Sterically Overcrowded Alkenes; a Stereospecific Photochemical and Thermal Isomerization of a Benzoannulated Bithioxanthylidene

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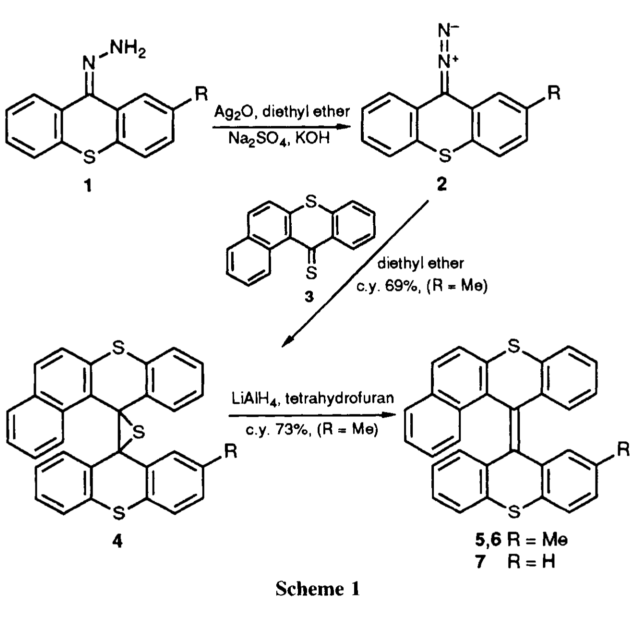
Enantiomerically pure sterically overcrowded 12*H*-benzo[*a*]thioxanthenyl-12-(2-'methyl-9'*H*-thioxanthene-9'-ylidene) shows a stereospecific photochemical and thermal isomerization of the *P-trans* into the *M-cis* isomer (and *vice versa*), with a large thermal isomerization barrier ($\Delta G^{\ddagger} = 28.6$ kcal mol^{-1}) (1 cal = 4.184 J), making this type of molecule especially suitable as the key structural unit for applications as chiroptical molecular switches.

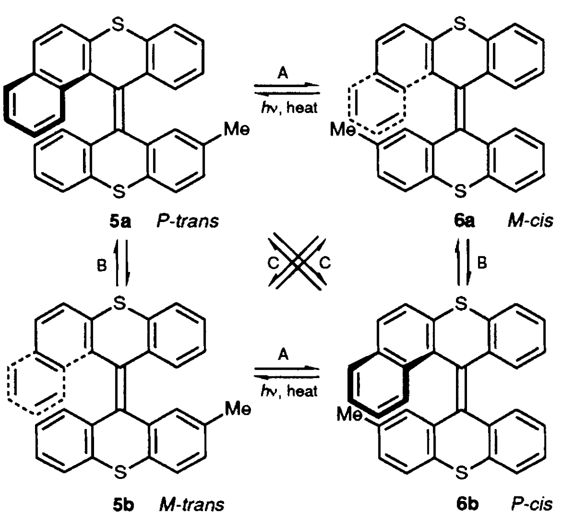
Sterically overcrowded alkenes[1] have evoked considerable interest owing to their intriguing thermochromic and photochromic properties.[2,3] The conformational behaviour of disubstituted bifluorenylidenes,[4] biacridanes,[5] bixanthylidenes[6] and bianthrones[7] has been extensively studied by dynamic NMR spectroscopic techniques, revealing the intrinsic chirality of these bis(tricyclic) structures. Resolution of these compounds would allow stereochemical studies by circular dichroism (CD) or chiral high performance liquid chromatography (HPLC) analysis. Recently, we have succeeded in resolving thioxanthene based alkenes; the first examples of thermally stable enantiomers of symmetrically overcrowded alkenes.[8,9] A racemization barrier of $\Delta G^{\ddagger} = 27.3$ kcal mol^{-1},[8] was found for 2,2'-dimethyl bithioxanthylidene, a remarkably high barrier compared with values reported for other bis(tricyclic) alkenes[4–7] ($\Delta G^{\ddagger} = 12$–22 kcal mol^{-1}). This can be described to the increase in bond length between the aryl moiety and the sulfur atom enhancing steric hindrance during the racemization process. Further conformational studies were hampered owing to the observation that racemization and *cis–trans* isomerization occur at the same rate.

