prepared from natural material) via chain extension with the phosphonate **16**[14] in dioxane (75% isolated yield). Natural and synthetic materials so obtained proved spectroscopically (300 MHz ^1H NMR, ^{13}C NMR) and chromatographically (TLC, HPLC) identical. Protecting-group removal (80% aqueous acetic acid) then afforded methyl pseudomonate C, indistinguishable from naturally derived material by high-field NMR and TLC analysis, which upon hydrolysis[2a] yields the title compound.

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(14) This material is readily accessible via esterification (dicyclohexylcarbodiimide, 4-(dimethylamino)pyridine) of bromoacetic acid with methyl 9-hydroxynonanoate, followed by Arbuzov reaction with trimethyl phosphite.[5c]

(15) Fellow of the Alfred P. Sloan Foundation, 1981-1985.

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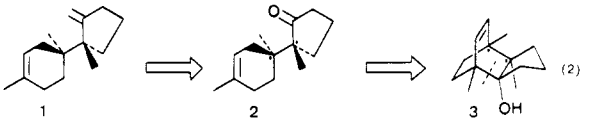
Stereoselective Synthesis of (±)-Trichodiene

Summary: A stereoselective synthesis of (±)-trichodiene (**1**) is described whose key step is the conversion of the tricyclic, homoallylic alcohol **3**, via β-fragmentation of its potassium alkoxide **3a**, to cyclopentanone **2**.

Sir: The naturally occurring bicyclic sesquiterpene hydrocarbon trichodiene (**1**), the biogenetic precursor of the biologically active trichothecanes, was first isolated in 1970 from the fungus *Trichothecium roseum* and its structure determined by degradation and spectroscopy.[1] Up to now, relatively few syntheses of **1** have been reported,[2] reflecting the general difficulty of controlling the stereochemistry of two adjacent chiral centres where there is free rotation about the common carbon-carbon bond. We present herein an effective solution to this problem in the context of a short, stereoselective synthesis of racemic trichodiene.

Recently, as a synthetic application of the β-fragmentation of potassium homoallylic alkoxides,[3] we reported the regioselective preparation of 1-(3-cyclohexenyl)-2-alkanones from 2-substituted bicyclo[2.2.2]oct-5-en-2-ols (eq 1).[4] Retrosynthetic analysis (eq 2) thus indicated that cyclopentanone **2**, a direct synthetic precursor of tri-

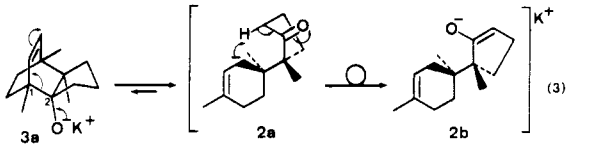
chodiene,[2a,c] would be formed analogously from the tri-



cyclic, homoallylic alcohol **3** in which the correct relative stereochemistry of the two relevant quaternary centers is already set up. An efficient preparation of **3** from 1,4-dimethyl-1,3-cyclohexadiene (**4**)[5] and the successful realisation of this synthetic strategy are outlined in Scheme I.

Diels-Alder reaction between **4** and 2-chloroacrylonitrile (1.5 equiv) in toluene containing hydroquinone at 90 °C during 60 h followed by hydrolysis[6] of the intermediate cycloadducts gave bicyclo[2.2.2]enone **5** (57%, bp 68-70 °C (10 mmHg)).[7] With lithium diisopropylamide (LDA) as base, two successive low temperature alkylations, methylation and then allylation, afforded dienone **6** (84%, bp 53-55 °C (0.05 mmHg)) with high stereoselectivity (≥95%[8]). The stereochemistry at C(3) is controlled by the second alkylation in which allyl iodide reacts exclusively at the less hindered face of the tetrasubstituted lithium enolate. Chemoselective and regioselective hydroboration of the monosubstituted alkenyl double bond in **6** with 9-borabicyclo[3.3.1]nonane (9-BBN) (1.1 equiv in tetrahydrofuran (THF) at 25 °C), oxidation with aqueous basic hydrogen peroxide, tosylation of the resulting keto alcohol, and treatment with lithium bromide (2.6 equiv) in acetone at reflux during 1.5 h then afforded bromo ketone **7** (77% from **6**, bp 88-90 °C (0.05 mmHg)). An intramolecular Barbier reaction[9] using lithium in THF at 0 °C in a sonicator[10] completed the synthesis of **3** (54%, bp 70-72 °C (0.05 mmHg)).[11]

