THE OXIDATION OF 4-(1-CYCLOHEXEN-1-YL)-MORPHOLINE WITH LEAD TETRAACETATE

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The oxidation of nitrogen compounds with lead tetraacetate has been revie-

wed recently by J. B. Aylward[1]. Aromatic anils[2] and aryldialkyl amines[3]

present the particular problem of the mode of formation of the aldehydic group

in a non-hydrolytic medium.

We thought that enamines could be opportune substrates to study the effect

of the presence of a nitrogen atom in the reaction between an unsaturated posi-

tion and lead tetraacetate, and to define the problem of the origin of the car-

bonyl groups which could be formed.

The reaction of 4-(1-cyclohexen-1-yl)-morpholine (I) in dry benzene at room

temperature with 1 mol. eq. of acetic acid-free lead tetraacetate was complete

within 20' and gave a mixture which was immediately distilled under vacuum to

yield a lower- and a higher-boiling fraction. The g.l.c. separation of the lower-

boiling fraction allowed the isolation of two products, N-acetyl-morpholine (II)

and 2-acetoxy-cyclohexanone (III). The g.l.c. separation of the higher boiling

fraction afforded 4-(1-cyclohexanon-2-yl)-morpholine (IV) and a mixture of two

compounds, which was chromatographed over silica-gel leading to the isolation of

one of them, 4-(2-acetoxy-1-cyclohexen-1-yl)-morpholine (V), b.p. 140°/4 mm Hg;

ν_{max} 1745 cm^{-1} (CHCl$_3$); m/e=225, 183, 182, 166, 165, 125, 110; in CDCl$_3$ signals

at δ=1,80-2,20 (4H, m, -C$\underline{H}_2$-C$\underline{H}_2$-), 2,06 (3H, s, -O-CO-C$\underline{H}_3$), 2,45 (4H, m,

-C$\underline{H}_2$-C=C-C$\underline{H}_2$-), 2,83 (4H, m, -C$\underline{H}_2$-N-C$\underline{H}_2$-), 3,73 (4H, m, -C$\underline{H}_2$-O-C$\underline{H}_2$-). The last

compound, which could never be obtained pure, had the molecular peak in the mass

spectrum (registered by g.l.c.-m.s.) at m/e=225, and fragmets which differed

from these of (V) only in the relative intensity of the peaks. In the IR spectrum

(CHCl$_3$) it showed a band at 1735 cm^{-1}; the acetoxy group resonated in the n.m.r.

(CDCl$_3$) at 1,97 δ and the olefinic hydrogen at 5,19 δ (multiplet). This sugge-

sted for it formula (VI). Table 1 shows the yield of compounds (II-VI) (Rea-

ction A)[4].

In the scope of confirming the structure of compounds (V) and (VI), 2-ace-

toxy-cycloxehanone (III) was treated with an equimolecular amount of morpholine

in diethyl ether solution in the presence of Linde 4 Å molecular sieves for

four days at room temperature[5] giving the results shown in Table 1 (Reaction B).

When reaction A was repeated at 15° avoiding any heating in the work-up

procedure, the g.l.c. investigation of the crude mixture showed, in addition to

compounds (II-VI) (30%), another product (70%). This could not be further puri-

fied as it was coverted completely into (II-VI) either by distillation or by

silica-gel chromatography. The investigation with the g.l.c.-m.s. tecnique showed

it had the molecular peak at m/e=285, and fragments at m/e=243, 225, 201, 183,

127. Its easy transformation into the final reaction mixture suggested formula

(VIII), derived by the introduction of two acetates on the enaminic double bond

of the starting material.

The derivation of the reaction products from (VIII) is shown in Scheme 1.

This compound could undergo an α-elimination to give (II) and (III), or a β-e-

limination to yield (V) and (VI).

The possible alternative formulation (IX) could not generate (V), since

gem-diacetates, once formed, restore promptly the starting ketone by Lewis acid

treatment, and do not give enolacetates[6].

Furthermore, the fact that both in reactions A and B compound (IV) derived

from (V) could be proved by the acid- or the basic-catalysed transformation

(V)→(IV). Hence, in the basic conditions of reaction B, morpholine acted as

nucleophile toward the carbonyl carbon of (V), allowing its transformation into.
(IV) and yielding also N-acetyl-morpholine (II); lead tetraacetate behaved in
reaction A as a Lewis acid giving the same results. In this case, compound (II)
derived exclusively from the α-elimination mechanism on (VIII).

A further confirmation of this reaction path derived by the observation that
under these conditions cyclohexanone is not attacked by lead tetraacetate.

It can be then concluded that the behaviour of the title aliphatic enamine
toward lead tetraacetate resembles closely that of some olefinic compounds[7].
In this case, the nitrogen atom gives an extra nucleophilicity to the β carbon,
activating the attack by the reagent.

Furthermore,this reaction is complementary to the hydroboration of enamines[8]
used for the dislocation of a ketonic group in complex molecules.

REFERENCES AND NOTES

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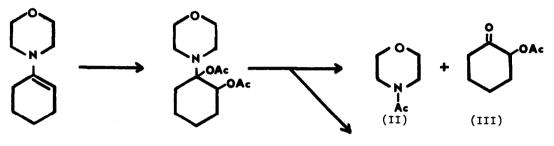
4) In some conditions, a small amount of (VII) could be isolated, owing to some
   further oxidation of (VI).

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TABLE 1

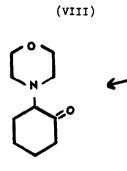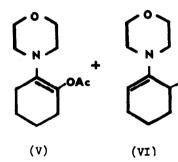| Compound	II	III	IV	V	VI
Reaction A	22*	10	49	7	10
" B	12	29	24	30	4

*Per cent yields determined by quantitative gaschromatography.

SCHEME 1

(I)   (VIII)

(II)   (III)

(V)   (VI)

(IV)

(VII)   (IX)