Stabilization of Reactive Aldehydes by Complexation with Methylaluminum Bis(2,6-diphenylphenoxide) and Their Synthetic Application

Keiji Maruoka, Arnel B. Concepcion, Noriaki Murase, Masataka Oishi, Naoki Hirayama, and Hisashi Yamamoto*

Contribution from the Department of Applied Chemistry, Nagoya University, Chikusa, Nagoya 464-01, Japan

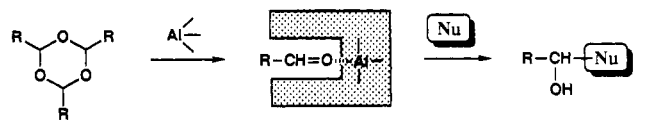
Received December 28, 1992

Abstract: Reactive aldehydes such as formaldehyde and α-chloro aldehydes can be successfully generated by treatment of readily available trioxane and α-chloro aldehyde trimers, respectively, with methylaluminum bis(2,6-diphenylphenoxide) (MAPH), and stabilized as their 1:1 coordination complexes with MAPH. The resulting CH_2=O·MAPH complex reacts with a variety of olefins to furnish ene-reaction products with excellent regio- and stereoselectivities. In addition, this complex as well as α-chloro aldehyde–MAPH complexes can be utilized as a stable source of gaseous formaldehyde and reactive α-chloro aldehydes, respectively, for the nucleophilic addition of various carbanions (organometallics, enolates, etc.). Formation of reactive aldehyde–MAPH complexes is firmly confirmed by ^{1}H NMR spectroscopy. A space-filling model of aldehyde–MAPH complexes implies that formaldehyde and α-chloro aldehydes coordinated with MAPH may be electronically stabilized by two parallel phenyl groups of aluminum ligands.

Introduction

Formaldehyde (gas) and α-chloro aldehydes are among the most reactive aldehydes and have been widely utilized in organic synthesis. For example, gaseous formaldehyde is indispensable as a highly reactive C_1-electrophile in a number of natural product syntheses[1] including a cytotoxic sesquiterpene, vernolepin,[2] paulownin,[3] and prostaglandins.[4] The synthetic utility of gaseous formaldehyde, in spite of its vast potential, is somewhat restricted because of its remarkably facile self-polymerization. The major barrier to its development has obviously been the difficulty associated with the generation of the reactive aldehydes. 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 the in situ generated formaldehyde with various olefins.[5] In view of their Lewis acidic conditions as well as the unstable formaldehyde–aluminum complexes, however, these methods are of limited interest and cannot be utilized for the nucleophilic addition of carbanions (organometallics, enolates, etc.) as often seen in natural product syntheses.[1-4] A similar drawback is also observed in α-chloro aldehydes. α-Chloro aldehydes belong to an important class of compounds in agricultural, medicinal, and polymer chemistry as reactive carbon electrophiles,[6] but their synthetic utility has been greatly limited due to the remarkably facile polymerization of the unstable α-chloroacetaldehyde monomers.[7] Indeed, only a 40–50% aqueous solution of α-chloroacetaldehyde is commercially available. 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: (1) the generation of reactive formaldehyde and α-chloro aldehydes from readily available trioxane and α-chloro aldehyde trimers,[8] respectively, and (2) the stabilization as formaldehyde- and α-chloro aldehyde–organoaluminum complexes to suppress self-polymerization by the exceptionally bulky aluminum ligands (Scheme I).[9] We wish to report our successful results of this study in which the utility of reactive aldehydes in organic synthesis is considerably increased as exemplified by further chemical transformation of reactive aldehyde–organoaluminum complexes with various nucleophiles.[10]

Scheme I



(R = H or CH_2Cl)

Results and Discussion

Stabilization of Formaldehyde. First, we examined the possibility of trapping gaseous formaldehyde with certain excep-

(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) Kraus, G. A.; Chen, L. *J. Am. Chem. Soc.* **1990**, *112*, 3464.

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

(5) (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.

(6) (a) Trippett, S.; Walker, D. M. *J. Chem. Soc.* **1961**, 1266. (b) Julia, M.; Bagot, J.; Siffert, O. *Bull. Chem. Soc. Fr.* **1973**, 1424. (c) Hagedorn, I.; Hohler, W. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 486. (d) De Nardo, M.; Collino, F. *Boll. Chim. Farm.* **1985**, *124*, 27. (e) Bednarski, M. D.; Simon, E. S.; Bischofberger, N.; Fessner, W.-D.; Kim, M.-J.; Lees, W.; Saito, T.; Waldmann, H.; Whitesides, G. M. *J. Am. Chem. Soc.* **1989**, *111*, 627. (f) Brockamp, H. P.; Kula, M. R. *Tetrahedron Lett.* **1990**, *31*, 7123. (g) Schmid, W.; Whitesides, G. M. *J. Am. Chem. Soc.* **1990**, *112*, 9670.

(7) Jira, R.; Kopp, E.; Moellering, W. In *Ullmanns Encyklopaedie Technischen Chemie; 4. Neubearbeitete und Erweiterte Auflage*; Bartholome, E., Biekert, E., Hellmann, H., Eds.; Verlag Chem.: Weinheim, 1975; Vol. 9, p 373. See also: Hatch, L. F.; Alexander, H. E. *J. Am. Chem. Soc.* **1945**, *67*, 688.

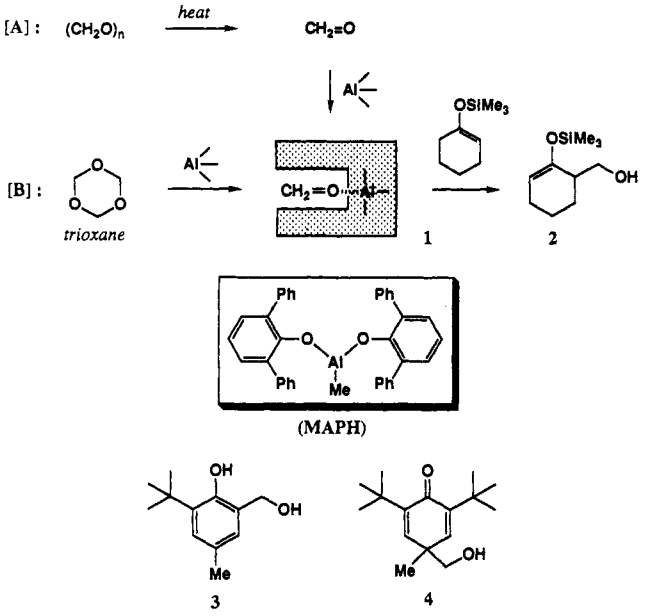
(8) (a) Ishizuka, M.; Wakasugi, T. *Eur. Pat.* 89-311506, Nov. 7, 1989. (b) Wakasugi, T.; Tonouchi, N.; Miyakawa, T.; Ishizuka, M.; Yamauchi, T.; Itsuno, S.; Ito, K. *Chem. Lett.* **1992**, 171. α-Chloro aldehyde trimers **1** and **3** were kindly provided from Kureha Chemical Industry Co., Ltd.

(9) Ab initio study of the CH_2=O·$TiCl_4$ complex. See: Branchadell, V.; Oliva, A. *J. Am. Chem. Soc.* **1992**, *114*, 4357.

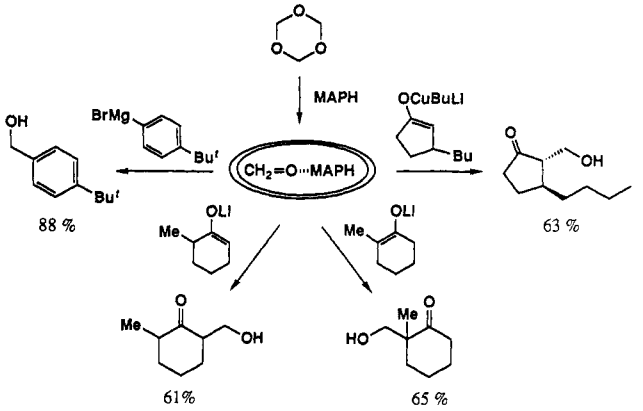
(10) Preliminary communication: Maruoka, K.; Concepcion, A. B.; Hirayama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 7422.

