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Bis-aluminated triflic amide promoted Diels–Alder reactions of α,β-unsaturated lactones

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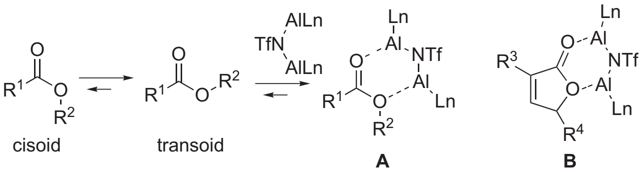
Abstract—The bis-aluminated triflic amides such as TfN[Al(Me)Cl]$_2$ and TfN[Al(*i*Bu)$_2$]$_2$, which are derived from triflic amide (1 mol) and aluminum reagent (2 mol), can efficiently promote the Diels–Alder reaction of α,β-unsaturated lactone derivatives as dienophiles. Selection of the ligand on aluminum of these Lewis acids should be important depending on the combination of dienophile and 1,3-diene.

α,β-Unsaturated aldehydes, ketones, and carboxylic acid derivatives are widely used as dienophiles in the Diels–Alder reaction.[1–4] However, the reaction of less reactive α,β-unsaturated lactones such as 5*H*-furan-2-one **2a**, 5,6-dihydropyran-2-one **2b** and their alkyl substituted derivatives suffer from a limitation of employable dienes even under Lewis acid mediated conditions.[4–7] For example, compared to reactions with reactive dienes such as cyclopentadiene, those with less reactive acyclic dienes were scarcely achieved. Moreover, no successful example of the Diels–Alder reaction with α-alkylated α,β-unsaturated lactones such as 3-methyl-5*H*-furan-2-one **2c** has been reported under either thermal or Lewis acid mediated conditions. Although thermal reactions of 5*H*-furan-2-one derivatives with various dienes have been studied, there remains problem in stereoselectivities (*endo* vs *exo* e.g.) of the cycloadducts.[8] Therefore, in place of the use of these α,β-unsaturated lactones, maleic anhydride analogs have been often used, although reduction of one of the two carbonyl groups of the cycloadducts would be required to obtain the desired products.[9]

Recently we reported that a bidentate Lewis acid efficiently promotes the intramolecular Diels–Alder (IMDA) reactions of triene systems having ester group linking diene and dienophile parts.[10] The IMDA reaction of such an ester tethered substrate is difficult to achieve under the thermal or common Lewis acid mediated conditions[11] because of the preference of transoid geometry,[12] while bis-aluminated triflic amides such as TfN[Al(Me)Cl]$_2$ generated in situ by mixing trifluoromethanesulfonamide (triflic amide, 1 mol) and dimethylaluminum chloride (2 mol) were found to strongly enhance the reactivity of the dienophile, presumably due to not only large oxophilic Lewis acidity of these bis-aluminated triflic amides,[10] but also a control of the conformation of ester moiety to be cisoid form **A** by the bidentate coordination (Scheme 1). Thus, it was expected that α,β-unsaturated lactones having cisoid-like ester structure would be also intensively activated through effective coordination to bis-aluminated triflic amide TfN(AlLn)$_2$ (**B** in Scheme 1). In this paper, we report that bis-aluminated triflic amide TfN(AlLn)$_2$ effects the Diels–Alder reaction of α,β-unsaturated lactones, in which selection of ligands on aluminum, for example, TfN[Al(Me)Cl]$_2$ versus TfN[Al(*i*Bu$_2$)]$_2$, are important depending on the combination of α,β-unsaturated lactone and 1,3-diene.



Scheme 1.

Keywords: Bis-aluminated triflic amide; Diels–Alder reaction; α,β-Unsaturated lactone.

