broadening of ^1H NMR peaks for groupings in the vicinity of the 9,10 bond in **1** and **1a**, in contrast to what is observed for prieurianin,[2] **2**, **3**, and many other compounds in this series suggests that steric congestion in this region has been alleviated in **1** and **1a** by cyclic hemiortho ester formation.

Experimental Section

^1H NMR spectra were run at 250 MHz on a Bruker WM-250 spectrometer. The assignments for hispidin A were checked by extensive decoupling. Other spectra were run as in earlier studies.[5] NMR parameters are given in Tables I and II.

Hispidin A (1) had UV [λ_{max} (EtOH) 213 nm (ϵ 12 000)], IR [($CHCl_3$) 3570 (OH), 3525 (OH), 3020 (C=CH), 1728 (ester), 1650 (C=C), 1380 (Me), 1210 (ester), 870 (furan) cm^{-1}], and mass (*m/e* 686, 635, 627, 626, 609, 594, 566, 527, 526, 509, 495, 484, 467, 449, 301, 241, 226, 209, 181, 167, 135, 83, 69, 55) spectra in accord with structure **1**.

Anal. Calcd for $C_{41}H_{56}O_{16}\cdot 2H_2O$: C, 58.57; H, 7.14. Found: C, 58.40; H, 7.00.

Hispidin A diacetate (1a), prepared from **1** with acetic anhydride and pyridine at 25 °C, had IR and mass (*m/e* 770, 728, 710, 682, 668, 640, 626, 611, 526, 512, 508, 343, 301, 283, 241, 226, 223, 209, 181, 167, 157, 135, 129, 83, 69, 55) spectra in accord with structure **1a**.

Anal. Calcd for $C_{45}H_{60}O_{18}\cdot 2H_2O$: C, 58.44; H, 6.93. Found: C, 58.55; H, 6.99.

Hispidin B (2) had IR [($CHCl_3$) 3590 (OH), 3010 (C=CH), 1760 (α,β-unsaturated lactone), 1725 (ester), 1645 (C=C), 1260 (ester), 1135 (*tert*-OH), 870 (furan) cm^{-1}] and mass spectra (see text) in accord with structure **2**.

Anal. Calcd for $C_{38}H_{48}O_{13}$: C, 64.04; H, 6.74. Found: C, 63.5; H, 7.1.

Hispidin B Acetate (2a). A small sample of **2** was treated with Ac_2O and pyridine at 25 °C; the mass spectrum of the resulting **2a** (amorphous) is described in the text.

Hispidin C (3), crystallized from methanol, had UV [λ_{max} (EtOH) 213 nm (ϵ 13 270)], IR [($CHCl_3$) 3590 (OH), 3020 (C=CH), 1760 (α,β-unsaturated lactone), 1730 (ester), 1645 (C=C), 1375 (Me), 1230 (ester), 1140 (*tert*-OH), 870 (furan), 775 (KBr, ethyl) cm^{-1}], and mass (*m/e* 672, 644, 626, 612, 595, 594, 586, 584, 566, 559, 548, 541, 513, 512, 481, 452, 435, 418, 354, 278, 243, 229, 225, 209) spectra in accord with structure **3**. Direct comparison (mixture melting point, chromatographic retention times, UV, and IR) with a sample of **3** from *Aphanamixis polystacha* established its identity.[6]

Hispidins A, B, and C demonstrated activities of $<1.0 \times 10^{-2}$, 2.9, and 17.0 μg/mL, respectively. Activity in the KB test system is defined as $ED_{50} \leq 20$ μg/mL.

Acknowledgment. This investigation was supported by Grant No. 5-R01-CA-22336-02, awarded by the National Cancer Institute, Department of Health, Education, and Welfare.

Registry No. 1, 75975-30-3; **1a**, 75975-31-4; **2**, 75975-32-5; **2a**, 75975-33-6; **3**, 70237-69-3.

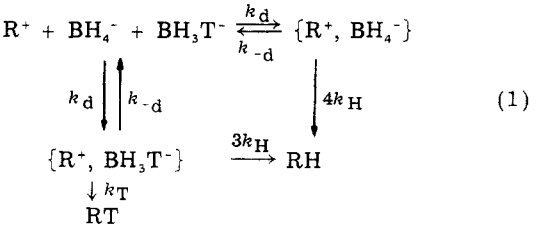
Communications

Tritium/Protium Discrimination in Reduction of Cyclopropenium Ion by Sodium Borohydride Does Not Identify the Rate-Determining Step[1]

Summary: Intramolecular isotope discrimination vitiates an attempt to deduce from the observation of a tritium isotope effect in borohydride reduction of a cyclopropenium ion that hydride transfer is at least partially rate determining.

