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Pentiptycene Chemistry: New Pentiptycene Building Blocks Derived from Pentiptycene Quinones

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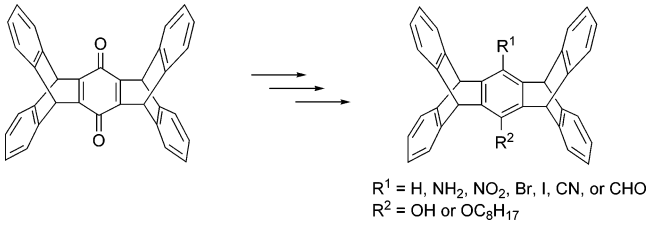
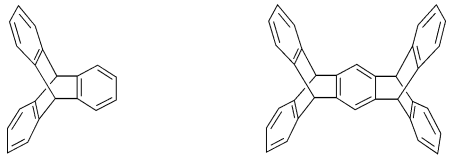


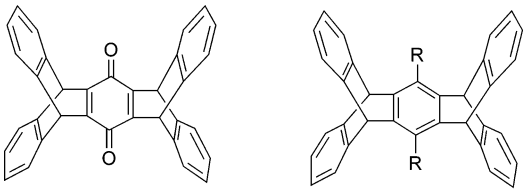
An efficient synthesis of new middle-ring disubstituted pentiptycenes from pentiptycene quinone is reported. One of the substituents is a bromo, iodo, amino, nitro, cyano, or formyl group and the other is a hydroxy or alkoxy group. These disubstituted pentiptycenes are potential building blocks for constructing novel pentiptycene-incorporated systems.

The three-dimensional rigid iptycene frameworks[1] such as triptycene (**1**) and pentiptycene (**2**) have found versatile usages in constructing molecules of both fundamental and practical importance.[2−7] One of the purposes for using the iptycene group(s) is to spatially isolate the functional moieties from the surroundings and to create intra- or intermolecular free volumes so that the desired properties (e.g., light-emitting efficiency and ability of free rotation) are enhanced.[4c,5−7] In this context, middle-ring functionalized pentiptycenes are particularly attractive, because pentiptycene is the smallest iptycene member that possesses a "spatially isolated" central phenyl ring.



1 **2**

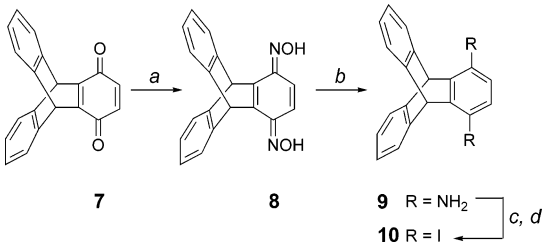
Regarding the polyaromaticity and high molecular symmetry of pentiptycene, the middle-ring derivatization would be more effective from the prefunctionalized precursors, particularly the readily prepared pentiptycene quinone **3**,[5,8] rather than from the parent pentiptycene **2**.[1] Indeed, two important pentiptycene building blocks, pentiptycene hydroquinone **4** and pentiptycene diacetylene **5**, have been derived from **3**.[5] However, an attempt



3 **4** R = OH; **5** R = CCH; **6** R = I

to prepare the diiodopentiptycene **6** from **3** by following the method for the conversion of the triptycene quinone **7** to the diiodotriptycene **10** via the intermeiates **8** and **9** (Scheme 1)

SCHEME 1[a]



[a] Key: (a) NH_2OH·HCl, EtOH; (b) $SnCl_2$, EtOH; (c) $NaNO_2$, HOAc, H_2SO_4, H_2O; (d) KI.

† National Taiwan University.

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(5) For examples of chemosensory materials, see: (a) Yang, J.-S.; Swager, T. M. *J. Am. Chem. Soc.* **1998**, *120*, 5321−5322. (b) Yang, J.-S.; Swager, T. M. *J. Am. Chem. Soc.* **1998**, *120*, 11864−11873. (c) Yang, J.-S.; Lin, C.-S.; Hwang, C.-Y. *Org. Lett.* **2001**, *3*, 889−892.

