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Novel Transformations of γ-Silyl Nitro Compounds

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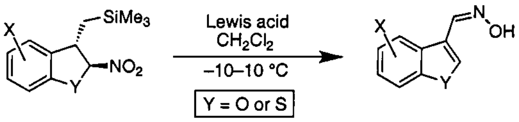
ABSTRACT



Introduction of a γ-silyl group into nitro compounds of dihydrobenzofuran, dihydrobenzo[*b*]thiophene, and dihydrofuran allowed new transformations to take place in the presence of a Lewis acid to give the corresponding α,β-unsaturated oximes or multisubstituted dihydrofurans, respectively, in good to excellent yields.

Many organosilicon compounds are stable under acidic and basic conditions.[1] Organosilyl groups, however, can exert α- and β-effects, which allow reactions to take place in a promoted or directed manner.[2] Reactions involving the γ-effect of silicon are limited,[3] such as in the Nef reaction,[4] $TiCl_4$-catalyzed arylation of 1,4-benzoquinones,[5] and norbornyl solvolyses.[6] In certain transformations, a γ-silyl group is eliminated from the substrate.[7] Examples include 1,4-elimination of γ-silyl alcohols by use of ceric ammonium nitrate[8] as well as ring opening of γ-silyl cyclopropyl[9] and cyclobutyl[10] ketones by Lewis acids. Herein, we report our new findings on the Lewis acid-catalyzed transformations of various γ-silyl nitro compounds[11] to benzofuran oximes, to benzo[*b*]thiophene oximes, and to multisubstituted dihydrofurans. These unprecedented transformations may involve complicated mechanisms.

Four commonly used Lewis acids, $AlCl_3$, $TiCl_4$, $BF_3{\cdot}OEt_2$, and $SnCl_4$, were chosen to catalyze the transformation of various γ-silyl nitro compounds.[11] Activity of these catalysts

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follows the order $AlCl_3 > TiCl_4 > BF_3{\cdot}OEt_2 > SnCl_4$.[12] First, we treated **1a**, prepared from the corresponding 2-nitrobenzofuran and trimethylsilylmethylmagnesium chloride, with a Lewis acid (2.0 equiv) in dichloromethane at −10 to 0 °C (Scheme 1). A stereoisomeric mixture of oximes **2a**[13] was obtained in 83−87% yield (see Table 1). The *E*/*Z* ratio of **2a** ranging from 1:1 to 1:6 was dependent upon the Lewis acids applied, among which $BF_3{\cdot}OEt_2$ gave the highest selectivity (1:6). We identified the structures and the configurations of the new compounds *E*- and *Z*-**2a** by spectroscopic methods and, especially, X-ray crystallography (see Figures 1(A) and (B)). In a control experiment under the same conditions, we found that the corresponding isopropyl nitro compound **1e** resulted in an inseparable complex mixture. This compound possessed a steric environment similar to that in **2a**, but without a *γ*-silyl group.

Scheme 1

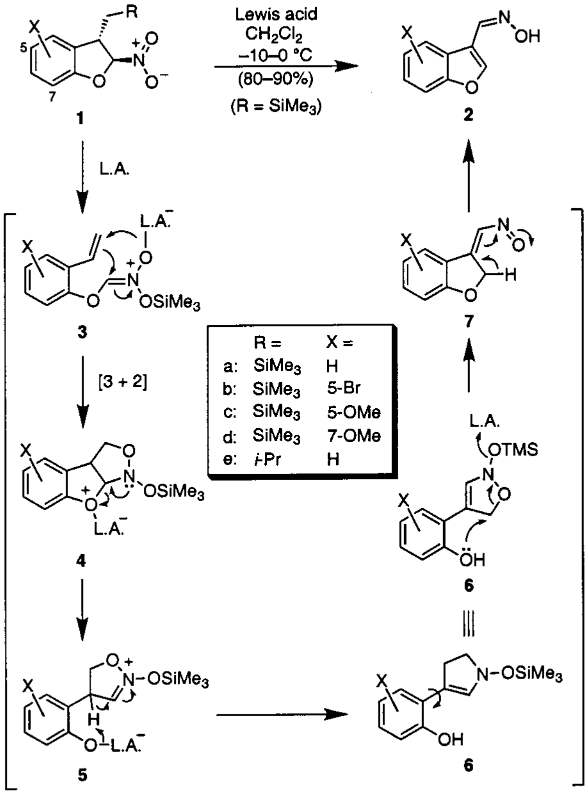

Table 1. Transformations of *γ*-Silyl Nitro Compounds **1a−d** to Oximes **2a−d** in CH_2Cl_2 by Various Lewis Acids (2.0 equiv) at −10−0 °C

