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MECHANISM OF THE ACETOXYLATION OF N-BENZYLNITRONES

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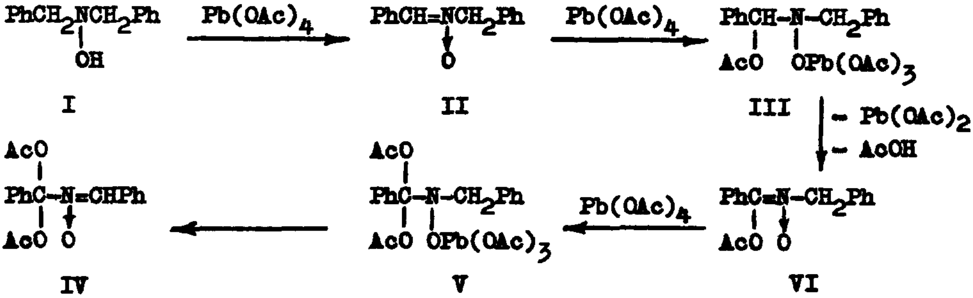
Recently on oxidizing N,N-dibenzylhydroxylamine (I) with lead tetraacetate Norman et al. (1) obtained a product which we had obtained earlier (2) by similar treatment of C-phenyl-N-benzylnitrone (II). Showing that formation of the nitrone (II) is the first step in the reaction of hydroxylamine (I) with $Pb(OAc)_4$, Norman et al. proposed a mechanism for the further reaction of nitrone (II) with $Pb(OAc)_4$ (see scheme 1).

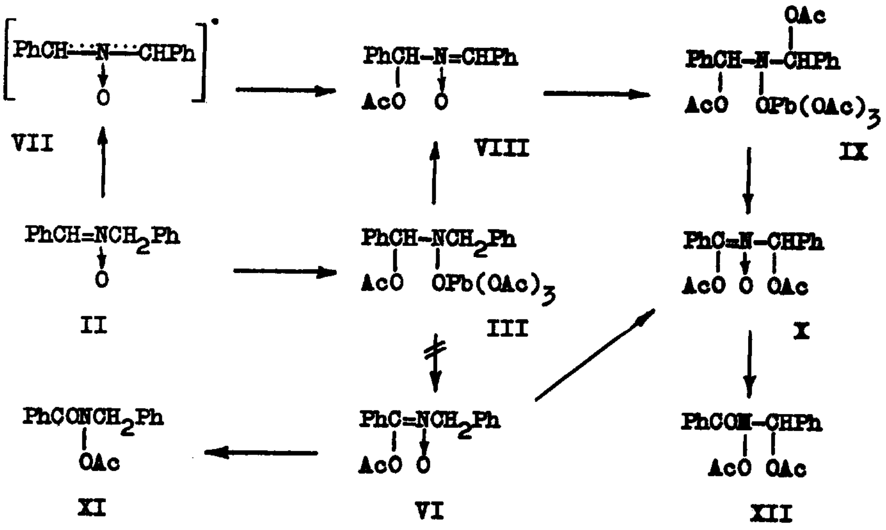


Scheme 1

However the mechanism is erroneous, for the following reasons. First, as we have shown in (3), apparently unknown to the English investigators, the reaction of aldonitrones with $Pb(OAc)_4$ is accompanied by acyl migration to the N-oxide oxygen and the final product from nitrone (II) has the structure of the diacylhydroxylamine (XII) but not of the nitrone (IV). Secondly, the mechanism depicted on scheme 1 is invalidated by our results with ^{14}C, described here.

The substance $Ph^{14}CH=N(O)CH_2Ph$ (II-^{14}C) was synthesized from $Ph^{14}CHO$ and N-benzylhydroxylamine according to conventional methods, the position of the label in the product being confirmed by hydrolysis of the latter to $Ph^{14}CHO$ and nonradioactive $PhCH_2NHOH$. The reaction of this labeled nitrone with 2 moles $Pb(OAc)_4$ (benzene, 20°) yielded diacylhydroxylamine (XII) where ^{14}C proved to be evenly distributed between the C atom of the benzoyl carbonyl and the α-C atom of the acetoxybenzyl group. This was borne out by hydrolysis of XII (refluxing with 10 % HCl under nitrogen) to benzoic acid and benzaldehyde, the molar radioactivities of which were in the ratio 52:47. The levelling of the isotopic composition of the azapropene carbons in II occurs just during the reaction with $Pb(OAc)_4$ and is not due to tautomerism of this compound since the ^{14}C distribution remained unchanged in the recovered II-^{14}C. These findings are inconsistent with Norman's scheme 1, where there is no stage with a symmetric intermediate, so that II-(methine-^{14}C) should afford compound (IV) containing all the radioactivity in the diacetoxybenzyl grouping.

