3-(Trimethylsilyl)oxetan-2-ones *via* enantioselective [2+2] cycloaddition of (trimethylsilyl)ketene to aldehydes catalysed by methylaluminoimidazolines

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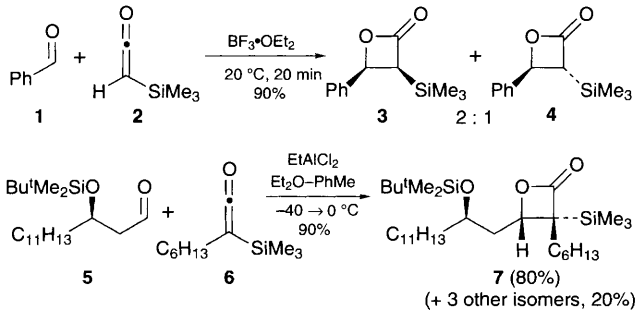
Enantioselective [2+2] cycloaddition of (trimethylsilyl)-ketene to aldehydes catalysed by methylalumino-imidazolines gives 3-(trimethylsilyl)oxetan-2-ones with up to 83% ee.

The [2+2] cycloaddition of a ketene to a carbonyl compound was first reported in 1911.[1] As a general synthetic route to oxetanones,[2,3] the method is limited by the instability of ketenes. However, in 1975 Zaitseva and co-workers[4] showed that (trimethylsilyl)ketene **2**, a readily available and stable ketene,[5] underwent [2+2] cycloaddition to achiral aldehydes in the presence of $BF_3{\cdot}OEt_2$ (Scheme 1). The modest *cis*-selectivity observed by Zaitseva was later improved by using aluminium-based Lewis acids.[6] Good diastereoselection is not restricted to trivial substrates: the [2+2] cycloaddition of hexyl(trimethylsilyl)ketene **6** with the enantiomerically pure β-silyloxyaldehyde **5** in the presence of $EtAlCl_2$ gave good yields, good 1,3-asymmetric induction and *cis*-stereoselectivity[7,8]. High levels of 1,2- and 1,3-asymmetric induction have also been observed recently in substrate-controlled cycloadditions of the simpler (trimethylsilyl)ketene catalysed by aluminium[9] and magnesium Lewis acids[10].

We now report the first catalytic, enantioselective [2+2] cycloadditions of achiral aldehydes **10a–e** with (trimethylsilyl)ketene **2** using enantiomerically pure methylaluminoimidazolines **9a–d** prepared from the appropriate bis-sulfonamides **8a–d** (Scheme 2 and Table 1). The reactions were performed according to the following general procedure:

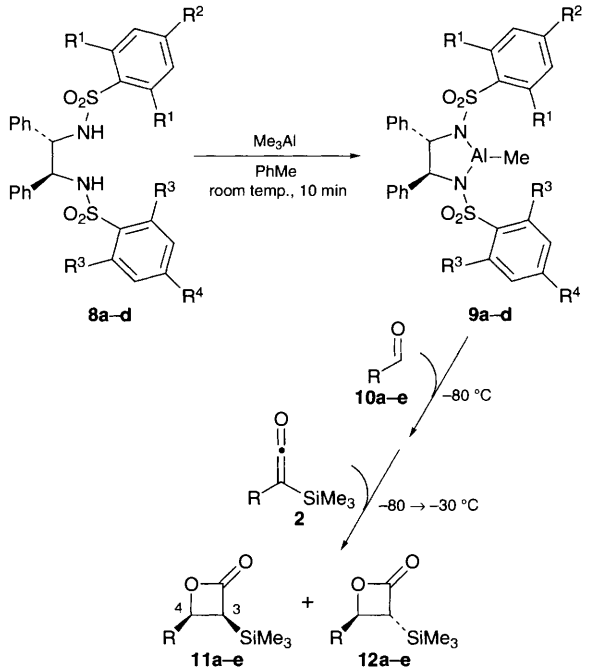
To a solution of the bis-sulfonamide **8** (0.15 mmol, 30 mol%) in dry toluene (4 ml), under nitrogen at room temperature was added trimethylaluminium (0.15 mmol) and the complex stirred at room temperature for 10 min. After cooling the catalyst to −80 °C, the aldehyde (0.5 mmol) in toluene (1 ml) was added. After 5 min (trimethylsilyl)ketene (0.55 mmol) in toluene (1 ml) was added dropwise. The reaction was stirred at −80 °C initially and then warmed gradually to −30 °C until complete consumption of the aldehyde as indicated by TLC, when it was quenched with water (1 ml). Standard aqueous workup followed by column chromatography (SiO_2, ether–hexanes) gave the pure *cis*-oxetanone **11** and recovered bis-sulfonamide ligand (up to 95% recovery).



Scheme 1

From Table 1 it can be seen that the cycloadditions occur in moderate to good yields with the *cis*-adducts **11** being formed preferentially in every case. Enantiomeric excesses range from 30–83% the most favourable substrates being aryl acetaldehydes **10c** and **10e** (entries 4, 8 and 12). Even the sterically non-hindered dodecanal **10b** was transformed to α-silyloxetanone **11b** in up to 48% ee (entries 7 and 15). Reaction times range from a few minutes up to 3 h and are heavily dependent on the nature of the catalyst but less so on the aldehyde. In many cases, the reactions progress with around 30 mol% of the catalyst. With the bis-trifluoromethylsulfonamide, 20 mol% of catalyst was sufficient but the enantioselectivity was poor. With less than 20 mol% catalyst the reaction did not go to completion.

