

Thermal Radical Cyclization of Non-Conjugated Aromatic Enyne-Allenenes: Synthesis of a Cyclobuta[*a*]naphthalene Skeleton

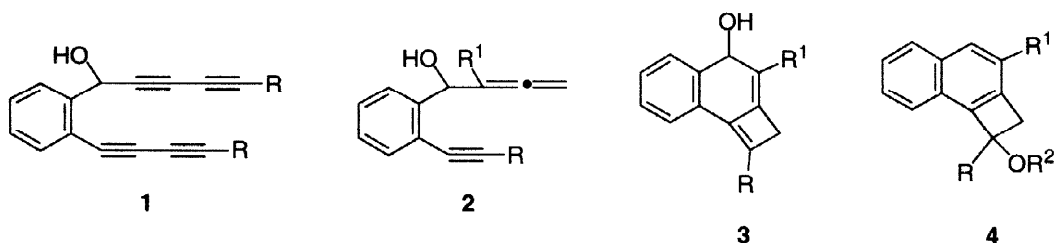
Chie Ikemoto, Tomikazu Kawano, and Ikuo Ueda*

The Institute of Scientific and Industrial Research, Osaka University, Mihogaoka, Ibaraki, Osaka 567-0047, Japan

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Abstract: The thermal cyclization of non-conjugated aromatic enyne-allenes (**2**) to form benzobicyclo[4.2.0]octatrienol (**3**) provides a simple and convenient procedure for the preparation of a cyclobuta[*a*]naphthalene skeleton (**4**). © 1998 Elsevier Science Ltd. All rights reserved.

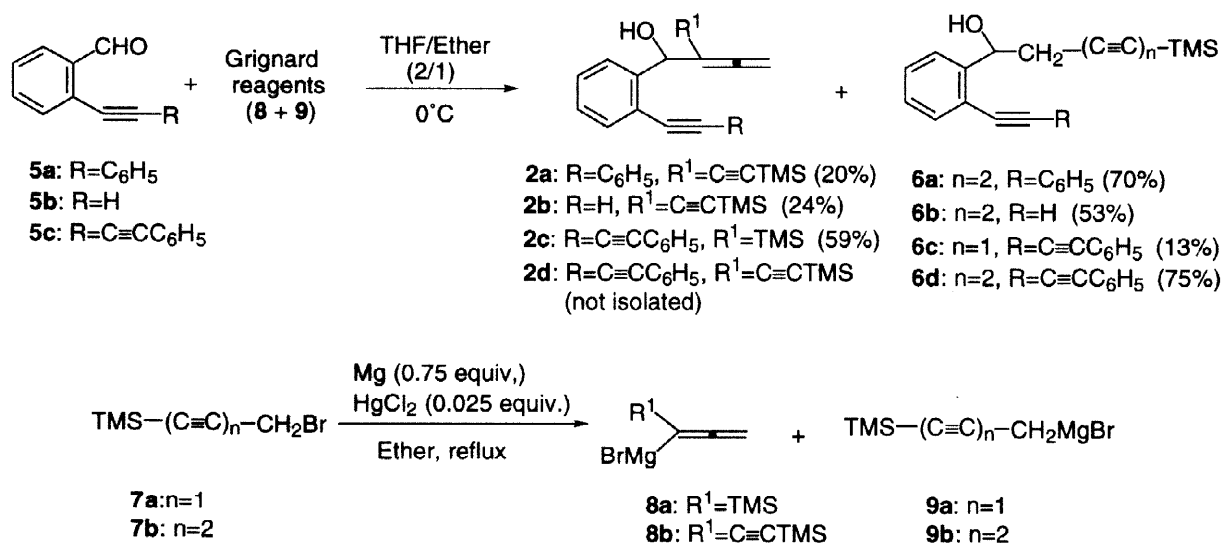
The thermal cycloaromatization of enediynes,¹⁾ enyne-cumulenes²⁾ and enyne-ketenes³⁾ by the Bergman, Myers-Saito and Moore cyclizations affords reactive biradicals which are now thought to play a critical role in the DNA-cleaving activity of an emerging class of powerful antitumor antibiotics. Furthermore, combinations of such biradical cycloaromatization protocols and subsequent radical cyclization will provide new synthetic pathways for the construction of complex molecules.⁴⁾ Thus, research in this area has been mainly focused on the synthesis of enediyne natural products and their synthetic analogs and the discovery of new synthetic pathways for the construction of polycyclic ring systems, particularly for the preparation of polyphenylenes and oligo(acenes). Recently, we have reported the thermal radical cycloaromatization of **1** to form 1,2-didehydrobenzene biradical intermediates.⁵⁾ In this paper, the thermal cyclization of **2** to yield 2,3-benzo-bicyclo[4,2,0]octa-1(8),2,5-trien-4-ols (**3**) which are converted into cyclobuta[*a*]naphthalene derivatives (**4**)⁶⁾ on treatment with silica gel or acid is described.



