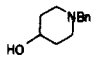
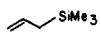
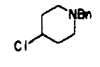
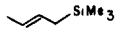
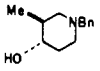
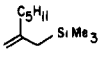
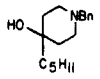
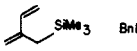
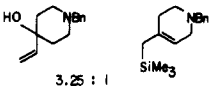
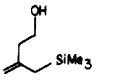
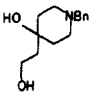
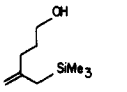
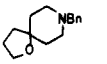
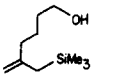
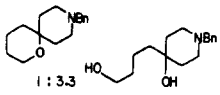
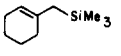
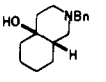
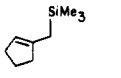
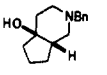
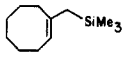
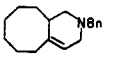
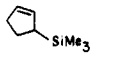
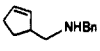
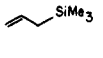
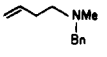
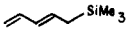
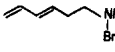
Table I. Reaction of Allysilanes with *N*-Alkylmethyleneiminium Salts in Water[a]

entry	allyl-silane	amine	temp, °C	time, h	prod.	yield, %[b]
1		$BnNH_2$·TFA	35	24		81
2		$BnNH_2$·HCl[c] LiCl	35	45		48
3		$BnNH_2$·TFA	45	48		54
4		$BnNH_2$·TFA	30	48		53
5		$BnNH_2$·TFA	25	24	 3.25 : 1	85
6		$BnNH_2$·TFA	25	4		100
7		$BnNH_2$·TFA	25	6		58
8		$BnNH_2$·TFA	25	6	 1 : 3.3	83
9		$BnNH_2$·TFA	35	48		94
10		$BnNH_2$·TFA	25	84		68
11		$BnNH_2$·TFA	25	82		62
12		$BnNH_2$·TFA	45	42		50
13		BnNHMe·TFA	50	68		76[d]
14		BnNHMe·TFA	45	65		95

[a] All reactions were run in 3.0–3.5 M aqueous solutions of the amine salt (1.0 equiv) using 1.1 equiv of the allylsilane and 2.3 equiv of 37% aqueous formaldehyde. [b] Isolated yields. [c] Reaction run in a 2.9 M solution of the amine salt in THF with 2 equiv of LiCl and 2.1 equiv of 37% aqueous formaldehyde. [d] 15% of BnNHMe recovered.

production occurred with 3-(trimethylsilyl)cyclopentene (entry 12). Even under forcing conditions, the product of aminomethano desilylation would not cyclize to a bicyclo[3.3.0] system. Tertiary homoallylamines could be prepared directly from acyclic allylsilanes by using a secondary amine salt (entries 13 and 14); however, these reactions were much slower relative to those cases employing primary amine salts (compare entries 1 and 13).

In summary, a generally useful synthesis of piperidines from primary amines, formaldehyde, and allylsilanes is now possible via an aminomethano desilylation–cyclization process. Further studies with iminium ions and allylsilanes are in progress.

Acknowledgment. This investigation was supported in part by a Grant from the National Science Foundation. The 300-MHz NMR instrument (Varian XL-300) used in the above studies was purchased with funds provided by the National Institutes of Health (Grant RR-1882).

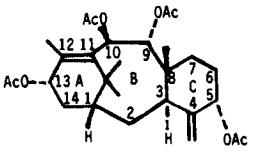
Synthesis of a Taxane Triene

Andrew S. Kende,* Stephen Johnson, Pauline Sanfilippo, John C. Hodges, and Louis N. Jungheim

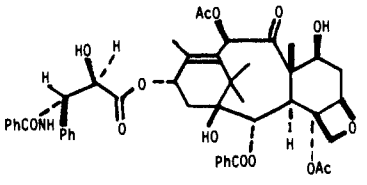
Department of Chemistry, University of Rochester Rochester, New York 14627

Received November 14, 1985

The highly oxygenated tricyclic structures of the taxane diterpenes[1] (e.g., taxusin, **1**)[2] and the powerful antitumor activities of certain members of this series (e.g., taxol, **2**)[3] have stimulated much recent effort toward their total synthesis. Despite the diversity of such approaches,[4] none have succeeded in constructing the complete carbon framework of the natural taxanes. We now report the first total synthesis of a racemic taxane triene comprising the *full and stereochemically correct carbon framework* of natural taxusin (**1**).



