

## The *threo*-Selective Reaction of Allenic Organometallic Compounds with Imines

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The reaction between the imines (**2**) and the allenic organometallic compounds (**3**) gives the *threo* adducts (**4**) with very high stereoselectivity, while the reaction with 9-but-2-enyl-9-borabicyclo[3.3.1]nonane gives the analogous *erythro* allylamines stereoselectively.

The development of new methods for acyclic stereocontrol is of major importance in synthetic organic chemistry. A number of excellent methods for controlling the relative stereochemistry in the oxygen containing acyclic system (**1a**) have been reported.<sup>1</sup> However, methods for preparing the nitrogen containing acyclic molecule (**1b**) stereoselectively are inadequate despite its frequent occurrence in many important natural products, *e.g.*, amino sugars and amino acids. We report that the reaction of the imines (**2**) with the allenic organometallic compounds (**3**) provides the *threo* adducts (**4**) with very high stereoselectivity. The results are summarized in Table 1.

Aliphatic imines produced the *threo* isomers exclusively (entries 1–11). Even the lithio derivative gave the *threo* adduct, though the yield was somewhat lower (entries 4 and 8). The use of ClTi(OPr<sup>i</sup>)<sub>3</sub> as 'M' gives the best selectivity and

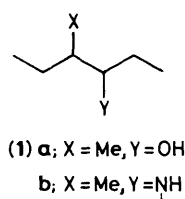


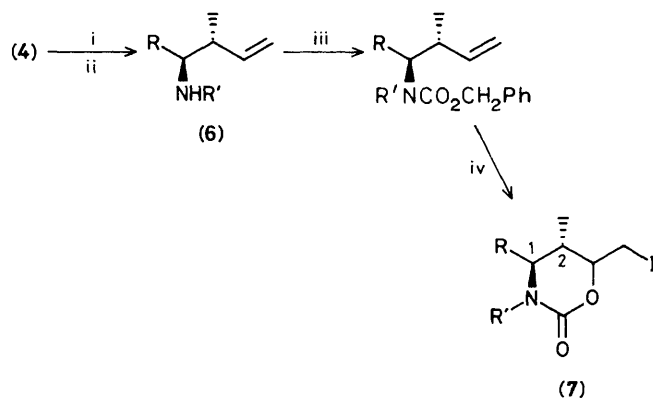
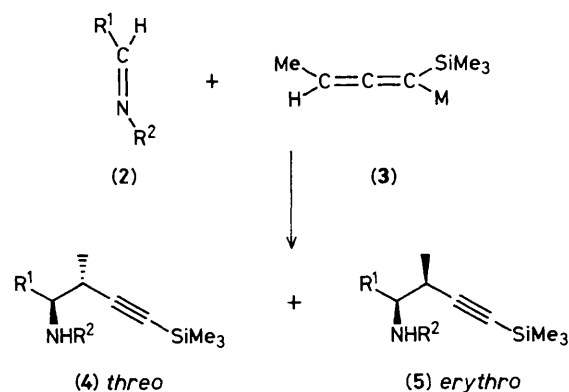
Table 1. *threo*-Selective reaction of (**2**) with (**3**).<sup>a</sup>

Entry	(2)		(3)	Isomer ratio		Total isolated yield, %
	R <sup>1</sup>	R <sup>2</sup>	M	(4)	(5)	
1	Et	CH <sub>2</sub> Ph	Ti(OPr <sup>i</sup> ) <sub>3</sub>	>99	—	95
2	Et	CH <sub>2</sub> Ph	B(OMe) <sub>n</sub> <sup>b</sup>	>99	—	21 <sup>c</sup>
3	Et	CH <sub>2</sub> Ph	AlEt <sub>3</sub>	>99	—	28
4	Et	CH <sub>2</sub> Ph	Li <sup>d</sup>	>99	—	65
5	Pr <sup>n</sup>	CH <sub>2</sub> Ph	Ti(OPr <sup>i</sup> ) <sub>3</sub>	>99	—	95
6	Pr <sup>n</sup>	Pr <sup>i</sup>	Ti(OPr <sup>i</sup> ) <sub>3</sub>	>99	—	57
7	Pr <sup>n</sup>	Pr <sup>i</sup>	AlEt <sub>3</sub>	>99	—	(80) <sup>e</sup>
8	Pr <sup>n</sup>	Pr <sup>i</sup>	Li <sup>d</sup>	>99	—	46
9	Pr <sup>i</sup>	Pr <sup>n</sup>	Ti(OPr <sup>i</sup> ) <sub>3</sub>	>99	—	64
10	Pr <sup>i</sup>	Pr <sup>n</sup>	AlEt <sub>3</sub>	>99	—	(90) <sup>e</sup>
11	Pr <sup>i</sup>	Pr <sup>i</sup>	Ti(OPr <sup>i</sup> ) <sub>3</sub>	>99	—	37
12	Ph	Ph	Ti(OPr <sup>i</sup> ) <sub>3</sub>	54	46	97
13	Ph	Ph	AlEt <sub>3</sub>	50	50	67
14	Ph	Ph	Li <sup>d</sup>	65	35	94
15	Ph	Pr <sup>n</sup>	Ti(OPr <sup>i</sup> ) <sub>3</sub>	81	19	95

