Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

N-Phenylation of N-Arylaminophthalimides with Triphenylbismuth and Cupric Acetate: A Convenient Synthesis of 1-Aryl-1-Phenylhydrazines

Yutaka Aoki [a], Yuko Saito [a], Takeshi Sakamoto [a] & Yasuo Kikugawa [a]

[a] Faculty of Pharmaceutical Sciences, Josai University, 1--1 Keyakidai, Sakado, Saitama, 350--0295, Japan

Published online: 04 Dec 2007.

To cite this article: Yutaka Aoki, Yuko Saito, Takeshi Sakamoto & Yasuo Kikugawa (2000) N-Phenylation of N-Arylaminophthalimides with Triphenylbismuth and Cupric Acetate: A Convenient Synthesis of 1-Aryl-1- Phenylhydrazines, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 30:1, 131-140, DOI: 10.1080/00397910008087300

To link to this article: http://dx.doi.org/10.1080/00397910008087300

SYNTHETIC COMMUNICATIONS, 30(1), 131–140 (2000)

N-PHENYLATION OF *N*-ARYLAMINOPHTHALIMIDES WITH TRIPHENYLBISMUTH AND CUPRIC ACETATE: A CONVENIENT SYNTHESIS OF 1-ARYL-1-PHENYLHYDRAZINES

Yutaka Aoki, Yuko Saito, Takeshi Sakamoto and Yasuo Kikugawa*

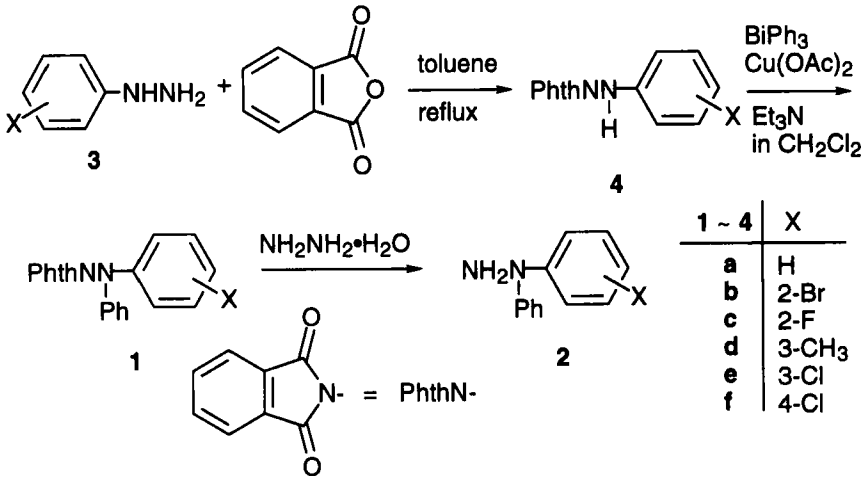
Faculty of Pharmaceutical Sciences, Josai University, 1-1 Keyakidai, Sakado, Saitama 350-0295, Japan

Abstract: Synthesis of 1-aryl-1-phenylhydrazines (**2**) from *N*-aryl-*N*-phenylaminophthalimides (**1**) which were synthesized by the phenylation of **1** with triphenylbismuth and cupric acetate is described.

In connection with a synthesis project currently underway in our laboratory, we required *N*-(*N*,*N*-diarylamino)phthalimides (**1**). It is well known that **1** are easily synthesized from 1,1-diarylhydrazines (**2**) and phthalic anhydride in refluxing toluene.[1] A survey of the existing methods often used for the synthesis of **2**

* To whom correspondence should be addressed.

revealed that condensation of a ring substituted acetanilide with a bromoarene by Ullmann reaction,[2] hydrolysis of the acetamide moiety, N-nitrosation, and finally reduction of the nitroso compound gave **2**. However, the nitrosation-reduction sequence is problematic because many nitrosoamines are known to be carcinogenic.[3]



On the other hand, it is convenient if **2** are synthesized from arylhydrazines (**3**). Because they are easily synthesized[4] and some of them are commercially available. As the direct regioselective phenylation of arylhydrazines is impossible, we carried out direct phenylation of the N-H of *N*-arylaminophthalimide (**4**) which were

prepared from **3** and phthalic anhydride in refluxing toluene, using triphenylbismuth and cupric acetate. Recently, many classes of N-H containing compounds are efficiently arylated by this combination.[5] However, all classes of N-H cannot always arylated and some modification of the method are necessary. We applied the literature method (Ph_3Bi, $Cu(OAc)_2$ and Et_3N in CH_2Cl_2)[6] for the phenylation of a new class of N-H containing **3** and could obtain **1** in high yield. The results are presented in Table 1. Compounds **1** were converted to **2** by deprotection of the phthalimide group with hydrazine hydrate as usual.[7] The results are presented in Table 2.

