HETEROCYCLIC ANALOGS OF PLEIADIENE.

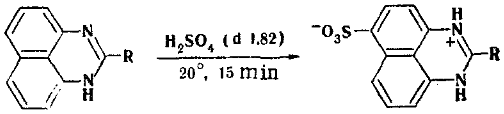
50.* SULFONATION OF PERIMIDINES, PERIMIDONES, AND 2,3-DIHYDROPERIMIDINES

A. F. Pozharskii, V. V. Kuz'menko,
V. N. Koroleva, and G. G. Yurchuk

UDC 547.856.7:542.945.245.2

The action of concentrated sulfuric acid on perimidine and 2-substituted perimidines, 1,3-dimethylperimidinium perchlorate, and the 1,3-dimethyl derivatives of perimidone and 2,3-dihydroperimidine gave the 6(7)-sulfonic acids of these compounds.

Up until now, virtually no study has been devoted to the sulfonic acids of the perimidine series. According to old patent data [2], perimidine-6(7)-sulfonic acid (IIa) is formed by refluxing 4-sulfo-1,8-naphthalenediamine with formic acid. We recently demonstrated in the case of perimidines that contain hydrophobic substituents in the 2 position (I, R = a high-molecular-weight alkyl or perfluoroalkyl group) that sulfonic acids of the II type can be obtained by sulfonation of perimidines with concentrated sulfuric acid [3]. In the present research we studied the sulfonation of perimidine itself (Ia) and simple 2-substituted perimidines (Ib,c), as well as 2,3-dihydroperimidine structures, for which we chose 1,3-dimethyl derivatives of perimidone and 2,3-dihydroperimidine.



Ia-c IIa-c

I-IIa R=H, b R=CH_3; c R=CF_3

Perimidines Ia-c, like the previously studied compounds [3], are sulfonated with surprising ease. The monosulfonic acids are formed in 80-95% yields 10-15 min after they are mixed with concentrated sulfuric acid at room temperature. The PMR spectra of the compounds are typical for 6(7)-monosubstituted perimidines, which compels us to assign the 6(7)-sulfonic acid structure to them. Thus, for example, the PMR spectrum of acid IIb contains four doublets belonging to the H_4, H_5, H_7, and H_9 protons and a triplet of the H_8 proton (Fig. 1). A doublet of the H_7 proton is found at weakest field at δ 7.78 ppm. This position of the signal of this proton is determined by the deshielding effect of the oxygen atoms of the peri-sulfo group, which is also observed in the spectra of peri-nitro- [4] and peri-acetylperimidine [5]. The J_0 value for the H_7 proton is 8.2 Hz. When the spectrum is recorded on an enlarged scale, it is apparent that the H_7 proton couples weakly with the meta H_9 proton, which shows up at δ 6.45 ppm. The H_5 and H_4 protons appear at 7.5 and 6.38 ppm, respectively.

In the case of more prolonged contact of I with sulfuric acid under the same conditions the compounds incorporate a second and, in part, third sulfo group. This process is conveniently observed by means of PMR spectroscopy (Fig. 2). A signal at δ 2.9 ppm is clearly apparent in the PMR spectrum (Fig. 2a) along with the peak of the protons of the CH_3 group of monosulfonic acid IIb (δ 2.7ppm) 30 min after mixing Ib with concentrated H_2SO_4. The intensity of the signal at 2.9 ppm gradually increases, whereas the intensity of the signal of monosulfonic acid IIb decreases (Fig. 2b). After 18 h, only the singlet of the CH_3

---

*See [1] for communication 49.

Rostov State University. Scientific-Research Institute of Physical and Organic Chemistry, Rostov-on-Don 344006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 691-696, May, 1980. Original article submitted November 12, 1979.

