

The facile and efficient Michael addition of indoles and pyrrole to α,β -unsaturated electron-deficient compounds catalyzed by aluminium dodecyl sulfate trihydrate $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ in water

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Aluminium dodecyl sulfate trihydrate $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ is easily prepared and can be used as a Lewis acid surfactant catalyst in water to conduct the highly efficient Michael addition of indoles and pyrrole to α,β -unsaturated electron-deficient compounds at room temperature.

Using aqueous media as a reaction solvent has attracted much attention in synthetic organic chemistry for several reasons.¹ In comparison with organic solvents, water is cheap, safe and reduces the use of harmful organic solvents and leads to the development of environmentally friendly chemical processes.² In addition, reactions in aqueous media illustrate unique reactivities and selectivities that are not usually observed in organic media.³

By the discovery of water-tolerant Lewis acids reported by Kobayashi and his co-workers, the reactions catalyzed by such acids have become feasible in aqueous media.⁴ Michael reactions promoted by Lewis acids have attracted much attention as one of the important carbon-carbon bond-forming reactions in organic synthesis and varieties of catalysts have been reported for this purpose which are used in organic solvents.⁵

Indole and pyrrole derivatives are important compounds that are found in many pharmacologically and biologically active compounds.⁶

In this article, we present the highly efficient Michael addition of indoles and pyrrole to α,β -unsaturated electron-deficient compounds in aqueous media using aluminium dodecyl sulfate $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ (Scheme 1) as a new Lewis acid surfactant catalyst. Aluminium dodecyl sulfate, $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ was prepared by the addition of hydrated aluminium nitrate or aluminium chloride to an aqueous solution of sodium dodecyl sulfate. The product was precipitated as a white powder compound in 83% yield. We have observed that $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ is not easily soluble in water and forms a turbid colloidal type solution. The elemental analysis of the isolated $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ gave satisfactory analytical results within the range of the experimental errors.⁷

By the use of catalytic amounts of $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$, addition of indole, 2-methylindole and *N*-methylindole to structurally diverse

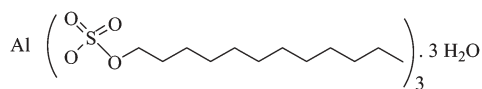
electron-deficient olefins proceeded efficiently in high isolated yields (Scheme 2). The results are presented in Table 1.

Michael addition of pyrrole, as an acid sensitive compound, to different electron-deficient olefins in the presence of this catalyst proceeded well in water and the Michael adducts were isolated in high yields (Table 1, entries 5, 6, 10, 14). Formation of any polymeric materials was not observed in the reactions presented in this study. These results show that $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ is a mild Lewis acid catalyst and may be used for Michael addition reactions using sensitive substrates.

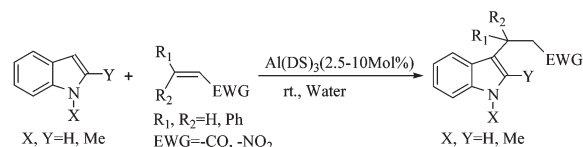
In order to show the strong catalytic effect of $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$, the reaction of indole and methyl vinyl ketone in the absence of $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ was also studied in water. We have observed that the desired Michael adduct (Table 1, entry 1) was produced in less than 20% yield after a prolonged reaction time (48 h). We have also studied the similar reaction in the presence of sodium dodecyl sulfate (SDS) in water. We have noticed that the reaction proceeded sluggishly and the desired Michael adduct was obtained in less than 20% yield after 24 h. These results showed that the combination of a Lewis acid moiety (cationic part) and a surfactant (anionic part) in $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ is important for the reactions to proceed in water. The Lewis acid part of the catalyst activates the substrate molecules and the surfactant part, affecting the solubility of the substrates in water at the same time. When these two factors are in play together, a drastic enhancement of the rates and the yields of the products is observed.

In Table 2, we have shown the catalytic activity of $[\text{Al}(\text{DS})_3]\cdot 3\text{H}_2\text{O}$ for Michael addition reactions in comparison with InCl_3 ,⁸ $\text{Sc}(\text{DS})_3$ ^{4d} and $\text{CeCl}_3\cdot 7\text{H}_2\text{O}-\text{NaI}$ ^{5a} catalysts used for the similar reactions in aqueous media.

In conclusion, in this study we have introduced a new effective non-corrosive Lewis acid surfactant combined catalyst for the efficient Michael addition of indoles and pyrrole to structurally diverse electron-deficient olefins at room temperature in aqueous media. By this protocol, pyrrole as an acid sensitive compound undergoes Michael addition reactions in high yields without any polymerization reactions occurring. These results show that the presented Lewis acid surfactant catalyst is a mild catalyst which is



Scheme 1



Scheme 2

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Table 1 Michael addition of indoles and pyrrole to electron-deficient olefins catalyzed by $\text{Al}(\text{DS})_3 \cdot 3\text{H}_2\text{O}$ in water^a

Entry	Substrate	Olefin	Product	Time (h)/Yield (%) ^b
1				24/20
2				0.8/97
3				0.7/95
4				1.5/96
5				2/85 ^c
6				2.5/88 ^d
7				12/88
8				12/86
9				10/81
10				10/89
11				48/71 ^e
12				48/66 ^e
13				48/54 ^e

Table 1 Michael addition of indoles and pyrrole to electron-deficient olefins catalyzed by $\text{Al}(\text{DS})_3 \cdot 3\text{H}_2\text{O}$ in water^a (continued)

Entry	Substrate	Olefin	Product	Time (h)/Yield (%) ^b
14				48/83 ^e

^a All products were identified by their IR, NMR and GC/MS spectra. ^b Isolated yield of the products after column chromatography; the purity was determined by GC. ^c Equimolar methyl vinyl ketone was used. ^d 2 equivalents of methyl vinyl ketone were used. ^e 10 mol % of the catalyst was used.

