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Resolution of Sterically Overcrowded Ethylenes; A Remarkable Correlation between Bond Lengths and Racemization Barriers.

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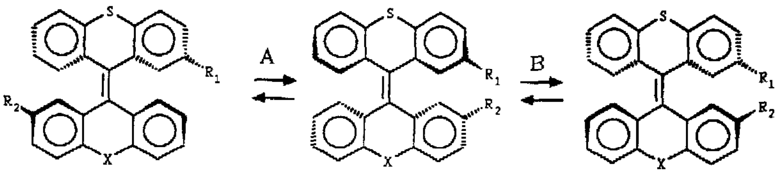
Abstract: The synthesis and resolution of 2-methyl-9H-thioxanthene-9-(9H-thioxanthen-9-ylidene) 1 and related structures 2-5, being the first examples of thermally stable optically active sterically overcrowded ethylenes, are reported. Substitution of the sulfur atom in the thioxanthene part of 1 with an X group (2, X = $C(CH_3)_2$; 3, NCH_3; 4, O) results in a change in racemization barrier (1, 27.4 kcal.mol $^{-1}$; 2, 25.1 kcal.mol $^{-1}$; 3, 21.3 kcal.mol $^{-1}$; 4, <20 kcal.mol $^{-1}$) depending upon the aryl-X bond lenghts.

Sterically overcrowded ethylenes[1] have attracted considerable attention due to their intriguing thermochromic and photochromic properties[2,3]. Investigations of the conformational behavior of disubstituted biacridanes[4], bixanthylidenes[5] and bianthrones[6] demonstrated that these compounds can adopt inherently dissymmetric chiral structures. As far as we know, no resolution of symmetrically overcrowded alkenes has been reported[7] and stereochemical studies have mainly been limited to NMR measurements. Recent attempts to resolve bifluorenylidenes by the use of tartaric acid derived chiral auxiliaries were unsuccessful because of low racemization barriers[8]. We now report the first successful resolution of thioxanthene based alkenes **1** - **3** and **5** and the observation of a remarkable correlation between racemization barriers and bond lengths in these molecules.

The alkenes **1**,**2**,**4** and **5** were synthesized using the thioketone-diazo coupling method[9,10] for the formation of the central double bond. 2-Methyl-9H-thioxanthenone hydrazone was oxidized to the diazo-compound (Ag_2O, CH_2Cl_2, -10 °C) and subsequently added to the appropriate thioketones[11]. The resulting episulfides were desulphurized with copper in boiling xylene to the alkenes in 70-80% yield based on the hydrazones[12] (Table 1). 10-Methyl-9H-acridane-9-thione failed to give **3** via this procedure. Alkene **3** was obtained via a one-pot Peterson olefination[13] sequence in 80% yield starting from 10- methyl-9H-acridane and 2-methyl-9H-thioxanthenone.

The methyl substituent (R_1) in the thioxanthene part of **1** - **4** was introduced to induce dissymmetry into the otherwise centrosymmetric structures.[14a] The methyl substituent apparently has no major influence on the basic *folded* structure as was demonstrated by X-ray analysis;[14b] twisted structures were not observed for **1** - **5** (NMR, HPLC, UV analysis).



1-5

figure 1

Table 1 Thioxanthene Based Overcrowded Ethylenes

Compound	X	R¹	R²	yield[a] (%)	$[\alpha]^{22}_{578}$ [b]	Φ_f [d]
1	S	CH_3	H	80	128	0.60
2	$C(CH_3)_2$	CH_3	H	76	103	0.37
3	NCH_3	CH_3	H	88	c	0.65
4	O	CH_3	H	70	-	0.48
5	S	CH_3	CH_3	68	280	0.72

a) Isolated yields based on 2-methyl-9H-thioxanthenone hydrazone for 1, 2, 4 and 5 and on 2-methyl-9H-thioxanthenone for 3.

b) n-hexane (c = 3.0 10^{-4} g/ml).

c) Optical rotation not accurately determined due to racemization at room temperature.

d) Fluorescence Quantum Yields relative to 9,10-diphenylanthracene.

