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Interplay of Twisting and Folding in Overcrowded Heteromerous Bistricyclic Aromatic Enes

Amalia Levy, P. Ulrich Biedermann, and Israel Agranat*

Department of Organic Chemistry, The Hebrew University of Jerusalem,
Jerusalem 91904, Israel

isria@vms.huji.ac.il

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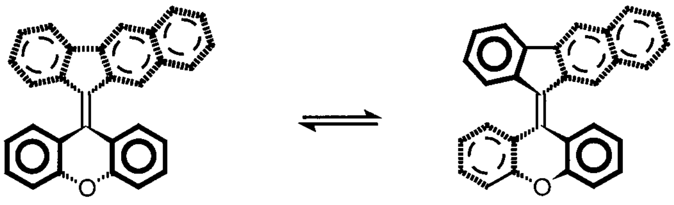
ABSTRACT



anti-folded **7**

twisted **7**

Fluorenylidenexanthenes 5–7 were synthesized by 2-fold extrusion diazo–thione couplings. 7 exhibited yellow crystals and purple (560 nm) solutions. ^{1}H NMR of 5 and 7 indicated subtle equilibria twisted (t) $\rightleftharpoons$ *anti*-folded (a) major/minor conformations. ^{13}C DNMR of 6 gave $\Delta G_c^{\ddagger}$(enantiomerization/inversion) $= 26.5$ kJ/mol and $\Delta G_c^{\ddagger}$(*E,Z*-topomerization) $= 82.0$ kJ/mol. PM3 calculations of 5 revealed minima a, t, ts (twisted/*syn*-folded), $\Delta\Delta H_f^\circ = 0.0, 14.1, 15.6$ kJ/mol, and transition states [t-ts], [a-ts], [t$_\perp$], [a-a*], $\Delta\Delta H_f^\circ = 16.3, 17.4, 82.2, 99.3$ kJ/mol.

The bistricyclic aromatic enes (**1**) have fascinated chemists since bifluorenylidene (**2**) and dixanthylene (**3**) were synthesized (1875, 1895) and thermochromism was revealed (1909) in bianthrone (**4**).[1−3] They can be classified into *homomerous* bistricyclic enes (**1**, X = Y) and *heteromerous* bistricyclic enes (**1**, X ≠ Y).[3] **2** is a fullerene fragment and a potential starting material for the preparation of buckybowls.[4] Thermochromic and photochromic bistricyclic enes serve as candidates for potential molecular switches.[5] Derivatives of **4** are topologically related to hypericin, present in St. John's Wort, an important antidepressant.[6] In bistricyclic enes, there are two principal modes of out-of-plane deformations: twisting around the double bond and out-of-plane bending.[7] The bending is realized by folding of the tricyclic moieties.[3,8] In addition, C_9 and $C_{9'}$ may be pyramidalized.[1,3] Bistricyclic enes are overcrowded in the fjord regions.[1,3] The nonplanarity of **1** may introduce chirality,[3,5,9,10] e.g., helicity of $C_9{=}C_{9'}$ and tripodal character of (substituted) folded tricyclic moieties. Bistricyclic enes resemble polycyclic aromatic hydrocarbons (PAHs): the majority of PAHs is also overcrowded and nonplanar and may adopt chiral conformations as global minima.[11] The major mode of deviation from planarity of **1** is strongly dependent on the bridges X, Y (bond lengths C−X and C−Y, distances $C_{4a}\cdots C_{10a}$), and on the size of the central rings.[3,12,13] Bifluorenylidene (**2**) with

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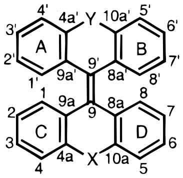
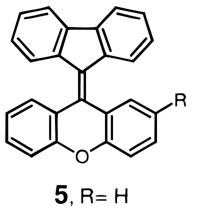
central five-membered rings is twisted (**t**) (pure twist ω = 31.9°),[3,14] while **1** with central six-membered rings are *anti*-folded (**a**) (folding dihedrals: dixanthylene (**3**)[3,15] 40.1°, ditelluroxanthylene (**1**, X, Y: Te)[16] 53.1°, and isopropylidene-bridged **1** (**1**, X, Y: CMe$_2$)[12] 53.0°). The dynamic processes of homomerous bistricyclic enes with central six-membered rings and of **2** have been extensively studied,[3,12,17] in contrast to the heteromerous bistricyclic enes series, where attention has been mostly limited to sulfur-bridged **1**.[13] The competition between twisting and folding intensifies in heteromerous bistricyclic enes with central five- and six-membered rings. An important case in point is 9-(9′*H*-fluoren-9′-ylidene)-9*H*-xanthene (**5**) (**1**, X: O, Y: −). The fluorenylidene moiety of **5** has an energetic propensity against folding, contrary to the xanthylidene moiety. Moreover, **5** is a potential push−pull system with its xanthylidene and fluorenylidene moieties serving as donor and acceptor, respectively. We report here on the interplay between twisting and folding in the conformational space of the heteromerous fluorenylidenexanthene series, including their dynamic stereochemistry.

