first-order rate of 11-*cis*-retinaldehyde isomerization was measured to be 2.4×10^{-6} s^{-1} at 65 °C in *n*-heptane. Under the same conditions the rate for the preformed *n*-butylamine Schiff base of 11-*cis*-retinaldehyde, prepared by stirring a 5% excess of *n*-butylamine with the aldehyde in dry ether followed by solvent evaporation, was 8.0×10^{-6} s^{-1} (Figure 2). Therefore Schiff base formation by itself does enhance the thermal isomerization of the retinaldehydes by approximately a factor of 3 under the conditions shown. However, this acceleration is not nearly what would be required to enable the isomerization reactions to proceed at room temperature, even after Schiff base formation was completed.

The effects of added bases on the isomerization rates of the Schiff bases was also investigated. The rates of isomerization of the *n*-butylamine Schiff base of 11-*cis*-retinaldehyde was measured in *n*-heptane in the presence and absence of either added *n*-butylamine or triethylamine (Figure 2). The addition of the amines led to a slowing down of the rate of isomerization, with the *n*-butylamine being more effective than the triethylamine in this regard (Figure 2). The isomerization rate constant in the presence of 50 mM *n*-butylamine was 4.9×10^{-7} s^{-1},, and in the presence of 50 mM triethylamine, it was 2.0×10^{-6} s^{-1}. In separate experiments we also found that, as would be anticipated, triethylamine markedly decreased the rate of isomerization of the *n*-butylamine Schiff base of 13-*cis*-retinal in chloroform. The preformed Schiff base (12 μM) was isomerized at 65 °C in chloroform passed through alumina with a first-order rate constant of 1.5×10^{-5} s^{-1}. The addition of 100 mM triethylamine slowed down the rate to 1.7×10^{-6} s^{-1}. The inhibitory effect of the added amines is probably due to the neutralization of trace amounts of acid catalysts in the medium. Finally, as expected, it was also found that acid catalysis rapidly brought the retinal Schiff bases into equilibrium. The half-life for the isomerization of 9.8 μM 11-*cis*-retinaldehyde Schiff base in chloroform by approximately 10 mM HCl is 7 min at 25 °C.

Acknowledgment. This work was supported by NIH Grant EY-04096.

Registry No. 13-*cis*-Retinaldehyde, 472-86-6; 11-*cis*-retinaldehyde, 564-87-4; butylamine, 109-73-9; 13-*cis*-retinaldehyde butylamine Schiff base, 51847-39-3; 11-*cis*-retinaldehyde butylamine Schiff base, 52647-48-0; *all-trans*-retinal, 116-31-4; triethylamine, 121-44-8.

Diastereoselective Addition of Electrogenerated Trichloromethyl and Dichloro(methoxycarbonyl)methyl Anions to α-Branching Aldehydes[1]

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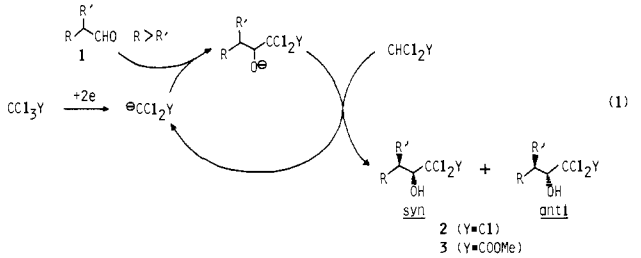
Previously we have reported a new electroreductive anionic chain reaction, in which aldehydes were converted into 1,1,1-trichloro-2-alkanols (**2**) with high current efficiency (eq 1).[2] The



(1)

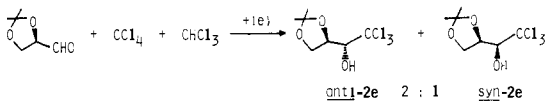
stereoconfiguration of products was classified by using "syn" and "anti" according to the definition of Masamune.[3] Similarly to

Table I. Diastereomeric Ratios and Yields of **2** and **3**

	R, R'	1	**2**, Y = Cl[a] syn:anti	yield, %[c]	**3**, Y = COOMe[b] syn:anti	yield, %[c]
a	R = Et; R' = Me		67:33[d]	89	90:10[d]	42
b	R = *i*-Pr; R' = Me		89:11[d]	76	~100:0[d]	25
c	R = *t*-Bu; R' = Me		~100:0[d]	49		
d	R = Ph; R' = Me		86:14[d]	60	~100:0[d]	36
e			33:67[e]	66	<5:95[f]	63
f			40:60[e]	52	<5:95[f]	55
g	R = *n*-Pr, R' = OAc		45:55[g]	76	17:83[g]	63

[a] Aldehyde:CCl_4:$CHCl_3$ = 1:1:10. [b] Aldehyde:CCl_3COOMe:$CHCl_2COOMe$ = 1:1:2. [c] Isolated yield based on aldehyde. [d] See ref 13. [e] See ref 15. [f] See ref 16. [g] See ref 17.

