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PRELIMINARY NOTE

1,1-Dihydroperfluoroalkylations of Nucleophiles with (1,1-Dihydroperfluoroalkyl)phenyliodonium Triflates

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SUMMARY

It was demonstrated that (1,1-dihydroperfluoroalkyl)phenyliodonium triflates (FMITS) served as very useful sources of 1,1-dihydroperfluoroalkyl cations. With a variety of nucleophiles, the corresponding fluoroalkyl derivatives were obtained.

1,1-Dihydroperfluoroalkyl groups have been of great interest in the field of medicines or light- and gas-fast azo dyes because of their unique properties [1-3]. However, the introduction of the fluoroalkyl groups into organic compounds was arduous. 1,1-Dihydroperfluoroalkyl anions or cations would be anticipated to be reactive species for the selective fluoroalkylations However, the anions were so unstable on account of easy eliminations of fluorine atoms at the β-positions that they could not be utilized as useful species [4].

The cations were difficult to generate due to the high electronegativity of fluorinated groups. This is understandable from the fact that 1,1-dihydroperfluoroalkyl halides possessed very little reactivity toward nucleophilic substitution [3,5]. The fluoroalkyl tosylates [6,7], mesylates [8], or o-nitrobenzenesulfonates [9,10] underwent nucleophilic reactions with amines or phenoxides only under drastic conditions. Even the more reactive triflates [11] or triclates [1] required very

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forcing conditions for alkylations to proceed. On the other hand, 1,1-dihydroperfluoroalkylation of carbanions has never been reported. The treatment of fluoroalkyl triflates with a carbanion afforded products resulting from the attack of the anion at the sulfur-sites of the triflates [12]. Furthermore, the fluoroalkylation of aromatic compounds has hardly been reported. Recently we have developed (1,1-dihydroperfluoroalkyl)-phenyliodonium triflates (FMITS-m) as the most reactive reagents of this type [13]. We now wish to report the fluoroalkylations of a variety of nucleophiles with FMITS reagents.

We found that FMITS reagents readily reacted with many kinds of nucleophiles under very mild conditions to give the corresponding fluoroalkyl compounds in varying yields. The results

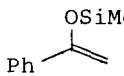
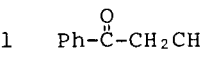
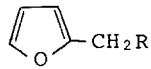
$$RfCH_2\text{-}\underset{\underset{Ph}{|}}{I}\text{-}OTf \xrightarrow{Nu^-} RfCH_2\text{-}Nu + PhI$$

FMITS-m (Rf=n-C_mF_{2m+1})

are summarized in Table 1. FMITS-1, -3, or -7 readily reacted with 2 molar proportions of aniline, N-ethylaniline, or phenylethylamine in methylene chloride at room temperature to produce N-dihydroperfluoroalkyl compounds in high or quantitative yields FMITS also reacted with equimolar aniline in the presence of equimolar collidine, as an acid trap of triflic acid liberated, to give the product quantitatively (Run 1b). FMITS-1 was treated with lithium phenoxide at 0 °C in methylene chloride to afford the trifluoroethyl ether in a good yield. Lithium phenylethoxide gave the corresponding ether as the sole product in 61 % yield. The fluoroalkylation of alkoxides by conventional methods was difficult because 1,1-dihydroperfluoroalkyl triflates had two reaction-sites, carbon- and sulfur-sites, and the major products resulted from the reaction at the latter site [14]. FMITS reacted with benzoic acid in the presence of equimolar collidine as a base at room temperature for 0.5 h to give the ester in a quantitative yield. On the other hand, FMITS reacted with a mercaptan without a base to produce the fluoroalkyl

