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1,3-Dichloro-tetra-*n*-butyl-distannoxane: a new application for catalyzing the direct substitution of 9*H*-xanthen-9-ol at room temperature

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1,3-Dichloro-tetra-*n*-butyl-distannoxane was firstly used to catalyze the direct substitution of 9*H*-xanthen-9-ol with indoles at room temperature to afford a class of 3-(9*H*-xanthen-9-yl)-1*H*-indole derivatives in good to excellent isolating yield. Moreover, other nucleophiles (such as diketone and pyrrole) could also proceed smoothly in this methodology. Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: 1,3-dichloro-tetra-*n*-butyl-distannoxane; xanthen-9-ol; nucleophiles; indoles

Introduction

1,3-Dihalo-tetra-alkyl-distannoxanes, having a unique ladder structure, are stable, easy-to-handle weak Lewis acids and have been employed as catalysts for various functional group transformations such as esterification, acetalization, and deacetalization. ($[ClBu_2SnOSnBu_2Cl]_2$ is commercially available from Aldrich Chem Co. Inc.) They are soluble in most organic solvents even though they have a large inorganic metaloxane core.[1] Distannoxane-catalyzed reactions usually proceed under almost neutral conditions and various functional groups can survive, especially for the strong Lewis acid catalyzed reaction of reactants with acid-sensitive functional groups. These merits have found a wide range of synthetic applications.[2–4] Generally, 1,3-dichloro-tetra-*n*-butyl-distannoxane exists as a dimer (Fig. 1). Owing to its high lipophilicity,[5] structural rigidity and multi-active catalytic centers (Sn **a**, Sn **b**, Fig. 1), 1,3-dichloro-tetra-*n*-butyl-distannoxane offers several advantages over alkali or other transesterification catalysts. [6,7] However, the study of this catalyst in direct substitution has never been explored before and thus provides a great opportunity for us to explore further.

In fact, the esterification between acid and alcohol is a dehydration reaction. For the nucleophilic substitution of alcohols, it is also a dehydrative process. A number of methods for the promotion of direct catalytic nucleophilic substitution of alcohols in organic solvents have been reported.[8–19] In previous articles, the reactions of xanthen-9-ol with nucleophilic reagents such as thiol, imide, indoles, and thiophene are promoted by acids or $BF_3.Et_2O$.[20–24] However, many of these procedures involve strong acidic conditions, low yields of products, and complex handling. For this reason, superior catalyst systems, which are cheap, easy to access, and stable in air, are desirable. Shun-jun Ji has recently found that indium tris(dodecyl sulfonate) [$In(DS)_3$], a strong Lewis acidic surfactant, can efficiently catalyze the reaction of 9H-xanthen-9-ol with various indoles in water.[25] Pier Giorgio Cozzi reported that the direct substitution of alcohol 'on water' without added Brønsted or Lewis acid is possible[26,27] (for the reaction of a ferrocenyl alcohol promoted by an indium salt, see Vicennati and Cozzi[28]) but this 'on water' reaction must be performed at 80 °C. As a continuation of our work on organotin compound,[29–32] we report herein that 1,3-dichloro-tetra-*n*-butyl-distannoxane, a new application, can efficiently catalyze the reactions of xanthen-9-ol **1** with indoles **2** at room temperature to give 3-(9*H*-xanthen-9-yl)-1*H*-indole derivatives **3** in good to excellent yield (Scheme 1).

Experimental

General

Xanthen-9-ol **1** was purchased from Acros (99%). Indoles were purchased from Shanghai Accela ChemBio Inc. (97%). 1,3-Dichloro-tetra-*n*-butyl-distannoxane ($[ClBu_2SnOSnBu_2Cl]_2$) was synthesized according to previously published protocols.[33] All other common solvents were purified using standard procedures. ^1H NMR and ^{13}C NMR were recorded on a Bruker 400 MHz or Varian Mercury 400 MHz spectrometer using $CDCl_3$ as solvent and tetramethylsilane (TMS) as the internal standard. Melting points were recorded on an electrothermal digital melting-point apparatus and were uncorrected. Elemental analyses were determined on a Yanaco CHN Corder MT-3 elemental analyzer.

