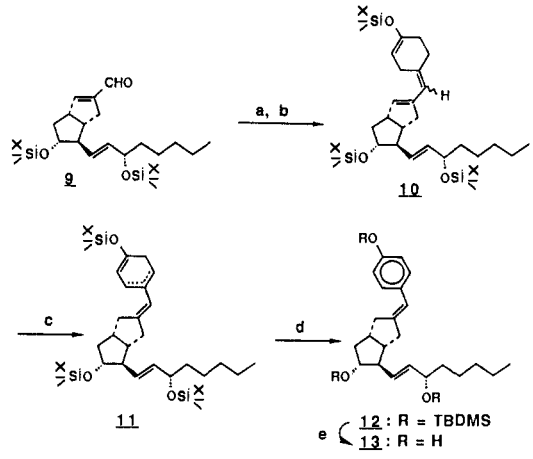
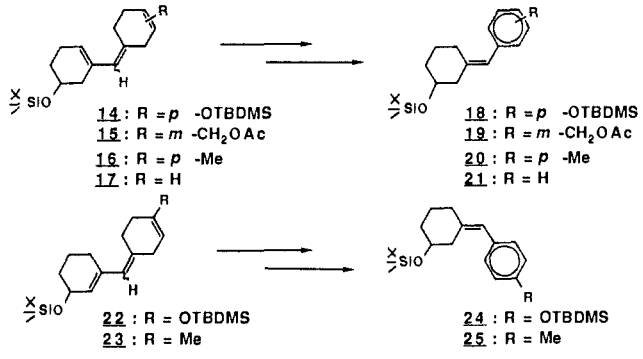
Scheme II[a]



[a] (a) TBDMSO—⟨⟩—SO_2Tol, *n*-BuLi, THF, −50 °C, then Ac_2O; (b) Na-Hg (5%), NaH_2PO_4, MeOH; (c) (naphthalene)$Cr(CO)_3$, acetone, 19 °C; (d) MnO_2, molecular sieves 4Å, benzene reflux; (e) *n*-Bu_4NF, THF, room temperature.

Scheme III



of the stereochemistry of the starting triene **2**, only **4** was expected to be formed stereospecifically (Scheme I).

As expected, treatment of **2** (*E*:*Z* = ca. 1:1) with (naphthalene)$Cr(CO)_3$ (20 mol %) in acetone at 19 °C for 22 h (argon atmosphere) afforded a mixture of **4** and **6** in a ratio of 8:1 (100%), which was then converted to **8** (*E*) in 87% yield as a single product by reaction with activated MnO_2. The *Z*-isomer was also prepared from **8** by photochemical technique. In comparison of **8** with the Z-isomer, the stereospecificity of the present reaction was unequivocally confirmed. **8** should be the versatile key intermediate for **13** and the related compounds.[9,11]

The methodology described above was further applied to **10** having the ω-chain. The enal **9**[10] was transformed into **10** (79%, *E*:*Z* = ca. 1:1). Treatment of **10** with (naphthalene)$Cr(CO)_3$ (20 mol %) in acetone at 18–20 °C for 2 h gave a mixture of the isomerized products **11**, which underwent aromatization to give **12** stereospecifically (58% overall yield from **10**). The stereospecificity was confirmed by the same technique as described above. **12** was converted to **13**[11] (89%) by treatment with fluoride anion (Scheme II).

Finally it was found that the six-membered ring compounds with an aryl-substituted exocyclic olefin **18** (73%), **19** (76%), **20** (79%), **21** (73%), **24** (73%), and **25** (88%) could be also obtained stereospecifically from the corresponding partially conjugated trienes **14**, **15**, **16**, **17**, **22**, and **23** (in every case, *E*:*Z* = ca. 1:1), demonstrating the generality of the present methodology (Scheme III).

In conclusion, we have developed the conceptually new method for the stereospecific synthesis of aryl-substituted exocyclic olefins by utilizing the room temperature 1,5-hydrogen shift of conjugated dienes catalyzed by (naphthalene)$Cr(CO)_3$ complex. Further studies are in progress.

