REACTION OF 2-THIOPYRROLIDONES WITH MONOCHLOROACETIC ACID AND ITS METHYL ESTER

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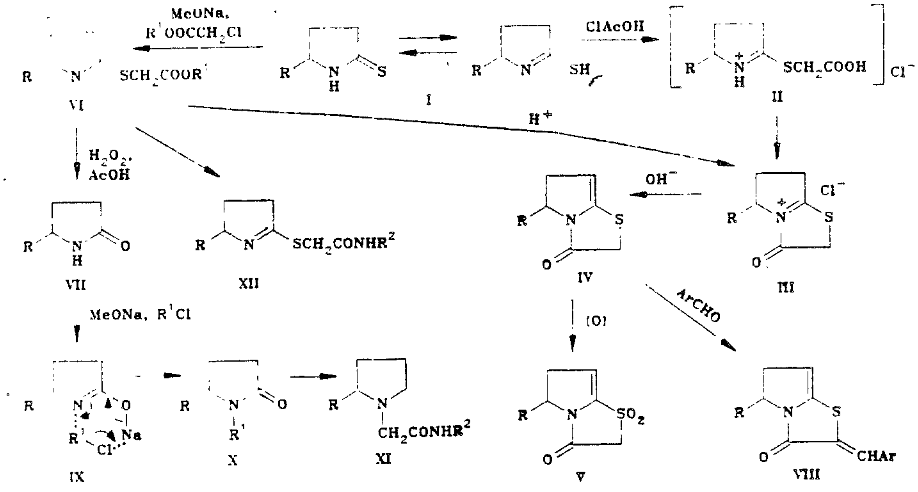
UDC 547.745'789.8.07:543.42

Calculations of the electronic structure of 5-alkyl-2-thiopyrrolidones and their oxygen analogs were carried out by the MO LCAO method in the CNDO/2 approximation. The obtained data were used to discuss the reactivity of the investigated compounds in the alkylation of monochloroacetic acid, leading, in the case of 2-thiopyrrolidones, to the formation of the corresponding thiazolinones.

Continuing our previously begun [1] investigations in studying the reactivity of 2-thio pyrrolidones, we carried out alkylation of 5-alkyl-2-thiopyrrolidones (I) and their oxygen analogs (VII) by monochloroacetic acid and its methyl ester. In the reaction of compound I with monochloroacetic acid in benzene, pyrrolidinyl[2,3]thiazolin-4-one chloride (III) was obtained in high yield:



I R=C_3H_7; VI R^1=H, CH_3; XI R^2=H; XII R^2=NH_2

Apparently, the reaction proceeds via a stage of formation of the intermediate product 5-alkyl-2-pyrrolidinylthioacetyl chloride (II) with its subsequent cyclization to compound III. The facileness of ring closure is probably due to the catalytic effect of hydrogen ions because of the hydrogen chloride evolved in the reaction process. The catalytic effect of the acids in the closure of the thiazole ring is indicated by the fact that when product I was heated with alkylating agents in methanol in the presence of sodium methylate only thioimido esters (VI) were formed, which were converted to chloride (III) when they were treated with hydrogen chloride. The composition and structure of compound III were established according to the data of elemental analysis and IR and proton NMR spectra. The proton NMR spectra of chloride III contained signals of the thiomethylene group (3.72 ppm, 2H, singlet), protons of the pyrroline ring (2.5-2.9 ppm, 4H, multiplet), and protons of the alkyl substituent (0.9-1.15 ppm, multiplet, 5-H). In addition, products of structure III obtained by both methods did not give a depression of the melting point of mixing samples. The presence of sulfide sulfur in base IV was confirmed by its conversion to the corresponding sulfone V during its oxidation by hydrogen peroxide in acetic acid. 5-Alkyl-2-pyrrolidone (VII) was obtained as a result of hydrolytic abstraction of the sulfur-containing group.

N. G. Chernyshevskii Saratov State University, Saratov 410026. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1690-1692, December, 1986. Original article submitted July 8, 1985; revision submitted November 5, 1985.

0009-3122/86/2212-1370$12.50

The high mobility of the hydrogen atoms of the thiomethylene group in compounds IV is manifested in their ability to react with aromatic aldehydes with the formation of arylidene derivatives of VIII.

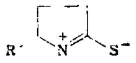
A comparison of the behavior of thiopyrrolidones I and their oxygen analogs VII in the alkylation showed that the analogs react with chloroacetic acid and its esters only in the presence of sodium methylate. Taking into account the lactim structure of Na salts of 2-pyrrolidones [2, 3], we can assume that, in this case, the alkylation proceeds with transfer of the reaction center through intermediate complex IX. In the absence of sodium methylate, an acylation process of 5-alkyl-2-pyrrolidones occurs.

To explain the higher reactivity of 2-thiopyrrolidones I than of 2-pyrrolidones VII in our considered reaction, we carried out a quantum-chemical calculation of their molecules by the MO LCAO method in the CNDO/2 approximation with standard parametrization [4]. The geometry of the pyrrolidone ring was chosen in the shape of an envelope where, according to data of x-ray diffraction analysis [5], the $C_{(4)}$ atom extends 0.18 Å from the plane. The C–S distance was varied from 1.72 (C=S) to 1.87 Å (C–S). The criterion for the correctness of the choice was the good agreement of the calculated dipole moment of unsubstituted 2-thiopyrrolidone with the experimental data (5.59 and 5.15 D).

