Preparation of Trifluoromethyl and Other Perfluoroalkyl Compounds with (Perfluoralkyl)trimethylsilanes

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The preparation of a variety of novel perfluoroalkyl-substituted compounds in high yields using easily prepared (perfluoroalkyl)trimethylsilanes (**1a-c**) is described. (Trifluoromethyl)-, (pentafluoroethyl)-, and (heptafluoropropyl)trimethylsilane, **1a-c**, respectively, react readily with carbonyl compounds, such as aldehydes and ketones, by a fluoride-initiated catalytic process. Fluoride-initiated addition of **1** to a carbonyl group generates an oxyanionic species which then further catalyzes the reaction. Even enolizable carbonyl compounds react cleanly under the reaction conditions. A study of the scope of the reactivity of **1a** toward other carbonyl groups in esters, lactones and an acid chloride was also carried out. Thus **1a** reacts cleanly with five- and six-membered ring lactones. However, unactivated esters do not react under the reaction conditions. The acid chloride reacts with **1a** to give a mixture of products.

Introduction

Organofluorine compounds have found rapidly increasing use in the areas of agrochemicals, pharmaceuticals, and fluoropolymers. A number of antiviral, antitumor, and antifungal agents have been developed in which fluorine substitution has been a key to their biological activity. Many organofluorine derivatives have been used as probes for studying biochemical processes. These applications stem from the fact that the introduction of fluorine into a molecule often leads to a significant change in its physical and chemical properties.[1] First, fluorine and hydrogen are comparable in size (the Van der Waal's radii of F and H are 1.35 and 1.1 Å, respectively). Thus, whereas a molecule and its fluoro analogues would be sterically almost indistinguishable to a guest molecule, their chemical behavior could be different from one another. Second, the high C-F bond energy, which averages about 116 kcal/mol, leads to enhanced thermal stability. Third, due to its high electronegativity, fluorine-containing molecules often show different chemical properties. In fact, the difluoromethyl(CF_2H) and difluoromethylene (CF_2) groups are considered isopolar and isosteric with the hydroxy (OH) and ether oxygen (O) groups, respectively.[2] Finally, fluorine substitution can increase lipid solubility, and this increases the rate of transport of biologically active compounds across lipid membranes. Thus, many perfluoroalkyl, especially trifluoromethyl-substituted, compounds have been examined for their ability to enhance transport rate in vivo.

Concomitant with an increased understanding of the behavior of organofluorine compounds,[1-3] considerable progress has also been made in the development of new synthetic methodologies.[4] A number of methods exist for the preparation of fluorinated and polyfluoroalkylated aromatic compounds.[5]

Trifluoromethyl-substituted compounds have been examined for their potential as biologically active drugs and agrochemicals.[6] Consequently, much effort has been put into developing more economical and efficient trifluoromethylating reagents using organometallic derivatives.

Trifluoromethylation of aromatics is readily achieved with a variety of methods most notably using trifluoromethylcopper,[7] sodium trifluoroacetate,[8] trifluoromethyl triflate,[9] bis(trifluoromethyl)mercury,[10] and other related reagents.[5,11] Although the literature abounds with examples of introducing perfluoroalkyl groups into carbonyl compounds through organometallic reagents of zinc,[12] calcium,[13] manganese,[14] magnesium,[15] silver,[14] and lithium[16] (eq 1), the procedures are seldom applicable to trifluoromethylation. Formation of difluorocarbene by α-elimination of metal fluoride is a serious side reaction (eq 2). Recently, electrochemical trifluoromethylation of carbonyl compounds was reported as a viable synthetic method. However, yields were poor with ketones and some aldehydes.[17a] Also use of (trialkylsilyl)(trifluoromethyl)diazenes as nucleophilic trifluoromethylating agents has been reported.[17b]

