Mass spectra of new groups of functionalized heterocycles 4.* 1-Alkyl-2-(alkylthio)pyrroles

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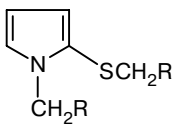
The electron impact-induced fragmentation of 1-alkyl-2-(alkylthio)pyrroles is accompanied by rearrangements of the molecular and fragment ions with ring expansion.

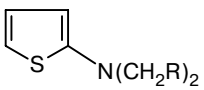
Key words: heterocycle, 1-alkyl-2-(alkylthio)pyrroles, mass spectra, electron impact, fragmentation, rearrangement.

Previously,[2] we showed that the main route of decomposition of 2-(organylthio)-1*H*-pyrroles under the action of electron impact is abstraction of the alkyl radical accompanied by expansion of the pyrrole ring to the 1,3-thiazine ring. Since the same six-membered ring is formed upon fragmentation of alkyl(2-thienyl)amines,[3] the spectra of the latter compounds are similar to the spectra of 2-(alkylthio)-1*H*-pyrroles in the m/z < 98 region.

This work is a study of the mass spectra of previously unknown 1-alkyl-2-(alkylthio)pyrroles (**1a—d**), synthesized by the route proposed in our recent studies,[4—6] *i.e.*, by deprotonation of allyl isothiocyanate on treatment with the complex superbase $Pr^i_2NK—Bu^tOLi$ and subsequent alkylation of the resulting pyrrole-2-thiol dianion. The spectrum of dibutyl(2-thienyl)amine (**2d**) was also recorded for comparison.



1a—d



2d

R = H (**a**), Me (**b**), Et (**c**), Pr (**d**)

Results and Discussion

It was found that the nature of the substituent R in compounds **1a—d** has a much greater influence on the pattern and degree of fragmentation of their molecular ions than that in 2-(alkylthio)-1*H*-pyrroles studied previously.[2] This is due to the fact that the main primary event in the fragmentation of the latter is the loss of the alkyl substituent. This results in generation of the ion with m/z 98, common to all of the compounds studied, whose further fragmentation follows the same route. In the case of compounds **1a—d**, a similar process gives ions with different substituents at the N atom; therefore, their further fragmentation routes are different.

The abstraction of the CH_2R group to give ion **A** is the fragmentation step common to all the compounds studied (Scheme 1, Table 1). Pyrroles **1b—d** also tend to undergo successive elimination of two $CH_2{=}CHR'$ olefin molecules (see Scheme 1, Table 1). The $[M - Me]^+$ ion present in the mass spectrum of **1a** has structure **A** (see Scheme 1). Since there are no active H atoms at any of the heteroatoms, the pyrrole ring cannot expand[7] to the thiazine ring to give structure **A′**. The further fragmentation of ion **A** follows three pathways (ejection of CS, H_2S, and methylisonitrile molecules) giving rise to ions **B**, **C**, and **D**, respectively.

In the case of derivative **1d**, elimination of the propyl radical R takes place, in addition to the elimination of the butyl group CH_2R. The intensity of the peak of the $[M - R]^+$ ion with m/z 168 is 12 times lower than the intensity of the $[M - CH_2R]^+$ ion peak with m/z 154 (see Table 1). The opposite situation is found in the mass spectrum of dibutyl(2-thienyl)amine (**2d**) (see Table 1), whose elemental composition is the same as that of **1d**. The intensities of the peaks of ions with m/z 154 and 168 are 9 and 35%, respectively, *i.e.*, elimination of the propyl radical from the *N*-butyl substituent predominates. This implies that in the molecu-

