Cu-Catalysed N-Arylation of Hydrazines with Bismuthanes: Synthesis and Pinacol or Imino-Pinacol Coupling of 4-Formylphenylhydrazines and their Phenylimine Derivatives

Olavi Loog, Uno Mäeorg*

Institute of Organic and Bioorganic Chemistry, University of Tartu, Jakobi 2, 51014, Tartu, Estonia
E-mail: uno.maeorg@ut.ee

Received 25 August 2004

Abstract: Acetal protected 4-formylphenylbismuthane was prepared and used for arylation of trisubstituted hydrazines. Formylphenylhydrazines, obtained after removal of acetal group, were used in coupling reaction to give diols containing two substituted hydrazino moieties and the coupling of corresponding phenylimine derivatives gave corresponding diamines.

Key words: hydrazine arylation, aldehydes, imines, pinacol coupling, diols

This work aims to extend the versatile hydrazines stepwise substitution strategy with direct introduction of arylaldehyde functionality and to use such substituted hydrazinoarylaldehydes and their imine analogues in pinacol or imino-pinacol coupling reactions.

Aldehydes play an important role in organic synthesis because they are easily convertible to different functionality or provide numerous ways for condensation and coupling reactions.[1] One well-known reaction of aldehydes is the pinacol coupling that is used to prepare vicinal diols.[2] Reaction of aldehydes with primary amines gives aldimines, which also can be coupled to form vicinal diamines.[3,4a] Vicinal diols and diamines both, especially in the homochiral form, are used as ligands in catalysts, as complexing agents, and as synthetic intermediates.[4]

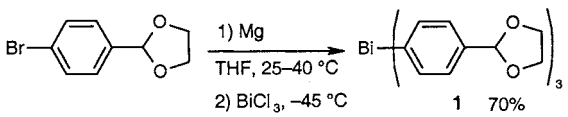
The hydrazine alkyl and aryl derivatives are found in drugs, pesticides, different types of reagents and constitute starting materials for the synthesis of heterocycles.[5a] One convenient way to obtain differentially substituted hydrazines is to use a directed stepwise substitution–deprotection strategy starting with a suitably protected hydrazine derivative.[5,6] In this strategy, arylbismuthanes have been used successfully for arylation of hydrazines.[7] Arylbismuthanes are quite versatile reagents for arylation,[8–12] but their synthesis is limited to aryl compounds substituted with groups tolerating lithiation or Grignard reagent preparations,[8b] and also the synthesis of arylbismuthanes with electron-withdrawing substituents is not so straightforward, although there are a few examples of such bismuthanes.[12b]

SYNLETT 2004, No. 14, pp 2537–2540
Advanced online publication: 20.10.2004
DOI: 10.1055/s-2004-835621; Art ID: G33404ST

Arylhydrazines and their derivatives (hydrazones, hydrazides) bearing an aldehyde group are relatively unknown compounds. For example, agaritinal, a derivative of 4-formylphenylhydrazine is often accompanied with agaritine[13] (a derivative of 4-hydroxymethylphenylhydrazine, which is considered a potential health risk) in mushrooms from genus Agaricus, at least one of which (*Agaricus bisporus*) is widely cultivated. Formylarylhydrazones have been used also as intermediates in the synthesis of compounds with non-linear optical properties,[14] hetero-diradicals[15] and heterocyclic compounds.[16] Other possible uses of formylphenylhydrazine derivatives include, for example, in photothermographic materials,[17] electrophotographic photoreceptors,[18] diagnostic agents for urobilinogen detection[19] and antibiotics.[20]

