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Vinyl-λ³-iodanes act as efficient sulfur atom acceptors: vinylic S_N2-based strategy for conversion of tertiary thioamides to amides

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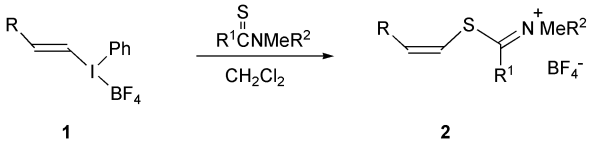
Exposure of tertiary thioamides to (*E*)-1-hexenyl(phenyl)-λ³-iodane results in vinylic S_N2 reaction to give the inverted (*Z*)-*S*-vinylthioimidonium salts, which under alkaline hydrolysis (Na_2CO_3 or K_2CO_3) selectively afford amides, while (*Z*)-*S*-vinyl thioesters are obtained in high yields *via* the hydrolysis under acidic conditions (HCl).

(*E*)-Alkenyl(phenyl)-λ³-iodanes **1** undergo vinylic S_N2 reactions under mild conditions because of the very high leaving group ability of phenyl-λ³-iodanyl groups.[1] The reaction affords (*Z*)-vinylic compounds with exclusive inversion of configuration.[2,3] Nucleophiles that undergo vinylic S_N2 reaction with (*E*)-alkenyl(phenyl)-λ³-iodanes **1** include halides,[2] dialkyl sulfides and selenides,[3a] phosphoroselenoates,[4a] dithiocarbamates,[4b] and carboxylic acids.[5] Formamides and acetamides with rather low nucleophilicity also act as good nucleophiles toward λ³-iodanes **1**, and afford (*Z*)-vinyl formates and (*Z*)-vinyl acetates, respectively, in a highly stereoselective manner.[6] Use of thioamides as nucleophiles, however, affords (*Z*)-enethiols stereoselectively, instead of (*Z*)-*S*-vinyl thiocarboxylates:[7] for instance, reaction of (*E*)-1-decenyl(phenyl)-λ³-iodane **1b** with thioacetamide in dichloromethane at room temperature results in formation of (*Z*)-1-mercaptodec-1-ene in 82% yield with exclusive inversion of configuration. This reaction involves the intervention of the highly labile (*Z*)-*S*-vinylthioimidonium salt, produced through nucleophilic attack by the sulfur atom of thioacetamide on (*E*)-1-decenyl-λ³-iodane **1b** from the side opposite the hyperleaving group PhI(BF_4) stereoselectively. Subsequent hydrolysis of the (*Z*)-*S*-vinylthioimidonium salt affords the retained (*Z*)-enethiol. The fact that, in the reaction with thioamides, (*E*)-alkenyl(phenyl)-λ³-iodane **1b** selectively captures the sulfur atom by forming (*Z*)-enethiols suggested to us that the λ³-iodane **1** could function as an agent for the conversion of thioamides to amides. We report herein on vinylic S_N2-based conversion of thioamides into amides, in which (*E*)-alkenyl(phenyl)-λ³-iodanes **1** act as efficient sulfur atom acceptor agents.

Diverse synthetic methods are available for the conversion of thioamides into amides.[8] These include oxidative conversion using hydrogen peroxide, *m*-chloroperbenzoic acid, diaryl telluroxide, manganese dioxide and (diacetoxyiodo)benzene, as well as hydrolytic conversion catalyzed by soft metal ions such as Cu(I), Ag(I) and Hg(II). Alkylation of thioamides followed by alkaline hydrolysis is an effective alternative for conversion into amides.

Exposure of tertiary thioamides to (*E*)-1-hexenyl(phenyl)-λ³-iodane **1a**, prepared from (*E*)-1-hexenylboronic acid by the BF_3-catalyzed reaction with (diacetoxyiodo)benzene *via* boron-λ³-iodane exchange in 82% yield,[9] results in vinylic S_N2 reaction to give the inverted (*Z*)-*S*-vinylthioimidonium salts **2** stereoselectively in >90% yields (Scheme 1). For instance, reaction of λ³-iodane **1a** with *N*,*N*-dimethylcyclohexanecarbothioamide in dichloromethane at 50 °C for 17 h gave (*Z*)-*S*-vinylthioimidonium tetrafluoroborate **2a** (98%) as a colorless oil.† A small vicinal coupling constant (J = 8.9 Hz) between the vinylic protons in ^{1}H NMR indicates a *cis* structure. The reaction is exclusively stereoselective to the limits of ^{1}H NMR detection with inversion of olefin geometry. As shown in Table 1, a variety of *N*,*N*-dimethyl and *N*-methyl-*N*-phenyl tertiary thioamides as well as cyclic *N*-methylpyrrolidine-2-thione afford S-vinylthioimidonium salts **2** in high yields.