The absolute configuration of the α-silyloxetanones **11a–e** was ascertained by desilyation with tetrabutylammonium fluoride in THF at −90 °C (90% yield) followed by hydrolysis with sodium hydroxide in methanol. The optical rotation of the resultant β-hydroxy acids was compared with authentic samples prepared by asymmetric reduction of the corresponding β-keto esters.[11,12]



8,9	R1	R2	R3	R4
a	Me	Me	Me	Me
b	Me	But	Me	But
c	Pri	Pri	Me	Me
d	Pri	Pri	Me	But

10,11,12	R
a	*c*-hex
b	$C_{11}H_{23}$
c	$PhCH_2$
d	$PhCH_2CH_2$
e	*p*-$MeOC_6H_4CH_2$

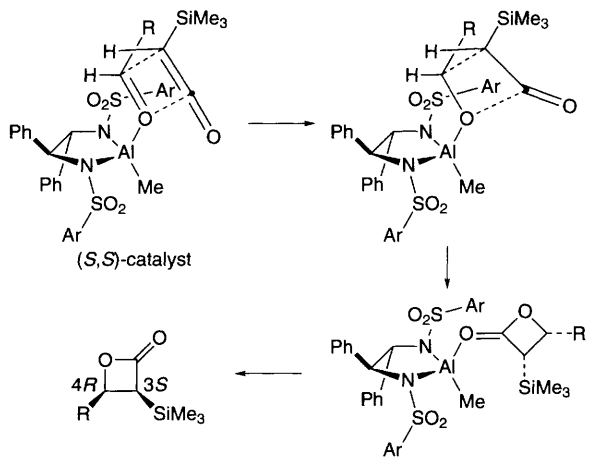
Scheme 2

The bis-sulfonamide ligands **8a–d** are easily synthesised in 90% yield from the enantiomerically pure 1,2-diphenylethane-1,2-diamine and the appropriate sulfonyl chlorides (NEt_3 and catalytic DMAP in dichloromethane).[13] *ortho* Substituents were essential for high enantio-induction but *para* substitution was also highly significant for some substrates (entries 1 and 4). The steric limits of the system are exceeded with bis-2,4,6-tri-*iso*-propylbenzenesulfonamide which is completely unreactive even with 100 mol% catalyst. However, non-C_2-symmetric catalysts such as **9c** and **9d** with a single tri-*iso*-propylbenzene-sulfonamide substituent gave selectivities that equalled or surpassed those obtained with the C_2-symmetric variants (entries 9–16).

Table 1 Asymmetric [2+2] cycloaddition of (trimethylsilyl)ketene to aldehydes

Entry	Catalyst **9** (equiv.)	Aldehyde **10**	Products (**11**:**12**)[a]	Yield (%)[b]	ee (%)[c]
1	**a** (0.44)	**c**	100:0	43	40
2	**a** (0.61)	**d**	100:0	43	44
3	**a** (0.98)	**a**	95:5	57	55
4	**b** (0.50)	**c**	83:17	56	83
5	**b** (0.30)	**d**	90:10	80	44
6	**b** (0.33)	**a**	85:15	32	68
7	**b** (0.29)	**b**	94:6	67	47[d]
8	**b** (0.30)	**e**	99:1	77	83[d]
9	**c** (0.29)	**c**	79:21	82	62
10	**c** (0.25)	**d**	90:10	85	30
11	**c** (0.51)	**a**	77:23	57	53
12	**d** (0.30)	**c**	75:25	72	82
13	**d** (0.29)	**d**	94:6	82	36
14	**d** (0.33)	**a**	69:31	43	67
15	**d** (0.30)	**b**	82:18	67	48[d]
16	**d** (0.29)	**e**	70:30	81	75[d]

[a] *cis*:*trans* ratios determined by ^1H NMR analysis of the crude reaction mixture. [b] Yields refer to isolated and purified cycloadducts. [c] ee determined by HPLC (Daicel Chiralpak AD; 2% isopropyl alcohol–hexane; 1.0 ml min^{-1}; 210 nm) unless otherwise stated. [d] ee determined by ^1H NMR analysis of the $CHSiMe_3$ doublet in the presence of 2 equiv. of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[23]



Scheme 3

The absolute stereochemistry of the cycloaddition can be rationalised in terms of the transition state shown in Scheme 3 which assumes a concerted but asynchronous reaction path involving a synperiplanar approach of a nucleophilic ketene to an electrophilic aldehyde coordinated to the Lewis acid. This synperiplanar approach (near coplanarity of the four participating atoms) and prior formation of the C–C bond are in accord with recent *ab initio*[14,15] and semi-empirical[16] calculations.

In conclusion we have accomplished the first catalytic asymmetric synthesis of 3-(trimethylsilyl)oxetan-2-ones *via* [2+2] cycloaddition of a silylketene with an aldehyde which, in effect, corresponds to an asymmetric aldol reaction. The stability of silylketenes offers distinct advantages in [2+2] cycloadditions compared with ketene itself.[17–19] Furthermore, we have extended the range of asymmetric reactions catalysed by bis-sulfonamide substituted metalloimidazolines which include the Diels–Alder cycloaddition,[13] aldol reactions,[13] allylmetallations,[20] nucleophilic additions of alkylzincs to aldehydes[21] and cyclopropanation.[22]

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