0002-7863/93/1515-3943$04.00/0

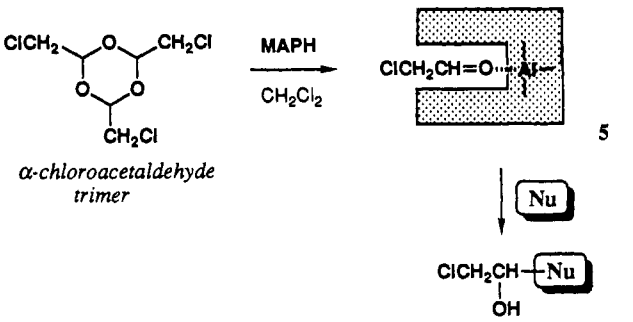
Scheme II



Scheme III



Scheme IV



tionally bulky organoaluminum reagents, and the formation of complex **1** was confirmed by the subsequent ene reaction with reactive olefins (path **A** in Scheme II). Attempted stabilization of gaseous formaldehyde with exceptionally bulky methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD)[11] in CH_2Cl_2 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%) (**3**) and 2,6-di-*tert*-butyl-4-(hydroxymethyl)-4-methyl-2,5-cyclohexadien-1-one (**4**) (18%). Switching aluminum reagents from MAD to methylaluminum bis(4-bromo-2,6-di-*tert*-butylphenoxide)[12] (MABR) suppressed the Friedel–Crafts alkylations without any ene-product formation. In marked contrast, however, methylaluminum bis(2,6-diphenylphenoxide) (MAPH)[12] 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 (**2**) in 61% yield after workup with saturated $NaHCO_3$. We then examined the stability of CH_2=O·MAPH complex and found that it was stable at 0 °C for 5 h and thereafter gradually decomposed at room temperature. These results were determined by the subsequent ene-reaction of the CH_2=O·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·MAPH complex and the yields of the ene-product **2** are as follows: 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).

Since the generation of gaseous formaldehyde by the thermal depolymerization of paraformaldehyde is often troublesome, we considered the possibility of direct formation of the CH_2=O·MAPH complex by cleaving paraformaldehyde with oxygenophilic MAPH. This proved to be difficult, however, in view of the low solubility of paraformaldehyde in CH_2Cl_2 solvent. The use of simple trioxane, which is easily soluble in CH_2Cl_2, offers major advantages as a formaldehyde source (path **B** in Scheme II). Indeed, treatment of trioxane with MAPH (3 equiv) in CH_2Cl_2 at 0 °C for 1 h successfully yielded the CH_2=O·MAPH complex, which gave a comparable result in a subsequent ene reaction [60% yield for **2**] to that from gaseous formaldehyde. The formation of this complex was further confirmed by subjection to ene reactions with various olefins (Table I). The used 2,6-diphenylphenol is readily removed chromatographically, since this nonpolar phenol comes off the column before the desired ene products. As substantiated in Table I, our method is obviously far superior in regioselectivity to previously known procedures[5] and shows strong preference for abstraction of hydrogen from CH_3 rather than from CH_2 or CH. Furthermore, this selectivity is independent of the reaction temperature (entries 1, 3, and 6). The notable chemoselectivity is also seen in the ene reaction of dihydrocarvone and geranyl acetate (entries 16 and 17). Even the basic amino functionality can be utilized without any difficulty (entry 19). In addition, the CH_2=O·MAPH complex is employable as a stable source of gaseous formaldehyde for the nucleophilic addition of various carbanions with high regio- and stereoselectivity, as illustrated in Scheme III. Consequently, it is no longer necessary to generate formaldehyde by the troublesome thermal depolymerization of paraformaldehyde.

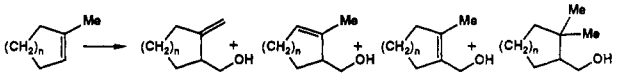
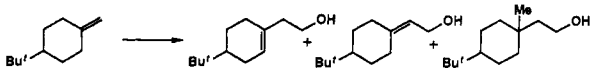
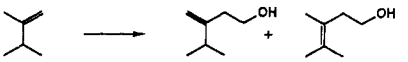
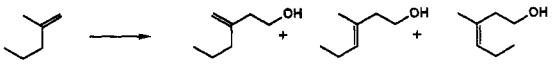
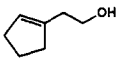
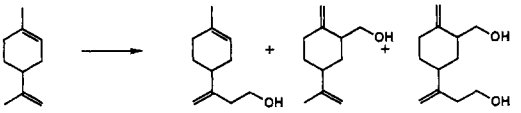
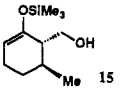
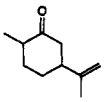
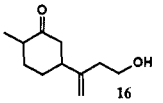
Stabilization of α-Chloro Aldehydes. Our observation of the stabilization of reactive, gaseous formaldehyde as a 1:1 coordination complex with MAPH in conjunction with the recent availability of stable α-chloro aldehyde trimer[8] has stimulated us to study the generation of reactive α-chloro aldehyde from the trimer and its stabilization as the MAPH complex **5** to suppress self-polymerization by the 2,6-diphenylphenoxy aluminum ligands (Scheme IV).

Reaction of α-chloroacetaldehyde trimer (1 equiv) with MAPH (3 equiv) in CH_2Cl_2 at 20 °C for 5 h yielded α-chloroacetaldehyde–MAPH complex **5**, which on subsequent treatment with lithium cyclohexenolate (as nucleophile) in THF at −78 °C gave rise to the aldol adduct 2-(2-chloro-1-hydroxyethyl)cyclohexanone in 83% yield. Attempted reaction of lithium cyclohexenolate in THF with α-chloroacetaldehyde trimer under similar reaction conditions gave none of the desired aldol adducts. The yield of α-chloroacetaldehyde–MAPH complex **5** is lowered on treatment of α-chloroacetaldehyde trimer with MAPH in CH_2Cl_2 at 20 °C

(11) (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. (c) Maruoka, K.; Saito, S.; Yamamoto, H. *Ibid.* **1992**, *114*, 1089.

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

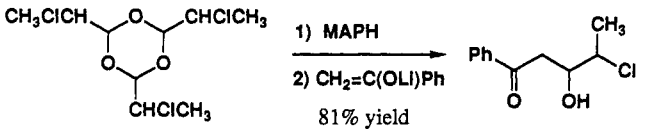
Table I. Reaction of Formaldehyde–Organoaluminum Complexes with Olefins

entry	olefin	reagent	conditions (°C, h)	products, % (ratio)
				
1	(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	(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 (44:21:35)
				
8		CH_2=O·MAPH[a]	0, 0.5	64 (100:0)
9		CH_2=O·$AlMe_2Cl$[b]	25, 12	96 (75:25)
				
10		CH_2=O·MAPH[a]	−78, 1	66 (70:24:6)
11		CH_2=O·$AlMe_2Cl$[b]	25, 18	89 (40:36:24)
12		CH_2=O·MAPH[a]	−78, 1	 88
				
13		CH_2=O·MAPH[a]	−78, 1	97 (72:28:0)
14		CH_2=O·$AlMe_2Cl$[d]	25, 1	89 (42:2:56)
15		CH_2=O·MAPH[a]	0, 0.5	 71
16		CH_2=O·MAPH[a]	0, 0.5	 90
				
17		CH_2=O·MAPH[a]	0, 0.5	86
18		CH_2=O·$AlMe_2Cl$[d]	25, 1	3[f]
				
19		CH_2=O·MAPH[c]	0, 1	67

[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 5a. [c] See ref 5b. [d] This ene reaction was carried out according to ref 5a. [e] The ene reactions at a higher temperature (~0 °C) showed similar selectivities. [f] Complex reaction mixtures were formed.

for shorter or longer reaction time (e.g., 3 or 10 h). Decreasing the stoichiometry of the complex **5** lowered the yields of aldol adducts (2 equiv, 70%; 1 equiv, 44%).

