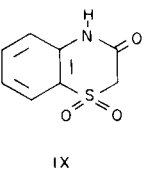
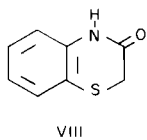
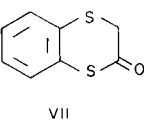
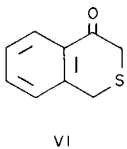
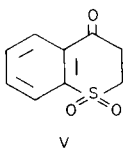
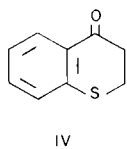
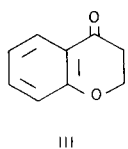
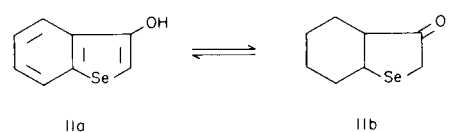
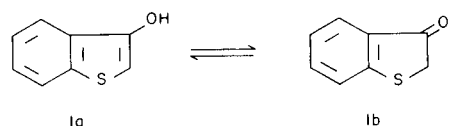


A Nuclear Magnetic Resonance Study of Sulfur and Selenium Analogs of Benzocyclanones

G. Grandolini, A. Ricci, N. P. Buu-Hoi and F. Périn

Istituto Chimica Farmaceutica, Università Degli Studi di Perugia,
and Institut de Chimie des Substances Naturelles du C.N.R.S.

In the course of our studies on the synthesis of complex heterocycles derived from various sulfur- and selenium-containing analogs of benzocyclanones (I), it was of importance to determine to what extent such oxo compounds display keto \rightleftharpoons enol tautomerism. 3-Hydroxythianaphthene (Ia), for instance, is able to react with carbonyl reagents such as arylhydrazines in its ketonic form Ib (2), although a study of its n.m.r. spectrum showed that in both neutral and acidic solvents it exists solely in its enolic form (3).



A similar study has now been done on 3-hydroxy-selenonaphthene (IIa) which we recently found (4) to undergo chemical reactions corresponding to its keto form (IIb), and on six oxo compounds derived from various sulfur benzoheterocycles; for the sake of comparison, chroman-4-one (III) was included in this research.

The sulfur-containing oxo compounds were: thianaphthene-2-one (IV) and the corresponding sulfone (V); isothiachroman-4-one (VI); 1,4-benzodithian-2-one (VII); 3-keto-2,3-dihydro-1,4-benzothiazine (VIII) and the corresponding sulfone (IX).

The nuclear magnetic spectra of these various substances were examined both in a neutral solvent (deuteriochloroform) and in a strongly acidic one (trifluoroacetic acid). The Table shows the chemical shifts corresponding: A, to the two methylene protons in position α to the carbonyl; B, to the two methylene protons α to the oxygen, sulfur, or selenium heteroatom; and C, to the aromatic proton situated in position *peri* to the carbonyl (where such a proton exists). Details of some of these spectra are given in Figures 1 to 10.

DISCUSSION OF RESULTS

Compound II.

(a) The spectra in deuteriochloroform and in trifluoroacetic acid are almost identical, the solvent effect being very small here.

(b) At variance with 3-hydroxythianaphthene (Ia), compound II exists in its *keto form* (IIb) in both of the solvents used. The singlet at 3.92-4.04 p.p.m. can be attributed to the protons of the sequence $-\text{Se}-\text{CH}_2-\text{CO}-$, as it is quite comparable to that found with 1,4-benzodithian-2-one (3.47-3.54 p.p.m.) and with isothiachroman-2-one (3.57-3.70 p.p.m.), although the paramagnetic effect of the selenium heteroatom on the chemical shift of the two neighboring methylene protons is greater than that of the sulfur heteroatom (account must also be taken of the difference in size and nature of the three heterocycles concerned).

(c) In the aromatic area of the spectra, the proton in position 4 is well resolved because of the influence of the electron-accepting carbonyl group in the *peri* position. This proton shows an *ortho* coupling ($J_{AB} = 7-10$ c.p.s.)

