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Double trap: A single product from the THF-initiated interception of a cyclopropylidene(oid) and its rearranged strained cyclic allene

Ernesto Esquivel-Amores, Kirstie Rogers, Luca R. Thamattoor, Dasan M. Thamattoor*

Department of Chemistry, Colby College, Waterville, ME 04901, USA

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ABSTRACT

The reaction of 1,1-dibromo-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**3**) with butyllithium in THF at ~ −70 °C, followed by quenching with water at room temperature, led to a complex mixture of products which included a trace amount of the unusual pyran derivative, 3-(5*H*-dibenzo[*a*,*c*][7]annulen-5-yl)-2-(phenanthren-9-yl)tetrahydro-2*H*-pyran (**6**). The X-ray crystal structure of **6** revealed a phenanthrene unit α to the oxygen and a dibenzocycloheptene moiety in the β position. The formation of **6** is mechanistically rationalized on the basis of the initially generated cyclopropylidenes(oid) (**4**/**5**) interacting with THF to form an oxonium ylid **7** which then undergoes a ring expansion to produce the pyran framework in **10**. Subsequent reaction of **10** with the strained dibenzocycloheptatetraene **2**, resulting from ring opening of **4**/**5**, leads to the observed product **6**. To the best of our knowledge, this work documents the first example of a cyclopropylidene(oid) and its ring-opened allene trapped into a single product.

1. Introduction

A few years ago, we reported the first crystal structure of a tetramer (**1**) formally derived from a strained cyclic allene (**2**) [1]. Compound **1** was serendipitously isolated in extremely low yield following the work-up of a Doering-Moore-Skattebøl (D-M-S) reaction [2–4] of 1,1-dibromo-1a, 9b-dihydro-1*H*-cyclopropa[*l*] phenanthrene (**3**) with butyllithium and $CuCl_2$ in THF at low temperature (Scheme 1). This process initially produces the cyclopropylidenoid **4** which can then ring-open to **2** either directly or via the free cyclopropylidene **5** [5].

In connection with our ongoing research program aimed at generating carbenes from cyclopropanated phenanthrenes [6–12], we recently repeated the D-M-S reaction of **3** with butyllithium in THF at ~ −70 °C, followed by quenching with water at room temperature (Scheme 2). A complex mixture of products, including the aforementioned tetramer **1**, was obtained. Interestingly, in the course of purifying the product mixture by column chromatography, we noticed that some of the column fractions contained well-defined, colorless crystals. The structure of the crystalline material was elucidated by X-ray diffraction studies which revealed that the compound was an unusual, sterically congested pyran derivative, 3-(5*H*-dibenzo[*a*,*c*] [7]annulen-5-yl)-2-(phenanthren-9-yl)tetrahydro-2*H*-pyran (**6**) [13]. The structure of **6** and a possible route to its formation by the THF-initiated sequential trapping **4**/**5** and **2** are described below.

2. Experimental

General notes: Tetrahydrofuran was dried by passage through two columns (2 ft x 4 in) of activated alumina. All other solvents and reagents were used as obtained from commercial sources. The synthesis of 1,1-dibromo-1a, 9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**3**) was carried out following our previously reported procedure [14]. Flash chromatography was performed on an automated system with pre-packed silica gel columns (70–230 mesh). NMR spectra were recorded in $CDCl_3$ at 500 MHz and 126 MHz for ^1H and ^{13}C nuclei respectively. The chemical shifts, recorded in δ ppm, are referenced to the signal of tetramethylsilane, set to 0.00 ppm. FTIR spectra were acquired with an attenuated total reflectance (ATR) accessory. Melting points were recorded on a digital hot plate and are uncorrected.

Synthesis of ***6***: A solution of 1,1-dibromo-1a,9b-dihydrocycpropa [*l*]phenanthrene (**3**) [14] (3.50 g, 10 mmol) in 80 mL of dry THF was prepared at room temperature, under argon, in an oven-dried, 250 mL three-necked round-bottom flask equipped with a teflon-

* Corresponding author.
E-mail address: dmthamat@colby.edu (D.M. Thamattoor).

