had been saturated, accompanied by partial reductive cleavage of the benzylic C–O bond of the sugar. Metallic ytterbium[17] led to a very clean and completely selective saturation of the central anthracene ring. One of the factors that complicated the reduction was the hydrolytic lability of the styryl enol ether double bond. This reactivity suggested the reduction conditions that were ultimately successful. Clean formation of **9**[16] took place in 88% yield by careful alternate addition of methanolic HCl and $NaBH_3CN$ to a solution of **8** in ethanol at 25 °C.[18] The pH of the mixture was kept at approximately 4.5 by monitoring the color of bromocresol green which had been added to the reaction mixture. Under these carefully controlled conditions the reaction was clean and did not result in loss of any of the protecting groups. The stereochemistry of the newly generated stereogenic center was confirmed by observing the NOE between the axial benzylic methine hydrogen and the methine proton adjacent to the methyl on the sugar.

Attention was focused on the introduction of the five-carbon chain. Several general approaches to this problem were evaluated; the higher degree of convergency that was attained with **6** made it the reagent of choice. Treatment of an equimolar mixture of **6** and stannylanthracene **10** with 0.06 equiv of $Pd_2(dba)_3{\cdot}CHCl_3$ and 0.12 equiv of triphenylphosphine[19] in THF at 70 °C for 48 h, with scrupulous exclusion of air, afforded 45–50% of **11**[16] along with ca. 15% of **9**. The stereogenic center on the side chain was introduced in good yield by addition of lithium dimethylcuprate to **11**.[12] The product (**12**;[16] 60% yield) was obtained as a single diastereoisomer, as determined by ^1H NMR at 300 MHz. This result was confirmed by ^1H NMR at 500 MHz on the quinone. The conversion of **12** to vineomycinone B2 methyl ester was accomplished in two steps. Oxidation of **12** with bis(pyridine) silver permanganate[20] in dichloromethane afforded anthraquinone **13**. All protecting groups were removed in a single operation by exposure of **13** to HCl in anhydrous methanol at 23 °C for 4 h to afford methyl ester **1** in 35% overall yield as a single isomer.[21] The synthetic material was identical with an authentic sample by spectroscopic comparison.[22]

To summarize, a general methodology for appending *C*-glycosyl units onto anthraquinones has been developed and has been used for a highly convergent synthesis of **1**. The ready availability of hydroxyanthraquinones suggests that this methodology is suitable for the synthesis of other, more complex members of this class of natural products.

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Supplementary Material Available: Reproductions of NMR and IR spectra for **1** (13 pages). Ordering information is given on any current masthead page.

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[17] Hou, Z.; Taniguchi, H.; Fujiwara, Y. *Chem. Lett.* **1987**, 305–308. The first application of ytterbium in the reduction of an aromatic ring was reported in 1978: White, J. D.; Larson, G. L. *J. Org. Chem.* **1978**, *43*, 4555–4556.

[18] (a) Horne, D. A.; Jordan, A. *Tetrahedron Lett.* **1978**, 1357–1358. (b) Hutchins, R. O.; Rotstein, D.; Natale, N.; Fanelli, J.; Dimmel, D. *J. Org. Chem.* **1976**, *41*, 3328–3329.

[19] Sheffy, F. K.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 7173–7175.

[20] Firouzabadi, H.; Sardarian, A. R. *Synthesis* **1986**, 946–948.

[21] Danishefsky and co-workers have reported that *epi*-vineomycinone B2 methyl ester is distinguishable from vineomycinone B2 methyl ester by ^1H NMR at 500 MHz in deuteriochloroform (ref 5).

[22] **1**: IR (neat) 3400 (br), 2930, 2860, 1735, 1630, 1440, 1375, 1260, 990, 970 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 13.22 (s, 1 H), 13.10 (s, 1 H), 7.92 (d, J = 8.0 Hz, 1 H), 7.86 (d, J = 7.7 Hz, 1 H), 7.81 (d, J = 8.0 Hz, 1 H), 7.70 (d, J = 7.7 Hz, 1 H), 4.95 (dd, J = 11.0, 2.0 Hz, 1 H), 3.86 (ddd, J = 11.1, 8.8, 5.0 Hz, 1 H), 3.71 (s, 3 H), 3.54 (dq, J = 8.8, 6.1 Hz, 1 H), 3.22 (dd, J = 9.2, 8.8 Hz, 1 H), 3.11 (d, J = 13.6 Hz, 1 H), 3.03 (d, J = 13.6 Hz, 1 H), 2.58 (d, J = 16.1 Hz, 1 H), 2.55 (d, J = 16.1 Hz, 1 H), 2.53 (ddd, J = 12.6, 5.0, 2.0 Hz, 1 H), 1.49 (ddd, J = 12.6, 11.1, 11.0 Hz, 1 H), 1.42 (d, J = 6.1 Hz, 3 H), 1.30 (s, 3 H); mass spectrum (20 eV) *m/e* (no M^+), 384 (57), 281 (20), 280 (18), 207 (100), 117 (14), 111 (12), 109 (13), 99 (31), 97 (28); exact mass calcd for $C_{21}H_{20}O_7$ 384.1095, found 384.1152.

