# DIRECT INTRODUCTION OF HETEROCYCLIC RESIDUES IN THE OXINDOLE RING

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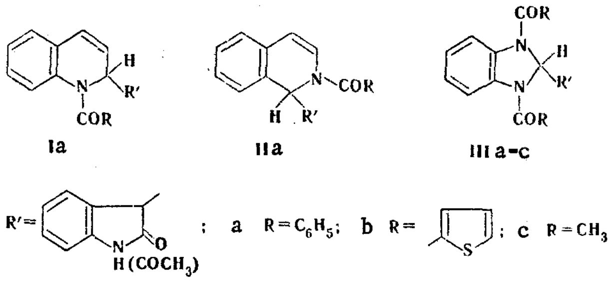
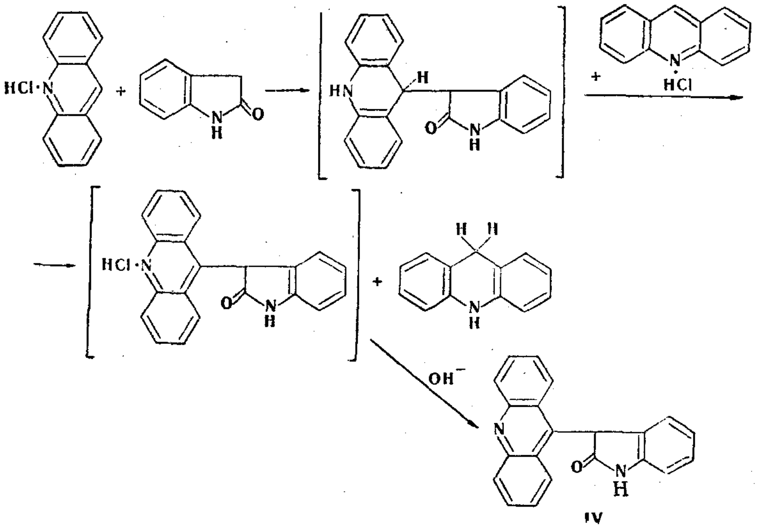
It has been reported [1] that salts of some N-acyloxyheteroaromatic cations hetarylate 1-methyloxindole in situ. It seemed extremely probable that the salts of more electrophilic N-acylheteroaromatic cations also can be used for the direct introduction of a heterocyclic residue in the oxindole ring, especially since similar salts have proved to be suitable for the hetarylation of the most diverse CH acids with $pK_a \leqslant 20$-$21$ [2].

In fact, we obtained the corresponding oxindole derivatives (I-III) by reaction of N-heteroaromatic bases with oxindole in acetic anhydride or an inert aprotic solvent in the presence of acyl halides:



A pyridine residue cannot be introduced in the oxindole ring by this method. When the reaction is carried out in acetic anhydride, in addition to hetarylation, acetylation of the oxindole fragment at the NH group rather than at the OH group (IIIc) occurs.



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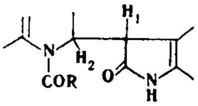
The introduction of an acridine residue in the oxindole ring is readily accomplished by reaction of protic acridinium salts, as in the acridinylation of indole and mimethylaniline [3].

Intense absorption bands at 1650-1750 $cm^{-1}$, which correspond to the carbonyl groups of N-acyl residues and an oxindole fragment, are observed in the IR spectra of I-III. In addition, the IR spectra of all I-IV contain absorption bands at 3300-3500 $cm^{-1}$, which are related to the oxindole NH group, whereas similar bands are absent in the spectrum of IIIc.

A quartet of an AB system formed by the signals of the $H_1$ and $H_2$ protons is present in the PMR spectra of I-III:



We assigned the doublet with δ 8.74 ppm to the $H_1$ proton and the doublet with δ 5.8-6.0 ppm to the $H_2$ proton. The weak-field singlet with δ 10.54 ppm was assigned to the resonance of the NH proton in the oxindole fragment in I-IV (a, b).

The mass spectra of the compounds obtained are similar in many respects and completely confirm their structure. In the first step of the fragmentation of the molecular ion, the amide bond in the heteroaromatic residue undergoes cleavage, as a result of which fragment ions with masses corresponding to an acyl residue and an $[M - \text{acyl}]^+$ ion appear in the spectrum, after which the interannular bond undergoes cleavage to give an ion with mass 132 (an oxindole fragment) or the ion of the corresponding heterocyclic residue.

## EXPERIMENTAL

The IR spectra of solutions of the compounds in chloroform were recorded with a UR-20 spectrometer. The mass spectra were obtained with Varian CH-6 and MAT-311 spectrometers under the following conditions: an accelerating voltage of 3 kV, a cathode emission current of 300 μA, an ionizing voltage of 70 eV, and an ion-source temperature of 80°C. The PMR spectra of solutions in $d_6$-dimethyl sulfoxide were recorded with a Varian XL-100 spectrometer at 100 MHz and room temperature with tetramethylsilane as the internal standard. Chromatography on Silufol was accomplished by elution with chloroform and development with iodine vapors and in UV light.

