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Reaction of Unstabilized Iodonium Ylides with Organoboranes

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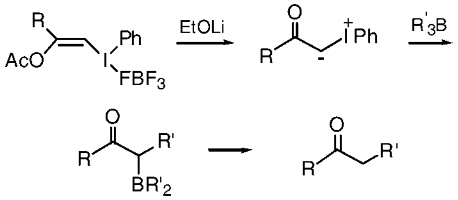
ABSTRACT



Exposure of monocarbonyl iodonium ylides, generated by the ester exchange of (*Z*)-(2-acetoxyvinyl)-λ^3-iodanes with EtOLi, to organoboranes results in a 1,2-shift of a carbon ligand from boron to the ylide carbons, which probably generates hitherto uncharacterized α-boryl ketones.

Onium ylides react with organoboranes and transfer a carbon ligand on boron to ylide carbanions via the intermediate formation of zwitterionic organoborane−ylide complexes. Group 15 (N, P, As) and 16 (S) onium methylides react with organoboranes to afford the corresponding homologated boranes.[1] Reaction of ethyl (dimethylsulfuranylidene)acetate with triphenylborane gives, after alkaline hydrolysis, ethyl phenylacetate in high yields.[1b] Recently, Shea and co-workers developed an efficient boron-catalyzed polymerization of dimethylsulfoxonium methylide yielding α-hydroxy polymethylene and block copolymers through living polyhomologations.[2]

On the other hand, reactions of group 17 onium ylides, especially iodonium ylides, with organoboranes are virtually unexplored, despite their extensive synthetic use in organic synthesis.[3] Dai and Yang reported an interesting alkyl group shift from boron to nitrogen in the reaction of [(*N*-tosylimino)iodo]benzene $PhI{=}NTs$ with trialkylboranes.[4] We are pleased to report herein the reaction of iodonium ylides with organoboranes, in which unstabilized monocarbonyl iodonium ylides **5** smoothly undergo a 1,2-shift of an alkyl or an aryl group from boron to ylide carbons under mild conditions. In marked contrast, no reaction was observed between stabilized iodonium ylides **1** and organoboranes.

β-Dicarbonyl and β-disulfonyl iodonium ylides, relatively stable species, enjoy rich chemistry in modern organic synthesis and serve as useful progenitors for the generation of carbenes.[3,5] The attempted reaction of the stable ylides **1** with triorganoboranes such as Ph_3B and Et_3B (THF/rt) did not show any evidence for formation of carbon ligand transfer product **3** but instead gave a small amount of O-phenylated ether **2** (Scheme 1). Formation of the enol ether **2** involves the well-known thermal 1,4-rearrangement with phenyl migration from iodine(III) to oxygen atom, which proceeds via the intermediacy of a spiro-Meisenheimer complex.[6] The stable β-dicarbonyl ylides **1** possess a highly delocalized

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(1) (a) Tufariello, J. J.; Lee, L. T. C. *J. Am. Chem. Soc.* **1966**, *88*, 4757. (b) Tufariello, J. J.; Lee, L. T. C.; Wojtkowski, P. *J. Am. Chem. Soc.* **1967**, *89*, 6804. (c) Musker, W. K.; Stevens, R. R. *Tetrahedron Lett.* **1967**, 995. (d) Koster, R.; Rickborn, B. *J. Am. Chem. Soc.* **1967**, *89*, 2782.

(2) (a) Shea, K. J.; Walker, J. W.; Zhu, H.; Paz, M.; Greaves, J. *J. Am. Chem. Soc.* **1997**, *119*, 9049. (b) Busch, B. B.; Paz, M. M.; Shea, K. J.; Staiger, C. L.; Stoddard, J. M.; Walker, J. R.; Zhou, X.-Z.; Zhu, H. *J. Am. Chem. Soc.* **2002**, *124*, 3636.

