Asymmetric [2 + 2] Cycloaddition of Ketene with Aldehydes catalysed by Chiral Bissulfonamide–Trialkylaluminium Complexes

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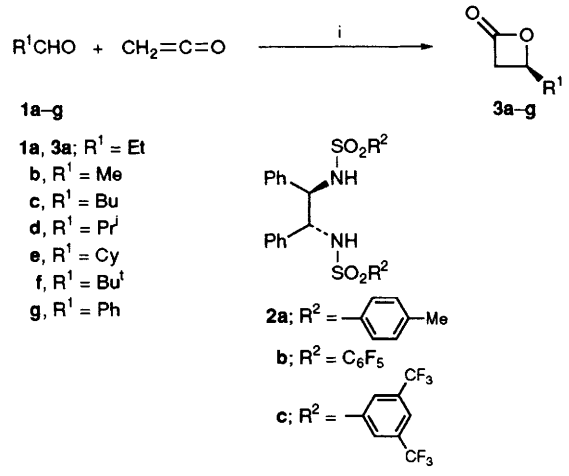
Asymmetric [2 + 2] cycloaddition of ketene with the aldehydes **1a–g**, catalysed by 10 mol% of C_2-symmetric bissulfonamide **2a–c**–R_3Al complexes afforded optically active 4-substituted oxetan-2-ones **3a–g** in up to 74% enantiomeric excess.

There is much current interest in the catalytic asymmetric synthesis of optically active functional compounds by using chirally modified Lewis acids as the catalyst.[1] Among those which are especially desirable are chiral oxetan-2-ones, because they serve as a monomer precursor for biodegradable copolyesters and as structural elements in pharmacologically interesting natural products.[2] Recently, we reported the first asymmetric [2 + 2] cycloaddition of ketene with aldehydes activated by a stoichiometric amount of 3,3′-bis(triphenylsilyl)-1,1′-binaphthalene-2,2′-diol –Me_3Al complex, yielding the optically active oxetan-2-ones.[2] However, the chemical and the optical yield greatly decreased when a catalytic amount of the chiral Lewis acid was employed. This was mainly ascribed to the deactivation of the catalyst *via* acylation of the diolate ligand by ketene. On the other hand, Lewis acids modified by chiral bissulfonamides have been investigated as useful chiral activators of aldehydes in several important organic transformations.[3] Therefore, we hoped that the ligated sulfonamide groups would resist the acylative deactivation by ketene because of their weak basicity. We report herein that the use of C_2-symmetric bissulfonamides **2a–c**–R^3_3Al complexes as the catalyst overcomes this problem (Scheme 1).



Scheme 1 *Reagents and conditions*: i, **2a–c**-R^3_3Al (10 mol%), toluene, −78 °C. Cy = cyclohexyl.

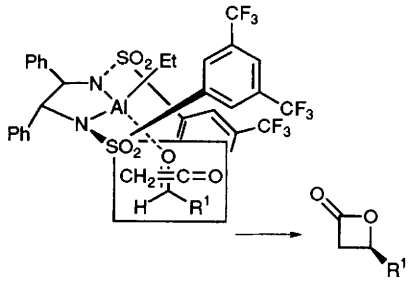
The [2 + 2] cycloaddition reactions were performed as follows (Scheme 1). To a stirred solution of the enantiopure bissulfonamide (*R,R*)-**2**–R^3_3Al complex[3] in dry toluene was added an aldehyde (10 equiv.) under nitrogen at −78 °C. After 10 min, gaseous ketene was bubbled into the mixture for several minutes. The reaction mixture was then stirred for 1 h at −78 °C. After usual work-up, the crude product was subjected to GC analysis to determine the yield and the e.e. The absolute configuration of the lactone **3e** was determined by conversion to the known 1-cyclohexylpropanol.[4]

