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Carbamoyl Radicals from Se-Phenylselenocarbamates: Intramolecular Additions to Alkenes

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Abstract: A series of 5 *exo*-trig cyclizations of carbamoyl radicals generated from readily available Se-phenylselenocarbamates is reported. Kinetic studies indicate that the rate constant of this cyclization exceeds $1 \times 10^8 \text{s}^{-1}$ in several cases. © 1998 Elsevier Science Ltd. All rights reserved.

Acyl radical cyclization has recently emerged as a useful tactic for ring construction in organic synthesis,¹ and successful variations on this theme include the use of alkoxycarbonyl² and imidoyl³ radical donors for producing lactones and cyclic amines, respectively. Less well-studied are carbamoyl radical additions to alkenes to afford lactam products.⁴ To date, acylcobalt salophen reagents are among the most common carbamoyl radical precursors in the literature.^{4a,b} In this report we disclose the use of Se-phenylselenocarbamates as convenient and effective alternative precursors for the production of carbamoyl radicals.

Scheme I



Initial efforts focused on accessing the requisite selenocarbamates via addition of PhSeH to the corresponding isocyanates followed by attempted radical cyclization mediated by either n-Bu₃SnH or TMS₃SiH. In all cases only formamide⁵ and amine products resulting from reduction and decarbonylation, respectively, were isolated. The predominance of rotamers unfavorable to ring formation in the intermediate secondary carbamoyl radicals is a possible reason for the failure of these substrates to cyclize.⁶ This would be particularly true if the interconversion of the reactive and unreactive carbamoyl radicals was slow on the scale of the radical lifetimes.^{7,8} In response to this difficulty, the corresponding tertiary carbamates ($R \neq H$) were then examined as a potential means for overcoming this putative conformational situation (Eq. (1)).



The more highly substituted selenocarbamates required for this study were best prepared in a slightly different fashion than was employed for the secondary carbamates. Thus, treatment of N-tosylamine 1 with triphosgene followed by addition of phenylselenol afforded the N-tosyl-Se-phenylselenocarbamate 2^9 in quite good yield. Exposure of this material to excess TMS₃SiH in refluxing toluene led in serviceable yield to the

Entry	Selenocarbamate	Conditions ^a	Product ^b	Yield (%)
1		А		68
2	TsN SePh	А	TSN	41 ^c
3	TsN SePh	Α	TSN	31
4	TsN SePh	Α	TsN	66
5	TsN SePh	В	TsN Ph	55
6	TsN SePh Ph Ph	В	TsN Ph	51
7	N SePh Ts O	A	TsN	45
8	N SePh	А	EtN	49

 Table I Radical Cyclization of Se-Phenylselenocarbamates

^a Conditions "A": TMS₃SiH, AIBN, toluene, reflux; Conditions "B": Bu₃SnH, (Bu₃Sn)₂, sunlamp, benzene, heat; Ref. 10. ^b Ref. 9. ^c Produced as a mixture of isomers.

expected butyrolactam 3.⁹ In contrast, Bu₃SnH afforded the corresponding formamide product along with lesser amounts of amine.¹¹ Other examples that illustrate the scope of this cyclization protocol are compiled in Table I. In most cases examined during this study, (TMS)₃SiH/AIBN in refluxing toluene provided superior yields of cyclized products, however, Bu₃SnH/(Bu₃Sn)₂/hv conditions proved most effective for securing the requisite lactams in Entries 5 and 6.¹² Typically, cyclization was effected on N-tosyl substituted substrates, but Nalkylselenocarbamates are also viable radical precursors as evidenced by the result in Entry 8, thus discounting any unusual electronic influence of the sulfonamide on the cyclization process.¹³



Inspection of the entries in Table I reveals that a range of 5-exo cyclizations can be achieved starting from selenocarbamates, unfortunately attempts to extend the process to the corresponding 6-exo cyclizations failed to deliver significant quantities of lactam products. An exception to this trend was the interesting formation of quinolone 4^9 via a tandem 6-endo cyclization-desulfonylation pathway (Eq. (2)).

Laser flash photolysis (LFP) studies of the radical precursors in Entries 5 and 6 of Table 1 demonstrated that the 5-*exo* radical cyclization reactions were quite fast. THF solutions of the precursors at ambient temperature were irradiated with 266 nm light from a Nd-YAG laser. Time-resolved UV-vis spectroscopy showed "instant" formation of the PhSe• radical (λ_{max} at 295 and 490 nm) as well as peaks we attribute to the products of the cyclization event. Specifically, peaks with λ_{max} at 315 nm and 334 nm were observed from the precursors in Entries 5 and 6, respectively, as expected for benzylic and diphenylalkyl radicals.¹⁴ The "instant" formation of the products requires that the cyclization reactions had rate constants exceeding $2x10^8s^{-1}$. Because aryl substitution on the ethenyl group results in increases of about 2 orders of magnitude in the rate constants for 5-*exo* radical cyclizations under similar conditions.¹⁶ Furthermore, the rate constants for the 5-*exo* cyclizations of carbamoyl radicals are more than an order of magnitude larger than the rate constants for cyclizations of carbano-centered radical analogs.¹⁷

In conclusion, readily available N-substituted Se-phenylselenocarbamates are useful precursors for carbamoyl radicals in 5-exo cyclizations.

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