Resolution of **1**,**2**, and **3** was achieved using HPLC with (+) polytriphenylmethylmethacrylate as a chiral stationary phase[15]. 2-Methyl-9H-thioxanthene-9-(9H-xanthen-9-ylidene) **4** could not be resolved, apparently due to a racemization barrier below 20 kcal.mol^{-1}.[16] The bithioxanthylidene **5**, containing methyl substituents in both halves of the molecule, was isolated as a cis-trans mixture (50/50 ratio). It could be separated in three forms; two cis enantiomers and one achiral centrosymmetrical trans form. The thermal racemization of these alkenes was determined by polarimetry in the temperature range 45-75 °C in p-xylene and followed first-order kinetics. The racemization barriers are summarized in Table 2.

Racemization of alkenes **1-4** (R_2 = H) can occur by two mechanisms (figure 1); rotation around the double bond (process a) and by movement of the aromatic moieties of upper and lower halves of **1-4** through the mean plane of the molecules (process b). The thermal isomerization of optically pure cis **5** (R_2 = CH_3), as determined by HPLC analysis, showed that cis/trans isomerization and racemization occurred at a comparable rate indicating that both processes have the same energy barrier (27.4 kcal.mol^{-1}). NMR studies on biacridanes[4], bixanthylidenes[5] and bianthrones[6] have also indicated the same value for these two isomerization processes.

Table 2 Racemization Barriers of Overcrowded Ethylenes

Compound	X	Aryl-X bond length[a] Å	racemization barrier kcal.mol^{-1}
1	S	1.77	27.4 ± 0.2
2	$C(CH_3)_2$	1.52	25.1 ± 0.3
3	NCH_3	1.42	21.3 ± 0.5[b]
4	O	1.38	< 20.0

a) The bond lengths for compounds 1 and 4 were taken from the X-ray structure of 4[14b], for 2 from the X-ray structure of 10H-anthracene-9-thione, 10,10 dimethyl[14b] and for 3 from the X-ray structure of 9-t-butyl-9,10-dihydroacridine.[17]

b) The racemization barrier was determined by calculation from the HPLC chromatogram: 15% of racemized material was found at 11.8 °C between the peaks of the enantiomers.[18]

A surprisingly high thermal racemization barrier of 27.4 kcal.mol^{-1} was found for 2-methyl-9H-thioxanthene-9-(9H-thioxanthen-9-ylidene) **1**, a value exceeding the barrier for bixanthylidenes[5] (18 kcal.mol^{-1}) as determined by ^{1}H NMR studies by 9.4 kcal.mol^{-1}!

Systematic modification of the atom X, bridging the aryl-moieties in the lower half of alkenes **1** - **4**, allowed a comparison of the racemization barriers and the aryl-X bond lengths. The data in Table 2 clearly indicate a remarkable correlation: a large increase in racemization barrier is found when the aryl-X bond is lengthened. This "remote bond length effect" can be explained by the fact that a longer aryl-X bond will force the two aromatic halves of the lower part of the molecule into the direction of the upper thioxanthene moiety. Since during racemization two peri H-peri H (H_1-H_1'; H_8-H_8') passages have to take place, the smaller aryl-aryl distance between the lower and upper halves will clearly enhance the steric barrier for this process.

Finally fluorescence measurements on alkenes **1** - **5** have been performed. The bithioxanthylidenes and the acridine substituted alkene **3** are strongly fluorescent compounds (see Table 1). As acridines and related compounds have found widespread application as fluorescent agents[19] the enantiomers of **1**, **3** and **5** could serve as novel chiral (helical) fluorescent probes.

In conclusion we have prepared the first optically active thermally stable symmetrically overcrowded ethylenes and have demonstrated the possibility to tune the racemization barrier by variation in a single bond.

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