lapses by internal return. It has been demonstrated in a number of cases that nucleophilic attack at the 4-position of 4-substituted *N*-acyl nitrenium ions by a variety of nucleophiles is a facile process.[19,20] The subsequent rearrangement reaction has not been reported in these systems but would seem to offer a reasonable explanation for the formation of **3**.[22]

The hydrolysis of *N*-(sulfonatooxy)-*p*-acetotoluidide[19a] in the presence of 0.5 M diethyl phosphate also proceeds with the formation of small amounts of previously undetected products. These materials have not yet been isolated in a pure form, but their chromatographic behavior is similar to that of **2** and **3**.

The demonstration that **1** can arylate simple phosphate diesters in aqueous solution may be important to an understanding of the in vivo activity of its polycyclic analogues. We will continue this study with an emphasis on the possible reactions of our model compounds with the phosphate backbone of oligonucleotides in aqueous solution.

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(22) A referee has suggested that **3** may be formed from traces of *N*-(sulfonatooxy)-2-chloroacetanilide present in the sample of **1**. We have not been able to detect this material nor have we detected any hydrolysis products which would have arisen from it.

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trans-2-Phenylcyclohexanol. A Powerful and Readily Available Chiral Auxiliary

Summary: The title alcohol has been shown to be a powerful and readily available chiral auxiliary for use in ene reactions of the derived glyoxylate ester.

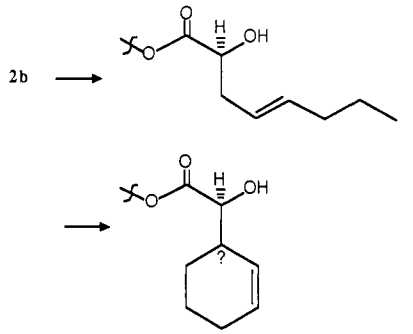
Sir: The control of stereochemistry through the use of asymmetric induction has evolved during the last decade to the point where it is now considered a viable tool within the synthetic arsenal. The chiral auxiliary 8-phenylmenthol (**1a**) has been shown to provide exceptional levels

1 a R = H
b R = OCCHO

2

of induction in a number of reaction processes.[1-3] However, a number of factors[4] combine to seriously limit accessibility to 8-phenylmenthol, and, in addition, access to its enantiomer is even more restricted. We report here that *trans*-2-phenylcyclohexanol (**2a**, PhCy-OH) can be used as a replacement for 8-phenylmenthol and that its preparation in optically active form by enzymatic hydrolysis of its acetate ester provides ready access to both enantiomers.

As part of an extensive investigation of chiral auxiliaries that might mimic the asymmetric induction abilities of 8-phenylmenthol, we investigated the ene reactions of the glyoxylate ester **2b** of *trans*-2-phenylcyclohexanol (PhCyOH, **2a**). Reaction of **2b** with 1-hexene under the



conditions previously found to be optimal for the glyoxylate of 8-phenylmenthol (1 equiv of $SnCl_4$, −78 °C, 1 h) provided a 78% yield of a single diastereomer of the homoallylic alcohol ene adduct by ^{13}C analysis.[5,6] Alternatively, a strictly thermal process (165 °C, 15 h, CH_2Cl_2) provided a 1:1 mixture of the two possible diastereomeric products. The catalyzed reaction of **2b** with cyclohexene also produced a single diastereomer, indicating excellent control of asymmetry at two chiral centers.

While the stereochemical outcomes of the reactions described above are similar to those observed when **1a** was used as chiral auxiliary, such is not the case in the reactions with *cis*- and *trans*-2-butene and with 1-(trimethylsilyl)-*cis*-2-butene where two chiral centers are formed. In these cases the level and direction of stereochemical control at the second center (C-3) differ markedly. Nonetheless, only two of the four possible diastereomers are observed from these reactions,[5] indicating excellent levels of asymmetric induction at C-2.

In addition to the differences noted above in terms of threo to erythro ratios, it was observed that *cis*-butene and *trans*-butene were essentially configurationally stable in the reactions with **2b** (20% isomerization after complete

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(5) A nearly equal mixture of diastereomeric ene adducts with this chiral auxiliary were obtained in the absence of the Lewis acid. These isomers are not as well resolved chromatographically as those with 8-phenylmenthol. In all cases, however, the diastereomers show distinct ^{13}C NMR absorptions. Since the minor diastereomers (epimeric at the secondary alcohol carbon) were not observable as products from any of the Lewis acid catalyzed reactions when ^{13}C analysis was carried out with a signal to noise ratio of at least 30:1, we can set a minimum level of induction at 95%.

(6) The structure of all new compounds proposed is based on analysis of ^{13}C and ^{1}H spectral data as well as either elemental analytical or high resolution mass spectral data.