With **3** in hand the key step was effected by treatment with potassium hydride (1.1 equiv) in hexamethylphosphoric triamide (HMPA) at 25 °C and then heating the thus formed potassium alkoxide **3a** at 140 °C during 1 h. Quenching (20% aqueous NH_4Cl) followed by an extractive workup led to the isolation of stereochemically pure **2** in 32% yield.[12,13] In analogy with previous work[4]



(1) (a) Nozoe, S; Machida, Y. *Tetrahedron Lett.* **1970**, 2671-2674. (b) *Tetrahedron* **1972**, *28*, 5105-5117.

(2) (a) Welch, S. C.; Prakaso Rao, A. S. C.; Wong, R. Y. *J. Org. Chem.* **1980**, *45*, 4077-4085. (b) Suda, M. *Tetrahedron Lett.* **1982**, *23*, 427-428. (c) Schlessinger, R. H.; Schultz, J. A. *J. Org. Chem.* **1983**, *48*, 407-408.

(3) For other synthetic applications, see: (a) Snowden, R. L.; Muller, B. L.; Schulte-Elte, K. H. *Tetrahedron Lett.* **1982**, *23*, 335-338. (b) Snowden, R. L. *Helv. Chim. Acta* **1983**, *66*, 1031-1038.

(4) Snowden, R. L.; Schulte-Elte, K. H. *Helv. Chim. Acta* **1981**, *64*, 2193-2202.

(5) Ruttimann, A; Wick, A.; Eschenmoser, A. *Helv. Chim. Acta* **1975**, *58*, 1450-1455.

(6) Evans, D. A.; Scott, W. L.; Truesdale, L. K. *Tetrahedron Lett.* **1972**, 121-124.

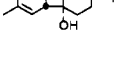
(7) Reactions involving air-sensitive reagents or substances were conducted under a N_2 atmosphere. Satisfactory spectroscopic data (IR, ^1H NMR, and MS) were obtained for each synthetic intermediate by using chromatographically purified and homogeneous samples.

(8) This lower stereoselectivity limit was determined by ^{13}C NMR spectral comparison of the crude reaction mixture with the C(3) epimer of **6**, independently prepared from **5**, with a similar high stereoselectivity, by inversion of the alkylation sequence.

(9) Blomberg, C.; Hartog, F. A. *Synthesis* **1977**, 18-30.

(10) Luche, J.-L.; Damiano, J.-C. *J. Am. Chem. Soc.* **1980**, *102*, 7926-7927.

(11) Another tertiary alcohol, tentatively assigned the tricyclic-[5.4.0.0^{2,6}] structure i, was also isolated in 11% yield.



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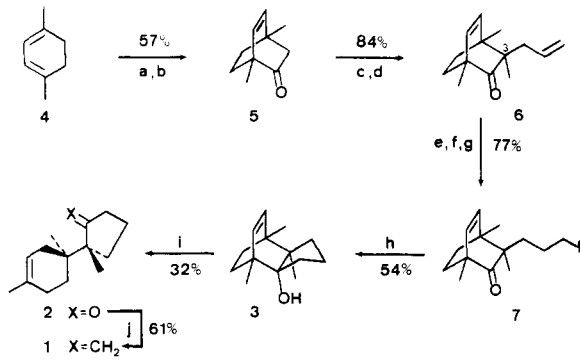
Scheme I[a]



