substitution of it by significant amounts of other solvents, e.g., 1,1-dichloroethane, generally resulted in increased complexity of the product mixture. (d) Trifluoroacetic acid was the best of several catalysts tried, and the optimum concentration at −15 °C was about 20%; higher concentrations favored formation of the trifluoroethyl ether **19** (see Table I) evidently produced by solvolysis of the *pro-C(11)* allylic hydroxyl group prior to cyclization. (e) Under the aforementioned preferred conditions the maximum yield was realized after a reaction time of about 24 h. Since the product composition remained unchanged when the mixture was kept at −15 °C for more than 1 week, it seemed that the desired dilution effect (see item b above) could be realized by adding daily increments of substrate over a period of 1 week.

From the information generated by the preliminary studies described above, preparative cyclizations were performed. Thus a solution of 209 mg of the silyl ether **8** in 5 mL of 1,1-dichloroethane was added in five equal portions over 23-h intervals to a stirred solution of 20% trifluoroacetic acid in trifluoroethanol at −15 °C. Each portion of substrate was added over a 10-min period and between additions the reaction mixture was allowed to stand in the freezer at −15 °C. After 51 h the solvents were removed at reduced pressure, and the residue was dissolved in 35 mL of methylene chloride and treated with 30 mL of 2 M methanolic KOH for 5 min at 23 °C. The crude product was acetylated (C_5H_5N, Ac_2O, 16 h, 22 °C), and the GC product analysis of the resulting mixture is shown in Table I. Purification[4b,d] gave 106 mg (58% yield) of material containing 97% of the desired products **5** (see Table I).

The same procedure was employed for the cyclization of the substrate **3** to give the product distribution shown in Table I. Purification[4a,d] afforded a 47% yield of material containing 90% of the desired products **5** (see Table I).

The product **5** was identified by GC (coinjection), NMR, and IR comparisions with authentic specimens[2a] of the interconvertible 17α and 17β epimers. Crystallization afforded the racemic 17β form [mp 108–110 °C lit.[2a] 108–110 °C) and the racemic 17α epimer,[5] mp 160–162 °C. Similarly, the more stable (17α) form of the 13α (C/D, cis) isomer **17** was compared with authentic material that had been converted, by ozonolysis followed by cyclodehydration of the resulting δ-diketone, into 11α-hydroxy-13α-progesterone, the structure of which was established by single-crystal X-ray diffraction analysis.[7] The D-homo structure **18**, which is a tentative assignment based on NMR and IR properties, is analogous to the presumed structure of a byproduct in the cyclization of **1**.[8] The constitution of the more stable, probably the 17β, form of the ether **19** has been established by ^{19}F NMR, IR, and mass spectral (M^+, m/e 398) analysis.

It is concluded from the results set forth in Table I that the vinylic fluoride terminated cyclization of substrate **8** is highly regio- and stereoselective, much more so than the methylacetylenic-terminated cyclization of **3**.

Acknowledgment. We are indebted to the National Institutes of Health and the National Science Foundation for support of this research. T.A.L. was the recipient of an NIH postdoctoral fellowship.

Registry No. 3, 58404-34-5; (±)-**5** (α isomer), 65166-73-6; (±)-**5** (β isomer), 58404-30-1; **7**, 79827-51-3; **8**, 79827-52-4; (*E*)-(+−)-**9**, 79827-53-5; (*Z*)-(+−)-**9**, 79827-54-6; **10**, 79827-55-7; **11**, 79827-56-8; **12**, 79827-57-9; **13**, 43001-29-2; (±)-**14**, 79839-10-4; (±)-**15**, 79827-58-0; (±)-**15** diketone derivative, 79827-59-1; (±)-**16**, 79827-60-4; (±)-**16** TMS ether, 79839-07-9; (±)-**17** (α-isomer), 79896-00-7; (±)-**17** (β-isomer), 79896-38-1; (±)-**18**, 79839-08-0; (±)-**19** (α isomer), 79839-09-1; (±)-**19** (β-isomer), 79896-39-2.

(7) Johnson, W. S.; Kapoor, V. M.; Schubert, U., unpublished studies.
(8) See footnote 4 of ref 3.

