Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 23–26

TETRAHEDRON LETTERS

Formation of an aromatic indenide anion in a bridge-annelated [2.2]metacyclophanene: a novel and stereoselective nucleophilic addition to an acenaphthylene derivative

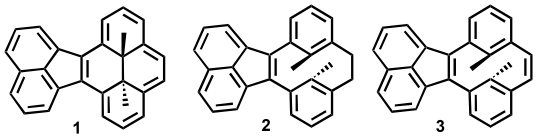
Pu Chen and Yee-Hing Lai*

Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543

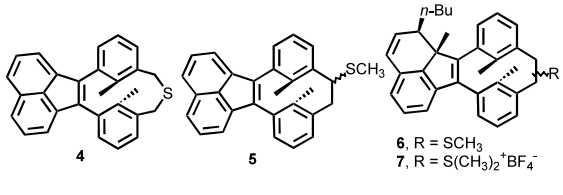
Received 1 October 2002; revised 30 October 2002; accepted 8 November 2002

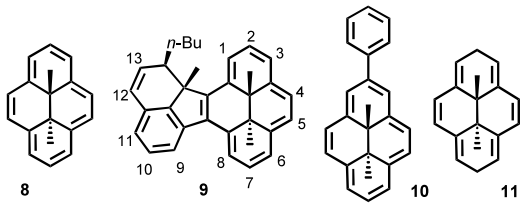
Abstract—Treatment of the acenaphthyleno-annelated thiacyclophanene **4** with *n*-butyl lithium followed by quenching with methyl iodide unexpectedly afforded the ring-contracted adduct **6**. A similar reaction between cyclophanene **2** and *n*-butyl lithium gave the adduct **14** indicating indirectly that in the former reaction the nucleophilic addition occurred after the Wittig-rearrangement of **4** to form the cyclophanene **13**. The relief of geometric strain in the [2.2]metacyclophanene moiety induced by acenaphthyleno-annelation is believed to be the driving force for the nucleophilic attack. The sulfonium salt **7** prepared by methylation of compound **6** underwent a spontaneous Hofmann-elimination, in the absence of a base, to give the intermediate cyclophanediene **18** which valence isomerized to the near-planar dihydropyrene **9**. © 2002 Elsevier Science Ltd. All rights reserved.

Nucleophilic attack on arenes being activated by the presence of a nitro group,[1–5] Lewis acid[6] or by coordination with a transition metal[7–14] is well documented. Benzene and inactivated arenes however are reluctant to undergo nucleophilic addition/substitution reactions. Nucleophilic alkylation of anthracene and phenanthrene by the anion generated from dimethyl sulfoxide have been reported.[15,16] Similar reactions of benzene and naphthalene with alkyllithiums however could only be achieved in low yields under drastic conditions.[17–19] To our best knowledge, there is no detailed report on nucleophilic addition reactions of non-alternant aromatic hydrocarbons.



The dihydropyrene **1**, synthesized by oxidation of cyclophanene **2** under photochemical conditions, failed to undergo valence isomerization to afford the cyclophanediene **3**.[20] This is attributed to unfavorable geometric strain induced in **3** due to bridge-annelation by acenaphthylene. An alternative route to **3** would be a ring contraction of thiacyclophanene **4** via a Wittig rearrangement–Hofmann elimination sequence.[21] In this communication we report a novel nucleophilic alkylation (addition) of the acenaphthylene moiety in **4**.





Keywords: acenaphthyleno-metacyclophanene; nucleophilic addition; geometric strain; indenide anion; aromatization.

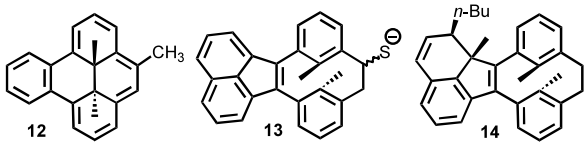
* Corresponding author. Tel.: +65-6874-2914; fax: +65-6779-1691; e-mail: chmlaiyh@nus.edu.sg

0040-4039/03/$ - see front matter © 2002 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(02)02517-0

