DOI 10.5012/bkcs.2010.31.04.1064

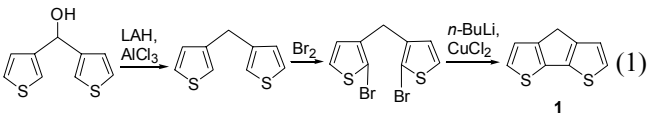
Short and Efficient Synthesis of Cyclopentadithiophene and Its Dialkylated Product

Ji Hae Park and Bun Yeoul Lee*

*Department of Molecular Science and Technology, Ajou University, Suwon 443-749, Korea. *E-mail: bunyeoul@ajou.ac.kr*
Received January 26, 2010, Accepted February 8, 2010

Key Words: Cyclopentadithiophene, Nazarov cyclization, Decarboxylation

Cyclopentadithiophene (CDT) is a key building block for the construction of a low band gap conjugated polymers, which has recently attracted much attention as a base material for heterojunction solar cells.[1] Zirconium and titanium complexes of cyclopentadienyl fused with a thiophene unit are also relevant in the development of a homogenous Ziegler catalyst.[2] The first synthesis of CDT was reported four decades ago (equation 1).[3] The synthetic route was rather lengthy and required use of hazardous chemicals such as lithium aluminum hydride and Br_2. Furthermore, the overall yield and atom economy for equation 1 were very low (theoretical atom economy, 8.0%; practical atom economy, 1.2%, overall yield, 15%), hampering a large scale synthesis of CDT by this route.

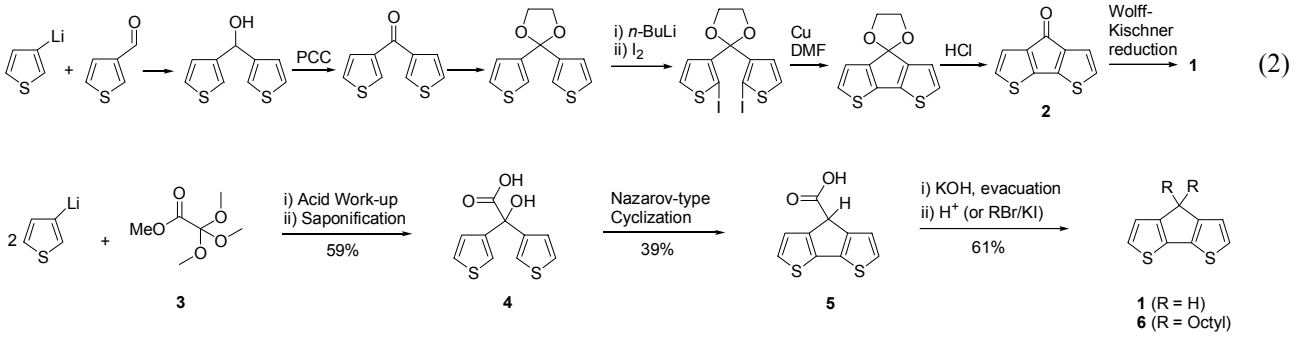


(1)

Recently, another route was reported, where cyclopenta[2,1-*b*;3,4-*b*']dithiophen-4-one (**2**) was reduced according to a Huang-Minlon modification of the Wolff-Kischner procedure (equation 2).[4] The reaction condition for the Wolff-Kischner reduction was harsh; treatment of slurry of **2** in ethylene glycol with potassium hydroxide and hydrazin hydrate for 8 h at 180 °C. Due to the slurry nature of the reaction medium and harsh conditions, the reported yield (65%) has not proved reproducible, instead fluctuating in lower values. Furthermore, synthesis of **2** is not straightforward, hampering a large scale synthesis, although some steps have been improved (equation 2).[5]

A short and efficient synthetic route for CDT is presently reported, which can allow a large scale synthesis of **1** (Scheme 1). A key step of the route is the Nazarov-type cyclization of a pentadien-3-ol system. The Nazarov cyclization has been efficiently employed in construction of cyclopentadiene systems[6] and is still an issue in the synthetic organic chemistry.[7] The Nazarov-type cyclization of **4** was previously reported in small scale employing three equivalents of $AlCl_3$ in benzene.[8] A problem in the previous report on the scaleable synthetic point is a synthesis of **4**.[9] Compound **4** was prepared by three steps. The first step was addition of 3-thienylmagnesium bromide to excess dimethyl oxalate; the yield was 53%. The second step was addition of 3-thienylmagnesium bromide to methyl 3-thienylglyoxalate obtained in the first step. The yield for the second step was low (29%). Saponification of the hydroxy ester with ethanolic KOH followed by the usual workup gave the desired compound **4**. 3-Thienylmagnesium bromide could not be made directly from 3-bromothiophene and magnesium, but was prepared from 3-thienyllithium, which required a tedious procedure.

