was recorded on a V.G. Micromass 7070H mass spectrometer. Optical rotation was recorded on a Perkin-Elmer Model 141 polarimeter. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on either a Bruker WM-250 (at 62.9 MHz for carbon) or an IBM 200SY (at 50.3 MHz for carbon) Fourier transform spectrometer. Chemical shifts (δ) in Table I were measured with respect to $CDCl_3$ (77.00 ppm) and are given with respect to Me_4Si.

Isolation of Cimilophytine. The alkaloidal residue (165 g) after the isolation of haplophytine was subjected to preliminary countercurrent separation in a 30-tube Craig countercurrent machine, between $CHCl_3$ (stationary phase) and McElvain's buffer (moving phase, pH 2.5). The crude base mixture (23.2 g) liberated from the buffer fractions by basification to pH 8.5 with ammonia was resubjected to partitioning in a 200-tube Craig countercurrent machine between $CHCl_3$ and McElvain's buffer, the pH of which was gradually varied from 6.5 to 1.2 over a period of 2 weeks. A total of 1200 × 10 mL fractions were collected. Fractions were combined on the basis of the TLC behavior of the alkaloids from the individual fractions. Fractions 771–800 were combined to give 1.03 g of material, which upon crystallization from $CHCl_3$–EtOH yielded cimilophytine (200 mg): mp 325 °C dec; $[\alpha]^{20}$ −84.9° (EtOH); λ_{max}^{EtOH} 228 (32 800), 266 (15 900), 300 (4000); λ_{max}^{KBr} 3425, 1751, 1621 cm^{-1}; for a proton NMR see text; high-resolution mass measurement, observed m/e 682.3018, $C_{38}H_{42}N_4O_8$ requires m/e 682.3002.

Hydrogenation of Cimilophytine: Formation of Tetrahydrocimilophytine and Its Methyl Ester (8). Cimilophytine (20 mg) in ethanol (8 mL) was hydrogenated over platinum oxide (2 mg) at room terperature and atmospheric pressure. The reaction, monitored by TLC, was stopped after 45 min, CH_2Cl_2 was added, and the mixture was filtered. The filterate gave on concentration gave a polar solid (18 mg); m/e 686 (M^+). Methylation of the solid in methanol with ethereal diazomethane and crystallization of the resulting product from $CHCl_3$–EtOH gave the methyl ester 8 as a colorless solid: mp 270 °C; ^1H NMR δ $CDCl_3$ 1.29 (t, 3 H, J = 7 Hz), 2.35 (s, 3 H), 3.3 (s, 3 H), 3.57 (s, 3 H), 6.29 (d of d, 1 H, J = 7, 1 Hz), 6.85 (d of d, 1 H, J = 8, 1 Hz), 7.04 (d of t, 1 H, J = 8, 1 Hz), 7.33 (s, 1 H), 7.54 (s, 1 H), 10.69 (s, 1 H), 11.38 (s, 1 H); MS, m/e (relative intensity) 700 (73, M^+), 682 (6, $M^+ - 18$), 669 (22, $M^+ - 31$), 657 (52), 429 (3), 255 (16), 168 (9).

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Microbially Mediated Enantioselective Ester Hydrolyses Utilizing *Rhizopus nigricans*. A New Method of Assigning the Absolute Stereochemistry of Acyclic 1-Arylalkanols

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The fungus *Rhizopus nigricans* has been used to effect the enantioselective hydrolysis of 22 acetates of acyclic 1-arylalkanols. The absolute stereochemistry of all the chiral alcohols formed can be accounted for by a rule which is based on the relative sizes of substituents on the carbinol carbon. The relative sizes of substituents deduced from these hydrolyses have been compared with those assigned from Horeau's method for the same compounds and found to be identical; i.e., a phenyl group or heterocyclic ring is always larger than an alkyl group. The use of *R. nigricans* to prepare chiral alcohols and use of the rule to predict their configuration constitute a new method of assigning the absolute stereochemistry of secondary alcohols. With minor modifications this method can also be used to prepare gram quantities of chiral alcohols of both configurations.