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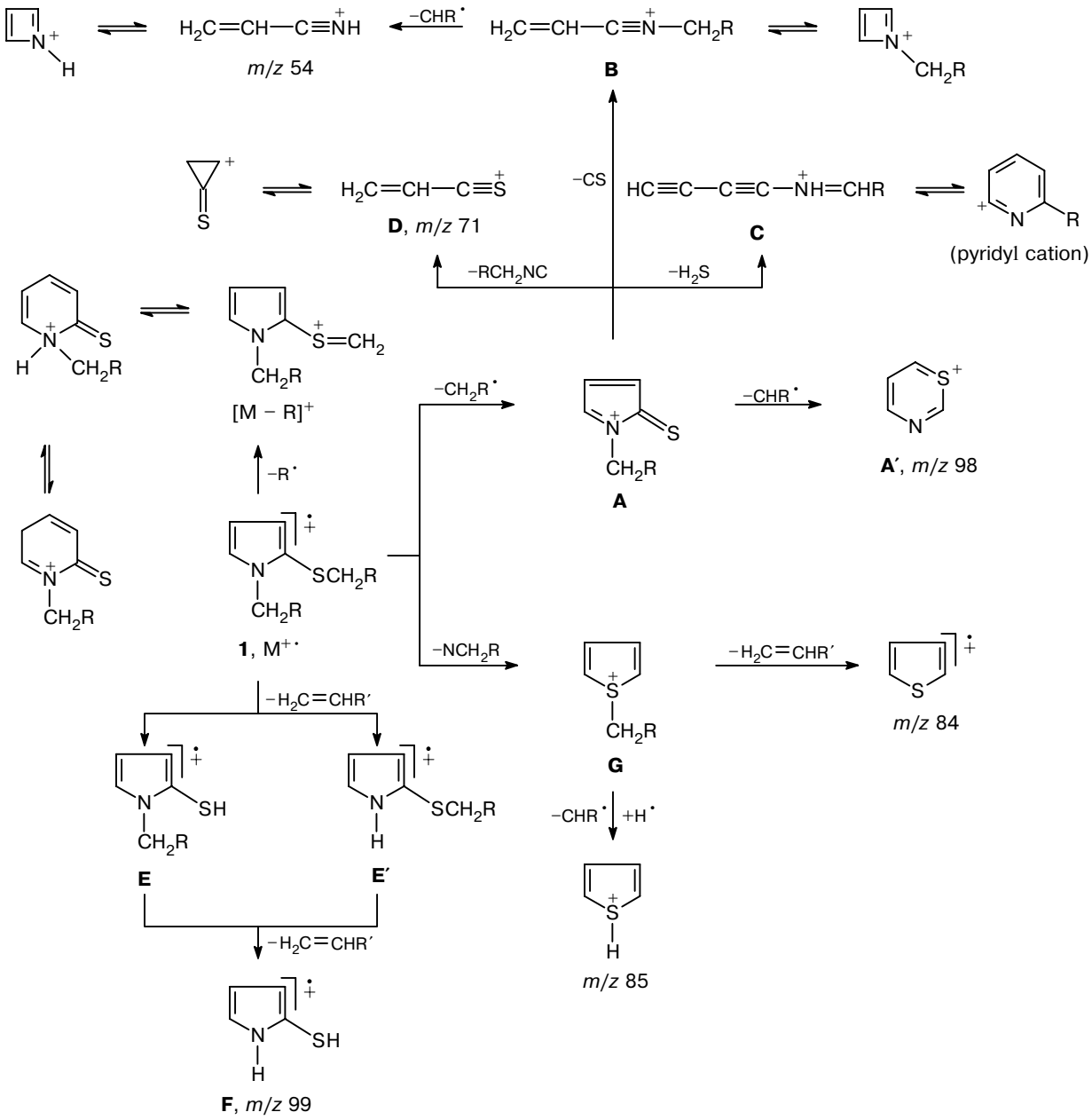
Scheme 1



lar ion derived from **1d**, the charge is concentrated on the sulfur rather than on the nitrogen atom, and the $^{\bullet}CH_2R$ substituent splits off from the exocyclic heteroatom.

Yet another route of primary fragmentation of the molecular ion derived from **1d** involves the loss of the NCH_2R group, resulting in odd-electron ion **G**. This ion loses a butene molecule or a butenyl radical, being thus converted into ions with *m/z* 84 and 85, respectively (see Scheme 1).

