Pergamon

Tetrahedron Letters 44 (2003) 6625–6627

TETRAHEDRON
LETTERS

Thermally induced cascade pericyclic reaction pathways from tetraene esters

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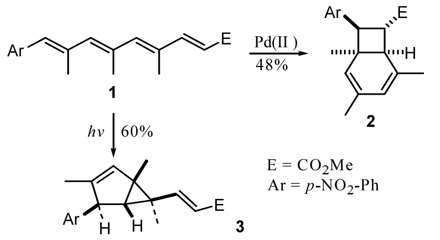
Received 2 June 2003; revised 27 June 2003; accepted 3 July 2003

Abstract—A novel thermally induced cascade pericyclic transformation of a tetraene ester into a complex tricyclic core is reported. This transformation is high yielding and highly selective.

During our continuing efforts directed towards the biomimetic synthesis of propionate derived natural products, we have become interested in the development of sterically hindered tetraene esters as flexible synthons for naturally occurring targets (Scheme 1).[1,2]



Scheme 1.

As previously discovered, tetraene **1** has a large degree of strain (as demonstrated by the >130° angle between C_4, C_5, C_6, and the 45° dihedral angle of the C_9–C_{10} single bond) which could provide the initial driving force for a variety of transformations (Fig. 1).[3]

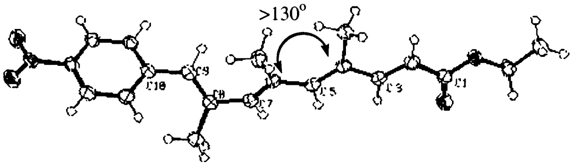
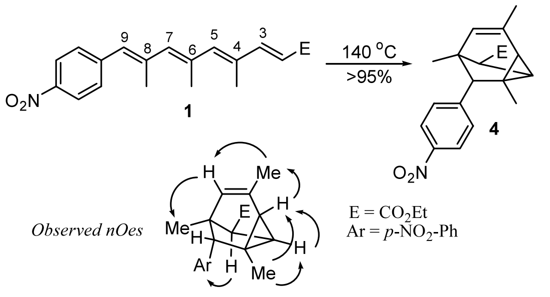


Figure 1. X-Ray analysis of tetraene ester **1**.

We would now like to report the interesting and high yielding transformation resulting from the thermal treatment of strained tetraene **1**. Thus, treatment of tetraene ester **1** at 140°C afforded the interesting tricyclo[3.2.1.0^{2,7}]oct-3-ene core structure **4** in excellent yield (95%) as a single diastereoisomer (Scheme 2). The structure was determined by a combination of NMR methods, including NOE and 2-D NMR analysis.



Scheme 2.

The structure was furthermore corroborated by chemical derivatisation into the corresponding dinitrobenzoate ester **5** (Scheme 3).

Benzoate ester **5** readily provided crystals suitable for X-ray analysis (Fig. 2).[4]

Formation of the tricyclic ester **4** can be explained by an isomerisation of the desired double bond to generate the required (*E*,*E*,*Z*,*E*)-tetraene ester **6**.[5] This ester can

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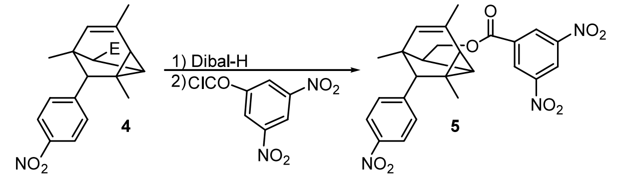
doi:10.1016/S0040-4039(03)01673-3



Scheme 3.

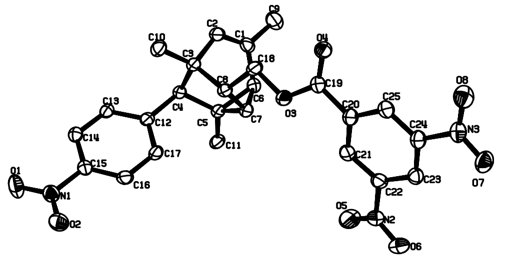
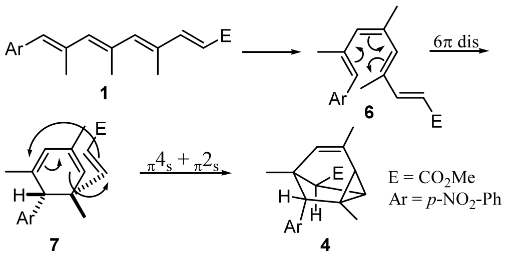


Figure 2. X-Ray analysis of tricyclic benzoate **5**.