Supplementary Material Available: Experimental data for **1–8**, spectral data for **18** and **24**, and synthetic routes to **14**, **15**, **16**, **17**, **22**, and **23** (5 pages). Ordering information is given on any current masthead page.

(8) Frankel, E. N. *J. Catal.* **1972**, *24*, 358.
(9) For selective deprotection of alcoholic and phenolic silyl ethers, see: Collington, E. W.; Finch, H.; Smith, I. J. *Tetrahedron Lett.* **1985**, *26*, 681.
(10) Mase, T.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1984**, *25*, 5087 (now commercially available from Nissan Chemical Industries, Ltd, Japan).
(11) Biological activities of **13** and the related compounds will be reported in due course.

Diastereoselective Photodeconjugation of α,β-Unsaturated Esters

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Ultraviolet light irradiation of aliphatic α,β-unsaturated esters having one hydrogen atom in the γ-position led to the corresponding deconjugated esters through a dienol intermediate.[2,3] This reaction was sufficiently general to be proposed as a synthetic procedure for the preparation of β,γ-unsaturated esters.[4] If the starting material bears one α-alkyl substituent, the dienol intermediate is prochiral, and we have shown precedently that enantioselective protonation of the α-carbon could be observed in an aprotic solvent containing small amounts of chiral aminoalcohols.[5] Thus, optically active β,γ-unsaturated esters were obtained through an asymmetric bimolecular reaction. A model involving a cyclic transition state was proposed to explain the chiral discrimination.[5b]

Photochemical studies of an intramolecular asymmetric induction in solution have been mainly restricted to photocycloadditions.[6,7] Thus, we chose to determine the importance of an

(1) As a former Corey's research group member, J.M. dedicates this paper in a tribute to E. J. Corey on the occasion of his 60th birthday.
(2) (a) Jorgenson, M. J. *Chem. Commun.* **1965**, 137. Jorgenson, M. J. *J. Am. Chem. Soc.* **1969**, *91*, 198. (b) Barltrop, J. A.; Wills, J. *Tetrahedron Lett.* **1968**, 4987. (c) Jorgenson, M. J.; Gundel, L. *Tetrahedron Lett.* **1968**, 4991. (d) Itoh, M.; Tokuda, M.; Kihara, K.; Suzuki, A. *Tetrahedron* **1968**, *24*, 6591. (e) Itoh, M.; Tokuda, M.; Seguchi, K.; Taniguchi, K.; Suzuki, A. *Kogyo Kagaku Zasshi* **1969**, *72*, 219.
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Table I. Intramolecular Chirality Induction in Photodeconjugation of **1a–e**

ester	run	solvent	T, °C	additive (equiv)	% yield	% de[a]	conf C_α[b]
1a	1	hexane	−78	MeOH (1)	80	19	*S*
1b	2	hexane	−78	MeOH (1)	80	0	
1c	3	hexane	−40	H_2O (saturated)	85	22	*S*
	4	CH_2Cl_2	−40	H_2O (saturated)	67	38	*S*
	5	MeOH	−40		56	55	*S*
1d	6	MeOH	+25		83	73	*R*
	7	hexane	−40	HN(*i*-Pr)$_2$ (0.1)	76	88	*R*
1e	8	MeOH	+25		81	68	*S*
	9	hexane	+25	HN(*i*-Pr)$_2$ (0.1)	78	70	*S*
	10	hexane	−40	HN(*i*-Pr)$_2$ (0.1)	80	85	*S*
	11	hexane	−78	HN(*i*-Pr)$_2$ (0.1)	82	88	*S*