[a] Reagents: (a) CH_2=C(CN)Cl, toluene, 90 °C; (b) $Na_2S \cdot 9H_2O$, EtOH, reflux, 24 h; (c) LDA, THF, −70 °C, then CH_3I, HMPA, −30 °C; (d) LDA, THF, −70 °C, then CH_2=$CHCH_2I$, HMPA, −60 °C; (e) 9-BBN, THF, then 30% aqueous H_2O_2, NaOH; (f) TsCl, C_5H_5N; (g) LiBr, acetone, reflux, 1.5 h; (h) Li, THF, 0 °C; (i) KH, HMPA, 140 °C, 1 h; (j) Ph_3P=CH_2, Me_2SO, 80 °C.

the reaction mechanism (eq 3) is believed to involve heterolytic cleavage of the allylic C(1)–C(2) bond in **3a** and rearrangement of the resultant allylic anion **2a** to the potassium enolate **2b**, which is subsequently protonated to afford **2**. Finally, Wittig methylenation as described[2c] furnished (±)-**1** in 61% yield.[14]

Registry No. (±)-**1**, 61505-17-7; (±)-**2**, 61375-52-8; (±)-**3**, 89398-34-5; **4**, 26120-52-5; (±)-**5**, 89398-35-6; (±)-**6**, 89398-36-7; (±)-**7**, 89398-37-8; CH_2=C(CN)Cl, 920-37-6; CH_2=$CHCH_2I$, 556-56-9.

(12) Spectroscopic data (IR, 360-MHz ^1H NMR, MS) of **2** are identical with those of an authentic sample provided by Professor R. H. Schlessinger. ^{13}C NMR ($CDCl_3$) δ 223.7 (s), 132.4 (s), 119.8 (d), 53.9 (s), 40.8 (t), 36.3 (s), 33.7 (t), 33.1 (t), 27.9 (t), 27.4 (t), 23.2 (q), 18.7 (t), 18.4 (q), 18.3 (q). For another stereoselective synthesis of **2**, see: Yamakawa, K.; Sakaguchi, R.; Nakanura, T.; Watanabe, K. *Chem. Lett.* **1976**, 991–992.

(13) The only moderate yield of **2** is believed to result in part from a competing alkoxide accelerated retro-Diels–Alder reaction of **3a**; isolation of 2-methyl-1-cyclopentanone from the reaction mixture supports this hypothesis. For a related precedent, see ref 4.

(14) ^1H and ^{13}C NMR spectra of (±)-**1** are identical with those of natural trichodiene provided by Professor D. E. Cane.

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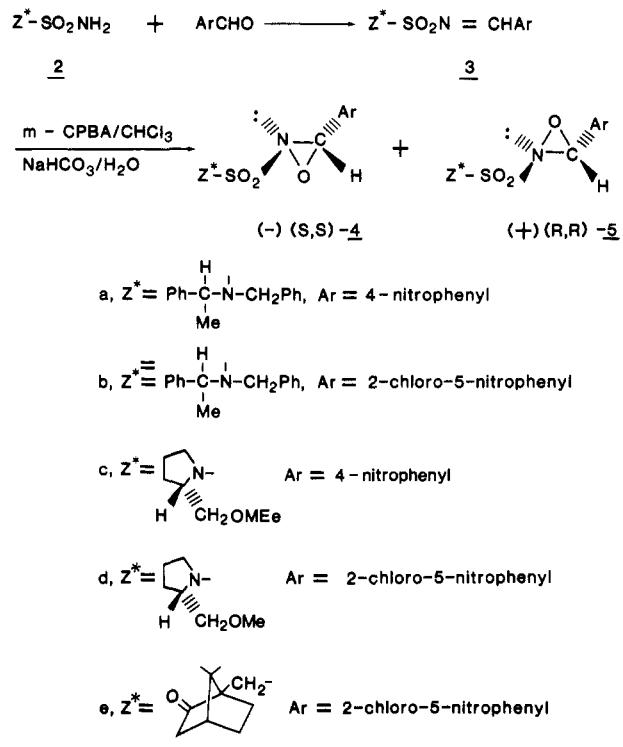
Chiral Sulfamides: Synthesis of Optically Active 2-Sulfamyloxaziridines. High Enantioselectivity in the Asymmetric Oxidation of Sulfides to Sulfoxides

Summary: The first synthesis of optically active 2-sulfamyloxaziridines **4a–d** and **5a–d**, which affords high enantioselectivity (38–68% ee) for asymmetric oxidations of sulfides to sulfoxides, is described.

