structure than that of the azo form. The creation of this cosphere is favored in water or water-like solvents or in the water-rich compositions of the aqueous binaries. In water–alcohol mixtures, $\Delta H°$ becomes negligibly small in compositions where little solvent structure remains and $\Delta G°_T$ is governed only by $\Delta S°$.

Whereas the breaks in the plots of $\Delta G°_T$ for PND and of $\bar{\nu}_{max}$ of TNS against the mole fraction of alcohol must result from changes in the solvent structure, we cannot be certain what that structural change is. The fact that so many properties of these mixtures and of solutes dissolved in them show extrema at 4–6 mol % *tert*-butyl alcohol and 10–15 mol % ethanol has led Franks[21] and Arnett[22] to propose that addition of the alcohols to water leads initially to increased structuring and that the extrema appear at compositions where further addition of alcohol caused breakdown of structure. Yaacobi and Ben-Naim[35] interpret the thermodynamics of solution of methane and ethane in ethanol–water mixtures in terms of reinforcement of water structure by ethanol only up to about 3 mol %, with a decrease in water structure between 3 and 20 mol %. By this interpretation, water structure is no longer important above 20 mol %. Proton chemical shift data show that addition of alcohol to water enhances hydrogen-bonded structure between 0 and 5 mol % *tert*-butyl alcohol[36,37] and 0 and 8 mol % ethanol.[38]

If it is assumed that alcohol–water mixtures containing more than 20 mol % ethanol and 6 mol % *tert*-butyl alcohol are unstructured, changes in the values of $\bar{\nu}_{max}$ for TNS and log K_T for PND in the unstructured compositions can be used to estimate the importance of solvent changes such as polarity on the probe properties. The excess changes observed in the water-rich compositions then give an estimate of the contribution of structural factors to the total change. Using the values of $\bar{\nu}_{max}$ for TNS and 1,7-ANS in ethanol–water shown in Figure 4 and extrapolating to 0 and 100% ethanol, we estimate contributions of 4.0 and 2.8 kcal/mol, respectively, to the total change in transition energy from solvent effects not related to structuring. The contributions associated with solvent structuring in this medium are 6.3 kcal/mol for TNS and 4.8 kcal/mol for 1,7-ANS. Using eq 6 and 7 to obtain similar extrapolated values of log K_T of PND in ethanol–water and *tert*-butyl alcohol–water, we estimate contributions to the total change in $\Delta G°_T$ of 1.6 kcal/mol from factors related to structuring and 2.7 kcal/mol from factors not related to structuring in ethanol–water mixtures. The corresponding contributions in *tert*-butyl alcohol–water are 2.0 and 1.9 kcal/mol, respectively. The estimates of contributions to the solvent effects due to the existence of solvent structure may be high, since properties of these mixtures that are related to polarity are not linear functions of mole fraction.

The anomalous solvent effect of TFE on both probes shows that in certain favorable cases, a hydrogen-bonding solvent can interact with dye solute by direct hydrogen bonding. The relatively high acidity and low basicity of the fluorinated alcohols reduce their self-association compared to the hydrocarbon alcohols[39] and thus increase their tendency to solvate dyes[24] and salts[25] by hydrogen bonding. The fact that $\bar{\nu}_{max}$ values of TNS in the hydrocarbon alcohols are correlated by δ and that the values for these alcohols fall on the same correlation line with aprotic solvents shows that self-association of the hydrocarbon alcohol dominates the solvent effect, and hydrogen-bonded solvent–dye interactions are not very important. The fact that a direct hydrogen-bonded interaction with the probes can shift their properties in the same direction as the indirect solvent–solvent hydrogen-bonding interaction may lead to confusing interpretations and emphasizes the importance of examining a wide range of solvent types and properties. It is most important in interpreting solvent effects to examine solvents in which there are not cross correlations between solvent properties, as is the case in many alcohol–water mixtures.