According to this methodology, **1** were obtained in two steps from **3** without synthesizing **2**, and **2** were easily obtained from **1**.

Table 1. Phenylation of **4** with $BiPh_3$-$Cu(OAc)_2$ in CH_2Cl_2 at room temperature

run	substrate	$BiPh_3$ (eq.)	$Cu(OAc)_2$ (eq.)	Et_3N (eq.)	time (h)	product (yield, %)
1	**4a**	1.1	1.0	1.0	4	**1a** (96)
2	**4b**	2.0	1.5	1.5	24	**1b** (99)
3	**4c**	2.0	1.5	1.5	24	**1c** (96)
4	**4d**	2.0	1.5	1.5	72	**1d** (82)
5	**4e**	2.0	1.5	1.5	24	**1e** (98)
6	**4f**	2.0	1.5	1.5	24	**1f** (97)

Table 2. Removal of phthaloyl group from **1** with $NH_2NH_2 \cdot H_2O$

run	substrate	time (h)	product (yield, %)
1	**1a**	6	**2a** (97)
2	**1b**	4	**2b** (83)
3	**1c**	6	**2c** (91)
4	**1d**	4	**2d** (83)
5	**1e**	6	**2e** (84)
6	**1f**	6	**2f** (70)

Experimental

All the melting points were determined with a Yanagimoto hot-stage melting point apparatus and are uncorrected. ^{1}H NMR spectra were measured at 270 MHz on a JEOL JNM-EX270 spectrometer with tetramethylsilane (Me_4Si) as an internal reference and $CDCl_3$ as the solvent. ^{1}H NMR spectral data are reported in parts per million (δ) relative to Me_4Si. IR spectra were recorded on a JASCO IR 810 spectrophotometer. Mass spectra were obtained with a JEOL JMX-DX 300 spectrometer with a direct inlet system at 70 eV. Elemental analyses were performed in the Microanalytical Laboratory of this University.

Synthesis of *N*-arylaminophthalimides (**4a**, **c** and **f**) was reported previously.[1] Other *N*-arylaminophthalimides (**4b**, **d** and **e**) were prepared similarly.

Table 3. Spectral data for phthaloyl compounds

compd.	IR [a] (cm^{-1})	MS (*m/z*)	^{1}H-NMR($CDCl_3$) δ ppm
1a	1790 1730 1590	314	7.07 (2H, t, *J*=7.5, Ar-H), 7.17 (4H, d, *J*= 8.0Hz, Ar-H), 7.25-7.34 (4H, m, Ar-H), 7.77-7.84 (2H, m, ArH), 7.88-7.95 (2H, m, Ar-H)
1b	1795 1740 1600	392	6.73 (2H, d, *J*=7.7Hz, Ar-H), 6.97 (1H, t, *J*=7.0 Hz, Ar-H), 7.14 (1H, dt, J_1=8.0Hz, J_2=2.0Hz, Ar-H), 7.24 (2H, dt, J_1=8.1Hz, J_2=2.0Hz, Ar-H), 7.34 (1H, dt, J_1=8.0Hz, J_2=2.0Hz, Ar-H), 7.66 (2H, dt, J_1=8.1Hz, J_2=2.0Hz, Ar-H), 7.77-7.85 (2H, m, Ar-H),7.88-7.95 (2H, m, Ar-H)
1c	1795 1740 1600	332	6.75 (2H, d, *J*=8.0Hz, Ar-H), 6.93 (1H, t, *J*=8.0 Hz, Ar-H), 7.06-7.31 (5H, m, Ar-H), 7.66 (1H, dt, J_1=8.0Hz, J_2=2.0Hz, Ar-H), 7.75-7.86 (2H, m, Ar-H), 7.88-7.98 (2H, m, Ar-H)
1d	1790 1740 1600	328	2.29 (3H, s, CH_3), 6.87-7.38 (9H, m, Ar-H), 7.76-7.87 (2H, m, Ar-H), 7.88-7.97 (2H, m, Ar-H)
1e	1795 1740 1590	348	6.87 (1H, dd, J_1=8.0Hz, J_2=2.0Hz, Ar-H), 6.96-6.99 (2H, m, Ar-H), 7.14-7.23 (2H, m, Ar-H), 7.34-7.36 (4H, m, Ar-H), 7.80-7.84 (2H, m, Ar-H), 7.92-7.95 (2H, m, Ar-H)
1f	1790 1740 1595	348	7.05-7.36 (9H, m, Ar-H), 7.80-7.85 (2H, m, Ar-H), 7.90-7.95 (2H, m, Ar-H)

