PROTONATED FORMS OF 2-(2-THIENYL)PYRROLES. INVESTIGATION BY MEANS OF ^{1}H NMR SPECTROSCOPY AND MNDO CALCULATIONS

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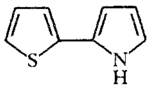
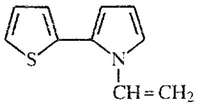
By means of ^{1}H NMR spectroscopy it was demonstrated that 2-(2-thienyl)pyrrole and its 1-vinyl-substituted derivatives are protonated by acids (HSO_3F, CF_3CO_2H, HCl, and HBr) at the C_5 atom of the pyrrole ring. The reaction with the superacid system $HSO_3F/SbF_5/SO_2$ leads to an equilibrium mixture of pyrrolium and thiophenium ions. The MNDO method was used to calculate the heats of formation (ΔH), charges, and partial electron densities of the highest occupied molecular orbitals (HOMO) of 2-(2-thienyl)pyrrole and its protonated forms. The calculated ΔH values of the thienylpyrrolium and pyrrolylthiophenium ions are in agreement with the experimentally established relationship.

The decrease in the reactivities of the simplest five-membered aromatic heterorings in electrophilic reactions in the order pyrrole > > furan > thiophene is well known [1, 2]; the difference in the activities of the first pair (six to seven orders of magnitude) is substantially greater than the difference for the second pair (one to three orders of magnitude). In earlier NMR studies [3, 4] we observed that 2-(2-furyl)pyrrole and substituted 2-(2-furyl)pyrroles are protonated by hydrogen halides to give equilibrium mixtures of pyrrolium and furanium cations. Quantum-chemical calculations (MNDO) demonstrated [5] that the reason for this unexpected fact is the equality of the heats of formation of the most stable planar forms of these cations. This means that the mutual effect of directly bonded heterorings when protonation takes place is so great that it is capable of leveling out such a great difference in the activities of the isolated fragments. For a better understanding of this phenomenon it was necessary to extend the range of activity of the investigated fragments in electrophilic reactions.

With this in mind, we used ^{1}H NMR spectroscopy to study the protonation of the following 2-(2-thienyl)pyrroles:



I



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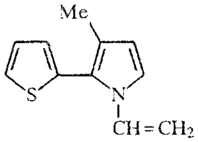

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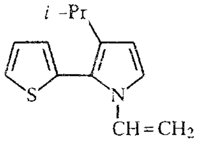

IV

Protonation was accomplished by means of HCl, HBr, CF_3COOH, and HSO_3F, as well as the superacid system $HSO_3F/SbF_5/SO_2$.

Using the MNDO method with complete optimization of the geometries involved we calculated the heats of formation and studied the electron and three-dimensional structures, as well as the internal rotation of 2-(2-thienyl)pyrrole (I) and its α-protonated forms. We performed similar calculations for 2-phenylpyrrole and its cations, which are formed in the protonation of the pyrrole or phenyl rings, as model compounds.

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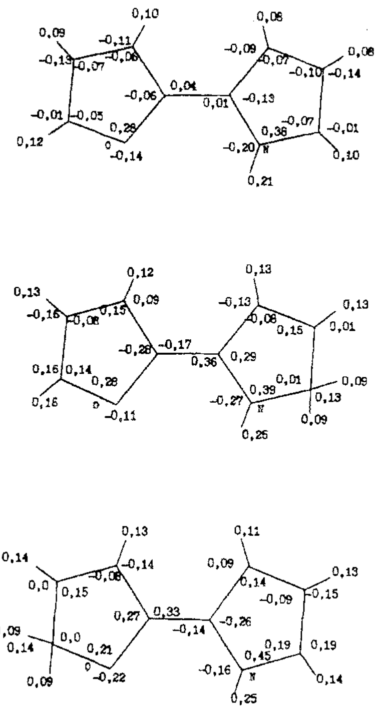