Treatment[†] of **4** with *n*-butyllithium followed by quenching with methyl iodide gave an orange-red oil. The mass spectrum of the product indicates a molecular ion at *m*/*z* 476–72 mass units higher than that of the expected compound **5**. This could in principle correspond to an addition of a butyl and a methyl group to **5**. Additional supporting evidence is the presence of a multiplet and a singlet at δ 0.6–1.3 (9 protons) and 1.88 (3 protons), respectively, in the ^{1}H NMR spectrum of the isolated product. This is assigned the structure **6** (see later discussion on compound **14**). Methylation[‡] of **6** with dimethoxycarbonium fluoroborate unexpectedly led directly to the isolation of a thick green oil with an electronic spectrum almost identical to that of compound **8**. This is thus consistent with the presence of a dihydropyrene unit in the product. A molecular ion observed at *m*/*z* 428–48 mass units (CH_3SH) lower than that of compound **6**—which further supports the above argument and the product is thus assigned the structure **9** (the proposed stereochemistry is derived from that of **6** and **14**; see later discussion).

The well-resolved aromatic proton signals in the ^{1}H NMR spectrum of **9** (Fig. 1(a)) could be readily assigned by decoupling experiments. Assignments of H10, 11, 12 and 13 are straightforward while H9, being deshielded by the dihydropyrene ring, shifts significantly downfield. H4 and 5 should in principle be non-equivalent but they appear unresolved as a relatively broad singlet centered at δ 8.60 similar to that observed for H4 and 5 (δ 8.67)[21] in the parent molecule **8**. H2 and 7 in **9** however are resolved. The two doublets of H3 and 6 respectively overlap in the region of δ 8.4–8.7 similar to the chemical shift (δ 8.62)[21] observed for H3 and 6 in **8**. H8 in the dihydropyrene moiety in **9**, being adjacent to the benzene ring, appears as the most deshielded proton.

The internal methyl protons of **9** are partly resolved and appear highly shielded at δ –4.00 and –4.01, respectively, indicating the presence of a strong diamagnetic ring current very similar to that of **10** (δCH_3 = –4.00, –4.03).[23] Interestingly, the external methyl protons appear as a singlet at δ 1.70 shifted significantly downfield compared to the chemical shift of the methyl protons of **11** (δ 0.97).[21] The molecular structure of **9** optimized by AM1 calculations[24] (Fig. 1(b)) indicates that the three methyl groups are at similar distances from the periphery of the 14π macroring with a similar projection stereochemistry above and below the plane of the dihydropyrene moiety. It is thus believed that the external methyl protons are deshielded significantly by the ring current of the dihydropyrene. This serves as a good 'external' probe to indicate the strong diatropicity of dimethyldihydropyrene **8**. The external methyl protons in **12**[25] observed at δ 2.61 are more deshielded compared to methyl protons of toluene (δ 2.31). The benzannelated system **12** however is much less diatropic than the parent **8**.[25]



There was no reported example of a nucleophilic addition on acenaphthylenes. In our attempt, treatment of acenaphthylene with *n*-butyllithium under similar conditions followed by quenching with methyl iodide mainly returned the starting material. It would thus be interesting to determine whether the nucleophilic addition leading to the isolation of **6** occurred in the thiacyclophanene **4** or the ring contracted cyclophane

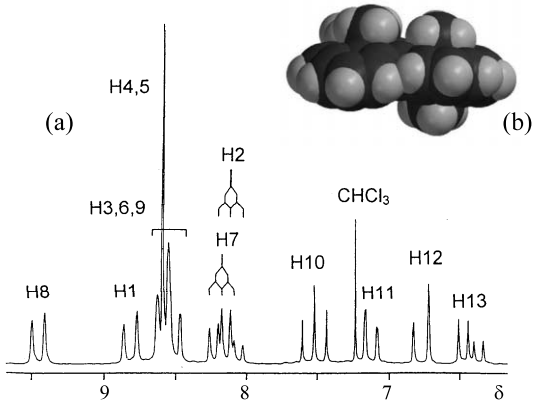
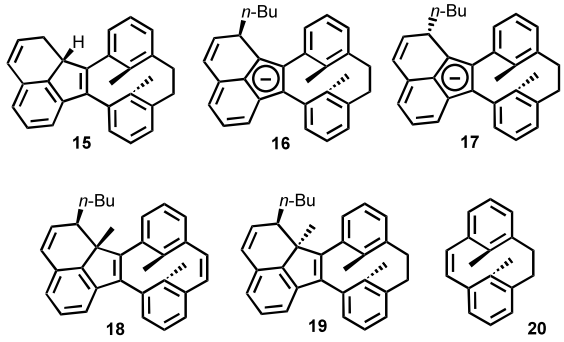


Figure 1. (a) A ^{1}H NMR spectrum of the aromatic protons of **9**. (b) The molecular structure of **9** optimized by AM1 calculations.

