Conformations of 3-Bromochromanones, -Thiachromanones, and -Thiachromanone Sulphones

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The nmr spectra of the heterocyclic protons of some chroman, thiachroman and thiachroman sulphone derivatives are discussed. It is concluded that the bromine atom probably occupies a pseudo-axial position in 3-bromochromanone but is pseudo equatorial in 3-bromothiachromanone and its sulphone. It is suggested that these different preferred conformations may be due to differing steric interactions between the bromine atom and the hetero atoms of the heterocyclic ring.

3-Bromo-1-thiachromanone sulphone (IIc) 6-methyl-1-thiaflavanone (VIb) and 6-methyl-1-thiaflavanone sulphone (VIc) disclosed ABX patterns in their nmr spectra, which were analyzed to obtain coupling constants for the heterocyclic protons. The 2,3-disubstituted compounds showed AB spectra from which couplings were obtained directly. The results are presented in Tables I and II.

TABLE I

Nmr and I.R. Spectra of 2- and 3-Substituted Chromanones, Thiachromanones and Thiachromanone Sulphones

Compound	Coupling Constants (Hz)		Solvent	I.R. (e)
	2,3-*trans*	2,3-*cis*		C=O (cm^{-1})
III	13.2 (a)	3.1 (a)	$CDCl_3$	1713 (c) (d)
IV	8.5 (a)		$CDCl_3$	1717 (c) (d)
V	---	1.8 (a)	$CDCl_3$	1713 (c) (d)
IIa	4.4 (b)	2.7 (b)	D_6 acetone	1689
Ia	---	---	---	1688
VIb	12.7	3.3	$CDCl_3$	1675
VIIb	10.1	---	D_6 acetone	1684
VIIIb	---	2.3	D_6 acetone	1679
IIb	8.6 (b)	3.1 (b)	CCl_4	1686
Ib	---	---	---	1676
VIc	12.5	3.2	$CDCl_3$	1693
VIIc	12.1	---	D_6 acetone	1702
IIc	11.9	4.4	D_6 acetone	1706
Ic	---	---	---	1690

(a) Ref. 1. (b) Ref. 5. (c) Ref. 4. (d) Other values have been reported (2) but were obtained using KBr discs, and therefore are not included here. (e) Chloroform solutions.

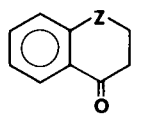
TABLE II

	Chemical Shifts (δ)		Geminal Coupling (Hz)	
	2H	3H		
VIb	4.67	3.17, 3.27	J3e3a	-16.5
VIIb	4.98	5.55		
VIIIb	4.97	5.20		
VIc	4.83	3.38, 3.93	J3e3a	-17.7
VIIc	5.05	5.70		
IIc	4.43, 4.91	5.78	J2e2a	-14.0

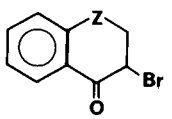
It can be seen that the 2,3-*trans* coupling in the sulphones does not vary significantly between the compounds observed, but has a high value consistent with diaxial coupling, and would indicate a strong preference for the conformation in which the bromine is equatorially oriented. This is in marked contrast to the oxygen series, where the value of the largest coupling observable changes from 13.2 in the flavanone (III) to about one-third of this value in 3-bromochromanone (IIa). This latter value would appear to be more consistent with a diequatorial, rather than a diaxial coupling.

The 2,3 coupling in the *trans* 3-bromoflavanone IV is also considerably less than that in the unbrominated flavanone, and could indicate either that the ring is distorted, or that a considerable mole fraction of the compound exists in the 2-phenyl axial 3-Br axial conformation (1). Similar results have been observed in the parent flavanones (2). The magnitude of the *trans* coupling also decreases in the thiachromanone series when the phenyl group is absent, but not to the same extent. 3-Bromothiachromanone would therefore appear to have less 3-Br axial character than its oxygen analogue.

Further evidence for the preferred conformations can be obtained from the 2-phenyl analogues. The product obtained by bromination of 6-methyl-1-thiaflavanone (VIb) at room temperature (5) is now shown to be the *trans* derivative (VIIb) while bromination in boiling acetic acid yielded a mixture of *trans* and *cis* isomers in the ratio of 2:1, as determined by nmr integration of the reaction products. Bromination of the thiaflavanone sulphone