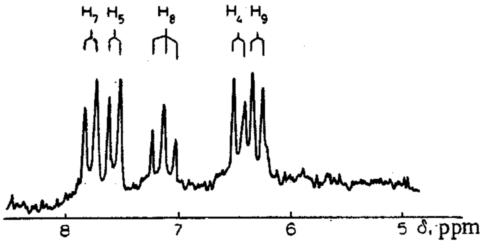


Fig. 1

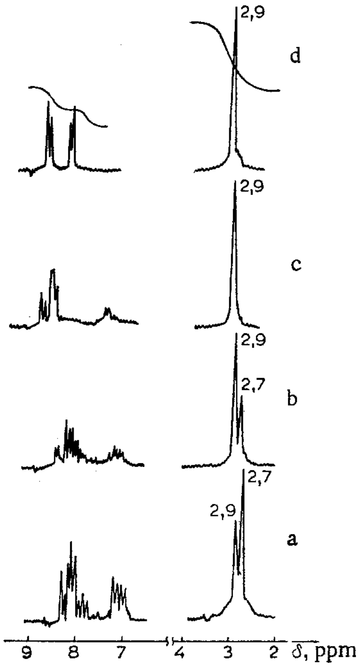


Fig. 2

Fig. 1. PMR spectrum of the ammonium salt of 2-methylperimidine-6(7)-sulfonic acid in DMSO.

Fig. 2. PMR spectrum of 2-methylperimidine: a) in concentrated H_2SO_4 30 min after mixing; b) the same after 3 h; c) the same after 18 h; d) in concentrated D_2SO_4 after 18 h.

group at δ 2.9 ppm remains (Fig. 2c). The chemical shifts of the protons of the 2-CH_3 groups in the di- and trisulfonic acids of perimidine are evidently identical, which also explains the presence of only one peak at δ 2.9 ppm in the PMR spectrum of the mixture. Judging from the fact that the overall intensity of the signals of the aromatic protons is 4.7 proton units after 18 h, Ib was converted during this time to a mixture consisting of ∿70% disulfonic acid and ∿30% trisulfonic acid. Unfortunately, we were unable to separate this mixture by a preparative method; however, one can obtain an idea regarding the structures of the resulting di- and trisulfonic acid derivatives by carrying out the same experiment in concentrated D_2SO_4. In this case the PMR spectrum of the mixture after 18 h consists of four singlets (Fig. 2d) with an overall intensity of two proton units, in addition to a singlet from the CH_3 group. Since the protons in the 5 and 8 positions in the perimidines never undergo substitution under the influence of electrophiles, there is no doubt that these singlets belong precisely to them, while the remaining protons in the molecule are exchanged by sulfo groups or deuterium. It is clear that any of the two possible trisulfonic acids should give two PMR signals from the nonequivalent H_5 and H_7 protons; on the other hand, the 6,7-disulfonic acid would give a singlet from the same protons, while the 4,7-disulfonic acid would give two singlets. On the basis of the facts set forth above it may be concluded that the second sulfonation of monosulfonic acids II proceeds with the formation of an asymmetrical 4,7-disulfonic acid. Since the formation of a 6,7-disulfonic acid evidently does not occur, it may be assumed that the third sulfonation takes place with the formation of 4,6,9-trisulfoperimidines. It should be noted that the third sulfonation is evidently reversible, since the intensity of the aromatic protons is ∿4.5 units in the PMR spectrum of a mixture of Ib with H_2SO_4 after 15 days.

The high selectivity of the monosulfonation of perimidines I at the 6(7) rather than the 4(9) position, in which there is also a large negative π charge [5], is evidently explained by the effect of the field created by the positively charged heteroatoms in the perimidinium cation and also by the mild reaction conditions. As one can see in the case of nitration of perimidines in an acidic medium [4], an appreciable amount of the ortho isomer is always formed along with the 6(7)-substitution product. This explanation specifies that perimidines are sulfonated in the cationic form. The latter seems completely natural if one takes into account the high basicities of I and II [6], as well as the strongly

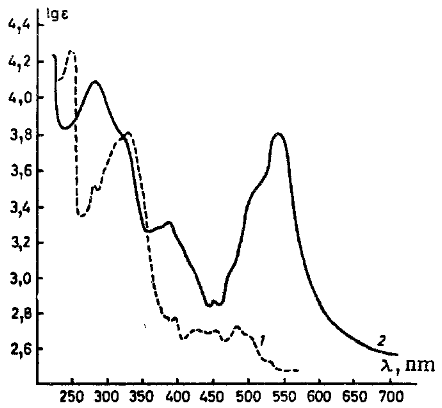
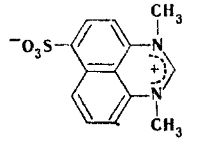
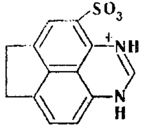