Table. Chemical Shifts

Formula	Protons A		Protons B		Proton C in TFAA
	in $CDCl_3$	in TFAA	in $CDCl_3$	in TFAA	
IIb	3.92 (s)	4.04 (s)	----	----	7.8 (m)
VII	3.47 (s)	3.54 (s)	----	----	----
VI	3.57 (m)	3.70 (m)	3.96 (m)	3.97 (m)	8.1 (m)
IV	3.20 (m)	3.56 (m) (4H)	2.90 (m)	3.56 (m) (4H)	8.15 (m)
		system A_2B_2		system A_2B_2	
V	3.62 (m) (4H)	3.86 (m) (4H)	3.62 (m) (4H)	3.86 (m) (4H)	non-deter- minable
	system A_2B_2	system A_2B_2	system A_2B_2	system A_2B_2	
III	2.80 (t) (2H) belonging to a system A_2X_2	3.02 (t) (2H) system A_2X_2	4.55 (t) (2H) belonging to a system A_2X_2	4.67 (t) (2H) system A_2X_2	8.0 (m)
VIII	3.58 (s)	3.60 (s)	----	----	----
IX	----	4.68 (s)			

s = singlet; t = triplet; m = multiplet. The chemical shifts are expressed in p.p.m.

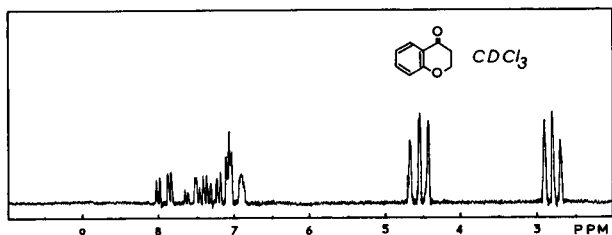


Figure 1

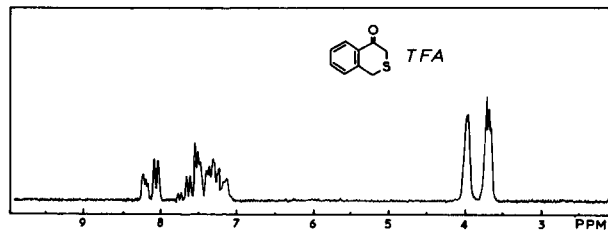


Figure 4

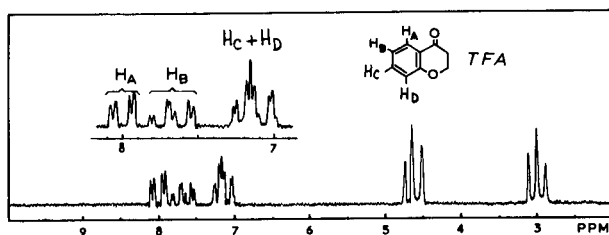


Figure 2

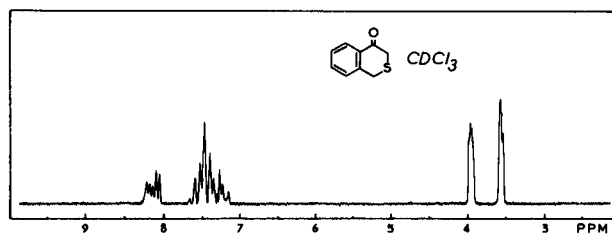


Figure 5

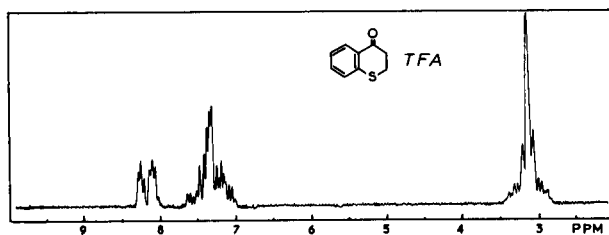


Figure 3

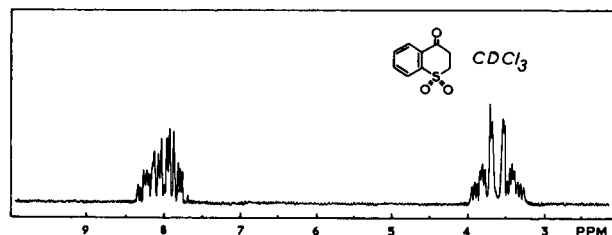


Figure 6

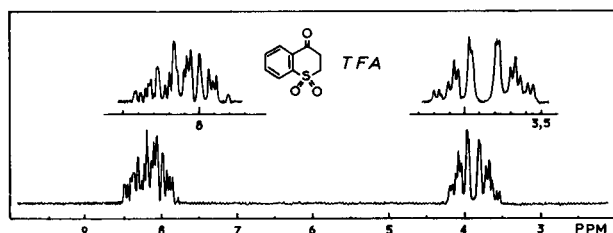


Figure 7

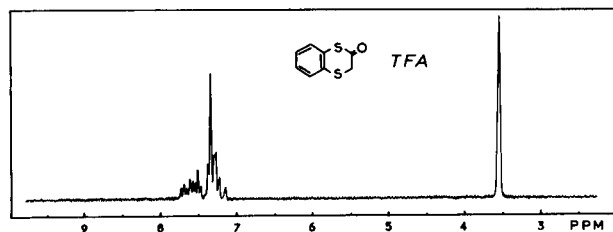


Figure 8

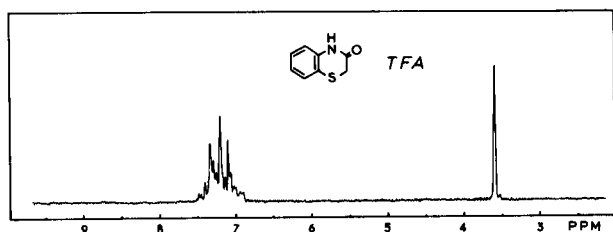


Figure 9

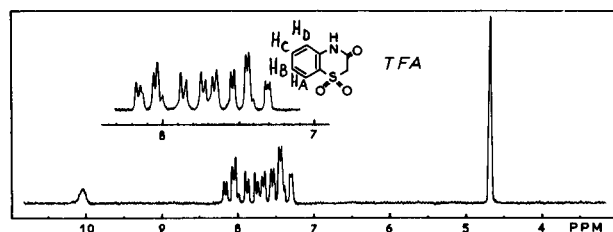


Figure 10

with the proton in position 5 and a *meta* coupling ($J_{AB} = 2-3$ c.p.s.) with that in position 6, the *para* coupling being negligible ($J = 0-1$ c.p.s.).

Compound VII.

In the spectrum in deuteriochloroform, the well-resolved peak at 7.6 p.p.m. corresponds probably to the proton in position 8 which undergoes the influence of the carbonyl group through the sulfur heteroatom in position 1. Here again, no enol form was detected.

Compound VI.

The proton in position *peri* to the carbonyl can be singled out from the other aromatic protons and appears