William S. Johnson,* Terry A. Lyle, G. William Daub
Department of Chemistry
Stanford University
Stanford, California 94305
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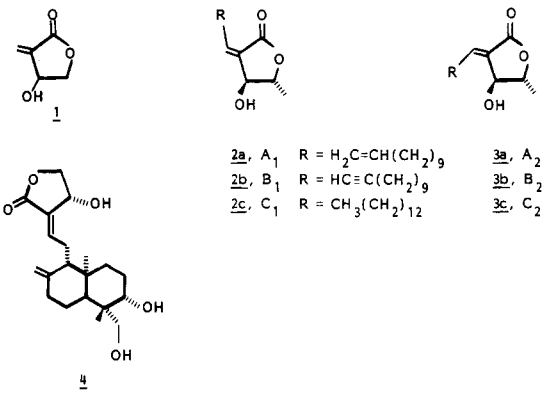
Stereochemistry of Deconjugative Alkylation of Ester Dienolates. Stereospecific Total Synthesis of the Litsenolides

Summary: Deconjugative protonations, alkylations, and aldol condensations of the dienolates from (*Z*)-2-alkenoates give the corresponding (*E*)-3-enoate products, whereas dienolates from (*E*)-2-enoates give mainly the (*Z*)-3-enoate products. These generalizations are exploited in stereospecific total syntheses of litsenolides A_2, B_2, and C_2.

Sir: The 3-alkylidene-4-hydroxy-2(3*H*)furanone (AHF) system is a common structural feature of polyoxygenated natural products, as exemplified by the compounds tulipalin B (**1**),[1] the litsenolides (**2**, **3**),[2] the mahubalactones,[3] the obtusilactones,[4] and andrographolide (**4**).[5] Despite the relative simplicity of the AHF moiety, no general synthesis of the AHF structure exists which offers control of substituent stereochemistry.[6]

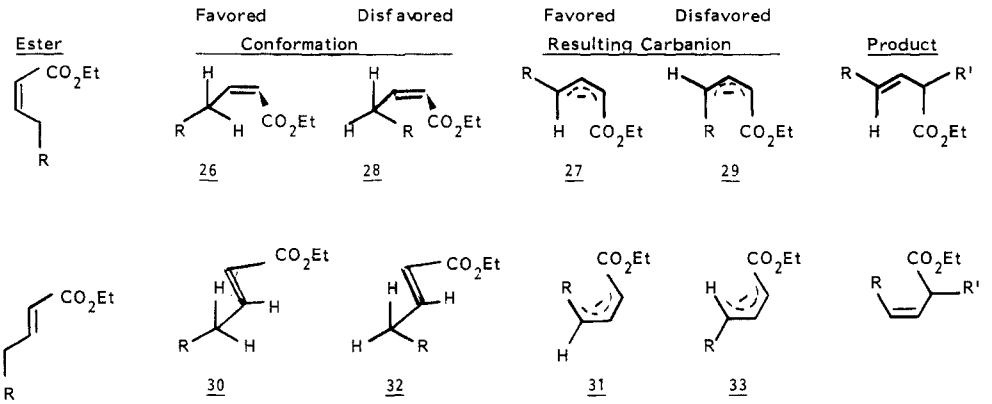


Our interest in devising a stereospecific route to the AHF system, with particular focus on the litsenolides, has led us to examine the stereochemistry of the deconjugative alkylation of the dienolate ions derived from pure geometric isomers of 2-alkenoate esters. Prior to this research it has been well established that such alkylations occurred

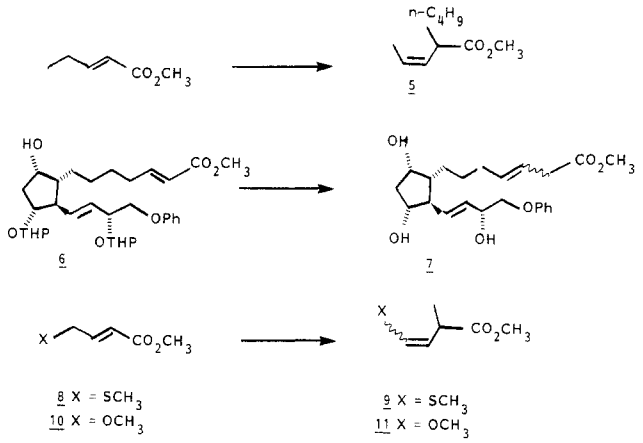
(1) Tschesche, R.; Kämmerer, F.-J.; Wulff, G. *Chem. Ber.* **1969**, *102*, 2057.
(2) Takeda, K.; Sakwawi, K.; Ishü, H. *Tetrahedron* **1972**, *28*, 3757.
(3) Martinez, J. C. V.; Yoshida, M.; Gottlieb, O. R. *Tetrahedron Lett.* **1979**, 1021.
(4) Niwa, M.; Iguchi, M.; Yamamura, S. *Chem. Lett.* **1975**, 655.
(5) Cava, M. P.; Chan, W. R.; Stein, R. P.; Willis, C. R. *Tetrahedron* **1965**, *21*, 2617 and references cited therein. The structure of andrographolide has recently been rigorously established by means of X-ray crystallographic analysis (Smith, A. B., III; Toder, B. H.; Carroll, P., private communication).
(6) The total synthesis of several Lauraceae lactones, including epilitsenolides C_1 and C_2, has been described recently by Rollinson, S. W.; Amos, R. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4114. References to earlier studies in this field are given in that paper; see also Corbet, J.-P.; Benezra, C. *J. Org. Chem.* **1981**, *46*, 1441. Wollenberg, R. H. *Tetrahedron Lett.* **1980**, 3139.

