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PHOTOCHEMICAL REARRANGEMENT OF VITAMIN B_6 OXIMES

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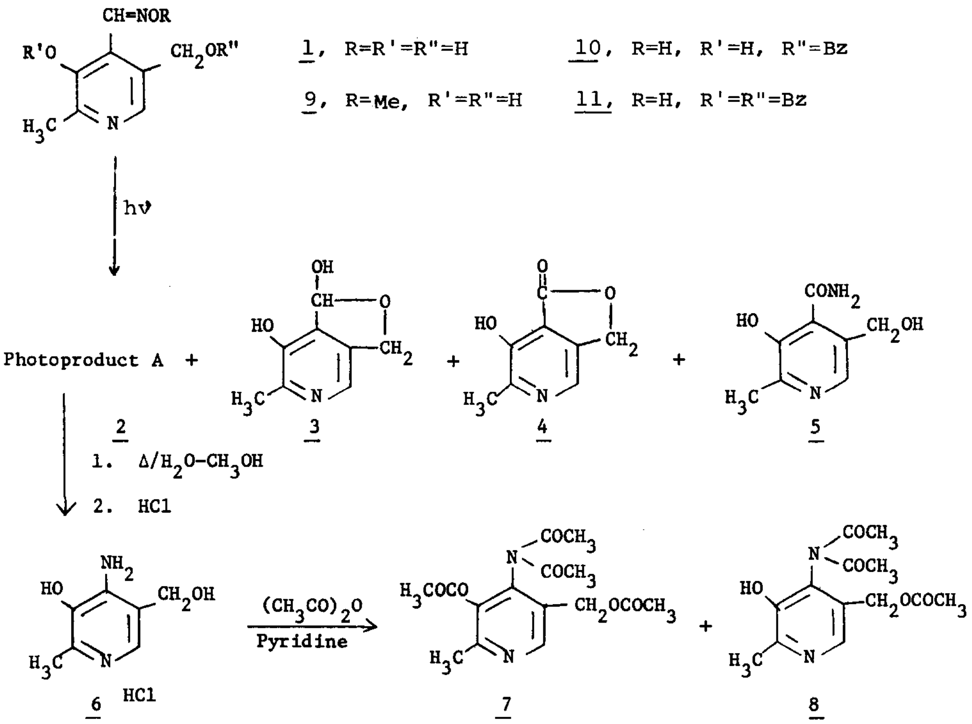
Photochemical rearrangements of oximes have received considerable attention in recent years. For example, Beckmann-type rearrangements,[1-7] syn-anti isomerization,[8,9] and conversion to oxazoles,[10] and nitriles[5,11] have been reported. In many cases, oxaziridines have been suggested as intermediates in photoreactions of oximes.[1-5]

We wish to report a unique conversion of pyridoxal oxime (1) to 4-amino-3-



Scheme 1

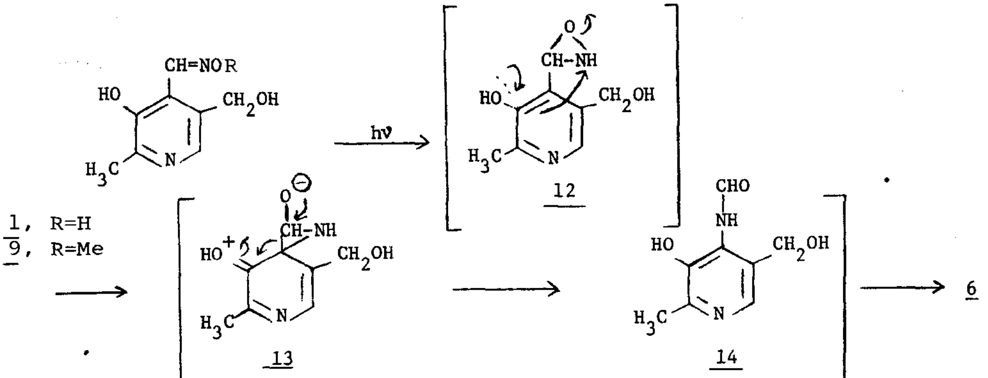
hydroxy-5-(hydroxymethyl)-2-methylpyridine hydrochloride (6) via a photochemical route (Scheme 1). This route, which represents a new photochemical transformation, is the first synthesis of the long-sought 4-amino analog of vitamin B_6.[12] The method should prove valuable for modifying vitamin B_6 in the 4-position, thus facilitating the synthesis of novel analogs for biological evaluation.