1



2

Directed-aldol $TiCl_4$-mediated coupling[5] of acetal **3**[6] with enol silane **4**[7] gave β-alkoxy ketones which on acid treatment gave 90%

(1) (a) Lythgoe, B. *The Alkaloids*; Manske, R. H. E. Ed.; Academic Press: New York, 1968; Vol. X, p 597. (b) Miller, R. W. *J. Nat. Prod.* **1980**, *43*, 425.

(2) (a) Miyazaki, M.; Shimizu, K.; Mishima, N.; Kurabayashi, M. *Chem. Pharm. Bull.* **1968**, *16*, 546. (b) Chan, W. R.; Halsall, T. G.; Hornby, G. M.; Oxford, A. W.; Sabel, W.; Bjamer, K.; Ferguson, G.; Robertson, J. M. *Chem. Commun.* **1966**, 923.

(3) Wani, M. C.; Taylor, M. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325.

(4) Recent approaches that have yielded tricyclic compounds include: (a) Martin, S. F.; White, J. B.; Wagner, R. *J. Org. Chem.* **1982**, *47*, 3190. (b) Shea, K. J.; David, P. D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 419. (c) Brown, P. A.; Jenkins, P. R.; Fawcett, J.; Russell, D. R. *J. Chem. Soc., Chem. Commun.* **1984**, 253. (d) Neh, H.; Blechert, S.; Schnick, W.; Jansen, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 905. (e) Holton, R. A. *J. Am. Chem. Soc.* **1984**, *106*, 5731. (f) Kojima, T.; Inouye, Y.; Kakisawa, H. *Chem. Lett.* **1985**, 323. A recent synthesis of a possible bicyclic biogenetic taxane precursor, verticillene, has been reported (Jackson, C. B.; Pattenden, G. *Tetrahedron Lett.* **1985**, 3393), but this system fails to cyclize to taxanes with acids (Begley, M. J.; Jackson, C. B.; Pattenden, G. *Ibid.* **1985**, 3397).

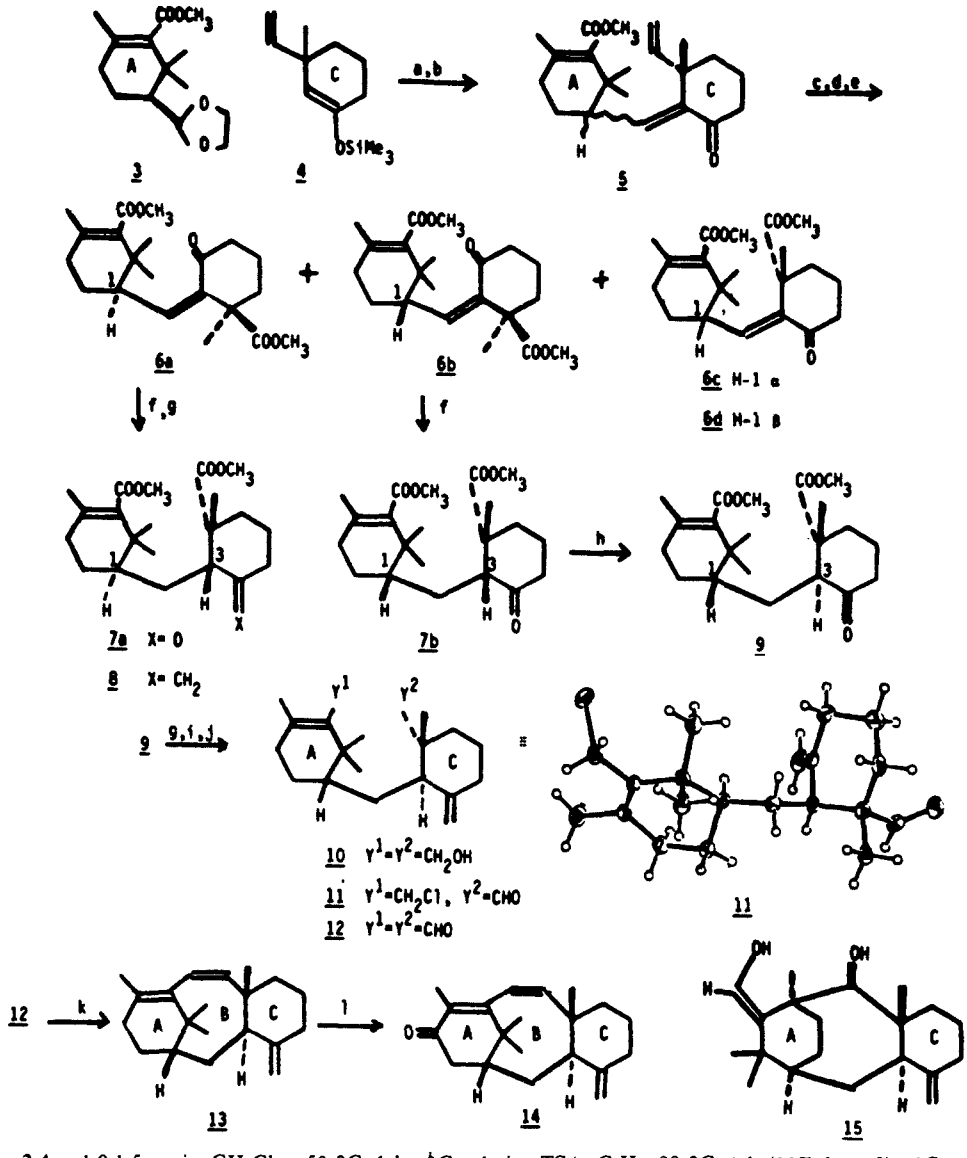
(5) Mukaiyama, T. *Org. React.* **1982**, *28*, 203.

