evaporated. The residue was passed through a short column of silica in hexane–ethyl acetate (3:1) to remove phosphine oxide. Evaporation yielded 0.66 g (85%) of 2-phenylbenzimidazole, mp 287 °C.[6] When the phosphinamide reagent is used, washing with water is sufficient to remove the (recoverable) phosphinamide.

The same procedure suffices to prepare simple amides, by using only a 1:1:1 stoichiometry (acid/amine/reagent) and affording similar or higher yields.

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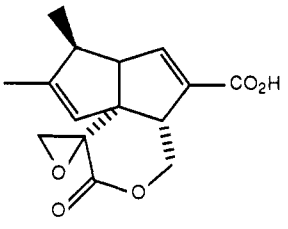
A Total Synthesis of Pentalenolactone E Methyl Ester via a [3 + 2] Annulation Strategy

Summary: An efficient total synthesis of the methyl ester of pentalenolactone E is accomplished via a [3 + 2] annulation process.

Sir: We have recently reported an efficient and general route to annulated cyclopentanones utilizing a stepwise [3 + 2] process.[2] This new strategy for the construction of five-membered rings relies on the in situ generation of a γ-oxo ester enolate **2** from β-(silyloxy)cyclopropyl esters **1**. The 1,3-bifunctional system (**2**), when combined with a two-carbon acceptor such as [α-(phenylthio)vinyl]-phosphonium salt **3**, leads to a cyclopentene which is readily converted to its cyclopentanone analogue.

In this report we describe the application of this methodology to the total synthesis of the methyl ester of pentalenolactone E,[3] **8**. This latter compound is a member



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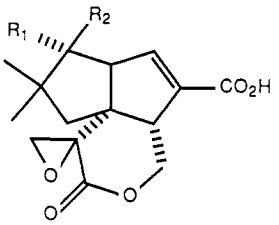
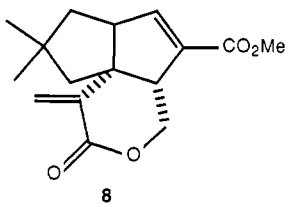


6 $R_1,R_2 = O$

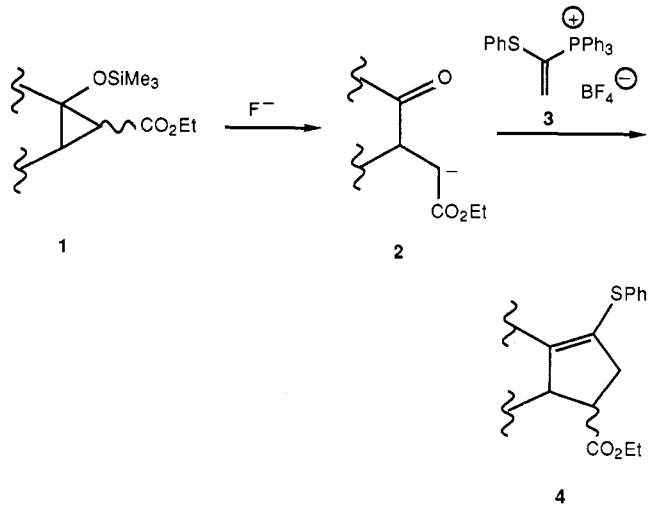
7 $R_2 = OH, R_1 = H$



8

of a class of lipophilic antibiotics isolated from culture broths of *Streptomyces* that also includes pentalenolactone **5** and the pentalenolactones G, **6**, and H, **7**. While several syntheses have been reported[4] for pentalenolactone E, **8**, the route described herein features an efficient one-pot cyclopentannulation process, ester differentiation leading to the γ-lactone, and a new sequence to the α,β-unsaturated methyl ester from the cyclopentanone.

Scheme I



1 **2** **4**

Our syntheses begins with the known[5] 4,4-dimethylcyclopentenone (**9**) which is reductively converted to its enol silyl ether regiospecifically.[6] Addition of *tert*-butyl diazoacetate[7] to the enol ether followed by ring-opening of the (silyloxy)cyclopropane with fluoride produces the α-alkylated cyclopentanone[8] **10** in 70% yield. We have found that the cyclopropanation route is far superior to the alkylation of the appropriate enolate with an α-halo *tert*-butyl ester in terms of yield and regiospecificity. Conversion of ketone **10** to its trimethylsilyl enol ether under thermodynamic control and cyclopropanation with ethyl diazoacetate produces the requisite (silyloxy)cyclopropane **11** in a yield of 65%.