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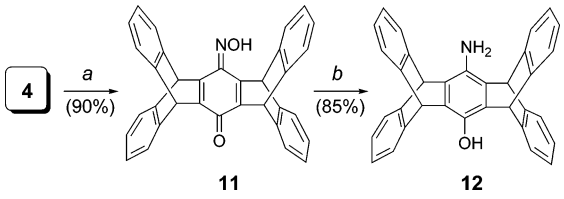
SCHEME 2 [a]



[a] Key: (a) $NH_2OH{\cdot}HCl$, THF, reflux; (b) $SnCl_2$, HCl, CH_2Cl_2, reflux.

was reported to be unsuccessful.[9] Apparently, the reactivity of **3** (an interior quinone) differs in some aspects from that of **7** (a peripheral quinone).

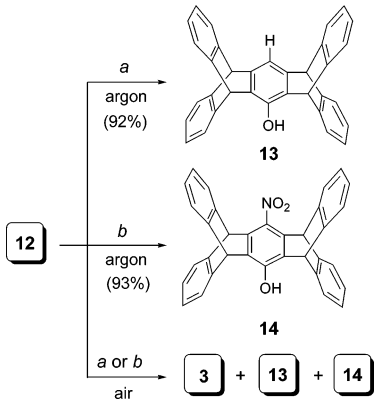
To expedite the pentiptycene as well as larger iptycene chemistry, methodologies for facile conversion of interior iptycene quinones to iptycene building blocks with more diversified functional groups are highly demanded. We report herein our first step toward this goal by converting **3** to several new functionalized pentiptycenes, in which iodo, bromo, amino, nitro, cyano, and formyl groups have been introduced for the first time in the middle ring. We have also shown that the reactivity of these building blocks is comparable to or better than that of the planar nonbulky aryl analogues.

We have reasoned that the poorer solubility of **3** vs **7** in ethanol might account in part for the failure of the conversion of **3** to **6** under the same conditions as that for **7** → **10** (Scheme 1).[9] Indeed, when the ethanol solvent was replaced by THF for the reaction of **3** and hydroxylamine in the presence of ca. 2 equiv of hydrochloric acid, the mono-oxime **11** was obtained in high yield (Scheme 2). It should be noted that the corresponding dioxime was not observed, even when the reaction was carried out with a large excess of hydroxylamine and a prolonged reaction time. This indicates that the carbonyl group in **11** is rather unreactive toward hydroxylamine. Reduction of **11** in dichloromethane by stannous chloride as expected affords the aminophenol **12**.

It is interesting to note that the amino group in **12** can be either removed to form the pentiptycene phenol **13** or converted to a nitro group (i.e., compound **14**) almost exclusively with the same reagents (*tert*-butyl nitrite and H_3PO_2) simply by controlling the concentration of reagents and the order they are added to the THF solution of **12** (Scheme 3). When the THF solution of **12** was first mixed with 3 equiv of H_3PO_2 and then slowly added with 1.5 equiv of *tert*-butyl nitrite, compound **13** was isolated with a high yield (92%), although a small amount of compound **14** was also obtained (∼2%). In contrast, compound **14** was the primary product (93%), and **13** became minor (∼2%) when **12** first reacted with an excess of *tert*-butyl nitrite (5 equiv or more) and then with 1 equiv of H_3PO_2. It should be noted that the yield of **14** decreased (82%) and that of **13** (10%) increased when the reaction was carried out in the absence of H_3PO_2. In addition, both reactions succeed only under deaerated conditions; otherwise, the quinone **3** could dominate the product with a yield (40−96%) depending on the concentration of *tert*-butyl nitrite and H_3PO_2.

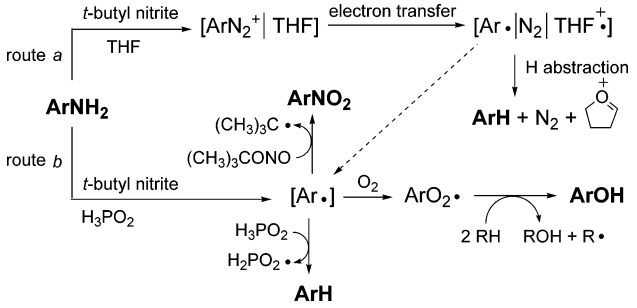
Although alkyl nitrites are well-known diazotizing reagents that lead to deamination for amines in THF,[10,11] to the best of our knowledge, no previous report has ever indicated that they

SCHEME 3 [a]



[a] Key: (a) (1) 3 equiv of $H_3PO_{2(aq)}$, THF, (2) 1.5 equiv of $(CH_3)_3CONO$; (b) (1) 5 equiv of $(CH_3)_3CONO$, THF, (2) 1 equiv of $H_3PO_{2(aq)}$.