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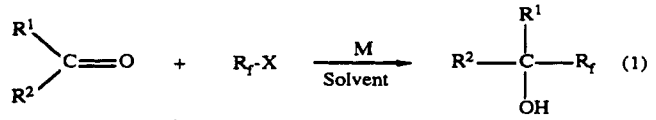
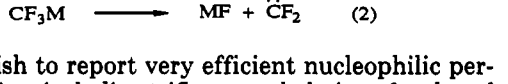


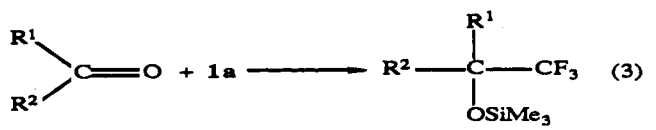
R^1 = H, Alkyl, Aryl
R^2 = Alkyl, Aryl
R_f = C_2F_5, C_3F_7, etc
M = Zn, Mg, Mn, Ca, Ag, Li
Solvent = DMF, THF



We not wish to report very efficient nucleophilic perfluoroalkylation, including trifluoromethylation of carbonyl compounds, using easily prepared (perfluoroalkyl)trimethylsilanes (1).[18] Over the years trimethylsilyl com-

$R_fSi(CH_3)_3$
1a: $R_f = CF_3$
1b: $R_f = CF_3CF_2$
1c: $R_f = CF_3CF_2CF_2$

pounds substituted with electron-withdrawing substituents, such as CN, I, Cl, Br, N_3, NCO, CNO, etc., have been used as synthetic reagents to attach these substituents to electron-deficient centers.[19] Reactions of these reagents are generally based on the hard–soft reactivity principle,[20] with the silicon acting as the hard acid and the electronegative substituent the soft base. Accordingly, the bond between the pseudohalide trifluoromethyl, for example, and the trimethylsilyl in **1a** should be sufficiently polarized with the trifluoromethyl group bearing substantial negative charge. If we consider the reaction of **1a** with a carbonyl group, the propensity of silicon to form strong bonds with the hard base oxygen can be a favorable thermodynamic process to drive the reaction (eq 3). The net result would

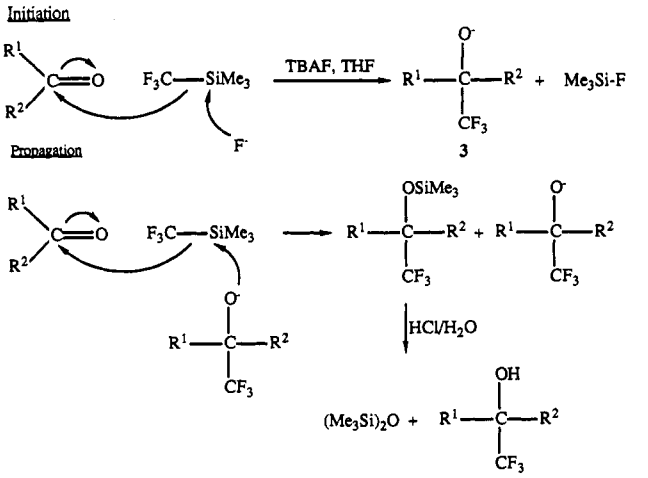


be the addition of **1a** across the carbonyl. Consequently we embarked on a study of (trifluoromethyl)trimethylsilane ($TMSCF_3$, **1a**) as a potential reagent for introducing the trifluoromethyl group into carbonyl compounds and found a long sought after simple and efficient trifluoromethide equivalent reagent.[21] Subsequently, we found that this reaction works equally well with higher perfluoroalkyltrimethylsilanes, such as **1b** and **1c**.