Chiral secondary alcohols of established absolute stereochemistry are remarkably versatile intermediates for the synthesis of a host of compounds, since there are many stereospecific reactions available for replacing the hydroxyl group with halogen, nitrogen, sulfur, or carbon. In order to take advantage of this versatility, we worked on the asymmetric synthesis of alcohols whose absolute stereochemistry would be predicted from the method of preparation. While there are purely chemical methods for preparing alcohols of high optical purity, the absolute stereochemistry of the products is not always predictable. There are, however, a number of enzymic or microbial methods which exhibit the desired product stereoselectivity. For example, Jones et al.[2] have recently described the use of horse liver alcohol dehydrogenase (HLAD) for the synthesis of a variety of alcohols with predictable configurations. Prelog and co-workers[3] carried out pioneering studies on the use of an oxido reductase present in *Curvularia falcata* to prepare chiral alcohols. From these studies they proposed a rule, based on the relative sizes of substituents flanking the carbonyl group to be reduced, which accounts for their observations. Prelog's rule was later shown also to rationalize the configurations of a variety of aromatic and heteroaromatic alcohols formed from the corresponding ketones and *Cryptococcus macerans* or *Sporobolomyces pararoseus*.[4] While this

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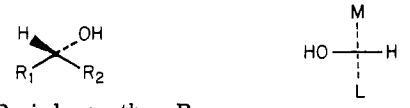
Table I. Select Summary of Substrates and Microorganisms Used for Enantioselective Hydrolyses

substrate	microorganism	config of alcohol formed	ref
1	*Brevibacterium ammoniagenes* (ATCC 6872)	*R*	17
a series of 3-acetoxylalk-1-enes	*Brevibacterium ammoniagenes* (ATCC 6872)	*R*	17
1-pentyl-2-propynyl acetate	*Brevibacterium ammoniagenes* (ATCC 6872)	*S*	6a
1-pentyl-2-propynyl acetate	*Candida cylindracea* esterase	*R*	6a
1-octyn-4-yl acetate	*Rhizopus nigricans* (ATCC 6227b)	*S*	18
3-acetoxycycloheptene	*Candida cylindracea*	*S*	19
cis- and *trans*-2-methylcyclohexyl acetates	*Bacillus subtilis* var. *niger*	*R*	6b
cis- and *trans*-3-methylcyclohexenyl acetates	*Bacillus subtilis* var. *niger*	*S*	6b
cis- and *trans*-1-decalols	*Bacillus subtilis* var. *niger*	*trans*-(1*R*) *cis*-(1*S*)	6c
cis- and *trans*-2-decalols	*Bacillus subtilis* var. *niger*	*trans*-(2*S*) *cis*-(2*S*)	6c
7-(2-*trans*-styryl-3-acetoxy-5-oxocyclopentyl)-*n*-heptanoic acid	*Saccharomyces* sp. 1375-143	3*R*	20
1	*Bacillus subtilis* var. *niger*	*S*	7a

method is valuable in a great many cases, it is not always applicable, since some ketones are not reduced by microorganisms. We therefore decided to explore possibilities for obtaining chiral alcohols of predictable configurations by enantioselective microbial hydrolysis of racemic esters. While such methods have been used to prepare optically active acids, particularly amino acids, from racemic esters,[5] only a few systematic studies of the inverse problem have been carried out: the resolution of alcohols by the enantioselective hydrolysis of their racemic esters. A selective survey of that literature is given in Table I, which shows that a variety of microbes can be used to prepare chiral alcohols. Of the studies in Table I only those by Oritani et al.[6] and Mori et al.[7] have systematically tried to determine the stereochemical preferences of the enzyme in order to predict the configuration of the alcohols formed. Both groups used *Bacillus subtilis* var. *niger* for their work. Oritani et al. employed a number of substituted cyclohexyl acetates as substrates and showed that the absolute stereochemistry of the resulting alcohol was dependent upon the substitution pattern on the cyclohexanol. Mori et al.[7a] examined the hydrolysis of a number of acetylenic esters and found that while the configuration of the carbinol formed in these compounds was consistent within the series, there appeared to be no obvious relation between the chirality of carbinol carbon in one series of substrates and in another. That is, no single principle was found that would correlate the configurations of the alcohols formed from different substrates. Since there have been relatively few studies of the microbes employed and their stereochemical preferences and since the potential value of the method appears to be great, we decided to use a different microorganism and to evaluate its ability to yield chiral aromatic alcohols. A variety of cyclic and acyclic aromatic acetates were employed as substrates since the absolute stereochemistry of the resulting alcohols had been previously established. In an initial survey[8] *Rhizopus nigricans* was shown to contain an esterase that was able to yield alcohols with configurations that appeared to exhibit a consistent pattern. On the basis of this survey of approximately a dozen compounds, we suggestd a rule based on the relative sizes of substituents on the carbinol carbon to account for our observations. The rule states that the enantiomer shown in Chart IA is the one most rapidly hydrolyzed. The hydrolysis of only three acyclic benzylic acetates had been examined in this survey, and hence many more had to be studied in order to test the rule. We have therefore systematically determined the configurations of the alcohols formed from the hydrolysis of 22 acyclic 1-arylalkanyl acetates and report those results here. The relative sizes of R_1 and R_2 and their electronegativities were varied. In addition, we have included a number of heterocyclic esters to determine the effect of heteroatoms on the stereochemical course of the reaction. Since the rule utilizes the relative sizes of substituents, we have selected compounds in which the relative sizes of the substituents in question have been assigned by Horeau's method[9] and by Mosher et al.[10] in a study of chiral reductions of the corresponding ketones. The relative sizes deduced from these methods have been compared and found to be identical.

