Synthesis of (*p*-Nitroaryl)diarylmethanes via Vicarious Nucleophilic Substitution of Hydrogen

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Abstract: (*p*-Nitroaryl)diarylmethanes are readily prepared via vicarious nucleophilic substitution of hydrogen in nitroarenes with carbanions of diarylmethyl *p*-chlorophenyl sulfide. These carbanions are efficient reagents for introduction of diarylmethyl substituents in the *para* position of nitroarenes via the VNS reaction. The reaction does not proceed *ortho* to the nitro group due to steric hindrances on the addition step.

Key words: carbanions, vicarious nucleophilic substitution of hydrogen, sulfides, nitroarenes, arylations

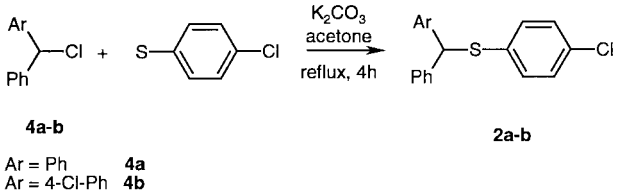
For studies on oxidation of nitrobenzylic carbanions we needed a series of substituted (*p*-nitroaryl)diarylmethanes **3**. Although there are many methods available for synthesis of triarylmethanes,[1-4] synthesis of (*p*-nitroaryl)diarylmethanes was reported only once by Katritzky via vicarious nucleophilic substitution of hydrogen (VNS) in nitrobenzene derivatives with carbanions of benzotriazoyl diarylmethanes.[5] In these compounds, the benzotriazoyl moiety served as a carbanion-stabilizing and leaving group, able to be eliminated in the course of the VNS reaction. Our experience in the VNS reaction indicated that ArS substituents are efficient carbanion-stabilizing and leaving groups,[6] thus carbanions containing such groups, for instance generated from $ArSCH_2CN$,[7] $PhSCH_2SPh$,[8] $(PhS)_3CH$,[9] etc., enter readily into this reaction. Nitroarenes can be also benzylated via VNS reaction with benzyl aryl sulfides.[10]

Thus, although benzhydrylation of nitroarenes via VNS reaction with carbanions of benzotriazoyl diarylmethanes was reported to proceed in good yields,[5] we set up to develop an alternative procedure using carbanions of benzhydryl sulfides **2**. We expected that **2** should be more available and be more effective in the VNS reaction with nitroarenes. Since in the preliminary experiments the expected reaction proceeded in good yield, a series of nitroaryl diarylmethanes **3** were prepared via reaction of benzhydryl *p*-chlorophenyl sulfides **2** with nitroarenes according to Scheme 1. Results of these reactions are given in the Table.

We have also attempted to use benzhydryl chloride **4a** as the carbanion precursor. However, the VNS reaction proceeded satisfactorily only at low temperature (−70 °C) in THF and gave **3a** and **3j** in moderate yields, 37% and 45%, respectively.

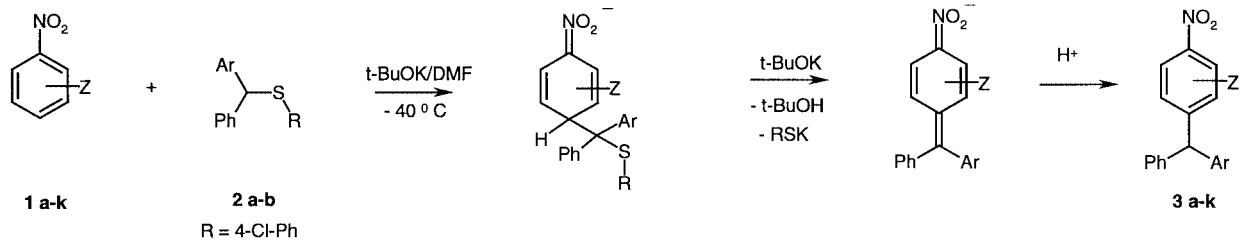
On the other hand, it was reported earlier that 9-chlorofluorene, an analogue of diphenylchloromethane gave good yields of the VNS products.[11]

Benzhydryl *p*-chlorophenyl sulfides **2** were used as the carbanion precursors since *p*-chlorophenylthiolate is a somewhat better leaving group than thiophenolate. Corresponding sulfides were prepared in the reaction of diarylchloromethanes with *p*-chlorothiophenol in K_2CO_3/acetone system (Scheme 2) in yields close to quantitative.