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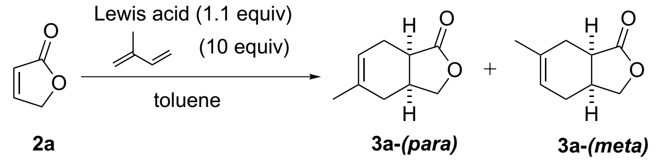
The Diels–Alder reaction of 5*H*-furan-2-one **2a** with isoprene was conducted under Lewis acid mediated conditions (Table 1). On using 1.1 equiv of TfN[Al(Me)Cl]$_2$ (**1a**), the reaction of **2a** with 10 equiv of isoprene proceeded at 60 °C within 6 h to give the adduct **3a** in 76% yield with excellent *para*-selectivity (*para*/*meta* > 20:1) (entry 1). By changing Cl ligand to methyl ligand on aluminum, thus with TfN(AlMe$_2$)$_2$ (**1b**), slightly lower yield (63% yield) and *para*-selectivity (*para*/*meta* = 9.5:1) of the adduct **3a** were observed. Furthermore, with TfN[Al(*i*Bu$_2$)]$_2$ (**1c**), which has more bulky two alkyl ligands, higher temperature and longer reaction time were required for the complete conversion of the dienophile **2a** to give the adduct **3a** in 52% yield (entry 3). On the other hand, monodentate Lewis acid Me$_2$AlCl, Tf$_2$NAl(Me)Cl, or TfN(Ph)[Al(Me)Cl] examined here did not effectively promote the reaction of **2a** with isoprene (entries 4–6). That is, contrary to the good result obtained by the use of the bidentate Lewis acid **1a** as shown in entry 1, when the reaction was conducted with 2.2 equiv of these Lewis acids, the Diels–Alder adduct **3a** was obtained in low yield (8–32%) along with the recovery of **2a** (23–31%) even after a longer reaction time. From these results, the bidentate bis-aluminated triflic amides **1** were found to be effective catalyst for the Diels–Alder reactions of α,β-unsaturated lactone **2a** with isoprene and the ligands on aluminum strongly influenced on its efficiency, as shown by the large difference between **1a** and **1c** in the reaction of **2a** with isoprene (entry 1 vs 3). It is also noted that efficiency of the bis-aluminated triflic amide **1**, in particular **1a** when compared with Tf$_2$NAl(Me)Cl or TfN(Ph)[Al(Me)Cl], cannot be explained simply by the Lewis acidity, rather the activation of the lactone **2a** due to the bidentate coordination is possibly important.

Based on the above result, the Diels–Alder reactions of α,β-unsaturated lactones **2a**–**c** with isoprene and 2,3-dimethylbutadiene catalyzed by bidentate bis-aluminated triflic amides **1** were carried out to see the effect of ligands on aluminum in each reaction (Table 2). As in the case with isoprene, the chloro/methyl derivative **1a** was found to efficiently accelerate the Diels–Alder reaction of the butenolide **2a** with 2,3-dimethylbutadiene to give the cycloadduct **4a** in 94% yield, while the use of the diisobutyl derivative **1c** gave **4a** in 43% yield after 24 h at 80 °C (entry 7 vs 8). Similarly, in the case of the six-membered unsaturated lactone **2b**, the Lewis acid **1a** rather than **1c** worked nicely in the Diels–Alder reaction with isoprene and 2,3-dimethylbutadiene to give the adducts **3b** and **4b** in 77% and 71% yields, respectively (entries 3 vs 4, 9 vs 10). On the other hand, in the reaction of less reactive α-methyl substituted butenolide **2c** with these acyclic dienes, the Lewis acid **1c** was found to be more effective than **1a** with respect to the yield of the adduct. For example, the adduct **3c** derived from **2c** and isoprene was obtained in 58% yield when the reaction was carried out with 1.1 equiv of **1c** for 24 h at 80 °C, while in 32% yield by using **1a** for 9 h at 80 °C (entries 5 vs 6). Similar tendency was also observed in the reaction of **2c** with 2,3-dimethylbutadiene (entries 11 vs 12). In addition to the results with cyclopentadiene described below, these results indicated that when the lactone (dienophile) reacts with diene slowly due to the steric reason as in the case of α-methyl substituted butenolide **2c**, polymerization of diene catalyzed by the Lewis acid proceeds and the rate of polymerization enhances as the Lewis acidity increases. Therefore, compared to **1c**, stronger Lewis acid **1a** was not always effective in the Diels–Alder reaction of **2c** with dienes. Efficiency of the bidentate Lewis acid such as **1c** for the Diels–Alder reaction of **2c** with these dienes should be noted, because there has been no report on a successful example of the Diels–Alder reaction of α-alkylated α,β-unsaturated lactones under both thermal and Lewis acid mediated conditions.[13]