Chart I. Absolute Stereochemistry of the Enantiomer That Yields (+)-α-Phenyladipic Acid in Horeau's Method



where R_1 is larger than R_2 where L is larger than M

Pirkle et al.[11] have recently proposed a relation between the elution order of related 1-arylalkanols from a chiral HPLC column and their absolute stereochemistry. The correlation was recently tested,[12] and it was shown that the configuration of the enantiomer preferentially retained on the column *differs* for cyclic and acyclic compounds.[12,13] Furthermore, some exceptions within a series were noted. In order to evaluate the reliability of the rule in assigning configurations of alcohols formed in these hydrolyses, we have compared such assignments with those made by using other methods.

Methods and Results

In general it is essential to employ purified enzymes if unambiguous data on the behavior of substrates or in-

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Table II

racemic acetate	% yield of recovd crude	abs stereochem of alcohol formed	% hydrolysis	ee[c]	specific rotations recorded,[b] deg: acetates	specific rotations recorded,[b] deg: alcohol	ref to abs stereochem
1A	94	*R* (1B)	45	79	−51.4 (*c* 4.22)	+42.9 (*c* 3.36)	4, 10, 21
2A		*S* (2B)		43		+25.4 (C)	4
3A	>67	*S* (3B)		51	−2.9 (*c* 1.55)	−8.6 (*c* 1.75)	4, 8
4A	57	*R* (4B)	39	45	−13.1 (*c* 2.38)	+16.8 (*c* 1.35)	10
5A	94	*R* (5B)	27	75	−10.9 (*c* 3.54)	+24.8 (*c* 1.29)	10
6A	33	*R* (6B)	10	44	−3.39 (*c* 1.9)	+9.8 (*c* 0.13)	10
7A	53	*R* (7B)	31	9	−0.8 (*c* 4.75)	+3.1 (*c* 1.5)	10
8A		*S* (8B)	23	8		+8.6 (*c* 4.25, B)	22
9A	100	*S* (9B)	24	59	−21.1 (*c* 7.2)	+99.1 (*c* 2.25)	23
10A	64	*R* (10B)	23	76	−2.0 (*c* 3.57)	−42.3 (*c* 1.86, E)	24
11A	27	*R* (11B)	11	46[a]	−7.3 (*c* 3.72)	−52.5 (*c* 1.1)	25, 26
12A		*R* (12B)	71	84	−79.6 (*c* 3.65)	+42.1 (*c* 2.94)	26, 27
13A		*R* (13B)	33	~100[a]	−6.8 (*c* 1.18)	+67.3 (*c* 0.4)	22
14A	68	*R* (14B)	44	94[a]	−34.9 (*c* 1.29)	+34.6 (*c* 1.2, M)	25
15A	56	*R* (15B)	57	93[a]	−35.5 (*c* 2.62)	+36.8 (*c* 1.44)	12, 14
16A		*R* (16B)	64	36		+8.33 (*c* 9.6)	15, 26
17A	90	*R* (17B)	44	22	−25.6 (*c* 5.08)	+5.0 (*c* 3.14)	15, 26
18A	70	*R* (18B)	78	22	−88.2 (*c* 2.73, E)	+14.7 (*c* 4.35, E)	28
19A	93	*R* (19B)	53	83	−90.5 (*c* 5.10, E)	+30.4 (*c* 6.70, E)	28
20A	100	*R* (20B)	43	~100	−82.7 (*c* 4.37, E)	+38.1 (*c* 1.65)	28
21A	72	*R* (21B)	61	73	+0.47 (*c* 8.48)	−20.2 (*c* 7.16)	29
22A	57	*S* (22B)	28	63	+3.07 (*c* 3.62)	−29.5 (*c* 2.63)	30

