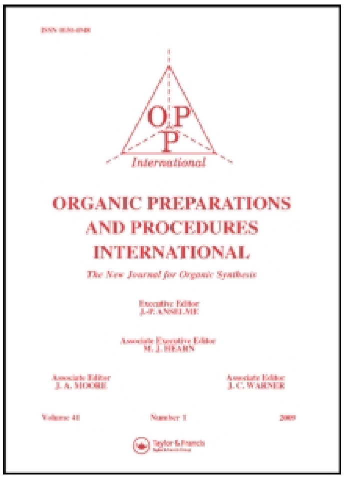

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SYNTHESIS OF 3,6-DI-(*tert*-BUTYL)FLUORENE BY NICKEL(0) CATALYZED COUPLING OF ARYL HALIDES

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SYNTHESIS OF 3,6-DI-(*tert*-BUTYL)FLUORENE BY NICKEL(0) CATALYZED COUPLING OF ARYL HALIDES

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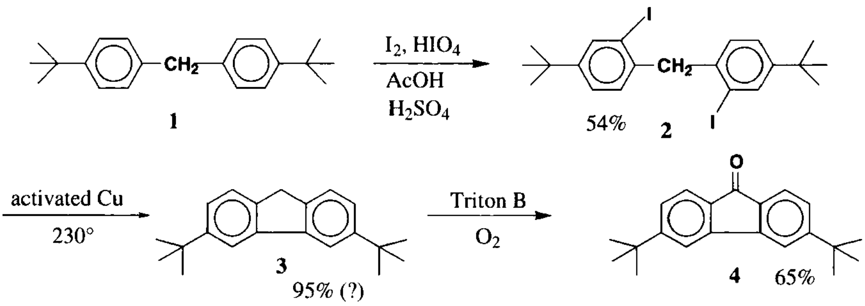
In the course of our investigations of fluorenyl substituted *m*-xylylenes, substantial amounts of 3,6-di-(*tert*-butyl)fluorenone were required. An obvious route is *via* the corresponding 3,6-di-(*tert*-butyl)fluorene. Unfortunately electrophilic substitution of fluorene occurs at 2- and 7-positions rather than the 3- and 6-positions. This led Kajigaeshi and coworkers[1] to synthesize the title compound from *p,p*'-di-(*tert*-butyl)diphenylmethane according to **Scheme 1**.



Scheme 1

While following this route, we encountered certain difficulties. The Ullmann reaction which requires high temperature, was not reproducible in our hands. There were also some inconsistencies in the Experimental Section, in particular for the iodination step. Here we provide full details as well as improvements in the synthesis of the fluorenone **4** including major modification at the coupling step.

The intramolecular coupling of the diiodide **2** was achieved using nickel(0) complex under mild conditions. The method was a combination of one originally developed by Semmelhack,[2] later modified by Kende[3] [*in situ* generation of the nickel(0) complex] and Kumada[4] [use of catalytic amount of the nickel(0) complex]. Thus *p,p*'-diphenylmethane[5] was iodinated with a mixture of periodic acid and iodine according to a literature procedure[6] to afford **2** in 83% yield. The diiodide was then coupled in the presence of *tetrakis*(triphenylphosphine)nickel(0) catalyst which was generated *in situ* from the air stable *bis*(triphenylphosphine)nickel(II) chloride (10 mol%), triphenylphosphine and zinc powder [to reduce nickel(II) to nickel(0)] in DMF. Fluorene **3** was obtained in 85% yield (**Scheme 2**).

$$\mathbf{2} \xrightarrow[\text{DMF, 70-75°}]{\text{Ni(0)}^{a}} \underset{85\%}{\mathbf{3}} \xrightarrow[\text{Bu}^{t}\text{OOH, rt}]{\text{PDC}} \underset{80\%}{\mathbf{4}}$$

a) $NiCl_2(PPh_3)_2$:PPh_3:Zn = 0.1:0.8:2.5 *or* $NiCl_2 \bullet 6H_2O$:PPh_3:Zn = 1:4 :1.2

Scheme 2

This coupling could also be achieved from *in situ* preparation of nickel(0) complex (*stoichiometric amount*) directly from nickel(II) chloride hexahydrate, triphenylphosphine and activated zinc.[7] Thus these results show that in addition to the formation of 6-, 7- and other larger rings, a 5-membered ring can also be formed using nickel(0) catalyst.[8] The 3,6-di-(*tert*-butyl)fluorene thus obtained was oxidized with a 1:1 mixture of PDC and *tert*-butylhydroperoxide[9] at room temperature to give 3,6-di-(*tert*-butyl)fluorenone in good yield (80%).

EXPERIMENTAL SECTION

^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 MHz instrument in $CDCl_3$. All chemical shifts are reported as δ values in parts per million downfield from TMS.

