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# Reaction of Benz[a]azulene with Dimethyl Acetylenedicarboxylate. Formation of a π-Bond Fixed Heptalene Derivative

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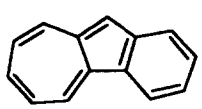
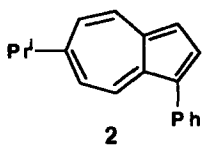
*Abstract:* Reaction of benz[a]azulene with dimethyl acetylenedicarboxylate (DMAD) in tetralin at 200 °C gave a new π-electron system, dimethyl benzo[a]heptalene-6,7-dicarboxylate and dimethyl indeno[1,2,3-cd]azulene-5,6-dicarboxylate. The reaction of a non-fused azulene, 6-isopropyl-1-phenylazulene, gave extremely different results indicating strong effects of the fused benzene ring on the reactivities of azulenes with DMAD. Coupling constants of the protons on the seven-membered ring and variable temperature $^1$H NMR of the heptalene indicated π-bond fixation of the molecule.

Since the azulene ring of benz[a]azulene (**1**) is well-known to be strongly perturbed by the fused benzene ring,[1] it is very interesting to know the reactivities of such perturbed azulene ring with various reagents. In spite of fundamental significance of benz[a]azulene as a fused azulene, reactions of **1** have been little studied because of its synthetic difficulties.[2] Recently, we have found an efficient synthetic method of **1**[3] by the application of our new azulene synthetic method.[4]

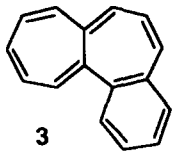
The reactions of non-fused azulenes with dimethyl acetylenedicarboxylate (DMAD) have been widely studied in non-polar solvents[5] or in polar solvents in the presence of ruthenium catalyst.[6] Only two examples have been known on the reaction of fused azulenes with the reagent.[7] Recently, the reaction of **1** with DMAD in the presence of ruthenium catalyst was reported to form a small amount of unstable [8+2] adduct and a trace of



**1**




**2**



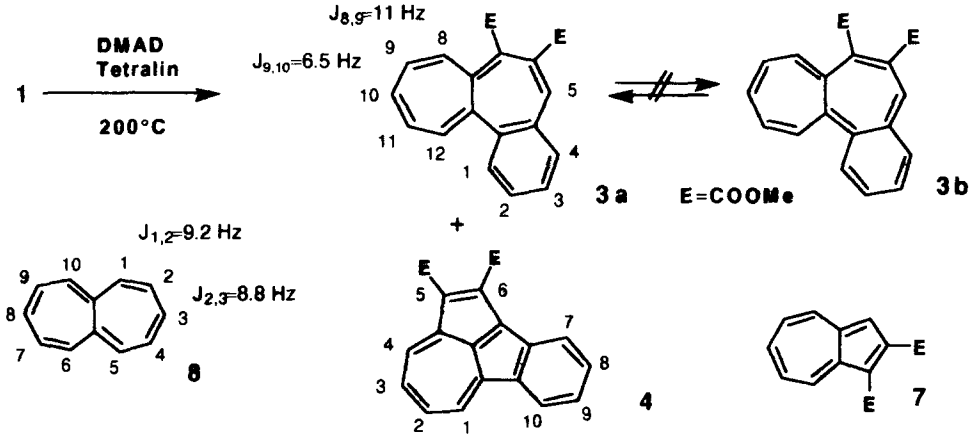
**3**

indenoazulene derivative.[6c] As a series of studies on the reactivities of **1**, we carried out the reaction of **1** with DMAD to form a benzo[a]heptalene derivative (**3a**) as a major product and found that the results were extremely different from those of the above report.[6c] To know specificity of fused azulene (**1**) on the reaction with DMAD, the reaction of a non-fused azulene, 6-isopropyl-1-phenylazulene (**2**), with DMAD under the same conditions was also studied. These results are reported here together with discussion on the structure of a new π-electron system, benzo[a]heptalene (**3**).

A solution of **1** (200 mg, 1.1 mmol) with DMAD (234 mg, 1.65 mmol) in tetralin (10 ml) was heated at 200 °C for 1 h. After being cooled to room temperature, the reaction mixture was charged on an alumina column and eluted with hexane to remove the solvent. Then, all the products were eluted out with ethyl acetate.

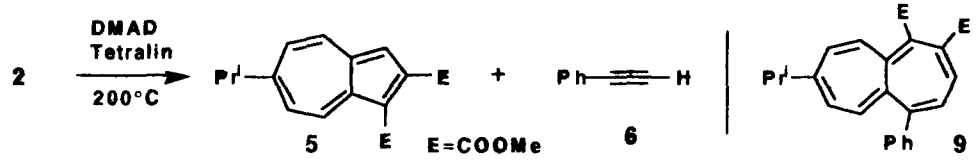
Isolation of the products with reversed phase preparative HPLC (ODS, 70% aqueous MeCN) gave a new π-electron system, dimethyl benzo[a]heptalene-6,7-dicarboxylate (**3a**)[8] (190 mg, 54% yield) and dimethyl indeno[1,2,3-cd]azulene-5,6-dicarboxylate (**4**)[9,10] (14.5 mg, 4.1%) (Scheme 1). All spectral data and results of elementary analyses of **3a** and **4** were consistent with the assigned structures. It is noteworthy that no formation of a dimethyl azulene-1,2-dicarboxylate derivative (**7**) was observed in this reaction.