The stage is set for the key cyclopentannulation reaction in which intermediate **11** is treated with potassium fluoride and 18-crown-6 in the presence of [α-(phenylthio)vinyl]-triphenylphosphonium tetrafluoroborate (**3**). The bicyclo [3.3.0]octene system[9] **12** is isolated in 95% yield as a 1:1 mixture of cis/trans stereoisomers. Chemoselective hydrolysis of the ethyl ester in methanolic hydroxide yields an enriched cis/trans (1.5/1) mixture of the carboxylic acid. It appears that during the basic hydrolysis there is some epimerization of the ester prior to hydrolysis. Attempts to directly epimerize the ester **12** with sodium ethoxide did not result in any changes in the 1:1 ratio of stereoisomers. The cis carboxylic acid could easily be separated from its trans isomer and was isolated in 57% yield. Reduction of the cis acid was affected with sodium

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(8) All new compounds gave correct elemental analyses or high resolution mass spectra and were fully characterized by 300-MHz ^{1}H NMR and ^{13}C NMR.
(9) 300-MHz ^{1}H NMR of pure cis methyl ester ($CDCl_3$): δ 1.03 (s, 3 H), 1.16 (s, 3 H), 1.43 (s, 9 H), 1.72 (d, 1 H, J = 14.2 Hz), 1.91 (d, 1 H, J = 14.2 Hz), 2.05 (dd, 1 H, J = 14.7, 3.8 Hz), 2.16 (d, 1 H, J = 14.7 Hz), 2.48 (AB, 2 H, J_{AB} = 15.0 Hz), 2.45–2.60 (m, 1 H), 2.96–3.14 (m, 2 H), 3.64 (s, 3 H), 7.16–7.31 (m, 5 H); mp 67–68 °C.

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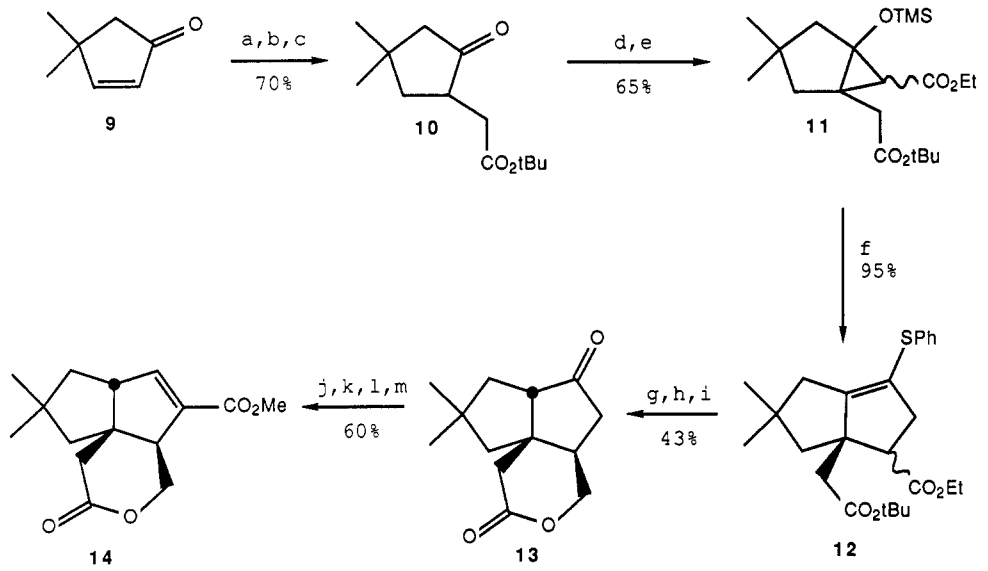
Scheme II[a]



[a] (a) Et_3SiH, $RhCl(PPh_3)_3$, PhH;[6] (b) (2.5 equiv) N_2CHCO_2-*t*-Bu, $CuSO_4$, PhH;[6] (c) Et_3NHF, THF, 25 °C; (d) Me_3SiCl, Et_3N, DMF, 135 °C; (e) 4 equiv of N_2CHCO_2Et, $CuSO_4$, PhH; (f) (2 equiv) **3**, (5 equiv) KF, (0.1 equiv) 18-crown-6, CH_3CN, 82 °C;[2] (g) $NaOH/H_2O$, MeOH, THF, 60 °C; (h) $ClCO_2Et$, Et_3N, THF; $NaBH_4$, THF/H_2O, room temperature; (i) TFA, $CHCl_3$; (j) C_4H_9N, *p*-TSA, PhH, 80 °C; (k) (10 equiv) $ClCO_2Me$, PhH, 80 °C; (l) (3 equiv) $NaCNBH_3$, MeOH, HCl, room temperature; (m) (1.1 equiv) MCPBA, CH_2Cl_2; K_2CO_3, THF, room temperature.