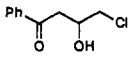
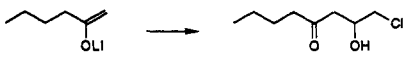
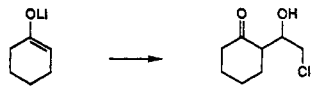
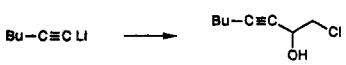
As revealed in Table II, the α-chloroacetaldehyde–MAPH complex **5** can be utilized as a stable source of α-chloroacetaldehyde for the nucleophilic addition of various carbanions under mild conditions. The reaction proceeds in a highly regioselective manner (entries 2 and 4). Similarly, stabilization of other α-chloro aldehydes with MAPH appears feasible.[8] For example, α-chloropropionaldehyde–MAPH complex can be generated from the corresponding α-chloro aldehyde trimer **6**and subsequently trapped with lithium 1-phenylethenolate to furnish aldol adduct **7** in 81% yield.



6 **7**

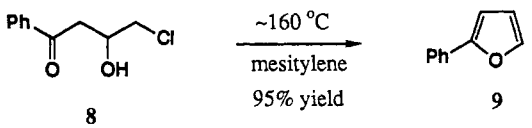
The versatility of functionalized chloro aldols in synthetic as well as heterocyclic chemistry serves as a stimulus for exploration of the potential applications of this methodology. Accordingly, we have devised a new stereoselective approach to furans by a

Table II. Reaction of α-Chloroacetaldehyde/MAPH Complex **5** with Various Nucleophiles[a]

entry	nucleophile	conditions (°C, h)	product	yield[b] (%)
1		−78, 0.5	 **8**	90
2		−78, 0.5		75
3		−78, 0.5	**10**	83[c]
4		−78, 0.5		74[d,e]
5		0, 4; 20, 1		57

[a] The α-chloroacetaldehyde/MAPH complex **5** (3 equiv) was prepared by treatment of α-chloroacetaldehyde trimer (1 equiv) with MAPH (3 equiv) at 20 °C for 5 h and subsequently reacted with nucleophiles under the indicated conditions. [b] Isolated yield. [c] Ratio of erythro/threo = 2:1. [d] The copper enolate was generated in situ on treatment of cyclohexenone with Bu_2CuLi in ether at −20 °C. [e] Ratio of erythro/threo = ~1:1.

direct cyclization of the chloro aldols.[13] Thus, heating of 4-chloro-3-hydroxy-1-phenyl-1-butanone (**8**) in mesitylene under reflux for 7.5 h led to the formation of 2-phenylfuran (**9**) in 95% yield.



8 **9**

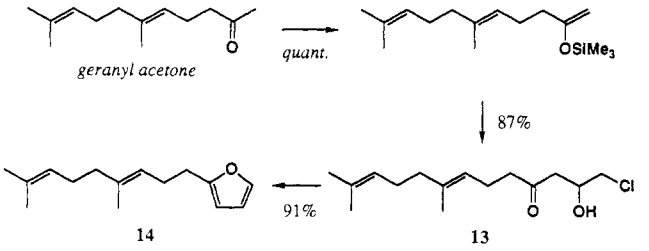
11

12

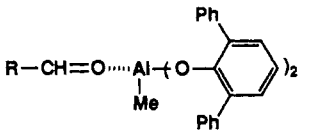
In a similar manner, 4-chloro-3-hydroxy-1-phenyl-1-pentanone (**7**) and *trans*-3-butyl-2-(2-chloro-1-hydroxyethyl)cyclohexanone (**10**) were transformed to the corresponding furans **11** and **12** in 83% and 71% yields, respectively, by heating at ~160 °C.

Hence, the present synthetic approach provides a new access to a facile synthesis of various furans (e.g., **14**) as flavor and fragrance compounds from readily available terpene ketones, as illustrated in Scheme V.[14]

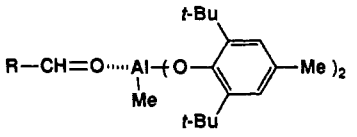
Scheme V



NMR Study of Aldehyde–MAPH Complexes. In order to verify the existence of hypothetical aldehyde–MAPH complexes, we carried out a ^1H NMR spectral study of the coordination complexes in $CDCl_3$. The CH_2=O signals of free formaldehyde monomer occurred at δ 9.60.[15] When trioxane was mixed with MAPH in a 1:3 molar ratio in $CDCl_3$ at 0 °C for 1 h, a CH_2=O···Al singlet was observed at δ 6.04 by room-temperature ^1H NMR analysis. The ^1H NMR measurement of the CH_2=O·MAPH complex at low temperature (−50 °C) showed a similar chemical-shift value (δ 5.85). In a similar manner, α-chloroacetaldehyde–MAPH complex **5**, generated from α-chloroacetaldehyde trimer and MAPH, showed a CH=O···Al triplet at δ 6.63 and a $ClCH_2$ doublet at δ 2.43. *Notably, there is always an upfield shift of aldehyde protons in the aldehyde–MAPH complexes from free aldehydes.* In fact, butyraldehyde–MAPH and pivalaldehyde–MAPH complexes, which were prepared simply by mixing of the corresponding aldehydes with MAPH in $CDCl_3$ at 0 °C, also exhibit CH=O···Al signals at δ 6.91 and 6.73, respectively, at room temperature. These results are in marked contrast to the low-temperature ^1H NMR data of pivalaldehyde–MAD and benzaldehyde–MAD complexes, where CH=O···Al peaks appear at δ 9.40 and 9.65, respectively, close to the normal values of free aldehydic protons. It should be added that the ^1H NMR measurement of these aldehyde–MAD complexes at room temperature gave only broad peaks.



aldehyde-MAPH complex



aldehyde-MAD complex

Since dimethylaluminum 2,6-diphenylphenoxide and methylaluminum bis(2-phenylphenoxide) as MAPH analogues are totally ineffective for the stabilization of formaldehyde in conjunction with the quite different behaviors of aldehyde–MAPH complexes in ^1H NMR spectroscopy, the origin of the remarkable effect of MAPH on such stabilization is worthy of comment. In a space-filling model of the α-chloroacetaldehyde–MAPH complex (Figure 1), each phenyl group of two phenoxy ligands is parallel to the other in front of the Lewis acidic aluminum so that the reactive α-chloroacetaldehyde carbonyl by coordination to MAPH is electronically stabilized by a sandwich structure between these two phenyl groups. This inference is in accord with the ^1H NMR data on the upfield shift of aldehydic protons in the aldehyde–MAPH complexes.

(13) Recent furan syntheses: (a) Mukaiyama, T.; Ishihara, H.; Inomata, K. *Chem. Lett.* **1975**, 527. (b) Kretchmer, R. A.; Laitar, R. A. *J. Org. Chem.* **1978**, *43*, 4596. (c) Bartlett, S.; Chambers, R. D.; Kelly, N. M. *Tetrahedron Lett.* **1980**, *21*, 1891. (d) Garst, M. E.; Spencer, T. A. *J. Org. Chem.* **1983**, *48*, 2442. (e) Minami, I.; Yuhara, M.; Watanabe, H.; Tsuji, J. *J. Organomet. Chem.* **1987**, *334*, 225. (f) Jansen, B. J. M.; Peperzak, R. M.; de Groot, Ae. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 549. (g) McCombie, S. W.; Shankar, B. B.; Ganguly, A. K. *Tetrahedron Lett.* **1987**, *28*, 4123. (h) Srikrishna, A.; Pullaiah, K. C. *Ibid.* **1987**, *28*, 5203. (i) Hiroi, K.; Sato, H. *Synthesis* **1987**, 811. (j) Sato, S.; Matsuda, I.; Izumi, Y. *Tetrahedron Lett.* **1987**, *28*, 6657. (k) Davies, H. M. L.; Romines, K. R. *Tetrahedron* **1988**, *44*, 3343. (l) Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 4407. (m) Marshall, J. A.; Robinson, E. D. *J. Org. Chem.* **1990**, *55*, 3450.

