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N-β-STYRYLAMIDINES - A NOVEL CLASS OF COMPOUNDS FROM AN ANOMALOUS BISCHLER-NAPIERALSKI REACTION*

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We like to report that an attempted $POCl_3$ cyclization of N-acetyl-β-(3,4-methylenedioxyphenyl)-β-N-pyrrolidinoethyl amine (I), m.p.112-114°[3] took an unexpected turn to afford in 50% yield the novel styrylamidine II, m.p. 117-119°, instead of the desired 3,4-dihydro-1-methyl-6,7-methylenedioxy-4-N-pyrrolidinoisoquinoline. The U.V. spectrum of II in 95% EtOH with a maximum at 328 mμ (log ϵ 4.37) was distinctly similar to that of trans-N-β-(3,4-methylenedioxystyryl) benzamide (IV)[4]. The NMR spectrum of II in $CDCl_3$ at 60 MC (TMS internal standard) showed the following signals: a) 4H multiplet at 1.88; b) 4H multiplet at 3.48; c) 3H singlet at 2.07; d) 1H doublet at 6.24 (J 13 cps); e) 1H doublet at 7.36; f) 2H singlet at 5.88, aromatics 2H, 6.73, 1H, 6.88 ppm. The trans-stereochemistry of II was derived from the agreement of the observed coupling constant of protons d and e with the value found (15 cps) for the olefinic protons in IV, which was significantly larger than the J value (8 cps), noted for the olefinic protons in 2-benzoyl-1-cyano-1,2-dihydroisoquinoline. Treatment of a $CDCl_3$ solution of II with D_2O at 25° led to significant loss of intensity of the methyl signal ($\sim$50% in 4 days), indicating that II was probably in equilibrium with the dienamine-enediamine III (not present in any detectable amount). This reaction, as monitored by NMR, did not alter other features of the spectrum of II. Exposure of II to hot mineral acid gave 6,7-methylenedioxy-2-(3,4-methylenedioxyphenyl) naphthalene[5], presumably via 3,4-methylenedioxyphenylacetaldehyde. Styrylamidine II was

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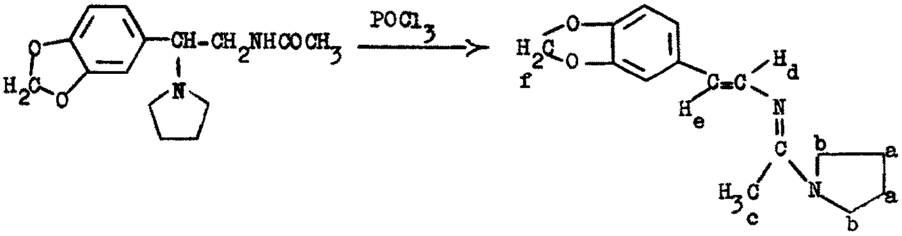
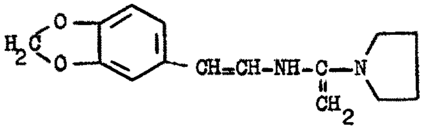
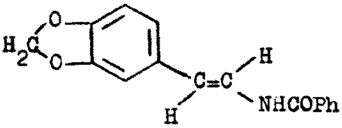
catalytically reduced with uptake of one mole of hydrogen, to afford the corresponding β-(3,4-methylenedioxyphenyl)-ethylamidine V, (HCl salt, m.p. 258-260°), with λ_{max} at 268 mμ (log ϵ 3.59) in close agreement with that found for I.



I II

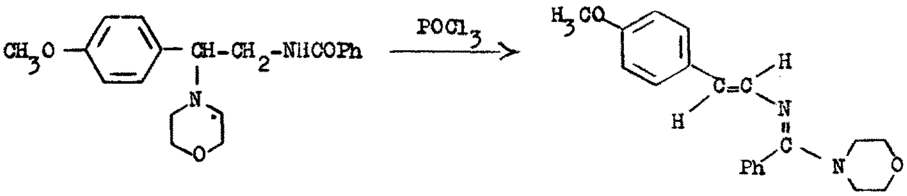


III



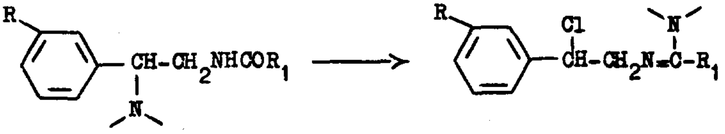
IV

N-Benzoyl-β-(4-methoxyphenyl)-β-N-morpholinoethylamine VI, m.p. 120-122°, was likewise transformed in 57% yield to the <u>trans</u>-N-styrylamidine VII, m.p.93-95°. Mild hydrolysis of VII by hot aqueous dioxane afforded N-β-(p-methoxystyryl) benzamide[6], m.p. 192°. Catalytic hydrogenation converted VII to the corresponding phenethylamidine, m.p. 45-47° (picrate, m.p. 145-146°), identical with an authentic sample prepared from N-benzoyl-β-(p-methoxyphenyl) ethylamine, m.p. 126-127° by $SOCl_2$ treatment, followed by reaction with morpholine. The arylvinyl amidine formation was a general reaction for amides of type I and VI, carrying electron-releasing groups in the <u>para</u> position to the side chain or their 2-furyl and 2-



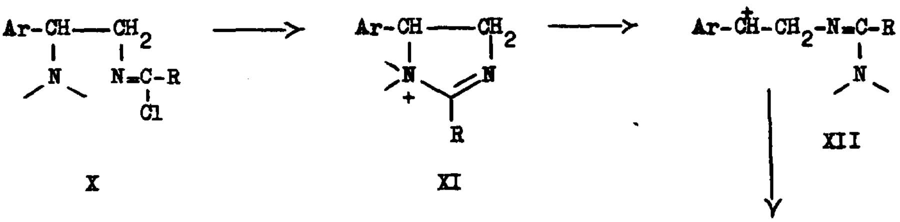
VI VII

thienyl analogues. In contrast, $POCl_3$ treatment of amides VIII led only to the chloro derivatives IX, which could not in general be transformed to styrylamidines.



VIII R = H, $-OCH_3$ IX R = H, $-OCH_3$

We believe that the reaction proceeds via the imino chloride X, the quaternary salt XI and the carbonium ion XII. In the case of amides I, VI and their 2-furyl and 2-thienyl analogues, XII eliminates a proton to form a styrylamidine, while the carbonium ion from VIII picks up a chloride ion to provide IX. This is in keeping with recently published results on the rates of formation of stilbenes in the acid-catalyzed dehydration of 1,2-diaryl ethanols[7].



X XI XII

II or IX

Attempts to prepare the novel β-styrylamidines by reaction of phenylacetaldehyde or β-bromostyrene with an amidine were unsuccessful; so was an attempt to eliminate halogen from the chloro compounds IX. However, since a variety of β-aryl-ethylenediamines and through them, their acyl derivatives, are readily accessible by a route developed earlier[8], their $POCl_3$ treatment constitutes an attractive synthesis of the hitherto unknown N-β-styrylamidines of type II.

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