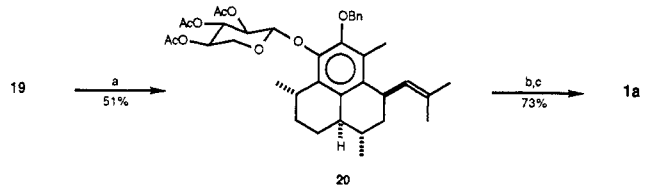
Scheme V[a]



[a] (a) 1α-Bromo-2,3,4-triacetyl-D-xylose[15] (8 equiv), AgOTf (8 equiv), tetramethylurea (10 equiv), CH_2Cl_2, 20 °C; (b) KOH, MeOH; (c) Li/NH_3-THF.

acid (Scheme III).[10] Selective benzylation of the phenolic hydroxy group then provided **14**. Silylation and DIBAL reduction of **14** gave rise to a mixture of **15** and **16**, which was separated by preparative TLC on silica gel (6:1 hexane/EtOAc).[11]

Oxidative removal of the benzylic methylene unit was accomplished by conversion of **15** to the aldehyde (PCC, CH_2Cl_2) followed by Baeyer–Villiger oxidation (Scheme IV) effected with MCPBA in chloroform (using Na_2HPO_4 as buffer).[12] It was found that desilylation of **17** with excess TBAF in THF could be made to proceed without hydrolysis of the formyl unit if the pH of the reaction mixture was adjusted to about 7 by the addition of acetic acid. Swern oxidation of the resulting alcohol gave **18** in excellent yield and without detectable aldehyde epimerization. Treatment of **18** with the dianion of isobutyric acid produced the expected β-hydroxy acid and also cleaved the formate ester. The product, without purification, was carried on to **19** by reaction with excess (dimethylamino)formaldehyde dineopentyl acetal[13] in warm chloroform containing a small quantity of 4,4′-methylenebis(2,6-di-*tert*-butylphenol).

Of a considerable number of glycosidation protocols which were investigated, that outlined in Scheme V provided the best results. Although it was necessary to employ a considerable excess of the bromo sugar, **20** could be obtained in acceptable yield and with good stereoselectivity. This material was identical with an authentic sample prepared from natural pseudopterosin C.[14] Deacetylation followed by cleavage of the benzyl unit with Li in NH_3 gave (−)-pseudopterosin A (**1a**) identical with material produced by hydrolysis of natural pseudopterosin C (**1c**).[2]

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Registry No. **1a**, 104855-20-1; **3** (epimer 1), 113161-35-6; **3** (epimer 2), 113161-49-2; **4** (epimer 1), 113161-36-7; **4** (epimer 2), 113161-50-5; **5** (epimer 1), 113161-37-8; **5** (epimer 2), 113216-82-3; **6**, 113161-38-9; **7**, 113161-39-0; **8**, 113161-40-3; **9**, 113161-41-4; **10** (epimer 1), 113161-42-5; **10** (epimer 2), 113216-83-4; **11**, 113161-43-6; **12**, 113216-81-2; **13** (epimer 1), 113161-44-7; **13** (epimer 2), 113216-84-5; **14** (epimer 1), 113161-45-8; **14** (epimer 2), 113216-85-6; **15**, 113180-37-3; **16**, 113299-29-9; **17**, 113180-38-4; **18**, 113161-46-9; **19**, 113161-47-0; **20**, 113161-48-1; $CH_3CH{=}C(OSiMe_3)CH{=}C(OSiMe_3)OMe$, 78133-88-7; Me_2CLiCO_2Li, 16423-62-4; $Me_2NCH(OCH_2CMe_3)_2$, 4909-78-8; (−)-(*S*)-limonene, 5989-54-8; 1α-bromo-2,3,4-triacetyl-D-xylopyranose, 3068-31-3.

Supplementary Material Available: Experimental and spectral data for compounds **4–9** and **11–20** (4 pages). Ordering information is given on any current masthead page.

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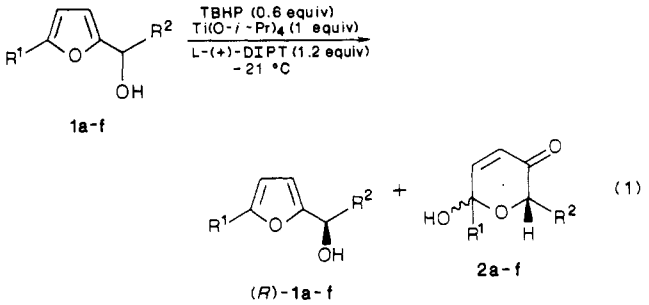
Preparation of Optically Active 2-Furylcarbinols by Kinetic Resolution Using the Sharpless Reagent

Summary: Enantioselective oxidation using TBHP and an asymmetric titanium–tartrate complex provides direct access to a variety of optically active 2-furylcarbinols.