Highly Diastereoselective Reactions of Ytterbium-Mediated Alkynyllithium and Alkynylmagnesium Reagents with Chiral 2-Acyl-1,3-oxathianes: Reversal of Diastereoselectivity

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Eliel has devised a chiral 2-acyl-1,3-oxathiane **1** employing (+)-pulegone as a chiral auxiliary and has utilized it for the synthesis of optically active tertiary alcohols **2** bearing a carbonyl function at the α-position.[1] The enantiomeric purity of **2** rests upon the diastereoselectivity of nucleophilic addition of a Grignard reagent to acyloxathiane **1** to give **3** according to Cram's chelate model **4**[1] (Scheme I).

Although this process is versatile for the synthesis of various optically active tertiary alcohols, only one enantiomer can be derived from one substrate **1**. The other enantiomer **5** could be obtained by means of an opposite face selective attack of an organometallic species giving diastereomeric **6** according to a chelate model 7. We have observed that use of lanthanide trichlorides to mediate addition of organolithium or -magnesium species can realize the above expectation. Precedence for a lanthanide-mediated reaction of alkyllithium and -magnesium reagents with carbonyl compounds comes from the work of Imamoto, who has disclosed extremely high nucleophilicity of alkylcerium and other organolanthanide reagents.[2,3] Since highly reactive organocerium reagents have been utilized in the synthesis of chiral amines from SAMP-hydrazones, both an alkyllithium and an alkylcerium reagent show the same diastereoselectivity.[4] Opposite diastereoselectivity caused by lanthanide reagents has been little studied.[5,6] This paper describes a reaction with extremely high diastereocontrol induced by ytterbium.

The reaction of 2-acyl-1,3-oxathiane **1** (R = Me, Et, Ph) with 1-pentynylcerium dichloride ($R'Li + CeCl_3 \rightarrow R'CeCl_2$; $R' = CH_3CH_2CH_2C{\equiv}C$) gives diastereomer **6** predominantly, in contrast to the selective formation of **3** by R′Li.[7] The reaction with $R'YbCl_2$ ($R'Li + YbCl_3$) shows better diastereoselectivity to give **6** exclusively;[8] $R'YCl_2$ ($R'Li + YCl_3$) behaves similarly. Results are summarized in Table I.

The reaction of **1** with 1-pentynylmagnesium bromide (R′MgBr) gives mainly **3**. Ytterbium-mediated reaction gives

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[1] (a) Eliel, E. L.; Morris-Natschke, S. *J. Am. Chem. Soc.* **1984**, *106*, 2937. (b) Lynch, J. E.; Eliel, E. L. *J. Am. Chem. Soc.* **1984**, *106*, 2943.

[2] Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392 and references cited therein.

[3] Application of organolanthanide reagents to organic synthesis: (a) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573 and references cited therein. (b) Hou, Z.; Fujiwara, Y.; Jintou, T.; Mine, N.; Yokoo, K.; Taniguchi, H. *J. Org. Chem.* **1987**, *52*, 3524. (c) Lee, T. V.; Channon, J. A.; Cregg, C.; Porter, J. R.; Roden, F. S.; Yeoh, H. T.-L. *Tetrahedron* **1989**, *45*, 5877. (d) Ukaji, Y.; Yoshida, A.; Fujisawa, T. *Chem. Lett.* **1990**, 157 and references cited therein.

[4] Denmark, S. E.; Weber, T.; Piotrowski, D. W. *J. Am. Chem. Soc.* **1987**, *109*, 2224.

[5] Kawasaki, M.; Matsuda, F.; Terashima, S. *Tetrahedron Lett.* **1985**, *26*, 2693.

[6] Recent review on diastereocontrolled nucleophilic addition to carbonyl compounds: Fujisawa, T.; Ukaji, Y. *Yuki Gosei Kagaku Kyokaishi* (*J. Synth. Org. Chem., Jpn.*) **1989**, *47*, 186.

