Et_2AlCl Complexes of an *N*-Acyloxazolidinone: NMR Investigation

Stephen Castellino* and Wesley J. Dwight

Department of Chemistry
North Dakota State University
Fargo, North Dakota 58105-5516

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Our interest in the solution structures of Lewis acid complexes and their reaction pathways has led us to spectroscopically investigate the intermediates formed between **1** and various Lewis acids. In a previous report, we characterized the 1:1 $SnCl_4$ chelate of **1** by NMR.[1] Surprisingly, this dynamically stable chelate produces only modest facial and endo selectivity in Diels–Alder additions, as reported by Evans.[2] Optimum selectivity for these reactions was observed with 1.4 equiv of R_2AlCl (R = Me, Et) as the Lewis acid promoter.[3] Furthermore, the selectivity was found to be dependent upon the stoichiometry of the aluminum Lewis acid. To account for these experimental observations, Evans proposed that upon addition of 1 equiv of R_2AlCl, a 1:1 complex (**2**) was formed. The addition of a second equivalent of Lewis acid resulted in a redistribution reaction that produced a dialkyl aluminum cation, which formed the chelate **3** (Scheme I). This chelate accounted for the increased reactivity and high selectivity observed. Redistribution reactions of this type have been proposed but have not been well characterized in solution.[4]

We initiated our investigation by performing "titration" experiments with Et_2AlCl and **1**. At −80 °C with 1 equiv of Lewis acid, a single species is observed by ^1H and ^{13}C NMR with chemical shifts distinct from the "free" oxazolidinone (Figure 1a).[5] The addition of Et_2AlCl beyond 1 equiv results in the observation of a *second* set of resonances by ^1H and ^{13}C with a concomitant decrease in signal intensity of the initially formed species (Figure 1b). When the ratio of Et_2AlCl to **1** reaches 2:1, only the second species formed is observed (Figure 1c). Upon addition of >2 equiv of the Lewis acid, two additional sets of resonances are observed. These latter sets are due to the two diastereomers of **4**, which arise from the 1,4-conjugate addition of an ethyl group to the oxazolidinone (Scheme I). This reaction pathway is enhanced by the use of >2 equiv of the Lewis acid or elevated temperatures. The observation of conjugate addition in the presence of excess Lewis acid has previously been reported.[6]

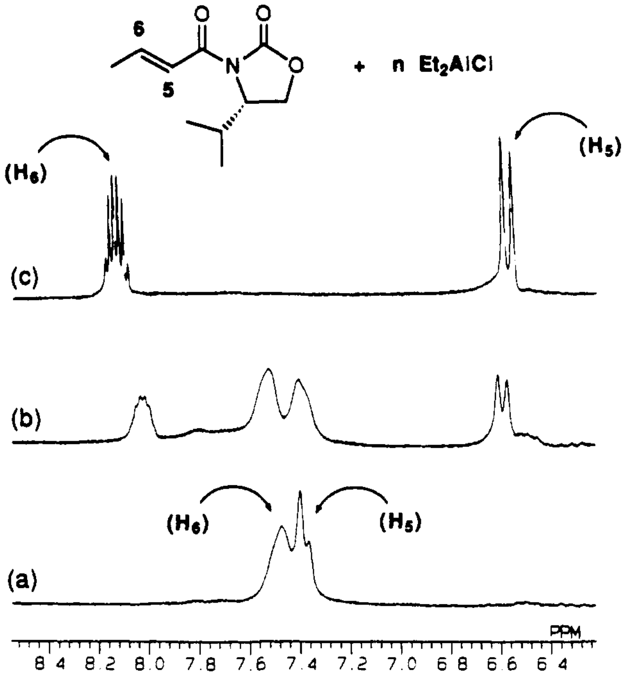
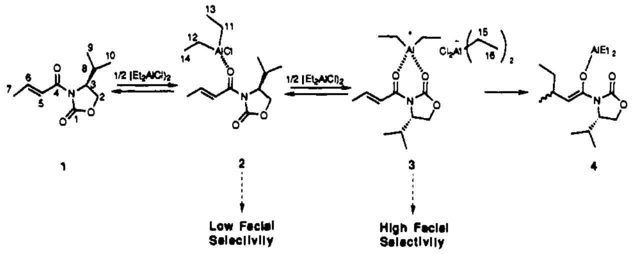


