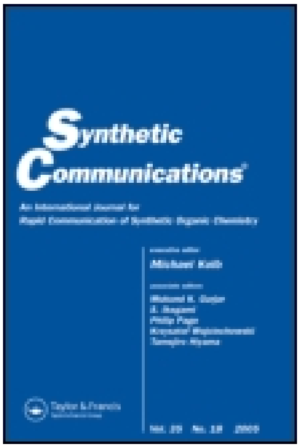

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Indium Tris(dodecyl Sulfonate) [In(DS)$_3$]–Catalyzed Formation of 3-(9*H*-Xanthen-9-yl)-1*H*-indole Derivatives in Water at Room Temperature

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Abstract: In(DS)$_3$ catalyzes formation of 9*H*-xanthen-9-ol with indoles at room temperature in water to afford a class of 3-(9*H*-xanthen-9-yl)-1*H*-indole derivatives in high yields.

Keywords: indium tris(dodecyl sulfonate), indole, water, xanthen-9-ol

INTRODUCTION

In previous articles, the reactions of xanthen-9-ol with nucleophilic reagents such as thiol,[1] imide,[2] indoles,[3,4] and thiophene[5] promoted by acids or $BF_3 \cdot Et_2O$[4] have been reported. However, many of these of these procedures involved strong acidic conditions, low yields of products, and complex handling. For this reason, superior catalyst systems, which are cheap, easy to access, and in stable air, are desirable.

Recently, organic reactions that can be carried out in aqueous media have become one of the most challenging areas in organic synthesis because of the environmental benefits and favorable effects of water on chemical transformations.[6] In particular, reactions mediated by indium in aqueous media are of

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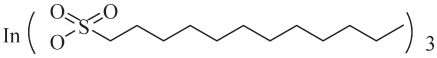
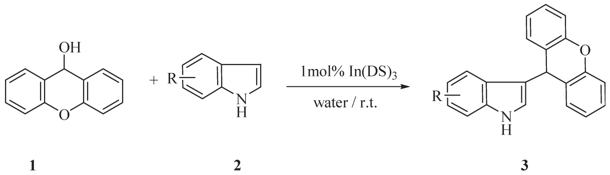


Figure 1. The structure of In(Ds)$_3$.



Scheme 1.

current interest for their considerable applications in organic synthesis.[7,8] Lewis acid–surfactant–combined catalysts (LASC) have been easily prepared, developed, and applied to Lewis acid–catalyzed organic reactions in water. These catalysts have been successfully used for various typical carbon–carbon bond-forming reactions such as aldol, allylation, Mannich-type reactions, and Michael addition in water.[9] The LASCs consist of Lewis acidic metal cations such as indium(III) and amphiphilic anions such as dodecyl sulfonate and form stable colloidal dispersions in the presence of organic substrates in water. As a continuation of our work on indoles,[10] here we report that indium tris(dodecyl sulfonate) [In(DS)$_3$] (Fig. 1), a new LASC, effectively catalyzes the reactions of xanthen-9-ol **1** with indoles **2** in water to give 3-(9*H*-xanthen-9-yl)-1*H*-indole derivatives in high yields (Scheme 1).

RESULTS AND DISCUSSION

First, the reaction of 9*H*-xanthen-9-ol **1** with indole **2a** was tested as a model reaction in the presence of various catalysts in water (Table 1). When In(DS)$_3$

Table 1. Reaction of indole **2a** with **1** catalyzed by different catalysts in water[a]

Entry	Catalysts	Time (h)	Yield (%)[b]
1	In(DS)$_3$	1	96
2	InCl$_3$	1	86
3	Fe(DS)$_3$	1	96
4	Sm(DS)$_3$	1	93
5	Yb(DS)$_3$	1	94
6	—	1	—

[a] These reactions were performed using 1 mol% catalysts.
[b] Isolated yield.

was used as a catalyst, the reaction proceeded smoothly to afford the desired product 3-(9*H*-xanthen-9-yl)-1*H*-indole **3a** in 96% yield (Table 1, entry 1). As shown Table 1, this reaction can also be catalyzed by $InCl_3$ to give the desired product **3a** in good yield in water (Table 1, entry 2). Among various dodecyl sulfonates such as $Fe(DS)_3$, $Sm(DS)_3$, and $Yb(DS)_3$ employed in this reaction, $In(DS)_3$ and $Fe(DS)_3$ are more effective in terms of reaction yields than the others (Table 1, entries 3–5).