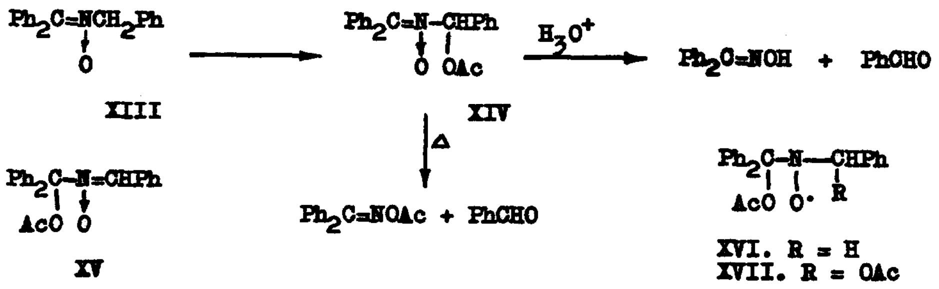
A mechanism consistent with the results of the isotopic experiments is represented in scheme 2. Its distinctive feature is the formation of the symmetric intermediate (IX), which eliminating AcOH and $Pb(OAc)_2$, transforms into the diacetoxynitrone (X) which rearranges to the final product (XII) as the result of acyl O,O' migration. Although formation of symmetric IX explains the observed levelling of the isotopic composition, the results in themselves do not permit a choice between two possible paths for the conversion of II into IX (II → III → VIII → IX or II → VII → VIII → IX). In the case of N-arylnitrones of both the aldo and the keto series the only object of attack on treatment with $Pb(OAc)_4$ is the nitrone grouping, so that the primary step is formation of a bond between acetoxyl and the C atom of the nitrone (4). If C-phenyl-N-benzylnitrone would have undergone a similar reaction, then it should have first yielded the adduct (III) which would have decompose to AcOH, $Pb(OAc)_2$ and monoacetoxynitrone (VIII). The latter would then have add a second mole of $Pb(OAc)_4$ to afford IX and further X. An alternative conversion of III to X, including the decomposition of III to VI as proposed by Norman et al. (1), must be rejected, because it does not provide for the formation of a symmetrical particle.



Scheme 2

It is well known, however, that in some compounds [see, for instance, (1)] the N-benzyl group is readily oxidized by Pb(OAc)$_4$ with loss of a methylene hydrogen and one could thus expect that in N-benzylnitrones this group would compete with the nitrone grouping as primary object of attack. If so, then transformation of nitrone (II) into the monoacetoxynitrone (VIII) would have proceeded through azaallylic radical (VII) (or corresponding anion) during formation of which the observed levelling of the isotopic composition would have taken place. The two mechanisms (II → III → VIII or II → VII → VIII) could be discriminated by means of the isotopic composition of monoacetoxynitrone (VIII) obtained from II-(methine-^{14}C). However, all our attempts to isolate compound (VIII) were fruitless, the reaction of II with 1 mole of Pb(OAc)$_4$ invariably leading to an equimolar mixture of the starting compound (II) and the end product (XII).

We therefore attempted to solve this problem by using C,C-diphenyl-N-benzylnitrone (XIII), which should yield the structural isomers (XIV) or (XV) on attack by Pb(OAc)$_4$ of its benzyl or nitrone groupings, respectively. We were able to obtain a monoacetoxy derivative of XIII on slowly adding to its benzene solution 1 mole of Pb(OAc)$_4$ in abs. benzene; yield 67 %, m.p. 116-118° (from ether - petroleum ether mixture). The spectral parameters of the product (including ^{13}C NMR spectrum) and the chemical properties (hydrolysis by aq. HCl at 20° to benzaldehyde and benzophenonoxime; thermolysis to O-acetylbenzophenonoxime and benz-



aldehyde) were in accord with formula (XIV) but not formula (XV).

Intermediate formation of the monoacetoxynitrone (XIV) occurs also when the nitrone (XIII) is reacted with excess $Pb(OAc)_4$, i.e. under conditions when it undergoes fargoing conversion [cf. (4)]. This was demonstrated by ESR, the spectrum (3_N x 3_H; a_N 14.5, a_H 8.2 ersteds) immediately upon mixing the reagents corresponding to the nitroxyl (XVI), changed in a few minutes to another (3_N x 2_H; a_N 13.9, a_H 1.1 ersteds) corresponding to the nitroxyl (XVII). The latter spectrum in turn appeared immediately on mixing solutions of $Pb(OAc)_4$ and acetoxynitrone (XIV). The radicals thus play the part of nitrone traps.

Owing to the different steric hindrances of the C=N bond in ketonitrone (XIII) and aldonitrone (II) the above proof that the primary object of $Pb(OAc)_4$ attack is the benzyl group cannot be automatically carried over to the latter compound. However, as can be seen from the formation of the nitroxyls (XVI and XVII) and the ease of fission of C,C,N-triphenylnitrone by lead tetraacetate (4), steric hindrances in C,C-diarylnitrones should not be very large. We believe therefore, that in the first stage of the conversion of II to XII the formation of VII is more probable than of III.

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