Procedure for the Reaction of Xanthen-9-ol with Various Nucleophiles Catalyzed by 1,3-Dichloro-tetra-*n*-butyl-distannoxane

A mixture of xanthen-9-ol **1** (0.040 g, 0.2 mmol), **2a** (0.024 g, 0.2 mmol), 1,3-dichloro-tetra-*n*-butyl-distannoxane (2.3 mg, 0.002 mmol), and dichloromethane (0.5 mL) was stirred in a tube at room temperature until the disappearance of the starting **2a** (6.0 h, checked by thin-layer chromatography, TLC). After standing for

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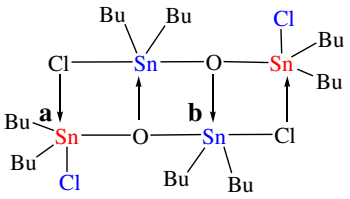
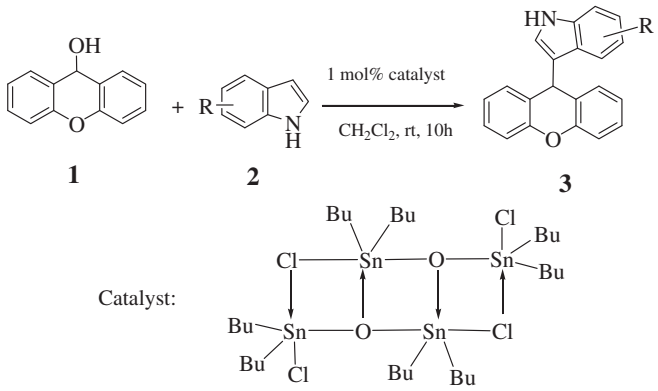


Figure 1. The structure of 1,3-dichloro-tetra-*n*-butyl-distannoxane.



Scheme 1. The reaction of xanthen-9-ol with indoles catalyzed by 1,3-dichloro-tetra-*n*-butyl-distannoxane.

10 h, the reaction mixture was directly purified by flash chromatography to afford the pure product **3a** (0.058 g, yield 98%). 3-(9*H*-Xanthen-9-yl)-1*H*-indole **3a**: m.p. 142–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 5.59 (s, 1H, CH), 6.94–7.40 (m, 13H), 8.04 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.4 (C–O_{arom}), 136.8 (C–N_{arom}), 129.5 (C_{arom}), 127.8 (C_{arom}), 125.9 (C_{arom}), 124.5 (C_{arom}), 123.2 (C_{arom}), 122.9 (C_{arom}), 122.2 (C_{arom}), 120.4 (C_{arom}), 119.7 (C_{arom}), 116.4 (C_{arom}), 111.3 (C_{arom}), 35.6 (CH); anal. calcd for $C_{21}H_{15}NO$: C 84.82, H 5.08, N 4.71; found C 84.54, H 4.65, N 4.56.

All other 3-(9*H*-Xanthen-9-yl)-1*H* substituted indole derivatives were prepared by the same method. And the corresponding products were characterized by ^{1}H NMR, ^{13}C NMR, and elemental analysis.

2-Methyl-3-(9H-xanthen-9-yl)-1H-indole **3b**: m.p. 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 2.30 (s, 3H, CH_3), 5.58 (s, 1H, CH), 6.82–7.23 (m, 12H), 7.72 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.3 (C–O_{arom}), 135.4 (C–N_{arom}), 132.3 (C_{arom}), 129.4 (C_{arom}), 127.7 (C_{arom}), 124.2 (C_{arom}), 123.1 (C_{arom}), 121.2 (C_{arom}), 119.5 (C_{arom}), 118.9 (C_{arom}), 116.2 (C_{arom}), 115.3 (C_{arom}), 110.3 (C_{arom}), 33.8 (CH), 12.0 (CH_3); anal. calcd for $C_{22}H_{17}NO$: C 84.86, H 5.50, N 4.50; found C 84.58, H 5.28, N 4.51.