as a system of peaks because of the *ortho* and *meta* couplings. The two singlets at 3.97 and 3.70 p.p.m. can be assigned to the methylene group located next to the benzene ring and to the methylene group next to the carbonyl, respectively, on grounds of comparison with the spectra of the previous substance. The width of these singlets could be due to some long range effect.

Compound IV.

In TFAA, the proton *peri* to the carbonyl appears as a doublet at 8.15 p.p.m. and is coupled with the other aromatic protons. The multiplet at 3.16 p.p.m. corresponding to the two methylenes can be ascribed to the non-equivalence of the latter; this is even more apparent in the spectrum in deuteriochloroform, where the corresponding, non-resolvable signal is of the type A_2B_2 . A study of IV had already been made by Martin (5).

Compound V.

Here it was impossible to identify the proton *peri* to the carbonyl, because of an equal influence of the sulfone group on the proton in position 8: these two protons gave, therefore, superimposed signals.

Compound III.

The spectrum of this compound in trifluoroacetic acid is much better resolved than in the case of thiochroman-4-one. (a) The aromatic region shows distinct signals for the proton H_A (8.0 p.p.m.) and H_B (7.67 p.p.m.), the chemical shift of the proton H_A toward the weaker field being due to the influence of electron-accepting carbonyl in *peri*; H_A is *ortho*-coupled with the proton H_B ($J_{AB} = 8$ c.p.s.) and *meta*-coupled with the proton H_C ($J_{AC} = 2$ c.p.s.). H_B is *ortho*-coupled with H_A and H_C , and *meta*-coupled with H_D , and H_D and H_C behave in a similar way, although their peaks partly superimpose each other. (b) Whilst the two methylenes are only slightly non-equivalent in the spectrum of thiochroman-4-one, the two methylenes of this compound produce an A_2X_2 spectrum, the methylene adjacent to the carbonyl appearing at 3.02 p.p.m. and the one adjacent to the oxygen heteroatom at 4.67 p.p.m.