Efficiency of the bulky bidentate Lewis acid **1c** was found remarkable in the reaction of **2c** with reactive cyclopentadiene (Table 3). Thus, in the presence of **1c**,

Table 1. Effect of Lewis acid on the Diels–Alder reaction of **2a** with isoprene



Entry	Lewis acid	Temp (°C)	Time (h)	Yield[a] (%)	*para*/*meta*[b]
1	TfN[Al(Me)Cl]$_2$ (**1a**)	60	6	76	>20:1
2	TfN(AlMe$_2$)$_2$ (**1b**)	60	3	63	9.5:1
3	TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	80	24	52	7.3:1
4[c,d]	Me$_2$AlCl	60	9	32	5.4:1
5[c,e]	Tf$_2$NAl(Me)Cl	60	7	28	2.7:1
6[c,f]	TfN(Ph)[Al(Me)Cl]	60	7	6	ND[g]

[a] Isolated yield.

[b] Determined by isolated yield.

[c] 2.2 equiv of Lewis acid was used.

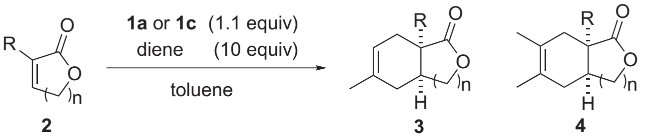
[d] Recovery of **2a**, 30%.

[e] Recovery of **2a**, 23%.

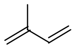
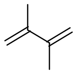
[f] Recovery of **2a**, 31%.

[g] *meta*/*para* ratio was not determined.

Table 2. The Diels–Alder reaction of **2** with acyclic dienes promoted by **1a** and **1c**

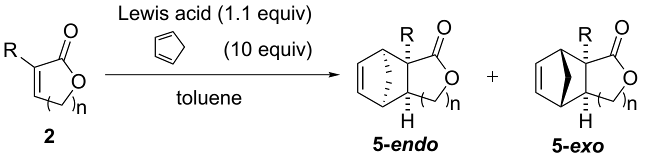


2a: n = 1, R = H **2b**: n = 2, R = H **2c**: n = 1, R = Me

Entry	2	Diene	Lewis acid	Temp (°C)	Time (h)	Product	Yield[a] (%)	*para*/*meta*[b]
1	**2a**		TfN[Al(Me)Cl]$_2$ (**1a**)	60	5	**3a**	76	>20:1
2	**2a**		TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	80	24	**3a**	52	7.3:1
3	**2b**		TfN[Al(Me)Cl]$_2$ (**1a**)	60	6	**3b**	77	8.4:1[c]
4	**2b**		TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	60	24	**3b**	38	8.5:1[c]
5	**2c**		TfN[Al(Me)Cl]$_2$ (**1a**)	80	9	**3c**	32	5.9:1
6	**2c**		TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	80	24	**3c**	58	4.1:1
7	**2a**		TfN[Al(Me)Cl]$_2$ (**1a**)	60	3	**4a**	94	
8	**2a**		TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	80	24	**4a**	43	
9	**2b**		TfN[Al(Me)Cl]$_2$ (**1a**)	60	24	**4b**	71	
10	**2b**		TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	60	24	**4b**	46	
11	**2c**		TfN[Al(Me)Cl]$_2$ (**1a**)	60	10	**4c**	31	
12	**2c**		TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	80	24	**4c**	42	

[a] Isolated yield.
[b] Determined by isolated yield.
[c] Determined by ^{1}H NMR (300MHz).

Table 3. Effect of Lewis acid on the Diels–Alder reaction of **2** with cyclopentadiene



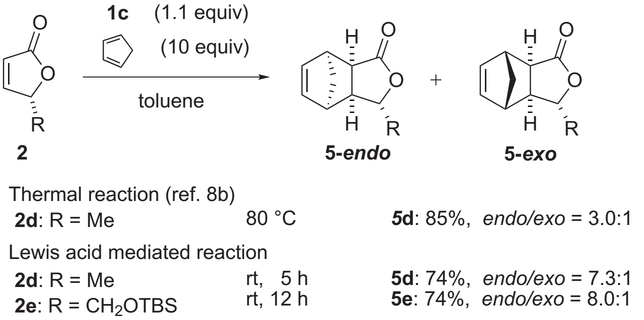
2a: n = 1, R = H **2b**: n = 2, R = H **2c**: n = 1, R = Me

