

MULTIPLE RADICAL ADDITIONS STARTING WITH IMINYL RADICALS DERIVED
FROM SULPHENYLIMINES.

Jean Boivin, Eric Fouquet, and Samir Z. Zard*
Laboratoire de Synthèse Organique associé au C.N.R.S.
Ecole Polytechnique, 91128 Palaiseau, France

Summary. Iminyl radicals obtained by tri-*n*-butylstannane induced cleavage of *S*-phenyl sulphenylimines readily cyclise onto suitably located double bonds. The intermediate carbon centered radical can be trapped by a variety of electron-poor olefins thus providing an entry into synthetically useful pyrroline derivatives.

During the last decade organic chemistry has been considerably enriched by new synthetic methods based on radical intermediates generated under smooth and controlled conditions¹. This emergence was made possible by an increasing refinement in the understanding of the mechanisms and kinetics underlying these processes. However, most of the attention of synthetic chemists has focused on carbon-centered radicals, probably because of the somewhat more complex behaviour of nitrogen- and oxygen-centered radicals and a lack of mild methods for generating them.

In a previous communication² we reported a convenient method giving access to iminyl radicals based on the fragmentation of *S*-aryl sulphenylimines by tin radicals under very gentle conditions. These precursors are easily obtained from the corresponding carbonyl derivatives³. We have found iminyl radicals to be sufficiently reactive to add smoothly, in an intramolecular fashion, to a γ,δ double bond before premature quenching by tri-*n*-butylstannane, which would have simply given the unsubstituted imine (and, of course, the parent carbonyl compound after work-up). In this way various mono- or bicyclic pyrrolines (including spiro derivatives) were obtained in generally good yields. This is in sharp contrast to aminyl radicals which add rather sluggishly to olefins unless their reactivity is enhanced by protonation or by complexation with a transition metal⁴.

In this Letter, we describe an extension of this new methodology in which the intermediate carbon radical is trapped with an appropriate electron-poor olefin before final quenching by *n*-Bu₃SnH, as illustrated in the Scheme below. Thus slow addition (4-5 hours) of tri-*n*-butylstannane and a catalytic amount of AIBN to a solution of sulphenylimine **1** (prepared by the method of Morimoto et al.⁵) and methyl acrylate (5 equiv.) in refluxing cyclohexane gave cyclisation-addition product **4a**⁶ in 83% yield, along with small amount of **4b** resulting from double addition to methyl acrylate.

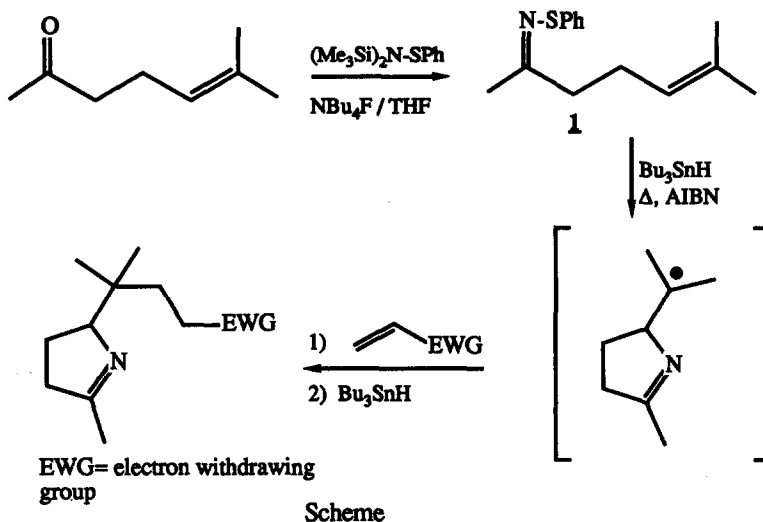


Table: Reaction of Sulphenylimines **1**, **2**, and **3** with *n*-Bu₃SnH in the presence of activated olefins.

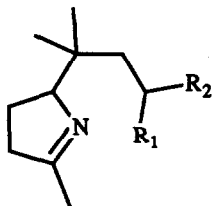
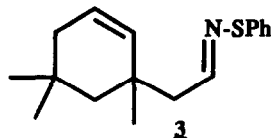
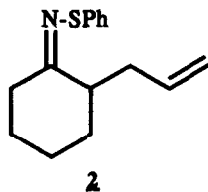
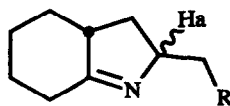
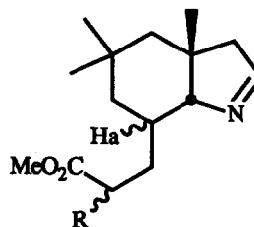
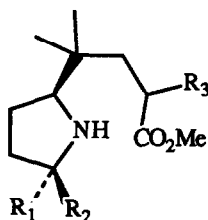
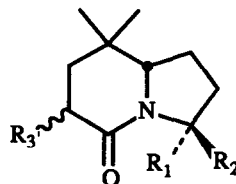
Sulphenylimine (1 mmol.)	Olefin (mmol.)	Yields (%)			
		A	B	C	D
1	CH ₂ =CHCO ₂ Me (5)	4a (83)	-	-	4b (12)
1	CH ₂ =C(CO ₂ tBu) ₂ (2)	4c (68)	(11)	-	-
1	CH ₂ =CHCN (5)	4d (60)	-	(15)	4e (8)
2	CH ₂ =C(CO ₂ tBu) ₂ (2)	5a+5b (65)	5c+5d (30)	-	-
3	CH ₂ =CHCO ₂ Me (5)	6a+6b (81)	(10)	-	(not determined)

A) Product of cyclisation-addition.

