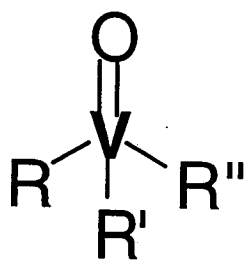
Denmark Group Meeting

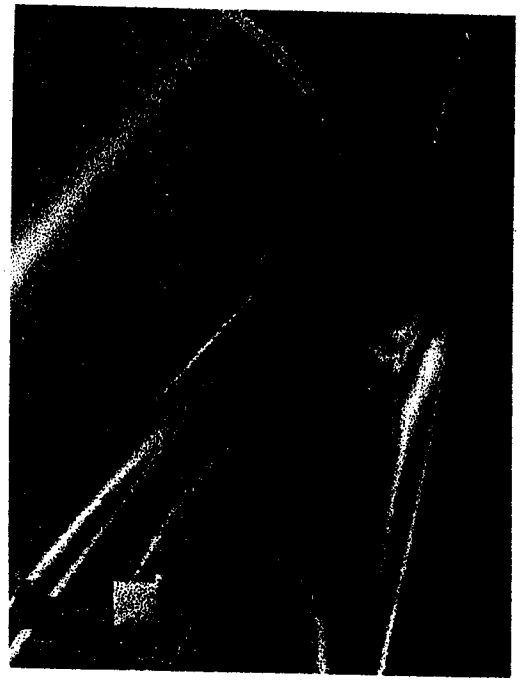
January 22, 2002

Tyson A. Miller

(Oxo)vanadium Catalysis



Basic Properties of Vanadium



Atomic # - 23
MW = 50.9415
[Ar] $3d^3\ 4s^2$
^{51}V (99.75%) - I = 7/2
^{50}V (0.25%) radioactive
Valences - 2, 3, 4, 5
mp - 1917 °C
bp - 3409 °C
$d^{18.7°C}$ - 6.11 g/ml

Scandinavian Goddess - "Vanadis" - beautiful multicolored compounds

Light gray or lustrous powder

Body-centered cubic crystals

Insoluble in water

Reacts with hot H_2SO_4, HF, HNO_3, aqua regia

Vanadium metal: 95% purity - $20 / lb.
99.9% purity - $100 / oz.

Discovered by del Rio in 1801 - A French chemist incorrectly declared that del Rio's new element was impure chromium; del Rio accepted his analysis. (It never pays to do that . . . .)
Rediscovered by Selström in 1830; Prepared nearly pure by Roscoe in 1867; Prepared ultra pure in 1927.

Minutae: V_2O_5 - Manufacture of yellow glass, inhibits UV transmission, depolarizer, dyeing, developer in photography
$VOSO_4$ - Manufacture of blue and green glass, dyeing
$VOCl_2$ - printing

Merck Index. 12th ed. Whitehouse Station: Merck & Co.; Inc. **1996**.
CRC Handbook of Chemistry and Physics. 72nd ed. Boca Raton: CRC Press, **1991**.
http://www.webelements.com/webelements/elements/text/V/key.html

WebElements: the periodic table on the world-wide web

http://www.webelements.com/

Key: element name / atomic number / symbol / 1997 atomic weight (mean relative mass)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
hydrogen 1 **H** 1.00794(7)																	helium 2 **He** 4.002602(2)
lithium 3 **Li** 6.941(2)	beryllium 4 **Be** 9.012182(3)											boron 5 **B** 10.811(7)	carbon 6 **C** 12.0107(8)	nitrogen 7 **N** 14.00674(7)	oxygen 8 **O** 15.9994(3)	fluorine 9 **F** 18.9984032(5)	neon 10 **Ne** 20.1797(6)
sodium 11 **Na** 22.989770(2)	magnesium 12 **Mg** 24.3050(6)											aluminium 13 **Al** 26.981538(2)	silicon 14 **Si** 28.0855(3)	phosphorus 15 **P** 30.973761(2)	sulfur 16 **S** 32.066(6)	chlorine 17 **Cl** 35.4527(9)	argon 18 **Ar** 39.948(1)
potassium 19 **K** 39.0983(1)	calcium 20 **Ca** 40.078(4)	scandium 21 **Sc** 44.955910(8)	titanium 22 **Ti** 47.867(1)	vanadium 23 **V** 50.9415(1)	chromium 24 **Cr** 51.9961(6)	manganese 25 **Mn** 54.938049(9)	iron 26 **Fe** 55.845(2)	cobalt 27 **Co** 58.933200(9)	nickel 28 **Ni** 58.6934(2)	copper 29 **Cu** 63.546(3)	zinc 30 **Zn** 65.39(2)	gallium 31 **Ga** 69.723(1)	germanium 32 **Ge** 72.61(2)	arsenic 33 **As** 74.92160(2)	selenium 34 **Se** 78.96(3)	bromine 35 **Br** 79.904(1)	krypton 36 **Kr** 83.80(1)
rubidium 37 **Rb** 85.4678(3)	strontium 38 **Sr** 87.62(1)	yttrium 39 **Y** 88.90585(2)	zirconium 40 **Zr** 91.224(2)	niobium 41 **Nb** 92.90638(2)	molybdenum 42 **Mo** 95.94(1)	technetium 43 **Tc** [97.9072]	ruthenium 44 **Ru** 101.07(2)	rhodium 45 **Rh** 102.90550(2)	palladium 46 **Pd** 106.42(1)	silver 47 **Ag** 107.8682(2)	cadmium 48 **Cd** 112.411(8)	indium 49 **In** 114.818(3)	tin 50 **Sn** 118.710(7)	antimony 51 **Sb** 121.760(1)	tellurium 52 **Te** 127.60(3)	iodine 53 **I** 126.90447(3)	xenon 54 **Xe** 131.29(2)
caesium 55 **Cs** 132.90545(2)	barium 56 **Ba** 137.327(7)	57-70 * lutetium 71 **Lu** 174.967(1)	hafnium 72 **Hf** 178.49(2)	tantalum 73 **Ta** 180.9479(1)	tungsten 74 **W** 183.84(1)	rhenium 75 **Re** 186.207(1)	osmium 76 **Os** 190.23(3)	iridium 77 **Ir** 192.217(3)	platinum 78 **Pt** 195.078(2)	gold 79 **Au** 196.96655(2)	mercury 80 **Hg** 200.59(2)	thallium 81 **Tl** 204.3833(2)	lead 82 **Pb** 207.2(1)	bismuth 83 **Bi** 208.98038(2)	polonium 84 **Po** [208.9824]	astatine 85 **At** [209.9871]	radon 86 **Rn** [222.0176]
francium 87 **Fr** [223.0197]	radium 88 **Ra** [226.0254]	89-102 ** lawrencium 103 **Lr** [262.1097]	rutherfordium 104 **Rf** [261.1088]	dubnium 105 **Db** [262.1142]	seaborgium 106 **Sg** [266.1219]	bohrium 107 **Bh** [264.1247]	hassium 108 **Hs** [269.1341]	meitnerium 109 **Mt** [268.1388]	ununnilium 110 **Uun** [271.1461]	unununium 111 **Uuu** [272.1535]	ununbium 112 **Uub** [277]		ununquadium 114 **Uuq** [289]		ununhexium 116 **Uuh** [289]		ununoctium 118 **Uuo** [293]

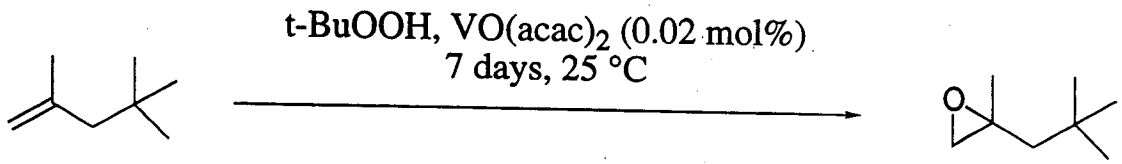
*lanthanoids	lanthanum 57 **La** 138.9055(2)	cerium 58 **Ce** 140.116(1)	praseodymium 59 **Pr** 140.90765(2)	neodymium 60 **Nd** 144.24(3)	promethium 61 **Pm** [144.9127]	samarium 62 **Sm** 150.36(3)	europium 63 **Eu** 151.964(1)	gadolinium 64 **Gd** 157.25(3)	terbium 65 **Tb** 158.92534(2)	dysprosium 66 **Dy** 162.50(3)	holmium 67 **Ho** 164.93032(2)	erbium 68 **Er** 167.26(3)	thulium 69 **Tm** 168.93421(2)	ytterbium 70 **Yb** 173.04(3)
**actinoids	actinium 89 **Ac** [227.0277]	thorium 90 **Th** 232.0381(1)	protactinium 91 **Pa** 231.03588(2)	uranium 92 **U** 238.0289(1)	neptunium 93 **Np** [237.0482]	plutonium 94 **Pu** [244.0642]	americium 95 **Am** [243.0614]	curium 96 **Cm** [247.0703]	berkelium 97 **Bk** [247.0703]	californium 98 **Cf** [251.0796]	einsteinium 99 **Es** [252.0830]	fermium 100 **Fm** [257.0951]	mendelevium 101 **Md** [258.0984]	nobelium 102 **No** [259.1009]

