

Literature Report 2012-06-12

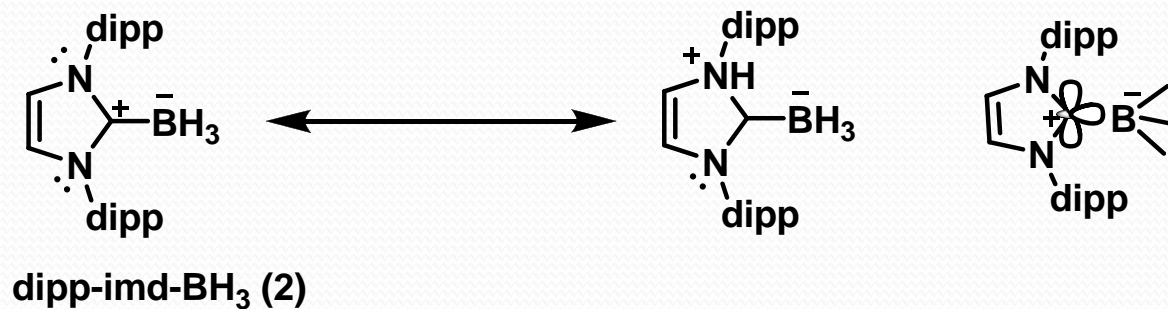
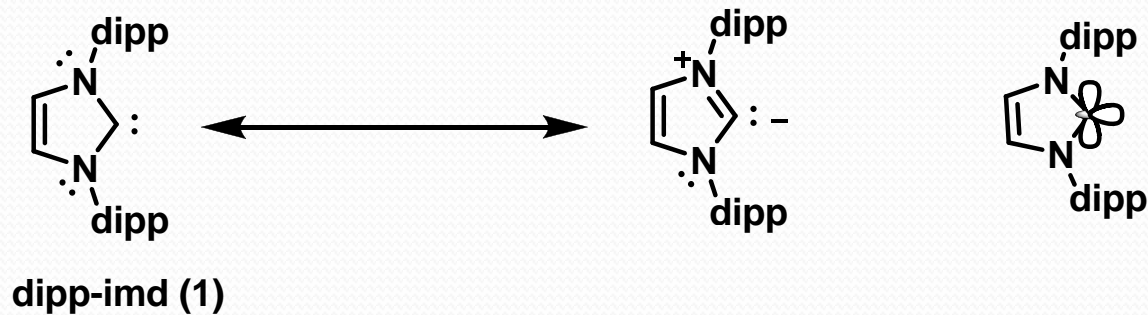
Duan, Y. Checker: Chen, M.-W.

NHC–Borane在还原反应中的应用

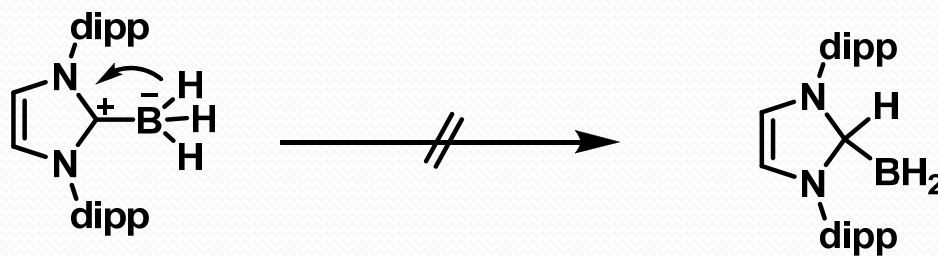
Lindsay, D. M. *et al*

Chem. Commun. **2010**, 46, 2474

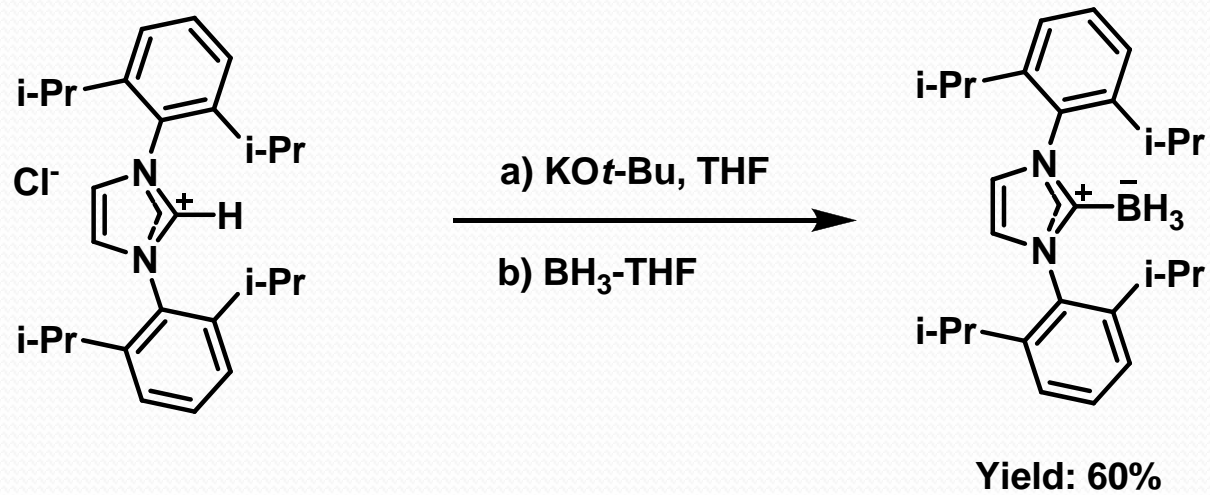
Selected resonance structures and simplified orbital pictures



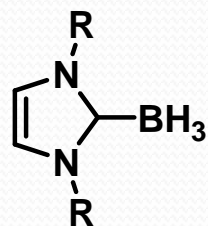
NHC-boranes, do not readily hydroborate themselves



