62 (dd, *J* = 6.8, 1.6 Hz, 2 H), 2.62 (s, 3 H), 2.15 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 168.9, 140.3, 138.3, 128.8, 126.9, 89.2, 26.9, 21.0.

MS (FAB): *m/z* (%): 191 (63) [M – OAc]$^+$, 251 (32) [M + H]$^+$, 273 (9) [M + Na]$^+$.

(4-Nitrophenyl)methylene Diacetate (2k)

TLC: R_f = 0.30 (hexane–EtOAc, 5:1); mp 126–128 °C (Lit.[30] 124–126 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (m, 2 H), 7.71–7.69 (m, 3 H), 2.16 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 148.9, 142.1, 128.1, 124.1, 88.6, 21.0.

MS (FAB): *m/z* (%): 276 (6) $[M + Na]^+$.

2-Furylmethylene Diacetate (2l)

TLC: R_f = 0.30 (hexane–EtOAc, 4:1); mp 52–54 °C (Lit.[31] 52–54 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (s, 1 H), 7.46 (dd, *J* = 2.0, 1.2 Hz, 1 H), 6.54 (m, 1 H), 6.40 (dd, *J* = 3.2, 2.0 Hz, 1 H), 2.14 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 148.1, 143.9, 110.6, 109.9, 83.7, 20.9.

MS (FAB): *m/z* (%): 139 (100) $[M – OAc]^+$, 198 (18) $[M]^+$, 221 (12) $[M + Na]^+$.

3-[Bis(acetyloxy)methyl]-4*H*-1-benzopyran-4-one (2m)

TLC: R_f = 0.12 (hexane–EtOAc, 3:1); mp 131–133 °C (Lit.[36] 131–132 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (dd, *J* = 8.0, 2.0 Hz, 1 H), 8.10 (d, *J* = 0.8 Hz, 1 H), 7.80 (d, *J* = 0.8 Hz, 1 H), 7.70 (m, 1 H), 7.48 (m, 1 H), 7.44 (m, 1 H), 2.15 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.0, 168.4, 156.2, 154.9, 134.2, 126.0, 125.7, 124.3, 119.7, 118.2, 85.2, 20.8.

MS (FAB): *m/z* (%): 217 (17) $[M – OAc]^+$, 277 (12) $[M + H]^+$, 299 (17) $[M + Na]^+$.

2-(4-Methoxyphenyl)-2-oxoethane-1,1-diyl diacetate (2n)

Colorless oil; TLC: R_f = 0.26 (hexane–EtOAc, 3:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.8 Hz, 2 H), 7.61 (s, 1 H), 6.96 (d, *J* = 8.8 Hz, 2 H), 3.89 (s, 3 H), 2.18 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.3, 169.0, 164.7, 131.6, 126.3, 114.4, 86.3, 55.8, 20.9.

MS (FAB): *m/z* (%): 207 (13) $[M – OAc]^+$, 267 (22) $[M + H]^+$, 289 (11) $[M + Na]^+$.

3-Phenylpropane-1,1-diyl Diacetate (2o)

Colorless oil; TLC: R_f = 0.40 (hexane–EtOAc, 5:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (m, 2 H), 7.20 (m, 3 H), 6.84 (t, *J* = 5.6 Hz, 1 H), 2.72 (m, 2 H), 2.11 (m, 2 H), 2.06 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2, 140.7, 128.7, 128.5, 126.4, 90.3, 34.9, 29.9, 21.0.

MS (FAB): *m/z* (%): 237 (10) $[M + H]^+$, 259 (11) $[M + Na]^+$.

2-Phenylpropane-1,1-diyl Diacetate (2p).

Colorless oil; TLC: R_f = 0.27 (hexane–EtOAc, 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (m, 5 H), 6.90 (d, *J* = 6.0 Hz, 1 H), 3.18 (m, 1 H), 2.06 (s, 3 H), 1.97 (s, 3 H), 1.36 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2, 169.0, 140.2, 128.6, 128.5, 127.3, 92.2, 43.1, 21.0, 20.9, 15.3.

MS (FAB): *m/z* (%): 177 (57) $[M – OAc]^+$, 237 (8) $[M + H]^+$, 259 (7) $[M + Na]^+$.

3,4,5-Trimethoxybenzaldehyde (1a); Typical Procedure for Deprotection of *gem*-Diacetates

Diacetate **2a** (298 mg, 1 mmol) and TiF_4 (12.4 mg, 0.10 mmol) were added to a screw-capped vial. H_2O (2.00 mL) was added and the mixture was stirred at 60 °C. When the reaction was complete, the resulting mixture was dissolved in CH_2Cl_2 (40 mL), and the soln was washed with 5% aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography [silica gel, pentane–Et_2O (2:1)] to give a white solid; yield: 181 mg (92%). All the products listed in Table 3 are known and commercially available. Spectral data were identical to those previously reported.

(3,4,5-Trimethoxyphenyl)methylene Diacetate (2a); Typical Procedure for Ti(IV)-Catalyzed Synthesis of *gem*-Diacetates from Dimethyl Acetals

Dimethyl acetal **4a** (484 mg, 2.00 mmol) and TiF_4 (12.3 mg, 0.10 mmol) were added to a screw-capped vial under argon. Ac_2O (0.57 mL, 6.00 mmol) was added, and the mixture was stirred at r.t. until the reaction was complete. The resulting solid mixture was dissolved in CH_2Cl_2 (40 mL), and the soln was washed with 5% aq $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography [silica gel, hexane–EtOAc (3:1)] to give (3,4,5-trimethoxyphenyl)methylene diacetate (**2a**) as a white solid; yield: 505.6 mg (85%). 3,4,5-Trimethoxybenzaldehyde (**1a**) was also obtained as a white solid byproduct; yield: 12.6 mg (2.6%).

(Pentene–Et_2O was used for the column chromatography of volatile products. Spectral data for the products were identical to those for **2a**, **2e**, **2f, 2h**, and **2j** as reported above.)

(4-Methoxyphenyl)methylene diacetate (2q)

TLC: R_f = 0.27 (hexane–EtOAc, 5:1); mp 60–62 °C (Lit.[37] 60–62 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (s, 1 H), 7.46 (d, *J* = 8.8 Hz, 1 H), 6.92 (d, *J* = 8.8 Hz, 1 H), 3.82 (s, 3 H), 2.11 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 160.8, 128.4, 128.0, 114.2, 90.0, 55.6, 21.1.

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