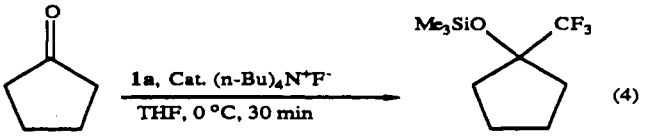
Results and Discussion

Initially, we attempted reactions of a carbonyl compound, such as cyclopentanone, with $TMSCF_3$ in the presence of a variety of Lewis acids, such as, $F_3B{\cdot}OEt_2$, ZnI_2, $TiCl_4$, Et_2AlCl, $EtAlCl_2$, and $SnCl_4$. However, ^{19}F NMR spectra of the reaction mixtures in all cases showed no trace of the trifluoromethylated product. We then considered the possibilities of activating the silicon–carbon

Scheme I



bond under nucleophilic conditions. Silicon is known to form strong bonds with oxygen and fluorine. Many reactions of silicon compounds using fluoride ion as the mediator are well known.[19] Hiyama and co-workers[22] recently reported a series of fluoride-initiated carbonyl addition reactions of a variety of α-halo carbanions derived from α-halo organosilicon compounds. From the vibrational spectra and force field calculation data for **1a** and its perdeuterated analogue, Eujen[23] pointed out the apparent weakness of the Si–CF_3 bond in these and other silanes containing CF_3 groups. We therefore envisaged that a similar carbonyl addition could occur with perfluoroalkyltrimethylsilanes (**1a–c**) under fluoride catalysis. Indeed, when cyclopentanone was treated with **1a** in THF in the presence of a catalytic quantity (2 mol %) of tetra-*n*-butylammonium fluoride trihydrate[24] (TBAF) at 0 °C, ^{19}F and ^{13}C NMR spectra of the reaction mixture showed quantitative formation of the trifluoromethylated adduct (eq 4). Subsequently, we found that **1a** adds equally well



(4)

to a wide variety of aldehydes, ketones, and enones and is generally unaffected by moisture.[21] The resulting trimethylsilyl ethers are hydrolyzed by aqueous acid to give trifluoromethylated carbinols in excellent overall yield. The results of the reaction of **1a** with aldehydes, ketones, and an enone are summarized in Table I. In the case of hindered ketones, such as 2-adamantanone and estrone methyl ether, the reaction was sluggish. Nevertheless, trifluoromethylated adducts were obtained on prolonged reaction. In the case of 2-cyclohexen-1-one, 1,2-addition predominates (>90%). Shortly after submission of our communication,[21] a paper describing a new synthesis of trifluoromethyl-substituted phenols and anilines by the addition of triethyl- and tri-*n*-butyl(trifluoromethyl)silane to quinones appeared in the literature.[26] Most recently, **1a** has been used for the synthesis of trifluoropyruvic acid

(18) (Trifluoromethyl)trimethylsilane (**1a**) was prepared by a modification (see the Experimental Section) of the published procedure: Ruppert, I.; Schlich, K.; Volbach, W. *Tetrahedron Lett.* **1984**, *25*, 2195. Also see: Pawelke, G. *J. Fluorine Chem.* **1989**, *42*, 429. Attempts to utilize more readily available phosphorus compounds, such as Ph_3P, $(MeO)_3P$, and $(EtO)_3P$ for this reaction gave no trace of **1a**.

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Table I. Fluoride Ion Induced Trifluoromethylation of Carbonyl Compounds with (Trifluoromethyl)trimethylsilane (1a)