[†] A solution of *n*-butyllithium (3.80 mmol) in hexane was added dropwise to a solution of **4** (1.00 g, 2.56 mmol) in dry THF (50 ml) at 0°C under nitrogen. After 10 min, excess methyl iodide was added until the brown color was discharged. Water and dichloromethane were added, and the organic layer was separated, washed and evaporated. The residue was chromatographed on silica gel using hexane/dichloromethane (1:1) as eluant to yield **6** (a bright orange-red oil) as a mixture of isomers, 1.06 g (87%). ^{1}H NMR δ 6.9–7.8 (m, 9H), 6.65 (dd, 1H, J=4.7, 5.6 Hz), 6.15 (d, 1H, J=5.6 Hz), 3.6–3.9 (m, 1H), 3.16 (dd, 1H, J=1.2, 2.4 Hz), 2.6–2.8 (m, 1H), 2.19, 2.13 (s, total 3H), 1.88 (s, 3H), 0.6–1.2 (m, 10H), 0.85, 0.72 (s, total 6H); MS ($M^{\bullet+}$) *m*/*z* 476 (14), 462 (41), 413 (100), 398 (18), 357 (38), 326 (59), 163 (21). M_r calcd for $C_{24}H_{36}S$ 476.2537, found (MS) 476.2535. Anal. calcd for $C_{34}H_{36}S$: C, 85.66; H, 7.61. Found: C, 85.23; H, 7.66.

[‡] A solution of **6** (0.54 g, 1.13 mmol) in dry dichloromethane (5 ml) was added slowly to a stirred suspension of dimethoxycarbonium fluoroborate[22] (0.36 g, 2.2 mmol) in dry dichloromethane (5 ml) at –30°C under nitrogen. After the addition, the mixture was allowed to warm to rt and stirred for 2 h. Water and dichloromethane were added and the organic layer was separated, dried and evaporated. The green residue was chromatographed on silica gel using hexane as an eluant to yield **9** as a thick green oil, 82 mg (16%); ^{1}H NMR δ 9.46 (d, 1H, J=7.8 Hz), 8.83 (d, 1H, J=8.2 Hz), 8.60 (s, 2H), 8.60 (dd, 2H, J=7.0 Hz), 8.53 (d, 1H, J=7.8 Hz), 8.18 (t, 1H, J=7.6 Hz), 8.13 (t, 1H, J=7.8 Hz), 7.53 (t, 1H, J=7.4 Hz), 7.13 (d, 1H, J=7.4 Hz), 6.78 (d, 1H, J=9.8 Hz), 6.43 (dd, 1H, J=9.4 Hz, J=9.4 Hz), 1.70 (s, 3H), 0.6–1.3 (m, 10H), –4.00, –4.01 (s, 6H); MS ($M^{\bullet+}$) *m*/*z* 428 (21), 413 (100), 398 (34), 357 (47), 356 (31), 341 (35), 326 (67), 163 (49). M_r calcd for $C_{33}H_{32}$ 428.2504, found (MS) 428.2506. Anal. calcd for $C_{33}H_{32}$: C, 92.47; H, 7.53. Found: C, 92.12; H, 7.73.

13 formed after an initial Wittig rearrangement. Thus, the cyclophanene **2**[20] was treated with *n*-butyllithium followed immediately by quenching with methyl iodide.[§] The product **14** (the assigned stereochemistry will be discussed later) was obtained as pale yellow oil. A molecular ion at *m*/*z* 430 was observed in its mass spectrum supporting the addition of a butyl and a methyl group to **2** in the reaction. The above observation suggests that a Wittig-rearrangement of **4** occurred first to afford compound **13** before the nucleophilic addition took place.



