STUDIES IN THE IMIDAZOLE SERIES

LVIII.* DEBENZYLATION OF N-BENZYL-SUBSTITUTED 1H-PYRROLO[1,2-a]IMIDAZOLES AND 4H-PYRROLO[1,2-a]BENZIMIDAZOLES

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The debenzylation of N-benzyl-substituted 1H-pyrrolo[1,2-a]imidazoles and 4H-pyrrolo-[1,2-a]benzimidazoles under the influence of sodium in liquid ammonia was studied. From the IR and PMR spectra it was established that the compounds obtained have the structures of 7H-pyrrolo[1,2-a]imidazole and 3H-pyrrolo[1,2-a]benzimidazole derivatives. The debenzylation of 2,3-diphenyl-4-benzylpyrrolo[1,2-a]benzimidazole proceeds with the simultaneous reduction of the pyrrole ring and the formation of 1H-2,3-dihydro-2,3-diphenyl-pyrrolo[1,2-a]benzimidazole.

The synthesis of N-alkyl (aryl, aralkyl)-substituted 1H-pyrrolo[1,2-a]imidazoles [2-4] and 4H-pyrrolo-[1,2-a]benzimidazoles [2,5-8] has been described. In order to obtain derivatives of the indicated hetero-cycles without substituents attached to the nitrogen atom of the imidazole ring, we studied the debenzylation of several N-benzyl-substituted 1H-pyrrolo[1,2-a]imidazoles and 4H-pyrrolo[1,2-a]benzimid**a**zoles. The reactions were carried out using sodium (4-8 g-atom) in liquid ammonia, as described for removal of the benzyl group in the imidazole series [9] and other nitrogen-containing heterocycles [10]. The corresponding debenzylated derivatives of pyrrolo[1,2-a]imidazole (VI and VII) and pyrrolo[1,2-a]benzimidazole (XIX and XX), the structures of which could be established by means of IR and PMR spectroscopy, were obtained as a result of debenzylation of 1-benzyl-6-(p-tolyl)- and 1-benzyl-2,3,6-triphenylpyrrolo[1,2-a]imidazoles (II and III) and 1-benzyl-6-phenyl (or p-methoxyphenyl)pyrrolo[1,2-a]benzimidazoles (XIII and XIV).

A study of the IR spectra of VI, VII, XIX, and XX showed that they do not contain an NH group and consequently are not derivatives of 1H-pyrrolo[1,2-a]imidazole and 4H-pyrrolo[1,2-a]benzimidazole. It remained to assume that, at the instant that the $N-CH_2C_6H_5$ bond is reduced, a proton migrates from the imino group of the imidazole ring to the α or β position of the pyrrole ring.

For the solution of this problem we studied the PMR spectra of the debenzylated compounds (VI, VII, XIX, and XX) and of a number of N-substituted 1H-pyrrolo[1,2-a]-imidazoles (II-V) and 4H-pyrrolo[1,2-a]-benzimidazoles (XIII-XVIII). It was established that the PMR spectra of the 1-alkyl(aryl, aralkyl)-sub-stituted 1H-pyrrolo[1,2-a]-imidazoles (II-V, Table 1) are characterized by the presence of proton signals at 5.13-5.50 ppm (the 7 position), 6.44 ppm (the 2 position), and 6.52-6.81 ppm (the 3 position). The signals of the proton in the 5 position of the two-ring compounds are found in the spectra along with the signals of the protons of the benzene ring of the substituents at 6.7-7.5 ppm. In the PMR spectra of 4-alkyl(aralkyl)-pyrrolo[1,2-a]benzimidazoles (XVI-XVIII) the signals of the protons in the 3 position are observed at 5.55-5.59 ppm, while the signals of the proton in the 1 position are observed at 6.9-8.0 ppm along with the signals of the protons of the benzene rings of the three-ring compounds and the substituents.

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^{*}See [1] for communication LVII.

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TABLE 1. Chemical Shifts in the PMR Spectra of Pyrrolo[1,2-a]-imidazole and Pyrrolo[1,2-a]benzimidazole Derivatives



Our assignment of the chemical shifts of the protons in the pyrrolo[1,2-a]-midazole and pyrrolo[1,2-a]-benzimidazole rings is in agreement with the results of other investigators of the PMR spectra of pyrrole derivatives [11] and pyrrolo[1,2-a]-benzimidazole derivatives [12], in which the signals of the protons of the α position of the pyrrole ring appear at weaker field than the signals of the β protons.