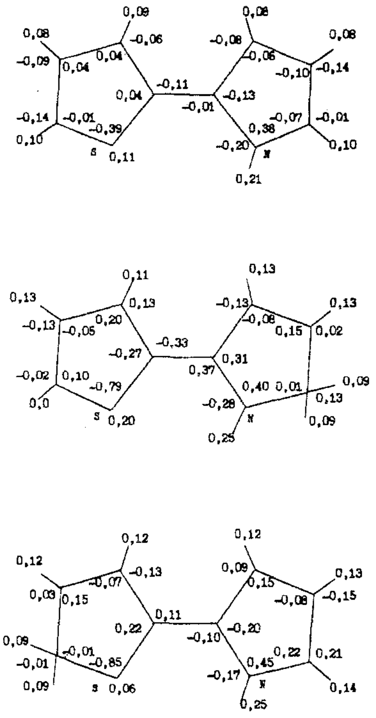
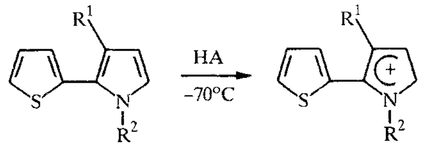


Fig. 1 Fig. 2

Fig. 1. Total charges and π charges (presented within the rings) on the atoms of 2-(2-furyl)pyrrole and its protonated forms.

Fig. 2. Total charges and π charges (presented within the rings) on the atoms of 2-(2-thienyl)pyrrole and its protonated forms.

Our experiments showed that at −70°C the only reaction product, regardless of the substituents in the pyrrole ring and the nature of the acid (except for the superacid system) are 2-(2-thienyl)pyrrolium cations:

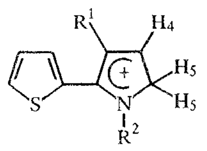


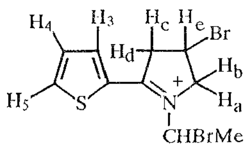
I-IV I-IVA

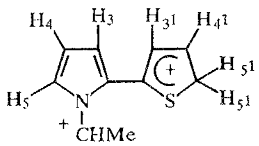
R^1 = H, Me, *i*-Pr; R^2 = H, CH=CH$_2$; A = SO$_3$F, CF$_3$CO$_2$, Cl, Br

As in the case of furylpyrroles [3, 4], an increase in the temperature of the sample to 0°C (in CF_3COOH) and 20°C (in HSO_3F) does not change the form of the NMR spectra of all of the investigated compounds. A substantial difference from the behavior of furylpyrroles is the fact that even in the case of the reaction with hydrogen halides at high temperatures the pyrrolium ions remain the only reaction products (although, admittedly modified due to the addition of HCl or HBr to the vinyl group).

TABLE 1. Parameters of the ^1H NMR Spectra of the Cations .....


I-IVA, IIC


IIB


IID

N	R^1	R^2	H_4	CH_2-5	H_3'	H_4'	H_5'	R^1	R^2
IA	H	H	8,03	5,12	8,27	7,50	8,27	7,35	
IIA	H	$CH=CH_2$	7,93	5,38	8,27	7,63	8,43	7,22	5,93 (H_A) 5,75 (H_B) 7,49 (H_C)
IIA	H	$CHClCH_3$	8,06	5,36	8,42	7,62	8,53	7,40	6,65 (CH) 2,24 (CH_3)
IIA	H	$CHBrCH_3$	8,13	5,46	8,49	7,66	8,58	7,46	6,80 (CH) 2,46 (CH_3)
IIIA	Me	$CH=CH_2$	7,70	5,23	8,30	7,67	8,30	2,50	5,72 (H_A) 5,49 (H_B) 7,43 (H_C)
IVA	*i*-Pr	$CHClCH_3$	7,78	5,24	8,19	7,60	8,34	3,05 (CH) 1,37 $(CH_3)_2$ 1,06	6,49 (CH) 2,18 (CH_3)
IIB			5,10 (H_e)	4,68 (H_a) 5,20 (H_b)	8,35	7,63	8,63	5,10 (H_c) 4,05 (H_d)	6,80 (CH) 2,28 (CH_3)
IIC	H	CH^+-CH_3	8,57	5,77	9.21	8,18	8,81	7,91	9,82 (CH^+) 3,46 (CH_3)
IID			7,68	8,71 (H_5)	8,23	9,02	5,63 (CH_2-5')	8,45	10,06 (CH^+) 3,58 (CH_3)

