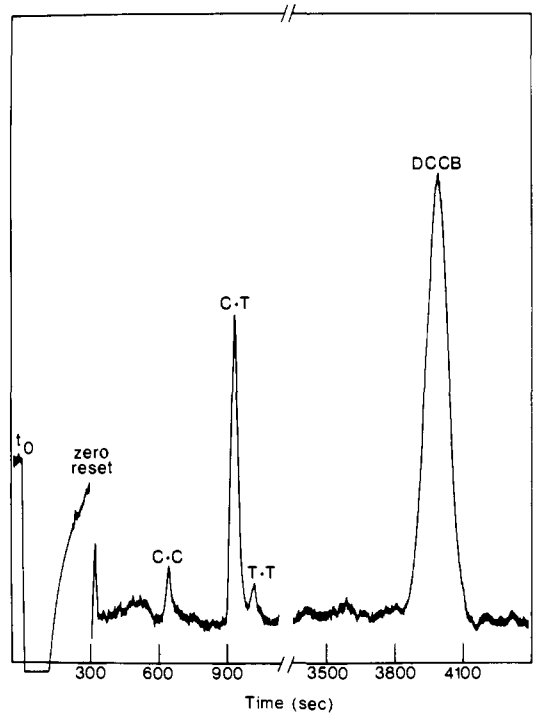

Figure 1. Gas chromatogram of reactant and product mixture after 10 pulses of irradiation at 8.2 J/cm^2 of 0.267 torr of *cis*-3,4-dichlorocyclobutene. The chromatogram was taken on a 10-ft × 0.25-in. β,β'-oxydipropionitrile column at 70 °C, with a detector temperature of 200 °C and an amplifier setting of 2 × 10^{-11} A/mV F.S. Sample was injected at t_0. The peak at 300 s is a column impurity.

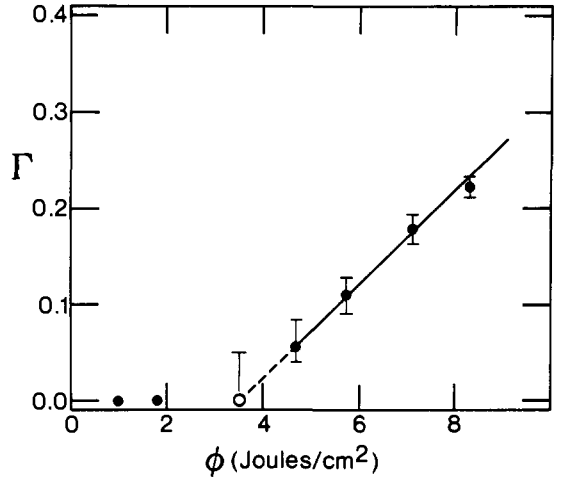

Figure 2. Fraction of forbidden products vs. laser fluence. The open circle is the measurement of Danen et al.[8]

The observation that the conversion per pulse increases with reactant pressure indicates that collisions play a major role in the reaction mechanism. This behavior is expected even at low pressures for the following reason. Isomerization reactions are unique in that, unlike fragmentation reactions, the nascent products cannot dissipate their energy (in excess of 60 kcal/mol for CC and TT)[4] except through collisions and radiation. Collisions of vibrationally hot products with excited reactants lead to further reaction, the products of which are able to continue the "energy chain". The length of this chain, and hence the conversion per pulse, should increase with reactant pressure. The expected effect of the buffer gases is to shorten the chain, reduce Γ, and increase the CC/TT ratio by lowering the energy content of the molecules involved.

It has been conjectured that vibrational excitation of the reactant can result in symmetry forbidden products being formed in a concerted process on the ground electronic surface. The production of a large fraction of the sterically unfavorable CC isomer (CC/TT > 1) argues against such a concerted mechanism in the present study.[4a] More likely explanations for the forbidden products are either direct formation of CC and TT from a biradical intermediate[12] or secondary isomerization of vibrationally hot CT formed in a concerted step. We note that secondary absorption of photons by the nascent primary product is unlikely to be important because of the collisional nature of the mechanism. Additional studies are in progress to elucidate further the mechanism.

Acknowledgment. We thank Professor John Brauman for very helpful discussions. Support by the National Science Foundation (Grant CHE78-07998) is gratefully acknolwedged.

(12) Stephenson, L. M., Jr.; Brauman, J. I. *Acc. Chem. Res.* **1974**, *7*, 65.

