β-Hydroxysulfoximine-Directed Simmons-Smith Cyclopropanations. Synthesis of (-)- and (+)-Thujopsene

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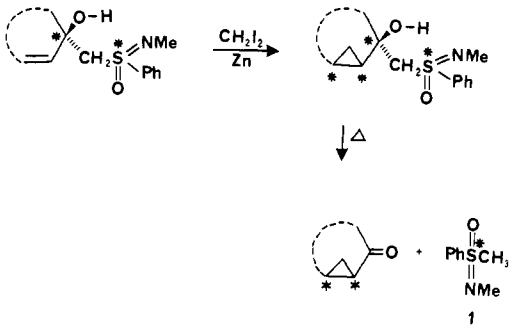
(-)-Thujopsene (**10**), a tricyclic sesquiterpene, was originally isolated from the wood oil of the Japanese Hiba tree[1] and has since been found in many conifers belonging to the natural order Cupressales.[2a] Its structure[2] and absolute configuration[3] were determined, and subsequently four total syntheses of (±)-**10** have been reported.[4] In the first of these Dauben and Ashcraft[4a] found that (±)-dihydromayurone (**8**) could be readily converted to (±)-**10**. We felt that **8** would be an exemplary target for a new cyclopropyl ketone optical activation method based on Simmons-Smith reactions of resolved "allylic" β-hydroxysulfoximines derived from cyclic enones (Scheme I).

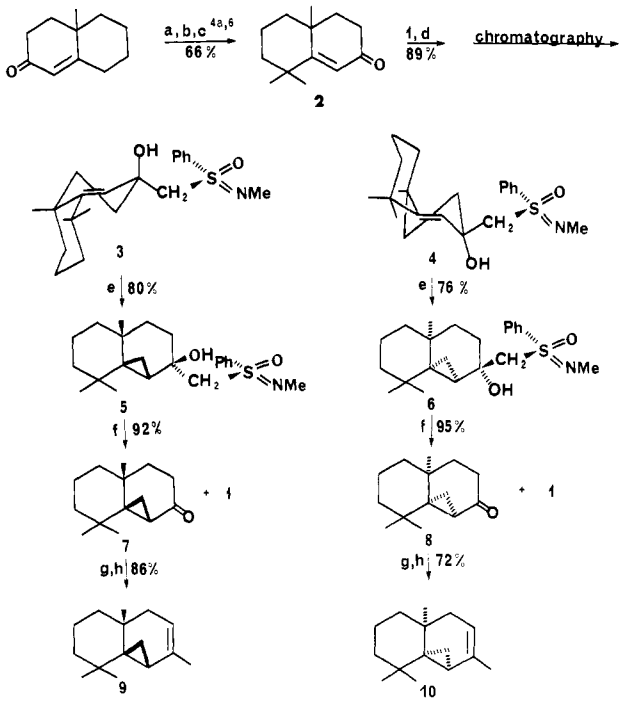
The sequence of reactions utilized in the thujopsene synthesis is outlined in Scheme II. Addition of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine (**1**)[5] as its lithium derivative to (±)-4a,8,8-trimethyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (**2**)[4a,6] (THF, -78 °C, 1 h) provided two major diastereomeric adducts (**3**, **4**) along with a single minor one (from "axial" addition) in 83% combined yield (ratio 12:7:1). These allylic β-hydroxysulfoximines were readily separated by column chromatography on silica gel; **3** was isolated as a crystalline solid (mp 109-110 °C, $[\alpha]^{25}_D$ -133.9° (*c* 1.24, $CHCl_3$))[7] and **4** as a gum ($[\alpha]^{25}_D$ +33.1° (*c* 1.06, $CHCl_3$)).[8] Treatment of diastereomer **3** with a 30-fold excess of Simmons-Smith reagent (Zn(Ag), CH_2I_2, Et_2O, reflux, 72 h)[9] provided cyclopropylcarbinol **5** as a crystalline solid (mp 88-91 °C, $[\alpha]^{25}_D$ +34.4° (*c* 1.04, $CHCl_3$)) in 80% yield after flash chromatography. Diastereomer **4** reacted more sluggishly, requiring a 50-fold excess (72 h) to produce the desired cyclopropanated diastereomer **6** in 76% yield as a crystalline material (mp 101-103 °C, $[\alpha]^{25}_D$ +7.3° (*c* 1.18, $CHCl_3$)). Analytical HPLC and ^{13}C NMR indicated that the Simmons-Smith reaction was stereospecific in the introduction of the cyclopropane ring. Other results in our laboratory have indicated unequivocally that the cyclopropanation occurs cis to the hydroxyl group of allylic β-hydroxysulfoximines.[10]