0022-3263/82/1947-0163$01.25/0

Chart I



at the 2- rather than 4-position.[7] However, in most such instances, there was no information about the stereochemical correspondence between the double bond geometry in the starting 2-alkenoate and in the product. The few examples that did comment on this matter indicated no clear-cut trend. Thus Koyama in 1972 reported that alkylation of methyl (*E*)-2-pentenoate with KNH_2 or $NaNH_2$ and *n*-BuI gave 20–33% yields of a single unconjugated ester assigned structure **5**.[8] On the other hand, Hayashi described in 1980 that protonation of the lithium dienolate from *E*-ester **6** gave 60% of a 1:1 mixture of the *E* and *Z* isomers of ester **7**.[9] Earlier studies from this



laboratory have shown that the lithium enolate from *E*-ester **8** gives good yields of alkylation products **9** in which the new double bond stereochemistry is approximately 1:1 *E*/*Z*.[10] However, Zimmerman has observed that similar alkylation of the methoxy analogue **10** produces only the *Z* isomer of ester **11**.[11] In the somewhat different cases studied by Pfeffer and Silbert, C-2 alkylation or protonation of the dianion of (*E*)-2-hexenoic acid showed little stereospecificity, although protonation of the dianion of the *Z* acid did yield predominantly the *E* isomer of 3-hexenoic acid.[12]

To resolve these ambiguities we have systematically examined the stereochemical outcome of the deconjugative discharge of the lithium dienolates of a series of unsaturated esters under standard reaction conditions.[13] The stereochemical results are listed in Table I. Taken with the scattered literature data previously cited,[14] this study permits us to propose the following simple rules and rationales to predict the stereochemical outcome of these synthetically useful reactions when carried out under our standard protocols.

1. Electrophilic discharge of the Li dienolate from the ester of a (*Z*)-2-alkenoate (disubstituted double bond) leads stereospecifically to the (*E*)-3-alkenoate ester.

2. Electrophilic discharge of the Li dienolate from the ester of an (*E*)-2-alkenoate (disubstituted double bond) leads stereospecifically to the (*Z*)-3-alkenoate ester unless the C-4 carbon bears a substituent larger than CH_3, beyond which the reaction becomes increasingly stereorandom.

3. Alkylation (or protonation) of a Li dienolate from either a (*Z*)- or (*E*)-3-alkenoate ester is stereospecific, with retention of precursor double bond position and geometry.

The observed inversion of stereochemistry in the conversion of the 2-*Z* to the 3-*E* series is consistent with stereoelectronic control (orbital overlap) in formation of the intermediate carbanion. We propose that the energy of the transition state leading to this species is controlled by the energy of the developing carbanion ("product development control"). As a result, the conformation of each starting ester which leads to the minimum energy stereoisomer of the developing carbanion is the one that lies on the preferred transition-state pathway. In the case of the 2-*Z* precursor, deprotonation occurs from conformation **26** to yield directly the minimum energy carbanion stereoisomer **27**, which gives rise to the observed 3-*E* product. The alternative 2-*Z* precursor conformation **28** would lead to enolate **29**, which is unfavorable because of severe 1,3-allylic strain between R and $COOC_2H_5$ (Chart I).

The striking preference for 3-*Z* products from 2-*E* precursors, except when C-4 substitution is large, may have a similar origin. Stereoelectronic control here would dic-

(7) Rathke, M. W.; Sullivan, D. *Tetrahedron Lett.* **1972**, 4249; Herrmann, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2433.

(8) Koyama, H.; Kogure, K.; Mori, K.; Matsui, M. *Agric. Biol. Chem.* **1972**, *36*, 793.

(9) Hayashi, M.; Arai, Y.; Wakatsuka, H.; Kawamura, M.; Konishi, Y.; Tsuda, T.; Matsumoto, K. *J. Med. Chem.* **1980**, *23*, 525.

(10) Kende, A. S.; Constantinides, D.; Lee, S. J.; Liebeskind, L. *Tetrahedron Lett.* **1975**, 405.