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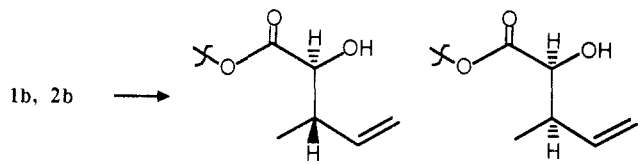

	threo	erythro
	threo/erythro	
glyoxylate	*cis*-butene	*trans*-butene	1-(trimethylsilyl)-*cis*-2-butene
1b	8:1	15:1	1:15
2b	6:1	1.6:1	1:2.5

conversion) while isomerization in the presence of **1b** is more rapid than the ene reaction. These observations are consistent with contrasting reaction pathways. We postulate that both proceed through an intermediate carbocation but that in the case of 8-phenylmenthol glyoxylate, reversal to starting materials from this species is faster than progression on to product while these relative rates are reversed with 2-phenylcyclohexanol glyoxylate. Alternatively, it is possible that the reaction with **2b** is a concerted process.

Because the auxiliary remains connected to the substrate after the ene reaction, the stereochemical analyses described above could be conducted with racemic **2a**. For application in asymmetric induction processes, a practical resolution of this alcohol is required. While **1a** has been resolved[7] via its half-phthalate ester salt with either brucine or strychnine to provide both enantiomers and prepared in 72% enantiomeric excess by hydroboration of 1-phenylcyclohexene with monoisopinocampheylborane,[8] neither of these approaches would appear to be a viable method for the production of large quantities of optically active **2a**. We have found that enzymatic hydrolysis (hog liver esterease, pH 7.8 phosphate buffer[9]) of the acetates derived from racemic **2a** is complete at 50% conversion, providing optically pure (−) alcohol ($[\alpha]_D$ −56.3°, lit.[8] $[\alpha]_D$ −55.5°), while the (+) enantiomer remained as the ester ($[\alpha]_D$ +6.2°) from which it can be freed by simple hydrolysis ($[\alpha]_D$ +54.5°). Reesterification of the (−) alcohol provided acetate with $[\alpha]_D$ −6.2°. Thus, each enantiomers can be obtained in an optically pure state, within experimental error.[10]

We anticipate that *trans*-2-phenylcyclohexanol will serve as an effective substitute for 8-phenylmenthol in many of the asymmetric induction processes where the latter has been used successfully. In this regard, we have found that similar levels of asymmetric induction are obtained in the reactions of the ene reactions of the *N*-sulfinylcarbamates of **2a** and **1a** and that the reactions of the former proceed in higher chemical yield.[12] PhCy-OH can be readily prepared by the copper-catalyzed opening of cyclohexene oxide[13] and we expect rapid and widespread acceptance of this new chiral auxiliary.

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A New Method for the Preparation of γ,δ-Unsaturated Ketones via Claisen Rearrangement

Summary: Thermal rearrangement of monosodium salts of 3-(allyloxy)crotonates derived from primary and secondary allylic alcohols and of disodium salts of 3-(allyloxy)-2-alkenoic acids affords γ,δ-unsaturated ketones.

Sir: We previously reported[1] a convenient alternative to the traditional "allyl vinyl ether Claisen rearrangement" sequence[2] for the synthesis of γ,δ-unsaturated aldehydes. The method is experimentally simple to perform and avoids mercury catalysis which is generally required for the preparation of allyl vinyl ethers. In this paper, we disclose an extension of the method that allows the synthesis of γ,δ-unsaturated ketones.

Autenrieth[3] was the first to show that a variety of nucleophiles displace chloride from both isomers of 3-chlorocrotonic acid. We found that the corresponding reaction with allylic alkoxides provides a general method for the preparation of 3-(allyloxy)crotonic acids (Table I). Good yields of the derived adducts **2** were obtained when an allylic alcohol[4] was heated with 2.20 equiv of sodium hydride and 1.15 equiv of 3-chlorocrotonic acid (**1**)[5] in THF at 65 °C for 4 h. When the sodium salts of these carboxylic acids were heated to 200–215 °C under reduced pressure (15 mm) in a Kugelrohr apparatus (method A), the desired γ,δ-unsaturated ketones **3** distilled from the reaction mixture (Scheme I).[6]

Some Claisen rearrangements were found to be accelerated by carbanion formation,[7] and the dianions of allylic acetoacetates undergo Carroll rearrangement at room

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(4) Although 3-chlorocrotonic acid reacts more rapidly with alcohols then the betaine described in ref 1, the reaction is again limited to primary and secondary alcohols.
(5) A mixture of *cis*- and *trans*-3-chlorocrotonic acid prepared by a modification of the procedure of Jones et al. (Jones, D. E.; Morris, R. O.; Vernon, C. A.; White, R. F. M. *J. Chem. Soc.* **1960**, 2349) was used. A mixture of PCl_5 in benzene was treated with 0.5 molar equiv of ethyl acetoacetate at 25 °C for 14 h followed by 7.5 molar equiv of water for 24 h. The benzene layer was separated and the crude product was sublimed (45–50 °C, 4 mm); 43% yield.
(6) Under these conditions, Claisen rearrangement of the carboxylates of **2** apparently occurs followed by decarboxylation to the corresponding enolates. These enolates are protonated, although the proton source is not certain, and ketones distill from the reaction mixture in a high state of purity.
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