4-Acetoxy-3-(9*H*-xanthen-9-yl)-1*H*-indole **3c**: m.p. 154–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 2.20 (s, 3H, CH_3), 5.68 (s, 1H, CH), 6.86–7.38 (m, 12H), 8.35 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 169.4 (CH_3–C=O), 151.1 (C–O_{arom}), 143.8 (C–N_{arom}), 135.5 (CH_3–C=O–O–C_{arom}), 128.9 (C_{arom}), 128.7 (C_{arom}), 127.6 (C_{arom}), 125.7 (C_{arom}), 124.1 (C_{arom}), 123.3 (C_{arom}), 122.5 (C_{arom}), 122.2 (C_{arom}), 116.1 (C_{arom}), 113.2 (C_{arom}), 109.1 (C_{arom}), 36 (CH), 20.7 (CH_3); anal. calcd for $C_{23}H_{17}NO_3$: C 77.73, H 4.82, N 3.94; found C 77.68, H 4.33, N 3.78.

4-Chloro-3-(9*H*-xanthen-9-yl)-1*H*-indole **3d**: m.p. 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 5.36 (s, 1H, CH), 6.82–7.13 (m, 12H), 8.18 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.8 (C–O_{arom}), 130.2 (C–N_{arom}), 127.8 (C_{arom}), 127.1 (C_{arom}), 126.3 (C_{arom}), 126.0 (C_{arom}), 125.6 (C_{arom}), 124.7 (C_{arom}), 123.1 (C_{arom}), 122.7 (C_{arom}), 122.4 (C_{arom}), 121.5 (C_{arom}), 119.7 (C_{arom}), 116.5 (C_{arom}), 110.1 (C_{arom}), 109.8 (C_{arom}), 101.3 (C_{arom}), 34.2 (CH); anal. calcd for $C_{21}H_{14}ClNO$: C 76.02, H 4.25, N 4.22; found C 76.31, H 3.95, N 3.87.

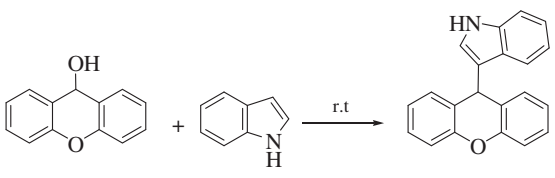
4-Methyl-3-(9*H*-xanthen-9-yl)-1*H*-indole **3e**: m.p. 183–191 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 2.00 (br, s, 3H, CH_3), 5.71 (s, 1H, CH), 6.73–7.22 (m, 12H), 8.04 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 150.9 (C–O_{arom}), 131.1 (C–N_{arom}), 129.2 (C_{arom}), 127.7 (C_{arom}), 126.1 (C_{arom}), 125.7 (C_{arom}), 125.0 (C_{arom}), 123.1 (C_{arom}), 122.4 (C_{arom}), 121.7 (C_{arom}), 116.2 (C_{arom}), 109.2 (C_{arom}), 36.2 (CH), 21.3 (CH_3); anal. calcd for $C_{22}H_{17}NO$: C 84.86, H 5.50, N 4.50; found C 84.62, H 5.37, N 4.42.

5-Chloro-3-(9*H*-xanthen-9-yl)-1*H*-indole **3f**: m.p. 142–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 5.37 (s, 1H, CH), 6.79–7.21 (m, 12H), 7.87 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.4 (C–O_{arom}), 135.1 (C–N_{arom}), 129.3 (C_{arom}), 127.9 (C_{arom}), 126.9 (C_{arom}), 125.4 (C_{arom}), 124.3 (C_{arom}), 124.13 (C_{arom}), 123.24 (C_{arom}), 122.58 (C_{arom}), 120.19 (C_{arom}), 119.03 (C_{arom}), 116.5 (C_{arom}), 112.3 (C_{arom}), 35.4 (CH); anal. calcd for $C_{21}H_{14}ClNO$: C 76.02, H 4.25, N 4.22; found C 75.97, H 3.76, N 3.94.

