protonated neutral phosphate is the reactive species. Protonation makes the diester electronically equivalent to a triester, and their similar ^{15}N isotope effects indicate a similar degree of bond breaking to the leaving group in the transition states of these two processes. The reaction in these cases is associative, with only ~25–32% bond cleavage in the transition state if one uses the value of 1.0028 as representing a fully broken bond.

The alkaline hydrolysis of phosphodiesters is an S_N2 process. The value for the ^{15}N isotope effect suggests that the P–O bond is ~57% broken in the transition state. The isotope effect data imply a less associative transition state for this reaction than for the alkaline triester or acidic diester hydrolysis.

Although the maximum isotope effect representing total bond cleavage is somewhat uncertain, comparisons within this series of reactions allow one to observe with a good degree of precision subtle differences in the transition states in the continuum of phosphoester reactions. Because the ^{15}N isotope effect is a secondary one and reaction coordinate motion does not make a contribution, it is a better measurement of P–O bond order in the transition state than the primary ^{18}O isotope effect. This method should be a useful tool for probing transition-state bond breaking in other reactions as well.

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Generation of a Stable Formaldehyde–Organoaluminum Complex and Its Synthetic Utility

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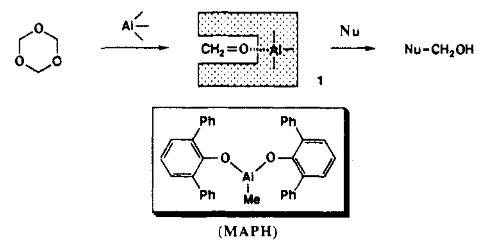
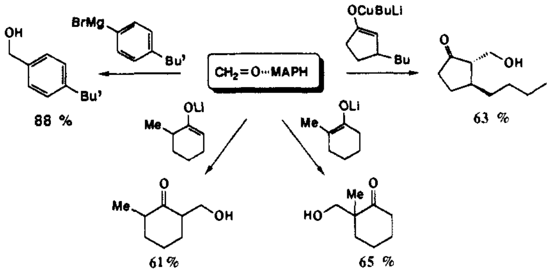
Formaldehyde (gas) is undoubtedly one of the most highly reactive C_1 electrophiles in organic synthesis, as demonstrated in a number of natural product syntheses[1] including a cytotoxic sesquiterpene, vernolepin,[2] and prostaglandins.[3] The synthetic utility of gaseous formaldehyde, in spite of its vast potential, is somewhat restricted because of its remarkably facile self-polymerization. Recent extensive efforts by Snider et al. have resulted in the development of expedient methods, i.e., the generation of formaldehyde from paraformaldehyde catalyzed by Me_2AlCl or Me_3Al and the successful trapping of in situ generated formaldehyde with various olefins.[4] In view of their Lewis acidic conditions as well as the unstable formaldehyde–aluminum complexes, however, these methods cannot be utilized for the nucleophilic addition of carbanions (organometallics, enolates, etc.) as often seen in natural product syntheses.[1-3] In this context, we have been interested for some time in the possibility that certain exceptionally bulky, oxygenophilic organoaluminum reagents might be highly effective because of their two different capabilities, the generation of formaldehyde from readily available trioxane and its stabilization as a formaldehyde–organoaluminum complex to suppress self-polymerization by the exceptionally bulky aluminum ligands (Scheme I). In this communication we report our initial results from this study.

