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Stereoselective Cyclotrimerization of Enantiopure Iodonorbornenes Catalyzed by Pd Nanoclusters for C_3 or C_{3v} Symmetric *syn*-Tris(norborneno)benzenes

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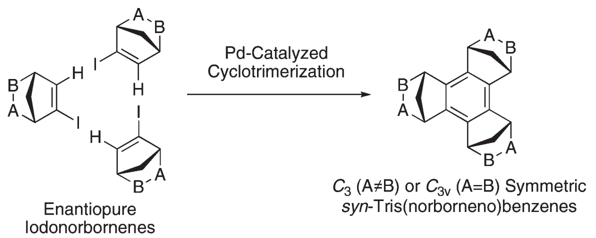
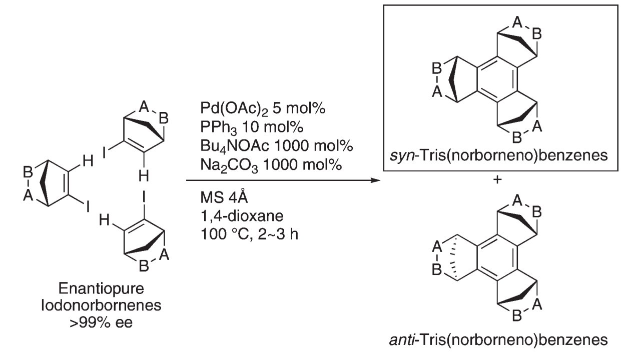


C_3 or C_{3v} symmetric enantiopure *syn*-tris(norborneno)benzenes with various functional groups were synthesized through Pd-catalyzed cyclotrimerization of enantiopure iodonorbornenes. The generality of Pd-catalyzed cyclotrimerization for *syn*-tris(norborneno)benzenes were well-demonstrated.

syn-Tris(norborneno)benzenes have been recently utilized as synthetic intermediates for syntheses of C_3 or C_{3v} symmetric buckybowls[1] or as cup- or basket-shaped host molecules to encapsulate guest molecules.[2] According to these recent applications, *syn*-tris(norborneno)benzenes with a variety of functional groups are recognized as molecules for new materials or their precursors. *syn*-Tris(norborneno)benzenes are prepared through cyclotrimerization of norbornene derivatives, where both desired *syn*- and undesired *anti*-isomers are generally obtained.[3,4] In most of the reported examples such as Cu-mediated or Pd-catalyzed cyclotrimerization, undesired *anti*-isomers were obtained as a major product. Given such background, one of the important issues in this area is the development of a general method for selective formation of *syn*-tris(norborneno)benzenes. We have recently reported Pd-catalyzed cyclotrimerization of enantiopure iodonorbornenes to prepare C_3 symmetric enantiopure *syn*-tris(norborneno)benzenes under Pd-nanocluster conditions (Scheme 1).[5] In this paper, we report the applicability of this Pd-catalyzed cyclotrimerization reaction to prepare C_3 or C_{3v} symmetric *syn*-tris(norborneno)benzenes with various functional groups.

SCHEME 1. Pd-Catalyzed Cyclotrimerization of Enantiopure Iodonorbornenes



Standard reaction conditions for Pd-catalyzed cyclotrimerization of enantiopure iodonorbornenes are shown in Scheme 1. 5 mol % of $Pd(OAc)_2$, 10 mol % of PPh_3, 1000 mol % of Bu_4NOAc, 1000 mol % of Na_2CO_3, and molecular sieves 4 Å were suspended in 1,4-dioxane. The

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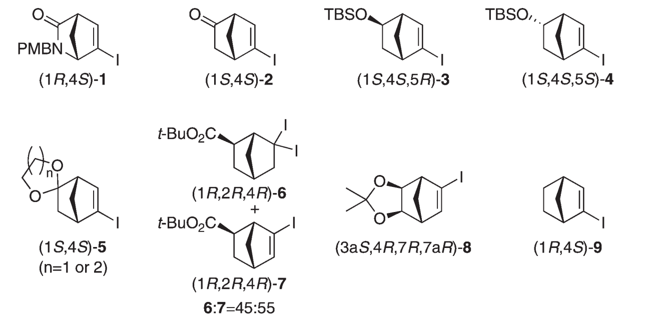

FIGURE 1. Enantiopure iodonorbornenes.