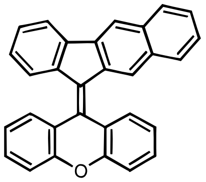


1

2, X,Y: —
3, X,Y:O
4, X,Y:C=O



5, R= H
6, R= CH(CH$_3$)$_2$



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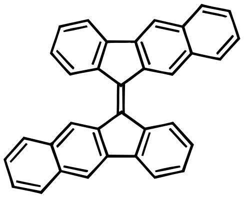

(*E*) **-8**

The substrates of the present study were 2-isopropyl-9-(9′*H*-fluoren-9′-ylidene)-9*H*-xanthene (**6**) and 9-(11′*H*-benzo-[*b*]fluoren-11′-ylidene)-9*H*-xanthene (**7**), as well as **5**.[18,19] For **6** and **7**, Barton's 2-fold extrusion process for the synthesis of highly hindered olefins was applied.[20] In principle, both the diazofluorene/xanthenethione and the fluorenethione/diazoxanthene coupling could be adopted. The former route was preferred due to the convenience of the relative stabilities of the reactants (aromatic dipolar structures) and their reactivities as carbon nucleophiles and carbon electrophiles, respectively, in the diazo/thione coupling. The method is especially suitable for heteromerous bistricyclic enes. Reaction of 2-isopropyl-9*H*-xanthene-9-thione (prepared from the respective ketone[21] and Lawesson reagent[22]) with 9-diazo-9*H*-fluorene in boiling benzene (2 h) gave dispiro[9*H*-fluoren-9,2′-thiirane-3′,9″-(2″-isopropyl)-9″*H*-xanthene] in 60% yield. Treatment of the thiirane with Ph$_3$P in boiling benzene (5 h) followed by fast column chromatography (3×) on silica gel gave **6** as a purple film (unstable in air) in 36% yield. Reaction of 11-diazo-11*H*-benzo[*b*]fluorene[23] and 9*H*-xanthene-9-thione in boiling benzene (45 h) led directly to **7**. The product was purified by repeated triturations and recrystallizations with cyclohexane−acetone. It was obtained as yellow crystals, free of the red side-products (*E*)- and (*Z*)-bis(11*H*-benzo[*b*]fluoren-11-ylidene) (**8**).[24] Sublimation at 180−190 °C/0.05 Torr gave yellow single crystals of **7**, mp 221−222 °C. When the diazo/thione reaction was interrupted after 7 h, the intermediate dispiro-thiirane could be isolated, yellow crystals, mp 178−179 °C. The UV/vis spectra of **5**−**7** in solution have visible absorptions at 533, 557, and 560 nm, respectively, as compared with 450 nm in **2** and 508 and 530 nm in (*E*)-**8** and (*Z*)-**8**. The purple color of **5**−**7** indicated that in solution, fluorenylidenexanthenes, adopt twisted conformations (reduced HOMO−LUMO gap). In the solid-state, yellow **7** is *anti*-folded, while in solution it turns purple, indicating a preferred twisted conformation.[25] The ^{1}H NMR chemical shifts of the fjord regions protons support these conclusions. ^{1}H NMR spectroscopy has been used to distinguish qualitatively among twisted, *anti*-folded, and *syn*-folded conformations of homomerous **1** in solution.[16] In a twisted conformation, these protons (H_1, H_8, $H_{1'}$, $H_{8'}$) appear at low aromatic field, e.g., δ 8.39 in **2**,[26] while in an *anti*-folded conformation, these protons appear at high aromatic field, e.g., δ 7.15 in **3**, and δ 6.80 in **1** (X, Y: Te).[16] This shielding effect is attributed to the diamagnetic ring currents of the opposing aromatic rings.[27] The fjord regions protons of **5** appear at low aromatic field δ 8.13 (H_1, H_8) and δ 7.89 ($H_{1'}$, $H_{8'}$), pointing at a twisted conformation. Consistently,