Table 2 Comparison of the reaction of indole with methyl vinyl ketone catalyzed by $[\text{Al}(\text{DS})_3] \cdot 3\text{H}_2\text{O}$ with the other catalysts used for this reaction

Entry	Catalyst	Time (h)	Yield (%)
1	$[\text{Al}(\text{DS})_3] \cdot 3\text{H}_2\text{O}$	0.8	97
2	$\text{Sc}(\text{DS})_3$ ^{4d}	1	98
3	InCl_3 ⁸	3	90
4	$\text{CeCl}_3 \cdot 7\text{H}_2\text{O} - \text{NaI}$ ^{5a}	2	96

suitable for Michael addition reactions using acid sensitive compounds.

Full investigations of the stability of this compound in aqueous media under different conditions and its new catalytic applications in organic reactions are underway in our laboratories.†

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Notes and references

† *General procedure* for the Michael addition of indole derivatives to α,β -unsaturated carbonyl compounds: The indole (1 mmol), the α,β -unsaturated carbonyl or nitro compound (2 mmol) and $[\text{Al}(\text{DS})_3] \cdot 3\text{H}_2\text{O}$ (2.5–10 mol %) were added to water (10 ml). The reaction mixture was stirred at room temperature for the appropriate time (Table 1, monitored by TLC). Et_2O (10 ml) was added to the mixture with stirring. The ethereal phase was separated and dried over Na_2SO_4 . Evaporation of the solvent gave the crude desired product. Further purification was performed by column chromatography, eluting with the appropriate solvents to give the Michael adducts in 54 to 97% isolated yields. The purity of the purified products was also determined by GC.

- (a) *Organic Synthesis in Water*, (Ed.: P. A. Grieco), Blackie Academic and Professional, London, 1998; (b) C.-J. Li and T.-H. Chan, *Organic Reactions in Aqueous Media*, John Wiley & Sons, New York, 1997.
- P. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, 1998.
- (a) S. Kobayashi, Y. Mori, S. Nogayama and K. Manabe, *Green Chem.*, 1999, **1**, 175; (b) B. Cornils, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1575.
- (a) S. Kobayashi, K. Manabe and S. Nagayama, in *Modern Carbonyl Chemistry*, (Ed.: J. Otera), Wiley-VCH, Weinheim, 2000; (b) K. Manabe and S. Kobayashi, *Chem. Commun.*, 2000, 669; (c) K. Manabe, Y. Mori, T. Wakabayashi, S. Nagayama and S. Kobayashi, *J. Am. Chem. Soc.*, 2000, **122**, 7202; (d) K. Manabe, N. Aoyama and S. Kobayashi, *Chem. Commun.*, 2001, 174; (e) S. Kobayashi, S. Nagayama and T. Busujima, *J. Am. Chem. Soc.*, 1998, **120**, 8287.

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- 5 (a) G. Bartoli, M. Bartolacci, M. Bosco, G. Foglia, A. Giuliani, E. Marcantoni, L. Sambri and E. Torregiani, *J. Org. Chem.*, 2003, **68**, 4594; (b) M. Bandini, P. G. Cozzi, M. Giacomini, P. Melchiorre, S. Selva and A. U. Ronchi, *J. Org. Chem.*, 2002, **67**, 3700.
- 6 (a) P. Arya, R. Joseph and D. T. H. Chou, *Chem. Biol.*, 2002, **9**, 145; (b) H.-C. Zhang, H. Ye, A. F. Moretto, K. K. Brumfield and B. E. Maryanoff, *Org. Lett.*, 2000, **2**, 89.
- 7 **Preparation of Al(DS)₃·3H₂O from Al(NO₃)₃ and sodium dodecyl sulfate:** To a solution of sodium dodecyl sulfate (9 mmol, 2.6 g) in water (75 ml) was added a solution of Al(NO₃)₃·9H₂O (3 mol, 1.126 g) in water (25 ml) at room temperature. White precipitates appeared immediately and the mixture was stirred for another 20 min. The white solid was separated by filtration and was washed with water (2 × 30 ml). Drying of the isolated solid under diminished pressure (–20 torr, 24 h) gave the desired compound as a white powder in 83% yield, 2.185 g, mp 216 °C, ¹H NMR (250 MHz, DMSO) δ = 0.85 (t, 9H, *J* = 7.5 Hz), 1.14–1.48 (54H, m), 2.51 (m, 6H), 3.31–3.71 (m, 6H). ¹³C NMR (63 MHz, DMSO) δ = 13.88, 22.05, 25.48, 28.68, 28.76, 29.00, 30.5, 31.25, 60.19, 65.51, 72.20. IR (Kerr) = 1175, 1315 cm^{–1}. Anal.; calcd. for Al(DS)₃·3H₂O: requires C, 49.3%; H, 9.2%; S, 11%; Al, 3.02%; found, C, 49.45%; H, 9.1%; S, 10.98%; Al, 2.96%.
- 8 J. S. Yadav, S. Abraham, B. V. S. Reddy and G. Sabitha, *Synthesis*, 2001, 2165.