Element symbols and names: symbols, names, and spellings are those recommended by IUPAC (http://www.iupac.org/). After controversy, the names of elements 101-109 are now confirmed (Pure & Appl. Chem., 1997, 69, 2471–2473). Names have yet to be proposed for the elements 110–112, 114, 116, and 118, those used here are IUPAC's temporary systematic names (Pure & Appl. Chem., 1979, 51, 381–384). In the USA and some other countries, the spellings aluminum and cesium are normal while in the UK and elsewhere the usual spelling is sulphur.
Atomic weights (mean relative masses): Apart from the heaviest elements, these are IUPAC 1997 values (Pure & Appl. Chem., 1999, 71, 1593–1607). Elements for which values are given in brackets have no stable nuclides and are represented by 5-figure values for the longest-lived isotope. The elements thorium, protactinium, and uranium have characteristic terrestrial abundances and these are the values quoted. The last significant figure of each value is considered reliable to ±1 except where a larger uncertainty is given in parentheses.
Periodic table organisation: for a justification of the positions of the elements La, Ac, Lu, and Lr in the WebElements periodic table see W.B. Jensen, "The positions of lanthanum (actinium) and lutetium (lawrencium) in the periodic table", J. Chem. Ed., 1982, 59, 634–636.
Group labels: the numeric system (1–18) used here is the current IUPAC convention. For a discussion of this and other common systems see: W.C. Fernelius and W.H. Powell, "Confusion in the periodic table of the elements", J. Chem. Ed., 1982, 59, 504–508.

 For updates to this table see http://www.webelements.com/webelements/support/media/pdf/. Version date: 30 July 2001.

http://www.webelements.com/webelements/support/media/pdf/

First Metal Catalyzed Epoxidation

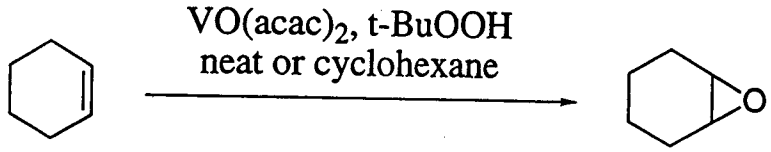


44% conversion
quantitative yield

also seen with acetoacetonates of Cr, V, MoO_2

Indictor, I.; Brill, W.F. *JOC* **1965** *30* 2074.

Kinetics of Vanadium Catalyzed Epoxidation of Cyclohexene



Average rates measured in the first 1-4% of reaction
Catalyst - 0.00005 to 0.001 M
Peroxide - 0.027 - 0.5 M
Alkene - 0.0875 - 1.8 M

$$\text{rate} = \frac{k\,[Vo]}{(1/[P]\,Kp) + 1} \qquad Km = 1/Kp$$

k = limiting specific rate (obs. at high ratio of [P]/[V]
[Vo] = total conc. of vanadium
[P] = conc. of hydroperoxide
Kp = vanadium/hydroperoxide association constant

Table I. Typical Kinetic Data for the Vanadium-Catalyzed Epoxidation of Cyclohexene with *t*-Butyl Hydroperoxide. Solvent, Cyclohexene

Temp, °C	[Catalyst] × 10^4 [a]	[BuO_2H]	Rate × 10^4 [b]
42.1	12.10	0.452	246
	6.00		117
	2.00		39.1
	0.61		12.5
34.1	2.22	0.452	15.9
		0.0452	6.43
	1.11	0.452	7.85
		0.0452	3.44
	1.05	0.226	6.11
		0.0452	3.39
31.0	1.10	0.452	11.4
		0.226	9.45
		0.135	8.54
		0.0904	6.98
		0.0452	4.51
		0.0271	3.34
36.0	1.11	0.452	16.5
		0.226	14.5
		0.135	12.3
		0.0904	10.4
		0.0452	7.05
		0.0271	4.72
41.3	1.03	0.452	23.0
		0.226	18.0
		0.135	16.2
		0.0904	13.5
		0.0452	9.10
		0.0271	6.05
50.6	1.04	0.452	34.1
		0.226	29.7
		0.135	23.7
		0.0904	21.3
		0.0452	14.2
		0.0271	9.86

[a] Total concentration of $VO(acac)_2$ added. [b] Rates in M min^{-1} extrapolated to zero *t*-BuOH.

Table II. Kinetic Data for the Vanadium-Catalyzed Epoxidation of Cyclohexene with *t*-Butyl Hydroperoxide.[a] Solvent, Cyclohexane

[Olefin]	Rate × 10^3 [b]	k_2[c]
1.795	2.69	3.19
0.897	1.37	3.28
0.449	0.630	2.98
0.180	0.253	2.99
0.0875	0.109	2.66
	k_2 (av) 3.02 ± 0.20	

[a] Reactions at 41.3°. Hydroperoxide, [P], = 0.181 M. Total concentration of $VO(acac)_2$, $[V_0]$, = 5.62 × 10^{-4} M. [b] Rates in M min^{-1}, extrapolated to zero *t*-BuOH. [c] Calculated second-order rate constant (in l. $mole^{-1}$ min^{-1}), $(1/V_0)\{1/K[P]) + 1\}$(rate/[olefin]), where K is taken as 11.6 M^{-1} (see Table III).

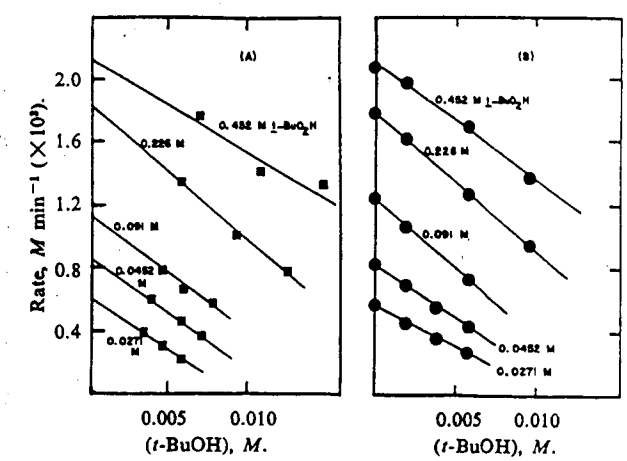


Figure 1. Extrapolation of rate data to zero *t*-butyl alcohol (epoxidation reactions in cyclohexene, 41.3°; $[VO(acac)_2]_{initial}$ 1.04 × $10^{-4}M$): (A) observed rates, (B) rates calculated from eq 3; parameters taken from Table III and Figure 4. Note the close approach to linearity with the calculated rates.

1st order in catalyst, 1st order in alkene
peroxide - low - rate ~ [P]
high - levels off and approach limiting value ~ [cat.]

Gould, E.S.; Hiatt R.R.; Irwin, K.C. *JACS* **1968** *90* 4573.

Kinetics of Vanadium Catalyzed Epoxidation of Cyclohexene

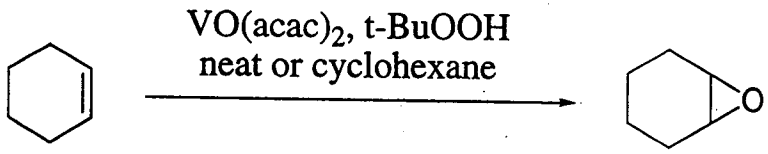


Table III. Limiting Specific Rates (k) and Association Constants (K_p) of Vanadium-Hydroperoxide Complex, VP[a]

Temp, °C	k, min^{-1}	K_p, M^{-1} [b]
24.1	7.30 ± 0.04	15.3 ± 2.0
31.0	12.1 ± 0.2	13.2 ± 1.0
36.0	17.2 ± 0.4	12.4 ± 0.9
41.3	24.7 ± 2.0	11.6 ± 0.8
50.6	39.3 ± 1.3	10.3 ± 0.7

[a] Evaluated from intercepts and slopes of Hofstee-type plots (Figure 2); solvent, cyclohexene. [b] K_p = [VP]/[V][P], where P is hydroperoxide, and V is hydroperoxide-free vanadium.