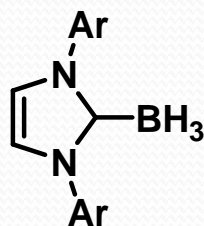
The synthesis of NHC-boranes



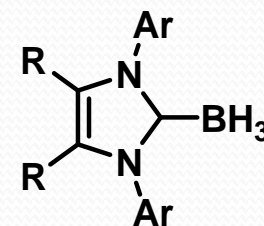
Select examples of NHC-boranes



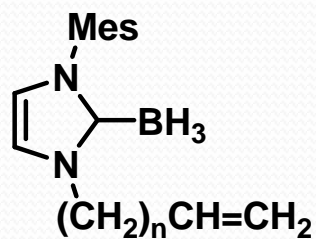
R = CH(CH₃)₂
R = adamantyl



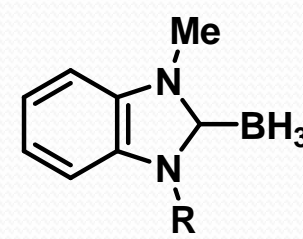
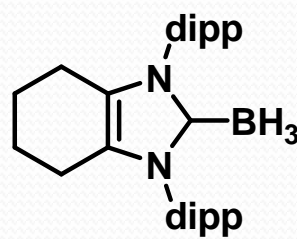
Ar = 4-ClC₆H₄
Ar = 4-*t*-Bu-2,6-Me₂C₆H₂



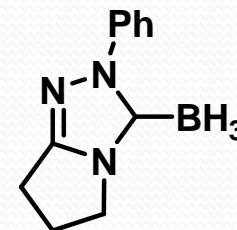
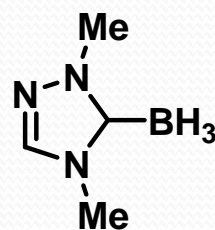
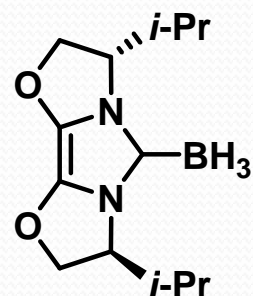
R = CN
R = Cl



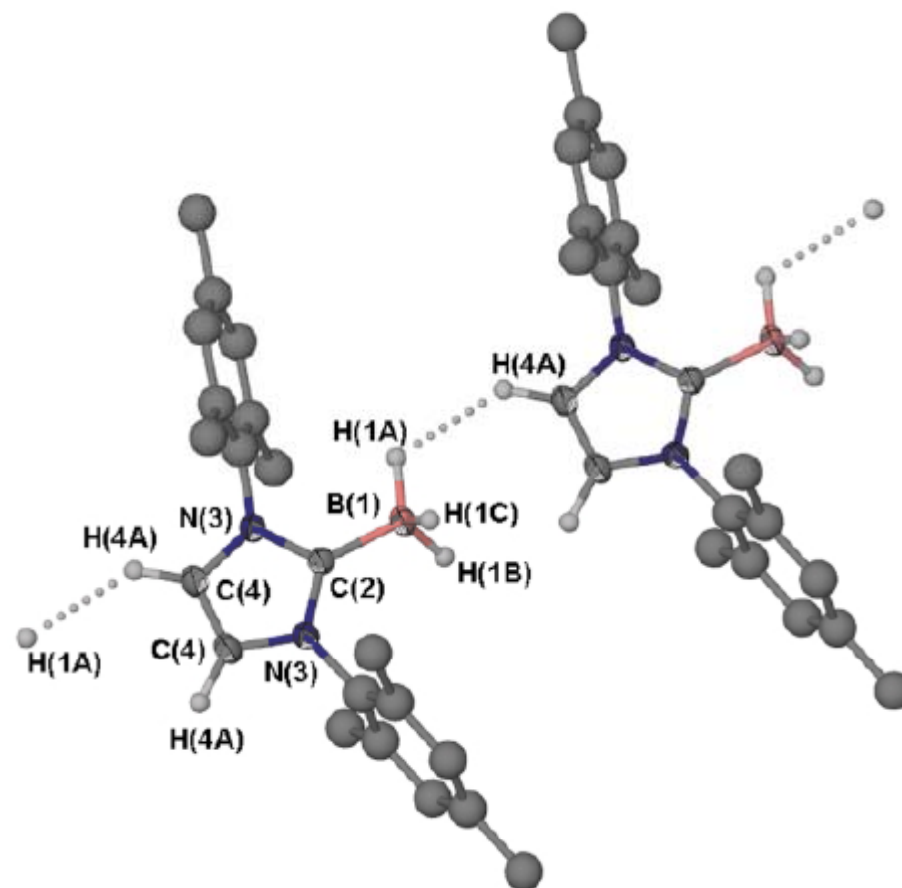
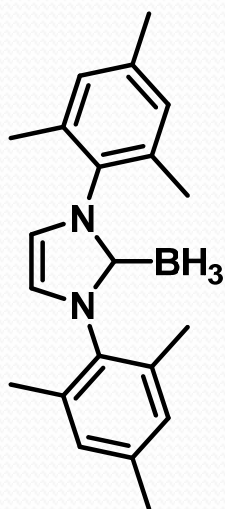
n = 1, 2



R = CH₂CH=CH₂
R = CH₃

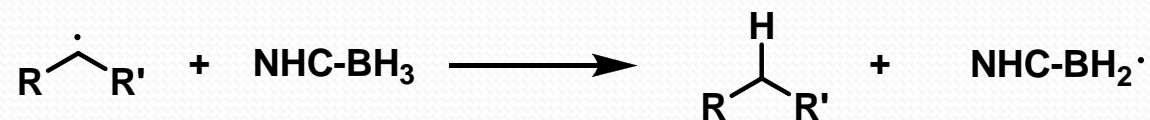
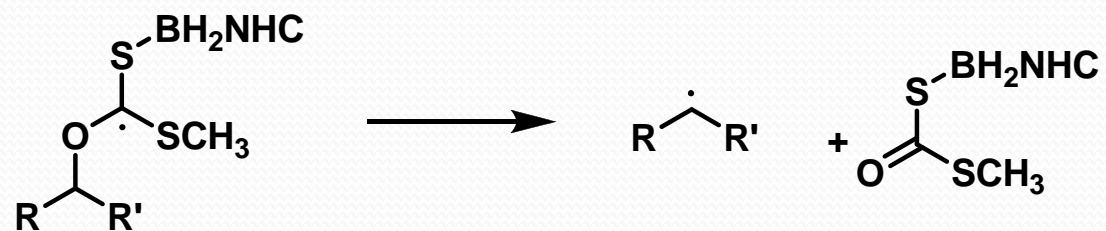
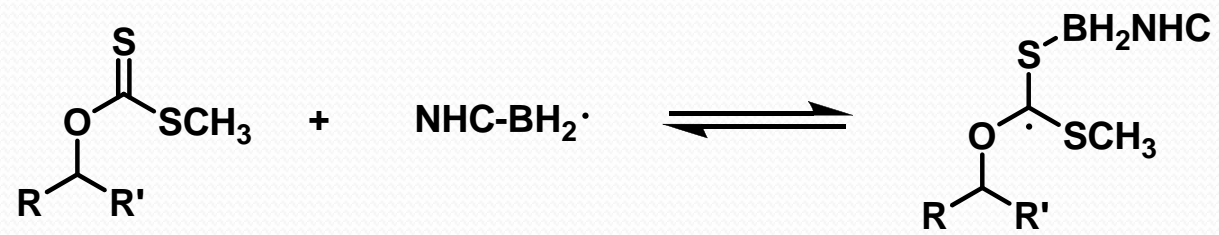


