

FLUORIDE-INDUCED 1,2-ELIMINATION OF *o*-TRIMETHYLSILYL-
PHENYL TRIFLATE TO BENZYNE UNDER MILD CONDITIONS

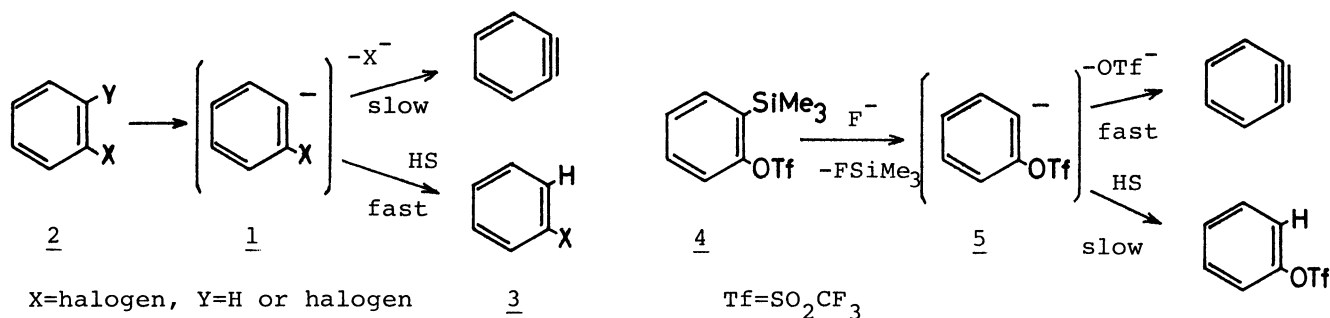
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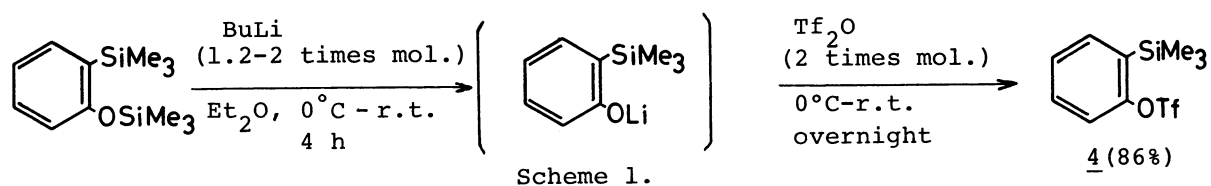
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Fluoride-induced 1,2-elimination of *o*-trimethylsilylphenyl triflate provided a convenient route to benzyne under mild conditions where detriflation from an intermediary aryl anion appeared to occur in preference to protonation even in the presence of alcohols.

In spite of the utility of benzyne in organic synthesis, the methods of its generation under mild condition from readily available chemicals are relatively limited,¹⁾ one of which is dehalogenation from anionic intermediate (1, X=halogen) which is usually generated by deprotonation from aromatic halogen compounds (2, X=halogen, Y=H) with strong bases or by metal-halogen exchange of *ortho* dihalogen-substituted benzenes (2, X, Y=halogens) with lithium or magnesium. The highly basic condition of these reactions is however unfavorable in the cases where the molecule contains base-sensitive functional groups, and protonation to 1 gives halobenzenes (3) under protic conditions and usually appears to occur in preference to benzyne formation. In the course of our study in the synthetic application of perfluoroalkanesulfonic esters, we intended to prepare *o*-trimethylsilylphenyl triflate (4) for generating anionic intermediate (5) by fluoride-induced desilylation under neutral condition followed by elimination of triflate group to give benzyne, which could be considered to occur in preference to protonation to 5 because of the excellent leaving group property of triflate group.²⁾



o-Trimethylsilylphenyl triflate (4)³⁾ was readily prepared by dropping excess molar amounts of butyllithium and subsequent triflic acid anhydride to *o*-trimethylsilylphenoxytrimethylsilane⁴⁾ in ether which is obtained in high yield by two steps from *o*-chlorophenol (Scheme 1). Triflate (4) is quite stable liquid and readily purified by distillation under reduced pressure.