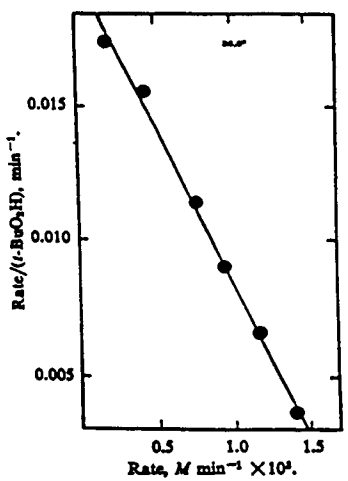


Figure 2. Hofstee-type plot, rate/[hydroperoxide] *vs.* rate (epoxidation in cyclohexene, 36.0°; $[VO(acac)_2]_{total}$ 1.11 × 10^{-4} M). Rates adjusted to zero t-BuOH. The slope of the least-squares line shown indicates an association constant of 11.8 M^{-1} for the vanadium–hydroperoxide complex. The intersection of this line with the abscissa (at 0.001985 M min^{-1}) corresponds to a specific rate of heterolysis, k, of 17.8 min^{-1}.

Table IV. Typical Kinetic Data for t-Butyl Alcohol Inhibition of the Vanadium-Catalyzed Epoxidation of Cyclohexene with t-Butyl Hydroperoxide at 41.3°

[P], M [a]	[A], $M \times 10^{3}$ [b]	[V$_0$], $M \times 10^{4}$ [c]	Rate (obsd) $\times 10^{3}$ [d]	Rate (calcd) $\times 10^{3}$ [e]
0.452	10.37	1.08	1.47	1.37
0.226	5.55	1.08	1.41	1.35
	8.85		1.10	1.04
	12.05		0.81	0.81
0.181	5.07	1.04	1.18	1.21
	8.65		0.85	0.89
	11.22		0.70	0.70
0.091	4.33	1.04	0.78	0.86
	7.45		0.58	0.62
0.045	3.76	1.10	0.63	0.58
	5.46		0.48	0.48
	6.72		0.38	0.40
0.027	3.16	1.10	0.47	0.42
	4.45		0.32	0.35
	5.57		0.27	0.24

[a] t-BuO$_2$H. [b] t-BuOH, average value. [c] Total concentration of VO(acac)$_2$ added. [d] Rates in M min^{-1}. [e] Rates calculated using eq 3. Values of k and K_p taken from Table III. K_i = 119 M^{-1}. K_i' = 2.1 × 10^4 M^{-2}.

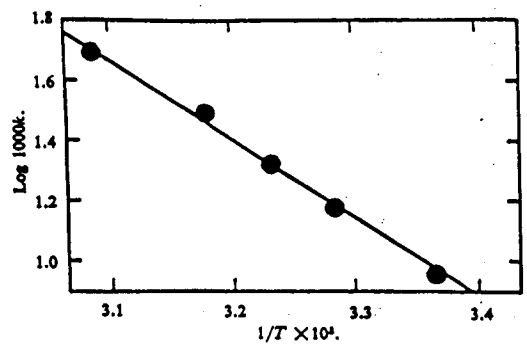


Figure 3. Arrhenius plot, log k *vs.* $1/T$, for the rate-determining step in the epoxidation of cyclohexene with t-butyl hydroperoxide in the presence of added VO(acac)$_2$ (solvent cyclohexene). From the slope of this plot, a $\Delta H^{\ddagger}$ value of 12.7 ± 0.4 kcal/mole and a $\Delta S^{\ddagger}$ value of −19.9 ± 1.9 eu were obtained.

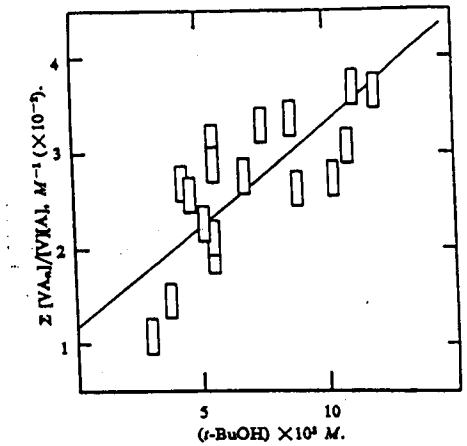


Figure 4. Variation of the ratio $\Sigma[VA_n]/[V][A]$ with concentration of t-BuOH. $\Sigma[VA_n]$, the total of alcohol-bound vanadium, is obtained by measuring the decrease in epoxidation rates as measured quantities of t-butyl alcohol are added (see ref 14). Epoxidation reactons in cyclohexene, 41.3°. The intercept of the least-squares line shown gives a value of 119 M^{-1} for the association constant of the 1:1 vanadium–alcohol complex, VA. The slope of this line gives the value 2.1 × 10^4 M^{-2} for the association constant of VA$_2$. K_i = 119 M^{-1} K_i' = 2.1 × 10^4 M^{-2}

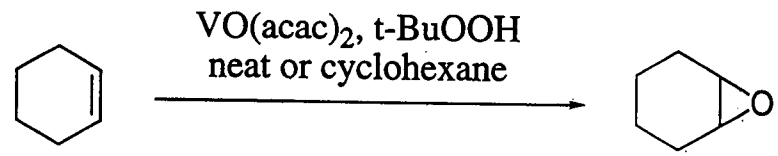
$$\text{rate} = \frac{k[V_0]}{(1/[P]K_p)(K_i[A] + K_i'[A]^2 + 1) + 1} \quad (3)$$

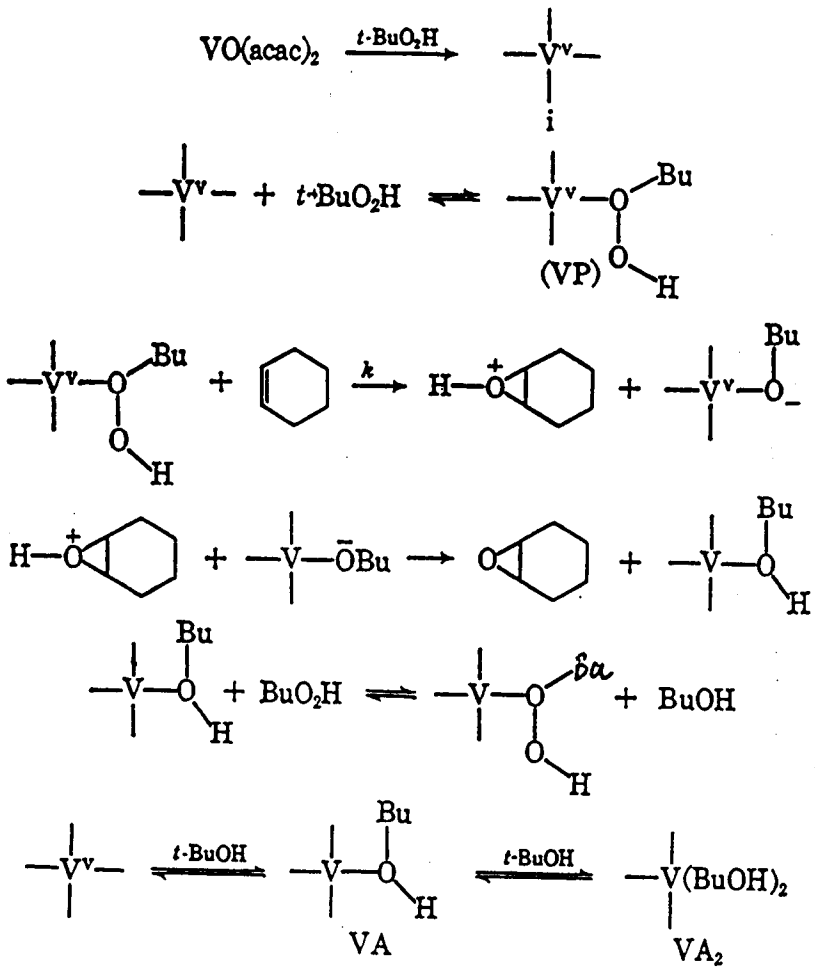
$$\frac{\Sigma[VA_n]}{[V][A]} = \frac{[P]K_p[([V_0]k/\text{rate}) - 1] - 1}{[A]}$$

High uncertainties in Kp disallow estimate in $\Delta H_{association}$.
Likelihood that VA and VA_2 inhibits the reaction.

Gould, E.S.; Hiatt R.R.; Irwin, K.C. *JACS* **1968** *90* 4573.

Proposed Mechanistic Scheme





catalyst activation; rapid, irreversible (5)

complex formation; rapid, reversible, K_p (6)

heterolysis; rate-determining (7)

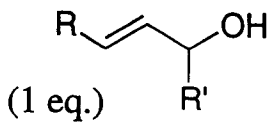
proton transfer; rapid (8)

ligand exchange; rapid, reversible (9)

inhibition; reversible, K_I and K_I' (10)

Gould, E.S.; Hiatt R.R.; Irwin, K.C. *JACS* **1968** *90* 4573.

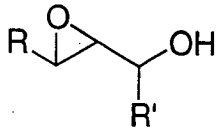
Epoxidation of Allylic Alcohols



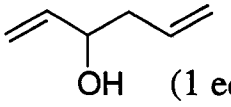
(1 eq.)

R = alkyl
R' = alkyl, H

t-BuOOH (0.14 - 1.5 eq.)
$VO(acac)_2$ (0.14 - 1 mol%)
THF (2 g = 2.25 mL)
80 - 100°C, 30 - 60 min.

