

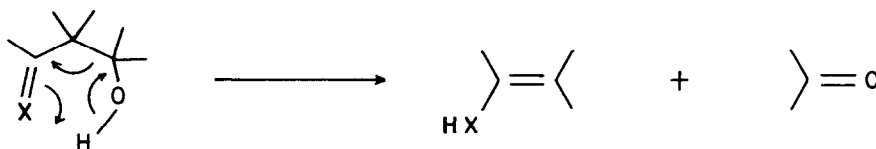
A NOVEL RETRO-ENE REACTION
THE FRAGMENTATION OF N-BENZYL-2-BENZOYL-2-METHYLPROPANIMINE

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Summary N-Benzyl-2-benzoyl-2-methylpropanimine treated with nucleophiles undergoes a fragmentation reaction that can be envisaged as a retro-ene reaction via the formation of an intermediate hemiketal

Fragmentation reactions of the retro-ene type have been the subject of extensive studies^{1,2} Thus, many β,γ -unsaturated alcohols undergo the fragmentation shown in Scheme I



SCHEME I

Many examples of this general reaction in which $X = \text{CR}_2$ and $X = \text{O}$ (thermal retro-aldol condensation) have been reported³ However there are very few in which $X = \text{NR}$ ^{4,5} In most of these cases the $\text{C}=\text{N}$ double bond is part of an heterocyclic system Some open-chain compounds have also been studied For instance, Pollack and Cooper⁶ reported the retro-aldol reaction of diacetone alcohol catalyzed by primary aliphatic amines In this case the reaction proceeds via an

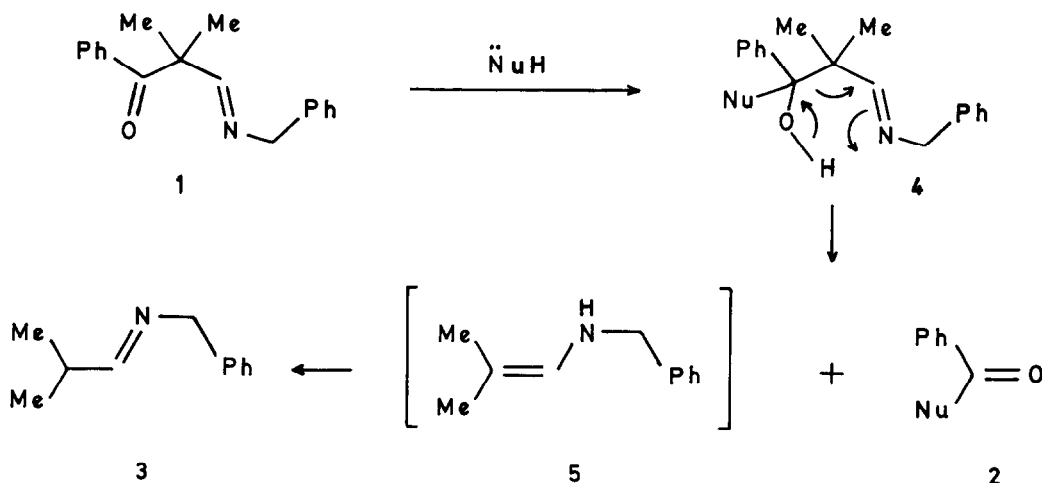
imine intermediate.

We report here a novel retro-ene-type fragmentation in the reaction of N-benzyl-2-benzoyl-2-methylpropanimine with nucleophiles.

Imine 1 was synthesized by treatment of α -benzylisobutyraldehyde with an equimolecular amount of benzylamine in dry ether under nitrogen. After evaporation of solvent, n.m.r. and i.r. spectra of the crude reaction mixture showed 100% conversion to the monoimine 1⁷. The imine 1 could be purified by vacuum distillation and is stable if stored in the absence of moisture and under nitrogen.

Reaction of imine 1 in methanol at reflux temperature under nitrogen for one hour yields methyl benzoate 2 (Nu= MeO) and N-benzyl-2-methylpropanimine 3 quantitatively. This imine was identified by its i.r. and n.m.r. spectra and also by independent synthesis from isobutyraldehyde and benzylamine⁸.

The reaction can be interpreted as involving nucleophilic attack of methanol at the carbonyl group with formation of an hemiketal 4 (Scheme II) which in the reaction medium fragments to methyl benzoate and the enamine 5 which tautomerizes to the observed imine 3.



SCHEME II

The proposed mechanism is substantiated by the following a) The reac-

tion can be carried out in methanol (d_4) which was been treated with anhydrous Na_2CO_3 in order to eliminate traces of acid⁹. b) Under these conditions reaction of imine 1 shows two new resonances in the n.m.r. spectrum. The new signals at 1.6 δ and 4.0 δ can be assigned to the enamine 5 on the basis of the calculated chemical shifts. Also as the reaction proceeds these new resonances decrease and those corresponding to the imine 3 increase. After 24 hours the reaction products are indistinguishable with those obtained in acidic methanol.

As far as we are aware this is the first reported observation of a non-stabilized enamine of the type 5 shown. Trapping experiments are under way to capture the proposed intermediate.

An alternative mechanism involving initial hydrolysis of the monoimine has also been considered and ruled out on the grounds that α -benzoylisobutyraldehyde does not transform under these reaction conditions.

A similar reaction could account for the rapid decomposition of monoimine 1 in moist ether solution, at room temperature. In this case, 1 yields quantitatively benzylammonium benzoate and isobutyraldehyde. Nucleophilic attack by water to the carbonyl group followed by fragmentation of the intermediate would yield benzoic acid and the enamine 5 which may hydrolyze in the reaction medium to benzylamine and isobutyraldehyde. The benzylammonium benzoate, formed by reaction of benzoic acid with benzylamine, precipitates from the ether solution as white crystals.

The fragmentation reaction described shows a clear dependence on the nucleophilicity of the reagent. Thus, under similar experimental conditions to those given above, treatment of 1 with ethanol proceeds with a significantly lower rate and the reaction with t-butanol fails. These results are in accord with a mechanism in which the first step is the formation of the hemiketal.

The fragmentation of imine 1 is not unique and preliminary results show that the reaction can be extended to other molecules and nucleophiles.

Acknowledgement

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and i.r. data n.m r. (Cl₄C) δ 1.5 (6H, s, 2CH₃), 4.6 (2H, d, CH₂), 7.2 (8H,
m, aromatic), 7.8 (3H, m, CH and 2H aromatic ortho CO), i r. (neat) 1680
(C=O), 1650 (C=N) cm⁻¹
- 8 - n m r. (Cl₄C) δ 1.1 (6H, d, 2CH₃), 2.4 (1H, m, CH(CH₃)₂), 4.5 (2H, d, CH₂),
7.3 (5H, m, aromatic), 7.6 (1H, m, CH=N)
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