

Highly Efficient Alkylation of Epoxides with R_3Al/H_2O Systems Based on the Double Activation of Epoxy Oxygens

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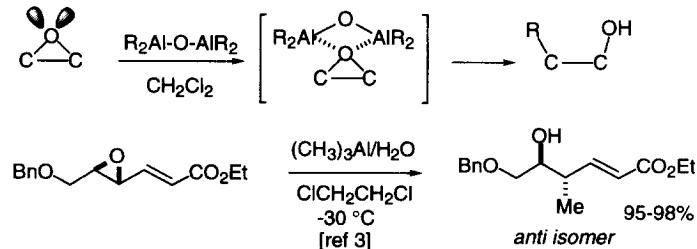
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Abstract: Alkylation of epoxides can be effected with trialkylaluminum/water system, which is much superior to the parent trialkylaluminum. Bidentate bis(dialkyl)aluminoxanes and their hypothetical analogues seem to be active species for the double activation of epoxy substrates. Such double-activation ability is emphasized using several synthetic examples in comparison with the corresponding monodentate derivatives. The double coordination complex formation of bidentate $(Me_2Al)_2O$ is characterized with THF by 1H and ^{13}C NMR spectroscopy.

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Recently we elucidated a pivotal role of methylalumoxane (MAO) as cocatalyst to generate highly active homogeneous metallocene catalysts (*i.e.*, Kaminsky catalysts)¹ for cationic olefin polymerizations, where the bidentate Al-O-Al unit of MAO is crucially important for activating a metallocene ligand effectively.² This new finding prompted us to examine the following two points: (i) the alkylation ability of bis(dialkyl)aluminoxanes toward epoxy substrates as a new type of efficient alkylation agents; (ii) comparison of this reactivity with that of the previously reported Me_3Al/H_2O system on the selective methylation of γ,δ -epoxy acrylates (Scheme I).³

Scheme I



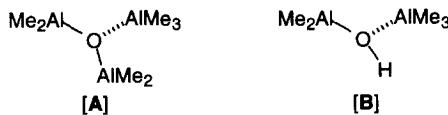
The requisite $(Me_2Al)_2O$ can be readily prepared by mixing Me_3Al (2 equiv) with H_2O (1 equiv) in CH_2Cl_2 at 0 °C for 30 min.⁴ Treatment of 3-phenylpropene oxide with the *in situ* generated $(Me_2Al)_2O$ in

Table I. Alkylation of Epoxides with Modified Al Reagents ^a

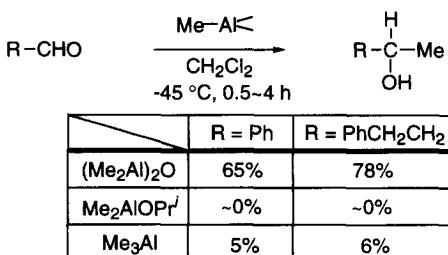
entry	epoxide	Al reagent (equiv)	condition (°C, h)	alkylation product	% yield ^b (ratio)
1		Me ₃ Al (1~2)	-45, 3		trace
2		Me ₂ AlOAlMe ₂ (1)	-45, 3		65 (76:15:9)
3		Me ₂ AlOPr ⁱ (1~2)	-45, 3		trace
4		Me ₃ Al + H ₂ O (2:1)	-45, 3		71 (88:5:7)
5		Et ₃ Al (1)	-30, 8	(R = Et)	2
6		Et ₂ AlOAlEt ₂ (1)	-30, 8		59 (18:9:73) ^c
7		Et ₃ Al + H ₂ O (2:1)	-30, 8		71 (22:19:59) ^c
8		Me ₃ Al (1)	-20, 4		trace
9		Me ₂ AlOAlMe ₂ (1)	-20, 4		68 (64:36)
10		Me ₂ AlOPr ⁱ (1)	-20, 4		trace
11		Me ₃ Al + H ₂ O (2:1)	-20, 4		73 (73:27)
12		Me ₃ Al (1~5)	-30, 6		0~13
13		Me ₂ AlOAlMe ₂ (2)	-30, 6		14
14		Me ₂ AlOPr ⁱ (5)	-30, 6		trace
15		Me ₃ Al + H ₂ O (4:2)	-20, 3		63
16		Me ₃ Al + H ₂ O (10:5)	-30, 6		79
17		Me ₂ AlOAlMe ₂ (2) + MeAl (2)	-20, 3		48
18		Me ₃ Al (3~6)	-20, 3		23~34
19		Me ₂ AlOAlMe ₂ (3)	-20, 3		92
20		Me ₂ AlOPr ⁱ (3)	-20, 3		trace
21		Me ₃ Al + H ₂ O (6:3)	-20, 3		92
22		Et ₂ AlOAlEt ₂ (3)	-20, 3	(R = Et)	trace
23		Et ₃ Al + H ₂ O (6:3)	-20, 3		26
24		Me ₃ Al (3)	-20, 3		15
25		Me ₂ AlOAlMe ₂ (3)	-20, 3		87
26		Me ₂ AlOPr ⁱ (3)	-20, 3		trace
27		Me ₃ Al + H ₂ O (6:3)	-20, 3		94
28		Et ₂ AlOAlEt ₂ (3)	-20, 3	(R = Et)	trace
29		Et ₃ Al + H ₂ O (6:3)	-20, 3		42