Formation of benzyne from triflate(4) induced by the nucleophilic attack of fluoride ion at silicon was investigated by trapping benzyne intermediate with furan in the form of 1,4-dihydronaphthalene-1,4-endo-oxide(6). After dropping 4 to a solution of furan containing various fluorides, the reaction mixture was stirred for an appropriate time at room temperature until 4 was consumed. As shown in Table 1, yields of 6 are independent of the dropping time of 4, namely independent of the rate of benzyne formation(Runs 1-3). Fifteen times molar amounts of furan with tetramethylammonium fluoride in HMPT is enough to trap benzyne almost quantitatively (Run 4), while decreased solubility of fluoride ion resulted in a slower reaction rate in furan compared with in HMPT(Run 5). Slower reactions of the triflate(4) were observed with less soluble potassium and caesium fluorides(Runs 6-8). An optimum condition was obtained in acetonitrile with tetrabutylammonium fluoride(1.5 times mol.) and furan(4 times mol.) to yield 61% of 6(Run 9), which is much better than the results in the thermal decomposition of benzenediazonium 2-carboxylate(36% and 51% yields of 6 with 4 and 7 times molar amounts of furan, respectively⁵). Fluoride ion is needed at least stoichiometrically for desilylation(Run 10).

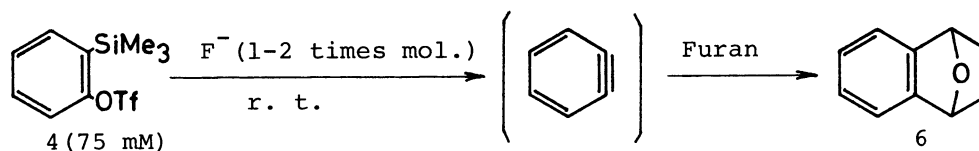


Table 1. Reactions of Triflate(4) with Furan at Room Temperature

Run	F ⁻ reagents	Solvents	Molar Ratio 4:Furan:F ⁻	Dropping Time(min)	Reaction Time(h)	Yields ^{a)} 6(%)
1	Me ₄ NF	HMPT	1:4:2	15	4	42 ^{b)}
2	"	"	"	2	2	51
3	"	"	"	45	2	56
4	"	"	1:15:2	5-105	2.5	86-96
5	"	Furan	1:excess:2	5	114 ^{c)}	76
6	KF	HMPT	1:4:2	5	15	34
7	KF-18-Crown-6	Benzene	"	5	22 ^{d)}	No reaction
8	CsF	HMPT	"	110	44	42
9	Bu ₄ NF	CH ₃ CN	1:4:1.5	5	3.5	61
10	Me ₄ NF	HMPT	1:4:0.1	5	22	- ^{e)}

a) Determined by GLC. b) Isolated yields. c) 88% conversion under reflux.

d) Under reflux. e) Not detected by GLC.

The excellent leaving group property of triflate in benzyne formation was clearly demonstrated in the comparison of the results of the triflate(4) with those of *o*-trimethylsilylphenyl chloride(7) by Cunico *et al.*⁶⁾ (Table 2). Chloride(7) gave lower yields of 6 accompanying chlorobenzene(3, X=Cl) and 2-trimethylsilylfuran (9) which were formed as a result of proton-abstraction of aryl anion(1, X=Cl) from furan, where triflate(4) gave always better yields of 6 without any by-product of phenyl triflate(8, X=OTf) or 9. Higher reactivity of 4 compared with 7 is apparent in the reactions with potassium fluoride(Runs 7 and 8). Runs 3 and 4 indicated that fast elimination of triflate ion occurs even in the reactions with hydrated fluorides, while elimination of chloride ion is much slower than protonation.

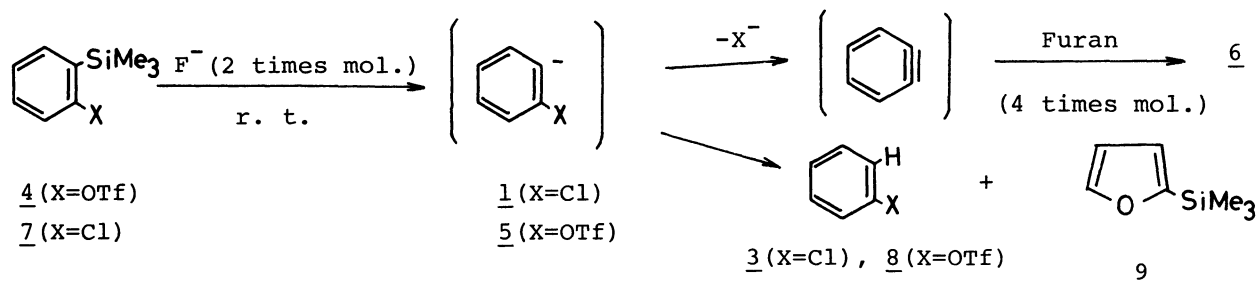


Table 2. Comparison of Reactivity of Triflate(4) with Chloride(7)

