

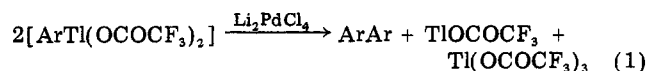
Biaryl Synthesis via Coupling of Arylthallium Bis(trifluoroacetates) with a Catalytic Amount of Lithium Tetrachloropalladate

Richard A. Kjonaas* and David C. Shubert

Department of Chemistry, Fort Hays State University,
Hays, Kansas 67601-4099

Received October 13, 1982

We report here a convenient and efficient synthesis of symmetrical biaryls by treating arylthallium bis(trifluoroacetates) with a catalytic amount (0.10 molar equiv) of lithium tetrachloropalladate (Li_2PdCl_4) as generalized in eq 1. This method involves very mild conditions—room



temperature for 5 days or refluxing tetrahydrofuran (THF) (67 °C) for 5 h. It will tolerate air, moisture,¹ and even carboxyl groups (Table I, entry f). In most cases, isolation of the product is achieved by aqueous workup followed by filtration through a small amount of silica gel to remove the residual traces of thallium salts.

Several research groups have observed the formation of biaryls as side products in reactions that involve arylthallium(III) compounds and a palladium(II) salt.² Another group³ reported that they obtained yields of 12–70% of four different biaryls by treating the corresponding thallium(III) compounds with a stoichiometric amount of PdCl_2 and sodium acetate in refluxing acetic acid. One of those biaryls, biphenyl, was also prepared with less than a stoichiometric amount of palladium(II) salt. Until now, however, there has been no report of the coupling of substituted arylthallium(III) compounds with a catalytic amount of a palladium(II) salt.

The coupling method reported herein complements existing biaryl syntheses.^{4–9} Those methods that involve Grignards⁵ and aryl lithiums are applicable only when acidic and electrophilic functional groups are absent. The Ullman reaction⁶ involves high temperatures and requires the use of aryl iodides. Most of the dehydromerization^{4,7} methods are of limited synthetic utility because of low yields, the formation of difficult to separate mixtures of products, and because they work best with electron-rich substituents. Some methods are extremely sensitive to air and moisture.⁸ A method involving the use of aryl mercuric salts requires refluxing pyridine (115 °C) for several hours.⁹

Our method too has drawbacks and limitations. It involves the use of highly toxic thallium compounds,¹⁰ and

(1) The addition of 2 molar equiv (with respect to starting material) of water had no effect on the reaction.

(2) For example: (a) Spencer, T.; Thorpe, F. G. *J. Organomet. Chem.* 1975, 99, C8–C10. (b) Larock, R. C.; Fellows, C. A. *J. Am. Chem. Soc.* 1982, 104, 1900–1907.

(3) Uemura, S.; Ikeda, Y.; Ichikawa, K. *J. Chem. Soc. D* 1971, 390–391. See also; Henry, P. M. *J. Org. Chem.* 1970, 35, 3083–3086.

(4) McKillop, A.; Turrell, A. G.; Young, D. W.; Taylor, E. C. *J. Am. Chem. Soc.* 1980, 102, 6504–6512 and numerous references therein.

(5) (a) Taylor, S. K.; Bennett, S. G.; Heinz, K. J.; Lashley, L. K. *J. Org. Chem.* 1981, 46, 2194–2196. (b) Hayashi T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* 1982, 104, 180–186.

(6) (a) Fanta, P. E. *Chem. Rev.* 1964, 64, 613–632. (b) Cornforth, J.; Sierakowski, A. F.; Wallace, T. W. *J. Chem. Soc., Chem. Commun.* 1979, 294–295.

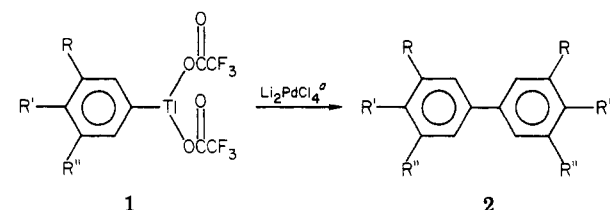
(7) Musgrave, O. C. *Chem. Rev.* 1969, 69, 499–531.

(8) Semmelhack, M. F.; et al. *J. Am. Chem. Soc.* 1981, 103, 6460–6471.