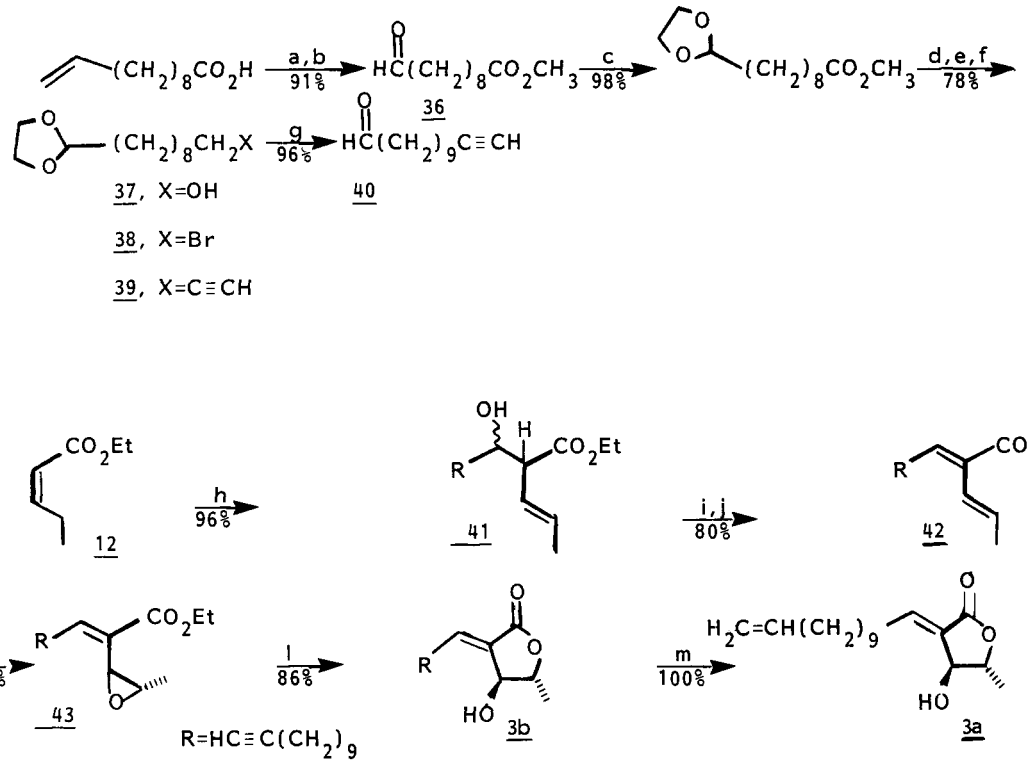
(11) Zimmerman, M. P. *Synth. Commun.* **1977**, *7*, 189.

(12) Pfeffer, P. W.; Silbert, L. D. *J. Org. Chem.* **1971**, *36*, 3290.

(13) (a) All (*E*)-2-enoate esters were prepared from the condensation of the appropriate aldehyde and triethylphosphonoacetate. The (*Z*)-2-enoate esters were prepared from the *cis*-2-enoic acids (EtI, K_2CO_3, THF, reflux), which in turn were obtained as described (Rappe, C. *Org. Synth.* **1973**, *53*, 123). (b) To a solution of 1.1 equiv of lithium diisopropylamide/hexamethylphosphoramide in THF at −78 °C is introduced via syringe the 2-enoate ester. After 30 min, the appropriate alkylating agent is added. After the mixture is stirred for 15 min at −78 °C, the reaction is quenched by the addition of H_2O. Extraction with Et_2O, concentration of the organic material in vacuo, and distillation affords the desired 3-enoate ester. Purity of all products and quantitation of product ratios was determined by 400-MHz ^1H NMR on distilled reaction products.

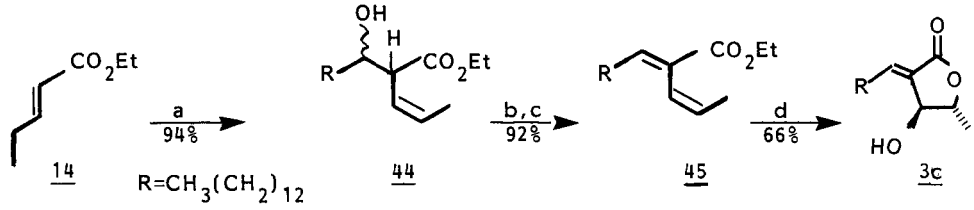
(14) After completion of this research, a note appeared describing the deconjugative protonation of (*E*)- and (*Z*)-2-enoate esters; our results compare favorably with those reported: Krebs, E.-P. *Helv. Chim. Acta* **1981**, *64*, 1023.

