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CYCLISATION OF IMINE RADICALS DERIVED FROM SULPHENYLIMINES: A SIMPLE ACCESS TO Δ^1-PYRROLINES.

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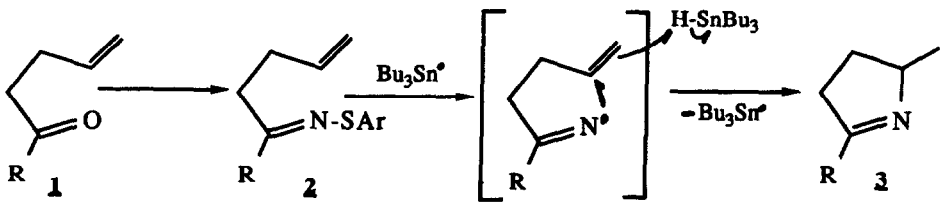
Summary. Treatment of various sulphenylimines containing a γ,δ–double bond with tri-n-butylstannane affords the corresponding pyrroline derivatives in good yield.

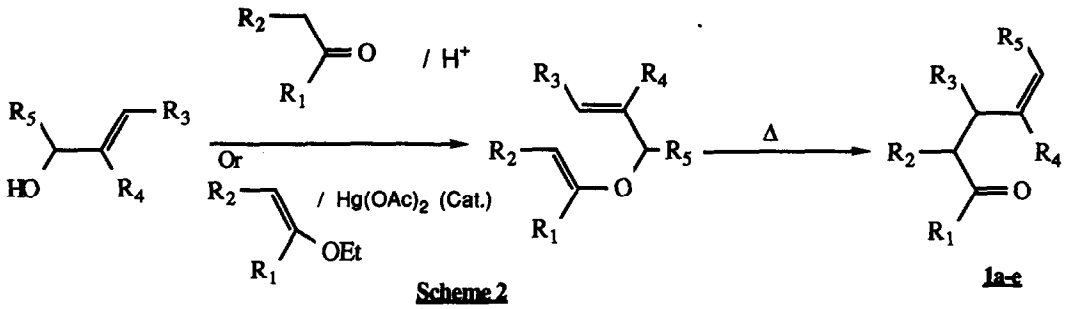
Internal capture of aminyl radicals[1], especially as the protonated or transition metal-complexed species[2], has frequently been used as an entry into various nitrogen heterocyclic systems. Iminyl radicals in contrast have received little attention from synthetic chemists. This appears to be due in the main to the lack of a convenient and mild source of these reactive intermediates. Most of the existing methods are based on non-chain pyrolytic or photochemical reactions which are ill-suited for preparative work[3]. A notable exception however is the reduction of N-chloroketimines with tri-n-butylstannane, used by Poutsma and Ibraria[4] to generate iminyl radicals needed in a mechanistic study. This approach, however, is restricted to the few accessible N-chloroketimines.

In this Letter, we describe an alternative procedure which allies the advantages of radical chain reactions based on stannane chemistry with the ready availability of sulphenylimines such as 2 or 3. Unlike N-chloroketimines, sulphenimides are readily accessible by a number of methods[5], generally from the corresponding carbonyl derivative or, in some cases, through the oxime[6]. They are easily purified by crystallisation or by chromatography. The high thiophilicity of the stannyl radicals as well as the relative weakness of of the N-S bond in these systems [5] should constitute a powerful driving force in favour of the formation of the iminyl radical (scheme 1).



