Synthesis J. Choi et al. Special Topic

Synthesis of Tribenzotropone by Ring Expansion of Phenanthrene-9,10-dione

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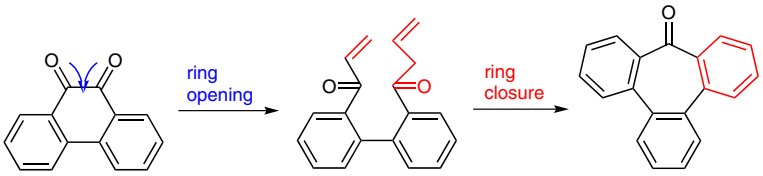

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Abstract Tribenzotropone was efficiently synthesized by a ring-expansion method from readily available phenanthrene-9,10-dione via a ring-opened diketone as a key intermediate; the diketone was prepared by nucleophilic addition of allyl and vinyl groups, followed by an oxidative ring-opening reaction with lead(IV) acetate. Ring closure by an intramolecular Diels–Alder reaction and subsequent dehydrogenation produced tribenzotropone in 38% overall yield. Ring closure by a Morita–Baylis–Hillman reaction, on the other hand, produced a dibenzo-fused nonanedione in 22% overall yield.

Key words annulations, cycloadditions, Diels–Alder reactions, fused-ring systems, ring expansion

Tropone is an unusual carbonyl compound with a relatively high dipole moment of 4.17 D (c.f. acetone, 2.91 D), in which a dipolar resonance structure contributes to the non-benzenoid aromatic character of the molecule.[1] Tropone has been extensively studied as a material for liquid crystals because of its polarity and planarity.[2–4] Tribenzotropone (**1**; 9*H*-tribenzo[*a*,*c*,*e*][7]annulen-9-one) on the other hand, is peculiar in that all the alkene moieties in the seven-membered ring are incorporated into fused benzene rings (Figure 1). Structurally, the molecule deviates from planarity to reduce its angular strain as well as the unfavorable steric interactions between the *ortho*-hydrogen atoms;[5,6] consequently, the carbonyl group participates in various reactions, including reduction and nucleophilic addition.[7,8] There have been reports on modifications of the carbonyl group of tribenzotropone to give materials for use as thermochromic dyes[8] or as photo- or thermoresponsive molecular switches.[9,10]

Tropones have been synthesized either by oxidation of cycloheptanones or by ring-expansion of benzene derivatives.[1,11] The synthesis of tribenzotropone (**1**) is more challenging due to the presence of three fused benzene rings. Even though the oxidation of tribenzocycloheptatriene and the rearrangement of the diazonium salt of 9-(2-aminophenyl)-9*H*-fluoren-9-ol have been reported to produce **1**, the preparations of the necessary substrates required multistep sequences with difficulties or poor yields.[5,6] On the other hand, the Diels–Alder reaction of furan with an alkyne derived from dibenzosuberone is an excellent approach to the synthesis of tribenzotropone (**1**), giving a 31% overall yield in five steps.[12] We surmised that the ring-expansion of a benzo-fused cyclohexanone might constitute another efficient synthetic path to benzotropone. In a continuation of our ring-expansion study, we were able to demonstrate an easy and practical synthesis of tribenzotropone (**1**) from readily available phenanthrene-9,10-dione (**4**).[13,14] We herein disclose the details of our ring-expansion study.

