PLANCHE REARRANGEMENT IN INDOLINES WITH ACCEPTOR SUBSTITUENTS. 2.* PYRROLIDONE RING FORMATION FROM THE REACTION BETWEEN 1,3,3-TRIMETHYL-ω-CYANOMETHYLENEINDOLINE AND o-AMINOPHENOL

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It was found that when 1,3,3-trimethyl-ω-cyanomethyleneindoline was condensed with o-aminophenol in polyphosphoric acid, a complex heterocyclic system containing a pyrrolidone ring was formed as a result of the Planche rearrangement.

In a previous report we established that the reaction between 1,3,3-trimethyl-ω-cyanomethyleneindoline (I) and o-phenylenediamines yielded, via the Planche rearrangement, 2-methyleneindolines having methylbenzimidazoline substituents in position 3 rather than position 2 of the indoline ring [1].

It was considered worthwhile examining the reaction between nitrile I and o-aminophenol under the same conditions. The reaction could be expected to afford benzoxazole salt III, a Planche rearrangement product, rather than compound II [1]. Typically, these salts are very readily hydrolyzed, a reaction which proceeds with the breaking of the C–O bond [2, 3]. In our case, therefore, N-acyl-o-aminophenol IV could be expected to form. It is well known that 2-methyleneindolines having both phenol and amide groups as substituents can form more complex heterocyclic systems as a result of intramolecular addition of OH or NH groups at the exocyclic double bond [4-6]. In the case of indoline IV two alternative structures, V and VI, are possible.

The ^1H and ^{13}C NMR spectra indicated that a complex heterocyclic system was formed. For example, the PMR spectrum of the compound revealed signals from two very different methyl groups at 1.30 and 1.60 ppm, as well as a CH_2 signal in the form of two doublets (AB system: 2.41; 2.88, J = 18 Hz). In the ^{13}C NMR spectrum the sp^3 hybridized $C_{(2)}$ atom signal at 90.9 ppm was of particular interest. By comparing the chemical shift value of this signal with the similar shift for methylbenzimidazole derivatives of 2-methyleneindoline [1] and setting it against the ^{13}C spectra of similar compounds [6], it became evident that an N–C–N triad was present in the synthesized substance. On the basis of the above findings we were able to lend our support to structure V in preference to the other possible cyclic structure. PMR spectra recorded in the presence of a Lanthanide Shift Reagent ($Eu(fod)_3$) corroborated the occurrence of this structure. Coordination (LSR) took place at the carbonyl oxygen. When the LSR was added, the observed order of Lanthanide induced shifts (LIS) was in complete agreement with structure V: $C_{(3)}-CH_3$ 1.6 ppm; $C_{(2)}-CH_3$ 3.4 ppm; $N-CH_3$ 2.6 ppm; CH_2 6.6 and 7.6 ppm. The IR spectrum of the compound exhibited bands centered around 1670 cm^{-1}, which is quite typical of a pyrrolidone ring carbonyl group.

*For Communication 1, see [1].

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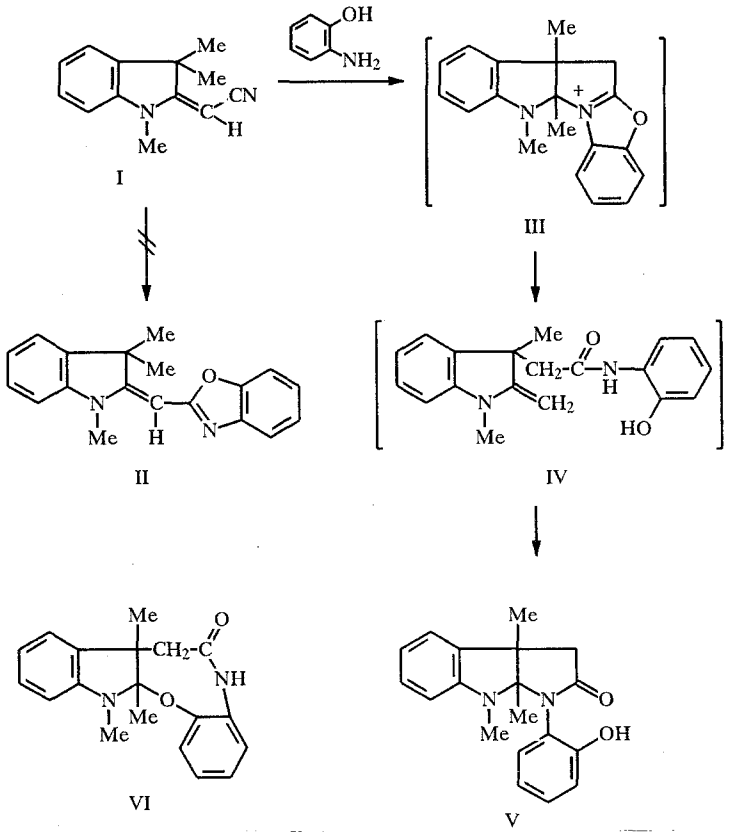
TABLE 1. PMR Spectra of Compounds V and VII

