FRAGMENTATION OF 2- AND 4-(2-FURYL)PYRIDINES UNDER THE INFLUENCE OF ELECTRON IMPACT

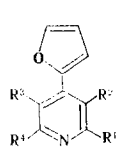
P. I. Zakharov, V. G. Zaikin,
A. I. Mikaya, P. K. Radzhan,
A. T. Soldatenkov, and N. S. Prostakov

UDC 547.821.4'721:543.51

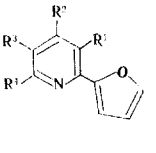
The dissociative ionization of 12 compounds of the 2- and 4-(2-furyl)pyridine series that contain methyl, ethyl, and n-propyl groups in various positions of the pyridine ring was investigated. It was established that the intensity of the $[M-H]^+$ ion peak depends only slightly on the mutual orientation of the alkyl groups and the furyl grouping, while the probability of cleavage of the furan ring with ejection of CO and HCO• particles is very sensitive to these structural factors. Cleavage of the pyridine ring leads to the development of $[M-HCN]^+$ and $[FuCN]^+$ ions.

Furan derivatives have diversified biological activity [1], and this to a considerable extent explains the intensive development of the chemistry of these compounds [2]. At the same time, little study has been devoted to furylpyridines, and the literature contains only a few reports dealing with the synthesis and study of their properties [2-6], although derivatives that have a wide spectrum of physiological activity have already been found in this group of substances [7-10].

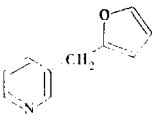
In this connection it seems timely to study the mass-spectral behavior of furylpyridines for the utilization of the principles obtained to establish the structures of newly synthesized furylpyridines, to identify them directly in reaction mixtures, and to determine the accompanying impurities. Until recently, only the fragmentation of 3-furylpyridines had been investigated [5]. The present communication is devoted to an examination of the dissociative ionization of 2- and 4-(2-furyl)pyridines (I-XII) that contain alkyl substituents in the pyridine ring [for comparison, we also studied the fragmentation of furylpyridylmethane (VII) [11]].



II–IV, VIII, X–XII



I, V, VI, IX



VII

I, II $R^1=R^2=R^3=R^4=H$; III $R^1=R^4=CH_3$, $R^2=R^3=H$; IV $R^1=R^4=H$, $R^2=R^3=CH_3$; V $R^1=R^3=H$, $R^2=R^4=CH_3$; VI $R^1=R^3=CH_3$, $R^2=R^4=H$; VIII $R^1=R^4=H$, $R^2=R^3=C_2H_5$; IX $R^1=R^3=C_2H_5$, $R^2=R^4=H$; X $R^1=R^2=CH_3$, $R^3=H$, $R^4=C_2H_5$; XI $R^1=R^4=n\text{-}C_3H_7$, $R^2=R^3=H$; XII $R^1=CH_3$, $R^2=C_2H_5$, $R^3=H$, $R^4=n\text{-}C_3H_7$.

The mass spectra of the indicated compounds are presented in Table 1.

Under the influence of electron impact, I-IX give stable molecular ions (M^+), the peaks of which in most cases have the maximum intensities in the mass spectra. The presence of an ethyl substituent in the α position relative to the nitrogen atom (X) decreases the intensity of the M^+ peak somewhat, while the presence of a propyl substituent (XI and XII) decreases it sharply (Table 1); this is similar to the mass-spectral behavior of alkyl-substituted pyridines [12, 13].

Peaks of $[M-H]^+$ ions, which have appreciable intensities, are observed in the mass spectra of all of the investigated furylpyridines. In the spectrum of 2-furylpyridine I the ratio of the intensities of the $[M-H]^+$ and M^+ ions exceeds this ratio in the mass spectrum of 4-furylpyridine II by a factor of more than 1.5. This fact can be explained by the possibility of stabilization of the $[M-H]^+$ ion due to cyclization of the β-carbon atom of the furan ring and the nitrogen atom of the pyridine ring, which is possible only in the case of I (Scheme 1, pathway A).

Patrice Lumumba Peoples' Friendship University, Moscow 117923. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 769-774, June, 1982. Original article submitted April 7, 1981; revision submitted September 25, 1981.