(6) Acetal **3** was prepared from 2,6-dimethylcyclohexenone by the following 10 steps in 21% yield. Conjugate addition of CH_2=$CHMgBr$ (1.4 equiv, 0.1 equiv of CuI, Et_2O–THF, −78 °C, 2.5 h) and trapping with CH_3I (4 equiv, 1 equiv of HMPA, −78 to 25 °C, 16 h, 78%), then α-chlorination (1.2 equiv of SO_2Cl_2, CCl_4, catalytic pTSA, 10–25 °C, 12 h), and HCl elimination (3 equiv of LiCl, 3 equiv Li_2CO_3, DMF, 100 °C, 2 h, 75%) gave 2,2,6-trimethyl-3-vinyl-5-cyclohexenone. Reaction with the anion of Me_3SiCH_2Cl (1.5 equiv of Me_3SiCH_2Cl, 1.5 equiv of sec-BuLi, THF/TMEDA, then addition of enone at −55 °C and warming to 25 °C for 2 h) followed by direct hydrolysis (90% HCOOH, 25 °C, 1.5 h) gave 90% of a dienal which was oxidized (1.1 equiv of $NaClO_2$, 2:1 H_2O–dioxane, 1.3 equiv of NH_2SO_3H, 0–25 °C, 1.5 h) and reacted with excess CH_2N_2 in ether (0 °C, 30 m) to give 69% of methyl 2,2,6-trimethyl-3-vinyl-5-cyclohexenecarboxylate. Vinyl cleavage (2.6 equiv of *N*-methyl-morpholine *N*-oxide (NMO), 0.02 equiv of OsO_4, 2:1 Me_2CO–H_2O, 25 °C, 16 h, bisulfite workup, followed by 1.1 equiv of $NaIO_4$ in 1:1 Me_2CO-H_2O, 25 °C, 30 m) gave 63% of noraldehyde which was converted in 95% yield (glycol, pTSA, C_6H_6, reflux) to acetal **3** (C, 65.88; H, 8.65).

(7) Cf.: House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.

0002-7863/86/1508-3513$01.50/0

Scheme I



[a] 2 equiv of $TiCl_4$, 3:4 = 1.0:1.5 equiv, CH_2Cl_2, −50 °C, 1 h. [b] Catalytic pTSA, C_6H_6, 80 °C, 1 h (90% from **3**). [c] Catalytic OsO_4, 3 equiv of NMO, aqueous Me_2CO, 25 °C, 24 h; 1.1 equiv of $NaIO_4$, aqueous Me_2CO, 25 °C, 1 h. [d] 1.3 equiv of $NaClO_2$, 1.5 equiv of NH_2SO_3H, aqueous dioxane, 10 → 25 °C, 30 min. [e] CH_2N_2, Et_2O, −50 → 25 °C, 15 min (61% from **5**). [f] H_2 (1 atm), 5% Pd–C, EtOH, 25 °C (95%). [g] Zn/CH_2Br_2/$TiCl_4$, THF/CH_2Cl_2, reflux, 18 h (60%). [h] K_2CO_3, MeOH, 4 days, 25 °C, then CH_2N_2, Et_2O, 0 °C (66%). [i] 6 equiv of *i*-Bu_2AlH, 3:1 hexane–Et_2O, 0 °C, 1.5 h (90%). [j] 2.1 equiv of $(COCl)_2$, 4.2 equiv of Me_2SO, CH_2Cl_2–Me_2SO, −70 → 25 °C (85%). [k] $TiCl_3$, Zn–Cu, DME, 1 h, reflux, add dilute **12** over 24 h, reflux 18 h (20%). [l] 10 equiv of CrO_3/dimethylpyrazole, CH_2Cl_2, −25 °C, 3 h (44%).

