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# REACTION OF 2,3-DIOXOPYRROLO[2,1-*a*]ISOQUINOLINES WITH o-PHENYLENEDIAMINE

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*Reaction of 1,2,3,4-tetrahydroisoquinoline enaminoamides with oxalyl chloride gives 2,3-dioxpyrrolo[2,1-a]isoquinolines which react with o-phenylenediamine to give spiro benzimidazolines or condensed quinoxalines, depending on the conditions used.*

We have previously obtained 2,3-dioxopyrrolo[2,1-*a*]isoquinolines [1], which are promising synthons [2]. At present, condensed dioxopyrrolines are known principally as dienophiles and reactions of their carbonyl groups have been very little studied. With the preparation of new polycyclic systems in mind, we have studied the reactions of 2,3-dioxopyrrolo[2,1-*a*]isoquinoline with o-phenylenediamine at the dicarbonyl system [3].

The starting 2,3-dioxo-5,5-dimethyl-8,7-$(R^1)_2$-1-$R^2$-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolines IIa-d are prepared by treating the enamines Ia-d with oxalyl chloride. By using the tertiary amides Ib-d as starting materials we have broadened the scope of the previously described reaction [1].

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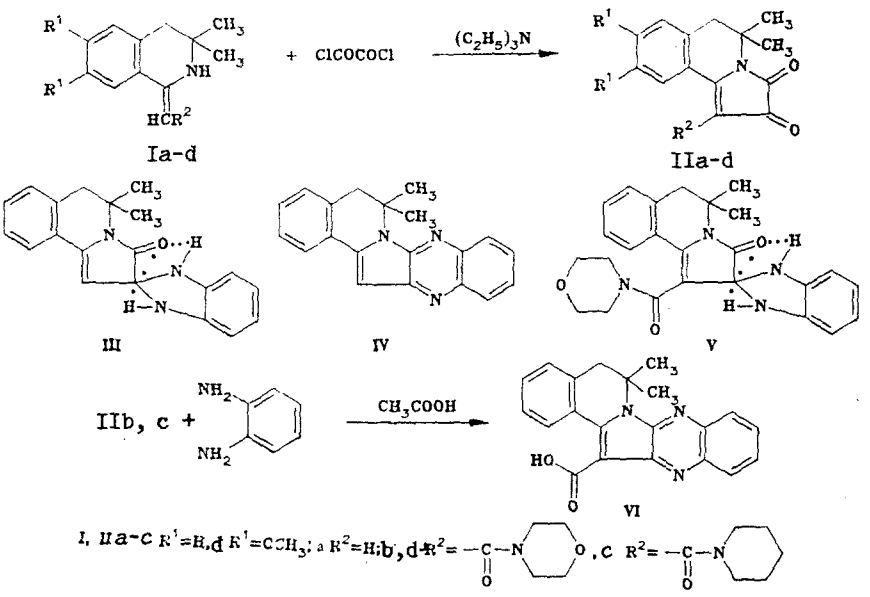

It has been reported [3] that the structure of the reaction products of dioxopyrrolines with o-phenylenediamine depends upon the conditions used. When refluxed in alcoholic solution in the presence of traces of HCl the main products are usually spiro benzimidazolines but when refluxed in acetic acid they are condensed quinoxalines.

In fact, treatment of IIa with o-phenylenediamine in refluxing ethanol with traces of HCl gives the spiro compound III, whereas in glacial acetic acid the product is IV with traces of III (monitored by TLC). Reaction of the tertiary amide IIb in ethanol gives the expected product V, but in glacial acetic acid the amide group is unexpectedly readily hydrolyzed to give the carboxylic acid VI (Table 1). The same acid VI is formed from amide IIc under the same conditions.

Hydrolysis of amides IIb, c apparently occurs in both cases via protonation in glacial acetic acid of one of the nitrogen atoms of the quinoxalino[2,3-b]pyrrole, which activates the amide carbonyl group.

TABLE 1. Data for Synthesized Compounds

| Compound | Empirical formula | mp, °C | PMR spectrum,* δ, ppm | | | | Yield, % |
|---|---|---|---|---|---|---|---|
| | | | 6H, s, $(CH_3)_2C_3$ | 2H, s 4-H | Ar, m | other protons | |
| IIb | $C_{19}H_{20}N_2O_4$ | 196...198 | 1,48 | 2,87 | 7,00...7,80 | 3,14...3,76 (m, $4CH_2$) | 93 |
| IIc | $C_{20}H_{22}N_2O_3$ | 215...216 | 1,53 | 2,84 | 6,93...7,80 | 3,24...3,54 (m, $2CH_2N$); 1,53 (br. s, $3CH_2$) | 76 |
| IId | $C_{21}H_{24}N_2O_6$ | 173...174 | 1,14 | 2,60 | — | 6,44 (s, 5-H); 6,91 (s, 8-H); 3,30...3,91 (14H, m $2CH_3O$ and $4CH_2$) | 70 |
| III | $C_{20}H_{19}N_3O$ | 268...269 | 1,27 | 2,76 | 6,90...7,85 | 6,31 (1H, s, 1-H); 11,45(s, NH); 11,71 (s, NH) | 47 |
| IV | $C_{20}H_{17}N_3$ | 134...135 | 1,73 | 2,86 | 6,87...8,07 | — | 66 |
| V | $C_{25}H_{26}N_4O_3$ | 315...317 | 1,30 | 2,74 | 6,77...7,67 | 2,94...3,70 (m, $4CH_2$); 11,41 (s, NH); 11,72 (s, NH) | 53 |
| VI | $C_{21}H_{17}N_3O_2$ | 222...224 | 1,33 | 2,80 | 6,73...8,50 | 11,20 (s, OH) | —** |

