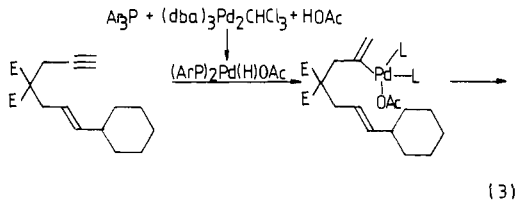
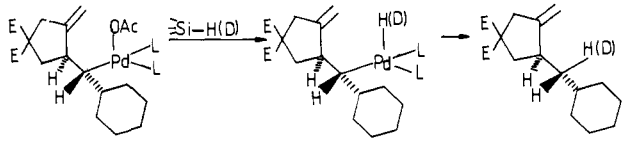
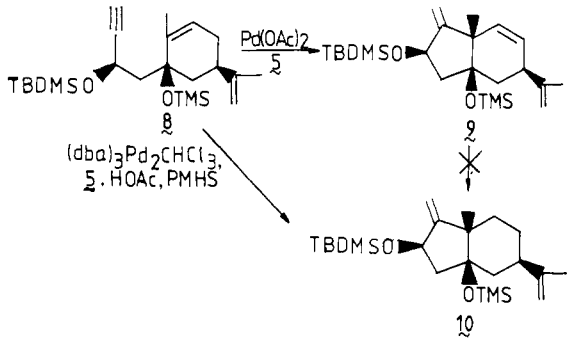


(3)



results are obtained by using triethylsilane or PMHS. In entry 3, some problems encountered in the chromatographic separation of dba resulted in a slightly lower yield. Third, allylic acetates are compatible (entries 4 and 5)—an observation also consistent with Pd(0) not being the active catalyst. Fourth, substituents on the acetylene (entry 6) as well as olefin (entries 1–5 and 7) are tolerated. Fifth, high diastereoselectivity may be observed. The product of entry 6 is a single diastereomer which has been tentatively assigned as trans on the basis of mechanistic considerations. Sixth, six-membered rings may be formed (entry 8). Seventh, the best yields are derived by a slow addition of 1 equiv of acetic acid via syringe pump to a reaction mixture containing the enyne, silane, catalyst, and ligand, all at room temperature. Normally, this reaction is complete within 6 h. This approach for reductive cyclization nicely complements the previous Pd(2+) enyne cyclizations to dienes by permitting chemoselective adjustment of the oxidation pattern. For example, it is now easy to convert **8** to either **9** or **10** but it would not be trivial to try to chemoselectively reduce **9** to **10**. The method also provides



diastereoselective incorporation of deuterium into methylene groups and can serve as a diastereoselective approach to highly substituted cyclopentanes. Mechanistically, this reaction is most consistent with involving a $L_2Pd(H)OAc$ (**11**) species which forms from **4** and acetic acid. To our knowledge, addition of a weak acid like acetic to Pd(0) has not been reported although the additions of strong acids are well-known.[9] An attempt to detect such a species by NMR spectroscopy by simply mixing **4**, ligand, and HOAc led to no observable differences in the spectrum from the reactants—a fact implying **11** can only form in an equilibrium which favors starting materials.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health General Medical Sciences for their generous support of our programs. A NATO Science Fellowship administered by the Royal Norwegian Council for Scientific and Industrial Research and a leave of absence from the University of Oslo provided support for part of the stay of F.R.

(8) D. Jebaratnam has established the utility of this ligand in other work; unpublished observations in these laboratories. Also see ref 5b.

(9) Maitlis, P. M.; Espinet, P.; Russell, M. J. H.; *Compr. Organomet. Chem.* **1982**, *6*, 250–252, 340–342.