^a Alkylation of epoxides was carried out by treatment of epoxides in CH₂Cl₂ with alkylaluminum reagents under the given reaction conditions. ^b Isolated yield. ^c The simple reduction product, 3-phenylpropanol was also obtained in 11% yield.

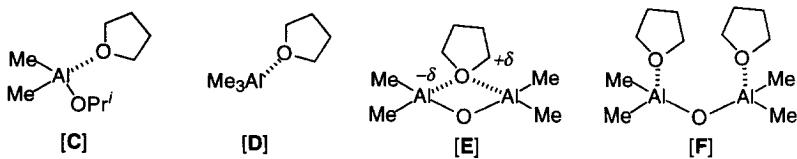
CH_2Cl_2 at -45°C for 3 h afforded a mixture of 2-methyl-3-phenyl-1-propanol, 1-phenyl-2-butanol, and 4-phenyl-2-butanol in 65% yield in a ratio of 76:15:9 (entry 2 in Table I). In contrast, alkylation of this epoxide with simple Me_3Al (1~2 equiv) under similar conditions produced only trace amounts of methylation products (entry 1). Furthermore, use of $\text{Me}_2\text{AlOPr}^i$ (1~2 equiv) as a monodentate counterpart of $(\text{Me}_2\text{Al})_2\text{O}$ resulted in almost total recovery of the starting epoxide (entry 3). Notably, $\text{Me}_3\text{Al}/\text{H}_2\text{O}$ system at low temperature⁵ was found to be some more reactive than $(\text{Me}_2\text{Al})_2\text{O}$ (entry 4).³ A similar tendency was observed with ethyl analogues (entries 5~7 in Table I). These results clearly demonstrate that the bidentate Al catalyst, $(\text{R}_2\text{Al})_2\text{O}$ strongly enhances the reactivity of epoxy oxygen toward alkyl transfer via the double electrophilic activation of epoxy moiety. Even more reactive species derived from the $\text{Me}_3\text{Al}/\text{H}_2\text{O}$ system at low temperature might be ascribed to the partial generation of hypothetical bidentate reagents of type [A] or [B], where epoxides would be activated and then alkylated via pentacoordinated aluminum species.^{5~7} Other selected examples are also included in Table I.



Our system is also applicable to the carbonyl alkylation experiments as illustrated by the methylation of benzaldehyde and 3-phenylpropanal with a series of methylaluminum reagents.