Fig. 3. Electronic absorption spectra of 1,3-dimethyl-2,3-dihydroperimidine: 1) in H_2SO_4 (1:1), λ_{max} (log ε): 236 (4.48), 280 (3.58), 300 (3.65), 315 (3.77), 334 (3.81), 390 (2.77), 400 (2.77), 425 (2.69), 460 (2.7), 490 (2.72), 520 (2.58), 530 nm (2.52); 2) in concentrated H_2SO_4, λ_{max} (log ε): 224 (4.22), 285 (4.09), 325 (3.8), 372 (3.28), 385 (3.31); 450 (2.86), 480 (3.1), 520 (3.56), 540 nm (3.8).

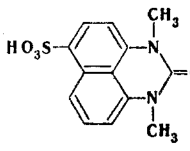
acidic medium in which the process is carried out. In addition, we established that 1,3-dimethylperimidinium perchlorate is sulfonated by concentrated H_2SO_4 with the same ease as in the sulfonation of perimidines I-II to give the 6(7)-sulfonic acid, which is isolated from the reaction mixture in the betaine form (III).



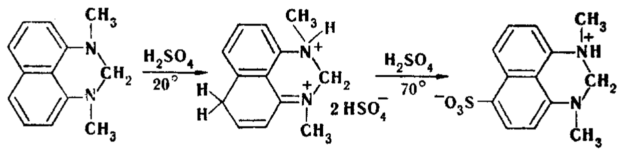
III



IV



V



VI VII VIII

$$\mathrm{III} \xrightarrow[\Delta]{\mathrm{NaOH}} \mathrm{V} + \mathrm{VIII}$$

If the para positions in perimidines I are occupied, sulfonation may also take place in the 4(9) positions, and the reaction proceeds under conditions that are just as mild. We demonstrated this in the case of aceperimidine, which was converted to sulfonic acid IV in 73% yield. The sulfonation of 1,3-dimethylperimidone to acid V also proceeds readily. Despite the very low basicities of the perimidones [7], the reaction in this case also evidently proceeds through the cation formed by protonation of the amide oxygen atom. The fact that the colorless 1,3-dimethylperimidone takes on the red-yellow color that is characteristic of perimidines and their cations when it is added to concentrated H_2SO_4 constitutes indirect evidence for this.

Somewhat unexpectedly, 1,3-dimethyl-2,3-dihydroperimidine (VI) was the only one of all of the investigated compounds that did not undergo sulfonation at room temperature. We were able to obtain sulfonic acid VIII only by heating VI with concentrated H_2SO_4 at 70°C. The relative inertness of VI to concentrated sulfuric acid is due to the formation under these conditions of dication VII, in which one of the heteroatoms and the para carbon atom of the naphthalene ring are protonated. The data from UV and PMR spectroscopy, in particular,

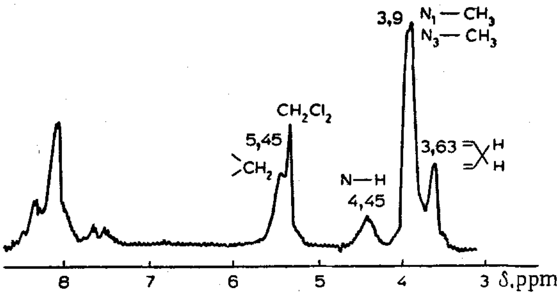


Fig. 4. PMR spectrum of 1,3-dimethyl-2,3-dihydroperimidine in concentrated H_2SO_4.

constitute evidence in favor of this. Whereas VI is colorless in neutral media and in media with moderate acidity, its color changes to dark-crimson in concentrated H_2SO_4. This change is accompanied by a pronounced change in the electronic absorption spectrum (Fig. 3). The PMR spectrum of VI in concentrated H_2SO_4 (Fig. 4) contains, in addition to a signal of the heteroring CH_2 group at 5.45 ppm, a singlet at δ 3.63 ppm with an intensity of two proton units, which is related to the CH_2 group of the protonated naphthalene ring. The weak splitting of the signals of the N–CH_3 groups indicates their nonequivalence, while the broadness of the signal of the heteroring CH_2 group constitutes evidence for coupling of these protons with the proton of the NH group (the signal of the latter appears at δ 4.45 ppm).