N-Hydroxypyridine-2-thione Carbamates as Aminyl and Aminium Radical Precursors. Cyclizations for Synthesis of the Pyrrolidine Nucleus

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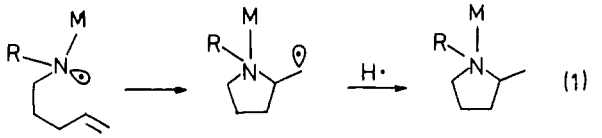
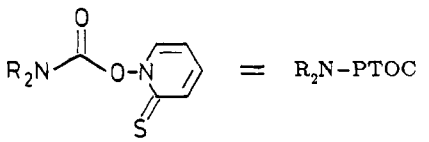
Recently there has been a growing interest in the applications of radical cyclization reactions in organic synthesis. Intramolecular C–C bond-forming reactions involving attack of a carbon radical on an alkene or alkyne have been used in the preparation of various carbocyclic and heterocyclic systems.[1] Neutral (aminyl, **1**) and protonated or complexed (aminium, **2**) nitrogen-centered radicals with δ-ϵ double bonds, while less well studied, can cyclize to give pyrrolidines (eq 1).[2] In this paper we demonstrate that *N*-



(1)

1 M = lone pair
2 M = H^+ or metal ion

hydroxypyridine-2-thione carbamates (**3**) are convenient sources



3, PTOC = ((1H)–pyridine–2–thione)oxycarbonyl

for both aminyl radicals and aminium cation radicals for intramolecular N–C bond-forming reactions. The ease of preparation of these precursors[3] and the mild conditions under which they produce either type of nitrogen-centered radical offer advantages over other routes to these radicals.[5]

The cyclization of *N*-butyl-4-pentenylaminyl radical (**5**) was studied as a model reaction.[7] Reactions were initiated by visible irradiation (150 W, tungsten filament lamp); after initiation, the radical chain processes shown in Scheme I were possible. Precursor **4** can react with a carbon-, tin-, sulfur-, or silicon-centered radical to give, after a decarboxylation step, radical **5**. Aminyl radical **5** can cyclize, apparently reversibly (see below), to carbon

(1) Examples are given in the following: *Selectivity and Synthetic Applications of Radical Reactions, Tetrahedron Symposium in Print, No. 22*; *Tetrahedron* **1985**, *41*, 3887–4303. Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon: Oxford, 1986.

(2) (a) Stella, L. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 337–350. (b) Surzur, J.-M. In *Reactive Intermediates*, Abramovitch, R. A., Ed.; Plenum: New York, 1982; Vol. 2, Chapter 2. (c) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, Essay 4.

(3) The preparation of carbamates **3** has been reported;[4a] the synthetic reactions are similar to those used in the preparation of *N*-hydroxypyridine-2-thione esters.[4b]

(4) (a) Newcomb, M.; Park, S.-U.; Kaplan, J.; Marquardt, D. J. *Tetrahedron Lett.* **1985**, *26*, 5651–5654. (b) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901–3924.

(5) Other routes to nitrogen-centered radicals involve radical chain reactions of *N*-chloroamines,[2a,b,6a] or *N*-nitrosamines,[6b] often in the presence of Brønsted or Lewis acids, the decomposition of tetrazenes,[6c] or the anodic oxidation of lithium dialkylamides.[6d]

(6) (a) Neale, R. S. *Synthesis* **1971**, 1–15. (b) Chow, Y. L.; Perry, R. A.; Menon, B. C.; Chen, S. C. *Tetrahedron Lett.* **1971**, 1545–1549. (c) Michejda, C. J.; Campbell, D. H.; Sieh, D. H., Koepke, S. R. In *Organic Free Radicals*; Pryor, W. A., Ed.; ACS Symposium Series 69, American Chemical Society: Washington, DC, 1978, pp 292–308. (d) Bauer, R.; Wendt, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 202–203.

(7) Alkylpentenylaminyl radicals from reactions of *N*-chloramines,[2a,b,8a] a tetrazene,[6c,8b] and lithium dialkylamides[8c,d] have been studied.

