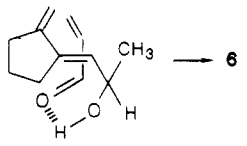
The intermolecular cycloaddition shows a remarkable reversal of diastereofacial selectivity in going from *N*-phenylmaleimide to acrolein as the dienophile. The formation of adduct **5** (eq 2) corresponds to the facial selectivity suggested previously based upon experimental and theoretical studies.[14] The opposite facial selectivity observed in the formation of **6** may arise by the OH group serving as an "internal acid catalyst" in which event **23** corresponds to the most reasonable model for the transition state.



23

The ability to impose control upon the course of organic reactions represents an important strategy to achieve chemo-, regio-, and diastereoselectivity. The present results highlight the versatility of the hydroxy group in such a role for both transition-metal and thermal reactions to provide ready access to polycyclic structures from totally acyclic building blocks in a simple consecutive two-step sequence.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for their generous support of our programs.

Supplementary Material Available: Spectral data for compounds **4–6**, **7** (X = $C(CO_2CH_3)_2$), **8** (X = $C(CO_2CH_3)_2$), **8** (X = NCH_2Ph), **9**, **10** (X = $C(CO_2CH_3)_2$), **10** (X = NCH_2Ph), **11**, and **13–18** (4 pages). Ordering information is given on any current masthead page.

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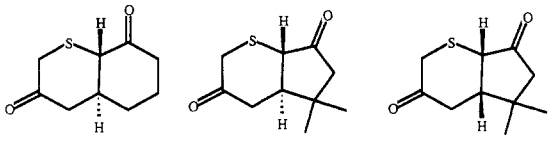
Synthesis of Optically Active Thiadecalins and Thiahydrindans by a Proline-Catalyzed Intramolecular Michael Reaction

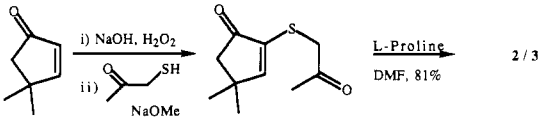
Summary: The *trans*-thiadecalindione **1** and the *trans*- and *cis*-thiahydrindandiones **2** and **3** were prepared from the corresponding α-thio enones **4** and **5** by a proline-catalyzed intramolecular Michael process. The optically pure enantiomers of **1** were obtained by fractional crystallization, allowing the assignment of an enantiomeric excess of 19–28% for the Michael reaction depending on reaction conditions. Additionally, thiadecalindione **1** was reduced by actively fermenting bakers' yeast to provide exclusively the product **7** resulting from reduction of the thiopyran ring carbonyl group.

Sir: During work directed toward the synthesis of compounds that contain medium-sized rings, we needed to synthesize the sulfur-containing diketones **1** and **2/3**. Because our strategy was to first bridge the sulfur ring with an optically active carbon chain and then to desulfurize to produce a medium-sized ring, it was desirable to acquire the heterocycles **1** and **2/3** in optically active form.



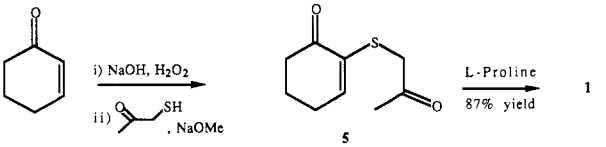
1 **2** **3**

Toward this end, 4,4-dimethylcyclopent-2-enone[1] was epoxidized in 60% yield with basic hydrogen peroxide[2] and the resulting epoxide opened regioselectively with mercaptoacetone.[3] Spontaneous dehydration then gave the crystalline enone **4**, in 75% yield.[4] The enone was stirred in dry dimethylformamide at 60 °C with 1 equiv of L-proline to give the diastereomeric sulfides **2** and **3** in approximately a 1:1 ratio (81%). The diastereomers were separated by silica gel chromatography and identified by the ^1H NMR coupling constants of the ring junction protons [**2**, J = 11.5 Hz, $[\alpha]_D$ −21.6° (c 3.60, $CHCl_3$); **3**, J = 8.0 Hz, $[\alpha]_D$ −19.9° (c 2.27, $CHCl_3$)]. Attempts to discern the enantiomeric excess of these compounds using various chiral shift reagents proved inconclusive.