2, methyl 2,2-dichloro-3-hydroxyalkanoates (**3**) were obtained in reasonable yields by the electroreduction of mixtures of aldehydes, methyl trichloroacetate, and methyl dichloroacetate (eq 1).[4] In our continuing study on the utilization of **2** in organic synthesis, we have found that the electrogenerated trichloromethyl anion adds to 2,2-dimethyl-1,3-dioxolane-4-carboxaldehyde with moderate diastereoselectivity (eq 2).[8] This result prompted us to



(2)

anti-2e 2 : 1 syn-2e

investigate the diastereoselectivity of addition of electrogenerated trichloromethyl and dichloro(methoxycarbonyl)methyl anion to various aldehydes branching at the α-position.

A general procedure of the reaction is as follows: A solution of tetraethylammonium *p*-toluenesulfonate in 60 mL of DMF was placed in a divided cell equipped with carbon-rod electrodes. To the catholyte was added 0.01 mol of carbon tetrachloride, 0.1 mol of chloroform, and 0.01 mol of aldehydes. The catholyte was electrochemically reduced with a constant current of 0.1 A. After 0.02*F* of electricity was passed (5.33 h), the product was isolated by distillation or column chromatography. All the products gave satisfactory results in elemental and spectroscopic analyses.

The yield and diastereoselectivity are summarized in Table I. In the reaction with trichloromethyl anion, the aldehydes **1a-d** mainly yield syn isomers (R > R'), whereas the main products obtained from aldehydes **1e-g** are called anti isomer, since the main chain is the carbon chain. The ratio of syn/anti of **2a-c** increased in the order of bulkiness of α-substituent R (*t*-Bu > *i*-Pr > Et). No anti isomer was formed in the reaction of **1c**. The stereochemistry of the addition of trichloromethyl anion to aldehydes has not been known so far, but tribromomethyl anion generated by rather complex methods has been known to show similar stereoselectivity.[9]

The noteworthy results in the present study are that the addition of dichloro(methoxycarbonyl)methyl anion to α-branching aldehydes always shows excellent stereoselectivity. Since dichloro(methoxycarbonyl)methyl anion is hardly generated by the

(1) Electroorganic Chemistry. 76.
(2) Shono, T.; Ohmizu, H.; Kawakami, S.; Nakano, S.; Kise, N. *Tetrahedron Lett.* **1981**, *22*, 871.
(3) Masamune, S.; Ali, S. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 557.
(4) (a) Products **3** have also been obtained by the reaction of aldehydes with alkyl trichloroacetates using Grignard reagents[5a] or Zn[5b] or with alkyl dichloroacetate using a strong base.[6] In these methods, however, low temperature is necessary, and in the latter case, only limited types of esters and aldehydes are usable. (b) It has been reported that dichloro(ethoxycarbonyl)methyl anion, cathodically generated from ethyl trichloroacetate, adds to cyclic ketones to yield ring-expanded products.[7]
(5) (a) Villieras, J.; Castro, B. *Bull. Soc. Chim. Fr.* **1968**, 246. (b) Castro, B.; Villieras, J.; Ferracutti, N. *Ibid.* **1969**, 3521.
(6) (a) Normant, N. *J. Organomet. Chem.* **1975**, *100*, 189. (b) Timmler, H.; Wegler, R. *Chem. Ber.* **1967**, *100*, 2362.
(7) Karrenbrock, F.; Schafer, H. J. *Tetrahedron Lett.* **1978**, 1521.
(8) Shono, T.; Ohmizu, H.; Kise, N. *Tetrahedron Lett.* **1982**, *23*, 4801.
(9) (a) Furet, C.; Servens, C.; Pereyre, M. *J. Organomet. Chem.* **1975**, *102*, 423. (b) Mukaiyama, T.; Yamaguchi, M.; Kato, J. *Chem. Lett.* **1981**, 1505.