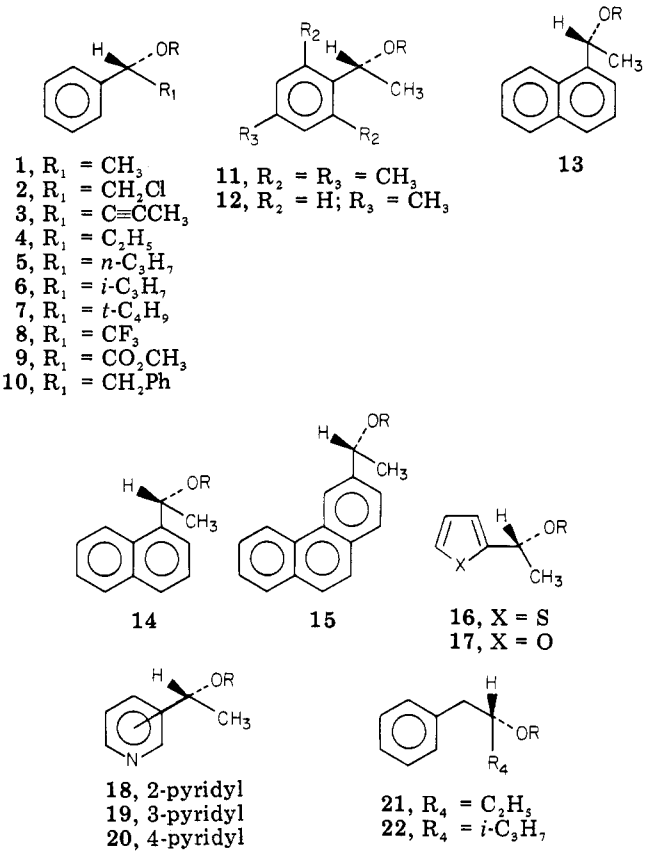
[a] The ee values were calculated from data on the HPLC resolution of the corresponding acetate on a Pirkle chiral column. [b] The solvent was $CHCl_3$ unless indicated otherwise: B = benzene, C = cyclohexane, E = ethanol, M = methanol. [c] Enantiomeric excess.

hibitors are desired. The proposal to employ an entire organism, with its wide range of hydrolytic enzymes, for investigating the effects of structural changes on the stereochemical course of a hydrolytic reaction is therefore subject to dangers which can be minimized but never completely eliminated. The possibility that a substrate will be hydrolyzed fortuitously be another enzyme to yield the antipodal alcohol may be small, but it must not be dismissed. Although we have not encountered a situation where this has actually occurred, we suggest that, where possible, configurations deduced from these hydrolyses should be confirmed by using one of the other available methods.

The following procedure was worked out to alert us to possibly anomalous situations. A group of four to six flasks of sterile potato dextrose medium were inoculated at the same time with a recent liquid culture of the organism and grown for 6–8 days, or until growth of the mass of mycelium appeared to stop. One of the flasks was used to hydrolyzed a standard sample of (±)-1A to establish the presence and activity of the unkown esterase. Information on the activity of the enzyme was used to vary the reaction times of other substrates in order to obtain approximately 30–50% hydrolysis. The unreacted acetate and alcohol formed were extracted and separated by column or thick-layer chromatography and their specific rotations measured. The specific rotation of the recovered acetate was determined to verify that the absolute configuration of the enantiomer in excess differed from that present in excess in the alcohol.