5-Bromo-3-(9*H*-xanthen-9-yl)-1*H*-indole **3g**: m.p. 184–186 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 5.49 (s, 1H, CH), 6.92–7.49 (m, 12H), 8.02 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.3 (C–O_{arom}), 135.3 (C–N_{arom}), 129.2 (C_{arom}), 127.9 (C_{arom}), 127.6 (C_{arom}), 125.2 (C_{arom}), 124.1 (C_{arom}), 123.2 (C_{arom}), 122.1 (C_{arom}), 120.2 (C_{arom}), 116.5 (C_{arom}), 113.0 (C_{arom}), 112.7 (C_{arom}), 35.4 (CH); anal. calcd for $C_{21}H_{14}BrNO$: C 67.04, H 3.75, N 3.72; found C 66.89, H 3.49, N 3.62.

5-Methoxy-3-(9*H*-xanthen-9-yl)-1*H*-indole **3h**: m.p. 176–178 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 3.67 (s, 3H, CH_3O), 5.50 (s, 1H, CH), 6.78–7.24 (m, 12H), 7.89 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 153.9 (CH_3–O–C_{arom}), 151.4 (C–O_{arom}), 131.9 (C–N_{arom}), 129.5 (C_{arom}), 127.7 (C_{arom}), 126.4 (C_{arom}), 124.4 (C_{arom}), 123.3 (C_{arom}), 123.1 (C_{arom}), 120.4 (C_{arom}), 116.3 (C_{arom}), 112.2 (C_{arom}), 111.9 (C_{arom}), 101.6 (C_{arom}), 55.7 (CH_3O), 35.6 (CH); anal. calcd for $C_{22}H_{17}NO_2$: C 80.71, H 5.23, N 4.28; found C 80.43, H 4.98, N 4.12.

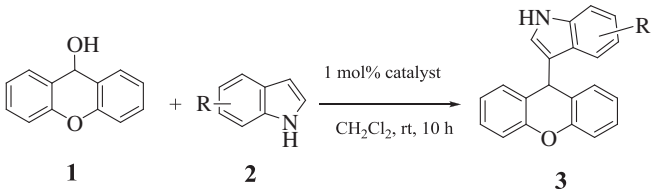
Table 1. Parameters screening of the reaction of xanthen-9-ol **1** with indole **2a**[a]

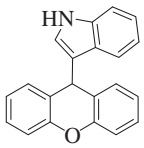
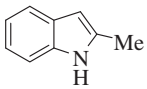
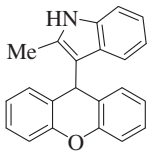
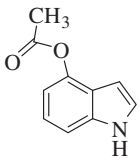
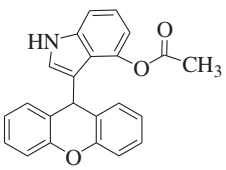
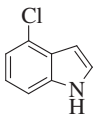
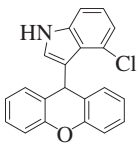
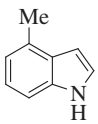
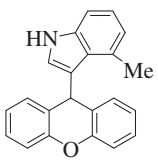
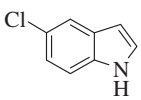
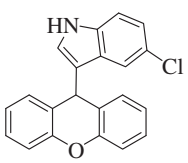
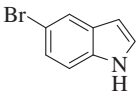
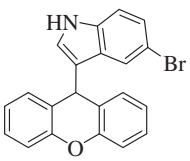


Entry	Solvent	Catalyst (1 mol%)	*t* (h)	Yield (%)[b]
1	H_2O	—	96	—
2	THF	—	72	32
3	CH_2Cl_2	—	48	40
4	CH_2Cl_2	Bu_2SnO	10	71
5	CH_2Cl_2	Bu_2SnCl_2	10	85
6	CH_2Cl_2	$[ClBu_2SnOSnBu_2Cl]_2$	10	98
7	H_2O	$[ClBu_2SnOSnBu_2Cl]_2$	48	22

[a]All reactions were carried out at room temperature.
[b]Isolated yields.

