The Preferred Conformation of 9-Alkylthioxanthenes

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Summary Chemical shift and long-range coupling data indicate that the alkyl groups of 9-alkylthioxanthenes prefer the *a'* conformation.

IT has recently been shown [1,2] that 9-alkyl-9,10-dihydroanthracenes preferentially exist with the *meso*-substituent [the substituent at C(9)] in the pseudo-axial (*a'*) position. Taylor and Proctor[3] have recently shown a similar behaviour for 9-alkylacridanes. We now report the assignment of stereochemistry to 9-alkylthioxanthenes. Both the chemical shifts of the alkyl groups and the allylic [H–C(9)–C=C–C(1,8)–H] couplings support the assignment of the alkyl groups to the *a'* array.

The following were prepared by the reaction of butyllithium with thioxanthene followed by alkylation of the carbanion with the appropriate alkyl halide: 9-methylthioxanthene (I),[4] 9-ethylthioxanthene [(II), m.p. 49—50°], 9-isopropylthioxanthene [(III), m.p. 52·5—53·0°]. The t-butyl derivative [(IV), m.p. 156—157°] was prepared by the reaction of thioxanthylium perchlorate with t-butyllithium, the previous procedure having afforded poor yields. The resonance (100 MHz, $CDCl_3$, Me_4Si) of the methyl group of (I) is a doublet, δ 1·40 (J 7·0 Hz) p.p.m. The methyl group of (II) is a triplet, δ 0·80 (J 7·2 Hz) p.p.m., while the methylene resonance is a multiplet centred at δ 1·73 p.p.m. The methyl resonance of (III) is a doublet, δ 0·76 (J 6·8 Hz) p.p.m., while the methine resonance is a multiplet centred at δ 2·22 p.p.m. The singlet arising from the t-butyl group of (IV) occurs at δ 0·90 p.p.m. The similarity between these values and those of the corresponding 9,10-dihydroanthracene derivatives[1] suggest a similar, *i.e. a'*, environment for the alkyl groups of both systems.

An unequivocal evaluation of the effect of increasing the size of the C(9) alkyl group upon the conformational distribution of 9-alkylthioxanthenes (and, undoubtedly, similar systems) can be obtained by determining the effect of changing the alkyl group upon the allylic coupling between 9-H and the aryl protons, *a'* coupling more strongly than *e'*. Irradiation of the aryl region (*vide infra*) causes the 9-H signal to decrease in band width at half height by the following amounts: (I) 21%; (II), 16%; (III), 14%; (IV),

22% (all values ±1·5%). These data indicate that, while (I) is conformationally inhomogeneous,[4] (II) and (III) are both essentially *a'*. The increase in the coupling in passing to (IV) indicates that in (IV) 9-H occupies a position more *a'* than do the 9-H protons in (II) and (III). This reflects a flattening of the central ring [relative to (II) or (III)] resulting from repulsions between the t-butyl group *and* the sulphur atom and its *a'* non-bonding electron pair. Such a distortion has also been noted for 9-t-butyl-9,10-dihydroanthracene.[1,2]

The irradiation frequencies used to achieve maximum decoupling of the 9-H and aryl protons vary only slightly for (I)—(IV). However, the actual values [δ 7·26 for (I), 7·21 for (II), 7·16 for (III), and 7·18 p.p.m. for (IV), all ±0·01 p.p.m.] support the view that 1-H and 8-H are being decoupled since we have demonstrated (unpublished results) that an *a'* alkyl group will cause slight shielding of a substituent at C(1), the extent of shielding being related (in a manner similar to that demonstrated above) to the nature of the alkyl group. Thus, the changes in the "half band widths" are considered significant and *not* the result of varying degrees of decoupling in different experiments. Finally, each "% change" is the average result of *at least* ten determinations (sweep width 100 Hz).

These results support the assumption inherent in the arguments of Michaelis *et al.*,[5] *i.e.*, that Methixene (an anticholinergic agent, 9-[(*N*-methyl-3'-piperidyl)methyl]thioxanthene) prefers the *a'* conformation. They also indicate a similarity, between the conformational preferences of 9-alkyl-9,10-dihydroanthracenes,[1,2] 9-alkylacridanes,[3] and 9-alkylthioxanthenes.

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