seems particularly appealing for large-scale operations and for different substrates; with the emergence of a considerable number of new RTILs,[3, 11] it should be possible to design RTILs with high selectivity for specific substrates. The possibility of using nonpolar solvents with high boiling points or water instead of diethyl ether, and supported RTIL in hollow-fiber membranes will allow this technology to reinforce its environmentally benign character and become attractive for industrial application.

Experimental Section

For the batch studies, the cell indicated in Figure 1 was used without pumps. The ionic liquid 1-*n*-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]) was immobilized in the porous structure of a polyvinylidene fluoride (PVDF) hydrophilic membrane (Gelman Sciences, FP Vericel, pore size 0.45 μm) by filtration in vacuo and placed in a metallic net (i.d. 1.65 cm) located between side A ($V = 30$ mL) and side B ($V = 30$ mL) of the cell. The amines (1:1:1 molar mixture) hexylamine (470 μL), DIIPA, (500 μL) and TEA (500 μL), and *n*-decane (400 μL; internal standard) in diethyl ether (30 mL) were added to side A of the cell. *n*-Decane (400 μL; internal standard) was added to diethyl ether (30 mL) in side B of the cell. The transport of amines to side B at room temperature was monitored by GLC by taking samples from side A and B of the cell at defined time intervals (15, 30, 60, 120, 240, 360 min). The recovery of each amine was determined by comparison of the areas of the peaks of each amine with those of *n*-decane and relative to the areas initially observed in side A.

For continuous operation conditions, the cell indicated in the Figure 1 was used, with each side of the cell connected to a piston pump (FMI lab pump, model QSY) to promote the circulation in each side. The RTIL [bmim][PF_6] was immobilized as indicated above. The amines (1:1 molar mixture) DIIPA (100 mL) and TEA (100 mL) in diethyl ether (5 L) were circulated with a flow rate of 1 mL/min in side A of the cell. Diethyl ether (5 L) was circulated with a flow rate of 1 mL min^{-1} in side B of the cell. Both solutions were renewed every 2 days. The transport of each amine to side B was monitored by sequentially collecting samples from the outlet tube of side B every 12 h. During the 14 days of continuous operation, 23 samples were collected with a total volume of 20410 mL. The DIIPA/TEA ratio was determined for each sample by GLC. Eighteen samples (15460 mL) were fractionally distilled to afford a mixture of DIIPA/TEA (250 mL; 89.2:10.8, determined by GLC); ^{1}H and ^{13}C NMR spectral data were identical to those of authentic samples. The distilled diethyl ether fraction and the remaining six samples contained a mixture of DIIPA/TEA (142.2 mL (81.6:18.4) and 105.7 mL (80.9:19.1), respectively, ratio determined by GLC analysis with *n*-decane as internal standard).

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Lewis Acid Controlled Regioselective 1,2 and 1,4 Reaction of α,β-Unsaturated Carbonyl Compounds with Ti^{IV} Enolates Derived from α-Diazo β-Keto Carbonyl Compounds**

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The addition of nucleophiles to α,β-unsaturated carbonyl compounds is a fundamental transformation in organic synthesis. Since there are two reaction sites in the α,β-unsaturated carbonyl functional group, this addition reaction can only be of practical synthetic utility in organic synthesis if one

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can control the selectivity for the two possible regioisomers.[1] There are several factors that control the regioselectivity (1,2 vs 1,4 addition). These include the attacking nucleophiles,[2] solvent,[3] temperature,[4] steric bulk,[5] and transition-metal additives.[6, 7] In general, the softness or hardness of the nucleophiles is of primary importance. Hard nucleophiles, such as alkyl lithium compounds, give predominantly 1,2 addition, whereas soft nucleophiles, such as the anion of the activated methylene compounds, give primarily 1,4 addition products.[8]

