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Tetrahedron Letters 46 (2005) 8195–8197
Tetrahedron Letters

A convenient synthesis of biphenylene

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Received 5 September 2005; revised 15 September 2005; accepted 19 September 2005

Abstract—An efficient one-pot reaction for the synthesis of biphenylene **1** starting from biphenyl is reported. The final product was prepared from commercially available, cheap materials in moderate yet very competitive yield. Biphenyl was *ortho*-lithiated to 2,2′-dilithiobiphenyl **2**, which was then coupled to biphenylene.

Biphenylene **1** was first prepared by Lothrop[1] in 1941 by an Ullman reaction of 2,2′dibromo- or 2,2′diiodobiphenyl and was for many years the only known derivative of cyclobutadiene fused to benzene. This compound, formally the dibenzo-derivative of cyclobutadiene, has been investigated thoroughly in the following years due to its interesting chemical properties and theoretical relevance to the discussion of aromaticity.[2] Many alternative protocols have been developed for its synthesis, but the known procedures for the preparation of **1** are unsatisfactory because they either use expensive starting materials or they afford **1** only in small amounts. A summary of the known, preparative useful synthetic routes which are not based on vacuum-pyrolysis is given in Scheme 1.

Starting from **I**, **II**,[3] and **III**,[4] an aryne intermediate is formed via elimination reactions, which dimerizes to biphenylene. With the exception of the procedure starting from **II**, the yields of biphenylene formation are generally low, and compound **II** has to be prepared in four steps from *o*-nitroaniline in approximately 54% yield. The standard method nowadays for the synthesis of **1** is a protocol described in *Organic Synthesis* starting from commercially available anthranilic acid **III**, which leads to **1** in 21%–30% yield.[4] During this preparation, however, explosive benzenediazonium-2-carboxylate is an intermediate. Although it is not necessary to isolate this substance, it is a hazardous material which should be a driving force to replace it in the laboratory. Other preparations starting from **V**,[5] **VI**,[1] and **VII**[6] employ transition metal mediated coupling reactions of 2′,2′-dihalogenated derivatives of biphenyl. A method mainly developed by Vollhardt and co-workers uses a cobalt mediated alkyne coupling reactions of *o*-dialkynylbenzenes, for example, *o*-diethynylbenzene **IV**,[7] with other alkynes. This procedure is valuable for substituted biphenylene derivatives, but presumably too expensive for the synthesis of the parent compound **1**. Other ways to synthesize biphenylene rely on vacuum-pyrolysis,[2,8] with the typical drawbacks of an often troublesome preparation of starting materials, low yields, and the problem to synthesize larger amounts of the desired product.

We are interested in the transition metal mediated C–C activation of biphenylene in stoichiometric as well as catalytic reactions.[9] The NHC (*N*-heterocyclic carbene) stabilized nickel complex $[Ni_2(Im^{i\text{-}Pr})_4(COD)]$ ($Im^{i\text{-}Pr}$ = 1,3-di(*iso*-propyl)imidazole-2-ylidene), for example, is the currently most active catalyst known for the insertion of diphenylacetylene into the 2,2′ bond of biphenylene to yield 9,10-di(phenyl)phenanthrene. Although biphenylene is commercially available,[10] it is expensive, which reflects the difficulties of the preparation. Since, we rely on a feedstock of **1** in our laboratory, we developed a new, efficient and easily achievable synthetic approach to **1**, in which commercially available, inexpensive biphenyl is directly coupled in the 2,2′-position. Our work was inspired by the report of the coupling reaction starting from **VII**.[6] We report here the first synthesis of **1** starting directly from unsubstituted biphenyl in a convenient one-pot procedure.

Biphenyl was selectively bis-*ortho*-metalated using stoichiometric amounts of *n*-BuLi and tetramethyl-ethylenediammine (TMEDA)[11] and 2,2′-dilithiobiphenyl was

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Keywords: Biphenylene; Biphenyl; One-pot synthesis.

