Tetrahedron Letters, Vol.31, No.41, pp 5927-5930, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

VINYL RADICAL GENERATION WITH SELENOBORANE AND ITS APPLICATION TO CYCLIZATION REACTION OF ENYNES

Tadashi Kataoka, Mitsuhiro Yoshimatsu, Hiroshi Shimizu, and Mikio Hori*
Gifu Pharmaceutical University, 6-1 Mitahora-higashi 5-chome, Gifu 502, Japan

Abstract: Tris(methylseleno)- and tris(phenylseleno)boranes added to acetylenes to afford methylseleno- and phenylseleno-substituted Z-vinylselenides in high yields. The addition reactions proceeded by way of free radicals and were applied to cyclization reactions of enyne compounds. The radical cyclization provided pyrrolidine derivatives diastereoselectively.

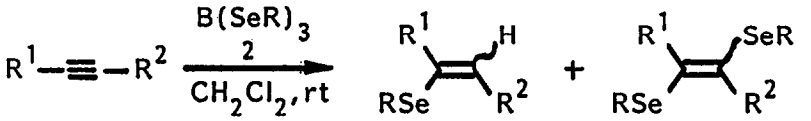
Construction of five- and six-membered rings through the intramolecular addition of carbon free radicals to carbon-carbon multiple bonds is well documented.[1] The intramolecular capture of vinyl radicals with double bonds forms exo-methylene substituted five- and six-membered rings. Recently, Oshima et al. reported that enyne compounds reacted with Et_3B-R_3SnH or Et_3B-RSH to give vinyl stannane-[2] or vinyl sulfide-substituted five-membered rings.[3] However, the Et_3B-RSeH system did not give satisfactory results.[4]

On the other hand, vinyl selenides can be transformed to other groups, [5] and various methods have been devised for their preparation. One of the simplest methods of access to vinyl selenides is the addition of selenols to acetylenes,[6] but selenols have defects in handling because of their bad smell and easy oxidation to diselenides. We sought a better reagent for hydroselenation of acetylenes and selected $(RSe)_3B$ as candidates, which have been utilized for selenoacetalization of aldehydes and ketones.[7] We describe here that $(RSe)_3B$ causes the free radical addition to the acetylenic bonds to form vinyl selenides and that this reaction can be successfully applied to the cyclization of enynes into the vinyl selenide-substituted cyclic compounds.

Hydroselenation of acetylenes took place readily with 0.5 equivalent of tris(methylseleno)borane or tris(phenylseleno)borane in CH_2Cl_2 to give (Z)-vinylselenides stereoselectively at room temperature. Results are summarized in Table I. $(RSe)_3B$ added to the terminal acetylenic carbon regio- and stereoselectively to give (Z)-vinyl selenides. The addition reactions proceeded even by use of 1/3 equivalent of $(RSe)_3B$. In the cases of dimethyl acetylenedicarboxylate (DMAD)(**1b**) and phenylacetylene (**1c**), two phenylseleno groups were introduced in the vicinal and trans modes affording (E)-1,2-bis(phenylseleno)-alkenes, **4b** and **4c**, respectively. Acetylenic alcohol **1d** did not give a satisfactory result, but alkyl acetylenes **1e** and **1f** afforded the corresponding vinylselenides. Although disubstituted acetylenes gave no adduct under the similar reaction conditions, diphenylacetylene gave the adduct **3g** by use of a catalytic amount of trifluoroacetic acid.

The reaction of $(MeSe)_3B$ with methyl propiolate (**1a**) in $CDCl_3$ was performed by the NMR spectroscopy in order to investigate the reaction intermediates. The reaction did not proceed under an argon atmosphere but proceeded in the presence of oxygen or air.

However, the reaction would not progress by the radical chain mechanism, because enough oxygen was necessary to complete the reaction. The ^{1}H NMR spectrum showed a singlet olefinic signal at δ 7.65 due to 3-H and no signal due to 2-H. The ^{11}B NMR spectrum showing