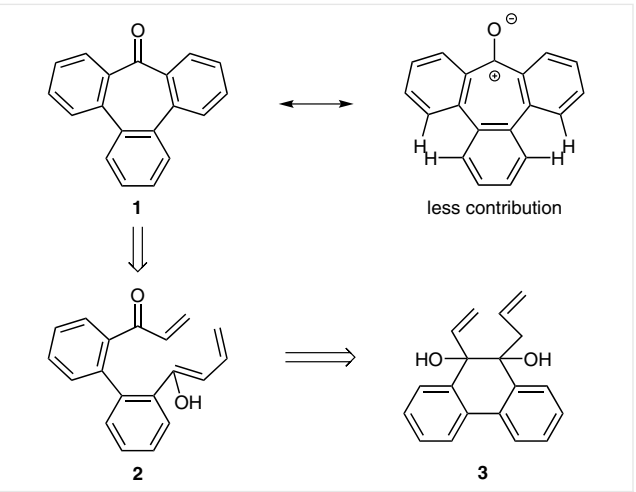
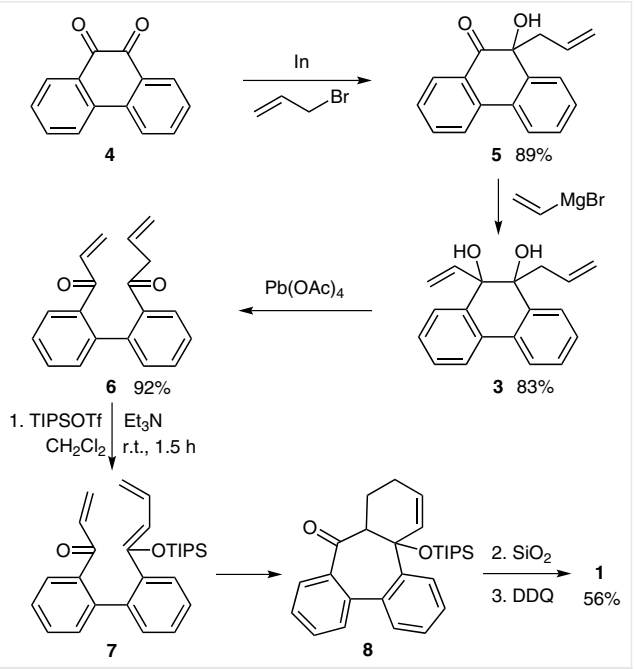


Figure 1 Disconnection approach to tribenzotropone (**1**) by means of an intramolecular Diels–Alder reaction

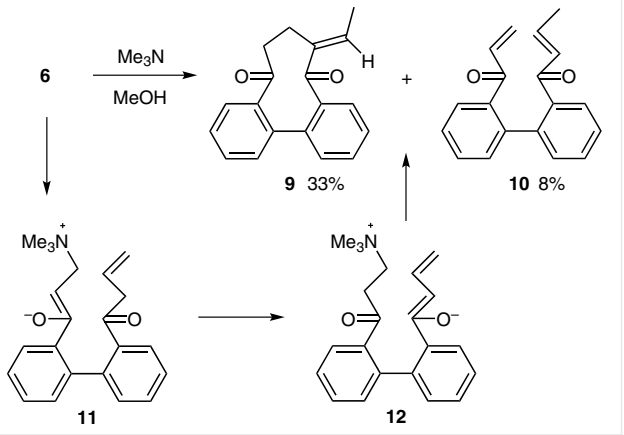
As delineated in the disconnection strategy shown in Figure 1, we planned to use the intramolecular Diels–Alder reaction of ketone **2** as the key step to install the benzo-fused tropone skeleton;[15] ketone **2**, in turn, might be obtained by the oxidative ring-opening reaction of diol **3**.[13,14] Readily available phenanthrene-9,10-dione (**4**) was used as the starting material, in which the cyclohexanedione core underwent ring-expansion after incorporation of two alkenyl tethers (Scheme 1). A mild and selective indium-mediated addition of an allyl group to dione **4** produced hydroxy ketone **5** in 89% yield.[16] The addition of vinylmagnesium bromide (3 equiv) provided dihydrophenanthrene-9,10-diol **3**, with vinyl and allyl substituents, in 83% yield. Only one diastereomer was obtained, according to thin-layer chromatography and ^{13}C NMR spectrometric analysis. We expected the *anti*-diol to be formed as a result of chelation control of the neighboring hydroxy group in the Grignard addition, but it was not necessary to assign the stereochemistry of the product. Oxidation of diol **3** by lead(IV) acetate proceeded efficiently to give the ring-opened diketone **6** in 92% yield.



Scheme 1 Synthesis of tribenzotropone (**1**) from readily available phenanthrene-9,10-dione (**4**) by introduction of C_3 and C_2 units, oxidative ring opening, intramolecular Diels–Alder reaction, and oxidation

