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THE THERMAL REARRANGEMENT OF N-ARYL-ISOXAZOLINE-3-ONES

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N-aryl-isoxazoline-3-ones rearrange quantitatively to N-aryl-oxazoline-2-ones when heated to about 150°.

2-Phenyl-5-methyl-isoxazoline-3-one (① ,* $R_1=R_2=H$), mp 34-36°, ν_{CO} 1670 cm^{-1}; λ_{max} 262 nm (ϵ 10.200); τ ca.2.50, broad 5H-multiplet; 4.43, 1H-quartet, J=0.9 cps; 7.72, 3H-doublet, J=0.9 cps, was prepared according to Matter et al. (1) who mention its rearrangement to an unknown isomer. When 100 mg samples of ① , $R_1=R_2=H$, sealed in ampoules under vacuum, were immersed in an oil bath of 150°, quenched in ice water after various time intervals, and finally analyzed by NMR-spectroscopy, first order rearrangement to an isomer of mp 90-91° was observed. Its spectral properties, ν_{CO} 1775 cm^{-1}; λ_{max} 247.5 nm (9800); τ ca. 2.60, broad 5H-m; 3.45, 1H-q. J=1.5 cps; 7.88, 3H-d. J=1.5 cps; suggested the assignement of structure ② , $R_1=R_2=H$, subsequently confirmed by the following synthesis:

Five mmoles each of phenylisocyanate and lactic aldehyde diethyl acetal (2) (③ , $R_2=H$), were heated to 100° for 20 min. with a trace of pyridine, yielding 90% urethane ④ , $R_1=R_2=H$, bp 100-110°; ν_{CO} 1700 cm^{-1}; ca. 2.8,

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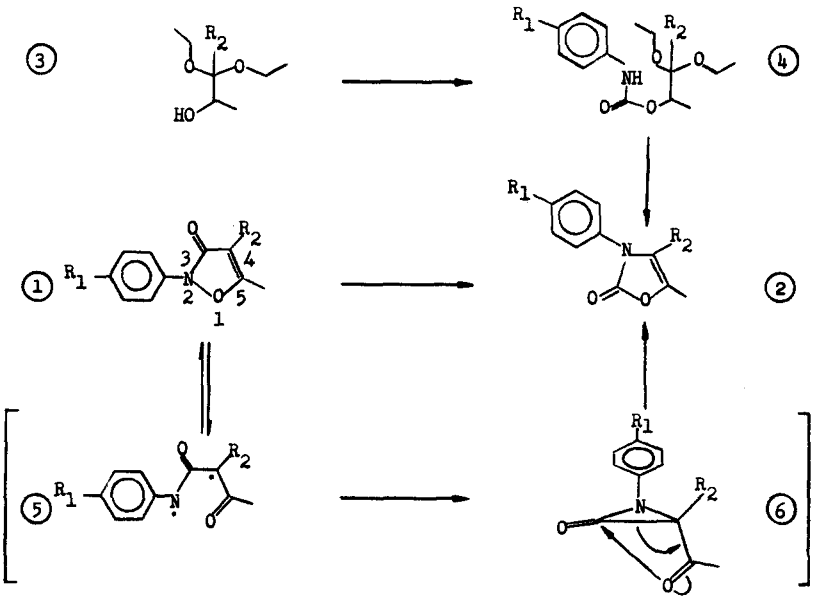
*Satisfactory elemental analyses were obtained for all compounds. IR-spectra were run in methylene chloride, UV-spectra in methanol and NMR-spectra in deuterochloroform at 60 or 100 Mc with tetramethylsilane as an internal standard.



broad 6H-m; 5.08, 1H-8-line-multiplet; 5.55, 1H-d. J=5 cps; 6.36, 4H-m.; 8.70, 3H-d. J=6.3 cps; 8.80, 6H-m. A solution of the urethane (4.0 mmoles) in 5 ml conc. H_2SO_4 was kept at 20° for 10 min. to effect cyclization to a crystalline product (yield 50%), indistinguishable from ② , $R_1=R_2=H$, in its mp, spectroscopic as well as chromatographic behaviour.

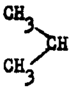
The N-O-bond is known (3) to undergo homolysis with great ease. It seems therefore reasonable to assume breaking of this bond in the first step of the rearrangement of ① . In addition, the resulting diradical ⑤ profits from conjugative stabilization.

Recoupling of ⑤ to the α-lactam ⑥ parallels the formation of an azirine in the rearrangement of 3,5-diphenylisoxazole (4). A four centre rearrangement of ⑥ , similar to the one described by Sheehan et al. (5) in the sodium hydride-catalyzed rearrangement of certain α-chloroanilides leads to the final product ② .

Table 1 shows the kinetic data of the rearrangement of three N-aryl-isoxazoline-3-ones. Clean first order kinetics were observed with all compounds through at least four half-lives, assuming complete rearrangement to ② . After 10 half-lives, compounds other than ② were essentially absent according to thinlayer chromatography.

TABLE 1

Thermal rearrangement rates of N-aryl-isoxazoline-3-ones ①

R_1	R_2	Temperature (°C)	$10^5.k$ (sec^{-1})	$\Delta H^{\neq}$ (kcal/mole)	$\Delta S^{\neq}$ (e.u.)
H	H	121.7 ± 0.2 135.0 ± 0.2 148.8 ± 0.2	1.05 ± 0.01 4.25 ± 0.04 17.2 ± 0.3	33.4 ± 0.3	+ 3.0
F	H	119.8 ± 0.2 149.6 ± 0.2	2.2 ± 0.1 44 ± 1	32.1	+ 1.5
H	 $(CH_3)_2CH$	149.6 ± 0.2 164.3 ± 0.2	8.14 ± 0.20 32.5 ± 0.5	33.9	+ 2.5

As expected for the mechanism described above, the activation entropy terms listed in table 1 are small. The similarity of k, $\Delta H^{\neq}$ and $\Delta S^{\neq}$ for R_1=H or F, and R_2=H or isopropyl, respectively, indicates a negligible sensitivity of the rate-determening step towards polar and steric alterations, again compatible with the proposed mechanism.

The inducement of this rearrangement by photochemical means will be reported later.

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