

Understanding Anionic Chugaev Elimination in Pericyclic Tetracene Formation

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Article history:

Received

Received in revised form

Accepted

Available online

Key words: 3,3-Sigmatropic rearrangement, elimination, aromatisation, DFT Study, Chugaev, thiotetracene

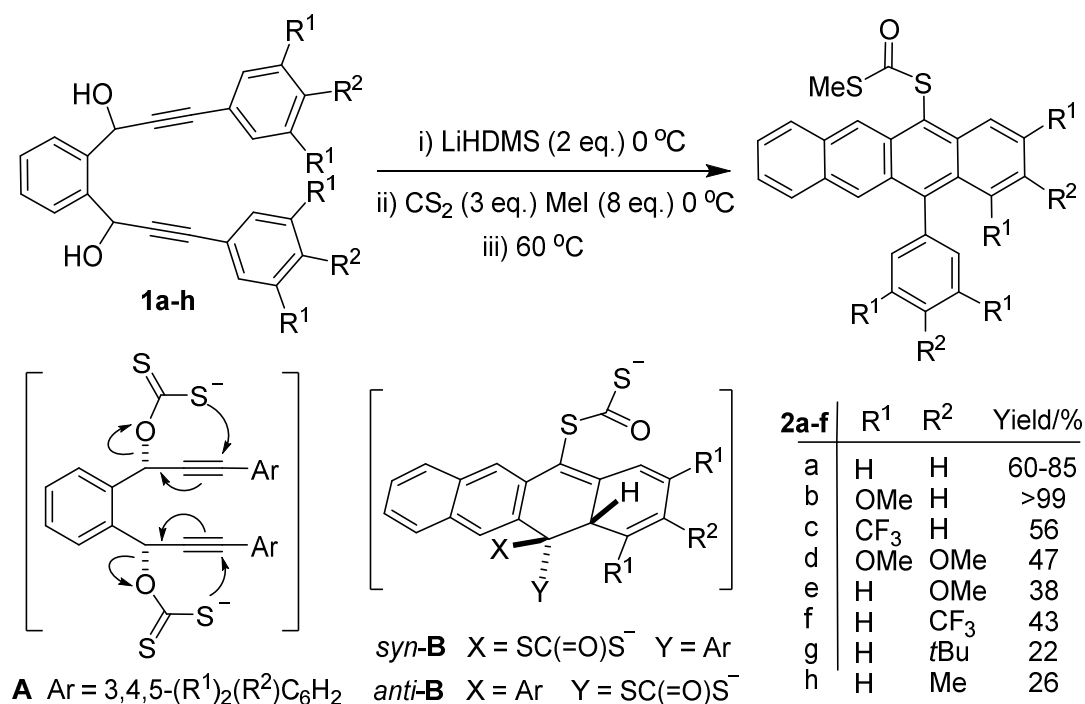
Abstract: The reaction pathway for the formation of tetracenes from the diols $1,2\text{-C}_6\text{H}_4(\text{CHOHC}\equiv\text{C}\text{Ar})_2$, LiHDMS, CS_2 and MeI has been modelled by computational methods at the CBS-QB3 level of theory. Comparison of $\text{PhCHOC}(=\text{S})\text{YCCPh}$ ($\text{Y} = \text{S}^-$ or SMe) indicates a slight kinetic advantage for the anionic system towards [3,3]-sigmatropic rearrangement [$E_{\text{act}}(\text{calc.})$ 19.7 vs 21.8 kcal mol⁻¹]. Using anthracene-based models, 10-{SC(=O)Y}-4a,10-dihydroanthracene ($\text{Y} = \text{S}^-$ or SMe), allows direct comparison of both *syn* and *anti*-manifolds in the neutral vs. anionic Chugaev elimination. *Syn* elimination of $[\text{HSC}(=\text{O})\text{S}]^-$ is distinctly favoured [$E_{\text{act}}(\text{calc.})$ 11.4 kcal mol⁻¹] vs. *syn* elimination of neutral methylated $\text{HSC}(=\text{O})\text{SMe}$ [$E_{\text{act}}(\text{calc.})$ 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 photoelectric¹ and thermoelectric devices.² Unlike lower acene homologs, which are widely available, tetracenes must be synthesized. While many synthetic strategies have been devised³ 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 Lin⁴ 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 $[\text{HSC}(=\text{O})\text{S}]^-$ from *syn*- and *anti*-**B**. The