Scheme I



Scheme II



Attempted reaction of exceptionally bulky methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD)[5] in CH_2Cl_2 with gaseous formaldehyde followed by addition of 1-(trimethylsiloxy)-1-cyclohexene resulted in formation of the Friedel–Crafts alkylation products, 2-*tert*-butyl-6-(hydroxymethyl)-4-methylphenol (42%) and 2,6-di-*tert*-butyl-4-(hydroxymethyl)-4-methyl-2,5-cyclohexadienone (18%). Switching aluminum reagents from MAD to methylaluminum bis(4-bromo-2,6-di-*tert*-butylphenoxide)[6] suppressed the Friedel–Crafts alkylations without any ene-product formation. In marked contrast, however, methylaluminum bis(2,6-diphenylphenoxide) (abbreviated to MAPH) is capable of forming a 1:1 coordination complex **1** with formaldehyde, as confirmed by the subsequent ene reaction with 1-(trimethylsiloxy)-1-cyclohexene, giving the desired 6-(hydroxymethyl)-1-(trimethylsiloxy)-1-cyclohexene in 61% yield after workup with saturated $NaHCO_3$.[7] We then examined the stability of the $CH_2{=}O{\cdot}MAPH$ complex and found that it was stable at 0 °C for 5 h and thereafter gradually decomposed at room temperature.[8] The use of simple trioxane as a formaldehyde source offers major advantages. Indeed, treatment of trioxane with MAPH (3 equiv) in CH_2Cl_2 at 0 °C for 1 h successfully yielded the $CH_2{=}O{\cdot}MAPH$ complex, which was confirmed by subjection to ene reactions with various olefins (Table I). Our method is obviously far superior in regioselectivity to previously known procedures.[4] The eminent chemoselectivity is also seen in the ene reaction of dihydrocarvone and geranyl acetate (entries 9 and 10). In addition, the $CH_2{=}O{\cdot}MAPH$ complex can be utilized as a stable source of gaseous formaldehyde for the nucleophilic addition of various carbanions, as illustrated in Scheme II. Consequently, it is no longer necessary to generate form-

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(1) (a) Angelo, J.; Stork, G. *J. Am. Chem. Soc.* **1974**, *96*, 7114. (b) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1973**, *38*, 3244. (c) Lucast, D. H.; Wemple, J. *Synthesis* **1976**, 724.

(2) (a) Grieco, P. A.; Hiroi, K. *J. Chem. Soc., Chem. Commun.* **1972**, 1317. (b) Grieco, P. A.; Hiroi, K. *Tetrahedron Lett.* **1973**, 1831; **1974**, 3467. (c) Grieco, P. A.; Noguez, J. A.; Masaki, Y. *Ibid.* **1975**, 4213. (d) Grieco, P. A.; Nishizawa, M.; Burke, S. D.; Marinovic, N. *J. Am. Chem. Soc.* **1976**, *98*, 1612.

(3) (a) Stork, G.; Isobe, M. *J. Am. Chem. Soc.* **1975**, *97*, 4745. (b) Stork, G.; Isobe, M. *Ibid.* **1975**, *97*, 6260.

(4) (a) Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, *104*, 555. (b) Snider, B. B.; Cordova, R.; Price, R. T. *J. Org. Chem.* **1982**, *47*, 3643. (c) Snider, B. B.; Phillips, G. B. *Ibid.* **1983**, *48*, 2789. (d) Snider, B. B. In *Selectivities in Lewis Acid Promoted Reactions*; Schinzer, D., Ed.; Kluwer Academic Publishers: London, 1989; pp 147–167.

(5) (a) Maruoka, K.; Itoh, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 4573. (b) Maruoka, K.; Araki, Y.; Yamamoto, H. *Ibid.* **1988**, *110*, 2650. (c) Maruoka, K.; Itoh, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *Ibid.* **1988**, *110*, 3588.

(6) Maruoka, K.; Nonoshita, K.; Banno, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 7922; **1990**, *112*, 316.

(7) Since dimethylaluminum 2,6-diphenylphenoxide and methylaluminum bis(2-phenylphenoxide) as MAPH analogues are totally ineffective for this purpose, the origin of the remarkable effect of MAPH for stabilizing formaldehyde is worthy of comment. In a space-filling model of MAPH, two phenyl groups are parallel to each other in front of the Lewis acidic aluminum so that formaldehyde by coordination to MAPH is electronically stabilized by a sandwich structure between these two phenyl groups.

(8) These results were determined by the subsequent ene reaction of the $CH_2{=}O{\cdot}MAPH$ complex (3 equiv) with 1-(trimethylsiloxy)-1-cyclohexene at −78 °C for 1 h. The reaction conditions for generation of the $CH_2{=}O{\cdot}MAPH$ complex and the yields of the ene product follow: 61% (0 °C, 1 h); 48% (0 °C, 3 h); 52% (0 °C, 5 h); 16% (25 °C, 1 h); 2% (25 °C, 24 h).