Sir: 2-Furylcarbinols (**1**) have been recognized as versatile compounds in organic synthesis.[1] There is, however, no general method for preparation of optically active **1**.[2] We wish to report here that the Sharpless reagent for asymmetric kinetic resolution of secondary allylic alcohols[3] can be used for the resolution of racemic **1**, thus providing a highly efficient method for preparation of optically active **1** (eq 1).[4] Though the oxidation of **1** using *tert*-butyl



hydroperoxide (TBHP) catalyzed by early transition metals to provide racemic **2** has been reported,[5] this example is the first in which the oxidation is carried out in

(10) (a) Taylor, S. K.; Hockerman, G. H.; Karrick, G. L.; Lyle, S. B.; Schramm, S. B. *J. Org. Chem.* **1983**, *48*, 2449. (b) Taylor, S. K.; Davisson, M. E.; Hissom, B. R., Jr.; Brown, S. L.; Pristach, H. A.; Schramm, S. B.; Harvey, S. M. *J. Org. Chem.* **1987**, *52*, 425.

(11) Since chemoselective oxidation of the benzylic hydroxy group of the diol corresponding to **15** should be possible, the silylation of the other hydroxy group would appear to be unnecessary. However, we elected to postpone attempts to close the last ring of the system stereoselectively in order to first determine whether the isobutenyl moiety could be successfully introduced. We thus required a means of separating the C-1 epimers and this was most easily accomplished through the derivatives **15** and **16**.

(12) (a) Nakatsubo, F.; Cocuzza, A. J.; Keeley, D. E.; Kishi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 4835. (b) Gammill, R. B.; Hyde, B. R. *J. Org. Chem.* **1983**, *48*, 3863.

(13) Aristoff, P. A.; Johnson, P. D.; Harrison, A. W. *J. Org. Chem.* **1983**, *48*, 5341.

(14) Compound **20** was prepared from **1c** by using methods derived from the work of Fenical [(i) BnBr, K_2CO_3, DMSO; (ii) Ac_2O/pyr].

(15) *Methods in Carbohydrate Chemistry*; Whistler, R. L., Wolfrom, M. L., BeMiller, J. N., Shafizadeh, F., Eds.; Academic: New York/London, 1962; Vol. 1, p 183.

(1) Piancatelli, G.; Scettri, A.; Barbadoro, S. *Tetrahedron Lett.* **1976**, 3555. Piancatelli, G.; Scettri, A. *Tetrahedron Lett.* **1977**, 1131. Laliberté, R.; Mêdawar, G.; Lefebvre, Y. *J. Med. Chem.* **1973**, *16*, 1084. Georgiadis, M. P. *J. Med. Chem.* **1976**, *19*, 346. DeShong, P.; Ramesh, S.; Elango, V.; Perez, J. J. *J. Am. Chem. Soc.* **1985**, *107*, 5219.

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(3) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

(4) For other examples of kinetic resolution using the Sharpless reagent, see the following. β-Hydroxy sulfides and α-acetylenic alcohols: Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589. β-Hydroxy amines: Miyano, S.; Lu, L. D.-L.; Viti, S. M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 4350.

(5) Ho, T.-L.; Sapp, S. G. *Synth. Commun.* **1983**, *13*, 207.

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Table I. Kinetic Resolution of 1 Using TBHP, L-(+)-DIPT, and Ti(O-*i*-Pr)$_4$[a]

run		substrate 1 R^1	R^2	time, h	slow-reacting (i.e., recovered) enantiomer (*R*)-1[b] yield,[c] %	% ee	$[\alpha]^{25}_D$ (c, $CHCl_3$)	oxidation product 2: yield,[d] %
1	a	H	Me	24	32	>95[e]	+20.8° (1.27)	53
2[f]	b	H	*n*-Am	25	42	>95[g]	+13.8° (1.07)	53[h]
3	c	H	*i*-Pr	25	39	>95[g]	+18.1° (1.04)	55
4	d	H	*t*-Bu	40	41	6[g,i]		58
5	e	H	Ph	40	42	>99[j]	+6.9° (1.13)	44
6	f	Me	*n*-Am	6	40	>95[g]	+7.8° (1.01)	55

[a] The reaction was carried out by using TBHP (0.6 equiv), L-(+)-DIPT (1.2 equiv), and Ti(O-*i*-Pr)$_4$ (1.0 equiv) in CH_2Cl_2 at −21 °C. [b] Absolute configurations were proven by correlation with the corresponding (*R*)-α-hydroxy acids[9] by the following sequence: (1) Ac_2O, C_5H_5N; (2) $NaIO_4$, $RuCl_3 \cdot H_2O$ (cat.), CCl_4–CH_3CN–H_2O (2:2:3); (3) NaOH, H_2O–MeOH. [c] Isolated yields. [d] Determined by ^1H NMR analysis of the crude reaction mixture. [e] Determined by ^1H NMR analysis of the corresponding acetate in the presence of (−)-Pr(DPPM)$_3$ (detection limit ca. 95% ee). [f] The resolution was also effected by using 20% catalyst in the presence of molecular sieves, affording (*R*)-**1b** with >95% ee in 38% isolated yield.[7] [g] Determined by ^1H NMR analysis of the corresponding MTPA ester (detection limit ca. 95% ee). [h] Anomeric mixture of 2:1 ratio. [i] Absolute configuration was not determined. [j] Determined by HPLC analysis of the corresponding benzoate using CHIRALPAK OT(+) (Daicel Chemical Industries, Ltd.).

an enantioselective manner.