X-ray crystallographic study



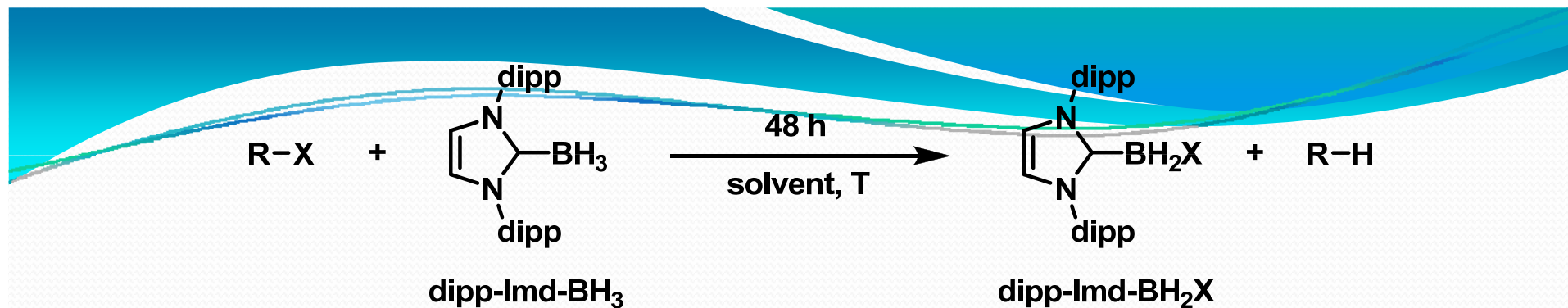
Clyburne, J. A. C. *et al Chem. Commun.* **2003**, 1722

A new class of boron-centered radical



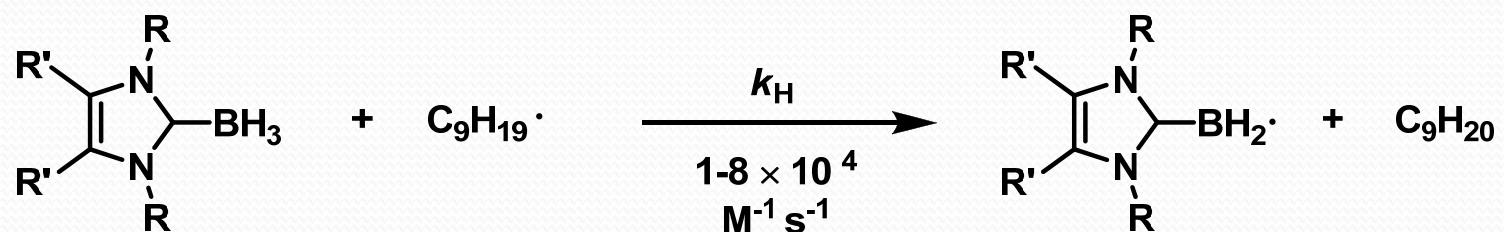
Curran, D. P. *et al J. Am. Chem. Soc.* **2009**, *131*, 11256

J. Am. Chem. Soc. **2010**, *132*, 2350



Entry	RX	equiv	solvent	T (°C)	Prod, X =	yield	¹¹ B NMR (CDCl ₃ , δ)
1	C ₁₂ H ₂₅ Cl	1	PhCF ₃	140	Cl	ND	-18.7
2	CCl ₄	64	CCl ₄ /CDCl ₃	80	Cl	84	-18.7
3	C ₁₂ H ₂₅ Br	1.5	toluene	140	Br	70	-23.0
4	CBr ₄	1	C ₆ D ₆	80	Br	56	-23.0
5	C ₁₂ H ₂₅ I	1	C ₆ D ₆	180	I	90	-33.0
6	C ₄ H ₉ I	1	PhH	180	I	100	-33.0
7	C ₁₂ H ₂₅ OTs	1.5	toluene	140	OTs	70	-11.4
8	C ₁₂ H ₂₅ OMs	1.5	toluene	140	OMs	60	-11.0
9	C ₁₂ H ₂₅ OTf	1.5	1,4-dioxane	25	OTf	ND	-8.8

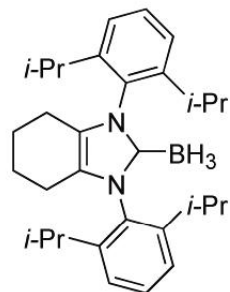
Estimated rate constants for hydrogen abstraction



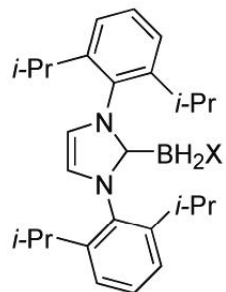
Lacote, E. *et al Org. Lett.* **2010**, 12, 2998

The rate constants k_H for hydrogen-atom transfer

Less reactive than 1

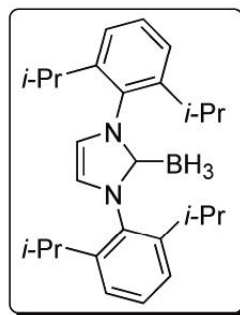


9
 $k_H < 1 \times 10^4$



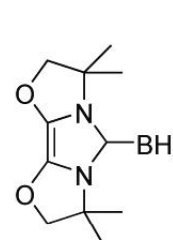
3, X = SC(O)SMe
10, X = Cl
both $k_H < 1 \times 10^4$

