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Short Note

5,6-Diphenyl-1,3,4,7-tetra-*p*-tolyl-1,3,3a,7a-tetrahydropentaleno[1,2-*c*]furan

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Abstract: The reaction of (*Z*)-5-phenyl-1,3-di-*p*-tolylpent-2-en-4-yn-1-ol (**1**) with trimethylsilyl chloride in dichloromethane at ambient temperature gave a dimeric ether compound **2** in 30% yield. Subsequently, heating **2** in toluene under refluxing temperature rendered the title compound quantitatively. The structure of this tricyclic-fused compound was characterized using NMR, mass spectroscopy, and X-ray crystallography. This unique linear tricyclic fused furan framework is reported for the first time.

Keywords: pentaleno[1,2-c]furan; tricyclic fused rings; heterocycle

1. Introduction

Derivatives of cyclopenta[a]pentalenes (**I**) are a family of tricyclic compounds composed of three fused cyclopentane rings, and such a skeleton is found in natural products [1–5]. However, the corresponding heterocycles, such as pentaleno[1,2-*c*]pyrrole (**II**) or pentaleno[1,2-c]furan (**III**), are less studied (Figure 1). Amongst, Lycopalhine A with an aza-heterocycle is the only natural product found in fawcettiminetype Lycopodium alkaloid [6,7]. For the furan derivative **III,** it has never been reported either in natural products or in synthetic targets.

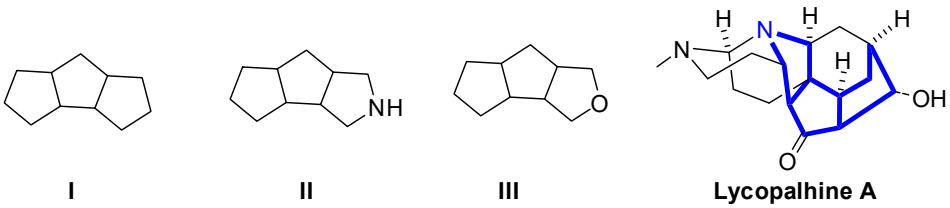

Figure 1. Structures of linear tricyclic 5/5/5 ring systems and Lycopalhine A.

Several synthetic approaches and reactions leading to derivatives of **I** and **II** have been developed in the past [1–5,8–10]. In a previously work, we investigated whether treatment of pent-1-en-3-yn-1-ol (**IV**) with anilines in the presence of Lewis acid provided the tricyclic compound **VI** directly (Scheme 1) [11]. Presumably, the substitution of aniline with **IV** followed by dimerization took place to give **V**, which then underwent cascade cyclization to yield the tricyclic pentaleno[1,2-*c*]pyrrole ring systems **VI**. Compound **VI** was able to proceed the dehydrogenation to render the fully conjugated pentaleno[1,2-c]pyrrole molecule **VII**. The success of this methodology is the formation of dimeric intermediate **V**, giving the desired carbon framework.