In this paper we report the synthesis and resolution of the benzoannulated bithioxanthylidene derivatives, *trans*-**5** and *cis*-**6** 12*H*-benzo[*a*]thioxanthenyl-12-(2-'methyl-9'*H*-thioxanthene-9'-ylidene), which show remarkable stereospecific photochemical and thermal isomerization processes (Schemes 1 and 2). These feature, might largely improve the properties of the recently described chiroptical molecular switch based on two chiral forms of a sterically overcrowded alkene.[10]

The synthesis of **5**, **6** and **7** is based on the thioketone–diazo



Scheme 1



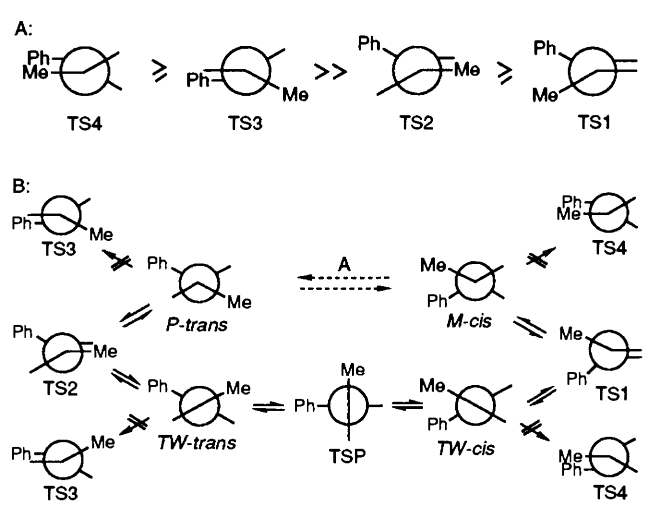
Scheme 2

coupling method for the formation of the central double bond (Scheme 1).[11] 2-Methyl-9*H*-thioxanthene-9-one-hydrazone **1**[12] was oxidized to the corresponding diazo-compound **2** (Ag_2O, diethyl ether, room temp.) and subsequently 12*H*-benzothioxanthene-12-thione **3**[13] was added. The resulting episulfides **4** were desulfurized by reduction with $LiAlH_4$[14] to afford the alkenes as a mixture of *trans*-**5** and *cis*-**6** (ratio 50:50, chemical yield 73%).†

Pure *trans*-alkene **5** (28% yield) was obtained after two crystallizations from ethanol. The *cis* and *trans* isomers are easily distinguished by their ^{1}H NMR spectra. The methyl singlet at δ 2.00 in *trans*-**5**, is shifted upfield to δ 1.58 in *cis*-**6** owing to the shielding effect of the naphthalene moiety. The mixture of **5** and **6** was separated into the four stereoisomers *P-trans* **5a**, *M-trans* **5b**, *M-cis* **6a**, and *P-cis* **6b** using HPLC with (+)-poly(triphenylmethylmethacrylate) as a chiral stationary phase[15] (Scheme 2).

The relative configurations of all four isolated isomers could be assigned using CD and ^{1}H NMR spectroscopy.[16] One pair of CD spectra closely resembled the CD spectra obtained for the enantiomers of the unsubstituted derivative **7** (with a hydrogen atom replacing the methyl group in **5**), while for the other isomers a significantly changed CD pattern was found. Because interactions between the *cis*-methyl functionality and the neighbouring naphthyl moiety in **6** will change the geometry of the aromatic system, and, therefore, the CD spectrum,[17] the *cis* configuration was assigned to the fractions with the altered CD spectra.‡ This correlation was confirmed by ^{1}H NMR analyses using the large separation in absorption for the methyl groups in **5** and **6** (see above).