(35) M. Yaacobi and A. Ben-Naim, *J. Solution Chem.*, **2**, 425 (1973).
(36) R. G. Anderson and M. C. R. Symons, *Trans. Faraday Soc.*, **65**, 2550 (1969).
(37) D. N. Glew, H. D. Mak, and N. S. Rath, *Chem. Commun.*, 264 (1968).
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Communications to the Editor

Derivation of (+)- and (−)-C_{17}-Juvenile Hormone from Its Racemic Alcohol Derivative *via* Fungal Metabolism

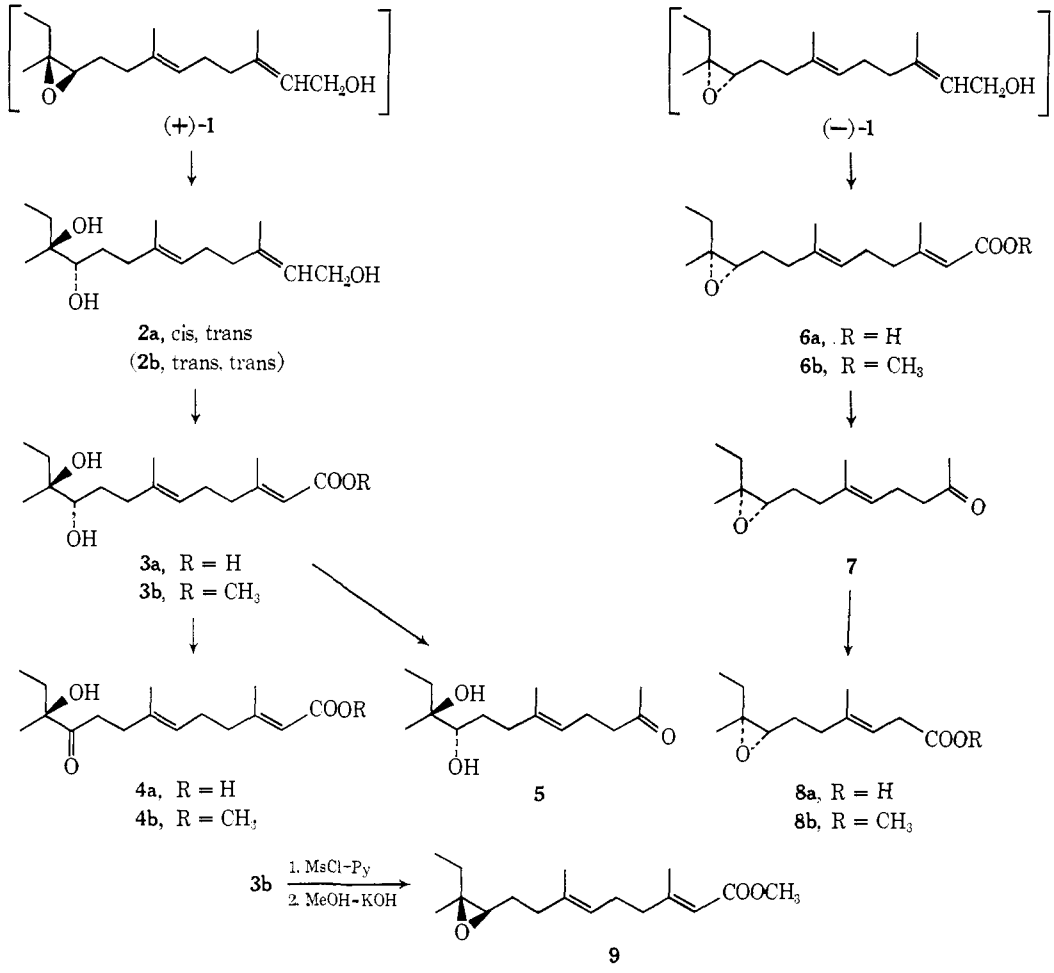
Sir:

In our metabolic studies with *Helminthosporium sativum*, a racemic mixture of 10,11-epoxyfarnesol has been transformed into (−)-10,11-dihydroxyfarnesoic acid,[1] which was then chemically converted into an enantiomeric pair of C_{16}-juvenile hormone (JH).[2] Novel trans and cis hydration mechanisms of the racemic epoxide were also investigated.[3] These results can be utilized for optical resolution of racemic epoxy isoprenoids, which is difficult to carry out by the usual resolution methods. In this communication, we describe a derivation of an enantiomeric pair of C_{17}-JH from its racemic alcohol derivative *via* fungal metabolism. The difference of the metabolic processes between the enantiomers of 10,11-epoxyhomofarnesol is also shown, being compared with those of 10,11-epoxyfarnesol.

