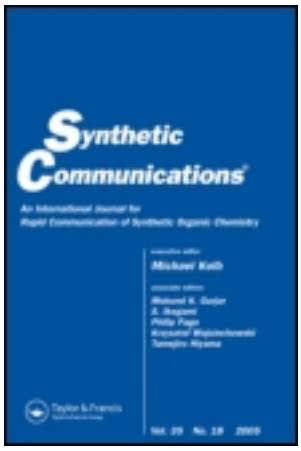


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

# ortho-(Substituted Silyl)phenylsydnones via a Novel Sydnone to Phenyl Ring, Lithiation-Induced Silicon Migration

Kenneth Turnbull [a] & Douglas M. Krein [a]

[a] Chemistry Department , Wright State University , Dayton, Ohio, USA

Published online: 17 Aug 2006.

To cite this article: Kenneth Turnbull & Douglas M. Krein (2003) ortho-(Substituted Silyl)phenylsydnones via a Novel Sydnone to Phenyl Ring, Lithiation-Induced Silicon Migration, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:12, 2061-2067, DOI: 10.1081/SCC-120021032

To link to this article: http://dx.doi.org/10.1081/SCC-120021032

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016



SYNTHETIC COMMUNICATIONS®
Vol. 33, No. 12, pp. 2061–2067, 2003



# *ortho*-(Substituted Silyl)phenylsydnones via a Novel Sydnone to Phenyl Ring, Lithiation-Induced Silicon Migration

**Kenneth Turnbull* and Douglas M. Krein**

Chemistry Department, Wright State University, Dayton, Ohio, USA

## ABSTRACT

3-(2-Bromophenyl)sydnone (**5**) reacts with LDA then substituted chlorosilanes to form the corresponding 4-silylsydnones **6**, which rearrange to the novel ortho-silylphenylsydnones **8** on treatment with *n*-butyllithium.

*Key Words:* Sydnones; Silyl rearrangement.

*Correspondence: Kenneth Turnbull, Associate Professor, Chemistry Department, Wright State University, 3640 Colonel Glenn Highway, Dayton, Ohio 45435, USA; Fax: (937) 775-2717; E-mail: kenneth.turnbull@wright.edu.

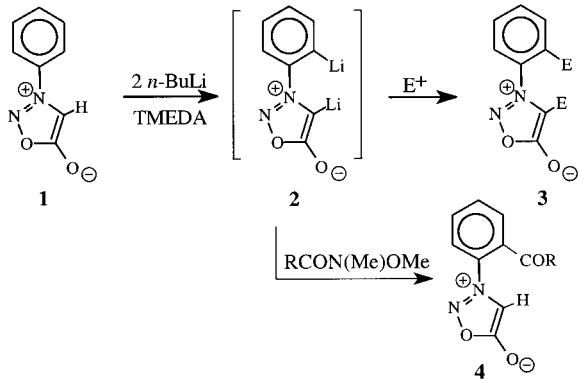


DOI: 10.1081/SCC-120021032 0039-7911 (Print); 1532-2432 (Online)