(9) Kretzmer, R. A.; Glowinski, R. *J. Org. Chem.* 1976, 41, 2661–2662.

(10) For a discussion of the toxicity of thallium and recommended laboratory procedures, see: Taylor, E. C.; McKillop, A. *Acc. Chem. Res.* 1970, 3, 338–346.

Table I. Coupling of Arylthallium Bis(trifluoroacetates) with Lithium Tetrachloropalladate



compd	R	R'	R''	isolated yield, %
a	H	H	H	88
b	H	CH_3	H	97
c	H	<i>n</i> -Bu	H	86
d	H	<i>t</i> -Bu	H	72
e	H	CH_2O	H	89 (96) ^b
f	H	$(\text{CH}_2)_3\text{CO}_2\text{H}$	H	90
g	CH_3	CH_3	H	81
h	<i>i</i> -Pr	H	<i>i</i> -Pr	66
i	H	Cl	H	20

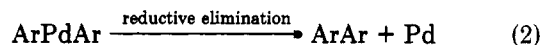
^a In each case 0.10 molar equiv (with respect to 1) was used. All reactions were carried out in refluxing THF for 5 h. Essentially the same results were obtained when carried out at 25 °C for 5 days. ^b Starting material 1e was contaminated with 7% of the ortho isomer. Thus an 89% yield of 2e based on the gross weight of thallated anisole is a 96% yield based on the net amount of 1e.

the reaction fails when there is a substituent in the ortho position. Thus we were unable to couple either thallated methyl benzoate or thallated *p*-xylene. The reaction also failed with thiophene bis(trifluoroacetate) and, as indicated in Table I, thallated chlorobenzene gave a low yield of coupled product. Thallated bromo- and iodobenzene were even less productive.

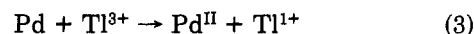
Despite their toxicity, arylthallium bis(trifluoroacetates) are an attractive starting material and they greatly enhance the utility of this coupling procedure. A large variety of them can be prepared in high yield, and, in many cases, it is possible to select the position of thallation by varying the reaction conditions.¹¹

Although 0.10 molar equiv of Li_2PdCl_4 was used in each experiment, the reaction appears to be suited to much smaller amounts of catalyst. When 1b was treated with only 0.010 molar equiv of Li_2PdCl_4 and refluxed 36 h, a 90% yield of 2b was obtained. Only a trace of 2b was detected after 36 h when the catalyst was omitted.

None of our experiments were directed toward the determination of a mechanism. Reductive elimination (eq 2) of a diaryl palladium species, however, is thought to be



common among coupling reactions involving palladium.¹² If reductive elimination occurs in the palladium(II)-catalyzed coupling of arylthallium compounds, the catalyst could then be regenerated from zerovalent palladium by the reduction of part of the thallium(III) (eq 3) that would



have resulted from the initial transmetalation. Such a regeneration was recently suggested for another reaction involving aryl thallium(III) compounds.^{2b}

(11) (a) McKillop, A.; Hunt, J. D.; Zelesko, M. J.; Fowler, J. S.; Taylor, E. C.; McGillivray, G.; Kienzle, F. *J. Am. Chem. Soc.* 1971, 93, 4841–4844. (b) Taylor, E. C.; Kienzle, F.; Robey, R. L.; McKillop, A.; Hunt, J. D. *Ibid.* 1971, 93, 4845–4850. (c) To obtain para-thallated toluene free from its ortho isomer, see: McKillop, A.; Fowler, J. S.; Zelesko, M. J.; Hunt, J. D.; Taylor, E. C.; McGillivray, G. *Tetrahedron Lett.* 1969, 2423–2426. (12) Trost, B. M. *Tetrahedron* 1977, 33, 2615–2649 (see p 2642).

Experimental Section

Materials. The arylthallium bis(trifluoroacetates) were prepared by established procedures.¹¹ Thallium and thallium compounds are extremely toxic and should be handled with utmost care.¹⁰ Thallium trifluoroacetate (94%) was obtained from Aldrich Chemical Co. and was used without further purification. THF was stored at reflux with sodium metal and benzophenone in a recycling solvent still. Li_2PdCl_4 was prepared by dissolving PdCl_2 and LiCl in water (heating is required), evaporating the water, and heating in vacuo at 100 °C until a red-purple solid was obtained.

