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# AZA-CLAISEN REARRANGEMENTS IN THE 2-ALLYLOXY SUBSTITUTED OXAZOLE SYSTEM

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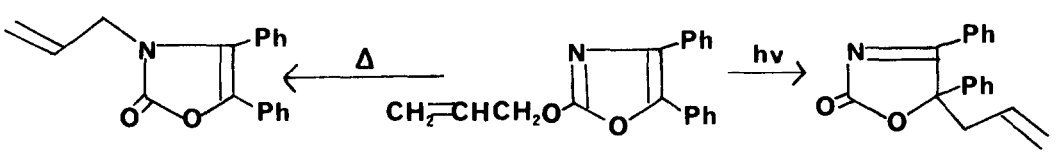
Abstract Thermolysis and photolysis of several 2-allyloxy substituted 4,5-diphenyloxazoles results in a sigmatropic reorganization to give substituted oxazolin-2-ones.

3,3-Sigmatropic rearrangements have found substantial utility in the methodology of synthetic organic chemistry.[1-3] For example, the Claisen rearrangement of allyl vinyl ethers, and compounds of related structure, to γ,δ-unsaturated carbonyl compounds is a reaction of both mechanistic significance and great synthetic value.[1,4] Although a number of reactions which appear to involve an aza-oxa-[3,3] sigmatropic shift have been reported in the literature,[5-9] a study of the scope and synthetic applications of these Claisen analogues has been quite limited One factor which has probably impeded the study of this type of reorganization is the difficulty in preparing the requisite starting materials. Accordingly, we decided to use 2-allyloxy substituted oxazoles as a model for elucidating some of the structural features associated with the 3,3-sigmatropic reorganization of allyl O-imino ethers This communication summarizes some of our observations in this area

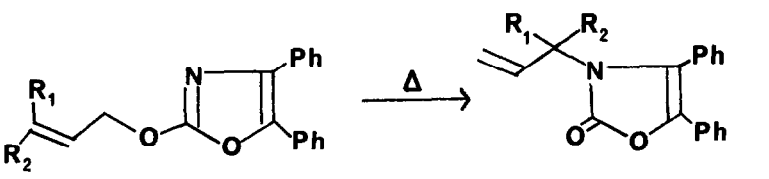
A series of 2-allyloxy substituted 4,5-diphenyloxazoles were readily prepared by treating 2-chloro-4,5-diphenyloxazole[10] with the appropriate allyl alkoxide. In the simplest case, the 2-allyloxy substituted heterocycle 1 rearranged completely on heating to 3-allyl-4,5-diphenyl-4-oxazolin-2-one (2), mp 82-83°C, NMR ($CDCl_3$,90 MHz) δ 3.99-4.14 (m, 2H), 4 87-5 24 (m, 2H), 5 54-5 98 (m, 1H) and 7 11-7.61 (m, 10H). The identity of 2 was verified by comparison with an authentic sample prepared from the reaction of 4,5-diphenyl-4-oxazolin-2-one with allyl bromide in the presence of sodium hydride. In marked contrast to the




2 1 3

thermal results, the photolysis of oxazole 1 gave rise to 5-allyl-4,5-diphenyl-3-oxazolin-2-one (3), mp 100-101°C, NMR ($CDCl_3$,90 MHz) δ 3.20 (dd, 1H, J=14 0 and 6 0 Hz), 3.55 (dd, 1H, J=14.0 and 6.0 Hz), 4.93-5.26 (m, 2H), 5.35-5.82 (m, 1H) and 7.27-8.00 (m, 10H), uv (cyclohexane) 266 nm (ε 17500), m/e 277 ($M^+$), 237 and 129.

