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1,2-CYANOSELENENYLATION OF OLEFINS. REACTION OF ENAMINES WITH PHENYL SELENOCYANATE[1]

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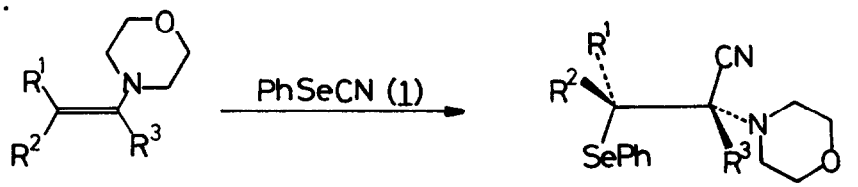
Summary: The first 1,2-cyanoselenenylation of carbon-carbon double bond has been achieved by the reaction of six enamines derived from ketones or aldehydes with phenyl selenocyanate in ethanol. The products, 2-phenylseleno-1-aminocarbonitriles, were obtained in 81-98% yield with complete regio- and stereospecificity.

Among many useful synthetic reactions involving organoselenium reagents[2], 1,2-addition across carbon-carbon double bonds is an extremely powerful synthetic method leading to the formation of various organic compounds including heterocycles.[3-10] Nucleophiles used in this methodology have been halides[3], hydroxide[4], alkoxide[5], carboxyl[5,6], urethane[7], amines[8], sp^2-carbon[9], and sulfur[10] and reagents such as benzeneselenenyl trifluoroacatate,[6c] benzeneselenenyl halides[3,5,6a,7,8,9], and N-phenylselenophthalimide[4a,b] have been most successfully employed. To date, however, cyanide ion, a versatile nucleophile for carbon-carbon bond formation as well as functional group interconversion, has not been utilized as a nucleophile in the selenenylation of olefins. Even in the case of phenyl selenocyanate (1), merely efficient oxyselenenylation has been observed with a variety of olefins in the presence of a metal catalyst: in no cases have products arising from 1,2-cyanoselenenylation been reported.[4d]

In an extension of our convenient synthesis of 1,[11] we have studied its reaction with enamines (2) and have found that 1 undergoes facile 1,2-cyanoselenenylation with 2 to provide 2-phenylseleno-1-aminocarbonitriles (3) in high yields. Herein we wish to report some examples of this potentially useful reaction.



2 3

Phenyl selenocyanate (1) is a chromatographically stable liquid.[11] While it is totally inert toward unactivated olefins or carbonyl compounds, it shows remarkable reactivity toward these compounds in the presence of metal catalysts[4d] or tri-n-butylphosphine.[12] It was nonetheless expected that 1 might react with highly nucleophilic olefins, such as enamines, under selected conditions without assistance of additional materials. In an initial experiment, a variety of aprotic solvents were examined for the reaction between 1 and 1-(E-1-propenyl)-morpholine (2a). Of these, dichloromethane gave the most satisfactory results; a sluggish but clean reaction occurred at ambient temperature to provide a single adduct (3a) in 62% yield after column chromatography. Surprisingly, however, the reaction took place almost instantaneously when 1 was added to a solution of 2a in anhydrous ethanol at room temperature; spectrally pure crystals of 3a precipitated immediately from the reaction mixture. After the precipitate had been collected, a second crop of 3a was obtained from the concentrated mother liquor by silica-gel chromatography. The combined yield of 3a was 95% yield. It is worth mentioning here that no products arising from 1,2-ethoxyselenenylation were detected by NMR. The presence of a cyano group in 3a was clearly demonstrated by IR(2210 cm^{-1}) and by ^{13}C-NMR(δ=115.01).

Reactions of other enamines (2b-f) were performed in an analogous manner. As shown in Table I, with the exception of 2c and 2e, the reactions were instantaneous in ethanol and provided nearly quantitative yields of 3 for enamines derived from ketones(2d and 2f) or aldehydes(2a and 2b).[14] While the observed relatively slow reaction rate of 2c can be attributed to the steric congestion at the β-position, it appears that substantial rate reduction of 2e must be caused by the electron-withdrawing property of the phenyl group.

More intriguing is the observation that each reaction in the Table afforded a single adduct within the limit of ^{13}C-NMR detectability. This suggested that the reaction is both regiospecific and sterospecific. This may be most simply illustrated by the reaction of 2a. The ^{1}H-NMR spectrum of 3a unequivocally precluded the possibility of the other regioisomer; the chemical shifts of H-1 and H-2(numbering based on nomenclature) were δ=3.36 and 3.59, respectively. One would predict the chemical shift of H-2 to be a much smaller value for the other regioisomer. Upon irradiation of the doublet due to the methyl group(δ=1.43, J= 7.0 Hz), H-1 and H-2 formed an AB quartet with a coupling constant of 10.8 Hz. Assuming that in the most stable conformation of 3a the two bulky substituents (methyl and morpholino groups) would exist in trans configuration, the large coupling of the protons(10.8Hz) may suggest the stereochemistry of 3a as shown in structure 3(R^1=R^3=H, R^2=Me).[15] Although this may indicate the stereochemical course of the reaction to be 1,2-anti-addition across the enamine double bond,[16] definitive evidence must await further investigation.