yield of enones **5** as a 2:1 mixture of two *Z* and two *E* isomers.[8] Selective vinyl cleavage gave the corresponding enone diesters **6** separable by Si gel chromatography into the two pure diester *Z* isomers (**6a,b**), whereas the two enone diester *E* isomers (**6c,d**) could not be separated. Consequently our initial determination of stereochemistry was achieved from unambiguous transformations of the two *Z* isomers, but the mixture of *E* isomers was subjected to the same transformations and the desired ("natural") diastereomer isolated at the diol **10** stage.

The higher R_f enone diester *Z* isomer **6a** was quantitatively hydrogenated over Pd–C to a single ketone diester **7a** which was methylenated under modified Tebbe conditions[9] to yield the crystalline methylene diester **8**,[10] mp 113–114.5 °C. Single-crystal X-ray analysis revealed that **8** had the wrong ("nonnatural") stereochemistry at both C-1 and C-3 relative to the C-10β-methyl substituent (taxane numbering).[11] Hydrogenation of the lower R_f enone diester *Z* isomer **6b** gave a single ketone diester **7b** which was assumed to have the "wrong" C-3β stereochemistry by analogy with **7a**. Fortunately, epimerization of **7b** with K_2CO_3–MeOH gave a 4:1 ratio favoring the desired C-3α isomer **9**.

Methylenation of **9** as above followed by reduction with *i*-Bu_2AlH gave the crystalline diol **10**[12] as thin plates, mp 150–152 unsuitable for X-ray analysis. Swern oxidation converted **10** to dialdehyde **12**[13] in 85% yield. When the Me_2SO in the Swern oxidation was moist, up to 40% of a crystalline byproduct was formed. This proved to be chloro aldehyde **11** (mp 86–88 °C)

(8) The two *Z* isomers exhibited alkene proton doublets centered at δ 5.54 and 5.64, respectively, whereas the two *E* isomers showed these doublets centered at δ 6.90 and 6.99. All structures shown gave satisfactory combustion or mass spectrometric analyses.

(9) Lombardo, L. *Tetrahedron Lett.* **1982**, 4293. Lombardo, L.; Mander, L. N. *J. Org. Chem.* **1983**, *48*, 2298.

(10) **8** (400 MHz, ^1H NMR, $CDCl_3$, partial) δ 4.84 (1 H, s), 4.68 (1 H, s), 3.75 and 3.69 (each 3 H, s), 1.64 (3 H, s), 1.22, 0.98, and 0.96 (each 3 H, s).

(11) Details of the X-ray structures will accompany our full paper. We are grateful for Dr. J. C. Huffman (Molecular Structure Center, Indiana University) for the X-ray analysis of chloroaldehyde **11**.

(12) **10**: 300-MHz, ^1H NMR ($CDCl_3$, partial) δ 4.78 (1 H, s), 4.61 (1 H, s), 4.20 and 4.10 (2 H, AB, J = 12 Hz), 3.54 and 3.44 (2 H, AB, J = 12 Hz), 1.76 (3 H, s), 1.08 (3 H, s), 0.88 (6 H, s); OH at δ 1.5 (exchanged D_2O).

(13) **12**: 400-MHz, ^1H NMR ($CDCl_3$, partial) δ 10.11 (1 H, s), 9.46 (1 H, s), 4.81 (1 H, s), 4.70 (1 H, s), 2.09 (3 H, s), 1.23, 1.08, and 0.94 (each 3 H, s); MS found 302.2231.

which on X-ray analysis fully confirmed the preceding and subsequent stereochemical assignments.[11] Hydrogenation of the two enone diester *E* isomer mixture (**6c,d**) followed by C-3 epimerization, methylenation, and *i*-Bu_2AlH as described also gave ca. 10% of pure diol **10**.