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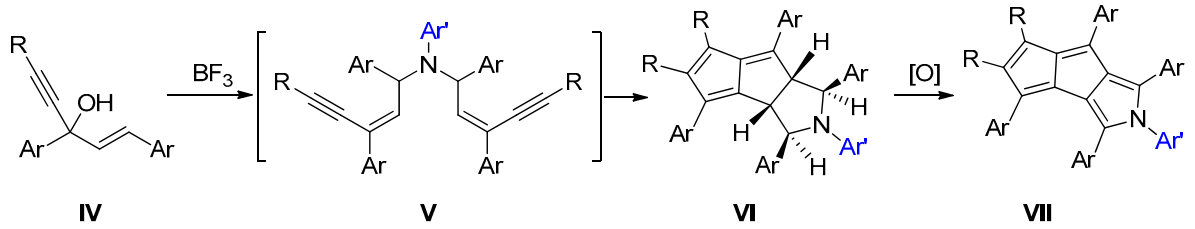
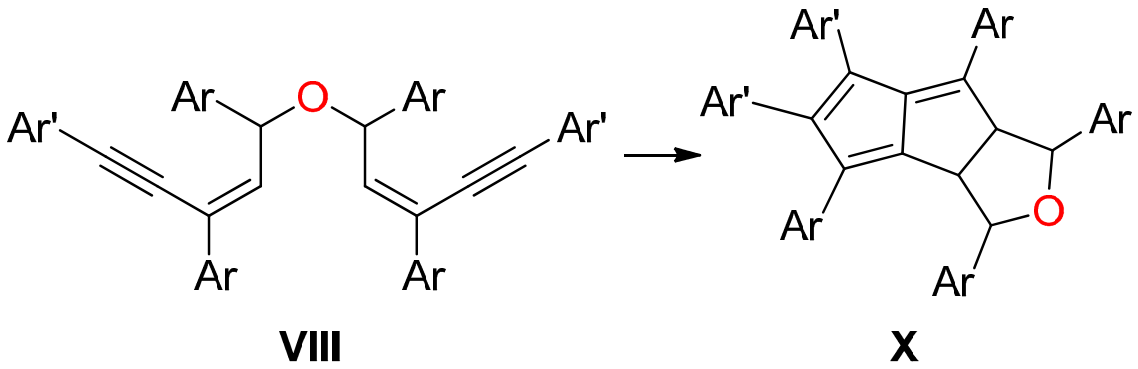


Scheme 1. Synthetic scheme leading to pentaleno[1,2-c]pyrrole **VII**.

Based on the above observations, we envisioned that if one can have an ether analog **VIII**, then it might undergo a similar cascade cyclization, which would eventually lead to the desired furan derivative **X** (Scheme 2). Here, we would like to demonstrate this idea and to obtain the tricyclic pentaleno[1,2-*c*]furan molecule.

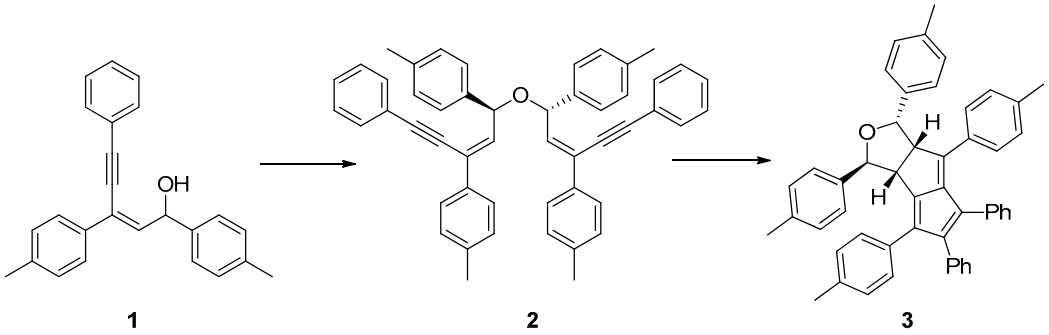


Scheme 2. Proposed approach leading to the target molecule.

2. Results

2.1. Synthesis of Dihydropentaleno[1,2-c]furan 3

Scheme 3 illustrates the synthetic approach leading to the target molecule **3**. The synthetic sequence commenced from the readily available pent-2-en-4-yn-1-ol 1, which was prepared according to our previously reported procedure by the addition of phenylacetylide to (*E*)-1,3-di-p-tolylprop-2-en-1-one followed by acid-catalyzed rearrangement [11,12]. Treatment of 1 with trimethylsilyl chloride at room temperature provided the dimeric ether **2** in 30% yield [13]. The reactant was totally consumed, giving various products, as indicated using a TLC analysis. Attempts to improve the yield of **2** was in vain even with the use of various Lewis acids such as $TiCl_4$, BF_3, and Me_3SiBr. Upon chromatographic purification, compound **2** was obtained as viscous liquid in 30% yield. Thermal heating of **2** in toluene quantitatively rendered the target molecule 3 as a brown solid. Unlike the aza-analog VI, compound **3** did not undergo dehydrogenation reaction to form a fully conjugated system.