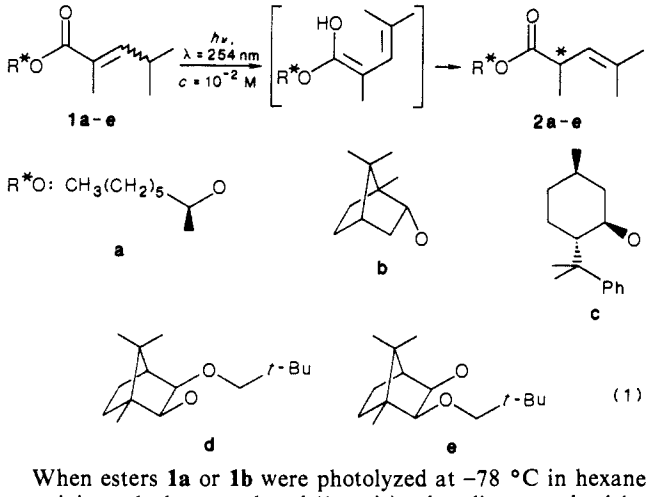
[a] de's were determined on a 80 MHz NMR for esters **2a,b** in the presence of Eu(hfc)$_3$ and on a 300 MHz NMR for esters **2c–e**. [b] Configuration of C_α of **2a–e** was determined by chemical correlations. These esters were hydrogenated on PtO_2 and compared with analogous esters obtained from (*S*)-(+)-2,4-dimethylpentanoic acid.[9]

Table II. Double Asymmetric Induction in Photodeconjugation of **1a–e** and Enantioselective Photodeconjugation of **1f**

ester	run	solvent	T, °C	additive (equiv)	% yield	% de[a]	conf C_α[b]
1a	12	hexane	−78	(−)-ephedrine (0.1)	78	9	*R*
	13	CH_2Cl_2	−78	(−)-ephedrine (0.1)	83	19	*R*
	14	CH_2Cl_2	−78	(+)-ephedrine (0.1)	78	17	*S*
1b	15	CH_2Cl_2	−78	(−)-ephedrine (0.1)	85	33	*R*
	16	CH_2Cl_2	−78	(+)-ephedrine (0.1)	83	11	*S*
1c	17	CH_2Cl_2	−40	(−)-ephedrine (0.1)	63	10	*S*
	18	CH_2Cl_2	−40	(+)-ephedrine (0.1)	46	64	*S*
1d	19	CH_2Cl_2	−40	(−)-ephedrine (0.1)	88	67	*R*
	20	CH_2Cl_2	−40	(+)-ephedrine (0.1)	86	31	*R*
1e	21	CH_2Cl_2	−40	(−)-ephedrine (0.1)	80	28	*S*
	22	CH_2Cl_2	−40	(+)-ephedrine (0.1)	78	72	*S*
1f	23	CH_2Cl_2	−78	(+)-ephedrine (0.1)	63	20[c]	*S*

[a,b] See Table I. [c] ee; from ref 5b.

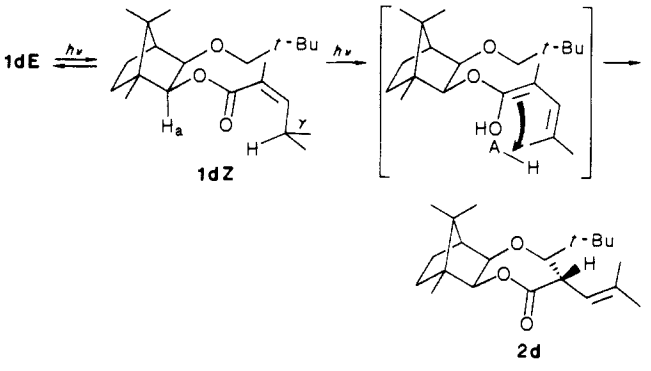
intramolecular asymmetric induction during the protonation step of a photodienol. For this purpose, the photodeconjugation of chiral esters of 2,4-dimethyl-2-pentenoic acid was investigated (eq 1, Table I). We have also examined the effect of a double asymmetric induction[8] when these esters were irradiated in the presence of a chiral aminoalcohol (Table II).