In the reactions of **1a** with ketene catalysed by R^3_3Al complexes of **2a–c** (Table 1, runs 1–5), optically active **3a** was obtained in good yields with up to 33% e.e., Et_3Al complex of **2c** giving the highest e.e. The reactions of aldehydes **1b–g** catalysed by the **2c**–Et_3Al complex also afforded the oxetanones **3b–g** (runs 6–11) in up to 74% e.e. The bulky aldehydes such as **1e** and **1g** gave the higher enantioselectivities compared with those of the small aldehydes **1a–c**. In all of these cycloaddition reactions, acylation of the catalyst by ketene did not occur. Furthermore, the preferred enantiomers were those produced *via* the addition of ketene from the *re*-face of the aldehydes.

Table 1 Cycloaddition of ketene with aldehydes **1a–g** catalysed by chirally modified Lewis acids[a]

Run	Aldehyde **1** (R^1)	Catalyst **2**-R^3_3Al	Product **3**	Yield (%)[b]	Ee (%)[b]	Abs. config.[c]
1	**1a** (Et)	**2a**-Me_3Al	**3a**	13	0	—
2	**1a** (Et)	**2b**-Me_3Al	**3a**	94	10	*S*
3	**1a** (Et)	**2c**-Me_3Al	**3a**	55	20	*S*
4	**1a** (Et)	**2c**-Et_3Al	**3a**	77	33	*S*
5	**1a** (Et)	**2c**-Bu^i_3Al	**3a**	72	23	*S*
6	**1b** (Me)	**2c**-Et_3Al	**3b**	59	30	*S*
7	**1c** (Bu)	**2c**-Et_3Al	**3c**	82	41	*S*
8	**1d** (Pr^i)	**2c**-Et_3Al	**3d**	76	56	*R*[d]
9	**1e** (Cyclohexyl)	**2c**-Et_3Al	**3e**	75[e]	74	*R*[d,f]
10	**1f** (Bu^t)	**2c**-Et_3Al	**3f**	77	65	*R*[d,g]
11	**1g** (Ph)	**2c**-Et_3Al	**3g**	11[h]	14[i]	*R*[d]

[a] All reactions were performed using 10 mol% of the chirally modified Lewis acids in toluene at −78 °C. [b] Determined by GC analysis using an ASTEC Chiraldex G-TA column [0.25 mm (i.d.) × 20 m, column temperature: 70 °C **3a** and **3b**, 105 °C **3c**, 100 °C **3d**, 125 °C **3e**, 80 °C **3f**, carrier gas: He]. [c] For the determination of the absolute configurations, see ref. 2. [d] Change in *R* and *S* nomenclature is due to the change of the priority order of the substituents. [e] Isolated yield. [f] Determined by comparison of the specific rotation sign of the 1-cyclohexylpropanol derived from the (−)-**3e** with the reported data.[4] [g] Determined by comparison of the specific rotation sign with the reported data.[5] [h] Isolated yield of the 1-phenylpropane-1,3-diol derived from the adduct. [i] Determined by HPLC analysis of the 1,3-diol derived from the adduct (column: Daicel Chiralcel OB, eluent: 10% propan-2-ol in hexane).



Scheme 2

A steric model depicted in Scheme 2 may explain the observed enantioselectivity. The aldehydes **1a–g** seem to coordinate to the catalyst by use of the lone pair electrons of the carbonyl oxygen in a manner *anti* to the substituent R^1 as suggested by Nevalainen[6] for a simple diazaaluminolidine–formaldehyde complex. The bulky aldehydes prefer such a configuration to avoid the steric repulsion between the bulky R^1 group and the diazaaluminolidine moiety, resulting the higher selectivities compared with that of the small aldehydes. Then, the nucleophilic attack of ketene to the activated aldehydes[7] proceeds preferentially from the *re*-face to avoid the bulky bis(trifluoromethyl)phenyl group which is located *anti* to the nearby phenyl group of the catalyst relative to the plane of the diazaaluminolidine ring.[1(*i*)]

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