Sir: It was recently reported[2] that the preparation of labeled sterculic acid, by dropping the corresponding cyclopropenium perchlorate into Me_2SO containing tritium-labeled sodium borohydride (26.7 mCi/mmol) at 5 °C, led to a product which had "incorporated 6.8 times less label than was present in the sodium borohydride". The product therefore presumably had a specific activity of 3.93 mCi/mmol. From this it was concluded that "the reaction is not solely diffusion controlled. The cation–hydride approach must be somewhat reversible with hydride transfer at least partially rate determining". The observed tritium discrimination is, however, consistent with either hydride transfer or diffusion as wholly rate determining, as we show below.

The two-step scheme incorporating diffusion and hydride transfer is shown in eq 1. Here it is assumed that the diffusion rate constants exhibit no isotope effect. Rate expressions for formation of RH and RT are given by eq 2, where secondary isotope effects have been neglected so



(1)

$$d[RH]/dt = 4k_H[\{R^+, BH_4^-\}] + 3k_H[\{R^+, BH_3T^-\}] \quad (2a)$$

$$d[RT]/dt = k_T[\{R^+, BH_3T^-\}] \quad (2b)$$

that k_H and k_T each refer to transfer of a specific hydrogen isotope from any species of borohydride ion. Equation 3

$$(d[RH]/d[RT]) = 4(k_H/k_T)([\{R^+, BH_4^-\}]/[\{R^+, BH_3T^-\}]) + 3(k_H/k_T) \quad (3)$$

is formed from the ratio of eq 2a to eq 2b. Now we take the ion pairs to be present at steady-state concentrations, yielding eq 4a; multiplication of numerator and denominator by $(0.25k_H)$ and definition of $\alpha = (k_{-d}/4k_H)$ produces eq 4b. The quantity α is useful because its value signifies

$$([\{R^+, BH_4^-\}]/[\{R^+, BH_3T^-\}]) = [(k_{-d} + 3k_H + k_T)/(k_{-d} + 4k_H)]([BH_4^-]/[BH_3T^-]) \quad (4a)$$

$$([\{R^+, BH_4^-\}]/[\{R^+, BH_3T^-\}]) = ([\alpha + 0.75 + (k_T/4k_H)]/[\alpha + 1])([BH_4^-]/[BH_3T^-]) \quad (4b)$$

the rate-determining step: as α approaches infinity, hydride transfer becomes completely rate determining, while as α approaches zero, diffusion becomes completely rate

(1) This research was supported by grants from the National Institutes of Health (Kansas) and the Consejo Nacional de Investigaciones Cientificas y Tecnológicas (Costa Rica).

(2) Pawlowski, N. E.; Sinnhuber, R. O. *J. Org. Chem.* **1980**, *45*, 2735.

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determining. Combination of eq 4b and 3 gives eq 5.

$$(d[RH]/d[RT]) = (k_H/k_T) \times \left[([BH_4^-]/[BH_3T^-])\left(\frac{4[\alpha + 0.75 + (k_T/4k_H)]}{\alpha + 1}\right) + 3\right] \quad (5)$$

To the approximation that $([BH_4^-]/[BH_3T^-])$ is constant,[3] eq 5 can be integrated and solved for α. From the specific activities, we can calculate that $([RH]/[RT]) \simeq 7400$ and $([BH_4^-]/[BH_3T^-]) \simeq 1090$. Insertion of these into the expression for α provides eq 6, which contains two unknown quantities, α and (k_H/k_T).

$$(4\alpha/3) = [(k_H/k_T) - 1.9]/[1.7 - (k_H/k_T)] \quad (6)$$

To investigate the extent to which the observed isotope discrimination determines α, we must consider what values of k_H/k_T and α simultaneously satisfy eq 6. We note that if $k_H/k_T = 1.9$, $\alpha = 0$ and diffusion is wholly rate determining, while if $k_H/k_T = 1.7$, $\alpha = \infty$ and hydride transfer is wholly rate determining. Both 1.9 and 1.7, and any intermediate value, are physically acceptable values for k_H/k_T, so α is not determined by the observations.

The same result may be derived qualitatively from eq 1 by noting that isotope discrimination may occur intramolecularly in reaction of the $\{R^+, BH_3T^-\}$ ion pair whether it is formed reversibly (hydride transfer rate determining) or irreversibly (diffusion rate determining). The observation of Pawlowski and Sinnhuber[2] does show that for the hydride transfer process, the tritium isotope effect is in the range $k_H/k_T = 1.7$–1.9, a significant and interesting result.

Acknowledgment. We are glad to thank Professor N. E. Pawlowski for his patient help in clarifying this paper.

Registry No. Sodium borohydride, 16940-66-2; cyclopropenium ion, 19553-81-2.

(3) Commonly less than 10% of the sodium borohydride was consumed: personal communication from Professor Norman Pawlowski.

