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A Novel System Consisting of Low-Valent Vanadium and Diethyl Phosphonate or Triethyl Phosphite for the Highly Stereoselective Reduction of *gem*-Dibromocyclopropanes

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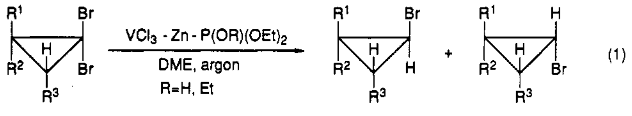
A variety of reductants based on the redox properties of transition metal complexes have been developed for the reduction of organic halides.[1] One-electron reduction has synthetic potential for the generation of radical intermediates. Vanadium species in low oxidation states serve as versatile one-electron reductants,[2-4] but their synthetic utility in this respect has been limited. In a previous paper, we demonstrated that vanadium(II) chloride promotes the regioselective radical addition of bromotrichloromethane to terminal olefins.[5] This method is not applicable to less-reactive halides. The efficiency of the one-electron transfer system depends on the redox potential of both the vanadium complexes and the radicophiles. We herein report that a combination of a low-valent vanadium species and either diethyl phosphonate (commercially named diethyl phosphite) or triethyl phosphite is effective for the highly stereoselective reduction of *gem*-dibromocyclopropanes. Such selectivity has been realized with only a few reductants.[6]

Reduction of 1,1-dibromo-2-phenylcyclopropane (**1a**) with the vanadium(II) species[7] generated from vanadium(III) chloride and zinc in the presence of diethyl phosphonate in dimethoxyethane afforded *cis*-1-bromo-2-phenylcyclopropane (**2a**) and a small amount of the *trans*-isomer (**3a**) (eq 1, Table I). High stereoselectivity was attained with this reduction system. It should be noted that no debromination occurred in the absence of either of the components. An increase in the amount of zinc or diethyl phosphonate raised the yield of 1-bromo-1-phenylcyclopropanes, although further reduction to phenylallene occurred. Triethyl phosphite was found to work as well as diethyl phosphonate.



(1)

1a R^1=Ph, R^2=R^3=H **2** **3**
1b R^1=CN, R^2=Me, R^3=H
1c R^1=CO_2Me, R^2=Me, R^3=H
1d R^1=Ph, R^2=Me, R^3=H
1e R^1=H; R^2, R^3=$(CH_2)_4$

Similar stereoselective debrominations were achieved with other *gem*-dibromocyclopropanes **1**, except for *gem*-dibromocyclopropane **1c**. Cyano or methoxycarbonyl substitution on the cyclopropane ring resulted in more facile reduction.

It is important to note that a catalytic reduction reaction with high stereoselectivity was achieved when the amount of vanadium(III) chloride was decreased (Table I). $CpV(CO)_4$ gave higher stereoselectivity and a higher yield than VCl_3 in the stereoselective monodebromination of **1a** with zinc and diethyl phosphonate. These findings indicate that a reversible redox cycle involving a low-valent vanadium species formed in situ is operating with zinc.

Some conclusions about the reaction mechanism can be made. A combination of diethyl phosphonate and triethylamine efficiently reduces *gem*-dibromocyclopropanes and α-bromo α,β-unsaturated carbonyl compounds,[8] but a similar ionic mechanism is probably not operating in our case because triethyl phosphite produces the vanadium-containing reductant system with equal ease. A low-valent vanadium species generated from vanadium(III) chloride and zinc has been reported to induce the reductive coupling of carbonyl compounds.[2f,g] Stoichiometric reactions have also been reported for the coupling of allylic bromides mediated by VCl_3-$LiAlH_4$[2d] and the reduction of alkyl halides with $CpV(CO)_3H^-$,[3] in which a radical chain mechanism is operative. In our case, the radical formed via such a one-electron reduction seems to be converted either to the monobromocyclopropane or, through further one-electron reduction, to a carbanion.[9] The latter intermediate is likely to lead to the formation of phenylallene. The greater facility of the reduction of the cyclopropanes bearing an electron-withdrawing group is considered to be based on the resulting difference in redox potential.