(14) *The Chemistry of Heterocyclic Flavoring and Aroma Compounds*; Vernin, G., Ed.; Ellis Horwood: Chichester, 1982.

(15) Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Structuraufklarung Organischer Verbindungen mit Spectroskopischen Methoden*; Springer-Verlag: Heidelberg, 1976.

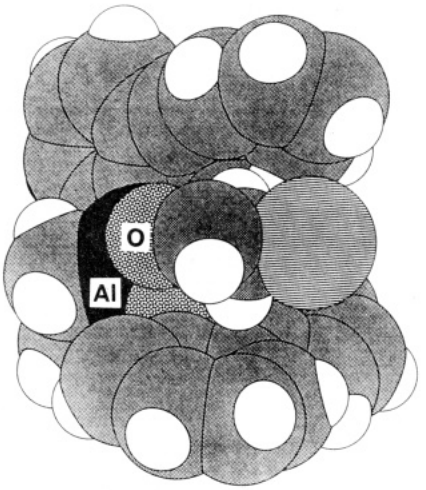


Figure 1. Space-filling model of the α-chloroacetaldehyde–MAPH complex, where the Al and CO oxygen are specifically labeled.

Conclusions

This study illustrates the generation of reactive aldehydes (formaldehyde and α-chloro aldehydes) from readily available trioxane and α-chloro aldehyde trimers and their stabilization as formaldehyde–MAPH and α-chloro aldehyde–MAPH complexes to suppress self-polymerization by two 2,6-diphenylphenoxy aluminum ligands. The resulting aldehyde–MAPH complexes are highly useful as a stable source of reactive aldehydes for further chemical transformation in selective organic synthesis since they react with a variety of nucleophiles such as olefins and carbanions with high selectivity. Consequently, the bulky organoaluminum reagent MAPH may play an important role as an artificial enzyme for recognition and stabilization of aldehydes. A more sophisticated design of aluminum ligands and a more detailed characterization of aldehyde recognition by their artificial enzymes are subjects of our ongoing study.

Experimental Section

Preparation of Olefins. 1-(Trimethylsiloxy)-3-methyl-1-cyclohexene was prepared according to a literature procedure.[16] *N*-Geranyl-*N*-methylaniline was synthesized by treatment of *N*-methylaniline with genanyl bromide and NaH in THF.

Preparation of MAD. To a solution of 2,6-di-*tert*-butyl-4-methylphenol (2 equiv) in CH_2Cl_2 was added at room temperature a 2 M hexane solution of Me_3Al (1 equiv). The methane gas (~2 equiv) evolved immediately. The resulting colorless solution was stirred at room temperature for 1 h and used as a solution of MAD in CH_2Cl_2 without any purification. Other modified organoaluminum reagents such as MABR, methylaluminum bis(2-phenylphenoxide), and dimethylaluminum 2,6-diphenylphenoxide were prepared in situ from Me_3Al and the corresponding phenols in CH_2Cl_2 at room temperature for 1 h.

Generation of Formaldehyde. The gaseous formaldehyde was generated by the thermal depolymerization of paraformaldehyde (dried over phosphorus pentoxide under vacuum) at 150 °C and introduced to the flask containing CH_2Cl_2 at –78 °C. Use of higher temperature should be avoided because small amounts of protic impurities can be transferred into the reaction mixture.

Attempted Trapping of Formaldehyde with MAD. To a solution of MAD (1 mmol) in CH_2Cl_2 (5 mL) was added at –78 °C a solution (~2 mL) of formaldehyde in CH_2Cl_2. The mixture was stirred at –78 °C for 15 min and 1-(trimethylsiloxy)-1-cyclohexene (0.5 mmol) was added at this temperature. The reaction mixture was stirred at –78 °C for 1 h and at –40 °C for 4 h. This was poured into 1 N HCl and extracted with CH_2Cl_2. The organic layers were washed with brine. The combined CH_2Cl_2 extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel to furnish 2-*tert*-butyl-6-(hydroxymethyl)-4-methylphenol (**3**) (156 mg, 42%) and 2,6-di-*tert*-butyl-4-(hydroxymethyl)-4-methylcyclohexa-2,5-dien-1-one (**4**) (90 mg, 18%).

(16) Boeckman, R. K. *J. Am. Chem. Soc.* **1974**, *96*, 6179.

2-*tert*-Butyl-6-(hydroxymethyl)-4-methylphenol:[17] 200 MHz ^{1}H NMR ($CDCl_3$) δ 7.52 (1H, s, ArOH), 7.04 (1H, d, J = 2.5 Hz, Ar-H), 6.70 (1H, d, J = 2.5 Hz, Ar-H), 4.77 (2H, d, J = 6 Hz, CH_2O), 2.25 (3H, s, CH_3), 1.41 (9H, s, *t*-Bu); IR (liquid film) 3375 (OH), 2957, 2922, 2872, 1482, 1449, 1391, 1360, 1235, 1206, 862 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.36; H, 9.52. 2,6-Di-*tert*-butyl-4-(hydroxymethyl)-4-methylcyclohexa-2,5-dien-1-one: ^{1}H NMR ($CDCl_3$) δ 6.83 (2H, m, Ar-H), 4.37 (2H, d, J = 6.5 Hz, CH_2O), 2.94 (1H, t, J = 6.5 Hz, OH), 1.25 (9H, s, *t*-Bu), 1.20 (3H, s, CH_3), 0.97 (9H, s, *t*-Bu); IR (liquid film) 3441 (OH), 2961, 2872, 1671, 1634, 1456, 1366, 1227, 1190, 936, 916, 884 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.99; H, 10.63.

Preparation of Formaldehyde–MAPH Complex. (a) From Gaseous Formaldehyde. To a solution of 2,6-diphenylphenol (3 mmol) in CH_2Cl_2 (15 mL) was added at room temperature a 2 M hexane solution of Me_3Al (1.5 mmol). The methane gas evolved immediately. The resulting colorless solution was stirred at room temperature for 1 h to furnish a solution of MAPH in CH_2Cl_2. Then a CH_2Cl_2 solution (~2 mL) of gaseous formaldehyde, generated by the thermal depolymerization of paraformaldehyde, was introduced to a solution of MAPH in CH_2Cl_2 at –78 °C and used as a solution of CH_2=O·MAPH complex in CH_2Cl_2 for subsequent ene reactions.

(b) From Trioxane. A solution of MAPH (1.5 mmol) in CH_2Cl_2 (10 mL) was prepared exactly as described above. To this was added a solution of trioxane (0.5 mmol) in CH_2Cl_2 (0.2 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h and used as a solution of CH_2=O·MAPH complex in CH_2Cl_2 for subsequent reactions without any purification.

Ene Reaction of 1-(Trimethylsiloxy)-1-cyclohexene.[5c] To a solution of the CH_2=O·MAPH complex (1 mmol, prepared from gaseous formaldehyde) in CH_2Cl_2 (10 mL) was added 1-(trimethylsiloxy)-1-cyclohexene (0.5 mmol) at –78 °C, and the resulting mixture was stirred at –20 °C for 5.5 h. The solution was then poured into saturated $NaHCO_3$ and extracted with CH_2Cl_2. Evaporation of solvents and purification of the residue by column chromatography on silica gel (ether/hexane = 1:3) gave 6-(hydroxymethyl)-1-(trimethylsiloxy)-1-cyclohexene (**2**) (61 mg, 61% yield) as a colorless oil: 200 MHz ^{1}H NMR ($CDCl_3$) δ 4.92 (1H, dd, J = 2.8, 4 Hz, CH=), 3.64 (2H, d, J = 6.2 Hz, CH_2O), 2.46 (1H, br s, OH), 2.30 (1H, m, CHC=C), 2.01 (2H, m, CH_2C=C), 1.38–1.85 (4H, m, CH_2CH_2), 0.22 (9H, s, $Si(CH_3)_3$); IR (liquid film) 3375 (OH), 3048, 2932, 2841, 1663, 1252, 1179, 909, 845 cm^{-1}. Anal. Calcd for $C_{10}H_{20}O_2Si$: C, 59.95; H, 10.06. Found: C, 59.98; H, 10.20.