4

Next, cyclohex-2-enone was epoxidized, as above, in 67% yield and treated with mercaptoacetone[3] to give the sulfur-functionalized enone **5** as a yellow oil in 54% yield. Enone **5** underwent cyclization in dry dimethylformamide at room temperature for 48 h with 1 equiv of L-proline to give exclusively the trans isomer **1** as a white solid [87%, $[\alpha]_D$ −58.7° (c 0.71, $CHCl_3$)].



5

On a somewhat larger scale 5 g of **5** was kept with L-proline at −15 °C for 7 days. The optical rotation of the product **1** was −85° (c, 0.90, $CHCl_3$), which was raised to −296° (c 1.23, $CHCl_3$) upon recrystallization from THF. Two further recrystallizations gave material of optical rotation −311° (c 1.01, $CHCl_3$), which did not change upon further recrystallization (overall yield ~45%).

The 300-MHz ^1H NMR spectra of the recrystallized and racemic compounds were then analyzed by using the chiral shift reagent tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III), [Eu(hfc)$_3$]. The racemic material showed marked splitting of nearly every signal, while no splitting or shoulders were observed for the triply recrystallized material. Since a prepared

(1) Magnus, P. D.; Nobbs, M. S. *Synth. Commun.* **1980**, *10*, 273.
(2) House, H. O.; Wasson, E. I. in *Organic Syntheses*; Wiley: New York, 1976; Collect. Vol. 4, p 552.
(3) Hromatka, V. O.; Engle, E. *Monatsh. Chem.* **1948**, *78*, 29.
(4) (a) Schultz, A. G.; Kashdan, D. S. *J. Org. Chem.* **1973**, *38*, 3814. (b) Tobias, M. A.; Strong, J. G.; Napier, R. P. *J. Org. Chem.* **1970**, *35*, 1709.

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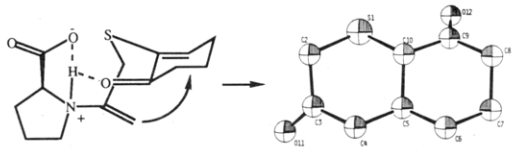
"90% ee" solution of **1** exhibited visible shoulders for many of its peaks in the Eu(hfc)$_3$ spectrum, we conclude that the optical purity of **1** is ≥95%. On the basis of the assumption that recrystallized **1** exhibiting a rotation of −311° is optically pure, an enantiomeric excess of 19% can be assigned for the cyclization conducted at room temperature, and a value of 28% for the reaction conducted at −15 °C. When **5** was cyclized by using unnatural D-proline, and the product recrystallized twice from THF, a compound identical in all respects with **1** but having a rotation of +307° (*c* 0.975, $CHCl_3$) was obtained.

The recrystallized compound (−)-**1** was then subjected to single-crystal X-ray structure analysis.[5] The diffraction data was refined to an unweighted residual value of 0.059 for the structure **1** with the absolute configuration shown below (C-5 and C-10 having the *S* configuration). A model

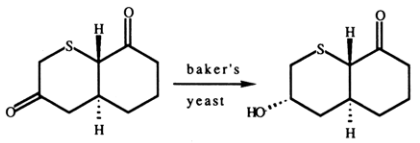


6 **1**

similar to that proposed by Agami[6] for the intramolecular aldol reaction of Hajos and Parrish[7] can be used to explain the stereoselectivity of this intramolecular Michael process. In our model (**6**), an enamine-like adduct between proline and the side-chain ketone is initially formed. Hydrogen bonds between the protonated nitrogen of the amino acid and the enone carbonyl then direct the Michael addition preferentially to one face of the carbocyclic ring.

Our next problem became the regioselective differentiation of the ketone groups of the bicyclic products. Initial attempts at monoreduction (one hydride equivalent of L-selectride, $LiAlH_4$, or $NaBH_4$) produced mixtures of ketols, diols, or starting material. The attempted monoketalization with ethylene glycol also showed poor selectivity. Discrimination between the two ketones was achieved by use of actively fermenting bakers' yeast.