As seen from Figures 1 and 2, a change of solvent to deuteriochloroform has very little influence on the spectrum, except for small variations in the chemical shifts.

Compound VIII.

In the spectrum of this compound in TFAA (Figure 9), the aromatic protons appear as a complex multiplet at 7.2 p.p.m., which is due to the fact that neither the -NH-group nor the sulfur heteroatom is able to exert a sufficient deshielding effect on the respective *peri* protons to separate their signals from the rest (the multiplet formed by the aromatic protons appears more clearly as an A_2B_2 system in the spectrum in deuteriochloroform).

Compound IX.

Unlike for the previous compound, the spectrum in TFAA (Figure 10) clearly shows the double doublets corresponding to H_A (8.1 p.p.m) and H_D (7.35 p.p.m.), with, in between, the superimposed multiplets corresponding to H_B and H_C ($J_{AB} = 7.5$ c.p.s. and $J_{AC} = 2$ c.p.s.). The signal of the imine proton appears at 10 p.p.m., and that of the methylene is shifted to 4.68 p.p.m. because of the combined effects of the carbonyl and sulfone groups.

CONCLUSION

Apart from their intrinsic interest, the above n.m.r. data provide evidence for the non-existence of the enolic forms of all the oxo compounds investigated, in both acidic and neutral media; this feature might prove useful in the interpretation of their chemical reactions and their light absorption spectra.

EXPERIMENTAL

Preparation of Compounds.

"3-Hydroxyselenonaphthene" was prepared according to Lesser and Weiss (6), 1,4-benzodithian-2-one according to Ricci and Negri (7), isothiachroman-4-one according to von Braun and Weissbach (8), and chroman-4-one according to Powell (9); the method used for the synthesis of thiachroman-4-one and its sulfone was that of Arndt (10), and for that of compounds VIII and IX, that of Claasz (11).

n.m.r. Studies.

The spectra were determined on a Varian A-60 apparatus, with tetramethylsilane as internal reference.

Acknowledgment.

Our thanks are due to Prof. V. Bellavita for his interest in and encouragement for this work, and to the authorities of the University of Perugia for a Fellowship to one of us (F.P.).

REFERENCES

- (1) N. P. Buu-Hoi, V. Bellavita, A. Ricci, J. P. Hoeffinger and D. Balucani, *J. Chem. Soc. (C)*, 47 (1966); N. P. Buu-Hoi, A. Martani, A. Croisy, P. Jacquignon and F. Pèrin, *ibid.*, 1787 (1966); A. Ricci, N. P. Buu-Hoi, P. Jacquignon and M. Dufour, *J. Heterocyclic Chem.*, 2, 300 (1965).
- (2) E. W. McClelland and J. L. D'Silva, *J. Chem. Soc.*, 227 (1932); C. E. Dalglish and F. Mann, *ibid.*, 653 (1947); N. P. Buu-Hoi and G. Saint-Ruf, *Israel J. Chem.*, 1, 369 (1963).
- (3) N. P. Buu-Hoi, V. Bellavita, A. Ricci and G. Grandolini, *Bull. Soc. Chim. France*, 2658 (1965).
- (4) N. P. Buu-Hoi, G. Saint-Ruf, A. Martani, A. Ricci and D. Balucani, *J. Chem. Soc., (C)*, 1968 (in the press).
- (5) R. H. Martin, N. Defay, F. Geerts-Errard, P. H. Givan, J. R. Jones and R. W. Wedel, *Tetrahedron*, 21, 1833 (1965).
- (6) R. Lesser and R. Weiss, *Ber.*, 45, 1838 (1912).
- (7) A. Ricci and M. Negri, *Ann. Chim. (Italia)*, 50, 1066 (1960).
- (8) J. von Braun and K. Weissbach, *Ber.*, 62, 2416 (1929).
- (9) S. G. Powell, *J. Am. Chem. Soc.*, 45, 2710 (1923).
- (10) F. Arndt, *Ber.*, 56, 1278 (1923); *ibid.*, 58, 1626 (1925).
- (11) M. Claasz, *ibid.*, 45, 751 (1912).

Received December 13, 1967

Perugia, Italy and
91-Gif-sur-Yvette, France