

DIRECTED ORTHO METALATION OF SILYLOXYBENZAMIDES.

ANION INDUCED O → C SILICON REARRANGEMENT

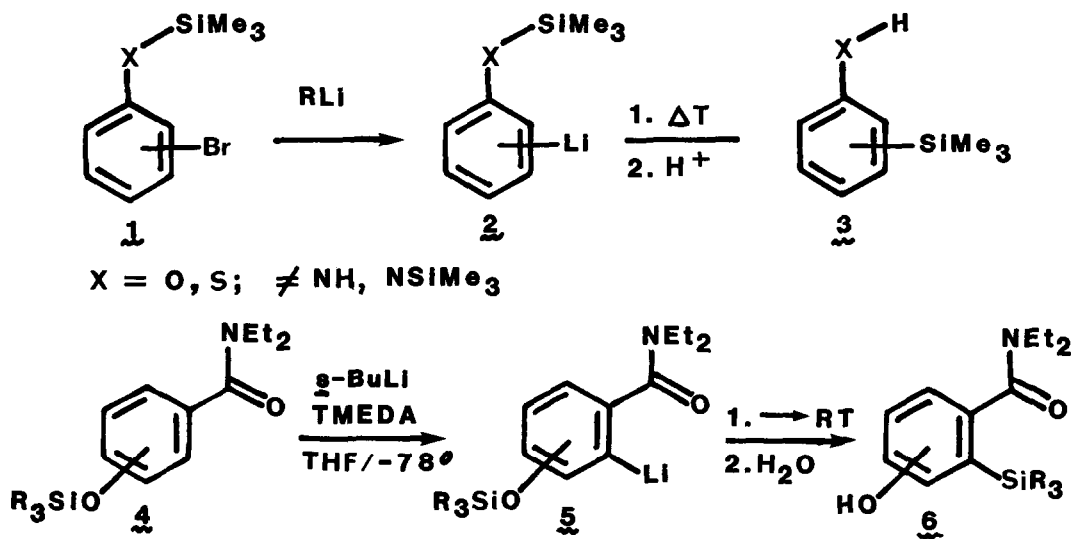
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Summary: Trialkylsilyloxybenzamides 4, o- and m-OSiR₃ undergo directed ortho metalation-mediated silicon rearrangement to salicylamides 6, 6- and 3-OH by intra- and inter-molecular mechanisms respectively.

Metal-halogen exchange of bromo-substituted trialkylsilyl phenols, to a less extent thiophenols, but not anilines, 1 → 2, triggers an anionic O → C 1,3-silyl rearrangement to produce corresponding aromatic ring silylated derivatives 3 (Scheme).¹ Evidence from cross-over experiments on 1 (X = O) indicates an intramolecular mechanism for ortho-bromo and an intermolecular pathway for the corresponding para-bromo trialkylphenoxysilanes.² We report preliminary results concerning O → C silicon migration of silyloxybenzamides 4 to silylated salicylamides 6 induced by directed ortho metalation (5)³ and provide mechanistic evidence for this rearrangement.⁴



Scheme

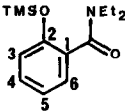
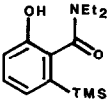
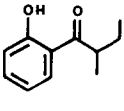
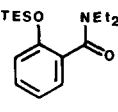
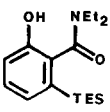
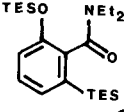
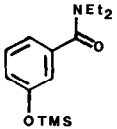
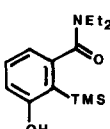
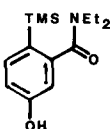
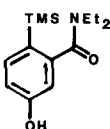
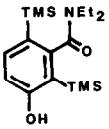
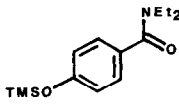
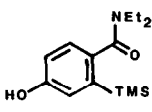
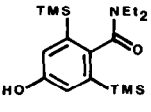
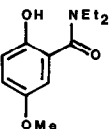
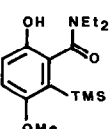
In an attempt to develop a general synthesis of 6-substituted salicylamides by *in situ* phenol protection, N,N-diethylsalicylamide⁵ was O-metalated (1 equiv \underline{s} -BuLi/TMEDA/THF/-78°C/1 h) and treated with TMSCl (1 equiv) to generate the silyloxybenzamide intermediate 4a which was subjected to a second metalation under identical conditions and quenched with an excess of MeI (-78°C → RT). 6-Trimethylsilylsalicylamide (6a) was obtained in 45% yield. A similar result (55% of 6a) was observed when the metalation was allowed to proceed for only 10 min and the MeI quench was carried out at -90°C. In order to provide evidence for the O → C silicon rearrangement, pure 4a was separately prepared⁶ and subjected to the metalation procedure (-78° or -90°C) without adding the external electrophile. This resulted in the formation of the silylated salicylamide 6a (68%) together with o-hydroxyvalerophenone (2%) (Table) from NEt₂ displacement by \underline{s} -BuLi. These experiments suggested that the rate of silicon rearrangement from the ortho-lithiated species derived from 4a is very rapid⁷ compared to that of its reaction with methyl iodide.⁸

The triethylsilyloxybenzamide 4b⁶ underwent the silicon rearrangement less cleanly to give compounds 6b and its O-silylated product while the corresponding *t*-butyldimethyl derivative underwent extensive decomposition with no evidence for the formation of the rearrangement product 6c, 2-OH, R = *t*-BuMe₂.

