improve our knowledge of support effects in heterogeneous catalysis. Additional studies are in progress to elucidate the details of this tautomerization as well as the reactivity of these new compounds.

Acknowledgment. We gratefully acknowledge the National Science Foundation for support of this work (Grant No. CHE 8106096). R.E.S. thanks the University of Minnesota for an Institute of Technology Corporate Associate fellowship (1980–1982).

Registry No. 1, 79085-63-5; **2**, 83333-39-5; **3**, 83312-29-2; **4**, 73230-19-0; **5**, 83333-40-8; $CF_3SO_3CH_3$, 333-27-7; $PPN[Ru_5N(CO)_{14}]$, 83312-28-1; CF_3SO_3H, 1493-13-6.

Supplementary Material Available: List of the atomic coordinates and thermal parameters and the observed and calculated structure factors (8 pages). Ordering information is given on any current masthead page.

Sterochemical Variations in the Cyclocondensation of Aldehydes with Siloxydienes. An Application to the Erythronolide Series

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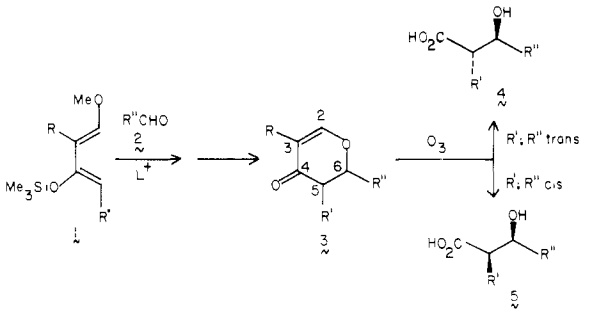
Received June 21, 1982

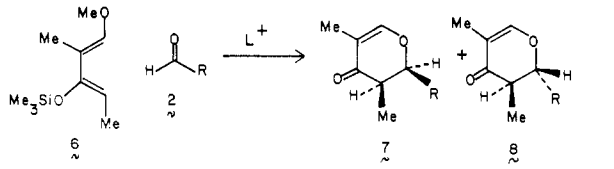
Recently, we reported on the Lewis acid (L^+) catalyzed reactions of aldehydes with siloxydienes.[1] For many applications the value of the reaction will be closely linked to the stereochemical control, which can be exercised at positions 5 and 6 of **3**. Below,



we report that this stereochemical outcome is subject to considerable influence by changing the Lewis acid catalyst. As a result of this finding, solutions to the synthesis of threo- (**4**) and erythro- (**5**) β-hydroxy acids *from the some substrates*, under very simply executed conditions, are now available.

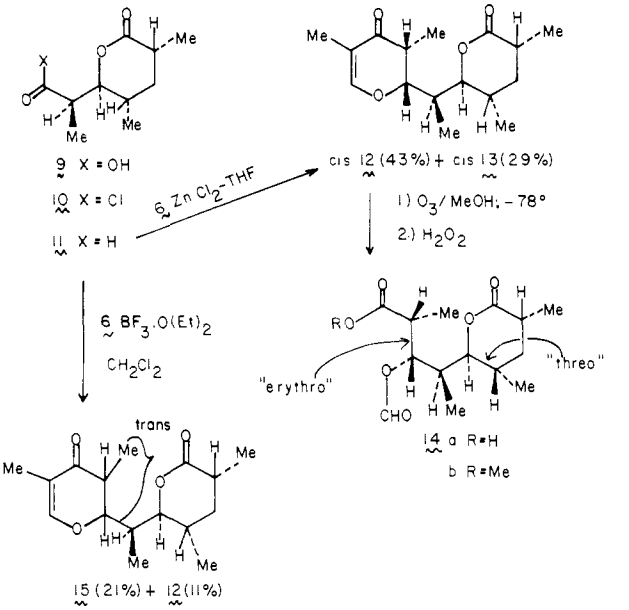
The silyloxydiene **6**[3] was chosen for this study because of its ready availability and stereochemical homogeneity. In examination of its reactions with a range of aldehydes under a wide variety of conditions, an important and remarkable discovery was realized. When the reaction was carried out with $BF_3{\cdot}OEt_2$ as the catalyst in methylene chloride (−78 °C), consistent trans (i.e., threo) selectivity was noted as shown in Table I (see entries A).