starting material	Lewis acid	product	overall yield (%)	*E*/*Z* ratio
1a	$AlCl_3$	**2a**	84	1:1
1a	$TiCl_4$	**2a**	87	1:2
1a	$BF_3{\cdot}OEt_2$	**2a**	83	1:6
1a	$SnCl_4$	**2a**	86	1:2
1b	$AlCl_3$	**2b**	82	1:1
1b	$TiCl_4$	**2b**	90	1:2
1b	$BF_3{\cdot}OEt_2$	**2b**	85	1:5
1b	$SnCl_4$	**2b**	82	1:3
1c	$AlCl_3$	**2c**	83	1:1
1c	$TiCl_4$	**2c**	88	1:2
1c	$BF_3{\cdot}OEt_2$	**2c**	80	1:5
1c	$SnCl_4$	**2c**	81	1:2
1d	$AlCl_3$	**2d**	85	1:1
1d	$TiCl_4$	**2d**	90	1:6
1d	$BF_3{\cdot}OEt_2$	**2d**	80	1:5
1d	$SnCl_4$	**2d**	81	1:2

The speculative mechanism shown in Scheme 1 may account for the intriguing transformation. *γ*-Silyl nitro compound **1a** first undergoes fragmentation upon Lewis catalysis. The resultant nitronate **3a**[14] holds an ideal geometry for an intramolecular [3 + 2] cycloaddition.[14,15] Then ring opening of cycloadduct isoxazolidine **4a** followed by proton transfer in **5a** affords isoxazoline **6a**. In situ cyclization−ring opening takes place in **6a** to give α,*β*-unsaturated nitroso intermediate **7a**. Finally **7a** undergoes tautomerization to produce oxime **2a**.

We successfully extended the newly developed transformation[16] to dihydrobenzofurans with an electron-withdrawing (e.g., Br) or -donating group (e.g., OMe) attached to the

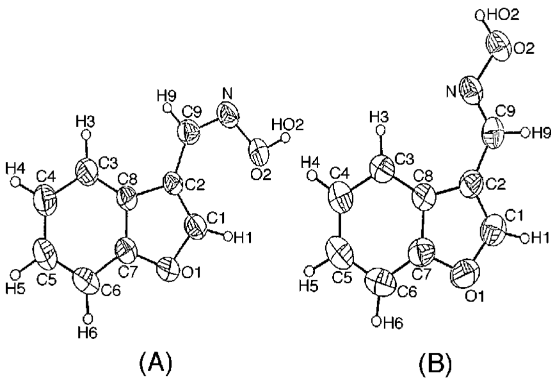

Figure 1. Crystal structures of oximes **2a**: (A) for the *Z*-isomer; (B) for the *E*-isomer.

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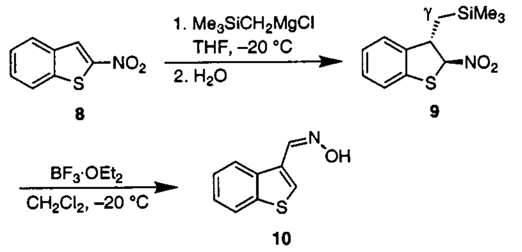
(16) **Standard Procedure for the Lewis Acid-Catalyzed Transformation of *γ*-Silyl Nitro Compounds.** A solution of a *γ*-silyl nitro compound (1.0 equiv) in dichloromethane (2.0 mL/mmol) was treated with $BF_3{\cdot}OEt_2$ (2.0 equiv). It was stirred at −78 to 0 °C until no starting material was left as shown by TLC. The reaction mixture was quenched with water (2.0 mL) at 0 °C and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with saturated aqueous NaCl (10 mL), dried over $MgSO_4$ (s), filtered, and concentrated under reduced pressure. The residue was purified by use of column chromatography on silica gel to provide the desired product with purity >99.9%.

benzene nucleus. Thus nitro compounds **1b**,**c**,**d** reacted with a Lewis acid to produce **2b**,**c**,**d**[13] in up to 80−90% yield (Scheme 1 and Table 1).