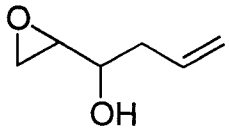


7 - 97% conversion (80-90's)
51 - 100% yield (80-90's)



(1 eq.)

t-BuOOH (0.1 eq.)
$VO(acac)_2$ (0.25 mol%)
THF (2 g = 2.25 mL, 17.7 M)
80°C, 30 min.



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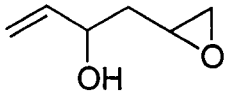
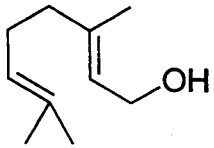


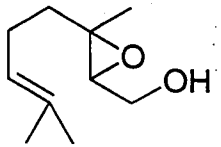
4 : 1

77% conversion, 92% yield

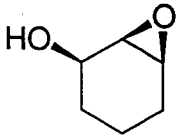


$VO(acac)_2$ (1.4 mol%)
t-BuOOH (1.1 eq.)
refluxing benzene, 4 hr.

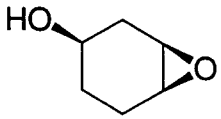
93% yield, 98% regiopure



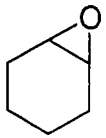
allylic-OH > homoallylic-OH > alkene



200
(98/2)



10
(98/2)



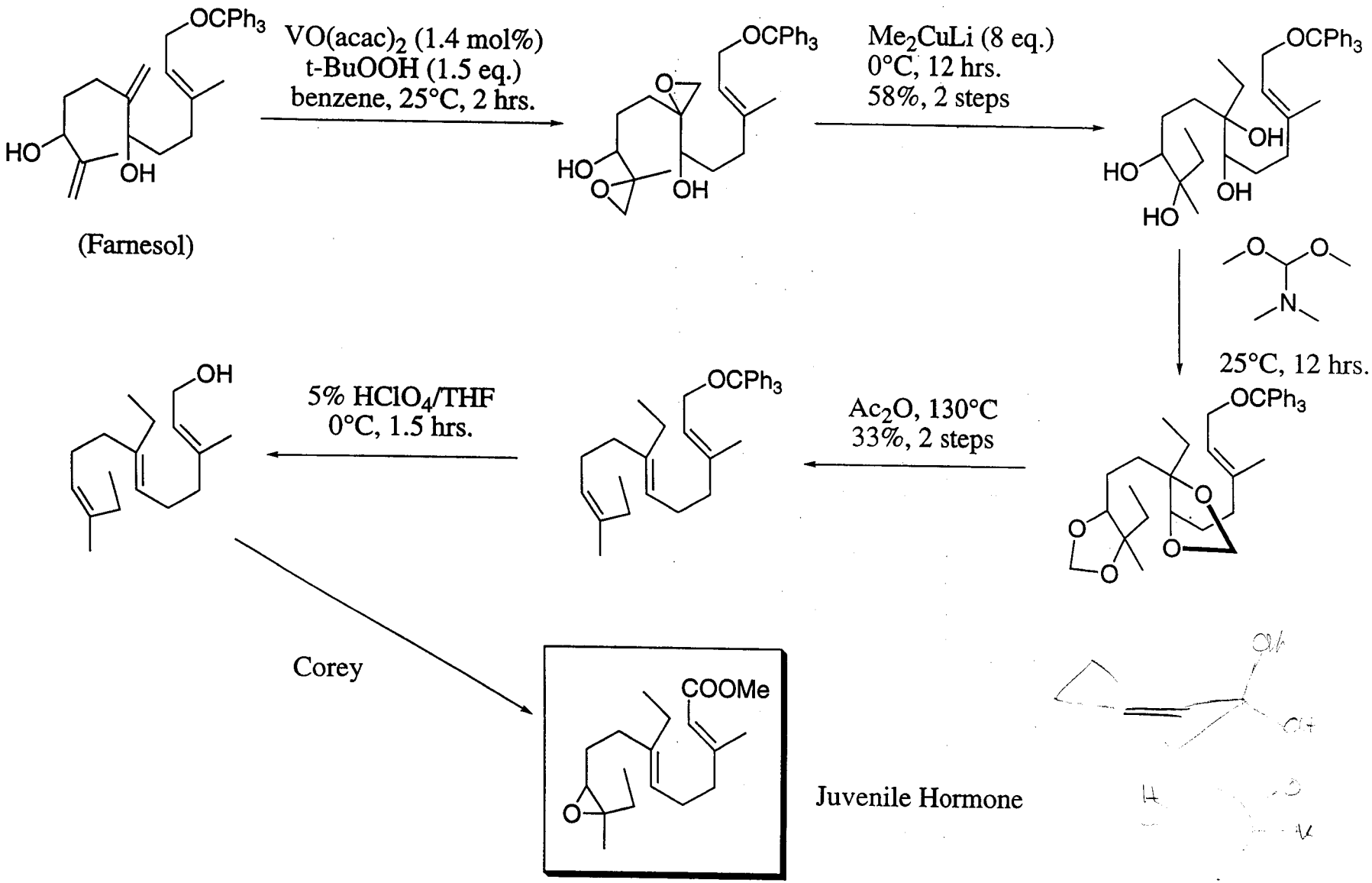
1

green >> deep red >> yellow >> light green
(V) (O-O)

Later publication comments that RT°C and 1.5 eq. t-BuOOH is a better condition.

Sheng, M.N.; Zajacek, J.G. *JOC* **1970** *35* 1839.
List F.; Kuhnen, L. *Erdol. Kohle.* **1967** *20* 192.
Sharpless K.B.; Michaelson, R.C. *JACS* **1973** *95* 6136.

Formal Synthesis of *dl*-C_{18} *Cecropia* Juvenile Hormone



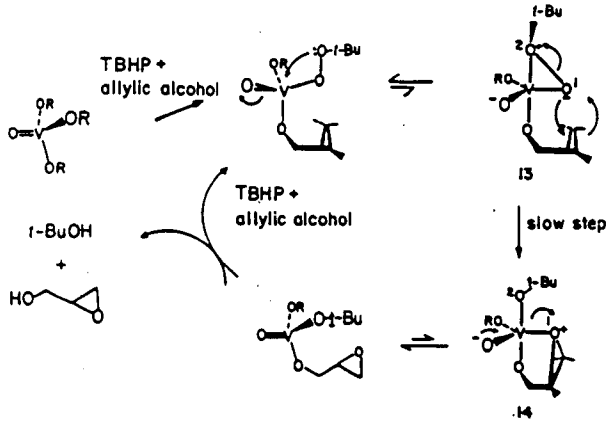
Tanaka, S; Yamamoto, H.; Nozaki, H.; Sharpless, K.B.; Michaelson, R.C.; Cutting, J.P. *JACS* **1974** *96* 5254.
Corey, E.J.; Katzenellenbogen, J.A.; Gilman, N.W.; Roman, S.A.; Erickson, B.W. *JACS* **1968** *90* 5618.

Proposed Mechanism of Epoxidation

Table I. Stereochemistry of Epoxidation of Acyclic Allylic Alcohols.[a]

Allylic alcohol		*threo*	*erythro*
 9	V^{+5}, TBHP	20	80
	MCPBA	60	40
 10	V^{+5}, TBHP	5	95
	MCPBA	45	55
 11	V^{+5}, TBHP	29	71
	MCPBA	64	36
 12	V^{+5}, TBHP	71	29
	MCPBA	95	5

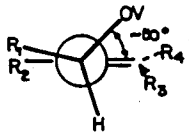
Scheme III. Possible Mechanism for the Vanadium-Catalyzed Epoxidations.



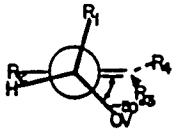
Scheme IV. Predicted O-C-C=C Dihedral Angles

for V^{+5}, TBHP epoxidations:

~50°



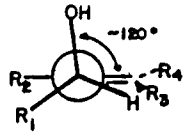
15, leads to *threo* product



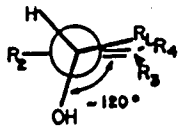
16, leads to *erythro* product

for peroxy acid (MCPBA) epoxidations:

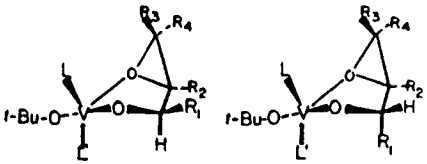
~120°



17, leads to *threo* product

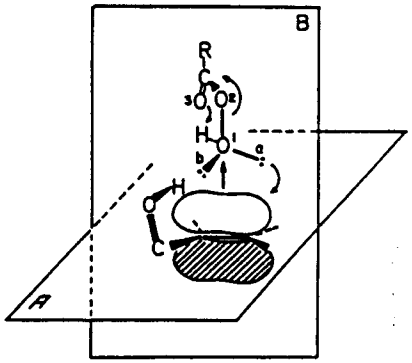


18, leads to *erythro* product



14 (*erythro*) 14(*threo*)

Scheme V. Consideration of Stereoelectronic Effects in Peracid Epoxidations of Allylic Alcohols.