Scheme 1

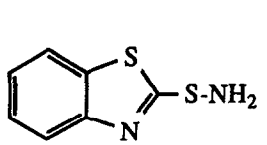
Sulphenylimines **2a-e**, obtained in reasonable yields (43-68%) by direct condensation of carbonyl derivatives **1a-e** with 2-benzothiazolyl- sulphenamide **4**, were first chosen for this study. Sulphenamide **4** is a stable crystalline solid, easily prepared from 2-mercaptobenzothiazole, ammonia and sodium hypochlorite[7]. The starting γ,δ-unsaturated ketones and aldehydes **1a-e** are themselves readily available through a Claisen rearrangement as shown in scheme 2. The preparation of aldehydes **1a**, **1b**, and **1c** required prior isolation of the corresponding intermediate allyl vinyl ether, obtained through the mercuric acetate catalysed reaction of geraniol, cinnamyl alcohol, and isophorol respectively with ethyl vinyl ether[8]. Ketone **1d** and aldehyde **1e** were directly produced from cyclohexanone and cyclohexanecarboxaldehyde respectively by heating with allyl alcohol in the presence of a little acid[9].



Scheme 2

1a-e

As a precaution against premature reduction of the iminyl radical, the stannane was slowly added to the substrate. Thus, addition over 4-5 hours of tri-n-butylstannane to a refluxing solution of the sulphenylimine **2a** in cyclohexane produced pyrroline **5a** in 70% yield as a 1:5 mixture of cis and trans isomers. Similarly, **2b** gave **5b** in 61% yield with a slightly better selectivity (cis:trans ratio 1:9).



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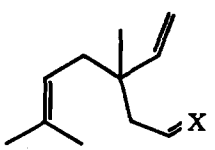
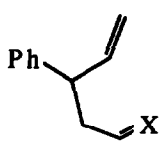
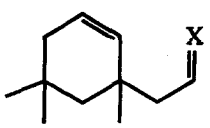


1,2 or 3a



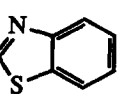
1,2 or 3b



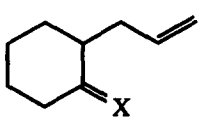
1,2 or 3c

1 , X= O

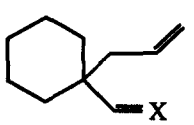
2 , X= N-S



3 , X= N-SPh

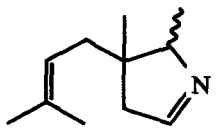


1,2 or 3d

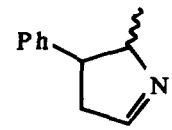


1,2 or 3e

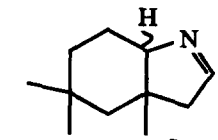
Bicyclic and spiro systems are also easily accessible by this approach. Thus, cyclisation of the imine radical from 2c and 2d afforded the corresponding bicyclic pyrrolines 5c and 5d in 70% and 73% yield respectively. The former was essentially the cis isomer (cis:trans ratio approx. 95:5) whereas the latter consisted of comparable amounts of the two diasterioisomers (45:55). Finally reduction of sulphenylimine 2e with the stannane gave the spiro pyrroline 5e in excellent yield (94%).



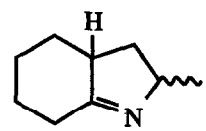
5a



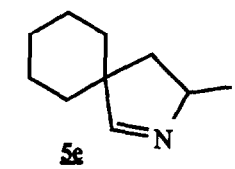
5b



5c



5d



5e

The analoguous S-phenyl sulphenylimines 3b and 3e also undergo a clean reductive radical cyclisation on treatment with tributylstannane. These derivatives are conveniently obtained by a procedure developed by Morimoto and co-workers [10] using a fluoride catalysed condensation of N,N-bis (trimethylsilyl)-phenylsulphenamide with ketones and aldehydes. Through this variant, compounds 5b and 5e were produced in 55% and 71% yield respectively.

As illustrated by the above examples, iminyl radicals are sufficiently electrophilic to undergo rapid cyclisation, unlike aminyl radicals, which add only sluggishly to unactivated double bonds and usually require protonation or complexation with a transition metal. In addition, the presence of the imine moiety in the cyclised products offers a powerful handle for their further regiospecific elaboration, especially when the synthetic possibilities of the imine-enamine tautomerism are taken into consideration. This aspect, in combination with the potential of radical reaction for introducing new carbon-carbon bonds[11], should make this approach quite attractive for the synthesis of alkaloids and related substances. Further extensions and applications of this new method are currently under study.

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