Racemic C_{17}-JH has been synthesized in fairly large

(1) Y. Suzuki and S. Marumo, *Chem. Commun.*, 1199 (1971); *Tetrahedron Lett.*, 1887 (1972).
(2) Y. Suzuki, K. Imai, S. Marumo, and T. Mitsui, *Agr. Biol. Chem.*, **36**, 1849 (1972).
(3) Y. Suzuki, K. Imai, and S. Marumo, *J. Amer. Chem. Soc.*, **96**, 3703 (1974).

Scheme I



scale to be used in this work.[4] The synthetic product contained 23% 2-cis isomer, and, since metabolizing this stereoisomeric mixture with the fungus would lead to contamination of the desired acidic 2-trans metabolites by the corresponding 2-cis ones, the synthetic C_{17}-JH was converted into the alcohol derivative by reduction ($LiAlH_4$) of the ester group. We had established earlier that racemic *cis,trans*-10,11-epoxyfarnesol was metabolized only into (−)-*trans,trans*-10,11-dihydroxyfarnesoic acid and not into the cis,trans acid. Thus, the racemic trans,trans,cis and cis,trans,cis mixture of 10,11-epoxyhomofarnesol (**1**) was shaken with the precultured mycelia of *Helminthosporium sativum* in the modified Czapek-Dox medium in the same way as in the case of epoxyfarnesol.[1] The extent of the metabolism was checked by tlc, and agitation of the culture was stopped when the substrate disappeared. Chromatographic separation (silica gel) of the ethyl acetate extracts of the culture filtrate gave seven metabolites (Scheme I), *i.e.*, three neutral compounds, **2a** (yield 13.5%), **5** (5.9%), and **7** (3.4%), and four acidic ones, **3a** (20.6%), **4a** (1.3%), **6a** (1.9%), and **8a** (2.4%), which were purified as their methyl esters.

3b (oil); $C_{17}H_{30}O_4$, *m/e* 280 ($M^+ - H_2O$); $[\alpha]_D$ −10.2° (*c* 1.1, MeOH); ir (CCl_4) 3500 (OH), 1725 cm^{-1} (ester); nmr ($CDCl_3$) δ 0.94 (t, $J \approx 7.5$ Hz, C_{11}-CH_2CH_3), 1.09 (s, C_{11}-CH_3), 1.62 (bs, C_7-CH_3), 1.96 (bs, two OH), 2.15 (bs, C_3-CH_3), 3.38 (dd, $J \approx 2.5$, 10.0 Hz, C_{10}-CH), 3.71 (s, $COOCH_3$), 5.17 (bs, C_6-H), 5.70 (bs, C_2-H). These spectra are unequivocally indicative of **3b** being methyl (−)-*trans,trans*-10,11-dihydroxyhomofarnesoate. Conversion of **3b** into optically active C_{17}-JH was achieved by mesylation (mesyl chloride in pyridine) followed by base treatment (MeOH-KOH). The product (**9**) showed nmr and ir spectra completely identical with those of C_{17}-JH.[4,5] The optical rotation of **9**, $[\alpha]_D$ +11.7° (*c* 0.6, MeOH), is quite close to that of (10*R*,11*S*)-C_{18}-JH (+12.2°) reported by Loew and Johnson,[6] indicating that the (+)-C_{17}-JH prepared in the present work must have a fairly high optical purity. This chemical conversion also established the absolute stereochemistry of **3b** to be 10*S*,11*S*.

