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THE OXIDATION OF COMPOUNDS CAPABLE OF IMINE-ENAMINE TAUTOMERISM WITH LEAD TETRAACETATE

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Abstract—Compounds capable of imine-enamine tautomerism react preferentially via their enamine tautomer giving a 2-acetoxyaldehyde which equilibrates with the starting imine. This derives from the extra nucleophilicity of the β-carbon of the enamine tautomer. The reaction of the imine isomer to form an aryl- or an alkylnitrenoid species is a minor pathway.

INTRODUCTION

In previous papers[1] we reported the results of the oxidation of aromatic anils with lead tetraacetate (LTA). These substrates were shown to be cleaved by the oxidant to form the benzylic radical R-ϕ-$\dot{C}$H-OAc and an arylnitrenoid species. Other papers[2] reported that the oxidation of enamines with LTA gives as the primary reaction product a diacetate 1 which undergoes an α- or a β-elimination reaction forming a 2-acetoxyketone 2 or an enolacetate-enamine 3 which gives the corresponding 2-aminoketone 4 (Scheme 1).

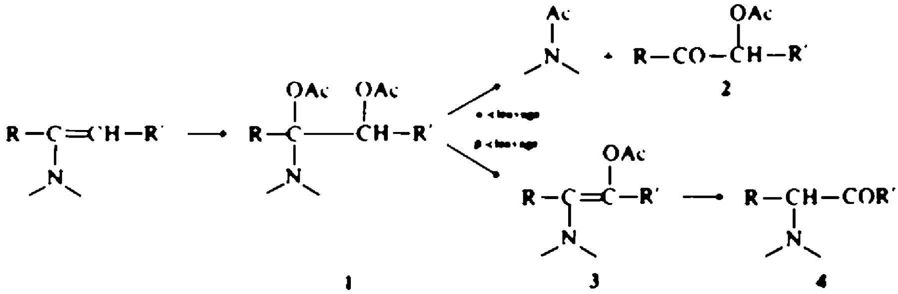
These data suggested the possibility of a comparison between the reactivity of the $>C{=}C{-}N<$ and the $>C{=}N{-}$ groups toward LTA, using substrates which can give rise to imine-enamine tautomerism under the action of Lewis acids.[3]

Compound 5, oxidised with 1·2 mol eq of LTA at room temperature, gave N-acetylcyclohexylamine 6 (38%), the acetoxyimine 7 (33%) and small amounts (<10%) of cyclohexylaldehyde, cyclohexylamine, cyclohexanone and N,N'-dicyclohexylurea. Compound 7 was prepared from 2-acetoxycyclohexylaldehyde and cyclohexylamine.

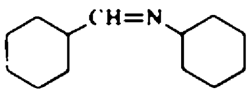
The imine 8, oxidised in the same conditions, gave 6 (17%), 2-acetoxy-n-heptaldehyde 9 (28%), the acetoxyimine 10 (16%) and small amounts (<10%) of n-heptaldehyde, cyclohexylamine and cyclohexanone. The preparation of 10 was performed as for 7.

The oxidation of the imine 11 gave again 9 (18%), azobenzene 12 (27%) and n-heptaldehyde (36%).

Azobenzene 12 was also formed in the oxidation of the



SCHEME 1



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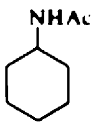

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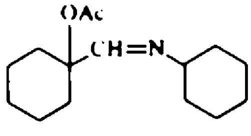

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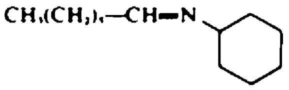

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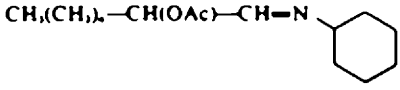
$CH_3(CH_2)_4{-}CH(OAc){-}CHO$

9



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anil **13** in 7% yield. Other products were acetophenone (35%), phenacyl acetate (53%) and traces of aniline.

The imine **14** was recovered after the LTA treatment in 57% yield. Benzaldehyde, cyclohexanone and cyclohexylamine were also formed in poor yield.

The enamine **15**, oxidised with 1·2 mol eq of LTA, gave a mixture of morpholine, acetylbenzoin **16** and a thermolabile product which had MS peaks at *m/e* 323 (M⁺), 281, 237, 236, 131, 120, 91 and 42. By chromatography a 92% yield of **16** was obtained. These data, and the observation that the NMR spectrum of the reaction mixture after evaporation of morpholine had the signals of **16**, together with a singlet at δ 1·96 corresponding to an acetate group and a multiplet at δ 3–4 which indicated a morpholino group allowed to indicate formula **17** for the thermolabile reaction product. The NMR spectrum showed that **16** and **17** were 43% and 47% of the mixture. Compound **17** was shown by GLC-MS and NMR to be formed also in the reaction of **16** with morpholine in diethyl ether at reflux in the presence of Linde 4 Å molecular sieves in 28% yield.

The results observed in the oxidation of the first two imines **5** and **8** are considerably different from those obtained from aromatic anils. Only a minor part of the reaction occurs via a $>C{=}N-$ bond fission. To this reaction path are ascribed the production of the aldehydes and a cycloalkylnitrenoid species with subsequent formation of the aliphatic amine and cyclohexanone according to the reactivity of alkylnitrenes.[4] The most part of the reaction course derives by the enamine reactivity of these molecules. This can be explained by LTA catalysis of the imino-enamino tautomerism (**18** ⇄ **19**) of these molecules acting as Lewis acid.[5] The enamino form (**19**) is oxidised by LTA faster than the imino form **18** and its fate is shown in Scheme 2.