On the other hand, the complexation of Lewis acids with the carbonyl oxygen atom can dramatically affect the properties of the α,β-unsaturated carbonyl compounds.[9] For example, both the reactivity and the selectivity of the Diels–Alder reaction of α,β-unsaturated carbonyl compounds with dienes could be greatly enhanced by Lewis acids.[10] Lewis acids play an indispensable role in organic chemistry, especially in catalytic asymmetric synthesis. Herein we report the Lewis acid promoted nucleophilic addition of the $TiCl_4$-derived enolate of β-keto α-diazo carbonyl compounds to α,β-unsaturated carbonyl compounds. We found that by choosing appropriate Lewis acids, it is possible to control the selectivity for either 1,2 or 1,4 addition.

The Ti enolate **1a** or **1b** was generated by treating the β-keto α-diazo carbonyl compounds with $TiCl_4/Et_3N$ in anhydrous CH_2Cl_2 at $-78\,^{\circ}C$ (Scheme 1).[11] When the enolate **1a** reacts with enone **2a** at $-78\,^{\circ}C$, a mixture of 1,2- and 1,4-addition products (60:40) was isolated in 70% yield (Table 1, entry 1). If the enone **2a** was stirred with another equivalent of $TiCl_4$ in CH_2Cl_2 before adding to the enolate **1a**, the 1,4-addition product was obtained as the major product (1,2/1,4 17:83) (Table 1, entry 4). If the enone **2a** was activated with $SnCl_4$ (1 equiv) instead of $TiCl_4$, the selectivity for 1,4 addition was further enhanced (1,2/1,4 5:95; Table 1, entry 5). On the other hand, when the enone **2a** was activated with $BF_3\cdot OEt_2$, the 1,2-addition product became predominant (1,2/1,4 83:17; Table 1, entry 2). The activation of enone with $Ti(OiPr)_4$ further enhanced the selectivity for 1,2 addition (1,2/1,4 96:4; Table 1, entry 3). For Ti enolate **1b**, a similar enhancement of regioselectivity was observed (Table 1, entries 6–10).

When enone **2b** was employed as the substrate, the direct reaction with the Ti enolate **1a** gave equal amounts of 1,2- and 1,4-addition products (Table 1, entry 11). $TiCl_4$ activation of the enone significantly enhanced 1,4 addition (1,2/1,4 1:99; Table 1, entry 14), whereas $BF_3\cdot OEt_2$ did not affect the selectivity for 1,2 addition (1,2/1,4 49:51; Table 1, entry 12). Evidently, the steric bulk of the phenyl group in enone **2b** overrides the activation of $BF_3\cdot OEt_2$ for the carbonyl group.[5a] However, activation by $Ti(OiPr)_4$ can still enhance the selectivity for the sterically less favored 1,2 addition (1,2/1,4 76:24; Table 1, entry 13).

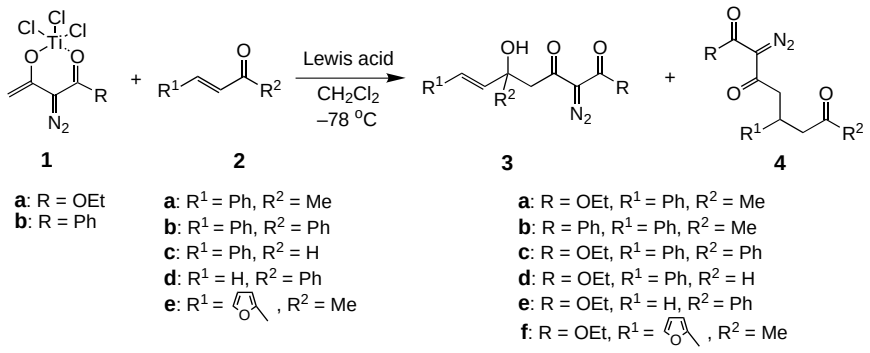
For enal **2c**, only the 1,2-addition product was isolated, even in the $TiCl_4$-activated reaction (Table 1, entries 15, 16). The high reactivity of the aldehyde carbonyl group is the determining factor in controlling the regioselectivity in this case. On the other hand, for the enones **2d** and **2e**, similar control of diastereoselectivity as that for **2a** and **2b** was observed (Table 1, entries 17–22).

