(30), 234 (16), 233 (14), 220 (29), 219 (80), 218 (39), 205 (16), 204 (13), 188 (88), 173 (61), 151 (20), 150 (20) 149 (66), 132 (27), 128 (22), 127 (20), 117 (38), 116 (25), 115 (35), 105 (32), 91 (31), 77 (46).

LITERATURE CITED

1. S. Motoki, C. Urakawa, A. Kano, V. Fushimi, T. Hirano, and K. Murato, Bull. Chem. Soc. Jpn., 43, 809 (1970).
2. A. A. Stolyarchuk, Yu. N. Furman, V. L. Pikalov, Z. F. Solomko, and V. S. Tkachenko, Khim.-Farm. Zh., 9, 19 (1975).
3. L. K. Mushkalo, I. B. Dzvinchuk, and N. N. Mushkalo, Ukr. Khim. Zh., 45, 231 (1979).
4. A. K. El-Shafei, H. S. El-Kashef, and A. M. El-Khawage, Indian J. Chem., Vol. No. 21B, 655 (1982).
5. R. C. Harris and J. M. Straley, French Pat. No. 4537757; Chem. Abstr., 73, 100054 (1970).
6. N. N. Mushkalo, N. O. Markova, and L. K. Mushkalo, Vestn. Kazan. State Univ., No. 21, 31 (1980).
7. T. V. Stupnikova, B. M. Zemskii, R. S. Sagitullin, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 3, 291 (1982).
8. T. G. Chmilenko, Z. F. Solomko, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 4, 525 (1977).
9. A. N. Kost, P. A. Sharbatyan, P. B. Terent'ev, Z. F. Solomko, V. S. Tkachenko, and L. G. Gergel', Zh. Org. Khim., 8, 2113 (1972).

REACTIONS OF 4,5-DIAMINO-3-METHYL-1-PHENYLPYRAZOLE WITH DIARYLIDENEACETONES

V. D. Orlov, Kh. Kiroga, A. Marrugo, N. N. Kolos, and S. V. Iksanova

UDC 547.572.773.892.07: 543.422.25

The reaction of 4,5-diamino-3-methyl-1-phenylpyrazole with dibenzylideneacetone and its 4,4'-derivatives has been studied; the reactions lead to aromatic 1H-2,3-dihydropyrazolo[5,4-b]1,5-diazepine derivatives. The reaction pathway has also been identified.

The reactions of aromatic and heterocyclic 1,2-diamines with α,β-unsaturated ketones constitute a direct method for the synthesis of annelated 2,3-dihydro-1,5-diazepines [1-3]. In a preceding communication [4], it was shown that 4,5-diamino-3-methyl-1-phenylpyrazole also reacts with chalcones in acidic media to give 1H-2,3-dihydropyrazolo[5,4-b]-1,5-diazepine derivatives.

Continuing these investigations, we have examined the reaction of 4,5-diamino-3-methyl-1-phenylpyrazole (I) with diarylideneacetones. In the case of the reaction of diamine I with symmetrically substituted diarylideneacetone derivatives (R = R^1), pure dihydropyrazolodiazepine derivatives (II-VII, XVIII) are obtained in excellent yield; non-symmetrical ketones (R ≠ R^1), on the other hand, give mixtures of two isomeric dihydropyrazolodiazepines, which are difficult to separate (the formation of mixtures was suggested, first of all, by the relatively low melting points of the products which were obtained, and, secondly, by analysis of their PMR spectra).

The structures of the newly synthesized compounds II-XX were confirmed on the basis of their elemental analyses and spectral characteristics (Tables 1-3). For example, the IR

A. M. Gor'kii Khar'kov State University, Khar'kov 310077.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1563-1567, November, 1987. Original article submitted June 2, 1986.