The imidonium salts **2** are labile and highly susceptible to hydrolysis with moisture (Scheme 2); exposure of **2a** to THF–H_2O (10:1) at room temperature for 4 h results in the hydrolysis to give a mixture of the amide **3a** (R^1 = *c*-C_6H_{11}, R^2 = Me, 71%) (probably with liberation of (*Z*)-1-mercapto-1-hexene) and (*Z*)-*S*-vinyl thiocarboxylate **4a** (R = Bu^n, R^1 = *c*-C_6H_{11}, 29%). Use of alkali metal carbonates (M_2CO_3: M = Na, K, Rb, Cs) as an additive not only accelerates the hydrolysis but also increases the selectivity for amide formation (Table 2): thus, Na_2CO_3 or K_2CO_3 in THF gave a high yield of the amide **3a** (>90%) within 20 min at room temperature (Table 2, entries 2 and 3), along with the formation of (*Z*)-*S*-vinyl thiocarboxylate **4a** in less than 8% yield. Formation of thioamide (14–17%) was observed when the hydrolysis was carried out in the presence of



1 **2**

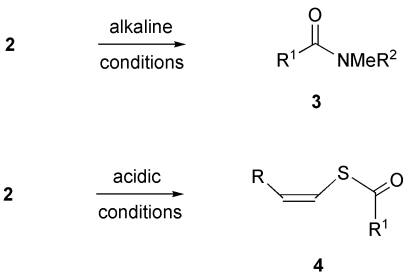
1a R = *n*-C_4H_9, **1b** R = *n*-C_8H_{17}

Scheme 1

Table 1 Synthesis of (*Z*)-*S*-vinylthioimidonium tetrafluoroborates **2** *via* vinylic S_N2 reaction of vinyl-λ³-iodane **1a** with thioamides[a]

	Thioamide			Product [yield (%)][b]
Entry	R^1	R^2	*T*/°C (*t*/h)	**2**
1	*c*-C_6H_{11}	Me	50 (17)	**2a** (98)
2	Bu^n	Me	25 (48)	**2b** (92)
3	*c*-C_5H_9	Me	50 (14)	**2c** (91)
4	Ph	Me	25 (32)	**2d** (92)
5	*p*-MeC_6H_4	Me	25 (47)	**2e** (92)
6	*p*-ClC_6H_4	Me	25 (55)	**2f** (95)
7	Bu^n	Ph	50 (15)	**2g** (97)
8	Ph	Ph	50 (15)	**2h** (94)
9	–$(CH_2)_3$–		50 (13)	**2i** (93)

[a] Reactions were carried out using a thioamide (1.1 equiv.) in dichloromethane under N_2. [b] Isolated yields.



Scheme 2

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Table 2 Hydrolysis of (*Z*)-*S*-vinylthioimidonium tetrafluoroborates **2** to amides **3** under basic conditions[a]

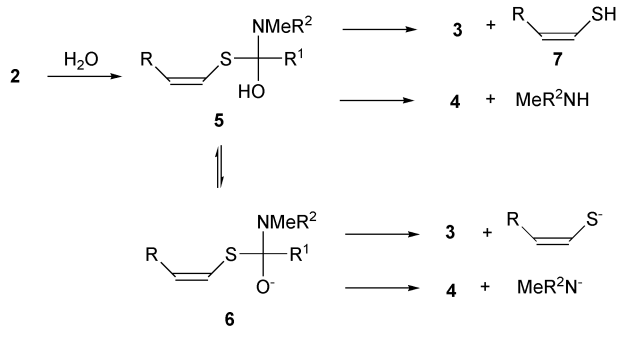
				Product [yield (%)][b]	
Entry	**2**	Base (equiv.)	*t*	**3**	**4**
1	**2a**	Li_2CO_3 (1)[c]	20 min	70	30
2	**2a**	5% Na_2CO_3 (1)	20 min	92 (79)	8
3	**2a**	5% K_2CO_3 (1)	20 min	92 (67)	8
4	**2a**	5% Rb_2CO_3 (1)[de]	20 min	79	4
5	**2a**	5% Cs_2CO_3 (1)[d]	20 min	83	3
6	**2a**	AgOAc (2)[c]	20 min	87 (58)	13
7	**2b**	5% Na_2CO_3 (1)	20 min	89	9
8	**2c**	5% Na_2CO_3 (1)	20 min	88	11
9	**2d**	5% Na_2CO_3 (2)[d]	4 h	83 (82)	—
10	**2d**	AgOAc (1.2)[f]	3 h	86 (86)	13
11	**2e**	5% K_2CO_3 (2)[d]	3 h	80	—
12	**2e**	AgOAc (1.2)[f]	3 h	85	9
13	**2f**	5% K_2CO_3 (2)[d]	2 h	80	5
14	**2g**	5% Na_2CO_3 (1)	20 min	84	4
15	**2h**	5% Na_2CO_3 (1)	30 min	83	13
16	**2i**	5% K_2CO_3 (2)	30 min	81	—
17	**2i**	AgOAc (1.2)[f]	4 h	88	—

[a] Unless otherwise noted, reactions were carried in THF at room temperature under nitrogen. [b] Yields were determined by ^{1}H NMR. Isolated yields are shown in parenthesis. [c] In THF–H_2O (2:1). [d] Thioamides were obtained in 14–20% yields. [e] Reaction temperature: 0 °C. [f] In THF–H_2O (4:1).