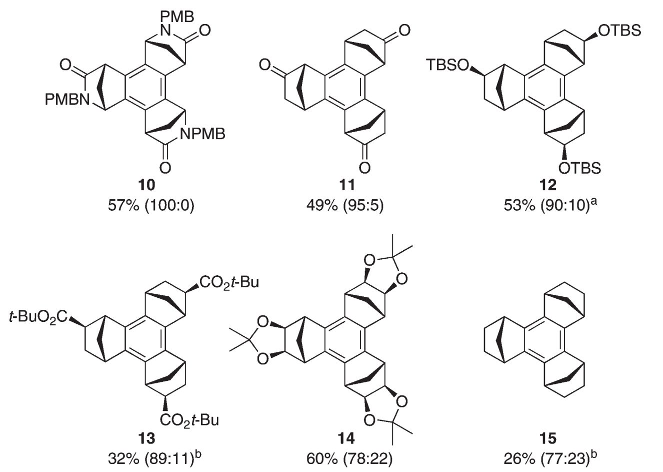

FIGURE 2. Yield and *syn*/*anti* ratio of tris(norborneno)benzenes. [a]Ratio after conversion to **11**. [b]^{1}H NMR ratio.

mixture was heated at 100 °C for a few minutes, which generates small size of Pd-nanoclusters (~3.5 nm).[5] An enantiopure iodonorbornene was added, and the reaction mixture was stirred at 100 °C for 2−3 h. Cyclotrimerization of enantiopure iodonorbornenes shown in Figure 1 were examined. The obtained *syn*-tris(norborneno)benzenes and their yield (*syn*/*anti*) are summarized in Figure 2. In the case of cyclotrimerization of **1** (PMB = *p*-methoxybenzyl), *syn*-isomer **10** was obtained in 57% yield exclusively without formation of the *anti*-isomer. Although cyclotrimerization of **2**, **3**, **6** + **7**, **8**, and **9** afforded mixtures of *syn*- and *anti*-isomers, *syn*-isomers were obtained as the major products with high *syn*-selectivity. Cyclotrimerization of **2** with a carbonyl group afforded **11** in 49% yield with a *syn*/*anti* = 95:5 ratio.[6] Similarly, **12** was synthesized by cyclotrimerization of **3** with a TBS ether (TBS = *t*-BuMe$_2$Si) at the *exo* position in 53% yield with a *syn*/*anti* = 90:10 ratio.[6] On the other hand, cyclotrimerization of **4** with a TBS ether at the *endo* position resulted in a complex mixture without formation of tris(norborneno)benzene. We have previously reported that iodonobornenes **5** do not undergo cyclotrimerization, either.[5b] These results suggest that a substituent at the *endo* position in norbornene skeleton prevents cyclotrimerization.[5b] A mixture of *gem*-diiodonorbornane **6** and iodonorbornene **7** can be directly subjected to cyclotrimerization to afford **13** in 32% yield (*syn*/*anti* = 89:11), similarly to the preparation of **11** as previously reported.[5b] Pure iodonorbornene derivatives are prepared by treatment with *t*-BuOK from a mixture of *gem*- diiodonorbornane and iodonorbornene in other cases (see the Supporting Information). However, treatment of **6** and **7** by such a strong base causes epimerization of the α-position of the alkoxycarbonyl group. Direct utility of a mixture of *gem*-diiodonorbornane and iodonorbornene for this cyclotrimerization is advantageous for base-sensitive substrates. Thus-prepared *syn*-tris(norborneno)benzenes **10**−**13** are all C_3 symmetric enantiopure compounds.

Use of an enantiopure iodonorbornene is valuable even for preparation of C_{3v} symmetric *syn*-tris(norborneno)benzenes since cyclotrimerization of racemic iodonorbornenes could prefer *anti*-isomer formation.[4a] As expected, cyclotrimerization of **8** afforded *syn*-**14** as a major product in 60% yield (*syn*/*anti* = 78:22).[7] The *syn*-selectivity of **14** is lower than those of C_3 symmetric ones. To check the stereoselectivity, the reaction of nonsubstituted iodonorbornene **9** was also investigated to give similar *syn*/*anti* = 77:23 ratio in 26% yield.[7]

Desired *syn*-isomers were obtained as a major product in every example as expected. Observed *syn*/*anti* selectivity caused by substituents ranges from 100:0 to 77:23. As a general trend, higher *syn*-selectivity is observed for C_3 symmetric tris(norborneno)benzenes than C_{3v} symmetric ones. Judging from the difference on the selectivity between the C_3 and C_{3v} symmetric compounds as well as the substituents effect, symmetrical palladacycle species, which derive from a dimer of iodonorbornenes, could be generated as the intermediate in the side reaction pathway for *anti*-isomers.[8] Although the formation of *anti*-isomer is undesired, it will help us to elucidate the reaction mechanism of cyclotrimerization.

