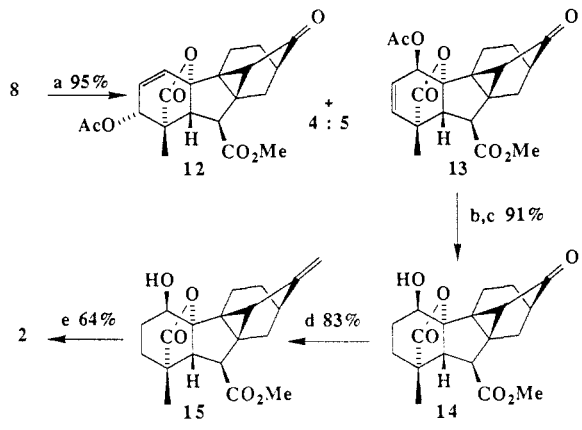
Scheme II



[a] Reagents and conditions: (a) LiOAc, HMPT, 4 °C, 72 h; (b) K_2CO_3, MeOH, 24 °C, 15 min; (c) H_2, Rh-Al_2O_3, EtOAc, 1 atm, 24 °C, 6 h; (d) CH_2Br_2, $TiCl_4$, Zn, CH_2Cl_2, 24 °C, 5 min; (e) *n*-PrSLi, HMPT, 24 °C, 1.5 h.

iodolactone **4**, mp 131-3 °C, $[\alpha]^{25}_D$ -370° (*c* 0.096),[8] which was ozonolyzed to norketone **5**, mp 131-3 °C, $[\alpha]^{25}_D$ -361° (*c* 0.088). Formation of the 9,15-cyclogibberellane skeleton was then effected by an intramolecular alkylation reaction mediated by potassium hydride, to afford **6**, mp 167-8 °C, $[\alpha]^{25}_D$ -153° (*c* 0.094). Subsequent reaction with diphenylboron bromide[9] not only removed the protecting group from the 3β-hydroxyl but also reestablished the desired A-ring/19β→10 lactone structure, thereby forming **7** [colorless oil, $[\alpha]^{25}_D$ -41° (*c* 0.023)]. Although the basis of this apparently contrathermodynamic isomerization[10] has not yet been elucidated, it appears to be general for this type of compound, and the saving of three steps greatly enhances the efficiency of these gibberellin to antheridiogen interconversions. Deletion of the functionality in ring A was effected by hydrogenolysis/hydrogenation of mesylate **8**, $[\alpha]^{25}_D$ +41° (*c* 0.016), following which, several attempts were made to convert the resulting ketone **9**, $[\alpha]^{25}_D$ -81° (*c* 0.006), into the target ester **10** by means of a Wittig reaction.[11] Although the formation of **11** (arising from a retrograde Michael reaction)[3] in addition to **10** came as no surprise, the recovery of ether soluble material was only ca. 20%.[12] The problem was satisfactorily resolved by employing the Lombardo modification[13] of the Oshima-Nozaki procedure,[14] which afforded **10** in 87% yield as a colorless oil, $[\alpha]^{21}_D$ -65° (*c* 0.008). Comparison of its ^{1}H NMR spectrum with that of the natural substance revealed a close correspondence in the chemical shifts associated with the respective methylene and H(6) resonances, but in conformity with expectations arising from earlier spectroscopic analyses,[5] the signals associated with H(5) and H(15) in **10** occurred at approximately 0.5 ppm higher field relative to the *A. mexicana* antheridiogen; i.e., assuming the same basic structure, the differences were consistent with the presence of a 1β-hydroxy function in the latter compound.

Confirmation of structure **2** for the new antheridiogen was established as outlined in Scheme II by treating mesylate **8** with lithium acetate in HMPT, which afforded a 4:5 mixture of the oily S_N2 and syn-S_N2' products **12** $[\alpha]^{21}_D$ -190° (*c* 0.012), and **13** $[\alpha]^{21}_D$ -280° (*c* 0.015), respectively.[15] Hydrolysis of the latter followed by hydrogenation gave hydroxy ketone **14**, mp 220-1 °C, $[\alpha]^{25}_D$ -103° (*c* 0.013), and thence the desired olefinic ester **15** as a colorless foam $[\alpha]^{21}_D$ -50° (*c* 0.003) by methylenation as before[13] (once again the Wittig reaction proved to be unsatisfactory). The trimethyl silyl ether of this product was identical by GC/MS with that of the methyl ester derived from natural material,[16] while the parent acid **2**, mp 213-4 °C, $[\alpha]^{21}_D$ -72° (*c* 0.013, MeOH), [derived by treatment of **16** with lithium propanethiolate in HMPT][17] afforded a virtually identical ^{1}H NMR spectrum with that obtained from an authentic sample.[16,18]