β-Hydroxysulfoximines undergo a retro reaction upon mild thermolysis to regenerate the carbonyl moiety and the starting sulfoximine.[11] Diastereomer **6** was thermolyzed neat in a Kugelrohr oven at 100 °C under water-aspirator vacuum, and resolved (+)-dihydromayurone (**8**) was sublimed into the collection bulb as it was generated. This tricyclic ketone was isolated in

Scheme I



Scheme II



a = MeI, KO-*t*-Bu, *t*-BuOH; b = NH_2NH_2, Na, $(HOCH_2CH_2)_2O$; c = $Na_2Cr_2O_7$, HOAc; d = *n*-BuLi, THF, -78 °C; e = CH_2I_2, Zn(Ag), Et_2O; f = 100 °C; g = MeMgBr, Et_2O; h = TsOH, PhH, reflux

95% yield after flash chromatography as a crystalline solid (mp 103-104 °C, $[\alpha]^{25}_D$ +70.5° (*c* 0.78, $CHCl_3$)) exhibiting physical parameters and spectral data in accord with the published values.[4c,12] The optical purity of (+)-**8** was 94% based on the reported $[\alpha]^{25}_D$ +75.4° ($CHCl_3$)[12a] for material prepared from naturally occurring (+)-mayurone. Diastereomer **5** was thermolyzed in an identical manner to give in 92% yield the enantiomeric (-)-dihydromayurone (**7**) as a crystalline material (mp 105-106 °C, $[\alpha]^{25}_D$ -72.2° (*c* 1.06 $CHCl_3$)).

It has been previously reported that (±)-**8** could be converted into (±)-thujopsene (**10**) by addition of methylmagnesium bromide, followed by dehydration during workup with saturated ammonium chloride.[4a] In our hands dehydration did not occur under these conditions. However, reaction of (+)-**8** with methylmagnesium bromide (Et_2O at reflux, 30 min, then saturated aqueous NH_4Cl quench) followed by dehydration of the cyclopropylcarbinol (benzene, catalyzed by *p*-TsOH, reflux, 1 h) cleanly provided, after flash chromatography, a 72% yield of (-)-**10** as a colorless oil with $[\alpha]^{25}_D$ -103.9° (*c* 1.02, $CHCl_3$) plus spectral data and physical constants in agreement with the published values.[2a] An optical purity of 94% can be deduced from the highest reported $[\alpha]^{25}_D$, -110° (*c* 2.0, $CHCl_3$).[2a] Reaction of (-)-**7** under

(1) Yano, M. *J. Soc. Chem. Ind. Jpn.* **1913**, *16*, 443. Uchida, S. *Ibid.* **1928**, *31*, 501.
(2) (a) Norin, T. *Acta Chem. Scand.* **1961**, *15*, 1676 and references cited therein. (b) Nozoe, T.; Takeshita, H.; Itô, S.; Ozeki, T.; Seto, S. *Chem. Pharm. Bull.* (Tokyo) **1960**, *8*, 936. (c) Sisido, K.; Nozaki, H.; Imagawa, T. *J. Org. Chem.* **1961**, *26*, 1964. (d) Kobayashi, H.; Nagahama, S.; Akiyoshi, S. *Bull. Chem. Soc. Jpn* **1961**, *34*, 1123.
(3) Enzell, C. *Acta Chem. Scand.* **1962**, *18*, 1553. Norin, T. *Ibid.* **1963**, *17*, 738.
(4) (a) Dauben, W. G.; Ashcraft, A. C. *J. Am. Chem. Soc.* **1963**, *85*, 3673. (b) Büchi, G.; White, J. D. *Ibid.* **1964**, *86*, 2884. (c) Mori, K.; Ohki, M.; Kobayashi, A.; Matsui, M. *Tetrahedron* **1970**, *26*, 2815. (d) Anderson, P. L. *Diss. Abstr. B* **1967**, *28*, 91.
(5) Optical purity 98% based on $[\alpha]^{25}_D$ +184° (*c* 3, acetone) for (*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine. All rotations are corrected for the optical purity of the sulfoximine.
(6) Enzell, C. *Tetrahedron Lett.* **1962**, 185.
(7) Satisfactory analytical and spectral data were obtained for all new compounds.
(8) The indicated absolute configurations of **3** and **4** can be directly inferred via the stereospecific transformations utilized in converting them into compounds of known absolute stereochemistry, **10** and its enantiomer **9**.
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(10) Johnson, C. R.; Barbachyn, M. R., unpublished results. For a review of Simmons-Smith reactions directed by oxygen coordination see: Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1972**, *20*, 1.
(11) Johnson, C. R.; Zeller, J. R. submitted for publication.
(12) (a) Chetty, G. L.; Dev, S. *Tetrahedron Lett.* **1965**, 3773. (b) Itô, S.; Endo, K.; Honma, H.; Ota, K. *Ibid.* **1965**, 3777.