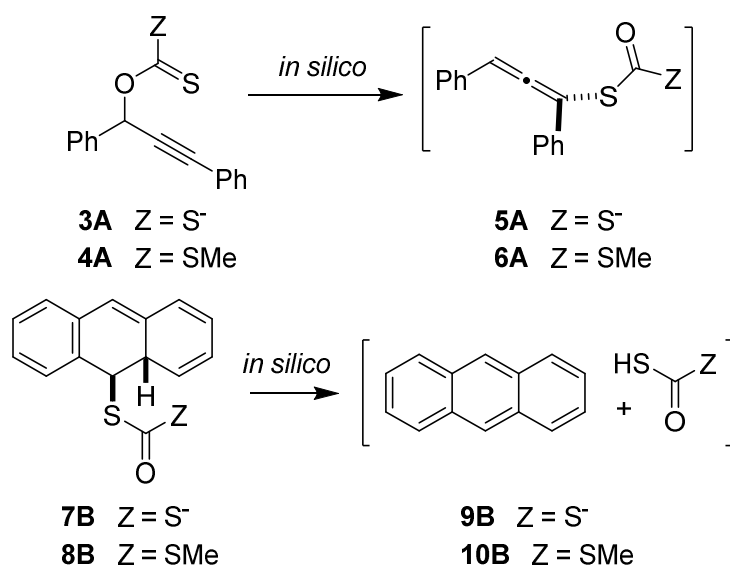
electronic properties of substituents R^1 and R^2 clearly moderate the requirements (i-ii) – For example, compare the quantitative yield realized for **2b** vs. those for **2d** and **2e**. Finally, the situation is further complicated by potential additional access to **2** via elimination of neutral leaving groups from *anti*-**B** where Y is [HSC(=O)SMe].



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**).

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).



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

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 bounds⁹ on B3LYP calculated energies, the geometries were further optimized and Gibbs Free Energies calculated using the CBS-QB3¹⁰ 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 $\delta E_{\text{act}}(\text{calc})$ of 16.1 kcal mol⁻¹ corresponds to an effective rate advantage of >10¹⁰ at 60 °C.¹¹ The [3,3]-sigmatropic rearrangements have very similar $\delta E_{\text{act}}(\text{calc})$ energies of ~20 kcal mol⁻¹, and these calculations suggest that the reverse step back to **3A/4A** is highly endoergic with $\delta E_{\text{act}}(\text{calc})$ energies of ~40 kcal mol⁻¹.

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

Starting point	Process	Endpoint	$E_{\text{act}}(\text{calc})$ (kcal mol ⁻¹)	$\Delta G_{\text{f}}^{\circ}(\text{calc})$ (kcal mol ⁻¹)
3A	[3,3]-sigmatropic rear.	5A	+19.7	-20.7
4A	[3,3]-sigmatropic rear.	6A	+21.8	-19.9
7B	<i>syn</i> -elimination	9B	+11.4	-27.3
8B	<i>syn</i> -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 R¹) 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, CF₃ and *t*Bu volumes are 30.4, 39.8 and 73.5 Å³ respectively¹²) or they had strong electronic effect (σ -0.27, +0.42, -0.10 respectively¹³) we also prepared **2h** bearing a methyl group with modest average (21.6 Å³, 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

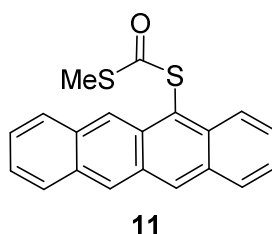
higher level CBS-QB3 (Supporting Information). A similar situation was found for the hydroxide induced E2 elimination from *anti*-**8B** except in this case a barrier of ~ 10 kcal mol⁻¹ was attained. It should be noted that these vacuum calculations poorly describe base-induced E2 elimination, since 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 offers a viable alternative for *anti* B-type diastereomers that are predicted to be otherwise unreactive.