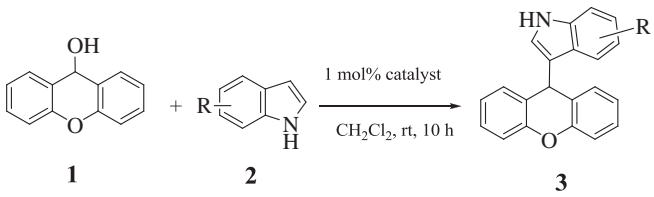
Table 2. Reactions of xanthen-9-ol **1** with indoles **2a–l** catalyzed by 1,3-dichloro- tetra-*n*-butyl-distannoxane[a]

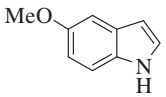
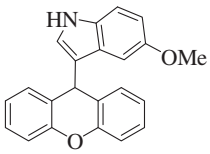
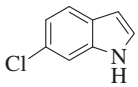
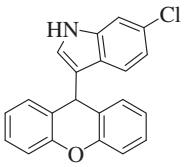
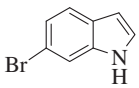
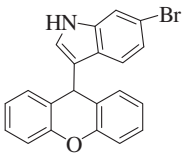
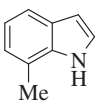
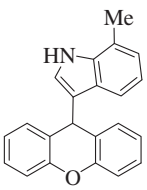
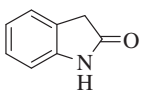


Entry	Indole	Product	Yield (%)[b]
1	 **2a**	 **3a**	98
2	 **2b**	 **3b**	>99
3	 **2c**	 **3c**	97
4	 **2d**	 **3d**	85
5	 **2e**	 **3e**	94
6	 **2f**	 **3f**	92
7	 **2g**	 **3g**	88

(Continues)

Table 2. *(Continued)*



Entry	Indole	Product	Yield (%)[b]
8	 **2h**	 **3h**	85
9	 **2i**	 **3i**	92
10	 **2j**	 **3j**	97
11	 **2k**	 **3k**	83
12[c]	 **2l**	—	—

[a]All reactions were carried out using a catalytic amount of 1,3-dichloro-tetra-*n*-butyl-distannoxane (1 mol%) at room temperature.
[b]Isolated yields.
[c]A small amount of oxidative byproduct (9*H*-xanthen-9-one) (yield 13%) and a large amount of reductive byproduct (9*H*-xanthene) (yield 42%) of xanthen-9-ol **1** were obtained.

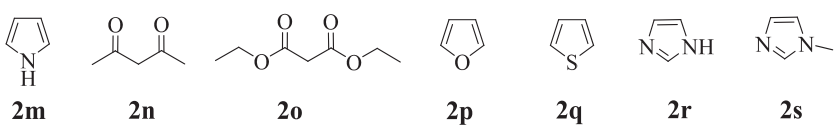
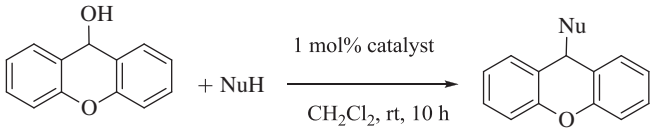
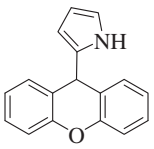
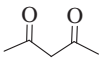
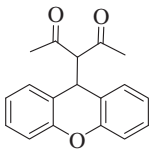
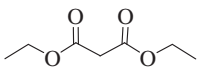
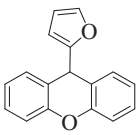
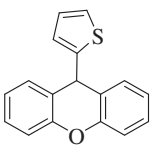
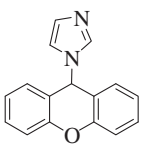


Figure 2. Nucleophiles **2 m–s** employed in the direct nucleophilic substitution of xanthen-9-ol.