Erythro-Selective Aldol Reaction via Tris(dialkylamino)sulfonium Enolates[1]

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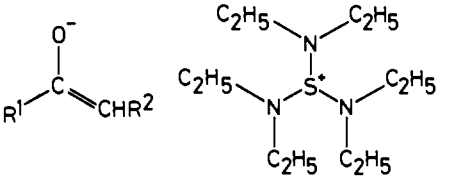
Recently we have demonstrated that reaction of an enol silyl ether and tris(diethylamino)sulfonium (TAS) difluorotrimethylsiliconate as a fluoride ion source, generates the TAS enolate depicted in structure **1**.[2] The anionic moiety in **1** in THF

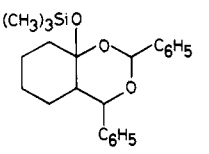


1

solvent has proved to possess negligible bonding interaction with the TAS countercation and acts as a highly nucleophilic species.[1,2] We report here a stereoselective aldol reaction of such a TAS enolate (Scheme I), which provides a new means for acyclic stereoselection.[3]

Aldol reaction of the TAS enolate **1** and aldehyde substrates does not take place smoothly, because the equilibrium of eq 2 in Scheme I lies so far to the left.[2,4] In addition, the aldol anion **5** in certain cases reacts with another aldehyde molecule to give the enolate/aldehyde 1:2 condensation product.[5] However, the silyl fluoride **4** or enol silyl ether **2** present in the reaction system can trap effectively the aldol anion **5** to give the aldol silyl ether **6** (eq 3 or 4).[6] Thus, when a mixture of an (*E*)- or (*Z*)-enol silyl

(1) Superanions. 3. Part 2: Noyori, R.; Nishida, I.; Sakata, J. *Tetrahedron Lett.* **1980**, *21*, 2085.
(2) Noyori, R.; Nishida, I.; Sakata, J.; Nishizawa, M. *J. Am. Chem. Soc.* **1980**, *102*, 1223.
(3) Review: Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2.
(4) Ingold, C. K. "Structure and Mechanism in Organic Chemistry", 2nd ed.; Cornell University Press: Ithaca, 1969; Chapter 13.
(5) For instance, the reaction of 1-(trimethylsiloxy)cyclohexene and benzaldehyde afforded the adduct i.



i

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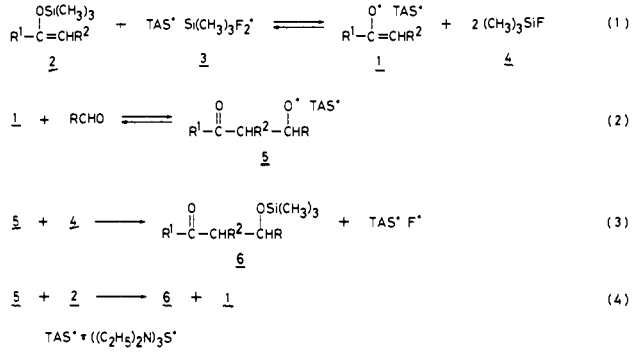
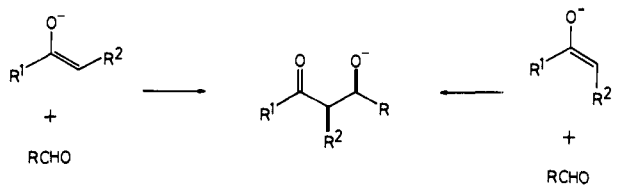
Scheme I



Scheme II

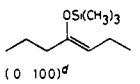
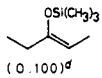
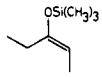
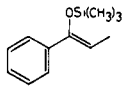
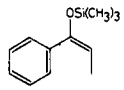
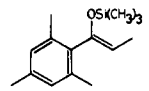
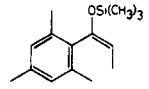


ether **2**, an aldehyde (1.1–1.4 equiv), and a catalytic amount (0.01–0.1 equiv) of TAS difluorotrimethylsiliconate (**3**)[7] in THF was allowed to stand at low temperatures, the corresponding β-trimethylsiloxy ketone **6** was obtained. In some cases addition of an excess amount of the silyl fluoride **4** (up to 10 equiv) was required to obtain **6** in high yield. Removal of the silyl group with dilute hydrochloric acid afforded the β-hydroxy ketone. The stereochemical assignment (threo or erythro[8]) was made by ^{1}H NMR, particularly using the well-accepted $J_{threo} > J_{erythro}$ relationship.[10] Some representative reactions are summarized in Table I.