Regiocontrol by Lewis acids has also been observed for cyclic enones. Without the activation of the Lewis acid, the reaction of Ti enolate **1a** with cyclohexenone **5b** (Scheme 2) gave a mixture of 1,2- and 1,4-addition products in low selectivity (1,2/1,4 67:33; Table 2, entry 4). $TiCl_4$ activation gave almost only 1,4-addition product (1,2/1,4 1:99; Table 2, entry 7), whereas $BF_3\cdot OEt_2$ activation slightly increases the amount of 1,2-addition product obtained (1,2/1,4 86:14; Table 2, entry 5). When the enone was activated with $Ti(OiPr)_4$, the 1,2-addition product is greatly increased (1,2/1,4 99:1; Table 2, entry 6). For cyclopentenone **5a**, the reaction without Lewis acid activation gave a mixture of unidentified products (Table 1, entry 1). $TiCl_4$ activation gave the

Table 1. Regioselective nucleophilic addition of Ti enolate **1** with α,β-unsaturated carbonyl compounds **2**.

Entry	1	2	Lewis acid[a]	t [h]	3	4	3/4[b]	Yield [%][c]
1	**a**	**a**	none	6	**a**	**a**	60:40	70
2	**a**	**a**	$BF_3\cdot OEt_2$	8	**a**	**a**	83:17	67
3	**a**	**a**	Ti(O*i*Pr)4	8	**a**	**a**	96:4	78
4	**a**	**a**	$TiCl_4$	6	**a**	**a**	17:83	63
5	**a**	**a**	$SnCl_4$	10	**a**	**a**	5:95	50
6	**b**	**a**	none	8	**b**	**b**	50:50	42
7	**b**	**a**	$BF_3\cdot OEt_2$	9	**b**	**b**	76:24	48
8	**b**	**a**	$Ti(OiPr)_4$	8	**b**	**b**	94:6	60
9	**b**	**a**	$TiCl_4$	9	**b**	**b**	22:78	75
10	**b**	**a**	$SnCl_4$	8	**b**	**b**	0:100	58
11	**a**	**b**	none	9	**c**	**c**	50:50	71
12	**a**	**b**	$BF_3\cdot OEt_2$	8.5	**c**	**c**	49:51	83
13	**a**	**b**	$Ti(OiPr)_4$	8	**c**	**c**	76:24	90
14	**a**	**b**	$TiCl_4$	8	**c**	**c**	1:99	73
15	**a**	**c**	none	7	**d**	**d**	100:0	50
16	**a**	**c**	$TiCl_4$	5	**d**	**d**	100:0	71
17	**a**	**d**	none	8.5	**e**	**e**	40:60	73
18	**a**	**d**	$Ti(OiPr)_4$	8.5	**e**	**e**	76:24	82
19	**a**	**d**	$SnCl_4$	8.5	**e**	**e**	0:100	76
20	**a**	**e**	none	8	**f**	**f**	71:29	78
21	**a**	**e**	$Ti(OiPr)_4$	8	**f**	**f**	100:0	81
22	**a**	**e**	$SnCl_4$	8	**f**	**f**	0:100	54

[a] Lewis acid (1 equiv) was used to activate the substrate. [b] The product ratio was determined by ^1H NMR spectroscopic analysis (400 MHz) and was confirmed by separation by column chromatography. [c] Yield of isolated products.