Whereas all the above-listed fragment ions present in the mass spectrum of **1d** could arise from the initial structure of the $M^{+\bullet}$ molecular ion, the other fragments are formed from the isomeric form, $[M']^{+\bullet}$, in which the pyrrole ring has expanded to the dihydropyridine ring with involvement of the α-methylene group of the alkyl substituent at the N atom (Scheme 2). Indeed, it was shown previously[2] that 2-(alkylthio)-1*H*-pyrroles do not tend to undergo bond cleavage between the heterocycle and the 2-substituent, *i.e.*, the $[M - SCH_2R]^+$ ion is not formed, whereas in the spectrum of **1d**, the intensity of the peak of this ion with *m/z* 122 is equal to 76%. A similar difference between the spectra of dialkyl(2-thienyl)amines and their 3- or 5-methyl de-

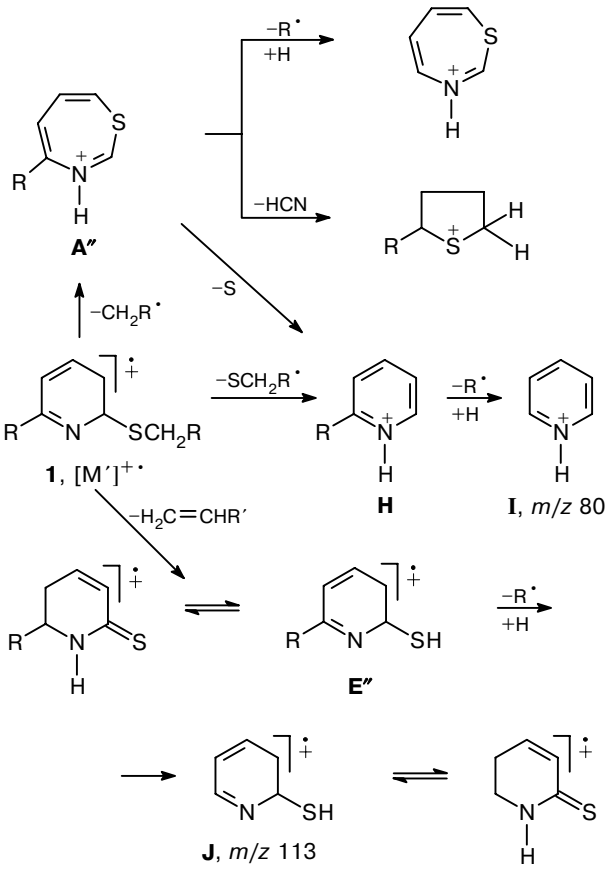
Table 1. Mass spectra of 1-alkyl-2-(alkylthio)pyrroles **1a—d** and dibutyl(2-thienyl)amine **2d** (at 60 V)

Ion	*m/z* (I_{rel} (%))				
	1a	**1b**	**1c**	**1d**	**2d**
$[M]^{+\bullet}$	127	155	183	211	211
	(100)	(67)	(59)	(90)	(32)
$[M - R]^+$	—	140	154	168	168
		(2)	(2)	(4)	(35)
$[M - CHR]^{+\bullet}$	—	127	141	155	155
		(15)	(91)	(66)	(15)
$[M - 2\ CHR]^{+\bullet}$	—	99	99	99	99
		(8)	(100)	(95)	(21)
$[M - CH_2R]^+$	112	126	140	154	154
	(97)	(100)	(80)	(47)	(9)
$[(M - CH_2R) - H_2S]^+$	78	92	106	120	—
	(36)	(17)	(7)	(4)	
$[(M - CH_2R) - CHR]^+$	—	98	98	98	98
		(32)	(68)	(44)	(7)
$[M - SCH_2R]^+$	—	94	108	122	122
		(8)	(22)	(76)	(8)
$[(M - CHR) - R + H]^{+\bullet}$	—	—	113	113	113
			(29)	(100)	(6)
$[(M - R) - CHR]^{+\bullet}$	—	—	112	112	112
			(28)	(79)	(100)
$[(M - CH_2R) - HCN]^+$	85	*	**	127	127
	(20)			(26)	(2)
$[(M - SCH_2R) - R + H]^+$	—	—	80	80	80
			(13)	(23)	(18)
$[(M - CH_2R) - CS]^+$	68	82	96	110	—
	(24)	(4)	(1)	(9)	
$[M - NCH_2R]^+$	—	112	126	140	—
		(4)	(11)	(7)	
Other ions, *m/z*					
85	***	(5)	(6)	(5)	—
84	—	(5)	(7)	(9)	—
72	—	(4)	(18)	(12)	(2)
71	(16)	(13)	(20)	(18)	(3)
57	—	—	—	(18)	(6)
54	—	(17)	(28)	(26)	(3)
45	(25)	(12)	(21)	(16)	(5)
43	—	—	(27)	(4)	(3)
42	(13)	(3)	(8)	(4)	(2)
41	(10)	(4)	(35)	(47)	(13)
39	(24)	(13)	(28)	(25)	(7)