Table 3. The S_N1-type reaction of xanthen-9-ol with other nucleophiles[c] catalyzed by 1,3-dichloro-tetra-*n*-butyl distannoxane[a]



Entry	Nucleophiles	Product	Yield (%)[b]
1	 **2m**	 **3m**	96
2	 **2n**	 **3n**	88
3[d]	 **2o**	—	—
4	 **2p**	 **3p**	<5
5	 **2q**	 **3q**	<5
6	 **2r**	 **3r**	<5
7[e]	 **2s**	—	—

[a]All reactions were carried out using a catalytic amount of 1,3-dichloro-tetra-*n*-butyl-distannoxane (1 mol%) at room temperature.
[b]Isolated yields.
[c]The amounts of all these nucleophiles were 2 equiv.
[d]The oxidative byproduct 9*H*-xanthen-9-one was obtained with 51% yield.
[e]48 h.

6-Chloro-3-(9*H*-xanthen-9-yl)-1*H*-indole **3i**: m.p. 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 5.48 (s, 1H, CH), 6.88–7.27 (m, 12H), 7.90 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.3 (C–O_{arom}), 137.2 (C–N_{arom}), 129.4 (C_{arom}), 128.2 (C_{arom}), 127.9 (C_{arom}), 124.4 (C_{arom}), 124.1 (C_{arom}), 123.3 (C_{arom}), 123.2 (C_{arom}), 120.6 (C_{arom}), 120.5 (C_{arom}), 116.5 (C_{arom}), 111.2 (C_{arom}), 35.5 (CH); anal. calcd for $C_{21}H_{14}ClNO$: C 76.02, H 4.25, N 4.22; found C 75.79, H 3.97, N 4.10.

6-Bromo-3-(9*H*-xanthen-9-yl)-1*H*-indole **3j**: m.p. 155–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 5.47 (s, 1H, CH), 6.87–7.41 (m, 12H), 7.89 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.3 (C–O_{arom}), 137.7 (C–N_{arom}), 129.4 (C_{arom}), 128.0 (C_{arom}), 124.7 (C_{arom}), 124.1 (C_{arom}), 123.2 (C_{arom}), 123.1 (C_{arom}), 121.0 (C_{arom}), 120.6 (C_{arom}), 116.5 (C_{arom}), 115.9 (C_{arom}), 114.2 (C_{arom}), 100.0 (C_{arom}), 35.5 (CH); anal. calcd for $C_{21}H_{14}BrNO$: C 67.04, H 3.75, N 3.72; found C 66.85, H 3.40, N 3.51.

7-Methyl-3-(9*H*-xanthen-9-yl)-1*H*-indole **3k**: m.p. 185–187 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 2.41 (s, 3H, CH_3), 5.52 (s, 1H, CH), 6.86–7.22 (m, 12H), 7.85 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 151.4 (C–O_{arom}), 136.3 (C–N_{arom}), 129.5 (C_{arom}), 127.7 (C_{arom}), 125.5 (C_{arom}), 124.5 (C_{arom}), 123.1 (C_{arom}), 122.7 (C_{arom}), 122.6 (C_{arom}), 121.0 (C_{arom}), 120.4 (C_{arom}), 119.9 (C_{arom}), 117.5 (C_{arom}), 116.3 (C_{arom}), 35.7 (CH), 16.6 (CH_3); anal. calcd for $C_{22}H_{17}NO$: C 84.86, H 5.50, N 4.50; found C 84.61, H 5.29, N 4.39.