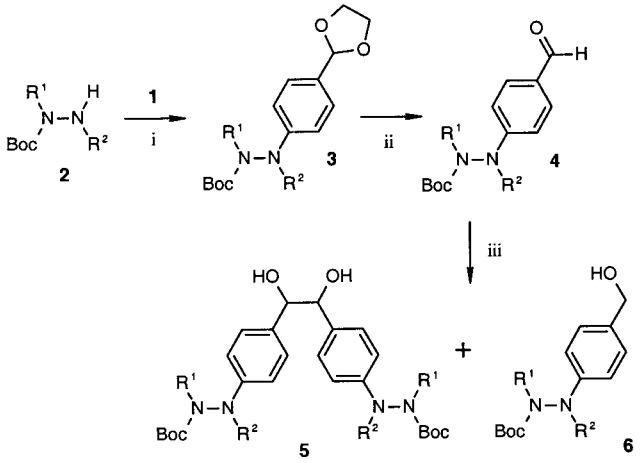
Preparative methods for formylarylhydrazine derivatives involve, for example, reduction of 4-cyanophenylhydrazine derivatives with DIBALH to the corresponding aldehydes.[15] In another method,[14] substituted phenylhydrazone is metallated with *t*-BuLi and then treated with PhN(Me)CHO. 4-Formylhydrazobenzenes formed as a result of nontypical alkyl-nitrogen cleavage when acetamidomethyl substituted diaryl azocompounds were treated with KOH in alcohol.[21] Also, a few other, more specific, methods have been described.[16,22]

Here we describe the synthesis of aryl bismuthane **1** from 4-bromophenyl-1,3-dioxolane[23] and its use for arylation of three substituted hydrazines. The aryl bismuthane **1** is obtained in good yield via standard aryl Grignard chemistry using a slightly modified method described by Combes and Finet[25] under mild conditions in the final step (Scheme 1).[26]



Scheme 1 Synthesis of arylbismuthane **1**.

Arylation of hydrazines with **1** in the presence of $Cu(OAc)_2$ and Et_3N[9d] proceeded under mild conditions and gave good yields for trisubstituted hydrazines[27] (see Table 1, compounds **3a**–**c**).[28] When 1,2-diacetylhydrazine was used, the arylation gave complicated mixture of unidentified products. Acetal group removal from com-



Scheme 2 Arylation of substituted hydrazines with **1** and pinacol coupling of hydrazinobenzaldehydes **4**. *Conditions*: i) $Cu(OAc)_2$, Et_3N, CH_2Cl_2; ii) TsOH, THF–H_2O; iii) Mn, Cp_2TiCl_2, 2,4,6-Me_3Py·HCl, THF (or in entry a′: Zn/Cu, EtOH, Δ).

pounds **3a**–**c** proceeded in high yields by treatment with substoichiometric amounts of TsOH in aqueous THF.[29] Under these conditions, Boc groups, even on the same nitrogen in **3b**, were not affected.

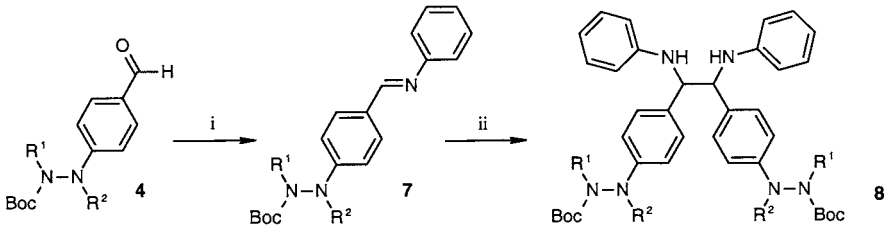
Treatment of **4a** with Zn/Cu couple[30] in ethanol (entry a′) resulted mainly in the formation of simple reduction product **6a**.[31] Coupling of hydrazinobenzaldehydes under the conditions described by Gansäuer and Bauer[32] gave the corresponding diols **5a**–**c**[33] in moderate yields and with moderate (**5a**,**b**) to good (**5c**) diastereoselectivity.

Long reaction times and moderate yields are probably due to the bulky substituents in the hydrazino moiety. For example, the lowest yield and longest reaction time were observed for cases in which all three substituents in hydrazine were Boc groups (entry 2). Long reaction times may also be responsible for the moderate diastereoselectivity observed.[35]

The coupling of phenylimine derivatives[36] **7a** and **7b** to the corresponding diamines were then investigated. Treatment with Zn/Cu couple[31] gave diamines in 71% and ca. 29% yields, respectively, but with no diastereoselectivity.[37]

It should be noted that attempts to remove two or three Boc groups attached to one hydrazino moiety in products **5b**, **6a**, **6b**, **8a** simultaneously under different deprotection conditions[38] led in all cases to degradation or polymerisation.[39] Hence it is advisable that the hydrazine derivative into which the 4-formylphenyl group is to be introduced is selected so that there is no further need for removal of Boc groups. Alternatively, different protecting groups (for example Z) should be considered.