The thermal racemization of the unsubstituted 1,2-benzo-annulated bithioxanthene **7** was followed by polarimetry at 75–85 °C in *p*-xylene and showed first-order kinetics, with a racemization barrier of 28.6 kcal mol^{-1}, the highest value obtained so far for optically stable sterically overcrowded alkenes.[8,10] Placing a methyl group on the 2′-position of **7** (creating **5** or **6**) is supposed to have no influence on the isomerization barrier in analogy with related bistricyclic systems.[5–9] For the methyl substituted analogues **5** and **6**, the thermal isomerization process was followed by HPLC. Heating of the *P-trans* isomer **5a** in isooctane at 96 °C, revealed a stereospecific isomerization to the *M-cis* form **6a**, indicating a *cis–trans* isomerization accompanied by a simultaneous reversal of helicity (process A, Scheme 2). No other isomers could be detected, even after heating at 96 °C for 20 h. The same isomerization pathway was found upon irradiation of the *P-trans* isomer **5a** at 300 nm in hexane.§ Similar stereospecific thermal and photochemical processes leading to **5b** were observed starting from the optically pure *P-cis* isomer **6b**.



Scheme 3 A: Transition states for **5** and **6**. B: Mechanism for the *P-trans*-**5a** to *M-cis*-**6a** isomerization.

This remarkable thermal and photochemical behaviour can be rationalized using the mechanisms proposed by Agranat and Tapuhi for the isomerization of bistricyclic ethylenes (Scheme 3).[5–7] The rate determining 'highest free energy transition states' (TS1, TS2, TS3 and TS4) are achieved during 'edge passage', *i.e.* movement of two aromatic moieties along each other. The barriers of these processes are determined by steric hindrance between the different groups in the vicinity of the central double bond. The *cis–trans* isomerization can only occur *via* the perpendicular twisted form (TSP), which is considered to have a lower free energy.

Comparing the four rate-determining transition states, which can be constructed for **5** and **6**, no large energy difference is expected for TS1 and TS2, because of the relatively small influence of a methyl group at the 2′ position. The free energy of TS3 and TS4 will, however, be strongly increased owing to severe steric hindrance that will occur during edge passage of the large non-flexible naphthyl moiety. Based on these considerations, the preferred isomerization pathway for the *P-trans*-**5a** to *M-cis*-**6a** conversion is as shown in Scheme 3. The naphthyl ring is not able to pass the benzene groups, in the opposite part of the molecule. Therefore, the reaction paths involving TS3 or TS4, which would lead to the formation of *M-trans* **5b** and *P-cis* **6b** *via* processes B and C in Scheme 2, are not observed.¶

The stereospecific photochemical and thermal-isomerization processes described here make enantiomerically pure **5** and **6** especially suitable for the construction of chiroptical molecular switches based on inherent dissymmetric olefins.[10] In these systems the photochemically addressed *cis–trans* isomerization is reflected in the *M-cis* to *P-trans* ratio, which can be detected by chiroptical techniques such as CD or optical rotatory dispersion (ORD). No other isomerization processes should occur. The molecules described above perfectly fit in this profile; only process A (Scheme 2) occurs

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† All new compounds gave satisfactory spectroscopic and analytical data.

‡ *CD data* in n-hexane $\lambda(\Delta\varepsilon)$: *M*-**5**: 197 (76.2), 211 (53.2), 229 (−99.5), 254 (−12.6), 292 (30.2), 320 (17.4), 355 (−7.9). *M*-**6**: 195 (68.6), 213 (41.4), 229 (−93.5), 250 (−41.4), 297 (33.0), 320 (26.2), 360 (−4.6). *M*-**7**: 194 (65.5), 213 (56.2), 228 (−104.1), 252 (−16.5), 293 (28.6), 321 (20.4), 352 (−6.3).

§ Quantum yield for racemization of **7**: $\Phi_r = 0.25$ (300 nm, n-hexane).

¶ A comparable stereospecific isomerization scheme can be drawn for the *M-trans–P-cis* interconversion.

photochemically. Furthermore, these compounds are thermally stable, no isomerizations can be detected at room temperature. If, however, thermal isomerizations should occur at elevated temperatures then again only process A will take place. Information will be lost, but in contrast to previous systems[10] no permanent damage will be inflicted upon the switch, since *M-cis* and *P-trans* are still the only isomers present. Investigations towards a thermostable chiroptical switch based upon the isomerization processes described here are currently underway.

We thank the 'Stichting Technische Wetenschappen' (STW) and the Dutch Foundation for Scientific Research (NWO) for their financial support.

Received, 30th October 1992; Com. 2/05824C

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