* Superimposed on the peak of the $[M - 2\ CHR]^{+\bullet}$ ion with *m/z* 99.
** Superimposed on the peak of the $[(M - CHR) - R + H]^{+\bullet}$ ion with *m/z* 113.
*** Superimposed on the peak of the $[(M - CH_2R) - HCN]^+$ ion with *m/z* 85.

rivatives (the former do not eliminate the $NAlk_2$ substituent,[3] while for the methyl-substituted analogs, the contribution of this process is substantial[1]) is due to the expansion of the thiophene ring to the thiazine ring.[1] The fact that ion **H** with *m/z* 122 does really contain a pyridine ring rather than a pyrrole ring is confirmed by its further fragmentation: ion **H** loses a propene molecule rather than a butene molecule, being thus converted into the protonated molecular ion of pyridine **I** with *m/z* 80 (see Scheme 2). The ejection of the butene molecule from $[M']^{+\bullet}$ derived from compound **1d** affords ion **E″**. This ion loses a propene molecule to give the pseudo-molecular ion of 2-mercapto-1,2-dihydropyridine **J** with *m/z* 113; the peak of this ion has the maximum intensity in the spectrum of **1d**.

Scheme 2



Analysis of further fragmentation routes of the $[M - CH_2R]^+$ ion with *m/z* 154 shows that this structure differs from the structure of **A** formed upon decomposition of **1a**. Indeed, the intensity of the peaks due to ions **B** $[154 - CS]^+$ and **C** $[154 - H_2S]^+$, produced from ion **A**, is low (see Scheme 1, Table 1). Conversely, high intensity is observed for the ion peaks with *m/z* 127 (26%) and 112 (79%) arising upon elimination of the HCN and C_3H_6, respectively, from the ion with *m/z* 154. Both processes can be understood assuming that the ion with *m/z* 154 has a thiazatropilium structure **A″** (see Scheme 2), which results from detachment of the $^{\bullet}CH_2R$ substituent from the S atom of the $[M']^{+\bullet}$ isomer of the molecular ion.

The fragmentation of the propyl derivatives **1c** follows a similar pattern, typical of the butyl analog **1d**. The ethyl-containing compound **1b** occupies an intermediate position; it decomposes by pathways typical both of the methyl analog **1a** (*e.g.*, ejection of the H_2S molecule from the $[M - CH_2R]^+$ ion) and of higher homologs.

The mass spectra of all compounds studied, except for **1a**, exhibit a peak of the thiazine ion with *m/z* 98, whose fragmentation has been discussed in detail previously.[2]

Thus, fragmentation of 1-alkyl-2-(alkylthio)pyrroles is accompanied by rearrangements of the molecular and fragment ions with ring expansion.

Experimental

Mass spectra were recorded on an LKB-2091 GC/MS instrument with ionizing voltages of 10 and 60 V using the chromatographic system of sample injection into the ion source (source temperature 240 °C, a 38-m long glass capillary column with the SE-54 phase, vaporizer temperature 270 °C; the rate of heating from 60 to 270 °C was 16 °C min^{-1}). IR spectra were measured on a Specord IR-75 spectrophotometer in thin film; ^{1}H NMR spectra were run on a Varian EM-390 spectrometer (90 MHz, ~20% solutions in CCl_4, Me_4Si as the internal standard).

