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Unusual Rotamer Equilibria in Solution and Atropisomerism in 9-(1,3-Dioxolan-2-yl)-1,2,3,4-tetrafluorotriptycene

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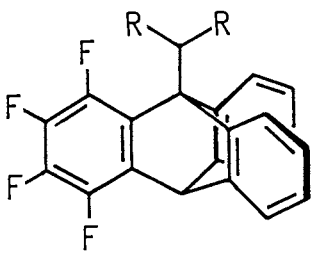
The title compound exists as a 1:1 mixture of ap and ±sc rotamers at equilibrium in $CDCl_3$. The origin of the unusually high population of the ap rotamer was explored by molecular mechanics calculations. The two rotamers were separately isolated as crystals by selective crystallization.

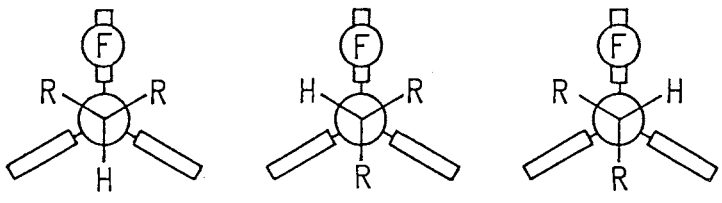
Conformational equilibria are subject to various factors of electronic and steric origin. Observation of apparently abnormal behavior of conformational equilibria has often led to a new idea of intramolecular interaction or revealed unique conformational states of the molecules. Studies of rotamer equilibria about the bridgehead-to-substituent bond in 9-substituted triptycene derivatives have afforded abundant information on various types of interaction between the substituent at the bridgehead and the one at the peri position of the triptycene skeleton, taking advantage of the high rotational barrier about the bond.[1)]

In this article, we report on the unusual rotamer populations in 9-(1,3-dioxolan-2-yl)-1,2,3,4-tetrafluorotriptycene (**2**) and on the results of molecular mechanics calculations to elucidate the origin of this anomaly and finally on the realization of atropisomerism in **2** taking advantage of the unique behavior.

During the attempts to synthesize 1,2,3,4-tetrafluorotriptycene-9-carbaldehyde (**1**), we had a chance to prepare compound **2**, the ethylene acetal of **1**.[2)] Three rotamers are possible about the bridgehead-to-substituent bond as shown by the Newman projections in Scheme 1, although the +sc and -sc rotamers can not be distinguished by NMR. Internal rotation around this bond is not only quite slowon the NMR time scale but also somewhat slow on the laboratory time scale. The



2: R,R=OCH_2CH_2O
3: R=OCH_3
4: R=CH_3



ap *+sc* *-sc*

Scheme 1.

Table 1. Conformational Equilibria[a)]

Compd	Solvent	K(±sc/ap)	%ap
2	C_6D_{12}	0.65±0.02	61
	C_6D_6	0.86±0.02	54
	$CDCl_3$	1.00±0.02	50
	CD_3CN	1.38±0.02	42
3	C_6D_{12}	36 ±2	2.7
	C_6D_6	25 ±2	3.8
	$CDCl_3$	32 ±2	3.0
	CD_3CN	15.5±1.0	6.1

a) Measured at 26 °C by ^1H NMR (500 MHz).

Table 2. Calculated steric energy differences between rotamers and their component terms (kcal mol^{-1}) and dipole moments (D) by MM2

	2		3	
$\Delta H°$(ap-±sc)[a)]	-0.41		1.65	
ΔE_s(ap-±sc)	0.62		2.10	
Compression	0.10		0.24	
Bending	0.08		0.31	
Stretch-Bend	0.03		0.02	
van der Waals				
1, 4-	-0.07		-0.11	
other	0.16		0.21	
Torsional	0.51		-0.24	
Coulombic	-0.19		1.66	
	ap	±sc	ap	±sc
Dipole Moment	4.51	3.63	5.72	3.54

a) Calcd from the data in $CDCl_3$ in Table 1 assuming $\Delta S°=R\ln 2$.

^1H NMR spectrum of rotamerically equilibrated **2** in $CDCl_3$ at 26 °C indicates that **2** exists as a mixture of two rotamers, ap and ±sc, in a ratio of 1:1 (Table 1). That is, ap-**2** is more stable than either of ±sc-**2**, which seems intuitively unusual on both steric and electrostatic grounds.

