H/D ISOTOPE EXCHANGE IN 9-R-sym-OCTAHYDRO-10-OXONIA(CHALCOGENONIA)ANTHRACENE PERCHLORATES

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The method of controlled H/D isotope exchange in acid media has been used to study the effect of the heteroatom and the substituents in 9-R-sym-octahydro-10-oxonia(chalcogenonia)anthracene perchlorates on the mobility of hydrogen atoms in the α-methylene units of alicyclic rings condensed with heteroaromatic rings. It has been established that in a group of aryl-substituted salts the mobility of the hydrogen atoms increases in the series $S^+ < O^+ < Se^+$, which corresponds to a decrease in thermodynamic stability of the chalcogenopyrylium cations. In a group of unsubstituted salts ($R = H$) the order of reactivity of the methylene groups is $O^+ < S^+ < Se^+$ and corresponds to the increasing orbital electrophilicity and complexing ability of these cations.

A large number of reactions of pyrylium and chalcogenopyrylium salts resulting from the high mobility of the hydrogen atoms in α- and γ-alkyl substituents are known. These compounds readily undergo condensations with aromatic aldehydes, certain heterocyclic ketones, dimethylformamide, ethyl orthoformate, diazo compounds, and nitrous acid and can exchange hydrogen atoms for metal atoms [1-7]. Despite the large number of studies which have been conducted in this area, an unexpected outcome was the virtual absence of information in the literature on the effect of the heteroatom in a chalcogenopyrylium ring on the mobility of hydrogen atoms in α- and γ-alkyl substituents.

It is unlikely that certain indirect findings relating to this question, for example, differences in the reactivities of pyrylium and chalcogenopyrylium salts that have the same composition during their condensation with aromatic aldehydes [6, 7], are of relevance. These reactions have multiple stages and the observed differences in their rates and yields of required products may be due not so much to the ability of the cations of these salts to undergo deprotonation but to differences in the reactivity of intermediates such as anhydro bases.

In the present study we have attempted to fill a gap in the chemistry of chalcogenopyrylium salts by investigating H/D isotope exchange in 9-R-sym-octahydro-10-oxonia(chalcogenonia)anthracene perchlorates (I, II). The exchange reactions were carried out by heating solutions of compounds I and II in a mixture of deuterated acetic and trifluoroacetic acids. By using the strong trifluoroacetic acid in large excess, which reacts with the anhydro bases virtually instantaneously, it was possible to exclude the effect of their variable reactivity on the rate of the processes and to make a sufficiently reliable assessment of the mobility of the hydrogen atoms in the α-methylene groups from the degree of H/D exchange (see scheme on top of following page).

By analyzing the data presented in Table 1, it is possible to arrange the compounds studied in the following order of decreasing reactivity of the methylene groups: IIc > Ic > Ib > Ia > IIa > IIb. It should be pointed out that in the group of unsubstituted salts I the degree of isotope exchange increases in the series $O^+ < S^+ < Se^+$, while in the group of aryl-substituted salts II there is a different order: $S^+ < O^+ \ll Se^+$.

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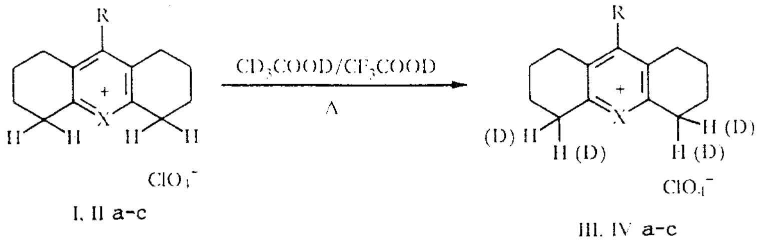
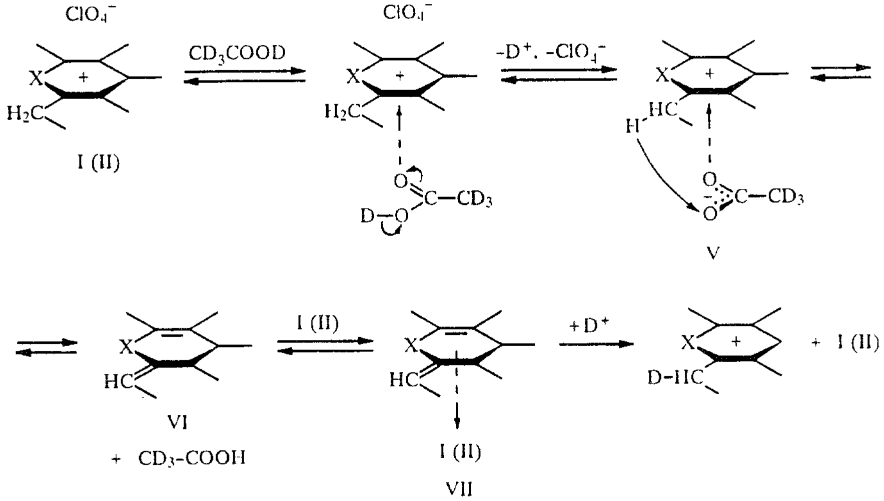