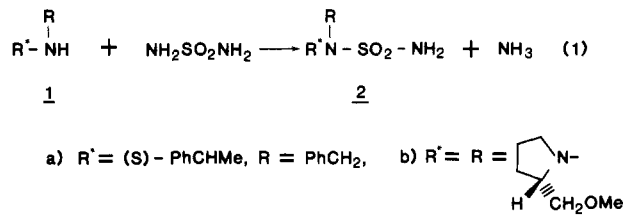
Sir: Although sulfamides ($R_2NSO_2NH_2$) have been known and studied for many years,[1] there are only a few synthetic procedures employing these reagents.[2] Furthermore, there

Scheme I



appear to be no optically active examples of these compounds. As part of a program to explore chiral sulfamides in organic synthesis we report the first examples of optically active sulfamides and their application to the synthesis of chiral 2-sulfamyloxaziridines **4a–d** and **5a–d** (Scheme I). Chiral 2-sulfamyloxaziridines are a new class of asymmetric oxidizing agents that afford the best enantioselectivity (38–68% ee) of any reagent for the oxidation of sulfides to sulfoxides.

Chiral sulfamide **2a**, 78% yield, mp 89–90 °C; $[\alpha]_D$ −22.0° (*c* 2.28, $CHCl_3$), was prepared by heating equivalent amounts of (−)-(*S*)-*N*-(α-methylbenzyl)-*N*-benzylamine (**1a**)[3] and sulfamide ($NH_2SO_2NH_2$) in dry dimethoxyethane for 3 days as described by McManus et al. (eq 1).[5] With



(+)-(*S*)-2-(methoxymethyl)pyrrolidine (**1b**)[6] this procedure gave only a 51% yield of sulfamide **2b**, mp 60–62 °C; $[\alpha]_D$ −3.46° (*c* 2.0, $CHCl_3$) after 5 days. However, the yield of **2b** was improved to 66% when the two reagents were heated in the absence of the solvent for 24 h (90 °C for

(1) For reviews on the chemistry of sulfamic acids that include discussions of sulfamides, see: (a) Spillane, W. J. *Int. J. Sulfur Chem.* **1973**, *8*, 469. (b) Benson, G. A.; Spillane, W. J. *Chem. Rev.* **1980**, *80*, 151. (c) Andersen, K. K. *Compr. Org. Chem.* **1979**, *3*, 363.

(2) Sulfamides have been primarily used in the synthesis of heterocyclic systems. In addition to the examples given in ref 1: (a) 1,2,6-Thiadiazirine 1,1-dioxides, Wright, J. B. *J. Org. Chem.* **1964**, *29*, 1905. Elguero, J.; Ochoa, C.; Stud, M.; Estaban-Calderon, C.; Martienz-Ripoll, M. *Ibid.* **1982**, *47*, 536. (b) Thiadiazine 1,1-dioxides, Timberlake, J. W.; Hodges, M. L. *J. Am. Chem. Soc.* **1973**, *95*, 634.

(3) This amine was prepared according to the procedure of Anderson and Santi[4] except that (−)-(*S*)-α-phenylethylamine (Hexcel) was used in the place of the racemic amine; $[\alpha]_D$ −39.9° (neat).

(4) Anderson, R. T., Jr.; Santi, D. V. *J. Med. Chem.* **1976**, *19*, 1270.

(5) McManus, J. M.; McFarland, J. W.; Gerber, C. F.; McLamore, W. M.; Laubach, G. D. *J. Med. Chem.* **1965**, *8*, 766.

(6) Enders, D.; Eichenauer, H. *Chem. Ber.* **1979**, *112*, 2933.

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