SYNTHESIS AND PROPERTIES OF ENAMINE DERIVATIVES OF 1-METHYL-2-PHENYL-5-PYRROLONE AND 5-THIOPYRROLONE

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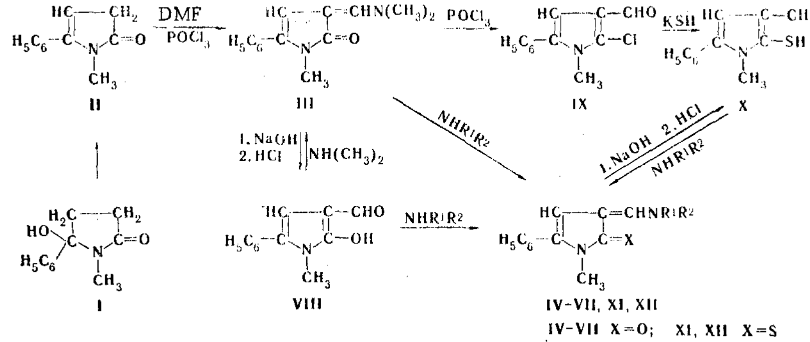
The corresponding dimethylaminomethylene derivative, from which a number of similar compounds were synthesized by reaction with amines, was obtained by the reaction of 1-methyl-2-phenyl-2-hydroxy-5-oxotetrahydropyrrole with dimethylformamide in the presence of phosphorous oxychloride. The formyl derivatives of 1-methyl-2-phenyl-5-pyrrolone and 5-thiopyrrolone were obtained, and the UV and IR spectra of the enamines of these compounds were studied.

It has been shown [1] that N-substituted succinimides readily form the corresponding 2,5-dichloro-3,4-diformylpyrroles on reaction with dimethylformamide (DMF) in the presence of phosphorus oxychloride. It seemed of interest to introduce pyrrole derivatives containing one oxo group into this reaction. For, this, we synthesized 1-methyl-2-phenyl-2-hydroxy-5-oxotetrahydropyrrole (I) [2], which is readily dehydrated in the presence of phosphorus oxychloride to give 1-methyl-2-phenyl-5-pyrrolone (II). The latter reacts at −20 to −30°C with the Vilsmeier reagent to give 1-methyl-2-phenyl-4-dimethylaminomethylene-5-pyrrolone (III), which is isolated as a salt.



Compound III undergoes transamination, which proceeds particularly readily in the case of strongly basic amines (Table 1), and is hydrolyzed on treatment with alcoholic alkali to give a salt of 1-methyl-2-phenyl-4-formyl-5-hydroxypyrrole (VIIIa). Acidification of an aqueous suspension of this salt gave 1-methyl-2-phenyl-4-formyl-5-hydroxypyrrole (VIII), which, on reaction with amines in benzene, forms the same compounds (III-VII) that were obtained in the transamination (Table 1).

Compound III reacts with excess phosphorus oxychloride to give 1-methyl-2-phenyl-4-formyl-5-chloropyrrole (IX), which is similar to what is observed for pyrazolone and α-pyrrolone derivatives [3, 4]. Compound IX reacts with reagents that are characteristic for the aldehyde group, and the chlorine atom is readily substituted on reaction with potassium hydrosulfide. The resulting aldehyde of mercaptopyrrole (X) reacts with amines to give 4-aminomethylene derivatives (XI, XII).

The UV spectra of III-VII depend only slightly on the nature of the solvent. This is especially the case for monosubstituted aminomethylene derivatives, which attests to the low polarization of the α,β-unsaturated $>N-CH=C-C=X$ system, in contrast to sulfur-containing compounds (XI, XII).

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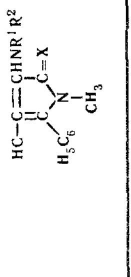
TABLE 1



Compound	X	R¹	R²	mp, °C (from heptane)	Empirical formula	Found, %			Calc., %			Yield, % *	λ_{max}, nm (lg ε)		$\nu_{>N-CH=C-C=X}$ cm⁻¹ (chloroform)
						C	H	N	C	H	N		cyclohexane	ethanol	
III	O	CH_3	CH_3	163	$C_{14}H_{16}N_2O$	73,5	7,0	12,4	73,7	7,0	12,3	51	384(4,2)	374(3,80)	1665
IV	O	H	H	147—148	$C_{12}H_{12}N_2O$	71,7	5,9	—	72,0	6,0	14,0	(68)	368	366(3,86)	1673
V	O	H	CH_3	150	$C_{13}H_{14}N_2O$	72,9	6,6	12,9	73,0	6,5	13,1	54(65)	378(4,6)	374(3,85)	1670
VI	O	H	C_6H_5	198—199	$C_{18}H_{16}N_2O$	78,5	6,1	10,5	78,3	5,8	10,2	19	—	402(4,44)	1668
VII	O	$(CH_2)_5$		113—114	$C_{17}H_{20}N_2O$	75,7	7,4	10,5	76,1	7,5	10,4	16(95)	378(4,2)	376(4,3)	1665
XI	S	CH_3	CH_3	134—135	$C_{14}H_{16}N_2S$	S 13,0	—	11,4	S 13,1	—	11,5	72 —	468(3,83)	424(3,6)	1627
XII	S	H	C_6H_5	165—166	$C_{18}H_{16}N_2S$	S 10,8	—	9,6	S 10,9	—	9,6	80 —	475(3,93)	462(4,16)	1642

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* The yields from VIII or X are presented, while the yields in parentheses are those from III.