I, III) R = H; II, IV) R = $C_6H_4OCH_3$-p; a) X = O; b) X = S; c) X = Se

Attempts to establish a correlation between the reactivity of the α-methylene groups in compounds I and II and the position of their proton signals in the PMR spectra proved unsuccessful. Thus, for example, the positions of the $H_{4,5}$ signals in the spectra of salts Ib, c and IIb, c, which have different reactivities, almost coincide. The slight differences between the spectra of salts Ia, Ib and IIa, IIb also do not provide any explanation for their differing reactivities. All this may suggest that the degree of isotope exchange in salts I and II under these experimental conditions does not depend on the degree of polarity of the C–H bonds in their α-methylene groups.

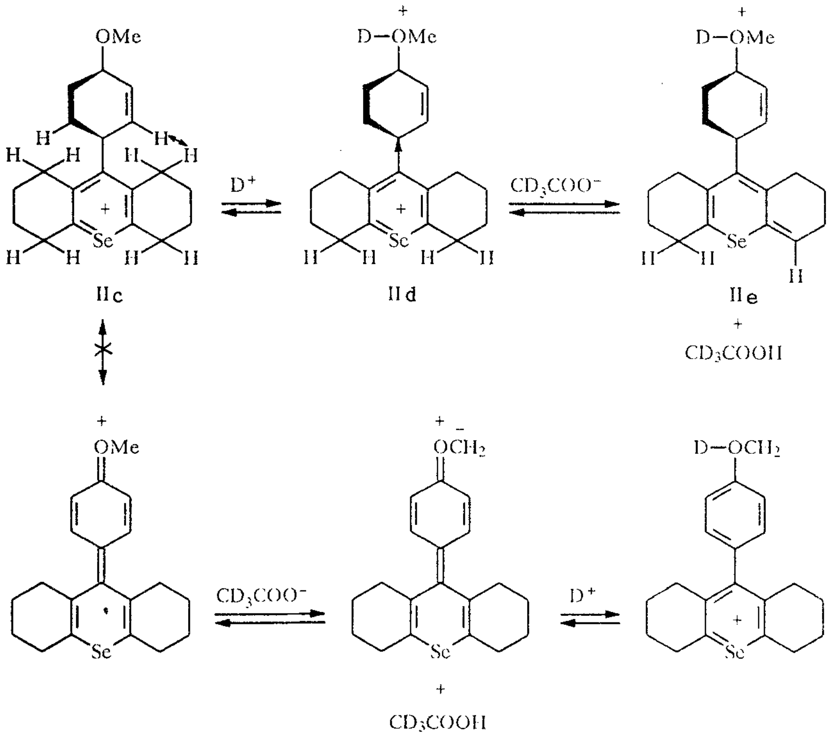
Comparison of these results with the known physicochemical properties of the compounds studied proved more fruitful. It was found that the increase in degree of isotope exchange in the series Ia < Ib < Ic corresponds to the increase in orbital electrophilicity of their cations [8] and hence in an increased tendency to form molecular complexes with n- and π-electron donors [9]. The influence of these factors on the rate of reaction becomes clear if isotope exchange is represented by the following sequence of reaction stages:



The increasing ability of heteroaromatic cations (pyrylium < thiopyrylium < selenopyrylium) to form complexes with deuteroacetic acid should aid its dissociation and hence accelerate exchange of the weakly basic perchlorate anion for the acetate anion, which can capture a proton. Formation of molecular complexes VII by the resulting anhydro bases VI should displace the equilibrium to the right, inhibiting the replacement of a proton and conversely increasing the probability of inserting deuterium. We assume that the combined effect of these factors is responsible for the variation in the degree of H/D isotope exchange that occurs in compounds I.