The requirement for diethyl phosphonate or triethyl phosphite as a key component of the reductant system suggests that the coordination of the phosphorus raises the reduction capability. A ^{51}V NMR ligand exchange experiment on $CpV(CO)_4$ reflected such a coordination: the vanadium signal was shifted to higher field (by 6 ppm) when $CpV(CO)_4$ (15 mM) was treated with 100 equiv of $P(OEt)_3$ for 12 h in dimethoxyethane and dichloromethane-d_2 (1:1). The complexation appears to increase the steric bulk of the reductant, which is thus compelled to attack the less-hindered bromine atom selectively.[6c] Furthermore, diethyl phosphonate is assumed to serve as a hydrogen source,[10] possibly from within the coordination

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Table I. Reduction of *gem*-Dibromocyclopropanes

			$P(OR)(OEt)_2$		conditions		yields, %[a]			
1	VCl_3 equiv	Zn equiv	R	equiv	temp (°C)	h	**2** + **3**	(**2**/**3**)	phenylallene	recovered **1**, %[a]
1a	1	1	H	1	rt	60	20	(95:5)	5	49
	0	1	H	1	rt	60	0		0	95
	1	1	–		rt	100	0		0	95
	1	0	H	1	rt	60	0		0	87
	1	3	H	1	rt	60	40, 37[b]	(93:7)	28	0
	1	1	H	3	rt	60	28	(91:9)	10	57
	1	1	Et	1	rt	60	17	(91:9)	0	74
	0.1	1	H	1	rt	120	45	(93:7)	0	45
	0.3	1	H	1	rt	18 days	66	(94:6)	0	15
	0.1[c]	1	H	1	rt	100	78	(97:3)	0	0
1b	1	1	H	1	rt	60	66	(90:10)		30
	1	1	–		rt	60	0			98
	1	2	H	1	rt	30	99, 78[b]	(89:11)		0
	1	1	Et	1	rt	60	74	(87:13)		21
	0.1	1	H	1	rt	72	72	(95:5)		0
1c	0.1	1	H	1	rt	50	70,[d] 50[b]	(39:61)		9[d]
	0.03[c]	1	H	1	rt	24	71[d]	(38:62)		2[d]
1d	1	2	H	1	80	90	31	(90:10)		62
1e	2	2	H	2	80	72	74	(1:>99)		0
	2	2	Et	1	rt	72	57, 42[b]	(1:>99)		38

[a] GLC yields unless otherwise stated. [b] Isolated yield. [c] $CpV(CO)_4$ was used instead of VCl_3. [d] NMR yield.

sphere. Diethyl phosphonate and triethyl phosphite are considered to contribute to the efficiency of the stereoselective reduction.

Diethyl phosphonate/low-valent vanadium and diethyl phosphonate/triethylamine are two complementary reducing agents that operate by one-electron and two-electron transfer mechanisms, respectively. Further investigations on reductive transformations with the system are now in progress.

Experimental Section

Stoichiometric Reduction. A representative experimental procedure is as follows. A suspension of vanadium trichloride (0.157 g, 1.0 mmol) and activated zinc (0.196 g, 3.0 mmol) in dimethoxyethane (2 mL) was stirred at rt for 10 min under argon. After 1,1-dibromo-2-phenylcyclopropane (**1a**, 0.276 g, 1.0 mmol) and diethyl phosphonate (0.138 g, 1.0 mmol) were added, the mixture was stirred at rt for 60 h. Ether (10 mL) was added to the resulting mixture, which was filtered, washed with brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (10:1 v/v) to give the *cis*- and *trans*-1-bromo-2-phenylcyclopropanes (**2a** and **3a**) (Table I). The reductions of the other *gem*-dibromocyclopropanes were carried out similarly, and the results are listed in Table I. The structures of the monobromocyclopropanes thus obtained were assigned by comparison of their spectral or GLC (1.2 m, 20% PEG 20M column, 100–150 °C) data with those of authentic samples.[8a]

Catalytic Reduction. A representative experimental procedure is as follows. A suspension of vanadium trichloride (15.7 mg, 0.1 mmol) and activated zinc (65.4 mg, 1.0 mmol) in dimethoxyethane (2 mL) was stirred at rt for 10 min under argon. After 1,1-dibromo-2-phenylcyclopropane (**1a**, 0.276 g, 1.0 mmol) and diethyl phosphonate (0.138 g, 1.0 mmol) were added, the mixture was stirred at rt for 120 h. Workup in a manner similar to that described above gave the corresponding monobromocyclopropanes (**2a** and **3a**) (Table I). The catalytic reductions of the other *gem*-dibromocyclopropanes were carried out similarly, and the results are listed in Table I.

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