Stability of Formaldehyde–MAPH Complex. To a solution of MAPH (1 mmol) in CH_2Cl_2 (10 mL) was added at –78 °C a CH_2Cl_2 solution (~2 mL) of gaseous formaldehyde. The resulting CH_2=O·MAPH complex in CH_2Cl_2 was stirred at –78 to 25 °C for 15 min to 24 h and treated with 1-(trimethylsiloxy)-1-cyclohexene (0.5 mmol) at –20 °C. Stirring was continued at –20 °C for a few hours. The solution was then poured into diluted HCl and extracted with CH_2Cl_2. Evaporation of solvents and purification of the residue by column chromatography on silica gel (ether/hexane = 1:1) afforded 2-(hydroxymethyl)cyclohexanone in the yields indicated as follows: 61% (–78 °C, 15 min); 60% (0 °C, 15 min); 45% (0 °C, 3 h); 50% (0 °C, 5 h); 19% (25 °C, 1 h); 2% (25 °C, 24 h).

General Procedures for Ene Reactions. To a solution of the CH_2=O·MAPH complex (1.5 mmol, prepared from trioxane) in CH_2Cl_2 (15 mL) was added olefin (0.5 mmol) at –78 °C, and the resulting mixture was stirred under the conditions indicated in Table I. The solution was then poured into diluted HCl and extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel (ether/hexane as eluants) to furnish ene products. The used 2,6-diphenylphenol can be readily removed chromatographically from the crude products, since this nonpolar phenol comes off the column before the desired ene products.

2-(Hydroxymethyl)-1-methylenecyclopentane:[5a] ^{1}H NMR ($CDCl_3$) δ 5.00 (1H, m, CH=), 4.90 (1H, m, CH=), 3.59 (2H, d, J = 6.4 Hz, CH_2O), 1.45–2.75 (8H, m, cyclopentyl and OH); IR (liquid film) 3343 (OH), 3073, 2953, 2870, 1651, 1435, 1075, 1026, 882 cm^{-1}. Anal. Calcd for $C_7H_{12}O$: C, 74.96; H, 10.78. Found: C, 74.90; H, 10.93.

2-(Hydroxymethyl)-1-methylenecyclohexane:[5a] ^{1}H NMR ($CDCl_3$) δ 4.79 (1H, m, CH=), 4.65 (1H, m, CH=), 3.45–3.75 (2H, d, J = 6.4 Hz, CH_2O), 1.20–2.40 (8H, m, cyclopentyl and OH); IR (liquid film) 3333 (OH), 3079, 2930, 2857, 1646, 1447, 1028, 887 cm^{-1}. Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.15; H, 11.31.

2-(4-*tert*-Butyl-1-cyclohexenyl)ethanol:[5b] ^{1}H NMR ($CDCl_3$) δ 5.55 (1H, m, CH=), 3.68 (2H, t, J = 6 Hz, CH_2O), 2.24 (2H, t, J = 6 Hz,

(17) Baldwin, J. E.; Cacioli, P.; Reiss, J. A. *Tetrahedron Lett.* **1980**, *21*, 4971.

OCH_2CH_2C=), 1.05–2.15 (8H, m, cyclohexenyl and OH), 0.88 (9H, s, *t*-Bu); IR (liquid film) 3344 (OH), 2963, 2886, 2842, 1475, 1435, 1393, 1364, 1048 cm^{-1}. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.08; H, 12.26.

3-Isopropyl-3-buten-1-ol:[5a] ^1H NMR ($CDCl_3$) δ 4.84 (2H, d, J = 24 Hz, CH_2=), 3.73 (2H, t, J = 6.6 Hz, CH_2O), 2.33 (2H, t, J = 6.6 Hz, CH_2CO), 2.27 (1H, heptet, J = 6.6 Hz, CHC=C), 1.68 (1H, br s, OH), 1.05 (6H, d, J = 6.6 Hz, $2CH_3$); IR (liquid film) 3333 (OH), 3087, 2963, 2876, 1642, 1466, 1048, 891 cm^{-1}. Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.85; H, 12.50.

Ene Reaction with 2-Methyl-1-pentene. The isomeric ratio of three ene products, 3-propyl-3-buten-1-ol, (*E*)-3-methyl-3-hexen-1-ol, and (*Z*)-3-methyl-3-hexen-1-ol, was determined to be 70:24:6 by capillary GLC analysis in comparison with authentic samples.[5a]

2-(1-Cyclopentenyl)ethanol:[5a] ^1H NMR ($CDCl_3$) δ 5.49 (1H, m, CH=), 3.73 (2H, t, J = 6.2 Hz, CH_2O), 1.50–2.48 (9H, m, $(CH_2)_3$ and OH); IR (liquid film) 3337 (OH), 3046, 2950, 2894, 2847, 1445, 1048, 1022 cm^{-1}. Anal. Calcd for $C_7H_{12}O$: C, 74.96; H, 10.78. Found: C, 74.94; H, 11.03.

Ene Reaction with Limonene. The isomeric ratio of three ene products, 3-(4-methyl-3-cyclohexenyl)-3-buten-1-ol, (5-isopropyl-2-methylenecyclohexyl)methanol, and [3-(hydroxymethyl)-4-methylenecyclohexyl]-3-buten-1-ol, was determined to be 72:28:0 by capillary GLC analysis in comparison with authentic samples, which were prepared according to the literature procedure.[5a] 3-(4-Methyl-3-cyclohexenyl)-3-buten-1-ol: ^1H NMR ($CDCl_3$) δ 5.41 (1H, s, CH=), 4.87 (2H, d, J = 13.6 Hz, CH_2=), 3.72 (2H, t, J = 6.4 Hz, CH_2O), 2.35 (2H, t, J = 6.4 Hz, CH_2CO), 1.37–2.23 (8H, m, CH, CH_2, and OH), 1.66 (3H, s, CH_3); IR (liquid film) 3322 (OH), 3083, 2963, 2919, 2836, 1640, 1437, 1046, 891, 799 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.50; H, 11.01.

Ene Product 15 from 3-methyl-1-(trimethylsiloxy)-1-cyclohexene: ^1H NMR ($CDCl_3$) δ 4.97 (1H, t, J = 4 Hz, CH=), 3.80 (1H, dd, J = 4, 10.8 Hz, CHO), 3.64 (1H, dd, J = 6, 10.8 Hz, CHO), 2.46 (1H, br s, OH), 2.03 (2H, m, CH_2C=C), 1.87 (1H, m, CHC=C), 1.64 (2H, m, CH_2), 1.28 (1H, m, CH), 1.03 (3H, d, J = 6 Hz, CH_3), 0.22 (9H, s, $Si(CH_3)_3$); IR (liquid film) 3406 (OH), 2959, 2926, 2847, 1667, 1252, 1184, 912, 847, 756 cm^{-1}. Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C, 61.60; H, 10.28.

Ene product 16 from dihydrocarvone: ^1H NMR ($CDCl_3$) δ 4.92 (2H, dd, J = 1, 7.2 Hz, CH_2=), 3.73 (2H, t, J = 6.6 Hz, CH_2O), 2.33 (2H, dt, J = 1, 6.6 Hz, CH_2CO), 1.22–2.50 (9H, m, CH, CH_2 and OH), 1.04 (3H, d, J = 6.4 Hz, CH_3); IR (liquid film) 3490 (OH), 2932, 1711 (C=O), 1449, 1049, 897 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.22; H, 10.11.

Ene product 17 from geranyl acetate: ^1H NMR ($CDCl_3$) δ 5.33 (1H, t, J = 7 Hz, CH=), 4.91 (2H, d, J = 26.8 Hz, CH_2=), 4.59 (2H, d, J = 7 Hz, C=CCH_2O), 3.52 (2H, d, J = 7.6 Hz, CH_2O), 2.27 (1H, quintet, J = 7.6 Hz, CHCO), 2.04 (3H, s, CH_3C=O), 1.94–2.11 (2H, m, CH_2), 1.69 (6H, d, J = 2.2 Hz, $2CH_3$), 1.38–1.58 (3H, m, CH_2 and OH); IR (liquid film) 3420 (OH), 2936, 1740 (C=O), 1445, 1368, 1235, 1024, 953, 893 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.97; H, 10.04.