Sharpless, K.B.; Verhoeven, T.R. *Aldrichchimica Acta* **1979** *12* 63.

First Vanadium Catalyzed Asymmetric Epoxidation of Allylic Alcohols

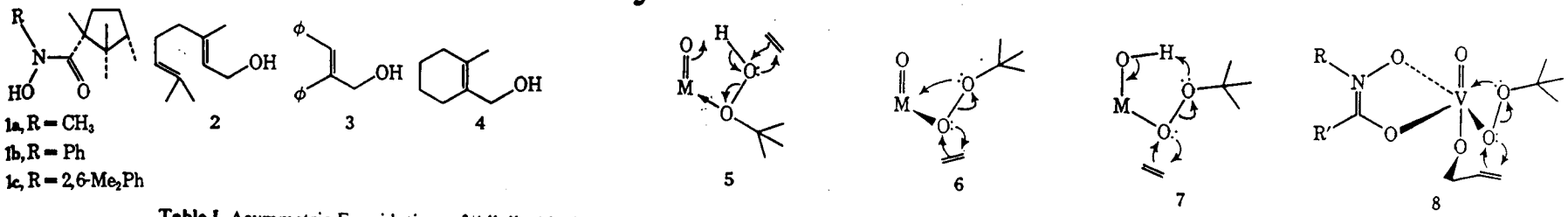


Table I. Asymmetric Epoxidations of Allylic Alcohols[a]

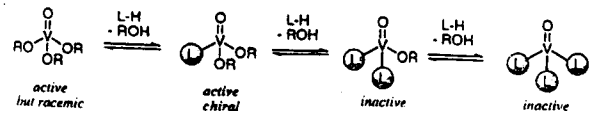
Hydroxamic acid (equiv)[b]	Allylic alcohol	°C	% ee[c]	% conversion[d]
1 **1a** (5)	**2**	−78 → 25	17	83
2 **1a** (3)	**3**	−78 → 25	10	100
3 **1a** (5)	**3**	−78 → 25	21	80
4 **1a** (10)	**3**	−78 → 25	18	22
5 **1b** (4)	**2**	−78 → 25	19	100
6 **1b** (4)	**2**	25	17.5	100
7 **1b** (5)	**2**	25	30	86
8 **1b** (5)	**2**	−78	—	0
9 **1b** (7)	**2**	−78 → 25	10	10
10 **1b** (1)	**3**	−78 → 25	<8	100
11 **1b** (2)	**3**	−78 → 25	8	100
12 **1b** (3)	**3**	−78 → 25	22.5	100
13 **1b** (5)	**3**	−78 → 25	50	30
14 **1b** (5)	**3**	25	40	84
15 **1b** (5)	**4**	25	40	87
16 **1b** (5)	**4**	−10	44	75
17 **1c** (3)	**2**	0	5	70
18 **1c** (4)	**2**	0	19	55
19 **1c** (5)	**2**	0	—	0

[a] All reactions were performed with 1 mmol of allylic alcohol and 2.5 mg (1%) of $VO(acac)_2$ catalyst in 20 mL of toluene under a nitrogen atmosphere. When the appropriate amount of hydroxamic acid was added to these solutions they immediately turned from green to reddish brown in color. Stirring was continued at room temperature for 15 min then, after cooling, 2 equiv of *tert*-butyl hydroperoxide (90+%, Lucidol) was added dropwise. During addition of the hydroperoxide the solution turned ruby red and this color persisted even after warming to room temperature. Reactions were monitored by TLC and acetylation was accomplished in situ by addition of pyridine and acetic anhydride. Acetylation was allowed to proceed for 2 h at room temperature and workup (see ref 5b) afforded the crude epoxyacetates which were purified by PLC and or microdistillation. [b] The figure in parentheses refers to the equivalents of hydroxamic acid added based on the amount of $VO(acac)_2$ catalyst. [c] The enantiomeric excess (ee) was determined by ^1H NMR using Eu-OPTISHIFT II [$Eu(hfbc)_3$] chiral shift reagent on the epoxyacetates (see ref 13 for estimated rotations of the three epoxyacetates). [d] The percent of epoxy alcohol product plus the percent of unreacted allylic alcohol equals 100%. In cases of 100% conversion the isolated yields of epoxy acetates ranged from 70 to 90%.

Hydroxamates of vanadium are not isolable, but best ee as of 1979.

Michaelson, R.C.; Palermo, R.E.; Sharpless, K.B. *JACS* **1977** *99* 1990.

Binaphthyl Hydroxamic Acids



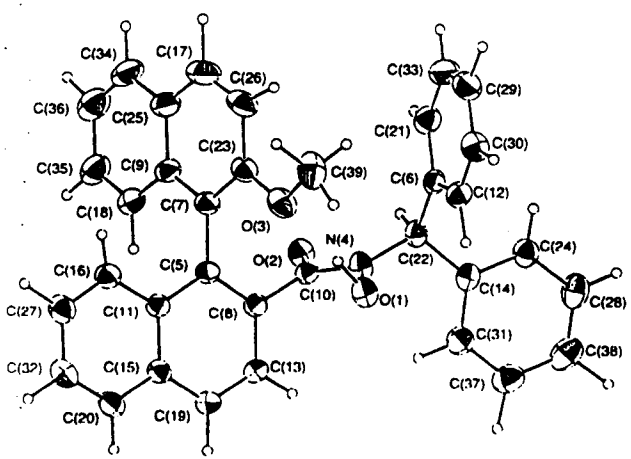


Fig. 2. ORTEP drawing of ligand 1c.

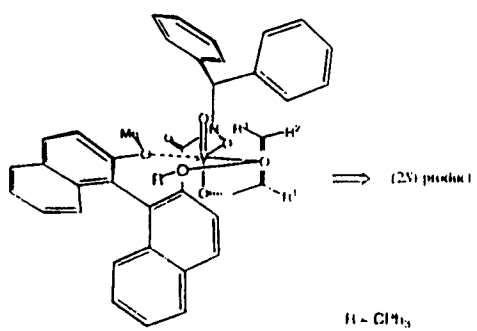
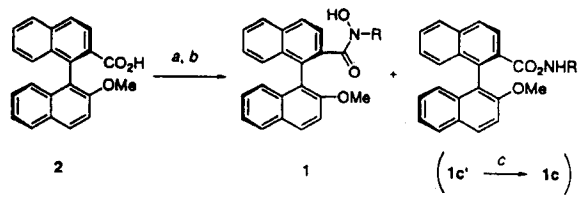


Fig. 3. Proposed transition states of asymmetric epoxidation.

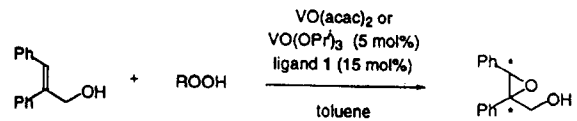
Scheme 1[a]



hyroxamic acid	yield from 2 (%)
1a (R = cyclohexyl)	84
b (R = Bn)	72
c (R = $CHPh_2$)	89

[a] Key: (a) $(COCl)_2$, cat.DMF, CH_2Cl_2; (b) 3, NEt_3, CH_2Cl_2; (c) *t*-BuLi, THF, −78 to 0 °C.

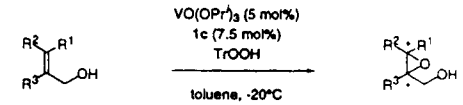
Table 1. Catalytic Enantioselective Epoxidation of *trans*-2,3-Diphenyl-2-propenol[a]

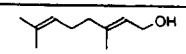
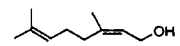
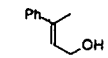
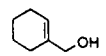
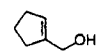
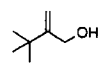


entry	catalyst	ROOH[b]	conditions (°C, h)	ee[c] (%)
1	$VO(acac)_2$/1a	CHP	0, 6 days	25
2	1b	CHP	0, 8 days	54
3	1c	CHP	0, 19	65
4	$VO(OPr^i)_3$/1c	CHP	0, 3	68
5		TBHP	−40, 10	40
6		TrOOH	−20, 68	86
7[d]		TrOOH	−20, 24	83
8[e]		TrOOH	−20, 24	73

[a] Unless otherwise noted, the reaction was carried out in toluene in the presence of vanadium complex (5 mol %) and 1 (15 mol %). The isolated yield in each entry was around 80%. [b] CHP = cumenehydroperoxide, TBHP = *tert*-butyl hydroperoxide, TrOOH = triphenylmethyl hydroperoxide. [c] The absolute configuration of the major enantiomer in each run was 2*S*,3*S*, and the ee values were determined by chiral HPLC (column, OD-H) analysis. [d] 7.5 mol % of 1c. [e] 6.0 mol % of 1c.