The availability of **2** by means of this synthesis will greatly expedite investigations into the biological role of this intriguing substance, while the discovery of yet a further skeleton for this class of phytohormones not only injects considerable further interest into the area but also provokes contemplation of a possible alternative hypothesis for the biosynthetic origin of **1** based on an analogue of **2**. The consolidation of the synthetic methodology and augmentation of the spectroscopic data base also enhances prospects for the elucidation of the structures possessed by further antheridiogens obtained from other ferns.[19]

Supplementary Material Available: Characterization data for compounds **10** and **15** (1 page). Ordering information is given on any current masthead page.

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(12) This result indicated that little of the initial adduct had closed to the oxaphosphetane and proceeded to the normal product. It was possible to glean further amounts of **10** by heating the aqueous layer with DBU, however, suggesting that the missing material could be accounted for by the water soluble betaine.
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(16) We gratefully acknowledge the cooperation of Dr. J. E. Nester, Professor N. Takahashi, and Dr. H. Yamane in providing spectroscopic data, and to Professor J. MacMillan and Dr. J. E. Nester for conducting ^{1}H NMR and GC/MS comparisons. The gibberellin substrates utilized in this project were generously donated by Abbott Laboratories and ICI Plant Protection.
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Isotope Effects on Isotope Effects. Failure of the Rule of the Geometric Mean as Evidence for Tunneling[1]

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Received February 1, 1988

We showed in earlier work that secondary β-tritium isotope effects in eliminations from 2-arylethyl derivatives are often larger than expected on the basis of rehybridization of the C-H(T) bond from sp^3 to sp^2 as the system progresses along the reaction coordinate.[2-4] We suggested that a contribution of tunneling to the secondary isotope effect could be responsible for this discrepancy and presented calculations showing that a significant tunnel correction results when the bending motions of the non-

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Table I. Secondary Tritium Isotope Effects in E2 Reactions of $ArCLTCH_2X$ and $ArCL_2CH_2X$ (L = H or D) at 50 °C

reaction	k_H/k_T	k_D/k_T	$(k_H/k_T)_{calcd}$[c]
1[a] + EtONa/EtOH	1.204 ± 0.015	1.0314 ± 0.010	1.106 ± 0.033
2[b] + *t*-BuOK/*t*-BuOH	1.191 ± 0.012	1.0274 ± 0.008	1.092 ± 0.026

[a] 2-Phenylethyltrimethylammonium bromide. [b] 2-(*p*-Chlorophenyl)ethyl tosylate. [c] From the relation $k_H/k_T = (k_D/k_T)^{3.26}$ (ref 8 and 9).

transferred hydrogen are coupled with the stretching motion of the transferred hydrogen. The calculations also predict that the tunnel correction to the secondary tritium isotope effect should be diminished when the transferred atom is deuterium rather than protium. We report here experimental evidence that this is indeed the case.

The experiments were modeled after the earlier ones by using 2-arylethyl derivatives tracer labeled with tritium in the β-position. The resulting mixture can undergo the following elimination reactions

$$ArCL_2CH_2X + RO^- \xrightarrow{2k_1} ArCL{=}CH_2 + ROL + X^-$$

$$ArCLTCH_2X + RO^- \begin{cases} \xrightarrow{k_2} ArCL{=}CH_2 + ROT + X^- \\ \xrightarrow{k_3} ArCT{=}CH_2 + ROL + X^- \end{cases}$$

When L = H, $k_1/k_3 = (k_H/k_T)_{sec}$, and when L = D, $k_1/k_3 = (k_D/k_T)_{sec}$. We determined $(k_H/k_T)_{sec}$ and $(k_D/k_T)_{sec}$ in the manner previously described[2] for the reactions of 2-phenylethyltrimethylammonium ion (**1**) with ethoxide in ethanol and 2-(*p*-chlorophenyl)ethyl tosylate (**2**) with *tert*-butoxide in *tert*-butyl alcohol, both at 50 °C. The results are given in Table I.