6b (oil); $C_{17}H_{28}O_3$, *m/e* 280 (M^+); $[\alpha]_D$ −12.8° (*c* 0.2, MeOH). The spectral data (nmr and ir) were completely identical with those of C_{17}-JH, showing that the (−)-hormone (as a free acid) has been directly obtained as the result of fungal metabolism. The optical rotation measured was slightly larger than the reported one (−11.7°) of (−)-C_{18}-JH,[6] suggesting that **6b** must be in a highly pure state. Both enantiomers of C_{17}-JH were thus obtained *via* the fungal metabolic action on the racemic alcohol derivative.[7]

(4) K. Mori, A. Sato, and M. Matsui, *Agr. Biol. Chem.*, **36**, 1931 (1972).

(5) A. S. Meyer, H. A. Schneiderman, E. Hanzmann, and J. H. Ko, *Proc. Nat. Acad. Sci. U. S.*, **60**, 853 (1968).

(6) P. Loewa nd W. S. Johnson, *J. Amer. Chem. Soc.*, **93**, 3765 (1971).

(7) Improvement of the low yield of (−)-C_{17}-JH from the culture filtrate by optimizing the metabolic conditions was not pursued, owing to an insufficient amount of the synthesized substrate. Attempts to derive chemically (−)-C_{17}-JH from methyl (−)-10,11-dihydroxyhomofarnesoate (**3b**) by the procedure carried out successfully in the case of C_{16}-JH (halogenation or mesylation of the C_{11}-hydroxyl, followed by base treatment) have failed.

The structures of the other five metabolites were determined by spectral analysis. Metabolite **2a**, oil, $[\alpha]_D$ −8.3° (*c* 1.1, MeOH), was concluded to be (10*S*, 11*S*)-*cis*,*trans*-dihydroxyhomofarnesol, which is most probably the hydration product of the minor 2-cis substrate. **2a** might have come partly from the major 2-trans substrate by the action of a trans–cis isomerase, as was found in the metabolic course of epoxyfarnesol.[8] Metabolite **4b**, oil, $[\alpha]_D$ −6.6° (*c* 0.2, MeOH), was identified as methyl (11*S*)-*trans*,*trans*-10-oxo-11-hydroxyhomofarnesoate, which was clearly an oxidation product of **3a** at C_{10}. Terminal oxidation of an allylic carboxylate in **3a** gave an alternate metabolite **5**, oil, $[\alpha]_D$ −13.8° (*c* 0.7, MeOH), to which the structure (9*S*,10*S*)-*trans*-dihydroxyhomogeranylacetone was assigned. By a similar oxidation, **6a** was converted into (9*S*,10*R*)-*trans*, *cis*-epoxyhomogeranylacetone (**7**), oil, $[\alpha]_D$ −27.9° (*c* 0.3, MeOH). Two-carbon degradation of **7** gave *trans*-*cis*-7,8-epoxy-4,8-dimethyl-dec-3-enoic acid (**8a**). Although the exact optical rotation of **8b** was not measured owing to its small value, the distinct negative sign in ORD indicated the absolute stereochemistry to be 7*S*,8*R*.

The seven metabolites may be placed in two groups by their structural characteristics, the first group (**2a**, **3a**, **4a**, **5**) having a glycollic moiety, and the second group, the epoxide-containing compounds (**6a**, **7**, **8a**). Metabolic conversion of the racemic substrate into these two groups of compounds could be reasonably explained by postulating two metabolic pathways. Namely, the glycollic compounds would be originally derived from the (+)-enantiomer of the substrate, (+)-**1**, which is hydrated enzymatically in the trans manner with nucleophillic attack at the C_{10} position. This hydration is essentially the same as in the case of (+)-epoxyfarnesol.[3] On the other hand, (−)-epoxy compounds would be derived from the (−)-enantiomer, (−)-**1**, the epoxy ring being resistant to hydration by the hydrase of the fungus. This difficulty for the fungus in hydrating (−)-**1** may be ascribed to the steric effect of an ethyl in place of the methyl group at the C_{11} position of (−)-epoxyfarnesol, which had been established to undergo cis hydration to produce optically minus glycol.[3] The juvenile hormone activity of the enantiomers, **6b** and **9**, should prove to be quite interesting, and the bioassay is under way.