Silicon rearrangements were also observed for the *m*- and *p*-silyloxybenzamides 4c and 4d.^{5,6} Yields of major products 6c, 6d and 6e (bracketed in Table) were only slightly changed by *in situ* preparation of 4c and 4d. The results with the *m*-silyloxybenzamide 4c shows poorer regioselectivity for metalation in between the two functions compared to the corresponding *m*-anisamide.³ The methoxy salicylamide 4e smoothly rearranged into the contiguously substituted aromatic 6f.

Crossover experiments demonstrated that the rearrangement of 4a proceeds by an intermolecular mechanism. Lithiation of a 1:1 molar ratio of 3-deuterated 4a (95% d₁)⁹ and the triethylsilyloxybenzamide 4b resulted in the formation of 3-deuterated 6a (31%) and 3-deuterated 6b (19%) salicylamides which respectively showed 50±5% and 40±5% d₁ content at C-3 (400 MHz NMR, MS).¹⁰ An identical crossover experiment using 2-deuterated 4c (84% d₁)¹¹ and N,N-diethyl 3-triethylsilyloxybenzamide resulted in the formation of 2-deuterated 6c (16%)¹¹ and N,N-diethyl 2-triethylsilyloxy-3-hydroxybenzamide (11%) which showed 82±5% and 0±5% d₁ content respectively thus strongly suggesting that the silicon migration in the

TABLE. Anionic Silicon Rearrangement of Silyloxy-benzamides^a

Benzamide	Products ^b yield, c%		
 4a	 6a	 2	68^d
 4b	 6b	 10	47 (45)
 4c	 6c	 6d	58 (62)
		 5	5 (16)
		 4	4 (11)
 4d	 6e	 11	78 (62)
 4e	 6f		(76)

^aTMS = SiMe₃, TES = SiEt₃. ^bAll products showed analytical and spectral (IR, NMR, MS) data consistent with the assigned structures. ^c6a, 6c, and 6f were chemically correlated (MeI/K₂CO₃/acetone) with silylated anisamides prepared by directed ortholithiation-silylation.¹¹ ^dYields are of purified (chromatographed, distilled) materials. Yields in brackets correspond to those obtained by *in situ* preparation of 4a-d and the TMS derivative of 4e. ^e21% of starting 4a was recovered.

m-silyloxy system 4c occurs via an intramolecular mechanism. These results thus parallel the behavior of p-Br and o-Br silyloxybenzenes 1, $X = 0$.²

In summary, initial cases of a directed metalation induced $O \rightarrow C$ silicon rearrangement proceeding via inter- and intra-molecular pathways have been observed. Methodological extensions and synthetic applications are under study.¹²

References and Footnotes

1. Review: Habich, D.; Effenberger, F. Synthesis, 1979, 841. Recent work: Heinicke, J.; Nietzschmann, E.; Tzschach, A. J. Organometal. Chem. 1983, 243, 1.
2. Simchen, G.; Pfletschinger, J. Angew. Chem, Int. Ed. Engl. 1976, 15, 428.
3. Beak, P.; Snieckus, V. Accts. Chem. Research, 1982, 15, 306.
4. The n-BuLi induced $O \rightarrow C$ silicon rearrangement of π -(R_3SiOPh) $CrCO_3$ complexes constitutes a recent and sole example in which the o-lithiated species is not formed by metal-halogen exchange: Fukui, M.; Ikeda, T.; Iishi, T. Tetrahedron Lett. 1982, 1605.
5. Hydroxybenzamide precursor of 4a and 4e were prepared by a new method involving anionic rearrangement of aryl carbamates, see Sibi, M.P.; Snieckus, V. J. Org. Chem. 1983, 48, 1935. Precursors of 4b-d were obtained by BBr_3 demethylation ($CH_2Cl_2/-78^\circ C$) of the corresponding anisamides.
6. Compounds 4a, 4c, 4d were prepared from the corresponding phenols (excess $HN(SiMe_3)_2/40^\circ C/6$ h), distilled (bulb-to-bulb) and, due to moisture sensitivity, used immediately in metalations. 4b was prepared ($Et_3SiCl/Et_3N/PhH/reflux$) and similarly handled.
7. Silicon migration in 2, $X = 0$, o-Li has been observed even at $-100^\circ C$: Arai, I.; Park, K.H.; Daves, G.D. J. Organometal. Chem. 1976, 121, 25. For a temperature dependence study, see ref. 2.
8. However, interception of 5 by deuteration ($EtOD/-78^\circ C \rightarrow RT$) is feasible as evidenced from the formation of N,N-diethyl 6-deuterosalicylamide (80% yield, 80% d_1 by 400 MHz NMR and MS).
9. Prepared from N,N-diethyl O-phenylcarbamate by sequential metalation, deuteration, anionic rearrangement⁵ and silylation.⁶
10. Analytical standards of 3-deuterated 6a and 6b and 2-deuterated 6c were obtained by separate silicon rearrangement experiments.
11. N,N-Diethyl 2-deuterio-5-methoxybenzamide was prepared according to Mills, R.J.; Snieckus, V. J. Org. Chem. 1983, 48, 1565 and converted into 2-deuterio 4c by demethylation⁵ and silylation.⁶
12. We thank NSERC Canada for continuing financial support of our research. 400 MHz spectra were obtained at the Southwestern Ontario NMR Centre funded by a major installation grant from NSERC Canada.

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