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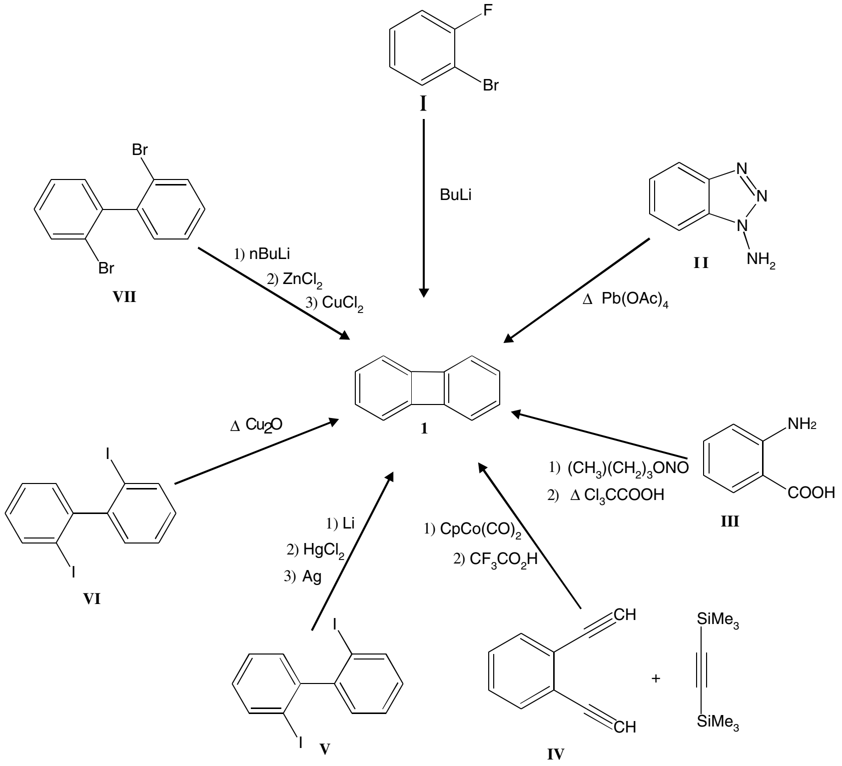
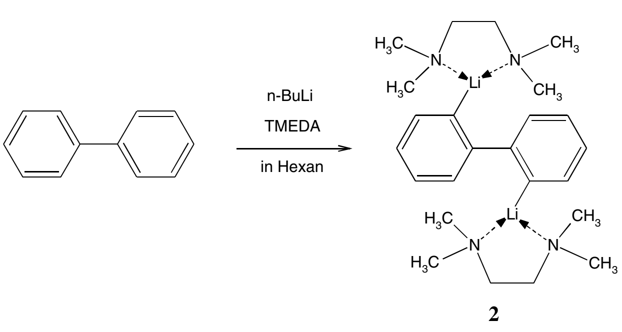
doi:10.1016/j.tetlet.2005.09.124



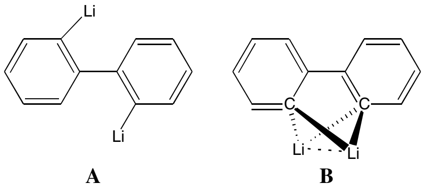
Scheme 1. Synthetic routes to biphenylene not based on vacuum-pyrolysis methods.

obtained as the TMEDA-adduct **2** in the first step of the new developed synthesis (Scheme 2).[12,13]

The first lithiation is preferred in *ortho*-position due to inductive and solvating effects of the phenyl rings, which affect both the transition-state and monolithiated product. MNDO calculations performed on different monolithiated products of biphenyl revealed an intramolecular stabilizing interaction between the vicinal phenyl ring and the lithium atom in the *ortho*-lithiated product, which stabilizes this compound by approximately 9.7 kcal/mol with respect to the *meta* and *para* substituted isomers.[11] The second lithiation step leads selectively to the 2,2′-dilithiobiphenyl in good yields. This selectivity also accounts to stabilizing interactions between vicinal phenyl rings and the lithium atoms in conformer **A**, as well as an stabilizing lithium–lithium interaction in conformer **B** (Scheme 3).



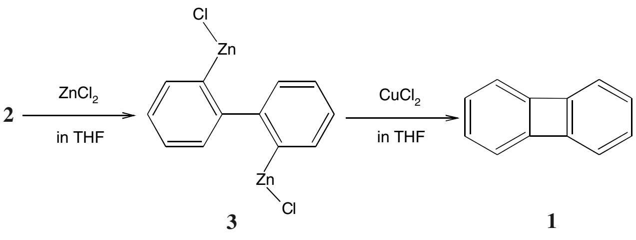
Scheme 2.