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016



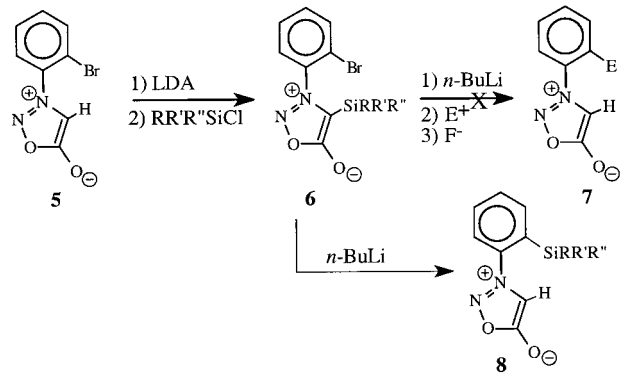





*Scheme 1.*

Recently, we have demonstrated that the sydnone ring is an effective director of *ortho*-lithiation.[1] Therein, treatment of 3-phenylsydnone (**1**) with 2.2 equiv. of *n*-BuLi in the presence of N,N,N′,N′-tetramethylethylenediamine (TMEDA) provided the putative dilithio intermediate **2** which could be trapped with reactive electrophiles to yield the disubstituted sydnones **3**[1] or with Weinreb's amides to afford the *o*-acyl species **4** regiospecifically (Sch. 1).[2] The latter result was of particular interest since much of our previous work had utilized *ortho*-substituted arylsydnones as precursors to differently substituted sydnones,[3] to fused ring sydnones[4] or to various heterocycles.[5] However, the utility of this approach as a general route to *ortho*-substituted arylsydnones is limited since only weak electrophiles show this selectivity. Accordingly, there was a need for a lithiation protocol which would provide the desired *o*-substituted species without competitive reaction at the sydnone 4-position. We postulated that this goal could be achieved by a sequence involving protection of the sydnone 4-position of 3-(2-bromophenyl)sydnone (**5**) as a silyl moiety (to yield **6**), metal-halogen exchange followed by reaction with an electrophile, and removal of the protective group with fluoride ion (to yield **7**) (Sch. 2).

Preparation of the 4-silyl species **6** was achieved in 79–85% yield using LDA then the appropriate chlorosilane. However, all attempts to effect halogen-metal exchange, followed by reaction with an electrophile, led to product mixtures, the major component of which was the corresponding *o*-silylated compound **8**. Indeed, excellent yields (80–89%) of these novel sydnones were forthcoming on treatment of **6** with *n*-butyllithium in the absence of an electrophile, even at temperatures as low as −100°C (Table 1). Apparently, the rearrangement of **6** to **8** is very facile




*Scheme 2.*

***Table 1.*** Preparation of the 4-silyl species **6** and conversion to their *o*-silyl congeners **8**.

| Compound | *R*, *R*′, *R*″ (in **6** & **8**) | Yield (%) of **6**[a] | M.p. (°C) of **6** | Yield (%) of **8**[a] | M.p. (°C) of **8** |
|---|---|---|---|---|---|
| a | Me, Me, Me | 85 | 124–126 | 87 | 43–44 |
| b | $^{i}$Pr, $^{i}$Pr, $^{i}$Pr | 81 | 143–145 | 89 | 78–80 |
| c | Me, Me, $^{t}$Bu | 83 | 116–118 | 85 | 91–93 |
| d | Ph, Ph, $^{t}$Bu | 79 | 108–110 | 80 | 102–104 |

[a]All compounds were fully characterized by IR, $^{1}$H NMR, $^{13}$C NMR, and combustion analysis.

and is unaffected by steric encumbrance around the silicon atom. The driving force is presumably the greater thermodynamic stabilty of the sydnone anion. Thus, upon exposure to *n*-butyllithium, the bromosilylsydnone **6** undoubtedly undergoes metal-halogen exchange to form the corresponding unstable *ortho*-anion which attacks the 4-silyl moiety, leaving the more stable sydnone anion. Protonation on work-up affords the appropriate *ortho*-silylsydnone **8**.

The identities of the products were confirmed by satisfactory combustion analyses, the presence of the sydnone C=O stretching vibration at $\sim$1750 cm$^{-1}$ and the singular sydnone ring C-H stretching vibration at $\sim$3150 cm$^{-1}$ in their infrared spectra, as well as the expected chemical shifts and splitting patterns in their proton and carbon NMR spectra.

Overall, we have developed a useful preparation of *ortho*-silylarylsydnones **8** which, due to the probable lability of the *ortho*-silyl moiety, likely would be inaccessible by conventional preparations involving manipulations with the appropriate *ortho*-substituted aniline derivatives. Accordingly, we intend to explore further the scope and limitations of the present discovery as a route to novel *ortho*-substituted arylsydnones.



## EXPERIMENTAL

### General Procedure for the Preparation of 3-(2-Bromophenyl)-4-(substituted silyl)sydnones 6

To a stirred solution of 3-(2-bromophenyl)sydnone (**5**) [1.00 g, 4.15 mmol] in dry THF (100 mL) at −78°C was added lithium diisopropylamide · monotetrahydrofuran [3.04 mL, 4.56 mmol, 1.5 M in cyclohexane] dropwise under an atmosphere of dry nitrogen. After 0.5 h, the appropriate silyl chloride (4.98 mmol) was added and, after an additional 1 h, the mixture was allowed to warm to 0°C whereupon it was quenched with saturated brine (100 mL), then extracted with $CH_2Cl_2$ (3 × 100 mL). The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo to yield an impure oil which was purified by column chromatography ($SiO_2$, $CH_2Cl_2$:hexane (4:1) as eluant), followed by recrystallization ($CH_2Cl_2$:hexane) to afford colorless crystals of the title compound.

