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Understanding anionic Chugaev elimination in pericyclic tetracene formation

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ABSTRACT

The reaction pathway for the formation of tetracenes from the diols 1,2-C_6H_4(CHOHC≡CAr)$_2$, LiHDMS, CS_2 and MeI has been modelled by computational methods at the CBS-QB3 level of theory. Comparison of PhCHOC(=S)YCCPh (Y=S^- or SMe) indicates a slight kinetic advantage for the anionic system towards [3,3]-sigmatropic rearrangement [E_{act}(calcd) 19.7 vs 21.8 kcal mol^{-1}]. Using anthracene-based models, 10-{SC(=O)Y}-4a,10-dihydroanthracene (Y=S^- or SMe), allows direct comparison of both *syn* and *anti*-manifolds in the neutral versus anionic Chugaev elimination. *syn*-Elimination of [HSC(=O)S]$^-$ is distinctly favoured [E_{act}(calcd) 11.4 kcal mol^{-1}] versus *syn* elimination of neutral methylated HSC(=O)SMe [E_{act}(calcd) 27.5 kcal mol^{-1}]. The smaller barrier to *syn* elimination of the anionic leaving group is in accord with the low temperature conditions required for this Chugaev reaction (60 °C) and suggests a general advantage in carrying out Chugaev eliminations in anionic manifolds.

1. Introduction

Tetracene and its substituted analogues are attractive fragments for the development of both photoelectric[1] and thermoelectric devices.[2] Unlike lower acene homologs, which are widely available, tetracenes must be synthesized. While many synthetic strategies have been devised[3] these can be step intensive and the consolidated yields are often further compromised by isolation and scale-up issues associated with poor acene solubility. One potential method for overcoming these difficulties is through the use of cascade processes whereby the tetracene target is attained by a series of pericyclic reactions. Examples of such approaches can be found in the work of Lin[4] and Liu.[5]

In 2015 we described the one-pot transformation of diols **1** to the thiolated tetracenes **2** via a cascade based on xanthate formation (Scheme 1).[6] The reactivity of this system was in accord with the initial step in the cascade being triggered from the anionic intermediate **A**, as the isolable di-SMe analogue of **A** (the xanthate attained by MeI dialkylation), was inert toward rearrangement to **2** at high temperatures (up to 250 °C). Both the [3,3] sigmatropic rearrangements resulting from **A** and the subsequent 6π electrocyclic rearrangements needed to access the cyclization precursor **B** have stereospecific requirements; *anti*-**1** leading to *syn*-**B** and conversely *syn*-**1** providing *anti*-**B** as a consequence of Woodward–Hoffman selectivities. The potential final yields of the tetracenes **2** thus depend on: (i) the *syn*:*anti* ratio in the initial sample of **1** and (ii) the relative efficacy of elimination of the [HSC(=O)S]$^-$ from *syn*- and *anti*-**B**. The electronic properties of substituents R^1 and R^2 clearly moderate the requirements (i–ii)—For example, compare the quantitative yield realized for **2b** versus those for **2d** and **2e**. Finally, the situation is further complicated by potential additional access to **2** via elimination of neutral leaving groups from *anti*-**B** where Y is [HSC(=O)SMe].

2. Results and discussion

Previously we have found DFT computational methods useful tools in determining thiocarbonyl reaction pathways in the Newman–Kwart rearrangement.[7] We chose to model the behaviour of **A** and **B** with in silico studies of truncated model systems **3**–**4A** and **7**–**8B**, respectively (Scheme 2).