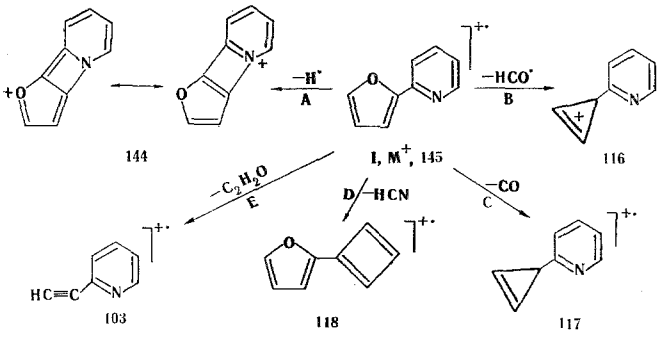
0009-3122/82/1806-0581$07.50

TABLE 1. Mass Spectra (70 eV) of Furylpyridines I-XII*

Compound	m/z values (relative intensities of the ion peaks in percent of the maximum peak)
1	2
2-(2-Furyl)pyridine (I)	146 (10), 145 (100), 144 (49), 143 (19), 118 (28), 117 (63), 116 (55), 106 (11), 105 (10), 104 (8), 103 (11), 102 (10), 101 (16), 100 (13), 93 (14), 92 (16), 91 (42), 90 (50), 89 (58), 81 (13), 80 (18), 79 (23), 78 (49), 77 (19), 76 (16), 75 (15), 74 (12), 73 (9), 71 (17), 70 (10), 69 (22), 67 (19), 66 (22), 65 (28), 64 (41), 63 (62), 62 (38), 61 (21), 57 (25), 56 (12), 55 (26), 54 (12), 53 (37), 52 (39), 51 (49), 50 (41)
4-(2-Furyl)pyridine (II)	146 (10), 145 (100), 144 (30), 117 (22), 116 (23), 90 (9), 89 (11), 78 (8), 63 (11), 51 (10)
2,6-Dimethyl-4-(2-furyl)pyridine (III)	174 (10), 173 (100), 172 (30), 158 (9), 146 (8), 145 (43), 144 (40), 143 (9), 131 (15), 130 (17), 128 (5), 118 (9), 117 (8), 116 (8), 115 (14), 106 (9), 105 (8), 104 (11), 103 (22), 102 (17), 101 (5), 99 (5), 94 (6), 93 (18), 92 (20), 91 (20), 90 (6), 89 (14), 88 (8), 87 (11), 86 (9), 81 (5), 80 (6), 79 (22), 78 (23), 77 (66), 76 (22), 75 (26), 74 (22), 73 (5), 67 (8), 66 (18), 65 (45), 64 (45), 63 (77), 62 (35), 61 (22), 55 (8), 54 (11), 53 (49), 52 (55), 51 (85)
3,5-Dimethyl-4-(2-furyl)pyridine (IV)	174 (11), 173 (100), 172 (26), 170 (5), 160 (11), 159 (18), 158 (12), 147 (5), 146 (9), 145 (26), 144 (98), 143 (18), 142 (9), 132 (5), 131 (11), 130 (30), 129 (7), 128 (11), 119 (11), 118 (5), 117 (14), 116 (11), 115 (30), 104 (5), 103 (12), 102 (7), 91 (18), 89 (7), 79 (5), 78 (11), 77 (26), 76 (6), 75 (7), 74 (5), 65 (11), 64 (5), 63 (14), 62 (6), 53 (9), 52 (11), 51 (21)
2,4-Dimethyl-6-(2-furyl)pyridine (V)	174 (10), 173 (100), 171 (5), 158 (7), 149 (6), 145 (16), 144 (19), 130 (6), 115 (5), 93 (8), 92 (7), 91 (6), 83 (6), 81 (6), 79 (8), 78 (6), 77 (10), 71 (6), 69 (7), 65 (7), 55 (11), 52 (5), 51 (7)
3,5-Dimethyl-2-(2-furyl)pyridine (VI)	174 (11), 173 (100), 172 (33), 147 (6), 145 (14), 144 (65), 143 (8), 130 (7), 119 (16), 117 (5), 116 (9), 92 (7), 90 (6), 79 (5), 78 (12), 65 (6), 63 (6), 58 (6), 52 (5), 51 (11)
(2-Methyl-5-pyridyl) (2-furyl)-methane (VII)	174 (12), 173 (100), 172 (17), 159 (9), 158 (18), 146 (11), 145 (89), 144 (51), 143 (7), 142 (5), 131 (10), 130 (31), 118 (10), 117 (25), 116 (35), 115 (6), 106 (5), 105 (26), 104 (10), 103 (12), 91 (6), 90 (20), 89 (20), 81 (30), 78 (8), 77 (13), 65 (12), 64 (7), 62 (6), 54 (13), 53 (7), 52 (22), 51 (9)