Finally, we have investigated the vertical excitation energies of the first singlet (S) and triplet (T) excited states of the tetracenes **2** by time-dependant DFT methods. Time-dependent DFT methods can provide estimates of the excitation energy from the electronic ground state to the first (or higher) excited state, including singlet and sometimes triplet excited states for closed-shell singlet ground states. It does this by simulating vertical transposition of one electron from an occupied orbital of the ground state to an unoccupied orbital of the ground state. Provided the excitation is dominated by HOMO-to-LUMO character then estimates of the energies of unoccupied singlet (S) and triplet (T) excited states of the system can be attained. These values are of major interest in the design of efficient singlet fission solar cells; discovered in 1965,¹⁴ this particular photovoltaic system is attractive as formally one photon can provide two excitons. In order to maximize the likelihood of singlet fission occurring it is desirable to have the ratio of the excitation energies of the triplet and singlet state (S/T, Table 2) similar to that of the parent tetracene (C₁₈H₁₂), which is common to most of the devices that have been prepared thus far.¹ The energies calculated for both tetracene and the substituted analogues **2a-h** are presented in Table 2. These values suggest that certain derivatives (**2a**, **2g**) are attractive for further investigation in singlet fission OPV devices.

Table 2. Calculated singlet (S) and triplet (T) in substituted **2a-h** and parent tetracene (C₁₈H₁₂).

Compound	S state (eV)	T state (eV)	S/T	Compound	S state (eV)	T state (eV)	S/T
tetracene	2.748	0.842	3.26	2a	2.648	0.935	2.83
2b	2.627	1.530	1.72	2c	2.936	1.530	1.92
2d	2.580	1.008	2.56	2e	2.663	1.020	2.61
2f	2.744	1.114	2.46	2g	2.725	0.905	3.01
2h	2.607	0.949	2.75	11 ^a	3.086	1.551	1.99

^a Compound **11** is:



3. Conclusions

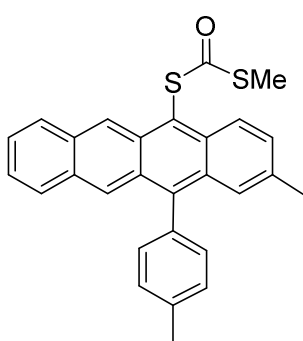
DFT (CBS-QB3) studies are in accord with the conversion of *anti* diols **1** upon treatment with LiHDMS, CS₂ and MeI to intermediates (**B**) arising from cascading [3,3]-sigmatropic rearrangements and 6 π -electrocyclizations. Conversion of intermediate **B** to the final tetracene **2** is favoured when *syn* anionic

Chugaev elimination is realized [$E_{\text{act}}(\text{calc})$ 11.4 kcal mol⁻¹]. Elimination of the neutral xanthate is of prohibitive energy cost [$E_{\text{act}}(\text{calc})$ 27.5 kcal mol⁻¹]. In the absence of *syn* elimination processes *anti* elimination is only viable in the presence of an external base. The barrier to this was estimated to be ca. 10-14 kcal mol⁻¹ but was limited by the level of theory that could be employed.