The erythro aldols obtained as the major product were kinetically controlled ones. The fluoride ion catalyzed reaction of cyclopentanone enol silyl ethers and isobutyraldehyde at −78 °C produced the erythro adduct almost exclusively (entry 2). Under these reaction conditions, there was no apparent erythro to threo isomerization; the threo counterpart did not isomerize either. When the reaction was carried out at an elevated temperature, the degree of the stereoselectivity was reduced to some extent (entry 3; compare also entries 4 and 5). Stereochemical integrity (*E* or *Z*) of the enol silyl ethers or TAS enolate is unaffected under these conditions. Thus it is evident that the aldol reaction of the TAS enolates, irrespective to the configuration, form the erythro adducts in a stereoselective fashion (Scheme II).

Among various significant differences between the aldol chemistry of the ordinary Lewis acid coordinated enolates and of the TAS enolates, perhaps the most important is the origin of the diastereoselection. The Lewis acid complexed enolates are considered to react with aldehydes by a pericyclic process via the metal-linked six-membered-ring transition states of type **7** (M = metallic species).[10-16] Here the kinetic aldol stereoselection is

Table I. Aldol Reaction via TAS Enolates[a]

entry	enol silyl ether (*E*/*Z* ratio)[b]	aldehyde (equiv)	conditions: **4**, equiv	conditions: temp, °C (time)	% yield of product[c] (erythro/threo)[d]
1		$(CH_3)_2CHCHO$ (1.3)	10	−78 (8 h)	67[e] (100 0)[f]
2		$(CH_3)_2CHCHO$ (1.3)	10	−78 (35 min)	67[e] (100 0)[f]
3		$(CH_3)_2CHCHO$ (1.3)	10	−20 → −30 (12 h)	80 (89 11)
4	 (0 100)[d]	C_6H_5CHO (1.1)	–	−70 (30 min)[g]	65 (86 14)
5		C_6H_5CHO (1.3)	10	0 (5 min)[h]	90 (73 27)
6	 (0.100)[d]	C_6H_5CHO (1.2)	10	−78 (2 h)	89 (86 14)
7	 (70 30)[d]	C_6H_5CHO (1.3)	7	−78 (2 h)	84 (63 37)
8	 (1 99)	C_6H_5CHO (1.3)	–	−75 (1 h)	75 (95 5)
9	 (91 9)	C_6H_5CHO (1.3)	–	−73 (1 h)	78 (94 6)
10	 (2 98)	C_6H_5CHO (1.1)	–	−78 (4 h)	77[e] (95 5)
11		$(CH_3)_2CHCHO$ (1.4)	–	−70 (11 h)	25[e,i] (95 5)
12	 (97 3)	C_6H_5CHO (1.1)	–	−78 (4 h)	65[e] (95 5)
13		$(CH_3)_2CHCHO$ (1.2)	–	−70 (11 h)	17[e,i] (95 5)

[a] All reactions were carried out by using 0.1 equiv of **3** as a fluoride ion source. [b] Determined by GLC. [c] Determined by ^{1}H NMR using tetrachloroethane (δ 5.98) as an internal standard. [d] Determined by ^{1}H NMR analysis. [e] Isolated yield. [f] NMR signals due to threo isomer were not observed. [g] **3**: 0.01 equiv. [h] **3**: 0.05 equiv. [i] The reaction was very slow. A considerable amount of the starting material was recovered.

(6) (a) Kleschick, W. A.; Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247. (b) Noyori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *Ibid.* **1977**, *99*, 1265. See footnote 13.

(7) Middleton, W. J. U.S. Patent 3 940 402, 1976.

(8) The threo/erythro nomenclature for the relative configuration of compounds possessing two adjacent asymmetric centers is now in some confusion, because in many cases chemical or even formal correlation between these compounds and threose or erythrose is quite difficult. We propose the following straightforward procedure to clear this confusion. When such a diastereomeric compound is cleaved at the single bond which links the two asymmetric carbons, two prochiral, trigonal radicals are produced. Here two diastereomeric modes are possible for the recombination. The products arising from the *re* face/*re* face or *si* face/*si* face combination are referred to as threo diastereomers, and the recombination through *re*/*si* or *si*/*re* interaction affords the erythro isomers. This nomenclature procedure accommodates the customary naming for aldols[9] in most cases and, more conveniently, is applicable to the related diastereomeric compounds other than aldols (even for substances containing more than two asymmetric carbons) in which unambiguous selection of the *skeletal backbone*[9] is difficult.

