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Nickel-catalyzed organozinc-induced unexpected 1,3-migration of *tert*-butyl from sulfur to carbon in *N-tert*-butanesulfinyl iminoacetates

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ABSTRACT

The nickel-catalyzed reaction for an unexpected 1,3-migration of *tert*-butyl from sulfur to carbon, upon treatment of functionalized *N-tert*-butanesulfinyl iminoacetate in the presence of organozinc reagent, was developed. The generality has been explored by considering the flexibility in the structure of each reactive component, organozinc halide and *N-tert*-butanesulfinyl iminoacetate.

The carbon–carbon bond-forming reaction catalyzed by either a nickel or palladium catalyst between organometallic reagents and electrophiles is a powerful tool for constructing complex natural and unnatural organic molecules in the last decades.[1] Among these organometallic reagents, organozinc halides represent an optimal compromise in terms of reactivity and wide functional group tolerance. Most of them have been used for the alkylation of alkyl electrophiles,[2] aldehyde, ketone,[3] α,β-unsaturated carbonyl compounds,[4] and imines[5] (*N*-sulfonyl imines[6]) in mild conditions. Recently, some new types of reactions (e.g., formation of *E*-stilbenes by witting-type reaction via organozinc halides with high selectivity and excellent yield) have also been developed.[7]

The *N*-sulfur imines, one of the most versatile intermediates, have been extensively used in organic synthesis. Especially, the commercially available chiral *N-tert*-butanesulfinamide is widely used due to its excellent diastereocontrol and the mild conditions for its cleavage.[8,9] The direct additions of Grignard, organolithium, and aryl boron reagents to *N*-sulfur imines represent the most reliable methods to prepare enantiopure amines, α- and β-amino acids, and α- and β-amino phosphonates.[10,11] Unfortunately, these reagents usually could not be tolerant to the labile functional groups of nucleophiles. In order to find a general approach to prepare amino acids bearing some unusual substituents, we are interested in exploring this challenging reaction by using organozinc halides with glyoxylate *N-tert*-butanesulfimine catalyzed by $Ni(acac)_2$. Surprisingly, when the *N-tert*-butanesulfinyl iminoacetate was treated with organozinc reagent in the presence of nickel, instead of the desired product (nucleophilic addition) which was only detected as a small amount, the predominant product was the unexpected product which was generated by the 1,3-migration of *tert*-butyl group from sulfur to carbon. To our best knowledge, this is the first example of a 1,3-migration of *tert*-butyl from sulfur to carbon that occurred in this system. Herein, we wish to report this novel 1,3-migration which was achieved by organozinc halides with *N-tert*-butanesulfinyl iminoacetate catalyzed by $Ni(acac)_2$ (Scheme 1).

In order to investigate the scope and limitations of this novel 1,3-migration, various functionalized zinc reagents and catalysts had been executed. When organozinc iodides were used, it was found that all the reactions achieved good to excellent yields in the presence of 10 mol % $Ni(acac)_2$ (Table 1, entries 1–13) in a mild reaction condition. We had also tested the organozinc bromides instead of iodide and found that bromides were active enough to obtain the desired products in this condition (entries 3 and 15), although the yield was relatively low for benzylzinc bromide (entry 14). Intensive screening revealed that the unexpected migration was generated in lower yield (25%) when Et_2Zn was used in the same conditions.

The effects of the catalysts on this reaction were studied using n-$C_3H_7CH_2ZnI$ as a substrate. As shown in Table 1, $Ni(acac)_2$ gave the best result with the 10 mol % loading (entries 1 and 16–19). Interestingly, in the absence of $Ni(acac)_2$, the reaction could continued to take place although the yield was relatively lower (entry 20). Consequently, catalysts may play an important role regarding the reaction efficiency and the reactivity.