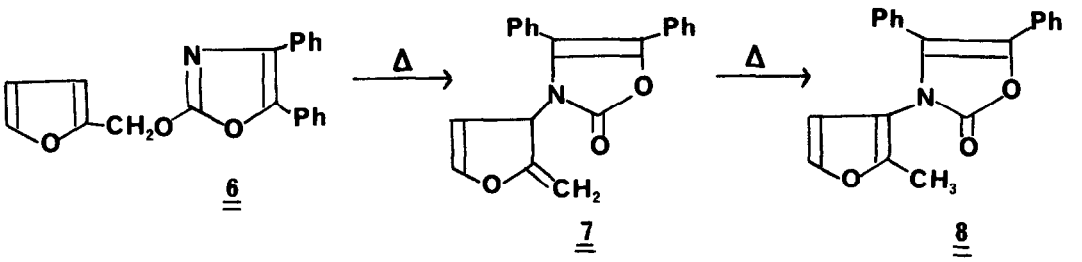
To test for the inversion of the allyl moiety which occurs in concerted 3,3-sigmatropic processes, the rearrangement of 2-[(2-butenyl)oxy]-4,5-diphenyloxazole (4a) was studied. Heating a sample of 4a in benzene at 155°C resulted in the formation of 3-(1-methylallyl)-4,5-diphenyl-4-oxazolin-2-one (5a). Subjection of the closely related oxazole 4b to similar thermolysis conditions produced oxazolinone 5b in quantitative yield,[11] NMR ($CDCl_3$,90 MHz) δ 1.05 (s, 6H), 4.80-5.08 (m, 2H), 6.05 (dd, 1H, J=16 and 10.0 Hz) and 7.12-7 68 (m, 10H). The formation of the 1,1-dimethyl-2-propenyl substituted isomer 5b is only compatible with the 3,3-sigmatropic rearrangement route.[12]




4a ; $R_1 = H$ ; $R_2 = CH_3$
4b ; $R_1 = R_2 = CH_3$

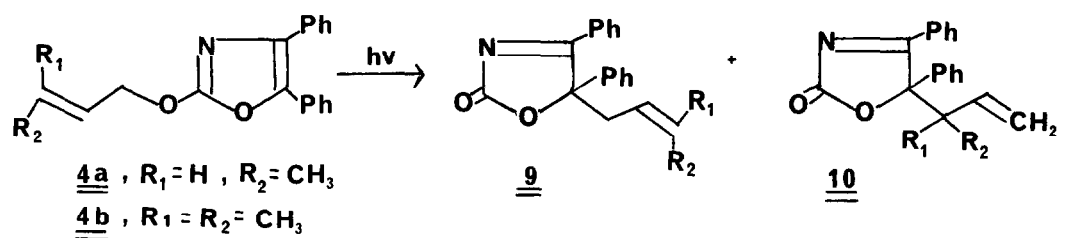
5a ; $R_1 = H$ ; $R_2 = CH_3$
5b ; $R_1 = R_2 = CH_3$

Further examples which would support the generality of these rearrangements were sought. With this in mind, we investigated the thermal behavior of 2-[(furfuryl)oxy]-4,5-diphenyloxazole 6. Heating a sample of 6 at 80°C for 6 hr gave 2-methyl-3-(4,5-diphenyl-4-oxazolin-2-one)furan 8, mp 161-162°C, NMR ($CDCl_3$,90 MHz) δ 2.21 (s, 3H), 5.97 (d, 1H, J=2.0 Hz), 6.23 (d, 1H, J=2.0 Hz) and 7 2-8 0 (m, 10H). When the thermolysis of 6 was carried out at a lower temperature and for shorter periods of time, the product derived from a 3,3-sigmatropic shift (i.e. 7, mp 85-86°C, NMR ($CDCl_3$,90 MHz) δ 4 05 (bs, 1H), 4 35 (bs, 1H), 5.70 (bd, J=6 0 Hz), 6 15 (t, 1H, J=1.5 Hz), 6.21 (dd, 1H, J=6.0 and 1.5 Hz), 7.3-8.0 (m, 10H)) could be isolated in high yield. This compound was readily converted to 8 on further heating or by stirring with a trace of acid.