Scheme 3. Synthesis of dihydropentaleno[1,2-*c*]furan **3**.

2.2. Characterization

Mass spectrum of compound **3** shows a $[M + H]^+$ ion at m/z = 659.328, which is in consistent with the molecular formula of $C_{50}H_{42}O$. Besides the signals for aromatic region, the ^{1}H NMR of **3** in $CDCl_3$ illustrates four signals corresponding to the protons on the furan ring. Among them, three sets of signals do show coupling interactions to each other, and there are signals at δ 5.33 (d, *J* = 7.7 Hz, *H*-1), 4.69 (dd, *J* = 7.7 Hz, 6.0 Hz, *H*-7a), and 4.27 (d, *J* = 6.0 Hz, *H*-3a), indicating that these protons are seated in *cis* fashion (Figure 2). On the other hand, a shift at δ 5.51 appears to be a singlet, which is assigned to be *H*-3 *trans* to the above-mentioned protons (Figure 2 and Figure S1 in Supplementary Materials). Based on ^{1}H NMR assignment, the relative configuration along the furan ring is concluded. Nevertheless, this observation is further confirmed using X-ray crystallography (see Section 2.3). In addition, four singlets due to the methyl groups of tolyl moieties were observed at δ 2.37, 2.29, 2.14, and 2.12, respectively. All these information readily support the structure proposed.

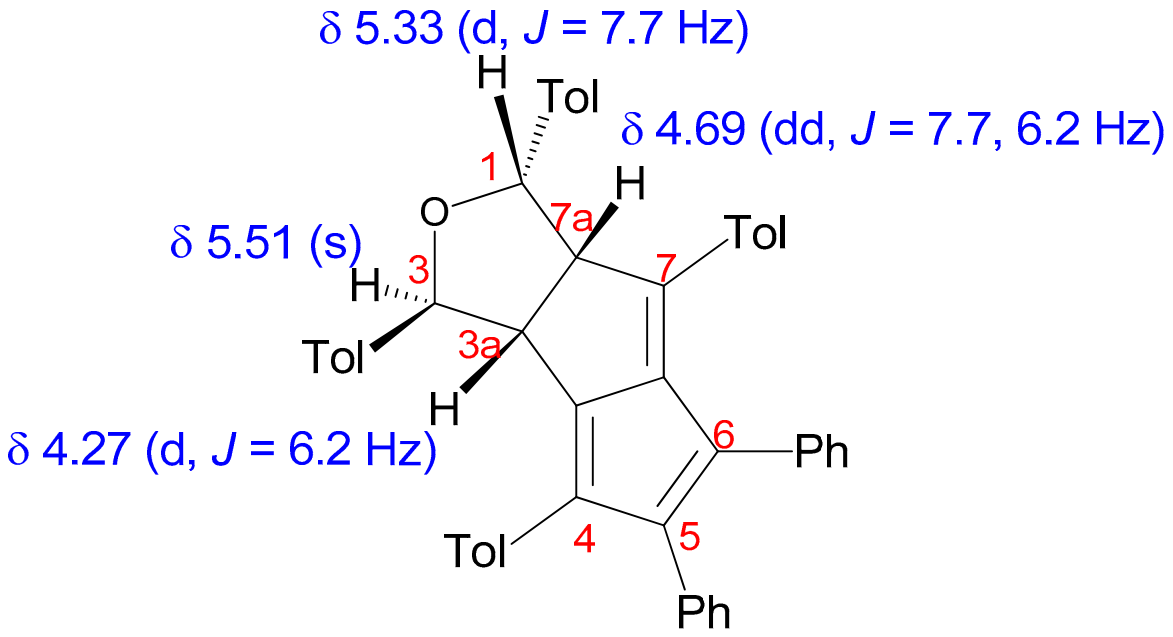


Figure 2. ^{1}H NMR assignment for protons on the furan ring (numbers given for carbons are according to the nomenclature).

