Tetrahedron Letters No.52, pp. 4833-4836, 1965. Pergamon Press Ltd.
Printed in Great Britain.

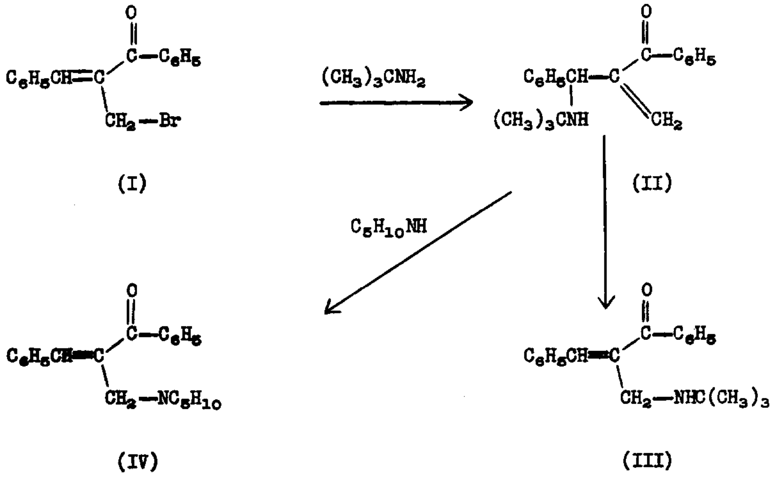
MOBILE KETO ALLYL SYSTEMS. I. REARRANGEMENTS IN THE SYNTHESIS OF α-[(N-T-BUTYLAMINO)-METHYL]-CHALCONE

Richard P. Rebman and Norman H. Cromwell
Avery Laboratory of Chemistry, University of Nebraska
Lincoln, Nebraska

(Received 23 October 1965)

Examples of allylic rearrangement accompanying bimolecular nucleophilic substitution on primary allylic halides are rare (1,2) and allylic rearrangement of allylic amines is apparently unknown (3). We have found that *trans* α-(bromomethyl)-chalcone (I) (from the reaction of N-bromosuccinimide with *trans*-α-methylchalcone in carbon tetrachloride containing benzoylperoxide) in solvent pentane reacts with two molar equivalents of t-butylamine to give exclusively, in high yield, the rearranged substitution product, α-α[-(N-t-butylamino)-benzyl]-acrylophenone (II), which under the proper conditions may be induced to rearrange quantitatively to the thermodynamically more stable isomeric form, α-[(N-t-butylamino)-methyl]-chalcone (III).

The latter rearrangement has been found to proceed by two mechanisms. Although II is reasonably stable with respect to isomerization either in the crystalline state or in solvent pentane, in solvent chloroform (and other slightly polar solvents) it readily rearranges to III. Even in solvent pentane, however, II reacts readily with added t-butylamine to give the isomeric form III. The addition of other amines, such as piperidine, to II in solvent pentane gives amine exchange in addition to rearrangement yielding, in this case, α-[(N-piperidino)-methyl]-chalcone (IV).



The uv. spectrum (95% ethanol) of I, m.p. 79°C, showed λmax, 257 mμ (13,700); 290 mμ (13,800). The n.m.r. (4) spectrum (CCl_4) showed a complex multiplet (10 H) centered at τ2.4 (aromatic protons), a singlet (1 H) at τ2.91 (benzal proton), and a singlet (2 H) at τ5.50 (α-bromomethyl protons).

Anal. Calcd. for $C_{16}H_{13}BrO$:C,63.80; H,4.36; Br,26.53. Found: C,63.83; H,4.64; Br,26.26.

The uv. spectrum (isooctane) of II, m.p. 69°C, showed λmax, 243 mμ (11,900). The n.m.r. spectrum ($CDCl_3$) showed a complex multiplet (10 H) centered at τ2.4 (aromatic protons), two singlets (1 H each) at τ3.68 and τ4.28 (vinyl protons), a singlet (1 H) at τ4.85 (benzyl proton), and a singlet (10 H) at τ8.92 (t-butylamino protons, C-H and N-H).

Anal. Calcd. for $C_{20}H_{23}NO$: C,81.87; H,7.90; N,4.77. Found: C,81.83; H,7.85; N,4.86.

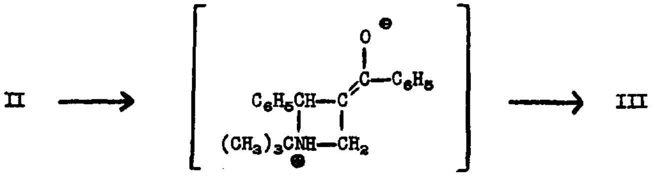
The uv. spectrum (isooctane) of III, m.p. 105°C, showed λmax, 255 mμ (11,500); 283 mμ (16,100). The n.m.r. spectrum ($CDCl_3$) showed a complex multiplet (10 H) centered at τ2.4 (aromatic protons), a singlet (1 H) at τ2.71 (benzal proton), a singlet (2 H) at τ6.28 (α-N methylene protons), and a singlet (10 H) at τ8.83 (t-butylamino protons, C-H and N-H).

Anal. Found for III: C,81.80; H,7.71; N,4.92.

The uv. spectrum (95% ethanol) of IV, m.p. 72°C, showed λmax, 250 mμ (14,100); 285 mμ (13,900). The n.m.r. spectrum (CCl_4) showed a complex multiplet (10 H) centered at τ2.4 (aromatic protons), a singlet (1 H) at τ2.85 (benzal proton), a singlet (2 H) at τ6.56 (α-N methylene protons), a doublet (4 H) centered at τ7.6 (α-N piperidine ring protons), and a singlet (6 H) centered at τ8.55 (β- and γ-N piperidine ring protons).

Anal. Calcd. for $C_{21}H_{23}NO$: C,82.59; H,7.59; N,4.59. Found: C,82.60; H,7.61; N,4.74.

A preliminary investigation of the kinetics of the amine-unassisted rearrangement of II to III shows first-order kinetics with a very low energy of activation, Ea 6 k. cal./mole, and a very low negative entropy of activation, ΔS*, -66 cal./deg./mole, in deuteriochloroform in the range of 35.5°C. to 41.5°C., which suggests a highly polar, cyclic transition state in which C-N bond-making is well ahead of C-N bond breaking (5,6).



The electron delocalization provided by the carbonyl group undoubtedly facilitates these allylic rearrangements. The scope, mechanisms, and full details of these reactions will be reported in subsequent papers.

Acknowledgment. - - - This work was supported in part by a research grant from the National Science Foundation G-20149 and in part by a research grant from the U. S. Public Health Service, National Cancer Institute, G-2931.

REFERENCES

1. F. G. Bordwell, F. Ross, and J. Weinstock, J. Am. Chem. Soc. 82, 2878 (1960).
2. R. H. DeWolfe and W. G. Young in S. Patai, The Chemistry of Alkenes, Vol. 1, p. 691. John Wiley and Sons, New York, 1964.
3. Idem, Chem. Rev. 56, 753 (1956).
4. The n.m.r. data were obtained on a Varian A-60 instrument, and are expressed as τppm. chemical shift, using tetramethylsilane (τ,10.0) as internal standard.
5. E. S. Gould, Mechanism and Structure in Organic Chemistry, Henry Holt and Co., New York, 1960, p. 178-181.
6. A. A. Frost and R. G. Pearson, Kinetics and Mechanism, John Wiley and Sons, New York, 1961, 2nd Ed., p. 137.