yield. This latter lactone was then saponified with 2.4 equiv of $NaOH/H_2O/t$-BuOH followed by the addition of a catalytic amount of $RuCl_3$ and 3.3 equiv of $NaIO_4/H_2O$ for 24 h.[7] Acidification of this reaction mixture followed by extraction and esterification produces keto ester **4** in 76% overall yield from lactone **3**. Intramolecular Claisen condensation of keto ester **4** with 2.5 equiv of $NaN(SiMe_3)_2$ in refluxing THF (1h for addition, 1h reflux) followed by quenching with $ClPO(OEt)_2$/TMEDA gives bicyclic keto enol phosphate **5a** in 71% yield.[8] Selective reduction of the ketone group of intermediate **5a** with $NaBH_4$/EtOH followed by reductive deoxygenation of the diethyl phosphate moiety with $Li/EtNH_2/Et_2O$ in the presence of t-BuOH[9] affords bicyclic ketone **5b** in 34% yield after oxidation with H_2CrO_4 in acetone.[10,11]

A Wittig reaction on ketone **5b** with $Ph_3P{=}CHOCH_3$ in Me_2SO[12] followed by hydrolysis produces an epimeric mixture of aldehydes. Stereoselective alkylation of this epimeric mixture of aldehydes with allyl bromide using Ph_3CK in DME[13] to generate the respective enolate anion followed by reduction of the resulting product with $NaBH_4$/EtOH at −10 °C produces alcohol **6** in 33% overall yield from ketone **5b**. Esterification of alcohol **6** with n-BuLi in THF/TMEDA (4:1, respectively) followed by addition of $ClPO(NMe_2)_2$ gives the corresponding phosphate ester. Selective hydroboration of the monosubstituted alkene with disiamylborane/THF followed by oxidation with $H_2O_2/NaOH$ produces a primary alcohol–phosphate ester.[14] Reduction of the latter with $Li/EtNH_2/Et_2O$ in the presence of t-BuOH[9] affords alcohol **7** in 69% overall yield from alcohol **6**. Intramolecular Prins reaction was effected by oxidation of alcohol **7** with PCC/CH_2Cl_2[15] to give tricyclic enone **8** in 67% yield. Wolff–Kishner reduction[16] of enone **8** produces crystalline hydrocarbon **9** in 64% yield. Reduction of enone **8** with $NaBH_4$/EtOH gives a single isomeric alcohol. Sequential treatment of this alcohol with $NCS/Ph_3P/THF$[17] followed by reduction of the intermediate chlorides with $LiAlH_4$ in refluxing THF affords a mixture of hydrocarbon **9** and (±)-seychellene (**10**) (6:94 ratio, respectively) in 23% overall yield from enone **8**. The spectral data of **10** (IR, NMR) were identical with those reported for the natural product.[1,3]

Reduction of enone **8** with $NaBH_4$/EtOH followed by reduction of the exocyclic alkene with $Li/EtNH_2/Et_2O$ in the presence of t-BuOH gives a single isomeric alcohol. Oxidation of this alcohol with PCC/CH_2Cl_2[15] produces ketone **11** in 79% overall yield from enone **8**. Conversion of ketone **11** to a p-toluenesulfonylhydrazone and treatment of this derivative with NaH/DMF[18] at 140 °C for 1h affords hydrocarbon **1** in 54% overall yield from ketone **11**. The NMR spectral data of hydrocarbon **1** [80 MHz NMR (C_6D_6) δ 0.70 (s, 3, CH_3), 0.83 (s, 3, CH_3), 0.88 (d, 3, J = 6.7 Hz, CH_3CH), 0.99 (s, 3, CH_3), 0.55 (dt, cyclopropyl H)] are significantly different than those reported for natural cycloseychellene.[2,19] We conclude that the NMR spectrum and the structure of natural cycloseychellene should be reinvestigated and revised. We report the NMR characterization of synthetic **1** and natural cycloseychellene in the accompanying paper.

