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How steric effects favor thiepins over their benzene sulfide tautomers at theoretical levels?

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ABSTRACT

The change of enthalpies, energy differences, activation energies and equilibrium constants (at 298 K), for valence tautomerizations between 2,7-di(X)benzene sulfides (B_{X-X}) and 2,7-di(X)thiepins (T_{X-X}), also between 2-*tert*-butyl-7-(X)benzene sulfide (B_{X-Y}) and 2-*tert*-butyl-7-(X)thiepin (T_{X-Y}), are estimated at *ab initio* (MP2/6-311++G**, HF/6-311++G**) and DFT (B3LYP/6-311++G**) levels, where X = H, Me, Et, *i*-Pr, and Y = *t*-Bu. For X = H, benzene sulfide (B_{H-H}) is more stable than thiepin (T_{H-H}) ($\Delta H = 6.37$ kcal mol^{-1}), in the above B_{X-X}/T_{X-X} series. Likewise, $B_{H\text{-}t\text{-}Bu}$ is more stable than $T_{H\text{-}t\text{-}Bu}$ ($\Delta H = 5.62$ kcal mol^{-1}), in B_{X-Y}/T_{X-Y} series. In contrast, for X = Me, Et, and *i*-Pr, steric effects shift the equilibrium in favor of T_{X-Y} in such a way that K_{eq} for $B_{i\text{-}Pr\text{-}t\text{-}Bu}/T_{i\text{-}Pr\text{-}t\text{-}Bu}$ is about 10^9 times greater than that for $B_{H\text{-}t\text{-}Bu}/T_{H\text{-}t\text{-}Bu}$. The B3LYP/6-311++G** calculated activation energies for inversions of thiepins to their mirror images, show higher energy barriers for all the T_{X-Y} thiepins, compared to their corresponding T_{X-X} analogues. Magnetic (NICS) criterion indicates virtual non-aromaticity for all T_{X-X} and T_{X-Y} thiepins, but extreme antiaromaticity for all their corresponding inversion transition states.

1. Introduction

Heterocyclic 8-π-electron systems, heteropins, have long been a subject of interest [1]. Among these seven-membered rings, the chemistry of thiepin (T_{H-H}) has been an area of challenge, due to its thermal instability [2]. Syntheses of simple thiepins have often failed, due to their facile sulfur extrusions, through benzene sulfide intermediates [3,4]. Evidently this process is followed by a sequence of reactions involving several intermediates in which the number of sulfur atoms increases, ending with benzene and a stable form of sulfur [5]. Overcoming the problem of finding stable thiepins is approached by placing different types of substituents around the carbon skeleton of thiepins. The synthesis of thieno[3,4-*d*]thiepin [6] and later 2,7-di-*tert*-butyl thiepin [5] are examples of achieving simple stable thiepins. The electronic effects of substituents appear of little importance for stabilizing thiepins [7], while their steric effects play a greater role [5]. Molecular modelings indicate a considerable sensitivity of thiepins stability on the substitutions attached at the positions 2 and 7 [1]. Here a systematic theoretical study is adopted to probe the steric effects by introducing gradually enlarging substituents on the parent thiepins at 2 and 7 positions, for two series of valence tautomerizations involving B_{X-X}/T_{X-X} and B_{X-Y}/T_{X-Y} systems, using HF, MP2 and B3LYP methods, with 6-31G* and 6-311++G** basis sets (X = H, Me, Et, *i*-Pr and Y = *t*-Bu) (Fig. 1a). The steric effects on the thiepins (T_{X-X} and T_{X-Y}) inversions are also investigated at B3LYP/6-311++G** level of theory (Fig. 1b).

2. Computational methods

All calculations are carried out using the Gaussian 98 or 03 suites of programs [8]. Structures are optimized at HF/6-31G* [9], MP2/6-31G* [10] and B3LYP/6-31G* [11,12] levels of theory. The optimized structures are characterized by frequency calculations using HF and B3LYP methods where 0 and 1 imaginary frequencies indicate minima and transition states, respectively. Single point calculations are performed at B3LYP/6-311++G**//B3LYP/6-31G*, MP2/6-311++G**//MP2/6-31G* and HF/6-311++G**//HF/6-31G* levels of theory. The minimum energy pathways and transition-state structures are calculated using quadratic synchronous transit (QST2) [13]. Nucleus independent chemical shift (NICS) calculations [14] are performed using the gauge independent atomic orbitals method (GIAO/B3LYP/6-311++G**//B3LYP/6-31G*) [15]. Evidently, the geometrical center of the ring's heavy atoms serve as the most easily defined reference point, which is referred as the standard NICS location (NICS(0)) and is used along with that at 1 Å above the plane of the ring (NICS(1)).

