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SIGMATROPIC TAUTOMERISM BETWEEN N-ALLYL-3-ISOXAZOLIN-5-ONES AND 4-ALLYL-2-ISOXAZOLIN-5-ONES

Yasuo Makisumi and Takashi Sasatani

Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, Japan

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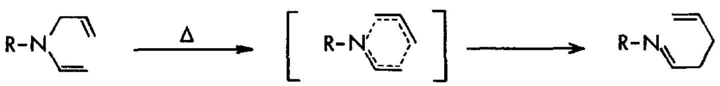
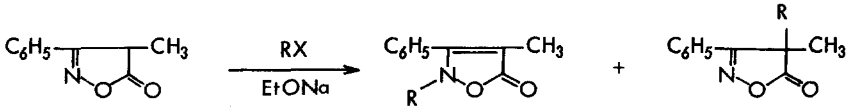
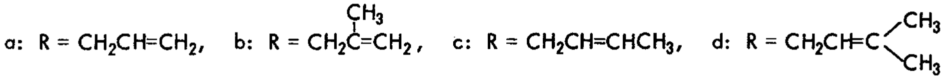
In continuation of our studies of 3,3-sigmatropic reactions, we have discovered the facile amino-Claisen rearrangement of the N-allyl-enamine system in pyrazolin-5-ones (1). Recent reports (2, 3, 4) on the analogous examples of the amino-Claisen rearrangement prompt a preliminary report of our work on the sigmatropic tautomerism between N-allyl-3-isoxazolin-5-ones and 4-allyl-2-isoxazolin-5-ones.



N-Allyl-enamine compounds II were prepared by alkylation of 3-phenyl-4-methylisoxazolin-5-one (I) with allylic halides in the presence of sodium ethoxide (5). In this reaction, I reacted as an ambident anion to afford N-allyl-3-phenyl-4-methyl-3-isoxazolin-5-ones (IIa-d) and 4-allyl-3-phenyl-4-methyl-2-isoxazolin-5-ones (IIIa-d) in the ratio of about 2 : 1. The structures of these products were determined by IR and UV spectral analyses as shown in Table I. II showed the IR bands of C=C-C=O and the UV absorption characteristic of Δ^3-isoxazolin-5-one (7) and III exhibited the C=O band and the UV absorption characteristic of Δ^2-isoxazolin-5-one (7). Moreover, the IR ($CHCl_3$) and NMR ($CDCl_3$, 60 MHz) spectra showed that the γ-substituted allyl group had not isomerized during reaction.



I IIa-d IIIa-d



a: $R = CH_2CH{=}CH_2$, b: $R = CH_2\overset{CH_3}{\overset{|}{C}}{=}CH_2$, c: $R = CH_2CH{=}CHCH_3$, d: $R = CH_2CH{=}C\begin{matrix}CH_3\\CH_3\end{matrix}$

TABLE I
IR and UV Spectral Data of Isoxazolin-5-ones

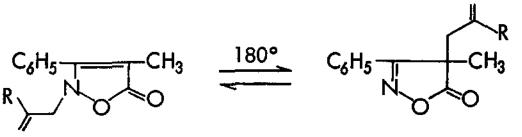
	$\nu_{C=C-C=O}^{CHCl_3}$ cm^{-1}		λ_{max}^{EtOH} mμ (log ε)		$\nu_{C=O}^{CHCl_3}$ cm^{-1}	λ_{max}^{EtOH} mμ (log ε)
IIa	1730	1637	248 (4.00) 283 (3.98)	IIIa	1796	256.5 (4.07)
IIb	1728	1633	245.5 (3.98) 286 (3.98)	IIIb	1795	259 (4.10)
IIc	1727	1635	247 (3.98) 282 (3.96)	IIIc	1796	255.5 (4.06)
IId	1725	1636	244.5 (3.99) 284 (3.97)	IIIc'	1787	254 (4.03)
				IIId	1791	255.5 (4.06)

Amino-Claisen rearrangements of the N-allyl compound IIa, b.p. 115° (0.05 mm), and the N-methallyl compound IIb, b.p. 134° (0.05 mm), were examined by heating at 180° for 1 hr. Thus, IIa and IIb rearranged to the 4-allyl compound IIIa, b.p. 114-115° (0.2 mm), and the 4-methallyl compound IIIb, b.p. 120° (0.15 mm), respectively, over 95% yields, along with the recovery (ca. 1%) of the unreacted IIa, b.