We also obtained sulfonic acid VIII by disproportionation [8] of betaine III under the influence of 10% alkali. We were unable to obtain the second product of this reaction, viz., 1,3-dimethylperimidone-6(7)-sulfonic acid (V).

Sulfonic acids II, IV, and VIII, which exist in the form of crystal hydrates, are evidently betaines, in which form they are depicted in the schemes given above. This is indicated by the presence in their IR spectra of a band at 1660-1670 cm^{-1}, which is characteristic for the $\nu_{C=\overset{+}{N}<}$ stretching vibrations of the heteroring in perimidinium cations (compare this with the $\nu_{C=\overset{+}{N}<}$ band at 1680 cm^{-1} in the spectrum of genuine betaine III). The IR spectra of all of the sulfo derivatives contain intense bands of stretching vibrations of SO_3^- groups at 1040, 1170, and 1250 cm^{-1}.

One can also form a judgment regarding the structures of the sulfonic acids to a certain extent from their solubilities in water. Compounds II, IV, and VIII, like betaine III, are moderately or slightly soluble in water. On the other hand, sulfonic acid V is extremely soluble, and we were able to isolate it only in the form of the ammonium salt. The di- and trisulfonic acids of 2-methylperimidine are also quite soluble in water. Thus, it may be assumed that the presence of a nonionized sulfo group in the molecule leads to high solubility of the compounds in water.

Considering the ease of sulfonation of perimidines with concentrated H_2SO_4, we hoped that they would also undergo sulfonation with milder agents, particularly pyridine sulfotrioxide. However, I-III remained unchanged when they were heated with pyridine sulfotrioxide at 110°C for 7 h.

EXPERIMENTAL

The UV spectra of the compounds were recorded with an SF-4A spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-467 spectrometer with hexamethyldisiloxane as the internal standard (or methylene chloride for measurements in H_2SO_4).

Perimidine-6(7)-sulfonic Acid (IIa). A 0.5-g (3 mmole) sample of perimidine was added in portions to 5 ml of concentrated H_2SO_4, and the dark-green mixture was stirred for 15 min. It was then poured over 30 g of ice, and the precipitate that formed in 1 h was removed by filtration and washed with water and acetone to give 0.6 g (81%) of yellow-green prisms with mp > 330°C (from a large volume of water). PMR spectrum (d_6-DMSO), δ: 7.95

(1H, d, J = 8.2 Hz, 7-H), 7.75 (1H, d, J = 7.5 Hz, 5-H), 7.5 (1H, s, 2-H), 7.35 (1H, t, 8-H), 6.55 (1H, d, J = 7.5 Hz, 4-H), and 6.47 ppm (1H, d, J = 8.2 Hz, 9-H). IR spectrum: 1035, 1170, 1253 (SO_3^-); 1670 ($\mathrm{C{=}\overset{+}{N}H}$); 2400-3250 cm^{-1} ($>\overset{+}{\mathrm{N}}\mathrm{H}$). Found: C 49.9; H 4.0; N 10.3; S 12.1%. $C_{11}H_8N_2O_3S$. Calculated: C 49.6; H 3.8; N 10.5; S 12.0%.

2-Methylperimidine-6(7)-sulfonic Acid (IIb). This compound was similarly obtained in 80% yield. The pale-yellow needles (from a large volume of water) darkened at 290-340°C without melting. PMR spectrum (DMSO), δ: 7.78 (1H, d, J = 8.2 Hz, 7-H), 7.5 (1H, d, J = 7.5 Hz, 5-H), 7.12 (1H, t, 8-H), 6.45 (1H, d, J = 8.2 Hz, 9-H), and 6.38 ppm (1H, d, J = 7.5 Hz, 4-H). IR spectrum: 1030, 1163 (SO_3^-); 1660 cm^{-1} ($\mathrm{C{=}\overset{+}{N}H}$). UV spectrum, λ_{max} (log ε): 324 (3.79) (in CH_3OH); 347 nm (3.86) (in 0.1 N NaOH). Found: C 54.4; H 3.6; N 10.5; S 12.0%. $C_{12}H_{10}N_2O_3S$. Calculated: C 54.9; H 3.8; N 10.7; S 12.2%. The ammonium salt of the 6(7)-sulfonic acid, which was quite soluble in water, alcohol, and DMSO, was obtained by dissolving with ammonia. It was purified by reprecipitation from aqueous solution (two to three drops of NH_4OH were added to the water, since the salt is readily hydrolyzed to the sulfonic acid when it is refluxed in water) after refluxing with activated charcoal by the addition of acetone. The pale-green crystals gradually darkened at 280-340°C.