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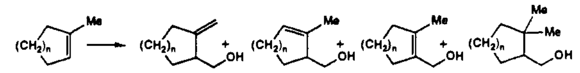
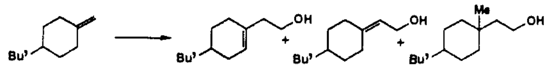
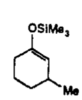
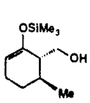
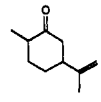
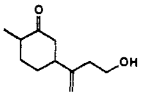
Table I. Reaction of Formaldehyde–Organoaluminum Complexes with Olefins

entry	olefin	reagent	conditions (°C, h)	products (ratio)
				
1	a, n = 1	CH_2=O·MAPH[a]	-78, 1	61% (100 : 0 : 0 : 0)[e]
2		CH_2=O·$AlMe_2Cl$[b]	0, 0.17	73% (75 : 25 : 0 : 0)
3	b, n = 2	CH_2=O·MAPH[a]	-78, 1	80% (100 : 0 : 0 : 0)[e]
4		CH_2=O·$AlMe_2Cl$[b]	0, 0.17	92% (41 : 59 : 0 : 0)
5		CH_2=O·$AlMe_3$[c]	25, 0.25	56% (7 : 0 : 25 : 68)
				
6		CH_2=O·MAPH[a]	-78, 1	71% (100 : 0 : 0)[e]
7		CH_2=O·$AlMe_3$[c]	25, 0.25	71% (44 : 2) : 35)
8		CH_2=O·MAPH[a]	0, 0.5	 71%
9		CH_2=O·MAPH[a]	0, 0.5	 90%
				
10		CH_2=O·MAPH[a]	0, 0.5	86%
11		CH=$_2$O·$AlMe_2Cl$[d]	25, 1	3%[f]

[a] The CH_2=O·MAPH complex (3 equiv) was prepared by treatment of trioxane (1 equiv) with MAPH (3 equiv) at 0 °C for 1 h and subsequently reacted with olefins under the indicated conditions. [b] See ref 4a. [c] See ref 4b. [d] This ene reaction was carried out according to ref 4a. [e] The ene reactions at higher temperature (~0 °C) showed similar selectivities. [f] Complex reaction mixtures were formed.

aldehyde by the troublesome thermal depolymerization of paraformaldehyde.

Supplementary Material Available: Representative experimental procedures for ene and aldol reactions with the CH_2=O·MAPH complex and table of five additional ene reactions (2 pages). Ordering information is given on any current masthead page.

High Reactivity, Regioselectivity, and Endo Stereoselectivity of Vinylboranes in Diels–Alder Reactions

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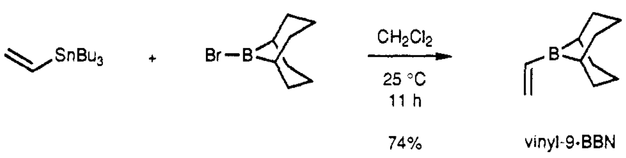
Chemists have long believed that a trivalent boron atom, with its empty p orbital, should behave in a fashion similar to that of traditional organic electron-withdrawing groups.[1] This idea is synthetically attractive when applied to the activation of Diels–Alder dienophiles, because the product boron compounds can be transformed into alcohol, ketone, amine, or alkane products, none of which can usually be produced by a direct Diels–Alder reaction. However, Diels–Alder reactions on vinylboron derivatives are very rare and the known examples do not exhibit either high reactivity or general synthetic utility. In 1963, Matteson[2] reported the reaction of vinylboronic esters with cyclopentadiene at 90–100 °C and isoprene at 130–140 °C. Vinyldichloroborane reacts with cyclopentadiene in low yield at 80 °C.[3,4] In an evaluation of ketene equivalents, Evans reported the low reactivity of vinylboronic esters with 1,3-cyclohexadiene derivatives, with long reaction times at 200 °C required.[5] Due to the necessarily strenuous reaction conditions, other examples are lacking.

We were interested in experimentally assessing how a *dialkyl*boron group compares to carbonyl groups in its effects on reactivity. The recent utilization of diarylboron groups in anion chemistry[6,7] made it surprising that there were no reports of successful[8] Diels–Alder reactions on vinyl*boranes*. We report here that a dialkylboron group is dramatically more activating than esters and boronic esters in normal Diels–Alder reactions and that vinylboranes are exceptionally reactive, regioselective, and stereoselective dienophiles. We anticipate that excellent synthetic applicability should result.