The reliability of various density functional theory (DFT) models is already evaluated for the study of bond dissociation energies,

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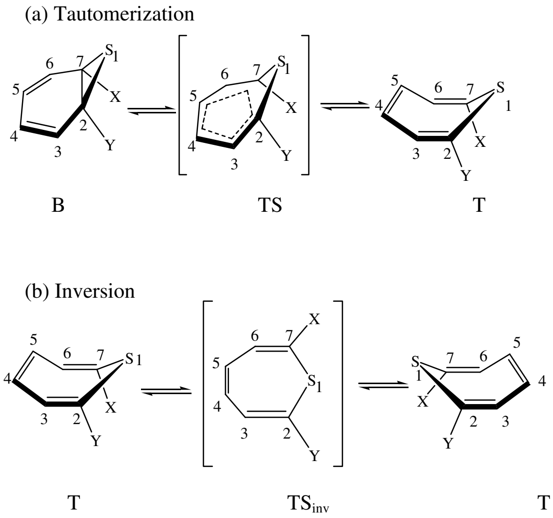

X	Y	B	T
H	H	$B_{H\text{-}H}$	$T_{H\text{-}H}$
Me	Me	$B_{Me\text{-}Me}$	$T_{Me\text{-}Me}$
Et	Et	$B_{Et\text{-}Et}$	$T_{Et\text{-}Et}$
i-Pr	*i*-Pr	$B_{i\text{-}Pr\text{-}i\text{-}Pr}$	$T_{i\text{-}Pr\text{-}i\text{-}Pr}$
H	*t*-Bu	$B_{H\text{-}t\text{-}Bu}$	$T_{H\text{-}t\text{-}Bu}$
Me	*t*-Bu	$B_{Me\text{-}t\text{-}Bu}$	$T_{Me\text{-}t\text{-}Bu}$
Et	*t*-Bu	$B_{Et\text{-}t\text{-}Bu}$	$T_{Et\text{-}t\text{-}Bu}$
i-Pr	*t*-Bu	$B_{i\text{-}Pr\text{-}t\text{-}Bu}$	$T_{i\text{-}Pr\text{-}t\text{-}Bu}$

Fig. 1. (a) Valence bond tautomerizations between benzene sulfides to their corresponding thiepins. (b) Thiepins ring inversions to their corresponding mirror images.

heats of formation, and geometrical parameters [16–18]. B3LYP/6-311++G** is selected as our method of choice for giving geometries and vibrational frequencies most consistent to those obtained at the MP2 level [19]. Also, the NBO population analysis on optimized structures are accomplished at B3LYP/6-311++G**//B3LYP/6-31G* level [20].

3. Results and discussion

Enthalpies, energy barriers and structures for valence tautomerizations of benzene sulfides ($B_{X–X}$ and $B_{X–Y}$), to their corresponding thiepins ($T_{X–X}$ and $T_{X–Y}$) are calculated at HF, MP2, and B3LYP levels, using 6-311++G** basis set, for X = H, Me, Et, and *i*-Pr, while Y = *t*-Bu (Fig. 1 and Tables 1 and 2). Thermodynamics as well as thiepin inversions and related aromaticities and geometries are discussed below.

3.1. Thermodynamics

Table 2
The calculated NICS (total) values (ppm) at the ring centers, NICS(0) and 1 Å above the plane of the rings, NICS(1), for $T_{X–X}$ and $T_{X–Y}$ species and their corresponding planar transition states for inversion (TS_{inv} and TS'_{inv}) at GIAO-B3LYP/6-311++G**//B3LYP/6-31G* level

Structure	Substituent (X)	Species	NICS(0)	NICS(0.5)	NICS(1)
$T_{X–X}/TS_{inv}$	H	T	0.34	−1.25	−2.25
		TS_{inv}	25.08	23.77	19.33
	Me	T	−0.64	−1.69	−2.35
		TS_{inv}	17.37	16.30	13.02
	Et	T	−1.16	−2.39	−3.02
		TS_{inv}	16.74	16.03	13.21
	i-Pr	T	0.89	0.11	−0.95
		TS_{inv}	17.44	16.77	13.79
$T_{X–Y}/TS'_{inv}$	H	T	−1.08	−2.56	−3.73
		TS'_{inv}	21.76	20.56	16.63
	Me	T	−1.11	−1.76	−2.66
		TS'_{inv}	17.96	16.87	13.49
	Et	T	−0.85	−1.57	−2.99
		TS'_{inv}	17.80	16.69	13.27
	i-Pr	T	−1.62	−2.87	−3.44
		TS'_{inv}	18.73	17.73	14.42