Ene product 18 from *N*-geranyl-*N*-methylaniline: ^1H NMR ($CDCl_3$) δ 7.20 (2H, t, J = 6.5 Hz, *m*-Ar-H), 6.67 (3H, d, J = 6.5 Hz, *o,p*-Ar-H), 4.86 (2H, d, J = 26 Hz, CH_2=), 3.22–3.54 (4H, m, CH_2N and CH_2O), 2.91 (3H, s, CH_3N), 2.21 (1H, m, =CCH), 1.67 (3H, s, =CCH_3), 1.06–1.61 (8H, m, CH, CH_2, and OH), 0.94 (3H, d, J = 6.2 Hz, CH_3); IR (liquid film) 3385 (OH), 2928, 2870, 1601, 1507, 1374, 747, 693 cm^{-1}. Anal. Calcd for $C_{18}H_{29}NO$: C, 78.49; H, 10.61; N, 5.09. Found: C, 78.47; H, 10.59; N, 4.98.

Reaction with Grignard Reagent. To a solution of the CH_2=O·MAPH complex (1.5 mmol, prepared from trioxane) in CH_2Cl_2 (15 mL) was added at –78 °C a 0.62 M ethereal solution of (4-*tert*-butylphenyl)-magnesium bromide (2.4 mL, 1.5 mmol). The resulting solution was stirred at –78 °C for 1.5 h, at –40 °C for 1 h, and at 0 °C for 1 h. The mixture was poured into diluted HCl and extracted with CH_2Cl_2. The combined extracts were dried, concentrated, and purified by column chromatography on silica gel to furnish (4-*tert*-butylphenyl)methanol (72 mg, 88% yield):[18] TLC R_f = 0.15 (ether/hexane = 1:1); ^1H NMR ($CDCl_3$) δ 7.38 (4H, m, Ar-H), 4.67 (2H, d, J = 5 Hz, CH_2O), 1.73 (1H, t, J = 5 Hz, OH), 1.32 (9H, s, *t*-Bu); IR (liquid film) 3333 (OH), 2963, 2905, 2869, 1364, 1042, 1015 cm^{-1}. Anal. Calcd for $C_{11}H_{26}O$: C, 80.44; H, 9.82. Found: C, 80.48; H, 9.96.

(18) Cristol, S. J.; Bindel, T. H. *J. Org. Chem.* **1980**, *45*, 951.

Aldol Reaction with Lithium 2-Methylcyclohexenolate. To a solution of the CH_2=O·MAPH complex (1.5 mmol, prepared from trioxane) in CH_2Cl_2 (15 mL) was added at –78 °C a solution of lithium 2-methylcyclohexenolate in THF, which was prepared from 2-methyl-1-(trimethylsiloxy)-1-cyclohexene (0.5 mmol) and a 1.5 M ethereal solution of MeLi (0.55 mmol) in THF (2 mL) at 0 °C for 20 min. The resulting mixture was stirred at –78 °C for 1 h and at 0 °C for 2 h. The solution was then poured into diluted HCl and extracted with CH_2Cl_2. The combined extracts were dried, concentrated, and purified by column chromatography on silica gel (ether/hexane = 2:1 as eluant) to furnish 2-(hydroxymethyl)-2-methylcyclohexanone (46 mg, 65% yield) as a colorless oil:[19] TLC, R_f = 0.21 (ether/hexane = 2:1); ^1H NMR ($CDCl_3$) δ 3.51 (2H, d, J = 6 Hz, CH_2O), 1.40–2.75 (9H, m, cyclohexyl and OH), 1.20 (3H, s, Me); IR (liquid film) 3458 (OH), 2938, 2869, 1701 (C=O), 1046 cm^{-1}. Anal. Calcd for $C_8H_{14}O_2$: C, 67.58; H, 9.92. Found: C, 67.68; H, 10.07.

Aldol Reaction with Lithium 6-Methylcyclohexenolate. To a solution of the CH_2=O·MAPH complex (1.5 mmol, prepared from trioxane) in CH_2Cl_2 (15 mL) was added at –78 °C a solution of lithium 6-methylcyclohexenolate in THF, which was prepared from 6-methyl-1-(trimethylsiloxy)-1-cyclohexene (0.5 mmol) and a 1.5 M ethereal solution of MeLi (0.55 mmol) in THF (2 mL) at 0 °C for 20 min. The resulting mixture was treated as described above to furnish 2-(hydroxymethyl)-6-methylcyclohexanone (43 mg, 61% yield; isomeric ratio = 2.4:1) as a colorless oil:[20] ^1H NMR ($CDCl_3$) δ 3.55–3.85 (2H, m, CH_2O), 1.25–2.80 (9H, m, cyclohexyl and OH), 1.19 (3H, d, J = 7 Hz, Me), 1.03 (3H, d, J = 5.5 Hz, Me); IR (liquid film) 3417 (OH), 2934, 2869, 1704 (C=O), 1456, 1048 cm^{-1}. Anal. Calcd for $C_8H_{14}O_2$: C, 67.58; H, 9.92. Found: C, 67.62; H, 9.99.

Conjugate Addition/Alkylation of 2-Cyclopentenone. To a suspension of CuI (137 mg, 0.72 mmol) in ether (2 mL) was added at –20 °C a 1.6 M hexane solution of BuLi (0.9 mL, 1.44 mmol). The mixture was stirred at –20 °C for 20 min and treated with 2-cyclopentenone (41 mg, 0.5 mmol) at this temperature for 10 min. The in situ generated copper enolate of 3-butylcyclopentanone in ether/hexane was then transferred via cannula to a solution of the CH_2=O·MAPH complex (1.5 mmol, prepared from trioxane) in CH_2Cl_2 (15 mL) at –78 °C. The whole mixture was stirred at –78 °C for 30 min and worked up with saturated NH_4Cl. The crude products were chromatographed on a silica gel column by using a 1:2 mixture of ether and hexane as eluant to give *trans*-3-butyl-2-(hydroxymethyl)cyclopentanone (53 mg, 63% yield) as a colorless oil: ^1H NMR ($CDCl_3$) δ 3.90 (1H, dd, J = 3.8, 11.2 Hz, CHO), 3.68 (1H, ddd, J = 3.8, 6.2, 11.2 Hz, CHO), 2.02–2.50 (3H, m, CH_2C(=O)CH), 1.18–2.02 (10H, m, CH, CH_2, and OH), 0.92 (3H, t, J = 6.2 Hz, CH_3); IR (liquid film) 3447 (OH), 2957, 2928, 2872, 2860, 1740 (C=O), 1406, 1159, 1051 cm^{-1}. Anal. Calcd for $C_{10}H_{17}O_2$: C, 70.97; H, 10.12. Found: C, 70.77; H, 10.32.

Preparation of α-Chloroacetaldehyde–MAPH Complex. A solution of MAPH (1.5 mmol) in CH_2Cl_2 (10 mL) was prepared as described above. To this was added a solution of α-chloroacetaldehyde trimer (118 mg, 0.5 mmol) in CH_2Cl_2 (0.2 mL) at 20 °C. The mixture was stirred at 20 °C for 5 h and used as a dark yellow solution of $ClCH_2$-CH=O·MAPH complex in CH_2Cl_2 for subsequent reactions without any purification.