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$\delta(\mathbf{5}) - \delta(\mathbf{3})$ (H_1, H_8) = +0.98 ppm, reflecting a change from *anti*-folded **3** to twisted **5**. However, $\delta(\mathbf{5}) - \delta(\mathbf{2})$ ($H_{1'}$, $H_{8'}$) = −0.50 ppm indicates presumably an equilibrium, in solution, between the dominant twisted conformation and the minor *anti*-folded conformation. In **7**, $\delta(H_1) = 8.07$ and $\delta(H_8) = 8.23$, while the fjord regions benzo[*b*]fluorenylidene protons appear at $\delta(H_{10'})$ 8.40 (s) and $\delta(H_{1'})$ 7.85−7.91. For comparison, $\delta(H_{10}, H_{10'}) = 9.10$ (s) and $\delta(H_1, H_{1'}) = 8.46$ (dd) in twisted (*Z*)-**8** and $\delta(H_{10}, H_{10'}) = 9.90$ (s) and $\delta(H_1, H_{1'}) = 8.63$ (dd) in twisted (*E*)-**8**. Note that $\delta(\mathbf{7}, H_{10'}) - \delta((E)\text{-}\mathbf{8}, H_{10'}) = -0.50$ ppm. This difference is interpreted in terms of an equilibrium between the major twisted conformation and the minor *anti*-folded conformation of **7**, as compared with pure twisted (*E*)-**8.** In the ^{13}C NMR spectra of **5**, $\delta(\mathbf{5}) - \delta(\mathbf{3}) = +9.2$ ppm (C_9) and $\delta(\mathbf{5}) - \delta(\mathbf{2}) = -10.0$ ppm ($C_{9'}$) are noteworthy. These differences between the heteromerous **5** and the respective homomerous **2** and **3** indicate certain contributions of aromatic xanthenylium-fluorenide structures to twisted **5**.

In bistricyclic enes, three dynamic processes were observed:[3] (a) *E*,*Z*-isomerization; (b) conformational inversion, i.e., inversion of the helicity in twisted **1** or inversions of the boat conformations in the central rings of folded **1**; (c) *syn*,*anti*-isomerization. Enantiomerizations may be considered in all three processes. A DNMR study[28] of the conformational behavior of **6** revealed two dynamic processes: conformational inversion *and* *E*,*Z*-topomerization (Figure 1). The prochiral methyl groups of **6** appear at 295 K as a single doublet at 1.23 ppm ($J = 6.9$ Hz) (^1H NMR) and as one singlet at 24.0 ppm (^{13}C NMR), in $CDCl_3$, indicating a fast exchange process. The low-temperature dynamic experiment was run in $CDFCl_2$,[29] monitoring the ^{13}C NMR signals of the prochiral methyl carbons. Coalescence was observed at 134 ± 2 K, with $\Delta\nu = 57$ Hz, giving $\Delta G_c^‡$(enantiomerization/inversion) = 26.5 ± 0.5 kJ/mol. In the aromatic region, the ^{13}C NMR spectrum of **6** in $CDCl_3$ contained 26 signals: 13 due to the fluorenylidene carbons and 13 due to the xanthylidene carbons, indicating a slow *E*,*Z*-topomerization exchange. Upon heating, coalescences of some of the carbon signals of the fluorenylidene moiety were observed. For $C_{2'}$ and $C_{7'}$ (δ = 127.33 and 127.37 at 295K), $T_c = 357.3$ K, and $\Delta\nu_c = 3.4$ Hz, giving $\Delta G_c^‡(E, Z)$ = 82.1 kJ/mol.[30] For $C_{4'}$ and $C_{5'}$ (δ = 119.40 and 119.35 at 295 K), $T_c = 357.3$, $\Delta\nu_c = 3.6$ Hz, giving $\Delta G_c^‡(E, Z)$ = 81.8 kJ/mol. In toluene-d_8, the pair of signals at 141.09 and 141.14 ppm coalesced at $T_c = 363.5$ K, $\Delta\nu_c = 5.1$ Hz, giving $\Delta G_c^‡(E, Z)$ = 82.3 kJ/mol. The barrier for *E*,*Z*-topomerization of **6** is 82.0 ± 0.4 kJ/mol. The very low barrier of the conformational inversion of **6** and its inequality with the barrier for *E*,*Z*-topomerization are noted. These results contrast sharply with the conformational behavior of homomerous bistricyclic enes with central six-membered rings,[3] which indicated essentially identical barriers for *E*,*Z*-isomerization, and conformational inversion (e.g., in 2,2′-diisopropyldixanthylene, $\Delta G_c^‡$ = 74.9 kJ/mol) and a common highest transition state.[21]