a) KBr.

Table 4. Spectral data for hydrazines

compd.	IR [a] (cm^{-1})	MS (*m/z*)	^{1}H-NMR($CDCl_3$) δ ppm
2a	3345 3060 1590	184	4.15 (2H, brs, NH_2), 6.98 (2H, tt, J_1=6.8 Hz, J_2=1.6Hz, ArH), 7.17-7.34 (8H, m, ArH)
2b	3350 3060 1600	262	4.20 (2H, brs, NH_2), 6.82 (1H, t, *J*=7.3 Hz, Ar-H), 6.88 (2H, dd, J_1=8.8Hz, J_2= 1.1Hz, Ar-H), 7.10-7.18 (1H, m, Ar-H), 7.20 (2H, t, *J*=7.1Hz, Ar-H), 7.31-7.36 (2H, m, Ar-H), 7.67 (1H, d, *J*=7.7Hz, Ar-H)
2c	3350 3070 1600	202	4.15 (2H, brs, NH_2), 6.85 (1H, t, *J*=7.3 Hz, Ar-H), 6.97 (2H, d, *J*=7.7Hz, Ar-H), 7.08-7.26 (5H, m, Ar-H), 7.30-7.38 (1H, m, Ar-H)
2d	3350 3050 1600	198	2.32 (3H, s, CH_3), 4.15 (2H, brs, NH_2), 6.81 (1H, d, *J*=7.3Hz, Ar-H), 6.96 (1H, t, *J*=7.0Hz, Ar-H), 7.03 (2H, d, *J*=7.0Hz, Ar-H), 7.14-7.32 (5H, m, Ar-H)
2e	3350 3070 1585	218	4.10 (2H, brs, NH_2), 6.85 (1H, d, *J*=7.7 Hz, Ar-H), 7.02 (1H, d, *J*=7.5Hz, Ar-H), 7.07-7.17 (2H, m, Ar-H), 7.17-7.27 (3H, m, Ar-H), 7.34 (2H, d, *J*=7.5Hz, Ar-H)
2f	3350 3075 1590	218	4.25 (2H, brs, NH_2), 7.03 (1H, t, *J*=7.0 Hz, Ar-H), 7.10-7.24 (6H, m, Ar-H), 7.31 (2H, t, *J*=7.0Hz, Ar-H)

a) Neat.

Table 5. Physical constants and microanalytical data for phthaloyl compounds

compd.	mp (°C) (solvent)	molecular formula	found (%) (calc.)		
			C	H	N
1a	160-161 (AcOEt)	$C_{20}H_{14}N_2O_2$	76.26 (76.42)	4.66 (4.49)	8.87 (8.91)
1b	237 (acetone)	$C_{20}H_{13}N_2O_2Br$	60.95 (61.09)	3.54 (3.33)	7.11 (7.12)
1c	169 (AcOEt)	$C_{20}H_{13}N_2O_2F$	72.08 (72.28)	4.23 (3.94)	8.45 (8.43)
1d	114 (AcOEt)	$C_{21}H_{16}N_2O_2$	76.97 (76.81)	5.05 (4.91)	8.53 (8.53)
1e	82-84 (pet. ether)	$C_{20}H_{13}N_2O_2Cl$	68.73 (68.87)	3.92 (3.76)	7.98 (8.03)
1f	122-124 (ben.- hex.)	$C_{20}H_{13}N_2O_2Cl$	69.11 (68.87)	3.96 (3.76)	8.08 (8.03)

4b: mp 217~218 °C (CH_2Cl_2). *Anal.* Calcd for $C_{14}H_9BrN_2O_2$: C, 53.02; H, 2.86; N, 8.83. Found: C, 53.00; H, 3.04; N, 8.85.