Figure 1. H_5 and H_6 chemical shifts of **1** as a function of Et_2AlCl stoichiometry at −80 °C. (a) **1** and 1 equiv of Et_2AlCl; (b) **1** and 1.5 equiv of Et_2AlCl; (c) **1** and 2 equiv of Et_2AlCl.

Scheme I



The assignment of the initially formed species (1 equiv of Et_2AlCl) to complex **2** is based on ^{13}C data (Table I). C-4 and C-6 experience downfield shifts of approximately 3.5 and 11.9 ppm, respectively, while C-5 is shifted upfield by 3.7 ppm. C-1 does not experience a downfield shift but rather a slight upfield shift. These data are consistent with aluminum complexation *preferentially* at the acyl carbonyl group and activation of C-6 toward nucleophilic attack. The chemical shift perturbation of C-1 may be due to changes in conformer populations associated with C–N bond rotations.[7]

The species formed when 2 equiv of Et_2AlCl are present is assigned to **3**. Analysis of the ^{13}C data reveals similar chemical shift perturbations for the acyl fragment of C-4, C-5, and C-6 (Table I). However, the magnitude of the chemical shift differences ($\Delta\delta$) is increased. Most notable is C-6, which now is shifted downfield by approximately 23 ppm relative to the free oxazolidinone. C-1, C-2, and C-3 in the oxazolidinone ring are also shifted downfield by 6.4, 5.6, and 2.2 ppm, respectively. A comparison of these chemical shifts with those of the previously reported $SnCl_4$:**1** chelate indicates similar chemical shift perturbations from **1** for all 10 carbons.[1] The largest difference

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[1] Castellino, S. *J. Org. Chem.* **1990**, *55*, 5197.

[2] Evans, D. A.; Chapman, K. T.; Bisaka, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238.

[3] The use of 1.5 equiv of $RAlCl_2$ for optimum selectivity in Diels–Alder reactions with structurally similar chiral auxiliaries has been reported: (a) Oppolzer, W.; Rodriguez, I.; Blagg, J.; Bernardinelli, G. *Helv. Chim. Acta* **1989**, *72*, 123. (b) Boeckman, R. K.; Nelson, S. G.; Gaul, M. D. *J. Am. Chem. Soc.* **1992**, *114*, 2258.

[4] (a) Snider, B. B.; Zhang, Q. *J. Org. Chem.* **1991**, *56*, 4908. (b) Means, N. C.; Means, C. M.; Bott, S. G.; Atwood, J. L. *Inorg. Chem.* **1987**, *26*, 1466. (c) Snider, B. B.; Rodini, D. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, *37*, 3927. (d) Wakatsuki, K.; Matsubayashi, G.; Tanaka, T. *Org. Magn. Reson.* **1973**, *5*, 423. (e) Matsubayashi, G.; Wakatsuki, K.; Tanaka, T. *Org. Magn. Reson.* **1971**, *3*, 703. (f) Eisch, J. J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. A., Abel, E. W., Eds.; Pergamon: London, 1982; Vol. 1, Chapter 6.