We can prepare **4** by reacting methyl 2,2,2-trimethoxyacetate (**3**) with two equivalents of 3-thienyllithium, generated from 3-bromothiophene in hexane by bromo-lithio exchange reaction using *n*-BuLi.[10] Compound **3** can be prepared inexpensively from dimethyl oxalate in 50 g scale.[11] Employing nonpolar hexane solvent in both the lithiation reaction and the subsequent carbonyl attack reaction is crucial for a good yield. Yield is poor (~30%) when THF is used instead of hexane. The trimethyl orthoester group is easily converted to a carboxylic acid group by acidic work-up (1 N HCl) and subsequent saponification reaction. The saponificated product is soluble in water and most of side products can be removed by washing with diethyl ether. The ^{1}H and ^{13}C NMR spectra indicate that the crude product obtained in this procedure is sufficiently pure to proceed to the next Nazarov-type cyclization. In the ^{1}H NMR spectrum ($CDCl_3$), only three signals are observed at 7.39, 7.31, and 7.17 ppm and only six signals are observed at 177.89, 141.80, 126.75, 126.31, 123.52, and 76.81 ppm in the ^{13}C NMR



(2)

Scheme 1. A short and efficient synthetic route for CDT

spectrum. Crude compound **4** is obtained in 15-g scale in this way in ~60% yield. In the previously reported Nazarov-type cyclization of **4**, 3 equivalents of $AlCl_3$ were used in a large amount of dry benzene (35 mL/g-**4**). The reported high yield (75%) was not reproducible in our laboratory, but it was ~40% in many trials.[8] Work-up procedure was also very tedious; lots of solid were formed and so filtration was not easy. A new condition is developed for the cyclization. Polyphosphoric acid acts as an acid catalyst, and the cyclization occurs to give the desired compound **5** in ~40% yield. The work-up procedure is simple and can be applied in a large scale synthesis. Clean compound can be obtained by passing through a short pad of silica gel eluting with ethyl acetate. Even though the yield for the cyclization is moderate, this cyclization is atom-economically advantageous over the intramolecular oxidative coupling of the dibromo-compound used in equation 1 or Ulmann coupling of diiodo-compound shown in equation 2.

In a previously reported method, the decarboxylation of **5** was achieved by very harsh conditions: dissolving **5** (0.6 g) in quinoline (25 mL) and heating the solution in the presence of copper powder (0.5 g) at 238 °C (reflux) for 4 h.[8] A new mild decarboxylation condition is set up. When compound **5** is treated with KOH in dimethylsulfoxide (DMSO), deprotonation occurs to yield a carboxylate anion. Under a vacuum, the carboxylate anion liberates CO_2 gas to be a cyclopentadienyl-type anion of CDT. In the reaction carried out in the NMR cell using DMSO-d_6, a clean conversion of a pair of doublet thiophene signals at 7.41 and 7.17 ppm (J = 5.2 Hz) to another pair of doublet signals at 6.82 and 6.40 (d, J = 5.2 Hz) ppm is observed. The targeted **1** can be obtained by protonation on the generated cyclopentadienyl-type anion of CDT in ~60% yield. The generated cyclopentadienyl-type anion of CDT can be also directly converted, in overall ~60% yield, to more valuable dioctyl CDT (**6**) by the treatment of two equivalents of octyl bromide and a catalytic amount of KI.

Experimentals

General remark. Hexane, benzene, and THF were distilled from benzophenone ketyl. Pyridine was dried by keeping over molecular sieves. Dimethyl sulfoxide (dmso) was used as it was received without further purification. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian Mercury Plus 400 apparatus.

Synthesis of 3. Synthesis of the compound in 50 g scale was reported but it required a tedious fractional distillation step to remove some side products.[11] A more convenient method was developed which did not generate any side product to allow purification just by simple vacuum distillation. Thus, methyl 2,2-dichloro-2-methoxyacetate (25.0 g, 0.144 mmol), anhydrous methanol (50 mL), pyridine (41 mL), and anhydrous diethyl ether (70 mL) were mixed. The resulting solution was stirred overnight at room temperature. Addition of diethyl ether (100 mL) resulted in two phases. The upper phase was collected and additional diethyl ether (50 mL) was added to the lower phase. White solid precipitated which was filtered off. The solid was washed with diethyl ether (50 mL × 2). Organic phases were combined and washed with saturated aqueous $CuSO_4$ solution (200 mL). The collected organic phase was dried over anhydrous $MgSO_4$ and the solvent was removed using a rotary evaporator. After pyridine was discarded by vacuum distillation at ~30 °C/0.4 mmHg, the product was collected at 40 ~ 50 °C/0.4 mmHg (21.5 g, 91%). ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 3.35 (s, 9H) ppm. ^{13}C NMR ($CDCl_3$) δ 165.80, 110.71, 52.98, 50.97.