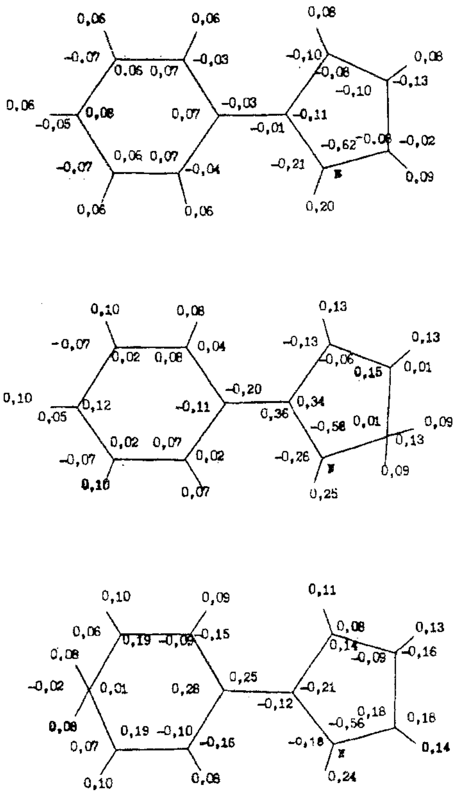
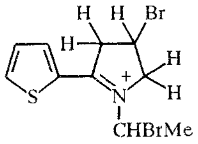


Fig. 3. Total charges and π charges (presented within the rings) on the atoms of 2-(2-phenyl)pyrrole and its protonated forms.

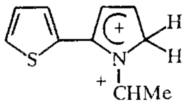
Carrying out the reaction of pyrrole II with HBr at 0°C (or increasing the temperature of the sample in the spectrometer sensor from −70°C to 0°C) leads to the addition of a second molecule of HBr to the protonated pyrrole ring and the formation of 1-(1-bromoethyl)-4-bromo-3,4-dihydro-2-(2-thienyl)-5H-pyrrolium cation (IIB):



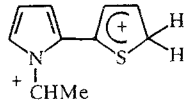
IIB

Again, in contrast to furylpyrroles, the thiophene ring does not participate in the reaction.

The results of the reaction of 1-vinyl-2-(2-thienyl)pyrrole $HSO_3F/SbF_5/SO_2$ radically differ those described. The spectrum of the mixture obtained at −70°C contains signals of three compounds, of which two dications were reliably identified, viz., the 5-H-2-(2-thienyl)-1-(1-ethania)pyrrolium cation (IIC) and the 5H-2-[1-(ethania)-2-pyrrolyl]thiophenium cation (IID) in a ratio of 2:1.



IIC



IID

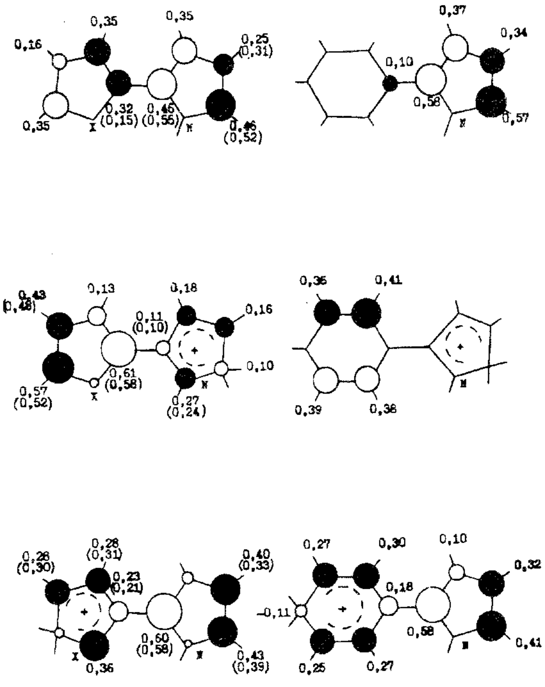
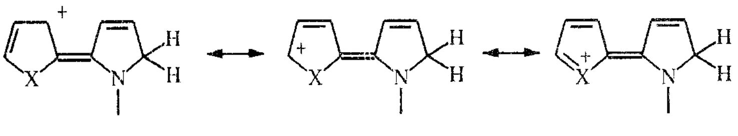


Fig. 4. Structures of the HOMO of the cis conformers of 2-furyl- (X = S) and 2-thienylpyrroles (X = O), as well and 2-phenylpyrrole, and their protonated forms. The values in parentheses pertain to X = S for the cases in which they differ from the values corresponding to X = O.