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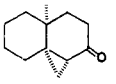
Table I. Production of Optically Active Cyclopropyl Ketones

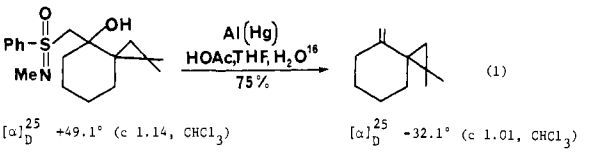
entry	method[a]	cyclopropyl ketone	$[\alpha]_D^{25}$ ($CHCl_3$), deg
1	A		+160.6 (*c* 2.17) −164.9 (*c* 2.33)
2	B		+15.3 (*c* 2.04) −15.5 (*c* 1.28)
3	A		+47.3 (*c* 0.51) −50.8 (*c* 1.31)
4	A		+162.3 (*c* 0.63) −171.9 (*c* 1.11)
5	A		+97.7 (*c* 1.76) −95.3 (*c* 1.47)
6	B		+215.3 (*c* 1.08) −214.5 (*c* 1.02)
7	A		+101.4 (*c* 2.09)

[a] Method A sequence: (1) addition of 1 to enone (yields ~95%); (2) separation of diastereomeric enone adducts by medium-pressure liquid chromatography on silica gel with EtOAc/hexanes (combined recovery 85–96%); (3) cyclopropanation (yields 77–96%); (4) thermal release of cyclopropyl ketone (yields 73–98%). Method B sequence: (1) addition of 1 to enone (yields ~95%); (2) cyclopropanation (yields 91–98%); (3) chromatographic separation (as above) of cyclopropanated adducts (combined recovery 65–98%); (4) thermal release of cyclopropyl ketones (yields 60–75%).

identical conditions gave, after chromatography, an 86% yield of the unnatural enantiomeric (+)-thujopsene (**9**) as a colorless oil, $[\alpha]^{25}_D$ +107.6° (*c* 2.04, $CHCl_3$) (98% optically pure). Alternatively the β-hydroxysulfoximines **5** and **6** were desulfurized with Raney nickel[13] and dehydrated to obtain the same products (**9** and **10**), but in reduced yield (~56%).

This new methodology for the optical activation of cyclopropyl ketones represents a viable alternative to other resolution[14] or asymmetric induction[15] techniques. Additional examples are shown in Table I. Generally both enantiomers are obtained in high optical purity, and the resolving reagent **1** can be readily recovered. In some instances, e.g., Table I, entries 2 and 6, it was found to be more expedient to separate the diastereomers after cyclopropanation. As anticipated, the method when applied to enones in which the carbonyl is acyclic presents special problems. The addition of **1** to 1-(1-cyclohexenyl)ethone (Table I, entry 7) provided readily separable diastereomeric adducts. Each of these pure diastereomers with nonrigid carbinol sites underwent the Simmons–Smith reaction to give two cyclopropyl diastereomers. From the enone adduct of lower R_f one of the cyclopropyl diastereomers was obtained pure by chromatography and thermolyzed to the ketone noted in Table I.

The resolved cyclopropanated adducts and ketones are amenable to further elaboration, e.g., **8** → **10** and eq 1, allowing for extensions of the utility of the method. Work is continuing on the exploration of the β-hydroxysulfoximine moiety as a chiral directing group in other additions to neighboring alkenes.