Table 2. Catalytic Epoxidation of Various Substituted Allyl Alcohols in the Presence of $VO(OPr^i)_3$/1c[a]



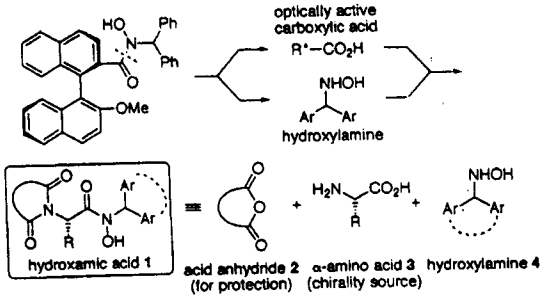
entry	allylic alcohol	yield (%)[b]	ee (%)[c]	config.(2,3)[d]
1		80	66	(*S*,*S*)
2		87	41	(*S*,*R*)
3		70	78	(*S*,*S*)
4		96	91	(*S*,*S*)
5		61	87[e]	(*S*,*S*)
6		59	94[e]	(*S*,*S*)
7		14	71	(*S*,*S*)
8		19	38	(*S*,*R*)
9		53	39	(2*S*)
10		16	40	(2*S*)

[a] The epoxidation was conducted at −20 °C for 2−3 days in toluene in the presence of $VO(OPr^i)_3$ (5 mol %) and 1c (7.5 mol %), but the reaction time (entries 7−10) was 1 week. [b] Isolated yield. [c] Determined by chiral HPLC (column, OD-H) analysis. [d] Determined by comparison of reported optical rotation. [e] Determined by chiral GLC (column, β-TA) analysis.

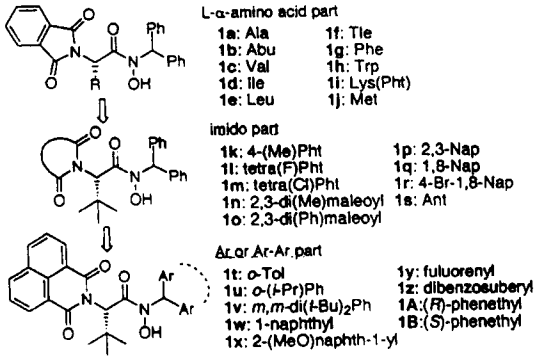
Murase, N.; Hoshino, Y.; Oishi, M.; Yamamoto, H. *JOC* **1999** *64* 338.
Hoshino, Y.; Murase, N.; Oishi, M.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **2000** *73* 1653.

α-Amino Acid Based Ligands

Scheme 1. Design of an α-Amino Acid-Based Hydroxamic Acids as a Ligand



Scheme 2. Iterative Positional Optimization Approach



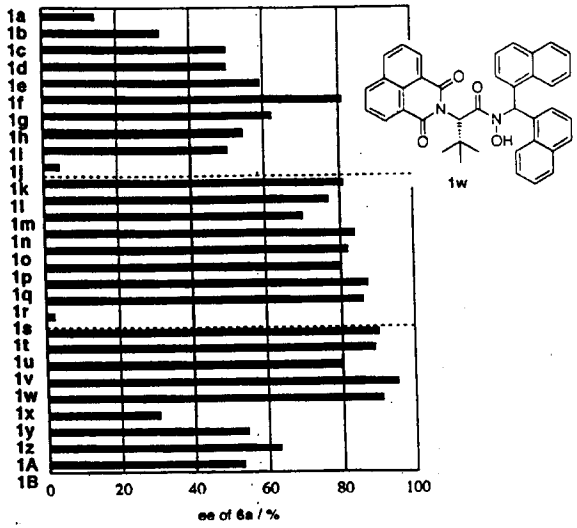


Figure 1. Enantioselectivities of epoxy alcohol **6a**.

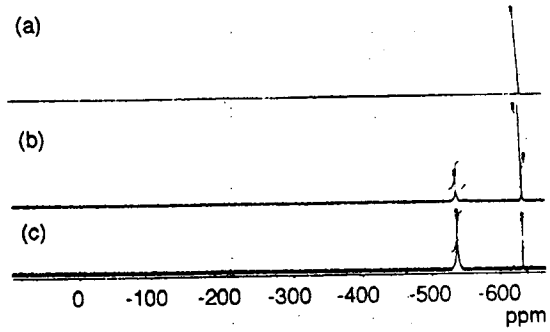


Figure 2. ^{51}V NMR spectra in benzene-d_6 at room temperature ($VOCl_3$, 0 ppm): (a) $VO(O\text{-}i\text{-}Pr)_3$, (b) $VO(O\text{-}i\text{-}Pr)_3$ and ligand **1w** (molar ratio, 1:1), and (c) $VO(O\text{-}i\text{-}Pr)_3$ and ligand **1w** (molar ratio, 1:1.5).

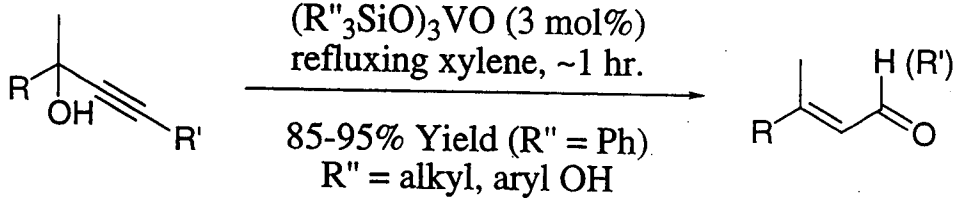
Table 1. The Asymmetric Epoxidation of Various Allylic Alcohols in the Presence of $VO(O\text{-}i\text{-}Pr)_3$ (1 mol %) and Hydroxamic Acid **1w** (1.5 mol %)[a]

entry	epoxy alcohol 6	time (h)	yield (%)[b]	ee (%)[c]
1		6	96	95
2[g]		6	93	96
3[h]		15	99	86
4[i]	**6a**	6	98	91
5	**6b**	6	97	95
6	**6c**	5	82	93[d]
7	**6d**	6	95	81[d]
8	**6e**	3	97	78[d]
9	**6f**	70	94	83[d]
10	**6g**	80	58[e]	87
11	**6h**	1 week	71[f]	76
12	**6i**	24	80	82[d]

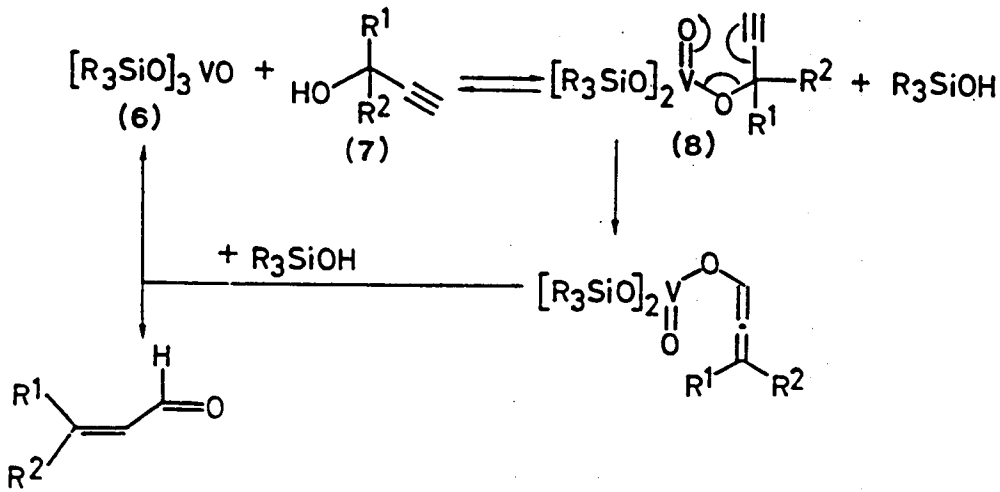
[a] All reactions were carried out at 0 °C in the presence of 1.5 equiv of *tert*-butylhydroperoxide and 1 mol % of vanadium catalyst prepared in situ by mixing $VO(O\text{-}i\text{-}Pr)_3$ and ligand **1w** (V/ligand 1:1.5) unless otherwise noted. [b] Isolated yield by column chromatography. [c] Determined by HPLC analysis with a chiral column (Chiral OD-H) unless otherwise noted. [d] Determined by GLC analysis with a chiral stationary phase column (β-TA). [e] The aldehyde was obtained in 9% yield as a byproduct. The allyl alcohol was recovered in 8% yield. [f] The allyl alcohol was recovered in 21% yield. [g] The reaction was conducted under an atmosphere of dry argon. [h] 0.1 mol % of $VO(O\text{-}i\text{-}Pr)_3$ and 0.15 mol % of **1w** were used. [i] 1.1 mol % of **1w** was used.

Hoshino, Y.; Yamamoto, H. *JACS* **2000** *122* 10452.