1: **a**: R = OEt; **b**: R = Ph

2: **a**: R^1 = Ph, R^2 = Me; **b**: R^1 = Ph, R^2 = Ph; **c**: R^1 = Ph, R^2 = H; **d**: R^1 = H, R^2 = Ph; **e**: R^1 = , R^2 = Me

3: **a**: R = OEt, R^1 = Ph, R^2 = Me; **b**: R = Ph, R^1 = Ph, R^2 = Me; **c**: R = OEt, R^1 = Ph, R^2 = Ph; **d**: R = OEt, R^1 = Ph, R^2 = H; **e**: R = OEt, R^1 = H, R^2 = Ph; **f**: R = OEt, R^1 = , R^2 = Me

Scheme 1. Lewis acid promoted nucleophilic addition of Ti enolate **1** with α,β-unsaturated carbonyl compounds **2**.

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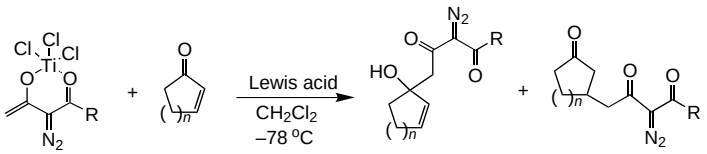


1 **5** **6** **7**

a: R = OEt **a**: *n* = 1 **a**: R = OEt, *n* = 1
b: R = Ph **b**: *n* = 2 **b**: R = OEt, *n* = 2
c: R = Ph, *n* = 2

Scheme 2. Lewis acid promoted nucleophilic addition of Ti enolate **1** with cyclic enones **5**.

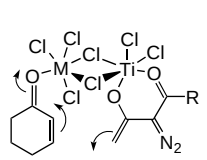
Table 2. Regioselective nucleophilic addition of Ti enolate **1** with cyclic enones **5**.

Entry	1	5	Lewis acid[a]	*t* [h]	6	7	6/7[b]	Yield [%][c]
1	**a**	**a**	none	8	**a**	**a**	–	–[d]
2	**a**	**a**	$BF_3 \cdot OEt_2$	6.5	**a**	**a**	–	–[d]
3	**a**	**a**	$TiCl_4$	7	**a**	**a**	0:100	45
4	**a**	**b**	none	8	**b**	**b**	67:33	63
5	**a**	**b**	$BF_3 \cdot OEt_2$	8	**b**	**b**	86:14	40
6	**a**	**b**	$Ti(OiPr)_4$	8.5	**b**	**b**	99:1	68
7	**a**	**b**	$TiCl_4$	7	**b**	**b**	1:99	52
8	**b**	**b**	none	8	**c**	**c**	70:30	51
9	**b**	**b**	$BF_3 \cdot OEt_2$	8.5	**c**	**c**	100:0	31[e]
10	**b**	**b**	$TiCl_4$	8.5	**c**	**c**	19:81	47
11	**b**	**b**	$SnCl_4$	8	**c**	**c**	0:100	34[e]

[a] Lewis acid (1 equiv) was used to activate the substrate. [b] The product ratio was determined by ^1H NMR spectroscopic analysis (400 MHz) and was confirmed by separation by column chromatography. [c] Yields of isolated products. [d] The reaction gave a complex mixture, 1,4-addition product could be isolated in low yield. [e] Considerable amounts of starting materials were recovered.

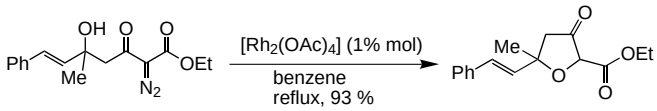
1,4-addition compound as the sole product (Table 1, entry 3). The 1,2-addition product could not be isolated when the reaction was activated with $BF_3 \cdot OEt_2$. This is believed to be a result of the low stability of the 1,2-addition product **6a**.