Standard 1

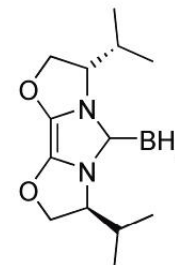


1, dipp-lmd-BH₃
 $k_H = 2 \times 10^4$

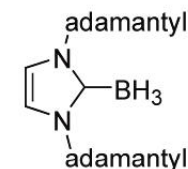
Similar reactivity to 1



11
 $k_H = 2 \times 10^4$

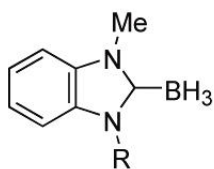


12
 $k_H = 2 \times 10^4$

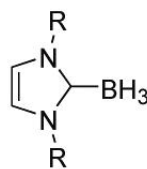


13
 $k_H = 2 \times 10^4$

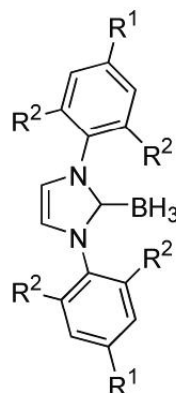
More reactive than 1



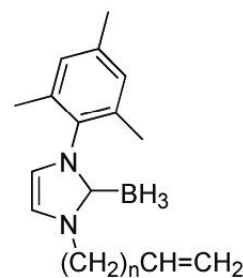
14a, R = CH₂CH=CH₂
 $k_H = 5 \times 10^4$
14b, R = CH₃
 $k_H = 7 \times 10^4$



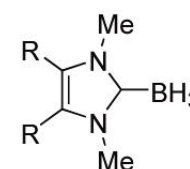
15a, R = CH(CH₃)₂
 $k_H = 5 \times 10^4$
15b, R = cyclohexyl
 $k_H = 7 \times 10^4$
15c, diMe-lmd-BH₃
R = CH₃, $k_H = 8 \times 10^4$



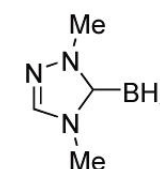
16a, R¹ = Cl; R² = H
 $k_H = 5 \times 10^4$
16b, R¹ = *t*-Bu; R² = CH₃
 $k_H = 5 \times 10^4$



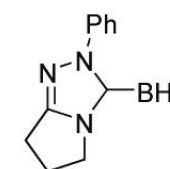
17a, n = 1
 $k_H = 6 \times 10^4$
17b, n = 2
 $k_H = 6 \times 10^4$



18a, R = CN
 $k_H = 6 \times 10^4$
18b, R = Cl
 $k_H = 6 \times 10^4$

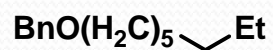
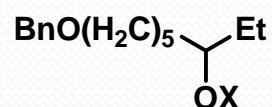
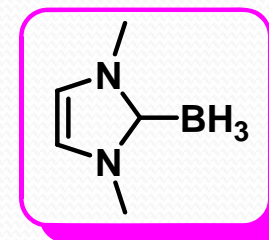
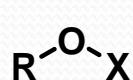


19, diMe-Tri-BH₃
 $k_H = 8 \times 10^4$



20
 $k_H = 6 \times 10^4$

Deoxygenations of Xanthates and Thionocarbonates



14, X = C(S)SMe

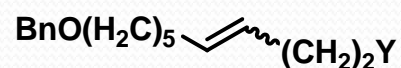
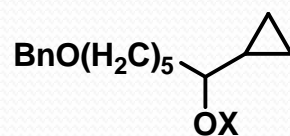
A

19, 79%

14, X = C(S)SMe

B

19, 81%



20, Y = H

21, Y = SC(=O)SMe

A) 1 equiv of AIBN, 80 °C, 2 h.

B) 1 equiv of Et₃B, rt, 2 h.