Acknowledgment. We thank the Robert A. Welch Foundation (Grants No. E-518 and E-183) for support of this research program. We also thank Dr. S. Dev for his helpful discussions.

Registry No. (±)-**1**, 79083-63-9; (±)-*cis*-**2**, 79201-57-3; (±)-*trans*-**2**, 79201-58-4; (±)-**3**, 79201-59-5; (±)-**4**, 79201-60-8; (±)-**5a**, 79201-61-9; (±)-**5b**, 79201-62-0; (±)-**6**, 79201-63-1; (±)-**7**, 79201-64-2; (±)-**8**, 79201-65-3; (±)-**9**, 79201-66-4; (±)-**10**, 24568-69-2; (±)-**11**, 79201-67-5; 2,5-dimethylcyclohexanone, 932-51-4.

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(19) Copies of the IR, 220-MHz NMR (C_6D_6), and mass spectra were obtained from Dr. B. M. Lawrence, Director of Research and Development, R. J. Reynolds Tobacco Co. We thank Dr. Lawrence for providing these spectra.

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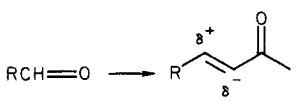
Branching Strategy in Organic Synthesis. 2. Reversal of Olefin Polarization with Concomitant Carbon–Carbon Bond Formation[1]

Summary: Vinyl sulfones are smoothly converted to α,β-unsaturated nitriles on exposure to KCN/dicyclohexyl-18-crown-6 in refluxing *tert*-butyl alcohol.

Sir: The delineation of new strategies for the construction of carbon skeleton branch points is fundamental to the development of synthetic organic chemistry. One approach to the construction of such branch points is to elaborate a specificially functionalized olefin.[2] This approach is limited, however, by the general observation that the olefin so prepared is negatively polarized in the direction of chain growth. This polarization is illustrated by the classical aldol condensation.



It is on occasion desirable in developing the branching of an olefin-containing carbon skeleton to switch chain growth to the opposite end of the olefin. This usually necessitates reversal of olefin polarization. While methods to temporarily effect such reversal (umpolung[3]) have been

(1) For part 1 in this series, see: Taber, D. F.; Gunn, B. P. *J. Org. Chem.* **1979**, *44*, 450.
(2) Faulkner, D. J. *Synthesis* **1971**, 175.

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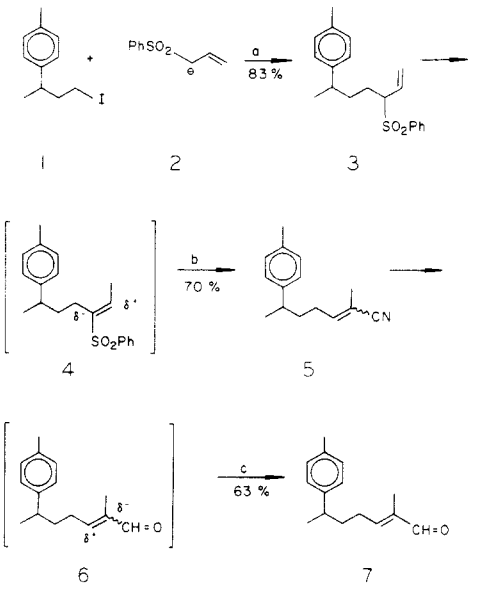
Scheme I

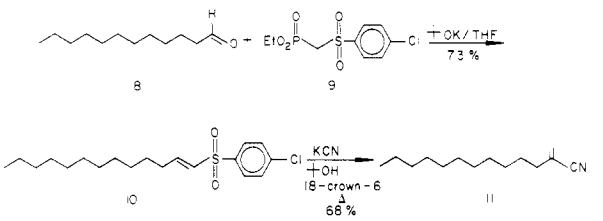


a) THF, -78° → RT, 30 min. b) KCN, dicyclohexyl 18-crown-6, potassium *t*-butoxide, methylene blue, *t*-butanol, reflux, argon, 18h. c) Dibal, hexane, RT, 3h; 5% aqueous HCl, RT, 5 min.