In 1,2,3,4-tetrafluoro-9-isopropyltriptycene (**4**), the equilibrium population of the ap rotamer was found to be 10% in $CDCl_3$ at ambient temperature,[3)] indicating that the rotamer equilibrium is fundamentally determined by steric effects. Replacement of the two methyl groups by methoxyl groups results in 9-dimethoxymethyl-1,2,3,4-tetrafluorotriptycene (**3**),[2)] where the population of the ap rotamer dropped to 3.0%. As OCH_3 is less bulky than CH_3, the population of the ap rotamer would be expected to increase on going from **4** to **3** if only the steric effect is considered. Thus the electrostatic repulsion between the 1-F and OCH_3 groups exceeds the steric factor in determining the equilibrium.

Comparison of these data with those of **2** clearly indicates that the population of the ap rotamer in **2** is abnormally high. In order to obtain further information, we examined the solvent effects on the equilibria in **2** and **3**. The results are shown in Table 1. As the solvent becomes more polar, the population of the ap rotamer increases in **3** but decreases in **2**, although the extent of the change is small in either compound.

In order to explore the origin of these anomalies, we performed molecular mechanics calculations on these compounds using the modified MM2 program.[4)] The total steric energy differences between the rotamers, their component terms, and the magnitudes of the dipole moments are listed in Table 2 and the ORTEP drawings of the optimized geometries are shown in Fig. 1. As for the energy differences between the rotamers, the absolute values of the calculated total steric energy differences are somewhat different from the observed enthalpy differences but the tendency that the ap rotamer is relatively more stabilized in **2** than in **3** is reproduced. Examination of the component terms reveals that the Coulombic term significantly contributes to the destabilization of the ap rotamer in **3** while it is

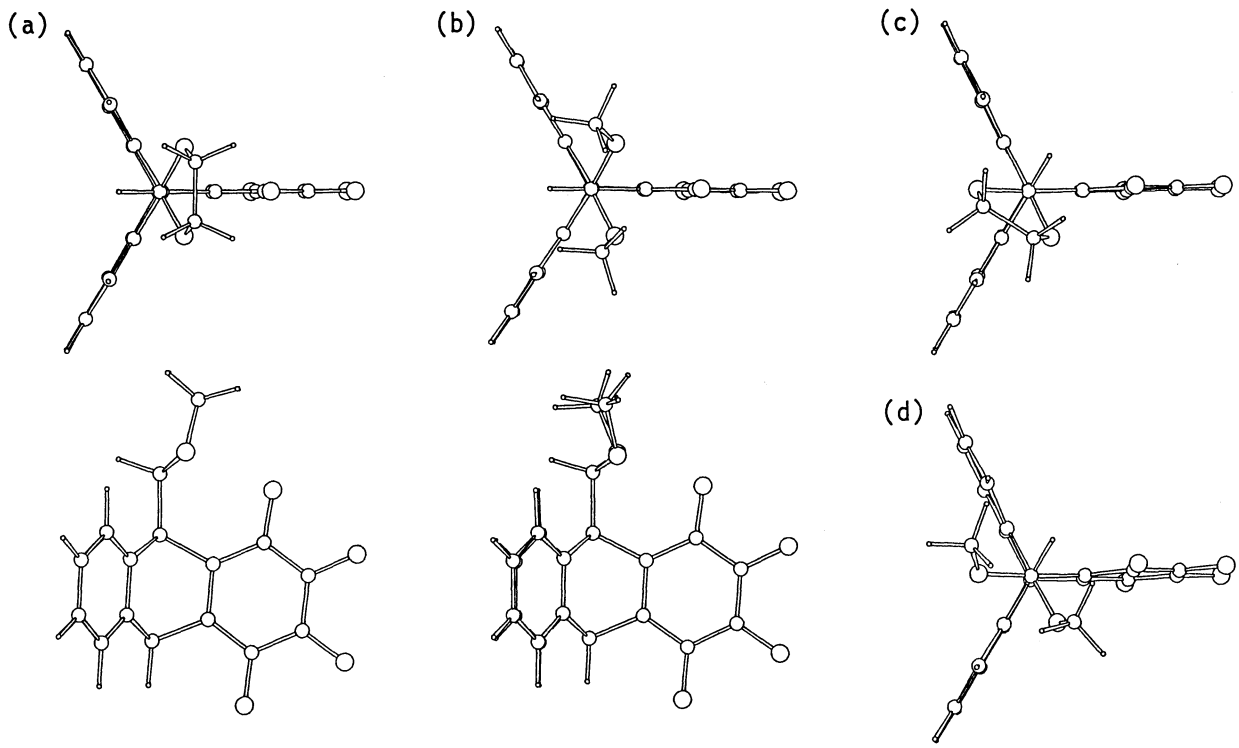


Fig. 1. Optimized geometries (MM2) of (a) ap-**2**, (b) ap-**3**, (c) +sc-**2**, and (d) +sc-**3**.