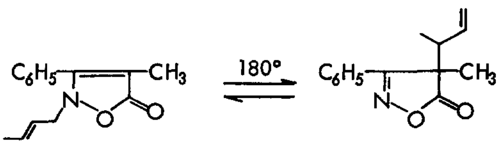
To test for the inversion of the allyl moiety which occurs in concerted cyclic processes, rearrangement of the N-crotyl compound IIc, b.p. 124-126° (0.04 mm); ν 966 cm^{-1} (-CH=CH-), was studied. Heating IIc at 180° for 1 hr afforded a sole product, 4-(a-methylallyl)-3-phenyl-4-methyl-2-isoxazolin-5-one (IIIc'), b.p. 114-116° (0.15 mm), which had the $-CH=CH_2$ group at 999 and 923 cm^{-1} and the IR and UV absorptions characteristic of Δ^2-isoxazolin-5-one as shown in Table I. This result demonstrates complete inversion of the allyl moiety. However, the yield of IIIc' did not increase over 45% even prolonged heating of IIc at 180° and the ratio of the unreacted IIc to IIIc' showed the constant value of 54 : 46, suggesting the presence of a thermal equilibrium between IIc and IIIc' via cyclic processes.

When IIIc' was heated at 180°, a sole rearranged product, identical with IIc, was isolated in 52% yield and the ratio of IIc to the unreacted IIIc' showed the constant value of 54 : 46. Thus, the sigmatropic tautomerism between IIc and IIIc' via the amino-Claisen and the Cope rearrangements was proved. Cope rearrangements of IIIa and IIIb were also tested by heating at 180° for 1 hr and the expected products IIa and IIb were isolated in about 1% yields, along with the unreacted IIIa and IIIb (over 95% recovery).

These sigmatropic tautomerisms show that Δ^2-isoxazolin-5-ones are thermodynamically more stable than Δ^3-isoxazolin-5-ones. The shift of the equilibrium of IIc $\rightleftharpoons$ IIIc' would be interpreted as a result of the destabilization of IIIc' due to the steric interaction of the a-methyl on allyl group. Such phenomena were

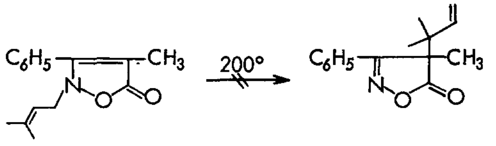


IIa,b 1 : 99 IIIa,b

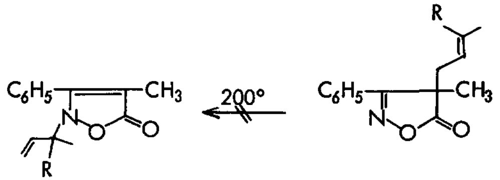


IIc 54 : 46 IIIc'

observed in the following reactions. Heating the N-(γ,γ-dimethylallyl) compound IId, b.p. 143° (0.008 mm); τ 8.62, 8.35 (s, gem di-Me), 6.03 (d, J = 7.5 Hz, N-CH_2), 4.93 (m, -CH=), at 200° resulted in the quantitative recovery of the unreacted IId and amino-Claisen product, 4-(α,α-dimethylallyl) compound IIId', in which a large destabilization due to steric interaction of α-gem-dimethyl was presumed, was not detected. Moreover, the 4-crotyl compound IIIc, m.p. 81-82°; ν 967 cm^{-1} (-CH=CH-), and the 4-(γ,γ-dimethylallyl) compound IIId, b.p. 123-125° (0.03 mm); τ 8.55, 8.42 (s, gem di-Me), 7.32 (d, J = 7.5 Hz, CH_2), 5.17 (m, -CH=), were stable on heating at 200° and the corresponding Cope rearrangement products, N-(α-methylallyl) and N-(α,α-dimethylallyl) compounds IIc' and IId' were not detectable.



IId IIId'



IIc,d' IIIc,d

Katritzky and his co-workers (7, 9) have reported the spectral studies on the prototropic tautomerism of pyrazolin-5-ones and isoxazolin-5-ones and suggested a similar tendency in the tautomeric composition of both the systems.

In comparison with the exclusive amino-Claisen rearrangement of 2-allyl-1-phenyl-3-pyrazolin-5-ones to the corresponding 4-allyl-2-pyrazolin-5-ones (1), the results described here suggest that the difference of the thermal stability between the Δ^2- and Δ^3-pyrazolin-5-ones is relatively larger than that between the Δ^2- and Δ^3-isoxazolin-5-ones.

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