developed,[4] methods to effect permanent reversal have not in general been addressed.[5] To be truly useful, reversal of polarization should be coupled with carbon–carbon bond formation, to attach a readily modifiable functional group at the growing end of the olefin. We report such a method, based on the facile conversion of a vinyl sulfone to an α,β-unsaturated nitrile.[6]

This approach is illustrated by a simple synthesis of the sesquiterpene aldehyde nuciferal **7**[7,8] (Scheme I).[9] Thus, **3**, readily prepared by alkylation[10] of allyl phenyl sulfone (**2**) with iodide **1**,[8e] can be equilibrated with potassium *tert*-butoxide in *tert*-butyl alcohol to α,β-unsaturated sulfone **4**. The polarization of **4** is that commonly encountered in synthetic schemes, bond formation having been effected at the more negative end of the olefin. Addition of cyanide ion to the sulfone, followed by the elimination of potassium arenesulfinate,[6] effects reverrsal of olefin polarization, with concomitant carbon–carbon bond formation. After conversion of the nitrile to the stereoelectronically more demanding aldehyde,[11] this reversed polarization allows smooth equilibration of **6** to the desired *E* olefin **7**. This constitutes a new method for specific construction of a trisubstituted olefin.[2]

In its simplest incarnation, this approach allows the facile construction of an α-methylene nitrile from an aldehyde.[12] This is not a trivial conversion, involving as it



does formation of three new bonds to a single carbon.[16] It should be noted that this offers an efficient and conceptually novel entry to the α-methylene acid functionality common to many physiologically active terpene derivatives.

As the addition of cyanide ion to a vinyl sulfone appears to have not previously been investigated, we have briefly explored the generality of this transformation. As indicated, even very hindered olefins (e.g., **13**[9,17]) react smoothly.[18a]

Cyclic sulfones (e.g., **14**), although more sluggish,[18a,b] are also converted efficiently to the corresponding nitriles.

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(11) Marshall, J. A; Andersen, N. H.; Johnson, P. C. *J. Org. Chem.* **1970**, *35*, 186.

(12) Preparation of Sulfone **10**: To 531 mg (1.63 mmol) of phosphonate **9**[13] in 2 mL of dry THF in a 10-mL flame-dried round-bottom flask was added under argon at room temperature with magnetic stirring 158 mg (1.41 mmol) of potassium *tert*-butoxide. After 15 min, dodecanal **8** (200 mg, 1.09 mmole in 1 mL of THF was added, after which stirring was continued for 4 h. The reaction mixture was diluted with 5% aqueous HCl and extracted with CH_2Cl_2. The organic extract was dried over magnesium sulfate, filtered, concentrated in vacuo, and chromatographed on 10 g of TLC grade silica gel with 1% ethyl acetate in petroleum ether to give recovered aldehyde (R_f (10% EtOAc/hexane) 0.45), 54 mg, and sulfone **10** (R_f (10% EtOAc/hexane) 0.33), 207 m g (73%): ^{1}H NMR δ 0.86 (bt, 3 H), 1.25 (m, 18 H), 2.22 (m, 2 H), 6.26 (d, J = 16 Hz, 1 H), 6.96 (dd, J = 7, 16 Hz, 1 H), 7.44 (d, J = 9 Hz, 2 H), 7.76 (d, J = 9 Hz, 2 H); IR 2950, 2850, 2705, 1705, 1450, 1325, 1145, 1080 cm^{-1}; mass spectrum, 358 (6), 356 (15), 231 (8), 229 (20), 180 (45), 177 (47), 96 (100). Anal. Calcd: C, 63.91; H, 8.19. Found: C, 63.94; H, 8.19. Preparation of Nitrile **11**: Sulfone **10** (180 mg, 0.5 mmol), dicyclohexyl-18-crown-6[14] (19 mg, 0.05 mmol), powdered KCN (326 mg, 5.0 mmol), methylene blue[15] (10 mg), and *tert*-butyl alcohol (2 mL) were combined in a 10-mL round-bottom flask, a reflux condensor was attached, and the mixture was refluxed under argon with magnetic stirring for 2.5 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic extract was dried over Na_2SO_4, filtered, concentrated in vacuo, and chromatographed on 5 g of TLC grade silica gel with 2% ethyl acetate in petroleum ether to give recovered sulfone (32 mg) and nitrile **11** (R_f (10% EtOAc/hexane) 0.58), 58 mg (68%): ^{1}H NMR δ 0.86 (bt, 3 H); 1.1–1.7 (m, 18 H), 2.22 (t, J = 7 Hz, 2 H), 5.62 (s, 1H), 5.76 (s, 1 H); IR 2920, 2855, 2220, 1630, 1455, 855 cm^{-1}; mass spectrum, 207 (7), 206 (10), 192 (13), 178 (47), 164 (72), 150 (100), 136 (87). Anal. Calcd: C, 81.08; H, 12.16. Found: C, 81.30; H, 12.25.

