ORGANIC
LETTERS

2001
Vol. 3, No. 11
1629−1632

Electrophilic Aromatic Substitutions of Silylated Furans and Thiophenes with Retention of the Organosilyl Group

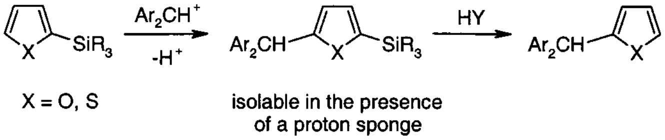
Mirjam Herrlich, Nathalie Hampel, and Herbert Mayr*

Department Chemie der Ludwig-Maximilians-Universität München,
Butenandtstrasse 5-13 (Haus F), D-81377 München, Germany

hmy@cup.uni-muenchen.de

Received March 8, 2001

ABSTRACT

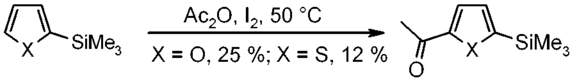


The influence of trialkylsilyl groups on the nucleophilic reactivities of furans and thiophenes is determined by kinetic experiments.

Arylsilanes usually react with electrophiles to give arenes in which the electrophile occupies the position to which the silyl group was previously bonded.[1] This orientation has been explained by the well-known β-stabilizing effect of silicon.[2] In contrast to this general statement, examples have been reported in which electrophilic aromatic substitution of arylsilanes proceeds with retention of the silyl group.[3]

Ishibashi and co-workers, for example, found that the reaction of trimethylphenylsilane with methyl chloro(methylthio)acetate in the presence of tin(IV) chloride did not give *ipso*-substitution but a mixture of disubstituted benzenes.[4] In a recent review, Keay has described the use of organosilyl moieties as blocking groups in furan chemistry, which can easily be introduced and replaced by electrophiles via *ipso*-substitution.[5a] However, in 1948 Benkeser reported that electrophilic acetylations of 2-(trimethylsilyl)furan and 2-(trimethylsilyl)thiophene do not proceed with *ipso*-substitution but take place at the 5-position (Scheme 1).[5b]

Scheme 1. Acetylation of 2-(Trimethylsilyl)furan and -thiophene.



It was the goal of this work to investigate the influence of organosilyl groups on the reactivity of heteroarenes by kinetic and product studies.

Treatment of the 2-silylfurans **1a**−**d** (1.3−1.5 equiv) with the triflate of the dianisylcarbenium ion **2a** gave the furans **4** and **5** in a 2:8 to 3:7 ratio. A higher **4**/**5** ratio was generally observed with the triflate of the ferrocenylphenylcarbenium ion **2b** as the electrophile (Table 1, upper half).

Though the formation of **4** and **5** was initially rationalized by direct displacement of the silyl group in **1a**−**d**, another reaction mechanism is suggested by experiments conducted

---

[1] Weber, W. P. In *Silicon reagents for the Organic Synthesis*; Springer-Verlag: Berlin, 1983; Vol. 14; Chapter 8, pp 114−128.

[2] For reviews, see: Apeloig, Y. In *Heteroatom Chemistry: ICHAC-2*; Block, E., Ed.; VCH: New York, 1990; pp 27−46. Apeloig, Y. In *The Chemistry of Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; J. Wiley & Sons: Chichester, 1998; Vol. 1, Chapter 2, pp 57−225. Lambert, J. B.; Zhao, Y.; Emblidge, R. W.; Salvador, L. A.; Liu, X.; So, J.-H.; Chelius, E. C. *Acc. Chem. Res.* **1999**, *32*, 183−190. Siehl, H.-U.; Müller, T. In *The Chemistry of Silicon Compounds*; Rappoport, Z., Apeloig, Y., Eds.; J. Wiley & Sons: Chichester, 1998; Vol. 2, Chapter 12, pp 595−701.