0009-3122/87/2311-1254$12.50

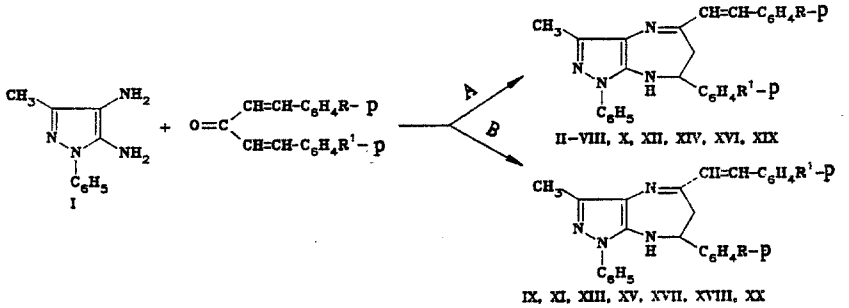
TABLE 1. Substituted 2,3-Dihydro-1H-pyrazolo[5,4-b]-1,5-diazepines

Compound	T_{mp}, °C	Heating time, h	UV spectrum (in methanol), λ_{max}, nm (log ε)	ν_{NH}	Found N, %	Molecular formula	Calc. N, %	Yield, %
II	178	4	388 (4,32), 284 (4,34), 248 (4,20)	3364	14,0	$C_{27}H_{24}N_4$	13,9	80
III	162—163	3	385 (4,32), 289 (4,31), 248 (4,25)	3384	12,9	$C_{29}H_{28}N_4$	13,0	64
IV	167	3	387 (4,40), 291 (4,33), 247 (4,33)	3399	12,1	$C_{29}H_{28}N_4O_2$	12,1	64
V	189—190	2	392 (4,35), 289 (4,38), 248 (4,24)	3367	11,9	$C_{27}H_{22}Cl_2N_4$	11,8	61
VI	195—196	2	393 (4,35), 289 (4,33), 249 (4,25)	3377	9,9	$C_{27}H_{22}Br_2N_4$	10,0	56
VII	282	5	435 (4,30), 318 (sh.), 271 (4,35)	3395	17,3	$C_{27}H_{22}N_6O_4$	17,0	20
VIII	190 (dec)	1	387 (4,35), 286 (4,39), 248 (4,33)	3368	13,1	$C_{28}H_{26}N_4$	13,4	25
VIII : IX (1 : 1)*	93	3	385, 286, 248	3362	13,3	$C_{28}H_{26}N_4$	13,4	84
X : XI (1 : 1)	96	3	385, 290, 248	3362	12,8	$C_{28}H_{26}N_4O$	12,9	54
XII : XIII (1 : 2)	152—154	4	390, 279, 253	3370	11,7	$C_{33}H_{28}N_4$	11,7	72
XIV	181—182	1	388 (4,37), 284 (4,39), 248 (4,30)	3364	12,6	$C_{27}H_{23}ClN_4$	12,8	27
XIV : XV (1 : 1)	67	1,5	391, 286, 249	3247	12,7	$C_{27}H_{23}ClN_4$	12,8	90
XVI : XVII (1 : 1)	74	1,5	392, 286, 247	3242	11,8	$C_{27}H_{23}BrN_4$	11,6	92
XVIII	180—181	1	436 (4,35), 313 (4,18), 248 (4,25)	3389	15,5	$C_{27}H_{23}N_5O$	15,6	93
XIX : XX (1 : 2)	212	2,5	397, 281, 252	3401	14,5	$C_{28}H_{25}N_5O_3$	14,6	71
XXI	156—158	3	311 (3,69), 263 (4,16), 241 (4,21)	3403	16,5	$C_{22}H_{22}N_4$	16,5	70

*The characteristics of the isomeric mixtures are given; the ratios of isomers produced are shown in parentheses.

TABLE 2. Calculated Data for a Planar Molecule of 1-Phenyl-4-cinnamalamino-5-aminopyrazole

Electronic transition	UV spectral band	Calculated		Experimental		Transition localization, %						Change in electron density, e					
		E, eV	f	E, eV	f	N	pyrazolyl	C=N	C=C	1-C_6H_5	C_6H_5 (syn)	N	pyrazolyl	C=N	C=C	1-C_6H_5	C_6H_5 (syn)
0→1	1	3,11	0,83	3,19	0,48	13	27	29	20	1	10	−0,21	−0,35	0,28	0,19	0,0	0,09
0→2		4,06	0,37			8,4	33,7	21,8	14,1	13,9	7,9	−0,10	−0,34	0,33	0,16	−0,1	0,06
0→3	2	4,29	0,30	4,36	0,72	17,4	40,1	4,1	3,1	32,8	2,5	−0,28	−0,08	−0,05	−0,02	0,45	−0,01
0→4		4,48	0,08			4,0	13,9	1,2	2,0	69,2	9,6	−0,07	−0,16	−0,01	0,0	0,24	0,0
0→5		4,68	0,10			3,4	27,9	9,5	15,1	27,5	16,6	−0,02	−0,11	0,09	0,03	0,13	−0,12