The synthesis of **2** is outlined in Scheme 1; starting materials (**5**) were prepared by methods described in the literature.^{5,7)} Although Grignard reagents prepared from **7**⁸⁾ and magnesium metal in the presence of anhydrous mercury(II) chloride in ether contain mainly **9**,⁹⁾ the reaction under refluxing ether was shown to yield

a mixture of **8**, which may be thermodynamically stable, and **9** in a product ratio of about 1 to 1. Reaction of **5** with Grignard reagents (**8** and **9**) produced *in situ* was achieved smoothly by use of a (2:1) mixed solvent of THF and ether at 0 °C. When **5a-c** were treated with the corresponding Grignard reagents, the desired products (**2a-c**)¹⁰ were obtained along with byproducts (**6a-c**) which were separated by silica gel column chromatography. The yields of **2a-c** are given in Scheme 1. When compound **5c** was subjected to the reaction with the Grignard reagents (**8b** and **9b**), a new product (**3d**) was obtained without isolating **2d** along with **6d**. Compound **3d** was purified by column chromatography on silica gel with a (10 : 1) mixture of hexane and ethyl acetate as an eluent at lower temperature than 5 °C. When **3d** was subjected to the almost same purification conditions at room temperature, cyclobuta[*a*]naphthalene derivative (**4d**) was obtained in a quantitative yield. Treatment of **3d** with methanol in the presence of a catalytic amount of pyridinium *p*-toluenesulfonate in anhydrous THF afforded **4e** in 72% yield. The structure of **3d**, **4d** and **4e** was determined on the basis of elementary analyses and spectral data.

Scheme 1 .

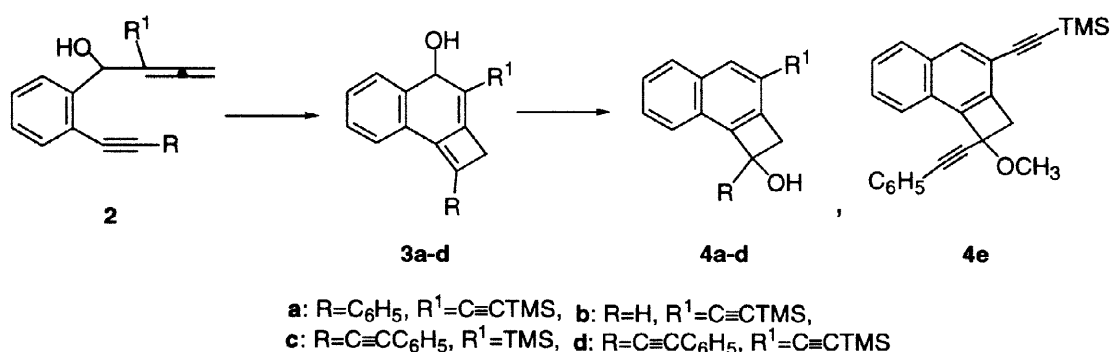


Thermolysis of **2a-d** was carried out in the presence of one equivalent of 1,4-cyclohexadiene, a hydrogen donor, in purified benzene. As compounds **3** were easily converted into **4** on silica gel in benzene (water content: ≤0.2%), the reaction mixtures containing **3** were chromatographed on silica gel with benzene as an eluent to isolate **4** as final products (Table 1). When **2a** was stirred at 30 °C for 24 h, **4a** was obtained in 93% yield. Reaction of **2c** at 60 °C for 11 h afforded **4c** in 79% yield. Interestingly, **2d** underwent thermal radical cyclization at such a low temperature as 0 °C to yield **3d**, which was converted into **4d** on silica gel in benzene. On the other hand, reaction of **2b** at 60 °C for 24 h afforded unchanged **2b** in a recovery yield of more than 90% with a small amount of unidentified products. Heating **2b** at 80 °C for 24 h afforded only dark-brownish decomposition products. In this case, the biradical generated from yne-allene cyclization may be too unstable to yield the final product.