The results of the oxidation of various **1** in which a substituent R^2 is a primary, secondary, or tertiary alkyl group or an aromatic group, using TBHP (0.6 equiv), Ti(O-*i*-Pr)$_4$ (1 equiv), and L-(+)-DIPT (1.2 equiv), are summarized in Table I. It can be seen from Table I that highly efficient kinetic resolution occurs in all cases except for **1d**, which has a sterically demanding tertiary alkyl group. When L-(+)-DIPT is employed, the slow-reacting enantiomer is always that shown in eq 1, i.e., when the hydroxyl group is up, the furan ring is on the left. Thus this system adds another example of the feature of predictability with the parent process for kinetic resolution of allylic alcohols.[6] Noteworthy also is the fact that the kinetic resolution of **1** also proceeds effectively by using 20% catalyst in the presence of molecular sieves (see footnote *f* in Table I).[7] In the present reaction, the oxidation products **2** are readily separable by column chromatography on silica gel since (*R*)-**1** and **2** have quite different R_f values on silica gel. However, the isolation of (*R*)-**1** can be carried out more conveniently by treating the crude mixture with base (NaOH, Et_2O, H_2O).[8] Under these conditions, **2** is converted into an unidentified very polar product or products (R_f 0 (hexane–Et_2O, 2:1)).

A typical experimental procedure is represented by preparation of (*R*)-**1b**: To a solution of Ti(O-*i*-Pr)$_4$ (3.68 mL, 12.3 mmol) in CH_2Cl_2 (60 mL) was added L-(+)-DIPT (3.12 mL, 14.8 mmol) at −20 °C. After being stirred for 10 min, the solution was cooled to −30 °C, and racemic **1b** (2.07 g, 12.3 mmol) in CH_2Cl_2 (3 mL) and TBHP (1.99 mL, 7.41 mmol, 3.73 M in CH_2Cl_2) were added to the system. The solution was stirred at −21 °C for 25 h and poured into a mixture of 10% tartaric acid solution (0.5 mL), Et_2O (20 mL), and NaF (3 g). The mixture was stirred vigorously for 3 h at room temperature, and the resulting white precipitate was filtered through a pad of Celite. The filtrate was concentrated to give an oil, which was dissolved in Et_2O (100 mL) and treated with 1 N NaOH (50 mL) for 30 min at 0 °C with vigorous stirring. The ethereal solution was washed with brine, dried ($MgSO_4$), and concentrated to give an oil, which was passed through a short silica gel column to afford (*R*)-**1b** (872 mg, 42% yield).

As starting racemic carbinols **1** can be readily prepared in large quantity from furfural and Grignard reagents, or 2-furyllithium and aldehydes, the optically active compounds **1** are now readily available asymmetric starting materials. Application of the optically active **1** in natural product synthesis and in material science are in progress in our laboratory.

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(6) Thus far, no exception has been reported; cf. ref 4.
(7) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.
(8) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(9) Newman, P. *Optical Resolution Procedures for Chemical Compounds*; Optical Resolution Information Center: New York, 1981; Vol. 2, Part 1.

Molecular Complex Evaluation. A Simultaneous Assay of Binding Using Substrate Mixtures

Summary: An experimental method is described that allows the simultaneous measurement of the extent of molecular complex formation between a ligand and a mixture of different potential substrates. The method is operated by chemically binding the ligand to a polyacrylamide resin and adding a mixture of potential substrates to the resin. By measurement of the concentrations of the substrates both before and after addition of the resin, the decrease in bulk solution concentration of those substrates that bind to the resin-bound ligand can be observed. By determination of the loading of the ligand on the resin, association constants can be determined, assuming competitive binding. As an application of the assay, ristocetin and vancomycin were used as ligands and binding to a number of dipeptides was measured and compared with association constants measured in free solution by a standard titration assay.

Sir: Measurement of association constants (K_a) is an important part of the study of the complexes formed between ligands and substrates (hosts and guests).[1] Common methods of K_a determination involve monitoring the change in some property (UV extinction coefficient, NMR chemical shift, etc.) during the titration of a ligand with a substrate. Disadvantages of the titration method include

(1) Review: Connors, K. A. *Binding Constants*; Wiley: New York, 1987.

0022-3263/88/1953-1587$01.50/0