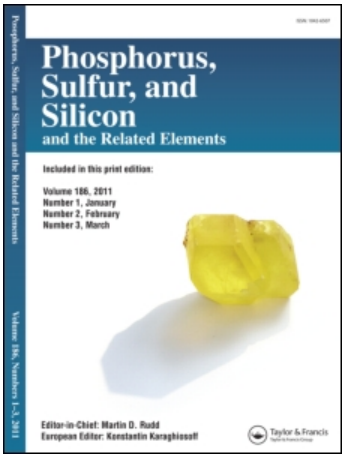

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BASE-CATALYZED HYDROGEN-DEUTERIUM EXCHANGE IN BENZO DERIVATIVES OF FIVE-MEMBERED AROMATIC HETEROCYCLES VI. ISOTOPE EFFECT IN 1-BENZOTHIAZOLE, BENZOXAZOLE, BENZOSELENAZOLE, BENZOTHIOPHENE, BENZOFURAN AND BENZOSELENOPHENE

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BASE-CATALYZED HYDROGEN-DEUTERIUM EXCHANGE IN BENZO DERIVATIVES OF FIVE-MEMBERED AROMATIC HETEROCYCLES

VI. ISOTOPE EFFECT IN 1-BENZOTHIAZOLE, BENZOXAZOLE, BENZOSELENAZOLE, BENZOTHIOPHENE, BENZOFURAN AND BENZOSELENOPHENE

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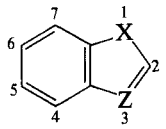
The rates of the base-catalyzed hydrogen–deuterium exchange at C-2 and the reverse in 1-benzothiazole, benzoxazole, benzoselenazole, benzothiophene, benzofuran and benzoselenophene are reported. Also the primary hydrogen isotope effects are discussed. In good agreement with our previous papers, the data obtained can be explained by assuming that in these reactions several effects were involved by the heteroatoms considered and that none of these decidedly and constantly outweighs the others. Furthermore, the rate-limiting steps were found to be different not only between the two compound series, but also in the same aza derivative series.

INTRODUCTION

In our previous papers,[1–5] the base-catalyzed hydrogen–deuterium exchange at position 2 in some benzo derivatives of five-membered aromatic heterocycles was studied.

In these investigations was demonstrated that the heteroatoms were able to transmit the substituent effects from the benzo ring to position 2 of the five-membered ring.[1,2,5] The heteroatoms considered (N, O, S and Se) also revealed a different and sometimes contradictory ability to stabilize the α-carbanion.[3–5]

In order to elucidate the role of the heteroatoms in these reactions, the base-catalyzed hydrogen–deuterium (and vice versa) exchange at position 2 and the primary hydrogen isotope effects for 1-benzothiazole, benzoxazole, benzoselenazole, benzothiophene, benzofuran and benzoselenophene are reported and discussed in this paper.



X = O, S, Se.
Z = N, CH.

RESULTS

The second order rate constants for base-catalyzed hydrogen–deuterium exchange at position 2 (k_H), their relative values, the same rate constants for the reverse exchange (k_D) and the primary hydrogen isotope effects (k_H/k_D) for the above-mentioned compounds are shown in the following table.

DISCUSSION

Careful examination of the rate constant values for base-catalyzed hydrogen–deuterium exchange at

TABLE

The second order (1 mol^{-1} sec^{-1}) rate constants for the base-catalyzed hydrogen–deuterium exchange at C-2 (k_H) and the reverse exchange (k_D); the primary hydrogen isotope effects (k_H/k_D); the relative second order rate constants for the three compounds of each series[a]

Compound	X	Z	k_H	k_D	k_H/k_D	Rel. k_H
benzothiazole	S	N	[b]1.2×10^{-4}	5.7×10^{-5}	2.1	
benzoxazole	O	N	[b]2.4×10^{-3}	6.0×10^{-4}	4.0	$k_S:k_{Se}:k_O = 1:4:20$
benzoselenazole	Se	N	[b]4.9×10^{-4}	9.7×10^{-5}	5.1	
benzothiophene	S	CH	[b]2.3×10^{-7}	2.6×10^{-7}	0.9	
benzofuran	O	CH	[b]5.8×10^{-8}	4.8×10^{-8}	1.2	$k_{Se}:k_O:k_S = 1:2:7$
benzoselenophene	Se	CH	3.3×10^{-8}	4.0×10^{-8}	0.8	

[a] Substrate concentration 10^{-1} M; solvent deuteromethanol or methanol; sodium methoxide 10^{-1} to 1 M; temperature 25°C (±0.1).
[b] These values were reported from the previous papers.[1–5]

position 2 (k_H) confirms some of our previous conclusions.[4,5]

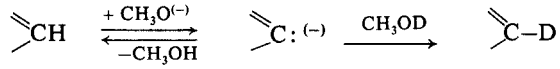
In fact, while the relative rates of hydrogen–deuterium exchange at C-2 for benzothiazole, benzoselenazole and benzoxazole ($k_S:k_{Se}:k_O$) are 1:4:20, the same relative rates for benzoselenophene, benzofuran and benzothiophene ($k_{Se}:k_O:k_S$) are nearly 1:2:7. In particular, for the latter case it is surprising that the selenium heteroatom appears to be less effective than the oxygen and sulphur heteroatoms in the stabilization of the α-carbanion.

