Alder reaction between **5a** or **5b** and dienophile **6b** (120–150 °C) is selective in favor of **7a** and **7b** by a ca. 2:1 ratio relative to the undesired regioisomer **11**. However, dienes **5c** and **5d** afford approximately 1:1 mixtures of both regioisomers, while **5e** reacts slowly to give a 4:1 mixture in favor of the wrong isomer **11e**.

With the proper choice of diene substituents, a synthetically useful ratio of adducts **7** can now be obtained by the intermolecular Diels–Alder route. Furthermore, cleavage of the activating *N*-chloroacetyl group is easily accomplished with methanolic carbonate. Thus, crystalline **12a** can be obtained in ~50% overall yield from **6b**.

Methods for introduction of cytochalasin ring A functionality are under active investigation and will be described in due course.

Acknowledgment. This work was supported by the National Institutes of Health (CA 17918-02).

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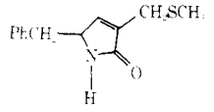

i

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(11) NMR spectrum of **10** (R = $COCH_2Cl$): 270-MHz NMR ($CDCl_3$) δ 7.32 (5 H, m), 5.64 (1 H, dt, *J* = 9, 3 Hz), 5.56 (1 H, dt, *J* = 9, 3 Hz), 4.65 (2 H, s), 4.32 (1 H, ddd, *J* = 8, 3, 2 Hz), 3.07 (1 H, dd, *J* = 13, 3 Hz), 2.75 (1 H, dd, *J* = 13, 8 Hz), 2.71 (1 H, dd, *J* = 9, 6 Hz), 2.52 (1 H, br t, *J* = 9 Hz), 2.31 (1 H, m), 2.13 (1 H, m), 1.40 (3 H, d, *J* = 7 Hz), 0.83 (3 H, d, *J* = 7 Hz). NMR spectrum of **10** (R = H): 270-MHz NMR ($CDCl_3$) δ 7.22 (5 H, m), 5.77 (1 H, dt, *J* = 9, 3 Hz), 5.65 (1 H, dtd, *J* = 9, 3, 1 Hz), 5.48 (1 H, br s), 3.41 (1 H, ddd, *J* = 10, 5, 4 Hz), 2.96 (1 H, dd, *J* = 14, 4 Hz), 2.76 (1 H, dd, *J* = 10, 7 Hz), 2.57 (1 H, m), 2.52 (1 H, dd, *J* = 14, 10 Hz), 2.34 (2 H, m), 1.36 (3 H, d, *J* = 7 Hz), 1.22 (3 H, d, *J* = 7 Hz).
(12) Compound **10** has been prepared by a different route by G. Stork et al. (personal communication, G. Stork).
(13) NSF Predoctoral Fellow, 1975–1978.

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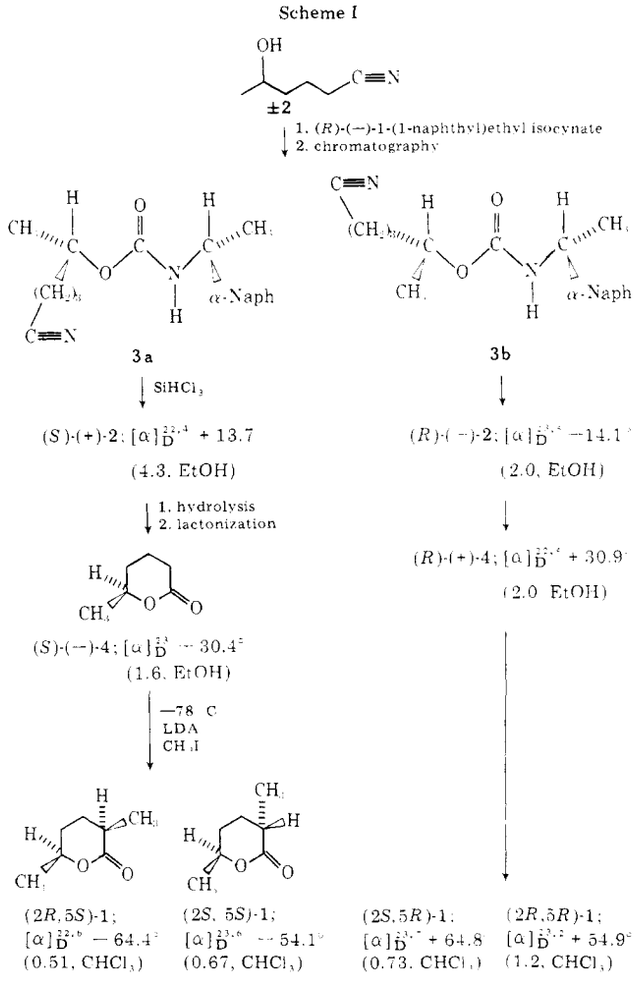
Synthesis of the Carpenter Bee Pheromone. Chiral 2-Methyl-5-hydroxyhexanoic Acid Lactones