Modifications in Size and Electronegativity of R_1 and R_2. The relative sizes and electronegativities of R_1 and R_2 were varied as shown for compounds **1A–15A** (Chart II) to determine the influence of these parameters on the stereochemical course of the reaction. The results are given in Table II and show that chiral alcohols are obtained in each case. Their enantiomeric excess (ee) varied from 8% to 100%, and it is immediately apparent that the larger ee's are found in those alcohols which show the greatest differences in the relative sizes of R_1 (aryl) and R_2 (alkyl), i.e., naphthyl or phenanthryl vs. methyl. The

Chart II[a]



[a] A, R = Ac; B, R = H.

smallest ee is obtained where R_1 and R_2 are phenyl and *tert*-butyl, respectively, which are close in size. There is little change in the observed ee's on changing R_2 from methyl to ethyl to propyl to isopropyl vs. that of a constant R_1 (phenyl). The relation between ee and the extent of hydrolysis is discussed below. The electronegativity of R_2 does have an effect on the ee since the size of the CF_3 group

is usually assumed to be only slightly larger (the radii of the H and F are 0.32 and 0.72, rspectively) than a methyl group, while the ee of the fluoro alcohol is significantly lower than that of the CH_3 analogue. A similar decrease in ee was not observed for an electronegative carbomethoxyl group, compound **9A**.

As no information was available on the effect of the presence of a heteroatom in R_1 on the course of the hydrolysis, we examined compounds **16A–20A**. The configuration of the carbinol formed in each case was the same as that of **1B**; i.e., the presence of an atom of nitrogen, sulfur, or oxygen did not alter the stereochemical course of the hydrolysis.

Hydrolysis of two acetates, **21A** and **22A**, of nonbenzylic alcohols provided chiral alcohols with the configurations shown in Table II. Thus, the enzyme is clearly able to distinguish between two differently substituted methylene groups.

Absolute Stereochemistry of 15A–17A. The absolute stereochemistry of **15B** has not been rigorously determined, but it has been tentatively assigned by two methods. Sugimoto et al.[14] reduced the corresponding ketone with sodium borohydride in the presence of bovine serum albumin. These investigations have shown that this procedure generally yields chiral alcohols enriched in the *S* enantiomer. A second assignment[12] is based on the empirical observation that in a series of acyclic 1-arylalkanols the enantiomer shown in Chart IA (where R_1 = aryl and R_2 = alkyl) is preferentially retained on a chiral HPLC column. The absolute stereochemistry of the enantiomer formed in excess in our hydrolyses in consistent with assignments based on both methods.

The absolute stereochemistry of the 2-thienyl ethanol (**16B**) was assigned by Červinka et al.[15] using a method (reduction of the ketone with a complex of $LiAlH_4$ and (−)-quinine) that had been shown empirically to yield the *R* enantiomer. We confirmed their assignment by oxidizing a sample of the (−)-acetate **16A** (prepared by microbial reduction of the corresponding ketone with *Cryptococcus macerans*[4] followed by acetylation) to methyl (*S*)-*O*-acetyl lactate of known absolute stereochemistry by using the ruthenium tetraoxide oxidation procedure recently described by Sharpless et al.[16] The same oxidation procedure was also used to convert a sample of (+)-**17A** (recovered from enzymic hydrolysis) to methyl (*S*)-*O*-acetyl lactate. The absolute stereochemistry of **17B** previously assigned [15] by using Horeau's method was thus verified.

Table III. Hydrolysis of 1A as a Function of Time

time of hydrolyses, h	% total recovery (acetate + alcohol)	% hydrolysis obsd	ee	
			alcohol	recovd acetate
0.5	~100	28	98	20
1.0	94	45	79	43
2.0	~100	56	76	54
4.0	~100	63	74	63
8.0	~100	67	67	68
16.0	~100	77	46	86