SCHEME 4



can effectively convert alkylamines or arylamines to the corresponding nitro species. Thus, the efficient reaction of **12** → **14** has raised our interests in finding how the reagents of *tert*-butyl nitrite and H_3PO_2 react with simple arylamines. In this context, we have investigated the corresponding reactions of 4-aminophenol, 4-chloroaniline, and 2-aminoanthraquinone. The control experiments have shown that in the absence of H_3PO_2 all three compounds reacted with *tert*-butyl nitrite in THF to form only the deaminated products (68−72%), as reported in the literature.[10] Under the same conditions for the reaction of **12** → **14**, a mixture of the deaminated (26−32%) and nitro-substituted (50−58%) products were observed for the former two cases but still only the deaminated product (85%) was generated for the latter one. Apparently, the unique pentiptycene scaffold plays an important role in accounting for the high efficiency of the amino → nitro transformation in **12**.

A radical mechanism has long been proposed for the decomposition of diazotized arylamines mediated by neutral organic solvents or the powerful reducing agent H_3PO_2.[10−12] Thus, the combination of THF and H_3PO_2 in the above reactions should also involve the intermediate of aryl radicals (Ar•). Indeed, the formation of **3**, **13**, and **14** from **12** can be attributed to the reaction of the pentitpycene radical **15** with O_2, H_3PO_2, and *tert*-butyl nitrite, respectively (route b in Scheme 4). A larger yield in nitroarene formation for **12** vs anilines might be a result of a greater stability for **15** than the planar phenyl radicals. It

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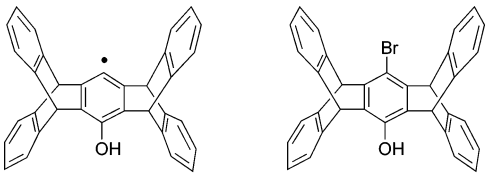
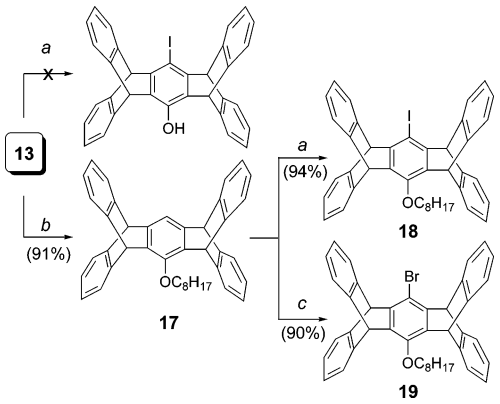
has been shown that the bulky iptycene groups can kinetically stabilized a reactive center such as a triplet carbene to a large extent.[7a] The discrepancy in nitroarene fromation between **12** and anilines in conditions without H_3PO_2 might indicate that the THF-promoted Ar• (route a in Scheme 4) is generally not able to escape out of the solvent cage before it abstracts hydrogen atom from the oxidized THF molecule (i.e., a radical cage mechanism[13]), but **15** appears to be an exception (the dashed arrow in Scheme 4) again due to its greater stability. Further characterization of **15** and its analogues is in progress in our laboratory.



15 **16**

It is also known that the combination of alkyl nitrites and copper(II) halides can convert arylamines to aryl halides.[12] However, the reaction of **12** with *tert*-butyl nitrite and $CuBr_2$ led to **14** instead of bromopentiptycene **16**. A replacement of $CuBr_2$ by KI as the halogen source for the reaction was also unsuccessful, because a mixture of unseparable products was formed. Unseparable mixtures were also obtained when **13** was subjected to the iodination conditions of I_2/Ag_2SO_4.[14] Nonetheless, the iodopentiptycene **18** can be readily prepared by using the O-alkylated derivatives of **13**, such as compound **17**, as the substrate (Scheme 5). The corresponding bromopentiptycene **19** can also be generated from the reaction of **17** and NBS.[15]