(3) (a) Koser, G. F. In *The Chemistry of Functional Groups, Supplement D*; Wiley: New York, 1983; Chapter 18. (b) Varvoglis, A. *Synthesis* **1984**, 709. (c) Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431. (d) Varvoglis, A. *The Organic Chemistry of Polycoordinated Iodine*; VCH: New York, 1992. (e) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523.

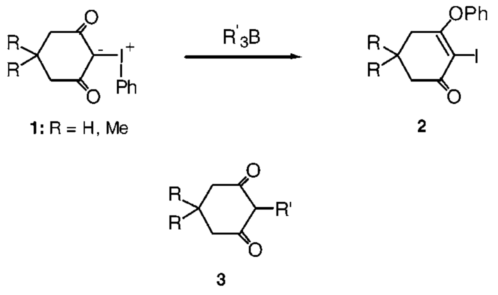
(4) Yang, R.-Y.; Dai, L.-X. *Synthesis* **1993**, 481.

(5) (a) Moriarty, R. M.; Prakash, O.; Vaid, R. K.; Zhao, L. *J. Am. Chem. Soc.* **1989**, *111*, 6443. (b) Hadjiarapoglou, L.; Spyroudis, S.; Varvoglis, A. *J. Am. Chem. Soc.* **1985**, *107*, 7178. (c) Moriarty, R. M.; Bailey, B. R.; Prakash, O.; Prakash, I. *J. Am. Chem. Soc.* **1985**, *107*, 1375. (d) Muller, P.; Fernandez, D. *Helv. Chim. Acta* **1995**, *78*, 947.

(6) Takaku, M.; Hayashi, Y.; Nozaki, H. *Tetrahedron* **1970**, *26*, 1243.

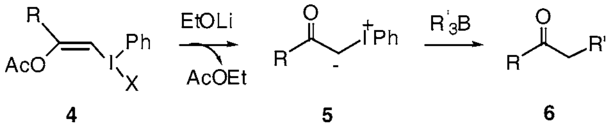
10.1021/ol0495669 CCC: $27.50

Scheme 1



ylidic carbanion directly bound to the strongly electron-withdrawing phenyliodonio group.[7] Consequently, they exhibit relatively low nucleophilicity, which in turn renders these ylides inactive toward organoboranes.

Scheme 2



4a: R = n-C_8H_{17}, X = BF_4, **4b**: R = n-C_8H_{17}, X = Br
4c: R = $Ph(CH_2)_3$, X = BF_4, **4d**: R = t-Bu, X = BF_4

Recently, we found that the ester exchange reaction between (Z)-(2-acetoxyvinyl)-λ^3-iodanes **4** and EtOLi resulted in quantitative generation of the unstable monocarbonyl iodonium ylides **5** in THF at −78 °C, with the liberation of ethyl acetate (Scheme 2).[8] In contrast to the stabilized iodonium ylides **1**, the monocarbonyl iodonium ylides **5** are moderately nucleophilic in nature and act as alkylidene transfer agents to carbonyl compounds and activated imines to yield α,β-epoxy ketones and 2-acylaziridines stereoselectively in good yields.[9] The ylides **5** undergo transfer of a carbon ligand from boron to ylide carbons by the reaction with triorganoboranes. Thus, exposure of the monocarbonyl iodonium ylide **5a** ($R = n$-C_8H_{17}), derived in situ from (Z)-(2-acetoxyvinyl)-λ^3-iodane **4a** by ester exchange with EtOLi (1.3 equiv) in THF at −78 °C for 10−20 min, to Et_3B (1.3 equiv) at −78 °C for 1 h and then at room temperature for 0.5 h under argon afforded ethylated ketone **6a** in 86% yield (Table 1, entry 1).[10] Secondary alkyl and aryl groups are also transferred from boron to ylide carbons. Comparison of the results of entries 4 and 5 in Table 1 indicates that only one alkyl group in the trialkylborane is active in the reaction. With use of triethylaluminum instead of Et_3B, ketone **6a** was obtained in 46% yield.