Scheme I[a]



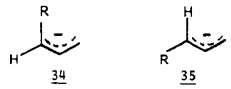
[a] a, MeOH, H_2SO_4 (cat.), Δ, 4 h; b, O_3 in 1:1 MeOH/CH_2Cl_2, 0 °C, then Me_2S; c, $HOCH_2CH_2OH$, C_6H_6, *p*-TsOH (cat.), $-H_2O$, Δ, 10 h; d, LAH, Et_2O, 0 °C → room temperature, 3 h; e, 1.3 equiv of Ph_3P, 1.3 equiv of CBr_4, THF, room temperature, 2 h; f, HC≡CH, *n*-BuLi, HMPA, THF, -78 °C → 0 °C, 8 h; g, aqueous acetone, *p*-TsOH (cat.), Δ, 12 h; h, LDA, HMPA, THF, **40**, -78 °C, 20 min; i, 1.05 equiv of MsCl, 1.5 equiv of Et_3N, CH_2Cl_2, 0 °C, 15 min; j, 2 equiv of KH, THF 0 °C → room temperature, 12 h; k, 1 equiv of mCPBA, 1 equiv of K_2CO_3, CH_2Cl_2, 0 °C, 2 h; l, 2 N H_2SO_4 (cat.), THF, Δ, 8 h; m, H_2, 1 atm, 5% Lindlar catalyst, EtOAc, 1 h.

Scheme II



[a] a, LDA, HMPA, THF, -78 °C, *n*-$C_{13}H_{27}CHO$, 20 min; b, 1.05 equiv of MsCl, 1.5 equiv of Et_3N, CH_2Cl_2, 0 °C, 15 min; c, 1 equiv of KH, THF, 0 °C → room temperature, 12 h; d, 0.2 equiv of OsO_4, 1.05 equiv of NMO, 2 equiv of *t*-BuOH, aqueous acetone, room temperature, 24 h, then 10% aqueous HCl, room temperature, 4 h.

tate competition between 2-*E* precursor conformation **30**, leading to the 3-*Z* carbanion **31**, vs. conformation **32** leading to the 3-*E* carbanion **33**. Whereas the energy difference between these alternative starting conformations **30** and **32** is probably negligible, such may not be the case for the developing dienolate carbanions **31** and **33**. There is extensive evidence, both experimental and theoretical, that for the crotyl anion system the cis form **34** is usually more stable than the trans form **35**.[15]

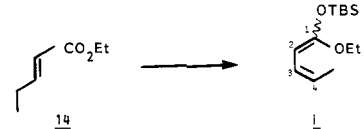


Whether this is the result of greater $A^{1,2}$ strain than of $A^{1,3}$ strain because of the 133° CCC angle of the allyl anion unit,[16] or because of the proposed "aromaticity" of the cis crotyl anion,[15b] is not clear. However, to the extent that our dienolate anion systems resemble the crotyl anion model, greater stability is expected for the 3-*Z* carbanion **31** than for its stereoisomer **33**. On this basis, preferential deprotonation of conformer **30** would be anticipated.[17]

(15) (a) Bates, R. B.; Beavers, W. A. *J. Am. Chem. Soc.* **1974**, *96*, 5001 and references cited therein. (b) Schleyer, P. v. R.; Dill, J. D.; Pople, J. A.; Hehre, W. J. *Tetrahedron* **1977**, *33*, 2497 and references given therein.

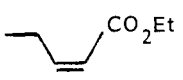
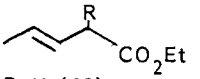
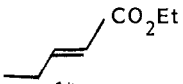
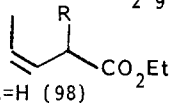
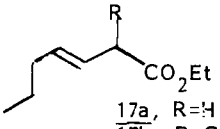
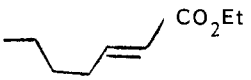
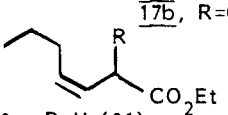
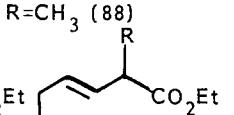
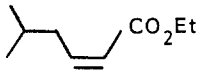
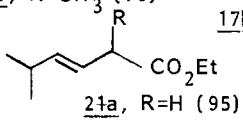
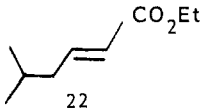
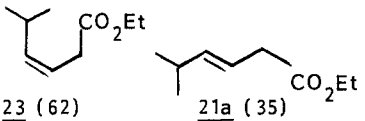
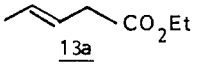
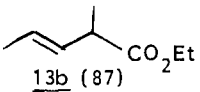
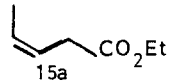
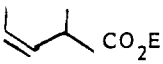
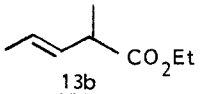
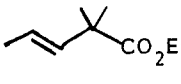
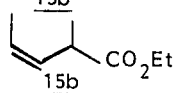
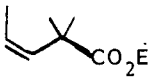
(16) Boerth, D. W.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 750. Meyer, A. Y.; Chrinovitzky, M. *J. Mol. Struct.* **1972**, *12*, 157.

(17) Kinetic deprotonation of **14** followed by quenching with *t*-$BuMe_2SiCl$ afforded a single α,β-unsaturated ketene acetal (**i**).