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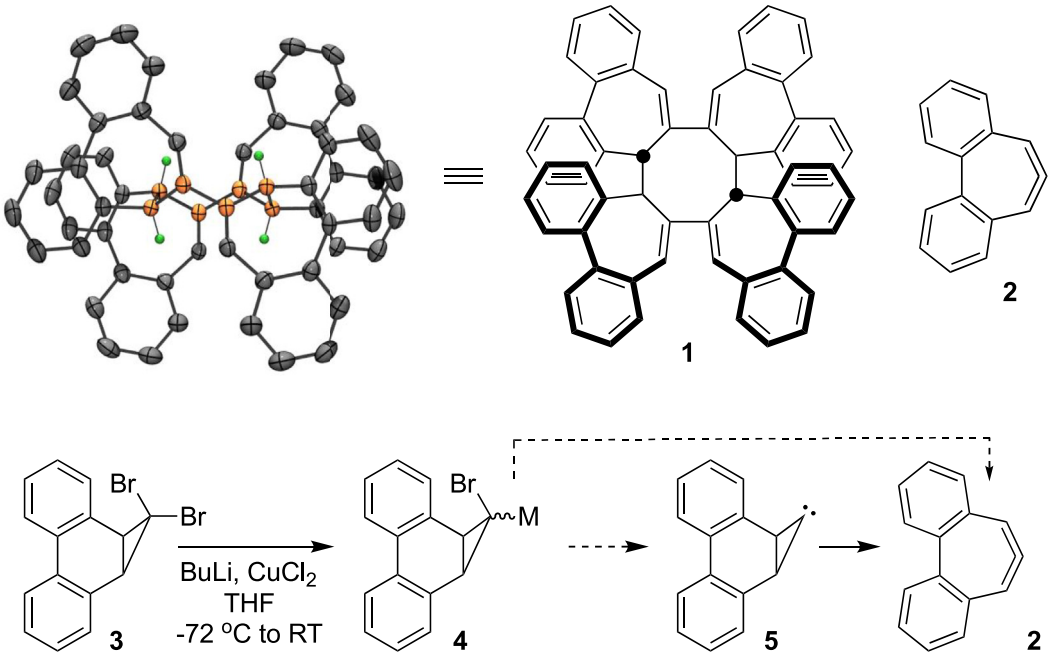
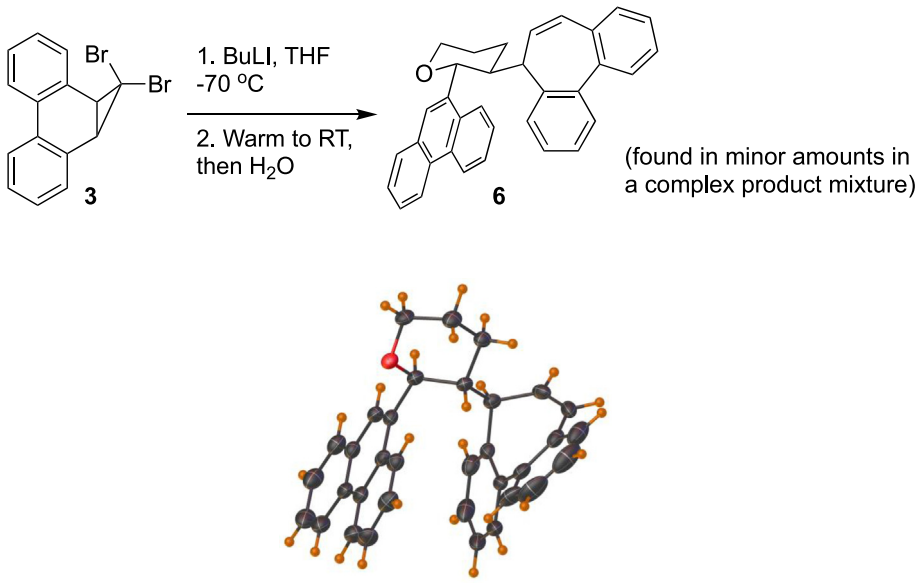


Scheme 1. The Doering-Moore-Skattebøl reaction of the *gem*-dibromocyclopropane **3**.



