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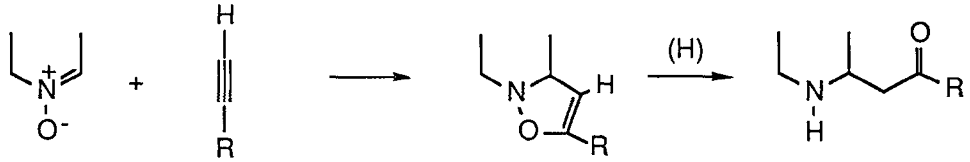
A NEW EFFICIENT SYNTHESIS OF β-AMINOKETONES *VIA* Δ^4-ISOXAZOLINES.

Vincent Mancuso and Claude Hootelé*
Université Libre de Bruxelles, Faculté des Sciences, CP 160,
Laboratoire de Chimie Organique, 50, Av. F.D. Roosevelt, B-1050 Bruxelles, Belgique.

Summary : β-aminoketones are prepared in good yield by hydrogenolysis (Pd/C) of the N-O bond of Δ^4-isoxazolines obtained by 1,3-dipolar cycloaddition of nitrones with alkynes.

In recent years, the thermal [3+2] dipolar cycloadditions have been increasingly used to prepare precursors for the synthesis of a number of compounds(1-7). The cycloaddition of nitrones with alkenes affords isoxazolidines with predictable regio- and stereochemistry and constitutes a general methodology for the synthesis of alkaloids of various classes(1,8).

On the other hand, the nitrone-alkyne cycloadditions are far less popular mainly because most of the resulting Δ^4-isoxazolines are known to be thermally labile compounds(2,9,10) ; they are, however, attractive derivatives as they can be viewed as masked β-aminoketones. We have developped such a synthesis of β-aminoketones *via* the following sequence:



The condensations of nitrones 1 and 2 (Table 1) with a series of alkynes (R = phenyl, n-pentyl, chloromethyl, (E)-styryl) were performed in refluxing chloroform, benzene or 1,1,1-trichloroethane and afforded regiospecifically the expected(6,11) 5-substituted isoxazolines as evidenced by ^{1}H and ^{13}C NMR measurements. The vinyl hydrogen at C4 appears as a doublet (J = 2 Hz) in the range 4.5-5.5 ppm, in agreement with expected values(2). As anticipated, 1-phenyl-1-buten-3-yne reacted specifically on the triple bond.

The reductive scission of the N-O bond in Δ^4-isoxazolines is a poorly documented reaction(2). It was indeed found that the hydrogenolytic cleavage can be cleanly performed in the presence of Pd/C in ethanol ; the anticipated β-aminoketones were obtained in good yield after column chromatography purification. In most cases, the corresponding cis-s-cis enaminone derivative(12) (10-20%) was also isolated from the reaction mixture.

This new, two-step procedure for the preparation of β-aminoketones offers an alternative pathway for the synthesis of members of this important class of compounds.

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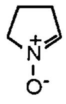
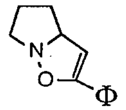
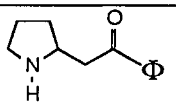
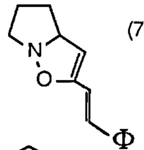
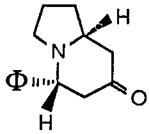
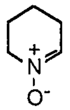
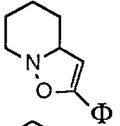
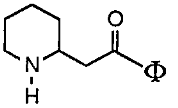
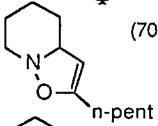
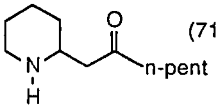
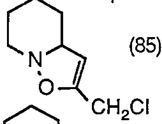
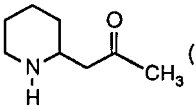
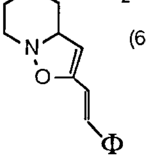
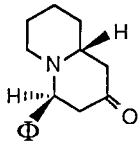
* Research Associate of the National Fund for Scientific Research (Belgium).

Table 1. Synthesis of β-aminoketones *via* Δ^4-isoxazolines from nitrones 1 and 2.

Nitrone	Isoxazoline (% yield)[a]		^{1}H NMR[b] C4-H (δppm)	β-aminoketone (% yield)[a]	
 1		(70)[f]	5.06		(60)
		(76)[e]	4.82		(52)[d]
 2		(81)[c,e]	5.28		(86)
		(70)[g]	4.52		(71)
		(85)[e]	5.0		(50)
		(65)[e]	5.0		(35)

a. Yields based on isolated, pure compounds with exception of the chloroderivative ; the yield of the latter was determined by ^{1}H NMR spectroscopy on the crude reaction product ; yields have not been systematically optimized. All compounds isolated gave satisfactory spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR and mass spectra).

b. Recorded on a Bruker WM 250 in $CDCl_3$ with TMS as internal standard.

c. m.p. : 66-67°C (pentane).

d. m.p. : 74-75°C (hexane).

e, f, g. The condensation was performed in refluxing $CHCl_3$(e), C_6H_6(f), CH_3CCl_3(g).

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