The previously unknown 9-vinyl-9-borabicyclo[3.3.1]nonane (vinyl-9-BBN)[9] was easily synthesized by treatment of a 1.0 M solution of *B*-bromo-9-BBN in methylene chloride with 1 equiv of vinyltributyltin, followed by distillation of the reaction mixture [bp 28–30 °C (0.25 mm)]. Vinyl-9-BBN can be kept for weeks in a freezer under an inert atmosphere and is extremely pyrophoric.



The reactions of vinyl-9-BBN with some simple dienes are summarized in Table I. In contrast to the reactions of butadiene or isoprene with methyl acrylate,[10] nitroethylene,[11] phenyl vinyl sulfone,[12] dibutyl vinylboronate,[2] or even vinylboronic esters substituted with a second electron-withdrawing group,[13] all requiring prolonged heating at 100–150 °C, the Diels–Alder reactions of vinyl-9-BBN with butadiene and isoprene were both >80% complete in a day at 25 °C! Based on the bimolecular rate constant determined by NMR (Table I), vinyl-9-BBN is 200 times more reactive than methyl acrylate with butadiene.[14] Vinyl-9-BBN is still less reactive than Lewis acid complexed dienophiles[10] and α,β-unsaturated Fischer carbene complexes,[15] but among simple neutral substituents, the activating effect of a dialkylboron

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(1) Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228.

(2) Matteson, D. S.; Waldbillig, J. O. *J. Org. Chem.* **1963**, *28*, 366.

(3) Coindard, G.; Braun, J. *Bull. Chim. Soc. Fr.* **1972**, 817.

(4) In our hands, acid-catalyzed reactions of dienes in the presence of dihalovinylboranes are a severe problem.

(5) Evans, D. A.; Scott, W. L.; Truesdale, L. K. *Tetrahedron Lett.* **1972**, 121. Evans, D. A.; Golob, A. M.; Mandel, N. S.; Mandel, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 8170.

(6) Pelter, A.; Buss, D.; Colclough, E. *J. Chem. Soc., Chem. Commun.* **1987**, 297. Pelter, A.; Singaram, B.; Williams, L.; Wilson, J. W. *Tetrahedron Lett.* **1983**, *24*, 623.

(7) Cooke, M. P., Jr.; Widener, R. K. *J. Am. Chem. Soc.* **1987**, *109*, 931.

(8) Reference 3 reports a failed attempt.

(9) In all cases, ^1H and ^{13}C NMR and mass spectral data were consistent with the assigned structures. The "para" regiochemistry of **2** was established by oxidation (H_2O_2/NaOH and then pyridinium dichromate) and *p*-toluenesulfonic acid catalyzed equilibration to a mixture of 4-methyl-2-cyclohexenone and 4-methyl-3-cyclohexenone. See: Kinney, W. A.; Crouse, G. D.; Paquette, L. A. *J. Org. Chem.* **1983**, *48*, 4986. The stereochemistry and regiochemistry of **4–9** were assigned after oxidation to the corresponding alcohols. ^1H-Decoupling experiments on the alcohols corresponding to **4** and **5** established connectivity consistent only with 5-methyl-3-cyclohexenol isomers. The 5-methyl-3-cyclohexenol isomer corresponding to **4** was assigned the cis stereochemistry on the basis of coupling constants to the carbinol proton of 11.5, 9.7, 5.6, and 3.5 Hz. The 1,2,3,5,6,7,8,8a-octahydronaphthalen-2-ol corresponding to **6** was assigned the given stereochemistry on the basis of coupling constants to the carbinol proton of 11.6, 9.3, 5.3, and 3.4 Hz. The carbinol protons of the minor alcohol isomers corresponding to **5** and **7** were located 0.16 and 0.19 ppm downfield from those of the major isomers, respectively, and both displayed four smaller, incompletely resolvable coupling constants totaling ≈18 Hz.

(10) Inukai, T.; Kojima, T. *J. Org. Chem.* **1967**, *32*, 872.

(11) Kaplan, R. B.; Shechter, H. *J. Org. Chem.* **1961**, *26*, 982.

(12) Carr, R. V. C.; Paquette, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 853.

(13) Martinez-Fresneda, P.; Vaultier, M. *Tetrahedron Lett.* **1989**, *30*, 2929.

(14) A value of 1.6×10^{-8} M^{-1} s^{-1} for the reaction of 1,3-butadiene with methyl acrylate at 25 °C may be extrapolated from literature data.[10]

(15) Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 6726.

0002-7863/90/1512-7423$02.50/0