15, X = C(S)SMe

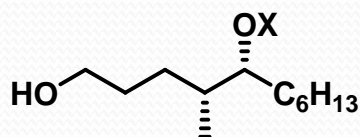
A

20, 52%; 21, 17%

15, X = C(S)SMe

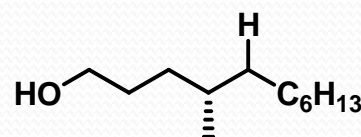
B

20, 63%; 21, 22%



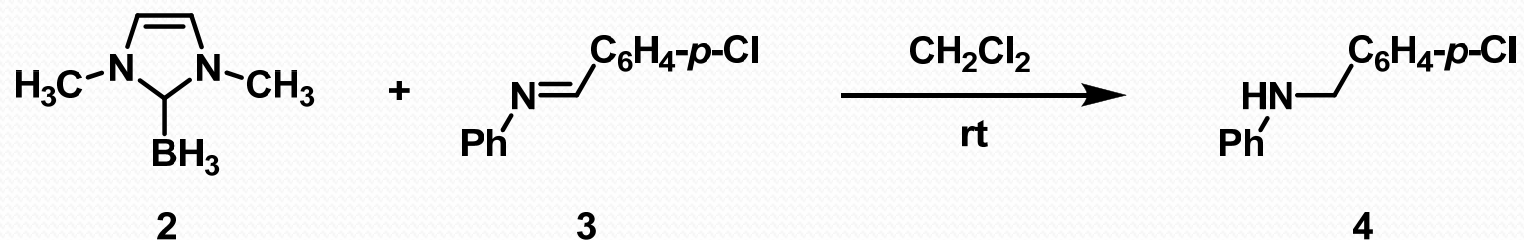
X = C(=S)OPh

A



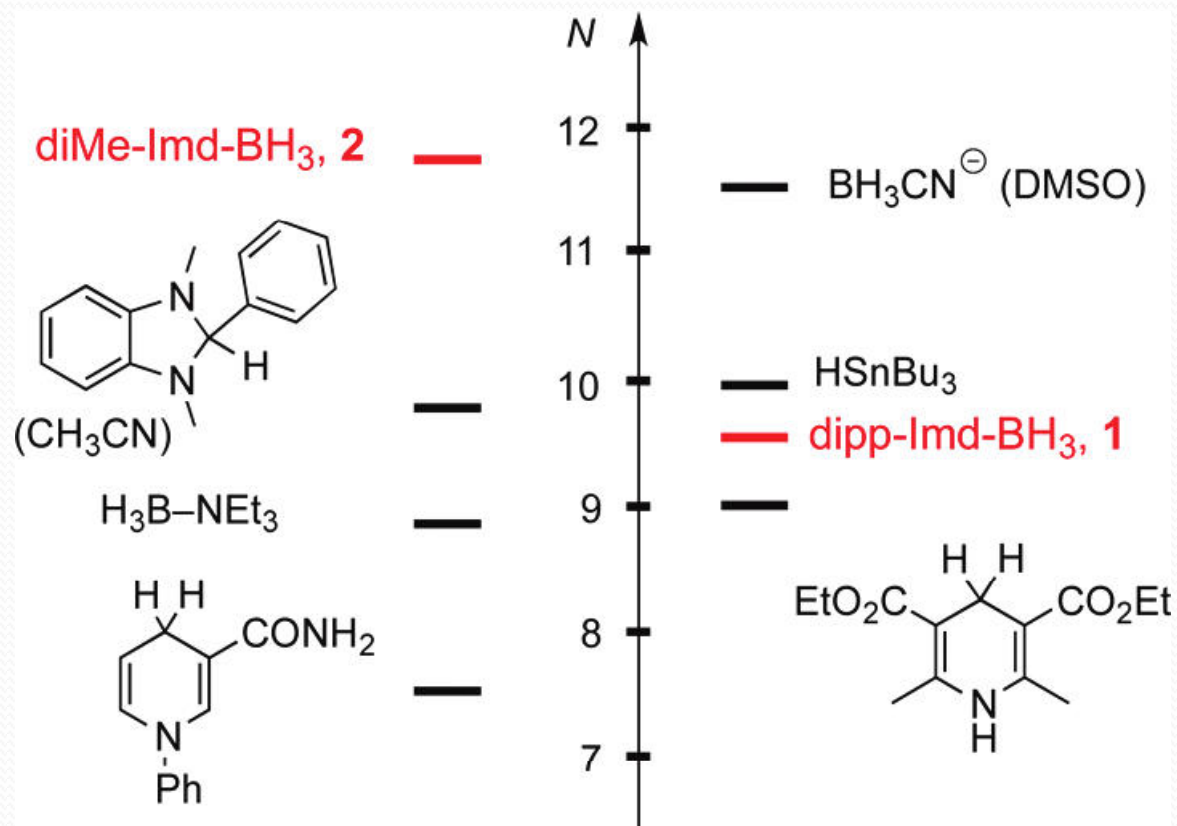
68%

N-Heterocyclic carbene boranes are good hydride donors



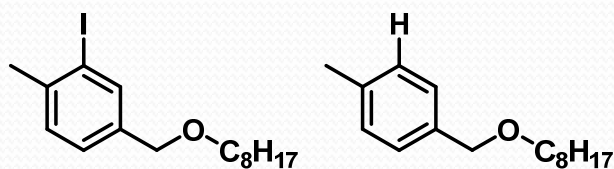
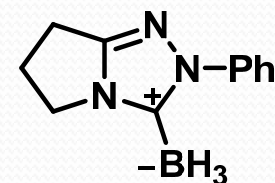
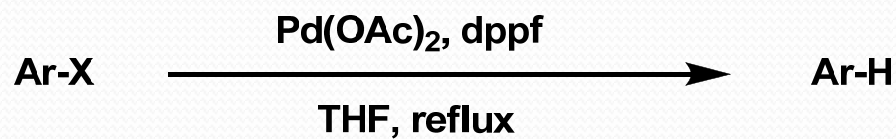
Entry	Equiv HOAc	Equiv 2	T	Yield (%)
1	0	1.3	24 h	--
2	1.3	1.3	1.5 h	84%
3	1	0.7	16 h	86%
4	1	0.5	16 h	94%
5	1	0.33	3 d	86%

Nucleophilicity parameters N of some hydride donors

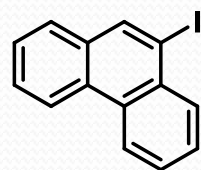


Mayr, H. *et al Org. Lett.* **2012**, *14*, 82

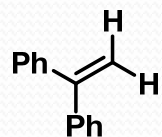
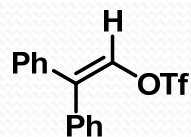
Scope of the palladium-mediated reduction of C_{sp2}-X bonds



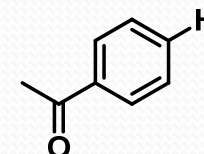
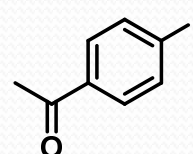
Yield: 70%



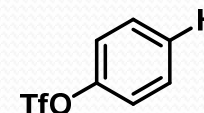
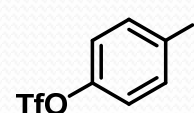
Yield: 67%