[5] Spectra were recorded at 400, 100, or 104 MHz for ^1H, ^{13}C, or ^{27}Al, respectively, using either a 5- or a 10-mm broad-band probe. The variable temperature control unit was calibrated for both probes against a methanol standard. ^1H and ^{13}C chemical shifts are referenced to methylene chloride. ^{27}Al chemical shifts are referenced to $Al(H_2O)_6$ (0.0 ppm) as a secondary standard. For 5-mm NMR experiments, samples were 0.1 M in **1** (0.7 mL CD_2Cl_2), and quantities of Et_2AlCl ranged from 9–23 μL. Errors in measuring quantities of Lewis acid or **1** are estimated to be ±10%. ^1H and ^{13}C chemical shifts were assigned on the basis of coupling constant analysis, selective decoupling experiments, and homo- and heteronuclear correlation experiments. All materials were carefully purified and handled by techniques appropriate for air- and moisture-sensitive materials.

[6] (a) Ruck, K.; Kunz, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 694. (b) Kunz, H.; Pees. K. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1168. Also see: Ruck, K.; Kunz, H. *Synlett* **1992**, 343 and ref 4a.

[7] The possibility of a 2:2 complex for species **2** in which the acyl oxygens are coordinated to the aluminum centers in the bridging Et_2AlCl dimer cannot be ruled out based on the solution ^1H and ^{13}C NMR data.

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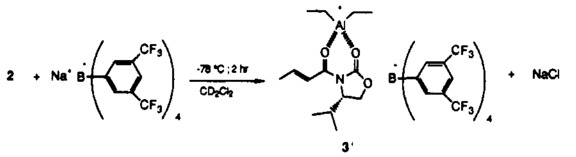
Table I. ^{13}C NMR Chemical Shift Data for **1** and Aluminum Alkyl Complexes at −80 °C

C	**1**, δ	**2**, δ	**3**, δ	3′, δ
C-1	154.6	152.1	161.0	160.7
C-2	63.8	63.9	69.5	68.8
C-3	59.0	59.3	61.2	61.6
C-4	165.2	168.7	171.1	170.7
C-5	122.3	118.6	117.8	116.4
C-6	146.5	158.4	169.2	172.2
C-7	18.6	20.0	21.1	21.4
C-8	29.2	28.1	29.9	30.2
C-9[a]	18.0	17.5	17.2	17.1
C-10[a]	14.9	13.7	13.6	13.2
C-11[b]	*c*	0.6	−1.7	−1.7
C-12[b]		0.6	−1.8	−1.7
C-13[d]	*c*	8.5	7.3	7.3
C-14[d]		8.5	7.7	7.5
C-15			3.1	
C-16			8.9	

[a] Assignments for C-9 and C-10 may be interchangeable. [b] Assignments for C-11 and C-12 may be interchangeable. [c] The ^{13}C chemical shifts for uncomplexed Et_2AlCl in CD_2Cl_2 are 2.9 (CH_2) and 7.8 (CH_3) ppm at −80 °C. [d] Assignments for C-13 and C-14 may be interchangeable.

between the two chelates is at C-6, which is shifted downfield by 18.4 ppm in the $SnCl_4$ chelate compared to 23 ppm for the 2:1 Et_2AlCl:**1** complex **3**. The ^{13}C spectrum also shows the presence of three sets of ethyl resonances, which is consistent with the two diastereotopic ethyl groups for **3** and a set of resonances for the magnetically equivalent ethyl groups of the aluminate anion (Table I). Attempts to characterize the aluminum intermediates by ^{27}Al NMR were not successful due to the low symmetry of the aluminum centers and low sample temperatures.[8]

Further conformation of the formation of the aluminum chelate **3** was gained by generating this intermediate through a separate pathway. The addition of 1 equiv of Et_2AlCl to the oxazolidinone **1** at −78 °C followed by 1 equiv of sodium tetrakis(bis(3,5-trifluoromethyl)phenyl) borate[9] (Na TFPB) produces **3′**, which has chemical shifts very similar to those of the intermediate derived from the addition of 2 equiv of Et_2AlCl to **1**, (eq 1; Table I).