Aldol Reaction with Lithium Cyclohexenolate. To a solution of the $ClCH_2CH$=O·MAPH complex (1.5 mmol, prepared from α-chloroacetaldehyde trimer) in CH_2Cl_2 (15 mL) was transferred at –78 °C a solution of lithium cyclohexenolate in THF, which was prepared from 1-(trimethylsiloxy)-1-cyclohexene (85 mg, 0.5 mmol) and a 1.4 M ethereal solution of MeLi (0.39 mL, 0.55 mmol) in THF (2 mL) at 0 °C for 20 min. The resulting mixture was stirred at –78 °C for 30 min, poured into diluted HCl, and extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel (ether/hexane = 1:1 to 3:2 as eluants) to furnish a mixture of *erythro*- and *threo*-2-(2-chloro-1-hydroxyethyl)cyclohexanone (73 mg, 83% yield) as a colorless oil: ^1H NMR ($CDCl_3$) δ 4.24 (q, J = 5 Hz, erythro CHO), 3.94 (m, threo CHO), 3.45–3.77 (2H, m, CH_2Cl), 2.27–2.76 (3H, CHC=O and CH_2C=O); IR (liquid film) 3490 (OH), 2942, 2865, 1705 (C=O), 1620, 1451, 1273, 1132 cm^{-1}.

The erythro/threo ratio was determined to be 2:1 by the reductive conversion to the known 2-(1-hydroxyethyl)cyclohexanone[21] with catalytic AIBN/Bu_3SnH in benzene under reflux. 2-(1-Hydroxyethyl)cyclohexanone: ^1H NMR ($CDCl_3$) δ 4.26 (m, erythro CHO), 3.93 (m, threo CHO), 3.64 (d, J = 4 Hz, threo OH), 2.71 (d, J = 5 Hz, erythro OH).

(19) Hirano, F.; Wakabayashi, S. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2579.
(20) Kobayashi, S. *Chem. Lett.* **1991**, 2187.
(21) Curran, D. *J. Am. Chem. Soc.* **1983**, *105*, 5826.

4-Chloro-3-hydroxy-1-phenyl-1-butanone (8): ^{1}H NMR ($CDCl_3$) δ 7.90–8.01 (2H, m, Ar-H), 7.40–7.65 (3H, m, Ar-H), 4.45 (1H, m, CHO), 3.68 (2H, d, J = 6.5 Hz, CH_2Cl), 3.37 (1H, br s, OH), 3.29 (2H, d, J = 5 Hz, CH_2C=O); IR (liquid film) 3456 (OH), 1682 (C=O), 1597, 1449, 1217, 1053, 756, 733, 691 cm^{-1}. The structure **8** was confirmed by conversion to a known dechlorination product, 3-hydroxy-1-phenyl-1-butanone,[22] with catalytic AIBN/Bu_3SnH in benzene under reflux.

1-Chloro-2-hydroxy-4-octanone: ^{1}H NMR ($CDCl_3$) δ 4.25 (1H, quintet, J = 5 Hz, CHO), 3.54 (2H, d, J = 5 Hz, CH_2Cl), 3.20 (1H, br s, OH), 2.70 (2H, d, J = 5 Hz, $OCCH_2C$=O), 2.43 (2H, t, J = 7 Hz, CH_2C=O), 1.55 (2H, m, CH_2), 1.29 (2H, m, CH_2), 0.88 (3H, t, J = 7 Hz, CH_3); IR (liquid film) 3438 (OH), 2961, 2934, 2874, 1709 (C=O), 1381, 1046, 750, 702 cm^{-1}. The structure was confirmed by conversion to a known dechlorination product, 2-hydroxy-4-octanone,[23] with catalytic AIBN/Bu_3SnH in benzene under reflux.

***trans*-3-Butyl-2-(2-chloro-1-hydroxyethyl)cyclohexanone (10).** The title compound was prepared as a ~1:1 erythro/threo mixture according to the procedure of conjugate addition/alkylation sequence of 2-cyclopentanone with Bu_2CuLi and CH_2=O·MAPH complex. These isomers can be separated by column chromatography on silica gel (ether/hexane = 1:2 to 1:1 as eluants).

Trans-erythro isomer: ^{1}H NMR ($CDCl_3$) δ 3.93 (1H, m, CHO), 3.60–3.79 (2H, m, CH_2Cl), 2.58 (1H, dd, J = 2.2, 10 Hz, CHC=O), 2.39 (2H, m, CH_2C=O), 1.21–2.17 (12H, m, CH, CH_2, and OH), 0.91 (3H, br t, CH_3); IR (liquid film) 3428 (OH), 2957, 2932, 2875, 1698 (C=O), 1088, 911, 735 cm^{-1}.

Trans-threo isomer: ^{1}H NMR ($CDCl_3$) δ 4.08 (1H, m, CHO), 3.52–3.80 (2H, m, CH_2Cl), 2.73 (1H, br s, OH), 2.51 (1H, t, J = 8.2 Hz, CHC=O), 2.35 (2H, m, CH_2C=O), 1.17–2.08 (11H, m, CH and CH_2), 0.90 (3H, br t, CH_3); IR (liquid film) 3420 (OH), 2957, 2932, 2876, 1698 (C=O), 1468, 1429, 1228, 910, 733, 702 cm^{-1}.

The structure **10** was confirmed by conversion to a known dechlorination product, *trans*-3-butyl-2-(1-hydroxyethyl)cyclohexanone,[24] with catalytic AIBN/Bu_3SnH in benzene under reflux.

Alkylation with Lithium Hexylide. To a solution of the $ClCH_2$-CH=O·MAPH complex (1.5 mmol, prepared from α-chloroacetaldehyde trimer) in CH_2Cl_2 (15 mL) was transferred at −78 °C a solution of lithium hexylide in ether, which was prepared from 1-hexyne (49 mg, 0.6 mmol) and a 1.6 M hexane solution of BuLi (0.34 mL, 0.55 mmol) in ether (2 mL) at 0 °C for 20 min. The resulting mixture was stirred at −78 °C for 10 min, at 0 °C for 4 h, and at 20 °C for 1 h. This was poured into diluted HCl and extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel (ether/hexane = 1:3 as eluant) to furnish 1-chloro-3-octyn-2-ol (46 mg, 57% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 4.55 (1H, m, CHO), 3.65 (2H, m, CH_2Cl), 2.35 (1H, br d, J = 6 Hz, OH), 2.20 (2H, dt, J = 1, 6 Hz, $CH_2C{\equiv}C$), 1.42 (4H, m, CH_2CH_2), 0.87 (3H, t, J = 7 Hz, CH_3); IR (liquid film) 3360 (OH), 2959, 2934, 2874, 2236, 1468, 1429, 1065, 1007 cm^{-1}. The structure was confirmed by conversion to a known dechlorination product, 3-octyn-2-ol,[25] with catalytic AIBN/Bu_3SnH in benzene under reflux.

4-Chloro-3-hydroxy-1-phenyl-1-pentanone (7). To a solution of MAPH (1.5 mmol) in CH_2Cl_2 (15 mL) was added a solution of α-chloropropionaldehyde trimer (140 mg, 0.5 mmol) in CH_2Cl_2 (0.5 mL) at room temperature. The mixture was stirred at room temperature for 5 h and used as a solution of α-chloropropionaldehyde/MAPH complex in CH_2Cl_2. This was cooled to −78 °C, and a solution of lithium 1-phenylethenolate in THF, which was prepared from 1-phenyl-1-(trimethylsiloxy)ethene (96 mg, 0.5 mmol) and a 1.4 M ethereal solution of MeLi (0.39 mL, 0.55 mmol) in THF (2 mL) at 0 °C for 30 min, was transferred to the above solution. The resulting mixture was stirred at −78 °C for 30 min, poured into diluted HCl, and extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4, concentrated, and purified by column chromatography on silica gel (ether/hexane = 1:2 to 1:1 as eluants) to furnish a 1:1 mixture of *erythro*- and *threo*-4-chloro-3-hydroxy-1-phenyl-1-pentanone (86 mg, 81% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.92–8.01 (2H, d, J = 6.5 Hz, Ar-H), 7.41–7.65 (3H, m, Ar-H), 4.23 (1H, m, CHO), 4.13 (1H, quintet, J = 7 Hz, CHCl), 3.45 (1H, br s, OH), 3.41 (1H, dd, J = 2.5, 17.5 Hz, CHC=O), 3.26 (1H, dd, J = 10, 17.5 Hz, CHC=O), 1.58 (3H, d, J = 7 Hz, CH_3); IR (liquid film) 3470 (OH), 1682 (C=O), 1449, 1215, 754, 733, 691 cm^{-1}. The structure **7** was confirmed by conversion to a known dechlorination product, 3-hydroxy-1-phenyl-1-pentanone,[26] with catalytic AIBN/Bu_3SnH in benzene under reflux.