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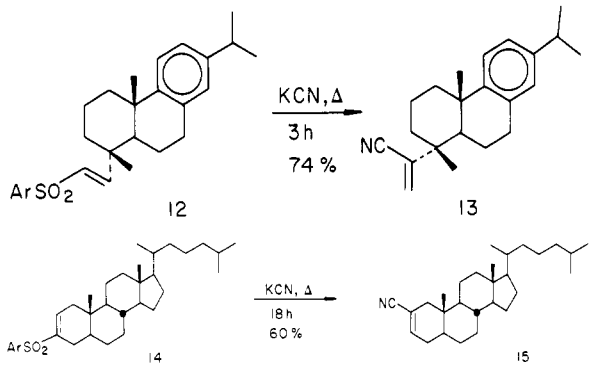
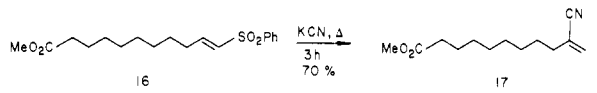
(17) (a) Sulfone **12** was prepared by condensation (NaH, Me_2SO, N_2, 80 °C 2 h) of phosphonate **9** with the corresponding aldehyde, which was in turn prepared by reduction (BH_3/THF) and oxidation (Jones reagent) of dehydroabietic acid. (b) Sulfone **14** was prepared by oxidation (H_2O_2/AcOH, Δ) of the corresponding sulfide, which was in turn prepared by $TiCl_4$-mediated condensation of *p*-chlorothiophenol with cholestanone: Mukaiyama, T.; Saigo, K. *Chem. Lett.* **1973**, 479. (c) Sulfone **16** was prepared by the addition of benzenesulfonyl iodide to methyl undecylenate, followed by dehydrohalogenation with triethylamine: Liu, L. K.; Chi, U.; Jen, K.-Y. *J. Org. Chem.* **1980**, *45*, 406.

(18) (a) The conditions of ref 12 were used. (b) Reaction time was extended to 18 h.



Finally, as exemplified by ester **16**, the reaction conditions are compatible with base-labile functionality.[18a]



Given the variety of established routes to vinyl sulfones,[19] we expect this method for carbon–carbon bond formation to be of general application. We also expect that reversal of olefin polarization, especially with concomitant carbon–carbon bond formation, will be an increasingly important concept in carbon skeleton assembly.

Acknowledgment. This investigation was supported by the National Institutes of Health, GM 15431. We acknowledge support from Biomedical Research Support Grant RR-05424 for MS and NMR instrumentation.

Registry No. 1, 43208-94-2; 2, 16212-05-8; 3, 79328-72-6; 4, 79328-73-7; 5, 79328-74-8; 7, 18744-24-6; 8, 112-54-9; 9, 40137-12-0; 10, 79328-75-9; 11, 79328-76-0; 12, 79328-77-1; 13, 79328-78-2; 14, 79356-96-0; 15, 79356-97-1; 16, 79328-79-3; 17, 79328-80-6; dehydroabietinal, 13601-88-2.

