

비대칭적으로 삼고리화된 벤젠의 합성

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Synthesis of Unsymmetrical Trisannelated Benzenes

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요 약. 2,3,4,5,6,7,8,9,10,11-데카하이드로-1H-사이클로펜타[*l*]페난트렌 (**1c**)과 1,2,3,4,5,6,7,8,9,10-데카하이드로사이클로헥사[*e*]-*as*-인다센 (**1d**) 같이 비대칭적으로 삼고리화된 벤젠을 합성하였다. 합성의 접근방법으로 사이클로펜탄온과 사이클로헥산온의 존재하에 무수 CuCl_2 를 촉매로 사용하여 미리 형성된 바이사이클로헥실리덴-2-온 (**3**), 바이사이클로헥실-1'-엔-2-온 (**4**) 과 바이사이클로펜틸리덴-2-온(**5**) 같은 엔온들의 효율적인 축합 반응을 사용하였다.

주제어: 삼고리화된 벤젠, 무수 CuCl_2

ABSTRACT. Synthesis of unsymmetrical trisannelated benzenes such as 2,3,4,5,6,7,8,9,10,11-decahydro-1H-cyclopenta[*l*]phenanthrene (**1c**) and 1,2,3,4,5,6,7,8,9,10-decahydrobenz[*e*]-*as*-indacene (**1d**) is described. The synthetic approach involves efficient condensation of pre-formed enones such as bicyclohexyliden-2-one (**3**), bicyclohexyl-1-en-2-one (**4**) and bicyclopentyliden-2-one (**5**) in the presence of cyclopentanone and cyclohexanone using anhydrous CuCl_2 as a catalyst.

Keywords: unsymmetrical trisannelated benzene, anhydrous CuCl_2

Copper (II) chloride (CuCl_2) is often utilized as an electron transfer oxidative reagent¹ and can also participate in the self-condensation of ketones.² In this report, the condensation of ketones such as cyclopentanone and cyclohexanone in the presence of unsaturated ketones such as **3**, **4** and **5** in the presence of a catalytic amount of anhydrous CuCl_2 was considered. These reactions lead to the preparation of **1a** (Trindan), **1b** (DTP), **1c** and **1d** (Fig. 1).

It has been noted that the presence of **1a** and **1b** in nylon 66 produce a fluorescence emission.³ The photochemical properties of many films such as phthalate and siloxan, have been modified by the

addition of a few percent of DTP **1b** in their composition.⁴ While the condensation approach has been used in the preparation of **1a** and **1b** (which have identical-sized rings about the core benzene), no communications for the preparation of **1c** and **1d** (which have different-sized rings about

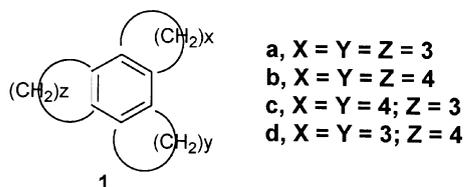


Fig. 1.

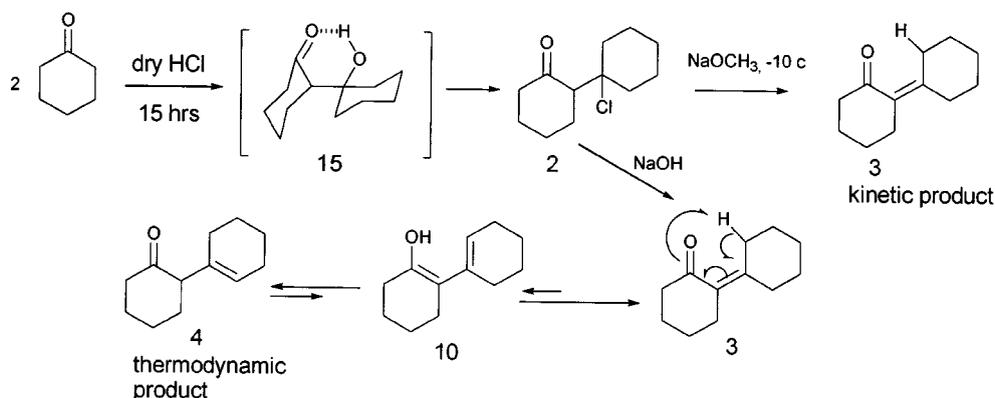


Fig. 2.