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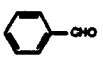
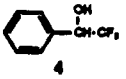
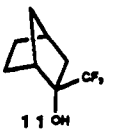
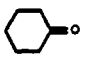
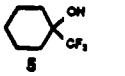
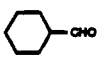
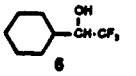
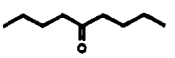
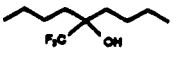
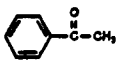
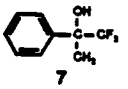
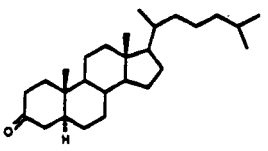
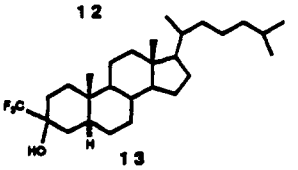
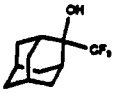
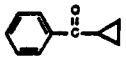
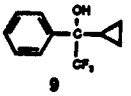
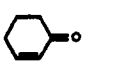
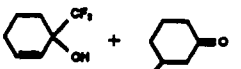
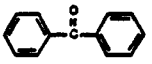
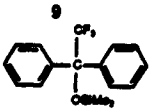
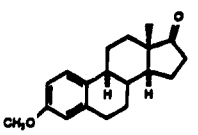
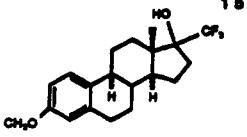
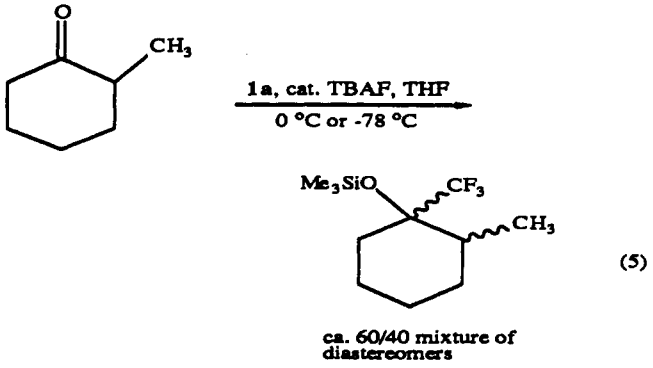
	 4	85		 11	92
	 5	77			
	 6	80		 12	87
	 7	74		 13	83[a]
	 8	72			
	 9	81		 14 + 15	60
	 10	88		 16	62[b]

[a] Only one stereoisomer was obtained. [b] Obtained as a mixture of 90% product (one isomer) and 10% starting ketone.

monohydrate ($CF_3(CO)COOH$)[27] based on our method.[21]

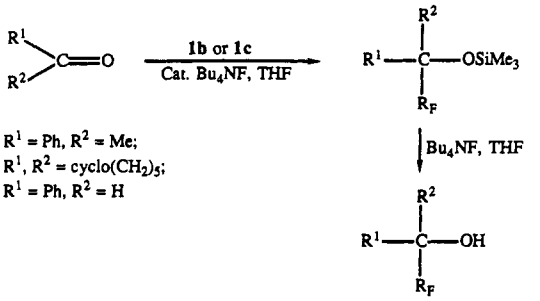
The proposed mechanism for the reaction, depicted in Scheme I, involves fluoride ion initiation (indicated by the irreversible formation of fluorotrimethylsilane) to afford the trifluoromethylated oxyanion **3**, which then catalyzes the subsequent reaction. Support for this mechanism comes from the observation that other oxyanionic species, such as potassium *tert*-butoxide and sodium trimethylsilanolate (Me_3SiONa),[25] are also effective catalysts. Steric hindrance in the carbonyl compound, however, is a limiting factor in the reactions of **1a** under these conditions. For example, extremely hindered ketones, such as 1,7,7-trimethylbicyclo[2.2.1]heptan-2-one, 3,3-dimethylbicyclo-[2.2.1]heptan-2-one, and di-1-adamantyl ketone gave only traces (<1%) of the respective trifluoromethylated adducts. An attempt was also made to ascertain if the carbonyl addition of **1a** proceeds diastereoselectively. Thus, 2-methylcyclohexanone was treated with **1a** in the presence of catalytic TBAF at 0 °C as well as at −78 °C. Surprisingly, however, the ratio of the two diastereomers remained unchanged (ca. 60/40).[28]



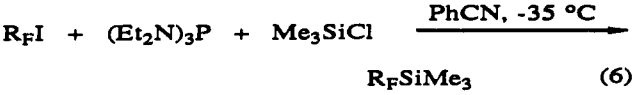
(5)