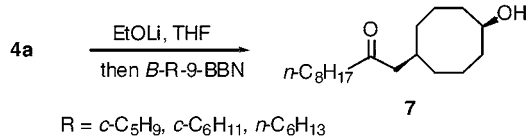
Table 1. Reaction of Monocarbonyl Iodonium Ylides **5** with Organoboranes[a]

entry	λ^3-iodane **4**	borane	ketone **6**	yield (%)[b]
1	**4a**	Et_3B	**6a**	86[c]
2	**4a**	n-Bu_3B	**6b**	68 (72)[c]
3	**4a**	s-Bu_3B	**6c**	76
4	**4a**	$(c$-$C_5H_9)_3B$	**6d**	96
5	**4a**	$(c$-$C_5H_9)_3B$	**6d**	15[d]
6	**4a**	$(c$-$C_6H_{11})_3B$	**6e**	74
7	**4a**	$[Ph(CH_2)_2]_3B$	**6f**	67
8	**4a**	Ph_3B	**6g**	67
9	**4a**	$(p$-$MeC_6H_4)_3B$	**6h**	50
10	**4b**	Ph_3B	**6g**	73
11	**4c**	n-Bu_3B	**6i**	73
12	**4c**	$(c$-$C_5H_9)_3B$	**6j**	69
13	**4d**	n-Bu_3B	**6k**	62[c]

[a] Reaction was carried out using 1.3 equiv of an organoborane in THF at −78 °C for 1 h and then at room temperature for 0.5 h under argon. [b] Isolated yields. [c] GC yields. [d] With use of organoborane (0.33 equiv).

In the Brown group, 9-borabicyclo[3.3.1]nonane (9-BBN) is used as a nonmigrating blocking group on tetrasubstituted borate complexes, for instance, in the α-alkylation of α-bromo ketones and esters.[11] The reaction of monocarbonyl iodonium ylide **5a** with B-cyclopentyl-9-BBN, however, resulted in an exclusive migration of the cyclooctyl−boron bond rather than the desired cyclopentyl−boron bond to give the hydroxy ketone **7** in 51% yield (Scheme 3). With B-cyclohexyl- and B-n-hexyl-9-BBN, selective formation of **7** was also observed in 37 and 46% yields, respectively.[12]

Scheme 3



Reaction of iodonium ylides **5** with catecholborane undergoes the boron-to-carbon 1,2-shift of hydrogen to give methyl ketones **8**:[1d] thus, exposure of **5a** to catecholborane

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[7] For the Hammett substituent constant ($\sigma_p = 1.37$) of $Ph(BF_4)I$−, see: Mironova, A. A.; Maletina, I. I.; Iksanova, S. V.; Orda, V. V.; Yagupolskii, L. M. *Zh. Org. Khim.* **1989**, *25*, 306.

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[9] (a) Ochiai, M.; Kitagawa, Y. *Tetrahedron Lett.* **1998**, *39*, 5569. (b) Ochiai, M.; Kitagawa, Y. *J. Org. Chem.* **1999**, *64*, 3181. (c) Ochiai, M.; Kitagawa, Y. *J. Synth. Org. Chem. Jpn.* **2000**, *58*, 1048.

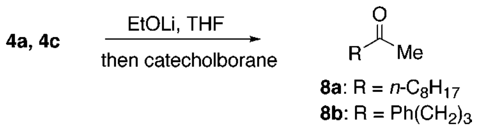
[10] **Experimental Procedure. 6a** (Table 1, entry 1)**:** To a stirred solution of (Z)-(2-acetoxy-1-decenyl)(phenyl)(tetrafluoroborato)-λ^3-iodane (**4a**)[8] (37 mg, 0.075 mmol) in THF (3.7 mL) was added a 0.58 M THF solution of EtOLi (0.167 mL, 0.097 mmol) at −78 °C under argon, and the mixture was stirred for 20 min. After addition of a 1.06 M hexane solution of Et_3B (0.92 mL, 0.097 mmol), the mixture was stirred for 1 h at −78 °C and 0.5 h at room temperature. The reaction mixture was quenched with water and extracted with dichloromethane. The organic phase was washed with brine and dried over anhydrous Na_2SO_4. The yield of **6a** was determined by GC analysis using an FFS ULBON HR-1 capillary column (0.25 mm × 50 m).

