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FRAGMENTATION IN HYPOIODITE AND THE RELATED ALKOXYL RADICAL-INVOLVING REACTIONS OF ALCOHOLS WITH NITROGEN ATTACHED TO THE β-CARBON. [1)]

Hiroshi Suginome, Hiroaki Umeda and Tadashi Masamune,
Department of Chemistry, Faculty of Science,
Hokkaido University, Sapporo, Japan.

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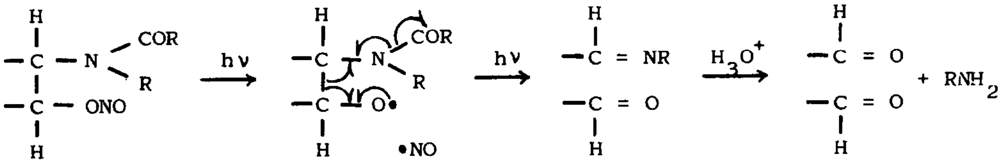
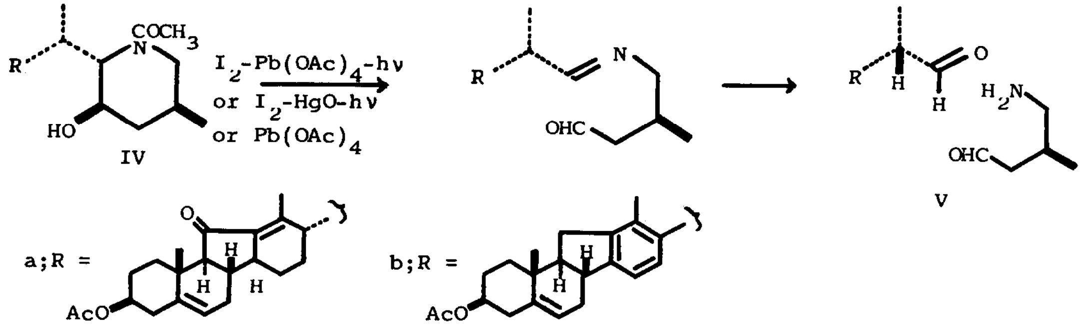
We have previously reported [2)] that the generation of alkoxyl radicals (partial formula II) by the irradiation of nitrite esters (partial formula I) with amide type nitrogen attached to the β-carbon of the nitrito group caused the cleavage of α,β carbon-carbon bond of this group and yielded aldehydes in substantial amounts after chromatography through an acidic column, as indicated in the scheme.

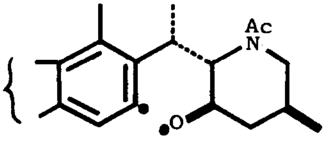


I II III

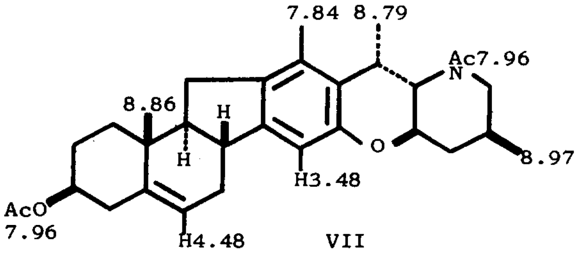
We have now found that this double β-scission can better be achieved by alternative procedures which generate alkoxyl radicals either photochemically or oxidatively, i.e., either by hypoiodite reaction [3,4)] or by lead tetraacetate oxidation. [5)]

For example, hypoiodite reaction of 3-O,N-diacetyl-3β,23β-dihydroxy-22,27-imino-11-oxojerva-5,13(17)-diene (IVa) [2)] with $Pb(OAc)_4$-I_2 reagent effected to produce 56% of pure aldehyde (Va), identical with a specimen obtained by nitrite photolysis [2)], and none of the other products were formed as proved by TLC. $Pb(OAc)_4$ oxidation of IVa was similarly found to be a clean reaction and afforded





VI



VII

61% of pure crystalline aldehyde (Va). Products and yields in the fragmentation reactions of IVa and 3-O,N-diacetylveratramine (IVb) [6], m.p. 272-273° under various conditions are shown in the TABLE. We also found that irradiation of IVb in the presence of HgO and I_2 [7] gave even better results and yielded a new aldehyde (Vb), m.p. 157-159°, with a yield as high as 73%, together with another new compound VII, m.p. $>$ 300° (9%). VII is formulated as an ether (VII), formed by the intramolecular combination of alkoxylaryl biradical (VI), by the NMR, (see assignments (τ) of signals in the formula), Mass spectrum (M^+, 491), U.V. (λmax 280, 286, 289 mμ (ε 5960, 6260, 6380)), and I.R. (no OH, 1736 cm^{-1}, OAc, 1629 cm^{-1}, N-Ac). Unexpectedly, the double β-scission product (V) was also obtained when IVa or IVb was shaken with HgO and I_2 in the dark at room temperature and the yield of V increased in the presence of pyridine as a base. Although the former result might be taken as evidence that the cleavage of C-C bond in IVa or IVb proceeds, at least to some extent, through a polar intermediate or a transition state of

TABLE

Yields of Products (%)

Reagents	Substrate		Aldehyde	Ketone	Recovered	Conditions
$Pb(OAc)_4-I_2$	a)	IVa	46	4	0	Cyclohexane
-hν	b)	IVb	56	0	0	80°, $\frac{1}{2}$hr
$Pb(OAc)_4$	c)	IVa	61	0	26	Benzene
	c)	IVb	23	0	22	80°, 4hr
$HgO-I_2$-hν	d)	IVa	50	0	21	Cyclohexane
	e)	IVb	73	0	5	80°, 3hr
$HgO-I_2$ dark	f)	IVa	11	1	58	Cyclohexane
	g)	IVb	25	0	45	Room Temp., 72hr
$HgO-I_2$	h)	IVa	35	0	38	Cyclohexane
-pyridine dark						Room temp., 70hr
$HgO-I_2$	i)	IVa	0	0	All recovered	Cyclohexane
$-C_6H_5SH$ dark						Room temp., 72hr

a) 450 W Hg arc lamp, $Pb(OAc)_4$ (4.5), I_2 (1.7)
b) 450 W Hg arc lamp, $Pb(OAc)_4$ (3.0), I_2 (1.8)
c) $Pb(OAc)_4$ (1.7)
d) 450 W Hg arc lamp, HgO (1.9), I_2 (2.8)
e) 150 W Hg arc lamp, HgO (1.9), I_2 (2.8)
f) HgO (1.7), I_2 (2.6)
g) HgO (1.3), I_2 (2.4)
h) pyridine (4), HgO (1.8), I_2 (2.6)
i) HgO (1.5), I_2 (2.0), thiophenol (2.0)

Arabic numerals in brackets denote molar proportions of reagents relative to substrates.

polar character [8), this possibility is excluded since the cleavage is entirely suppressed when thiophenol is added to the solution of substrate-HgO-I_2 in the dark. Therefore, it is concluded that the present fragmentation proceeds through a homolytic mechanism as in the case of nitrite photolysis. [2)

The fragmentation described here should prove useful in removing the piperidine ring from veratram alkaloids under mild non-basic conditions. A further advantage of this procedure over ionic fragmentation [9) is that the removal of the piperidine ring can readily be achieved in the compounds in which the imino-nitrogen of the heterocyclic ring is blocked by an acyl group and that the original configuration of a hydrogen attached to α-carbon (C_{20}) of potential formyl carbon is retained in the products.

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