Employing compound **15** as a reference, the cyclophanene **2** is estimated to have a strain energy of about 60 kJ mol^{-1} based on AM1 calculations.[24] This is believed to derive from an unfavorable geometry in the cyclophane moiety due to the annelation of the acenaphthylene unit. The driving force is to partially relieve the strain via a nucleophilic attack of the *n*-butyl anion to afford perhaps the intermediate aromatic indenide anion **16** before a methyl iodide quench resulted in the formation of product **14**. In comparison **16** is estimated to be about 8 kJ mol^{-1} more stable than its corresponding isomer **17**.[24] Even the adducts **14**, or **6**, are believed to be geometrically very favorable. This explains why the sulfonium salt **7** formed initially by methylation of **6** underwent a spontaneous elimination to give the intermediate cyclophanediene **18** which valence isomerized to the near-planar dihydropyrene **9**. This is one of very few examples of such a Hofmann-elimination, commonly used in the preparation of [2.2]metacyclophanenes or [2.2]metacyclophanedienes, observed in the absence of a base.

[§] A solution of *n*-butyllithium (0.1 mmol) in hexane was added to slowly to a solution of **2**[20] (25 mg, 0.07 mmol) in dry THF (10 ml) at 0°C under nitrogen. After 20 min, excess methyl iodide was added and the red color was discharged. The reaction mixture was then diluted with water and extracted with dichloromethane. The organic layer was separated, washed, dried and evaporated. The crude product was chromatographed on silica gel to give **14** as a pale yellow oil, 10 mg (33%). ^{1}H NMR δ 6.9–8.0 (m, 9H), 6.65 (dd, 1H, J=4.9, 5.6 Hz), 6.15 (d, 1H, J=5.6 Hz), 3.0–2.5 (m, 4H), 1.85 (s, 3H), 0.7–1.3 (m, 10H), 0.86, 0.73 (s, total 6H); MS ($M^{\bullet+}$) *m*/*z* 430 (17), 416 (34), 415 (85), 400 (13), 360 (29), 359 (100), 358 (21), 344 (25), 329 (27), 164 (12), 163 (24). Anal. calcd for $C_{33}H_{34}$: C, 92.04, H, 7.96. Found: C, 91.72; H, 7.44. Calcd for $C_{33}H_{34}$ 430.2661, found (MS) 430.2662.

The external methyl and *n*-butyl protons of **14** appear at δ 1.85 and 0.7–1.3, respectively, in its ^{1}H NMR spectrum. These data are almost identical to those observed for **6**. The chemical shifts of the external methyl protons in **6** (δ 1.88) and **14** (δ 1.85) are significantly deshielded compared to that of the methyl protons in **11** (δ 0.97).[21] The presence of an SCH_3 group in **6** results in many stereoisomers and thus **14** is used as a reference in the following discussion. The two isomers **14** and **19** could be derived from the same intermediate **16**. From their optimized structures (Fig. 2) derived from AM1 calculations,[24] **14** is estimated to be more stable by about 7 kJ mol^{-1}. The external methyl protons in **14** are in close proximity to one of the benzene rings and would be appreciably deshielded. The structures **6** and **14** are assigned accordingly (thus the structure of **9** assigned earlier). Another evidence to support the formation of only one isomer of **14** (or **6**) is the fact that only one pair of internal methyl signals at δ 0.86 and 0.73 (δ 0.85 and 0.72 for **6**) was observed similar to the chemical shift of the methyl protons in **20** (δ 0.79).[26]

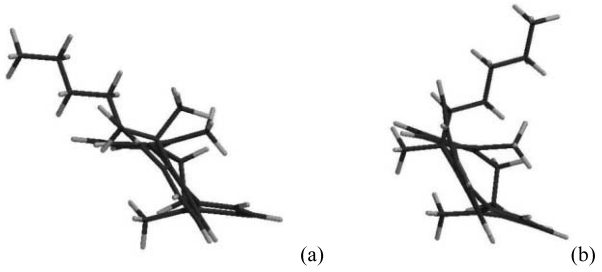


Figure 2. The molecular structures of (a) **14** and (b) **19** optimized by AM1 calculations.

[2.2]Metacyclophane, [2.2]metacyclophanene and [2.2]metacyclophanediene systems are known to sustain some degree of geometric strain. Many bridge-annelated derivatives of these compounds have also been reported. We however have shown that bridge-annelation by an acenaphthylene unit would increase the geometric strain in the cyclophane moiety of **2** significantly and this resulted in a novel and stereoselective nucleophilic addition reaction, observed for the first time in an acenaphthylene derivative. Our work has also provided a unique example **9** with methyl protons stereochemically positioned in the shielding and deshielding zone, respectively, of a strongly diatropic annulene.