Scheme 2

The VNS reaction with bulky carbanions of **2** proceeded exclusively in the *para* position to the nitro group. When the *para* position was occupied, as for example in *p*-nitrobiphenyl, the VNS reaction did not occur. On the other



Scheme 1

Table

Nitroarene	Z	CH–acid	Ar	VNS Product Yield (%)
1a	H	**2a**	phenyl	**3a** 95
1b	2-F	**2a**	phenyl	**3b** 98
1c	2-Cl	**2a**	phenyl	**3c** 93
1d	2-MeO	**2a**	phenyl	**3d** 89
1e	2-I	**2a**	phenyl	**3e** 52
1f	2-*t*-BuO	**2a**	phenyl	**3f** 76
1g	3-Cl	**2a**	phenyl	**3g** 74
1h	3-MeO	**2a**	phenyl	**3h** 78
1i	3-MeO	**2b**	4-chlorophenyl	**3i** 62
1j	3-CN	**2a**	phenyl	**3j** 72
1k	$(CH)_4$[a]	**2a**	phenyl	**3k** 90

[a] 1-Nitronaphthalene

hand, the reaction of **2** with *p*-chloronitrobenzene gave **3a**, the product identical to that of VNS in nitrobenzene, in 39% yield. Since Br is less susceptible towards nucleophilic substitution in nitrobenzene, reaction of $\mathbf{2}^-$ with *p*-bromonitrobenzene gave product **3a** in 22% yield and the starting nitroarene was partially recovered (26%). In these reactions, we did not detect the VNS products in *ortho* position to the nitro group in the reaction mixture. The reaction mixture contained large amounts of tars. In these cases, **3a** was formed via substitution of the halogen followed by reductive elimination of ArS group from the S_NAr product.

Absence of the VNS products in *ortho* position can be rationalized by steric hindrances in addition of the bulky carbanions of **2** in the vicinity of the nitro group, or in the *ß*-elimination of ArSH from the eventually formed 5^H adduct. To clarify this point, $\mathbf{2}^-$ was reacted with 4-bromo-2-fluoronitrobenzene in which fluorine is highly susceptible towards nucleophilic substitution (Scheme 3). Since formation of products of S_NAr of halogen *ortho* to the nitro group with $\mathbf{2}^-$ was not observed, one can conclude that actually the bulky **2** is unable to add in the vicinity of the nitro group of nitrobenzene. In this reaction, three products were actually formed in overall yield (approx 50%) whereas the starting nitroarene was totally consumed. In the reaction mixture we were able to identify **3b**, the product of S_NAr of bromine followed with reductive elimination of ArSH; **3f**, the product of S_NAr of fluorine with butoxide anion and 4-bromine with $\mathbf{2}^-$ followed with reductive elimination of ArSH; and **3l**, the product of S_NAr of fluorine with *p*-chlorothiophenolate anion and 4-bromine with $\mathbf{2}^-$ followed with reductive elimination of ArSH. Sequence of the S_NAr reactions leading from 4-bromo-2-fluoronitrobenzene to **3f** and **3l** was not clarified.

Mps were uncorrected. ^{1}H NMR spectra were recorded with a Varian Gemini 200 (200 MHz) or Bruker AMX (500 MHz) instruments. Chemical shifts are reported in ppm relative to TMS as internal standard; coupling constants *J* are in Hz. LSIMS HR and EIMS were done on an AMD 604 spectrometer. For column chromatography, silica gel 230−400 mesh (Merck) was used. DMF was distilled over CaH_2 and stored over molecular sieves. Potassium *tert*-butoxide (reagent grade) was purchased from Fluka and was handled in a dry box under Ar. Starting nitroarenes, *p*-chlorothiophenol and benzhydryl chloride **4a** were commercial products. Other benzhydryl chlorides were prepared according to the standard pathway: aroylation of benzene with 4-chlorobenzoylchloride,[12] reduction of the ketone with $NaBH_4$,[13] and exchange of OH for Cl with HCl.[14]

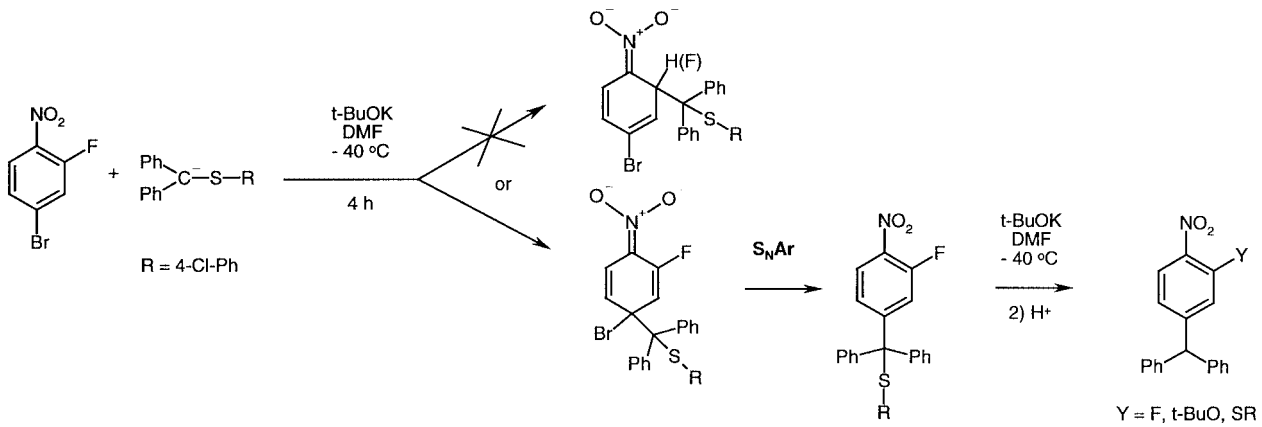
Satisfactory combustion analyses within ± 0.4 were obtained for all compounds **2a**, **3a**−**l**.