Spectroscopic properties identified the C3-C4 olefin to have *Z* geometry. However the orientation about C1-C2 could not be determined: NMR (400 MHz, $CDCl_3$) δ 0.18 (s, 6 H), 0.95 (s, 9 H), 1.32 (t, *J* = 7 Hz, 3 H), 1.67 (dd, *J* = 6.60 Hz, *J'* = 1.75 Hz, 3 H), 3.84 (q, *J* = 7 Hz, 2 H), 4.51 (d, *J* = 10.83 Hz, 1 H), 5.09 (ddq, *J* = 1.06 Hz, *J'* = 10.86 Hz, *J''* = 6.98 Hz, 1 H), 6.09 (ddq, *J* = 10.86 Hz, *J'* = 10.86 Hz, *J''* = 1.57 Hz, 1 H).

Table I[13]

ester	electrophile	product(s) (% yield)
 12	H_2O	 13a, R=H (98)
	CH_3I	13b, R=CH_3 (90)
	$n\text{-}C_{13}H_{27}CHO$	13c, R=$n\text{-}C_{13}H_{27}CH(OH)$ (95)
	$HC{\equiv}C(CH_2)_9CHO$	13d, R=$HC{\equiv}C(CH_2)_9CH(OH)$ (96)
 14	H_2O	 15a, R=H (98)
	CH_3I	15b, R=CH_3 (90)
	$n\text{-}C_{13}H_{27}CHO$	15c, R=$n\text{-}C_{13}H_{27}CH(OH)$ (94)
	$HC{\equiv}C(CH_2)_9CHO$	15d, R=$HC{\equiv}C(CH_2)_9CH(OH)$ (85)
 16	H_2O	 17a, R=H (99)
	CH_3I	17b, R=CH_3 (88)
 18	H_2O	 19a, R=H (81)
	CH_3I	19b, R=CH_3 (78)
		 17a, R=H (13)
		17b, R=CH_3 (14)
 20	H_2O	 21a, R=H (95)
	CH_3I	21b, R=CH_3 (89)
 22	H_2O	 23 (62) 21a (35)
 13a	CH_3I	 13b (87)
 15a	CH_3I	 15b (89)
 13b	CH_3I	 24 (90)
 15b		 25 (84)

Where R exceeds CH_3 in size, the data of Bothner-By et al.[18] suggest that rotamers resembling conformation **32** would begin to compete significantly with **30** and lead to a minimum energy deprotonation pathway toward anion conformation **33**.

In order to develop a stereospecific synthesis of the litsenolides, it was necessary to show that these rules also hold for the aldol condensation. The limited data of Table I suggest this to be the case, and this finding has been exploited in the following synthesis of litsenolides A_2 and B_2 (Scheme I) and C_2 (Scheme II).

Esterification of 10-undecenoic acid (CH_3OH, catalyst H_2SO_4, reflux, 4 h) followed by ozonolysis (O_3 in 1:1 CH_3OH/CH_2Cl_2, 0 °C, Me_2S) gave aldehyde ester **36**.[19] Protection of the aldehyde as the dioxolane ($HOCH_2CH_2OH/C_6H_6$, catalyst pTsOH–H_2O, reflux, 3 h) and subsequent reduction of the ester function ($LiAlH_4$, Et_2O, 0 → 25 °C, 3 h) gave alcohol **37**, mp 24.5–25 °C, which was readily transformed to the corresponding bromide **38** (1.3 equiv of Ph_3P, 1.3 equiv of CBr_4, THF, room temperature, 2 h). Reaction of bromide **38** with

(18) Bothner-By, A. A.; Naar-Colin, C.; Günther, H. *J. Am. Chem. Soc.* **1962**, *84*, 2748.

(19) All numbered intermediates give IR, NMR, and analytical composition and/or mass spectral data in complete accord with the desired structures.

lithium acetylide (HC≡CH, *n*-BuLi, THF/HMPA, −78 → 0 °C, 8 h) gave the acetylene **39**. Mild acid hydrolysis of the acetal (aqueous Me_2CO, catalyst *p*-TsOH, reflux, 12 h) gave the requisite 11-dodecynal side-chain synthon **40**[20] in 69% overall yield from 10-undecenoic acid.