Synthetic Utility of the Method. In addition to our desire to develop a new method for assigning the configurations of secondary alcohols, we also hoped that our procedure would be suitable for the preparation of sufficient material for synthetic studies. It was therefore important to increase the amount of alcohol formed per unit of medium. The data in Table II were obtained by using approximately 200–400 mg of substrate and an incubation time of 2–16 h for a culture of *R. nigricans* grown on 250 mL of culture medium (potato dextrose). Clearly, ten 1-L Erlenmayer flasks each containing 250 mL of medium can be processed readily to obtain 0.5–1.0 g of a chiral alcohol. However, before resorting to a brute force approach, some time was spent in determining whether the microorganism obtained from 250 mL of medium could hydrolyze several times the 0.5 mL (400 mg) of substrate usually employed. The substrate chosen was **1A**, primarily because of its availability and convenience. The work described is not intended to be exhaustive but merely to indicate some of the successful approaches that have been explored. When the reaction time was decreased, we found that approximately 50% of the substrate was hydrolyzed in 1 h. The observed rate then slowed down, perhaps because of differences in the hydrolysis rate of the two enantiomers or because of changes in the activity of the enzyme. If a higher substrate concentration was used, i.e., more than 2 mg/mL, the percent hydrolysis decreased. However, somewhat greater amounts of alcohol could be obtained from 1.0 mL of substrate, if the medium was diluted with an equal volume of water. The amount of *R* alcohol formed could also be increased if, after addition of the usual 0.5 mL of substrate, a second and then a third addition (0.5 mL) of substrate was made after 1 and 4 h, respectively. These modifications of the original procedure increased the amount of alcohol formed per unit of medium used by a factor of 3–4. While this approach was not pursued further, the above study of the hydrolysis of **1A** (Table III) also indicated that the method could be used to prepare alcohols of either configuration (see below) with a high ee.

The range of the ee values observed in these hydrolyses was in part related to the percent hydrolysis: smaller conversions of the acetate yield larger ee values for the alcohol. The ee of the alcohol was also related to differences in the hydrolysis rates of the two enantiomers. In the above study of alcohols formed from hydrolysis of acetates and one benzoate, we had satisfactory ee's in most cases. While we have not explored the effect of varying the structure of the acid on the ee of the alcohol, it is apparent that this variable should be examined when the acetate is hydrolyzed with low enantioselectivity.

We have investigated some methods to increase optical purities. The simplest approach was to reacetylate the chiral alcohol isolated from a single hydrolysis and to recycle this material. When this was done with a sample of

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1B (75% ee), the ee of the alcohol formed was increased to 96%. When alcohols are needed that are enriched in the enantiomer not formed in the enzymic hydrolysis, that enantiomer can be prepared either by inverting the configuration of the alcohol obtained by using a previously described chemical method[4] or by running the hydrolysis to approximately 75% completion. When this was done for **1A**, the recovered acetate was enriched in the *S* enantiomer (86% ee). The *S* alcohol can readily be prepared from the acetate.

Discussion

Each of the results in Table II can be accounted for by the proposed rule and the assumption that an aryl group is always R_1, i.e., effectively larger, while the alkyl group corresponds to R_2 (Chart IA). With this assumption the configuration of a new 1-arylalkanol can readily be predicted. However, in order to be able to extend the method to other classes of compounds, we were interested in determining whether this ordering in the sizes of substituents was unique. Horeau and co-workers[9] have established a general method of assigning the absolute stereochemistry of numerous secondary alcohols and have investigated the ability of their method to account for the absolute stereochemistry of the above 1-arylalkanols. The method, given in detail in ref 9, relates the enantiomer of α-phenylbutyric acid formed in excess with the relative sizes of substituents as shown in Chart IB. The studies of Horeau et al. have shown that the absolute stereochemistry of these compounds can be accounted for if it is assumed that an aromatic group is always larger (R_L) than an alkyl group (R_M), including *tert*-butyl. Thus Horeau's method and ours require identical assumptions concerning the relative sizes of aromatic and alkyl substitutents. Unfortunately, there is no information available on the effect on Horeau's method of introducing a nitrogen or sulfur near the carbinol carbon.

Mosher et al.[10] have assigned the relative sizes of alkyl and aryl groups in the same 1-arylalkanols by examining the absolute stereochemistry of the major enantiomer formed from the reduction of the corresponding ketones with an optically active Grignard reagent ((+)-1-chloro-2-methylbutane). From an analysis of the steric interactions in the transition state and of the known absolute stereochemistry of the reagent and product, they were able to attribute effective sizes to the various alkyl groups compared to a phenyl substituent. These assignments are consistent with those determined by Horeau et al. and those deduced from our enantioselective hydrolyses and the proposed rule.