2.3. Crystallography

The solid state structures of **3** was determined using a single-crystal X-ray diffraction analysis to reveal the structural details including the stereochemistry. ORTEP plot of **3** is shown in Figure 3A, and the relevant structural parameters are summarized in Table S5. The molecule comprises three fused five-member rings, namely furan ring (O1, C1, C2, C9, C10; A ring), cyclopentene ring (C2, C3, C4, C8, C9; B ring), and cyclopentadiene ring (C4, C5, C6, C7, C8; C ring). All bond lengths and bond angles in 3 are in normal ranges, as expected (Table S3 in Supplementary Materials).

The furan ring adopts an envelope conformation, which is supported by the observation of both torsional angles of O1-C10-C9-C2 and O1-C1-C2-C9 in [14.63(14)°] and [26.83(14)°], respectively (Table S5 in Supplementary Materials). The two fused cyclopentene/pentadiene rings (B and C rings) are almost coplanar (Figure 3B), as evidenced by the smaller torsional angles around both B and C rings (Table S5 in Supplementary Materials). Hydrogen atoms at C1, C2, and C9 are all pointed to the same side, i.e., *cis* to each other, whereas the hydrogen at C10 is seated to the opposite side. This is consistent with NMR spectroscopic analysis.

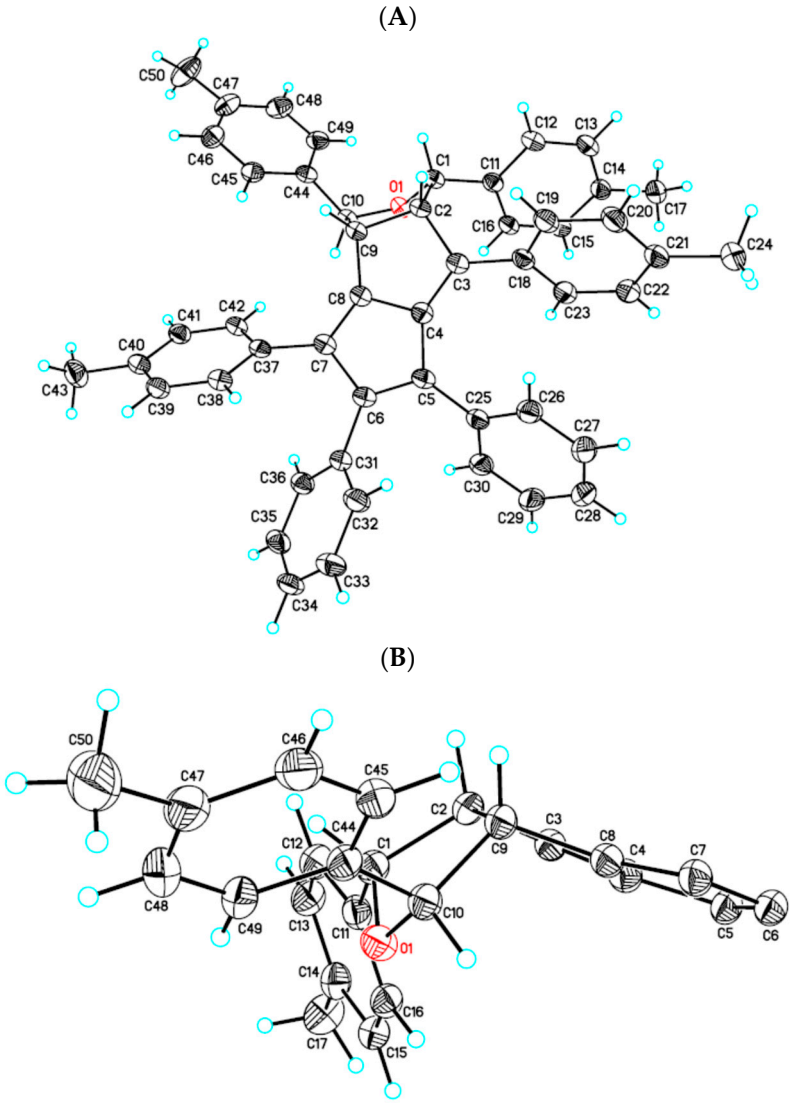


Figure 3. (**A**) ORTEP plot of **3**; (**B**) side view of three-fused rings (aryl rings at C3, C5, C8, and C7 are omitted for clarity) showing 30% probability atomic displacement ellipsoids.

3. Materials and Methods

3.1. General