then undergo the desired thermal 6π disrotatory electrocyclisation to generate cyclohexadiene **7**,[6] which undergoes a final intramolecular Diels–Alder reaction to generate the tricyclic structure **4** (Scheme 4).[7]

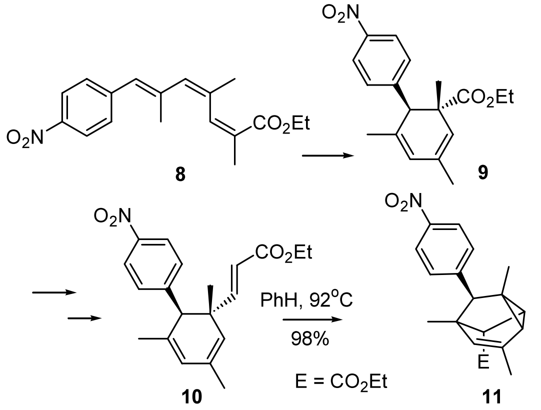


Scheme 4.

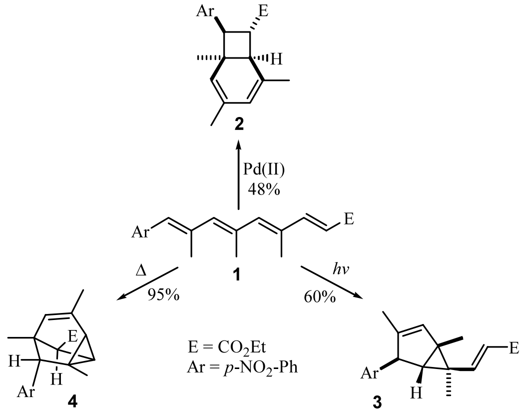
Recently Trauner et al. described a stepwise approach to a diastereoisomer of **4**. In their strategy, the (*E*,*Z*,*Z*)-triene ester **8** was prepared, which underwent electrocyclisation to afford the cyclohexadiene ester **9**.[8] This ester was further elaborated to the 5-vinyl-1,3-cyclohexadiene **10** which subsequently underwent a thermally induced intramolecular Diels–Alder reaction to yield the tricyclic ester **11** (Scheme 5).[9] Although this multi-step approach was high yielding, it required the construction of the (*E*,*Z*,*Z*)-triene ester **8** as starting material, which introduces a greater degree of complexity compared to our approach via an all (*E*)-tetraene. Thus, we believe our approach to be simpler and overall higher yielding.

In summary we have discovered a novel thermally induced tandem pericyclic process, which yields a novel complex core structure. This process provides an efficient route to this class of compound with an as yet to be determined potential.

This new thermal process further exemplifies the diversity of high yielding synthetic possibilities originating from this class of highly strained polyene esters, by simple modification of the reaction conditions (Scheme 6). We are now working on ways to expand the synthetic and mechanistic scope of these transformations, and at the same time explore new synthetic transformations.



Scheme 5.



Scheme 6.

Acknowledgements

We thank Dr. T. D. W. Claridge and Dr. B. Odell for NMR assistance, and the EPSRC for funding John Moses.

References

1. Moses, J. E.; Baldwin, J. E.; Marquez, R.; Adlington, R. M.; Cowley, A. R. *Org. Lett.* **2002**, *4*, 3731.
2. Moses, J. E.; Baldwin, J. E.; Marquez, R.; Adlington, R. M.; Claridge, T. W. C.; Odell, B. *Org. Lett.* **2003**, *5*, 661.
3. The atomic coordinates for **1** are available on request from the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW (Deposition number CCDC 190072). The crystallographic numbering system differs from that used in the text; therefore any request should be accompanied by the full literature citation of this paper.

4. The atomic coordinates for **5** are available on request from the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW (Deposition number CCDC 190073). The crystallographic numbering system differs from that used in the text; therefore any request should be accompanied by the full literature citation of this paper.
5. (a) Doering, W. V. E.; Belfield, K. D.; He, J. *J. Am. Chem. Soc.* **1993**, *115*, 5414; (b) Doering, W. v. E.; Kitagawa, T. *J. Am. Chem. Soc.* **1991**, *113*, 4288.
6. Woodward, R. B.; Hoffman, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, 1970; p. 53.
7. (a) Fujita, R.; Watanabe, K.; Yoshisuji, T.; Hongo, H.; Matsuzaki, H. *Chem. Pharm. Bull.* **2001**, *49*, 900; (b) Chou, T. C.; Jiang, T. S.; Hwang, J. T.; Lin, C. T. *Tetrahedron Lett.* **1994**, *35*, 4165.
8. Beudry, M.; Trauner, D. *Org. Lett.* **2002**, *4*, 2221.
9. Ng, M. S.; Beudry, M.; Trauner, D. *Org. Lett.* **2003**, *5*, 1701.