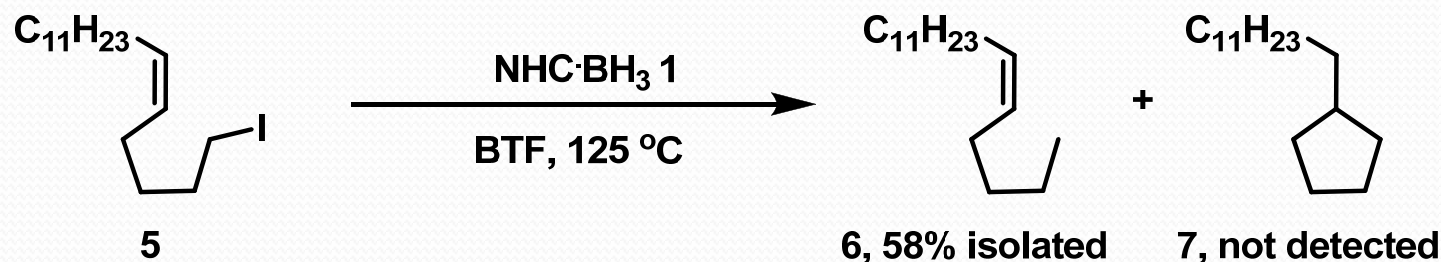
Yield: 90%



Conv: 100%

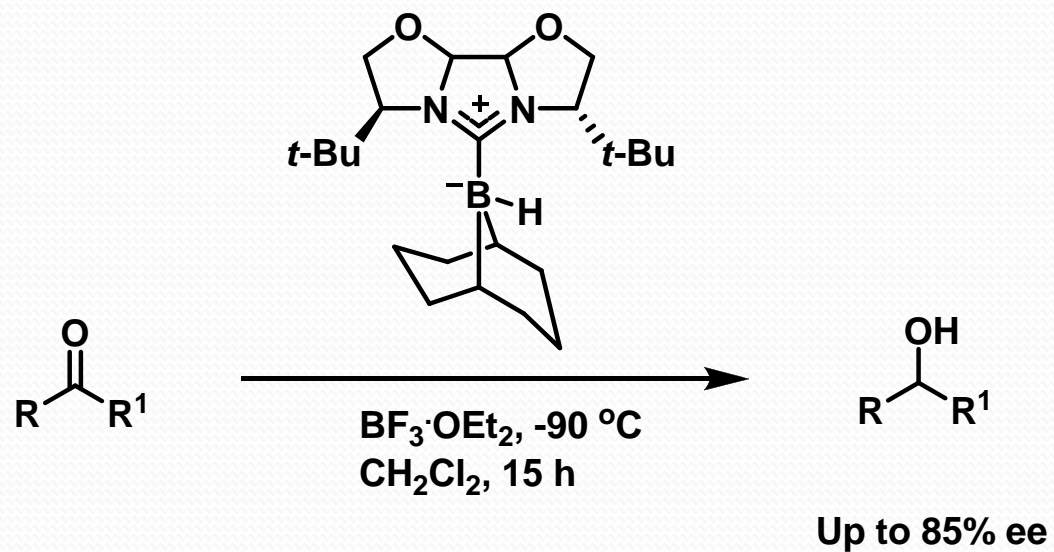


Conv: 100%



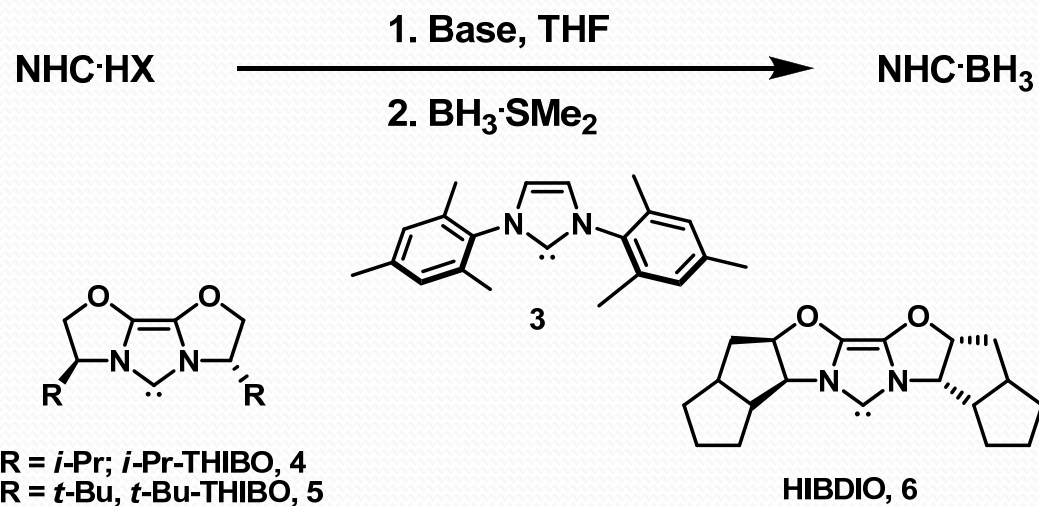
Finally, reduction of cyclizable probe iodide **5** provided only the open chain product **6** in 58% isolated yield (Scheme 1). Cyclized product **7** could not be detected by GC in the crude reaction mixture. Previous experiments have shown that **1** is a rather modest hydrogen donor,^[4] so any radical formed from **5** should have cyclized much more rapidly than it was reduced. This result firmly rules out the intermediacy of radicals in thermal reductions of primary iodides.

Applications in the asymmetric reduction of ketones



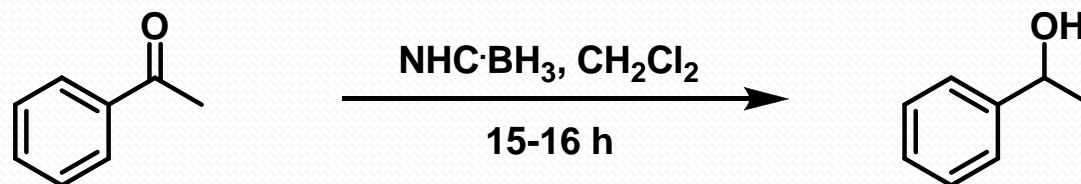
Lindsay, D. M. *et al Chem. Commun.* **2010**, 46, 2474

Synthesis of NHC–borane complexes



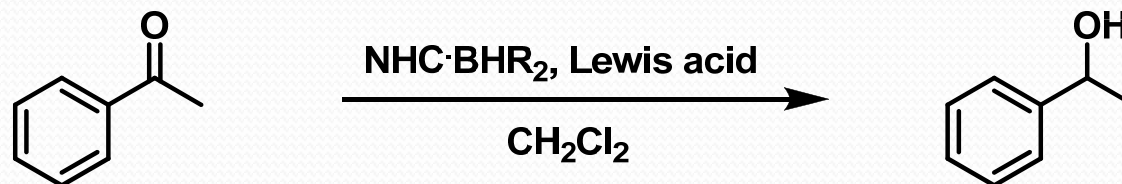
Entry	NHC·HX	Base	NHC·BH ₃	Yield (%)
1	3·HPF ₆	KHMDS	3·BH ₃	88
2	4·HOTf	<i>n</i> -BuLi	4·BH ₃	96
3	5·HOTf	<i>n</i> -BuLi	5·BH ₃	95
4	6·HOTf	<i>n</i> -BuLi	6·BH ₃	46