the benzene) have been reported.^{5,6} Therefore, synthesis of unsymmetrical-trisannellated benzenes such as **1c** and **1d** is an active area of investigation. Several approaches to the synthesis of symmetrical and unsymmetrical trisannellated benzene have been described.^{7,8} However, all of those methods involve either multiple steps or use very unstable starting materials.⁹⁻¹³ The major modification between our adopted strategy vs. other reported sequences is the occurrence of a facile initial condensation to form **3**, **4** or **5** followed by the establishment of the two other cycles (benzene and the third annealed cycle) late in the sequence. For the synthesis of **1c** and **1d**, the preparation and characterization of the α , β and β , γ -unsaturated ketones **3**, **4** (Fig. 2) and **5** (Fig. 3) was accomplished. Byproduct **6**, was obtained as a trace in the Claisen condensation of cyclopentanone (Fig. 3). The unsaturated ketone **3** formed as a kinetic product from reaction of NaOCH₃ over chloro-ketone **2** at -10°C. The chloro-ketone **2** in order was prepared from acid condensation of cyclohexanone presumably, via constructive β -hydroxy-ketone **15**. In the other experiment the chloro-ketone **2** reacted with 2N NaOH to offer unsatur-

ated ketone **3**, further reaction of **3** throughout the suprafacial [1,5]-H sigmatropic rearrangement via enol intermediate **10** mostly intend to convert to the unsaturated ketone **4** as a thermodynamic product (Fig. 2).

Because of unfavorable strained geometry of [1,5]-H sigmatropic rearrangement for cyclopentanone, practically only compound **5** and **6** were formed and separated. From PTLC (Fig. 3). Subsequently, these unsaturated ketones were treated with cyclopentanone or cyclohexanone in the presence of a catalytic amount of anhydrous CuCl₂. The mechanism of the trimerization reaction of ketones was examined by comparison of the separate reactions of cyclohexanone with **3** or **4** and with **5**.

The fact that both experiments lead to a successful synthesis of **1b** and **1a**, suggests that the mechanism of preparation of **1c** and **1d** also reasonably goes through a similar sequence such as that depicted in Fig. 4. The enol **10** further reacted with other molecule of cyclopentanone to give unstable keto-alcohol **11**. Dehydration of **11** leads to the preparation of unsaturated ketone **12**. The favorable concerted [1,7]-H rearrangement of **12** leads to the formation of trienol **13**. Pericyclic reaction after dehydration of **14** leads to the synthesis of **1c** (Fig. 4).

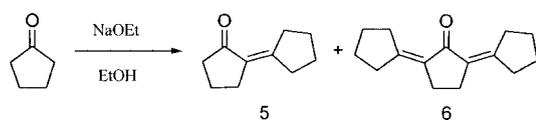


Fig. 3.

3 or 4+Cyclohexanone→1b DTP

5+Cyclohexanone→1a Trindan

The di- and tri-anions of these transannellated benzene, have been used as the ligands in the