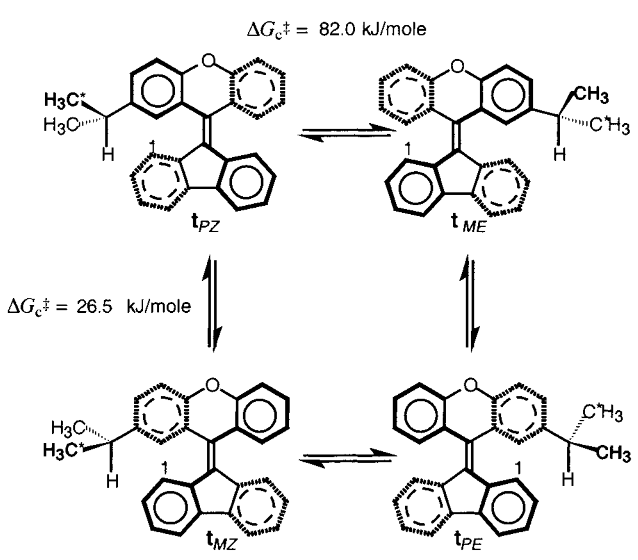

Figure 1. Conformational inversion and *E*,*Z* topomerization of **6**.

Table 1. Conformations of **5** Calculated by PM3

[a]		Min/ TS	ΔH_f° kJ/mol	$\Delta\Delta H_f^\circ$ kJ/mol	ω[b] [°]	folding [°] A-B	folding [°] C-D	$C_9{=}C_{9'}$ [Å]	$C_1\cdots C_{1'}$ [Å]	$H_1\cdots H_{1'}$ [Å]
a	C_s	Min	435.6	0.0	0.0	46.3	14.9	1.351	2.99	2.47
t	C_2	Min	449.7	14.1	41.4	5.2	2.5	1.372	3.04	2.43
ts	C_1	Min	451.2	15.6	39.0	18.8	4.4	1.370	3.02, 3.11[c]	2.75, 1.76[d]
[**t**-**ts**]	C_1	TS	452.0	16.3	40.3	11.4	3.5	1.371	3.01, 307[c]	2.63, 1.99[d]
[**a**-**ts**]	C_1	TS	453.0	17.4	32.4	34.8	9.0	1.363	3.11, 3.22[c]	2.78, 1.64[d]
[**t**$_\perp$]	C_{2v}	TS	517.8	82.2	90.0	0.0	0.0	1.447	4.13	3.82
[**a**-**a***]	C_s	TS	535.0	99.3	0.0	4.7	40.8	1.370	2.88	1.71

[a] Conformation: **a**: *anti*-folded; **t**: twisted; **ts**: twisted/*syn*-folded. [b] Pure twist of central ethylene group. [c] $C_8\cdots C_{8'}$. [d] $H_8\cdots H_{8'}$.

A semiempirical study of the conformational space of **5** using the PM3 method[31] revealed three minima and four transition states (Table 1). The C_s *anti*-folded conformation **a** is the global minimum in PM3. The C_2-twisted conformation **t** is a local minimum, 14.1 kJ/mol higher in energy than **a**. The conformational energies of twisted conformations of bistricyclic enes are probably overestimated.[3] Thus, an equilibrium favoring **t-5** over **a-5** in solution is reasonable. The C_1-twisted/*syn*-folded conformation **ts** is a local minimum with relative energy of 15.6 kJ/mol. **t** and **ts** interconvert via the transition state [**t-ts**] with 16.3 kJ/mol relative energy. **a** and **ts** are separated by a barrier of 17.4 kJ/mol, [**a-ts**], the highest transition state for the lowest energy mechanism for inversion of **a** or enantiomerization of **t** (Figure 2). The orthogonally twisted transition state [$\mathbf{t}_\perp$] for *E*,*Z*-isomerization of substituted **5** is a diradical with relative energy 82.2 kJ/mol. The transition state [**a-a***] facilitates an alternative single step pathway for inversion of **a-5**, which preserves the C_s symmetry. According to PM3, an *E*,*Z*-isomerization, or topomerization of substituted **a-5** would proceed in the following five steps:

$$\mathbf{a}_{EP} \xrightleftharpoons{[\mathbf{a\text{-}ts}]_{EP}} \mathbf{ts}_{EP} \xrightleftharpoons{[\mathbf{t\text{-}ts}]_{EP}} \mathbf{t}_{EP} \xrightleftharpoons{[\mathbf{t}\perp]} \mathbf{t}^{*}_{ZM} \xrightleftharpoons{[\mathbf{t\text{-}ts}]_{ZM}} \mathbf{ts}_{ZM} \xrightleftharpoons{[\mathbf{a\text{-}ts}]_{ZM}} \mathbf{a}_{ZM}$$

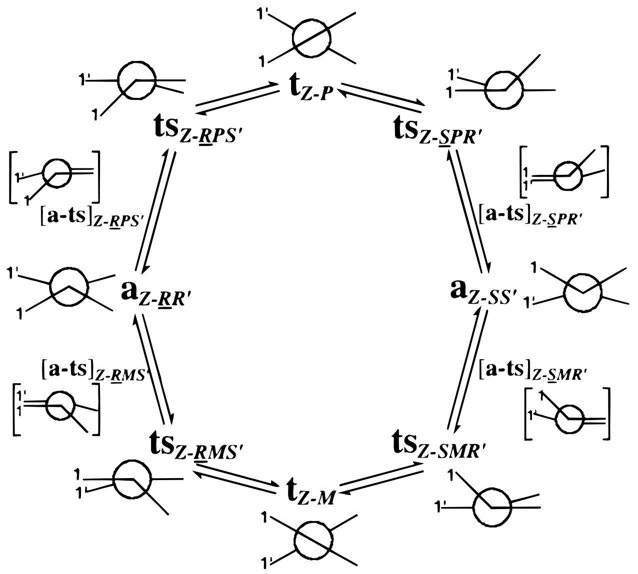

Figure 2. Mechanism for conformational inversion of **5** (PM3).

E,*Z*-Isomerization of **t-5** is a single step. The PM3 calculated energy of the transition state [$\mathbf{t}_\perp$]-**5**, 82.2 kJ/mol, is in excellent agreement with the experimental *E*,*Z*-topomerization barrier ($\Delta G_c^{\ddagger}$) in **6**, 82.0 kJ/mol. The *E*,*Z*-barrier is significantly lower than in **2**, 104 kJ/mol (DNMR), 104.6 kJ/mol (PM3).[32] This is attributed to an aromatic dipolar stabilization of [$\mathbf{t}_\perp$]-**5** versus [$\mathbf{t}_\perp$]-**2** and to an enhanced destabilization of **t-5** (ω = 41.4°) versus **t-2** (ω = 31.9°). The PM3 calculated energy of the transition state [**a-ts**]-**5** for conformational inversion of **a-5**, 17.4 kJ/mol, is lower than the experimental barrier ($\Delta G_c^{\ddagger}$) for enantiomerization of **6**, 26.5 kJ/mol.

In conclusion, the heteromerous fluorenylidenexanthenes serve as an illustration of the interplay of folding and twisting in overcrowded bistricyclic enes. The twisted purple conformations are considered the thermochromic modifications. There exists a subtle equilibrium in **7** between the yellow conformation and the thermochromic purple conformation at ambient temperatures. The two distinct dynamic processes of twisted bistricyclic enes, the enantiomerization and the *E*,*Z*-isomerization, were determined in the single compound, **6**. The experimental and computational elucidation of the dynamic stereochemistry of fluorenylidenexanthene (**5**) revealed the lowest enantiomerization/conformational inversion barrier in bistricyclic enes.

Supporting Information Available: ^{1}H and ^{13}C NMR data for **5**−**7** and ^{13}C DNMR results for **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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