Acknowledgements

This work was supported by the National University of Singapore (NUS). Assistance from the technical staff of the Chemical and Molecular Analysis Centre, Department of Chemistry, NUS, is gratefully acknowledged.

References

1. Makosza, M.; Winiarski, J. *Acc. Chem. Res.* **1987**, *20*, 282–289.
2. Chupakhin, O. N.; Charushin, V. N.; van der Plas, H. C. *Tetrahedron* **1988**, *44*, 1–34.
3. Terrier, F. In *Nucleophilic Aromatic Displacement: the Influence of the Nitro Group*; Feuer, H., Ed. Organic Nitro Chemistry Series; VCH Publishers: New York, 1991.
4. Makosza, M. *Synthesis* **1991**, 103–111.
5. Chupakhin, O. N.; Charushin, V. N.; van der Plas, H. C. *Nucleophilic Aromatic Substitution of Hydrogen*; Academic Press: San Diego, 1994.
6. Lin, J. R.; Kanazaki, S.; Kashino, S.; Tsuboi, S. *Synlett* **2002**, 899–902.
7. Miura, M.; Nomura, M. *Top. Curr. Chem.* **2002**, *219*, 211–241.
8. Koo, S. H.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1995**, *117*, 3389–3404.
9. *New Applications of Organometallic Reagents in Synthesis*; Seyferth, D., Ed.; Elsevier: New York, 1976; Vol. 1, pp. 361–395.
10. *Transition Metal Organometallics in Organic Synthesis*; Alper H., Ed.; Academic Press: New York, 1978; Vols. I and II.
11. Lai, Y.-H.; Tam, W.; Vollhardt, K. P. C. *J. Organomet. Chem.* **1981**, *216*, 97–103.
12. Semmelhack, M. F.; Clark, G. R.; Garcia, J. L.; Harrison, J. J.; Thebtaranonth, Y.; Wulff, W.; Yamashita, A. *Tetrahedron* **1981**, *37*, 3957–3965.
13. Pearson, A. J. *Metallo-Organic Chemistry*; Wiley-Interscience: New York, 1985.
14. Semmelhack, M. F. *Organometallics in Synthesis: A Manual*; Schlosser, M., Ed. Organoiron and Organochromium Chemistry. John Wiley-VCH: Chichester, 2002.
15. Russell, G. A.; Weiner, S. A. *J. Org. Chem.* **1966**, *31*, 248–251.
16. Nozaki, H.; Yamamoto, Y.; Nisimara, T. *Tetrahedron Lett.* **1968**, *9*, 4625–4626.
17. Dixon, J. A.; Fishman, D. H. *J. Am. Chem. Soc.* **1963**, *85*, 1356–1357.
18. Dixon, J. A.; Fishman, D. H.; Dudinyak, R. S. *Tetrahedron Lett.* **1964**, *5*, 613–616.
19. Eppley, R. L.; Dixon, J. A. *J. Am. Chem. Soc.* **1968**, *90*, 1606–1612.
20. Lai, Y.-H.; Chen, P.; Dingle, T. W. *J. Org. Chem.* **1997**, *62*, 916–924.
21. Mitchell, R. H.; Boekelheide, V. *J. Am. Chem. Soc.* **1974**, *96*, 1547–1557.
22. (a) Borch, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5303–5305; (b) Borch, R. F. *J. Org. Chem.* **1969**, *34*, 627–629.
23. Mitchell, R. H.; Chaudhary, M.; Dingle, T. W.; Williams, R. V. *J. Am. Chem. Soc.* **1984**, *106*, 7776–7779.
24. AM1 calculations were performed using the commercial Spartan 5.1.3 software.
25. Mitchell, R. H.; Yan, J. S. H.; Dingle, T. W. *J. Am. Chem. Soc.* **1982**, *104*, 2560–2571.
26. Blaschke, H.; Ramey, C. E.; Calder, I.; Boekelheide, V. *J. Am. Chem. Soc.* **1970**, *92*, 3675–3681.