(1)

3′

Minor chemical shift differences can be attributed to the effects of the borate and aluminate counterions. The addition of sodium tetraphenyl borate to complex **2** does not result in the redistribution transformation which produces the aluminum cation chelate **3**. In addition, the use of 2 equiv of $Al(CH_3)_3$ or 1 equiv of the aluminum trialkyl and NaTFPB does not produce **3**; only the 1:1 complex **2** is observed.

Preliminary synthetic experiments have established that Diels–Alder additions between **1** and cyclopentadiene are *catalyzed* by Et_2AlCl/NaTFPB (0.1–0.25 equiv). Excellent yields are achieved (85–90%), although the endo/exo selectivity (22:1) and the endo facial selectivity (4.5:1) are not as high as those reported by Evans[2] for the use of 1.4 equiv of Et_2AlCl.[10] This loss in selectivity may be attributed to the higher reactivity of **3′**, as indicated by the large Δδ at C-6. The relative reactivities of **2** and **3** were estimated by Evans to be 1:100 and appear to be reflected in the magnitude of the deshielding at C-6 upon complexation. Using these Δδs as a measure of enhanced electrophilicity, the order of reactivity for the complexes studied is: **3′** > **3** > $SnCl_4$ chelate ≫ **2**. Less than a stoichiometric amount (0.03–0.1 equiv) of NaTFPB in the presence of the 1:1 complex **2** also catalyzes the Diels–Alder addition with cyclopentadiene.[11]

In summary, we have characterized by NMR the two intermediates **2** and **3** which were previously proposed as the reactive intermediates in the dialkylaluminum chloride-promoted Diels–Alder reaction between **1** and cyclopentadiene. Perhaps of more significance is the observation that the diethylaluminum cation chelate **3′** can be prepared by the addition of NaTFPB to Et_2AlCl and **1**. Substoichiometric amounts of Et_2AlCl/NaTFPB *catalyze* the Diels–Alder addition between **1** and cyclopentadiene through intermediate **3′**, while greater than 1 equiv of Et_2AlCl is required to *promote* the cycloaddition with intermediate **3**. The use of catalytic Lewis acids, such the dialkyalumiunum cation, holds great promise for highly selective chelation control additions. Studies are in progress to gain further insight into formation of the aluminum cation complexes and their application to highly selective synthetic transformations.

Acknowledgment. We wish to thank Professor Evans for supplying us with oxazolidinone samples and the Ethyl Corp. for the generous gift of aluminum alkyls. Acknowledgment is made to the donors of the Petroleum Research Fund (22530-G4), administered by the ACS; NIH (GM47630-01); and the NSF-EPSCoR program for financial support. The NMR spectrometer was supported by a grant from the Air Force Office of Scientific Research (AFOSR-87-0036).

Supplementary Material Available: ^{13}C stack plots of stoichiometry experiments between **1** and Et_2AlCl; ^{13}C stack plot of **3**, **3′**, and $SnCl_4$:**1** chelate (3 pages). Ordering information is given on any current masthead page.

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(8) (a) Akitt, J. W. *Prog. Nucl. Magn. Reson. Spectros.* **1989**, *21*, 1. (b) van Vliet, M. R. P.; van Koten, G.; de Keijser, M. S.; Vrieze, K. *Organometallics* **1987**, *6*, 1652.

(9) (a) Bahr, S. R.; Boudjouk, P. *J. Am. Chem. Soc.*, in press. (b) Iwamoto, H.; Sonoda, T.; Kobayashi, H. *Tetrahedron Lett.* **1983**, *24*, 4703.

(10) Reaction conditions similar to those in ref 2 were employed except that only 5 equiv of diene was added, and the reaction solutions were allowed to stir for 12 h at −78 °C prior to the quenching of the reaction with aqueous NH_4Cl. Reaction conditions have not been optimized.

(11) Reaction conditions have not been optimized: for 0.05 equiv NaTFPB, endo/exo selectivity = 42:1, endo facial selectivity = 8.2:1, and yield = 90%.