Heating a sample to −10°C leads to disappearance of the signals of the compound with an unestablished structure, which, is evidently an unstable (kinetic) product of β protonation of the pyrrole ring, as well as to reverse change in the ratio (i.e.) of the dications cited above.

It is apparent from the experimental data that, in contrast to furylpyrrolium ions, the 2-(2-thienyl)pyrrolium ions formed as a result of α protonation of the pyrrole ring do not undergo substantial changes in excess HCl. One can specify two probable reasons for this.

The first probable reason is the high invulnerability of thienylpyrrolium rings relative to deprotonation because of the great ability of the sulfur atom to form an onium state [2]. In this case it follows from an examination of the mesomeric structures that, when X = S, the positive charge of the protonated pyrrole ring may be more delocalized than when X = O. This is confirmed by the changes in the calculated total charges on the O and S heteroatoms when pyrrolium ions are formed: the increase in the positive charge on the sulfur atom is 0.09, while the decrease in the negative charge on the oxygen atom is only 0.03.



We have previously observed [6] that the width of the signal of the protons of the 5-CH_2 group in the ^1H NMR spectrum may serve as a criterion for the stability of pyrrolium cations. In the case of intermolecular exchange of these protons with the medium the signal broadens with an increase in the temperature. For example, this kind of broadening occurs in the spectra of 2-alkyl- and 2-phenylpyrrolium ions [6]; in this case an increase in the temperature of the sample to +10°C does not change the width of the signal of the protons of the $5CH_2$ group for the IA-IVA cations in HCl.

As far as the second probable reason for the experimentally observed phenomenon is concerned, one might assume the existence of a higher barrier in the protonation of the thiophene ring. In this case the formal transfer of a proton from the protonated pyrrole ring to the thiophene ring, in contrast to the furan analogs, will be impeded. It is most likely that the joint action of these two factors is the reason for the experimentally observed phenomenon.

Protonation of the pyrrole ring by the usual acids at low temperatures is determined, as in the protonation of furylpyrroles, not by the magnitudes of the charges on the atoms (it is apparent from Figs. 1-3 that the charge on C_5 is minimal) but rather by the contributions of the atomic orbitals in the highest occupied molecular orbitals (HOMO). It follows from Fig. 4 that the greatest contribution to the HOMO is made by the p_z orbitals of the C_5 and C_2 atoms. The latter is not protonated because of steric hindrance.

A qualitatively different picture is observed in the reaction of 1-vinyl-2-(2-thienyl)pyrrole (II) with $HSO_3F/SbF_5/SO_2$. The existence of three reaction products at -70°C proves that, in addition to orbital control, charge (kinetic) control is also operative. The C_5 atom of the thiophene ring and the C_4 atom of the pyrrole ring have the highest charges in the thienylpyrrole I molecule. These atoms are the most likely centers for attack by a hard acid. Evidence in favor of this is also provided by the disappearance, when the sample is heated to -10°C, of signal of an unidentified compound (which, however, may be considered with high likelihood to be a product of β protonation in the pyrrole ring). Dication IID, with a protonated thiophene ring, is retained at -10°C, and its percentage even increases. This is in complete agreement with the calculated heats of formation (Table 2), which show that the thienylpyrrolium and pyrrolylthiophenium ions have quite close thermodynamic stabilities.

At the same time, calculations of the model cations formed in the protonation of 2-phenylpyrrole reveal a very large difference in the heats of formation of the phenylpyrrolium and pyrrolylphenonium ions (~ 55 kJ/mole). We have previously shown that 2-phenylpyrroles are protonated exclusively in the pyrrole ring upon reaction with any (including super-strong) acids [7]. Thus the results that we obtained demonstrate, first, that they reflect the adequacy of the method used to make the calculations and, second, that they explain the observed experimental facts.

Detailed calculations with complete optimization of the geometry of the conformers of 2-(2-thienyl)pyrrole and its protonated forms with the construction of the internal-rotation potential curves were carried out by the MNDO method. The most important calculated parameters are presented in Tables 2-4 and Figs. 1-5. For comparison, the analogous parameters of the 2-(2-furyl)pyrrole molecule and its protonated forms from [5] are also presented there.