(8) (a) Broka, C. A.; Eng, K. K. *J. Org. Chem.* **1986**, *51*, 5043–5045. (b) Maeda, Y.; Ingold, K. U. *J. Am. Chem. Soc.* **1980**, *102*, 328–331. (c) Tokuda, M.; Yamada, Y., Takagi, T.; Suginome, H.; Furusaki, A. *Tetrahedron Lett.* **1985**, *26*, 6085–6088. (d) Tokuda, M.; Yamada, Y.; Takagi, T.; Suginome, H. *Tetrahedron* **1987**, *43*, 281–296.

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Scheme I

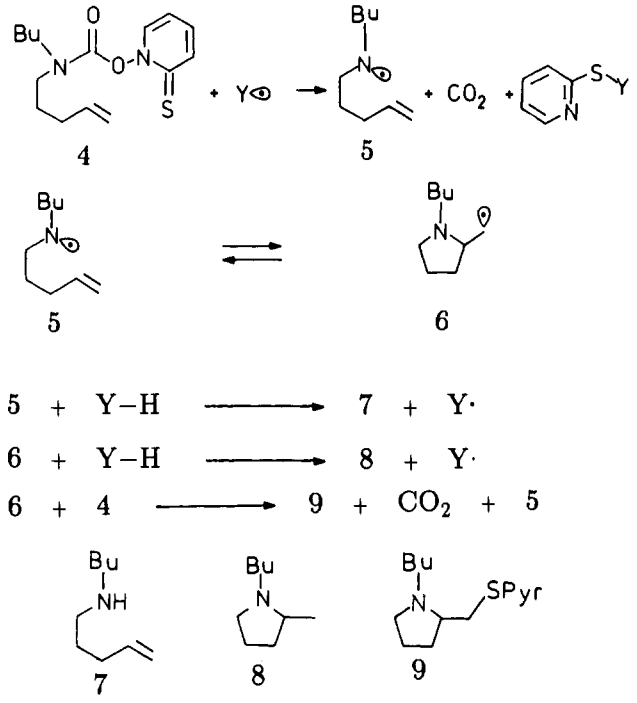


Table I. Yields of Products from Reactions of **4** in Benzene at 25 °C[a]

hydrogen donor (concn, M)		acid (concn, M)		rel % yields			total yield, %[b]
				7	8	9	
t-BuSH	(0.02)	none		100	0	0	80
n-Bu_3SnH	(0.1)			73	27	0	62
Ph_3SiH	(*c*)			40	60	*d*	50
none		CH_3CO_2H	(0.3)	20	0	80	70
t-BuSH	(0.11)		(0.1)	67	33	0	70
	(0.11)		(0.3)	25	75	0	75
	(0.11)		(0.9)	30	70	0	75
	(0.4)		(0.9)	40	60	0	70
	(2.8)		(0.9)	86	14	0	70
none		CF_3CO_2H	(0.5)	0	0	100	90
t-BuSH	(0.05)		(0.13)	0	100	0	78

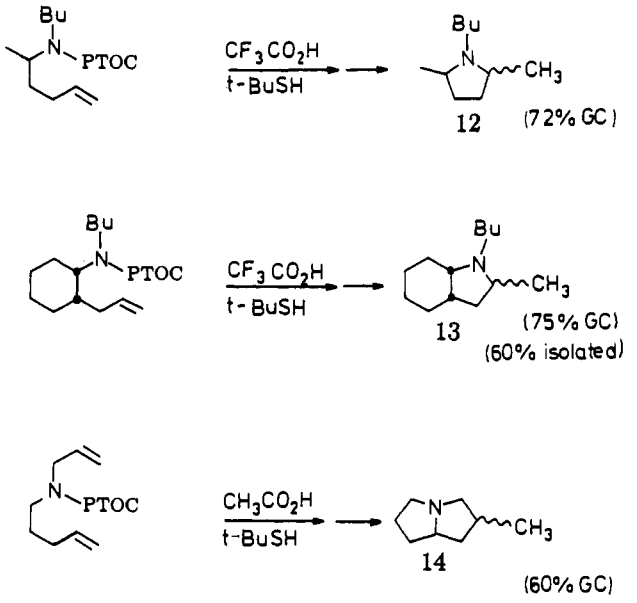
[a] The initial concentration of carbamate **4** was 0.01 M for all experiments except those run with CF_3CO_2H wherein the initial concentration was 0.04 M. [b] Absolute yields determined by GC. [c] Concentrations ranged from 0.11 to 1.09 M. [d] Product **9** was detected by TLC but was difficult to separate from the silane by GC.