Table I



	R	method	7, % yield	8, % yield
a	n-C_5H_{11}-	A[4]	21	69
		B[5]	91	2
b	Ph-	A	23	68
		B	78	<2[6]
c		A	17[7]	73[7]
		B	91[8]	<2[6]
d	$Ph(CH_2)_3$-	A	17	64
		B	83	<2[6]
e	$PhCH_2OCH_2$-	A	17	68
		B	66	24

Scheme I



However, when the reaction was carried out in tetrahydrofuran with zinc chloride as the catalyst, virtually complete cis (i.e., erythro) specificity was observed (see entries B). The only departure from this trend is that shown as entry e, method B, wherein cis specificity is eroded. The translatability (by ozonolysis) of dihydro-γ-pyrones to protected Reformatsky-type products of the types **4** and **5** had already been established[1b] and was again exploited in the synthesis of **14**. Application to a more complex setting was undertaken before exploring the mechanistic implications of these observations in detail. Toward that goal we prepared, according to Masamune,[2a,b] the lactonic aldehyde **11** (Scheme I) in two steps from the (Prelog–Djerassi) lactonic acid **9**. It will be recalled[1b] that **9** is prepared by a simple route,[1b] whose first step in the threo selective process shown as entry c, method A. Whereas the synthesis of **9** by our disconnective strategy required access to the threo series, the conversion of **11** → **12** requires fostering of the erythro modality (see arrows in structure

(1) (a) Danishefsky, S.; Kerwin, J. F., Jr.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358. (b) Danishefsky, S.; Kato, N.; Askin, D; Kerwin, J. F., Jr. *Ibid.* **1982**, *104*, 360. (c) Danishefsky, S.; Kerwin, J. F., Jr. *J. Org. Chem.* **1982**, *47*, 3803. (d) Danishefsky, S.; Kobayashi, S.; Kerwin, J. F., Jr. *Ibid* **1982**, *47*, 1981.

(2) (a) Masamune, S.; Hirama, M.; Mori, S.; Ali, Sk.A.; Garvey, D. S. *J. Am. Chem. Soc.* **1981**, *103*, 1568. (b) Masamune, S. In "Organic Synthesis Today and Tomorrow"; Trost, B. M., Hutchinson, D. R., Ed.; Pergamon Press: New York, 1980; pp 197–215.

(3) Danishefsky, S.; Yan, C.-F.; Singh, R. K.; Gammill, R. B.; McCurry, P. M., Jr.; Fritsch, N.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 7001.

(4) Method A: (1) **2** (0.1 M, CH_2Cl_2), **6** (1.1 equiv), $BF_3{\cdot}OEt_2$ (1.0 equiv) −78 °C, 1–2 h → aqueous $NaHCO_3$; (2) TFA catalyst (CCl_4) room temperature, 5 min.

(5) Method B: (1) **2** (0.1 M, THF), **6** (2.0 equiv), anhydrous $ZnCl_2$ (1.0 equiv) room temperature, 24–48 h, → aqueous $NaHCO_3$; (2) TFA catalyst (CCl_4), room temperature, 5 min.

(6) None of **8** was detected (NMR, TLC (SiO_2)) in the crude product mixture or isolated upon chromatographic purification.

(7) Only a single diastereomer (Cram adduct) was isolated.

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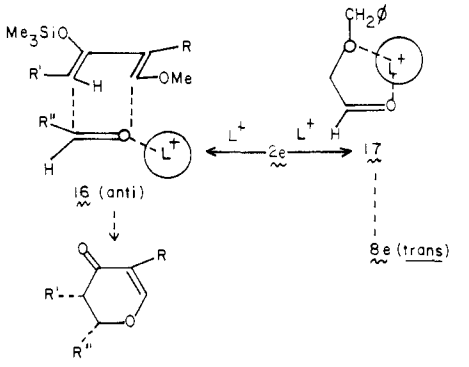
14). Accordingly, cyclocondensation of **11** with **6** was carried out with zinc chloride in tetrahydrofuran. There were obtained two cis isomers in a combined yield of 72%. *The major product (43%, mp 188–187 °C) is the cis "Cram"[9] system* **12**.[10] There was also obtained (29%) another *cis*-dihydro-γ-pyrone, which is presumably[11] the "anti-Cram" isomer **13**.