Once again, this occurrence is in considerable disagreement with the conclusions of some previous papers, in which the following reactivity order was observed: O < S < Se. Frequently, this order of reactivity was ascribed to the d-orbital overlap by the sulphur and selenium, or, alternatively, to polarization phenomena. However, as previously suggested, in principle one cannot exclude that some other effects can be involved including: electronegativity, aromaticity and transmission of substituent effects.[3–6]

In our opinion, the contradictory behaviour observed in these reactions by the heteroatoms examined provides a further proof that none of the activities normally considered effective in these and in similar reactivities (electronegativity, aromaticity and transmission of substituent effects, d-orbital conjugation, polarization phenomena) is operative. At least, we think we can again conclude that none of the above-mentioned effects decidedly and constantly outweighs the others.[4,5]

These conclusions can be indirectly confirmed also by the examination of the primary hydrogen isotope effect values (k_H/k_D). While these values for benzothiophene, benzofuran, benzoselenophene and benzothiazole were low (from nearly 1 to 2), the same values for benzoxazole and benzoselenazole were higher (respectively 4 and nearly 5).

In accordance with the previous studies on this matter and the mechanism proposed for these reactions by several authors, these occurrences indicate that the rate-limiting steps were different. In particular the proton transfer may be preceded by an equilibrium due to back protonation. The rate of



reprotonation may or may not be slower than the rate of replacement of hydrogen by deuterium, high or low primary hydrogen isotope effects being observed respectively. Furthermore, even the determination of the tritium isotope effect cannot give further and unequivocal information.[6–8]

In consideration of these facts, the primary hydrogen isotope effect values (k_H/k_D) reported in the table clearly show that the rate-limiting steps were different not only between the two compound series (benzothiazole, benzoxazole, benzoselenazole and benzothiophene, benzofuran, benzoselenophene), but also in the same aza derivative series.

For these reasons, we feel it can be concluded that the contradictory behaviour observed in our investigations can also be related to the differences in the rate-limiting steps; this is particularly true for the aza derivative heterocycles.

As a general conclusion, we think that the base-catalyzed hydrogen–deuterium exchange studies are not always and completely informative on the stabilities of the carbanions, above all in the case in which the rate-limiting steps in the reactions of the substrates compared are different.

In consideration of these assumptions, in our opinion, a large quantity of conclusions drawn on this matter by several authors and based on over-simplified investigations should be more carefully reconsidered.[6]

Further investigations are in progress in our laboratories in an attempt to clarify the details of the heteroatom activities.

EXPERIMENTAL

The ^{1}H nmr spectra were recorded on a Perkin-Elmer R 12 B spectrometer, using TMS as internal standard.

1-Benzothiazole, benzoxazole, benzoselenazole, benzothiophene and benzofuran were commercial products and were purified by standard methods for use in kinetic measurements of isotopic exchange. 1-Benzoselenophene was kindly supplied by Prof. M. Renson.

The 2-deuterated derivatives were prepared from the above-mentioned compounds by base-catalyzed (with sodium methoxide) hydrogen–deuterium exchange in monodeuteromethanol. The isotopic exchange was monitored by ^{1}H nmr spectroscopy and was nearly quantitative in all cases. The crude products obtained by usual procedures were purified by standard methods for use in kinetic measurements.

The experimental conditions for kinetic measurements of isotopic exchange were the same reported in detail in the previous papers.[1-5] In this connection, see also the table of this paper.

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REFERENCES AND NOTES

1. O. Attanasi, G. Bartoli and P. E. Todesco, *Tetrahedron* **32**, 399 (1976); and references therein.
2. O. Attanasi, G. Bartoli and P. E. Todesco, *J. Heterocyclic Chem.* **13**, 1021 (1976); and references therein.
3. O. Attanasi, *J. Heterocyclic Chem.* **14**, 95 (1977); and references therein.
4. O. Attanasi, *Gazz. Chim. Ital.* **107**, 359 (1977); and references therein.
5. O. Attanasi, *Studi Urbinati*, 129 (1976); and references therein.
6. J. A. Elvidge, J. R. Jones, C. O'Brien, E. A. Evans and H. C. Sheppard, *Adv. Heterocyclic Chem.* **16**, 1 (1974); and references therein.
7. W. J. Albery and J. R. Knowles, *J. Am. Chem. Soc.* **99**, 637 (1977).
8. E. Buncel and C. C. Lee, *Isotopes in Organic Chemistry* (Elsevier Scientific Publishing Company, Amsterdam, 1976), Vol. 2.