Summary: 5-Cyanopentan-2-ol was resolved by chromatographic separation of diastereomeric carbamate derivatives. Hydrolysis and lactonization of each enantiomer afforded optically pure δ-methyl-δ-valerolactone, which was methylated to give cis and trans isomers of 5-hydroxyhexanoic acid lactone. One of the cis enantiomers is the carpenter bee pheromone.

Sir: As a prelude to a future account of a convenient and general synthetic approach to enantiomerically pure γ-substituted γ-lactones or δ-substituted δ-lactones, we describe the synthesis of all four stereoisomers of 2-methyl-5-hydroxyhexanoic acid lactone (**1**). One (presumably)[1] of the enantiomers of the *cis*-lactone is the major volatile component of the carpenter bee sex attractant.[2]

Our synthetic approach was designed to utilize a racemic intermediate that could be predictably and conveniently resolved into its enantiomers using our recently described broad-spectrum chromatographic method.[3] As shown in Scheme I, racemic 5-cyanopentan-2-ol (**2**), prepared by the method of Colonge et al.,[4] was converted to diastereomeric cyanocarbamates **3a** and **3b** by reaction with (*R*)-(−)-1-(1-naphthyl)ethyl isocyanate.[5] These diastereomers are easily separable by automated multigram HPLC[6] (acidic alumina; 2:1 $CHCl_3$–hexane) and the enantiomerically pure cyano alcohols were retrieved quantitatively by silanolysis with trichlorosilane.[7] Basic hydrolysis of the enantiomeric cyano alcohols and subsequent lactonization afforded the corresponding enantiomers of δ-methyl-δ-valerolactone **4**. Low-temperature methylation (LDA–methyl iodide) of the enan-

Scheme I



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tiomers of lactone **4** afforded a 1:1 mixture of the GLC-separable (Carbowax, 150 °C) cis and trans isomers of **1**.[8] Since the methylation sequence has no effect upon the stereochemistry of the configurationally known δ carbon of **4**,[9] the absolute configurations of the four stereoisomers of **1** are established. Even had the absolute configuration of **4** not been previously assigned,[9] it could have been assigned from the elution order of the diastereomeric carbamates **3a** and **3b**.[10] Moreover, the absolute configurations of the enantiomers of *cis*-**1** (and hence the *trans*-**1** as well) are assignable from the sense of the (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol induced NMR spectral nonequivalence.[11] This induced NMR nonequivalence allows facile NMR determination of the enantiomeric purity of *cis*-**1** (and thus *trans*-**1** as well); both enantiomers were enantiomerically pure by this criterion. Lactone **4** recovered by GLC from the methylation reaction mixture was of unchanged specific rotation.[12]

Acknowledgment. This work has been partially supported by grants from the National Institutes of Health and the National Science Foundation.

Supplementary Material Available: the experimental details of this work (4 pages). Ordering information is given on any current masthead.