Scheme 2. The reaction of **3** with butylithium at low temperature followed by quenching with water at room temperature gave pyran **6** in low yield. The single crystal X-ray structure of **6** is also shown.

coated magnetic stir bar and thermometer. The stirred solution was cooled in a Dry Ice – acetone bath to −70 °C and treated with butyllithium (4.5 mL of a 2.5 M solution in hexanes, 11.3 mmol) over 15 min by syringe. The temperature of the reaction mixture was maintained below −60 °C during addition of butyllithium. After completion of addition, stirring was continued overnight in the bath to allow the reaction mixture to gradually warm to room temperature. The reaction was quenched by the addition of water (50 mL) and the aqueous and organic layers were separated. The aqueous layer was extracted with dichloromethane (2 × 40 mL) and the combined organic layers were washed sequentially with water (2 × 40 mL) and brine (40 mL). The organic layer was dried over anhydrous sodium sulfate and filtered. Silica gel was added to the filtrate to adsorb the product mixture upon slow evaporation of solvent. Purification was performed by chromatography over silica gel using a gradient of ethyl acetate (0–15%) in hexanes as the eluent. Fractions containing the desired product, contaminated by various other impurities, were consolidated and re-purified by a second round of column chromatography under the same conditions as noted above. Slow evaporation of the column fractions eluting with 2% ethyl acetate in hexanes provided the pure product **6** (15 mg, 0.7% yield) as colorless crystals. The reaction also produced a complex mixture of byproducts similar to those we have reported previously [1]. The ^{1}H and ^{13}C NMR spectra of the product as well as its IR spectrum are given in the supplemental material. Melting point: 190–191 °C. R_f: 0.1 (stationary phase: silica gel on

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Table 1
Salient crystal structure data for **6**.

Formula	$C_{34}H_{28}O$
$D_{calc.}$/g cm^{-3}	1.240
Absorption m/mm^{-1}	0.073
Formula Weight	452.56
Color	Clear colorless
Shape	Block
Size/mm^3	0.29 × 0.26 × 0.18
T/K	173
Crystal System	Monoclinic
Space Group	$P2_1/n$
a/Å	14.1310(4)
b/Å	9.1119(3)
c/Å	18.8865(5)
α/°	90
β/°	94.7330(10)
γ/°	90
V/Å^3	2423.54(12)
Z	4
Z'	1
Wavelength/Å	0.71073
Radiation type	MoK_a
θ_{min}/°	2.829
θ_{max}/°	26.393
Measured Reflections	29282
Independent Reflections	4953
Reflections Used	4240
R_{int}	0.0240
Parameters	316
Restraints	0
Largest Peak	0.320
Deepest Hole	−0.217
GooF	1.021
wR_2 (all data)	0.1143
wR_2	0.1072
R_1 (all data)	0.0528
R_1	0.0437

aluminum; mobile phase: 98% hexanes/2% ethyl acetate).

X-Ray Diffraction Studies: A clear, colorless, block-shaped crystal of **6** with dimensions 0.29 mm × 0.26 mm x 0.18 mm was mounted with oil on a MiTeGen MicroMount. X-ray data were acquired at 173 K on a Bruker D8 Quest Eco diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71073 Å) and PHOTON 50™ CMOS (**c**omplementary **m**etal-**o**xide **s**emiconductor) detector. The Bruker Apex 3 suite of programs was used to collect diffraction data [15]. The data reduction software package Bruker SAINT+ [16] was used to integrate the frames with a narrow-frame algorithm and the multi-scan method (SADABS) [17] was used to correct the data for absorption effects. Processing of data was carried out with the Olex2 suite of programs [18]. The Bruker SHELXTL software package [19,20] was used to perform structure solution by direct methods and refinement by full-matrix least-squares on F^2. All non-hydrogen atoms were refined anisotropically with suggested weighting factors and the hydrogens were calculated on a riding model. The cif file was validated with the checkCIF/Platon facility of IUCr that was accessed with Olex2 [18]. X-ray graphics were also produced with Olex2 [18].