3,5-Diethyl-4-(2-furyl)pyridine (VIII)	202 (13), 201 (100), 200 (35), 199 (14), 198 (8), 189 (6), 188 (32), 187 (4), 186 (60), 185 (6), 184 (27), 177 (5), 174 (9), 173 (30), 172 (66), 171 (10), 170 (8), 162 (6), 159 (9), 158 (40), 157 (17), 156 (15), 154 (7), 150 (5), 149 (11), 148 (6), 147 (7), 146 (10), 145 (10), 144 (17), 143 (30), 142 (14), 141 (5), 131 (7), 130 (19), 129 (8), 128 (13), 127 (6), 119 (5), 118 (6), 117 (11), 116 (12), 115 (24), 107 (6), 105 (6), 104 (6), 103 (9), 102 (6), 93 (7), 92 (6), 91 (28), 89 (10), 81 (6), 79 (11), 78 (12), 77 (34), 76 (6), 75 (5), 67 (5), 66 (6), 65 (23), 64 (8), 63 (16), 55 (7), 54 (5), 53 (20), 52 (12), 51 (21)
3,5-Diethyl-2-(2-furyl)pyridine (IX)	202 (14), 201 (100), 200 (30), 187 (10), 186 (57), 184 (22), 174 (10), 173 (27), 172 (67), 171 (7), 159 (7), 158 (33), 157 (13), 156 (17), 149 (13), 146 (10), 145 (10), 144 (17), 143 (27), 142 (13), 131 (7), 130 (20), 129 (10), 128 (13), 127 (7), 117 (13), 116 (13), 115 (27), 107 (7), 105 (7), 104 (7), 103 (10), 102 (7), 93 (10), 92 (7), 91 (33), 89 (10), 81 (7), 79 (17), 78 (18), 77 (43), 76 (7), 66 (8), 65 (33), 64 (10), 63 (20), 55 (10), 54 (7), 53 (30), 52 (20), 51 (40)
2,3-Dimethyl-6-ethyl-4-(2-furyl)pyridine (X)	202 (14), 201 (88), 200 (100), 199 (12), 174 (8), 173 (34), 172 (10), 170 (11), 157 (6), 156 (5), 145 (6), 144 (14), 143 (5), 131 (6), 130 (8), 129 (6), 128 (9), 127 (5), 117 (9), 116 (11), 115 (25), 105 (5), 104 (5), 103 (10), 102 (8), 93 (6), 92 (6), 91 (24), 89 (10), 81 (6), 79 (8), 78 (12), 77 (30), 76 (8), 75 (8), 69 (6), 67 (6), 66 (6), 65 (22), 64 (10), 63 (24), 62 (6), 57 (8), 56 (5), 55 (14), 54 (8), 53 (20), 52 (15), 51 (36)
2,6-Di-n-propyl-4-(2-furyl)pyridine (XI)	229 (22), 228 (12), 215 (8), 214 (30), 204 (7), 202 (15), 201 (100), 200 (21), 199 (13), 198 (11), 187 (10), 186 (39), 185 (5), 184 (6), 173 (11), 172 (10), 171 (6), 170 (9), 159 (6), 158 (12), 157 (18), 156 (8), 145 (9), 144 (17), 143 (11), 142 (5), 141 (7), 131 (9), 130 (10), 129 (12), 128 (17), 127 (9), 117 (10), 116 (16), 115 (37), 105 (6), 103 (10), 102 (7), 101 (5), 95 (5), 93 (5), 92 (6), 91 (25), 89 (9), 81 (7), 79 (11), 78 (9), 77 (25), 76 (5), 69 (7), 67 (7), 65 (17), 64 (5), 53 (11), 57 (9), 55 (13), 53 (12), 52 (5), 51 (16)
2-Methyl-3-ethyl-6-n-propyl-4-(2-furyl)pyridine (XII)	230 (5), 229 (21), 228 (14), 215 (10), 214 (36), 202 (14), 201 (100), 200 (8), 198 (5), 187 (11), 186 (35), 184 (5), 173 (6), 172 (7), 170 (6), 158 (6), 157 (9), 144 (10), 129 (5), 128 (9), 117 (5), 116 (7), 115 (20), 103 (5), 91 (13), 89 (7), 78 (5), 77 (14), 76 (5), 75 (6), 65 (11), 64 (6), 63 (17), 62 (6), 55 (5), 53 (9), 52 (7), 51 (16)