The mechanism by which the 2-allyloxy substituted oxazole system undergoes photochemical reorganization (i.e $\underline{1} \xrightarrow{h\upsilon} \underline{3}$) is also of considerable interest. One possibility is that the reaction proceeds via two consecutive 3,3-sigmatropic shifts. This path was eliminated, however, by the finding that oxazolinones $\underline{2}$ and $\underline{5}$ undergo oxidative photocyclization on irradiation. Rigidly held stilbene moieties are known to yield phenanthrene derivatives on irradiation and provide excellent precedent for this transformation.[13] A second mechanistic scenario is that the rearrangement proceeds via a photoinduced 1,5-sigmatropic shift. In a third conceivable mechanism, the oxazolinone ring could be formed via a 3,5-sigmatropic rearrangement Finally, the photolysis could proceed via a cleavage-recombination path involving a pair of radical intermediates It should be noted that other examples of photochemical 1,5-migrations proceeding through a dissociation-reassociation path are known in the literature.[14]

Evidence concerning the mechanism of the photoreaction was obtained by studying the photolysis of oxazole $\underline{4a}$. With this system, direct irradiation produced $\underline{9a}$ (83%) and $\underline{10a}$ (17%) which could be separated by liquid chromatography. Similar results were obtained with oxazole $\underline{4b}$.[15] These results are most compatible with a mechanism involving C-O bond

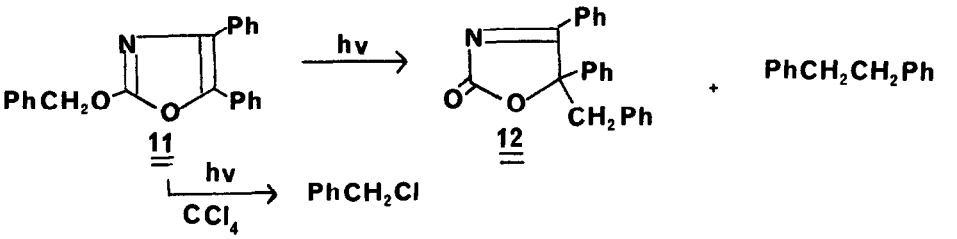


$\underline{4a}$ , $R_1 = H$ , $R_2 = CH_3$

$\underline{4b}$ , $R_1 = R_2 = CH_3$

scission to give a pair of radicals which undergo a subsequent recombination. The preferential formation of the 3-oxazolinone is to be expected since the transition state of these

systems prefers to localize the odd electron on the phenylated carbon. The product distribution (i.e. 9 vs. 10) on the allyl end reflects the greater steric hindrance to recombination of a tertiary site compared with a primary site.[16] Additional support for the cleavage-recombination path was obtained by carrying out the irradiation of 2-(benzyloxy)-4,5-diphenyloxazole 11. Photolysis of this compound produced oxazolinone 12




as well as bibenzyl The almost complete suppression of oxazolinone formation when the irradiation is carried out in carbon tetrachloride is consistent with the formation of a benzyl radical which is trapped by the solvent.[17]

Studies to probe more deeply the mechanistic details of these reactions are continuing

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(15) Compound 9b NMR ($CDCl_3$,90 MHz) δ 1 52 (s, 3H), 1 66 (s, 3H), 2.56 (d, 1H, J=7.0 Hz), 5 33 (t, 1H, J=7.0 Hz) and 7 2-7 7 (m, 10H), Compound 10b NMR ($CDCl_3$,90 MHz) δ 1.10 (s, 6H), 4.7-5.10 (m, 2H), 6.13 (dd, 1H, J=17 0 and 10 0 Hz) and 7.2-7 7 (m, 10H)
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(17) A free radical chain mechanism is an alternate mechanistic possibility However, the rearrangement to 12 did not occur when a sample of 11 was allowed to react with a source of benzyl radicals.

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