[11] (a) Brown, H. C.; Rogic, M. M.; Nambu, H.; Rathke, M. W. *J. Am. Chem. Soc.* **1969**, *91*, 2147. (b) Brown, H. C.; Nambu, H.; Rogic, M. M. *J. Am. Chem. Soc.* **1969**, *91*, 6855. (c) Hara, S.; Kishimura, K.; Suzuki, A. *Tetrahedron Lett.* **1978**, 2891.

[12] Reaction of B-n-hexyl-9-BBN with ethyl diazoacetate gives products derived from exclusive B-cyclooctyl bond migration. See: Hooz, J.; Gunn, D. M. *Tetrahedron Lett.* **1969**, 3455.

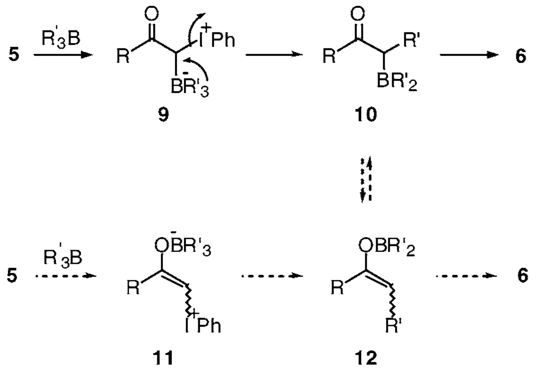
(1.3 equiv) in THF afforded 2-decanone **8a** in 66% yield (Scheme 4). Similarly, ylide **5c** gave 5-phenyl-2-pentanone **8b** (61%).

Scheme 4



The mechanism for the reaction of iodonium ylides **5** with organoboranes, which involves formation of α-boryl ketones **10**, is shown in Scheme 5. Initial formation of zwitterionic ylide−borane complexes **9**, followed by a rapid boron-to-carbon 1,2-shift of an alkyl group with concomitant reductive elimination of the hypernucleofuge, phenyliodonio group,[13] produces α-boryl ketones **10**. Subsequent hydrolysis affords ketones **6**. As an alternative process, formation of *O*-boron zwitterions **11** and the further intramolecular nucleophilic vinylic substitution[14] yielding *O*-boron enolates **12** should be considered; however, this pathway is not compatible with our results (See below).

Scheme 5

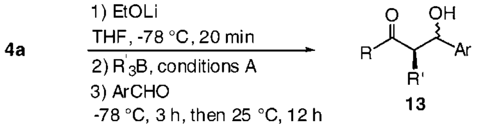


α-Boryl ketones have been proposed as intermediates in some reactions but have never been characterized.[15] Attempted synthesis of α-boryl ketones by the reaction of α-diazo ketones with tripropylborane resulted in exclusive formation of *O*-boron enolates.[16] Ab initio molecular orbital calculation shows that α-boryl ketone (Me_2BCH_2CHO) is more unstable than the isomeric boron enolate ($CH_2{=}CHOBMe_2$) by ca. 19 kcal/mol.[17] Interestingly, Abiko and Masamune reported the characterization of the intermediate α-boryl esters in the double aldol reaction of acetate esters.[18]

Importantly, deuterium experiments showed that when the reaction mixture of iodonium ylide **5a** with *n*-Bu_3B (−78 °C/1 h/THF) was quenched with MeOD at −78 °C, α-deuterated ketone **6b-α*d*** (59% D) was produced in 71% yield; however, quenching with MeOD after warming the reaction mixture to room temperature showed no deuterium incorporation in **6b** (87% yield). Similar results were obtained in the reaction with *s*-Bu_3B. These results probably suggest the involvement of the intermediate α-boryl ketone **10a** (R = *n*-C_8H_{17}, R′ = *n*-Bu) under our conditions, which is thermally unstable and easily decomposes to ketone **6b** below room temperature.[19] Formation of *O*-boron enolates **12** via intramolecular vinylic substitution of the zwitterions **11** or through a 1,3-boron shift of **10** does not seem to occur, because enolates **12** are known to be stable even at room temperature.[16,20]