2-(9*H*-Xanthen-9-yl)-1H-pyrrole **3m**: m.p. 109–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 5.23 (s, 1H, CH), 5.99–6.05 (m, 2H), 6.46–6.48 (m, 1H), 6.84–7.14 (m, 8H), 7.52 (br, s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 150.3 (C–O_{arom}), 150.2 (C–O_{arom}), 133.1 (C–N pyrrole), 128.4 (C_{arom}), 127.9 (C_{arom}), 127.1 (C_{arom}), 127.0 (C_{arom}), 122.3 (C_{arom}), 122.1 (C_{arom}), 122.0 (C_{arom}), 121.8 (C_{arom}), 117.1 (CH–N pyrrole), 115.6 (C_{arom}), 115.4 (C_{arom}), 106.9 (C pyrrole), 106.3 (C pyrrole), 36.2 (CH); anal. calcd for $C_{17}H_{13}NO$: C 82.57, H 5.30, N 5.66; found C 82.15, H 4.80, N 5.06.

3-(9*H*-Xanthen-9-yl)pentane-2,4-dione **3n**: m.p. 139–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 1.87 (s, 6H), 4.08–4.11 (d, 1H, CH, J = 12 Hz), 4.83–4.86 (d, 1H, CH, J = 12 Hz), 7.02–7.27 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 201.7 (CH_3–C=O), 153.3 (C–O_{arom}), 129.1 (C_{arom}), 128.40 (C_{arom}), 123.7 (C_{arom}), 123.4 (C_{arom}), 116.8 (C_{arom}), 73.8 (O=C–C–C=O), 40.2 (CH), 31.8 (CH_3); anal. calcd for $C_{18}H_{16}O_3$: C 77.12, H 5.75; found C 76.90, H 5.69.

Results and Discussion

In our initial study, we investigated the direct nucleophilic substitution of xanthen-9-ol **1** with indole **2a** by using the various reaction conditions (Table 1). As shown in Table 1, in the absence of catalyst, the reaction could not proceed in water at room temperature even prolonging reaction time to 96 h, but it could take place in organic solvent (THF or CH_2Cl_2) with low yield (entries 1–3, Table 1). When using organotin compound, because of the poor solubility of Bu_2SnO in CH_2Cl_2, the reaction could only afford the corresponding substituted product in more than the moderate level yield (entry 4). And changing the Bu_2SnO to the Bu_2SnCl_2, slightly better but not best result was obtained (entry 5). In order to improve the reaction yield further, we applied the high lipophilic 1,3-dichloro-tetra-*n*-butyl-distannoxane to catalyze this reaction. As a result, excellent reaction yield was obtained (entry 6). Nevertheless, this reaction was sluggish in aqueous media in the presence of 1 mol% 1,3-dichloro-tetra-*n*-butyl- distannoxane (entry 7). This may be due to its heterogeneous reaction.

To evaluate the generality of this reaction, using an optimized protocol, we performed the direct substitution of xanthen-9-ol **1** with various indoles **2a-l** (Table 2) in CH_2Cl_2 at room temperature promoted by 1 mol% 1,3-dichloro-tetra-*n*-butyl-distannoxane. As can be seen from the summarized results, except for indolin-2-one, all other substituted indoles could smoothly proceed to give the corresponding 3-(9-*H*-xanthen-9-yl)-1*H*-indole derivatives with high or excellent yield. Not only 4-substituted or 5-substituted indoles but also 6- or 7-substituted indoles showed high reactivity in our methodology (entries 3–11). Moreover, whether these substituents are electronic-withdrawing groups or electronic-donating groups, high yields of substituted products could be obtained. Upon closer inspection of the data in Table 2, we noticed that 4-chloroindole (Table 2, entry 4) gave a slightly lower yield than those of 5- and 6-chloroindoles (Table 2, entries 6 and 9). This may be ascribed to the indole 4-position steric hindrance and electronic-withdrawing effect for the electrophilic substitution in the place of the indole 3-position. Surprisingly, for the 4-acetoxy substituted indole, excellent yield could be afforded in this reaction system (Table 2, entry 3). Furthermore, almost quantitatively, product **3b** was obtained when using the 2-methyl indole (Table 2, entry 2). Nevertheless, for the indolin-2-one, two by-products – 9*H*-xanthen-9-one and 9*H*-xanthene, were obtained under this reaction condition with 13% and 42% yield (5 mg and 15 mg), respectively.