3. Results and discussions

*Structural analysis of **6***: The salient features of the X-ray crystal data are shown in Table 1. More detailed tables of bond lengths and angles are provided in the supplemental information. The structure, belonging to the monoclinic crystal system, was solved in the space group $P2_1/n$ (#14). The asymmetric unit consists of a single molecule with the unit cell volume corresponding to the presence of four molecules. An examination of the crystal structure reveals that the pyran ring in **6** adopts the familiar chair conformation with the two large substituent groups occupying adjacent equatorial positions trans to each other. The phenanthrene moiety is located on the carbon α to the oxygen whereas the dibenzocycloheptatriene substituent is on the β carbon. Furthermore, the pyran ring is linked to the seven-membered ring at the benzylic/allylic position. A segment of the crystal packing diagram, with the unit cell boundaries, is shown in Fig. 1. The diagram shows the layering of the phenanthrene units in the solid state. The ^{1}H NMR spectrum of **6** acquired at ambient temperature (see supplemental information) shows several signals that are substantially broadened. Perhaps such broadening might be attributed to the presence of the large substituents which impose significant conformational restrictions on the molecule. Those two substituents are unable to rotate past each other and are also likely to affect the ease with which the

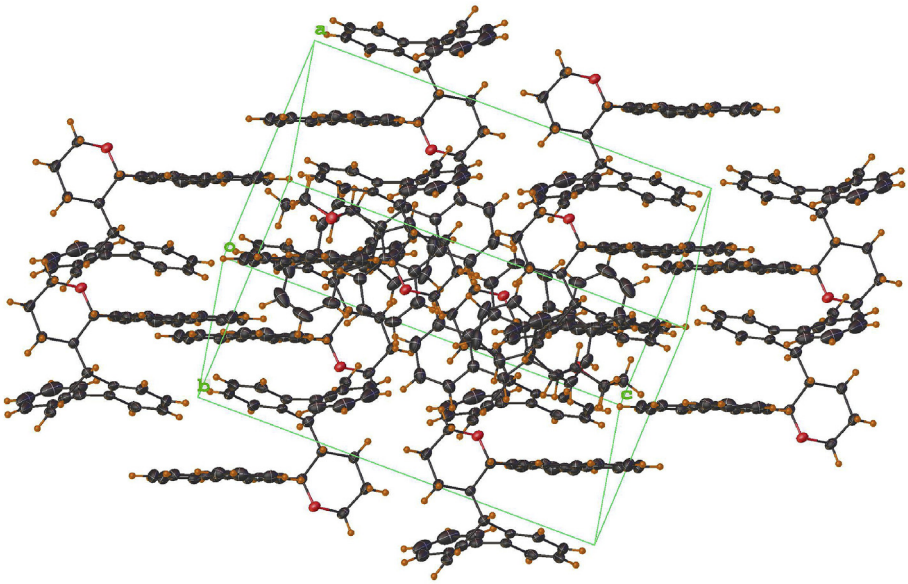

Fig. 1. A view of the crystal packing diagram of **6** with the unit cell shown. The layering of the phenanthrene units in the solid state can be also seen in the diagram.