(8) Y. Suzuki and S. Marumo, *Tetrahedron Lett.*, 5101 (1972).

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A Novel and Versatile Synthetic Reagent. The Monoalkyl Esters of Tetraalkylphosphorodiamidous Acid

Sir:

We wish to report the utility of alkyl esters of phosphorodiamidous acid (phosphorodiamidites) as a hitherto unrecognized class of convenient and versatile synthetic intermediates which may be utilized for the preparation of α,α-dichloroesters, α,α-dichlorophenyl alkanes, and trichloromethyl alkanes.[1]

The phosphorodiamidites, I, are conveniently synthesized from hexamethylphosphorus triamide (HMPT) by converting to the monochloro derivative,[2] II, followed by reaction of an ether solution of II with the appropriate alcohol in the presence of triethylamine as shown in eq 1. Compound II should be handled under

$$2P[NMe_2]_3 + PCl_3 \longrightarrow \underset{\text{II}}{3ClP[NMe_2]_2} \xrightarrow[Et_3N]{ROH} \underset{\text{I}}{[Me_2N]_2POR} \quad (1)$$

a dry nitrogen atmosphere as much as possible since it reacts rapidly with atmospheric moisture. *Caution:* II reacts explosively upon contact with water. The yields of I (based on HMPT) and boiling points are as follows: R = CH_3, 75%, bp 59–63° (40 Torr); R = Et, 77%, bp 42–43° (10 Torr); R = *i*-Pr, 66%, 61–62° (20 Torr); R = $PhCH_2$, 56%, 60–63° (0.01 Torr).[3]

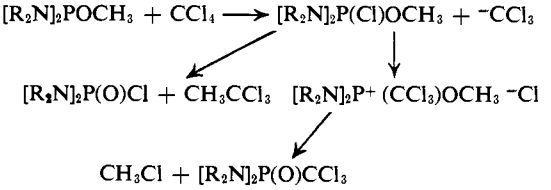
Upon addition of I (R = CH_3) to carbon tetrachloride even at 0° a very exothermic, almost explosive, reaction ensues yielding the products shown in eq 2.

$$[R_2N]_2POCH_3 + CCl_4 \longrightarrow \underset{\text{III}}{[R_2N]_2P(O)Cl} + [R_1N]_2P(O)CCl_3 + CH_3Cl + CH_3CCl_3 \quad (2)$$
$$\text{IV}$$

The products, with the exception of IV, were identified by comparison of nmr spectra and chromatographs with those of authentic compounds. Compound III was independently synthesized by treatment of a benzene solution saturated with chlorine with I. The yield of methyl chloride (15%) and 1,1,1-trichloroethane (85%) were determined by nmr using toluene as an internal standard. At high temperatures proportionately more methyl chloride was formed. A similar reaction of I (R = $PhCH_2$) yielded benzyl chloride (7%) and 1,1,1-trichloro-2-phenylethane (73%) although the reaction was considerably less exothermic.

We feel these results are best explained on the basis of the mechanism shown in Scheme I. The enchanced

Scheme I



reactivity of I over the corresponding trialkylphosphites, which give no detectable reaction at room temperature, is presumably due to an increase in the nucleophilicity of phosphorus in this system. Dialkoxy compounds, $[R_2N]P[OCH_3]_2$ (V), react only slowly at room temperature.

The reactions of phosphites with carbon tetrachloride have recently been reinvestigated by Cadogan and coworkers[5] who concluded that, in the absence of light

(1) Presented in part at the 167th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1974.
(2) H. Noth and H. J. Vetter, *Chem. Ber.*, **94**, 1505 (1961).
(3) An alternative method of synthesis of these compounds, the direct combination of hexamethylphosphorus triamide and alcohol,[4] was found to yield mixtures of amidites, diamidites, and phosphites which could not be conveniently separated.
(4) D. Houalla, M. Sanchez and R. Wolf, *Bull. Soc. Chim. Fr.*, 2368 (1965).
(5) R. E. Atkinson and J. I. G. Cadogan, *J. Chem. Soc., B*, 138 (1969).