Similarly, with the optimized conditions in hand, various substituted indoles were reacted with xanthen-9-ol to afford the corresponding 3-(9*H*-xanthen-9-yl)-1*H*-indole derivatives. The results are listed in Table 2. The products were obtained in high to quantitative yields in short reaction times. The reactions were clean and complete within 1.0–1.5 h with high regieoselectivity. Not only **2b–i** (Table 2, entries 2–9) but also the passivated indole derivative **2j** (Table 2, entry 10) worked well to give the 3-(9*H*-xanthen-9-yl)-1*H*-indole derivatives in good to high yields. However, when 3-methyl indole was used, no desired product was found.

Mechanistically, indole attacks an pyrylium ion, which is formed from an xanthen-9-ol in situ catalyzed by $In(DS)_3$, and then generates the corresponding product **3** (Scheme 2).

In conclusion, the present protocol provides a novel and highly efficient procedure for the synthesis of a class of compounds, 3-(9*H*-xanthen-9-yl)-1*H*-indoles, using a catalytic amount of $In(DS)_3$. The procedure offers several advantages including high yields, mild solvent, short reaction times, easily obtained catalyst, and simple experimental isolation procedures, which make it a useful procedure for the synthesis of 3-(9*H*-xanthen-9-yl)-1*H*-indole derivatives. In addition, the use of $In(DS)_3$ for other catalytic reactions in water is focus of ongoing studies.

EXPERIMENTAL

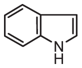
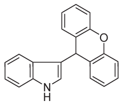
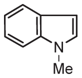
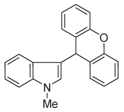
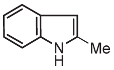
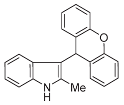
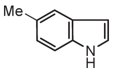
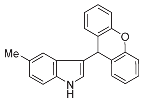
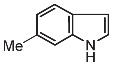
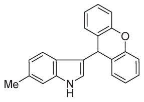
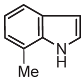
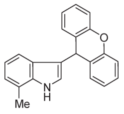
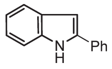
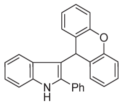
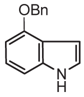
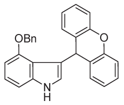
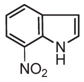
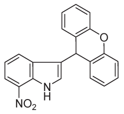
General

Melting points were recorded on an Electrothermal digital melting-point apparatus and are uncorrected. ^1H NMR (400-MHz) spectra were recorded on a Varian Mercury spectrometer in $CDCl_3$. IR spectra were obtained on a Nicolet FT-IR500 spectrophotometer using KBr pellets. High-resolution mass spectra were obtained using a GCT-TOF instrument.

Procedure for Synthesis of Indium Tris(dodecyl Sulfonate) [$In(DS)_3$][9c]

Sodium dodecylsulfonate (2.693 g, 9.90 mmol) was dissolved in H_2O (100 mL) at 70°C. To this, a solution of $InCl_3$ (0.725 g, 3.30 mmol) in H_2O

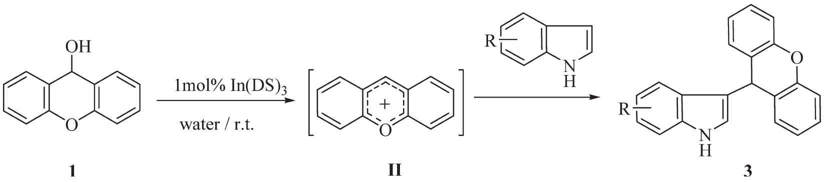
Table 2. Reactions of indole **2** with **1a–j** catalyzed by In(DS)$_3^a$

Entry	Indoles		Product		Time (h)	Yield (%)^b
1		**2a**		**3a**	1	96
2		**2b**		**3b**	1	83
3		**2c**		**3c**	1	82
4		**2d**		**3d**	1	81
5		**2e**		**3e**	1	90
6		**2f**		**3f**	1.5	85
7		**2g**		**3g**	1.5	98
8		**2h**		**3h**	1	82
9		**2i**		**3i**	1	97

[a] All reactions were carried out using a catalytic amount of In(DS)$_3$ (1 mol%) at room temperature.

[b] Isolated yields.

(l mL) was added at the same temperature. The mixture was cooled to room temperature, and the resulting precipitate was collected and purified by recrystallization from H_2O to give In(DS)$_3$ as a white solid (2.816 g, 99%). ^{1}H NMR (400 MHz, *d*-DMSO): δ 1.21–1.23 (m, 9H, CH_3), 1.64–1.777 (m, 48H), 1.92 (m, 6H, CH_2), 2.87 (m, 6H, CH_2), 3.54 (m, 6H, CH_2); ^{13}C NMR (100 MHz,



Scheme 2.

d-DMSO): 13.8, 22.0, 26.5, 28.6, 28.9, 29.0, 31.2, 52.4. The other new LASCs were prepared in a similar way.

