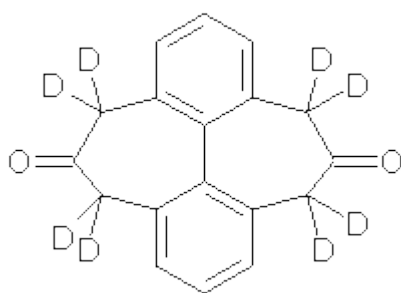


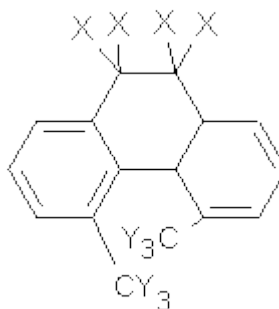
COMPUTED KINETIC ISOTOPE EFFECTS

Kinetic isotope effects (KIE) are a valuable tool for probing mechanisms without changing the potential energy surface. Their interpretation can sometimes be difficult – for example is a perdeutero group larger or smaller than the perhydro analogue?

O’Leary, Rablen and Meyer have examined two related molecules and their KIEs relating to stereoinversion.¹ **1** exhibits a normal isotope effect ($k_H/k_D = 1.06$) while **2** has an inverse isotope effect ($k_H/k_D = 0.880$). They optimized the structures and transition states (see Figure 1) for racemization of both compounds at B3LYP and MP2, and computed isotope effects based on the Biegeleisen-Mayer equation (which is based on reduced partition functions). The KIEs obtained from the two computational methods is very similar.



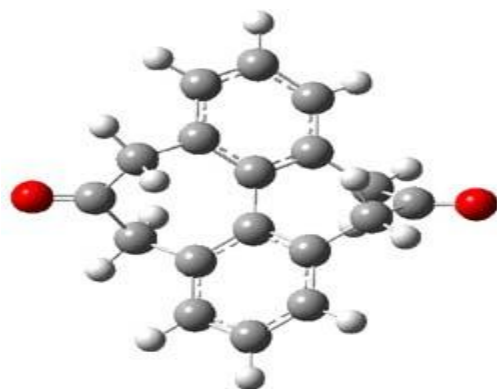
***d*₈-1**



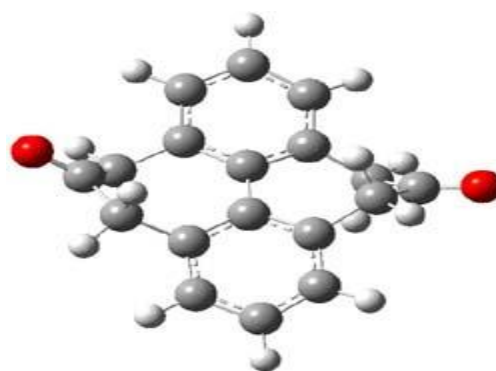
***d*₄-2: X=D, Y=H**

$d_6\text{-2}$: X=H, Y=D

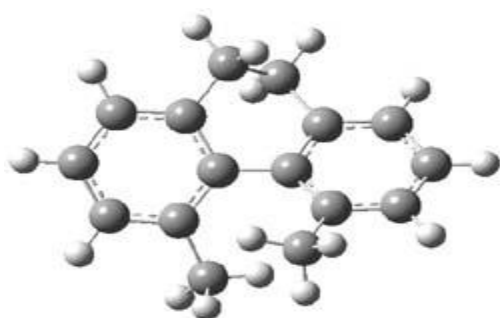
$d_{10}\text{-2}$: X=Y=D



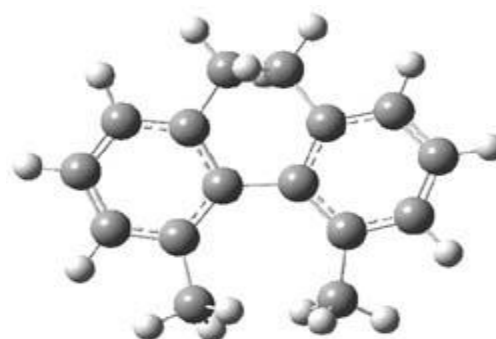
1



1TS



2



2TS

Figure 1. MP2/6-31G(d,p) optimized geometries of **1** and **2** and the transition states for their racemization.

The experimental and computed KIEs are listed in Table 1. The agreement between experiment and computation is excellent – suggesting that computations should be routinely employed when analyzing isotope effects.

Table 1. Experimental and computed KIEs for racemization of **1** and **2**.

	Expt	Comp
$d_8\text{-1}$	1.06	1.075
$d_6\text{-2}$	0.880	0.888
$d_4\text{-2}$	0.952	0.953
$d_{10}\text{-2}$	0.847	0.846

The authors decompose the isotope effects into enthalpic and entropic components and note that the interplay between these two can be subtle – sometimes one might dominate and other times the second term will dominate, and the terms can be cooperative or non-cooperative.

Source: <http://comporgchem.com/blog/?p=1515>