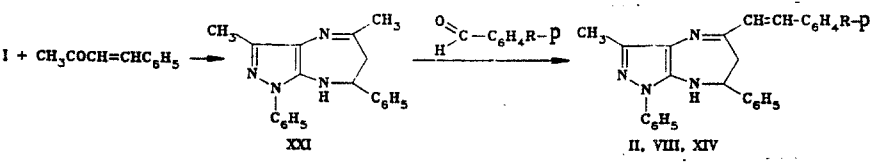
II R=R¹=H, III R=R¹=CH_3, IV R=R¹=OCH_3, V R=R¹=Cl, VI R=R¹=Br, VII R= =R¹=NO_2, VIII—XVIII R=H, VIII, IX R¹=CH_3, X, XI R¹=OCH_3, XII, XIII R¹=C_6H_5, XIV, XV R¹=Cl, XVI, XVII R¹=Br, XVIII R¹=NO_2, XIX, XX R=OCH_3, R¹=NO_2

spectra contained ν_{NH} bands at 3242-3377 cm^{-1}. The PMR spectra of these compounds exhibited sharp and distinct signals for the CH_2—CH fragment protons (ABX system), for the imino group proton (singlet), for the trans-vinyl group (AB system, J = 16.3-16.5 Hz), as well as multiplets for the aromatic protons. The mass spectrum of compound II exhibited a molecular ion peak.

The possible reaction pathways available for diamine I with unsaturated ketones, due to the presence of nonequivalent amino groups, have been discussed previously [4]; it was found that the azomethine bond of the seven-membered ring heterocycle is formed from the amino group which is located in the 4-position of the pyrazole ring. The absence of any fundamental differences between the synthesis conditions or spectral characteristics of the compounds summarized here and those reported earlier suggests that the scheme proposed earlier [4] for the reaction of I with diarylideneacetones is essentially correct.

The proposed scheme contains two alternative pathways (A and B) for asymmetrical diarylideneacetones; these result from the presence of nonequivalent cinnamoyl fragments in the ketones, which, in our opinion, is the main factor responsible for the formation of product mixtures. We were able to study the direction of the reaction of diamine I with these diarylideneacetones, as well as determine the composition of the product mixtures, via both chemical (independent syntheses) and spectral methods.

The starting material for the independent syntheses was 4,6-dimethyl-2,8-diphenyl-2,3-dihydro-1H-pyrazolo[5,4-b]diazepine (XXI); it was used to synthesize II, VIII, and XIV (Table 1):



Analysis of the IR spectra of compounds II-XXI clearly revealed that the ν_{NH} values could not be used to identify the isomers present, due to their low sensitivity to electronic effects exerted by the aromatic rings located in the 2- and 4-positions of the seven-membered ring.

In some individual cases the positions of the substituents in the dihydropyrazolodiazepines could be deduced from their electronic absorption spectra. These spectra are characterized by the presence of two well-resolved π-π^* bands in the 250-270 and 385-435 nm regions (Table 1). Quantum mechanical calculations (Table 2) indicated that the long wavelength band in these spectra is due to a one-electron 0 → 1 transition. This transition is accompanied by charge transfer from the imino group to the N=C—C=C fragment, via the pyrazoline ring; the phenyl radical in the styryl fragment is only negligibly excited in this transition (Table 2). In principle, therefore, the introduction of either weakly electron donating or electron withdrawing substituents R or R^1 should have very little effect on the λ_{max} values of the long wavelength band; this was confirmed experimentally (cf. spectra of compounds II-VI, Table 1). For the same reason, the spectra of different isomers produced in the reactions of diamine I with unsymmetrically diarylideneacetones overlap one another, making it difficult to identify the compounds. Only the introduction of a strongly electron withdrawing nitro group, which is able to facilitate the charge transfer transition discussed above, exerts a bathochromic shift on this band in the spectra of compounds VII,