In order to obtain insight into the mechanism of the thermal cyclization, reaction of **2a** was carried out under two conditions: one involves the reaction in the dark and the other involves the reaction under light. Reaction of **2a** in purified benzene with one equivalent of 1,4-cyclohexadiene for 24 h at 35 °C in the dark afforded **4a** in 90% yield. When the reaction of **2a** in deoxygenated THF was carried out under the same

conditions, **4a** was obtained in almost the same yield. On the other hand, the reaction of **2a** in benzene or THF, on irradiating with a 100-watt incandescent bulb, afforded only **4a** in good yields, respectively. Unfortunately compound **C** depicted in Scheme 2 was not established in the reaction mixtures obtained from these reactions.

Table 1. Thermal Cyclization Reaction of **2**.

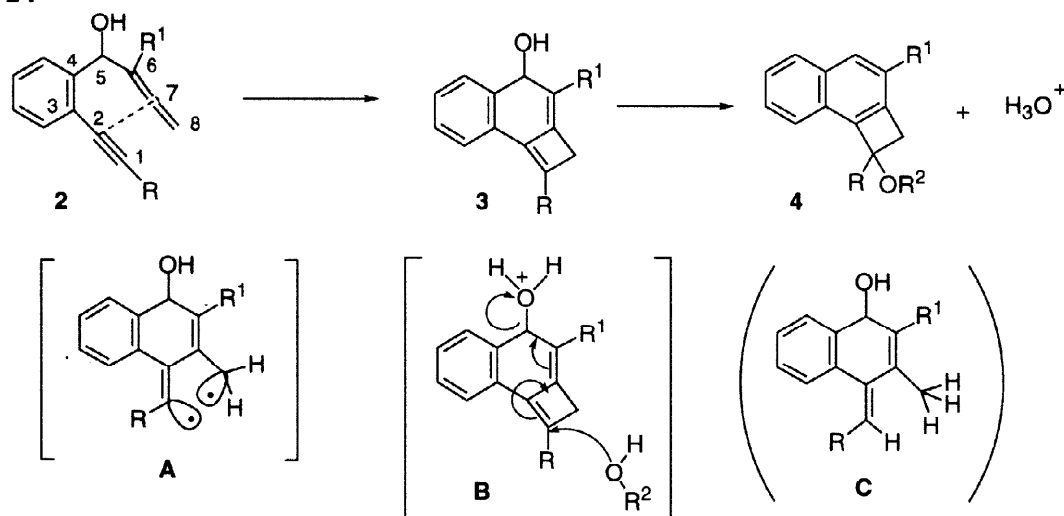


Entry	Starting material	Conditions ^{a)}		Product (%) ^{b)}
		Temp. /°C	Time/hour	
1	2a	35	24	4a (93)
2	2b	80	24	4b (n.d.) ^{c)}
3	2c	60	11	4c (79)
4	2d	0	0.5	4d (quant.)

a) Reaction of **2** in 2.5% (w/v) benzene solution was carried out in the presence of 1,4-cyclohexadiene (1 equiv.) under argon atmosphere. b) Formation of **3** was detected on TLC (silica gel, developing solvent: benzene); c) Isolated yield after treatment with silica gel chromatography. d) **4b** was not detected in the reaction mixture.

A proposed mechanism for the formation of the benzobicyclo[4.2.0]octatrienol (**3**) is presented in Scheme 2. The cyclization between the C2- and C7-positions at the initial step affords a biradical intermediate (**A**) which cyclizes to form **3**. An intermediate (**B**) formed by protonation of **3** undergoes elimination of water, aromatization and nucleophilic substitution to yield **4** as the final product. As the reaction occurs cleanly at low temperature in the dark, the cyclization reaction may be nonconcerted, involving the biradical intermediate (**A**).