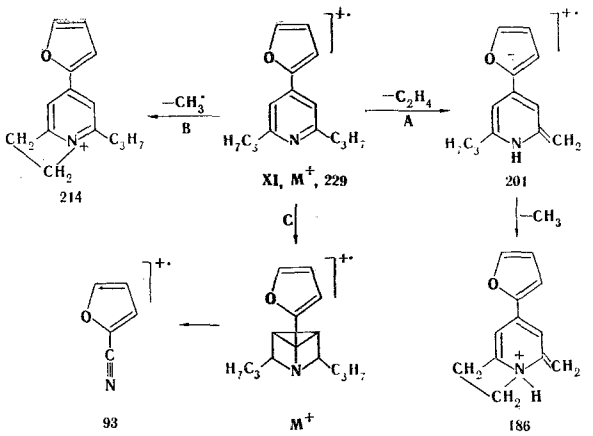
* The intensities of the peaks ≥5% of the maximum peak are indicated.

Scheme 1



A distinct dependence of the relative intensity of the $[M - H]^+$ ion peak on the mutual orientation of the alkyl and furyl substituents cannot be observed. Furylpyridines differ in this respect from the corresponding alkyl-substitutedphenylpyridines [14], in the mass spectra of which the relative intensity of the $[M - H]^+$ ion peak increases significantly when the phenyl and methyl substituents have a vicinal orientation. The pronounced increase in the relative intensity of the $[M - H]^+$ ion peak in the case of 2-ethyl-4-furylpyridine X is a consequence of the characteristic (for α-alkylpyridines) cleavage of the γ bond in the alkyl chain. In particular, the intense $[M - CH_3]^+$ ion peaks in the mass spectra of substituted 2,6-di-n-propyl- (XI) and 6-n-propyl-4-furylpyridines (XII) are due to this process (Scheme 2, pathway B). Competitive ejection of a hydrogen atom, which also occurs as a result of γ cleavage, is less favorable in the latter two cases.

Scheme 2



The above-noted pronounced decrease in the stabilities of the $M^{+\cdot}$ ions of XI and XII is evidently the result of the favorable [for α-alkylpyridines (alkyl $\geq C_3H_7$)] McLafferty rearrangement, which leads to ejection of a C_2H_4 molecule (Scheme 2, pathway A). The $[M - C_2H_4]^{+\cdot}$ ion peaks in these two cases have the maximum intensity.

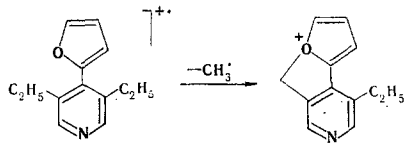
It is interesting to note that the absence in VII of a direct relationship between the pyridine and furan rings also leads to a significant decrease in the relative intensity of the peak of the $[M - H]^+$ fragment. This can be explained by the fact that competitive cleavage of the furan ring with the ejection of CO and HCO$^\cdot$ particles occurs, as will be shown below, with a higher probability in the molecular ion of VII.

The presence of alkyl substituents in the pyridine ring of furylpyridines III-XII leads to the development in their mass spectra of $[M - CH_3]^+$ ion peaks. The mechanism of the formation of these ions in the case of α-n-propyl-substituted furylpyridines (XI and XII) was examined above. A comparison of the mass spectra of ethyl-substituted furylpyridines VIII-X shows that $[M - CH_3]^+$ ion peaks with significant intensity are observed only in the case of VIII and IX, which contain ethyl substituents in the 1 or 4 position of the pyridine ring. The facile ejection of a CH_3 radical in these cases is evidently associated with cleavage of the ethyl group and the formation of a cyclic oxonium ion (Scheme 3).

The $[M - CH_3]^+$ ion peaks in the mass spectra of methyl-substituted furylpyridines III-VI have low intensities.