Scheme 3.

The reaction product can be isolated in approximately 47% yield and was characterized ^{1}H NMR spectroscopically. The synthesis of **1** does not require isolation of **2**. Although, we performed the synthesis of **1** in two separate steps with isolated **2**,[13,14] a one-pot procedure for the synthesis of **1** has the advantage of improved overall yield as well as avoiding the time consuming isolation of **2**.

In the second step, dilithium compound **2** was coupled with stoichiometric amounts of $ZnCl_2$ and $CuCl_2$ (Scheme 4).



Scheme 4.

The first step of this reaction requires the addition of anhydrous $\mathrm{ZnCl_2}$ to a solution of **2** in THF at −78 °C, which affords the corresponding zinc organyl **3**. Further addition of anhydrous $\mathrm{CuCl_2}$ at −78 °C leads to the coupling of **3** to biphenylene **1**.[6] After this step, the reaction mixture was hydrolyzed and the product was extracted with toluene. The crude product was recrystallized from pentane and purified by vacuum sublimation to give analytically pure **1** in the form of an off white, microcrystalline solid in 37% yield.[12] For the two-step synthesis, the yield was significantly lower (25–27%), mainly due to losses during the purification of **2**.

In conclusion, we enclosed an efficient one-pot reaction of biphenylene **1** starting from unsubstituted biphenyl. This reaction can be performed with commercially available, inexpensive starting materials to give biphenylene **1** in moderate yet competitive yield. This procedure is suitable for a 10–20 g scale preparation of biphenylene in short time.