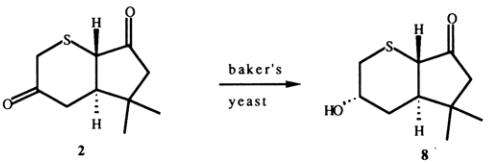
A broth of actively fermenting bakers' yeast was prepared according to the method of Ridley,[8] (−)-**1** was added,



1 **7**

and the suspension was stirred for 18 h. After silica gel chromatography the monoreduced product (−)-**7** was isolated as a crystalline solid (69%). Only the ketone contained in the thiopyran ring had been reduced. The structure and stereochemistry at the hydroxyl-bearing center were confirmed by single-crystal X-ray analysis.[9]

The corresponding *trans*-thiahydrindan **2** was also selectively reduced with bakers' yeast to give alcohol **8**, as a single diastereomer, in 59% yield.



2 **8**

From these studies one may conclude that either antipode of *trans*-diketothiadecalin **1** is available in optically pure form by an intramolecular Michael reaction catalyzed by D- or L-proline. The two chemically similar carbonyls of thiadecalin **1** can be differentiated by a stereoselective bakers' yeast reduction. Additionally, the diketothiahydrindans **2** and **3** can be produced in approximately a 1:1 ratio of cis and trans diastereomers. Thiahydrindan **2** can also be selectively reduced by bakers' yeast. Because of the versatility of sulfur-containing heterocycles, the compounds reported herein may prove to be useful optically active synthons in either ring expansion[10] or ring contraction[11] processes.

Acknowledgment. We are indebted to the donors of Petroleum Research Foundation, administered by the American Chemical Society, for their support of this work.

Supplementary Material Available: X-ray crystallographic data for compounds **1** and **7** (15 pages). Ordering information is given on any current masthead page.

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(5) X-ray structure data file for compound **1** are included in the supplemental data.

(6) (a) Agami, C.; Platzer, N.; Puchot, C.; Sevestre, H. *Tetrahedron* **1987**, *43*, 1091. (b) Agami, C.; Meynier, F.; Puchot, C.; Guilhem, J.; Pascard, C. *Tetrahedron* **1984**, *40*, 1031. (c) Agami, C.; Levisalles, J.; Puchot, C. *J. Chem. Soc., Chem. Commun.* **1985**, 441.

(7) (a) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615. (b) Hajos, Z.; Parrish, D. R. *Org. Synth.* **1984**, *63*, 26.

(8) Crumbie, R. L.; Deol, B. S.; Nemorin, J. E.; Ridley, D. D. *Aust. J. Chem.* **1978**, *31*, 1965.

(9) The X-ray structure data file for compound **7** are included in the supplemental data.

(10) (a) Vedejs, E.; Ried, J. G. *J. Am. Chem. Soc.* **1984**, *106*, 4617. (b) Vedejs, E.; Krafft, G. A. *Tetrahedron* **1982**, *38*, 2857.

(11) (a) Vedejs, E.; Singer, S. P. *J. Org. Chem.* **1978**, *43*, 4884. (b) Matsuyama, H.; Miyazawa, Y.; Takei, Y.; Kobayashi, M. *J. Org. Chem.* **1987**, *52*, 1703. (c) Casy, G.; Taylor, J. K. *J. Chem. Soc., Chem. Commun.* **1988**, 454.

(12) All new compounds reported herein were characterized by IR, NMR, and high resolution mass spectral analysis.

Redox Glycosidation via Thionoester Intermediates

Summary: Several steroidal glycosides were prepared via esterification with aldonic acids, Lawesson thionation, lithium triethylborohydride mediated reductive methylation, and silver(I)-catalyzed ring closure.

Sir: The efficient construction of oligosaccharides remains a glittering prize for synthetic organic chemists. Although the Koenigs–Knorr reaction in its many disguises has been the subject of intense scrutiny[1–3] over nearly one century, experimentally simple approaches to iterative glycoside

(1) For reviews on glycosidation chemistry, see: Kennedy, J. F.; White, C. A. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979; Vol. 5, p 755. Schaner, R. *Adv. Carbohydr. Chem. Biochem.* **1982**, *40*, 131.

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