**Scheme 1**




To compare the reactivities of **1** with non-fused azulene derivatives, the reaction of 6-isopropyl-1-phenylazulene (**2**)[11] with DMAD was carried out. The reaction of **2** (600 mg, 2.44 mmol) with DMAD (527 mg, 3.71 mmol) in tetralin (10 ml) under the same conditions gave dimethyl 6-isopropylazulene-1,2-dicarboxylate (**5**)[12] (250 mg, 36% yield) as a sole product together with recovered **2** (34%) (Scheme 2). Eliminated phenylacetylene (**6**) was detected by HPLC (retention time 1.60 min on an ODS column, 4.6 x 150 mm, 70% MeCN, flow rate 2 ml, monitored by 254 nm). No formation of heptalene derivatives such as **9** was observed in this reaction.

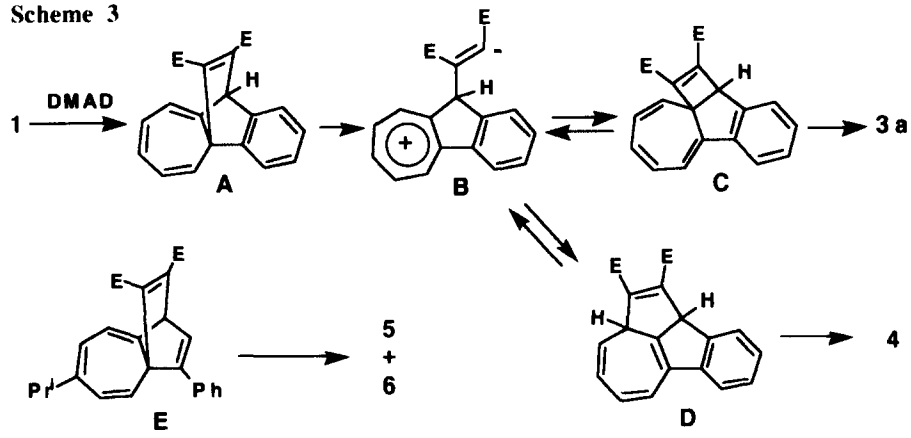
**Scheme 2**




Thus, it was found that benz[a]azulene (**1**) reacts with DMAD to give preferentially the heptalene derivative (**3a**) in a different mode from that of non-fused azulene (**2**). Reaction mechanism is considered to be almost the same as heptalene formation from azulene[5b] as follows (Scheme 3). Thus, the formation of an [8+2] cyclo-adduct (**A**) is supported on the consideration of orbital symmetry on the HOMO of **1** and the LUMO of DMAD.[13] The extreme different reaction mode of **1** form **2** seemed to be caused by difficult elimination of a highly strained molecule, benzyne, from an initially formed cyclo-adduct (**A**). Therefore, the intermediate (**A**) rearranged to another intermediate (**C**) through a dipolar intermediate (**B**). The intermediate (**C**) should be isomerized to **2** in the same manner proposed for the heptalene formation from azulene.[5b] The indenoazulene derivative (**4**) seemed to be formed by oxidation of an intermediate (**D**). On the other hand, the [8+2] intermediate (**E**) formed on the reaction of **2** with DMAD should eliminate easily stable phenylacetylene (**6**) to form **5** as a sole product.

It is well-known that the coupling constants of the vicinal ring protons of heptalene (**8**) (Scheme 1) are almost equal[14] because of its existence as an equilibrium mixture of bond isomers.[15] On the $^1$H NMR of **3a**, a large difference was observed in coupling constants between vicinal protons, H-8, H-9 ($J_{8,9}$ =11Hz) and H-9, H-10 ($J_{9,10}$ =6.5 Hz) (Scheme 1). This fact suggests that clear bond alternation is caused on the heptalene unit by the fused benzene ring to avoid an *o*-quinonoid structure (**3b**), that is, **3a** exists as a π-bond fixed structure (**3a**). Variable temperature $^1$H NMR of **3a** did not show significant spectral changes over the temperature range of -50 °C to +50 °C supporting above structure assignment.[16]