TABLE I 1,2-Cyanoselenenylation of Enamines (2) with Phenyl Selenocyanate (1)[a]

	2 or 3				3			
	R^1	R^2	R^3	Reaction time	Yield[b] (%)	M.p.[c] (°C)	ν(C≡N)[f] (cm^{-1})	^{13}C-NMR(C≡N)[g] (δ)
a	H	Me	H	5 min	95	121-2	2210	115.01
b	H	Et	H	5 min	98	106-7	2215	115.12
c	Me	Me	H	16 h	84	d	2210	114.69
d	H	$-(CH_2)_4-$		5 min	94	114-5	2200	117.07
e	Me(H)	H(Me)	Ph[e]	24 h	81	128-9	2210	116.20
f	Me(H)	H(Me)	Et[e]	5 min	96	d	2200	117.45

[a]The reaction was carried out at 22 °C under argon in anhydrous ethanol using equimolar ratio of 1 and 2. [b]Isolated yield. [c]Uncorrected. [d]Colorless viscous oil. [e]Stereochemistry unknown. [f]As KBr disc or liquid film. [g]In $CDCl_3$ with tetramethylsilane as internal standard.

Because of the remarkable regio- and stereospecificity and the high yield of the reaction, compounds 3 could then serve as useful precursors for a variety of functionalized organic molecules provided that the reaction could be extended to enamines having other amino groups. For example, if R^3=H, it can be regarded as a synthetic equivalent of biologically important dehydroamino acid.[17] Further studies along this line are now in progress.

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REFERENCES AND NOTES

1. Organoselenium Chemistry. Part 2. Part 1: reference 11.
2. For recent reviews on organoselenium chemistry, see; (a) D.L.J. Clive, Tetrahedron, 34, 1049(1978). (b) H.J. Reich, Acc. Chem. Res., 12, 22(1979). (c) H.J. Reich, "Oxidation in Organic Chemistry", Pt. C, W. Tarahanovsky, Ed. Academic Press, N.Y., 1978, p.1.
3. (a) G.H. Schmid and D.G. Garratt, Chem. Scr., 10, 76(1976). (b) D.R. Williams and K. Nishitani, Tetrahedron Lett., 21, 4417(1980). (c) D. Liotta and G. Zima, J. Org. Chem., 45, 2551(1980).
4. (a) P.A. Grieco, J.Y. Jaw, D.A. Claremon, and K.C. Nicolaou, J. Org. Chem., 46, 1215(1981). (b) K.C. Nicolaou, D.A. Claremon, W.E. Barnette, and S.P. Seitz, J. Am. Chem. Soc., 101, 3704(1979). (c) S. Uemura, A. Toshimitsu, T. Aoai, and M. Okano, J. Chem. Soc. Chem. Commun., 1979, 610. (d) A. Toshimitsu,

T. Aoai, S. Uemura, and M. Okano, J. Org. Chem., 45, 1953(1980).
5. (a) A.P. Kozikowski, K.L. Sorgi, and R.J. Schmiesing, J. Chem. Soc. Chem. Commun., 1980, 477. (b) K.C. Nicolaou, R.L. Magolda, W.J. Sipio, W.E. Barnette, Z. Lysenko and M.M. Joulie, J. Am. Chem. Soc., 102, 3784(1980). (c) K.B. Sharpless and R.F. Lauer, J. Org. Chem., 39, 429(1974).
6. (a) K.C. Nicolaou, S.P. Seitz, W.J. Sipio, and J.F. Blount, J. Am. Chem. Soc., 101, 3884(1979). (b) H.J. Reich and J.M. Renga, J. Org. Chem., 40, 3313 (1975). (c) H.J. Reich, J. Org. Chem., 39, 428(1974).
7. D.L.J. Clive, V. Farina, A. Singh, C.K. Wong, W.A. Kiel and S.M. Menchen, J. Org. Chem., 45, 2120(1980).
8. S.R. Wilson and R.A. Sawicki, J. Org. Chem., 44, 287(1979).
9. (a) D.L.J. Clive, G. Chittattn, and C.K. Wong, J. Chem. Soc. Chem. Commun., 1978, 441. (b) F. Rouessac, J. Zamarlik, Tetrahedron Lett., 22, 2643(1981).
10. (a) K.C. Nicolaou, W.E. Barnette, and R.L. Magolda, J. Am. Chem. Soc., 103, 3486(1981). (b) T.G. Back and S. Collins, J. Org. Chem., 46, 3249(1981). (c) D.G. Garratt, Can. J. Chem., 57, 2180(1979).
11. S. Tomoda, Y. Takeuchi, and Y. Nomura, Chem. Lett., 1981, 1069.
12. (a) P.A. Grieco, S. Gilman, and M. Nishizawa, J. Org. Chem., 41, 1485(1976). (b) M. Sevrin and A. Krief, J. Chem. Soc., Chem. Commun., 1980, 656. (c) P. A. Grieco and Y. Yokoyama, J. Am. Chem. Soc., 99, 5210(1977). (d) P.A. Grieco, Y. Yokoyama, and E. Williams, J. Org. Chem., 43, 1283(1978).
13. The structures of 3 were established by IR, proton- and carbon-NMR and elemental analysis.
14. The enamines 2 are stereochemically pure in all cases as shown by their proton-NMR data, although the stereochemistry of 2e and 2f are still ambiguous.
15. In this conformation of 3a, the dihedral angle between H-1 and H-2 is predicted to be 180°. This should result in relatively large coupling constant (5-12 Hz) according to the Karplus relationship; M. Karplus, J. Am. Chem. Soc., 85, 2870(1963). (b) S. Sternhell, Quart. Review, 1969, 236.
16. The stereochemistry of the starting enamine (2a) is E(trans).
17. β-Seleno-amino acids have been previously converted to the corresponding dehydro analogues by selenoxide syn-elimination; R. Walter and J. Roy, J. Org. Chem., 36, 2516(1971) and references cited therein. For a recent review on dehydroamino acids, see; U. Schmidt, J. Hausler, E. Ohler, and H. Poisel, Prog. Chem. Org. Nat. Prod., 37, 251(1979).

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