In conclusion, we have shown that 4-formylphenyl group could be introduced under mild conditions and in good



Scheme 3 Synthesis of phenylimine derivatives **7** and their imino-pinacol coupling. *Conditions*: i) $PhNH_2$, $MgSO_4$, CH_2Cl_2; ii) Zn/Cu, EtOH, Δ.

Table 1 Details for the Reactions in Scheme 2 and Scheme 3[a]

	R^1	R^2	**3**		**4**		**5** + **6**			**7**		**8**	
			Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield of **5** (%, *dl*/*meso*)	Yield of **6** (%)	Time (h)	Yield (%)	Time (h)	Yield (%, *dl*/*meso*)
a	Ph	Boc	28	96	3	92	23	65 (4:1)	(15)[b]	23	98	1	71 (1:1)
a′							29	8 (1:1)	65				
b	Boc	Boc	52	94	1.5	96	61	48 (4:1)	22	50	91	6	ca. 29[c] (1:1)
c	Ac	Ac	49	85	1	92	23	51 (10:1)	10	26	47[d]		

[a] Yields are for isolated materials. Ratios of *dl*/*meso* isomers were estimated on the basis of C_{18} HPLC and ^{1}H NMR; *dl* and *meso* isomers were assigned based on signals of benzylic protons in ^{1}H NMR spectra as described in the literature.[34]
[b] Yield estimated on the basis of C_{18} HPLC.
[c] Calculated on the basis of the yield of isolated material (44%), which contained ca. 15% of starting material **7b**.
[d] Initial yield of raw product was almost quantitative, but the attempts to crystallise the raw product and finally its purification by silica gel column chromatography lowered the yield considerably.

yields into trisubstituted hydrazines. We have also demonstrated that formylphenylhydrazines undergo coupling reaction to diols containing two substituted hydrazino moieties (**5a**–**c**) and the corresponding phenylimine derivatives undergo coupling to corresponding diamines (**8a**,**b**). In principle, numerous other trisubstituted hydrazines and also secondary amines/amides could be used as substrates and also bismuthanes of other benzaldehyde derivatives could be prepared and used in the similar manner for arylation.

Acknowledgment

This work was financially supported by the Estonian Science Foundation (No. 5255). We thank Dr Olga Tšubrik and Mr Aleksei Bredihhin for obtaining NMR spectra and Dr Ulf Ragnarsson for his encouragement and long-term support.