4d: mp 148~150 °C (AcOEt). *Anal.* Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.37; H, 4.99; N, 11.05.

4e: mp 178~180 °C (EtOH)(lit.[8] mp 180 °C).

Synthesis of *N*-(*N*-4-Chlorophenyl-*N*-phenylamino)phthalimide (1f); Typical Procedure:

A mixture of *N*-(*N*-4-chlorophenylamino)phthalimide (**4f**) (577 mg,

Table 6. HRMS data for hydrazines

compd.	molecular formula	found (calc.)
2a	$C_{12}H_{12}N_2$	184.0993 (184.1001)
2b	$C_{12}H_{11}N_2Br$	262.0091 (262.0106)
2c	$C_{12}H_{11}N_2F$	202.0906 (202.0906)
2d	$C_{13}H_{14}N_2$	198.1162 (198.1157)
2e	$C_{12}H_{11}N_2Cl$	218.0616 (218.0610)
2f	$C_{12}H_{11}N_2Cl$	218.0612 (218.0610)

2.12 mmol), triphenylbismuth (1.86 g, 4.23 mmol), cupric acetate (577 mg, 3.18 mmol), and triethylamine (321 mg, 3.18 mmol) in CH_2Cl_2 (30 ml) was stirred for 24 h at room temperature under Ar. After the reaction, the solution was diluted with AcOEt (15 ml) and was filtered with celite. The filtrate was evaporated under reduced pressure. The crude product was chromatographed on a column of silica gel with benzene-hexane (1:1) as an eluent to give **1f** (722 mg, 98%). Physical and spectral data for **1** are listed in Table 3 and 5.

Synthesis of 1-(3-Methylphenyl)-1-phenylhydrazine (2d); Typical Procedure:

To **1d** (1.02 g, 3.10 mmol) in EtOH (10 ml) was added $NH_2NH_2 \cdot H_2O$ (80%)(291 mg, 4.66 mmol) at room temperature. After refluxing the reaction mixture for 4 h, EtOH was evaporated under reduced pressure. To the residue benzene (5 ml) was added and insoluble material was removed by filtration. After evaporation of the filtrate, the crude product was chromatographed on a column of silica gel with benzene as an eluent to give **2d** (536 mg, 87%). Spectral and HRMS data for **2** are listed in Table 4 and 6.

References

1. Ohwada, A.; Li, H.; Sakamoto, T.; Kikugawa, Y. *Heterocycles*, **1997**, *46*, 225-233.
2. Weston, P. E.; Adkins, H. *J. Am. Chem. Soc.*, **1959**, *50*, 859-866; Ullmann, F. *Ber.*, **1903**, *36*, 2382-2384; Fanta, P. E. *Synthesis* , **1974**, 9-21.
3. Ferguson, L. N. *Chem. Soc. Rev.*, **1975**, *4*, 289-322.
4. Dufresne, C.; Leblanc, Y.; Berthelette, C.; McCooeye, C. *Synthetic Commun.*, **1997**, *27*, 3613-3624.

5. Barton, D. H. R.; Finet, J.-P.; Khamsi, J. *Tetrahedron Lett.*, **1986**, *27*, 3615-3618; Idem, *ibid.*, **1987**, *28*, 887-890; Barton, D. H. R.; Ozbalik, N.; Ramesh, M.*Tetrahedron Lett.*, **1988**, *29*. 857-860; Barton, D. H. R.; Finet, J.-P.; Khamsi, J. *Tetrahedron Lett.*, **1989**, *30*, 937-940; Arnauld,T.; Barton, D. H. R.; Doris, E. *Tetrahedron*, **1997**, *53*, 4137-4144; Combes, S.; Finet, J.-P. *Tetrahedron*, **1998**, *54*, 4313-4318.

6. Chan, D. M. T. *Tetrahedron Lett.*, **1996**, *37*, 9013-9016.

7. Greene, T. W.; Wuts, P. G. M. "*Protective Groups in Organic Synthesis*," Second Edition, John Wiley & Sons, Inc., 1990, pp 358-359.

8. Chattaway, F. D.; Vonderwahl, E. *J. Chem. Soc.*, **1915**, *107*, 1503-1509.

(Received in Japan 13 April 1999)