Diarylmethyl-4-chlorophenyl Sulfides 2a and 2b; General Procedure

To a stirred solution of *p*-chlorothiophenol (1.45 g,10 mmol) in acetone (20 mL) at r.t. K_2CO_3 (6.91 g, 50 mmol) was added, followed with dropwise addition of diarylmethane chloride **4** (10 mmol). The mixture was refluxed with stirring for 5 h. The inorganic solid was filtered off, washed with acetone (4 ×20 mL), and the solvent evaporated under reduce pressure. The residue was dissolved in CH_2Cl_2 (50 mL) and was passed through a small amount of silica gel. After evaporation of CH_2Cl_2, the product was sufficiently pure for our purposes.

(Diphenylmethyl)-4-chlorophenyl Sulfide (2a)

White crystals from EtOH, mp: 98−99 °C (Lit.[15] 101−102 °C).



Scheme3

[(4-Chlorophenyl)phenylmethyl]-4-chlorophenyl Sulfide (2b)
Orange oil, LSIMS(+) HR: calcd for $C_{19}H_{13}S^{35}Cl_2$ $(M-H)^+$: 343.01150. Found: 343.01182.

Reaction of Nitroarenes with 2a or 2b; General Procedure
t-BuOK (560 mg, 5 mmol) was dissolved in dry DMF (8 mL) under Ar and the solution was cooled to −40 °C. A solution of a nitroarene **1** (1 mmol) and a sulfide **2** (1 mmol) in DMF (2 mL) was added over 1.5 h. The reaction mixture was stirred at −40 °C to −50 °C for 4 h, then the reaction mixture was poured into ice-cooled dilute HCl (10%, 20 mL). After extraction with CH_2Cl_2 (4 x 10 mL), the combined organic layers were washed with aq NaOH (10%, 40 mL) to remove *p*-chlorothiophenol. The organic layer was dried ($MgSO_4$) and filtered through silica gel. Products were purified either by recrystallization from EtOH or by column chromatography on silica gel (hexane/EtOAc, 50:1), and then additionally recrystallized from EtOH.

4-(Diphenylmethyl)nitrobenzene (3a)
Purified by recrystallization to give pale yellow crystals, mp: 93−94 °C (Lit.[5] 95−97 °C).

2-Fluoro-4-(diphenylmethyl)nitrobenzene (3b)
Purified by column chromatography to give pale yellow crystals, mp: 58−59 °C (EtOH), (Lit.[5] 59−60 °C).

^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.98 (dd, 1H, *J* = 8.9, 8.0), 7.35−7.27 (m, 6H), 7.12−7.02 (m, 6H), 5.59 (s, 1H).

2-Chloro-4-(diphenylmethyl)nitrobenzene (3c)
Purified by recrystallization to give yellow crystals, mp: 82−83 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.81 (d, 1H, *J* = 8.4), 7.05−7.35 (m, 12H), 5.57 (s, 1H).

2-Methoxy-4-(diphenylmethyl)nitrobenzene (3d)
Purified by recrystallization to give pale yellow crystals, mp: 139−140 °C (Lit.[5] 142−144 °C).

^{1}H NMR (200 MHz, $CDCl_3$) δ*$_*$ = 7.78 (d, 1H, *J* = 8.4), 7.23−7.34 (m, 10H), 6.83 (d, 1H, *J* = 1.5), 6.76 (dd, 1H, *J* = 8.4, J = 1.7), 5.58 (s, 1H), 3.80 (s, 1H).

2-Iodo-4-(diphenylmethyl)nitrobenzene (3e)
Purified by recrystallization to give pale yellow crystals, mp: 109−110 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.81 (dd, 1H, *J* = 1.9, 0.6), 7.79 (d, 1H, *J* = 8.4), 7.31−7.35 (m, 4H), 7.25−7.29 (m, 2H), 7.19 (ddd, 1H, *J* = 8.4, 1.9, 0.6), 7.06–7.09 (m, 4H), 5.54 (s, 1H).