TABLE 3. PMR Spectra (δ, ppm, J, Hz) of Compounds II-XXI

Compound	NH, (s)	H_A, (d of d)	H_B, (d of d)	H_X (d of d)	H_α	H_β	CH_3	J_{AB}	J_{AX}	$J_{H_\alpha H_\beta}$
II	4,59	2,95	3,24	4,46	6,94	6,62	2,36	15,4	7,3	16,6
III	4,53	2,90	3,25	4,38	6,91	6,63	2,36	15,2	7,8	16,4
IV	4,52	2,88	3,22	4,37	6,83	6,61	2,35	15,4	7,1	16,6
V	4,58	2,98	3,16	4,50	6,89	6,56	2,35	15,2	7,4	16,6
VI	4,63	2,96	3,12	4,46	6,89	6,52	2,33	15,4	7,5	16,2
VIII/IX*	4,57	2,91	3,20	4,40	6,87/6,92	6,59/6,64	2,36	15,0	7,4	16,8
X/XI	4,54	2,93	3,26	4,43	6,88	6,65	2,36	15,2	7,8	16,0
XII/XIII	4,59	2,95	3,26	4,47	6,97/6,99	6,68/6,66	2,38	15,3	7,9	16,6
XIV	4,57	2,96	3,27	4,46	6,95	6,68	2,36	15,4	7,6	16,6
XIV/XV	4,56	2,97	3,16	4,44	6,86/6,89	6,53/6,59	2,32	15,2	7,5	16,4
XVI/XVII	4,57	2,99	3,21	4,46	6,91/6,94	6,55/6,63	2,36	15,2	7,3	16,2
XVIII	4,71	3,01	3,25	4,52	7,06	6,63	2,37	15,3	7,9	16,6
XIX/XX	4,80	2,96	3,25	4,42/ 4,65	7,07	6,56	2,35	15,0	6,9	16,4
XXI	4,54	2,80	2,91	4,48	—	—	2,30	15,0	7,0	—

*The chemical shift values of the R^1-group δ protons in compounds VII-XI are: 2.25; 2.23; 3.72; and 3.71 ppm, respectively; and 1.92 ppm for compound XXI. H_A, H_B, and H_X are the endocyclic protons (CH_2—CH fragment); H_α and H_β are the vinyl group protons.

XVIII, and XX, and thus makes it possible to assign their isomeric structures unequivocally.

The large differences observed in the λ_{max} values of the long wavelength bands in isomers XIX and XX make it possible to estimate the component ratio in this isomeric mixture based on its absorption spectrum. The calculations were made on the assumption that, if the compounds being compared contain identical or superimposable chromophoric systems (as is the case for compounds VII, XVIII, and XX), then the ε_{max} values for the long wavelength band will not differ significantly from one another. Based on this assumption, the ratio of isomers XIX and XX is 1:2.

The second band in the spectra of these compounds is assigned to a 0 → 3 transition, and is characterized by predominant localization of the transition energy on the pyrazole fragment. In the spectra of compounds II-XX, the λ_{max} position of this band is practically invariant, and is thus not useful for identification purposes.

Substitution of the aromatic ring located in the 2-position of the heterocycle has a very large effect on the chemical shift values of the NH and $C_{(2)}$—H group protons, whereas substitution of the aromatic ring in the styryl fragment induces changes in the δ values of the vinyl protons. The PMR spectra of mixtures of isomers (Table 3) therefore exhibit doubling of the signals corresponding to these protons (in the spectrum of the mixture of compounds VIII and IX, the methyl group signal is also doubled); this makes it possible to carry out the spectral assignments and also to determine the concentration of each isomer, based on the integrated intensities of the doubled signals.* It is noteworthy that the isomeric composition estimates obtained for the mixture of compounds XIX and XX ($R = OCH_3$, $R^1 = NO_2$) via the two methods, i.e., based on their electronic absorption and PMR spectra, were practically identical.

Reactions of unsymmetrical diarylideneacetones with 1,2-phenylenediamine and 5-phenyl-1,2-diaminoimidazole have already been studied [5, 6]. These processes have been shown to be highly regioselective: the formation of mixtures was observed only in the case of the reactions of ketones with R = H and R^1 = Cl or Br; in all other cases cyclization occurred at the unsubstituted cinnamoyl fragment. The processes are catalyzed by bases, with the first stage involving β-amination of the unsaturated ketone. This step is apparently suppressed by the introduction of electron donating substituents to the cinnamoyl fragment of the ketone. Ketones containing a nitro group are exceptions to this generalization; the decisive factor controlling their reaction pathway is the high thermodynamic stability of the final product, which is achieved when conjugation of the nitrophenyl radical is retained in the dihydroazepine product.

