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Reactions of a Novel Benzyne Annelated with Two Bicyclo[2.2.2]octene Units

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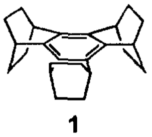
Abstract: Anthranilic acid **9** and *o*-dibromobenzene **14** annelated with two bicyclo[2.2.2]octene units were synthesized as the precursors for titled benzyne **3**. The generation of **3** was confirmed by trapping with furan and its derivative. In the absence of trapping agent, benzyne **3** generated by diazotization of **9** gave acridone **12** while that generated via lithiation of **14** dimerized to give BCO-annelated biphenylene **11**. The HOMO level of **11** is considerably raised as shown by cyclic voltammetry. © 1997 Elsevier Science Ltd.

Benzyne has been playing an important role as reactive intermediate in organic chemistry. Among its wide variety of reactions,[1] cycloaddition is particularly useful for construction of additional carbon skeletons. For example, cycloaddition to furan or pyrrole derivatives followed by elimination of the oxygen or nitrogen bridges has been proved as an excellent method for the synthesis of highly substituted polycyclic arenes.[2]

In the previous studies, we have synthesized benzenoid aromatics annelated with bicyclo[2.2.2]octene (abbreviated as BCO) frameworks such as **1**[3] and **2**.[4] It has been found that cationic species derived from **1** and **2** are remarkably stabilized by inductive and hyperconjugative effects, in addition to steric protection, by bicyclic σ-frameworks surrounding the π-systems.[3,4]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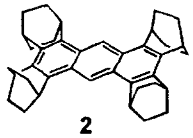
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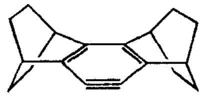
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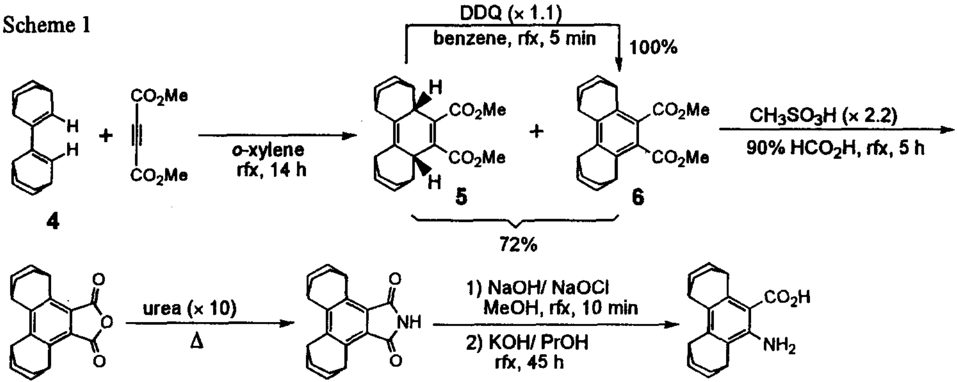
BCO-annelated benzyne **3** is expected as a versatile species for preparation of wider variety of polycyclic arenes having BCO frameworks, and its reactivity is of great interest. Here we report its generation and reactions.

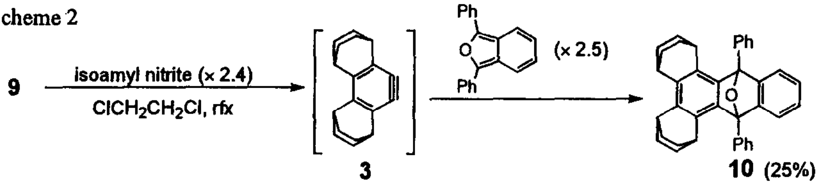
We first chose anthranilic acid **9** as the precursor for BCO-annelated benzyne **3**. The Diels-Alder reaction of **4**[5] with dimethyl acetylenedicarboxylate in refluxing *o*-xylene afforded a mixture of adduct **5** and dimethyl phthalate **6**. Adduct **5** was smoothly dehydrogenated by DDQ in refluxing benzene to give **6** quantitatively. Hydrolysis of **6** under acidic conditions afforded phthalic anhydride **7** as white precipitates, which were in turn heated with excess urea to give phthalimide **8**. Hofmann rearrangement of **8** followed by hydrolysis of the resulting urethane produced desired anthranilic acid **9**[6] (Scheme 1).