The same synthetic strategy was also applicable to the synthesis of 1-benzothiophene 3-oxime **10** from 2-nitro-1-benzothiophene (**8**, see Scheme 2). We added trimethylsilylmethylmagnesium chloride to nitrobenzothiophene **8** in THF at −20 °C. The resultant adduct **9** could be isolated, yet it was relatively unstable in comparison with the corresponding γ-silyl nitro compound **1**. Direct treatment of **9** with $BF_3{\cdot}OEt_2$ at −20 °C provided benzothiophene oxime **10**[13] in 61% overall yield.

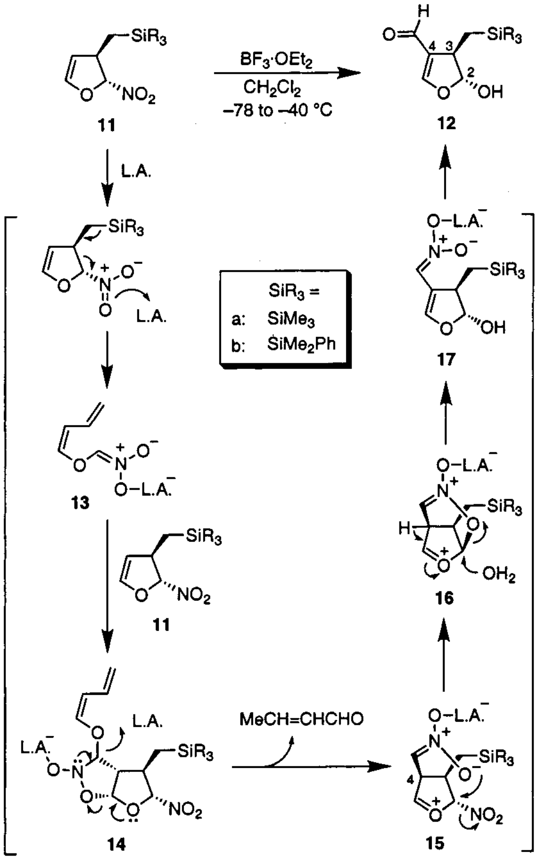
Scheme 2



Furthermore, we replaced the benzene nucleus in **1** with a C−C double bond and explored the acid-catalyzed transformations. Subsequently, γ-silyl nitro compounds **11a**,**b** were prepared in 73% and 81% yield, respectively, from the corresponding 2-nitrofuran and Grignard reagents by the procedure used for the conversion of **8** → **9**. Reaction of **11a**,**b** with $BF_3{\cdot}OEt_2$ (2.0 equiv) in CH_2Cl_2 at −78 to −40 °C for 15 min gave *trans*-3-formyl-4-silylmethyl-5-hydroxydihydrofurans **12a**,**b**,[13] respectively, as the major products and the corresponding cis isomers as the byproducts (Scheme 3). The overall yields ranged from 88 to 90%; the trans/cis ratios were 10:1, as determined by ^1H NMR spectrometry.

The speculative mechanism shown in Scheme 3 could be responsible for the unprecedented transformations. In the first step, acid-catalyzed fragmentation of γ-silyl nitro compounds of **11** takes place to give nitronate **13**. Reaction of **13** with the second molecule of **11** through a [3 + 2] cycloaddition would give the adducts **14**.[15] After extrusion of crotonaldehyde, an intramolecular cyclization could occur to the resultant nitronates **15** to produce unstable intermediates **16**. Hydrolysis[17] of **16** affords the targets **12** via nitronates **17**. In these transformations, the byproduct crotonaldehyde was detected by a GC-mass spectrometer.

Scheme 3



In conclusion, γ-silyl nitro compounds of various types underwent novel transformations upon Lewis acid catalysis. They were successfully applied in the syntheses of benzofuran and benzo[*b*]thiophene α,β-unsaturated oximes, and multisubstituted dihydrofurans.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **2a**−**d**, **10**, and **12a**,**b** in their *E*- and *Z*-forms as well as X-ray crystal data for *E*- and *Z*-**2a**,**b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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