*The mp of the isomeric mixtures do not change after recrystallization, which indicates that the isomeric ratios remain constant after recrystallization (Table 1).

The isomeric composition data (Table 1) indicates that the process under investigation has lower regioselectivity. Since this process is characterized by acid catalysis, it is possible that there is a change in the sequence of the different reaction steps. The first stage may involve formation of the azomethine derivative. This has been observed previously in the case of the reactions of 5,6-diamino-1,3-dimethyluracil with chalcones [7], where the azomethine derivatives were isolated. In the present investigation it was not possible to stop the reactions of diamine I with ketones at the first stage. However, when the reaction of diamine I with chalcone or dibenzylideneacetone was monitored spectrophotometrically, absorption bands at λ_{max} 370 and 380 nm, respectively, were observed; these probably belong to the azomethine intermediates formed in the first step. This is suggested by the excellent agreement of these values with the λ_{max} value of the long-wavelength band in azomethine XXII (370 nm), which was synthesized from diamine I and cinnamaldehyde, and which contains a similar chromophoric system.

In the azomethine intermediates obtained from unsymmetrical diarylideneacetones, there is less of a differentiation between the electronic states of the C=C bonds relative to the starting ketone (due to the lower electron withdrawing ability of a C=N group compared to a C=O group); this fact, in our view, explains the lower regioselectivity observed in our system.

Analyzing the PMR spectra of compounds II-XXI (Table 3), we note that the chemical shift and J constant values for the seven-membered ring protons are identical to the analogous characteristics observed in 2,4-diaryl-6-methyl-8-phenyl-2,3-dihydro-1H-pyrazolo[5,4-b]-1,5-diazepines [4]. It should also be noted that the structure of this heterocycle does not change upon replacement of the aryl ring in the 4-position by a styryl fragment, i.e., the tub-shaped conformation with an equatorial orientation of the aryl radical in the 2-position is retained.

EXPERIMENTAL

IR spectra of compounds II-XXI were measured on a Specord IR-75 spectrophotometer (for KBr pellets); electronic spectra were obtained on a Specord UV-VIS spectrophotometer (in methanol) at concentrations of $(2\text{-}3)\cdot10^{-5}$ M, while PMR spectra were recorded on a Bruker 200 MHz spectrometer for $CDCl_3$ solutions versus HMDS as internal standard; the mass spectrum of compound II was measured on a Varian MAT-311A spectrometer at an ionizing electron energy of 70 eV. Sample purities were followed by TLC on Silufol UV-254 plates using chloroform as eluent. Quantum mechanical calculations were carried out using a PPP-50 program with a standard set of parameters.

6-Methyl-4-styryl-2,8-diphenyl-2,3-dihydro-1H-pyrazolo[5,4-b]-1,5-diazepine (II). A solution of 0.6 g (3.2 mmole) I and 0.75 g (3.2 mmole) dibenzylideneacetone in a mixture of 10 ml methanol and 1 ml acetic acid was refluxed for 4 h. After cooling, the reaction mixture was neutralized with concentrated ammonia and left in the refrigerator for 1 h. The precipitate was removed by filtration to give 1 g (80%) of compound II, mp 178°C (from a mixture of hexane–benzene, 1:1). Found: M^+ 404. $C_{27}H_{24}N_4$. Calculated: M 404.

Compounds III-XXI were prepared in an analogous manner, varying only the heating times.

Condensation of Compound XXI with Aromatic Aldehydes. A solution of 0.5 g (1.6 mmole) compound XXI and 0.16 g (1.6 mmole) benzaldehyde in 10 ml methanol was mixed with 1 ml conc. HCl and refluxed 1 h, then cooled and neutralized with an ammonia solution. Compound II (0.2 g, 30%) was deposited in the form of light yellow crystals, mp 178°C (from a mixture of hexane–benzene, 1:1).

Compounds VIII and XIV were prepared in an analogous manner.