All operations were carried out under nitrogen. THF was purified by mechanically dispersed KOH (~50 g L^{-1}) and by distillation over $LiAlH_4$ in the presence of benzophenone under nitrogen. Butyllithium (1.6 *M* solution in hexane); Bu^{t}OK and allyl isothiocyanate were commercial preparations.

1-Methyl-2-(methylthio)pyrrole (**1a**) was prepared by the previously described procedure.[4]

1-Ethyl-2-(ethylthio)pyrrole (1b). A solution of Bu^{n}Li (0.10 mol) in 65 mL of hexane was added at −50 °C to a solution of diisopropylamine (0.10 mol) and Bu^{t}OK (0.10 mol) in 60 mL of THF; then, at −50 to −40 °C, a solution of allyl isothiocyanate (0.05 mol) in 40 mL of THF was added over a period of 30 min. The reaction mixture was stirred for 5 min at 15 °C, the temperature was decreased to −20 °C, and ethyl iodide (0.15 mol) was added (the temperature rose to 10 °C). The reaction mixture was stirred for 30 min at 40—45 °C and treated with ~60 mL of cold water. The organic layer was separated and the aqueous layer was extracted with ether and pentane. The combined organic fraction was dried with K_2CO_3, the solvents were evaporated under reduced pressure, and the residue was distilled *in vacuo* to give 3.3 g (42.6%) of 1-ethyl-2-(ethylthio)pyrrole (**1b**), purity 94% (GLC), b.p. ~40 °C (0.7 Torr), n_D^{20} 1.5122. Found (%): C, 61.77; H, 8.32; N, 9.17; S, 20.74. $C_8H_{13}NS$. Calculated (%): C, 61.89; H, 8.44; N, 9.02; S, 20.65. IR, ν/cm^{-1}: 610, 660, 720 vs, 760, 790, 880, 950, 965, 1000, 1030, 1040, 1060, 1080, 1100, 1120, 1200, 1260, 1280 vs, 1350, 1370, 1435, 1450, 1510, 2860, 2920, 2965, 3100. ^{1}H NMR, δ: 1.25 (dt, 6 H, 2 Me); 2.48 (q, 2 H, SCH_2); 3.96 (q, 2 H, NCH_2); 5.97 (m, 1 H, CH=); 6.18, 6.68 (both m, each 1 H, CH=).

1-Propyl-2-(propylthio)pyrrole (1c). A solution of Bu^{n}Li (0.10 mol) in 72 mL of hexane was added at −80 °C to a solution of diisopropylamine (0.10 mol) and Bu^{t}OK (0.10 mol) in 60 mL of THF; then, a solution of allyl isothiocyanate (0.05 mol) in 35 mL of THF was added dropwise at −30 to −25 °C over a period of 30 min. The reaction mixture was stirred for 10 min at 38—40 °C, cooled to 10 °C, and propyl iodide (0.15 mol) was added (the temperature rose to 20 °C). Then the mixture was heated to 40—45 °C, stirred for 75 min, cooled to ~20 °C, and ~60 mL of cold water was added. The organic layer was separated, the aqueous layer was extracted with ether and pentane, the combined organic fraction was dried with K_2CO_3, the solvents were removed under reduced pressure, and the residue was distilled *in vacuo* to give 5.3 g (58%) of 1-propyl-2-(propylthio)pyrrole (**1c**), b.p. ~70 °C (0.5 Torr), n_D^{20} 1.5208. Found (%): C, 65.75; H, 9.21; N, 7.49; S, 17.55. $C_{10}H_{17}NS$. Calculated (%): C, 65.52; H, 9.35; N, 7.64; S, 17.49. ^{1}H NMR, δ: 1.00 (dt, 6 H, 2 Me); 1.33—1.85 (m, 4 H, 2 β-CH_2); 2.50 (t, 2 H, SCH_2); 3.92 (t, 2 H, NCH_2); 6.00, 6.20, 6.68 (all m, each 1 H, CH=).