References

(1) Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; Wiley: New York, **1999**, 1197–1620.
(2) Reviews: (a) Robertson, G. M. In *Comprehensive Organic Synthesis*, Vol. 3; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, **1991**, 563. (b) Gansäuer, A.; Bluhm, H. *Chem. Rev.* **2000**, *100*, 2771.
(3) (a) Mercer, G. J.; Sigman, M. S. *Org. Lett.* **2003**, *5*, 1591; and references therein. (b) Alexakis, A.; Aujard, I.; Mangeney, P. *Synlett* **1998**, 873; and references therein.
(4) For reviews on vicinal diamines, see: (a) Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem. Int. Ed.* **1998**, *37*, 2580. (b) Bennani, Y. L.; Hanessian, S. *Chem. Rev.* **1997**, *97*, 3161. (c) See also: Matsubara, S.; Hashimoto, Y.; Okano, T.; Utimoto, K. *Synlett* **1999**, 1411. (d) Reedijk, J. *Chem. Commun.* **1996**, 801. (e) For vicinal diols see, in addition to ref.[2]: Kim, Y. H. *Acc. Chem. Res.* **2001**, *34*, 955. (f) Pietruszka, J.; Witt, A. *Synlett* **2003**, 91.
(5) (a) For a review see: Ragnarsson, U. *Chem. Soc. Rev.* **2001**, *30*, 205; and references therein. (b) Mäeorg, U.; Grehn, L.; Ragnarsson, U. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2626.
(6) (a) Brosse, N.; Jamart-Grégorie, B. *Tetrahedron Lett.* **2002**, *43*, 249. (b) Tšubrik, O.; Mäeorg, U. *Org. Lett.* **2001**, *3*, 2297.
(7) (a) Tšubrik, O.; Mäeorg, U.; Sillard, R.; Ragnarsson, U. *Tetrahedron* **2004**, *60*, 8363. (b) Loog, O.; Mäeorg, U.; Ragnarsson, U. *Synthesis* **2000**, 1591.
(8) For reviews on arylbismuthanes in combination with copper salts or metallic copper as N- and O-arylating reagents, see: (a) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400. (b) Elliott, G. I.; Konopelski, J. P. *Tetrahedron* **2001**, *57*, 5683. (c) *Organobismuth Chemistry*; Suzuki, H.; Matano, Y., Eds.; Elsevier: Amsterdam, **2001**. (d) Finet, J.-P. *Chem. Rev.* **1989**, *89*, 1487.
(9) (a) Shimi, K.; Boyer, G.; Finet, J.-P.; Galy, J.-P. *Lett. Org. Chem.* **2004**, *1*, 34. (b) Chatel, F.; Boyer, G.; Galy, J.-P. *Synth. Commun.* **2002**, *32*, 2893. (c) Sorenson, R. J. *J. Org. Chem.* **2000**, *65*, 7747. (d) Chan, D. M. T. *Tetrahedron Lett.* **1996**, *37*, 9013.
(10) (a) Aoki, Y.; Saito, Y.; Sakamoto, T.; Kikugawa, Y. *Synth. Commun.* **2000**, *39*, 131. (b) Barton, D. H. R.; Finet, J.-P.; Khamsi, J. *Tetrahedron Lett.* **1987**, *28*, 887. (c) Barton, D. H. R.; Finet, J.-P.; Khamsi, J. *Tetrahedron Lett.* **1986**, *27*, 3615.
(11) For the use of arylbismuthanes in arylation of hydrazine derivatives, see ref.[7] and ref.[10]
(12) Arylbismuthanes provide interest not only as arylating reagents but also as for example: (a) Therapeutic agents: Matano, Y.; Aratani, Y.; Miyamatsu, T.; Kurata, H.; Miyaji, K.; Sasako, S.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2511. (b) Building blocks for three-dimensional organometallics: Murafuji, T.; Nishino, K.; Nagasuke, M.; Tanabe, A.; Aono, M.; Sugihara, Y. *Synthesis* **2000**, 1208; and references therein.
(13) (a) Stijve, T.; Pittet, A. *Deutsche Lebensmittel-Rundschau* **2000**, *96*, 251; *Chem. Abstr.* **2000**, 133, 134478. (b) Chulija, A. J.; Bernillon, J.; Favre-Bovin, J.; Kaouadji, M.; Arpin, N. *Phytochemistry* **1988**, *27*, 929.
(14) Gompper, R.; Walther, P. *Tetrahedron* **1996**, *52*, 14607.
(15) Ionita, P.; Whitwood, A. C.; Gilbert, B. C. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1453.
(16) Slouka, J. *Pharmazie* **1971**, *26*, 466.
(17) Yanagisawa, H.; Ho, K. S. Eur. Pat. Appl. EP 1168066, **2002**; *Chem. Abstr.* **2002**, *136*, 61567.
(18) Nagata, M.; Kunieda, M.; Kanemaru, T. Jpn. Kokai Tokkyo Koho JP 2000314972, **2000**; *Chem. Abstr.* **2000**, *133*, 357222.
(19) Rittersdorf, W.; Rey, H.; Rieckmann, P. S. African ZA 6806903, **1969**; *Chem. Abstr.* **1970**, *72*, 29743.
(20) Takai, H.; Yoshida, M.; Iida, T.; Matsubara, I.; Shirahata, K. *J. Antibiot.* **1976**, *29*, 1253.
(21) Stodola, F. H. *J. Org. Chem.* **1972**, *37*, 178.
(22) (a) Vysochin, V. I.; Barkhash, V. A.; Vorozhtsov, N. N. *Zh. Obsh. Khim.* **1969**, *39*, 1607; *Chem. Abstr.* **1969**, *71*, 112563. (b) Russel, G. A.; Yao, C. F. *Heteroat. Chem.* **1993**, *4*, 433. (c) Wiley, R. H.; Irick, G. *J. Org. Chem.* **1959**, *24*, 1925. (d) Antibiotic XK-90 [*N*-acetyl-*N*′-(3-formyl-4-hydroxyphenyl)hydrazine] has been produced microbiologically from *Streptomyces chibasis*, see ref.[20]
(23) (a) 2-(4-Bromophenyl)-1,3-dioxolane was prepared from 4-bromobenzaldehyde (obtained from 4-bromotoluene by treatment with CrO_3/Ac_2O)[23b] in 66% yield (mp 33.5–34.0 °C).[24] (b) Lieberman, S. V.; Connor, R. *Org. Synth.* **1938**, *18*, 61.
(24) Hon, Y.-S.; Lee, C.-F.; Chen, R.-J.; Szu, P.-H. *Tetrahedron* **2001**, *57*, 5991.
(25) Combes, S.; Finet, J.-P. *Synth. Commun.* **1996**, *26*, 4569.
(26) A mixture of 2-(4-bromophenyl)-1,3-dioxolane (8.160 g, 35.6 mmol), Mg powder (0.909 g, 37.4 mmol) and THF (55 mL) was gently warmed to induce the reaction, keeping the reaction mixture temperature below 40 °C. The reaction mixture was stirred for 4 h at r.t. and cooled to –45 °C. A solution of $BiCl_3$ (3.370 g, 10.7 mmol) in THF (55 mL) was added over the period of 20 min at –45 °C. The mixture was stirred for 35 min at the same temperature and then allowed to warm to r.t. Sat. NH_4Cl solution and brine were added, the mixture was filtered through celite and the filter cake was washed with THF. The organic layer was separated and the water layer was extracted with Et_2O. The combined organic layer was dried ($MgSO_4$) and concentrated at reduced pressure. The residue was dissolved in the mixture of EtOAc and CH_2Cl_2 and eluted with EtOAc through a short pad of silica gel. Eluates were concentrated to about 1:3 of initial volume and about the same volume of hexane was then added. The precipitate was filtered and dried to give 4.74 g of light yellow fine crystals (mp 150.5–151.5 °C). Additional 0.16 g of product was obtained from the mother liquor by silica gel column chromatography (EtOAc–hexane). Overall yield 4.90 g (70%, purity by NMR >99%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.03 (m, 2 H), 4.10 (m, 2 H), 5.76 (s, 1 H), 7.47 (d, *J* = 8.0 Hz, 2 H), 7.74 (d, *J* = 8.2