Models **3**–**4A** (propargylic xanthate [3,3]-sigmatropic rearrangement) and **7**–**8B** (anthracene formation) were selected as they were small enough to be acceptable with higher level CBS-QB3 calculations, yet represent valid truncations of the real molecules. In fact the real world behaviour of **3**–**4A** mixtures has already been studied by us and formation of the allene **6A** confirmed.[6] To attain initial geometries on starting materials, products and transition states simple B3LYP/6-31+G(d,p)[8] DFT studies were carried out. However, because of known issues regarding energy error bounds[9]

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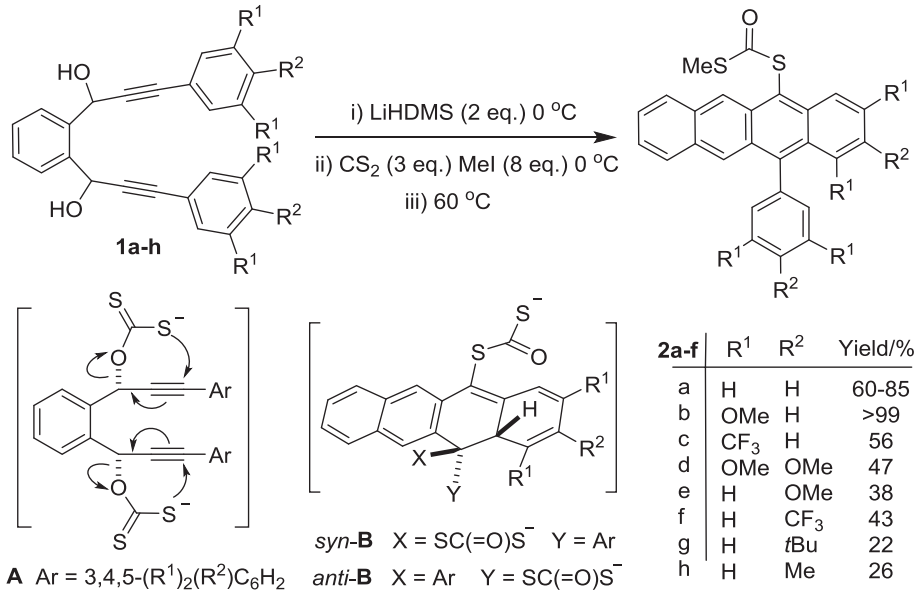
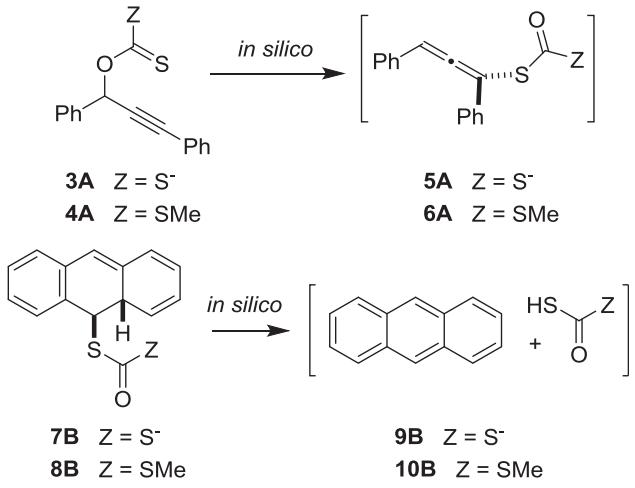


2a-f	R^1	R^2	Yield/%
a	H	H	60-85
b	OMe	H	>99
c	CF_3	H	56
d	OMe	OMe	47
e	H	OMe	38
f	H	CF_3	43
g	H	*t*Bu	22
h	H	Me	26

Scheme 1. Synthesis of substituted tetracenes **2** from diols **1** and the potential key steps In the cascade: [3,3] sigmatropic rearrangement (**A**) and Chugaev elimination of [HSC(=O)S]$^-$ (**B**).



