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Reaction of Monocarbonyl Iodonium Ylides with Activated Imines: Stereoselective Synthesis of *trans*- and *cis*-α,β-Aziridino Ketones

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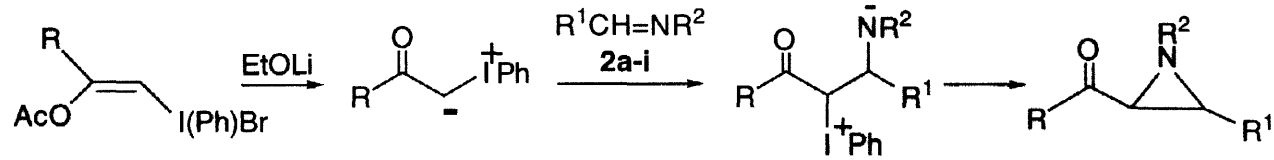
Abstract: Monocarbonyl iodonium ylides, generated *in situ* from *Z*-(2-acetoxyvinyl)iodonium salts via ester exchange reaction with EtOLi, undergo alkylidene-transfer reactions to activated imines yielding α,β-aziridino ketones. The aziridination of *N*-(2,4,6-trimethylbenzenesulfonyl)imines in THF affords *cis*-aziridines as a major product, while that of *N*-benzoylimines in THF-DMSO gives the *trans*-isomer stereoselectively. © 1998 Elsevier Science Ltd. All rights reserved.

In spite of the increasing interest in and research on iodonium ylides, the chemistry of unstabilized monocarbonyl iodonium ylides remains unknown.[1] Recently, we reported the first example for generation and characterization of monocarbonyl iodonium ylides: exposure of *Z*-(2-acetoxyvinyl)iodonium bromide **1** to EtOLi in THF at -78 ℃ results in ester exchange with the liberation of ethyl acetate to generate the monocarbonyl iodonium ylide **3**, which is stable up to -30 ℃ in THF but gradually decomposes at -20 ℃ to 1-bromo-2-decanone. The monocarbonyl iodonium ylide **3** acts as an alkylidene-transfer agent to carbonyl compounds, and the reaction with aldehydes in THF-DMSO gives α,β-epoxy ketones with *trans*-isomers as a major product.[2] We report herein a reaction of the monocarbonyl iodonium ylide **3** with activated imines **2**, which provides a stereoselective route for the synthesis of *trans*- and *cis*-α,β-aziridino ketones **5**.



1a,b **3a,b** **4** **5**

a: R = *n*-C_8H_{17}, **b**: R = *t*-Bu

No alkylidene-transfer reaction between the ylide **3a** and *N*-benzylideneaniline was observed. This is probably due to the low electrophilicity of the *N*-arylimines;[3] this reaction in THF-DMSO (12:1) at -30 ℃ gave a 1:1 mixture of *E*- and *Z*-10-eicosene-9,12-dione in 82% yield. The direct aziridination of C=N bonds took place when the activated *N*-sulfonylaldimines were employed.[3] Treatment of a THF solution of *Z*-(2-acetoxy-1-decenyl)(phenyl)iodonium bromide **1a** and *N*-(benzenesulfonyl)imine **2a** (R^1 = Ph, R^2 = SO_2Ph; 1.5 equiv) with one equiv of EtOLi at -78 ℃ (to room temperature) resulted in the formation of a stereoisomeric mixture of aziridine **5a** in 73% yield. The *trans*:*cis* ratio was determined to be 31:69 by ^1H NMR analysis (Table 1, Entry 1). The reaction presumably proceeds via intervention of the zwitterion **4** followed by the intramolecular reductive cyclization with liberation of iodobenzene. Introduction of the electron-donating *p*-MeO and *p*-Me groups on the benzenesulfonyl group of **2a** slightly increased the *cis*-selectivity, whereas that of the electron-withdrawing *p*-Cl substituent decreased the *cis*-selectivity. Use of *N*-(2,4,6-trimethylbenzenesulfonyl)imine **2b** led to the 85% *cis*-selectivity for the synthesis of aziridino ketone **5b** (Entry 2). Similar degree of *cis*-selectivity was observed in the reaction with other aromatic **2c-e** and aliphatic **2f** *N*-sulfonylaldimines. The reaction with vinyliodonium salt **1b** showed more than 90% *cis*-selectivity.