Hz, 2 H). ^{13}C NMR (50 MHz): δ = 65.3, 103.9, 128.5, 137.6, 156.3. Treatment of arylbismuthane **1** with TsOH in aq THF (see ref.[29]) gave corresponding bismuthane with free aldehyde groups; ^{1}H NMR and ^{13}C NMR spectra were identical with those described in ref.[12b]

(27) Hydrazine **2a** was prepared as described in ref.[7b] (82%, mp 104.5–105.5 °C). Hydrazine **2b** was prepared as described in ref.[5b] (78%, mp 109–110 °C).
Preparation of Hydrazine 2c. To the mixture of 1,2-diacetylhydrazine (0.382 g, 3.30 mmol) and MeCN (10 mL) were added Boc_2O (0.756 g, 3.46 mmol) in MeCN (5 mL) and then DMAP (0.010 g, 0.083 mmol) in MeCN (0.3 mL). The mixture was stirred at r.t. for 17 h under argon. The reaction mixture was then poured into the mixture of sat. NH_4Cl (10 mL) and brine (20 mL) and extracted with Et_2O. The combined organic layer was washed with the mixture of sat. NH_4Cl and brine (1:2), sat. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated. Column chromatographic separation (silica gel, EtOAc) of the residue gave **2c** as colourless oil (0.365 g, 51%), which crystallised on standing, mp 104–105 °C (purity by NMR >99%).

