Asymmetric [2 + 2] Cycloaddition of Ketene with Aldehydes Catalysed by Me_3Al Complexes of Axially Chiral 1,1'-Binaphthalene-2,2'-diol Derivatives

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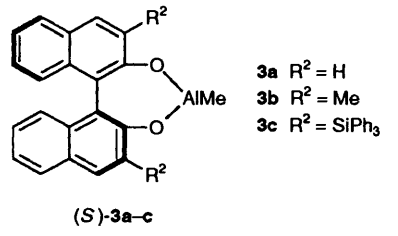
Asymmetric [2 + 2] cycloaddition of ketene **1** with the aldehydes **2a–f**, catalysed by axially chiral Lewis acids **3a–c** afforded optically active 4-substituted oxetan-2-ones **4a–f** in up to 56% enantiomeric excess (e.e.); the stereoselectivity of the reaction depended on the structure of the chiral Lewis acids and of the aldehydes, the order of addition of compounds **1** and **2** and on the solvents employed.

There is much current interest in the synthesis of optically active oxetan-2-ones which serve not only as a monomer of various biodegradable copolyesters,[1] but also as a structural element in pharmacologically interesting natural products.[2] Although the synthesis of oxetan-2-ones by Lewis acid-catalysed [2 + 2] cycloaddition of ketene with carbonyl compounds has been investigated, use of a chiral Lewis acid as an activator for this reaction has not been reported.[3] Here, we report the first asymmetric synthesis of 4-substituted oxetan-2-ones **4a–f** by the asymmetric [2 + 2] cycloaddition of ketene **1** with the aldehydes **2a–f**, catalysed by axially chiral 1,1'-binaphthalene-2,2'-diol derivatives–trimethylaluminium complexes **3a–c** (Scheme 1).



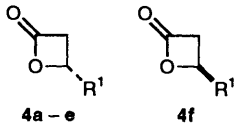
3a R^2 = H
3b R^2 = Me
3c R^2 = $SiPh_3$

(*S*)-**3a–c**

$CH_2=C=O$ + R^1CHO → (Toluene, −78 °C)

1 **2a–f**

2a, 4a R^1 = Et, **2b, 4b** R^1 = Me
2c, 4c R^1 = Pr, **2d, 4d** R^1 = Bu
2e, 4e R^1 = Pr^i, **2f, 4f** R^1 = Ph



4a–e **4f**

Scheme 1

In the stoichiometric reactions of the aldehyde **2a** with ketene catalysed by the chiral complexes **3a–c** (Table 1, runs 1–3), 4-ethyloxetan-2-one **4a** was obtained in fair to moderate yields with up to 56% enantiomeric excess (e.e.), compound **3c** giving the highest e.e. The reactions of the aldehydes **2b–f** also afforded the oxetanones **4b–f** (runs 7–11). The absolute configurations of these products were determined by comparison of the specific rotation sign of compound **4b**[4] or the known derivatives of compounds **4a**[5] and **4c–f**[6–8] with their reported data. On the other hand, almost no product was obtained using 10 mol% of complex **3c**[9] as the catalyst (run 4). Furthermore, the yield of compound **4a** greatly decreased when ketene was added to the catalyst solution a few minutes before the addition of the aldehyde (run 5). Since the [2 + 2] cycloaddition proceeds *via* nucleophilic attack of the ketene on the aldehyde which is activated by coordination to a Lewis acid,[10] the catalytic activity may be lost by the preferential coordination of ketene and/or the product oxetanone to the Lewis acid, preventing the ligation of the aldehyde. In addition, monoacetylation of the phenolic hydroxy groups of the catalyst by the ketene was observed in these reactions, which may also decrease the catalytic activity.

Interestingly, the preferred enantiomer depended on the structure of the catalysts (runs 1–3) and of the aldehydes (runs 3–10 *vs.* run 11). Differences in enantioselectivity between the catalysts **3a–c** may arise from differences in their stereoelectronic nature and/or a difference in the reactive species generated from them. The addition of ketene to the aldehyde **2f** catalysed by (*S*)-**3c** afforded the lactone (*S*)-**4f**, whereas the reactions of the aldehydes **2a–3e**, gave the lactones (*S*)-**4a–d** and (*R*†)-**4e** *via* ketene addition from the opposite π-face to that of compound **2f**. Although the origin of the reversal of the π-facial selectivity is unclear at present, a CPK molecular models study suggests that two coordination geometries of the aldehydes to the complex **3c** are probable (Schemes 2A and 2B). The structure of the aldehyde–**3c** complex depicted in Scheme 2A seems preferred, since there is less steric hindrance between the aldehyde R^1 group and the catalyst moiety (see below). The stereochemistry of the hetero-Diels–Alder reactions of compound **2f** with siloxy dienes has been explained using this model by Yamamoto and co-workers.[11] However, the approach of the ketene to the aldehydes in the manner shown in Scheme 2A suffers from the steric repulsion between the incoming ketene and the front triphenylsilyl group of the catalyst **3c**. Alternatively, the approach of the ketene to the aldehydes, as depicted in Scheme 2B, decreases this interaction, leading to the preferred enantiomer from the less bulky aldehydes **2a–e**. However, the relatively bulky aldehyde **2f** would experience difficulty coordinating as depicted in Scheme 2B because of the steric repulsion between the phenyl group of **2f** and the rear triphenylsilyl group. Therefore, the aldehyde **2f** may be forced to react with ketene in the manner shown in Scheme 2A to afford compound (*S*)-**4f** preferentially.