Identification of Coupling Products. All of the biaryls that were prepared have been previously reported. They were identified by IR (Perkin Elmer 700) and ^1H NMR (Varian EM360) spectroscopy and melting points (uncorrected).

General Coupling Procedure. To 2.00 mmol of thallated aromatic dissolved in 10 mL of THF in a flask equipped with a magnetic stirrer was added 0.20 mmol (52 mg) of Li_2PdCl_4 . The mixture was either left at 25 °C for 5 days or refluxed for 5 h. Both methods worked equally well. Evaporation of the THF was followed by the addition of 5 mL of water and extraction with three 5-mL portions of hexane unless otherwise noted below. The combined organic layers were dried (Na_2SO_4), and the volume was reduced to 2 mL by evaporation. All of the products were further purified by filtration through 0.5–8 g of silica gel followed by recrystallization. Product **2e** required column chromatography (see below).

4,4'-Dimethoxybiphenyl (2e). Following the general procedure, 1.07 g (2.00 mmol) of thallated anisole (this consisted of **1e** contaminated with 7% of the ortho isomer), 52 mg (0.20 mmol) of Li_2PdCl_4 , and 10 mL of THF were refluxed 5 h. Workup with chloroform instead of hexane was followed by column chromatography on 25 g of silica gel with chloroform as the eluent. Elution proceeded as follows: 50 mL, nil; 150 mL, 191 mg (89% based on crude thallated anisole, 96% based on **1e**) of **2e** as a white crystalline solid with spectral properties in agreement with those reported. Recrystallization from ether gave essentially all of the material back as white flakes: mp 173–175 °C (lit. mp 176–178 °C).

4,4'-Bis(3-carboxypropyl)biphenyl (2f). To a slurry of 0.959 g (2.00 mmol) of thallated 4-phenylbutyric acid¹³ and 10 mL of THF in a flask equipped with a magnetic stirrer was added 170 μL (2.2 mmol) of trifluoroacetic acid to give a homogeneous solution of **1f**. Addition of 52 mg (0.20 mmol) of Li_2PdCl_4 was followed by refluxing for 5 h. Most of the solvent was then removed by rotary evaporation. The resulting material was treated with 5 mL of 10% HCl and was washed with three 10-mL portions of ethyl acetate. Drying was achieved by evaporating the ethyl acetate, dissolving in 10 mL of methanol, and adding Na_2SO_4 . The methanol solution was then filtered through 1 g of silica gel to remove residual thallium salts. Part of the solvent was then evaporated so that **2e** would crystallize when cooled in an ice/NaCl bath. The white crystalline product was collected and extensively dried in an Abderhalden containing P_2O_5 . This resulted in 293 mg (90%) of **2f**: IR (Nujol mull) 2500–3500, 1685, 940 cm^{-1} ; ^1H NMR (acetone- d_6) δ 1.9 (m, 4 H), 2.33 (t, 4 H), 2.65 (t, 4 H), 7.27 (d, $J = 8$ Hz, 4 H), 7.53 (d, $J = 8$ Hz, 4 H); mp 170–174 °C (lit.¹⁴ mp 185 °C).

Acknowledgment. Financial assistance from FHSU through the Graduate Council Research Committee is gratefully acknowledged.

Registry No. **1a**, 23586-54-1; **1b**, 23586-55-2; **1c**, 67106-45-0; **1d**, 38579-34-9; **1e**, 28688-23-5; **1f**, 33930-55-1; **1g**, 23586-56-3; **1h**, 77212-88-5; **1i**, 23586-58-5; **2a**, 92-52-4; **2b**, 613-33-2; **2c**, 7641-81-8; **2d**, 1625-91-8; **2e**, 2132-80-1; **2f**, 6918-69-0; **2g**, 4920-95-0; **2h**, 4920-94-9; **2i**, 2050-68-2; Li_2PdCl_4 , 15525-45-8.

(13) The recrystallized product obtained in the thallation of 4-phenylbutyric acid is the mono(trifluoroacetate) rather than the bis(trifluoroacetate) (see ref 11b). It is completely insoluble in THF. Dissolution occurs within about 1 min when 1 molar equiv of trifluoroacetic acid is added.