Entry	2	Lewis acid	Temp (°C)	Time (h)	5	Yield[a] (%)	*endo*/*exo*[b]
1	**2c**	TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	Rt	4	**5c**	91	8.2:1
2	**2c**	TfN[Al(Me)Cl]$_2$ (**1a**)	Rt	12	**5c**	10	1.4:1
3	**2c**	TfN(AlMe$_2$)$_2$ (**1b**)	Rt	12	**5c**	19	4.8:1
4	**2c**	(Me$_2$Al)$_2$O	60	12	**5c**	13	3.1:1
5	**2c**	[(Me$_2$Al)$_2$O]$_2$SO$_2$	40	12	**5c**	12	ND[c]
6[d]	**2c**	Me$_2$AlCl	Rt	5	**5c**	12	2.5:1
7	**2a**	TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	Rt	13	**5a**	97	5.5:1
8	**2a**	TfN[Al(Me)Cl]$_2$ (**1a**)	Rt	4	**5a**	92	1.1:1
9	**2b**	TfN[Al(*i*Bu)$_2$]$_2$ (**1c**)	Rt	4	**5b**	99	7.8:1
10	**2b**	TfN[Al(Me)Cl]$_2$ (**1a**)	Rt	12	**5b**	68	4.5:1

[a] Isolated yield.
[b] Determined by isolated yield.
[c] *endo*/*exo* ratio was not determined.
[d] 2.2 equiv of Lewis acid was used.

α-methylated butenolide **2c** reacted with cyclopentadiene (10 equiv) at room temperature within 4h to give the corresponding adduct **5c** in excellent yield and with high *endo* selectivity (91%, *endo*/*exo* = 8.2:1) (entry 1). In contrast, the use of relatively strong Lewis acids **1a** or **1b**, remarkable decrease in the chemical yield of the cycloadduct **5c** (10% and 19%, respectively), was observed, possibly due to polymerization of cyclopentadiene and decomposition of **2c** by these Lewis acids prior to the Diels–Alder reaction (entries 2 and 3). Bidentate Lewis acid (Me$_2$Al)$_2$O[14a] and (Me$_2$AlO)$_2$-SO$_2$[14b] or monodentate Lewis acid such as Me$_2$AlCl were not effective for the Diels–Alder reaction of **2c** with cyclopentadiene giving rise to the adduct **5c** in low yield (entries 4–6). The bulky bidentate Lewis acid **1c** was also found to be more effective than the stronger Lewis acid **1a** in the reactions of the unsaturated lactone **2a**, **2b** with cyclopentadiene with respect to both chemical yield and *endo* selectivity of the adduct **5a**, **5b** (entries 7–10).[15]

Next, the Diels–Alder reactions of γ-substituted substrates **2d**, **2e** with cyclopentadiene were examined (Scheme 2). As shown in Scheme 2, it was reported that the thermal reaction of γ-methylated compound **2d** with



Scheme 2.

cyclopentadiene proceeded at 80 °C with complete π-facial selectivity to minimize steric influence of γ-methyl group, while the cycloadduct **5d** was obtained as an *endo*/*exo* mixture in a ratio of 3.0:1.[8b] The present bidentate Lewis acid **1c** was also an effective catalyst for the same reaction; that is, in the presence of **1c** the reaction of **2d** with cyclopentadiene proceeded at room temperature within 5 h to give the adduct **5d** in 74% yield with complete π-facial selectivity and a higher *endo* selectivity (*endo*/*exo* = 7.3:1). Similar result was observed in the reaction of γ-silyloxymethyl derivative **2e** with cyclopentadiene catalyzed by **1c** to give the adduct **5e** (74% yield, *endo*/*exo* = 8.0:1).

In conclusion, we have shown that the Diels–Alder reactions of α,β-unsaturated lactone derivatives including their α-methylated substrate with acyclic dienes and cyclopentadiene can be efficiently promoted by the bis-aluminated triflic amide, TfN[Al(Me)Cl]$_2$ and TfN[Al(iBu)$_2$]$_2$. Selection of these Lewis acids based on the ligand on the aluminum should be crucial to obtain high yield and high selectivity of the cycloadduct depending on the combination of α,β-unsaturated lactone and 1,3-diene.

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