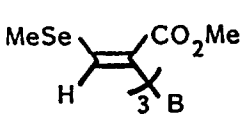
1 3 4

Table I Reactions with Acetylenes

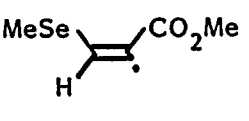
Acetylenes No.	R^1	R^2	Reagent R(Molar ratio)	Reaction Time(h)	Products (%yield)	$\frac{Z}{Z+E}$ x100 of 3 (%)
1a	H	CO_2Me	Me (0.5)	0.5	3a (100)	100
1a	H	CO_2Me	Ph (0.5)	0.5	3a (100)	100
1b	CO_2Me	CO_2Me	Me (0.5)	0.5	3b (75), 4b (trace)	100
1b	CO_2Me	CO_2Me	Ph (0.5)	0.5	3b (100)	92
1c	H	Ph	Me (0.6)	1	3c (61), 4c (18)	100
1c	H	Ph	Ph (0.5)	1	3c (79), 4c (12)	100
1d	H	CH(OH)Me	Me (0.6)	48	3d (9)	69
1d	H	CH(OH)Me	Ph (0.6)	48	3d (3.2)	100
1e	H	$(CH_2)_{11}Me$	Ph (0.6)	50	3e (72)	
1f	H	$(CH_2)_4Me$	Ph (0.5)	40	3f (31)	100
1g	Ph	Ph	Ph (0.5)*	72	3g (31)	
1h	H	CH_2SO_2Ph	Ph (0.5)	3	3h (97)	87

* catalytic amount of CF_3CO_2H

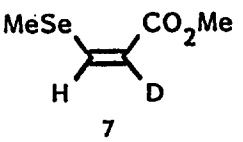
a peak at δ 19.07 indicates that the boron atom is not bound to the olefinic 2-C but to oxygen atom(s).[8] Thus, the intermediate is not a vinyl borane 5 but a vinyl radical 6, which abstracts a deuterium from $CDCl_3$ to give the 2-deuterioacrylate 7. Furthermore, this is supported by the mass spectrum of the product 7 with a molecular ion peak at m/z 243 corresponding to a molecular formula of $C_{10}H_9DO_2Se$. The radical addition of $(RSe)_3B$ to a triple bond is supported by the formation of 1,2-bis(phenylseleno)alkenes, 4b and 4c mentioned above and inhibition of cyclization with galvinoxyl described below.



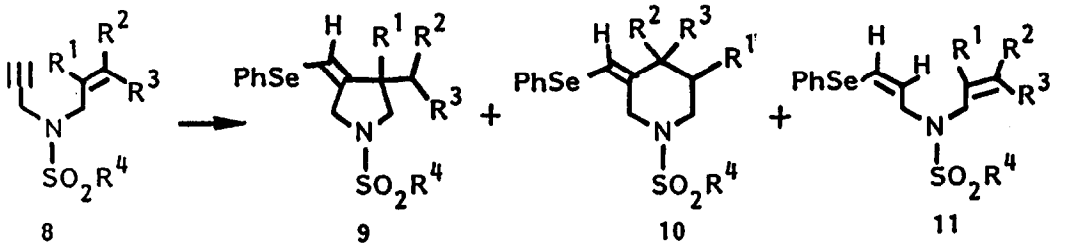
5



6



7

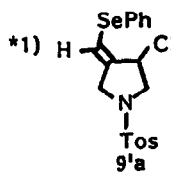


8 9 10 11

Table II

Synthesis of Selenomethylidene Substituted Pyrrolidine Derivatives

Compound No.	Enyne 8 R^1	R^2	R^3	R^4	Method (A or B)	Reaction Time(h)	Products (%yields)
8a	H	Ph	H	Tol	A	12	9a (90)*1
8a	H	Ph	H	Tol	B	1	9a (94)*2
8b	H	H	H	Ph	A	48	9b (51)
8b	H	H	H	Ph	B	4	9b (42), 10b(7)
8c	H	Me	Me	Tol	B	4	9c (quant.)
8d	Me	H	H	Tol	A	24	11d (18)



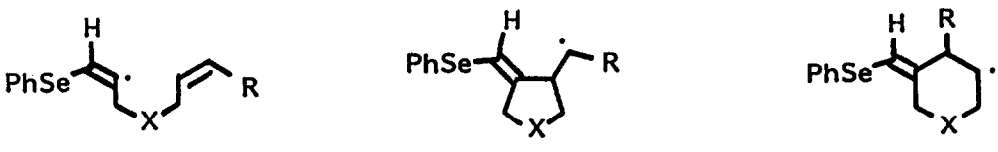
*1) 9'a (10%), *2) 9'a(4%)

Method A: no AIBN

Method B: 0.1eq AIBN

Next, we investigated application of the new vinyl radical generation reaction to cyclization of enyne compounds. Cyclization of N-cinnamyl-N-propargylsulfonamide 8a was conducted by two methods, with $B(SePh)_3$ (Method A) and with $B(SePh)_3$ and a catalytic amount of azobisisobutyronitrile (AIBN) (Method B) to provide pyrrolidine derivatives, 9a and 9'a in quantitative yield (Table II). On the other hand, N-allyl-N-propargyl derivative 8b by Method B provided a piperidine derivative 10b (7%) in addition to a pyrrolidine derivative 9b (42%).