(14) (a) Gildersleve, D. R.; Tute, M. S. Belg. Pat. 670 862; *Chem. Abstr.* 1966, 65, 8827f. (b) Diekmann, H.; Chang, C. K.; Traylor, T. G. *J. Am. Chem. Soc.* 1971, 93, 4068–4070.

Synthesis of Imines of α,β -Acetylenic Ketones

Paul Margaretha,* Clemens Schröder, Steven Wolff,¹ and William C. Agosta¹

Institut für Organische Chemie und Biochemie, Universität Hamburg, D-2000 Hamburg 13, Federal Republic of Germany

Received September 16, 1982

In order to extend our earlier studies of the photochemical behavior of imines of α,β -ethylenic ketones,² we were interested in preparation of simple aliphatic imines of α,β -acetylenic ketones. We found no report in the literature concerning these compounds³ and have now developed an exchange procedure that should be generally useful for their preparation from the corresponding alkyl alkynyl ketones.

As expected, attempts to react acetylenic ketones directly with primary amines gave enamino ketones as major products. Minor amounts of the desired imine were isolated when molecular sieves were employed. Thus, 3-pentyn-2-one (**1a**)⁴ and methylamine yielded 54% of **2** and only 5–15% of the ynimine **3** (Chart I). However, reasonable yields of ynimines **4a** and **4b** were obtained by the reaction of **1a** and **1b**⁵ with *N*-ethylidenecyclohexanamine (**5**)⁶ at 25 °C and 100 torr for 20 h. This method is superior to one previously described⁷ for saturated imines that uses isopropylideneamines and zinc chloride as a catalyst. With the aldimine **5** the reaction proceeds at room temperature and no catalyst is needed. The exchange is driven by continuous removal at low pressure of the acetaldehyde formed. These acetylenic imines could be fully characterized but were rather unstable on storage. *N*-Methyl imine **3** decomposed slowly even at –30 °C.

Since we had previously shown that α -fluorine substituents increase the reactivity of excited imines in cycloaddition reactions,^{2,8} we were also interested in preparing imines of alkynyl perfluoroalkyl ketones. These ketones have not been generally accessible, but we found that **1c,d** could be conveniently prepared from the corresponding perfluorocarboxylic acid and an excess of the Grignard-acetylide.⁹ Unfortunately these fluorinated ketones reacted with **5** to afford only minor amounts of acetylenic imines, as monitored by infrared spectroscopy; attempts to isolate these ynimines were unsuccessful.

Experimental Section

The following spectrometers were used: IR, Perkin-Elmer 297; UV, PE 200; ^1H NMR, Bruker WH-270 (270 MHz); ^{13}C NMR, Varian WP-80; mass spectrum, Varian CH7. Chemical shifts are reported in parts per million relative to internal Me_4Si . All boiling points are uncorrected. Elemental analyses were obtained in the analytical laboratory at the University of Hamburg.

3-Pentyn-2-ylidenemethanamine (3). Methylamine [prepared from methylammonium chloride (0.3 mol)] was added to

(1) The Rockefeller University, New York, NY.

(2) Margaretha, P. *Helv. Chim. Acta* 1978, 61, 1025.

(3) During the course of this work preparation of a single α,β -ynimine was reported in connection with a novel synthesis of ketones by way of imines: Marks, M. J.; Walborsky, H. M. *J. Org. Chem.* 1982, 47, 52.

(4) Braude, E. A.; Jones, E. R. H.; Sondheimer, F.; Toogood, J. B. *J. Chem. Soc.* 1949, 607.

(5) Wilson, J. W.; Stubblefield, V. S. *J. Am. Chem. Soc.* 1969, 90, 3423.

(6) Beekunis, G. E.; Thoma, J. A. Ger. Offen. 2 109 267; *Chem. Abstr.* 1971, 75, 140353.

(7) Haury, V. E. U. S. Pat. 2 692 284; *Chem. Abstr.* 1955, 49, 15946.

(8) Margaretha, P. *Helv. Chim. Acta* 1982, 65, 290.

(9) This general method has been used for synthesis of alkyl perfluoroalkyl ketones: Dishart, K.; Levine, R. *J. Am. Chem. Soc.* 1956, 78, 2268.