The Lewis acid controlled selectivity described above could be rationalized as follows. As the anion of the activated methylene compound, the Ti enolate **1** is considered to be a soft nucleophile.[8b] From ab initio calculations it is known that the complexation of the Lewis acid with the oxygen atom of an α,β-unsaturated carbonyl compound increases its carbonyl coefficient of LUMO relative to that of the remote β-carbon atom,[12] and hence the Lewis acid coordination should promote 1,2 addition. Therefore, $BF_3 \cdot OEt_2$ enhances the 1,2 selectivity. However, when enones are activated by $TiCl_4$ or $SnCl_4$,[13] there is another factor that overrides the Lewis acid activation for 1,2 addition. It is known that $TiCl_4$ can form dimeric structures that involve bridging chlorine atoms.[14, 15] Therefore we speculate that the complex **8** formed in the $TiCl_4$- or $SnCl_4$-activated reactions in which the two chlorine atoms serve as bridges for the two transition metals. Because of the steric proximity in this structure, 1,4 addition occurs much easier. Strong evidence to support this rationalization is that when $Ti(OiPr)_4$, which has no chlorine atoms for the bridging, is used as the activator, 1,2 addition was again greatly enhanced (Table 1, entries 3, 8 13, 18, 21; Table 2, entry 6).



8 (M = Sn or Ti)

Since the nucleophilic addition products bear diazo functionality, both 1,2- and 1,4-addition products can be subjected to further synthetically useful transformations.[16] For example, when **3a** was treated with $[Rh_2(OAc)_4]$ (1 mol %) in benzene, highly efficient chemoselective intramolecular insertion into the O–H bond occurs to give tetrahydrofuran derivative **9** as a mixture of two diastereomeric isomers in excellent yield (Scheme 3).



3a **9**

Scheme 3. $[Rh_2(OAc)_4]$-mediated intramolecular O–H insertion.

In summary, we have demonstrated that both 1,2 and 1,4 selectivity of the nucleophilic addition could be controlled by Lewis acids. Similar control of selectivity may be possible for other types of nucleophiles. Investigations along this line are underway in our laboratory.

Experimental Section

Typical procedure: $TiCl_4$ (209 mg, 1.1 mmol) and Et_3N (111 mg, 1.1 mmol) were added dropwise to a solution of **1a** (156 mg, 1 mmol) in anhydrous CH_2Cl_2 (10 mL) at –78 °C. The dark-red mixture was stirred at –78 °C for 1 h. $Ti(OiPr)_4$ (284 mg, 1 mmol) and **2a** (146 mg, 1 mmol) in anhydrous CH_2Cl_2 (2 mL) were added to this mixture. The reaction mixture was stirred for another 8 h and then quenched with saturated aqueous NH_4Cl (5 mL). The organic layer was separated; upon workup, a crude product was obtained which was purified by flash chromatography to yield major product **3a** as an oil (224 mg) and minor product **4a** as a white solid (10 mg, m.p. 68–69 °C) in 78% total yield. Simultaneously, **1a** (13%) and **2a** (19%) were recovered.

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First Evidence of Fast S–H···S Proton Transfer in a Transition Metal Complex**

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In the quest to control noncovalent interactions, S–H···S hydrogen bonds are attracting great interest. Despite the prevalence of the thiol group in cysteine residues and the potential importance of S–H···S bridging bonds in biology, little is known about this interaction.[1] Intermolecular S–H···S chains that play an organizing role in the solid state were found in X-ray structures of several compounds containing S–H groups.[2] The S–H···S hydrogen bonds are typically very weak, but may become moderately strong in particular compounds. Resonance[3] and charge[4] assistances have been put forward as being responsible for strong intramolecular S–H···S bonds. The greater acidity of dithiols relative to their monothiol analogues has been attributed to enhanced stabilization of the thiolate anion by an intramolecular $RS^-\cdots HSR$ hydrogen bond.[5] Evidence of S–H···S interactions in transition metal compounds are scarce,[6] although the acidity of the SH group should be enhanced when the sulfur atom is coordinated to a transition metal. Indeed, Sellmann et al. found strong intermolecular S–H···S bridges in the crystal structure of $[Ru(SH_2)(PPh_3)$ "S_4"].[6a] An influence of these bridges on the reactivity of the metal complexes has not been demonstrated, although intramolecular M–SH···hydride interactions have been proposed in the initial stage of the mechanism of hydride protonation.[7] Here we show that a fast S–H···S proton exchange takes place in bimetallic platinum complexes with bridging SH^- and S^{2-} ligands.

