Tetrahedron Letters,Vol.25,No.27,pp 2827-2830,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

SILICON IN BENZAMIDE DIRECTED ORTHO METALATION.

FORMATION AND REACTIONS OF BENZAMIDE BENZYNES

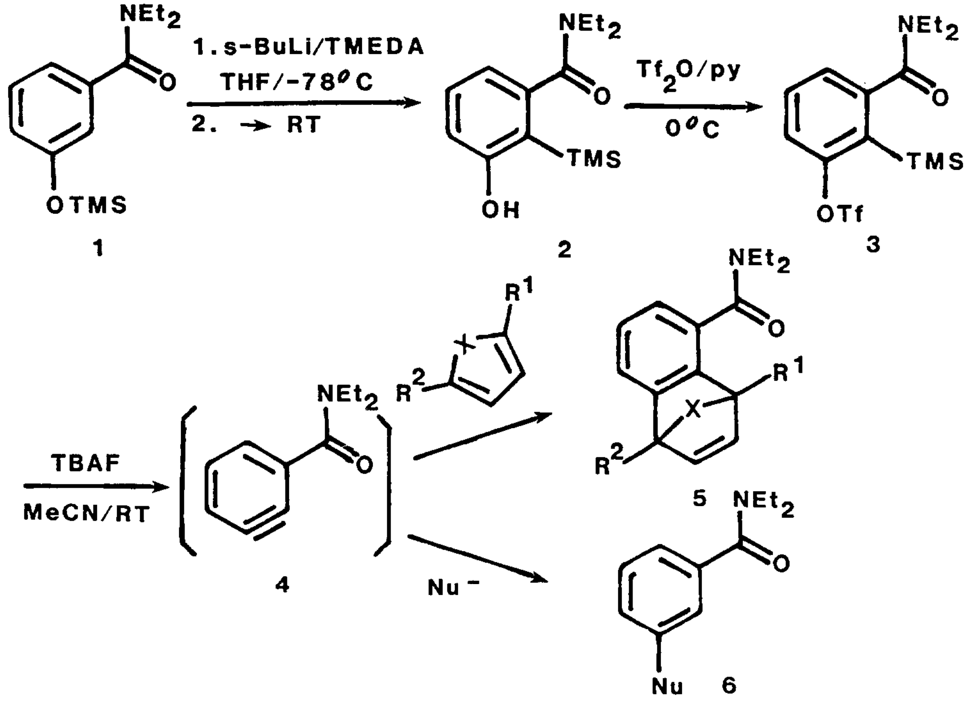
K. Shankaran and V. Snieckus*

The Guelph-Waterloo Centre for Graduate Work in Chemistry

The University of Waterloo, Waterloo, Canada N2L 3G1

Summary: 2-Trimethylsilyl-3-triflyl benzamide **3**, undergoes fluoride-mediated 1,2-elimination to give the benzyne intermediate **4** which is trapped by cycloaddition (**5**), and nucleophilic reactions (**6**).

The burgeoning synthetic advances in aliphatic silicon chemistry[1,2] have not been matched by activity in the aromatic silicon area[1,3] in spite of the firm physical organic footing provided long ago mainly by Eaborn and coworkers.[4] While investigating the use of silicon in context of benzamide directed metalation,[5] we uncovered an anion induced O → C silicon rearrangement, **1** → **2**.[6] Herein we report that 2 as its triflate **3** serves as a precursor to amide benzyne[7] **4** under the neutral mild conditions



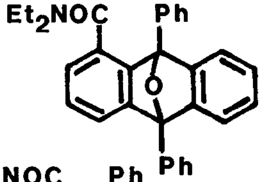
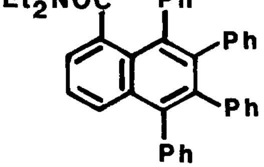
discovered by Kokayashi and coworkers.[8] The synthetically useful reactions of cycloaddition **(5)** and nucleophilic attack **(6)** are thereby derived which partially parallel those recently achieved by Meyers and coworkers using the benzyne corresponding to **4** derived from m-chlorophenyl oxazoline under strongly basic RLi metalation conditions.[9] These reactions offer new and useful synthetic methodological links to the rapidly evolving aromatic directed metalation strategy.[10]

The triflate **3**[11] was subjected to the benzyne-generating conditions[8] (1.5 equiv TBAF/MeCN/RT) in the presence of furan (4 equiv) to afford the cycloadduct **5**[12] in good yield **(Table 1).** Identical conditions with other reactive dienes led to cycloadducts **5b-d, 7,** and **8** in the yields shown. 2-Methylfuran gave a 1:1 mixture of **5c** and **5d** thus indicating absence of regioselectivity under these conditions. The adduct of **4** and tetraphenylcyclopentadienone underwent decarbonylation during purification to yield **8.**

When triflate **3** was subjected to the identical fluoride-induced elimination conditions in the presence of methanol (4 equiv) followed by acidic work up, the m-methoxybenzamide **6a** was obtained **(Table 2).** This result is consistent with the observations of Kobayashi[8] in the indication that either triflate elimination from the desilylated intermediate anion is fast in comparison with its protonation by the excess methanol or benzyne formation is the result of a concerted process. Similarly, reaction of **3** with TBAF and phenol, lithium thiophenoxide, N-trimethylsilyl aniline, and N-methyl-N-trimethylsilyl aniline provided the meta-substituted products **6b, 6c, 6d** and **6e** respectively in satisfactory yields. The formation of **6f** from the reaction of **4** with a silyl enol ether is suggestive of the potential of this method for the direct introduction of functionalized carbon substituents into meta positions. In contrast to the results of Meyers who showed that coordination of RLi reagents to the oxazoline directs kinetic ortho-nucleophilic attack,[9] the formation of **6** follows normal reactivity of benzynes with electron-withdrawing substituents[7] to form stabilized carbanions (thermodynamic control).