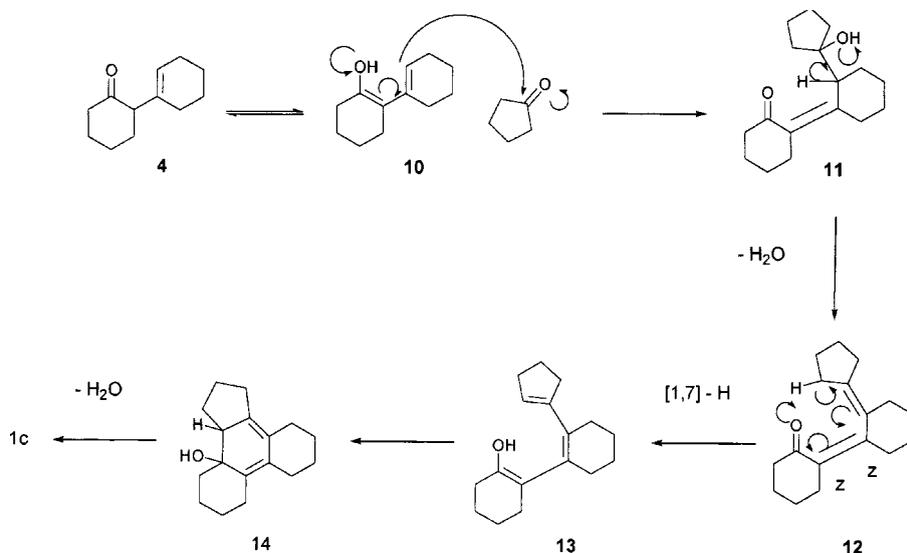
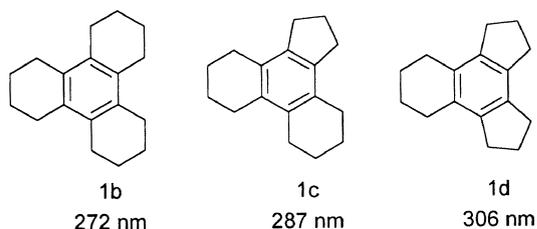


Fig. 4. Mechanism for trisannulation.

preparation of sandwich complexes with transition-metals.¹⁴

Previous UV studies have proved the effect of angularly annealed strained rings upon the aromaticity of benzene by examining the structures of **1a**, 1,2,3,4,5,6,7,8-octahydrocyclobuta[*e*]-as-indacene **7**, 1,2,3,4-dicyclobuta[5,6]cyclopentabenzene **8** and 1,2,3,4,5,6-hexahydrotricyclobuta[*a,c,e*]benzene **9** (Fig. 5).⁶ The alternating bond lengths of **9** were found to be negligible (less than 0.025 Å) and it was concluded that the benzene ring remains aromatic.¹⁵ The ultraviolet spectra of trisannulated benzenes **1b**, **1c** and **1d** (recorded in ethyl acetate) are particularly interesting. There is a general increase in λ_{\max} with an increase in the number of 5-membered annulated rings attached to the benzene rings as long as at least one of the annulated rings is still 6-membered (Fig. 6).

Fig. 5. All λ_{\max} (nm) recorded in isoctane except 9 which was recorded in (95%) ethanol.Fig. 6. λ_{\max} (nm) in EtOAc.

Experimental

Yields refer to isolated pure center cut from column chromatography or to the main band scratched from preparative TLC plate. Products were characterized by comparison with authentic sample (IR, NMR, GC, TLC, and mp). Melting points are uncorrected and determined by Mettler Fp5 melting point apparatus. IR spectra were obtained on a Shimadzu IR-470. All NMR data were recorded in CDCl_3 on Bruker 80 MHz and Bruker Avance 500-MHz spectrometers, the latter used particularly for ^{13}C NMR of **1c** and **1d**. [These samples gave 17 and 16 peaks, respectively, while one would predict 9 and 8 peaks, due to their possession of a C2 axis. The increase in the number of peaks may be some subtle conformational issue at play.]

TMS was used as an internal reference. High-resolution mass spectra were obtained from a Fisons Trio-1000 instrument.

2-(1-chlorocyclohexyl) cyclohexanone 2. Dry hydrogen chloride was bubbled through cyclohexanone (40 g, 42.2 mL, 476 mmol) contained in a water-cooled flask. After 15 hr the gas flow was stopped and the crystalline 2-(1-chlorocyclohexyl) cyclohexanone **2** (32 g, 71% isolated yield) collected by filtration.¹⁵ IR (CCl₄): 2870 (s), 1695 (vs), 1440 (s), 1375 (w), 1100-1300 (m), 880 (m) cm⁻¹.

