FORMATION OF 1H-2,3-DIHYDRO-2,2,4-TRIMETHYL-1,5-BENZODIAZEPINE FROM o-PHENYLENEDIAMINE AND ACETONE

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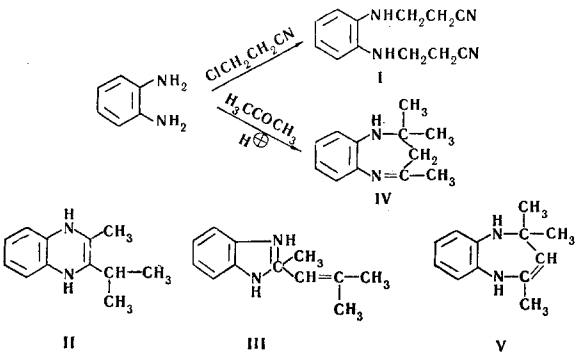
On the basis of a study of the UV, IR, PMR, and mass spectra and comparison with a sample of authentic structure it is shown that the product of the prototropic interaction of acetone with o-phenylenediamine has the 1H-2,3-dihydro-2,2,4-trimethyl-1,5-benzodiazepine structure.

Despite the numerous studies of the cyanoethylation of aromatic amines [1, 2], the monocyanoethyl derivative of o-phenylenediamine has not been reported. Braunholtz and Mann [3] obtained only N,N'-dicyanoethyl-o-phenylenediamine (I) by the action of acrylonitrile on this amine. There are data regarding the reaction of o-phenylenediamine with cyanoethyl ethers of phenol or β-naphthol [4], but no information regarding the structures of the compounds obtained was presented.

In attempts to obtain a monocyanoethylation product we carried out the reaction of o-phenylenediamine with an equimolar amount of β-chloropropionitrile, but only a dicyanoethylation product (I) was isolated under various conditions. If the condensation is carried out in acetone in the presence of triethylamine at 0-5°, the major reaction product is a substance of the composition $C_{12}H_{16}N_2$ with mp 124-125°. Control experiments indicated that β-chloropropionitrile and triethylamine only catalyze the condensation process as proton sources (due to splitting out of HCl). The formation of a compound with the composition $C_{12}H_{16}N_2$ by the reaction of o-phenylenediamine with acetone in the presence of hydrogen chloride was reported in 1905 by Ekeley and Wells [5], who assigned the 3-methyl-2-isopropyldihydroquinoxaline (II) structure to this compound. Later, Elderfield and co-workers [6] observed that 2-methylbenzimidazole is formed in the pyrolysis of this compound and therefore assumed that the 2-methyl-2-isobutenylbenzimidazoline structure (III) is more likely.



Mushkalo [7, 8] and Ried [9] found that o-phenylenediamine forms a compound of the same composition ($C_{12}H_{16}N_2$) by reaction with mesityl oxide and assigned the 1H-2,3-dihydro-2,2,4-trimethyl-1,5-benzodiazepine (IV) formula to it. The constants of our substance and the compounds studied by Mushkalo were

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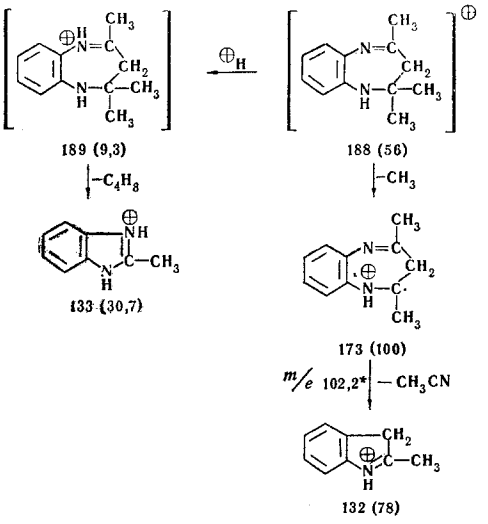
very close. This made it possible to assign structure IV to our substance, but the available data do not completely exclude alternative models II and III; we therefore deemed it necessary to carry out a more thorough study of the structure, especially because it was recently quite accurately proved that o-phenylenediamine forms 1,3-dibenzyl-2-phenylbenzimidazoline with benzaldehyde [10].