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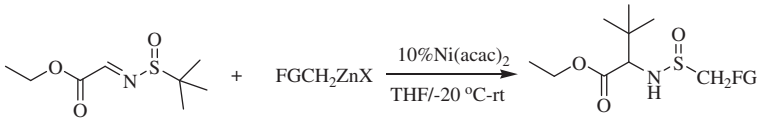
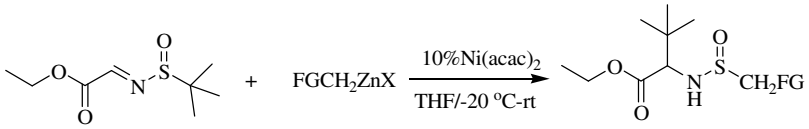


Scheme 1.

Table 1
Organozinc-induced 1,3-migration of *tert*-butyl from *N*-*tert*-butanesulfinyl iminoacetates[12]

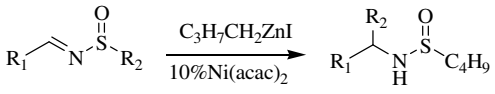


1 a~n **3** a~n

Entry[a]	FGCH$_2$–	X	Catalyst	*T* (°C)	Product	Y[b] (%)
1	CH_3CH_2	I	10% Ni(acac)$_2$	−20 to rt	**3a**	92
2	$C_2H_5CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3b**	88
3	*n*-$C_3H_7CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3c**	89
4	*n*-$C_4H_9CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3d**	81
5	*n*-$C_5H_{11}CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3e**	85
6	*n*-$C_9H_{19}CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3f**	76
7	$(CH_3)_2CH$	I	10% Ni(acac)$_2$	−20 to rt	**3g**	79
8	$(CH_3)_2CHCH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3h**	83
9	Cyclopentyl–	I	10% Ni(acac)$_2$	−20 to rt	**3i**	74
10	Cyclohexyl–	I	10% Ni(acac)$_2$	−20 to rt	**3j**	71
11	$BnOOC(CH_2)_2CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3k**	68
12	$CH_3OOC(CH_2)_2CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3l**	72
13	$BnOCH_2(CH_2)_2CH_2$	I	10% Ni(acac)$_2$	−20 to rt	**3m**	78
14	$PhCH_2$	Br	10% Ni(acac)$_2$	−20 to rt	**3n**	47
15	*n*-$C_3H_7CH_2$	Br	10% Ni(acac)$_2$	−20 to rt	**3c**	87
16	*n*-$C_3H_7CH_2$	I	20% Ni(acac)$_2$	−20 to rt	**3c**	87
17	*n*-$C_3H_7CH_2$	I	5% Ni(acac)$_2$	−20 to rt	**3c**	74
18	*n*-$C_3H_7CH_2$	I	10% In(OTf)$_3$	−20 to rt	**3c**	18
19	*n*-$C_3H_7CH_2$	I	10% Cu(OTf)$_2$	−20 to rt	**3c**	23
20	*n*-$C_3H_7CH_2$	I	None	−20 to rt	**3c**	61

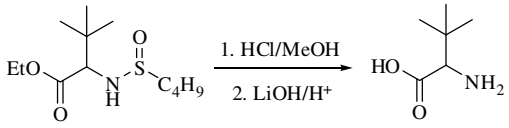
[a] 2.5 mmol alkyl zinc halides, 1 mmol *N*-*tert*-butanesulfinyl iminoacetate.
[b] Isolated yield.

Table 2
Influence of the *N*-sulfinyl imines on the reactivity



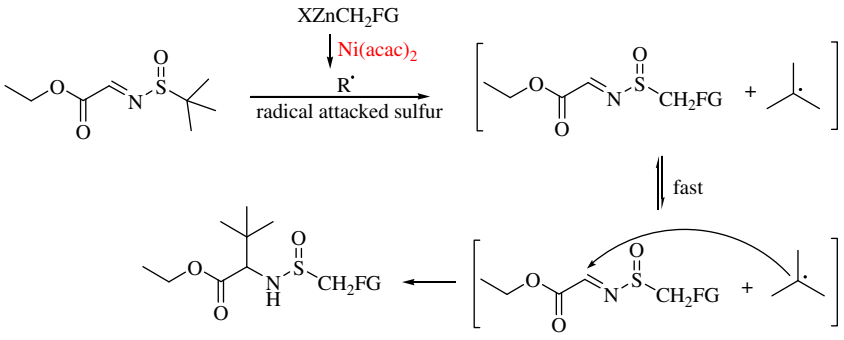
Entry	R_1	R_2	Y[a] (%)
1	Ph	*tert*-Butyl	0
2	Ph	*p*-$CH_3C_6H_4$	0
3	EtOOC	*p*-$CH_3C_6H_4$	0
4	EtOOC	*tert*-Butyl	89
5	MeOOC	*tert*-Butyl	84
6	PhOOC	*tert*-Butyl	71

[a] Isolated yield.