The primary addition product **20** gives by an α-elimination reaction[2] the 2-acetoxyaldehyde **21** which equilibrates with the starting material to give the acetoxyimine **22** and the unsubstituted aldehyde **23**. A direct β-elimination reaction from **20** to **22** could be a minor pathway.

The competition between the imine and the enamine atutomers is also apparent in the reaction of the substrates **11** and **13**. Here, azobenzene **12** is formed via a phenylnitrenoid as previously noted,[1] and 2-acetoxycarbonyl derivatives by α-elimination. The relevance of the "imine reactivity" of these substrates could be attributed to the necessity of an at least partial deconjugation of the double bond for the establishment of the equilibrium (**18** ⇄ **19**). In all these cases, the faster oxidation of the enamine tautomer over the imine isomer could be attributed to the extra nucleophilicity of its β-carbon making easier the attack by the electron deficient LTA molecule.

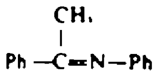
In the case of **16**, where an enamine form is not possible, the "imine reactivity" is apparent by the formation of the cyclohexylnitrenoid. The reaction products derive in fact by extraction of hydrogen to form

$CH_3(CH_2)_5-CH{=}N-Ph$

11

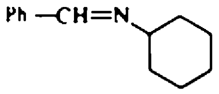
$Ph-N{=}N-Ph$

12



$Ph-C(CH_3){=}N-Ph$

13



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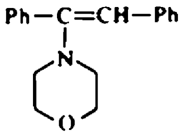

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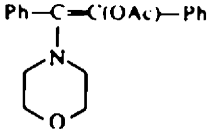
$Ph-CO-CH(OAc)-Ph$

16



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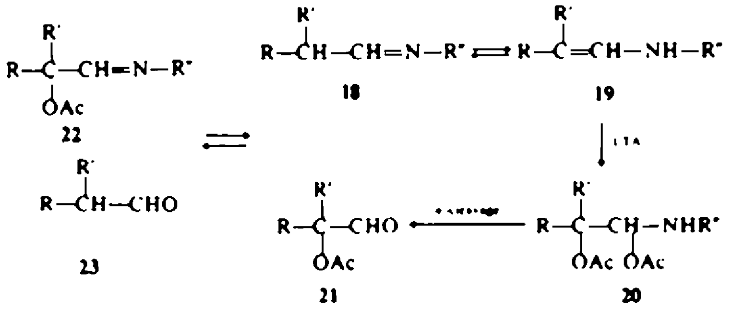

Scheme 2

the cyclohexylamino radical which is transformed either into cyclohexylamine or into cyclohexanone imine. The latter would be further oxidised to cyclohexanone.

EXPERIMENTAL

NMR spectra were recorded for solutions with a Varian NV14 instrument (TMS as internal standard). Analytical GLC was performed with a Varian 1740 gas chromatograph equipped with a glass column (6 ft × 0.3 in) packed with 3% SE 30 on Chromosorb W (oven temp 70–220°C, injection temp 200°C, flame ionisation detector temp 200°C, carrier gas N_2 at 26 ml/min), product yields were determined by tracing the curves on paper and cutting out and weighing the paper. MS spectra were obtained with a LKB 9000 (70 eV) GLC-linked instrument. Micro-analyses were obtained with a Perkin–Elmer Elemental Analyser 240.

Oxidation of the substrates. 1.2 Mol eq of acetic acid free LTA were added to 0.05 M solutions of the substrates in anhydrous benzene. After consumption of the oxidant the resulting suspension was filtered and evaporated to dryness under reduced pressure at room temperature and the residue was analysed by GLC-MS. A sample of the reaction of **5** with LTA was distilled at 0.8 mm/Hg. The fraction boiling at 130–170°C was collected, 2.17 g, and chromatographed on 65 g of silica gel G Merck eluting with n-hexane (25 ml fractions). Fractions 3–7 contained **7**, b.p. 160°C at 3 mm/Hg, ν_{max} 1730 cm^{-1}. Found C, 71.38, H, 10.35, N, 5.31. $C_{15}H_{25}NO_2$ requires C, 71.67, H, 10.03, N, 5.57%.

Preparation of compounds **7** *and* **10**. Compounds **7** and **10** were prepared by dropping simultaneously 50 ml of 0.1 M benzene solutions of the 2-acetoxyaldehydes and of cyclohexylamine in 100 ml of anhydrous benzene. After 18 h at room temperature and evaporation under reduced pressure the residue was distilled at 140°C at 3 mm/Hg to give **7** or **10**. For the latter, found C, 71.26, H, 10.61, N, 5.70. $C_{15}H_{27}NO_2$ requires C, 71.40, H, 10.74, N, 5.53%.

Attempted preparation of compound **17**. The solution of 1 g of **16** and 3 ml of morpholine in 40 ml of anhydrous diethyl ether was added to 4 g of Linde 4 Å molecular sieve and refluxed for 3 days. After filtration the solution was evaporated under reduced pressure at room temperature and analysed by GLC-MS and NMR.

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