Synthesis of Bicyclohexyliden-2-one 3. To a flame dried 50 mL round bottom flask was added compound **2** (10 g, 46.6 mmol) and NaOCH₃ (2.6 g Na in 40 mL absolute methanol) in -10 °C. The needle-like crystals of **2** were formed. The crude crystal was recrystallized from methanol-water (4:1v/v) in 88% yield m.p.=56-47 °C (m.p.=57 °C¹⁵). IR (KBr): 2920 (s), 2850 (s), 1670 (s), 1610 (s), 1440 (s) cm⁻¹ UV (CHCl₃): λ_{max} 245nm. ¹HNMR (CDCl₃): δ 1.2-2.8 (m, 18H).

Synthesis of Bicyclohexyl-1-en-2-one 4. The chloroketone **2** (10 g, 46.6 mmol) was well shaken with 50 mL 2N aqueous sodium hydroxide, the mixture was allowed to stand for 2hr, and then extracted with ether. The ether layer was washed with water, dried with MgSO₄ and the solvent was removed, leaving red oil, which was distilled at reduced pressure. The ketone was obtained as an oil (17 g, 93% isolated yield) b.p.=114-116 °C/_{3.5 mmHg} (114-116.6 °C)¹⁵ IR (CCl₄): 2940 (s), 1700 (vs), 1448 (m), 720 (m)cm⁻¹. ¹HNMR (CDCl₃): d 5.4 (m, 1H), 1.0-3.2 (m, 17H). UV(CHCl₃): λ_{max} 245, 306 nm.

Synthesis of Bicyclopentyliden-2-one 5. Sodium ethoxide (was freshly prepared, 3 g in 45 mL absolute ethanol) was added dropwise to cyclopentanone (40 g, 476 mmol) and the mixture allowed to stand for 2 days at -10 °C. The brown-reddish viscose solution was decanted from residue. The excess ethanol was removed by distillation. The residue was diluted by water. The organic layer was separated by extraction with ether, dried over MgSO₄, the ether removed and residue was distilled at reduced

pressure (4.64 g, 65% yield) (b.p.=88-90 °C/_{2 torr}¹⁶ IR (CCl₄): 2950 (vs), 2870 (s), 1695 (s), 1630 (vs) cm⁻¹, ¹HNMR(CDCl₃): δ 1.0-3.0 (m, 14H).

Synthesis of [1,1,3,1'] Tercyclopentan-2'-one 6. Was separated as a byproduct of compound **5** (Fig. 3) IR (neat): 2950 (vs), 2850(s), 1685(m), 1440(vs), 1610(vs), 1445(m), 1165-1300(s). ¹HNMR (CDCl₃): δ; 2.7(m, 4H), 2.3(m, 4H), 2.1(m, 4H), 1.5 (m, 8H).

Synthesis of 1,2,3,4,5,6,7,8,9,10,11,12-dodecahydrotriphenylene (DTP) 1b: A typical experimental procedure. The unsaturated ketone **3** (or **4**) (1.78 g, 10 mmol) was treated with cyclohexanone (0.98 g, 10 mmol) and the catalyst (CuCl₂) (0.27 g, 2 mmol) in a proportion of 1.1:1:0.2 mol, respectively. The cyclohexanone was added to the reaction mixture dropwise, the resulting mixture was refluxed at 155 for 2 hr. The color of solution was initially yellow orange, but after 15 to 20 min of refluxing changed to dark purple. During this period the HCl gas was evolved and white CuCl precipitate is formed. The crude reaction mixture was then extracted with ether and finally dried over anhydrous MgSO₄. After distillation of the volatiles, the residue was set aside. After 2-3 days, solid DTP **1b** formed in the reaction mixture and separated out as a solid. The crude crystalline mass was directly chromatographed over silica gel and eluted with petroleum ether, m.p.=229 °C (reported 230 °C¹⁷), (54% purified yield). IR (KBr): 2920 (vs), 2850 (s), 1445 (m), 1420 (m) cm⁻¹. UV (EtOAc): λ_{max}; 272 nm. ¹HNMR (CDCl₃): δ 1.73 (s, 12H), 2.53 (s, 12H). ¹³CNMR (CDCl₃): δ 132.4, 26.6, 22.6. Mass: m/e (relative intensity) 241(20), 240 (100), 239 (10), 198 (58), 141 (44), 91 (17); calcd for C₁₈H₂₄ m/e 240.1878, found 240.1875.