Scheme 2.

With optimal reaction condition in hand, a survey of various *N*-sulfinyl imines was carried out (Table 2). If the ethyl, methyl, and benzyl esters (entries 4–6) were applied, the 1,3-migration products were produced in high yields, while no desirable products could be detected if benzylimines and N-substituted sulfimines (entries 1–3) were used. By the removal of the *N*-sulfinyl and ethyl



Scheme 3. Plausible mechanism of 1,3-migration of *tert*-butyl catalyzed by Ni(acac)$_2$.

groups of compound **3c** under acidic condition (HCl/MeOH) followed by ester hydrolysis (LiOH), an important product *tert*-leucine would be afforded in 72% yield (Scheme 2). The spectroscopic and physical data of the synthetic *tert*-leucine were in excellent agreement with those reported.[13] Thus, this manipulation further unambiguously confirmed the structures of unexpected 1,3-migration products. A plausible reaction pathway is shown in Scheme 3. We proposed that the plausible reaction mechanism may be involved in a radical addition pathway, since the CH_2FG radical could be easily formed.[14] It was reasoned that the stabilized CH_2FG radical by $Ni(acac)_2$ attacks the sulfur and the single electron on the oxygen atom comes back to re-form the double bond of the sulfoxide. Meanwhile, the *tert*-Butyl radical generated attacks the imine to form a new C–C bond. Further study of the mechanism is underway.

In summary, nickel-catalyzed organozinc-promoted unexpected 1,3-migration of *tert*-butyl from sulfur to carbon in *N*-*tert*-butanesulfinyl iminoacetates had been described. The structures of these 1,3-migration products had been confirmed by converting to the corresponding *tert*-leucine. The further utilization of these 1,3-migration products will be reported in due course.

Acknowledgments

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12. *General procedure*: To a solution of ethyl *N*-(*tert*-butanesulfinyl)iminoacetate (205 mg, 1 mmol) and $Ni(acac)_2$ (10 mol %) in anhydrous THF (10 mL) was added a freshly prepared organozinc reagent (2.5 mL, 1 M in THF) at −20 °C under argon atmosphere. Then the mixtures were allowed to warm to room temperature. After being further stirred for another 6 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (4 mL) and diluted with EtOAc (30 mL) and brine (10 mL). The organic layer was separated and the aqueous phase was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (10 mL × 3), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by chromatography on silica gel (EtOAc/petroleum ether) to give mixtures of compounds. Compound **3c** (the ratio is 1:1 based on the GC value) as a colorless oil; IR (KBr) 3244, 2960, 2932, 2866, 1732, 1463, 1364, 1315, 1216, 1151 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.69 (d, J = 7.5 Hz, 1H), 4.45 (d, J = 7.8 Hz, 1H), 4.26–4.17 (m, 4H), 3.64 (d, J = 10.8 Hz, 1H), 3.54 (d, J = 9.6 Hz, 1H), 2.84–2.69 (m, 4H), 1.72–1.61 (m, 4H), 1.51–1.41 (m, 4H), 1.29 (m, 6H), 1.05–0.94 (m, 24H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 172.6, 66.5, 61.3, 61.2, 60.9, 56.2, 54.3, 34.9, 34.0, 26.7, 26.3, 25.2, 25.1, 21.9, 21.8, 14.2, 14.1, 13.8, 13.7; MS (ESI): 286 ($M+Na^+$); HRESIMS calcd for ($C_{12}H_{25}NNaO_3S + Na^+$): 286.1455, found 286.1448.
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