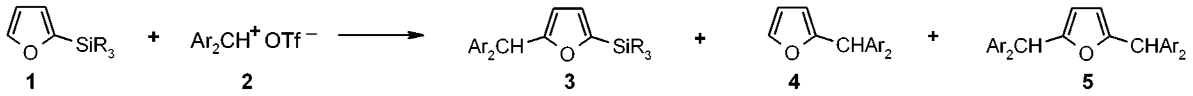
[3] For reviews, see: Bassindale, A. R.; Glynn, S. J.; Taylor, P. G. In *The Chemistry of Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; J. Wiley & Sons: Chichester, 1998; Vol. 2, Chapter 7, pp 382−388. Colvin, E. W. *Silicon in Organic Synthesis*; Butterworth: London, 1981. Fleming, I. In *Comprehensive Organic Chemistry*; Jones, N. D.; Ed.; Pergamon: Oxford 1979; Chapter 13, Vol. 3.

[4] Ishibashi, H.; Sakashita, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1953−1957.

[5] (a) Keay, B. A. *Chem. Soc. Rev.* **1999**, *28*, 209−215. (b) Benkeser, R. A.; Currie, R. B. *J. Am. Chem. Soc.* **1948**, *70*, 1780−1782.

10.1021/ol015810+ CCC: $20.00

Table 1. Reactions of Silylated Furans with Benzhydryl Cations (CH_2Cl_2)[a−c]



SiR3					ratio[d] 3	4	5	yield, %[e]
Reactions in the Absence of Proton Sponge								
SiMe3	**1a**	An_2CH^+	**2a**[f]	0 °C		29	71	85
		$FcPhCH^+$	**2b**[g]	rt		74	26	89
SiEt3	**1b**	An_2CH^+	**2a**	0 °C		26	74	99
		$FcPhCH^+$	**2b**	rt		80	20	72
SiBu3	**1c**	An_2CH^+	**2a**	0 °C		20	80	80
		$FcPhCH^+$	**2b**	rt		90	10	99
SiMe2*t*Bu	**1d**	An_2CH^+	**2a**	rt		31	69	84
		$FcPhCH^+$	**2b**	rt		91	9	72
Reactions in the Presence of Proton Sponge[h]								
SiMe3	**1a**	An_2CH^+	**2a**	−20 °C	93		7	57[i]
		$FcPhCH^+$	**2b**	0 °C	97		3	66[j]
SiEt3	**1b**	An_2CH^+	**2a**	−20 °C	99		1	72
		$FcPhCH^+$	**2b**	rt	99		1	77
SiBu3	**1c**	$FcPhCH^+$	**2b**	rt	99		1	63
SiMe2*t*Bu	**1d**	An_2CH^+	**2a**	−20 °C	100			64
		$FcPhCH^+$	**2b**	rt	100			71

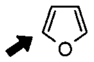
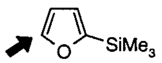
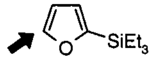
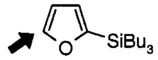
[a] An = *p*-$CH_3OC_6H_4$-. [b] Fc = ferrocenyl. [c] The reactions were performed as described in ref 8, but the workup was modified. It involved quenching with 15 mL of concentrated ammonia, separation of the two layers and extraction of the aqueous layers with CH_2Cl_2 (3 × 30 mL), washing of the combined organic layers with water, and, finally, drying over $MgSO_4$. [d] The ratios were determined from the ^1H NMR spectra of the crude products. [e] The yields with respect to **2** were determined from the ^1H NMR spectra of the crude products using mesitylene as an internal standard. For the calculation it was considered that 2 equiv of **2** is needed for the formation of **5**. [f] From **2a**-Cl and Me_3SiOTf, for **2a**-Cl, see: Schneider, R.; Mayr, H.; Plesch, P. H. *Ber. Bunsen-Ges. Phys. Chem.* **1987**, *91*, 1369−1374. [g] From **2b**-OAc and Me_3SiOTf, for **2b**-OAc, see: Mayr, H.; Rau, D. *Chem. Ber.* **1994**, *127*, 2493−2498. [h] 2 equiv of 2,6-di-*tert*-butylpyridine per mole of electrophile. [i] 39% of Ar_2CHOH from hydrolysis of **2** was identified in the crude product. [j] 20% of Ar_2CHOH from hydrolysis of **2** was identified in the crude product.

in the presence of 2,6-di-*tert*-butylpyridine as a proton sponge (Table 1, bottom). In all cases the disubstituted furan **3** is observed as the almost exclusive product, indicating that compounds **4** observed in the experiments without proton sponge are produced via protodesilylation of **3**. Since the bis-substitution products **5** are produced in very small amounts in the presence of the proton sponge, their formation in the absence of the hindered pyridine must be due to attack of the benzhydryl cations at **4** and not at **3**.