radical **6**. In the presence of a hydrogen atom donor (Y–H), radicals **5** and **6** can be trapped to give acyclic and cyclic products **7** and **8**, respectively. In competition with trapping by Y–H (or in the absence of Y–H), carbon radical **6** (but not aminyl radical **5**[4a]) can react with precursor **4** to give product **9** in a chain-propagating step.

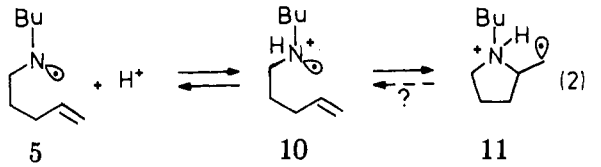
The yields of **7**–**9** from reactions of carbamate **4** in benzene at 25 °C are given in Table I (rows 1–3). The reactive H atom donor *t*-BuSH trapped **5** before cyclization occurred. In the presence of less reactive H atom donors, *n*-Bu_3SnH and Ph_3SiH, cyclic product **8** was formed; the insensitivity of the **7**/**8** ratio to the Ph_3SiH concentration suggests that a dynamic equilibrium between **5** and **6** obtained in the absence of a reactive H atom source.[9] Good yields of pyrrolidine products in reactions of simple δ,ε unsaturated aminyl radicals apparently reflect selective trapping of the cyclic carbon radical.[2]

Since the pK_a of dimethylaminium cation radical is about 7,[10] it appeared to be reasonable to attempt to protonate dialkylaminyl radicals with weak organic acids. Reaction of carbamate **4** in the presence of acetic acid[11] and *t*-BuSH gave improved yields of the pyrrolidine product **7**. A series of studies wherein the concentrations of acetic acid and *t*-BuSH were varied was conducted; representative results are collected in Table I. Since *t*-BuSH completely trapped neutral acyclic radical **5** in the absence of acid but pyrrolidine **8** was formed in the presence of acetic acid, we conclude that aminyl radical **5** was at least partially protonated by acetic acid in benzene to give aminium cation radical **10** (eq 2). Cyclization of **10** to **11** is faster than cyclization of **5** to **6** and/or the equilibrium constant for the protonated pair, if an equilibration between **10** and **11** is attained, is larger than that for the neutral pair.

Scheme II



PTOC = ((1H)–pyridine–2–thione)oxycarbonyl



The use of trifluoroacetic acid further improved the yield of pyrrolidine **8**. In the presence of *t*-BuSH and CF_3CO_2H, pyrrolidine **8** was formed in 78% yield by GC (52% isolated yield) and no acyclic amine **7** was detected. From the reaction of **4** in the absence of a hydrogen atom donor, the potentially useful thiopyridyl-substituted pyrrolidine **9** was isolated in 84% yield.

Reactions of δ,ε unsaturated aminium cation radicals formed from carbamates **3** under acidic conditions appear to be of general synthetic utility for formation of the pyrrolidine nucleus as illustrated by the unoptimized reactions shown in Scheme II. Stereoselectivity was observed in the formation of the 2,5-dimethylpyrrolidine **12** (trans:cis= 3:1) and in the perhydroindole **13** (isomer ratio = 3:1). The tandem cyclization of *N*-allyl-4-pentenylaminium cation radical to give the pyrrolizidine **14**[12] is similar to the reaction previously reported for the corresponding chloramine.[13] We are continuing to explore the applications of *N*-hydroxypyridine-2-thione carbamates for syntheses.