First of all, one must note the great agreement between the calculated parameters of 2-(2-thienyl)- and 2-(2-furyl)pyrrole and the cations formed by them. This also applies to the charge distributions (Figs. 1-3) and to the geometrical characteristics of the molecules, as well as the structures of the HOMO (Fig. 4). Virtually all of these parameters have close values. The most substantial differences are observed only for the heights of the barriers to internal rotation (BIR) of the furyl- and thienylpyrrolium ions. This will be examined in greater detail below.

The neutral molecules are characterized by an increase in the noncoplanarity of the rings in the substituent order furyl < thienyl < phenyl (Table 3). However, as we have previously demonstrated [5] on the basis of the data in [8], overestimation of the steric interactions between the nonbonded atoms by the CNDO method may lead to substantial distortion of the rotation potentials in systems with weakly expressed π conjugation. The data that we obtained are, at least, not in agreement with the results of *ab initio* calculations [9], which predict planar structure for furyl- and thienylpyrrole molecules, although they were obtained without optimization of the geometries. Of all of the protonated forms, only the 2-phenylpyrrolium cation is characterized by a significant interannular angle, while all of the rest of the cations are planar. The barriers to internal rotation in pyrrolium cations are also in agreement with this; the barrier to internal rotation for the 2-phenylpyrrolium cation is minimal.

An examination of the HOMO structure (Fig. 4) reveals profound differences between 2-phenylpyrrole and its heterocyclic analogs both in the neutral and cationic forms. In the starting 2-phenylpyrrole molecule the HOMO is localized virtually on the pyrrole ring, while in the cation with a protonated pyrrole ring, the AO of the phenyl fragment makes the principal contribution to the HOMO. The symmetry of the HOMO with respect to the $C_2-C_{2'}$ bond differs appreciably for the 2-phenylpyrrolium cation and the heteroaromatic ions. Thus, in all of the protonated forms, the HOMO is a bonding orbital, and it is an antibonding orbital only in the 2-phenylpyrrolium cation, which hinders interannular transfer of electron density. Thus a unified conjugation system is absent in this case. The structure and symmetry of the HOMO become similar to those for the pyrrolylfuranium and -thiophenium cation only in the case of hypothetical protonation of the benzene ring.

The problem of the relationship of barriers to internal rotation (BIR) in the protonated forms of the investigated compounds should be examined in greater detail, since their heights may serve as an estimate of the interannular conjugation.

TABLE 2. Heats of Formation (CNDO) of the Most Stable Conformers of 2-Furyl-, 2-Thienyl-, and 2-Phenylpyrroles,* kJ/mole

Configuration	Neutral molecule	Protonated form	
		N(+)**	2-substituent (+)***
	2-(2-furyl)pyrrole		
cis	87,32	738,43	740,57
trans	94,22	745,80	748,60
	2-(2-thienyl)pyrrole		
cis	249,55	908,21	903,39
trans	249,55	910,84	907,24
	2-phenylpyrrole		
	224,52	880,70	935,88

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*From the results of total optimization of the geometry.

**Protonated pyrrole ring.

***Protonated ring of the 2-substituent.

TABLE 3. Chief Parameters That Characterize Interannular Conjugation

	Order* of C_2-C_2'	Bond length, Å	Barrier height, kJ/mole	V_2, kJ/mole	Interplanar angle
		2-(2-furyl)pyrrole			
Neutral	1,02	1,45	—	2,51	12,7
N(+)	1,17	1,43	31,05	34,39	0
O(+)	1,38	1,40	80,84	85,48	0
		2-(2-thienyl)pyrrole			
Neutral	1,01	1,45	—	-2,93	54,8
N(+)	1,14	1,43	15,28	17,12	0
S(+)	1,49	1,38	88,07	86,94	0
		2-phenylpyrrole			
Neutral	0,98	1,47	—	-8,16	70,8
N(+)	1,07	1,46	2,47	2,93	38,6
Ph(+)	1,42	1,40	63,17	41,61	4,5

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*The bond order was determined as the sum of the squares of the elements of the density matrix that link the two atoms.