Sulfide-bridged aggregates with the Pt_2S_2 core have a rich chemistry.[8, 9] We proved that the reactivity of the Pt_2S_2 core is highly dependent on the nature of the terminal ligands.[9, 10] We have now synthesized of the monoprotonated complexes $[Pt_2\{Ph_2P(CH_2)_nPPh_2\}_2(\mu\text{-S})(\mu\text{-SH})]ClO_4$ ($n=2$, dppe (**1**); $n=3$, dppp (**2**)) by adding $HClO_4$ to a solution of the corresponding $[Pt_2(\mu\text{-S})_2P\cap P)_2]$ ($P\cap P$ = dppe or dppp) complex in benzene. The most remarkable spectroscopic feature of **1** and **2** is the equivalence of the four phosphorus nuclei at room temperature according to the ^{31}P NMR spectrum (Figure 1). The only analogous monoprotonated compound

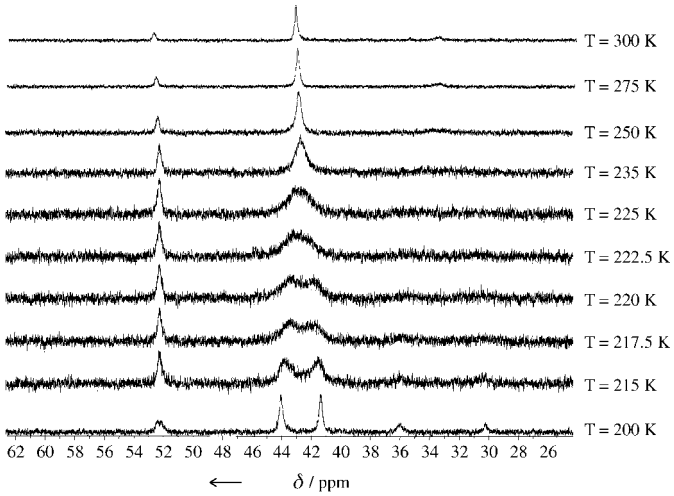

Figure 1. Variable-temperature $^{31}P\{^1H\}$ NMR spectra of **1**.

previously reported, namely, $[Pt_2(\mu\text{-S})(\mu\text{-SH})(PPh_3)_4]PF_6$, has two distinct environments about the P nuclei, as the SH group is *cis* to two phosphorus atoms and *trans* to the other two. Consequently, at room temperature, it shows two ^{31}P NMR signals with two distinct $^1J_{Pt,P}$ coupling constants.[8b, 11] Surprisingly, each of the monoprotonated complexes **1** and **2** shows only one pseudotriplet with the following apparent spectroscopic parameters in [D$_6$]acetone: $\delta_P = 42.8$ ppm and $^1J_{Pt,P} = 3108$ Hz for **1**, and $\delta_P = -3.3$ ppm and $^1J_{Pt,P} = 2960$ Hz for **2**.

We optimized the geometry of the model compounds $[Pt_2\{H_2P(CH_2)_nPH_2\}(\mu\text{-S})(\mu\text{-SH})]^+$ ($n=2$, dhpe (**1t**); $n=3$, dhpp (**2t**)) by B3LYP calculations.[12] Two conformations with a hinged Pt_2S_2 skeleton were found as minima in both complexes; they differ in the *endo* (**e**) or *exo* (**x**) orientation of the thiol proton (see Figure 2). As expected, two different Pt–P and two different Pt–S distances were found in all cases (e.g., in **1t(x)** Pt–P(*trans*-S) 2.338, Pt–P(*trans*-SH) 2.279, Pt–S 2.389, Pt–SH 2.465 Å), and this reflects the different *trans* influences of the sulfide and thiol ligands. The *exo* form is slightly more stable than the *endo* form, although the *exo*/

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