4. Experimental

The instrumentation, reagents and general preparations of diols **1** and tetracenes **2** have been previously described.⁶ Compound **1h** is known.⁵ Preparative details of new compound **2h** are given below. All calculations were carried out using Gaussian 09, Revision D.01¹⁵ with default settings. Initial structure searches for mapping of the reaction coordinate were run at the B3LYP/6-31+G(d,p)⁸ level of theory, and the resulting structures further optimized using CBS-QB3¹⁰ with 'tight' convergence and 'UltraFine' integration grid keywords specified. Transition-state structures were all characterized by a single imaginary vibrational frequency. Approximations for the HOMO eigenvalues of all tetracenes were calculated at the CAM-B3LYP/6-31G(d,p)¹⁶ level of theory. Values for the HOMO-LUMO gaps and energies of the first singlet and triplet excited states of all tetracenes were calculated using TD-SCF CAM-B3LYP/6-31G(d,p)¹⁶ with the tda (Tamm-Dancoff Approximation)¹⁷ keyword, taking the excitation energy of the first singlet excited state as the HOMO-LUMO gap.¹⁸ GaussView 5¹⁹ was used to generate all the 3D-molecular structure figures. Full details of the optimized geometries are given in the Supporting Information.

4.1 2-Methyl-12-(4'-methylphenyl)-5-(((methylthio)carbonyl)thio)-tetracene (**2h**)



From diol **1h** (80 mg, 0.18 mmol), LiHDMS (0.35 mL, 1.0 M in THF, 0.35 mmol), CS₂ (32 μ L, 40.6 mg, 0.53 mmol) and iodomethane (88 μ L, 202 mg, 1.42 mmol) to yield **2h** as an orange solid, 20.5 mg, 26% that could be recrystallized by liquid layering (pentane:ether). R_f 0.71 (7:3 pentane:ether). m.p. 136-138 °C, IR (CHCl₃): $\nu_{\text{max}}/\text{cm}^{-1}$ 3690, 3051, 3009, 2958, 2927, 2857, 2735, 1720, 1638, 1604, 1536, 1514, 1494, 1465, 1420, 1380, 1341, 1312, 1284, 1262, 1243, 11182, 1124, 1107, 1038, 1022, 972, 907, 881, 853, 823, ¹H NMR (500.1 MHz, CDCl₃): δ 9.34 (s, 1H), 8.63 (d, J = 9.1 Hz, 1H), 8.31 (s, 1H), 8.07 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 8.6 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.42 (ddd, J = 8.6, 6.4, 0.9 Hz, 1H, ArH), 7.40 (dd, J = 9.1, 1.6 Hz, 2H), 7.37 – 7.32 (ddd, J = 8.6, 6.4, 0.9 Hz, 1H, ArH), 2.60 (s, CH₃), 2.41 (s, 3H, CH₃), 2.29 (s, 3H, SCH₃), remaining signals could not be assigned due to extensive overlap of signals in the ¹H NMR, but where observed in COSY spectrum. ¹³C NMR (125.8 MHz, CDCl₃): δ 190.8 (C), 141.7 (C), 137.7 (C), 135.7 (C), 134.7 (C), 134.4 (C), 132.2 (C), 132.1 (C), 131.3 (C), 131.2 (CH), 130.6 (CH), 130.5 (C), 130.1 (C), 129.4 (CH), 128.7 (CH), 128.6 (CH), 127.1 (CH), 126.2 (CH), 126.2 (CH), 125.9 (CH), 125.6 (CH), 124.8 (CH), 119.7 (C), 22.1 (CH₃), 21.7 (CH₃), 13.8 (CH₃). UV-vis (CH₂Cl₂): λ_{max} 288.3 nm. MS (+ESI) calcd. for C₂₈H₂₂OS₂ m/z 439.1185 (M+H), found m/z 439.1197.

Acknowledgements

This project has received funding from the European Union's Seventh Programme for research, technological development and demonstration under grant agreement No 308768. JR thanks the Engineering and Physical Sciences Research Council (EPSRC) and European Thermodynamics Ltd for support of a studentship. LB thanks Dr. David Robinson for his advice and recommendations. All authors are grateful to the EPSRC UK NSCCS Computational Service for access facilities.

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