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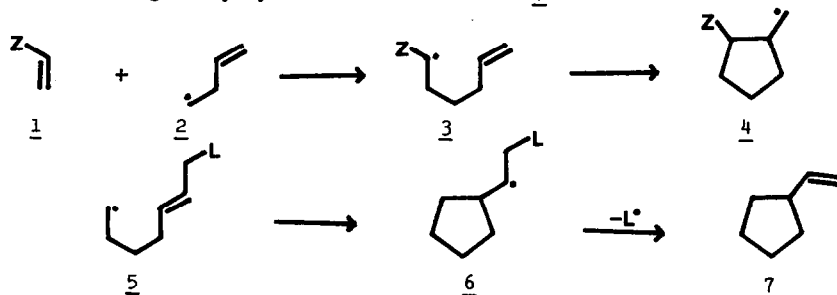
**RADICAL ANNULATION METHODOLOGY. 2-VINYLCYCLOPENTANE DERIVATIVE FORMATION
 BY A 3 + 2 CYCLOADDITION REACTION**

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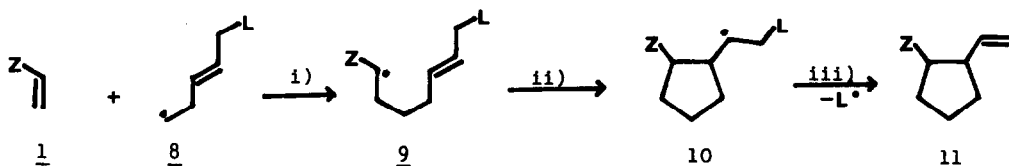
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Abstract: By thermally or photolytically induced decomposition of O-acyl derivatives of N-hydroxypyridine-2-thione or other thiohydroxamic esters, in the presence of an excess of electron deficient olefins, 2-vinylcyclopentane derivatives were obtained. This sequence of addition/cyclization/elimination reaction is mediated by a phenylthio radical.

Cyclopentane ring annulation by a 3 + 2 radical cycloaddition reaction of 3-butenyl type radical 2 to the electron deficient olefins 1 represents a useful methodology for the construction of polysubstituted cyclic molecules 4.¹⁻⁶ On the other hand a method for the free radical allylation by allyltributylstannanes⁷ or allyl t-butylsulphide⁸, involving the addition of a carbon radical onto a double bond with concomitant displacement of a radical from the allylic position, has been applied on the radical cyclization reactions.^{9,10} The cyclopentylmethyl radical 6, generated by 5-exo-cyclization of 5-hexenyl type radical 5 and possessing a good radical leaving group in the allylic position, undergoes a β -elimination affording vinylcycloalkane derivatives 7.^{3,5,6,9-11}

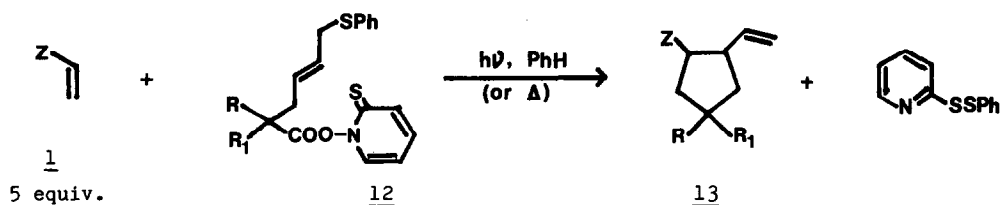


Our approach to the synthesis of highly functionalized vinylcyclopentane derivatives is based on the following known reactions: i) intermolecular addition of 3-pentenyl radical 8, ii) intramolecular cyclization of a 5-hexenyl type radical 9, and iii) β -elimination of a phenylthio radical from the cyclopentylmethyl radical 10, combining them in one reaction sequence which could be realized as one pot reaction. The reactivity of radical



intermediates and the ratio of reagents were appropriately selected making possible two regiocontrolled C-C bond formations. Thiohydroxamic esters were used as precursors of 3-pentenyl type radicals 8. The Barton decarboxylation procedure¹² was applied, because Curran generated 3-pentenyl type radical 8 by tributyltin hydride method and low yield of cyclic products were obtained.³ This sequence of radical cycloaddition reactions is terminated by elimination of a phenylthio radical which acts as a mediating species in this radical chain reaction.

Thiohydroxamic esters 12 were prepared in good yields as previously described.^{12,13} By thermally or photolytically induced decomposition of thiohydroxamic esters (such as a 0-acyl derivatives of N-hydroxypyridine-2-thione 12) in the presence of five-fold molar



excess of electron deficient olefins 1, 2-vinylcyclopentane derivatives 13 were obtained in 33-70% of isolated yields (50-90% g.c. yields).¹⁴ The reaction products show the spectral characteristics consistent with the proposed structures.¹⁵ The products and their yields are presented in the Table 1.