The data of quantum-chemical calculations (Fig. 1) are given in the form of molecular diagrams (the values of the charges on the atoms and the electron densities on the bonds are indicated in the form of Wiberg indices). A comparison of the electronic characteristics of the amide and thioamide groups in molecules VII and I showed that the negative charge on the nitrogen atom in compound I is almost half that in the case of oxygen analog VII. According to the data of the Wiberg indices, the degree of $N-C_{(2)}$ double bonding in the thioamide is higher than in the amide, and the C=S bond has the nature of an ordinary bond, while the double-bonding nature of the C=O group is retained.

The occupation values of the p_z orbitals of the nitrogen atom (1.83 in molecule VII and 1.65 in molecule I) also indicate the presence of conjugation of the electron pair of nitrogen with the C=S group, and there is no conjugation in the amide group.

From calculations, we see the significant contribution of the bipolar form



which explains the great facileness of alkylation of 2-thiopyrrolidones.

Methyl ester VI and ether X react facilely with ammonia and hydrazine hydrate [6], givi amides XI and hydrazides XII, respectively.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 instrument in mineral oil, with the liquid samp in a capillary layer. The proton NMR spectra were recorded on a Varian FT-80A instrument, and the internal standard was HMDS. The starting 5-alkyl-2-thiopyrrolidones were obtained by the method of [7].

Pyrrolidinyl[2,3]thiazol-4-one Chloride (III). To 7.15 g (0.05 mole) of 5-propyl-2-thiopyrrolidone (I) in 50 ml of dry benzene was added 5 g (0.05 mole) of monochloroacetic acid. The reaction mixture was heated for 30 min with stirring at 90°C. The precipitated crystals were separated, washed, and dried. Yield: 2.5 g (50%), mp 125-126°C (from benzene) IR spectrum: 1710 (C=O), 1640 (C=N), 640 cm^{-1} (C–S–C). Found, %: C 49.1, H 6.4, N 6.4, S 14.5. $C_9H_{14}ClNOS$. Calculated, %: C 49.2, H 6.4, N 6.4, S 14.6.

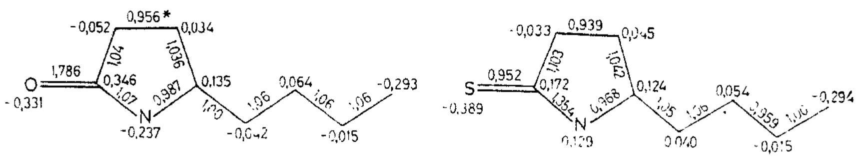


Fig. 1. Molecular diagrams of 5-butyl-2-pyrrolidone and 5-butyl-2-thiopyrrolidone.

5-Propyl-2-pyrrolidinylthioacetic Acid (VI). A solution of 3.1 g (0.02 mole) of 5-propyl-2-thiopyrrolidone in 10 ml of absolute methanol was added to a solution of sodium methylate (from 15 ml of absolute methanol and 0.45 g of metallic sodium). To the reaction mixture was added 2.6 g (0.02 mole) of monochloroacetic acid, the whole was heated on a water bath for 30 min, the precipitate was filtered, the solvent was removed, and the residue was fractionated in vacuo. Yield: 3.4 g (58%), bp 141-142°C (6.5 hPa). IR spectrum: 3400 (OH), 1690 (C=O), 640 cm^{-1} (C—S—C). Proton NMR spectrum: 12.05 (1H, s, OH); 3.70 (2H, s, CH_2), 2.91 (2H, tr, 3-CH_3), 0.9-1.3 ppm (protons of the alkyl substituent at $C_{(5)}$). Found, %: C 53.8, H 7.9, N 7.0, S 15.9. $C_9H_{15}NO_2S$. Calculated, %: C 53.7, H 7.5, N 6.9, S 15.8.

5-Arylidenepyrrolidinyl[2,3]thiazol-4-one (VIII). An alcoholic solution (30 ml) of 6.3 g (0.03 mole) of pyrrolidinyl[2,3]thiazol-4-one chloride and 4.5 g (0.03 mole) of N,N-dimethylbenzaldehyde with an addition of 1 ml of piperidine was boiled for 5 h. The solvent was evaporated, and acetone was added. Yield: 3.9 g(40%), mp 229-230°. IR spectrum: 1640 (C=N), 1710 cm^{-1} (C=O). Found, %: C 52.4, H 5.6, N 6.9, S 7.4. $C_{18}H_{22}N_2OS$. Calculated, %: C 52.1, H 5.3, N 6.7, S 7.7.

5-Propyl-2-oxo(thio)pyrrolidinylacetic Acid Hydrazide (XI, XII). A mixture of methyl 5-propyl-2-oxo(thio)pyrrolidinylacetate and hydrazine hydrate taken in an equimolecular amour was boiled for 30 min in a solution of isopropyl alcohol. It was left at 20°C for 48 h. The solvent was evaporated. Obtained: 2.2 g (50%) of compound XI, mp 84-86°C (from hexane). Found, %: C 54.3, H 8.6, N 21.7. $C_9H_{17}N_3O_2$. Calculated, %: C 54.2, H 8.5, N 21.1. Obtained: 2.4 g of compound XII (68%), bp 146-148°C (5 hPa). Found, %: C 51.72, H 7.7, N 19.4, S 14.4. $C_9H_{17}N_3OS$. Calculated, %: C 50.2, H 7.9, N 9.5, S 14.9.

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