The introduction of an aminomethylene group shifted the ν_{CO} sorption band by 40 cm^{-1} (ν_{CO} for 1-methyl-2-phenyl-5-pyrrolone in carbon tetrachloride is 1710 cm^{-1}). The monosubstituted enamines (IV, V, VII, and XII) are stabilized by an intramolecular hydrogen bond, as was demonstrated by a study of the concentration dependence. The frequency of the vibrations associated with the > N—CH = C—C = S grouping is lower than the frequency of the corresponding oxygen compound by 38 cm^{-1} in the case of XII (compare with VI) and by 26 cm^{-1} in the case of XI (compare with III). The difference in the shifts (12 cm^{-1}) between the monosubstituted enamine of the thiopyrrolone (XII) and the disubstituted compound (XI) may be associated with the fact that, in contrast to XII, which has the cis structure and is stabilized by an intramolecular hydrogen bond, XI apparently has the trans structure. The structure of these compounds and the structures of the aldehydes of 5-pyrrolone and 5-thiopyrrolone will be reported in greater detail at a later date.

EXPERIMENTAL

1-Methyl-2-phenyl-4-dimethylaminomethylene-5-pyrrolone (III). A 5-g (0.029 mole) sample of I in 25 ml of DMF was added with stirring at −30 to −20° to a mixture of 9.5 g (0.13 mole) of DMF and 8.4 g (0.033 mole) of phosphoruc oxychloride, and the mixture was stirred for 15-20 min, after which the light-yellow salt was removed by filtration, suspended in 75 ml of water, and neutralized with 10% sodium carbonate solution. The precipitate was removed by filtration, washed several times with small portions of ice water, and dried in a vacuum desiccator to give 4.5 g (76%) of III.

1-Methyl-2-phenyl-4-alkylaminomethylene-5-pyrrolones (IV-VII, Table 1). A benzene solution of III or VIII was refluxed with a three- to fivefold excess of the appropriate amine for 3-4 h and cooled. The reaction product was precipitated with ether and freed from the starting material by purification by column chromatography on aluminum oxide. Compound VI was also obtained in 72% yield by fusing I with diphenylformamidine.

1-Methyl-2-phenyl-4-formyl-5-hydroxypyrrole (VIII). A mixture of 1 g (4.4 mmole) of III and 0.18 g (4.5 mmole) of sodium hydroxide in 30 ml of 90% methanol was refluxed for 6 h and cooled. The precipitate was removed by filtration, and the filtrate was diluted with ether. The precipitate thus formed was combined with the bulk of the product. The sodium salt of VIII was washed thoroughly with chloroform and a small amount of ice water. After several reprecipitations from hot methanol solution by the addition of ether (the melting point of the salt was above 400°), the salt was suspended in a small amount of water and acidified with 10% hydrochloric acid. The precipitate was removed by filtration, washed with water, and dried to give 0.57 g (65%) of VIII with mp 112-113°, λ_{max} (in cyclohexane) 347 nm (3.67), λ_{max} (in ethanol) 359 nm (3.7), and ν_{CO} (in chloroform) 1667 cm^{-1}. Found: C 71.8; H 5.6; N 7.0%. $C_{12}H_{11}NO_2$. Calculated: C 71.6; H 5.5; N 7.0%.

1-Methyl-2-phenyl-4-formyl-5-chloropyrrole (IX). A mixture of 1 g (4.4 mmole) of III and 3 ml (33 mmole) of phosphorus oxychloride was refluxed for 8 h, cooled, and poured over ice. The ice mixture was made alkaline to pH 9-10 with 5% sodium hydroxide solution, and the precipitate was removed by filtration, washed with water, and dried to give 0.8 g (83%) of IX with mp 116° (from petroleum ether), λ_{max} (in cyclohexane) 272 nm (4.4), λ_{max} (in ethanol) 247 nm (4.5), and ν_{CO} 1666 cm^{-1}. Found: Cl 16.3; N 6.5%. $C_{12}H_{10}ClNO$. Calculated: Cl 16.2; N 6.4%. The oxime of IX had mp 149° (from ethanol). Found: Cl 15.0; N 11.6%. $C_{12}H_{11}ClN_2O$. Calculated: Cl 15.1; N 11.9%. The thiosemicarbazone of IX had mp 210° (from ethanol). Found: Cl 12.1; S 10.7%. $C_{13}H_{13}ClN_4S$. Calculated: Cl 12.1; S 10.5%.

1-Methyl-2-phenyl-4-alkylaminomethylene-5-thiopyrrolones (XI and XII, Table 1). A 1-g (4.6 mmole) sample of IX was dissolved in 80 ml of 80% methanol, 1.2 ml (9.2 mmole) of 50% aqueous potassium hydrosulfide solution was added, and the mixture was refluxed for 2 h. The solution was cooled, diluted with 100 ml of water, and filtered. The filtrate was acidified with 10% formic acid and again filtered. A 0.02-mole sample of dimethylamine hydrochloride or aniline hydrochloride was added to the resulting solution, and the precipitate (XI, XII) was separated, washed with water, dried, and crystallized from n-heptane.

1-Methyl-2-phenyl-4-formyl-5-mercaptopyrrole (X). This compound [1.45 g (67%)] was obtained from 2.9 g (0.01 mole) of XII by hydrolysis with alcoholic alkali under the conditions used for the synthesis of VIII and had mp 158-159°, λ_{max} (in cyclohexane) 380 nm (3.6), λ_{max} (in ethanol) 380 nm (3.6), and ν_{CO} 1670 cm^{-1}. Found: N 6.5; S 14.8%. $C_{12}H_{11}NOS$. Calculated: N 6.4; S 14.7%.

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