It is apparent from Table 3 that the BIR values in pyrrolium ion decrease substantially in the order furyl > thienyl > phenyl, which, in agreement with the data in [5], indicates a decrease in the stabilizing effect of these rings with respect to the pyrrolium cation. This principle does not apply in the alternative protonated forms, but one does clearly see an increase in the stabilizing effect of the pyrrole ring. Thus the height of the barrier to internal rotation of the pyrrolylfuranium ion is greater by a factor of 2.5 for the furylpyrrolium ion. A similar relationship for the pair of thienylpyrrole cations is ~6, where for the pair of phenylpyrrole cations is ~25.

The height of the barrier to internal rotation (BIR) in protonated bithienyl was previously [9] evaluated by dynamic NMR as being 49 kJ/mole, i.e., it was demonstrated that the delocalization of the electron density in this cation is higher than in the thienylpyrrolium ion but lower than in the pyrrolylthiophenium ion.

Expansion of the rotation potentials into a six-term Fourier series

$$\Delta E = E(\varphi) - E(0) = \sum_{i=1}^{6} 1/2\, V_i[1 - \cos(i\varphi)]$$

TABLE 4. Approximation by a Fourier Series of the Potential Rotation Relative to the Interannular $C_2-C_{2'}$ Bond in Substituted Pyrroles and Their Protonated Forms

	V_1	V_2	V_3	V_4	V_5	V_6
2-(2-furyl)pyrrole						
Neutral	6,53	2,51	0,71	-1,09	-0,08	0,08
N(+)	7,49	34,39	-0,46	-3,18	0,0	0,17
O(+)	2,85	85,48	0,21	-14,27	4,98	-4,81
2-(2-thienyl)pyrrole						
Neutral	-3,06	-2,93	0,0	-1,09	0,63	0,04
N(+)	1,01	17,12	2,34	-1,76	0,17	-0,08
S(+)	3,98	86,94	-7,74	-14,53	-0,04	3,01
2-phenylpyrrole						
Neutral	—	-8,16	—	-8,08	—	-3,60
N(+)	—	2,93	—	-5,11	—	-0,42
Ph(+)	—	41,61	—	-43,91	—	21,56

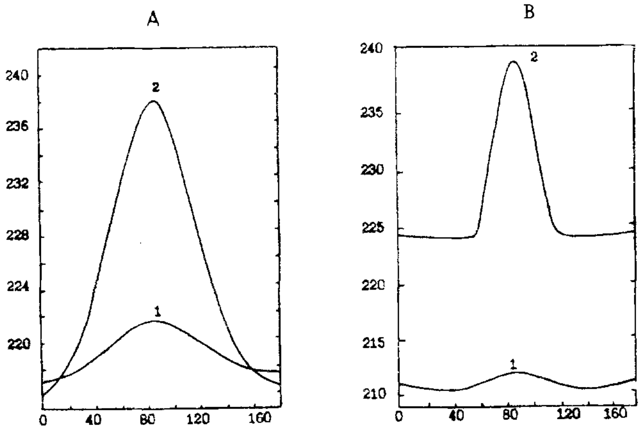

Fig. 5. Potential curves of the internal rotation of protonated 2-(2-thienyl)pyrrole (A) and 2-phenylpyrrole (B): 1) protonation in the pyrrole ring; 2) protonation in the substituent ring.

shows that the V_2 coefficient is the dominating parameter for all of the protonated forms of furylpyrrole and thienylpyrrole (Table 4). According to [10], this term describes the π contribution to the barrier to internal rotation (BIR). Consequently, in all of these cases the magnitude of the barrier is determined by $\pi-\pi$ conjugation. The rotation potential curves in the 2-phenylpyrrole cations seldom differ in form from those described above (Fig. 5). The V_2 coefficient does not dominate in the Fourier expansion. Thus in the indicated cations (at least in the 2-phenylpyrrolium ion) $\pi-\pi$ conjugation is not the factor that determines the internal rotation. This is also manifested in the lower order of the $C_2-C_{2'}$ bond.

EXPERIMENTAL

The cations were generated by mixing 0.02 g of the pyrrole with 0.2 g of the acid in equal volumes of CD_2Cl_2 (or liquid SO_2 in the case of the superacid system) in an NMR ampul at −70°C or by passage of a dry hydrogen halide into a solution of the pyrrole in CD_2Cl_2.

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