TABLE 1

1,1-Dihydroperfluoroalkylations with FMITS reagents

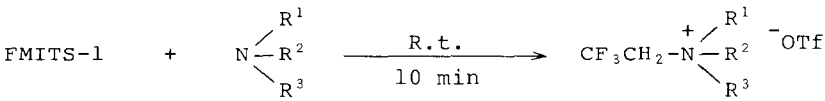
Run[a]	Substrate	FMITS -m	Base[b]	Solv.	Time (h)	Product[c]	Y.[d] (%)
1a	$PhNH_2$	m=1	A	CH_2Cl_2	1.5	$PhNHCH_2Rf$	92
1b	"	1	B	"	1	"	98
1c	"	3	A	"	1.5	"	96
1d	"	7	A	"	1.5	"	100
2	$PhNHEt$	1	A	"	1.5	$PhNEtCH_2Rf$	98
3	$PhCH_2CH_2NH_2$	1	A	"	1.5	$PhCH_2CH_2NHCH_2Rf$	85
4	PhOH	1	C	"	0.5	$PhOCH_2Rf$	79
5	$PhCH_2CH_2OH$	1	C	"	0.5	$PhCH_2CH_2OCH_2Rf$	61
6	PhCOOH	1	B	"	0.5	$PhCOOCH_2Rf$	99
7	n-$C_{12}H_{25}SH$	1	-	"	0.5	n-$C_{12}H_{25}SCH_2Rf$	80
8a	$CH_3CH(COOEt)_2$	1	D	DMSO[g]	1	$CH_3C(COOEt)_2CH_2Rf$	25
8b	"	7	D	" [g]	1	"	28
9	$PhCH_2CH_2MgBr$	7	-	Et_2O	0.5	$PhCH_2CH_2CH_2Rf$	36
10[e]		1	B	CH_2Cl_2	1		30
11[f]	Furan	7	B	Furan	24		52

[a] The reactions were carried out at room temperature except for Run 4 (0 °C), 5 (0 °C), and 11 (50 °C).
[b] A=another equivalent amount of the substrate, B=2,4,6-collidine, C=LiH, D=NaH.
[c] All the products showed spectral data (^1H- and ^{19}F-NMR, IR, and Mass) and elemental analyses in accord with the assigned structures.
[d] Isolated yields.
[e] After FMITS-1 was added into a solution of the silyl enol ether in CH_2Cl_2, the base was added into the solution.
[f] The reaction was carried out in a sealed tube.
[g] FMITS was added into a solution of sodium salt of diethyl methylmalonate in DMSO.

sulfide in a good yield. Finally we found that FMITS reacted with carbanions such as the sodium salt of diethyl methylmalo-

nate and with Grignard reagents to afford the desired products, though the yields were only moderate. Furthermore, FMITS reacted with a silyl enol ether to give a β-perfluoroalkyl carbonyl compound in 30% yield. Although FMITS did not react with non-activated aromatic compounds such as benzene, FMITS-7 was heated in furan at 50 °C in the presence of collidine to produce α-(dihydroperfluorooctyl)furan in 52% yield.

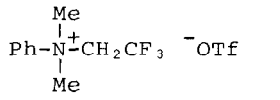
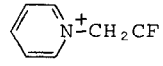
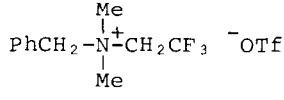
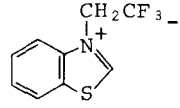
It was found that FMITS-1 rapidly reacted with an equivalent amount of a tertiary amine or a heterocyclic compound in methylene chloride at room temperature to give the corresponding fluoroalkyl ammonium or pyridinium triflate in excellent yields. The results are summarized in Table 2.



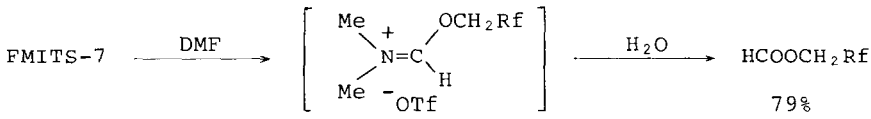
After a solution of FMITS-7 in dimethylformamide was allowed to stand for 5 h at room temperature, the usual post-treatment afforded 1,1-dihydroperfluorooctyl formate in 79% yield. It is reasonable that the formate was formed via the intermediate iminium salt followed by hydrolysis during the post-treatment.

TABLE 2

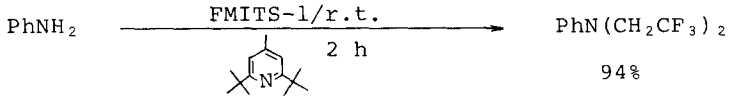
Reactions of tertiary amines and heterocyclic compounds with FMITS

Run	Product[a]	Y(%)[b]	Run	Product[a]	Y(%)[b]
1		89	3		83
2		89	4		84

[a] Isolated yields. [b] All the products showed spectral data in accord with the assigned structures.



Recently, it was shown that the bis(trifluoroethyl)amino group is particularly interesting in the pharmaceutical field [15]. FMITS reagents have made it possible to dialkylate primary amines in one step under very mild conditions. Aniline was allowed to react with 2 molar proportions of FMITS-1 in the presence of 2,6-di-t-butyl-4-methylpyridine as an acid trap in methylene chloride at room temperature for 2 h to give the dialkylaniline in 70% yield. Treatment with 3 molar proportions of FMITS-1 gave 94% yield of the product.



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