The somewhat unstable dialdehyde **12** in DME was added by syringe pump over 24 h to a refluxing suspension of McMurry Ti reagent from Zn–Cu and $TiCl_3$ in DME.[14] After a further 18 h at reflux, neutral workup and chromatography over Si gel/$AgNO_3$ using 15:1 hexane–ether gave the single taxane triene **13**[15] in 20% yield, accompanied by ca. 10% of a $C_{20}H_{32}O_2$ diene diol established by NMR and by X-ray analysis of its crystalline (enol) monoacetate as the stable enol **15**, arising from vinylogous reductive coupling of dialdehyde **12**[16] (Scheme I).

The convergent phase of our synthesis leads from acetal **3** in 10 steps and 5% yield to the key dialdehyde **12**, from which the sterically encumbered eight-membered B-ring can uniquely be formed by McMurry cyclization. To our knowledge this is the first direct cyclization of the taxane B-ring from any bicyclic seco-B intermediate. Moreover, triene **13** is not only the first synthetic compound containing the stereochemically correct taxane structure but offers attractive potential for taxusin synthesis. Thus **13** underwent selective allylic oxidation with CrO_3/2,5-dimethylpyrazole[17] to give enone **14**[18] in ca. 44% yield. Enone **14** with MCPBA (5 equiv, CH_2Cl_2, room temperature, 1 h) undergoes smooth epoxidation at the C-4 methylene group, suggesting fruitful possibilities for selective B- and C-ring functionalizations.[19]

(14) (a) McMurry, J. E.; Kees, K. L. *J. Org. Chem.* **1977**, *42*, 2655. (b) Review: McMurry, J. E. *Acct. Chem. Res.* **1983**, *16*, 405.

(15) **13**: 400-MHz, ^{1}H NMR, ($CDCl_3$, partial) δ 5.90 (1 H, br d, J = 11.6 Hz), 5.15 (1 H, d, J = 11.6 Hz), 4.86 (1 H, s), 4.64 (1 H, s), 1.72 (3 H, s), 1.07, 1.03, and 0.86 (each 3 H, s).

(16) Evidence for structure **15** will be detailed in our full paper.

(17) Salmond, W. G.; Barta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 2057.

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Ab Initio Predictions and Experimental Confirmation of Large Tunneling Contributions to Rate Constants and Kinetic Isotope Effects for Hydrogen Atom Transfer Reactions

Bruce C. Garrett

Chemical Dynamic Corporation
Columbus, Ohio 43220

Donald G. Truhlar*

Department of Chemistry, University of Minnesota
Minneapolis, Minnesota 55455

Joel M. Bowman

Department of Chemistry, Illinois Institute of
Technology, Chicago, Illinois 60616

Albert F. Wagner

Chemistry Division, Argonne National Laboratory
Argonne, Illinois 60439

Daniel Robie, Sivaram Arepalli, Nathan Presser, and Robert J. Gordon

Department of Chemistry
University of Illinois at Chicago
Chicago, Illinois 60680
Received November 8, 1985

The interpretation of kinetic isotope effects (KIE's) involves potential energy barrier heights, vibrational effects of stretches and bends, and competition between overbarrier and tunneling mechanisms.[1] In favorable cases, KIE's provide some of the most compelling evidence for or against detailed interpretations of the dynamics of reactive events. The present paper reports such a case in which the detailed question is the role of tunneling[2] in hydrogen atom transfer reactions in the gas phase. Since many features of H transfer are similar to proton and hydride transfer,[3] the role of tunneling in this kind of reaction has far reaching implications for reactions in solution as well as in gas-phase applications, such as combustion and atmospheric chemistry. In this communication we report new calculations and experiments on the bimolecular rate constant ratio k_3/k_4

$$O + HD \xrightarrow{3} OH + D$$

$$O + HD \xrightarrow{4} OD + H$$

which, together with earlier results[4-9] for k_1 and k_2

$$O + H_2 \xrightarrow{1} OH + H$$

$$O + D_2 \xrightarrow{2} OD + D$$

provide strong evidence for the dominance of tunneling in all four reactions at temperatures below 500 K.

The KIE's were measured in two complementary experiments. In the first study[6] k_1, k_2, and $k_3 + k_4$ were measured with a flash photolysis apparatus,[10] using atomic resonance fluorescence to monitor the decay of $O(^3P)$ in real time. In the new experiment the branching ratio k_3/k_4 was measured with a discharge flow apparatus using laser-induced fluorescence to determine the ratio of the steady-state concentrations of OH and OD products. Oxygen atoms were generated in a microwave discharge of N_2 containing 0.01% O_2 and combined far downstream with a mixture of either HD and N_2 or H_2, D_2, and N_2. The OH and OD fluorescence intensities observed with the H_2/D_2 mixtures were used to normalize the fluorescence ratio obtained with HD.

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