Reduction of acetophenone with NHC–borane complexes



Entry	NHC·HX	Lewis acid	T/°C	Yield (%)	Ee: (%)
1	3·BH ₃	--	rt	--	--
2	3·BH ₃	--	40	--	--
3	4·BH ₃	--	rt	44	14
4	4·BH ₃	--	0	10	36
5	4·BH ₃	Sc(OTf) ₃	-78	95	42
6	5·BH ₃	Sc(OTf) ₃	-78	92	50
7	6·BH ₃	Sc(OTf) ₃	-78	60	75

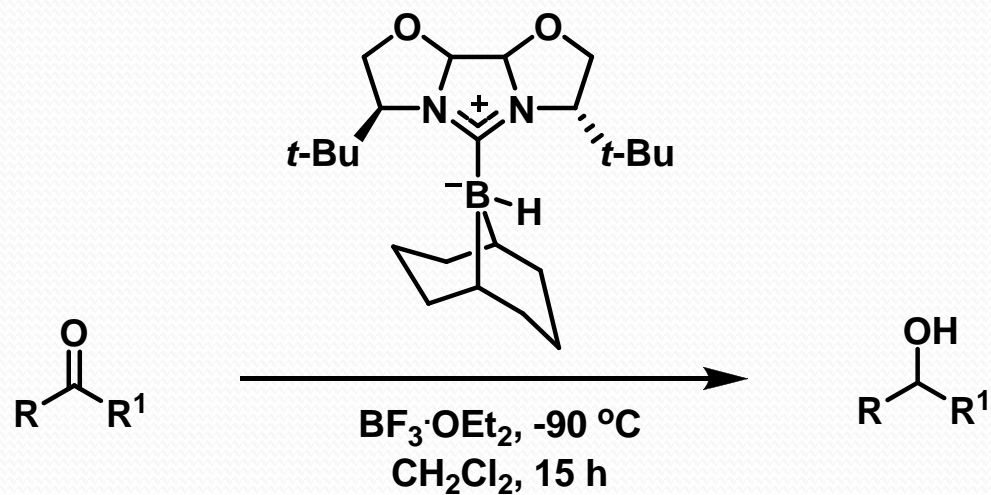
Asymmetric ketone reduction using NHC–dialkylborane complexes



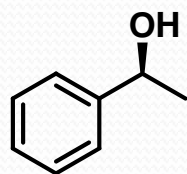
Entry	NHC·BHR ₂	T/°C	t/h	Yield (%)	Ee: (%)
1	3.9-BBN ^a	rt	24	15	--
2	4.9-BBN ^b	rt	15	40	34
3	4.9-BBN ^c	0	4	90	56
4	4.9-BBN ^c	-78	15	82	60
5	5.9-BBN ^c	-78	15	80	84
6	6.9-BBN ^c	-78	15	45	10

^a No Lewis acid additive. ^b 1 equiv. Sc(OTf)₃. ^c 1 equiv BF₃·OEt₂

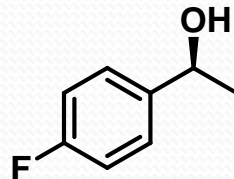
Asymmetric ketone reduction



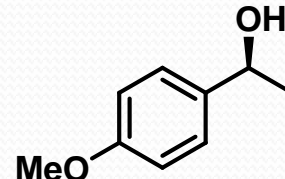
Up to 85% ee



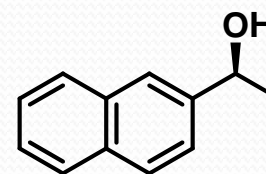
Ee: 84% (80%)



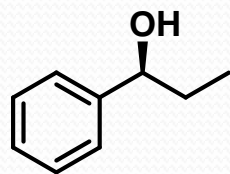
Ee: 85% (76%)



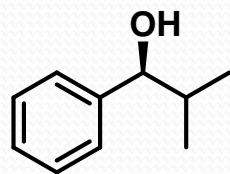
Ee: 59% (74%)



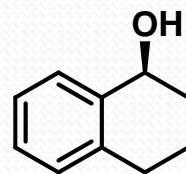
Ee: 71% (87%)



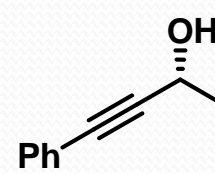
Ee: 63% (82%)



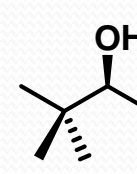
Ee: 24% (65%)



Ee: 0 (68%)

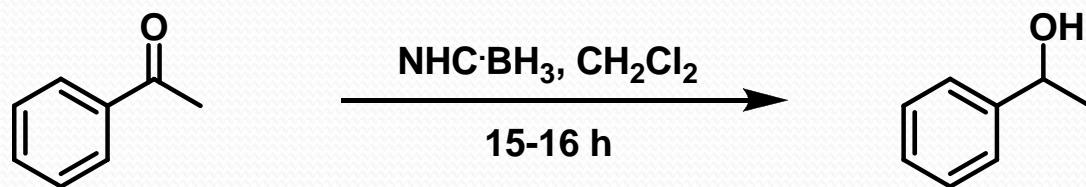


Ee: 70% (88%)