The complexing ability of the aryl-substituted salts II is much lower than in their unsubstituted analogs I. This is due not only to the lower electron-accepting ability of their cations but also to steric hindrance caused by the benzene rings that are not coplanar with the heterocycle. For this reason, the contribution of complexation factors to an increase in the rate of H/D exchange should be regarded as less important than for cations I. The magnitude of the exchange processes should at the same time depend to a greater extent on the state of the equilibrium V ⇄ VI, which is governed by the difference in thermodynamic stability between salt V and conjugated anhydro base VI. Unfortunately, accurate information on these values is absent from the literature. Nevertheless, by correlating certain indirect data, such as the delocalization energies of electrons in pyrylium and thiopyrylium cations [10] and also from a comparison of the reactivities of oxygen- and sulfur-containing anhydro bases [11], it may be assumed that the equilibrium (cation ⇄ anhydro base) is shifted to the right to a greater extent for a pyrylium salt than for its sulfur analog. This is likely to be responsible for the greater degree of exchange in compound IIa compared to compound IIb.

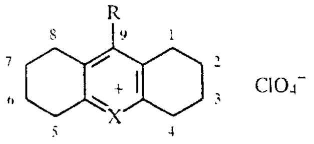
The key to establishing the cause of the large differences in CH acidity between compounds IIa and IIb and their selenium analog IIc is provided by comparing the results of isotope exchange in their α-methylene groups and aryl substituents. Attention may be drawn to the fact that the low reactivity of the methylene groups of compounds IIa and IIb matches a fairly high degree of H/D exchange in their methoxyl groups, while the anomalously high CH acidity of the methylene groups in compound IIc corresponds to the complete inability of the aryl substituent to undergo isotope exchange. These results taken together suggest that in the series of compounds IIa, IIb, and IIc there is a decrease in resonance interaction between the heterocycle and methoxyphenyl substituent, which is a consequence of the successive decrease in the degree of coplanarity between these molecular residues. This assumption can be substantiated from the results of quantum-chemical calculations [12] which suggest that the change from the pyrylium cation Ia to its sulfur analog Ib is accompanied by a convergence of the β-methylene groups of the alicycles because of an increase in the $C\beta-C\gamma-C\beta'$ angle by approximately 4°. In our view this trend should continue in the selenopyrylium cation. The steric convergence of the methylene groups, whose hydrogen atoms are mutually repelled by the ortho-proton of the aryl ring, should lessen the degree of molecular planarity and thus weaken the activating effect of the cationic section of the molecule on isotope exchange in the methoxyl group. It is quite probable that resonance interaction between the heterocycle and aryl substituent in selenopyrylium salt IIc is sterically hindered to such a degree that isotope exchange cannot occur in the methoxyl group. Conversely, there are opportunities for it to interact with electrophilic species such as a deuterium ion. Addition of the latter gives rise to a $-I$ effect from the substituent in the dication intermediate IId, which should assist deprotonation of the methylene groups and at the same time stabilize the resulting anhydro base IIe. In our opinion, it is this that is responsible for the anomalously high CH acidity of the methylene groups in cation IIc. For the pyrylium and thiopyrylium cations IIa and IIc activation of isotope exchange in the α-methylene groups through the formation of a dication intermediate is probably excluded because of a fairly high degree of π-electron interaction between the aryl substituents and cationic residues in the molecules.



From the combined results on the thermodynamic CH acidity of alkyl substituents in pyrylium and chalcogenopyrylium salts obtained in our study it may be concluded that the latter is determined not only by the effect of the heteroatom on the thermodynamic stability of the heterocyclic cations and conjugated anhydro bases but is also considerably dependent on the orbital electrophilicity of the cations and their steric structural features.