Although double coordination behavior of the bidentate bis-Al/epoxide complex is consistent with the above experimental findings, more direct evidence was obtained by ^{13}C and ^1H NMR spectroscopy using tetrahydrofuran (THF) as an ethereal substrate. Thus, the 75 MHz ^{13}C NMR measurement of the 1:1 $\text{Me}_2\text{AlOPr}^i/\text{THF}$ complex [C] in CDCl_3 at -50°C showed that the original signal of THF α -carbons at δ 67.87 shifted slightly to δ 68.45. This result implies the feeble Lewis acidity of $\text{Me}_2\text{AlOPr}^i$. The 1:1 $\text{Me}_3\text{Al-THF}$ complex [D] showed further downfield shift for the THF α -carbons (δ 69.18). In contrast, 1:1 bidentate $(\text{Me}_2\text{Al})_2\text{O/THF}$ chelation complex under similar conditions undergoes a further downfield shift for the THF α -carbons (δ 70.39), indicating the strong electrophilic activation of the THF α -carbons by intervention of the double coordination complex [E]. Complexation of THF with $\text{Me}_3\text{Al}/\text{H}_2\text{O}$ system at low temperature exhibited the THF α -carbons at δ 70.26, showing the similar electrophilic activation of the THF α -carbons as the complex [E].⁸ A similar tendency is also observed in the low-temperature ^1H NMR spectroscopy: δ 3.79 (free THF α -protons); δ 3.87 (THF α -protons of the complex [C]); δ 3.94 (THF α -protons of the complex [D]); δ 4.05 (THF α -protons of the complex [E]); δ 4.01 (THF α -protons of the complex with $\text{Me}_3\text{Al}/\text{H}_2\text{O}$ system).



In conclusion, we successfully demonstrated that the Lewis acidity of Me_2AlOR can be dramatically enhanced by forming bidentate bis-Al reagent, $\text{R}_2\text{Al-O-AlR}_2$ with two Al centers in an appropriate position using water as a desired spacer, and real active species derived from $\text{Me}_3\text{Al}/\text{H}_2\text{O}$ system at low temperature in selective ring opening of vinyl epoxides is different in nature from $(\text{Me}_2\text{Al})_2\text{O}$.

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References and Notes

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- (5) This reagent was prepared by adding a hexane solution of Me_3Al to a pre-cooled mixture of H_2O in CH_2Cl_2 at $-30\text{--}20$ °C. The methane gas evolution seems to be much slow compared to the case of $(\text{Me}_2\text{Al})_2\text{O}$ synthesis.
- (6) Pentacoordinate organoaluminum chemistry: (a) Ooi, T.; Kagoshima, N.; Maruoka, K. *J. Am. Chem. Soc.* **1997**, *119*, 5754. (b) Ooi, T.; Kagoshima, N.; Uraguchi, D.; Maruoka, K. *Tetrahedron Lett.* **1998**, *39*, 7105. (c) Ooi, T.; Furuya, M.; Maruoka, K. *Chem. Lett.* **1998**, 817. (d) Ooi, T.; Uraguchi, D.; Kagoshima, N.; Maruoka, K. *J. Am. Chem. Soc.* **1998**, *120*, 5327. (e) Maruoka, K.; Ooi, T. *Chem. Eur. J.* **1999**, *5*, 829.
- (7) A hypothetical species [A] would be generated by treatment of $(\text{Me}_2\text{Al})_2\text{O}$ with Me_3Al . Reaction of this species [A] (2 equiv) with cyclohexene oxide at -20 °C for 3 h gave *trans*-2-methylcyclohexanol in 48% yield (*cf.* entry 15: 63% yield with Me_3Al (4 equiv) and H_2O (2 equiv) under similar conditions). Hence, reactive species derived from the $\text{Me}_3\text{Al}/\text{H}_2\text{O}$ system at low temperature seem to be a mixture including Me_3Al , [A], and/or [B].
- (8) The 1:2 or 2:1 $(\text{Me}_2\text{Al})_2\text{O}$ -THF mixture exhibited the following chemical shifts for THF: ^{13}C NMR δ 69.79 (α -C); ^1H NMR δ 4.02 (α -CH) in the 1:2 mixture; ^{13}C NMR δ 70.39 (α -C); ^1H NMR δ 4.12 (α -CH) in the 2:1 mixture. Hence, two THF oxygens coordinate separately to two aluminum centers of $(\text{Me}_2\text{Al})_2\text{O}$ giving the complex [F] in the 1:2 mixture, while the double coordination complex [E] still predominates in the 2:1 mixture.