unimportant or rather favors ap in **2**. The ±sc rotamers are calculated to have almost the same dipole moments, while ap-**3** has a larger dipole moment than ap-**2**. The tendency of the solvent effects may be understood to some extent in terms of these calculated dipole moments.[6]

The differential behavior of **2** and **3** may be understood by considering the conformation of the acetal moieties. As shown in Fig. 1, the methyl carbons adjacent to the acetal oxygens in ap-**3** is more distant from each other and from 1-F than the methylene carbons in ap-**2** and therefore the C-O-C dipoles point more sharply to the tetrafluorobenzene ring and thus the repulsive electrostatic interaction would be larger in ap-**3** than in ap-**2**. With the similar reasoning the electrostatic repulsion in the ±sc rotamers would be larger in **2** than in **3**.

The presence of almost equal amounts of the two rotamers of **2** in solution suggests the possibility of separately isolating the rotamers as crystals by selective crystallization. Recrystallization of **2** from common solvents such as dichloromethane-hexane gives crystals comprising two rotamers where ±sc-**2** is usually predominant, presumably because of the slightly lower solubility and better crystallizability of the ±sc-**2**. Careful and slow recrystallization of **2** from dichloromethane-hexane at ambient temperature affords crystals consisting solely of the ±sc rotamer, mp 229-230 °C, while recrystallization from 2,2,4-trimethylpentane at 40-45 °C by slow evaporation of the solvent often affords crystals consisting solely of the ap rotamer, mp 230-231 °C.[7,8] Dissolution of the crystals in $CDCl_3$ at low temperatures and the ^1H NMR measurements at ca. 0 °C gave spectra of the pure

rotamers.[10] At higher temperatures, gradual isomerization took place and the classical kinetics monitored by ^{1}H NMR afforded the rate constant for the ±sc⟶ap isomerization of 4.5×10^{-4} s^{-1} at 26 °C which corresponds to $\Delta G^{\ddagger}$ of 22.1 kcal mol^{-1} and the half-life of ca. 13 min.[11]

The present case is the first example of atropisomerism in 9-s-alkyltriptycene derivatives[12] and also one of the rare cases where the rotamer interconversion is rather fast in solution at ambient temperature.

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References

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6) The large difference in dipole moments between the two rotamers of **3** is consistent with the increase of the ±sc rotamer in a polar solvent, while the small difference in **2** though ap-**2** has still a larger dipole moment than ±sc-**2** would not largely contradict the small decrease of the ±sc rotamer of **2** in a polar solvent.
7) Once the rotamerically pure crystals were obtained, either rotamer can be crystallized at will by adding a granule of the rotamer crystals to the solution as a seed.
8) The fact that the two rotamers have the same melting points may be an indication that the rotamer isomerization takes place in solid states as revealed recently in other triptycene compounds.[9] Details of the solid state behavior is under study.
9) G. Yamamoto, Chem. Lett., **1991**, 741.
10) ^{1}H NMR ($CDCl_3$, 0 °C, 500 MHz): ±sc-**2**: δ 4.05–4.52 (4H, m, ABCD, CH_2CH_2), 5.752 (1H, d, J_{HF}=1.6 Hz, 10-H), 6.435 (1H, d, J_{HF}=2.3 Hz, OCHO), 7.04–7.13 (4H, m, 6,7,14,15-H), 7.39–7.45 (2H, m, 5,16-H), 7.65–7.70 (1H, m, 8-H), 7.71–7.74 (1H, m, 13-H); ap-**2**: δ 4.30–4.36 (2H, m, AA'BB'), 4.45–4.51 (2H, m, AA'BB'), 5.782 (1H, d, J_{HF}=1.4 Hz, 10-H), 6.296 (1H, d, J_{HF}=4.9 Hz, OCHO), 7.03–7.13 (4H, m, 6,7,14,15-H), 7.39–7.45 (2H, m, 5,16-H), 7.75–7.81 (2H, m, 8,13-H).
11) The dynamic ^{1}H NMR study of **2** in C_6D_5Br gave the rate constant for the ±sc⟶ap conversion of 12.5 s^{-1} at 135 °C, which corresponds to $\Delta G^{\ddagger}$ of 22.1 kcal mol^{-1}. The activation parameters for the +sc ⇌ −sc process were obtained as follows by total lineshape analysis of the ^{1}H spectra in the 60–90 °C region: $\Delta H^{\ddagger}$=18.0±0.6 kcal mol^{-1}, $\Delta S^{\ddagger}$=0.3±1.7 cal mol^{-1} K^{-1}, $\Delta G^{\ddagger}$(350 K)=17.9 kcal mol^{-1}.
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