When esters **1a** or **1b** were photolyzed at −78 °C in hexane containing anhydrous methanol (1 equiv), a low diastereoselectivity of **2a** and **2b** was observed (runs 1 and 2). Such a result was not surprising if one considers the small steric differences induced by the alkoxy group on the two diastereofaces of the prochiral center in the photodienol obtained either from **1a** or **1b**.

Esters **1c–e**, where one diastereoface of the corresponding dienol is selectively crowded by the alkoxy group, were examined next. A diastereoisomeric excess (de) up to 55% could be obtained from the phenyl menthyl ester **1c**[10] (run 5). From more hindered esters

Scheme I. Intramolecular Chirality Induction in Photodeconjugation of **1d**



1d,e,[11] high selectivities (de = 88%) were obtained particularly in the presence of diisopropylamine (runs 7 and 11). The configuration of the major diastereoisomer **2c–e** suggested a rationalization according to Scheme I. In the ground state, the favored conformation of the ester adopts indeed a syn periplanar arrangement of the carbonyl group and the H_a–C–O bonds.[12] Furthermore, the photodienol is formed from the *Z* isomer in an s-cis conformation.[2-4] So, the results are best explained by a selective protonation of the photodienol[13] or the corresponding dienolate[3,13,14] on the less hindered side, in a conformation directly deduced from **1c–e** after a γ-hydrogen abstraction.[15]

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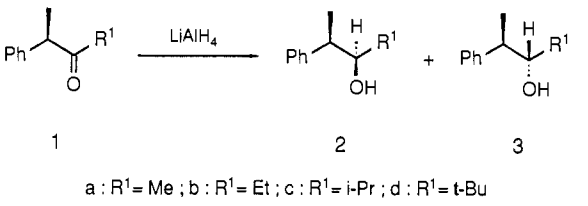
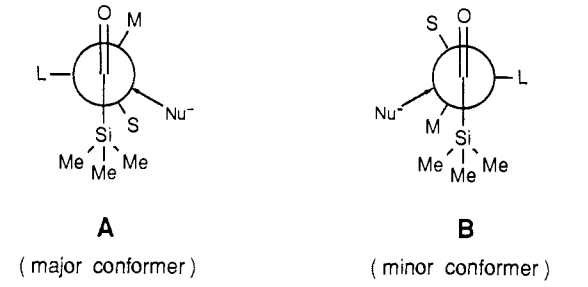
When esters **1a,b** were irradiated in the presence of ephedrine (runs 12-16), not only were the observed de very close to the ee obtained by irradiation of an achiral ester such as isopropyl 2,4-dimethyl-2-pentenoate **1f**[5b] (run 23) but also the configuration of the new asymmetric center could be deduced from the model proposed to rationalize enantioselectivities.[5b] When bulky esters **1c-e** were irradiated, the protonation, either with (+)- or (-)-ephedrine, occurs on the less hindered side. When the configuration of the new asymmetric center was expected to be the same, that is, either from the protonation of the less crowded face of the chiral dienol or as determined from the model developed for the enantioselective photodeconjugation of achiral esters in the presence of aminoalcohols (runs 18, 19, and 22), the de was similar to those observed in the absence of chiral additives. By contrast, where mismatched interactions were expected (runs 17, 20, and 21), the observed diastereoselectivities were considerably lowered.

Scheme I



Scheme II



High Diastereofacial Selectivity in Nucleophilic Additions to Chiral Acylsilanes[1]

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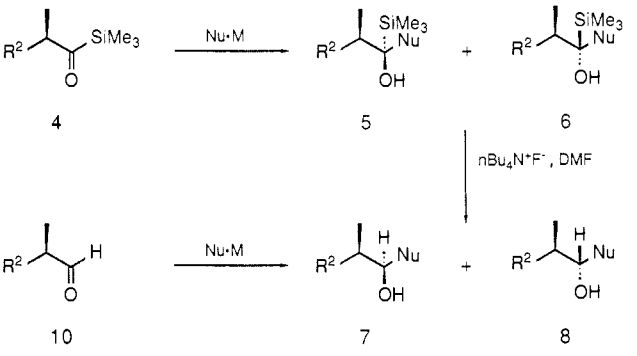
Asymmetric induction in nucleophilic additions to chiral aldehydes and ketones is a topic of great interest, and chiral aldehydes have been used more conveniently for the construction of many useful chiral synthons in natural product syntheses.[2] However, when the α-chiral carbonyl compounds have no ability to coordinate with metals, the 1,2-asymmetric induction is generally modest, and some more elegant approaches have been advanced recently.[2,3] In our case, it became necessary to explore more effective construction of syn moiety in the total synthesis of a new macrolide, rhizoxin.[4]