**3-(2-Bromophenyl)-4-(trimethylsilyl)sydnone (6a).** Using trimethylsilyl chloride (0.63 mL) in the general procedure. Found: C, 42.54; H, 4.20; N, 8.98. Calcd. for $C_{11}H_{13}BrN_2O_2Si$: C, 42.18; H, 4.18; N, 8.94; $\nu_{max}$ (KBr): 3093, 2961, 2899, 1729, 1418, 1252, 1217, 848, 765 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ 0.11 (s, 9H), 7.58 (m, 3H), 7.81 (m, 1H); $^{13}C$ NMR ($CDCl_3$): −2.08 (Si-($\underline{C}H_3)_3$), 106.29 (syd. C-4), 120.07, 128.00, 128.47, 133.33, 134.02, 135.46, 173.14 (syd. C=O) ppm.

**3-(2-Bromophenyl)-4-(triisopropylsilyl)sydnone (6b).** Using triisopropylsilyl chloride (1.06 mL) in the general procedure. Found: C, 51.46; H, 6.36; N, 6.99. Calcd. for $C_{17}H_{25}BrN_2O_2Si$: C, 51.38; H, 6.34; N, 7.05; $\nu_{max}$ (KBr): 3072, 2950, 2866, 1729, 1469, 1401, 1207, 1027, 884, 763, 645 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ 1.01 (d, 18H), 1.15 (septet, 3H), 7.55 (d, 3H), 7.78 (t, 1H); $^{13}C$ NMR ($CDCl_3$): 11.27 (Si-CH($\underline{C}H_3)_2$), 18.50 (Si-$\underline{C}$H($CH_3)_2$), 104.64 (syd. C-4), 120.84, 128.06, 128.14, 133.30, 134.21, 135.87, 173.85 (syd. C=O) ppm.

**3-(2-Bromophenyl)-4-(*tert*-butyldimethylsilyl)sydnone (6c).** Using *tert*-butyldimethylsilyl chloride (0.750 g) in the general procedure. Found: C, 47.31; H, 5.44; N, 7.89. Calcd. for $C_{14}H_{19}BrN_2O_2Si$: C, 47.33; H, 5.39;

N, 7.88; $\nu_{max}$ (KBr): 3095, 2931, 2859, 1739, 1478, 1409, 1253, 1217, 1033, 846, 824, 770 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ −0.35 (s, 3H), 0.23 (s, 3H), 0.93 (s, 9H), 7.55 (m, 3H), 7.77 (m, 1H); $^{13}C$ NMR ($CDCl_3$): −6.69, −7.13 (Si-[C($CH_3$)$_3$]($\underline{C}H_3$)$_2$), 18.37 (Si-[$\underline{C}$($CH_3$)$_3$]($CH_3$)$_2$), 26.70 (Si-[C($\underline{C}H_3$)$_3$]($CH_3$)$_2$), 105.31 (syd. C-4), 120.70, 128.15, 128.27, 133.26, 133.95, 135.68, 173.50 (syd. C=O) ppm.

**3-(2-Bromophenyl)-4-(*tert*-butyldiphenylsilyl)sydnone (6d).** Using *tert*-butyldiphenylsilyl chloride (1.29 mL) in the general procedure. Found: C, 60.30; H, 4.99; N, 5.82. Calcd. for $C_{24}H_{23}BrN_2O_2Si$: C, 60.12; H, 4.84; N, 5.84; $\nu_{max}$ (KBr): 3049, 2930, 2856, 1730, 1428, 1401, 1219, 1110, 858, 742, 704, 607, 506 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ −0.01 (s, 6H), 0.11 (s, 3H), 7.37 (m, 10H), 7.73 (m, 4H); $^{13}C$ NMR ($CDCl_3$): 19.00 (Si-[$\underline{C}$($CH_3$)$_3$]($C_6H_5$)$_2$), 26.51, 28.22 (Si-[C($\underline{C}H_3$)$_3$]($C_6H_5$)$_2$), 102.66 (syd. C-4), 119.89, 127.59, 127.84, 128.20, 129.49, 129.76, 130.58, 131.79, 132.42, 133.59, 134.73, 135.22, 135.67, 135.91, 173.56 (syd. C=O) ppm.