borohydride via its mixed anhydride.[10] Treatment of the resulting alcohol with trifluoroacetic acid in chloroform converts the vinyl sulfide to the ketone, hydrolyzes the *tert*-butyl ester, and catalyzes the lactonization to the crystalline ketolactone[11] **13**. The overall conversion of cis **12** to **13** can be effected in 75% yield.

While ketolactone **13** is a new precursor to pentalenolactone E methyl ester, a similar cyclopentanone was converted previously[4a] to the unsaturated methyl ester by a reduction-dehydration sequence in only 40% yield. We found that the most convenient route to the unsaturated ester[12] **14** involved the following sequence: (1) conversion to pyrrolidine enamine; (2) carbomethoxylation;[13] (3) conjugate reduction with sodium cyanoborohydride;[14] and (4) elimination of the pyrrolidine via its N-oxide in base.[15] The overall sequence was accomplished in 60% isolated yield. Compound **14** had been previously prepared by Paquette[4d] and converted to pentalenolactone E methyl ester[16] by methoxymagnesium carbonate followed by formalin in dimethylamine.

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Registry No. **3**, 69442-54-2; **9**, 22748-16-9; **10**, 109719-46-2; **11**, 109719-47-3; *cis*-**12**, 109719-48-4; *trans*-**12**, 109719-49-5; *cis*-**12** (acid), 109719-50-8; *trans*-**12** (acid), 109719-51-9; **13**, 109719-52-0; **14**, 83648-43-5.

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(11) 300-MHz ^1H NMR of **13** ($CDCl_3$): δ 0.90 (s, 3 H), 1.07 (s, 3 H), 1.75 (AB, 2 H, J_{AB} = 13.1 Hz), 1.80–1.86 (m, 1 H), 1.90 (ddd, 1 H, J = 13.1, 4.2, 1.1 Hz), 2.44 (ddd, 1 H, J = 18.0, 7.9, 1.9 Hz), 2.50–2.62 (m, 2 H), 2.63 (AB, 2 H, J_{AB} = 15.0 Hz), 2.75 (dd, 1 H, J = 18.0, 9.0 Hz), 4.11 (dd, 1 H, J = 11.9, 5.3 Hz), 4.44 (dd, 1 H, J = 11.9, 4.2 Hz); mp 108–109 °C.

(12) 300-MHz ^1H NMR of **14** ($CDCl_3$): δ 1.02 (s, 3 H), 1.06 (s, 3 H), 1.37 (dd, 1 H, J = 13.0, 5.9 Hz), 1.74 (AB, 2 H, J_{AB} = 13.5 Hz), 1.87 (dd, 1 H, J = 13.0, 9.4 Hz), 2.60 (AB, 2 H, J_{AB} = 14.4 Hz), 3.07–3.14 (m, 1 H), 3.17–3.20 (m, 1 H), 3.74 (s, 3 H), 4.44 (dd, 1 H, J = 11.8, 4.3 Hz), 4.50 (dd, 1 H, J = 11.8, 4.2 Hz), 6.83–6.84 (m, 1 H).

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(16) We have converted compound **14** to pentalenolactone E methyl ester employing methoxymagnesium carbonate and Eshenmosher's salt in yields between 40% and 50%. Our synthetic pentalenolactone methyl ester possessed ^1H NMR and ^{13}C NMR spectral data identical with literature[3] values.

Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by Polymer-Supported Chiral Amino Alcohols. Evidence for a Two Zinc Species Mechanism

Summary: Polymer-bound chiral amino alcohols (in particular, (dialkylamino)isoborneol) are excellent heterogeneous recyclable catalysts in the enantioselective alkylation of aromatic aldehydes with dialkylzinc.

Sir: The catalytic asymmetric alkylation of carbonyl compounds is a potentially important method for the preparation of enantiomerically pure alcohols. Oguni and Omi have recently reported[1] that the addition of diethylzinc to benzaldehyde was catalyzed by amines or alcohols such as (*S*)-leucinol to afford (*R*)-1-phenylpropanol in 48% ee. In our continuing studies[2-5] of

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