Synthesis of 4. Into a flask containing 3-bromothiophene (30.0 g, 0.184 mol) was added anhydrous hexane (225 mL). After the solution was cooled to −40 °C, *n*-BuLi (73.6 mL, 2.5 M in hexane, 0.184 mol) was added dropwise, and then anhydrous THF (15 mL) was added. The resulting white suspension was stirred for 10 min at −40 °C, and then allowed to warm to room temperature for 20 min. After the suspension was cooled to −78 °C, compound **3** (15.1 g, 0.0920 mol) was added in one portion with vigorous stirring. The solution was allowed to warm to room temperature for 40 min, during which time a solid precipitated. After water (150 mL) was added, the hexane phase was collected. The water phase was extracted further with diethyl ether (100 mL × 2). All the organic phases were combined and solvent was removed. The residue was dissolved in ethyl acetate (250 mL) and 1 N HCl (250 mL) was added. The resulting two phase solution was stirred for 20 min. Organic phase was collected and the water phase was extracted further with ethyl acetate (50 mL). The combined organic phases were washed with saturated aqueous Na_2CO_3 solution (20 mL). After the solution was dried over anhydrous $MgSO_4$, all volatiles were removed using a rotary evaporator to give an orange residue (~23 g). The residue was dissolved in methanol (92 g) dissolving KOH (10.2 g, 0.181 mol). The resulting solution was stirred for 3 h, until TLC indicated complete saponification. Water (150 mL) and diethyl ether (150 mL) were added. Water phase was collected, which was subsequently washed with diethyl ether (150 mL × 4). To a flask containing the water phase was added toluene (200 mL). H_2SO_4 (23 g, 0.23 mol) diluted with water (70 mL) was added dropwise while stirring vigorously. The organic phase was collected and the water phase was further extracted with toluene (50 mL × 2). After the combined organic phases were dried over anhydrous $MgSO_4$, solvent was removed using a rotary evaporator to give a residue that was solidified by evacuation (13.0 g, 59%). The ^{1}H and ^{13}C NMR spectra indicated that the purity of the crude product was satisfactory to proceed to the next step without further purification. ^{1}H NMR ($CDCl_3$) δ 7.39 (dd, J = 2.8, 1.2 Hz, 2H), 7.31 (dd, J = 5.2, 2.8 Hz, 2H), 7.17 (dd, J = 5.2, 1.2 Hz, 2H). The OH signal is missing due to broadening. ^{13}C NMR ($CDCl_3$) δ 177.89, 141.80, 126.75, 126.31, 123.52, 76.81.

Synthesis of 5. A CH_2Cl_2 solution (100 mL) dissolving **4** (11.3 g, 46.9 mmol) was added to polyphosporic acid (67 g, 85%) for 2 h at 50 °C with a syringe pump, and then the mixture was stirred at this temperature for 2 h. Ice (60 g) was added after cooling the mixture with ice bath and then ethyl acetate (100 mL) was added. After the mixture was filtered over Celite, the organic phase was collected. The water phase was extracted further with ethyl acetate (100 mL × 2). After the combined solution was dried over anhydrous $MgSO_4$, the solvent was removed using a rotary evaporator to give a tan-colored solid. Pure compound can be obtained by column chromatography on a short pad of silica gel eluting with ethyl acetate

(4.08 g, 39%). ^{1}H NMR ($CDCl_3$) δ 7.23 (d, J = 4.8 Hz, 2H), 7.21 (d, J = 4.8 Hz, 2H), 4.66 (s, 1H). The OH signal is missing due to broadening. ^{13}C NMR ($CDCl_3$) δ 174.92, 146.17, 139.19, 125.58, 123.46, 48.85.

Synthesis of 1. Compound **5** (1.00 g, 4.50 mmol) was dissolved in DMSO (20 mL), and KOH (0.505 g, 9.00 mmol) was added. The resulting solution was evacuated and then stirred overnight under a closed vacuum system. After overnight stirring, the system was briefly evacuated seven times in every 1 h. The solution was quenched with saturated NH_4Cl solution (30 mL) and then compound was extracted with hexane (20 mL × 3). After the solution was dried over anhydrous $MgSO_4$, solvent was removed using a rotary evaporator. Pure compound was obtained by column chromatography on silica gel eluting with hexane (0.430 g, 61%). ^{1}H NMR ($CDCl_3$) δ 7.19 (d, J = 4.8 Hz, 2H), 7.11 (d, J = 4.8 Hz, 2H), 3.57 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 149.63, 138.59, 124.50, 123.00, 32.07.