Scheme 2. Computational models used for the key [3,3] sigmatropic rearrangements and aromatizing elimination in the formation of the tetracenes of Scheme 1.

on B3LYP calculated energies, the geometries were further optimized and Gibbs Free Energies calculated using the CBS-QB3[10] composite method. The calculated energy barriers are given in Table 1. It is clear that in the anionic manifold a *syn* elimination of [HSC(=O)S]$^-$ is highly favoured over the equivalent *syn* elimination of HSC(=O)SMe; the δE_{act}(calcd) of 16.1 kcal mol^{-1} corresponds to an effective rate advantage of $>10^{10}$ at 60 °C.[11] The [3,3]-sigmatropic rearrangements have very similar δE_{act}(calcd) energies of ~20 kcal mol^{-1}, and these calculations suggest that the reverse step back to **3A**/**4A** is highly endoergic with δE_{act}(calcd) energies of ~40 kcal mol^{-1}.

Table 1
Calculated energy barriers (CBS-QB3) for [3,3]-sigmatropic rearrangement and eliminations

Starting point	Process	Endpoint	E_{act}(calcd) (kcal mol^{-1})	$\Delta G_f°$(calcd) (kcal mol^{-1})
3A	[3,3]-Sigmatropic rear	**5A**	+19.7	−20.7
4A	[3,3]-Sigmatropic rear	**6A**	+21.8	−19.9
7B	*syn*-Elimination	**9B**	+11.4	−27.3
8B	*syn*-Elimination	**10B**	+27.5	−25.7

This analysis is in accord with **1b** being the optimal substrate in our original work.[6] This compound is isolated with a high *anti*:*syn* ratio (favouring the formation of *syn*-**B** intermediates prior to elimination). It is also possible that the proximal oxygen (at R^1) also helps order the transition for the elimination via coordination of the lithium cation associated with the eliminating group. However, disentangling the specific electronic effects of all the substituents was not practical computationally. Indeed subtle changes can have significant effects in this system. For example, in our original system we had noted the distinctly poorer performance of the *para*-substituted phenyl derivatives (**1e**–**g**) compared to the parent **1a**. The difference in the *anti*/*syn* ratios of these compounds (~1:1 for **1e**–**g** vs 1.6:1 for **1a**) does not fully account for this. As the steric profile of para units in **1e**–**g** were either large (the OMe, CF_3 and *t*-Bu volumes are 30.4, 39.8 and 73.5 Å^3, respectively[12]) or they had strong electronic effect (σ −0.27, +0.42, −0.10, respectively[13]) we also prepared **2h** bearing a methyl group with modest average (21.6 Å^3, σ −0.17) steric and electronic parameters for **1h** (and with *anti*/*syn* ratio 1.9:1.0). Unexpectedly, the isolated yield of **2h** was also low (26%) compared to parent **2a** (60–85%) indicating the difficulties in fully understanding the substituent effects. We have also considered the possibility of eliminations from *anti*-**B** type structures (Scheme 1). In the highest yielding substrates (e.g., **1b** with *anti*/*syn* ratio of 1.9:1) even the residual *syn* diastereomer must be converted to the final tetracene by an *anti*-**B** type intermediate. However, despite an extensive computational search no reaction pathway for spontaneous *anti* elimination of either [HSC(=O)S]$^-$ or HSC(=O)SMe from the *anti*-analogues of **7B** and **8B** could be found. Simple E2 model elimination from *anti*-**7B** using hydroxide as a model for any alkoxide base present in the reaction mixture, provided a ca. 13 kcal mol^{-1} barrier to elimination at the B3LYP/6-31+G(d,p) level of theory but no convergence was attained with higher level CBS-QB3 (Supplementary data). A similar situation was found for the hydroxide induced E2 elimination from *anti*-**8B** except in this case a barrier of ~10 kcal mol^{-1} was attained. It should be noted that these vacuum calculations poorly describe base-induced E2 elimination, since the approach of hydroxide will lead to a lowering of energy due to charge-induced dipole interactions. These would be cancelled out in solution by the loss of similar anion-solvent interactions. While care must be taken in interpreting these B3LYP results they do suggest *anti* elimination