Changes of tautomerization enthalpies ($\Delta H_{B–T}$) and activation energies ($\Delta E^{\ddagger}_{B–T}$ and $\Delta E^{\ddagger}_{T–B}$) for $B_{X–X}/T_{X–X}$ and $B_{X–Y}/T_{X–Y}$ systems are calculated at three levels of theory: B3LYP/6-311++G**, HF/6-311++G** and MP2/6-311++G** (Table 1). A rather good numerical consistency is observed between the enthalpies and activation energies obtained at the B3LYP and MP2 levels, which differ with those obtained at the HF in a range of 0.38–2.57 kcal mol^{-1} for enthalpies and 5.8–13.37 kcal mol^{-1} for activation energies. Never-

Table 1
Change of enthalpies ($\Delta H_{B–T}$) and energy barriers ($\Delta E^{\ddagger}_{B–T}$ and $\Delta E^{\ddagger}_{T–B}$) in kcal/mol, for $B_{X–X}/T_{X–X}$ and $B_{X–Y}/T_{X–Y}$ tautomerization systems, at three levels of theory (B3LYP/6-311++G**, HF/6-311++G** and MP2/6-311++G**) along with the room temperature tautomerization equilibrium constants at B3LYP/6-311++G** and HF/6-311++G**, when X = H, Me, Et, *t*-Bu and Y = *t*-Bu

Systems	Tautomerization											Inversion	
	$\Delta H_{B–T}$			$\Delta E^{\ddagger}_{B–T}$ [a]			$\Delta E^{\ddagger}_{T–B}$ [b]			K_{eq}		$\Delta E^{\ddagger}_{inv}$	
	B3LYP	HF	MP2	B3LYP	HF	MP2	B3LYP	HF	MP2	B3LYP	HF	Thiepins	B3LYP
$B_{H–H}/T_{H–H}$	6.37	5.99	7.15	19.63	29.14	20.96	11.91	22.61	10.41	5.81×10^{-6}	3.70×10^{-5}	$T_{H–H}$	5.50
$B_{Me–Me}/T_{Me–Me}$	3.90	3.40	3.94	18.15	26.54	20.74	13.88	21.78	11.35	3.81×10^{-3}	1.07×10^{-2}	$T_{Me–Me}$	6.01
$B_{Et–Et}/T_{Et–Et}$	3.31	2.54	3.29	16.56	25.82	17.74	13.15	24.15	9.72	1.90×10^{-2}	6.71×10^{-2}	$T_{Et–Et}$	7.60
$B_{i\text{-}Pr\text{-}i\text{-}Pr}/T_{i\text{-}Pr\text{-}i\text{-}Pr}$	3.41	1.77	3.35	15.89	25.10	16.33	12.29	23.18	11.51	1.87×10^{-2}	2.0×10^{-1}	$T_{i\text{-}Pr\text{-}i\text{-}Pr}$	7.91
$B_{H\text{-}t\text{-}Bu}/T_{H\text{-}t\text{-}Bu}$	5.62	4.66	5.79	19.20	28.96	18.38	13.14	23.97	12.06	6.69×10^{-4}	2.33×10^{-3}	$T_{H\text{-}t\text{-}Bu}$	8.49
$B_{Me\text{-}t\text{-}Bu}$ /$T_{Me\text{-}t\text{-}Bu}$	−3.04	−4.96	−4.21	15.33	24.64	14.51	17.84	29.15	17.49	6.46×10^{3}	1.40×10^{5}	$T_{Me\text{-}t\text{-}Bu}$	8.78
$B_{Et\text{-}t\text{-}Bu}$ t/$T_{Et\text{-}t\text{-}Bu}$	−4.44	−6.76	−4.39	13.51	22.42	12.54	17.36	28.73	15.36	3.86×10^{4}	8.39×10^{5}	$T_{Et\text{-}t\text{-}Bu}$	9.33
$B_{i\text{-}Pr\text{-}t\text{-}Bu}/T_{i\text{-}Pr\text{-}\ t\text{-}Bu}$	−4.51	−7.05	−4.48	13.13	21.88	12.37	17.12	28.49	16.37	2.37×10^{5}	1.17×10^{7}	$T_{i\text{-}Pr\text{-}t\text{-}Bu}$	9.74

The inversion barriers of $T_{X–X}$ and $T_{X–Y}$, calculated at B3LYP/6-311++G**, are also presented. The energy data obtained at HF and B3LYP levels are corrected for zero point vibrational energy differences.

[a] Activation energy between a benzene sulfide and its corresponding tautomerization transition state ($TS_{X–X}$ or $TS_{X–Y}$).

[b] Activation energy between a thiepin and its corresponding tautomerization transition state ($TS_{X–X}$ and $TS_{X–Y}$).