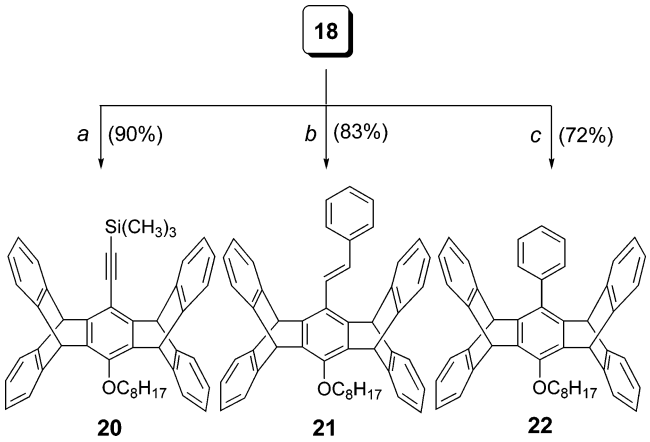
SCHEME 5 [a]



[a] Key: (a) I_2, Ag_2SO_4, EtOH, reflux; (b) K_2CO_3, KI, BrC_8H_{17}, acetone, reflux; (c) NBS, DMF, 80 °C.

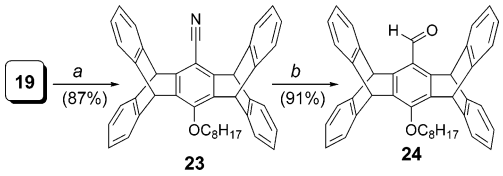
In view of the facts that the bulky pentiptycene group often affects the reactivity of its derivatives, as demonstrated by the difference in dioxime formation between **3** (Scheme 1) and **4** (Scheme 2) and that in the amino → nitro group transformation between **12** (Scheme 3) and substituted anilines,[10] the reactivity of **18** and **19** has been investigated. As shown in Scheme 6, a series of pentiptycene derivatives with extended π-conjugated

SCHEME 6 [a]



[a] Key: (a) $Pd(PPh_3)_4$, $HCCSi(CH_3)_3$, *i*-Pr_2NH, benzene, reflux; (b) $Pd(OAc)_2$, P(*o*-tolyl)$_3$, styrene, NEt_3, DMF, 90 °C; (c) $Pd(dba)_2$, $PhB(OH)_2$, PPh_3, Cs_2CO_3, 1,4-dioxane, 100 °C.

SCHEME 7 [a]



[a] Key: (a) CuCn, NMP, 200 °C; (b) (1) DIBAL-H, CH_2Cl_2, −20 °C, (2) HCl.

backbones (i.e., **20**−**22**) can be prepared from **18** when subjected to the standard conditions of the Sonogashira, Heck, and Suzuki reactions.[16] In addition, the bromo group in **19** can be replaced by a cyano group (i.e., **23**), which can be in turn reduced to a formyl group (i.e., **24**) (Scheme 7) according to the known procedures.[17,18] These results should ensure **18** and **19** as useful building blocks for the synthesis of more complicated pentiptycene derivatives.

In summary, efficient methods for converting the pentiptycene quinone **3** to several middle-ring functionalized pentiptycenes have been reported. The substituents range from the strong electron-withdrawing nitro and cyano group to the strong electron-donating amino and alkoxy groups. The same methodologies should also apply to the more extended iptycene quinones provided that solubility does not become an important issue. Since the functional groups in these disubstituted pentiptycenes allow for further derivatizations, our results should facilitate the development of iptycene-based materials.

Experimental Section

Four key synthetic steps, which for the preparation of compounds **11**−**14** are described in the following text, and the synthesis and characterization data of **17**−**24** are presented in the Supporting Information.

Synthesis of Compound 11. To a solution of **3** (6.0 g, 13.0 mmol) in 200 mL of THF was added hydroxylamine hydrochloride (3.6 g, 52 mmol) predissolved in 15 mL of water and 2 mL of

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concentrated $HCl_{(aq)}$ (37%). The mixture was heated to reflux for 3 days. The THF was then removed under reduced pressure, and the residue was then dissolved in CH_2Cl_2 and washed with brine. The organic layer was dried over anhydrous $MgSO_4$, and the filtrate was concentrated under reduced pressure. Column chromatography with CH_2Cl_2/hexane (1:1) as eluent afforded the orange solid of **11** with a yield of 90%. Further purification was not performed due to its poor stability: mp > 300 °C; IR (KBr) 1591 cm^{-1}; FAB-HRMS calcd for $C_{34}H_{21}NO_2$ (M^+) 475.1572, found 475.1583.