## General Procedure for the Preparation of 3-(2-(Substituted silyl)phenyl)sydnones 8

To a stirred solution of the appropriate 3-(2-bromophenyl)-4-(substituted silyl)sydnone **6** [5.00 mmol] in dry THF (150 mL) at −78°C was added *n*-butyllithium [3.67 mL, 5.5 mmol, 1.5 M in cyclohexane] dropwise under dry nitrogen. After 2 h, the mixture was allowed to warm to 0°C whereupon it was quenched with saturated brine (100 mL) then extracted with $CH_2Cl_2$ (3 × 100 mL). The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo to yield an impure oil which was purified via column chromatography ($SiO_2$, $CH_2Cl_2$: EtOAc (10:1) as eluant) followed by recrystallization ($CH_2Cl_2$: hexane) to afford colorless crystals of the title compound.

**3-(2-Trimethylsilylphenyl)sydnone (8a).** Using 3-(2-bromophenyl)-4-trimethylsilylsydnone (**6a**) [1.566 g] in the general procedure. Found: C, 56.61; H, 6.16; N, 11.83. Calcd. for $C_{11}H_{14}N_2O_2Si$: C, 56.38; H, 6.02; N, 11.95; $\nu_{max}$ (KBr): 3147, 3071, 2960, 2905, 1744, 1423, 1367, 1257, 941, 842, 767 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ 0.60 (s, 9H), 6.94 (s, 1H), 7.80 (d, 1H), 7.99 (t, 2H), 8.12 (d, 1H); $^{13}C$ NMR ($CDCl_3$): −0.81 (Si-($\underline{C}H_3$)$_3$), 97.18 (sydnone C-4), 124.62, 130.41, 131.43, 136.40, 136.59, 139.57, 168.73 (C=O) ppm.

**3-(2-Triisopropylsilylphenyl)sydnone (8b).** Using 3-(2-bromophenyl)-4-triisopropylsilylsydnone (**6b**) [1.986 g] in the general procedure. Found: C, 64.19; H, 8.24; N, 8.81. Calcd. for $C_{17}H_{26}N_2O_2Si$: C, 64.11; H, 8.23; N, 8.80; $\nu_{max}$ (KBr): 3121, 2950, 2868, 1753, 1463, 1424, 1363, 1252, 883,

773, 674 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ 0.95 (d, 18H), 1.11 (septet, 3H), 6.52 (s, 1H), 7.38 (d, 1H), 7.61 (t, 2H), 7.74 (d, 1H); $^{13}C$ NMR ($CDCl_3$): 12.09 (Si-[$\underline{C}H(CH_3)_2]_3$), 19.02 (Si-[$CH(\underline{C}H_3)_2]_3$), 97.81 (sydnone C-4), 126.27, 130.10, 130.80, 132.79, 138.12, 140.30, 168.59 (C=O) ppm.

**3-(2-*tert*-Butyldimethylsilyl)sydnone (8c).** Using 3-(2-bromophenyl)-4-*tert*-butyldimethylsilylsydnone (**6c**) [1.777 g] in the general procedure. Found: C, 60.62; H, 7.45; N, 10.28. Calcd. for $C_{14}H_{20}N_2O_2Si$: C, 60.84; H, 7.29; N, 10.13; $\nu_{max}$ (KBr): 3133, 2953, 2859, 1737, 1467, 1423, 1364, 1260, 1103, 939, 837, 773 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ 0.09 (s, 6H), 0.87 (s, 9H), 6.47 (s, 1H), 7.33 (d, 1H), 7.57 (t, 2H), 7.67 (d, 1H); $^{13}C$ NMR ($CDCl_3$): −5.33 (Si-[$\underline{C}(CH_3)_3](CH_3)_2$), 17.48 (Si-[$C(CH_3)_3](\underline{C}H_3)_2$), 26.88 (Si-[$C(\underline{C}H_3)_3](CH_3)_2$), 98.11 (sydnone C-4), 125.66, 130.18, 130.70, 134.59, 137.61, 139.69, 168.56 (C=O) ppm.