Synthesis of 6. To the cyclopentadienyl-type anion of CDT generated by decarboxylation of **5** (1.00 g, 4.50 mmol) using KOH (0.757 g, 13.5 mmol) according to the method described above were added octyl bromide (1.74 g, 9.00 mmol) and KI (25 mg, 0.15 mmol). The solution was stirred overnight at room temperature. Water (40 mL) was added and the product was extracted with hexane (20 mL × 3). After the solution was dried over anhydrous $MgSO_4$, solvent was removed using a rotary evaporator to give an oily residue. Pure compound was obtained by column chromatography on silica gel eluting with hexane (1.10 g, 61%). ^{1}H NMR ($CDCl_3$) δ 7.16 (d, J = 4.8 Hz, 2H), 6.94 (d, J = 4.8 Hz, 2H), 1.92-1.77 (m, 4H), 1.40-1.07 (m, 20H), 1.07-0.92 (m, 4H), 0.88 (t, J = 7.2Hz, 6H). ^{13}C NMR ($CDCl_3$) δ 158.14, 136.46, 124.49, 121.75, 53.48, 38.01, 32.14, 30.35, 29.69, 29.59, 24.86, 22.97, 14.48.

Acknowledgments. B. Y. Lee is grateful for LG Yonam foundation for the visiting scholarship.

References

1. (a) Zhu, Z.; Waller, D.; Gaudiana, R.; Morana, M.; Mülhlbacher, D.; Scharber, M.; Brabec, C. *Macromolecules* **2007**, *40*, 1981. (b) Zhang, M.; Tsao, H. N.; Pisula, W.; Yang, C.; Mishra, A. K.; Müllen, K. *J. Am. Chem. Soc.* **2007**, *129*, 3472. (c) Li, K.-C.; Huang, J.-H.; Hsu, Y.-C.; Huang, P.-J.; Chu, C.-W.; Lin, J.-T.; Ho, K.-C.; Wei, K.-H.; Lin, H.-C. *Macromolecules* **2009**, *42*, 3681. (d) Lee, S. K.; Cho, N. S.; Cho, S.; Moon, S.-J.; Lee, J. K.; Bazan, G. C. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 6873.
2. (a) De Rosa, C.; Auriemma, F.; Resconi, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 9871. (b) Senda, T.; Hanaoka, H.; Okado, Y.; Oda, Y.; Tsurugi, H.; Mashima, K. *Organometallics* **2009**, *28*, 6915.
3. Kraak, A.; Wersema, A. K.; Jordens, P.; Wynberg, H. *Tetrahedron* **1968**, *24*, 3381.
4. Coppo, P.; Cupertino, D. C.; Yeates, S. G.; Turner, M. L. *Macromolecules* **2003**, *36*, 2705.
5. (a) Lucas, P.; Mehdi, N. E.; Ho, H. A.; Belanger, D.; Breau, L. *Synthesis* **2000**, 1253. (b) Brzezinski, J. Z.; Reynolds, J. R. *Synthesis* **2002**, 1053. (c) Beyer, R.; Kalaji, K.; Kingscote-Burton, G.; Murphy, P. J.; Pereira, V. M. S. C.; Taylor, D. M.; Williams, G. O. *Synth. Met.* **1998**, *92*, 25. (d) Jordens, P.; Rawson, G.; Wynberg, H. *J. Chem. Soc. (C)* **1970**, 273.
6. (a) Threlkel, R. S.; Bercaw, J. E. *J. Organomet. Chem.* **1977**, *136*, 1. (b) Halterman, R. L.; Tretyakov, A. *Tetrahedron* **1995**, *51*, 4371. (c) Erker, G.; van der Zeijden, A. A. H. *Angew. Chem., Int. Ed.* **1990**, *29*, 512.
7. (a) Rieder, C. J.; Winberg, K. J.; West, F. G. *J. Am. Chem. Soc.* **2009**, *131*, 7504. (b) He, W.; Herrick, I. R.; Atesin, T. A.; Caruana, P. A.; Kellenberger, C. A.; Frontier, A. J. *J. Am. Chem. Soc.* **2008**, *130*, 1003. (c) Grant, T. N.; Rieder, C. J.; West, F. G. *Chem. Commun.* **2009**, 5676.
8. (a) Jeffries, A. T.; Moore, K. C.; Ondeyka, D. M.; Springsteen, A. W.; MacDowell, D. W. H. *J. Org. Chem.* **1981**, *46*, 2885. (b) Östman, B.; Sjöberg, S. *Tetrahedron Lett.* **1970**, *21*, 3137.
9. (a) Nyberg, K.; Östman, B.; Wallerberg, G. *Acta Chem. Scand.* **1970**, *24*, 1590.
10. Wu, X.; Chen, T. A.; Zhu, L.; Rieke, R. D. *Tetrahedron Lett.* **1994**, *35*, 3673.
11. Barrett, A. G. M.; Carr, R. A. E.; Attwood, S. V.; Richardson, G.; Walshe, N. D. A. *J. Org. Chem.* **1986**, *51*, 4840.