(28) **Typical Procedure**. CH_2Cl_2 (5 mL) and Et_3N (0.21 mL, 1.5 mmol) were added to the mixture of hydrazine (1.0 mmol), $Cu(OAc)_2$ (0.276 g, 1.5 mmol) and bismuthane **1** (0.985 g, 1.5 mmol) in oven-dried flask under argon. The reaction mixture was stirred at r.t. For the synthesis of **3b** additional amounts of $Cu(OAc)_2$ and Et_3N were added after 22 h and 48 h [respectively 0.186 g, 1.0 mmol + 0.091 g, 0.5 mmol of $Cu(OAc)_2$ and 0.1 mL, 1.0 mmol + 0.1 mL, 1.0 mmol of Et_3N]. For the synthesis of **3c** additional amounts of $Cu(OAc)_2$ (0.276 g, 1.5 mmol) and Et_3N (0.28 mL, 2.0 mmol) were added after 24 h. After indicated time (see Table 1) Et_2O and H_2O or in case of **3c** also brine were added. In case of **3a** only H_2O was added, the mixture was filtered through celite and the residue was rinsed with CH_2Cl_2. The organic layer was separated and the water layer was extracted with Et_2O and in case of **3a** also with CH_2Cl_2 or in case of **3c** also with EtOAc. The combined organic layer was washed with brine, dried ($MgSO_4$) and concentrated at reduced pressure. The residue was purified by silica gel column chromatography (EtOAc–hexane). Compound **3a**: Colourless oil (purity by NMR >95%). Compound **3b**: Colourless oil (purity by NMR >97%). Compound **3c**: Pale yellow oil (purity by NMR >98%).

(29) Acetal groups were removed similarly to the procedure described in ref.[24]; 0.4 equiv of TsOH were used in solvent mixture THF–H_2O 25:1. Compound **4a**: Colourless oil (purity by NMR >98%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.49 (s, 9 H), 1.52 (s, 9 H), 7.11–7.88 (m, 9 H), 9.94 (s, 1 H). ^{13}C NMR (50 MHz): δ = 28.16, 28.20, 82.9, 83.5, 121.2, 122.3, 125.7, 128.7, 130.4, 133.0, 141.0, 146.8, 152.5, 152.7, 190.9. Compound **4b**: Colourless crystals, mp 96.5–98.5 °C (purity by NMR >97%). Compound **4c**: Colourless oil (purity by NMR >98%).

(30) For the use of Zn/Cu couple in condensations of imines, see: (a) Vellemäe, E.; Tubrik, O.; Loog, O.; Mäeorg, S.; Mäeorg, U. *Proc. Estonian Acad. Sci. Chem.* **2003**, *52*, 91; *Chem. Abstr.* **2003**, *139*, 325020. (b) Sergeeva, E. V.; Rozenberg, V. I.; Antonov, D. Yu.; Vorontsov, E. V.; Starikova, Z. A.; Hopf, H. *Tetrahedron: Asymmetry* **2002**, *13*, 1121. (c) Shimizu, M.; Iida, T.; Fujisawa, T. *Chem. Lett.* **1995**, 609.

(31) The Zn/Cu couple was prepared and used as described in ref.[30a]; products were separated by silica gel column chromatography (EtOAc–hexane). Compound **6a′**: Colourless oil [purity by NMR >99%, by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >95%].

(32) Gansäuer, A.; Bauer, D. *J. Org. Chem.* **1998**, *63*, 2070.

(33) Compound **5a**: Off-white solid foam [purity by NMR >97%, by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >97%, *dl*/*meso* = 80:20]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.47 (s, 36 H), 3.04 [br s, -OH(*dl*)], 4.59 (*dl*, major) and 4.69 (*meso*, minor) (2 × s, 2 H), 6.97–7.50 (m, 18 H). ^{13}C NMR (50 MHz): δ = 28.2, 78.4, 82.4, 122.4, 123.0, 125.6, 127.2, 128.6, 137.1, 141.1, 141.4, 153.1. Compound **5b**: White solid foam [purity by NMR >97%, by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >98%, *dl*/*meso* = 80:20]. Compound **6b**: White solid foam [purity by NMR >98%, by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >97%]. Compound **5c**: White solid foam [purity by NMR >94% (ca. 5% Et_2O), by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >96%, by ^{1}H NMR *dl*/*meso* = 10:1]. Compound **6c**: White solid foam [purity by NMR >98%, by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >96%].

