Efficient synthesis of chrysanthemate precursor from chiral *p*-tolyl β-(trimethylsilyl)ethyl sulfoxide

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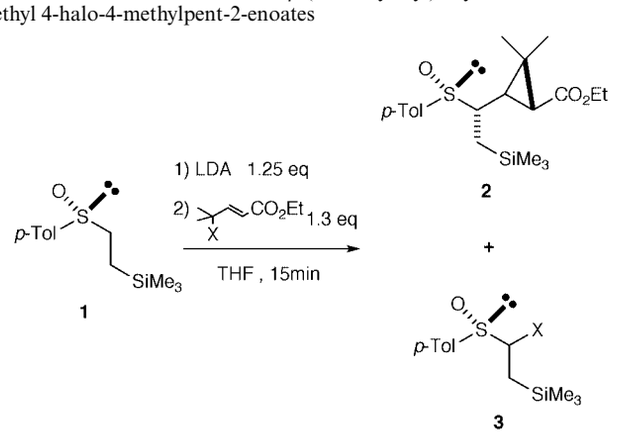
Reaction of α-lithio-β-silylethyl sulfoxide with ethyl 4-bromo- or 4-chloro-4-methylpent-2-enoate gives the cyclopropanecarboxylate as a single diastereomer which is converted to (1*R*)-*trans*-2-formyl-3,3-dimethylcyclopropanecarboxylate in high overall yield.

(1*R*)-*trans*-Chrysanthemate derivatives are more active than the (1*S*)-isomers to insects and less toxic to mammals. Asymmetric syntheses of chrysanthemate derivatives have been extensively studied;[1] *e.g.* catalytic asymmetric cyclopropanations of 2,5-dimethylhexa-2,4-diene with metal carbenoides using chiral ligands such as chiral Schiff bases, bisoxazolines, and salen complexes.[2] In particular, Masamune *et al*. have succeeded in achieving a good level of *trans*- and enantioselectivity using chiral bis(4,5-diphenyl-1,3-oxazolinyl)methane.[3] A diastereoselective synthesis of *cis*-chrysanthemates has been reported with moderate stereoselectivity through intramolecular cyclization using oxazolidinone as a chiral auxiliary.[4] Recently, we reported a highly stereoselective β-addition reaction of the α-sulfinyl carbanion derived from β-(trimethylsilyl)ethyl sulfoxide to α,β-unsaturated carbonyl compounds, and stereoselective intramolecular cyclization.[5] We now report an efficient stereoselective synthesis of a chrysanthemate precursor, ethyl *trans*-formyl-3,3-dimethylcyclopropanecarboxylate, using *p*-tolyl β-(trimethylsilyl)ethyl sulfoxide **1**.

The reaction of α-lithio-β-silylethyl sulfoxide[6] with ethyl 4-halo-4-methylpent-2-enoates was examined under various conditions. The results are summarized in Table 1.

A THF solution of *p*-tolyl β-(trimethylsilyl)ethyl sulfoxide **1** was treated with 1.25 equiv. of lithium diisopropylamide at −78 °C. After 5 min 1.3 equiv. of ethyl 4-bromo-4-methylpent-2-enoate was added rapidly and the mixture was stirred for 15 min. The reaction gave the cyclopropanecarboxylate **2**† and the brominated sulfoxide **3**‡ in 79 and 18% yields, respectively. Various reaction conditions have been tried to suppress the formation of **3** as shown in Table 1. When HMPA or copper iodide was added to the reaction mixture, the cyclization product **2** was obtained in 5 or 50% yield, respectively (entries 2 and 3). The reaction was carried out at −105 °C or at 0 °C giving **3** as a major product (entries 4 and 5). On the other hand, the cyclopropanecarboxylate **2** was formed in 84% yield without formation of the chlorinated compound when ethyl 4-chloro-4-methylpent-2-enoate was used (entry 6). The obtained cyclopropanecarboxylate **2** was found to be a single diastereomer. None of the other possible diastereomers was detected by ^{1}H NMR spectroscopy or HPLC analysis of the crude mixture. The *trans* configuration of **2** was assigned on the basis of the value of the vicinal coupling constant (5.4 Hz). Unfortunately, single crystals of **2** for the X-ray diffraction were not obtainable. Instead, the stereochemistry of the cyclopropanecarboxylate **4**,[5] obtained as a single diastereomer in a similar reaction between α-lithio-β-silylethyl sulfoxide and ethyl 4-bromobut-2-enoate, has been established by a single-crystal X-ray structure determination. Thus, the stereochemistry of **2** was reasonably assumed as (R_S,1′*R*,1*R*,2*R*) on the basis of the unequivocally confirmed stereochemistry of **4**.