On inspection of the PMR spectra of the debenzylated pyrrolo[1,2-a]imidazole (VI and VII) and pyrrolo[1,2-a]benzimidazole (XIX and XX) derivatives, it is seen that they do not contain signals corresponding to the protons in the 7 and 3 positions, respectively, while there are distinct signals with an intensity of two proton units at 4.64-4.70 ppm (VI and VII) and 5.15-5.38 ppm (XIX and XX), which should be assigned to the signals of the protons of the CH₂ group. Their location at comparatively weak field indicates the presence of systems of aromatic or conjugated double bonds next to the CH₂ group and is thus in agreement with the concept regarding their 7 and 3 positions, respectively.

Thus, it was established that VI and VII are 7H-pyrrolo[1,2-a]imidazole derivatives, while XIX and XX are 3H-pyrrolo[1,2-a]benzimidazole derivatives. The first of these compounds have not been reported, while the second are known only in the form of one representative -1,3,3-trimethylpyrrolo[1,2-a]benzimid-azole, obtained by the condensation of o-phenylenediamine with the nitrile of α, α -dimethyllevulinic acid [13].



It should be noted that this sort of isomerization has not been described in 1-substituted 2-alkyl(aryl)aminopyrroles or any other compounds with analogous structures.

The action of sodium (8.4 g-atom) in liquid ammonia on 2,3-diaryl-4-benzylpyrrolo[1,2-a]benzimidazoles, for example XV, results in reduction of the pyrrole ring along with debenzylation, and 2,3-dihydro-2,3-diphenyl-1H-pyrrolo[1,2-a]benzimidazole (XXI) is formed. The structure of XXI was confirmed by IR and PMR spectra: by the absence of a band from the valence vibrations of the NH group and by the presence of a multiplet from the signals of the protons of the hydrogenated pyrrole ring.



EXPERIMENTAL

The 1H-pyrrolo[1,2-a]imidazole (III-V, Table 1) [3,4] and 4H-pyrrolo[1,2-a]benzimidazole (XVI-XVIII) [6] derivatives were prepared as described previously.

<u>1-Benzyl-2-methyl-3-(p-methylphenacyl)imidazolium Bromide (1)</u>. This was obtained in 79% yield by the reaction of 1-benzyl-2-methylimidazole [9] with p-methylphenacyl bromide by the method in [14] and had mp 210-212°C (by precipitation by ether from absolute ethanol). Found %: Br 20.9. $C_{20}H_{21}BrN_2O$. Calculated %: Br 20.7.

<u>1-Benzyl-6-(p-tolyl)pyrrolo[1,2-a]imidazole (II)</u>. This was obtained in 47% yield by cyclization of I in ethanol in the presence of sodium ethoxide by the method in [4] and had mp 113-115° (decomp., from ethanol). Found %: C 83.5; H 6.3; N 9.6. $C_{20}H_{18}N_2$. Calculated %: C 83.9; H 6.3; N 9.8. The picrate had mp 199-201° (decomp., from acetic acid). Found %: N 13.6. $C_{20}H_{18}N_2 \cdot C_6H_3N_3O_7$. Calculated %: N 13.6.

 $\underline{2,3,6-\text{Triphenyl-7H-pyrrolo}[1,2-a]\text{imidazole (VII)}. This was obtained as described above in 36% yield by debenzylation of III. The colorless crystals melted at 247-249° (from anhydrous ethanol). Found %: C 86.2; H 5.5; N 8.2. C₂₄H₁₈N₂. Calculated %: C 86.2; H 5.4; N 8.4. The picrate had mp 251-252° (decomp., from dimethylformamide). Found %: C 64.0; H 4.0; N 12.6. C₂₄H₁₈N₂ · C₆H₃N₃O₇. Calculated %: C 63.9; H 3.7; N 12.1.$

<u>1-Benzyl-2-methylbenzimidazole (VIII)</u>. A. A solution of 27 g (0.109 mole) of the benzyl chloride salt of dimethylaniline in 15 ml of water and 13.2 g (0.1 mole) of 2-methylbenzimidazole [15] were added to a solution of 4.2 g (0.105 mole) of NaOH in 100 ml of water. The mixture was heated and worked up as described for 1-benzylbenzimidazole [16] to give 16.2 g (73%) of a product with bp 181-183° (3 mm) and mp 78-80° (from water). Found %: C 80.8; H 6.3; N 12.5. $C_{15}H_{14}N_2$. Calculated %: C 81.0; H 6.3; N 12.6. In [17] this compound is described in the form of the hydrochloride with mp 297° and the picrate with mp 197-199° in [18].

B. A solution of 99 g (0.5 mole) of N-benzyl-o-phenylenediamine [19] in 500 ml of acetic acid was refluxed for 5 h, poured into water, and neutralized with ammonium hydroxide. The base was extracted with chloroform, the solvent was removed by distillation, and the residue was vacuum-distilled to give 88 g (80%) of VIII with bp 181-183° (3 mm) and mp 78-80° (from water).