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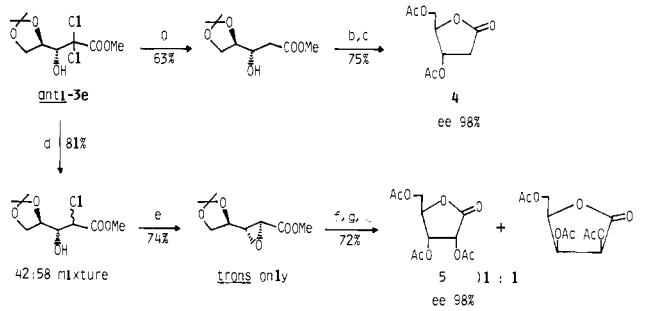
Scheme I[a]



[a] (a) +e, 0.3 A, 6F/mol, 0.2 M Me_4NCl/90% MeOH; (b) TFA, room temperature, 2 h; (c) Ac_2O/pyridine, room temperature, 3 h; (d) +e, 0.3 A, 3F/mol, 0.2 M NH_4NO_3/90% MeOH; (e) MeONa/MeOH, room temperature, 2 h; (f) KOH/H_2O-dioxane, reflux, 6 h; (g) dilute HCl, room temperature, 2 h.

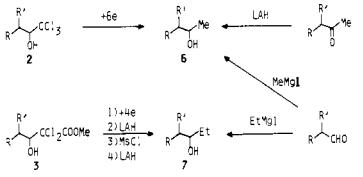
common chemical methods, the stereochemistry of the addition of this anion to aldehydes is hitherto unknown.[10] The easy electroreductive generation of dichloro(methoxycarbonyl)methyl anion and the almost exclusive formation of anti isomers from **1e**,**f**[12] are highly useful for the stereoselective synthesis of carbohydrates as exemplified by the syntheses of di-*O*-acetyl-2-deoxy-D-ribono-1,4-lactone (**4**) and tri-*O*-acetyl-D-ribono-1,4-lactone (**5**) from *anti*-**3e** (Scheme I).

(10) The addition of a zinc enolate to **1e** has been shown to be less selective than our results.[11]

(11) Murakami, M.; Mukaiyama, T. *Chem. Lett.* **1982**, 1271.

(12) (a) Fischer, H.; Baer, E. *J. Biol. Chem.* **1939**, *128*, 463. (b) English, J., Jr.; Griswold, P. H., Jr. *J. Am. Chem. Soc.* **1948**, *70*, 1390.

(13) The ratio was determined by ^1H NMR. In the compounds **2a-d** and **3a,b,d**, the chemical shifts of protons located on the carbon atom having a hydroxy group were as follows: **2a**, δ(syn) 3.96 (d, J = 2 Hz), δ(anti) 3.88 (d, J = 3 Hz); **2b**, δ(syn) 3.96 (br s), δ(anti) 3.85 (d, J = 6 Hz); **2c**, δ(syn) 4.15 (br s); **2d**, δ(syn) 4.21 (d, J = 2.5 Hz), δ(anti) 4.13 (d, J = 3 Hz); **3a**, δ(syn) 4.21 (d, J = 3 Hz), δ(anti) 4.10 (d, J = 6 Hz); **3b**, δ(syn) 4.30 (d, J = 6 Hz); **3d**, δ(syn) 4.47 (d, J = 6 Hz). The stereoconfiguration was determined by GLC analysis according to the reported methods.[14] Thus, **2** and **3** were transformed to alcohols **6** and **7**, respectively, and the retention time

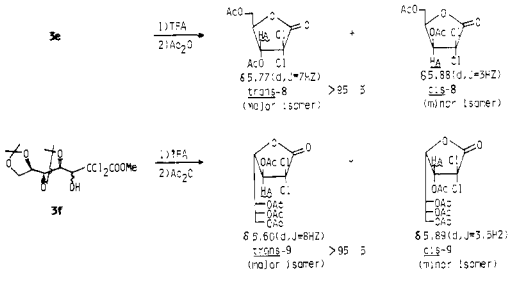


of each of these alcohols was compared with that of the authentic samples prepared by LAH reduction of ketones and the Grignard reaction of aldehydes. Since syn and anti isomers of each of the alcohols clearly showed different retention time, the stereoconfiguration could easily be identified.

(14) (a) Gault, Y.; Felkin, H. *Bull. Soc. Chim. Fr.* **1964**, 742. (b) Cram, D. J.; Elhafez, F. A. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828.