Table 1 Reaction of α-lithio-β-(trimethylsilyl)ethyl sulfoxide with ethyl 4-halo-4-methylpent-2-enoates

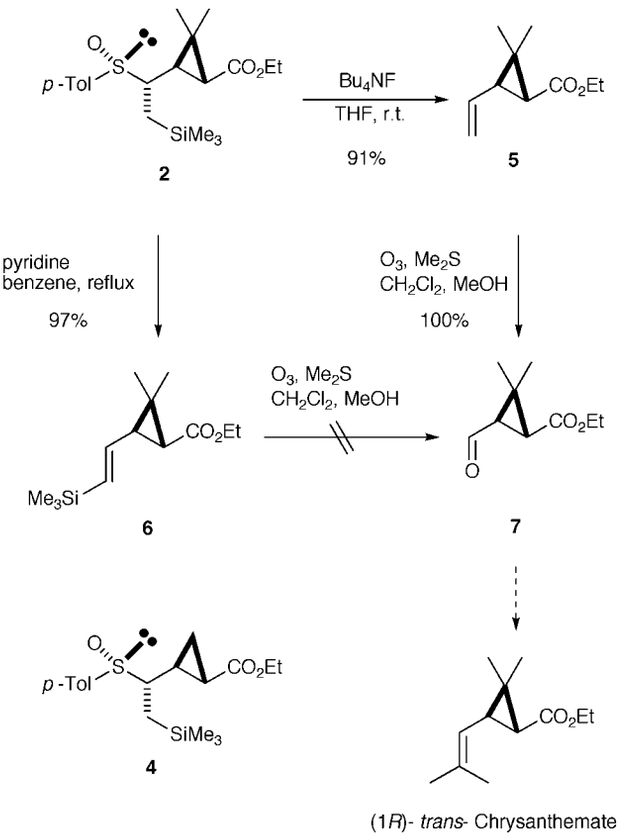


Entry	X	*T*/°C	Additive	Yield (%) **2**	**3**
1	Br	−78	—	79	18
2	Br	−78	HMPA	5	60[a]
3	Br	−78	CuI	50	45
4	Br	−105	—	24	64
5	Br	0	—	30	60
6	Cl	−78	—	84	0

[a] Sulfoxide **1** was recovered in 30% yield.

Remarkably, the chiral sulfoxide can completely control the stereochemistry of three consecutive chiral centers to be formed. The chiral sulfinyl group together with the β-trimethylsilyl group functions as a vinyl anion equivalent, not only inducing the stereoselectivity in the conjugate addition and cyclization reaction but also forming a double bond regioselectively from the product. Treatment of **2** with tetrabutylammonium fluoride in THF at room temperature afforded the β-eliminated compound **5** in 91% yield (Scheme 1). Thermal treatment of a benzene solution of **2** for 1 h in the presence of pyridine gave the product **6** as a mixture of *E* and *Z* isomers in a ratio of 63 : 37 in 97% yield.

We confirmed that no epimerization occurred during the conversion of **2** into homoallylic carboxylates **5** and **6** by the vicinal coupling constants in the ^{1}H NMR spectra. Ozonolysis of the vinylsilane **6** was not successful under various conditions. The olefin **5** was treated with O_3 in a mixture of CH_2Cl_2 and MeOH at −78 °C for 3 h and subsequently with Me_2S to give ethyl (1*R*)-*trans*-2-formyl-3,3-dimethylcyclopropanecarboxylate **7** quantitatively. The chemical shifts and the coupling constants of the ^{1}H NMR spectrum and the IR spectral data of **7** were in good accord with those reported.[7] The present procedure provides an efficient total synthesis of 1*R*-*trans*-chrysanthemates, since the aldehyde **7** can be easily transformed into them.[8]



Scheme 1

Notes and references

† The compounds **2**, **4**, **5** and **6** gave satisfactory microanalytical and spectroscopic (IR, ^{1}H NMR, ^{13}C NMR, *m*/*z*) data.

‡ Obtained in a diastereomer ratio of 59 : 41.

§ Selected data for **7**: TLC R_f = 0.69 (Hexane–AcOEt = 70 : 30); $[a]_D^{21.0}$ −29.3 (*c* 0.246, acetone); δ_H 1.25 (t, 3H, *J* = 7.1 Hz, -OCH_3), 1.32 (s, 3H, -CH_3), 1.40 (s, 3H, -CH_3), 2.41 (d, 1H, *J* = 4.5 Hz, -CO-CH-), 2.44 (dd, 1H, *J* = 2.0, 4.5 Hz, -CH-), 4.20 (q, 2H, *J* = 7.1 Hz, -OCH_2-), 9.60 (d, 1H, *J* = 2.0 Hz, -CHO); δ_C 14.3, 20.5, 21.6, 26.0, 30.9, 33.4, 60.4, 171.6; IR (neat) 2970, 1730, 1460, 1450, 1400, 1250, 1200, 1130, 1100, 1030 cm^{-1}; SIMS *m*/*z* (rel. intensity) 170.1 (M^+, 43), 149.1 (100), 113.0 (21), 57.0 (40), 28.0 (55); Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29; Found: C, 63.29; H, 8.51%.

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