Rb_2CO_3 or Cs_2CO_3. Use of AgOAc in THF–H_2O (2:1) is an effective alternative and afforded **3a** in 87% yield (Table 2, entry 6). Hydrolysis of the cyclic imidonium salt **2i** with K_2CO_3 gave an 81% yield of *N*-methyl-2-pyrrolidinone **3i**. The alkaline hydrolysis of the imidonium salts **2d–f** with aromatic R^1 group proceeds slowly and takes a longer reaction time than that of **2a–c** with aliphatic R^1 groups.

In marked contrast, hydrolysis of the imidonium salts **2** under acidic conditions is slow and selectively gives rise to (*Z*)-*S*-vinyl thiocarboxylates **4**: thus, treatment of **2a** with 10% aqueous HCl solution at room temperature for 11 h afforded the thiocarboxylate **4a** as a colorless oil in 81% yield, along with the formation of the amide **3a** (14%).[10] Under similar conditions, the imidonium salts **2c**, **2g** and **2h** gave the (*Z*)-*S*-vinyl thiocarboxylates **4c** (R = Bu^n, R^1 = *c*-C_5H_9), **4g** (R = R^1 = Bu^n) and **4h** (R = Bu^n, R^1 = Ph) in 81, 72 and 83% yields, respectively. Acidic hydrolysis accompanies the isomerization of the double bond geometry to a discernible extent by ^{1}H NMR: less than 5% for **4c** and **4g**, and 10% for **4h**.

Hydrolysis of the imidonium salts **2** under basic conditions probably involves the tetrahedral uncharged **5** and charged intermediates **6** (Scheme 3). Decomposition of **6** is a product determining step and selectively produces the amide **3** through C–S bond cleavage with liberation of (*Z*)-enethiol, because of the greater leavimg ability of a vinylthio group than that of an amino group. Formation of (*Z*)-enethiol **7** was confirmed by the hydrolysis (5% Na_2CO_3/THF/rt/25 min) of **2j** (R = *n*-C_8H_{17}, R^1 = *c*-C_6H_{11}, R^2 = Me), which afforded a mixture of (*Z*)-enethiol **7** (R = *n*-C_8H_{17}, 14%) and its dimer, (*Z*)-1-decenyl 1-mercaptodecyl sulfide[7] (72%), along with the formation of amide **3a** (81%) and thioester **4a** (6%). The extent of C–S bond cleavage decreases when the reaction was carried out under acidic conditions. Under acidic conditions, protonation to the tetrahedral intermediate **5** with formation of the conjugate acids would play an important role and the (*Z*)-*S*-vinyl thiocarboxylate **4** is produced selectively through protonation at the more basic nitrogen atom. Amide formation *via* S-protonation of **5** will be a disfavoured process.



Scheme 3

In the alkali metal carbonate-accelerated hydrolysis of **2**, changing the metal cation from Li to Na, K, Rb and Cs increases the selectivity for formation of the amide **3** over the thioester **4** (Table 1, entries 1–5). The results probably reflect differences in ionicity in the metal–oxygen bond, which increase in the order Li_2CO_3 < Na_2CO_3 < K_2CO_3 < Rb_2CO_3 < Cs_2CO_3.[11] An increased ionicity will result in a decrease in the rate of N-protonation of **5** leading to the formation of the thioester **4**.

In conclusion, a vinylic S_N2-based strategy provides a method for conversion of thioamides to amides, in which (*E*)-alkenyl(phenyl)-λ^3-iodanes serve as efficient sulfur atom acceptors. The basic hydrolysis of (*Z*)-*S*-vinylthioimidonium salts **2** involves selective C–S bond cleavage of charged tetrahedral intermediates **6**, whereas the acidic hydrolysis involves selective C–N bond cleavage of the conjugate acids of **5**.

Notes and references

† *Typical experimental procedure* for synthesis of (*Z*)-*S*-vinylthioimidonium tetrafluoroborates **2** (Table 1, entry 1): to a stirred solution of λ^3-iodane **1a** (0.27 mmol) in dichloromethane (5 mL) was added *N*,*N*-dimethylcyclohexanecarbothioamide (0.29 mmol) at room temperature under nitrogen and the mixture was warmed at 50 °C for 17 h. After cooling, the mixture was concentrated *in vacuo*. Purification of the crude product by repeated decantation with dichloromrthane–hexane gave (*Z*)-*S*-vinylthioimidonium tetrafluoroborate **2a** (98%) as a colorless oil: δ_H (300 MHz, $CDCl_3$, *J*/Hz) 0.93 (t, *J* 7.1, 3H), 1.2–1.8 (m, 10H), 1.90–2.05 (m, 4H), 2.31 (q, *J* 6.8, 2H), 3.09 (tt, *J* 11.6 and 3.2, 1H), 3.68 (s, 3H), 3.78 (s, 3H), 6.33 (br d, *J* 8.9, 1H), 6.38 (dt, *J* 8.9 and 6.8, 1H); ν_{max}(neat)/cm^{-1} 2931, 2859, 1607, 1453, 1150–1000; HRMS (FAB): calc. for $C_{15}H_{28}NS$ [(M − BF_4)$^+$], *m*/*z* 254.1942, found 254.1962.

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