propane-1,3-diol in THF followed by concentration of the solvent gave **6b** in 96% yield (Scheme II).

The typical procedure of the coupling reaction is as follows: A solution of the 5-bromouridine derivative 1 (0.3 mmol), the aryltin **6b** (0.34 mmol), and a catalytic amount of $Pd(PPh_3)_4$ (0.015 mmol) in toluene (5 mL) was refluxed with stirring for 1 day under argon atmosphere. The resulting mixture was concentrated in vacuo, and the residue was chromatographed on silica gel to isolate the desired product **7b**.

Next, we applied this procedure to several different nucleoside derivatives (Scheme III). The coupling reaction of the nucleoside derivatives, brominated or iodinated on the sp_2 carbons (**10a**,[6] **11a**,[6] and **12b**[13g]), with the aryltin **6b** also proceeded smoothly under similar conditions, giving the desired coupling products **10c**, **11c**, and **12c**, respectively, in high yields. The compounds **7b**, **10c**, **11c**, and **12c** are storable in the air at room temperature for more than several days. Deprotection of the silyl group and 2,2-dimethylpropane-1,3-diol gave water-soluble nucleosides bearing the $B(OH)_2$ group. These characteristics are highly promising to ^{10}B NCT.

It is now clear that the proper choice of catalyst and protecting group of boronic moiety and the protection of the sugar portion make it possible to combine the bifunctional organometallic compound with the multifunctional nucleoside derivatives. We are now in a position to prepare systematically a number of boron-containing nucleosides. Application of these new ^{10}B carriers for ^{10}B NCT is now in progress.

Acknowledgment. We thank the Iwaki Scholarship Foundation for partial support of this research.

Supplementary Material Available: Full characterization data for **6a**, **6b**, **7b**, **10c**, **11c**, and **12c** are provided along with a detailed procedure for the synthesis of ^{10}B-containing nucleosides (4 pages). Ordering information is given on any current masthead page.

A Regioselective Synthesis of Pyrroles via the Coupling of α,β-Unsaturated Imines with Esters or *N*,*N*-Dimethylformamide Promoted by $NbCl_3(DME)$

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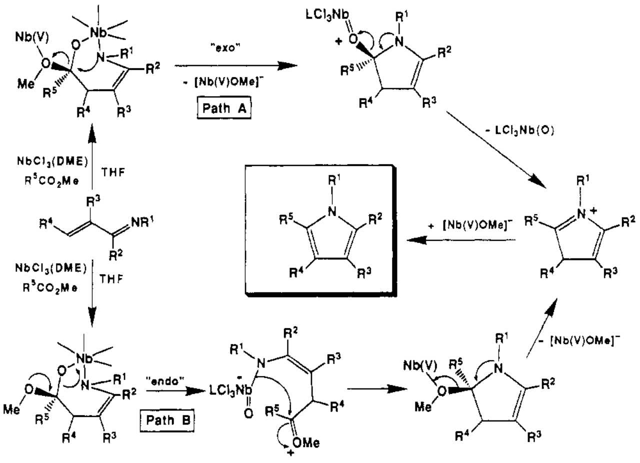
Summary: N-Substituted pyrroles are obtained when α,β-unsaturated imines are combined with $NbCl_3(DME)$ and an ester or *N*,*N*-dimethylformamide in tetrahydrofuran. The regiochemical outcome of the reaction is completely predictable.

Sir: Recently we described a synthesis of 2-amino alcohols via the coupling of aldimines with aldehydes or ketones promoted by the new reagent $NbCl_3(DME)$.[1] The metallaaziridine intermediate proposed can be considered as an N,C-dianion equivalent (Figure 1). Extension of this formalism to α,β-unsaturated imines suggested that such compounds could function as homoenolate[2] equivalents (Figure 1).[3] The two corresponding organometallic intermediates, C and D, bear structural resemblances to many early metal diene complexes.[4,5] These diene complexes are known to react with esters,[4] unlike the majority of early metal alkyls, including niobium metallaaziridines.[1] Therefore if either intermediate C or D were to react with an ester, an intermediate ketal would form, which could undergo an intramolecular ring closure leading to a pyrrole (Scheme I).[6]