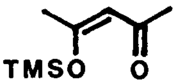
These results coupled with those of Meyers appear to hold promise for the development of new connections between aromatic directed metalation and benzyne chemistry with attendant benefits for synthetic aromatic chemistry.[13]

Table 1. Cycloaddition Reactions of Benzyne **4** [a]

Product	X	R^1	R^2	Yield,%	mp,°C
5a	O	H	H	63	75-76 (Et_2O-hexane)
5b	O	Me	Me	60	66 (Et_2O-hexane)
5c	O	H	Me	30	oil[b]
5d	O	Me	H	30	
7				56	61-62 (CH_2Cl_2-hexane)
8[c]				47	211-212 (EtOAc-hexane)

[a] All new compounds show analytical and spectral (IR, NMR, MS) data consistent with the assigned structures. Preparative tlc (SiO_2/pet ether-EtOAc, 65:35) was used for most purifications. Yields have not been optimized. [b] Unresolved 1:1 mixture of **5c** and **5d** (NMR ($CDCl_3$) δ 1.86, 1.92 for the bridgehead methyl groups). [c] Product of decarbonylation of the initial cycloadduct during ptlc.

Table 2. Reactions of Benzyne **4** with Nucleophiles[a]

Nu^-	Product	Nu	Yield, %
HOMe	**6a** [b]	OMe	41
HOPh	**6b**	OPh	43
LiSPh	**6c** [c]	SPh	62
TMSNHPh[d]	**6d** [e]	NHPh	70
TMSN(Me)Ph[d]	**6e** [c,e]	N(Me)Ph	83
	**6f** [e]	$CH(COMe)_2$	22

[a] See footnote a, Table 1. All products were oils with the exception of **6d**, mp 97-98°C (CH_2Cl_2-hexane). [b] Found to be identical with an authentic sample by direct comparison of spectroscopic and hplc properties. [c] Compounds **6c** and **6e** were shown to be different by spectroscopy (IR, NMR) and hplc behavior with the corresponding authentic o-isomers obtained by treatment of ortho lithiated N,N-diethylbenzamide with $(PhS)_2$ (Doadt, E.G.; Snieckus, V. unpublished results) and LiCu(CN)MeNPh (Iwao, M.; Reed, J.N.; Snieckus, V. J. Am. Chem. Soc. **1982**, **104**, 5531). [d] Prepared by modification of a literature method: Walton, D.R.M. J. Chem. Soc. C, **1966**, 1706. [e] Reaction was carried out in anhydr THF using 6 equiv of TBAF.

References and Footnotes

1. Colvin, E.W. Silicon in Organic Synthesis, Butterworths, London, **1981.**
2. Reviews: Paquette, L. Science, **1982,** 217, 793; Magnus, P. Aldrichimica Acta, **1980,** 13, 43; Chan, T.H.; Fleming, I. Synthesis, **1979,** 761; Colvin, E.W. Chem. Soc. Rev. **1978,** 7, 15; Rasmussen, J.K. Synthesis, **1977,** 91; Seyferth, D., Ed. New Applications of Organometallic Reagents in Organic Synthesis, Elsevier, Amsterdam, **1976;** Washburne, S.S. J. Organometal. Chem. **1976,** 123, 1.
3. Habich, D.; Effenberger, F. Synthesis, **1979,** 841.
4. Review: Eaborn, C. J. Organometal. Chem. **1975,** 100, 43.
5. Mills, R.J.; Snieckus, V. J. Org. Chem., **1983,** 48, 1565.
6. Billedeau, R.J.; Sibi, M.P. and Snieckus, V. Tetrahedron Lett. **1983,** 4515.
7. Reviews: Hoffman, R.W. Dehydrobenzene and Cycloalkynes, Academic Press, New York **1967;** Fields, E.K. in Organic Reactive Intermediates, S.P. McManus, Ed. Academic Press, New York **1973,** p. 449.
8. Himeshima, Y.; Sonoda, T.; Kobayashi, H. Chem. Lett. **1983,** 1211.
9. Meyers, A.I.; Pansegrau, P.D. Tetrahedron Lett., **1983,** 4935; Meyers, A.I.; Rieker, W. Tetrahedron Lett., **1982,** 2091.
10. Beak, P.; Snieckus, V. Accts. Chem. Research, **1982,** 15, 306.
11. Prepared by treating **1** with triflic anhydride (1.5 equiv) in pyridine solution at 0°C for 48 h followed by ptlc purification.
12. **5a** was converted (1. H_2/Pd-C/EtOH; 2. HCl/EtOH/reflux) into N,N-diethyl 1-naphthamide which was shown to be identical with an authentic sample by direct comparison.
13. We thank NSERC Canada for financial support of this research.

(Received in USA 5 January 1984)