Silylvanadate Catalyzed Rearrangements of α-Acetylenic Alcohols

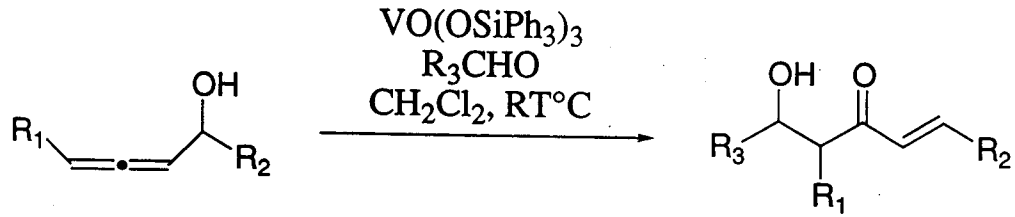


R = alkyl
R' = H, alkyl (one example, 92% yield)



Pauling, H.; Andrews, D.A.; Hindley, N.C. *Helv. Chim. Acta* **1976** *59* 1233.

Vanadium Catalyzed Additions of Allenic Alcohols and Aldehydes



Scheme 1. Proposed Additon of Allenic Alcohols and Aldehydes

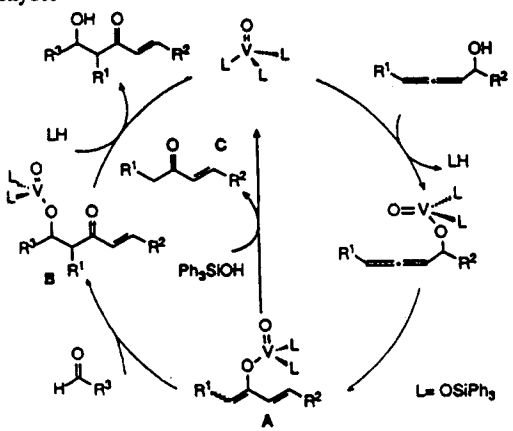


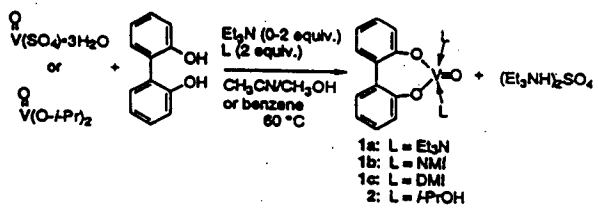
Table 1. Vanadium-Catalyzed Additions of Allenic Alcohols and Aldehydes[a]

Entry	Allenic alcohol	Aldehyde	Product	Yield[b]	Syn/Anti[c]
1	1	PhCHO	2	86%	80/20
2	1		6	83%	42/58
3	1		7	88%	67/33
4	1		8	86%	68/32
5	1		9	88%	70/30
6	1	C_3H_7CHO	10	79%	78/22
7	1		11	60% 71%[d]	80/20
8	1		12	61%	66/33
9	5	PhCHO	13	85%	-
10	5		14	70%	-
11	5		15	83%	-
12	5		16	64%	-

[a] In a typical procedure the reactions were carried out at room temperature in dichloromethane (2.5 M) employing 5 mol % of $VO(OSiPh)_3$, 1.2 equiv of aldehyde, and 1.0 equiv of allenic alcohol under an atmospheric pressure of argon. The reaction times varied from 24 to 48 h. [b] Isolated yield after flash chromatography. [c] The *syn/anti* ratio was determined by ^1H NMR. [d] The allenic alcohol was added slowly over a period of 6 h.

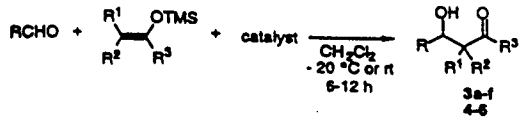
Trost, B.M.; Jonasson, C.; Wuchrer, M. *JACS* **2001** *123* 12736.

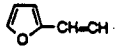
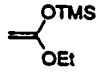
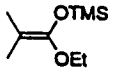
Mukaiyama-Type Aldol Additions



Scheme 1

Table 1. Aldol Reactions between Aldehydes and Enol Silanes Catalyzed by Various Oxovanadium(IV) Complexes



entry	R	enol silane	catalyst	d.r.[a]	yield, %[b]
1	Ph		1a	80/20 (40/60)[c]	53 (56)[c]
2			1a	80/20	50[d]
3			1a	74/26	12[e]
4			1a	80/20	10[f]
5			1b	90/10	72
6			1b'	90/10	93
7			1c	87/13	66
8			$SbCl_5$	50/50	57[g]
9			TMSOTf	50/50	91[g]
10	2-Naph		1b'	86/14 (35/65)[c]	95 (53)[c]
11	4-$MeOC_6H_4$		1b'	80/20 (43/57)[c]	78 (20)[c]
12	4-$NO_2C_6H_4$		1b'	76/23 (59/41)[c]	100 (76)[c]
13	Ph—≡		1b'	80/20	86
14			1b'	90/10	95
15	$Ph(CH_2)_2$		1b'	72/28	74
16	c-C_6H_{11}		1b'	60/40[h]	78
17	4-$NO_2C_6H_4$		1b'	—	91
18	Ph		1b'	—	62[h]
19	Ph		1b'	42/58	73[h]

Chen, C.-T.; Hon, S.-W.; Weng, S.-S. *Synlett* **1999** 816.

Catalytic Nucleophilic Acyl Substitution of Anhydrides

Scheme 1. Proposed Equilibrium between an Amphoteric Vanadyl Species and an Anhydride in the Catalytic Acylation of an Alcohol

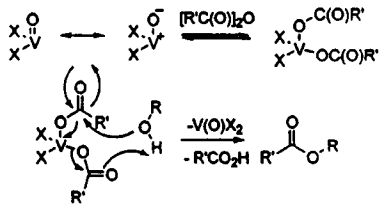
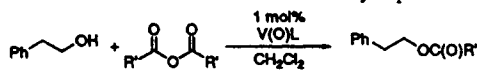


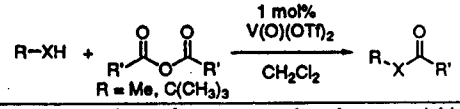
Table 1. Catalytic Acylations of 2-Phenylethanol with Various Anhydrides in the Presence of Various Vanadyl Species

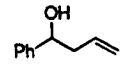
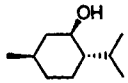
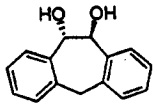
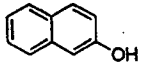
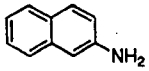
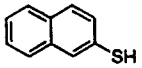


entry	V(O)L	anhydride (R')	time (h)	yield,[a] %
1	V(O)(acac)$_2$[b,c]	CH_3	5	85
2	V(O)Cl_3	CH_3	7.5	94
3	V(O)SO_4[c,d]	CH_3[e]	24	92
4	V(O)(OTf)$_2$	CH_3	0.5	98
5	V(O)(OTf)$_2$[f]	CH_3	0.75	98
6	V(O)(OTf)$_2$	CF_3	3	98
7	V(O)(OTf)$_2$	*i*-Pr	1	98
8	V(O)(OTf)$_2$	*tert*-Bu	11	99
9	V(O)(OTf)$_2$	*tert*-BuO	28	95
10	V(O)(OTf)$_2$	Ph	26	92
11	V(O)(OTf)$_2$	succinic	42	93
12	V(O)(OTf)$_2$	phthalic	96	75[g]

[a] Isolated yields. [b] Acetylacetonate. [c] Five mol % catalyst was used. [d] The trihydrate was used. [e] CH_3CN was used as solvent. [f] Catalyst was recovered from aqueous layer and reused for five consecutive runs. [g] Diphenethyl ester was isolated in 16%.

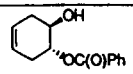
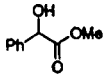
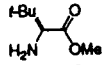
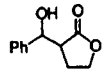
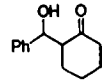
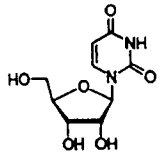
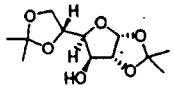
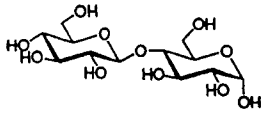
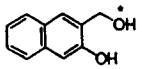
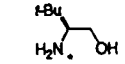
Table 2. Vanadyl Triflate-Catalyzed Acetylation and Pivalation of Alcohols, Amines, and Thiols



entry	substrate[a]	time, h	yield,[b] %
1	$Ph(CH_2)_2OH$	0.5 (11[c])	99 (99)
2	$PhCH{=}CHCH_2OH$	3.5[d] (72[c])	98 (85)
3		10 (24)	97 (97)
4		1 (96[c])	97 (84)
5		1 (5[e])	98 (95)
6		5 (36)	99 (99)
7		8 (42)	99 (99)
8		40 (96)	99 (98)
9	$(i\text{-Pr})_2NH$	3	97
10	*tert*-BuSH	12 (24)	99 (95)

[a] A total of 1.5 equiv of anhydride was used unless otherwise stated. [b] Isolated yields and characterized spectroscopically. [c] The data in parentheses correspond to pivalations. [d] A total of 2 equiv of anhydride was used. [e] A total of 3 equiv of anhydride was used. [f] THF was used as solvent. [g] Toluene was used as solvent.