*Spectra of IIb-d, IV taken in $CDCl_3$; III, V, VI in DMSO-$D_6$.

**With amides IIb and IIc the yields are 62 and 67%, respectively.

The structure of lactam III is confirmed by the vinylic proton signal (6.31 ppm) and two NH singlets (11.45 and 11.71 ppm) which shift to even lower field upon addition of $CF_3COOH$. A similar behavior was shown by V. The low field position of the two NH group protons is due to intramolecular association with a carbonyl group. The possibility of such an interaction in the spiro compounds III and V is sterically favored. The difference in chemical shifts of the two protons may be due to some disturbance of the symmetry, the pyrrolo[2,1-*a*]isoquinoline ring being not completely planar. In the quinoxaline IV the $C_1$–H proton is within the aromatic proton multiplet at 6.87-8.07 ppm whose integrated intensity corresponds to nine protons. The presence of the carboxyl group in VI is confirmed by the OH proton signal at 11.20 ppm, which disappears on addition of $D_2O$.

The IR spectra of the tertiary amides IIa-d in chloroform show absorption bands for the lactam carbonyl at 1705-1710 $cm^{-1}$, the carbonyl conjugated to the double bond (1745-1750 $cm^{-1}$, the amide carbonyl (1635-1640 $cm^{-1}$), and absorptoin in the region 1600-1610 $cm^{-1}$ for the C=C bond conjugated to the carbonyl group. Compounds III, V, and VI are insoluble in chloroform and their IR spectra were recorded in Vaseline mull. The imidazoline III shows broad absorption for C=O (1660 $cm^{-1}$), NH (3060 and 3150 $cm^{-1}$), and C=C near 1620 $cm^{-1}$. The spectrum of amide V is analogous to III but has an additional band near 1630 $cm^{-1}$ (amide C=O). The spectrum of the acid VI shows absorptoin bands at 1740 $cm^{-1}$ (C=O), 3040 $cm^{-1}$ (broad, associated OH group), and 1630 $cm^{-1}$ (double bond). Free OH bands were not observed, probably because of the formation of an intra- or intermolecular OH bond.

## EXPERIMENTAL

PMR spectra were recorded on an RYa 2310 (60 MHz) instrument with HMDS internal standard. IR spectra were taken on a UR-20 spectrophotometer. Chromatography was carried out on Silufol UV-254 plates in chloroform–acetone (9:1). Starting enamines Ia-d were synthesized by [4, 5] and compound IIa, as described in [1].

Data for IIb-d, III-VI are given in Table 1. All recrystallizations were from isopropanol. Elemental analytical data for C, H, and N agreed with that calculated.

**2,3-Dioxo-5,5-dimethyl-8,9-($R^1$)$_2$-1-$R^2$-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolines (IIb-d).** A mixture of Ib-d (10 mmoles) and triethylamine (2.76 ml, 20 mmoles) in dioxane (150 ml) was added over 40 min to oxalyl chloride (0.86 ml, 10 mmoles) in dioxane (50 ml). After 2 h the mixture was diluted with water (300 ml), and the precipitated solid filtered off, dried, and recrystallized.

**Spiro-[2H-benzimidazolinyl-2,2']-3-oxo-5,5-dimethyl-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline (III) and Spiro-[2H-benzimidazolinyl-2,2']-3-oxo-1-(N-morpholinocarbonyl)-5,5-dimethyl-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline (V).** o-Phenylenediamine (1.08 g, 10 mmoles) was added to a solution of IIa or IIb (10 mmoles), obtained by refluxing in ethanol (50 ml). Five to seven small bubbles of dry HCl were passed through, the product was refluxed for 2 h, and the precipitate filtered off, dried, and recrystallized.

**5,5-Dimethyl-2,3,5,6-tetrahydrobenz[g]quinoxalino[2,3-b]indolizine (IV) and 5,5-Dimethyl-1-carboxy-2,3,5,6-tetrahydrobenz[g]quinoxalino[2,3-b]indolizine (VI).** o-Phenylenediamine (1.08 g, 10 mmoles) was added to a solution of IIa or IIb (2.27 g, 10 mmoles) in glacial acetic acid (20 ml). The mixture was refluxed for 2 h, cooled, the solid filtered, dried, and recrystallized.

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