(9) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E. Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(10) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310.

(11) (a) Li^+: Kleschick, W. A.; Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247. (b) Li^+: Dubois, J. E.; Fellmann, P. *Tetrahedron Lett.* **1975**, 1225. Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 8109. Meyers, A. I.; Reider, P. J. *Ibid.* **1979**, *101*, 2501. Heathcock, C. H.; White, C. T. *Ibid.* **1979**, *101*, 7076. Heathcock, C. H.; Pirrung, M. C.; Buse, C. T.; Hagen, J. P.; Young, S. D.; Sohn, J. E. *Ibid.* **1979**, *101*, 7077. Masamune, S.; Ali, S. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem.* **1980**, *92*, 573. (c) Li^+, Mg^{2+}, Zn^{2+}: ref 10.

7 8

9 10

11 12

defined by the enolate configuration; the (*E*)-enolates produce the threo aldols selectively, and the (*Z*)-enolates afford the erythro isomers as the major product. On the other hand, reaction of the TAS enolates is characterized by the great negative charge buildup in the transition state (note that in the pericyclic transition-state **7** the charge is neutralized as a whole) and the absence of any cationic species capable of assembling the enolate anion and an aldehyde substrate. As a consequence, the extended transition states of type **8**[16–19] would be favored, since the electrostatic repulsion of the negatively charged oxygens is minimized through such atomic arrangement. We consider that the observed unique stereochemical outcome, *a moderate to very high level of erythro selection which is independent* of enolate geometry, indicates the operation of the mechanism involving the extended transition states.[17,19–21] In the case of the (*E*)-enolates, the transition-state **9** leading to the erythro aldol is favored over the diastereomeric threo transition-state **10**, because the latter suffers repulsive gauche R/R^2 interaction. The erythro transition-state **11** arising from a (*Z*)-enolate is stabilized relative to the threo transition-state **12** for the same reason.

Supplementary Material Available: Spectral and analytical data for the new compounds (1 page). Ordering information is given on any current masthead page.

(12) B^{3+}: Mukaiyama, T.; Inoue, T. *Chem. Lett.* **1976**, 559. Inoue, T.; Uchimaru, T.; Mukaiyama, T. *Ibid.* **1977**, 153. Fenzl, W.; Köster, R.; Zimmerman, H.·J. *Liebigs Ann. Chem.* **1975**, 2201. Masamune, S.; Van Horn, D.; Brooks, D. W. *Tetrahedron Lett.* **1979**, 1665. Van Horn, D. E.; Masamune, S. *Ibid.* **1979**, 2229. Hirama, M.; Garvey, D. S.; Lu, L. D.·L.; Masamune, S. *Ibid.* **1979**, 3937. Evans, D. A.; Vogel, E.; Nelson, J. V. *J. Am. Chem. Soc.* **1979**, *101*, 6120. Inoue, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 174.

(13) Al^{3+}: Jeffery, E. A.; Meisters, A.; Mole, T. *J. Organomet. Chem.* **1974**, *74*, 373. Maruoka, K.; Hashimoto, S.; Kitagawa, Y.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 7705. Nozaki, H.; Oshima, K.; Takai, K.; Ozawa, S. *Chem. Lett.* **1979**, 379.

(14) Ti^{4+}: (a) Mukaiyama, T.; Narasaka, K.; Banno, K. *Chem. Lett.* **1973**, 1011. Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503. (b) Chan, T. H.; Aida, T.; Lau, P. W. K.; Gorys, V.; Harpp, D. N. *Tetrahedron Lett.* **1979**, 4029.

(15) Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

(16) Dubois, J.·E.; Fort, J.·F. *Tetrahedron* **1972**, *28*, 1665.

(17) Murata, S.; Suzuki, M; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 3248.

(18) Mulzer, J.; Brüntrup, G.; Finke, J.; Zippel, M. *J. Am. Chem. Soc.* **1979**, *101*, 7723.

(19) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.