The temperature effects in the aldol condensations shown in Table 2 further support the thermally unstable nature of α-boryl ketones **10**. Treatment of a solution of α-boryl ketone **10a**, generated by the reaction of ylide **5a** with *n*-Bu_3B at −78 °C in THF, with benzaldehyde afforded a mixture of aldol products **13** in 56% yields, while aldol condensation after warming a solution of **10a** to −30 °C dramatically decreased the yield of **13** to 12% (Table 2, entry 2).[21] Furthermore, no aldols **13** were produced when a solution

Table 2. Temperature Effects in One-Pot Aldol Condensation[a]



entry	borane	conditions A T (°C)/t (h)	ArCHO (equiv)	yield (%)[b]	
				13	**6**
1	*n*-Bu_3B	−78/1	PhCHO (2)	56 (30:70)[c]	38
2	*n*-Bu_3B	−78/1, −30	PhCHO (2)	12 (51:49)[c]	26
3	*n*-Bu_3B	−78/1, 25	PhCHO (2)	0	68
4	*n*-Bu_3B	−78/1	*m*-ClC_6H_4CHO (2)	74 (50:50)[c]	38
5	*n*-Bu_3B	−78/1, 25	*m*-ClC_6H_4CHO (2)	0	93
6	*s*-Bu_3B	−78/2	PhCHO (1.3)	73 (50:50)[c,d]	16
7	(c-C_5H_9)$_3$B	−78/2	PhCHO (1.3)	62 (72:28)[c]	24

[a] Reaction was carried out using 1.3 equiv of EtOLi and organoborane in THF under argon. [b] Isolated yields. [c] Ratios of syn:anti. [d] Syn and anti aldols are 65:35 and 50:50 mixtures of diastereoisomers, respectively.

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(14) For nucleophilic vinylic substitution of vinyl-λ^3-iodanes, see: (a) Ochiai, M.; Oshima, K.; Masaki, Y. *J. Am. Chem. Soc.* **1991**, *113*, 7059. (b) Okuyama, T.; Takino, T.; Sato, K.; Ochiai, M. *J. Am. Chem. Soc.* **1998**, *120*, 2275. (c) Ochiai, M. *J. Organomet. Chem.* **2000**, *611*, 494.

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(19) Attempted detection of α-boryl ketones **10** in THF-d_8 by low-temperature NMR experiments was fruitless.

(20) For *Z*−*E* isomerization of boron enolates, see: (a) Evans, D. A.; Vogel, E.; Nelson, J. V. *J. Am. Chem. Soc.* **1979**, *101*, 6120. (b) Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099. (c) Masamune, S.; Mori, S.; Horn, D.; Brooks, D. W. *Tetrahedron Lett.* **1979**, 1665. (d) Boldrini, G. P.; Bortolotti, M.; Mancini, F.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1991**, *56*, 5820.

of **10a** was warmed to room temperature prior to the aldol condensations (Table 2, entries 3 and 5): in these cases, the ketone **6b** was obtained selectively in good yields.

In conclusion, we have shown that, in contrast to the stabilized iodonium ylides, the moderately nucleophilic monocarbonyl iodonium ylides undergo transfer of a carbon ligand from boron to ylide carbons by reaction with triorganoboranes. Most importantly, the reaction probably involves in situ generation of hitherto uncharacterized α-boryl ketones.

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Supporting Information Available: Detailed experimental procedures and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) For stereochemical assignments of aldols, see: (a) Stiles, M.; Winkler, R. R.; Chang, Y.; Traynor, L. *J. Am. Chem. Soc*. **1964**, *86*, 3337. (b) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc*. **1973**, *95*, 3310. (c) Heathcock, C. H.; Davidsen, S. K.; Hug, K. T.; Flippin, L. A. *J. Org. Chem.* **1986**, *51*, 3027.