The secondary k_H/k_T values are both substantial.[5] We pointed out earlier[2] that the fractionation factors of Hartshorn and Shiner[6,7] predict $k_H/k_T = 1.17$ at 50 °C for *complete* rehybridization. Since proton transfer is incomplete in the transition state, it is unlikely that rehybridization would be complete, so the actual contribution of rehybridization to k_H/k_T is probably well below 1.17. The k_D/k_T are very much smaller than the k_H/k_T and remain smaller when converted to k_H/k_T (last column of Table I) by the relationship[8,9]

$$k_H/k_T = (k_D/k_T)^{3.26} \quad (1)$$

This relationship is obeyed by the calculated *semiclassical* (without tunneling) primary (error ≤ 3.8%) and secondary (error ≤ 1.1%) isotope effects reported in ref 4. If masses are assumed to be in the ratio of reduced masses of C-H, C-D, and C-T instead of 1:2:3, the exponent in eq 1 becomes 3.34, but an exponent of ca. 6 is required to bring our calculated and directly measured k_H/k_T values into agreement. Any protium in the deuteriated substrate (<2% by NMR) would make k_D/k_T appear too large rather than too small.

That both measured $(k_H/k_T)_{sec}$ values in Table I are larger than predicted for rehybridization and larger than the $(k_H/k_T)_{sec}$ values calculated from $(k_D/k_T)_{sec}$ is consistent only with model calculations that include tunneling.[4] The disagreements between columns 2 and 4 of Table I also constitute violations of the rule of the geometric mean.[10] The principle behind the rule is that the isotope effect for a doubly labeled species should be very close to the product of the isotope effects for the corresponding singly labeled species. In other words, the two isotopes should exert their effects independently. This statement can be expressed algebraically in eq 2, where the subscript refers to the transferred and the superscript to the nontransferred atom

$$k_H^H/k_D^T = (k_H^H/k_H^T)(k_H^H/k_D^H) \quad (2)$$

But eq 2 can be true only if

$$k_H^H/k_H^T = k_D^H/k_D^T \quad (3)$$

The values in column 2 of Table I are k_H^H/k_H^T and in column 4 are k_D^H/k_D^T. It is evident that eq 3 does not hold and hence neither does eq 2. Specifically, k_D^H/k_D^T is less than k_H^H/k_H^T. Qualitatively similar effects of the mass of the transferred atom on secondary deuterium isotope effects have been observed in reactions involving NAD^+ and NAD^+ analogues,[11-13] but only in the nonenzymatic reactions[11] can one be reasonably sure that the hydride transfer is wholly rate determining. We continue to explore other predictions of the calculations.

(5) We believe our previously reported (ref 2) k_H/k_T for **1** + EtONa (1.259 ± 0.010 at 40 °C) is somewhat high, for the two present workers agree on a lower value (1.189 ± 0.008 at 40 °C, R.C.P., and the present value at 50 °C, M.A.).

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Triticones A and B, Novel Phytotoxins from the Plant Pathogenic Fungus *Drechslera tritici-repentis*

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Received February 18, 1988

Fungi of the genus *Drechslera* (*Helminthosporium*) attack a variety of plants.[1] The attack is usually chemical, and the disease symptoms are caused by plant toxins emanating from the fungal hyphae.[2] Phytotoxins produced by fungi are interesting for several reasons: they are often new structural types, they can be used in studying plant physiology, they can serve as models for new herbicides, and they can be used in screening programs for resistant plant strains.[3-5] *D. tritici-repentis* attacks crested wheat grass (*Agropyron cristatum*), quackgrass (*A. repens*), rye (*Secale cereale*), and wheat (*Triticum vulgare*), and the wheat disease is currently a major agricultural problem.[6] The symptons of fungal attack are lesions which appear as light to reddish brown elliptical spots 1-2 weeks after inoculation. These lesions suggest that *D. tritici-repentis* produces one or more phytotoxins, but no

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