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Corrigendum

Corrigendum to "A parallel combinatorial approach to locating homochiral Lewis acid catalysts for the asymmetric aza-Diels–Alder reaction of an imino dienophile" [Tetrahedron Lett. 39 (1998) 8905]☆

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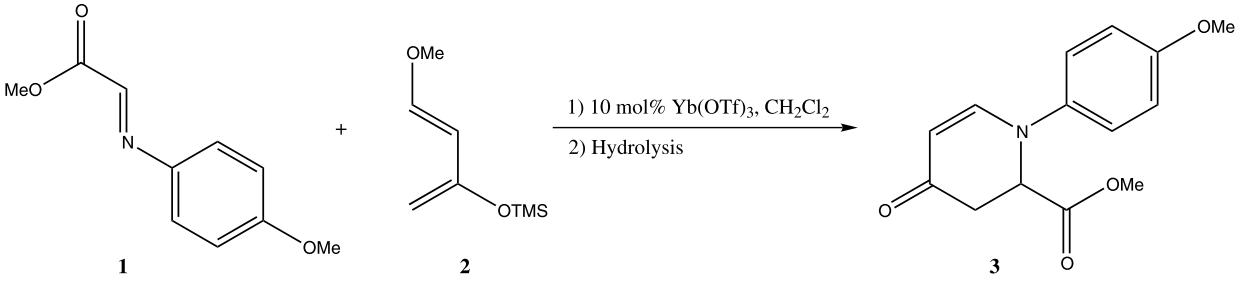
Unreproducibilty of the reported results

In 1998, we published[1] a paper in *Tetrahedron Letters* entitled 'A parallel combinatorial approach to locating homochiral Lewis acid catalysts for the catalytic asymmetric aza-Diels–Alder reaction of an imino dienophile.' The main findings of this paper were: (1) that $Yb(OTf)_3$ catalyses the reaction of imine **1** with diene **2** (Eq. (1)); (2) that a small scale combinatorial search method was used with a series of Lewis acids, chiral ligands, solvents and additives to locate new conditions for providing catalytic asymmetric induction in product **3**, providing a wide range of claimed levels of asymmetric induction; (3) the best reactions conditions were scaled up and produced the results summarised in Table 1, with the experimental and characterisation for **3** for the highest e.e. reaction, being as reported in the procedure below; and (4) e.e.s had been claimed to be determined by chiral HPLC using a Chiralcel OJ column (hexane:ethanol, 50:50, flow rate 1 ml/min, retention times 10.40 and 14.90 min).



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Ligands (1)

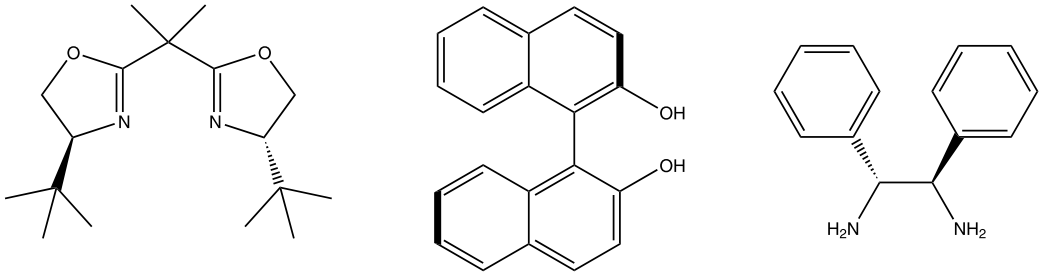

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Table 1. Scaled up reaction conditions and associated e.e.s

Lewis acid	Ligand	Additive	Solvent	Yield[a] (%)	E.e. (%)
MgI_2	**6**	2,6-Lutidine	MeCN	64	97[b]
$Yb(OTf)_3$	**6**	2,6-Lutidine	PhMe	60	87
$Cu(OTf)_2$	**6**	None	MeCN	58	86
$FeCl_3$	**4**	4 Å MS	CH_2Cl_2	67	92

[a] All yields unoptimised, after silica gel chromatography.
[b] For procedure and characterisation, see Ref. 1.