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Registry No. 1, 33993-53-2; **2**, 17299-44-4; **3**, 82198-83-2; **4**, 82198-84-3; **5**, 82198-85-4; **6**, 82262-78-0; **7**, 82262-79-1; **8**, 7129-16-0; **9**, 82262-80-4; **10**, 470-40-6; (+)-4,4,6-trimethylbicyclo[4.1.0]heptan-2-one, 82198-86-5; (−)-4,4,6-trimethylbicyclo[4.1.0]heptan-2-one, 82198-87-6; (+)-bicyclo[4.1.0]heptan-2-one, 82334-95-0; (−)-bicyclo[4.1.0]heptan-2-one, 58072-38-1; (+)-1,1-dimethylspiro[2.5]octan-4-one, 82198-88-7; (−)-1,1-dimethylspiro[2.5]octan-4-one, 82198-89-8; (+)-1,1-dimethylspiro[2.4]heptan-4-one, 82198-90-1; (−)-1,1-dimethylspiro[2.4]heptan-4-one, 82198-91-2; (+)-4a-methylperhydrocyclopropa[*d*]naphthalen-2-one, 82262-81-5; (−)-4a-methylperhydrocyclopropa[*d*]naphthalen-2-one, 82262-82-6; (+)-4,4-dimethylbicyclo[4.1.0]heptan-2-one, 82198-92-3; (−)-4,4-dimethylbicyclo[4.1.0]heptan-2-one, 82198-93-4; (+)-1-acetylbicyclo[4.1.0]heptane, 82198-94-5; 4,4a,5,6,7,8-hexahydro-4a-methyl-2-(3*H*)-naphthalenone, 826-56-2; methyl bromide, 74-83-9.

(13) Johnson, C. R.; Stark, C. J. *J. Org. Chem.* **1982**, 47, 1193.

(14) For example, partially resolved 2-cycloalken-1-ols have been cyclopropanated by the Simmons–Smith method followed by oxidation to optically active cyclopropyl ketones: Hill, R. K.; Morgan, J. W. *J. Org. Chem.* **1968**, *33*, 927. Lightner, D. A.; Jackman, D. E. *Tetrahedron Lett.* **1975**, 3051. A cyclopropyl ketone has been converted to an amine which was resolved with (−)-malic acid followed by regeneration of the ketone in optically active form: Zimmerman, H. E.; Hancock, K. G.; Licke, G. C. *J. Am. Chem. Soc.* **1968**, *90*, 1892.

(15) Enones have been transformed to optically active cyclopropyl ketones by using optically active oxosulfonium ylides: Johnson, C. R.; Schroeck, C. W. *J. Am. Chem. Soc.* **1968**, *90*, 6852. A cyclopropyl ketone of low ee has been obtained in a Simmons–Smith reaction of an enone in the presence of (−)-menthol: Sawada, S.; Oda, J.; Inouye, Y. *J. Org. Chem.* **1968**, *33*, 2141.

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Metathesis of Tungsten–Tungsten Triple Bonds with Acetylenes and Nitriles To Give Alkylidyne and Nitrido Complexes[1]

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We recently reported that $W(CCMe_3)(OCMe_3)_3$ will rapidly and catalytically convert an unsymmetric alkyne into a mixture containing the unsymmetric alkyne and the two possible symmetric alkynes (alkyne metathesis).[2] Although the catalyst is long-lived in the absence of air and water, we thought it possible that it is eventually deactivated by bimolecular decomposition of intermediate $W(CR)(OCMe_3)_3$ species to give $W_2(OCMe_3)_6$[3] or by some as yet undefined reaction involving β protons in the alkylidyne ligand. The fact that we found no evidence for bimolecular decomposition suggested to us that that $W_2(OCMe_3)_6$ would react with alkynes to give the alkylidyne complexes $W(CR)(OCMe_3)_3$. We report here that first, this is indeed the case, second, that alkylidyne complexes that contain β protons in the alkylidyne ligand can be isolated, and third, that nitriles also react with $W_2(OCMe_3)_6$ to give a mixture of $W(N)(OCMe_3)_3$ and $W(CR)(OCMe_3)_3$. This metathesis-like reaction of a W≡W bond is not only an excellent route to tungsten alkylidyne complexes but is a unique example of rapid cleavage of a W≡W bond at 25 °C by mild reagents.[4]

(1) Multiple Metal–Carbon Bonds. 27.

(2) (a) Wengrovius, J. H.; Sancho, J.; Schrock, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 3932. (b) Sancho, J.; Schrock, R. R. *J. Mol. Catal.* **1982**, *15*, 75.

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