The enolate of ethyl (*Z*)-2-pentenoate **12** was now generated under our standard conditions. Addition of 11-dodecynal (**40**) (1.0 equiv, −78 °C, THF, 20 min) to this enolate followed by neutral workup led to the 1:1 diastereomeric pair of 3-*E* isomers **41** in 94% yield. Mesylation of this mixture (**41**), using MsCl (1.05 equiv, 1.5 equiv of Et_3N, CH_2Cl_2, 0 °C, 15 min), gave a quantitative yield of the corresponding mesylates which, in common with their precursors, showed infrared ester carbonyl absorption at 1735 cm^{-1} and a strong 970-cm^{-1} peak for the 3-*E* double bond. After a survey of less stereospecific reagents,[21] we found that elimination of MsOH could be readily performed by treatment of the mesylates with KH (2.0 equiv, THF, 0 → 25 °C, 12 h, 80%) to give exclusively the single diene ester **42**.[22] Chemoselective epoxidation was readily accomplished (1.0 equiv of MCPBA, 1.0 equiv of K_2CO_3, CH_2Cl_2, 0 °C, 2 h, 86%) to yield the epoxide **43** where the trans stereochemistry at the epoxide ring could be unambiguously confirmed by 400-MHz NMR (J = 2.4 Hz).[23] Acid-catalyzed cyclization of the epoxy ester **43** (2 N H_2SO_4, THF, reflux, 8 h), possibly with participation of the ester carbonyl,[24] proceeded smoothly to give 86% yield of (±)-litsenolide B_2 (**3b**), having IR and NMR spectra identical with those reported.[25] Semihydrogenation (H_2, 1 atm, 5% Lindlar catalyst, EtOAc, 1 h) of **3b** quantitatively gave (±)-litsenolide A_2 (**3a**),[26] with properties again identical with those described. The overall yield of (±)-litsenolide B_2 from 11-dodecynal (**40**) by this sequence was 56% over five steps.

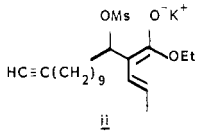
Confirmation of the stereochemical course of these reactions was obtained by an independent sequence leading to litsenolide C_2 from ethyl (*E*)-2-pentenoate (**14**). Condensation of the enolate from **14** as above with tetradecanal gave the diastereomeric pair of *Z* isomers **44** in 94% yield. Mesylation, followed by treatment with KH as described gave a single diene ester **45** having the expected 3-(*Z*) stereochemistry.[27] Osmylation at the disubstituted double bond (0.2 equiv of OsO_4, 1.05 equiv of NMO, 2 equiv of *t*-BuOH, aqueous acetone, 24 h)[28] followed by lactonization (2 N HCl, THF, room temperature, 4 h) gave in 66% yield (±)-litsenolide C_2 (**3c**), having IR, NMR, and mass spectra identical with those reported.[29] It is important to note that the osmylation/lactonization reaction sequence for the preparation of litsenolide C_2 (**3c**) could not be applied in analogous manner to the conversion of diene ester **42** to litsenolide B_2 (**3b**) because preferential osmylation at the acetylene bond took place.[30]

We conclude that the stereochemistry of deconjugative alkylation of dienolate esters is now well delineated, and that this knowledge forms the basis of a new, simple, stereospecific synthesis of AHF units from any suitable aldehyde precursor.[31]

Registry No. (±)-**3a**, 79980-79-3; (±)-**3b**, 79980-80-6; (±)-**3c**, 78340-32-6; **12**, 27805-84-1; **13a**, 3724-66-1; **13b**, 16489-03-5; **13c**, 79918-76-6; **14**, 24410-84-2; **15a**, 27829-70-5; **15b**, 58625-89-1; **15d**, 79918-77-7; **16**, 35066-42-3; **17a**, 54340-71-5; **17b**, 79918-78-8; **18**, 54340-72-6; **19a**, 79918-79-9; **19b**, 79933-08-7; **20**, 79918-80-2; **21a**, 79918-81-3; **21b**, 79918-82-4; **22**, 34993-63-0; **23**, 79918-83-5; **24**, 79918-84-6; **25**, 63860-08-2; **36**, 14811-73-5; **37**, 59014-59-4; **38**, 59014-60-7; **39**, 79918-85-7; **40**, 79918-86-8; **41** (isomer 1), 79918-87-9; **41** (isomer 2), 79918-88-0; **41** mesylate (isomer 1), 79933-09-8; **41** mesylate (isomer 2), 79918-89-1; **42**, 79918-90-4; **43**, 79918-91-5; **44** (isomer 1), 79918-92-6; **44** (isomer 2), 79918-93-7; **44** mesylate (isomer 1), 79918-94-8; **44** mesylate (isomer 2), 79918-95-9; **45**, 79918-96-0; i, 79918-97-1; iii, 79980-81-7; 10-undecenoic acid, 112-38-9; methyl 1,3-dioxolane-2-nonanoate, 79918-98-2; tetradecanal, 124-25-4.

(20) Compound **40**: IR (CCl_4) 3320 (s), 2960–2840 (s), 2710 (m), 1720 cm^{-1}; (s) NMR (400 MHz, $CDCl_3$) δ 1.24–1.70, 1.30 (m, bs, 16 H), 1.94 (t, J = 3 Hz, 1 H), 2.18 (dt, J = 3 Hz, J' = 7 Hz, 2 H), 2.41 (dt, J = 2 Hz, J' = 7 Hz, 2 H), 9.74 (t, J = 2 Hz, 1 H).