Acknowledgment. This work was supported by a grant from the National Science Foundation (CHE-85087076) and a

(9) The equilibrium we propose between **5** and **6** is in contradistinction to previous mechanistic conclusions.[7]

(10) Fessenden, R. W.; Neta, D. *J. Phys. Chem.* **1972**, *76*, 2857–2859.

(11) Despite the presence of δ-hydrogen atoms in animium cation radical **10**, a Hoffman–Löffler–Freitag reaction (δ-H atom abstraction) does not compete with cyclization; cf.: Surzur, J.-M.; Stella, L.; Tordo, P. *Bull. Soc. Chim. Fr.* **1975**, 1429–1430.

(12) We thank D. J. Marquardt for performing this reaction.

(13) Surzur, J.-M.; Stella, L. *Tetrahedron Lett.* **1974**, 2191–2194.

Biomedical Research Support Grant administered by Texas A&M University.

Supplementary Material Available: General method for synthesis of carbamates **3**, characterization of carbamates **3**, and general method for reactions of carbamates **3** (2 pages). Ordering information is given on any current masthead page.

Reaction of Allylstannanes with α,β-Unsaturated Acyliron Complexes: A Novel [3 + 2] Cycloaddition Reaction

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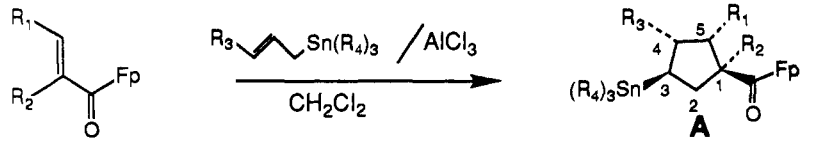
Recently, α,β-unsaturated acyliron complexes have emerged as valuable synthetic intermediates.[1] They undergo reactions such as Michael addition of nucleophiles[2] and Lewis acid catalyzed Diels–Alder reactions[3] readily. Also, they have seen recent application toward stereoselective synthesis.[1,3b,c] As part of a study to probe Lewis acid catalyzed reactions of acryloyliron complexes **1** with olefin and diene substrates,[3a] we recently initiated a study of the reactions of **1** with allylstannanes. As shown in Scheme I, this process catalyzed by aluminum chloride does not give the expected 5-hexenoyl species **4**[4] but provides the unexpected five-membered ring adduct **3**. We herein discuss preliminary results from studies of this remarkable reaction which potentially serves as a novel and useful method for cyclopentanoid synthesis.

Allyltributyltin reacts with acryloyliron complex **1** at −26 °C in the presence of 1 equiv of aluminum chloride to give the cyclopentanoid compound **3** in 42% yield. This appears to be a general reaction for five-membered ring formation as is evident from the examples provided in Table I. In two cases, the open-chain product analagous to compound **4** is observed (entries 8, 14). In all cases, only one stereoisomer is obtained as determined by ^{1}H NMR and ^{13}C NMR spectroscopy. Cis stereochemistry has been assigned to the reaction products based upon analysis of the ^{13}C–^{119}Sn coupling constants of selected compounds.[8] Optimum yields were obtained using freshly sublimed aluminum chloride as catalyst. Other catalysts were less effective for the five-membered ring-forming reaction. The acryloyl complex **1** is apparently unstable under the reaction conditions and decomposition competes with cycloaddition. This accounts for less than satisfactory mass balance seen in some cases.

