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A NITROGEN ANALOG OF THE CLAISEN REARRANGEMENT

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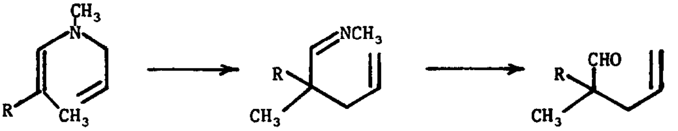
In surprising contrast to the Claisen rearrangement of allyl vinyl (or aryl) ethers (Eq. 1, X=O), relatively few examples of the amino-Claisen rearrangement (Eq. 1, X=NR) are known. Attempted rearrangement of N-allylaniline at 275° gave no o-allylaniline but only decomposition to propylene and aniline (1). Marcinkiewicz et al (2) proposed an explanation for this behavior and successfully predicted that N-allyl-1-naphthylamine would rearrange, but to date this is the only example of the rearrangement of an allyl aryl amine. The alkylation of certain enamines with allyl halides has been shown to involve initial N-alkylation followed by Claisen rearrangement of the ammonium salts (Eq. 1, $X=NR_2^+$) (3).

(Eq. 1)

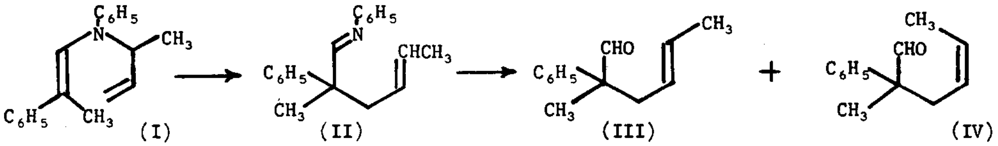
We have found that enamines prepared from N-allylamines and α-disubstituted aldehydes rearrange practically quantitatively on heating, and that consequently the amino-Claisen rearrangement in its most general form (4), the pyrolysis of N-allylvinylamines, is a facile and synthetically useful reaction. In the simplest case, N-allyl-N-methylisobutenylamine rearranged completely to N-methyl-2,2-dimethylpent-4-enimine on heating for one hr. at 250° in a sealed ampoule (Eq. 2, $R=CH_3$). The rearrangement could be followed by v.p.c. or by the appearance of the imine C-H in the n.m.r. spectrum. Hydrolysis of the imine gave the known aldehyde, 2,2-dimethylpent-4-enal (5), identified by its n.m.r. spectrum and the formation of the 2,4-dinitrophenylhydrazone, m.p. 117°. Similarly, the enamine from N-methyl-N-allylamine and α-phenylpropionaldehyde rearranged partly, on heating at 205° for 3 hr., to the N-methylimine of 2-methyl-2-phenylpent-4-enal (Eq. 2, $R=C_6H_5$). Hydrolysis gave the aldehyde, identical with a sample prepared by alkylation (6) of the piperidine enamine of α-phenylpropionaldehyde with allyl iodide.

To test for the inversion of the allyl moiety which occurs in concerted cyclic processes

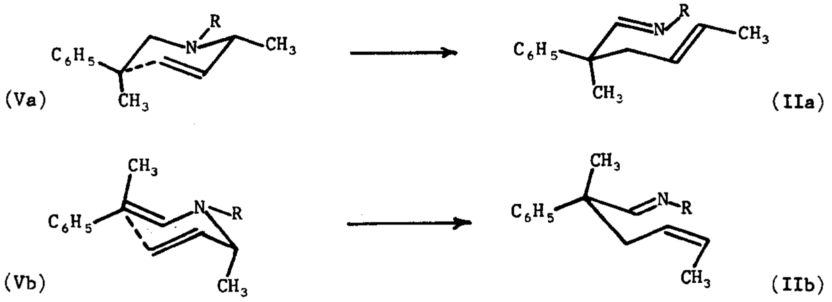


(Eq. 2)

the rearrangement of N-phenyl-N-(α-methallyl)-2-phenylpropenylamine (I) was studied. This enamine, b.p. 100-105° (0.05 mm.), was prepared from α-phenylpropionaldehyde and N-phenyl-α-methallylamine (7). The n.m.r. spectrum was consistent with (I); from the single olefinic proton absorption at 6.3 ppm the enamine is tentatively assigned the double bond geometry shown (8) since cis-trans mixtures of enamines from the same aldehyde show two peaks, at 6.3 and 6.1 ppm. Distillation at 170-175° effected complete rearrangement to the imine (II), which had a strong IR band at 10.4μ and distinctive n.m.r. absorption at 7.75 ppm (s) and 5.2-5.6 ppm (mult., 2H).



Hydrolysis of (II) with aqueous acid gave a mixture of aldehydes (III) and (IV) in the ratio 87:13, separated by preparative v.p.c. Structures were assigned from n.m.r. and IR spectra (the strong IR band at 10.4 μ in the trans isomer (III) is absent in (IV)) and were proven by independent synthesis, using the method of Stork and Dowd (9). These results demonstrate complete inversion of the allyl moiety. The formation of trans and cis isomers in a roughly 9:1 ratio parallels earlier results in the Claisen (10) and Cope (11) rearrangements, and is best accommodated by the conclusion reached in those cases that thermal rearrangements of diallylic systems proceed via four-center chair-like transition states (Va and Vb) with (Va), in which the methyl is equatorially substituted, preferred.



As a further test for the concerted nature of the rearrangement and as a probe of transition state geometry we have examined the rearrangement of optically active (I). Use of R-(+)-N-phenyl-α-methallylamine, $[\alpha]_D^{25}$ 2.64° ($CHCl_3$), in the preparation of (I) and subsequent rearrangement gave optically active (II). As required by conformations (Va) and (Vb), aldehydes (III) and (IV) have opposite configurations at the asymmetric center as well as at the double bond. (III), $[\alpha]_D^{25}$ +15.5°, and (IV), $[\alpha]_D^{25}$ -10.5°, were hydrogenated to the same saturated aldehyde, dextrorotatory from (III), levorotatory from (IV). The absolute configurations of (III), (IV), and (I) have been determined and are in agreement with the predictions of the four-center transition states (Va) and (Vb).

The rearrangement of N-allylenamines appears to be a general reaction involving a concerted cyclic process consistent with a four-center transition state. Since it provides a method of alkylating aldehydes without the use of an alkylating agent or strong base, it may prove of synthetic utility. Research on the optical yield is continuing.

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