Procedure: using magnesium(II) iodide and diamine **6**. To a solution of magnesium(II) iodide (29 mg, 0.10 mmol) and (1*R*,2*R*)-diphenylethylene diamine **6** (24 mg, 0.11 mmol) in acetonitrile (5 ml) was added 2,6-lutidine (0.01 ml, 0.11 mmol). After 30 min, imine **1** (200 mg, 1.04 mmol) was added in dry acetonitrile (10 ml), followed by diene **2** (0.25 ml, 1.29 mmol) after a further 30 min. The reaction mixture was stirred for 18 h, mixed with silica gel (2 g) and the solvent evaporated. The resulting solid was loaded onto a silica gel column and eluted with petroleum ether:ethyl acetate (1:2) to give enone **3** as a yellow solid (174 mg, 64%); $[\alpha]_D^{23} = -2.9$ (*c* 0.1 $CHCl_3$); ν_{max} (film, inter alia) 1740 (ester CO) and 1650 (ketone CO) cm^{-1}; λ_{max} (EtOH) 203 (ε 12,000), 239 (ε 7,520) and 341 (ε 15,100) nm; δ (^1H, $CDCl_3$, 400 MHz) 2.97 (1H, ddd, *J* 17, 2 and 1 Hz, CHH), 3.11 (1H, dd, *J* 17 and 7.5 Hz, CHH), 3.79 and 8.84 (each 3H, s, 2×OCH_3), 4.72 (1H, ddd, *J* 7.5, 2 and 1 Hz, N.CH.CH_2), 5.24 (1H, dd, *J* 17.5 and 1 Hz, N.CH:CH), 6.93 and 7.12 (each 2H, d, *J* 8 Hz, 2× ArCH), 7.43 (1H, dd, *J* 17.5 and 1 Hz, N.CH:CH); δ (^{13}C, $CDCl_3$, 100.7 MHz) 38.8 (CH_2), 53.4 (ArOCH_3), 56.0 (CO.OCH_3), 61.7 (N.CH), 102.3 (ArCH), 115.2 (ArCH), 122.3 (N.CH:CH), 138.6 (ArC.N), 150.5 (N.CH:CH), 170.8 (CO.OCH_3), 189.5 (CO.CH_2); *m*/*z* (CI, NH_3) 262.3 ($M+H^+$, base peak); Anal. $C_{14}H_{15}NO_4$ requires C, 64.1; H, 5.8; H, 5.3; found C, 64.2; H, 5.7; N, 5.6%.

In the interim since this communication, several workers have struggled to try to reproduce the following results: (1) the e.e.s shown in Table 1, though yields are reproducible. Typical e.e.s have been in the range varying from 0 to 55% using magnesium(II) iodide and ligand **6**, seemingly depending on how anhydrous the conditions are. The remaining entries fail to produce any asymmetric induction; (2) the optical rotation of −2.9 in the procedure above, for a material of 98% e.e., is incorrect, though the remainder of the characterisation data are correct.

In trying to understand the problems associated with these results, we have found the following: (1) pure racemic cycloadduct **3** has retention times of 34 and 49 min, respectively, for each enantiomer using a Chiralcel OD column (1 ml/min flow rate, IPA:hexane, 1:4); (2) using the asymmetric procedure reported by Jørgensen,[2] which he applied to the ethyl ester version of adduct **3**, the corresponding methyl ester cycloadduct **3** can be prepared in 87% e.e. (major peak at 34 min), 72% yield, $[\alpha]_D^{20} = +180$ (*c* 0.13, $CHCl_3$). Under identical conditions [CH_2Cl_2, $CuClO_4$·4MeCN, and (*R*)-Tol-Binap], but reproducing the Jørgensen ethyl ester reaction, we obtained 66% yield, 83% e.e. [89% yield and 72% e.e., $[\alpha]_D^{rt} = +181.7$ (*c* 0.82, $CHCl_3$) was reported by Jørgensen for the (*R*)-enantiomer[2]]. Hence, the major methyl ester enantiomer with the retention time of 34 min is therefore also (*R*), by correlation with this result.

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2. Yao, S.; Saaby, S.; Hazell, R. G.; Jørgensen, K. A. *Chem. Eur. J.* **2000**, *6*, 2435.