Elimination of CO and HCO$^\cdot$ particles from the $M^{+\cdot}$ ions occurs in the dissociative ionization of furylpyridines as a result of cleavage of the furan ring (Scheme 1, pathways B and C). The intensities of the

Scheme 3



VIII, M^+, 201 186

$[M - CO]^+$ and $[M - HCO]^+$ ion peaks and their ratios vary as a function of the nature and orientation of the substituents.

Cleavage of the furan ring in the dissociative ionization of furylpyridines I-XII also leads to ejection of C_2H_2O particles (Scheme 1, pathway E); however, the indicated process has a lower probability as compared with elimination of CO and HCO• particles, and the intensity of the $[M - C_2H_2O]^+$ ion peaks does not exceed 10-13%. Cleavage of the pyridine ring is additionally observed in the fragmentation of furylpyridines (Scheme 1, pathway D); ejection of an HCN molecule and the formation of an $[M - HCN]^+$ ion occur in this case. The appearance of an $[FuCN]^+$ fragment with m/z 93* is also observed in the mass spectra of some of the compounds (I, III, V, VI, and VIII-XI). Its formation in the fragmentation of III, VIII, and X, which contain a furyl substituent in the α position relative to the nitrogen atom, is evidently due to complex rearrangement of their molecular ions to, for example, an azaprismane structure (Scheme 2, pathway C), as in the case of the dissociative ionization of phenylpyridines [17, 18].

One should also note the formation of $[M - Fu]^+$ ions in the fragmentation of furylpyridines I-III due to cleavage of the carbon–carbon bond between the pyridine and furan rings. This process takes place particularly easily in the case of I, which contains a furyl substituent in the α position relative to the nitrogen atom. However, the introduction of alkyl groups in the pyridine ring (except in the case of IV) completely suppresses the formation of the $[M - Fu]^+$ fragment, evidently as a consequence of competitive fragmentation processes.

Cleavage of the $C-C_{pyr}$ bond is observed for VII, in which the furyl group is not directly bonded to the pyridine ring; the positive charge is localized on the furyl-containing part of the molecule, and $[CH_2Fu]^+$ ions [81 (30%)] are formed.

Thus the dissociative ionization of furylpyridines and their alkyl-substituted derivatives takes place primarily with elimination of a hydrogen atom, cleavage of the side alkyl chain, and fragmentation of the furyl and pyridine rings. The probability of the occurrence of these processes depends on the mutual orientation of the furyl and alkyl groups in the pyridine ring.

EXPERIMENTAL

The mass spectra of I-XII were obtained with an MKh-1303 spectrometer with a system for the direct introduction of the samples into the ion source at an ionizing voltage of 70 V and a sample-input temperature of 40-70°C. Furylpyridines I-XII were synthesized by the method in [11], and their purity and individuality were monitored by thin-layer chromatography (TLC) and gas–liquid chromatography (GLC); the structures of the substances were established on the basis of data from their IR, UV, and PMR spectra.

LITERATURE CITED

1. A. Williams, Furans, Synthesis and Applications, Noyes Data Corp., New York (1973).
2. É. Ya. Lukevits, Advances in the Chemistry of Furan [in Russian], Zinatne, Riga (1978).
3. H.-S. Ryang and H. Sakurai, J. Chem. Soc., Chem. Commun., 594 (1972).
4. P. Ribereau, G. Nevers, G. Queguiner, and P. Pastour, Compt. Rend., C, 280, 293 (1975).
5. L. Fisera, J. Lesko, J. Kovac, J. Hrabovsky, and J. Sura, Collect. Czech. Chem. Commun., 42, 105 (1977).
6. N. S. Prostakov, A. T. Soldatenkov, and V. O. Fedorov, Zh. Org. Khim., 15, 1109 (1979).
7. G. E. Wiegand, V. J. Bauer, S. R. Safir, D. A. Blickens, and S. J. Riggi, J. Med. Chem., 14, 214 (1971).
8. T. Caty, Japanese Patent No. 47392; Ref. Zh. Khim., 20N281P (1973).
9. D. M. Bailey, US Patent No. 3890335; Ref. Zh. Khim., 70124P (1976).
10. J. Szychowski, J. T. Wrobel, and A. Leniewski, Bull. Acad. Pol. Sci., Ser. Sci. Chim., 22, 383 (1974).
11. N. S. Prostakov, P. K. Radzhan, A. T. Soldatenkov, and A. I. Mikaya, Khim. Geterotsikl. Soedin., No. 3, 383 (1981).
12. R. A. Khmel'nitskii, P. B. Terent'ev, A. D. Polyakova, and A. N. Kost, Dokl. Akad. Nauk SSSR, 167, 1066 (1966).