All the chemicals were commercially purchased and used without further purification. Flash chromatography was performed using silica gel 230–400 mesh. 1,3,5-triarylpent-2-en-4-yn-1-ol **1** was prepared according to the reported procedure [11,12]. ^{1}H and ^{13}C NMR were recorded in a 400 MH_Z spectrometer in $CDCl_3$ referenced to TMS. Melting points were determined on a Fargo MP-1D instrument. Unless otherwise noted, all the reactions were performed without any special precautions.

3.2. Synthesis

3.2.1. (2Z,2′Z)[1′,3′-Ditolyl-5′-phenyl-pent-2′-en-4′-ynoxy]-1,3-ditolyl-5-phenyl-pent-2-en-4-yne **2**

A mixture of enynol **1** (33.8 mg, 0.1 mmol) and Me_3SiCl (0.5 mg, 4.6×10^{-3} mmol) in dichloromethane (1 mL) was stirred at room temperature for 20 h. Upon the consumption of enynol checked using TLC, water (5 mL) was added and extracted with ether (20 mL × 2). All extracts were combined, dried with anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was chromatographed on silica gel with elution of hexane/ethyl acetate (100:1). The desired product was collected and concentrated as brown

oil (19 mg, 0.03 mmol, 30%). ^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ 7.48 (d, *J* = 8.2 Hz, 4H), 7.44 (d, *J* = 8.2 Hz, 4H), 7.18–7.12 (m, 14H), 7.06 (dd, *J* = 7.9, 0.5 Hz, 4H), 6.54 (dd, *J* = 9.1, 0.5 Hz, 2H), 5.90 (d, *J* = 9.1 Hz, 2H), 2.32 (s, 6H), 2.28 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, CDCl3, 300 K): δ 138.4, 137.8, 137.1, 136.4, 134.3, 131.5, 129.2, 128.9, 128.0, 126.6, 126.2, 124.7, 123.1, 96.1, 86.3, 77.5, 21.1, 21.0. HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ Calcd. for $C_{50}H_{43}O$: 659.3314, found: 659.3310.

3.2.2. (5,6-Diphenyl-1,3,4,7-tetra-p-tolyl-1,3,3a,7a-tetrahydropentaleno[1,2-c]furan **3**