Conclusion

These studies have shown that a new method employing *R. nigricans* can be used to prepare chiral alcohols from their racemic acetates. The configurations of each of the alcohols has been assigned by using the proposed rule and the assumption that an aromatic ring (carbocyclic or heterocyclic) is effectively larger than an alkyl group. The product enantioselectivity exhibited by the enzyme present in *R. nigricans* can therefore be used for assigning the configurations of new 1-arylalkanols. The method can also be used to prepare gram or multigram quantities of these alcohols of either configuration for synthetic studies.

Experimental Section

General Methods. Melting points were determined by using a hot-stage apparatus; they are uncorrected. Proton magnetic resonance spectra were recorded on a Varian HR-220 instrument. Optical rotations were recorded on a Perkin-Elmer 241MC polarimeter. Preparative and analytical TLC work was performed on plates coated with silica gel F-254.

Microbial Hydrolyses. Diced potatoes (1.2 kg) in 4 L of distilled water were boiled for 2–4 h and filtered through cheesecloth. The volume of the solution was adjusted to 4 L, and 80 g of glucose was added. A 1-L Erlenmeyer flask containing 250 mL of this medium was inoculated with *R. nigricans* (ATCC 6227b) and shaken at 25 °C for 6–7 days or until growth of the mass of mycelium appeared to stop. The substrate (0.5 mL ~400 mg) was added as a liquid or as a solution in ~1 mL of THF, and the flask was shaken overnight (16 h) or, if the hydrolysis was rapid, until approximately 30–40% of the substrate had been hydrolyzed. The hydrolyses were monitored by TLC and ^{1}H NMR. The medium and mycelium were extracted three times with ethyl acetate, and the ethyl acetate extracts were concentrated. An estimate of the yield of unhydrolyzed acetate and alcohol is given in Table II. These yields varied considerably. Some losses were due to adsorption to the microorganism, but some were probably caused by metabolism of the alcohol. The percent hydrolysis was determined from an NMR measurement of the ratio of alcohol to acetate in the crude extract. The acetate and the alcohol were separated by thick-layer or column chromatography and their specific rotations measured. The data are summarized in Table II.

All the compounds used in this study were prepared by literature methods. The physical properties and ^{1}H NMR spectra of each compound were in good agreement with information in the literature. The enantiomeric excesses were usually obtained by comparing measured and literature specific rotations. For several compounds ee's were estimated from data on their resolution on a chiral Pirkle HPLC column.

The results of the time course of the hydrolysis of **1A** are summarized in Table III.

Registry No. (±)-**1A**, 50373-55-2; (*R*)-**1B**, 1517-69-7; (±)-**2A**, 79465-05-7; (*S*)-**2B**, 70111-05-6; (±)-**3A**, 79416-47-0; (*S*)-**3B**, 79416-50-5; (±)-**4A**, 83808-03-1; (*R*)-**4B**, 1565-74-8; (±)-**5A**, 86561-24-2; (*R*)-**5B**, 22144-60-1; (±)-**6A**, 86561-25-3; (*R*)-**6B**, 14898-86-3; (±)-**7A**, 86561-26-4; (*R*)-**7B**, 23439-91-0; (±)-**8A**, 85026-44-4; (*S*)-**8B**, 340-06-7; (±)-**9A**, 86561-27-5; (*S*)-**9B**, 21210-43-5; (±)-**10A**, 86561-28-6; (*R*)-**10B**, 41822-67-7; (±)-**11A**, 86561-29-7; (*R*)-**11B**, 1517-71-1; (±)-**12A**, 86561-30-0; (*R*)-**12B**, 42070-92-8; (±)-**13A**, 57573-90-7; (*R*)-**13B**, 42177-25-3; (±)-**14A**, 85880-67-7; (*R*)-**14B**, 52193-85-8; (±)-**15A**, 85880-68-8; (*R*)-**15B**, 84194-80-9; (±)-**16A**, 86561-31-1; (*R*)-**16B**, 86527-10-8; (±)-**17A**, 86561-32-2; (*R*)-**17B**, 27948-61-4; (±)-**18A**, 85880-66-6; (*R*)-**18B**, 27911-63-3; (±)-**19A**, 86561-33-3; (*R*)-**19B**, 7606-26-0; (±)-**20A**, 86561-34-4; (*R*)-**20B**, 27854-88-2; (±)-**21A**, 86527-08-4; (*R*)-**21B**, 29393-19-9; (±)-**22A**, 86527-09-5; (*S*)-**22B**, 67252-79-3.