Scheme I



Addition of *N*-allyl-α-methylcinnamaldehyde imine to a solution of $NbCl_3(DME)$ in dry ethyl acetate produced *N*-allyl-2,4-dimethyl-3-phenylpyrrole (Table I, entry 1). A similar reaction using *N*,*N*-dimethylformamide (DMF) gave *N*-allyl-3-phenyl-4-methylpyrrole (entry 2). *The electrophile need not be employed as the solvent in these re-*

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(1) Roskamp, E. J.; Pedersen, S. F. *J. Am. Chem. Soc.* **1987**, *109*, 6551.

(2) Werstiuk, N. N. In *Umpoled Synthons: A Survey of Sources and Uses in Organic Synthesis*; Hase, T. A., Ed.; John Wiley and Sons: New York, 1987, Chapter 6.

(3) When $NbCl_3(DME)$ and an α,β-unsaturated imine are reacted with an aldehyde or ketone, products resulting from carbon-carbon bond formation between the β-carbon of the imine and the carbonyl carbon are obtained (i.e., 2-aminotetrahydrofurans). Details of these reactions will be described elsewhere.

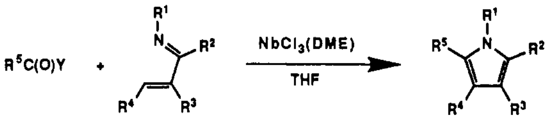
(4) (a) Yasuda, J.; Nakamura, A. *Angew Chem. Int. Ed. Engl.* **1987**, *26*, 723. (b) Yasuda, J.; Tatsumi, K.; Nakamura, A. *Acc. Chem. Res.* **1985**, *18*, 120.

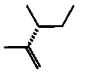
(5) Intermediate D has precedent in titanocene chemistry; Cohen, S. A.; Bercaw, J. E. *Organometallics* **1985**, *4*, 1006.

(6) We were led to consider path A from experiments with acylnitriles, which also produce pyrroles. The initially formed positive charge in path B would not be stabilized by the cyano substituent. However, we cannot rule out path B because the acylnitriles could be converted to esters by niobium alkoxides present from some ring opening of THF promoted by either Nb(III) or Nb(V). With respect to the last steps of the mechanism, ^1H NMR studies of the reaction in DMF-d_7 have demonstrated that pyrrole is formed *in situ* (i.e., before hydrolysis).

0022-3263/89/1954-4736$01.50/0

Table I



entry	R^1	R^2	R^3	R^4	R^5	Y	yield, %
1	$CH_2CH{=}CH_2$	H	Me	Ph	Me	OEt	29[a] (48)[b]
2	$CH_2CH{=}CH_2$	H	Me	Ph	H	NMe_2	58[a]
3	CH_2Ph	H	Me	Ph	H	NMe_2	50[a]
4	$CH_2CH{=}CH_2$	H	H	Ph	H	NMe_2	44[a]
5	n-Pr	H	Me	Ph	PhCH=CH	OMe	63[b]
6	$CH_2CH{=}CH_2$	H	Me	Ph	MeO_2CCH_2	OMe	40[b]
7	$CH_2CH{=}CH_2$	H	Me	Ph	CF_3	OMe	60[c]
8	$CH_2CH{=}CH_2$	H	Me	Ph	$HO(Me)CH(CH_2)_2$	*d*	78[b]
9	3,4-$(OMe)_2PhCH_2$	H	Me	Me	H	NMe_2	54[b]
10	$CH_2CH{=}CH_2$	Me	H	Ph	H	NMe_2	34[a]
11	$CH_2CH{=}CH_2$	H	$(CH_2)_3$		H	NMe_2	47[a]
12	$CH_2CH{=}CH_2$	H			H	NMe_2	44[b]

[a] $R^5C(O)Y$ employed as solvent. [b] $R^5C(O)Y$ employed as limiting reagent (see experimental for further details). [c] Excess of $R^5C(O)Y$ employed (500 equiv). [d] Starting with γ-valerolactone.