(*E*)-1-Chloro-8,12-dimethyl-2-hydroxy-7,11-tridecadien-4-one (13): ^{1}H NMR ($CDCl_3$) δ 5.07 (2H, t, J = 7.2 Hz, 2CH=), 4.28 (1H, quintet, J = 5.4 Hz, CHO), 3.58 (2H, d, J = 5.2 Hz, CH_2Cl), 2.73 (2H, d, J = 6.2 Hz, CH_2CO), 2.50 (2H, m, CH_2C=O), 2.28 (2H, quartet, J = 7.2 Hz, CH_2CC=O), 1.91–2.14 (4H, m, $2CH_2$), 1.62 and 1.68 (6H, s, $2CH_3$); IR (liquid film) 3440 (OH), 2967, 2917, 2857, 1713 (C=O), 1436, 1406, 1377, 1107, 1055 cm^{-1}. Anal. Calcd for $C_{15}H_{25}O_2Cl$: C, 66.04; H, 9.24. Found: C, 66.07; H, 9.54.

General Procedures for Furan Syntheses. Preparation of 2-phenylfuran (**9**) from 4-chloro-3-hydroxy-1-phenyl-1-butanone (**8**) is representative. A solution of chloro aldol **8** (40 mg, 0.2 mmol) in mesitylene (2 mL) was heated under reflux for 7.5 h. After being cooled to room temperature, the solution was directly applied to column chromatography on silica gel (ether/hexane = 1:100 as eluant) to furnish 2-phenylfuran (**9**)[13a] (27 mg, 95% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.65–7.71 (2H, m, Ar-H), 7.21–7.43 (3H, m, Ar-H), 7.42 (1H, d, J = 1.8 Hz, CHO), 6.66 (1H, d, J = 3.4 Hz, CH=CPh), 6.48 (1H, dd, J = 1.8, 3.4 Hz, CH=CO); IR (liquid film) 3117, 3075, 2926, 2855, 1609, 1506, 1480, 1279, 1219, 1157, 1009, 905, 760, 733, 691, 664, 594 cm^{-1}.

2-Methyl-5-phenylfuran (11):[13j] ^{1}H NMR ($CDCl_3$) δ 7.61–7.66 (2H, m, Ar-H), 7.21–7.40 (3H, m, Ar-H), 6.54 (1H, d, J = 3.2 Hz, CH=CPh), 6.06 (1H, d, J = 3.2 Hz, CH=C(Me)O), 2.37 (3H, s, CH_3); IR (liquid film) 2961, 2921, 1607, 1598, 1551, 1489, 1447, 1262, 1206, 1069, 1022, 785, 758, 691 cm^{-1}.

Furan 12: ^{1}H NMR ($CDCl_3$) δ 7.24 (1H, d, J = 2 Hz, =CHO), 6.26 (1H, d, J = 2 Hz, CH=CO), 2.56 (2H, t, J = 6.4 Hz, furyl-CH_2), 2.53 (1H, m, furyl-CH), 1.23–2.06 (10H, m, $5CH_2$), 0.92 (3H, t, J = 6.4 Hz, CH_3); IR (liquid film) 2930, 2859, 1507, 1456, 1445, 1223, 1040, 727, 714 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.90; H, 10.57.

2-((*E*)-4,8-Dimethyl-3,7-nonadienyl)furan (14). According to the general procedure, the title furan **14** was obtained in 58% yield accompanied by several side-reaction products. Reaction of chloro aldol **13** at higher temperature [dodecane reflux (~216 °C) for 1 h] resulted in the improvement of the product yield (91%). **14**: ^{1}H NMR ($CDCl_3$) δ 7.31 (1H, d, J = 1.8 Hz, CHO), 6.28 (1H, dd, J = 1.8, 3.2 Hz, CH=CO), 5.99 (1H, d, J = 3.2 Hz, CH=), 5.13 (2H, m, 2CH=), 2.65 (2H, dt, J = 2.6, 7.0 Hz, CH_2CO), 2.34 (2H, quintet, J = 7.4 Hz, CH_2CCO), 1.94–2.13 (4H, m, $2CH_2$), 1.60 and 1.69 (6H, s, $2CH_3$); IR (liquid film) 2967, 2921, 2857, 1500, 1449, 1377, 1262, 1150, 1107, 1078, 1010, 797, 727, 600 cm^{-1}. Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.51; H, 10.56.

^{1}H NMR Measurement of Aldehyde–MAPH Complexes. (a) From Trioxane or α-Chloroacetaldehyde Trimer. Preparation of $ClCH_2$-CH=O·MAPH in $CDCl_3$ is representative. To a solution of 2,6-diphenylphenol (148 mg, 0.6 mmol) in freshly distilled CH_2Cl_2 (2 mL) was added at 20 °C a 1 M hexane solution of Me_3Al (0.3 mL, 0.3 mmol). The resulting colorless solution was stirred at 20 °C for 1 h to furnish a solution of MAPH in hexane–CH_2Cl_2. Then the solvents were evaporated under vacuum. The residual liquid was diluted with $CDCl_3$ (1.8 mL), and a solution of α-chloroacetaldehyde trimer (24 mg, 0.1 mmol) in $CDCl_3$ (0.2 mL) was added at 20 °C. The mixture was stirred at 20 °C for 5 h and transferred by cannula to a 5-mm NMR tube at 20–25 °C. The 500 MHz ^{1}H NMR spectra were taken at 20 °C. $ClCH_2$-CH=O·MAPH complex: δ 6.63 (1H, t, J = 1.7 Hz, CH=O···Al), 2.43 (2H, d, J = 1.7 Hz, $ClCH_2$).

(b) From Butyraldehyde or Pivalaldehyde. Samples of the aldehyde–MAPH complexes in $CDCl_3$ were prepared by addition of these aldehydes to MAPH in $CDCl_3$ in a similar manner as described above. CH_3CH_2-CH_2CH=O·MAPH complex: δ 6.91 (1H, t, J = 1.3 Hz, CH=O···Al), 1.12 (2H, dt, J = 1.3, 7.6 Hz, CH_2C=O···Al), 0.47–0.66 (5H, m, CH_2-CH_3). t-Bu-CH=O·MAPH complex: δ 6.73 (1H, s, CH=O···Al), 0.06 (9H, s, t-Bu), −1.32 (3H, s, CH_3Al). The ^{1}H NMR measurement of the t-Bu-CH=O·MAPH complex at low temperature (−78 °C) showed similar δ values: δ 6.59 (1H, s, CH=O···Al), 0.05 (9H, s, t-Bu), −1.36 (3H, s, CH_3Al).

^{1}H NMR Measurement of Aldehyde–MAD Complexes in $CDCl_3$ at −50 °C. t-Bu-CH=O·MAD complex: δ 9.40 (1H, s, CH=O···Al), 1.25 (9H, s, t-Bu), −0.40 (3H, s, CH_3Al). PhCH=O·MAD complex: δ 9.65 (1H, s, CH=O···Al), 8.04–8.10 (2H, m, Ph-H), 7.76–7.86 (3H, m, Ph-H), −0.20 (3H, s, CH_3Al).

(22) Oare, D. A.; Henderson, M. A.; Sanner, M. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 132.
(23) Frimer, A. A.; Antebi, A. *J. Org. Chem.* **1980**, *45*, 2334.
(24) Suzuki, M.; Kawagishi, T.; Yanagisawa, A.; Suzuki, T.; Okamura, N.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1299.
(25) Marshall, J. A.; Wang, X. *J. Org. Chem.* **1991**, *56*, 960.
(26) Sato, T.; Matsuoka, H.; Igarashi, T.; Minomura, M.; Murayama, E. *J. Org. Chem.* **1988**, *53*, 1207.