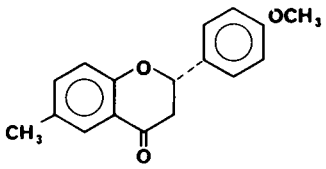


I

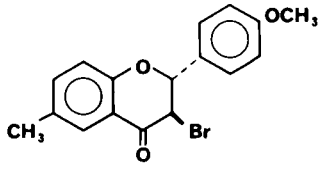


II

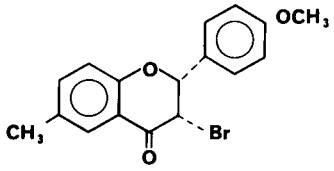
a Z = O
b Z = S
c Z = SO_2



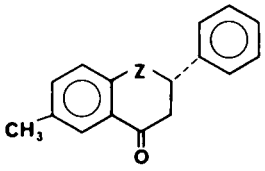
III



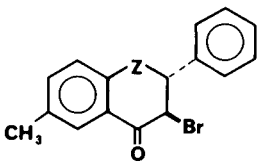
IV



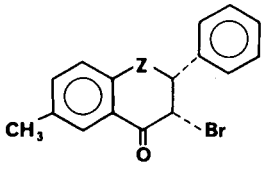
V



VI



VII



VIII

b Z = S
c Z = SO_2

(VIc) in either hot or cold acetic acid gave exclusively the *trans* isomer (VIIc) while flavanones are known to yield predominantly *cis* compounds on bromination with bromine in hot acetic acid (2 and 4). The thermodynamically favoured isomers thus vary from exclusively *trans* in the sulphones, through 2:1 *trans/cis* with sulphur, to predominantly *cis* when oxygen is the heterocyclic atom.

Katritzky and Zernai (5) have stated that infrared spectroscopy supports the conclusion that compounds of type II, where Z may be either S, O, or NSO_2-CH_3, possess conformations in which the halogen is predominantly axial, because the observed carbonyl frequencies are in good agreement with calculated values. The present infrared results (Table I) would suggest that the favoured conformations may also be inferred by comparison of the carbonyl region of brominated and unbrominated compounds, where small but significant differences are observed. In the thiaflavanone and thiaflavanone sulphones, an equatorial bromine would appear to increase the carbonyl absorption frequency by about 9 cm^{-1}, while the *cis* bromothiaflavanone (with 3-Br axial) shows little frequency change. Thiachromanone (Ib) has an absorption about 10 cm^{-1} lower than that of the 3-bromo derivative, while thiachromanone sulphone (Ic) similarly has an absorption 8 cm^{-1} less than that of its bromo derivative (IIc). This evidence would therefore tend to indicate a preference for equatorially, rather then axially, oriented bromine in 3-bromothiachromanone, and to this extent, the conclusions differ from Katritzky's general statement. Similarly, 3-bromothiachromanone sulphone may also be deduced to possess a predominantly equatorial bromine, which would be consistent with the nmr data. The carbonyl absorption of chromanone is essentially the same as 3-bromochromanone, but the differences for an axial or equatorial bromine are small in this series when measured in solution (4).

The tendency for bromine to occupy axial configurations in α-bromoketones is well known (6) and can be attributed to dipole-dipole repulsion between the carbonyl oxygen and halogen as in 2-bromocyclohexanone (7). In the present case, the difference in preferred conformation, with the bromine tending to be more equatorially situated, with $SO_2 > S > O$ may be due to differing 1,3-interactions between the bromine and heterocyclic atoms. In thiane 1-oxides there is evidence that the electron pair on sulphur may interact in a 1,3-diaxial fashion (8,9) while the bulky sulphone grouping (which has an axial oxygen) could similarly prevent the halogen from becoming axial. Also, it can be noted that models suggest that the presence of sulphur, with its longer C–S bonds, distorts the heterocyclic ring, forcing the carbonyl out of the plane of the aryl ring and accentuating the axial-like position in such a

way as to increase 1,3-diaxial interaction.

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EXPERIMENTAL

Preparation of Compounds.

3-Bromo-1-thiachromanone (IIb), (11) 3-bromochromanone (IIa), (12) and 3-bromothiachromanone sulphone (IIc), (10), were prepared by literature methods. 6-Methyl-1-thiaflavanone (VIb), 2,3-*trans*-3-bromo-6-methyl-1-thiaflavanone (VIIb), 6-methyl-1-thiaflavanone sulphone (VIc) and 2,3-*trans*-3-bromo-6-methyl-1-thiaflavanone sulphone (VIIc) were prepared by the method of Arndt (3,10).

2,3-*cis*-Bromo-6-methyl-1-thiaflavanone (VIIb).

This compound was obtained by carrying out the bromination in boiling acetic acid. Chromatography of the reaction product on silica gel and elution with benzene afforded the compound as pale yellow prisms, m.p. 84-85°.

Anal. Calcd. for $C_{16}H_{13}BrOS$: C, 57.7; H, 3.9; Br, 24.0. Found: C, 57.7; H, 3.9; Br, 24.0.

Further elution of the column gave the *trans* isomer, m.p. 120°, lit. (10) m.p. 120°.

Nmr spectra were obtained using Varian HA60 and A60 spectrometers at 60 MHz. Infra-red spectra were recorded on a Perkin Elmer 457 Spectrophotometer in chloroform solutions.

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