Scheme 1



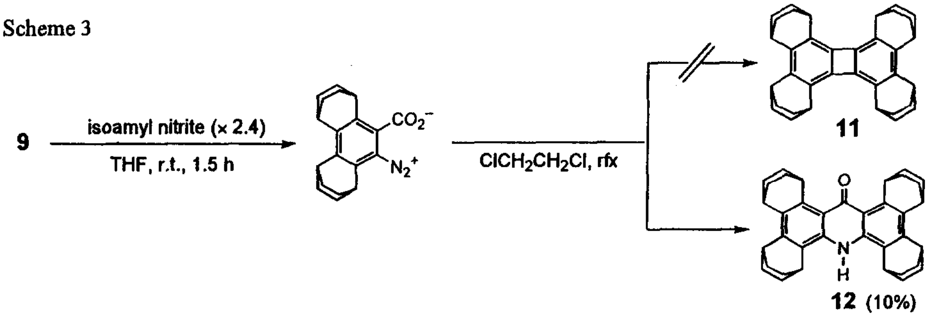
Diazotization of **9** by isoamyl nitrite in refluxing 1,2-dichloroethane in the presence of 2,5-diphenylisobenzofuran gave [4+2] adduct **10**,[7] which is the clear evidence for the generation of benzyne **3** (Scheme 2).

Scheme 2



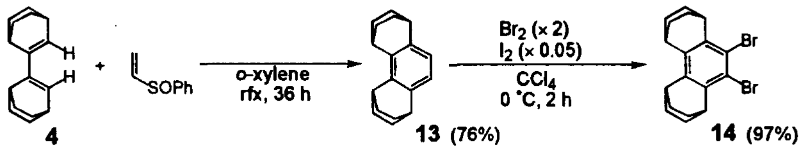
It is well-known that benzyne dimerizes to give biphenylene in the absence of trapping agents.[8] However, when compound **9** was diazotized in THF, and the resultant diazonium carboxylate was added to refluxing 1,2-dichloroethane, no detectable amount of biphenylene **11** was obtained. Instead, acridone **12**[9] fully annelated with BCO units was obtained as the only identified product in 10% yield (Scheme 3). Presumably, **12** arose from the reaction of benzyne **3** with unreacted anthranilic acid **9**.[10]

Scheme 3



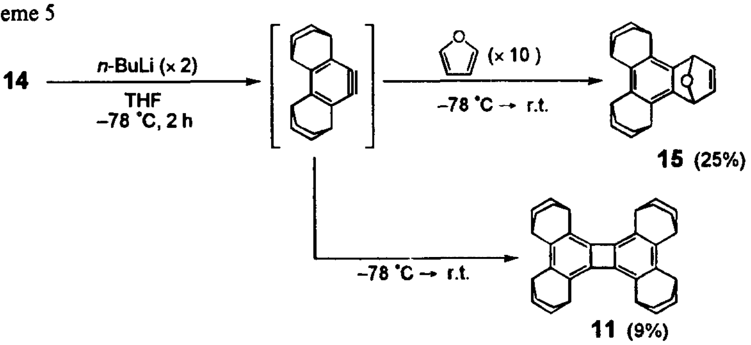
Besides anthranilic acids, *o*-dihalobenzenes have also been used for the benzyne precursors owing to their ready availability,[1] and *o*-dibromobenzene annelated with two BCO units **14** should be another source of benzyne **3**. As outlined in Scheme 4, the Diels-Alder reaction of **4** with phenyl vinyl sulfoxide[11] in refluxing *o*-xylene afforded bis-BCO-annelated benzene **13**.[12] Previously, we reported that tris-BCO-annelated benzene **1** exhibits a well-defined reversible oxidation wave at $E_{1/2}$ = +1.25 V vs Ag/Ag$^+$ upon cyclic voltammetry in acetonitrile.[3] In contrast, benzene **13** exhibited no oxidation wave under the same conditions. Bromination of **13** in carbon tetrachloride at 0 °C with a catalytic amount of iodine gave desired *o*-dibromobenzene **14**.[13]

Scheme 4



Treatment of **14** with two equivalents of butyllithium in the presence of excess furan gave adduct **15**,[14] and afforded biphenylene **11**[15] in the absence of diene (Scheme 5).

Scheme 5



The remarkable effect of BCO annelation upon the HOMO level of **11** was observed in its redox behavior. Previously, 1,2,3,4,5,6,7,8-octamethylbiphenylene has been reported to show only one reversible oxidation wave at $E_{1/2}$ = +0.78 V vs SCE in acetonitrile [16](calibrated to +0.40 V vs Fc/Fc$^+$ [17]). Compared to this, compound **11** exhibited a well-defined reversible oxidation wave at $E_{1/2}$ = +0.33 V vs ferrocene /ferricenium and an irreversible one at +1.03 V upon cyclic voltammetry in *o*-dichlorobenzene (Fig. 1). This fact indicates that **11** can yield a stable cation radical and a less stable dication upon consecutive oxidation. In fact, oxidation of **11** by NO$^+$SbCl$_6^-$ in dichloromethane gave a blue-violet solution, which exhibited an ESR spectrum composed of nine lines with relative intensities proportional to the coefficients in the binomial expansion (a_{H} = 0.12 mT, g = 2.003). This is supposedly due to the coupling of eight anti-protons[3] of the methylene bridge connected to the 2,3,6,7-positions of the biphenylene π-system.[16,18] After evaporation of the solvent, a blue solid was obtained, which was considered as cation radical salt **11**$^{+\bullet}$SbCl$_6^-$ since it provided the essentially same ESR spectrum upon dissolution in dichloromethane.

