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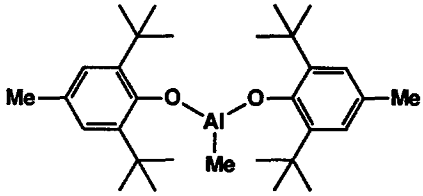
MOLECULAR RECOGNITION OF OXYGEN-CONTAINING SUBSTRATES WITH MAD

Keiji Maruoka, Shigeru Nagahara, and Hisashi Yamamoto*
Department of Applied Chemistry, Nagoya University, Chikusa, Nagoya 464-01, Japan

***Summary:** The binding behaviors of Lewis acidic MAD for various oxygen-containing substrates have been studied by low-temperature ^{13}C NMR analysis. Amides were found to more strongly coordinate to MAD than to aldehydes, esters, or ketones, while coordination of ethereal oxygens was rather weak.*

In a recent disclosure we introduced methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) as a Lewis acidic receptor and described its binding behavior for ether substrates.[1,2] It features a rapidly assembled and exceptionally bulky molecular cleft into which the sterically less hindered or electronically more labile of two different ethers is bound with unusually high selectivity, hitherto not attainable by the ordinary Lewis acids. Since organoaluminum compounds have a great tendency with various heteroatoms in organic molecules, particularly oxygen, to generate 1:1 coordination complexes,[3] we are interested in the binding behavior of MAD for various oxygen-containing substrates.[4] Here we wish to report our preliminary results of this study.



(MAD)

As oxygen-containing substrates, we utilized both aliphatic and aromatic aldehydes, amides, esters, ethers, and ketones with similar structural substituents. First, we took the low-temperature ^{13}C NMR spectra of these substrates and their coordination complexes with MAD in $CDCl_3$. For carbonyl and ethereal substrates, characteristic signals of carbonyl carbons and ethereal α-carbons can be measured, respectively. These data are listed in Table I.[5] The differences in the downfield shifts of carbonyl carbons of amides and esters by coordination to MAD were much smaller than those of aldehydes and ketones. This may be attributed to an electron releasing effect of the additional heteroatom (N, O) attached to the carbonyl groups which, in part, compensates for electron withdrawal of the complexed carbonyl oxygen. We then examined the binding behavior of MAD for combinations of other two different substrates by low-temperature ^{13}C NMR

Table I. Characteristic ^{13}C NMR Data for Free Substrates and their Complexes with MAD [a]

substrate	δ (free) / ppm [b]	δ (complex) / ppm	$\Delta\delta$ / ppm [c,d]	$\Delta\delta_{Al\text{-}Me}$ / ppm [c,e]
		carbonyl carbon		
PhCHO	192.97	201.68	8.71	2.60
$CH_3CH_2COCH_2CH_3$	213.10	236.04	22.94	4.60
$PhCOCH_2CH_3$	201.06	216.99	15.93	5.33
$CH_3CH_2CONMe_2$	173.70	176.39	2.69	5.18
$PhCONMe_2$	171.46	172.18	0.72	3.94
$CH_3CH_2COOCH_2CH_3$	174.86	184.53	9.67	4.36
CH_3CH_2COOPh	173.44	184.83	11.39	4.07
$PhCOOCH_2CH_3$	166.67	171.69	5.02	5.40
		α-methylene carbon		
$CH_3CH_2OCH_2CH_3$	66.19	64.67	-1.52	5.62
$PhOCH_2CH_3$	62.88	64.27	1.39	0.82

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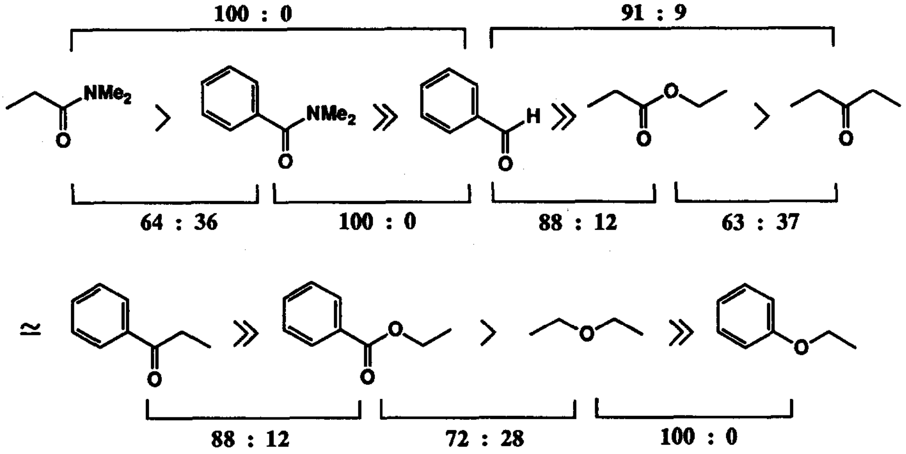
[a] Unless otherwise noted, oxygen-containing substrate (0.5 mmol) was mixed with 1 equiv of MAD in $CDCl_3$ (0.5 M solution) in a 5-mm NMR tube at 20-25 °C and the 125 MHz ^{13}C NMR spectrum was taken at -50 °C. [b] The term "δ (free)" refers to the chemical shift for free carbonyl carbons or free ethereal α-carbons. [c] In ppm downfield from free substrates. [d] $\Delta\delta = \delta$ (complex) - δ (free). [e] $\Delta\delta_{Al\text{-}Me} = \delta_{Al\text{-}Me}$ (complex) - $\delta_{Al\text{-}Me}$ (free MAD). $\delta_{Al\text{-}Me}$ (free MAD) = -9.09 ppm. In every cases, the downfield shifts were observed.

spectroscopy, and these results are summarized in Scheme I. For example, the 125 MHz ^{13}C NMR measurement of a mixture of 1 equiv each of MAD, *N,N*-dimethylpropionamide, and *N,N*-dimethylbenzamide in $CDCl_3$ (0.4 M solution) at -50 °C showed that the original signals of propionamide and benzamide at δ 173.70 and δ 171.46 shifted downfield to δ 176.39 and δ 172.18, respectively, in a ratio of 64:36. This ratio was also calculated based on the phenoxy carbons of free MAD and its complexes with amides.[6] The other complexation ratios for two different substrates were determined in a similar manner. As revealed in Scheme I, amides more strongly coordinate to Lewis acidic MAD than to aldehydes, esters, and ketones, while coordination of ethereal oxygens is rather weak.[7] The order in Scheme I implies that even the same functional groups showed different binding behaviors to Lewis acidic MAD depending on the types of substituents (aliphatic or aromatic) and their steric requirements.

Scheme I



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5. Unreproducible results were obtained in the case of aliphatic aldehydes such as propanal.
6. Two *N*-methyl carbons of amides can also be utilized to determine the complexation ratios. The 125 MHz ^{13}C NMR signals for free *N*-methyl carbons and their MAD complexes in $CDCl_3$ at -50 °C follow: *N,N*-dimethylpropionamide [$\delta_{N\text{-}Me}$ (free) = 35.20 and 36.99 ppm; $\delta_{N\text{-}Me}$ (complex) = 38.24 and 38.88 ppm]; *N,N*-dimethylbenzamide [$\delta_{N\text{-}Me}$ (free) = 35.11 and 39.57 ppm; $\delta_{N\text{-}Me}$ (complex) = 38.16 and 40.91 ppm].
7. Phenyl propionate has a similar binding capability to ethyl benzoate (complexation ratio = 52:48).

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