2-Trifluoromethylperimidine-6(7)-sulfonic Acid (IIc). This compound was similarly obtained in 91% yield. The yellow-orange crystals had mp > 300°C (dec., from alcohol with ether). PMR spectrum (DMSO), δ: 7.88 (1H, d, J = 8.2 Hz, 7-H), 7.58 (1H, d, J = 7.5 Hz, 5-H), 7.18 (1H, t, 8-H), 6.63 (1H, d, J = 7.5 Hz, 4-H), and 6.48 ppm (1H, d, J = 8.2 Hz, 9-H). IR spectrum: 1040, 1163, 1210 (SO_3^-); 1685 ($\mathrm{C{=}\overset{+}{N}H}$); 2400-3100 ($>\overset{+}{\mathrm{N}}\mathrm{H}$); 3390 cm^{-1} (H_2O). Found: C 45.1; H 2.4; N 8.9%. $C_{12}H_7F_3N_2O_3S$. Calculated: C 45.3; H 2.2; N 8.9%.

1,3-Dimethyl-6(7)-sulfonatoperimidinium Betaine (III). A 3-g (10 mmole) sample of 1,3-dimethylperimidinium perchlorate was added in portions at 20°C to 30 ml of concentrated H_2SO_4, and the mixture was stirred for 30 min. It was then filtered to remove a small amount of black flakes, and the filtrate was poured over 150 g of crushed ice. The resulting precipitate was removed by filtration and washed successively with water (to pH 7-8) and acetone to give 2.9 g (93%) of yellow prisms with mp > 350°C (from a large volume of water). PMR spectrum (CF_3COOH), δ: 8.0 (2H, m, 2,7-H), 7.7 (1H, d, J = 7.5 Hz, 5-H), 7.3 (1H, t, 8-H), 6.6 (1H, d, J = 7.5 Hz, 4-H), 6.2 (1H, d, J = 7.5 Hz, 9-H), 3.2 (3H, s, $N_3{-}CH_3$), and 3.1 ppm (3H, s, $N_1{-}CH_3$). IR spectrum: 1050, 1215 (SO_3^-); 1680 ($\mathrm{C{=}\overset{+}{N}H}$); 3400-3500 cm^{-1} (H_2O). Found: C 50.4; H 5.3; N 8.8; S 9.7%. $C_{13}H_{12}N_2O_3S\cdot 2H_2O$. Calculated: C 50.0; H 5.1; N 9.0; S 10.3%.

Aceperimidine-4(9)-sulfonic Acid (IV). This compound was obtained in 73% yield under conditions similar to those in the preparation of IIa. The yellow crystals had mp > 330°C (from CF_3COOH). IR spectrum: 1040, 1160, and 1240 (SO_3^-); 1660 ($\mathrm{C{=}\overset{+}{N}H}$); 2400-3180 cm^{-1} ($>\overset{+}{\mathrm{N}}\mathrm{H}$). Found: C 53.4; H 3.8; N 9.5; S 11.2%. $C_{13}H_{16}N_2O_3S\cdot H_2O$. Calculated: C 53.4; H 4.1; N 9.6; S 11.0%.

1,3-Dimethylperimidone-6(7)-sulfonic Acid (V). A 0.42-g (2 mmole) sample of 1,3-dimethylperimidone was added in portions to 5 ml of concentrated H_2SO_4, during which the solution turned bright-yellow. The mixture was stirred at 20°C for 15 min, after which it was poured over 30 g of ice, and the aqueous mixture was neutralized with ammonia and concentrated to a minimum volume. The ammonium salt of the 6(7)-sulfonic acid was removed by filtration and washed with ice water to give 0.6 g (96%) of slightly pinkish prisms with mp > 300°C (from water). PMR spectrum (d_6-DMSO), δ: 8.1 (1H, d, J = 9 Hz, 7-H), 7.8 (1H, d, J = 7.5 Hz, 5-H), 7.4 (1H, t, 8-H), 7.05 (4H, m, NH_4^+), 6.54 (2H, m, 4.9-H), 3.38 (3H, s, $N_3{-}CH_3$), and 3.23 ppm (3H, s, $N_1{-}CH_3$). IR spectrum: 1190, 1215 (SO_3^-); 1690 ($\mathrm{C{=}\overset{+}{N}H}$); 3450-3550 cm^{-1} (H_2O). Found: C 47.4; H 5.1; N 13.0; S 9.5%. $C_{13}H_{15}N_3O_4S\cdot H_2O$. Calculated: C 47.7; H 5.2; N 12.8; S 9.8%.