Table 3. Acetylation and/or Pivalation of Functionalized Substrates

entry	substrate[a]	time, h	yield,[b] %
1		0.5 (48[c])	99 (99)
2		2 (3)	96 (95)
3		0.5[d] (1.5)	100 (85)
4		12 (24)	95 (95)
5		6 (12)	100 (100)
6		96[e]	90
7		49[f]	75
8		60[e,g]	85
9	β-cyclodextrin	96[e]	90
10		3[h] (48)	95 (96)
11		2[h,i] (15)	60[j] (97)

[a] A total of 1.5 equiv of anhydride was used unless otherwise stated. [b] Isolated yields and characterized spectroscopically. [c] The data in parentheses correspond to pivalations. [d] A total of 2 equiv of anhydride was used. [e] A total of 3 equiv of anhydride was used. [f] Carried out at −5 °C. [g] No solvent was used. [h] Asterisk signifies the reactive site. [i] For effective monoacylation, 0.95 equiv of anhydride was used. [j] Diacetylated product was isolated in 10% yield.

1) VCl_3 and $V(OTf)_3$ were catalytically inactive >>> V=O necessary.
2) Tertiary alcohols are inactive (t-BuOH, Trityl-OH).

Chen, C.-T.; et al. *OL* **2001** *3* 3729.

Oxidative Coupling of Phosphonium Salts

Scheme 2

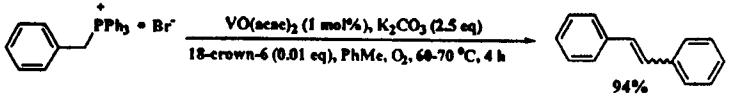
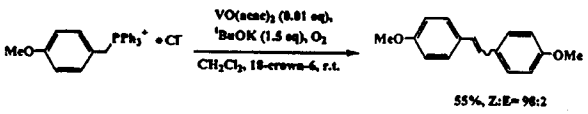


Table 1. Effect of Various Metal Catalysts in the Oxidative Coupling Reactions of Phosphonium Salts

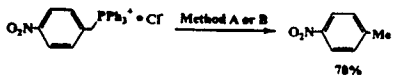
catalysts	yield/%[a]
none	31
$VO(acac)_2$	94
MnO_2	20
$Co(acac)_2$	50
$Mn(acac)_3$	40
$Ni(acac)_2$	50

[a] Isolated yields.

Scheme 3



Scheme 4



Scheme 5

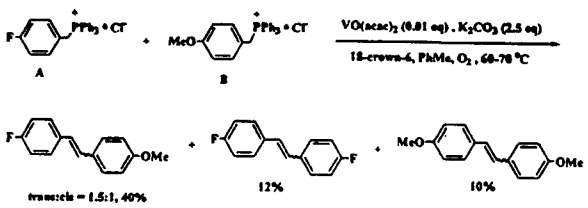
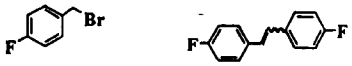
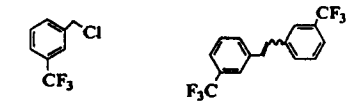
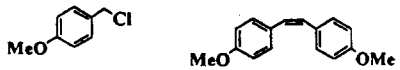
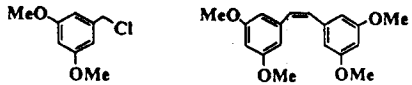
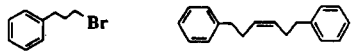
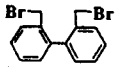
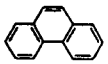


Table 2. Oxidative Coupling Reaction of Phosphonium Salts

entry	halides	products	reaction condition	yield/%[a]	Z/E
1			A[b]	93	1.7:1
2			A	83	1.6:1
3			A	84	1.3:1
4			A	75	1.3:1
5			B[c]	55	98:2
6			B	51.	>98:<2
7			B	78	98:2
8	$n\text{-}C_{12}H_{25}Br$	$C_{11}H_{23}$ $C_{11}H_{23}$	B	62	>98:<2
9			A	70	—
10	$Me\text{-}\overset{O}{\overset{\|\|}{C}}\text{-}CH_2Br$	no reaction	A or B	—	—

[a] Isolated yields. [b] Method A: PhMe, K_2CO_3 (2.5 equiv), 18-crown-6 (0.01 equiv), O_2 atmosphere, $VO(acac)_2$ (0.01 equiv), at 60–70 °C. [c] Method B: CH_2Cl_2, ^tBuOK (1.5 equiv), 18-crown-6 (0.01 equiv), O_2 atmosphere, $VO(acac)_2$ (0.01 equiv), at room temperature.

Shi, M.; Xu, B. *JOC* **2002** *67* 294.

Diastereoselective Pinacol Couplings of Secondary Aliphatic Aldehydes

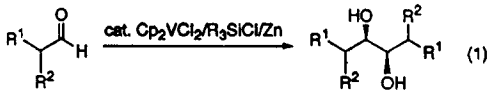
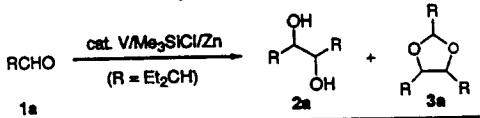


Table 1. Selectivity of the Formation of 1,2-Diol[a]



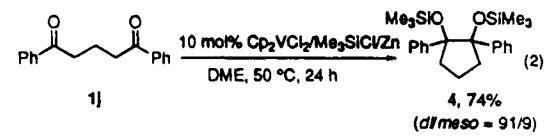
entry	cat.	solvent	yield, % (*dl/meso*) 2a	3a
1	$CpV(CO)_4$	DME	0	80 (63/37)
2	$CpV(CO)_4$	THF	78 (91/9)	0
3	Cp_2VCl_2	DME	0	82 (88/12)
4	Cp_2VCl_2	THF	100 (88/12)	0
5[b]	$CpV(CO)_4$	THF	100 (92/8)	0
6[b]	Cp_2VCl_2	THF	100 (96/4)	0
7[c]	Cp_2VCl_2	THF	74 (70/30)	0
8[d]	Cp_2VCl_2	THF	0	39 (89/11)

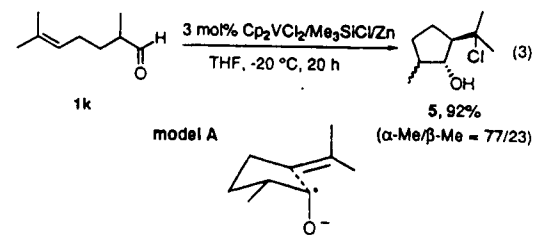
[a] Reaction conditions unless otherwise stated: aldehyde (2 mmol), catalyst (0.06 mmol), Zn (4 mmol), Me_3SiCl (4 mmol), solvent (7 mL), 20 °C, 13 h. [b] $PhMe_2SiCl$ was used instead of Me_3SiCl. [c] 40 °C. [d] −20 °C.

Table 2. $Cp_2VCl_2/R_3SiCl/Zn$-Induced Pinacol Coupling Reaction[a]

entry	aldehyde	coupling product	yield, %	[*dl/meso*]
1[b]	1b	2b	89	[91/9]
2[b]	1c	2c	71 (66)[c]	[90/10]
3	1d	2d	67 (66)[c]	[94/6]
4	1e	2e	100 (96)[c]	[85/15]
5	1f	2f	97	[50/50]
6	1g	2g	97	[64/36]
7	1h	2h	100	[56/44]
8	1i	2i	91	[57/43]
9[d]			17	[77/23]

[a] Reaction conditions unless otherwise stated: aldehyde (3 mmol), Cp_2VCl_2 (0.09 mmol), Zn (6 mmol), Me_3SiCl (6 mmol), THF (7 mL), 20 °C, 13 h. [b] $PhMe_2SiCl$ was used instead of Me_3SiCl. [c] Isolated yield (%). [d] −20 °C.





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Conclusion

1) Vanadium has been used successfully in catalysis.

2) Most of the useful organic reactions using vanadium catalysts are oxovanadium species (IV or V).
3) It's primary synthetic niche is oxidation, best with epoxidation of allylic alcohols.
4) Oxovanadium catalysts (V) are trigonal bipyramidal in structure and function via coordination/activation.
5) Lower valent vanadium catalysts (II, III) function by redox processes.
6) Reaction conditions using the catalyst are typically mild.

7) Reactions are first order with respect to catalyst.

8) Much improvement in selectivities is needed to provide proof of overall utility.

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