General Procedure for Synthesis of 3

A mixture of indole **2** (0.059 g, 0.5 mmol), **1a** (0.099 g, 0.5 mmol), In(DS)$_3$ (4.65 mg, 0.005 mmol), and water (2 mL) was stirred in a flask at room temperature until the disappearance of the starting **2** (1.0 h, checked by thin-layer chromatography, TLC). After standing for 1.0 h, the reaction mixture was filtered. Then the crude product was purified by flash chromatography to afford the pure product **3a** (0.143 g, yield: 96%).

Data

3-(9*H*-Xanthen-9-yl)-1*H*-indole, **3a:** mp 143–145°C (lit.[3a] 145°C); IR (KBr): ν 3429(NH), 3051, 2920, 2850, 1254, 749 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 5.55 (s, 1H, CH), 6.90–7.36 (m, 13H), 8.02 (br, s, 1H, NH). HRMS found: m/z 297.1157 (M$^+$); calcd. for $C_{21}H_{15}NO$: M, 297.1154.

1-Methyl-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3b:** mp 134–135°C; IR (KBr): ν 3426 (NH), 3040, 2929, 1250, 747 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ3.72 (s, 3H, CH$_3$), 5.54 (s, 1H, CH), 6.88–7.41 (m, 13H). HRMS found: m/z 311.1295 (M$^+$); calcd. for $C_{22}H_{17}NO$: M, 311.1310.

2-Methyl-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3c:** mp 187–189°C (lit.[3a] 196°C); IR (KBr): ν 3406 (NH), 3038, 2914, 1251, 748 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 2.36 (s, 3H, CH$_3$), 5.60 (s, 1H, CH), 6.85–7.27 (m, 12H); 7.82 (br, s, 1H, NH). HRMS found: m/z 311.1309 (M$^+$); calcd. for $C_{22}H_{17}NO$: M, 311.1310.

5-Methyl-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3d:** mp 134–136°C; IR (KBr): ν 3469 (NH), 3031, 2914, 1250, 751 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ

2.32 (s, 3H, CH_3), 5.52 (s, 1H, CH), 6.90–7.25 (m, 12H); 7.92 (br, s, 1H, NH). HRMS found: m/z 311.1296 (M^+); calcd. for $C_{22}H_{17}NO$: M, 311.1310.

6-Methyl-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3e:** mp 131–133°C; IR (KBr): ν 3428 (NH), 3036, 2915, 1252, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H, CH_3), 5.51 (s, 1H, CH), 6.78–7.25 (m, 12H); 7.89 (br, s, 1H, NH). HRMS found: m/z 311.1303 (M^+); calcd. for $C_{22}H_{17}NO$: M, 311.1310.

7-Methyl-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3f:** mp 186–187°C; IR (KBr): ν 3425 (NH), 3051, 2915, 2853, 1251, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H, CH_3), 5.54 (s, 1H, CH), 6.87–7.24 (m, 12H); 7.93 (br, s, 1H, NH). HRMS found: m/z 311.1311 (M^+); calcd. for $C_{22}H_{17}NO$: M, 311.1310.

2-Phenyl-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3g:** mp 236–238°C (lit.[3b] 219–221°C); IR (KBr): ν 3389 (NH), 3025, 1248, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.77 (s, 1H, CH), 6.82–7.65 (m, 17 H); 8.17 (br, s, 1H, NH), HRMS found: m/z 373.1485 (M^+); calcd. for $C_{27}H_{19}NO$: M, 373.1467.

4-(Benzyloxy)-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3h:** mp 144–146°C; IR (KBr): ν 3396 (NH), 3060, 2924, 1246, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.06 (s, 2H, CH_2), 5.93 (s, 1H, CH), 6.83–7.26 (m, 17H), 7.99 (br, s, 1H, NH). HRMS found: m/z 403.1569 (M^+); calcd. for $C_{28}H_{21}NO_2$: M, 403.1572.

7-Nitro-3-(9*H*-xanthen-9-yl)-1*H*-indole, **3i:** mp 181–182°C; IR (KBr): ν 3388 (NH), 1249, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.59 (s, 1H, CH), 6.71–8.36 (m, 12H), 9.92 (br, s, 1H, NH). HRMS found: m/z 342.1005 (M^+); calcd. for $C_{21}H_{14}N_2O_3$:M, 342. 1004.

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