On the other hand, use of *N*-benzoylimines instead of *N*-sulfonylimines resulted in predominant formation of

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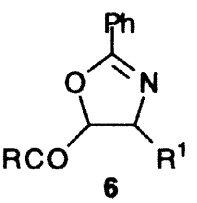
Table 1 Stereoselective Synthesis of α,β-Aziridino Ketones **5** from (β-Acetoxyvinyl)iodonium Bromides **1**[a]

Entry	1	Imine 2 (R^1, R^2)	Solvent	Conditions	α,β-Aziridino Ketone 5	Yield %[b]	Ratio[c]
1	**1a**	**2a** (Ph, SO_2Ph)	THF	-78℃→r.t.	**5a**	73	31:69
2	**1a**	**2b** (Ph, $SO_2C_6H_2$-2,4,6-Me_3)	THF	-78℃→r.t.	**5b**	73	15:85
3	**1a**	**2c** (*p*-MeC_6H_4, $SO_2C_6H_2$-2,4,6-Me_3)	THF	-78℃→r.t.	**5c**	82	18:82
4	**1a**	**2d** (*p*-ClC_6H_4, $SO_2C_6H_2$-2,4,6-Me_3)	THF	-78℃→r.t.	**5d**	76	18:82
5	**1a**	**2e** (2-Naphthyl, $SO_2C_6H_2$-2,4,6-Me_3)	THF	-78℃→r.t.	**5e**	80	16:84
6	**1a**	**2f** (*t*-Bu, $SO_2C_6H_2$-2,4,6-Me_3)	THF	-78℃→r.t.	**5f**	36	19:81
7	**1b**	**2b**	THF	-78℃→r.t.	**5g**	83	5:95
8	**1b**	**2c**	THF	-78℃→r.t.	**5h**	85	8:92
9	**1b**	**2d**	THF	-78℃→r.t.	**5i**	89	5:95
10	**1a**	**2g** (Ph, COPh)	THF-DMSO	-30℃, 2h	**5j**	68[d]	98: 2
11	**1a**	**2h** (*p*-ClC_6H_4, COPh)	THF-DMSO	-30℃, 2h	**5k**	66[e]	92: 8
12	**1b**	**2g**	THF-DMSO	-30℃, 2h	**5l**	72[f]	93: 7
13	**1b**	**2h**	THF-DMSO	-30℃, 2h	**5m**	69[g]	92: 8

[a] Reactions were carried out using one equiv of EtOLi and 1.5 equiv of an imine **2** in THF or THF-DMSO (12:1) under argon. [b] Isolated yields. [c] The *trans*:*cis* ratios, determined by ^1H NMR of the crude product. [d] *trans*-2-Oxazoline **6** (9%) was obtained. [e] 2-Oxazoline **6** (*trans*:*cis* = 67:33; 22%) was obtained. [f] *trans*-2-Oxazoline **6** (7%) was obtained. [g] *trans* -2-Oxazoline **6** (16%) was obtained.

the *trans*-α,β-aziridino ketones **5**; thus, reaction of the monocarbonyl iodonium ylide **3a** with *N*-benzoylimine **2g** in THF-DMSO (12:1) at -30 ℃ gave a 98:2 mixture of *trans*- and *cis*-α,β-aziridino ketones **5j** in 68% yield. In this reaction, however, intramolecular cyclization of the zwitterion **4** via attack of the nucleophilic oxygen may compete with the aziridine formation and a small amount of 2-phenyl-2-oxazoline **6** (R = *n*-C_8H_{17}, R^1 = Ph) was obtained as a by-product.[4] Similarly, *trans*-aziridines **5k-m** were prepared with high stereoselectivity (Entries 11-13).[5]



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In conclusion, our results demonstrated the monocarbonyl iodonium ylide **3** is nucleophilic in nature and undergoes stereoselective alkylidene-transfer reaction to the C=N bond of the activated aldimines.

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