Benzhydryl cations, which can be detected photometrically as described previously,[6] can be used as reference electrophiles to link the kinetic data of this work to reactivity data for other classes of compounds.[7] The increased reactivities of the 2-(trialkylsilyl)furans **1a**−**c** compared to furan (Scheme 2) do not reflect the activation of the *ipso*-position by trialkylsilyl but reflect the effect of the 2-silyl substituent on the reactivity of position 5.

The weak acceleration of electrophilic attack at the 5-position by 2-trimethylsilyl is in accord with the slightly negative value of $\sigma_p^+ = -0.09$[9] as well as with Apeloig's[10] conclusion that the carbenium ion stabilization of silyl groups is between that of alkyl groups and hydrogen.

Scheme 2. Rate Constants for the Attack of the Ferrocenylphenylcarbenium Ion **2b** at 2-Trialkylsilyl-Substituted Furans (20 °C, CH_2Cl_2)[a]

		k_2 / L mol^{-1} s^{-1}	k_{rel}
		0.0092^b	1.0
	**1a**	0.293	32
	**1b**	0.331	36
	**1c**	0.503	55

[a] The rate constants were determined photometrically as described in ref 6. [b] Partial rate constant. The actually measured rate constant is 0.0183 L mol^{-1} s^{-1}, from ref 8.

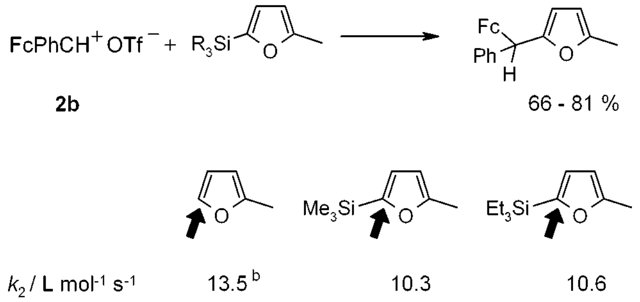
---

(6) For detailed information, see: Mayr, H.; Schneider, R.; Schade, C.; Bartl, J.; Bederke, R. *J. Am. Chem. Soc.* **1990**, *112*, 4446−4454.

(7) For reviews, see: Mayr, H.; Patz, M. *Angew. Chem.* **1994**, *106*, 990−1010; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938−957. Mayr, H.; Kuhn, O.; Gotta, M. F.; Patz, M. *J. Phys. Org. Chem.* **1998**, *11*, 642−654. Mayr, H.; Patz, M.; Gotta, M. F.; Ofial, A. R. *Pure Appl. Chem.* **1998**, *70*, 1993−2000.

To elucidate the effect of the trialkylsilyl groups on the rate of *ipso*-substitution,[11] we investigated the reactivities of 2-methyl-5-(trialkylsilyl)furans. The reactions occur exclusively with electrophilic attack at the silyl-substituted position and proceed with similar rates as with 2-methylfuran (Scheme 3).

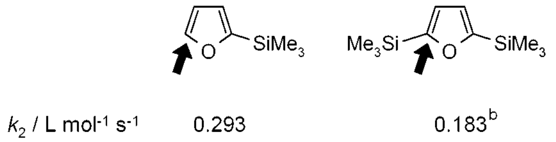
Scheme 3. Rate Constants of the Reactions of the Ferrocenylphenylcarbenium Ion **2b** with 2-Methyl-5-(trialkylsilyl)furans (20 °C, CH_2Cl_2)[a]



[a] The rate constants were determined photometrically as described in ref 6. [b] From ref 8.

The acceleration of the electrophilic attack by hyperconjugative stabilization of the resulting carbenium ion, which is observed in protodesilylations of silylated benzenes,[12] is obviously compensated by the steric shielding of the organosilyl group (Scheme 4).