A solution of **2** (66.9 mg, 0.2 mmol) in toluene was heated to reflux for 20 h. The reaction was monitored using TLC to the consumption of substrate. After the removal of the solvents, the residue was filtrated through silica gel with the elution of hexane. Upon concentration, the desired compound was obtained as a red solid (66.9 mg, 0.2 mmol, 100%). mp 202–203 °C; ^{1}H NMR ($CDCl_3$, 300 K) δ 7.35 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.10–7.06 (m, 5H), 7.02–6.96 (m, 7H), 6.92 (t, *J* = 7.8 Hz, 2H), 6.77 (t, *J* = 7.6 Hz, 4H), 6.50 (d, *J* = 8.4 Hz, 2H), 6.47 (d, *J* = 8.4 Hz, 2H), 5.51 (s, 1H), 5.33 (d, *J* = 7.8 Hz, 1H), 4.69 (dd, *J* = 7.7, 6.2 Hz, 1H), 4.27 (d, *J* = 6.2 Hz, 1H), 2.37 (s, 3H), 2,29 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 300 K):δ 154.6, 151.7, 147.8, 147.2, 138.8, 137.9, 136.7, 136.5, 136.3, 135.7, 135.3, 132.7, 131.7, 130.5, 130.3, 130.2, 129.1, 128.9, 128.5, 128.0, 127.5, 127.4, 127.2, 126.3, 125.9, 125.7, 125.5, 82.1, 81.4, 65.6, 50.1, 21.1, 21.1, 21.0, 20.9; HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ Calcd. for $C_{50}H_{43}O$: 659.3314, found: 659.3288.

3.3. Crystal Structure Determination

Crystals suitable for X-ray determination were obtained for **3** using recrystallization from dichloromethane and hexane at room temperature. Cell parameters were determined using a Bruker AXS D8 VENTURE, PhotonIII_C28 diffractometer. Crystal data of **3**: $C_{50}H_{42}O$, Mw = 658.83, Monoclinic, space group $P2_1/n$; *a* = 16.4711(10) Å, *b* = 9.1373(6) Å, *c* = 25.0870(15) Å, α = 90°, β = 106.575(3)°, γ = 90°; V = 3618.7(4) Å^3; Z = 4; $\rho_{calcd.}$ = 1.209 Mgm^{-3}; F(000) = 1400; Crystal size: 0.35 × 0.080 × 0.020 mm^3; reflections collected: 77656; independent reflections: 7628 [R(int) = 0.0644]; θ range 2.877 to 78.600°; goodness-of-fit on F^2 1.051; Final R indices [I > 2 sigma(I)] R1 = 0.0487, wR2 = 0.1259; R indices (all data) R1 = 0.0616, wR2 = 0.1365. The structure was solved using the SHELXS-97 program [13] and refined using the SHELXL-97 program [14] using full-matrix least-squares on F2 values. The X-ray crystallographic data for **3** have been deposited in the Cambridge Crystallographic Data Center with CCDC reference number 2341418. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (accessed on 19 March 2024), or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

4. Conclusions

We demonstrated a method for the synthesis of 5,6-diphenyl-1,3,4,7-tetra-*p*-tolyl-1,3,3a,7a-tetrahydropentaleno[1,2-*c*]furan, which is a compound composed of three fused five-member rings. The structure of the obtained compound was fully characterized using spectroscopic methods and X-ray single crystallography. Compound **3** is a derivative of pentalenes, which can be used as ligands for transition metal complexes or building blocks for organic synthesis.

Supplementary Materials: Table S1. Crystal data and experimental details for **3**; Table S2. Atomic coordinates and equivalent isotropic displacement parameters for **3**; Table S3. Bond lengths [Å] and angles [°] for **3**; Table S4. Anisotropic displacement parameters (Å^2 × 10^3) for **3**; Table S5. Selected bond distances (Å), bond angles (deg) and torsional angle (deg); Figure S1. ^{1}H NMR spectrum of compound **3** in $CDCl_3$; Figure S2. ^{13}C NMR spectrum of compound **3** in $CDCl_3$; and Figure S3. Mass spectrum of **3**.

Author Contributions: Conceptualization, S.-T.L.; methodology, investigation, and data collection, S.-K.C.; writing—original draft preparation, S.-T.L.; data checking and editing, S.-K.C. and S.-T.L.; X-ray data collection and refinement, Y.-H.L. supervision, S.-T.L. funding acquisition, S.-T.L. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: The data reported in this article can be obtained from the authors upon reasonable request.

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Conflicts of Interest: The authors declare no conflicts of interest.

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