**Scheme 3**

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3. Benz[a]azulene was synthesized in high yield by simultaneous removal of both substituents from 3-t-butyl-10-formylbenz[a]azulene by the treatment with 100% phosphoric acid at 140°C. The precursor was synthesized by the application of our new azulene synthetic reaction (ref. 4): Yasunami, M; Shinba, M; Sato, T; Yoshifuji, M; Takase, K. to be published.
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7. a) With cyclopent[cd]azulene: Diehl, H. and Hafner, K. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 107-108 b) With aceheptylene: Hafner, K.; Diehl, H.; Richarz W. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 108-109.
8. **3a:** Yellow micro crystals (Hexane-AcOEt), mp 152 °C; MS (DEI, 70 eV) *m/z* 320($M^+$, 100%); UV-Vis (MeOH) 220 nm(log ε 4.25), 254(4.03 sh), 276(4.20), 339(3.48 sh); IR ($CHCl_3$) 3030, 3010, 2952, 1722, 1718, 1435 $cm^{-1}$; $^1H$ NMR(600 MHz, $CDCl_3$) δ=3.67(3H, s, COOMe-7), 3.76(3H, s, COOMe-6), 6.09(1H, d, J=6.5 Hz, H-12), 6.25(1H, d, J=11.0 Hz, H-8), 6.43(1H, dd, J=11.0 and 6.5 Hz, H-9), 6.64(1H, dd, J=11.0 and 6.5 Hz, H-10), 6.68(1H, dd, J=11.0, and 6.5 Hz, H-11), 7.01(1H, d, J=7.5 Hz, H-1), 7.37(1H, d, J=8.0 Hz, H-4), 7.40(1H, dd, J=8.0 and 8.0 Hz, H-3), 7.45(1H, dd, J=8.0 and 7.5 Hz, H-2), 8.01(1H, s, H-5); $^{13}C$ NMR(150 MHz, $CDCl_3$) δ=51.62(COOMe-7), 52.27(COOMe-6), 121.16(C-7), 125.02(C-8), 128.47(C-3), 128.86(C-9), 129.79(C-1), 130.10(C-12), 130.40(C-4), 130.94(C-6), 131.52(C-2), 131.63(C-11), 131.73(C-10), 133.15(C-12a), 135.16(C-4a), 141.22(C-12b), 142.57(C-5), 146.31(C-7a), 166.82 (COOMe-7), 167.81(COOMe-6).
9. Only $^1H$ NMR data were reported by Rippert and Hansen consisting our results: ref. 6c.
10. **4**: Dark green needles (AcOEt), mp 188-190 °C; MS(DEI, 70 eV) *m/z* 318($M^+$, 100%); UV-Vis(MeOH) 212 nm(log ε 4.35), 277(4.27), 337(3.86 sh), 353(3.92), 386(3.59 sh), 447(3.50 sh), 657(2.63); IR(KBr) 1738, 1684, 1452, 1200 $cm^{-1}$; $^1H$ NMR(600 MHz, $CDCl_3$) δ=3.97(3H, s, COOMe-5), 4.11(3H, s, COOMe-6), 7.24(1H, dd, J=7.5 and 7.5 Hz, H-9), 7.44(1H, dd, J=7.5 and 7.5 Hz, H-8), 7.62(1H, d, J=7.5 Hz, H-7), 7.94(1H, d, J=7.5 Hz, H-10), 8.01(1H, dd, J=10.0 and 9.5 Hz, H-3), 8.26(1H, dd, J=10.0 and 9.2 Hz, H-2), 8.33(1H, d, J=9.2 Hz, H-1), 9.33(1H, d, J=9.5 Hz, H-4).$^{13}C$ NMR(150 MHz, $CDCl_3$) δ=51.51(COOMe-5), 52.60(COOMe-6), 118.00(C-10a or C-6a), 120.76(C-5,7), 123.26(C-10), 124.21(C-1), 124.85(C-9), 130.38(C-6a or C-10a), 131.27(C-8), 131.57(C-3), 138.92(C-6b, C-10c), 139.12(C-4), 139.41(C-2), 139.91(C-10b*), 141.13(C-4a*), 146.93(C-6*), 164.71(COOMe-5), 167.25(COOMe-6). * These signals are not determined.
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12. **5**: Violet needles (hexane), mp 69-70 °C; MS(DEI, 70 eV) *m/z* 286 ($M^+$, 90%), 255(100), 239(16), 228(19), 153(19), 115(19); IR(KBr) 2954, 1724, 1693, 1442, 1421, 1402, 1344, 1226, 1199 $cm^{-1}$; $^1H$ NMR(200 MHz, $CDCl_3$) δ=1.35(6H, d, J=6.9 Hz, $Pr^i$-Me), 3.11(1H, sept, J=6.9 Hz, $Pr^i$-CH), 3.95(3H, s, COOMe), 3.97(3H, s, COOMe), 7.37(1H, d, J=10 Hz, H-5), 7.39(1H, s, H-2), 7.47(1H, d, J=10.6 Hz, H-7), 8.37(1H, d, J=10 Hz, H-4), 9.33(1H, d, J=10.6 Hz, H-8); $^{13}C$ NMR(50 MHz, $CDCl_3$) δ=24.09($Pr^i$-Me), 39.86($Pr^i$-CH), 51.53(1-COOMe), 52.27(2-COOMe), 115.08(C-1), 117.70(C-3), 126.49(C-5), 138.70(C-6), 139.39(C-7), 140.08(C-2), 140.21(C-4), 140.84(C-3a, 8a), 163.98(C-8), 165.30(1-COOMe), 167.74(2-COOMe).
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