As described above, Pd-catalyzed cyclotrimerization of enantiopure iodonorbornens were generally applied to preparation of C_3 or C_{3v} symmetric *syn*-tris(norborneno)benzenes with various functional groups. The thus-obtained *syn*-tris(norborneno)benzenes possess amenable functional groups to prepare derivatives. They can be applied as synthetic intermediates to the synthesis of C_3- or C_{3v}-symmetric buckybowls as well as cup-shaped molecules.

Experimental Section

Representative Procedure of Pd-Catalyzed Cyclotrimerization. A suspension of Pd(OAc)$_2$ (11.3 mg, 0.050 mmol), PPh$_3$ (26.2 mg, 0.10 mmol), Bu$_4$NOAc (3.0 g, 10.0 mmol), Na$_2$CO$_3$ (1.1 g, 10.0 mmol), and molecular sieves 4 Å (293 mg) in 1,4-dioxane (15 mL) was heated at 100 °C for a few minutes under argon atmosphere. After the color of the solution changed to black, a solution of **8** (293 mg, 1.00 mmol) in 1,4-dioxane (5 mL) was quickly added to the solution at 100 °C. After being stirred for 2 h, the reaction mixture was cooled to ambient temperature. The reaction mixture was filtered through Celite, and the filter cake was washed with *t*-BuOMe/hexane(1:1). After evaporation of solvent, the residue was dissolved in *t*-BuOMe/hexane (1:1, 10 mL), and CH$_3$CO$_2$H (1.2 mL) was added. The organic layer was washed with ethylene glycol/water (1:2, 10 mL × 3), water (10 mL × 3), and brine, dried over Na$_2$SO$_4$, filtered through Celite, and evaporated. The crude product was purified by silica gel column chromatography (10−20% EtOAc/hexane) to give a

(6) We have previously reported that only *syn*-**11** or *syn*-**12** was formed by the cyclotrimerizations (see ref 5). Thorough scrutiny revealed that the minor *anti*-isomer was a contaminant in the product.

(7) Synthesis of **14** and **15** by Cu-mediated cyclotrimerization was reported in refs 3h (98%, *syn*/*anti* = 1:4) and 3e (100%, *syn*/*anti* = 1:3), respectively.

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mixture of *syn*- and *anti*-**14**. The mixture was separated by GPC (gel permeation chromatography) to give *syn*-**14** (77.1 mg, 47%) and *anti*-**14** (21.3 mg, 13%). *syn*-**14**: IR (KBr) ν 2983, 2917, 1382, 1264, 1206, 1162, 1065, 1023, 860 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.07−4.04 (6H, m), 3.24 (6H, s), 2.22 (3H, d, J = 9.8 Hz), 1.84 (3H, dt, J = 9.8, 1.5 Hz), 1.50 (9H, s), 1.29 (9H, s); ^{13}C NMR ($CDCl_3$) δ 136.1, 112.6, 81.5, 45.3, 42.6, 25.9, 24.4; HRMS (EI) m/z calcd for $C_{30}H_{36}O_6$ [M^+] 492.2512, found 492.2513. *anti*-**14**: IR (KBr) ν 2983, 2936, 1383, 1373, 1263, 1208, 1175, 1164, 1065, 1023, 860 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.17−4.13 (4H, m), 4.08−4.04 (2H, m), 3.26−3.20 (6H, m), 2.23 (3H, d, J = 9.5 Hz), 1.80 (2H, ddd, J = 9.5, 1.3, 1.3 Hz), 1.74 (1H, dt, J = 9.5, 1.5 Hz), 1.50 (9H, s), 1.285 (6H, s), 1.278 (3H, s); ^{13}C NMR ($CDCl_3$) δ 136.3, 136.2, 112.6, 81.5, 81.3, 45.4, 45.2, 45.1, 42.3, 42.0, 25.9, 24.4, 24.3; HRMS (EI) m/z calcd for $C_{30}H_{36}O_6$ [M^+] 492.2512, found 492.2506.

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Supporting Information Available: Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.