The required diene **7** for the intramolecular Diels–Alder reaction was prepared in situ by the reaction of diketone **6** with triisopropylsilyl triflate in the presence of triethylamine. The triisopropylsilyl group was selected to provide a stable silyl enol ether that would permit an efficient cycloaddition reaction to be performed at a high temperature. It was surprising that the intramolecular Diels–Alder reaction between the electron-rich diene and the electron-deficient dienophile proceeded even at room temperature within 1.5 hours to produce the cycloadduct **8**, which upon filtration through a short pad of silica gel gave an inseparable mixture of the desired tribenzotropone (**1**) and its dihydro analogue. The crude mixture was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to complete the oxidation to a benzene ring, thereby producing tribenzotropone (**1**) in 56% yield. This four-step ring-expansion strategy from phenanthrene-9,10-dione (**4**) offers an easy and efficient method for the synthesis of tribenzotropone (**1**) in 38% overall yield. The ring-opened diketone **6** is highly functionalized, and it was envisioned that other type of cyclization might lead to a medium-sized benzo-fused ring compound. The Morita–Baylis–Hillman reaction of diketone **6** on treatment with trimethylamine in methanol was used as a mild protocol to induce cyclization to form the nine-membered cyclic structure **9** (33% yield; Scheme 2).[13] A single stereoisomer was obtained under these conditions. An *E*-configuration was assigned to the alkene moiety of **9** on the basis of the magnetic anisotropy effect of the carbonyl group. The chemical shift of the vinylic proton was observed at δ = 6.17 ppm, whereas the *Z*-isomer (obtained as a mixture under reflux condition with triphenylphosphine in *tert*-butanol) showed a peak at δ = 5.19 ppm. The reaction is presumably initiated by conjugate addition of trimethylamine to form the transient intermediate **11**, which deprotonates the α-proton of the neighboring allyl ketone moiety to give the intermediate **12**. The α-alkylation of the dienolate by the β-carbon of the neighboring ketone, with trimethylamine as a leaving group, produced the nine-membered cyclic diketone **9** after migration of the terminal alkene to the conjugation site. Direct deprotonation of α-hydrogen in allyl ketone of **6** by trimethylamine is unlikely, if we consider the pK_a of its conjugated acid (<11), and therefore the possibility of intramolecular conjugate addition of the dienolate can be ruled out. The acyclic side-product **10** (8% yield) is believed to have been formed by the proton exchange of dienolate **12** with the α-hydrogen of the neighboring ketone, with concomitant elimination of trimethylamine.

In conclusion, we have demonstrated a practical ring-expansion strategy for constructing benzo-fused medium-sized ring compounds from readily available phenanthrene-9,10-dione (**4**) through the formation of diketone **6** by the introduction of vinyl and allyl tethers and oxidative ring-opening of the resulting diol **3**. The intramolecular Diels–Alder reaction of **6** followed by dehydrogenation produced tribenzotropone (**1**) in 38% overall yield from **4**. The intramolecular Morita–Baylis–Hillman reaction of **6** with trimethylamine, on the other hand, produced the dibenzo-fused nine-membered diketone **9** in 22% overall yield from **4**.



Scheme 2 Synthesis of the benzo-fused nine-membered dione **9** by the intramolecular Baylis–Hillman reaction of diketone **6**.

IR spectra were recorded on a Varian 2000 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VNMRS-400 spectrometer, in $CDCl_3$ with TMS as an internal reference. High-resolution mass spectrometry was performed by using a magnetic sector analyzer in a JEOL JMS-600W spectrometer. Solvents for extraction and chromatography were of reagent grade and were used as received. Column chromatography was performed with silica gel 60 (70–230 mesh) and a mixture of EtOAc and hexanes. Reactions were performed in a well-dried flask under argon unless noted otherwise.

10-Allyl-10-hydroxyphenanthren-9(10*H*)-one (5)

To a stirred solution of phenanthrene-9,10-dione (**4**) (3.00 g, 14.41 mmol) in DMF (80 mL) at 0 °C under argon were added allyl bromide (1.25 mL, 14.41 mmol), In (1.74 g, 15.1 mmol), and NaI (2.16 g, 14.41 mmol). The orange solution turned dark green at this point. The mixture was stirred at 0 °C for 15 min and then the reaction was quenched with 1 M aq HCl. The mixture was extracted with EtOAc and the extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography to give a light-yellow oil; yield: 3.20 g (12.79 mmol, 89 %); R_f = 0.49 (EtOAc–hexane, 1:4).