When the reaction was carried out in methylene chloride with BF_3·OEt_2 catalysis, a 2:1 mixture of trans-[12]: cis-**12** compounds was obtained. The stereochemistry of the major trans compound (see structure **15**) must be left unassigned vis-á-vis the Cram–anti-Cram diastereofacial issue.[9,13]

Thus, erythro (cis) specificity has been achieved in reaction of the complex **11** with **6** under the conditions of method B. We note that intrinsic diastereofacial[13,14] selection in addition reactions to **11** was never solved per se, even in the landmark Masamune synthesis.[2] The device of double stereodifferentiation[15,16] using a chiral (boron) enolate[17] was necessary to override the absence of inherent diastereofacial selectivity. The solution offered here lacks, for the moment, the element of auxiliary chiral guidance for the control of the diastereofacial problem available in the Masamune[17] and Evans[16] regimens.

Ozonolysis of **12** under the usual conditions[1b] gave the formate acid **14a**, best characterized as its methyl ester **14b**.[17,18] These structures embrace the chirality of carbons 1–9 of 6a-deoxyerythronolide.

The formation of cis products[19] corresponds, in cycloaddition terms, to an endo orientation of the R″ group of the aldehyde relative to the diene. It can be argued that this mode arises from the propensity of L^+ to complex with the basic aldehydo oxygen, anti to the R″ group (cf. **16**).[20] For steric or other reasons, the L^+ ensemble takes up the exo orientation in the pericyclic process. This would lead to *cis*-pyrone. In the case of aldehyde **2e**, a chelative bonding between L^+ and the two oxygen sites may result,[21] at least to some extent, in a syn-type of complex (cf. **17**). Exo addition of **17** would lead to trans product **8e**.



In the following paper mechanistic evidence regarding these reactions is gathered.

Acknowledgment. We acknowledge generous support from the American Cancer Society (Postdoctoral Fellowship to E.R.L., Grant No. PF-2020). The research was also supported by PHS Grant HL 25848. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale Unversity, which was supported by the NSF Chemistry Division Grant CHE 7916210.

Registry No. 2a, 66-25-1; **2b**, 100-52-7; **2c**, 33530-47-1; **2d**, 18328-11-5; **2e**, 60656-87-3; **6**, 82093-19-4; **7a**, 83378-97-6; **7b**, 83378-98-7; **7c**, 83378-99-8; **7d**, 83379-00-4; **7e**, 83379-01-5; **8a**, 83379-02-6; **8b**, 83379-03-7; **8c**, 80160-77-6; **8d**, 83379-04-8; **8e**, 83379-05-9; **9**, 80226-06-8; **10**, 83379-06-0; **11**, 83434-82-6; **12**, 83379-07-1; **13**, 83434-83-7; **14a**, 83379-08-2; **14b**, 83379-09-3; **15**, 83434-84-8; BF_3·Et_2O, 109-63-7; $ZnCl_2$, 7646-85-7.

Supplementary Material Available: Listing of IR, NMR, and mass spectra data for all new compounds (3 pages). Ordering information is given on any current masthead page.