9*H*-Xanthen-9-one: 5 mg, yield 13%; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 7.39–7.42 (m, 2H, Ph), 7.51–7.53 (d, 2H, Ph), 7.73–7.77 (m, 2H, Ph), 8.36–8.38 (m, 2H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 177.3 (C=O), 156.2 (C–O_{arom}), 134.9 (C_{arom}), 126.8 (C_{arom}), 124.0 (C_{arom}), 121.9 (C_{arom}), 118.0 (C_{arom}); anal. calcd for $C_{13}H_8O_2$: C 79.58, H 4.11; found C 79.67, H 4.16; ESI-MS calcd for $C_{13}H_8O$: 197.20 ($[M+H]^+$), found 197.27 ($[M+H]^+$). 9*H*-Xanthene: 15 mg, yield 42%; ^{1}H NMR (400 MHz, $CDCl_3$): δ_{ppm} 4.06 (s, 2H, CH_2), 7.01–7.07 (m, 4H, Ph), 7.17–7.22 (m, 4H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ_{ppm} 150.6 (C&bond;O_{arom}), 127.5 (C_{arom}), 126.2 (C_{arom}), 121.5 (C_{arom}), 119.2 (C_{arom}), 115.0 (C_{arom}), 26.5 (CH_2); ESI-MS calcd for $C_{13}H_{10}O$: 183.22 ($[M+H]^+$), found 183.07 ($[M+H]^+$).

The reason for this remains unclear at present. Previous articles have ever reported that Bu_2SnO can oxidize alcohols into their corresponding ketones.[34–36] Moreover, xanthen-9-ol **1** is easily oxidized in air. Thus, in our reaction system, the oxidative product was also obtained due to the co-action of the stannoxane catalyst and oxygen gas from air.

Next, we also examined the substitution of xanthen-9-ol with other nucleophiles in our protocol (Fig. 2). The results are summarized in Table 3. It was found that the high active nucleophiles, such as **2 m** and **2n**, could be smoothly substituted by xanthen-9-ol with high yields (Table 3, entries 1 and 2). However, in the case of diethyl malonate, no corresponding substituted product was obtained but resulted in the oxidative by-product 9*H*-xanthen-9-one (Table 3, entry 3). To test our protocol efficiency, we used the lower reactive furan, thiophene and imidazole nucleophiles. As a result, only trace amounts of corresponding substituted products were obtained, with a large amount of 9*H*-xanthen-9-ol left in these three cases catalyzed by 1,3-dichloro-tetra-*n*-butyl-distannoxane after 10 h (Table 3, entries 4–6). Unfortunately, the reaction could not proceed in our protocol, even with a prolonged reaction time, when using the *N*-methyl imidazole as a nucleophile (Table 3, entry 7). In addition, the low activity of benzhydrol was also examined and no product was obtained. This may be due to the very weak Lewis acidity of 1,3-dichloro- tetra-*n*-butyl-distannoxane catalyst.

Conclusion

In the present paper, a new application of 1,3-dichloro-tetra-*n*-butyl-distannoxane was explored for the direct nucleophilic substitution of xanthen-9-ol with several nucleophiles (indoles, pyrrole, diketone, etc.). Using 1 mol% 1,3-dichloro-tetra-*n*-butyl-distannoxane, the nucleophilic substitution of alcohol could efficiently proceed at room temperature and afford the corresponding product with high or excellent yield. Further asymmetric reaction on this direct substitution of xanthen-9-ol is in progress in our group.

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