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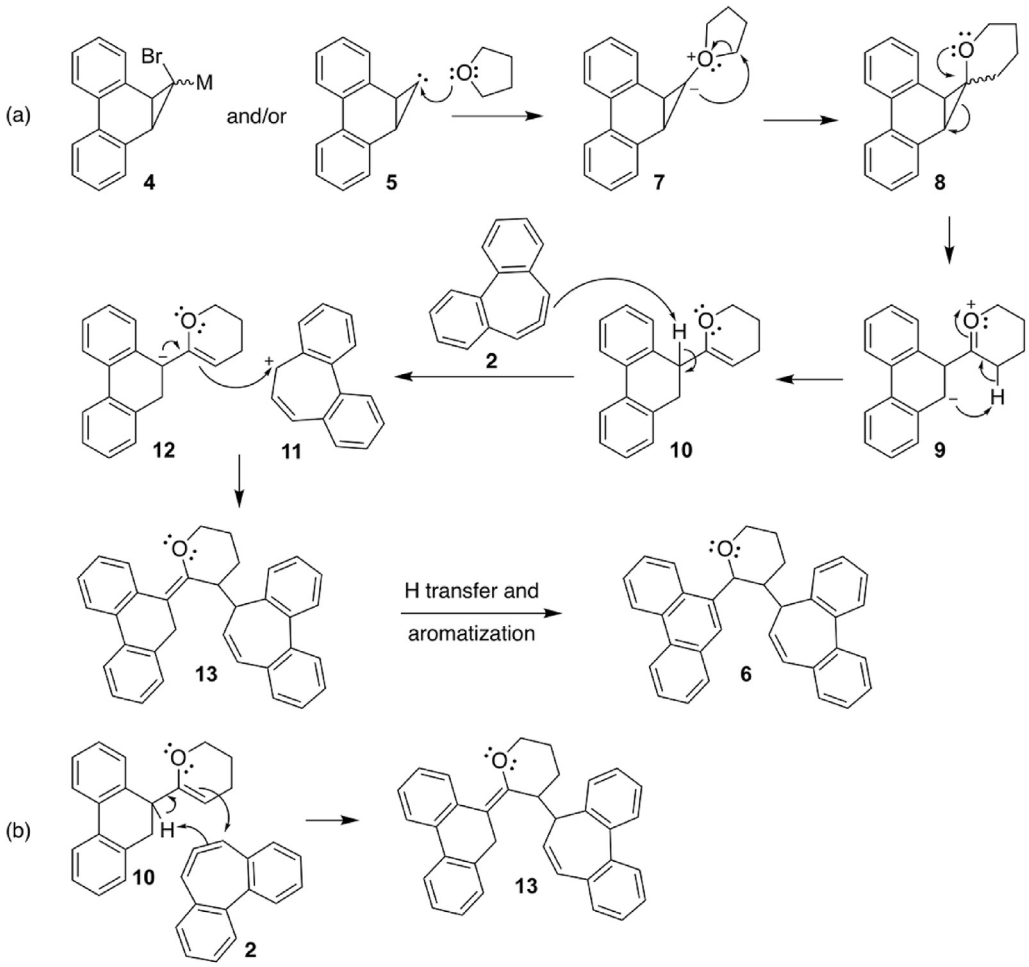

Scheme 3. (a) A postulated mechanism for the formation of pyran **6**. (b) An alternative route to **13** by an ene reaction between **10** and **2**.

pyran ring is able to undergo the conventional chair-to-chair ring flips.

A mechanistic rationale for the formation of ***6***: A plausible mechanism for the formation of **6** is proposed in Scheme 3. The parent cyclopropylidenes is known to favor a singlet ground state [21], and our DFT calculations [22] (B3LYP/6-31G*) [23–25] show that singlet **5** is also lower in energy than the triplet by about 11.3 kcal/mol after applying zero-point vibrational energy correction. Furthermore, it is known that singlet carbenes form oxonium ylids with THF which subsequently undergo ring expansion to pyrans [26–29]. By analogy, it is likely that **5** (and/or its surrogate carbenoid **4**) can also form the THF ylid **7** which can then rearrange to the pyran derivative **8**. Rupture of the cyclopropyl ring in spirocyclic **8**, assisted by the oxygen of the pyran, relieves strain to produce the putative zwitterionic intermediate **9**, and thence to the dihydropyran derivative **10**. This sequence essentially completes the interception of **4/5** by THF. It should be noted that **10** has an active hydrogen that is both allylic *and* benzylic. This could then set the stage for proton abstraction by the cyclic allene **2**, derived from **4/5**, to produce the resonance stabilized ions **11** and **12** (Scheme 3a). Combination of **11** and **12** would then form **13**. Alternatively, the formation of **13** may be accomplished in a single step via an ene reaction between **10** and **2** (Scheme 3b) [30]. Further aromatization of **13** by tautomerization can deliver the observed final product **6** [31].

4. Conclusions

This work describes the isolation and characterization of 3-(5*H*-dibenzo[*a*,*c*] [7]annulen-5-yl)-2-(phenanthren-9-yl)tetrahydro-2*H*-pyran (**6**), an unusual, sterically congested pyran derivative, obtained in trace amounts from the reaction of 1,1-dibromo-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**3**) with butyllithium in THF at low temperature, followed by quenching with water at room temperature. The formation of **6** is rationalized on the basis of the initially generated cyclopropylidene(oid) (**4/5**) interacting with THF to form an oxonium ylid **7** which then undergoes a ring expansion to produce the pyran framework in **10**. Subsequent reaction of **10** with the strained dibenzocycloheptatetraene **2**, resulting from ring opening of **4/5**, leads to the observed product **6**. To the best of our knowledge, this work documents the first example of a cyclopropylidene(oid) and its ring-opened allene trapped into a single product.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.molstruc.2018.01.061.

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