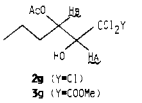
(15) The ratio was determined by isolation of each isomer with column chromatography on silica gel. The stereoconfiguration was confirmed by conversion of the products to known sugar compounds. Major isomers of **2e** and **2f** were identified to be anti isomers through their transformation to erythrose and mannose, respectively, by our previously reported method.[8] On the other hand, minor isomers gave threose and glucose suggesting that their configurations were syn.

(16) The ratio was determined by ^1H NMR of *O*-acetylated γ-lactones **8** and **9**, which were derived from **3e** and **3f**, respectively. The proton (H_A)

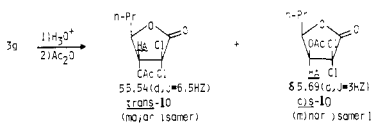


located on C-3 carbon of **8** and **9** showed two sets of doublets in the ratio of >95:5. The formation of di-*O*-acetyl-2-deoxy-D-ribono-1,4-lactone (**4**) from the major isomer of **3e** clearly showed that it was the anti isomer. The high similarity of the ^1H NMR of H_A of **8** with **9** suggested that the major isomer of **9** had a trans configuration at C-3 and C-4 positions. Hence, the major isomer of **3f** was assigned to be anti.

(17) The ratio was determined by ^1H NMR: **2g**, δ(syn, minor) 3.93 (br s, H_A), 5.55 (t, H_B, J = 7 Hz), δ(anti, major) 4.14 (d, H_A, J = 5 Hz), 5.29 (d t, H_B, J = 5, 8 Hz); **3g**, δ(syn, minor) 4.30 (br s, H_A), 5.49 (t, H_B, J = 7 Hz), δ(anti, major) 4.45 (d, H_A, J = 7 Hz), 4.95-5.22 (m, H_B). The fact



that the major isomer of **3g** was anti was suggested by comparing the ^1H NMR of H_A of *O*-acetylated γ-lactone **10** derived from **3g** with that of **8**. The



reasonable correlation of the ^1H NMR of **2g** with that of **3g** supported that the major isomer of **2g** was anti.

Synthesis of Macrocyclic Trichothecanoids: Baccharin B5 and Roridin E

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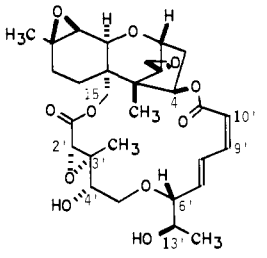
For the past few years, we have been investigating the synthetic opportunities afforded by the conformational preferences of macrocyclic compounds. One of the natural products under study in this context is the highly oxygenated trichlothecanoid baccharin B5 (**I**).[1] This stereochemically interesting compound is a potent antileukemic (T/C > 200) and is now being isolated in large quantities from a Brazilian shrub, *Baccharis megapotamica*, by NIH for evaluation as a chemotherapeutic agent. Baccharin is among the most complex of the roridin class of macrocyclic trichothecanoids whose simpler members include compounds such as roridin E (**2**).[2] Described here are the first[3] syntheses of



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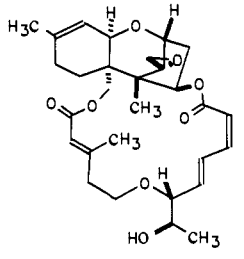

2

naturally occurring roridins in the form of syntheses of **1** and **2** starting from verrucarol and D-xylose. Of particular interest is the use of an achiral C1′-C5′ precursor and the establishment

(1) Kupchan, S. M.; Jarvis, B. B.; Dailey, R. G.; Bright, W.; Bryan, R. F.; Shizuri, Y. *J. Am. Chem. Soc.* **1976**, *98*, 7092. Kupchan, S. M.; Streelman, D. R.; Jarvis, B. B.; Dailey, R. G.; Sneeden, A. T. *J. Org. Chem.* **1977**, *42*, 4221. Jarvis, B. B.; Stahly, G. P.; Pavanasasivam, G.; Mazzola, E. P. *J. Med. Chem.* **1980**, *23*, 1054.

(2) Traxler, P.; Zurcher, W.; Tamm, Ch. *Helv. Chim. Acta* **1970**, *53*, 207. Matsumoto, M.; Minato, H.; Tori, K.; Ueyama, M. *Tetrahedron Lett.* **1977**, 4093.

(3) Previous synthetic work on the roridins: Tulshian, D. B.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1981**, *103*, 474. Roush, W. R.; Spada, A. P. *Tetrahedron Lett.* **1982**, 3773. Esmond, R.; Fraser-Reid, B.; Jarvis, B. B. *J. Org. Chem.* **1982**, *47*, 3358.

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