2-*tert*-Butoxy-4-(diphenylmethyl)nitrobenzene (3f)
To a solution of 2-*tert*-butoxynitrobenzene (195 mg, 1 mmol) and **2a** (311 mg, 1 mmol) in DMF (8 mL) cooled to −40 °C *t*-BuOK (250 mg, 2,2 mmol) dissolved in DMF (2 mL) was added over 1.5 h. The mixture was stirred at −40 °C to −50 °C for 4 h and then poured into cold water. After extraction with CH_2Cl_2 (4 x 10 mL), the combined organic layers were dried ($MgSO_4$) and filtered through silica gel. Products were purified via column chromatography (hexane) to give yellow crystals, mp: 86−87 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.66 (d, 1H, *J* = 8.9), 7.20−7.37 (m, 6H), 7.05−7.12 (m, 4H), 6.86−6.92 (m, 2H), 5.55 (s, 1H), 1.28 (s, 9H).

3-Chloro-4-(diphenylmethyl)nitrobenzene (3g)
Purified by recrystallization to give pale yellow crystals, mp: 86−87 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.27 (d, 1H, *J* = 2.4), 8.02 (dd, 1H, *J* = 8.5, 2.4), 7.01−7.34 (m, 11H,), 5.99 (s, 1H).

3-Methoxy-4-(diphenylmethyl)nitrobenzene (3h)
Purified by recrystallization to give yellow crystals, mp: 95−96 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.75 (dd, 1H, *J* = 8.4, 2.2), 7.68 (d, 1H, *J* = 2.2), 7.26−7.30 (m, 4H), 7.20−7.24 (m, 2H), 7.04−7.07 (m, 4H), 7.01 (d, 1H, *J* = 8.4), 5.93 (s, 1H), 3.81 (s, 3H).

4-[(4-Chlorophenyl)phenylmethyl]-3-methoxynitrobenzene (3i)
Purified by column chromatography to give white crystals, mp: 85−86 °C (Lit.[5] orange oil).

^{1}H NMR (200 MHz, $CDCl_3$) δ = 7.70−7.79 (m, 2H), 7.23−7.32 (m, 5H), 6.95−7.08 (m, 5H), 5.89 (s, 1H), 3.83 (s, 3H).

3-Cyano-4-(diphenylmethyl)nitrobenzene (3j)
Purified by recrystallization to give yellow crystals, mp: 97−98 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.51 (d, 1H, *J* = 2.4), 8.33 (dd, 1H, *J* = 8.8, 2.5), 7.05−7.40 (m, 11H), 6.03 (s, 1H).

4-(Diphenylmethyl)-1-nitronaphthalene (3k)
Purified by recrystallization to give pale yellow crystals, mp: 125−127 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.55 (d, 1H, *J* = 8.7), 8.14 (d, 1H, *J* = 8.5), 8.06 (d, 1H, *J* = 8.1), 7.72−7.48 (m, 2H), 7.36−7.25 (m, 6H), 7.13−7.04 (m, 5H), 6.31 (s, 1H).

Reaction of 4-Bromo-2-fluoronitrobenzene with 2a
t-BuOK (560 mg, 5 mmol) was dissolved in dry DMF (8 mL) under Ar and the solution was cooled to −40 °C. A solution of a 4-bromo-2-fluoronitrobenzene (220 mg, 1 mmol) and **2a** (1 mmol) in DMF (2 mL) was added over 1.5 h. The reaction mixture was stirred at −40 °C to −50 °C for 4 h and then was poured into ice-cooled diluted HCl (10%, 20 mL). After extraction with CH_2Cl_2 (4 x 10 mL), the combined organic layers were washed with aq NaOH (10%, 40 mL) to remove *p*-chlorothiophenol. The organic layer was dried ($MgSO_4$). The products were separated from tars by column chromatography on silica gel (hexane) to give a mixture of 3 substances as an orange oil (168 mg). According to TLC and EIMS, these products were identified as **3b, 3f** and **3l**.

5-(Diphenylmethyl)-2-nitrophenyl 4-chlorophenyl Sulfide (3l)
Compound **3j** (307 mg, 1 mmol) was stirred with 4-chlorothiophenol (144 mg, 1 mmol) and K_2CO_3 (630 mg, 5 mmol) in acetone (10 mL) at ambient temperature for 12 h. The workup was as for sulfides **2a** and **2b**.

The product was purified by column chromatography to give an orange oil, yield 328 mg, 76%.

^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.15 (d, 1H, *J* = 8.5), 7.19−7.26 (m, 10H), 7.00−7.07 (m, 1H), 6.84−6.91 (m, 4H), 6.75 (d, 1H, *J* = 1.8), 5.40 (s, 1H).

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