A methanolic solution of 1 (UV λ_{max}^{MeOH} 218, 260, 325 nm) was irradiated with a Hanovia 8A-1 quartz lamp until the spectrum changed to λ_{max}^{MeOH} 225, 275 nm. A crude hygroscopic photoproduct A was obtained, along with small quantities of at least three other compounds. During attempted purification and isolation, A was continuously converted to a stable product (λ_{max}^{MeOH} 228, 314 nm), which was isolated as the hydrochloride, m.p. 227-228° (over-all yield 45%), and its structure was shown to be 6 on the basis of elemental analysis and spectral data: MS M^+ at 154; NMR (D_2O) (δ) 2.40 (3) (CH_3), 7.83 (1) (6-H), I.R. ν_{KBr}^{max} 3365,3295, 3190 (OH's), 1640, 1623cm^{-1}. The structure of this compound was further confirmed by conversion into the tetraacetate 7, m.p. 126-7°, MS M^+ at 322; NMR ($CDCl_3$) (δ) 2.07 (3) (CH_3), 2.32 (3) (5-$OCOCH_3$), 2.48 (9) (3 and 4-$OCOCH_3$'s), 5.07 (2) (5-CH_2), 8.67 (1) (6-H). I.R. ν_{KBr}^{max} 1774, 1743, 1720 cm^{-1} ($OCOCH_3$'s). Partial deacetylation of 7 gave the triacetate, m.p. 156-157°, (M^+ at 280; NMR ($CDCl_3$) (δ) 2.058 (3) (CH_3), 2.12 (3) (5-$OCOCH_3$), 2.23 (3) (4—$COCH_3$), 2.42 (3) (4—$COCH_3$), 5.06 (2) (5-CH_2), 8.50 (1) (OH), 8.63 (1) (6-H). IRν_{KBr}^{max} 3260 (OH), 1766, 1741 and 1673 cm^{-1} (-$COCH_3$'s).

Two of the minor products of the photoreaction were isolated, and were identified as pyridoxal (3) and pyridoxic acid lactone (4). Another compound, m.p. 228-230°, isolated in very small quantity, showed in its mass spectrum a molecular ion at 182. It gave a positive Gibbs test, and its infrared absorption exhibited peaks at 3280, 3200, 1690 (C=O) cm^{-1}. These results indicated the structure 5 for this compound. No further work was done with 5, however, because of the paucity of the material.

In an attempt to elucidate the reaction mechanism as well as the general applicability of reaction, several experiments were carried out. Irradiation of 1 in *t*-BuOH, as well as of the methoxime 9 in methanol, provided *photoproduct A* (major), 3, and 4. Photolysis of the benzyloxy derivative 10 in methanol and subsequent heating of the crude product in aqueous methanol, followed by hydrolysis with 5N HCl, led to the isolation of 6 as the major compound. In contrast, similar treatment of the dibenzyloxy compound 11 gave no trace of 6. Also, photolysis[9] of isonicotinaldehyde oxime (syn), followed by heating of the crude photoproducts in aqueous methanol, yielded the corresponding *anti* isomer as the major product. No evidence for the formation of the corresponding 4-amino analog was found.

These results indicate the necessity of the presence of a hydroxyl group *ortho* to the aldoxime for this photochemical rearrangement. In view of this requirement and the fact that oxaziridines have been proposed as intermediates during photolysis of oximes,[1-5] we suggest the following mechanism for the conversion of 1 and 9 to 6:



Scheme 2

On the basis of this mechanism, the photoproduct A could be 12, a structure that could account for the observed instability of A. Work is now in progress to establish details of the scope and mechanism of the reaction.

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