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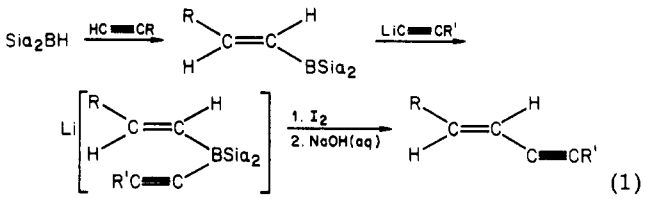
Stereospecific Synthesis of Conjugated Enynes from Alkenyldialkylboranes via Alkenylcopper Intermediates

Summary: Alkenylcopper intermediates, readily generated from alkenylboron derivatives of 9-borabicyclo[3.3.1]nonane (9-BBN), undergo coupling with 1-halo-1-alkynes to provide stereodefined conjugated enynes of high isomeric purity and in yields approaching quantitative.

Sir: Many insect sex pheromones contain a conjugated *cis,trans*-diene grouping.[1] Examples include bombykol,[2] megatomoic acid,[3] and the pheromones of the European grapevine moth[4] and the Egyptian cotton leafworm.[1b] Because conjugated *trans*-enynes are readily converted to the corresponding conjugated *cis,trans*-dienes by a simple hydroboration–protonolysis sequence,[4,5] the high-yield, stereospecific synthesis of conjugated enynes is a highly desirable goal.

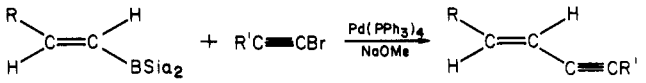
Several complex, relatively low-yield procedures have been developed for the synthesis of conjugated *trans*-enynes.[6] Some of these require a prior stereoselective synthesis of alkenyl halides.[7]

It would appear that a highly promising approach to such conjugated enynes involves alkenylborane intermediates. Thus, Negishi and co-workers developed a highly stereoselective (≥99%) synthesis of conjugated *trans*-enynes and utilized the method for the synthesis of two insect pheromones[5c,d] (eq 1). Perhaps the best synthesis to date,



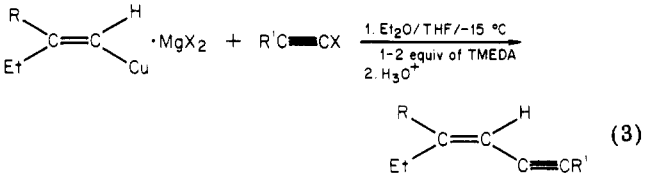
(1)

however, is that reported by Suzuki et al., utilizing the palladium-catalyzed reaction of 1-alkenylboranes with 1-halo-1-alkynes[8] (eq 2).



(2)

We were intrigued, however, by the report that alkenylcopper intermediates could be coupled to 1-halo-1-alkynes in the presence of 1–2 equiv of TMEDA to provide excellent yields of conjugated enynes[9] (eq 3).



(3)

Recently we developed a novel procedure for the conversion of alkenyldialkylboranes into the corresponding alkenylcopper compounds and reported their thermal decomposition to symmetrical 1,3-dienes[10] and their coupling to allylic halides to provide stereodefined 1,4-dienes[11] (eq 4).

(1) (a) Mayer, M. S.; McLaughlin, J. R. "An Annotated Compendium of Insect Sex Pheromones"; Florida Agricultural Experiment Stations Monograph Series No. 6, University of Florida, Gainesville, FL, Aug 1975. (b) Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845.
(2) Eiter, K. *Fortchr. Chem. Forsch.* **1970**, *28*, 204 and references cited therein.
(3) Silverstein, R. M.; Rodin, J. O.; Burkholder, W. E.; Gorman, J. E. *Science* **1967**, *157*, 85.
(4) Labovitz, J. N.; Henrick, C. A.; Corbin, V. L. *Tetrahedron Lett.* **1975**, 4209 and references cited therein.
(5) (a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 3834. (b) Zweifel, G.; Polston, N. L. *Ibid.* **1970**, *92*, 4068. (c) Negishi, E.; Lew, G.; Yoshida, T. *J. Chem. Soc., Chem. Commun.* **1973**, 874. (d) Negishi, E.; Abramovitch, A. *Tetrahedron Lett.* **1977**, 411.
(6) Descoins, C.; Samain, D. *Tetrahedron Lett.* **1976**, 745.
(7) Garwood, R. F.; Osakay, E.; Weedon, B. C. L. *Chem. Ind. (London)* **1962**, 1684.
(8) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, 3437.
(9) Normant, J. F.; Commercon, A.; Villieras, J. *Tetrahedron Lett.* **1975**, 1465.

0022-3263/81/1946-0645$01.00/0