Synthesis of 2,2'-Diiodo-4,4'-di-(*tert*-butyl)diphenylmethane (2).- To a solution of *p,p'*-diphenylmethane (8.91 g, 31.78 mmol), periodic acid dihydrate (2.90 g, 12.73 mmol) and iodine (6.46 g, 25.46 mmol) in glacial acetic acid (34 mL) was added water (5.5 mL) and H_2SO_4 (95%, 1.2 mL). The mixture was stirred and heated to 70-78° for 24 h. A brown oily liquid deposited at the bottom of the flask. The mixture was poured into ice-water and extracted with ether. The ether layer was washed with $NaHSO_3$ solution, Na_2CO_3, then water and brine. After drying ($MgSO_4$) rotary evaporation gave a light yellow residue (16.1 g) which was then chromatographed through an alumina column (hexane:benzene = 2:1). This gave a white semisolid (14.3 g, >83%) which was used without further purification. ^{1}H NMR: δ 7.86 (d, *J* = 2.0 Hz, 2H), 7.27 (dd, *J* = 2.0, 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 4.06 (s, 2H), 1.29 (s, 18H).

3,6-Di-(*tert*-butyl)fluorene (3).- **Method A**:[4] *bis*(Triphenylphosphine)nickel dichloride (0.141 g, 0.216 mmol), Zn powder (0.395 g, 6.05 mmol) and triphenylphosphine (0.453 g, 1.73 mmol) were placed in a 2-neck flask (100 mL) fitted with a stopcock adapter which was connected to a vacuum line. The flask was carefully evacuated and then filled with nitrogen. Degassed DMF (20 mL) was added and the mixture was heated using an oil bath (bath temp. 50-75°). After 1 h, a solution of diiodide **2** (1.15 g, 2.16 mmol) in 20 mL of DMF was added *via* a cannula and was allowed to stir at 70-75° for 24 h. It was then stirred at room temp. for an additional 24 h by which time the original green color had changed to reddish brown. The mixture was then treated with 1 N HCl, and extracted with diethyl ether. The ethereal layer was washed successively with water and brine and dried ($MgSO_4$). Rotary evaporation gave a solid (2.9 g) whose proton NMR revealed it to be the desired product (100% conversion) along with triphenylphosphine oxide and triphenylphosphine. Most of the phosphine oxide was removed by precipitation (hexane) and filtration. The filtrate was chromatographed through silica gel (hexane : benzene = 10 : 1) to afford the desired fluorene **3** (0.510 g, 85%).

Method B:[7] Nickel(II) chloride hexahydrate ($NiCl_2.6H_2O$, 0.283 g, 1.19 mmol), triphenylphosphine (1.25 g, 4.76 mmol) and activated zinc (~0.1 g, 1.5 mmol) (zinc was activated by treating with 10% HCl followed by washing successively with water and acetone and then drying) were placed in a 2-neck flask containing stirrer and a stopcock adapter. The flask was evacuated and filled with nitrogen. After addition of DMF (8 mL), the mixture was heated in an oil bath as above. After 1 h, a solution of diiodide **2** (0.68 g, 1.18 mmol) in DMF (3 mL) was added. After stirring for 24 h at 70-75°, the reaction mixture was treated as described above to afford a white solid whose proton NMR revealed it to be fluorene **3** (>90% conversion) along with triphenylphosphine oxide and triphenylphosphine. This mixture was taken up in THF and treated with 30% hydrogen peroxide to convert the phosphine to the phosphine oxide. Addition of saturated sodium sulfite solution (4 mL) followed by extraction (ether- hexane mixture), drying, filtration and rotary evaporation gave a residue which was triturated with hexane and filtered to remove most of the phosphine oxide. The filtrate was chromatographed as above to afford fluorene **3** (0.250 g, 76%). ^{1}H NMR: δ 7.82 (d, *J* = 1.6 Hz, 4,5-H, 2H), 7.45 (d, *J* = 8.0 Hz, 1,8-H, 2H), 7.34 (dd, *J* = 1.6, 8.0 Hz, 2,7-H, 2H), 3.81 (s, 2H), 1.42 (s, 18H).

3,6-Di-(*tert*-butyl)fluorenone (4).- The procedure was the same as that used for fluorene.[9] Thus from 3,6-di-(*tert*-butyl)fluorene **3** (2.36 g, 8.50 mmol), PDC (12.79 g, 34 mmol), celite (6 g), Bu^tOOH (70%, 4.38 g, 34 mmol) and benzene (70 mL) there was obtained 2.3 g (>95% conversion) crude yellow product. Recrystallization from a mixture of hexane and benzene gave pure **4** (yellow crystals, ~2 g, 80%). The compound sublimes at atmospheric pressure below its mp., mp. (sealed tube) 202-203° (lit[1] mp. 208-209°). ^{1}H NMR: δ 7.57 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 1.6 Hz, 2H), 7.30 (dd, J = 1.6, 8.0 Hz, 2H), 1.39 (s, 18H). ^{13}C NMR: δ 193.54, 158.74, 144.72, 132.46, 125.84, 124.01, 117.31, 35.62, 31.21. MS (m/z): 292 (M^+, 67), 277 (100). HRMS for $C_{21}H_{24}O$: found 292.18356, calcd. 292.18283. Compound **4** was also converted to precursors of *m*-xylylene diradicals.[10]

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