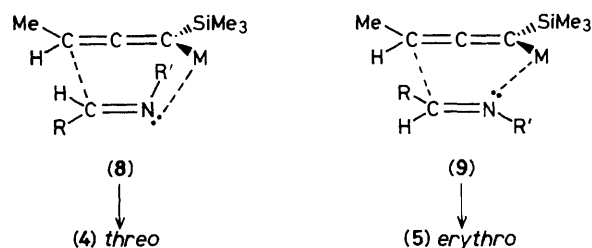
<sup>a</sup> All the reactions were carried at 1 mmol scale under N<sub>2</sub>. Compound (**3**) was prepared according to ref. 2. Treatment of 1-trimethylsilylbut-1-yne with Bu<sup>n</sup>Li (1.1 equiv.) in tetrahydrofuran at -78 °C followed by the addition of 'M' (1.1 equiv.) gave (**3**), where 'M' = ClTi(OPr<sup>i</sup>)<sub>3</sub>, B(OMe)<sub>3</sub>, or AlEt<sub>3</sub>. The imines were added to this mixture at -78 °C, and the reaction was quenched at room temperature. The isomeric allenic amines were not produced. The isomer ratio was determined by 400 MHz <sup>1</sup>H n.m.r. and <sup>13</sup>C n.m.r. spectroscopy. <sup>b</sup> Whether n = 3 (ate complex) or 2 (boronate) is not clear. <sup>c</sup> The reaction was sluggish with B(OMe)<sub>3</sub>. <sup>d</sup> 'M' was not added. <sup>e</sup> Yield of the crude product, determined by <sup>1</sup>H n.m.r. spectroscopy. The yield decreased at the isolation stage when AlEt<sub>3</sub> was used (*cf.* entry 3).

yield.<sup>4</sup> An increase in the steric bulk of the R<sup>1</sup> and R<sup>2</sup> groups made the reaction sluggish and resulted in lower yields (entries 6, 9, and 11). In contrast, aromatic imines resulted in low stereoselectivity (entries 12–15). The reason is not clear at present, but a similar observation has been reported for the reaction of aromatic aldehydes with allenic organometallic compounds.<sup>2</sup>

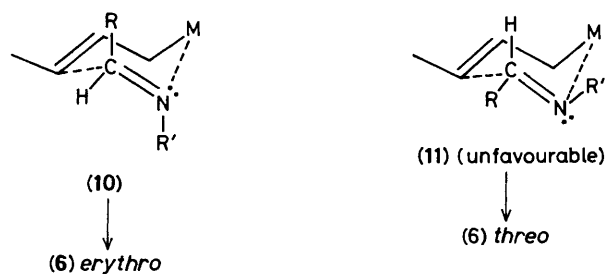
The structure of (**4**) and (**5**) was determined as follows (Scheme 1). Removal of the Me<sub>3</sub>Si group followed by selective reduction gave (**6**), which was converted into the iodocycliza-



Scheme 1. i, NaOMe–MeOH; ii, H<sub>2</sub>, catalyst Pd–BaSO<sub>4</sub>; iii, PhCH<sub>2</sub>OCOCI–Na<sub>2</sub>CO<sub>3</sub>; iv, I<sub>2</sub>.



Scheme 2

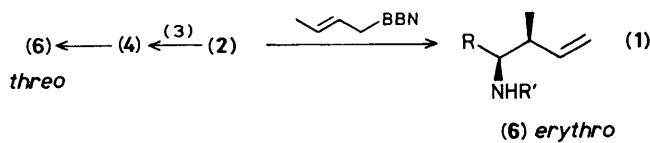


Scheme 3

tion product (7). Normally,  $J(1\text{-H}-2\text{-H})$  of (7) (*threo*) >  $J(1\text{-H}-2\text{-H})$  of the corresponding *erythro* isomer. Authentic samples of (6), (7), and their *erythro* isomers were prepared by the reaction of imines with but-2-enyl organometallic compounds.<sup>5</sup>

The very high *threo* selectivity can be explained as shown in Scheme 2.<sup>6</sup> Since the metal (M) can co-ordinate to the lone pair of the nitrogen atom with equal ease in both transition states, (8) and (9), the stereoselectivity must be determined by the steric interaction between the Me and R groups. Therefore, (4) is produced stereoselectively, and this selectivity is similar to that observed in the reaction of aldehydes.<sup>2</sup> On the other hand, the co-ordination of M to the lone pair has constraints in the six-membered cyclic transition states (10) and (11).<sup>5</sup> Thus, *erythro* allylamines are produced stereoselectively in the reaction with 9-but-2-enyl-9-borabicyclo[3.3.1]nonane (Scheme 3).<sup>5</sup>

In conclusion, we are now in a position to prepare both



BBN = 9-borabicyclo[3.3.1]nonan-9-yl.

isomers stereoselectively by choosing either allenic or allylic organometallic compounds, equation (1).

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- 6 It is known that imines exist in the *trans* configuration, C. G. McCarty, in 'The Chemistry of the Carbon-Nitrogen Double Bond,' ed. S. Patai, Interscience, London, 1970, p. 363.