[7] The diastereomer ratio (**3**/**6**) was determined by ^1H NMR analysis. The proton signal at C(2) of **3** (R = Me) appears at δ 4.96, and the corresponding proton of **6** (R = Me) is observed at δ 4.82. The intensity ratio of the two signals corresponds to the molar ratio of **3** and **6**. Moreover, optical rotations of the hydrolyzed products confirm the stereochemistry: Hydrolysis and successive reduction of **3** (R = Me; 34% de) gave (*R*)-2-methyl-3-pentyne-1,2-diol ($[\alpha]^{21}_D$ +0.33 ± 0.04°) whereas the same treatment of **6** (R = Me; 93% de) afforded the *S* isomer ($[\alpha]^{21}_D$ −0.75 ± 0.05°).

[8] $R'YbCl_2$ is prepared by the reaction of R′Li with $YbCl_3$. As the bond length of Yb–C is shorter than that of Ce–C, organoytterbium species make the chelate structure at the transition state compact, which may contribute to the high diastereoselectivity.

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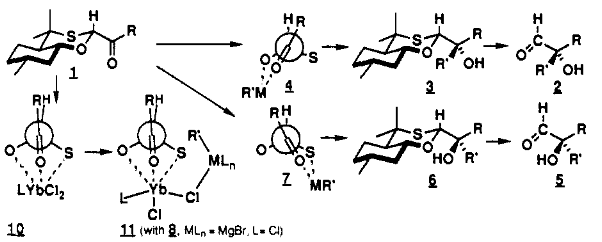
Table I. Reaction of 2-Acyl-1,3-oxathiane **1** with 1-Pentynylmetals (R'M)[a]

	1 (R = Me)		**1** (R = Et)		**1** (R = Ph)	
	M = Li	M = MgBr	M = Li	M = MgBr	M = Li	M = MgBr
R'M (equiv)	**3** + **6**[b] [**3**/**6**][c]	**3** + **6** [**3**/**6**]	**3** + **6** [**3**/**6**]	**3** + **6** [**3**/**6**]	**3** + **6** [**3**/**6**]	**3** + **6** [**3**/**6**]
R'M (2)	84 [74/26]	99 [66/34]	94 [75/25]	78 [84/16]	98 [91/9]	98 [97/3]
R'M (2) + CeCl$_3$ (3)	66 [11/89]	57 [10/90]	99 [7/93]	46 [38/62]	99 [44/56]	41 [38/62]
R'M (2) + YbCl$_3$ (3)	99 [3/97]	35 [2/98]	99 [2/98]	39 [1/99][d]	52 [6/94]	0
R'M (2) + YCl$_3$ (3)	63 [4/96]	18 [4/96]	99 [6/94]	99 [6/94]	56 [6/94]	0

[a] Experimental procedure is described in ref 9. [b] Yield (%). [c] Ratio was determined by ^{1}H NMR. [d] Chemical yield 99% (**3**/**6** = 0/100) when 5-min-aged R'MgBr + YbCl$_3$ reagent was used.

Scheme I



6 exclusively; however, the yield of product is low. Reactions with YCl$_3$- and CeCl$_3$-mediated species show high diastereoselectivity giving **6**. Results are included in Table I.[9]

Considerable attention has been focused on the reaction with YbCl$_3$-mediated Grignard reagents. A THF solution of R'MgBr was treated at 0 °C with a suspension of YbCl$_3$ in THF, and the mixture was immediately used in the reaction with **1** at −78 °C for 2 h, or the mixture was stirred at 0 °C for an aging period before reaction with **1**. Combinations of aging time, yield, and ratio **3**/**6**: 0 min, >99%, 0.2/99.8; 5 min, >99%, 0/100; 30 min, 78%, 0/100; 2 h, 39%, 0.4/99.6; 18 h, 0%. Reaction of **1** (R = Et) with a 2-h-aged reagent at 0 °C for 3 h gives **6** (95.4% de) quantitatively.

These results suggest the following: (1) Reaction of R'MgBr with YbCl$_3$ gives a reactive species R'MgBr·YbCl$_3$ (**8**) which shows high reactivity and diastereoselectivity. (2) Transmetalation giving (R'YbCl$_2$)$_2$ (**9**) proceeds slowly at 0 °C and is completed within 18 h; unchanged substrate **1** was recovered in the reaction with **9** at −78 °C. (3) Since the reaction of **1** with **8** proceeds smoothly at −78 °C but sluggishly with **9** at the same temperature, the nucleophilic reactivity of **8** is higher than that of **9**.