(8) An 8:1 mixture of the Cram and anti-Cram adducts.
(9) Cram, D. J.; Abd. Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828; Cram, D. J. Kopecky, K. R. *Ibid.* **1959**, *81*, 2748.
(10) We thank Dr. Richard D. Adams of the Department of Chemistry, Yale University, for carrying out the single-crystal X-ray structure determination, the full details of which will be published elsewhere.
(11) Epimerism at the C-4 (erythronolide numbering) stereocenter of **12** arising from epimerization of the α center in the aldehyde **11** prior to reaction with **6** could, in theory, lead to two diastereomeric Cram cis adducts. However, on quenching of the reaction at partial conversion only stereochemically homogeneous **11** was recovered, indicating **11** retains its stereochemical integrity under the reaction conditions, and we, therefore, infer **13** to be the result of anti-Cram addition to **11**.
(12) A single diastereomer.
(13) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; John, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.
(14) For another related breakdown in inherent diastereofacial selectivity in reactions of a closely related aldehyde see: Lu, L.-D. L. *Tetrahedron Lett.* **1982**, *23*, 1867.
(15) Heatcock, C. H.; White, C. T. *J. Am. Chem. Soc.* **1979**, *101*, 7076.
(16) Cf.: Evans, D. A.; Bartoli, J. *Tetrahedron Lett.* **1982**, 807.
(17) Masamune, S.; Choy, W., Kerdesky, A. J.; Imperiali, B. *J. Am. Chem. Soc.* **1981**, *103*, 1566.
(18) The alcohol corresponding to formate acid **14a** was reported by Masamune.[2a] Several attempts on our part to retrieve this alcohol by cleavage of this formate ester led to a mixture of products. Professor Masamune has described to us the instability of this compound to acidic and basic reagents. Our structural and stereochemical formulations of these compounds rest securely on the crystallographic determination of compound **12**[10] and full spectral characterization of both **14a** and **b**.
(19) Satisfactory IR, NMR, and mass spectra were obtained for all new compounds. The data are available in detail in the supplementary material.
(20) Studies of the protonation of aldehydes in superacid media show preferential, if not exclusive, anti orientation of the alkyl residue with respect to the carbonyl-associated proton (Brookhart, M.; Levy, G. C.; Winstein, S. *J. Am. Chem. Soc.* **1967**, *89*, 1735. Olah, G. H.; O'Brien, D. H.; Calin, M. *Ibid.* **1967**, *89*, 3582). The larger steric demand of the $ZnCl_2$·solvent catalyst used in this study would presumably increase this preference for anti orientation.
(21) Protonation of α-chloro-substituted aldehydes in superacid media shows a divergence from the preferred anti orientation.[20] The syn-protonated aldehyde is presumably stabilized by intramolecular hydrogen bonding between the α-choro substituent and the carbonyl-associated proton (Thil, L.; Riehl, J. J.; Rimmelin, P.; Sommer, J. M. *J. Chem. Soc., Chem. Commun.* **1970**, 591).

Mechanistic Variations in the Lewis Acid Catalyzed Cyclocondensation of Siloxydienes with Aldehydes

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Received June 21, 1982

The Lewis acid (L^+) mediated cyclocondensation of siloxydienes (**1**, Scheme I) with aldehydes (**2**) has been described both as to scope and pertinence.[1] With the particular diene, R = Me, (hereafter called diene **7**) a change in the 5–6 stereochemical relationship was achieved by manipulating the catalytic system.[2] In this communication we relate an investigation into the mechanisms of these processes.

Two limiting formulations are advanced for the cyclocondensation process. In the "pericyclic" model (a) cycloadduct **3** is directly produced. Its vinylogous ortho ester sytem suffers unraveling (by L^+) to afford **5**. It is the intent of the pericyclic model to formulate the process in the familiar framework of the classical all-carbon Diels–Alder process. In so doing it is well to take note that the precise issues of mechanistic nuance of that venerable "reference" process, not to mention the Lewis acid mediated variation,[3] await full elucidation.

(1) (a) Danishefsky, S.; Kerwin, J. F.; Jr.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358. (b) Danishefsky, S.; Kato, N.; Askin, D.; Kerwin, J. F.; Jr. *Ibid.* **1982**, *104*, 360. (c) Danishefsky, S.; Kerwin, J. F., Jr. *J. Org. Chem.* in press. (d) Danishefsky, S.; Kobayashi, S.; Kerwin, J. F., Jr. *Ibid.* **1982**, *47*, 1981.
(2) Danishefsky, S.; Larson, E. R.; Askin, D. *J. Am. Chem. Soc.* **1982**, *104*.

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