1-Butyl-2-(butylthio)pyrrole (1d). A solution of Bu^{n}Li (0.10 mol) in 75 mL of hexane was added at −60 °C to a solution of diisopropylamine (0.10 mol) and Bu^{t}OK (0.10 mol) in 60 mL of THF. At −30 to −20 °C, a solution of allyl isothiocyanate (0.05 mol) in 40 mL of THF was added dropwise over a period of 35 min. The reaction mixture was stirred for 15 min at 42—45 °C, cooled to 30 °C, and butyl iodide (0.15 mol) was added (the temperature rose to 47 °C). The reaction mixture was stirred for 40 min at 35—45 °C, 50 mL of DMSO was added, the mixture was stirred for 15 min, and treated with ~60 mL of cold water. The organic layer was separated, the aqueous layer was extracted with ether and pentane, the combined organic fraction was dried with K_2CO_3, the solvent was removed at a reduced pressure, and the residue was distilled *in vacuo* to give 9 g (89.6%) of 1-butyl-2-(butylthio)pyrrole (**1d**), b.p. 105—130 °C (0.5 Torr), n_D^{20} 1.5088. Repeated distillation gave 5.2 g of compound **1d** with b.p. 145—155 °C (15 Torr), n_D^{20} 1.5074. Found (%): C, 68.20; H, 10.15; N, 6.51; S, 15.14. $C_{12}H_{21}NS$. Calculated (%): C, 68.19; H, 10.01; N, 6.63; S, 15.17. IR, ν/cm^{-1}: 600, 700 vs, 745, 780, 860, 900, 1000, 1065, 1100, 1180, 1200, 1210, 1280 vs, 1360, 1370, 1420, 1450, 1460, 1500, 2860, 2920, 2950, 3100. ^{1}H NMR, δ: 0.94 (dt, 6 H, 2 Me); 1.10—1.75 (m, 8 H, 2 β,γ-CH_2); 2.50 (t, 2 H, SCH_2); 3.92 (t, 2 H, NCH_2); 5.98, 6.18, 6.62 (all m, each 1 H, CH=).

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References

1. L. V. Klyba, V. N. Bochkarev, L. Brandsma, B. A. Trofimov, O. A. Tarasova, V. Yu. Vvedenskii, and N. A. Nedolya, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 1560 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 1548].
2. L. V. Klyba, V. N. Bochkarev, L. Brandsma, N. A. Nedolya, and B. A. Trofimov, *Zh. Obshch. Khim.*, 1999, **69**, 1885 [*Russ. J. Gen. Chem.*, 1999, **69**, 1805 (Engl. Transl.)].
3. L. V. Klyba, V. N. Bochkarev, L. Brandsma, O. A. Tarasova, V. Yu. Vvedenskii, N. A. Nedolya, and B. A. Trofimov, *Zh. Obshch. Khim.*, 1999, **69**, 1881 [*Russ. J. Gen. Chem.*, 1999, **69**, 1801 (Engl. Transl.)].
4. N. A. Nedolya, L. Brandsma, H. D. Verkruijsse, and B. A. Trofimov, *Tetrahedron Lett.*, 1997, **38**, 7247.
5. L. Brandsma, N. A. Nedolya, and B. A. Trofimov, *Dokl. Akad. Nauk,* 1998, **358**, 196 [*Dokl. Chem.*, 1998 (Engl. Transl.)].
6. N. A. Nedolya, L. Brandsma, and B. A. Trofimov, *Zh. Org. Khim.,* 1998, **34**, 950 [*Russ. J. Org. Chem.*, 1998, **34**, 900 (Engl. Transl.)].
7. N. S. Vul´fson, V. G. Zaikin, and A. I. Mikaya, *Mass-spektrometriya organicheskikh soedinenii* [*Mass Spectrometry of Organic Compounds*], Khimiya, Moscow, 1986, 312 pp. (in Russian).

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