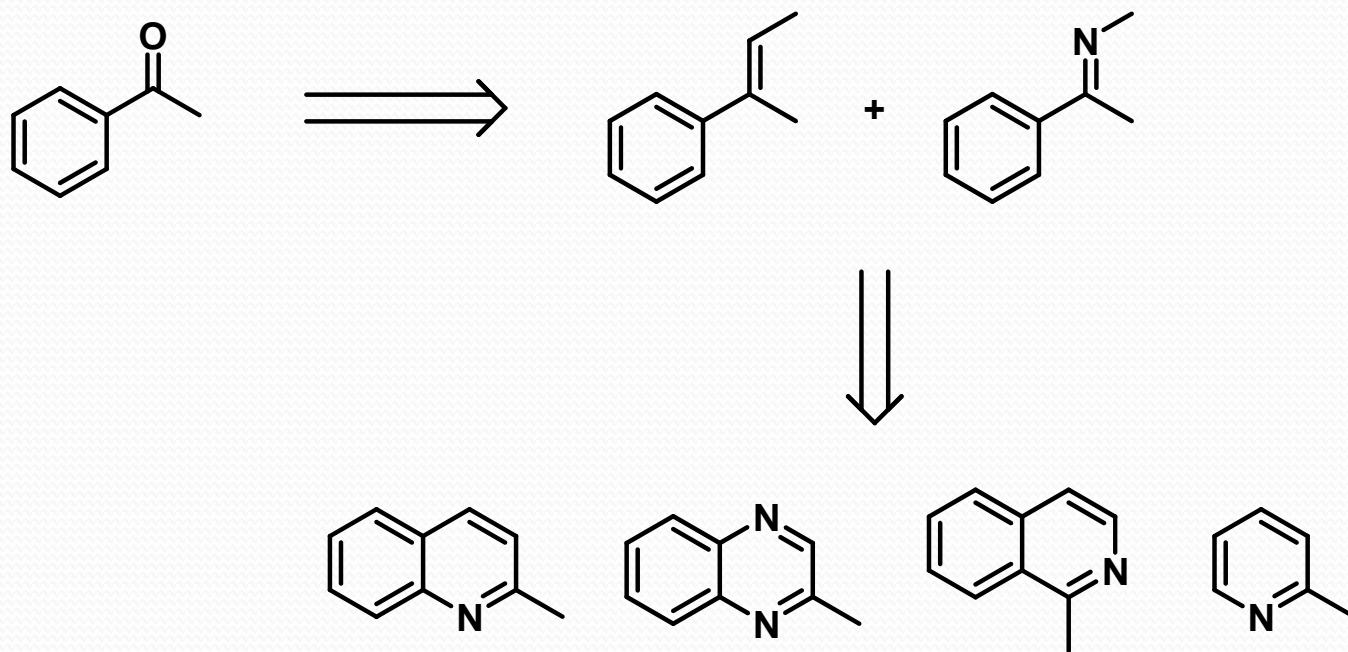


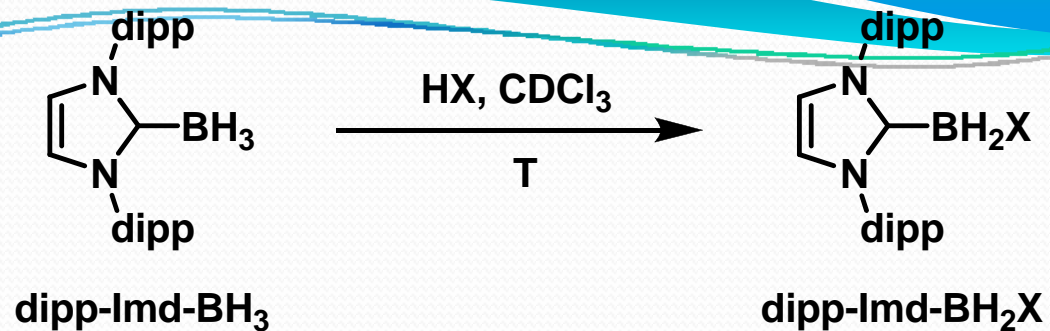
Ee: 62% (62%)

Summary



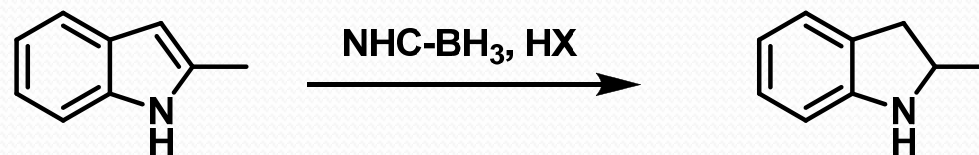
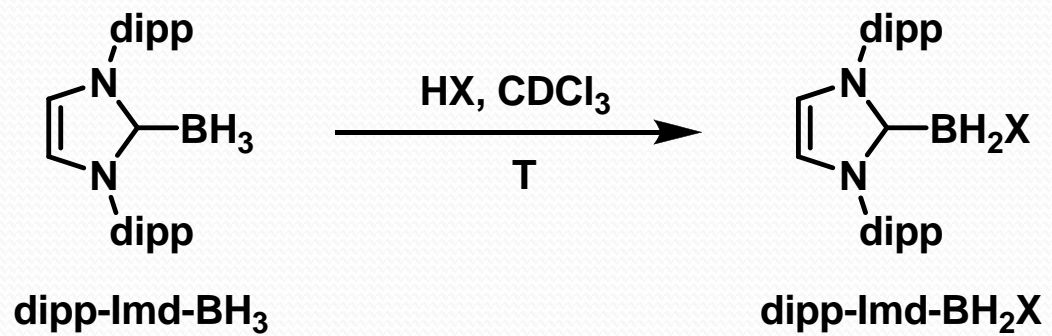
展 望







Entry	HX	pKa	T	Prod, X =	yield	^{11}B NMR (CDCl_3 , δ)
1	TfOH	-14	0	OTf	NMR	-8.8
2	HBr	-9	0	Br	NMR	-23.0
3	HCl	-8	0	Cl	81	-18.7
4	TsOH	-2.6	60	OTs	NMR	-11.2
5	MsOH	-2.6	0	OMs	88	-11.0
6	CF_3COOH	-0.6	25	OCOCF_3	85	-11.4
7	Cl_2CHCOOH	1.3	60	OCOCHCl_2	67	-11.1
8	NCCH_2COOH	2.5	60	OCOCH_2CN	24	-11.9

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For more than 40 years, there has been intense interest in the study of N-heterocyclic carbenes (NHCs), initially focused on empirical research, which led to the isolation of NHCs, and their concomitant impact in catalysis for organic synthesis. The ligating ability of NHCs equals or surpasses that of phosphanes in a range of transition metal-catalysed reactions, and the Lewis- and Brønsted basicity of NHCs has enabled their use as powerful organocatalysts.



In summary, we have synthesised a range of chiral and achiral NHC–borane and –organoborane complexes, and shown, in the first example of asymmetric synthesis using structurally well-defined chiral NHC–main group complexes, their potential in the asymmetric reduction of ketones. Work in our laboratory is ongoing to identify more effective chiral NHCs to apply the methodology to other C=X systems and to develop a catalytic, asymmetric variant of the reaction, and these studies will be described in due course.