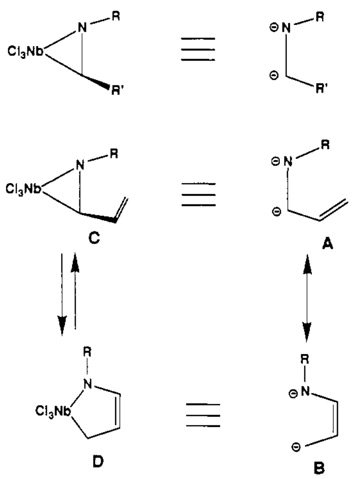


Figure 1.

actions (Table I). In general, it is used as the limiting reagent (see below). Lactones may also be used (entry 8).

One limitation of this method is that α-branched esters produce poor yields of pyrroles. Apparently this is a problem with the initial carbon–carbon bond-forming reaction since the major product isolated from these reactions is a 4,5-dihydropyrrole derived from self-condensation (tail to head) of the imine followed by deamination.[7] A second limitation we have observed is that the N-substituent on the imine cannot be α-branched. In such cases little or no reaction is observed.

Two important features of the above pyrrole synthesis are that the regiochemical outcome of the reaction is completely predictable and enolizable esters are tolerated.[8] Furthermore, we have demonstrated that the application of $NbCl_3(DME)$ in organic synthesis extends beyond its ability to supply two electrons for reductive cross-coupling reactions. After coupling has taken place, the new metal species can also promote selective reactions (e.g., deoxygenation, cyclization) based on features inherent to d^0 early transition metals (e.g., oxophilicity, Lewis acidity and rich coordination chemistry).[9]

A general experimental for the synthesis of pyrroles is provided below. All reactions were performed under an atmosphere of N_2.

Synthesis of Pyrroles. A dry 250-mL flask was charged with $NbCl_3(DME)$[10] (2.0 g, 6.9 mmol) and dry tetrahydrofuran (ca. 80 mL). The ester (4.6 mmol) in tetrahydrofuran (2 mL) was then added via syringe to the stirred mixture. After 5 min the α,β-unsaturated imine[11] (6.9 mmol) in tetrahydrofuran (ca. 2 mL) was added via syringe and stirring continued for 10 h. The reaction was poured into a separatory funnel, treated with potassium hydroxide (10% w/v, 75 mL), and extracted with ether (3 × 100 mL). The organics were combined, dried briefly over $MgSO_4$, and filtered, and the volatiles were removed in vacuo. The crude product was purified by either Kugelrohr distillation or flash chromatography[12] (silica gel, 230–400 mesh, hexane/ethyl acetate, the column was pretreated with 1% triethylamine before elution of the pyrrole).

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Supplementary Material Available: NMR, IR, and mass spectral data and C, H, N analysis information for pyrroles (9 pages). Ordering information is given on any current masthead page.

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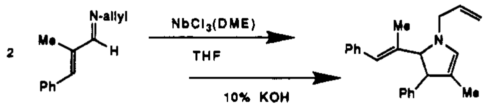
[7] For example:



[8] Recently dianions derived from N-(trimethylsilyl)allylic amines and N-(trimethylsilyl)-o-toluidine and monoanions derived from cuprate addition to methyl N,N-bis(trimethylsilyl)aminopropiolate have been used in the regioselective synthesis of pyrroles and other heterocycles: (a) Burns, S. A.; Corriu, R. J. P.; Huynh, V.; Moreau, J. J. E. *J. Organomet. Chem.* **1987**, *333*, 281. (b) Smith, A. B., III; Visnick, M. *Tetrahedron Lett.* **1985**, *26*, 3757. (c) Corriu, R. J. P.; Moreau, J. J. E.; Vernhet, C. *Ibid.* **1987**, *28*, 2963.

[9] For another example illustrating the importance of such secondary transformations, see; Hartung, J. B., Jr.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989**, *111*, 5468.

[10] $NbCl_3(DME)$ was prepared as described in ref 1. Alternatively, it may be purchased from the Aldrich Chemical Company.

[11] All imines were prepared by combining the appropriate aldehyde, amine, and excess $MgSO_4$ in dichloromethane and monitoring the reaction by ^1H NMR. The imines were purified by Kugelrohr distillation.

[12] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.