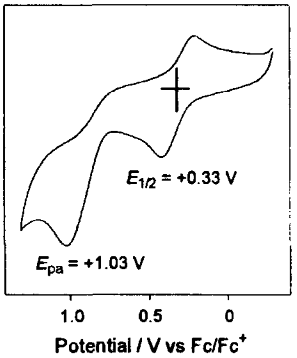


Fig. 1. Cyclic voltammogram of **11** in *o*-dichlorobenzene with Bu$_4$ClO$_4$ as a supporting electrolyte; scan rate. 0.1 V s^{-1}

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6. **9**: pale yellow solid; mp 203–206 °C (dec); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.84 (br, COOH), 3.60 (br s, 1H, CH), 3.32 (br s, 2H, NH_2), 3.28 (br s, 1H, CH), 3.23 (br s, 1H, CH), 3.19 (br s, 1H, CH), 1.68 (br m, 8H, CH_2), 1.21 (br m, 8H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.1, 141.6, 141.2, 140.1, 126.9, 124.9, 110.2, 31.2, 30.9, 28.4, 27.6, 26.4, 26.3, 25.6, 25.5; IR (KBr) ν_{max} 3473 (NH), 3368 (NH), 3000–2400 (br, CO_2H), 1655 (CO); HRMS calcd for $C_{19}H_{23}NO_2$ 297.1729, found 297.1716.
7. **10**: white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, 4H, Ar-H), 7.48 (dd, 2H, Ar-H), 7.47–7.40 (m, 6H, Ar-H), 7.07 (dd, 2H, Ar-H), 3.19 (br s, 2H, CH), 2.74 (br s, 2H, CH), 1.80–0.76 (br m, 16H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 141.5, 136.2, 135.8, 134.5, 129.8, 128.9, 128.3, 125.2, 121.8, 91.8, 29.3, 28.6, 26.2, 26.0, 25.3, 24.6; HRMS calcd for $C_{38}H_{34}O$ 506.2610, found 506.2631.
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9. **12**: pale yellow solid; mp > 400 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (br s, 1H, NH), 5.19 (br s, 2H, CH), 3.47 (br s, 2H, CH), 3.39 (br s, 2H, CH), 3.36 (br s, 2H, CH), 1.98–1.72 (br m, 16H, CH_2), 1.53–1.22 (br m, 16H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.1, 143.0, 142.9, 133.1, 132.4, 123.8, 115.9, 29.2, 28.9, 28.6, 27.7, 26.3, 26.0, 25.9, 25.6; IR (KBr) ν_{max} 3440 (NH), 1611 (CO); HRMS calcd for $C_{37}H_{41}NO$ 515.3188, found 515.3207.
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12. **13**: colorless crystal; mp 136–137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95 (s, 2H, Ar-H), 3.29 (br s, 2H, CH), 2.96 (br s, 2H, CH), 1.77 (br m, 8H, CH_2), 1.37 (br m, 8H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 137.7, 120.3, 34.4, 28.5, 26.4 (overlapped signals); MS *m/z* 238 (M^+)
13. **14**: colorless crystal; mp 176–178 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (br s, 2H, CH), 3.32 (br s, 2H, CH), 1.77 (br m, 8H, CH_2), 1.40 (br m, 4H, CH_2), 1.30 (br m, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 138.8, 119.0, 35.2, 29.1, 25.7, 25.2; MS *m/z* 394, 396, 398 (M^+)
14. **15**: white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (s, 2H, =CH–), 5.83 (s, 2H, CH), 3.21 (br s, 2H, CH), 3.08 (br s, 2H, CH), 1.76 (br m, 8H, CH_2), 1.50 (br m, 2H, CH_2), 1.34 (br m, 6H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 138.0, 134.0, 133.8, 80.7, 30.8, 28.5, 26.3, 26.03 (overlapped signals), 25.98; MS *m/z* 304 (M^+).
15. **11**: colorless crystal; mp > 400 °C; UV (CH_2Cl_2) λ_{max} 364 nm (log ε 3.75), 345 (3.64), 330 (3.32), 263 (4.54); ^{1}H NMR (300 MHz, CS_2–$CDCl_3$) δ 3.00 (br s, 4H, CH), 2.81 (br s, 4H, CH), 1.73 (br m, 16H, CH_2), 1.47 (br m, 8H, CH_2) 1.38 (br m, 8H, CH_2); ^{13}C NMR (75 MHz, CS_2–$CDCl_3$) δ 140.4, 136.6, 131.0, 31.3, 28.7, 26.4, 26.0; MS *m/z* 472 (M^+)
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