In conclusion, we have found for the first time that chiral Lewis acids **3a–c** catalyse the enantioselective [2 + 2] cycloaddition of ketene with aldehydes **2a–f** to yield the optically active 4-substituted oxetan-2-ones **4a–f** in moderate to good yields with up to 56% e.e., despite the fact that the reactant ketene was a small, rod-like molecule.

Experimental

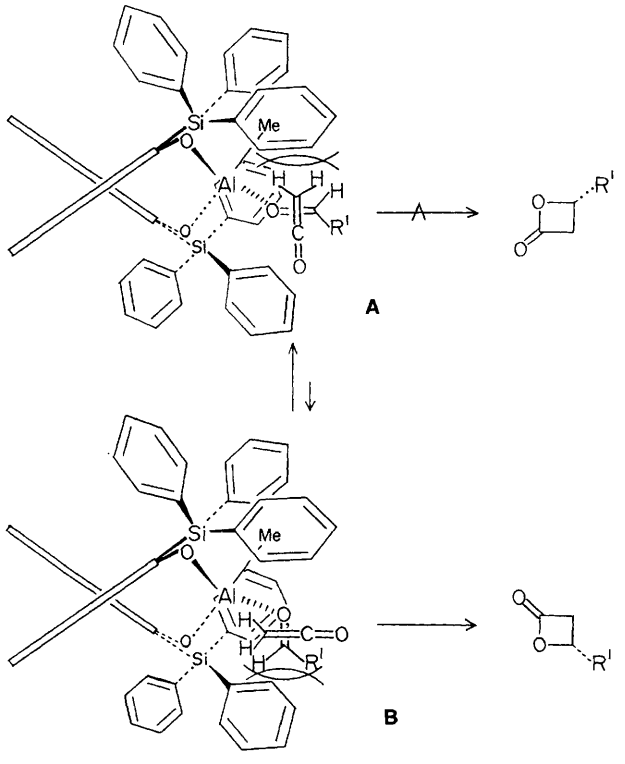
Representative Procedure (*run 1, Table 1*).—To a stirred

† Change in *R* and *S* nomenclature is due to the change of the priority order of the substituents.

Table 1 Cycloaddition of ketene **1** with the aldehydes **2a–f** catalysed by axially chiral Lewis acids (*S*)-**3a–c**

Run	Aldehyde 2 (R^1)	Catalyst 3 (R^2)	Product 4	Yield[a] (%)	E.e.[a] (%)	Abs. Confign.
1	**2a** (Et)	**3a** (H)	**4a**	45 (15[b])	36	*S*
2	**2a** (Et)	**3b** (Me)	**4a**	63	28	*R*
3	**2a** (Et)	**3c** ($SiPh_3$)	**4a**	67	56	*S*
4[c]	**2a** (Et)	**3c** ($SiPh_3$)	**4a**	< 5	—	—
5[d]	**2a** (Et)	**3c** ($SiPh_3$)	**4a**	33	45	*S*
6[e]	**2a** (Et)	**3c** ($SiPh_3$)	**4a**	91	20	*R*
7	**2b** (Me)	**3c** ($SiPh_3$)	**4b**	78	23	*S*
8	**2c** (Pr)	**3c** ($SiPh_3$)	**4c**	69	45	*S*
9	**2d** (Bu)	**3c** ($SiPh_3$)	**4d**	80	17	*S*
10	**2e** (Pr^i)	**3c** ($SiPh_3$)	**4e**	59	28	*R*
11	**2f** (Ph)	**3c** ($SiPh_3$)	**4f**	76[f]	21[g]	*S*

[a] Determined by GC analysis using an ASTEC Chiraldex G-TA column [0.25 mm (i.d.) × 20 m, column temperature: 70 °C (**2a** and **2b**), 85 °C (**2c**), 100 °C (**2e**), 105 °C (**2d**), carrier gas: He]. [b] Isolated yield. [c] **2a**:**3c** = 10:1, [**3c**] = 0.02 mol dm^{-3}. [d] Ketene was passed into the catalyst solution for a few minutes before the addition of compound **2a**. [e] Solvent: CH_2Cl_2. [f] Isolated yield of the 1-phenylpropane-1,3-diol derived from compound **4e**. [g] Determined by HPLC analysis of the 1,3-diol derived from compound **4f** (column: Daicel Chiralcel OB, eluent: 10% propan-2-ol in hexane).



Scheme 2

solution of optically pure (*S*)-1,1′-binaphthalene-2,2′-diol (1.0 g, 3.5 mmol) in dry toluene (100 cm^3) was added a hexane solution of Me_3Al (1.75 cm^3, 3.5 mmol; 2.0 mol dm^{-3}) under nitrogen at ambient temperature. After being stirred for 1 h, the solution was cooled to −78 °C and treated with the aldehyde **2a** (230 mg, 3.96 mmol). After 10 min, gaseous ketene (4.0 mmol) generated by pyrolysis of acetone according to the literature procedure [12] was bubbled into the mixture for several minutes. After this, the reaction mixture was stirred at −78 °C for 1 h and then treated with dilute HCl (10 cm^3; 0.5 mol dm^{-3}) and extracted with dichloromethane (100 cm^3 × 3). The combined extracts were washed with brine, dried (Na_2SO_4) and evaporated under reduced pressure until most of the solvent had been removed. The residue was subjected to bulb-to-bulb distillation (90 °C, 133 N m^{-2}) to yield (−)-**4a** (52 mg, 15%) as a colourless oil, $[\alpha]_D$ −11.5 (*c* 0.52 in $CHCl_3$). Compound (−)-**4a** exhibited ^1H NMR and IR spectra almost identical with the reported data for the racemic compound **4a**.[13] The rather low isolated yield may be due to the loss of the volatile and labile product **4a** during the isolation process, which is not optimized at present.

Acknowledgements

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