The sequence of radical chain reactions involving an addition/cyclization/elimination is initiated by decomposition of esters of N-hydroxypyridine-2-thione and 6-phenylthio-3-

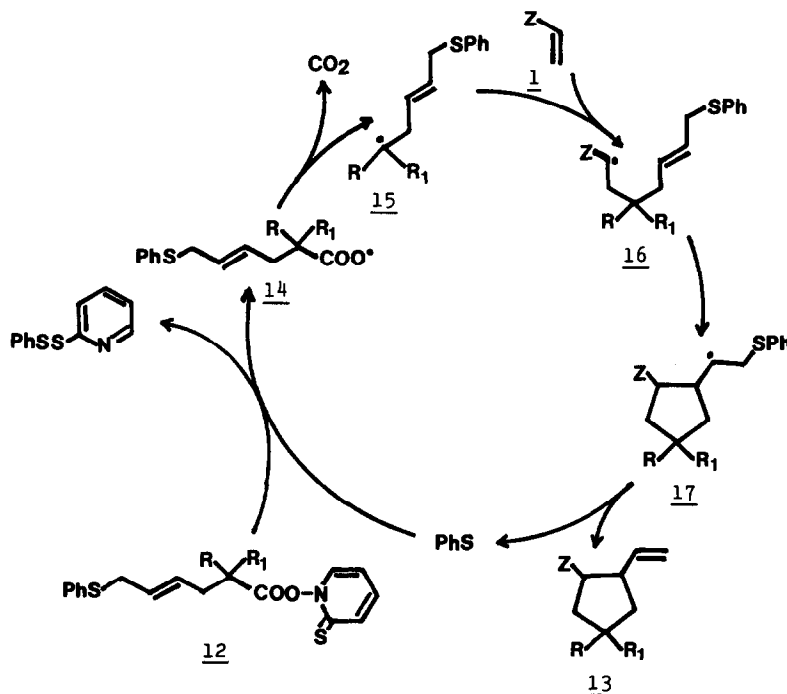


Table 1. 2-Vinylcyclopentanes obtained by the radical cycloaddition/elimination reaction

R	R ₁	Z	A	B	Method	Products ^{a)} and their isolated ^{b)} (and g.c.) ^{c)} yields in % ^{d)}	
H	C ₅ H ₉	CN	H	H	P		70 (90)
		COOEt	H	H	T		50 (76)
		COOEt	H	Me	P		40 (64)
H	PhCH ₂	CN	H	H	T ^{e)}		33 (50)
		COOEt	H	H	P		43 (71)
				H	P		37
	-(CH ₂) ₄ -	COOEt	H	H	P		41 (80)
		COMe	H	H	P		39 (89)
	-(CH ₂) ₅ -	CN	H	Me	P		58 (77)
		CHO	H	H	P		58 (89)

Method P: Irradiation of thiohydroxamic esters in benzene solution with a 200 W tungsten lamp (1 h).

Method T: Thermal decomposition of esters in boiling toluene (about 112°C, 1 h).

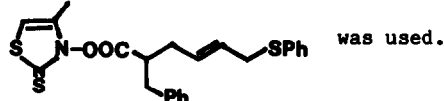
a) Mixtures of stereoisomers.

b) Isolated by chromatography using silica gel column and benzene as an eluent.

c) G.c. were performed using 5% OV-101 on Chromosorb WDMCS column.

d) Yields were not optimized. In some cases the experiments were repeated with reproducible yields of reaction products.

e) Thiohydroxamic ester



hexenoic acid 12. Addition of the phenylthio radical to the C=S bond of the starting ester 12 proceeds with a concerted or stepwise fragmentation reaction involving an intermediary carboxyl radical 14, and by its decarboxylation a 5-phenylthio-3-pentenyl radical 15 is generated. In the following step a regioselective addition of radical 15 to the radicophilic olefin 1 occurs. Using 5 equivalents of excess of olefin 1, the rate of addition of radical 15 to the electron deficient olefin 1 is more rapid than that for the addition to the starting thiohydroxamic ester 12. Thus by 5-exo-cyclization of radical 16, a cyclopentylmethyl radical 17 is formed. Bearing a phenylthio group in the β -position, radical 17 undergoes rapid fragmentation producing 2-vinylcyclopentane derivatives 13 and expelling the phenylthio radical as a chain carrying radical.

The synthetic value of this methodology is in the mild experimental conditions and the possibility that different functional groups can be tolerated without considerable influence on the yields of the reaction products.

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14. Typical experimental procedure: Thiohydroxamic esters were prepared in situ without isolation. The mixture of 2.4 mM of acyl chloride, 0.305 g (2.4 mM) of N-hydroxypyridine-2-thione, 0.213 g (2.7 mM) of pyridine and 0.062 g (0.3 mM) of 4-dimethylaminopyridine in 10 ml of benzene was stirred at room temperature during 15 min. in an argon atmosphere and protected from light. To the prepared ester solution 0.636 g (12 mM) of acrylonitrile (or other electron deficient olefin) was added and the reaction mixture was irradiated at r.t. by a 200 W tungsten lamp during 1 h (or refluxed in toluene for 1 h). After decomposition of 12 was completed an excess of solvent was removed by evaporation at reduced pressure and products were isolated by chromatography on silica gel column using benzene as an eluent.
15. Reaction products were characterized by *ir*, *nmr* and mass spectra and e.g. 2-vinyl-4-benzylcyclopentanecarbonitrile, has following spectral data: *ir*: 2920, 2240, 1640, 1600, 1495, 1455, 920, 750, 700 cm^{-1} ; $^1\text{H-NMR}$: 0.75-2.50 (m, 5H), 2.50-3.30 (m, 4H), 5.00-5.30 (m, 2H); 5.55-6.20 (m, 1H), 7.05-7.40 (m, 5H). *MS*: 211 (M^+), 184, 155, 117, 91 (100%), 77, 65.