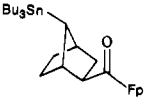
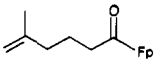
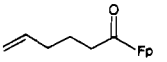
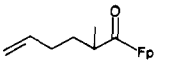
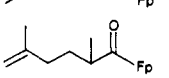
The mechanism we propose for this cycloaddition is outlined in Scheme I. First the aluminum chloride complexes with the acyliron giving the carbene complex **2**.[3a] The allylstannane then attacks the electrophilic carbene complex at C-2 giving the intermediate tin-stabilized carbocation **5**. This carbocation is stabilized by hyperconjugative interaction with the tributyltin group.[9] In the extreme, this interaction can be expressed by the nonclassical resonance form **5B**.[10] In **5B** there is significant electrophilic character at C-4 and C-5. Attack by the enolate at C-5 gives the five-membered ring compound **3**. Normally carbocations such as **5** destannylate to give olefins.[4,11] In this system, the favored pathway is cyclization. Here, iron donates significant electron density to the enolate in **5**, making it more reactive and making ring closure faster than with simple enolates.[12] The reaction efficiency also depends upon substituents at tin. The electron-donating alkyl groups provide better yields and faster reactions than the inductively electron-withdrawing phenyl groups.

This type of process has been observed in reaction of η^1-allyl transition-metal compounds with enones.[13] However, allenylsilanes are the only nontransition-metal systems which undergo

Table I. Reaction of α,β-Unsaturated Acylirons with Allystannanes



Fp = $Fe(CO)_2Cp$

entry	acyliron	allylstannane	catalyst	time/temp, °C	product	yield,[a,b] %
1	R_1, R_2 = H	allyltributyltin	$EtAlCl_2$	0.5 h/0	A: R_1, R_2, R_3 = H; R_4 = *n*-Bu	40
2	R_1, R_2 = H	allyltributyltin	$AlCl_3$	0.5 h/−26	A: R_1, R_2, R_3 = H; R_4 = *n*-Bu	42[6,15]
3	R_1, R_2 = H	allyltrimethyltin	$AlCl_3$	1.5 h/0	A: R_1, R_2, R_3 = H; R_4 = Me	27
4	R_1, R_2 = H	allyltriphenyltin	$AlCl_3$	24 h/25	A: R_1, R_2, R_3 = H; R_4 = Ph	8 (15)
5	R_1, R_2 = H	*trans*-crotyltributyltin	$AlCl_3$	1 h/0–25	A: R_1, R_2 = H; R_3 = Me; R_4 = *n*-Bu	52 (56)
6	R_1, R_2 = H	*trans*-cinnamyltributyltin	$AlCl_3$	2 h/25	A: R_1, R_2 = H; R_3 = Ph; R_4 = *n*-Bu	34 (45)
7	R_1, R_2 = H	cyclopent-2-enyltributyltin	$AlCl_3$	1 h/−78		27 (40)[7]
8	R_1, R_2 = H	methallyltributyltin	$AlCl_3$	5 min/−78		10
9	R_1 = H, R_2 = CH_3	allyltributyltin	$AlCl_3$	5 min/0	A: R_1, R_3 = H; R_2 = Me; R_4 = *n*-Bu	66 (91)
10	R_1 = H, R_2 = CH_3	*trans*-crotyltributyltin	$AlCl_3$	1 h/25	A: R_1 = H; R_2, R_3 = Me; R_4 = *n*-Bu	51 (87)
11	R_1 = CH_3, R_2 = H	allyltributyltin	$AlCl_3$	1 h/25	A: R_1 = Me, R_2, R_3 = H; R_4 = *n*-Bu	41 (58)
12	R_1, R_2 = H	allyltrimetylsilane	$AlCl_3$	24 h/25		31 (41)
13	R_1 = H, R_2 = CH_3	allyltrimethylsilane	$AlCl_3$	60 h/25		12 (77)
14	R_1 = H, R_2 = CH_3	methallyltributyltin	$AlCl_3$	5 min/−78		11 (57)

[a] The yields reflect compounds pure by TLC, ^{1}H NMR, and ^{13}C NMR analysis. The yields in parentheses are based on recovered starting material. [b] For a procedure see ref 5.

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