IR (KBr): 3487, 3082, 1700, 1612, 1483, 1454, 1384, 1291, 1257, 1207, 1085, 926, 764, 719, 640 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (d of A of ABq, J_{AB} = 13.6, J_d = 7.6 Hz, 1 H), 2.54 (d of B of ABq, J_{AB} = 13.6, J_d = 7.6 Hz, 1 H), 4.05 (s, 1 H), 4.86 (dd, J = 17.2, 1.6 Hz, 1 H), 5.04 (dd, J = 10.0, 0.8 Hz, 1 H), 5.63 (ddt, J_d = 17.2, 10.0, J_t = 7.9 Hz, 1 H) 7.38–7.46 (m, 3 H), 7.68–7.77 (m, 2 H), 7.83–7.89 (m, 1 H), 7.89–7.98 (m, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 49.0, 79.6, 119.5, 123.2, 124.0, 126.1, 127.3, 128.2, 128.4, 128.5, 129.0, 129.2, 131.4, 135.1, 137.5, 140.2, 202.9.

HRMS (CI): *m/z* calcd for $C_{17}H_{15}O_2$: 251.1072; found: 251.1070.

9-Allyl-10-vinyl-9,10-dihydrophenanthrene-9,10-diol (3)

To a stirred solution of hydroxy ketone **5** (1.07 g, 4.28 mmol) in THF (50 mL) at –78 °C under argon was added a 1 M solution of vinylmagnesium bromide in THF (12.8 mL, 12.8 mmol), and the mixture was stirred at –78 °C for 2 h. The reaction was quenched with 1 M aq HCl, the mixture was extracted with EtOAc, and the extracts were dried (K_2CO_3), filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography to give a light-yellow oil; yield: 0.99 g (3.56 mmol, 83%); R_f = 0.46 (EtOAc–hexane, 1:4).

IR (KBr): 3489, 3069, 1732, 1642, 1486, 1453, 1345, 1199, 1161, 1000, 924, 863, 745 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.31 (d of A of ABq, J_{AB} = 14.0, J_d = 6.0 Hz, 1 H), 2.32 (br s, 1 H), 2.67 (d of B of ABq, J_{AB} = 14.0, J_d = 8.8 Hz, 1 H), 2.70 (br s, 1 H), 4.95 (d, J = 17.6 Hz, 1 H), 5.03 (d, J = 9.2 Hz, 1 H), 5.05 (d, J = 10.4 Hz, 1 H), 5.34 (d, J = 16.8 Hz, 1 H), 5.59 (dddd, J_d = 17.6, 9.2, 8.8, 6.0 Hz, 1 H) 5.99 (dd, J = 16.8, 10.4 Hz, 1 H), 7.29–7.40 (m, 4 H), 7.45–7.49 (m, 1 H), 7.62–7.67 (m, 1 H), 7.68–7.74 (m, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 39.1, 78.3, 79.6, 115.4, 119.0, 123.5, 123.7, 124.4, 125.3, 127.8, 127.9, 128.0, 128.5, 132.0, 132.1, 133.5, 138.7, 139.3, 139.7.

HRMS (CI): *m/z* calcd for $C_{19}H_{17}O_2$: 277.1229; found: 277.1227.

1-(2′-Acryloylbiphenyl-2-yl)but-3-en-1-one (6)

To a stirred solution of diol **3** (1.12 g, 4.02 mmol) in MeCN (25 mL) at r.t. under argon was added $Pb(OAc)_4$ (2.00 g, 4.43 mmol), and the mixture was stirred at r.t. for 30 min. The reaction was quenched with 1 M aq HCl, the mixture was extracted with EtOAc. The extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography to give a yellow oil; yield: 1.02 g (3.70 mmol, 92%); R_f = 0.41 (EtOAc–hexane, 1:4).

IR (KBr): 3081, 1685, 1604, 1477, 1447, 1411, 1300, 1218, 1126, 1000, 924, 817, 766, 659 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38 (br s, 2 H), 4.97 (dd, J = 17.2, 1.6 Hz, 1 H), 5.09 (dd, J = 10.0, 1.6 Hz, 1 H), 5.75 (dd, J = 10.4, 1.2 Hz, 1 H), 5.86 (ddt, J_d = 17.2, 10.0, J_t = 6.8 Hz, 1 H), 6.17 (dd, J = 17.2, 1.2 Hz, 1 H), 6.52 (dd, J = 17.2, 10.4 Hz, 1 H), 7.14–7.22 (m, 2 H), 7.39–7.52 (m, 4 H), 7.61–7.68 (m, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 46.1, 118.3, 127.3, 127.6, 128.2, 128.7, 130.3, 130.6, 130.6, 130.7, 130.8, 131.1, 135.5, 138.0, 138.8, 139.6, 140.3, 195.1, 202.2.