The UV spectrum of our sample (λ_{max} 315 nm, log ε 3.40) was identical to that described for IV [11] and was typical for o-phenylenediamine derivatives. Bands corresponding to the NH group (3300 cm^{-1}) and C=N group (1640 cm^{-1}) can be isolated in the IR spectrum. The PMR spectrum has four singlets with an intensity ratio of 6:2:3:1 at 1.20, 2.15, 2.35, and 3 ppm, which corresponds to six protons from the methyl groups in the 2-position, two protons from the methylene group, three protons from the methyl group in the 3-position, and one proton from an imino group. Alternative structures II and III do not have a CH_2 group, and the isopropyl group of structure II (or an isomeric structure due to migration of the double bond within the ring) should have a splitting of signals from the methyl groups due to the methine proton, but this is not observed. Models of the V type are excluded for the same reasons.

The mass spectrum of $C_{12}H_{16}N_2$ also corresponds to structure IV.



In addition to the molecular peak with m/e 188 (58.6% of the maximum), there is also a peak with m/e 189 (9.3%) which corresponds to the M + 1 structure, formed as a result of molecular ion collision. The presence of such a particle is confirmed by the peak of a metastable ion with m/e 92.7, which corresponds to the 189 − 57 = 132 transition. The residue split off in the process is recorded by a peak with m/e 57. The most intense peak is one with m/e 173 ($M-CH_3$), which is characteristic for gem dialkyl compounds. Cleavage of CH_3CN occurs after this, which is confirmed by the peak of a metastable ion with m/e 102.2; correspondingly, the metastable ion with m/e 63.7 corresponds to cleavage of CH_3CN from the ion with m/e 133.

Thus it can be considered to be proved that o-phenylenediamine reacts with acetone in the presence of acidic agents to form (just as in the case with mesityl oxide) πH-2,3-dihydro-2,2,4-trimethyl-1,5-benzodiazepine (IV). In the case of β-chloropropionitrile one might expect the parallel formation of 2-oxo-1,2,4,5-tetrahydro-1,5-benzodiazepine, as occurs during the analogous reaction of o-phenylenediamine with acrylic acid [12], but this process did not occur under our conditions, as verified by chromatography of the reaction mass in a thin layer of aluminum oxide using reference spots of authentic structure (traces of the starting material and I were detected).

EXPERIMENTAL

The IR spectra in mineral oil were obtained with an IKS-22 spectrometer at 700-2000 cm^{-1} with an NaCl prism and at 2500-3400 cm^{-1} with an LiF prism.

The UV spectra were obtained with an SF-4 spectrophotometer.

The PMR spectra of 20% solutions in benzene with trimethylsilane as the internal standard were obtained with a JNM-3 spectrometer at 60 MHz.

The mass spectrum was obtained with an MKh-1303 spectrometer with input of the sample into the ion source.

N,N'-Dicyanoethyl-o-phenylenediamine (I). A mixture of 24.8 g (0.23 mole) of o-phenylenediamine and 30.8 g (0.23 mole) of β-chloropropionitrile was refluxed in 50 ml of alcohol for 15-16 h. The mixture was cooled, the solution was diluted with water, and 8 g of sodium hydroxide was added. The resulting precipitate was separated, washed with water, and steam distilled to remove unchanged o-phenylenediamine. The residuel I [3.5 g (14%)] was crystallized from aqueous alcohol and had mp 119° (compare with [3]). The distillate after steam distillation was evaporated to give 14 g of unchanged o-phenylenediamine.

1H-2,3-Dihydro-2,2,4-trimethyl-1,5-benzodiazepine (IV). o-Phenylenediamine [10.8 g (0.1 mole)] was dissolved in 50 ml of dry acetone, and 10.1 g (0.1 mole) of triethylamine was added. β-Chloropropionitrile [10.7 g (0.12 mole)] was added to the resulting mixture with cooling and stirring. The resulting precipitate of triethylamine salt was separated, and 9.69 g (52%) of benzodiazepine IV with mp 124-125° (from hexane) [7-9] was precipitated from the filtrate with hexane. This product was identical to the sample obtained by the method in [7] according to chromatography and the PMR spectra. Found %: C 76.76; H 8.46; N 15.15. $C_{12}H_{16}N_2$. Calculated %: C 76.59; H 8.51; N 14.9. UV spectrum (in ethanol): λ_{max} 315 nm, log ε 3.40 [9]. IR spectrum: 3300, 1640, 1225 cm^{-1}. PMR spectrum: singlets at 1.20 (6H), 21.15 (2H), 2.35 (3H), and 3.0 (1H) ppm.

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