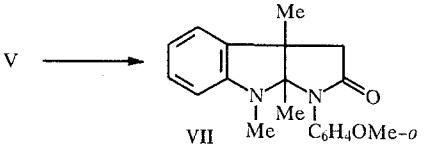
Compound (solvent)	$C_{(3)}$–CH_3, s	$C_{(2)}$–CH_3, s	N–CH_3, s	CH_2, d (J, Hz)	7-H, d (J, Hz)	Aromatic and other protons, ppm
V (C_6D_6)	0,83	1,24	2,26	2,41; 2,88 (18)	6,32	6,82...6,99 (7H, m, Ar); 8,33 (1H, m, OH)
V ($CDCl_3$)	1,30	1,60	2,61	2,71; 3,12 (18)	6,52	6,71...7,28 (8H, m, Ar, OH)
V (DMSO)	1,30	1,62	2,60	2,83; 3,44 (18)	—	6,49...7,51 (8H, m, Ar); 9,52 (1H, s OH)
V (CF_3COOD)	2,01	3,24	4,39	4,02 s	—	7,20...8,10 (9H s, Ar, OH)
VII ($CDCl_3$)	1,27; 1,28	1,48; 1,63	2,33; 2,58	2,66; 2,75; 2,96; 3,06 (16,6)	6,32; 6,48 (8,0)	3,34; 3,80 (3H, s, OCH_3); 7,09...7,30 (7H, m, Ar)
VII (CF_3COOD)	1,68	2,93	3,68	3,73	—	4,07 (3H, s, OCH_3); 6,81...7,72 (9H, m, Ar)

TABLE 2. ^{13}C NMR Spectra of Compounds V and VII

Compound (solvent0	N–CH_3	$C_{(2)}$–CH_3 ($=CH_2$)	$C_{(3)}$–CH_3	$C_{(3)}$	$C_{(2)}$	$C_{(10)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	Others and unidentified carbon atoms
V ($CDCl_3$)	15,3	27,2	20,7	48,7	90,9	40,6	104,9	133,0	146,0	171,9 (C=O); 152,6 (C_{12}); 121,5; 121,3; 116,0; 117,1; 118,5; 127,3; 128,4; 128,7
V (CF_3COOD)	35,9	15,6	23,2	58,8	198,8	46,0	117,2	140,7	145,2	120,4; 124,8; 125,2; 125,8; 128,3; 132,2; 133,1; 133,4; 150,3; 172,8 (C=O)
VII ($CDCl_3$)	16,8; 18,5	28,0; 29,2	22,4; 22,5	50,4; 50,5	92,5; 92,6	42,3; 42,7	105,6; 105,9	113,8; 135,0	148,3; 149,2	55,4; 55,8 (OCH_3); 112,1; 112,3; 117,8; 118,3; 120,6; 121,1; 122,8; 123,1; 125,2; 125,9; 128,4; 128,9; 130,2; 130,6; 132,3; 154,5; 156,7; 157,4; 172,6; 172,9 (C=O)
VII (CF_3COOD)	36,1	15,8	23,5	58,9	199,0	46,4	117,3	140,9	145,3	57,9 (OCH_3); 114,9; 124,1; 125,9; 127,9; 131,9; 133,1; 133,2; 133,4; 154,9; 179,4 (C=O)

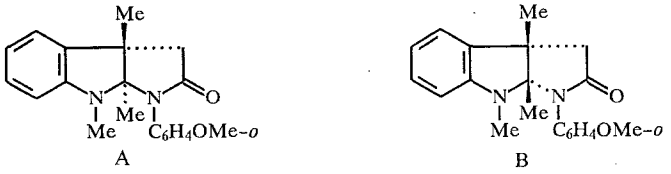


To obtain additional confirmation regarding the structure of compound V, we alkylated it with methyl p-toluenesulfonate in alkaline medium.