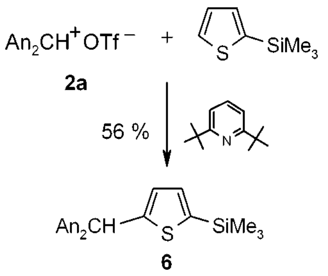
Scheme 4. Rate Constants for the Attack of the Ferrocenylphenylcarbenium Ion **2b** at 2-(Trimethylsilyl)furan and 2,5-Bis(trimethylsilyl)furan (20 °C, CH_2Cl_2)[a]



[a] The rate constants were determined photometrically as described in ref 6. [b] Partial rate constant. The actually measured rate constant is 0.366 L mol^{-1} s^{-1}.

Similar observations were made in electrophilic reactions of analogous thiophenes with the bis(*p*-anisyl)carbenium ion (**2a**). The reaction of the bis(*p*-anisyl)carbenium triflate **2a**·OTf⁻ with 2-(trimethylsilyl)thiophene in the presence of a proton sponge gave the 2,5-disubstituted thiophene **6** shown in Scheme 5 as the only isolable product.

Scheme 5. Reaction of 2-(Trimethylsilyl)thiophene with the Bis(*p*-anisyl)carbenium Ion **2a** (CH_2Cl_2)

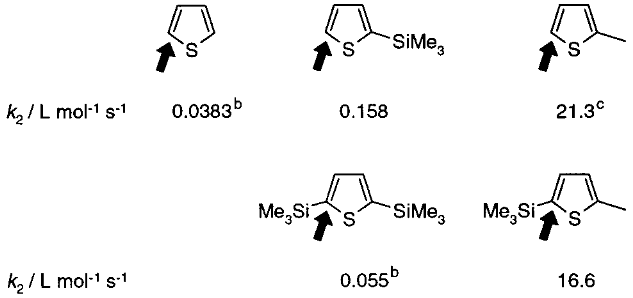


As in the furan series, introduction of the trimethylsilyl group into thiophene causes only a slight increase of reactivity, in accordance with the small σ_p^+ values of SiR_3.[9,13]

Similar substituent effects of 2-trimethylsilyl groups on the nucleophilic reactivities of furan and thiophene toward the tricarbonyliron-coordinated cyclohexadienylium ion have been reported.[14] Since these experiments have not been performed in the presence of a proton sponge, the site of initial electrophilic attack is not clear and the interpretation of these results may require revision.

The negligible kinetic "*ipso*"-effect derived from the comparison of 2-(trimethylsilyl)thiophene with 2,5-bis(trimethylsilyl)thiophene and from the comparison of 2-methylthiophene with 2-methyl-5-(trimethylsilyl)thiophene (Scheme 6) again suggests that the electronic acceleration of the *ipso*-attack by SiR_3 is compensated by steric retardation.

Scheme 6. Rate Constants for the Attack of Bis(*p*-anisyl)carbenium Ion **2a** at Differently Substituted Thiophenes (20 °C, CH_2Cl_2)[a]



[a] The rate constants were determined photometrically as described in ref 6. [b] Partial rate constants. The actually measured rate constants are 0.0767 and 0.110 L mol^{-1} s^{-1}, respectively. [c] From ref 8.

Introduction of a trialkylsilyl group to the 2-position of furan or thiophene hardly affects the reactivity of this position toward carbenium ions (*ipso*-attack), while the 5-position is somewhat activated. For that reason, carbocations preferentially attack the 5-position of 2-(trialkylsilyl)furans and

---

(8) Gotta, M. F.; Mayr, H. *J. Org. Chem.* **1998**, *63*, 9769−9775.

(9) Taylor, R. *Electrophilic Aromatic Substitution*; J. Wiley & Sons: Chichester, 1990; p 461.

(10) Apeloig, Y.; Stanger, A. *J. Am. Chem. Soc.* **1985**, *107*, 2806−2807.

(11) Brook, M. A.; Neuy, A. *J. Org. Chem.* **1990**, *55*, 3609−3616.

(12) Eaborn, C. *J. Organomet. Chem.* **1975**, *100*, 43−57.

(13) Glyde, E.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1632−1635.

(14) John, G. R.; Kane-Maguire, L. A. P.; Odiaka, T. I.; Eaborn, C. *J. Chem. Soc., Dalton Trans.* **1983**, 1721−1727.

-thiophenes to give 2,5-disubstituted heteroarenes which are protodesilylated in the absence of a proton trap.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

Supporting Information Available: Spectroscopic data for compounds **3** and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL015810+