In this communication, we report that α-chiral acylsilanes show exceptional diastereofacial preferences in nucleophilic additions followed by stereospecific protiodesilylation with F^- anion to afford Cram-type isomers **7**.

The important observation and explanation by Chêrest, Felkin, and Prudent that asymmetric induction increases markedly in the series of compounds **1** (R^1 = Me, Et, *i*-Pr, and *t*-Bu) as the size of R increases[5] suggests to us to start with an aldehyde equivalent having a bulky group R^1 (Scheme I), and, chiral acylsilanes[6] were selected to be one of the most ideal chiral carbonyl compounds because of the following three characteristic points; (1) the trimethyl silyl group may be bulky[7] enough to cause strong stereodifferentiation between A and B (Scheme II), (2) the silyl group can be stereospecifically replaced with hydrogen after nucleophilic additions, and (3) the acylsilanes and α-hydroxysilanes are both considered to be easy to handle and stable (Scheme III). Thus, α-chiral acylsilane **4** (R^2 = Ph)[8] was treated with *n*-BuLi in THF at -78 °C for 5 min, affording a mixture of α-hydroxysilanes[9] **5** and **6**. The diastereomer ratio was estimated to be >100:1.[10] Subsequent treatment of the crude α-hydroxysilanes with TBAF (n-$Bu_4N^+F^-$)[11,12] in DMF at room temperature gave the known desilylated products **7** and **8** in a ratio of >100:1.[13,14] For comparison, the syn and anti isomers **7** and **8** were obtained from the reaction of **10** (R^2 = Ph) and *n*-BuLi in a ratio of 5:1.[15] On the

Scheme III



(1) Dedicated to Prof. E. J. Corey of Harvard University on the occasion of his 60th birthday.

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(4) Nakada, M.; Urano, Y.; Kobayashi, S.; Ohno, M.; Iwasaki, S.; Okuda, S. *29th Symposium on the Chemistry of Natural Products*; Aug. 26-28, 1987; *Sapporo. Abstr.* p 110.

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(9) α-Hydroxysilanes were prepared and well characterized in the study of Brook rearrangement, see: Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77 and references cited therein.

(10) The ratio was determined by 400 MHz ^1H NMR analysis of the reaction mixture.

(11) TBAF (n-$Bu_4N^+F^-\cdot 3H_2O$, purchased from Aldrich) was used. TBAF (1 M solution in THF, Aldrich) was also effective. In THF, the reaction proceeded more slowly.

(12) During the present methdology was developed as an essential part for the total synthesis of a new macrolide, rhizoxin, a high stereoselective addition of nucleophiles to 2-(phenylthio)-3-phenyl-1-(trimethylsilyl)-1-propanone, see: Reich, H. J.; Holton, R. C.; Borkowsky, S. L. *J. Org. Chem.* **1987**, *52*, 314. This prompted us to publish our own results.[4]

(13) The ratio was determined by 400 MHz ^1H NMR and GLC analysis.

(14) For base-induced protiodesilylation of α-hydroxysilanes in cyclic system, see: Hudrlik, P. F.; Hudrlik, A. M.; Kulkarni, A. K.; *J. Am. Chem. Soc.* **1982**, *104*, 6809.

(15) (a) Of using crown ethers, see: Yamamoto, Y.; Maruyama, K.; *J. Am. Chem. Soc.* **1985**, *107*, 6411. (b) Of using R_4Pb, see: ref 3c.

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