*In the text and in the schemes the numbers that characterize the ions are the mass-to-charge ratios (m/z).

13. G. Vernin and J. Metzger, J. Chim. Phys., 71, 865 (1974).
14. A. I. Mikaya, A. T. Soldatenkov, V. O. Fedorov, V. G. Zaikin, and N. S. Prostakov, Zh. Org. Khim., 16, 1078 (1980).
15. P. I. Zakharov, V. P. Zvolinskii, A. T. Soldatenkov, A. P. Krapivko, and N. S. Prostakov, Zh. Org. Khim., 16, 2330 (1980).
16. H. M. Grub and S. Meyerson, Mass Spectrometry of Organic Ions, Academic Press, New York, Chapter 10 (1963).
17. P. B. Terent'ev, R. A. Khmel'nitskii, I. S. Khromov, A. N. Kost, I. P. Gloriozov, and M. Islam, Zh. Org. Khim., 6, 606 (1970).
18. V. P. Zvolinskii, P. I. Zakharov, L. A. Murugova, V. K. Shevtsov, G. A. Vasil'ev, A. V. Varlamov, and N. S. Prostakov, Zh. Org. Khim., 14, 2414 (1978).

EFFECT OF THE AGGREGATE STATE ON THE CONJUGATION IN THE 2-(2'-QUINOLYL)BENZOXAZOLE SYSTEM

N. A. Klyuev, P. B. Kurapov, G. G. Aleksandrov, and I. I. Grandberg

UDC 547.787.3'831:535.37:543.51+548.737

It was demonstrated by x-ray diffraction analysis, electronic spectroscopy, and mass spectrometry that the phase state and a decrease in the temperature of the solution have a substantial effect on the dihedral angle between the planes of the rings and the conjugation in the 2-(2'-quinolyl)benzoxazole molecule. The molecule is planar in the crystalline state, in the gas phase, and in solution at low temperature. The conjugation is maximal in these cases. The conjugation decreases when the compound is dissolved, and this is reflected in the character of the electronic absorption and emission spectra.

It is known [1] that the magnitude of the activation barrier (ΔE) for the conformers of bisheterocyclic analogs of biphenyl in the general case amounts to only 2-12 kcal/mole. Under these conditions the position of the equilibrium between the conformers is sensitive to various external factors [1, 2]. In particular, the magnitude of the dihedral angle between the planes of the aryl or hetaryl rings of a system with a structure of the biphenyl type and, consequently, the conjugation between them may depend on the aggregate state of the compound, the temperature, and the polarity of the solvent.

In order to study the effect of external factors on the conjugation in the 2-(2'-quinolyl)benzoxazole system (I) we obtained the electronic absorption and emission spectra of I at various temperatures in solutions and in the solid phase and made a detailed study of the character of the fragmentation of I under the influence of electron impact (the gas phase). We also determined the conformation of the I molecules in the crystal by means of x-ray diffraction analysis (XDA).

Thus in the case of a specific compound we have for the first time by means of various physicochemical methods traced how the aggregate state of the sample and the temperature of the solutions affect the conjugation in a system with a structure of the biphenyl type.

According to the XDA data, the 2-(2'-quinolyl)benzoxazole molecule is virtually planar in the crystal. The dihedral angle between the planes of the rings is only 1.1°. The maximum deviation of the C_9 and C_{13} atoms from the middle of the plane drawn through all of the nonhydrogen atoms is 0.03-0.04 Å, respectively (Tables 1 and 2 and Fig. 1). Thus in the solid phase the hetaryl rings of I constitute a planar system represented by the S-trans isomer. Maximum conjugation between the rings leads to a decrease in the length of the interannular C_7-C_8 bond (Fig. 1), which is 1.48(1) Å; this is 0.025 Å shorter than the central bond in biphenyl [3]. Sesqui character of the interannular bond was previously predicted for similar bisheterocyclic systems on the basis of the results of quantum-chemical calculations [4]. The principal geometrical parameters

K. A. Timiryazev Moscow Agricultural Academy, Moscow 127550. All-Union Scientific-Research Institute of Antibiotics, Moscow 113105. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 775-779, June, 1982. Original article submitted August 4, 1981.

0009-3122/82/1806-0585$07.50