It should be noted in conclusion that the results obtained on the relative mobility of the hydrogen atoms of the α-methylene groups in 9-R-sym-octahydro-10-oxonia(chalcogenonia)anthracene perchlorates correlates well with the results of [13]

TABLE 1. H/D Isotope Exchange in Salts Ia-c and IIa-c



Compound	$H_{4,5}$ for D after 70 h, %	H_{O-CH_3} for D after 70 h, %	Chemical shift, δ, ppm		E^*_{PC}, V [8]
			$H_{4,5}$	O—CH$_3$	
Ia	18	—	2,75	—	0,70
Ib	49	—	2,89	—	0,57
Ic	90	—	2,91	—	0,34
IIa	7	79	2,78	3,54	0,93
IIb	5	68	2,93	3,52	0,72
IIc	95**	0	2,98	3,50	0,63

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*Potentials of peaks in cathode reduction of cations I and II in acetonitrile.

**Result after 27 h.

on the relative reactivity of salts Ib and Ic in nitrosation processes and does not agree with the results of [6], in which pyrylium salt Ia was shown to have higher activity than Ib toward condensation with aromatic aldehydes.

EXPERIMENTAL

Isotope exchange was carried out by heating 5% solutions of salts I and II in a mixture of CF_3COOD and CD_3COOD (5:1) at 90°C in the tubes of a Varian FT-80A NMR spectrometer. Chemical shifts were measured on a δ (ppm) scale to an accuracy of 0.02 ppm. The internal standard used was HMDS. The degree of deuterium exchange was determined from the decrease with time of the integral intensity of the signals due to the α-methylene group protons. Salts I and II were synthesized according to the method of Abaev et al. [14].

REFERENCES

1. G. N. Dorofeenko, E. I. Sadekova, and E. V. Kuznetsov, Preparative Chemistry of Pyrylium Salts [in Russian], Izd. Rostov Univ., Rostov-na-Donu (1972), pp. 69, 160.
2. G. A. Reynolds and J. A. Allan, J. Org. Chem., **34**, 2376 (1969).
3. N. V. Khromov-Borisov and L. A. Gavrilova, Zh. Obshch. Khim., **32**, 86 (1962).
4. V. I. Boev and A. V. Dombrovskii, Khim. Geterotsikl. Soedin., No. 7, 881 (1981).
5. V. G. Kharchenko and S. N. Chalaya, Thiopyrans, Thiopyrylium Salts, and Related Compounds [in Russian], Izd. Saratov Univ., Saratov (1987), p. 123.
6. V. G. Kharchenko, T. I. Krupina, S. K. Klimenko, N. M. Yartseva, M. N. Berezhnaya, V. I. Milovanova, and N. N. Kozhevnikova, Khim. Geterotsikl. Soedin., No. 1, 64 (1974).
7. M. R. Detti, J. M. McKolvoy, and H. R. Luss, Organomet., No. 7, 1131 (1988).
8. N. T. Berberova, A. F. Blinokhvatov, A. S. Archegova, E. S. Klimov, A. V. Shpakov, and O. Yu. Okhlobystin, Khim. Geterotsikl. Soedin., No. 1, 47 (1991).
9. A. F. Blinokhvatov, Carbonyl Compounds in the Synthesis of Heterocycles [in Russian], Part 2, Izd. Saratov Univ., Saratov (1989), p. 15.
10. V. G. Kharchenko, A. D. Shebaldova, V. N. Kravtsova, N. S. Smirnova, and A. F. Pronin, Some Problems in the Chemistry of Diketones and Compounds Derived from Them [in Russian], Izd. Saratov. Univ., Saratov (1979), p. 66.

11. E. G. Kovalev, G. L. Rusinov, V. A. Anufriev, and L. G. Egorova, Khim. Geterotsikl. Soedin., No. 9, 1244 (1990).
12. K. K. Kalnin'sh and A. F. Blinokhvatov, Carbonyl Compounds in the Synthesis of Heterocycles [in Russian], Part 2, Izd. Saratov. Univ., Saratov (1992), p. 46.
13. S. K. Klimenko, N. N. Ivanova, N. N. Sorokin, A. F. Blinokhvatova, and T. V. Stolbova, Zh. Org. Khim., **26**, 403 (1990).
14. V. T. Abaev, A. F. Blinokhvatov, O. V. Markovtseva, and O. Yu. Okhlobystin, Khim. Geterotsikl. Soedin., No. 1, 51 (1991).