It is important to note that ytterbium plays the principal role in the control of diastereoselectivity of the reaction, in spite of the existence of two metal species, ytterbium and magnesium, in the reaction mixture. These observations suggested that the same type of diastereoselective reaction could proceed by the addition of a Grignard reagent to a mixture of **1** and YbCl$_3$. This expectation was realized in the addition of a THF solution of 1-pentynylmagnesium bromide to a 1/3 mixture of **1** and YbCl$_3$ in THF at −78 °C to give **6** (R = Me, 98.6% de) in quantitative yield.

Although the mechanism of reaction of **1** with Yb-mediated reagents has not been clearly understood, a possible mechanism to account for the high diastereoselectivity is depicted in chelate transition structure **11** (reaction with **8**; ML$_n$ = MgBr, L' = Cl) and **12** (reaction with **9**; ML$_n$ = YbCl$_2$, L' = R').[10,11]

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(9) (a) Typical procedure using CH$_3$CH$_2$CH$_2$C≡CYbCl$_2$: Finely pulverized YbCl$_3$·6H$_2$O (485 mg, 1.25 mmol) was heated to 150 °C under vacuum for 2 h. Then 4 mL of THF was added to the cooled material all at once with vigorous stirring. The mixture was sonicated. To this suspension, maintained at −78 °C, was added a THF solution of 1-pentynyllithium (R'Li, 0.83 mmol; 1.22 mL of 0.68 M solution), and the reaction mixture was stirred at −78 °C for 2 h. A THF solution of **1** (R = Et, 107 mg, 0.42 mmol in 4 mL of THF) was then added at −78 °C. The reaction mixture was stirred at −78 °C for 3 h and then quenched with saturated NH$_4$Cl solution. (b) Typical procedure using R'MgBr + YbCl$_3$: A THF solution of R'MgBr was added to a suspension of YbCl$_3$ in THF at 0 °C. The resultant mixture was stirred at 0 °C for 2 h and then used for the reaction with **1** at −78 °C as described above.

(10) Synergistic rate enhancement with both O and S (relative rate: 3-ethyl-4-heptanone/3-(phenylthio)-4-heptanone/3-methoxy-4-heptanone/1-methoxy-1-(phenylthio)-2-pentanone = 1/2.2/27/49, obtained by competitive reactions with MeYbCl$_2$) suggests that Yb coordinates with two O and one S to give **10**. As the S–C bond is longer than O–C, attack of R'Mg or R'Yb species to **10** from the less hindered side produces **6** via **11** or **12**.

(11) The activation energy of the reaction of dimeric RLi with a carbonyl compound is lower than that of the monomeric species: Kaufmann, E.; Schleyer, P. v. R.; Houk, K. N.; Wu, Y.-D. *J. Am. Chem. Soc.* **1985**, *107*, 5560.

Tungsten Nitrene Complexes Tp'W(CO)$_2$(NR)$^+$ (R = Ph, Bu^t) Generated from Amido Complexes Tp'W(CO)$_2$(NHR)

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Metal nitrene (or imido) chemistry has expanded[1] since olefin amination with d^0 osmium(VIII) reagents was achieved.[2] Zirconium nitrene monomers display insertion reactions[3] and activate CH bonds,[4] and a d^6 iridium nitrene, Cp*IrNBu^t, inserts a variety of electrophilic organic substrates.[5] Nonetheless, well-characterized electrophilic nitrene complexes remain elusive. Aziridine products form from nitrene transfer to cyclooctene after acylation of manganese porphyrin nitride with trifluoroacetic anhydride,[6] and tosyl nitrene insertion reactions have been mediated with metal porphyrins.[7,8] Group VI nitrene complexes such as X(dppe)$_2$W(NH)$^+$,[9] L$_2$Cl$_2$(CO)W(NPh),[10] and (Et$_2$NCS$_2$)$_2$Mo(NPh)$_2$[11] do

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(1) Nugent, W. A.; Mayer, J. M. *Metal-ligand Multiple Bonds*; Wiley-Interscience: New York, 1988.

(2) Chong, A. O.; Oshima, K.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 3420.

(3) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 8729.

(4) Cummins, C. C.; Baxter, S. M.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8731.

(5) Glueck, D. S.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 2719.

(6) Groves, J. T.; Takahashi, T. *J. Am. Chem. Soc.* **1983**, *105*, 2073.

(7) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1517.

(8) Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 6728.

(9) Bevan, P. C.; Chatt, J.; Dilworth, J. R.; Henderson, R. A.; Leigh, G. J. *J. Chem. Soc., Dalton Trans.* **1982**, 821.

(10) Bryan, J. C.; Geib, S. J.; Rheingold, A. L.; Mayer, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 2826.

0002-7863/90/1512-8190$02.50/0