

INTRAMOLECULAR CYCLOADDITIONS OF NITRILIMINES ON ACETYLENIC GROUPS

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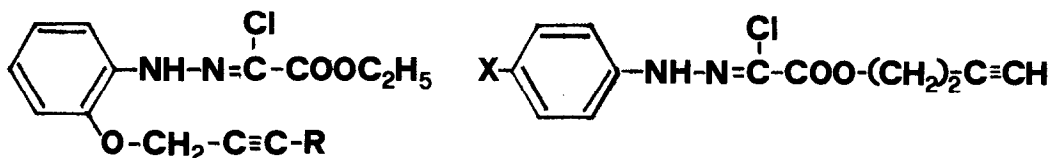
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Among the well known 1,3-dipolar cycloadditions, the intramolecular ones are not yet extensively investigated. To our knowledge, only few alkenyl or alkynyl nitrones⁽¹⁾ and azomethinimines⁽²⁾ were reported to give an intramolecular cyclo addition.

We now wish to describe the behaviour of nitrilimines generated from α -chloro-hydrazones bearing an acetylenic function. Two different kinds of substrates have been studied: i) compounds (Ia,b) where the halohydrazonic and acetylenic groups are connected through an aromatic ring ii) compounds (IIa,b) where the groups are connected through an aliphatic chain.



(Ia): R = H

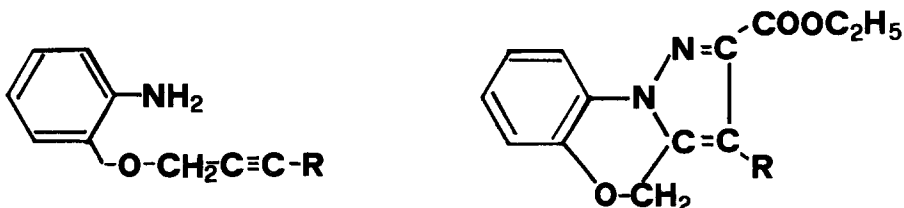
(Ib): R = C₆H₅

(IIa): X = Cl

(IIb): X = NO₂

The α -chloro-hydrazones (Ia) (m.p. 83°)⁽³⁾ and (Ib) (m.p. 75°) were prepared from the anilines (IIIa) and (IIIb) respectively by diazotization and coupling with ethyl α -chloro-acetoacetate. The anilines (IIIa)⁽⁴⁾ and (IIIb) (hydrochloride m.p. 191°) were obtained by reduction of the corresponding nitrocompounds⁽⁵⁾ with iron in boiling acetic acid.

Treatment of the α -chloro-hydrazone (Ia) with an equimolar amount of NaH in boiling dry tetrahydrofuran (96 hrs.) gave 2-carbethoxy-4H-pyrazolo[5,1-c][1,4]benzoxazine (IVa) (m.p. 100°, from n-hexane) in 40% yield. Treatment of the α -chloro-hydrazone (Ib) with triethylamine (ten fold excess) in boiling toluene for 60 hrs. gave the related 3-phenyl substituted derivative (IVb) (m.p. 112°, from n-hexane) in 59% yield.



(IIIa): R = H

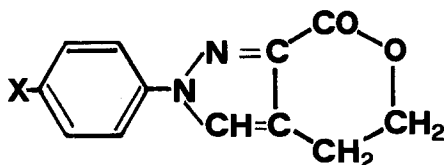
(IIIb): R = C₆H₅

(IVa): R = H

(IVb): R = C₆H₅

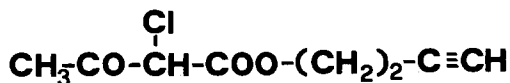
Compounds (Va,b) were obtained as follows. 3-Butynyl α -chloro-acetoacetate (VI) (b.p. 80°/0.2 mm) was prepared by reaction of 3-butynol with diketene and subsequent SO₂Cl₂ chlorination. Diazotization of the properly substituted anilines and coupling with the ester (VI) afforded the α -chloro-hydrazones (IIa) (m.p. 142°) and (IIb) (m.p. 175°).

Treatment of (IIa) and (IIb) with triethylamine (3 moles) in boiling toluene for 48 and 168 hrs. respectively followed by chromatography of the reaction mixtures (silica gel, eluent benzene) gave 1-p.chlorophenyl-4-(β -hydroxyethyl)-pyrazole-3-carboxylic acid lactone (Va) (m.p. 154°, from benzene) in 49% yield and 1-p.nitrophenyl-4-(β -hydroxyethyl)-pyrazole-3-carboxylic acid lactone (Vb) (m.p. 224°, from acetonitrile) in 25% yield. In both cases, some starting material was recovered.



(Va): X = Cl

(Vb): X = NO₂



(VI)

Structural assignments for the compounds (IVa,b) and (Va,b) are based on NMR data (see Table). The chemical shifts found for the pyrazolic hydrogens in (IVa) and (Va,b) agree with those reported for 4 and 5 position protons respectively.⁽⁶⁻⁹⁾

Table

Significative τ -values (CDCl_3) for pyrazole derivatives (IVa,b) and (Va,b).^(*)

Compound	aromatics	CH	OCH ₂	CH ₂
(IVa)	2.0(m)[1H];2.9(m)[3H]	3.31(s)	4.71(s)	---
(IVb)	2.0(m)[1H];2.7(m)[8H]	---	4.78(s)	---
(Va)	2.4(m)	2.12(s)	5.40(t)(J=6)	6.98(t)(J=6)
(Vb)	1.6(d)[2H];2.0(d)[2H] (J=9.5)	1.96(s)	5.52(t)(J=6)	6.92(t)(J=6)

(*) Coupling constants are given in cps.

The above results show that intramolecular cycloadditions of nitrilimines on acetylenic groups are possible. Ring closure of (Ia) and (IIa,b) to (IVa) and (Va,b) respectively is interesting on considering that it involves unconjugated alkynes, substrates which are known to be poorly reactive towards the nitrilimines.⁽¹⁰⁾ Furthermore, while the usual orientation of monosubstituted acetylenes in the intermolecular cycloadditions with nitrilimines is such as to afford 5-substituted pyrazoles,⁽⁹⁻¹¹⁾ obtainment of the 4-substituted pyrazoles (Va,b) reveals that in properly chosen substrates regiospecificity of monosubstituted acetylenes can be inverted.

References and remarks

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