3-(2-Benzoyl-1,2-dihydroisoquinol-1-yl)-2-oxindole (II). A mixture of 2.6 g (0.02 mole) of isoquinoline, 1.3 g (0.01 mole) of oxindole, and 1.4 g (0.01 mole) of benzoyl chloride in 10 ml of dry benzene was refluxed for 8 h, after which it was subjected to steam distillation, and the residue in the distillation flask was separated and recrystallized from 70% ethanol to give 0.5 g (14%) of a product with mp 190-191°C and $R_f$ 0.5. IR spectrum: 1650, 1700 (C=O), 3430 $cm^{-1}$ (NH). Found: C 78.6; H 4.6; N 7.3%. $C_{24}H_{18}N_2O_2$. Calculated: C 78.9; H 4.9; N 7.6%.

The compounds listed below were similarly obtained.

3-(1-Benzoyl-1,2-dihydroquinol-2-yl)-2-oxindole (I). This compound, with mp 190-191°C (from 70% ethanol) and $R_f$ 0.5, was obtained in 28% yield. IR spectrum: 1665, 1710 (C=O); 3425 $cm^{-1}$ (NH). Found: C 78.8; H 5.2; N 7.8%. $C_{24}H_{18}N_2O_2$. Calculated: C 78.9; H 4.9; N 7.6%.

3-(1,3-Dibenzoylbenzimidazolin-2-yl)-2-oxindole (IIIa). This compund, with mp 240-241 °C (from n-butanol) and $R_f$ 0.4, was obtained in 14% yield. IR spectrum: 1660, 1700 (C=O); 3428 $cm^{-1}$ (NH). Found: C 79.2; H 4.1; N 9.5%. $C_{29}H_{20}N_3O_3$. Calculated: C 79.0; H 4.4; N 9.2%.

3-[1,3-Di(2-thenoyl)benzimidazolin-2-yl]-2-oxindole (IIIb). This compound, with mp 2.62-263°C (from dimethylformamide) and $R_f$ 0.3, was obtained in 21% yield. IR spectrum: 1665, 1720 (C=O); 3435 $cm^{-1}$ (NH). Found: C 63.5; H 3.4; N 8.7; S 13.3%. $C_{25}H_{16}N_3O_3S_2$. Calculated: C 63.8; H 3.4; N 8.9; S 13.6%.

1-Acetyl-3-(1,3-diacetylbenzimidazolin-2-yl)-2-oxindole (IIIc). This compound, with mp 240-241°C (from n-butanol) and $R_f$ 0.4, was obtained in 22% yield. IR spectrum: 1650, 1670, and 1710 cm$^{-1}$ (C=O). PMR spectrum: 2.67 ($COCH_3$), 7.26 (oxindole H), 8.12 (benzimidazoline H), and 6.40-8.70 ppm (aromatic Protons). Mass spectrum, m/e values (peak intensities in percent): 89 (14.13); 90 (12.02); 91 (35.28); 92 (13.82); 93 (7.85); 97 (3.48); 101 (4.02); 102 (6.83); 103 (9.62); 104 (9.87); 105 (20.96); 106 (9.33); 107 (4.33); 108 (12.27); 115 (7.03); 116 (7.21); 117 (13.12); 118 (74.69); 119 (100); 120 (9.23); 122 (13.35); 128 (6.80); 129 (4.59); 130 (16.84); 131 (15.51); 132 (17.60), 133 (6.12); 142 (3.25); 143 (8.51); 144 (4.51); 146 (15.01); 147 (22.63); 159 (9.49); 160 (9.0); 161 (23.62); 162 (3.95); 171 (8.03); 173 (4.44); 174 (7.63); 189 (6.84); 203 (18.64); 204 (9.48); 265 (13.69); 288 (4.80); 290 (4.85); 307 (12.38); 308 (12.52); 349 (33.39); 350 (3.1). Found: C 66.5; H 5.0; N 11.0%. $C_{21}H_{19}N_3O_4$. Calculated: C 66.8; H 5.0; N 11.1%.

3-(9-Acridinyl)-2-oxindole (IV). A mixture of 3.2 g (0.015 mole) of acridine hydrochloride and 1 g (0.007 mole) of oxindole in 10 ml of dry dimethylformamide was heated at 100°C for 8 h, after which it was steam distilled, and the residue in the distillation flask was separated and recrystallized from n-butanol to give 1.2 g (55% based on oxindole) with mp 360-361°C and $R_f$ 0.5. IR spectrum: 1710 (C=O) and 3440 cm$^{-1}$ (NH). PMR spectrum: 10.40 (NH), 7.20 (oxindole H), and 6.87-8.32 ppm (aromatic protons). Mass spectrum: 31 (40.9); 36 (5.54); 38 (3.22); 40 (3.14); 43 (4.05); 44 (10.26); 51 (3.19); 63 (3.53); 73 (3.84); 76.1 (3.30); 77 (4.17); 89 (4.40); 93 (3.75); 104 (4.13); 105 (3.18); 113 (3.43); 126 (5.62); 128 (3.67); 133 (6.39); 134 (5.55); 140 (6.89); 141 (3.63); 151 (4.93); 152 (3.86); 155 (7.33); 167 (4.33); 177 (3.85); 178 (7.78); 179 (22.26); 180 (7.40); 193 (3.90); 253 (3.53); 254.3 (10.89); 255 (3.47); 264 (3.50); 266 (7.67); 267 (15.88); 268 (14.84); 282 (19.38); 283 (14.10); 293 (3.34); 308 (3.09); 309 (23.92); 310 (100); 311 (24.41); 312 (2.44). Found: C 81.4; H 4.2; N 8.9% $C_{24}H_{14}N_2O$. Calculated: C 81.3; H 4.5; N 9.0%.

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