This difference reflects the stability of the intermediate radicals II and III. Cyclization of the radical I initially formed in the 5-exo mode gives the exo-radical II

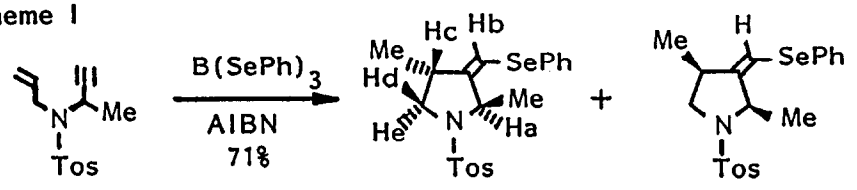


I II III

and ring closure in the 6-endo mode gives the endo-radical III. The benzyl radical II (R=Ph) is much more stable than the phenethyl radical III (R=Ph) in the reaction of **8a** and therefore the 5-exo products **9a** and **9a'** exclusively formed. In the case of **8b**, the secondary alkyl radical III (R=H) is more stable than the primary one II (R=H), but difference of stability between them is not so remarkable as that between II (R=Ph) and III (R=Ph). Consequently, cyclization of **8b** gives the pyrrolidine **9b** as a major product and piperidine **10b** as a minor one. The cyclization of enyne **8a** did not proceed in the presence of galvinoxyl.

Diastereoselectivity of this reaction was shown by cyclization of enyne **12** with $B(SePh)_3$ giving pyrrolidine derivatives **13a,b** with a ratio of diastereomers (**13a/13b**=4) (Scheme I).[9]

Scheme I



12 13a (4) 13b (1)

$B(SePh)_3$ and $B(SeMe)_3$ are new reagents for generation of RSe radical. We are currently investigating application of this methodology to the synthesis of carbocyclic compounds and biologically active compounds possessing the pyrrolidine ring.

REFERENCES

1. Reviews after 1986: (a) Giese, B. Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds; Baldwin, J. E. Ed.; Pergamon Press: Oxford, 1986. (b) Ramaiah, M. Tetrahedron, **1987**, 43, 3541. (c) Curran, D. P. Synthesis, **1988**, 417, 489.
2. (a) Stork, G.; Mook, R. Jr. Tetrahedron Lett., **1986**, 27, 4529. (b) Nozaki, K.; Oshima, K.; Utimoto, K. J. Am. Chem. Soc., **1987**, 109, 2547; (c) Stork, G.; Mook, R. Jr. ibid., **1987**, 109, 2829.
3. (a) Broka, C. A.; Reichert, D. E. C. Tetrahedron Lett., **1987**, 28, 1503. (b) Ichinose, Y.; Wakamatsu, K.; Nozaki, K.; Birbaum, J. L.; Oshima, K. Chem. Lett., **1987**, 1647.
4. Oshima, K.; Utimoto, K. Yuki Gosei Kagaku Kyokaishi, **1989**, 47, 40. [Chem. Abstr. **1989**, 111, 232885f.]
5. Comasseto, J. V. J. Organomet. Chem., **1983**, 253, 131.
6. (a) Wadsworth, D. H.; Detty, M. R. J. Org. Chem., **1980**, 45, 4611; (b) Comasseto, J. V.; Ferreira, J. V. J. Organomet. Chem., **1981**, 216, 287. (c) Renard, M.; Hevesi, L. Tetrahedron, **1985**, 41, 5939.
7. Clive, D. L. J. and Menchen, S. M. J. Org. Chem., **1979**, 44, 4279.
8. The chemical shift is reported in parts per million relative to the external reference boron trifluoride etherate. Good, C. D. and Ritter, D. M. J. Am. Chem. Soc., **1962**, 84, 1162; Hall, L. W.; Odom, J. D.; Ellis, P. D. ibid., **1975**, 97, 2527; McFarlane W.; Wrackmeyer B.; Noeth, H. Chem. Ber., **1975**, 108, 3831.
9. The ratio of diastereomers was determined by the intensities of an olefinic proton in the proton NMR spectrum. Cis- and trans-geometries of **13a** and **13b** were determined by measurement of the NOE difference spectrum. Irradiation of 4-methyl proton of **13a** increased the intensities of Hb, Hc, and He.

(Received in Japan 10 August 1990)