(20) Heathcock described the involvement of the extended transition state in the reaction of an onium enolate[6a] but withdrew this postulate later.[9]

(21) The mechanism of aldol reaction of zirconium enolates is in controversy. See: (a) Evans, D. A.; McGee, L. R. *Tetrahedron Lett.* **1980**, *21*, 3975. (b) Yamamoto, Y.; Maruyama, K. *Ibid.* **1980**, *21*, 4607.

A Triply Convergent Total Synthesis of *l*(−)-Prostaglandin E_2[1]

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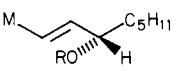
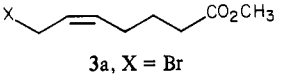
Received December 1, 1980

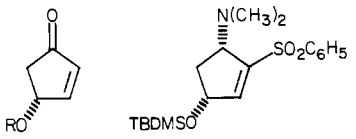
A highly desirable strategy for the synthesis of PGE_2 (**1**) involves a "triply convergent" approach. Formation of the C_{12}–C_{13} bond *and* the C_7–C_8 bond by the sequential addition of the easily available reagents **2**[2] and **3**[3] to a suitably activated, optically active



2a, M = Li
b, M = CuR
c, M = AlR_3
d, M = $Zr(Cp)_2Cl$



3a, X = Br
b, X = I



4 **5**

cyclopentene nucleus would constitute such a process. A substantial effort has been invested in using 4-alkoxycyclopent-2-enone (**4**) as the acceptor for such a conjugate-addition/alkylation sequence.[4] Although the conjugate-addition reaction (**2** + **4**) works well, subsequent enolate alkylation with the "upper side chain" reagent **3** is totally unsatisfactory.[4] At present, only indirect procedures are available for further elaboration of the resulting enolate to prostaglandin E_2 (**1**).[4] A general solution to this problem is now available through the use of chiral vinyl sulfone **5** as a substrate for the conjugate-addition/alkylation reaction.

Reaction of the optically active sulfide alcohol **6** [mp ca. 28 °C, $[\alpha]^{25}_D$ +116° (*c* 0.308, $CHCl_3$), 92% ee][5–9] with 3 equiv of

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‡A. P. Sloan Fellow, 1977–1979.

(1) Syntheses Via Vinyl Sulfones. 5. For paper 4, see J. Ponton, P. Helquist, P. C. Conrad, and P. L. Fuchs, *J. Org. Chem.*, **46**, 118 (1981).

(2) The chiral 15·(*S*)·*trans*·vinyl iodide precursor (prostaglandin numbering) to organolithium reagent **2a** is available either by classical resolution of the *trans*·halovinyl alcohol [A. F. Kluge, K. G. Untch, and J. H. Fried, *J. Amer. Chem. Soc.*, **94**, 7827 (1972)] or, more recently by enantioselective reduction of the *trans*·iodovinyl ketone with a chiral hydride reducing reagent [R. Noyori, I. Tomino, and M. Nishizawa, *J. Am. Chem. Soc.*, **101**, 5843 (1979)].

(3) (a) J. W. Patterson, Jr. and J. H. Fried, *J. Org. Chem.*, **39**, 2506 (1974); (b) J. Martel and E. Toromanoff, (Roussel·UCLAF), German Patent 2 121 361, 1970; (c) We thank Dr. Patterson for providing us the details of the experimental preparation for this material.

(4) For an in·depth discussion of the problem see (a) R. Davis and K. G. Untch, *J. Org. Chem.*, **44**, 3755 (1979); (b) J. Schwartz, M. J. Loots, and H. Kosugi, *J. Am. Chem. Soc.*, **102**, 1333 (1980).

(5) The racemic sulfide alcohol may easily be prepared on a *5-mol* scale by the method of Evans, Crawford, Fujimoto, and Thomas [*J. Org. Chem.*, **39**, 3176 (1977)].

(6) Evans and Thomas have developed a practical method for the resolution of alcohol **6** as its α·phenethylurethane derivative.[7] They have also assigned the absolute stereochemistry of the two enantiomers of alcohol **6**. [R. C. Thomas, Ph.D. Thesis, University of California, Los Angeles, CA, 1976.] We are very grateful to Professor Evans bringing this resolution procedure to our attention.

(7) Cleavage of the urethane is accomplished by the excellent procedure of Pirkle and Hauske [*J. Org. Chem.*, **42**, 2781 (1977)]. This method allows >90% recovery of the chiral α·phenethyl isocyanate for recycle purposes.

0002-7863/81/1503-2108$01.25/0