B) Product of cyclisation without addition.

C) Carbonyl compound resulting from the hydrolysis of the uncyclised imine.

D) Product of cyclisation-double addition to the activated olefin.

**4a** $R_1 = \text{CO}_2\text{Me}$, $R_2 = \text{H}$ **4b** $R_1 = \text{CO}_2\text{Me}$, $R_2 = (\text{CH}_2)_2\text{CO}_2\text{Me}$ **4c** $R_1 = R_2 = \text{CO}_2\text{tBu}$ **4d** $R_1 = \text{CN}$, $R_2 = \text{H}$ **4e** $R_1 = \text{CN}$, $R_2 = (\text{CH}_2)_2\text{CN}$ **5a** Ha α , $R = \text{CH}_2\text{CH}(\text{CO}_2\text{tBu})_2$ **5b** Ha β , $R = \text{CH}_2\text{CH}(\text{CO}_2\text{tBu})_2$ **5c** Ha α , $R = \text{H}$ **5d** Ha β , $R = \text{H}$ **6a** Ha α , $R = \text{H}$ **6b** Ha β , $R = \text{H}$ **6c** $R = (\text{CH}_2)_2\text{CO}_2\text{Me}$ **7a** $R_1 = \text{H}$, $R_2 = \text{Me}$, $R_3 = (\text{CH}_2)_2\text{CO}_2\text{Me}$ **7b** $R_1 = \text{CN}$, $R_2 = \text{Me}$, $R_3 = (\text{CH}_2)_2\text{CO}_2\text{Me}$ **8a** $R_1 = \text{Me}$, $R_2 = R_3 = \text{H}$ **8b** $R_1 = \text{Me}$, $R_2 = \text{H}$, $R_3 = (\text{CH}_2)_2\text{CO}_2\text{Me}$ **8c** $R_1 = \text{Me}$, $R_2 = \text{CN}$, $R_3 = \text{H}$

In the same manner, capture of the intermediate carbon radical with other electron-poor olefins such as methylene di-*t*-butyl malonate and acrylonitrile gave the corresponding adducts. These results are summarised in the Table. In each case the cyclised pyrrolines (**4c** and **4d** respectively) were obtained in good yield, accompanied in the case of acrylonitrile by small amount of double addition product **4e**. Methylene di-*t*-butylmalonate is much less prone to radical induced oligomerisation. Replacement of cyclohexane by benzene or chlorobenzene in the reaction of **1** with acrylonitrile did not alter the formation of the starting ketone (15%), arising from hydrolysis of the corresponding imine. This demonstrates that the latter comes from premature quenching by *n*-Bu₃SnH, and not from hydrogen abstraction from the solvent⁷.

Under the same conditions, sulphenylimine **2** afforded a transient primary carbon radical which was intercepted somewhat less efficiently with methylene di-*t*-butylmalonate to give a mixture of diastereoisomers **5a** and **5b** (total yield 65%, **5a/5b**= 1.5 : 1). In this case, premature quenching by tin hydride furnished significant amount of imines **5c** and **5d** (total yield 30%, **5c/5d**= 1.5:1). Sulphenylimine **3** also readily cyclised to an intermediate secondary carbon radical which further reacted smoothly with methyl acrylate to produce a diastereoisomeric mixture of **6a** and **6b** (total yield 81%, **6a/6b**= 2:1).

As an illustration of the chemical versatility offered by such pyrroline derivatives, a mixture of imines **4a** and **4b** (**4a/4b**= 85:15) was reduced by NaBH₃CN (3 eq.; 20°C, 15 min.) in acetic acid⁸ to give a mixture of lactam **8a** and amino-ester **7a** (total yield 85%), easily separated by chromatography. The latter cyclised into **8b** upon heating in refluxing toluene for one hour. Similarly the same mixture of **4a** and **4b** reacted with trimethylsilylcyanide⁹ in the presence of catalytic amounts of TiCl₄ in dichloromethane (20°C, 48 hrs) to afford, after work-up, the cyano lactam **8c** and the α -cyano amine **7b** (overall yield 88%). Interestingly, and because of steric shielding by the side chain, only one isomer is produced upon reduction by NaBH₃CN or addition of trimethylsilylcyanide to the imine. Other classical transformations of the imine moiety based, for example on the imine-enamine tautomerism or on the Mannich reaction, should lead to useful intermediates for the synthesis of various alkaloids. These further extensions are currently under study.

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- All new compounds gave satisfactory mass spectra and/or elemental analyses. Structures were established by i.r., and n.m.r. (¹H and ¹³C).
- In general, reaction conditions were not optimised. Variations in the rate of addition of n-Bu₃SnH and in the concentration of the olefinic trap should allow further improvement.
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