Condensation of Diamine I with Cinnamaldehyde. A solution of 0.3 g diamine I and 0.2 g cinnamaldehyde in a mixture of 10 ml methanol and 1 drop acetic acid was refluxed for 20 min. The crystalline precipitate was removed by filtration. Yield 0.4 g (80%) of compound XXII, mp 129-130°C (from methanol). Found: N 18.5%. $C_{19}H_{18}N_4$. Calculated: N 18.5%.

LITERATURE CITED

1. V. D. Orlov, N. N. Kolos, F. G. Yaremenko, and V. F. Lavrushin, Khim. Geterotsikl. Soedin., No. 5, 607 (1980).
2. V. D. Orlov, I. Z. Papiashvili, M. V. Povstyanoi, V. A. Idsikovskii, and O. M. Tsiguleva, Khim. Geterotsikl. Soedin., No. 1, 93 (1983).

3. V. D. Orlov, I. Z. Papiashvili, and P. A. Grigorov, Khim. Geterotsikl. Soedin., No. 5, 671 (1983).
4. V. D. Orlov, Kh. Kiroga, and N. N. Kolos, Khim. Geterotsikl. Soedin., No. 3, 363 (1987).
5. V. D. Orlov, N. N. Kolos, and V. F. Lavrushin, Khim. Geterotsikl. Soedin., No. 6, 827 (1981).
6. I. A. Papaishvili, Candidate's Dissertation, Chemical Sciences, Khar'kov (1983).
7. V. D. Orlov and I. Z. Papaishvili, Khim. Geterotsikl. Soedin., No. 2, 241 (1985).

SYNTHESIS AND STRUCTURE OF NONCONDENSED BICYCLIC THIAZOLIDINO-4-ONE DERIVATIVES

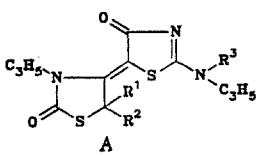
I. B. Levshin, V. V. Chistyakov, O. A. Anisimova, and Yu. N. Sheinker

UDC 547.789.5.07:543.51

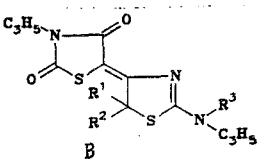
The synthesis of novel noncondensed bicyclic thiazolidin-4-one derivatives has been achieved. The bond between the thiazolidinone rings has been shown, using mass spectrometry, to be located at the 5–4' positions.

It has previously been demonstrated [1] that a noncondensed bicyclic thiazolidin-4-one derivative, namely, 2-acetylallylamino-4-oxo-5-(3-allyl-2-oxothiazolidin-4-ylidene)thiazoline (I), could be synthesized via condensation of an unstable intermediate, 2-acetylallylamino-thiazolin-4-one with 3-allylthiazolidin-2,4-dione in an acetic anhydride–acetic acid medium.

Based on the reactivity of the functional groups in the thiazolidin-4-one molecule, theoretically two isomers should be able to be formed, bonded to one another through either the 5–4' (A) or 4–5' positions (B).



A



B

I $R^1=R^2=H$, $R^3=COCH_3$; II $R^1=R^2=R^3=H$; III $R^1=R^2=CHPh$, $R^3=COCH_3$

In choosing between the alternative structures A and B in our previous paper [1], we relied on experimentally verified data concerning the greater reactivity of the methylene group in 2-acylamino thiazolidin-4-one derivatives with respect to aldol condensation reactions, compared to the reactivity of thiazolidin-2,4-dione derivatives [2]. This was supported also by the negative result obtained in the attempted self-condensation of 3-allylthiazolidin-2,4-dione upon refluxing in acetic anhydride or in a mixture of the latter with acetic acid. It was not possible, however, based on the data reported in [1], to reach an unequivocal conclusion concerning the site of addition of the two rings.

In order to confirm our assumptions concerning the structure of these compounds, and, furthermore, to establish the position of the double bond between the two rings, we have carried out a mass spectroscopic investigation of both the known compounds in this class (I-III [1]) as well as some new derivatives, which were prepared as a result of condensation

S. Ordzhonikidze All-Union Scientific Research Chemical-Pharmaceutical Institute, Moscow 119021. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1568-1571, November, 1987. Original article submitted March 5, 1986.

0009-3122/87/2311-1259$12.50