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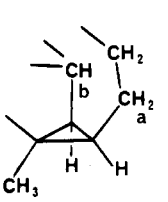
Cycloseychellene: A Structural Revision

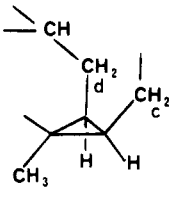
Summary: Investigation of the 400-MHz proton NMR spectra of the original structure **1** reported for cycloseychellene as well as the natural product leads to the conclusion that the actual carbon skeleton for natural cycloseychellene is represented as structure **2**.

Sir: Unequivocal synthesis of the molecule having the structure reported for cycloseychellene[1] produced a hydrocarbon, $C_{15}H_{24}$, the spectral properties and chromatographic behavior of which were unlike those of the natural product.[2] Since the synthesis was straightforward, we elected to remove this ambiguity by first interpreting the 400-MHz NMR spectrum of our synthetic material to ascertain that it is structure **1** and then interpreting the high-field NMR spectrum of natural cycloseychellene[3] as that of structure **2**.

The 400-MHz proton NMR spectra of **1** and **2** are shown in Figure 1. The synthetic and natural hydrocarbons are clearly distinct entities. The reasoning which distinguishes compound **1** from **2** is as follows. The synthesis of **1**[1] and the equilibration of **2** with seychellene,[1,2,4] a substance of certain structure, allows us to specify the essential carbon framework of compounds **1** and **2**. The difference between these two structures is localized with respect to the cyclopropyl ring. Appropriate partial structures which identify these compounds are **1A** and **2A**.



1A



2A

The assignments of the spectra are reduced to identifying the methylene and methine hydrogen atoms (a–d) adjacent to the cyclopropyl ring and determining whether there are three or four such protons in each structure. This seemingly trivial task is complicated by the fact that the cyclopropyl carbinyl protons exhibit unusual coupling patterns. The cyclopropyl resonances in structure **1** occur at δ 0.55 (a doublet of triplets) and 0.85 (a doublet). The doublet of triplets in the upfield resonance is collapsed to a doublet by decoupling a methylene group (a) at δ 1.87 to establish the cyclopropyl–methylene connectivity. The downfield cyclopropyl doublet is collapsed to a singlet by irradiation at δ 0.55. The coupling of ~0 Hz between the cyclopropyl and bridgehead proton (b) in structure **1** is the result of a 75° dihedral angle.[5] We point out that this geometrical decoupling can occur only if the adjacent group is a methine. An adjacent methylene group would have at least one significant J coupling into the cyclopropyl ring.

The spectrum of natural cycloseychellene features cyclopropyl resonances at δ 0.59 and 0.88. The fine structure in both cases is a four-line doublet of doublets. Decoupling the low-field cyclopropyl proton at δ 0.88 simplified the high-field cyclopropyl proton at δ 0.59 to a doublet and located the resonance at δ 1.656 as the last portion of an ABX spin system. The diastereotopic methylene protons (c) at δ 1.656 and 1.442 have dihedral angles of 40° and 80°, respectively, and show J couplings to the cyclopropyl resonance of 4 and 0 Hz.[5] Decoupling of the resonance at δ 1.442 and examination of the unperturbed pattern located another diastereotopic methylene group (d, δ 1.693 and 1.753). Decoupling the cyclopropyl resonance at δ 0.59 also confirms this assignment. The assessment of partial structure **1A** for natural cycloseychellene is completed when dihedral angles of 100° and 20° are found in a

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(3) Natural cycloseychellene (**2**, 0.0397 g) was reisolated from West Indian Patchouli Oil (7.857 g), Bruce Starke and Co., according to ref 2. This essential oil was obtained from Dr. B. M. Lawrence, R. J. Reynolds Tobacco Co. We thank Dr. Lawrence for this generous gift and copies of his spectra.

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