Scheme 2.



In conclusion, we have found that non-conjugated aromatic enyne-allene derivatives (**2**) undergo the thermal radical cyclization to yield benzobicyclo[4.2.0]octatrienols (**3**) in excellent yields which are synthetically useful precursors for the preparation of a cyclobuta[*a*]naphthalene skeleton (**4**).

Acknowledgments

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References and Notes

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- [10] All new compounds in this paper gave satisfactory IR, NMR, Mass spectra and elementary analyses. Selected physical data are as follows: **2a**: pale yellow oil; ¹H-NMR (400MHz, CDCl₃) δ: 7.61-7.58 (m, 1H), 7.54-7.51 (m, 3H), 7.38-7.33 (m, 4H), 5.82 (ddd, 1H, *J* = 3.8, 2.3, 2.3 Hz), 5.07 (dd, 1H, *J* = 13.4, 2.2 Hz), 5.00 (dd, 1H, *J* = 13.8, 2.2 Hz), 2.68 (d, 1H, *J* = 5.4 Hz), 0.125 (s, 9H). ¹³C-NMR (100MHz, CDCl₃) δ: 212.81, 142.69, 132.06, 131.55, 128.39, 128.34, 128.24, 127.63, 126.54, 123.22, 121.27, 99.95, 96.71, 94.71, 94.38, 87.14, 79.90, 72.43, -0.23. IR (CHCl₃) ν: 3400, 2155, 1935 cm⁻¹. EIMS *m/z*: 341 (M⁺), 342 [(M+H)⁺]. HRMS (EI) *m/z*: Calcd. for C₂₃H₂₁OSi (M⁺): 341.1362. Found: 341.1362. **3d**: yellow needles; mp. 141.5-142.2 °C (from hexane). ¹H-NMR (400MHz, CDCl₃) δ: 7.75-7.73 (m, 1H), 7.65-7.63 (m, 1H), 7.56-7.54 (m, 2H), 7.42-7.35 (m, 5H), 5.38 (d, 1H, *J* = 6.5 Hz), 3.59 (d, 1H, *J* = 14.4 Hz), 3.54 (d, 1H, *J* = 14.7 Hz), 2.28 (d, 1H, *J* = 6.8 Hz), 0.253 (s, 9H). ¹³C-NMR (100MHz, CDCl₃) δ: 144.24, 144.08, 138.77, 131.69, 129.77, 129.56, 128.97, 128.49, 128.10, 125.31, 124.21, 122.75, 118.00, 108.14, 102.00, 100.89, 99.44, 85.72, 69.67, 40.03, 0.068. IR (KBr) ν: 3400, 2140 cm⁻¹. FABMS *m/z*: 366 (M⁺), 349 [(M-OH)⁺]. *Anal.* Calcd for C₂₅H₂₂OSi: C, 81.91; H, 6.05. Found: C, 81.70; H, 5.77. **4d**: pale yellow foam; ¹H-NMR (400MHz, CDCl₃) δ: 7.98 (s, 1H), 7.96 (d, 1H, *J* = 8.5 Hz), 7.83 (d, 1H, *J* = 8.3 Hz), 7.56-7.52 (t-like, 1H), 7.48-7.43 (t-like, 1H), 7.42-7.40 (m, 2H), 7.29-7.25 (m, 3H), 3.98 (d, 1H, *J* = 13.7 Hz), 3.65 (d, 1H, *J* = 13.7 Hz), 2.84 (bs, 1H), 0.283 (s, 9H). ¹³C-NMR (100MHz, CDCl₃) δ: 142.50, 140.71, 134.57, 133.38, 131.79, 129.41, 128.49, 128.21, 127.94, 126.87, 126.02, 122.36, 121.93, 117.20, 101.53, 98.00, 88.84, 84.50, 70.09, 49.65, -0.014. IR (CHCl₃) ν: 3590, 2160 cm⁻¹. EIMS *m/z*: 366 (M⁺). HRMS (EI) *m/z*: Calcd. for C₂₅H₂₂OSi, (M⁺) 366.1426. Found: 366.1440.