<u>1,2-Dibenzylbenzimidazole (IX)</u>. This was obtained in 94% yield by benzylation of 2-benzylbenzimidazole, as described for VIII, and had mp 149-151° (from ethanol). Found %: C 84.7; H 5.8; N 9.5. $C_{21}H_{18}N_2$. Calculated %: C 84.5; H 6.1; N 9.4.

1-Benzyl-2-methyl-3-phenacylbenzimidazolium Bromide (X). This was obtained in 82% yield by the reaction of VIII with phenacyl bromide in acetone by the method in [5] and had mp 255-256° (decomp., from water). Found %: C 65.2; H 4.8; Br 18.7; N 6.7. $C_{23}H_{21}BrN_2O$. Calculated %: C 65.5; H 5.0; Br 19.0; N 6.7.

<u>1-Benzyl-2-methyl-3-(p-methoxyphenacyl)benzimidazolium Bromide (XI)</u>. This was obtained in 77% yield from VIII and p-methoxyphenacyl bromide, as in the case of X, and had mp 237-239° (decomp., from methanol). Found %: C 63.5; H 5.0; Br 18.2; N 5.9. $C_{24}H_{23}BrN_2O_2$. Calculated %: C 63.8; H 5.1; Br 17.7; N 6.2.

1,2-Dibenzyl-3-phenacylbenzimidazolium Bromide (XII). This compound, like X, was obtained in 76% yield from IX and phenacyl bromide and had mp 198-199° (decomp., from water). Found %: C 70.4; H 5.1; Br 16.0; N 5.4. $C_{29}H_{25}BrN_2O$. Calculated %: C 70.0; H 5.1; Br 16.1; N 5.6.

<u>2-Phenyl-4-benzylpyrrolo[1,2-a]benzimidazole (XIII)</u>. This was obtained in 92% yield by the cyclization of X in water in the presence of sodium bicarbonate by the method in [5] and had mp 123-124° (decomp., from ethanol). Found %: C 85.8; H 5.7; N 8.8. $C_{23}H_{18}N_2$. Calculated %: C 85.7; H 5.6; N 8.7.

 $\frac{2-(p-Methoxyphenyl)-4-benzylpyrrolo[1,2-a]benzimidazole (XIV). Like XIII, this was obtained in 95\% yield by cyclization of XI and had mp 159-160° (decomp., from dimethylformamide). Found %: C 81.6; H 5.9; N 8.0. C₂₄H₂₀N₂O. Calculated %: C 81.8; H 5.7; N 7.9.$

2,3-Diphenyl-4-benzylpyrrolo[1,2-a]benzimidazole (XV). Like XIII, this was obtained in 94% yield by cyclization of XII and had mp 157-158° (decomp., from ethanol-dimethylformamide (1:1)]. Found %: C 87.7; H 5.5; N 7.2. $C_{29}H_{22}N_2$. Calculated %: C 87.4; H 5.6; N 7.0.

<u>2-Phenyl-3H-pyrrolo[1,2-a]benzimidazole (XIX)</u>. Minute lumps of sodium [1.3 g (0.6 g-atom)] were added with stirring to a solution of 2.1 g (0.07 mole) of XIII in 250 ml of liquid ammonia. The reaction mass was stirred for 10 min, 3.3 g (0.6 mole) of NH₄Cl was added, and the ammonia was removed by evaporation in air. Water (100 ml) was added to the solid residue, and the precipitate was filtered and washed with water to give 0.9 g (60%) of a product with mp 217-218° (decomp., from methanol). Found %: C 82.6; H 5.3; N 12.1. $C_{16}H_{12}N_2$. Calculated %: C 82.7; H 5.2; N 12.1.

 $\underbrace{2,3-\text{Dihydro}-2,3-\text{diphenyl-1H-pyrrolo}[1,2-a]\text{benzimidazole (XXI)}. \text{ Very fine lumps of sodium [1.5 g} (0.65 g-atom)] were added to a suspension of 3.1 g (0.077 mole) of finely ground XV in 500 ml of liquid ammonia. The reaction mass was stirred for 10 min and worked up as described for the preparation of XIX to give 1.4 g (58%) of colorless crystals with mp 193-194° (from ethanol) that were slightly soluble in ether and insoluble in water. PMR spectrum (in CDCl₃): 4.55 ppm (1-CH₂), 4.13 ppm (multiplet, 2-CH, 3-CH), 6.9-8.1 ppm (C₆H₅, C₆H₄). Found %: C 85.2; H 5.8; N 8.8. C₂₂H₁₆N₂. Calculated %: C 85.1; H 5.8; N 9.0.$

The PMR spectra were recorded with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard: the spectra of II-IV, VI, VII, and XV in $CDCl_3$, of V and XVI in CCl_4 , of XIII, XIV, XIX, and XX in dimethyl sulfoxide, and of XVII and XVIII in $CHCl_3$ were obtained.

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