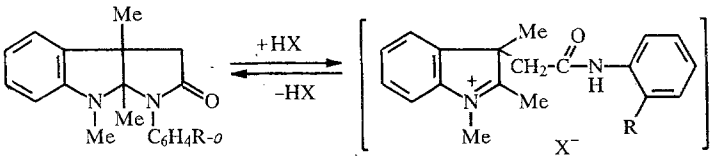


Methoxy group analysis in the resultant compound VII, in conjunction with the characteristic OMe group signal in the ^{1}H and ^{13}C NMR spectra (3.80 and 55.8 ppm, respectively), provided unambiguous confirmation that a free phenol group was present in compound V.

It was interesting that all the signals in the ^{1}H and ^{13}C NMR spectra of compound VII were split, a fact that can be explained by the existence of two diastereoisomers for compound VII.



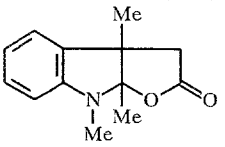
Addition of deutero methanol to a solution of compounds V and VII in deutero chloroform did not bring about deutero exchange of the methyl group at position 2, even when these compounds were kept in the solvents for 7 days. This indicated that the pyrrolidone ring is extremely stale in neutral media. At the same time, in ^{13}C NMR spectra recorded in deuterized trifluoroacetic acid the $C_{(2)}$ atom signal in compounds V and VII appeared at 198.8 and 190.0 ppm, respectively, which suggested that the pyrrolidone ring is destroyed in acid medium.



V, VII

The splitting of signals mentioned above was not, of course, observed in either the PMR or ^{13}C NMR spectra for compound VII in deuterized trifluoroacetic acid.

Our attempts to cyclize nitrile I under the same conditions with certain other anilines, including 2-amino-5-nitrophenol, proved unsuccessful. In every case the lactone VIII obtained in previous works [1, 4] was isolated.



VIII

EXPERIMENTAL

IR spectra were taken in KBr tablets on a UR-20 instrument; ^1H and ^{13}C NMR spectra were recorded on Bruker (100 MHz) and Varian (200 MHz) spectrometers in $CDCl_3$, C_6D_6, DMSO and CF_3COOD, internal standard TMS. Lanthanide shift reagent, commercial $Eu(fod)_3$, NPO Reagent.

Elemental analysis data on C, H, and N compounds V and VII and methoxy group analysis findings were in agreement with calculated values.

2,3,3a,8a-Tetrahydro-N-(2-hydroxyphenyl)-2-oxo-3,8,8a-trimethylpyrrolo[2,3-b]indole (V, $C_{19}H_{20}N_2O_2$). A sample of 2.6 g (13 mmoles) of nitrile I and 1.42 g (13 mmoles) of o-aminophenol were added to polyphosphoric acid at 100°C. The reaction mixture was then kept for 4 h at 180-190°C, cooled to 100°C, poured into water and neutralized with ammonia to pH 7-8. After extraction with chloroform, drying with sodium sulfate and evaporation of the solvent, the resultant oil was crystallized from heptane. Yield 1.44 g (36%), mp 178-180°C. IR spectrum: 1670, 1600 cm^{-1}.

2,3,3a,8a-Tetrahydro-N-(2-methoxyphenyl)-2-oxo-3a,8,8a-trimethylpyrrolo[2,3-b]indole (VII, $C_{20}H_{22}N_2O_2$). A mixture of 0.2 g of p-toluenesulfonic acid, 0.0386 g (0.69 mmoles) of potassium hydroxide and 2.1 g (0.69 mmoles) of indoline V in 5 ml of absolute alcohol was boiled for 1 h, then poured into 20 ml of water. After extraction with chloroform, drying with sodium sulfate and evaporation of the solvent, the resultant oil was crystallized from petroleum ether. Yield 0.87 g (40%), mp 143-145°C.

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