Synthesis of Compound 12. A mixture of **11** (6.0 g, 12.6 mmol), $SnCl_2$ (7.2 g, 38.0 mmol), 200 mL of CH_2Cl_2, and 2 mL of concentrated HCl aqueous solution in a 500-mL flask was heated to reflux for 16 h. The CH_2Cl_2 was then removed under reduced pressure, and the residue was then dissolved in ethyl acetate (ca. 4 L, due to a very poor solubility) and washed with 10% $NaOH_{(aq)}$. The organic layer was filtered through a layer of silica gel, and the filtrate was concentrated under reduced pressure to afford the white solid of **12** with a yield of 85%. Further purification was not performed, and the NMR spectra were not determined due to the very poor solubility: mp > 300 °C; IR (KBr) 1022, 1260, 3386, 3399, 3446 cm^{-1}; FAB-HRMS calcd for $C_{34}H_{23}NO$ (M^+) 461.1780, found 461.1787.

Synthesis of Compound 13. To a solution of **12** (0.5 g, 1.1 mmol) in 25 mL of THF at rt was added 0.6 mL of 50% $H_3PO_{2(aq)}$ (5.5 mmol) under argon. The mixture was stirred till it became a homogeneous solution. The solution was heated to 40 °C, and then a solution of *tert*-butyl nitrite (0.2 mL, 90%, 1.5 mmol) in 5 mL of THF was slowly added. The mixture was kept at 40 °C for 16 h. The THF was then removed under reduced pressure, and the residue was then dissolved in CH_2Cl_2 and washed with 10% $NaOH_{(aq)}$. The organic layer was dried over anhydrous $MgSO_4$, and the filtrate was concentrated under reduced pressure. Column chromatography with EA/CH_2Cl_2/hexane (1:1:7) as eluent afforded the white solid of **13** with a yield of 92%: mp > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (s, 2H), 5.72 (s, 2H) 6.94−6.99 (m, 8H), 7.19 (s, 1H), 7.33−7.38 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.1, 54.1, 113.1, 123.4 (2C), 125.0 (2C), 129.1, 144.2, 145.0, 145.6 (2C); IR (KBr) 1252, 3421 cm^{-1}; FAB-HRMS calcd for $C_{34}H_{22}O$ (M^+) 446.1671, found 446.1674.

Synthesis of Compound 14. To a solution of **12** (1.0 g, 2.2 mmol) in 50 mL of THF at rt was added 1.4 mL of *tert*-butyl nitrite (90%, 10.5 mmol) under argon. The mixture was stirred until it became a homogeneous solution, and then 0.4 mL of 50% $H_3PO_{2(aq)}$ (3.7 mmol) was slowly added. The mixture was kept at rt for 16 h. The THF was then removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 and washed with 10% $NaOH_{(aq)}$. The organic layer was dried over anhydrous $MgSO_4$ and the filtrate was concentrated under reduced pressure. The crude product was recrystallized from $CHCl_3$/MeOH to afford the yellow solid of **14** with a yield of 93%: mp > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 (s, 2H), 5.91 (s, 2H), 6.98−7.02 (m, 8H), 7.36−7.42 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.0, 49.8, 123.5, 124.4, 125.6, 125.7, 131.6, 138.2, 138.8, 143.9, 144.3, 147.6; IR (KBr) 1248, 1352, 1522 cm^{-1}; FAB-HRMS calcd for $C_{34}H_{21}NO_3$ (M^+) 491.1521, found 491.1528.

Acknowledgment. We thank the National Science Council of Taiwan, Academia Sinica, and CNST/UST for financial support.

Supporting Information Available: Experimental procedures and characterization data for compounds **17**−**24** and ^{1}H and ^{13}C NMR spectra of **13**, **14**, and **17**−**24**. This material is available free of charge via the Internet at http://pubs.acs.org.

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