HRMS (CI): *m/z* calcd for $C_{19}H_{17}O_2$: 277.1229; found: 277.1225.

9*H*-Tribenzo[*a*,*c*,*e*][7]annulen-9-one (1)

To a stirred solution of diketone **6** (0.50 g, 1.81 mmol) in CH_2Cl_2 (30 mL) at r.t. under argon were added TIPSOTf (0.6 mL, 2.15 mmol) and Et_3N (0.25 mL, 2.00 mmol). The mixture was stirred at r.t. for 1.5 h, then filtered through a short pad of silica gel. The filtrate was concentrated under reduced pressure. The crude product was dissolved in CH_2Cl_2 (20 mL), and treated with DDQ (0.41 g, 1.81 mmol). The mixture was stirred at r.t. for 1.5 h, and then the reaction was quenched with H_2O. The mixture was extracted with CH_2Cl_2, and the extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure (single spot in TLC). The crude product (0.42 g) was purified by trituration with hexane to give a white solid; yield: 0.26 g (1.03 mmol, 57%); mp 177–178 °C; R_f = 0.53 (EtOAc–hexane, 1:4).

IR (KBr): 2934, 1734, 1662, 1602, 1489, 1439, 1367, 1313, 1272, 1167, 1063, 927, 895, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.52 (m, 4 H), 7.57–7.63 (m, 2 H), 7.64–7.69 (m, 4 H), 7.71–7.75 (m, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 126.5, 128.0, 128.3, 129.1, 131.1, 131.4, 136.7, 137.1, 143.0, 198.7.

HRMS (CI): *m/z* calcd for $C_{19}H_{13}O$: 257.0966; found: 257.0968.

(6*E*)-6-Ethylidene-7,8-dihydro-5*H*-dibenzo[*a*,*c*][9]annulene-5,9(6*H*)-dione (9) and (2*E*)-1-(2′-acryloylbiphenyl-2-yl)but-2-en-1-one (10)

To a stirred solution of diketone **6** (0.43 g, 1.60 mmol) in MeOH (25 mL) at r.t. under argon atmosphere was added Me_3N (0.12 g, 1.90 mmol), and the mixture was stirred at r.t. for 4 h. The reaction was quenched with H_2O and the mixture was extracted with $CHCl_3$. The extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography to give cyclic diketone **9** [yield: 0.15 g (0.53 mmol, 33%)] and acyclic diketone **10** [yield: 0.04 g (0.13 mmol, 8%)].

9

Yellow oil; R_f = 0.36 (EtOAc–hexane, 1:4).

IR (KBr): 3073, 2928, 1674, 1611, 1438, 1375, 1289, 1236, 1120, 995, 885, 764, 649 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.53 (dd, *J* = 7.2, 1.2 Hz, 3 H), 2.12–2.20 (m, 1 H), 2.61 (ddd, *J* = 13.2, 6.4, 4.0 Hz, 1 H), 2.68 (ddd, *J* = 13.2, 10.8, 6.4 Hz, 1 H), 2.85 (ddd, *J* = 14.4, 10.8, 6.8 Hz, 1 H), 6.17 (q, *J* = 7.2 Hz, 1 H), 7.11–7.15 (m, 1 H), 7.24–7.28 (m, 1 H), 7.37–7.42 (m, 1 H), 7.43–7.47 (m, 1 H), 7.47–7.55 (m, 3 H), 7.79–7.82 (m, 1 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.8, 23.9, 40.4, 126.1, 127.2, 128.0, 128.2, 129.4, 130.3, 131.4, 131.6, 136.3, 138.1, 139.4, 139.4, 139.7, 141.0, 199.7, 203.2.

HRMS (CI): *m/z* calcd for $C_{19}H_{17}O_2$: 277.1229; found: 277.1222.

10

Yellow oil; R_f = 0.48 (EtOAc–hexane, 1:4).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.78 (d, J_d = 6.8 Hz, 3 H), 5.70 (d, *J* = 10.4 Hz, 1 H), 6.16 (d, *J* = 17.2 Hz, 1 H), 6.27 (d, *J* = 15.6 Hz, 1 H), 6.51 (dd, *J* = 17.2, 10.4 Hz, 1 H), 6.77 (dq, J_d = 15.6, J_q = 6.8 Hz, 1 H) 7.14–7.22 (m, 2 H), 7.36–7.48 (m, 4 H), 7.52–7.62 (m, 2 H).

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1381045.

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