Synthesis of 2,3,4,5,6,7,8,9-Octahydro-1H-trindane (Trindan) 1a. In a similar experiment, as described for **1b** cyclopentanone (0.84 g, 10 mmol) was reacted with unsaturated ketone **5** (1.5 g, 10 mmol) and CuCl₂ (0.27 g, 2 mmol). After standing for 2-3 days, trindan **1a** separated out of the reaction mixture. The crude mass (1.3 g) was recrystallized from H₂O: EtOAc, mp=96 °C (lit = 97.5-98 °C)⁵, (0.93g, 47% purified yield). ¹HNMR: δ 2.94-2.51 (t, 12H, J=7.3Hz), 2.32-1.82 (m, 6H).

^{13}C NMR displayed only 3 peaks, δ 137.3, 31.1, 25.3. MS: m/e 199 (56), 198 (89), 197 (100), 170 (95), 169 (94), and 155 (84); calcd. for $\text{C}_{15}\text{H}_{18}$ m/e 198.1408, found 198.1406.

Synthesis of 2,3,4,5,6,7,8,9,10,11-decahydro-1H-cyclopenta [I] phenanthrene 1c. An identical procedure applied for the synthesis of **1c** where-upon pre-formed ketone **4** (1.96 g, 11 mmol) was treated with cyclopentanone (0.84, 10 mmol) in the presence of CuCl_2 (0.27 g, 2 mmol). The crude product was purified by silicagel column, the solvent used as eluent was petroleum ether (43% isolated yield). IR (CCl_4): 2920 (s), 2830 (m), 1430 (m) cm^{-1} . UV (EtOAc): λ_{max} : 287 nm. ^1H NMR (CDCl_3): δ 1.3-3.4 (m, 22H). ^{13}C NMR (CDCl_3): δ 141.6, 140.7, 140.1, 138.2, 133, 131.2, 31.8, 31.7, 27.9, 27.7, 27.5, 27.2, 26.1, 23.9, 23.7, 23.6, 23.3. [The sample gave 17 peaks, while one would predict 9 peaks, due to its possession of a C2 axis. The increase in the number of peaks may be some subtle conformational issue at play.]. Mass: m/e (relative intensity); 227 (33), 226 (100), 225 (51), 199 (91); calcd for $\text{C}_{17}\text{H}_{22}$ m/e 226.1721, found 226.1727.

Synthesis of 1,2,3,4,5,6,7,8,9,10-decahydrobenz[e]-as-indacene 1d. Similarly, for the synthesis of **1d**, cyclohexanone (0.98 g, 10 mmol) was added to a mixture of bicyclopentyliden-2-one **5** (1.65 g, 11 mmol) and catalytic CuCl_2 (0.27 g, 2 mmol). The crude product was purified by silicagel column the solvent used as eluent was petroleum ether (38% isolated yield). IR (CCl_4): 1920 (vs), 1985 (s), 1430 (m) cm^{-1} . UV (EtOAc): λ_{max} 306 nm. ^1H NMR (CDCl_3): δ 1.8-2.2 (m, 12H), 2.6-2.9(m, 8H). ^{13}C NMR(CDCl_3): δ 141.4, 140.6, 138.1, 136.9, 132.9, 131.1, 31.9, 31.8, 31.6, 31.5, 29.6, 27.3, 26.1, 25.5, 23.8, 23.7. [The sample gave 16 peaks, while one would predict 8 peaks, due to its possession of a C2 axis. The increase in the number of peaks may be some subtle conformational issue at play.]. Mass: m/e (relative intensity); 213 (26), 212 (100), 211 (43), 184 (94), 183 (65); calcd for $\text{C}_{16}\text{H}_{20}$ m/e 212.1565,

found m/e 212,1561.

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