**3-(2-*tert*-butyldiphenylsilyl)sydnone (8d).** Using 3-(2-bromophenyl)-4-*tert*-butyldiphenylsilylsydnone (**6d**) [2.397 g] in the general procedure. Found: C, 72.15; H, 6.13; N, 6.79. Calcd. for $C_{24}H_{24}N_2O_2Si$: C, 71.97; H, 6.04; N, 6.99; $\nu_{max}$ (KBr): 3150, 3064, 2961, 2859, 1761, 1467, 1428, 1368, 1255, 1106, 938, 837, 703 $cm^{-1}$; $^1H$ NMR (200 MHz; $CDCl_3$): $\delta$ 1.14 (s, 9H), 5.86 (s, 1H), 7.51–7.30 (m, 11H), 7.72 (m, 2H), 8.18 (d, 1H); $^{13}C$ NMR ($CDCl_3$): 19.12 (Si-[$\underline{C}(CH_3)_3$] $(C_6H_5)_2$, 28.79 (Si-[$C(\underline{C}H_3)_3](C_6H_5)_2$), 98.09 (sydnone C-4), 126.58, 127.81, 129.83, 130.77, 131.55, 132.33, 135.37, 135.62, 138.16, 140.86, 167.92 (C=O) ppm.

## REFERENCES

1. Turnbull, K.; Krein, D.M. The sydnone ring as an *ortho*-director of lithiation. Dilithiation of 3-phenylsydnone and trapping by electrophiles. Tetrahedron Lett. **1997**, *38*, 1165.
2. Turnbull, K.; Sun, C.; Krein, D.M. The sydnone ring as an *ortho*-director of lithiation. 2. Dilithiation of 3-phenylsydnone and regiospecific *o*-aryl acylation using N-methoxy-N-methylamides. Tetrahedron Lett. **1998**, *39*, 1509.
3. (a) Turnbull, K. J. Bromination of sydnones. I. Reaction with 3-arylsydnones containing electron-donors on the aryl ring. Heterocycl. Chem. **1985**, *22*, 965; (b) Hodson, S.J.; Turnbull, K. J. Bromination of sydnones. II. Bromination of 3-(2-aminophenyl)sydnone and related compounds. Heterocycl. Chem. **1985**, *22*, 1223; (c) Turnbull, K. Debromination of 3-aryl-4-bromosydnones with sodium borohydride. Synthesis **1986**, 334; (d) Turnbull, K.; Blackburn, T.L.; Esterline, D.T. Bromination of sydnones. III. Bromination of 3-(2-substituted-phenyl)sydnones and subsequent

side chain modification. J. Heterocycl. Chem. **1990**, *27*, 1259; (e) McChord, K.L.; Tullis, S.A.; Turnbull, K. Debromination of 4-bromo-3-arylsydnones with sodium sulfite. Synth. Commun. **1989**, *19*, 2249.

4. (a) Preston, P.N.; Turnbull, K. Approaches to the synthesis of compounds containing fused mesoionic rings. J. Chem. Soc., Perkin Trans. 1 **1977**, 1229; (b) Burson, W.C., III; Jones, D.R.; Turnbull, K.; Preston, P.N. Intramolecular aza-wittig routes to sydnoquinoxalines. Synthesis **1991**, 745; (c) Saljoughian, M.; Turnbull, K. Acid induced reactions of a sydnone ketoxime. J. Heterocycl. Chem. **1988**, *25*, 1817; (d) Turnbull, K.; Krein, D.M. Formation of 4-hydroxy-4-substituted sydno[3,4-a](4*H*)indoles *via* dilithiation of 3-(2-bromophenyl)sydnone. Synthesis **1996**, 1183.
5. (a) Gelvin, C.R.; Turnbull, K. Sydnones as masked hydrazines for heterocycle formation: reactions of 3-(2-substituted phenyl)sydnones with HCl. Helv. Chim. Acta **1992**, *75*, 1931; (b) Marx, J.A.; Turnbull, K. Formation of 1-bromocarbonylindazoles *via* cleavage of 4-bromo *ortho*-substituted arylsydnones with HBr. Tetrahedron Lett. **1993**, 239.

Received in the USA October 3, 2002

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016