Run	X	F ⁻ reagents	Solvents	Yields of Products (%)		
				6	3 or 8	9
1	OTf	Me ₄ NF	HMPT	56	-	-
2	Cl ^{a)}	"	"	31	12	12
3	OTf	Me ₄ NF·4H ₂ O	HMPT	23	-	-
4	Cl ^{a)}	Et ₄ NF·4H ₂ O	DMSO	trace	90	-
5	OTf	Me ₄ NF	Furan	76	-	-
6	Cl ^{a)}	"	"	32	39	29
7	OTf	KF	HMPT	34	-	-
8	Cl ^{a)}	"	"	No reaction		

a) Taken from Ref. 6.

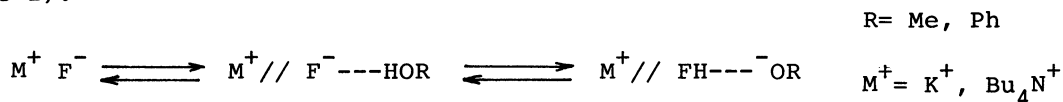
Benzyne formation from triflate(4) with fluoride ion was confirmed even in alcoholic media (Table 3). The reaction with 4 times molar amounts of methanol in

Table 3. Reactions of Triflate(4) with Methanol and Phenol at Room Temperature

Run	F ⁻ reagents ^{a)}	Solvents	Molar ratio 4 : ROH	Reaction Time (h)	Yields (%) of PhOR (R=Me or Ph)
1	Bu ₄ NF	CH ₃ CN	1 : 4 (MeOH)	2	60 (PhOMe)
2	"	"	1 : 4 (PhOH)	48 ^{b)}	38 (PhOPh)
3	"	CH ₃ OH	1 : excess (MeOH) ^{c)}	37 ^{d)}	34 (PhOMe)
4	KF	"	"	15	No reaction
5	"	"	"	42.5 ^{e)}	"

a) 1.5 times molar amounts. b) 53% conversion. c) 77 mM solution. d) 83% conversion with two unidentified by-products. e) Under reflux condition.

acetonitrile with tetrabutylammonium fluoride gave 60% yield of anisole, and the reaction with phenol under similar conditions gave 38% of diphenyl ether but with much slower reaction rate compared with methanol. Furthermore, an excess amount of methanol reduced the reaction rate and no reaction occurred with potassium fluoride in methanol even under reflux condition. These preliminary results indicate that the nucleophilicity of fluoride ion would be greatly affected by the counter cations or the amount and kind of alcoholic solvents surrounding fluoride ion (Scheme 2).



Scheme 2.

Synthetic application of this benzyne synthon under mild conditions and mechanistic investigation of the benzyne formation are now under progress.

References

- 1) R. W. Hoffmann, "Dehydrobenzene and cycloalkynes," Academic Press New York (1967); E. K. Fields, "Organic Reactive Intermediates," ed by S. P. McManus, Academic Press New York (1973), p.449.
- 2) A relative leaving ability of trifluoromethanesulfonyloxy group has been proved to be more than 10^8 times larger than that of chloride. See P. J. Stang, M. Hanack, and L. R. Subramanian, *Synthesis*, 1982, 87.
- 3) *O*-Trimethylsilylphenyl triflate (4); bp 70 °C/2 mmHg; IR(neat): ν_{max} 2980, 1420, 1255, 1210, 1145 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 0.4(9H, s), 7.1-7.5(4H, m); $^{19}\text{F-NMR}$ (CCl_4 , CCl_3F): δ 78.0(s).
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- 5) L. F. Fieser and M. J. Haddadin, *Can. J. Chem.*, 43, 1599(1965).
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(Received May 23, 1983)