Acknowledgements

Financial support of the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

References and notes

1. Lothrop, W. C. *J. Am. Chem. Soc.* **1941**, *63*, 1187.
2. See, for example: (a) Shepherd, M. K. *Cyclobutarenes—The Chemistry of Benzocyclobutene, Biphenylene, and Related Compounds*; Elsevier: Amsterdam, 1991; (b) Toda, F.; Garatt, P. *Chem. Rev.* **1992**, *92*, 1685.
3. Campbell, C.-D.; Rees, C. W. *J. Chem. Soc. (C)* **1969**, 742.
4. Logullo, F. M.; Seits, A. H.; Friedman, L. *Org. Synth. Coll.* Vol. 5, 1973, 54.
5. Wittig, G.; Herwig, W. *Chem. Ber.* **1954**, *87*, 1511.
6. Iyoda, M.; Kabi, S. M. H.; Vorashinga, A.; Kuwatani, Y.; Yoshidi, M. *Tetrahedron Lett.* **1998**, *39*, 5393.
7. Berris, B. C.; Lai, Y. H.; Vollhardt, K. P. C. *J. Chem. Soc., Chem. Commun.* **1982**, 953.
8. (a) Brown, R. F. C.; Browne, N. R.; Coulsten, K. J.; Eastwood, F. W.; Irwine, M. J.; Pullin, D. E.; Wiersum, U. E. *Aust. J. Chem.* **1989**, *42*, 1321; (b) Brown, R. F. C.; Coulsten, K. J.; Eastwood, F. W.; Vogel, K. *Aust. J. Chem.* **1988**, *41*, 1687; (c) Suhr, H.; Henne, P. *Liebigs Ann. Chem.* **1977**, 1610; (d) Barry, M.; Brown, F. C.; Eastwood, F. W.; Gunawaranda, D. A.; Vogel, K. *Aust. J. Chem.* **1984**, *37*, 1643.
9. Schaub, T.; Radius, U. *Chem. Eur. J.* **2005**, *11*, 5024.
10. For example: Aldrich no. 321958; 100 mg: 45.10€ (catalog 2005–2006).
11. Neugebauer, W.; Kos, A. J.; von Rague Schleyer, P. *J. Organomet. Chem.* **1982**, *228*, 107.
12. *Synthesis of biphenylene* **1**: All air/moisture sensitive manipulations were performed using standard Schlenk-line ($\mathrm{N_2}$) and dry-box (Ar) techniques. Solvents were predried and refluxed over sodium (THF, TMEDA, toluene, and pentane) and $\mathrm{N_2}$. Solvents were distilled at atmospheric pressure prior to use. N-BuLi (192.5 mL, 314 mmol: 16% in hexane) was added at room temperature to a stirred solution of biphenyl (20.0 g, 129 mmol) in dry TMEDA (47.1 mL, 314 mmol). The solution was stirred for 3 days at room temperature and all volatiles were removed afterwards in vacuo. The red residue was suspended in THF (400 mL) and a solution of anhydrous $\mathrm{ZnCl_2}$ (41.8 g, 306 mmol) dissolved in THF (280 mL) was added at −78 °C. The resulting mixture was stirred for 90 min at −78 °C, anhydrous $\mathrm{CuCl_2}$ (51.8 g, 386 mmol) was added, and the resulting suspension was stirred for 3 h at −78 °C and 1 day at room temperature to give a deep green solution. This solution was hydrolyzed with 4 M hydrochloric acid (267 mL), and the product was extracted twice with toluene (2 × 500 mL). The combined organic phases were washed twice with water (200 mL), dried over anhydrous sodium sulfate and all volatile material were removed in vacuo. The product was extracted with pentane (500 mL) from the remaining residue and the extract was stored at −40 °C overnight to give a yellowish precipitate, which was filtered off at −40 °C. The mother liquid was concentrated to 50–70 mL and stored at −40 °C for a second crop of crude product. The combined fractions were sublimed in vacuo (10^{-3} Torr) at 150 °C to afford 7.40 g (37%) biphenylene as an off white substance. $\mathrm{C_{12}H_8}$ [152.2 g/mol]. Calcd (found): C, 94.70 (94.37); H, 8.78 (8.68). EI/MS m/z (%): 152 (100) = $[\mathrm{M}^+]$, 76 (20) = $[\mathrm{M}]^{2+}$. ^{1}H NMR ($\mathrm{C_6D_6}$): $\delta = 6.40$ (m, 4H, Ar–*H*), 6.55 (d, 4H, Ar–*H*). ^{13}C NMR ($\mathrm{C_6D_6}$): $\delta = 118.50$ (Aryl–C_i), 128.90 (Aryl–C_o), 152.70 (Aryl–C_m).
13. *Synthesis of 2.2′-dilithiobiphenyl* **2**: *N*-BuLi (192.5 mL, 314 mmol: 16% in hexane) was added at room temperature to a stirred solution of biphenyl (20.0 g, 129 mmol) in dry TMEDA (47.1 mL, 314 mmol). The solution was stirred for 3 days at room temperature to give a yellow precipitate and a red solution. The precipitate was filtered off, washed twice with hexane (20 mL), and dried in vacuo. The filtrate was stored at −40 °C overnight to obtain a crop of yellow crystals of the TMEDA adduct (**2**·TMEDA) of **2**. These were filtered off at −78 °C, washed with cold hexane (−78 °C, 60 mL), and dried in vacuo. The overall yield of the combined fractions is 24.4 g (47%). ^{1}H NMR ($\mathrm{C_6D_6}$): $\delta = 1.76$ (s, 8H, N–CH_2), 1.83 (s, 24H, N–$(\mathrm{C}H_3)_2$), 7.18 (s, 4H, $\mathrm{C_{Ar}}$–H_m), 7.49 (m, 2H, $\mathrm{C_{Ar}}$–H_o), 8.48 (q, 2H, $\mathrm{C_{Ar}}$–H_p).
14. *Synthesis of biphenylene* **1** *starting from* **2**·*TMEDA*: Complex **2** · TMEDA (24.4 g, 61.2 mmol) was dissolved in 200 mL THF at −78 °C and a solution of anhydrous $\mathrm{ZnCl_2}$ (19.9 g, 145 mmol) in 180 mL THF was added. After addition, a white precipitate started to form and after 90 min stirring, anhydrous $\mathrm{CuCl_2}$ (19.9 g, 148 mmol) was added. The mixture was stirred for another 3 h at −78 °C and for 1 day at room temperature. Afterwards it was hydrolyzed with 4 M hydrochloric acid (127 mL), and the product was extracted with toluene (3 × 250 mL). The combined extracts were washed twice with water (150 mL) and dried over anhydrous sodium sulfate. All volatile material was removed in vacuo to obtain a dark yellow crude product. Pure biphenylene was obtained by sublimation at 150 °C in vacuo (10^{-3} Torr) on a water cooled sublimation finger to afford 5.30 g (55%) of an off white solid.