References and Notes

(1) Although the report[2] of the identification of *cis*-**1** as the major component of the sex attractant contains no chiroptic data, it is reasonable to assume that the natural material is chiral and not racemic. In the absence of such data, we cannot state which enantiomer of *cis*-**1** corresponds to the natural material. Toward this end, samples of the stereoisomers are available for testing.
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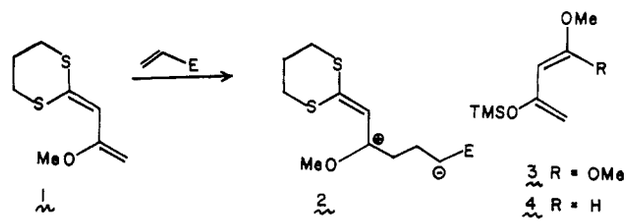
Diels–Alder Reactions of 1,1-Dimethoxy-3-trimethylsilyloxy-1,3-butadiene

Summary: The title compound has been shown to be a powerful diene in Diels–Alder reactions with electron-deficient dienophiles. In these processes, it functions as a directed synthetic equivalent of $^+COCH_2COCH_2^-$. The contrast in behavior between this diene and that of 2-(2-methoxy)allylidene-1,3-dithiane, which has a high tendency to afford Michael addition products with highly electrophilic olefins, is particularly striking.

Sir: Recently we investigated the feasibility of cycloaddition reactions of diene **1** with potential dienophiles.[1] We found that the generality of Diels–Alder cycloadditions of **1** was undermined by its tendency to afford simple Michael addition products with highly electrophilic olefins such as benzoquinone and dimethyl acetylenedicarboxylate. Cycloaddition reactions were observed only with less electrophilic olefins such as methyl vinyl ketone.

It seemed likely that strong electrophiles might react with the powerfully nucleophilic **1** via its "s-trans" conformer, thereby affording an intermediate of the type **2**, wherein cyclyzation would be noncompetitive with proton transfer as a means of charge dissipation.



It seemed worthwhile to pursue this line of study. Thus, the general proposition of using heavily functionalized dienes which might endow their Diels–Alder adducts with convenient access points for orderly future elaborations has, potentially, considerable possiblities in the design of synthetic strategy.[2-4] During the course of our studies, addressed to correcting the limitations of diene **1** described above, Brassard and coworkers[5] reported the preparation of diene **3** and homologues thereof by a method similar to that which we used for the preparation of **4**.[6] Of particular interest to us was the finding that compound **3** and its homologues gave cycloaddition products with several naphthoquinones. No other Diels–Alder reactions of **3** were described. Since we had found that reaction of compound **1** with the parent 1,4-benzoquinone afforded a benzofuran which was clearly derived from Michael addition and proton transfer,[1] we have examined the general enophilicity of compound **3**. Below we report that this substance is, in fact, an excellent diene for Diels–Alder reactions and its use allows for the facile elaboration of aromatic and alicyclic systems bearing extensive functionality.

Compound **3** reacted with dimethyl acetylenedicarboxylate in benzene. After 30 min under reflux[7] there was isolated an 89% yield of dimethyl 3-methoxy-5-hydroxyphthalate (**5**), mp 141–143 °C.[8] The unraveling of the presumed adduct **5a** is apparently instantaneous under these conditions. Similarly, compound **3** reacts with 1,4-benzoquinone (C_6H_6; room temperature; 15 min). The crude adduct was treated with pyridine–acetic anhydride (reflux; 12 h), thereby affording a 78% yield of 1-methoxy-3,5,8-triacetoxynaphthalene (**6**),[8] mp 172–173 °C.

It will be recalled that, with these two potential dienophiles, compound **1** gave high yields of products derived from simple 1,4-addition. Diels–Alder reaction of compound **3** with 1,3-dicarbomethoxyallene (C_6H_6; reflux; 1 h) afforded a 72% yield of the differentiated homophthalate derivative, **7**[8] (mp 70–72 °C). Similarly, a 74% yield of methyl 2-methoxy-4-hydroxybenzoate (mp 150–151 °C; lit.[9] 152–153 °C) was obtained after cycloaddition of **3** with methyl propiolate.

Thus, through this methodology, one elaborates in a single step a benzene ring in the form of a resorcinol monomethyl ether. The condition of the process with unsymmetrical dienophiles is that the methoxy group emerges ortho to that function which dominates their regiochemical sense of addition.

Cycloaddition of compound **3** with maleic anhydride occurs essentially instantaneously (neat; 0 °C). Trituration with ether gave a 95% yield of compound **9**,[8] mp 152–153 °C. No acidic

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