(34) For 1,2-diols see: (a) Tsukinoki, T.; Kawaij, T.; Hashimoto, I.; Mataka, S.; Tashiro, M. *Chem. Lett.* **1997**, *26*, 235; and references therein. (b) For 1,2-diamines ^{1}H NMR, see: Eisch, J. J.; Kaska, D. D.; Peterson, C. J. *J. Org. Chem.* **1966**, *31*, 453. (c) ^{13}C NMR: Periasamy, M.; Srinivas, G.; Karunakar, G. V.; Bharathi, P. *Tetrahedron Lett.* **1999**, *40*, 7577.

(35) Gansäuer and Bauer (see ref.[32]) found that in order to obtain good *dl*-selectivity, the concentration of aldehyde must be kept low, which was achieved by its very slow addition.

(36) Compounds **7a**–**c** were obtained by treatment of compounds **4a**–**c** with aniline (1.2–2.0 equiv) in CH_2Cl_2 at r.t. in the presence of $MgSO_4$ followed by filtration through the pad of celite and concentration at reduced pressure. Compound **7a**: Slightly yellow viscous oil (purity by NMR >98%). Compound **7b**: Light yellowish solid, mp 133–134 °C (purity by NMR >99%). Compound **7c**: Colourless oil (purity by NMR >95%).

(37) The Zn/Cu couple was prepared and used as described in ref.[30a]; products were purified by silica gel column chromatography (EtOAc–hexane). Compound **8a** (1:1 mixture of *dl*- and *meso*-isomers): Colourless oil [purity by NMR >94% (ca. 4% Et_2O), by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >97%]. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.40–1.57 (m, 36 H), 4.49 [br, 3 H, *dl*-NCH (1 H) and NH (2 H)], 4.88 (br s, 1 H, *meso*-NCH), 6.42–7.50 (m, 28 H). ^{13}C NMR (50 MHz): δ = 28.2, 61.8 (*meso*), 63.3 (*dl*), 82.4, 113.9 (*meso*), 114.2 (*dl*), 118.0 (*meso*), 118.3 (*dl*), 122.7, 125.6, 127.6, 127.7, 128.6, 129.1, 129.2, 135.4 (*meso*), 137.0 (*dl*), 141.0, 141.3, 146.5, 147.0, 153.0. Compound **8b** (1:1 mixture of *dl*- and *meso*-isomers): Colourless glass [purity by NMR >82% (ca. 15% **7b**), by C_{18} HPLC (MeOH–H_2O, UV 254 nm) >86%].

(38) Deprotection conditions for Boc groups which were probed: (a) CF_3COOH in CH_2Cl_2, see for example: Mäeorg, U.; Pehk, T.; Ragnarsson, U. *Acta. Chem. Scand.* **1999**, *53*, 1127. (b) Aq HCl in CH_3CN. (c) $BF_3{\cdot}Et_2O$ in HOAc, see: Hiskey, R. G.; Beacham, L. M. III; Matl, V. G.; Smith, J. N.; Williams, E. B. Jr.; Thomas, A. M.; Wolters, E. T. *J. Org. Chem.* **1971**, *36*, 488. (d) $SnCl_4$ in EtOAc, see: Miel, H.; Rault, S. *Tetrahedron Lett.* **1997**, *38*, 7865.

(39) Similarly, it has been found that removal of Boc groups from 1,2-di-Boc-1,2-diarylhydrazines under usual conditions resulted in cleavage of the N–N bond, to give rise to the corresponding arylamines: Kim, K.-Y.; Shin, J.-T.; Lee, K.-S.; Cho, C.-G. *Tetrahedron Lett.* **2004**, *45*, 117.