(21) In contrast to KH, Et_3N elimination of mesylate was not stereoconvergent, giving alkylidene isomers in the same proportion as the diastereomer ratio in **41**. Thus with KH a discrete enolate ii might be assumed to form which has lost its stereochemical integrity.



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(22) Compound **42**: IR (CCl_4) 3320 (s), 3025 (w), 2930 (s), 2860 (s), 1725 (s), 1650 (w), 970 cm^{-1} (s); NMR (400 MHz, $CDCl_3$) δ 1.20–1.58 (m, 17 H), 1.84 (dd, J = 7.2 Hz, J' = 1.4 Hz, 3 H), 1.94 (t, J = 2 Hz, 1 H), 2.18 (dt, J = 2.5 Hz, J' = 7 Hz, 2 H), 6.03 (qd, J = 6.8 Hz, J' = 16.2 Hz, 1 H), 6.15 (d, J = 15.9 Hz, 1 H), 6.57 (t, J = 7.4 Hz, 1 H).

(23) Booth, J. "Progress in NMR Spectroscopy"; Pergamon Press: Oxford, 1969; Vol. 5, pp 185–6.

(24) Stork, G.; Borch, R. *J. Am. Chem. Soc.* **1964**, *86*, 935.

(25) Compound **3b**: NMR (400 MHz, $CDCl_3$) δ 1.24–1.58, 1.34 (m, d, J = 7 Hz, 18 H), 1.92 (t, J = 2.5 Hz, 1 H), 2.18 (dt, J = 2.5 Hz, J' = 7 Hz, 2 H), 2.40 (m, 2 H), 4.49 (dq, J = 2.2 Hz, J' = 6.8 Hz, 1 H), 4.55 (m, 1 H), 6.98 (dt, J = 2 Hz, J' = 7.7 Hz, 1 H).

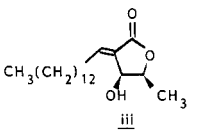
(26) Compound **3a**: NMR (400 MHz, $CDCl_3$) δ 1.18–1.78, 1.33 (m, d, J = 7 Hz, 18 H), 2.03 (bq, J = 7 Hz, 2 H), 2.40 (m, 2 H), 4.32 (dq, J = 2.3 Hz, J' = 6.5 Hz, 1 H), 4.57 (m, 1 H), 4.91–5.04 (m, 2 H), 5.93 (tdd, J = 6.5 Hz, J' = 10.3 Hz, J'' = 10.3 Hz, 1 H), 7.02 (dt, J = 1.7 Hz, J' = 7.8 Hz, 1 H).

(27) Compound **45**: IR (CCl_4) 3020 (m), 2940 (s), 2860 (s), 1725 (s), 1630 cm^{-1} (m); NMR (400 MHz, $CDCl_3$) δ 0.87 (J = 6.7 Hz, 3 H), 1.18–1.49, 1.24 (m, bs, 25 H), 1.51 (dd, J = 2 Hz, J' = 7.1 Hz, 3 H), 2.07 (dt, J = 7.3 Hz, J' = 7.3 Hz, 2 H), 4.17 (q, J = 7 Hz, 2 H), 5.75 (dq, J = 12.1 Hz, 6.5 Hz, 1 H), 5.96 (bd, J = 11.3 Hz, 1 H), 6.78 (t, J = 7.4 Hz, 1 H).

(28) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

(29) Compound **3c**: NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 6.7 Hz, 3 H), 1.01–1.56, 1.34 (m, d, J = 6.7 Hz, 29 H), 2.39 (m, 2 H), 4.49 (dq, J = 2.1 Hz, J' = 6.4 Hz, 1 H), 4.52 (m, 1 H), 6.97 (dt, J = 1.7 Hz, J' = 7.8 Hz, 1 H).

(30) Application of our epoxidation–lactonization sequence to diene ester **45** leads in 80% yield to (±)-epilitsenolide C_2 (iii), which gave spectroscopic data identical with those reported by Katzenellenbogen (ref 6).



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Andrew S. Kende,* Bruce H. Toder[32]

Department of Chemistry
University of Rochester
Rochester, New York 14627

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2-[(Acylamino)methyl]-6-methylpyrimidin-4(3*H*)-ones. Novel Precursors for the Synthesis of Imidazo[1,5-*a*]pyrimidines and Imidazo[4,5-*b*]pyridines

Summary: 2-[(Acylamino)methyl]-6-methylpyrimidin-4-(3*H*)-ones, which are synthesized from β-aminocrotonamide and ethyl *N*-acylglycinates, have been found to be novel and versatile precursors for the synthesis of imida-