1,3-Dimethyl-2,3-dihydroperimidine-6(7)-sulfonic Acid (VIII). A mixture of 0.5 g (2.5 mmole) of 1,3-dimethyl-2,3-dihydroperimidine and 5 ml of concentrated H_2SO_4 was stirred at 70-75°C for 1 h, after which it was cooled and poured over 30 g of ice. The aqueous mixture was treated with ammonia (to pH 2-3), and the resulting precipitate was removed by filtration and washed with water to give 0.6 g (81%) of pale-yellow prisms with mp > 330°C (from water). PMR spectrum (CF_3COOH), δ: 8.3 (1H, m, 7-H), 7.88 (1H, d, J = 8.0 Hz, 5-H), 7.1 (2H, m, 4,8-H), 6.48 (1H, d, J = 8.0 Hz, 9-H), 4.48 (2H, s, CH_2), 2.98 (3H, s, N_3–CH_3), and 2.88 ppm (3H, s, N_1–CH_3). IR spectrum: 1050, 1170, and 1250 (SO_3^-); 2670 ($>\overset{+}{N}H$); 3490, 3560 cm^{-1} (H_2O). Found: C 52.7; H 5.3 N 9.4; S 11.0%. $C_{13}H_{14}N_2O_3S \cdot H_2O$. Calculated: C 52.7; H 5.4; N 9.5; S 10.8%.

Disproportionation of 1,3-Dimethylperimidinium-6(7)-sulfonic Acid. A solution of 1.8 g (5.8 mmole) of 1,3-dimethyl-6(7)-sulfonatoperimidinium in 50 ml of 10% NaOH was stirred at 90°C for 1 h; the pink precipitate that began to form after 15 min was removed after the reaction mixture was cooled at the end of this heating period. The precipitate was dissolved in water, and the aqueous solution was acidified to pH 1 with concentrated HCl. The gray precipitate was separated and washed with water and alcohol. The yield of a mixture of V and VIII was 1.3 g (73%). The mixture was completely soluble in hot water and 5% HCl, and it therefore could not be separated by the usual method. Recrystallization from water gave 0.6 g (36.5%) of sulfonic acid VIII, which was identical to the sample described above with respect to the results of elementary analysis and its physicochemical properties. An insoluble black product was formed when the mother liquor from the crystallization was evaporated to isolate V.

LITERATURE CITED

1. N. A. Klyuev, A. F. Pozharskii, A. B. Belikov, and V. M. Adanin, Khim. Geterotsikl. Soedin., No. 5, 686 (1980).
2. German Patent No. 264292; Chem. Zentralblatt, II, 1351 (1913).
3. A. F. Pozharskii, I. V. Borovlev, G. G. Yurchuk, O. M. Bagrova, Yu. I. Vasilenok, and V. N. Lagunov, Khim. Geterotsikl. Soedin., No. 4, 550 (1980).
4. A. F. Pozharskii and V. N. Koroleva, Khim. Geterotsikl. Soedin., No. 4, 550 (1975).
5. A. F. Pozharskii, I. V. Borovlev, and I. S. Kashparov, Khim. Geterotsikl. Soedin., No. 4, 543 (1975).
6. A. F. Pozharskii and I. S. Kashparov, Khim. Geterotsikl. Soedin., No. 1, 111 (1970).
7. I. V. Borovlev and A. F. Pozharskii, Khim. Geterotsikl. Soedin., No. 6, 833 (1978).
8. A. F. Pozharskii and I. S. Kashparov, Khim. Geterotsikl. Soedin., No. 6, 860 (1972).