Next, we considered extending this reaction to introduce other perfluoroalkyl groups, such as pentafluoroethyl and heptafluoro-*n*-propyl, for which the corresponding (perfluoroalkyl)trimethylsilanes, **1b** and **1c**, were required. Attempts to prepare these hitherto unreported compounds by reaction of corresponding (perfluoroalkyl)lithium with Me_3SiCl resulted in very low yields of **1b** (5%) and **1c** (15%). Also, the volatile nature of these compounds made their isolation quite difficult. Much better yields were obtained, however, when a modified procedure of Ruppert et al.[18] was used (eq 6, see the Experimental Section). These compounds reacted readily with carbonyl compounds under fluoride initiation (Scheme II and Table II). The products are best isolated as the carbinols. Fur-

Scheme II



17: $R_F = C_2F_5$, R^1 = Ph, R^2 = Me
18: $R_F = C_2F_5$, R^1, R^2 = cyclo$(CH_2)_5$
19: $R_F = C_2F_5$, R^1 = Ph, R^2 = H
20: R_F = n-C_3F_7, R^1 = Ph, R^2 = Me
21: R_F = n-C_3F_7, R^1, R^2 = cyclo$(CH_2)_5$
22: R_F = n-C_3F_7, R^1 = Ph, R^2 = H



(6)

$R_F = C_2F_5$: 50%

$R_F = C_3F_7$: 68%

(27) Broicher, V.; Geffken, D. *Tetrahedron Lett.* **1989**, *30*, 5243.

Table II. Fluoride Ion Induced Pentafluoroethylation and Heptafluoropropylation of Carbonyl Compounds

carbonyl compound	product	overall yield (%)
	with **1b**	
$PhCOCH_3$	**17**	81
	**18**	82
PhCHO	**19**	86
	with **1c**	
$PhCOCH_3$	**20**	78
	**21**	81
PhCHO	**22**	66

Table III. Reaction of Lactones 23a–d with 1a

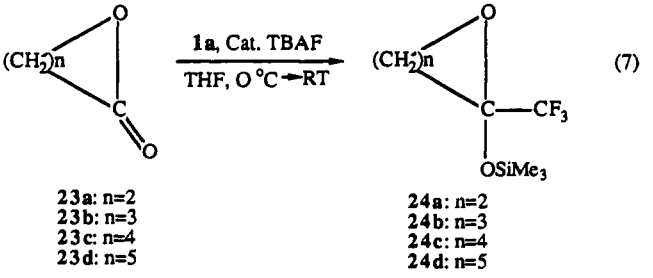
lactone	product(s)	yield (isolated), %
23a	**24a**	*a*
23b	**24b**	70
23c	**24c**	75
23d	**24d + 25 + 26**	*b*

[a] Product decomposed during distillation. [b] Yield of **24d** was not determined.

thermore, we did not observe formation of silyl enol ethers with any of the enolizable aldehydes and ketones in the reactions with the silanes **1**. In contrast (difluoromethyl)dimethylphenylsilane ($PhMe_2SiCHF_2$) reacts with carbonyl compounds under these conditions to give only silyl enol ethers.[22] It was suggested[22] that destabilization of the negative charge at the α-carbon in the difluoromethyl carbanion made it basic enough to induce enolization.[22,29]

Having established that (perfluoroalkyl)trimethylsilanes are versatile reagents to prepare perfluoroalkyl-substituted carbinols from aldehydes and ketones, we set out to explore a number or other reactions of the silane **1a** with substrates containing other carbonyl functional groups.[28]

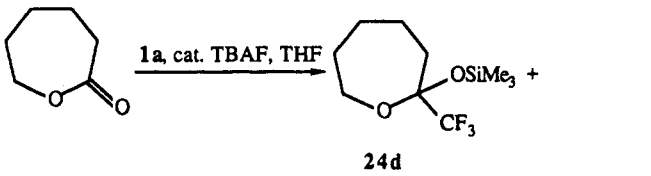
We first examined lactones for their reactivity toward **1a** under fluoride catalysis in THF. Indeed, **1a** adds smoothly to lactones **23** under these conditions (eq 7), but only the silylated hemiketals **24b** and **24c** could be isolated cleanly (Table III). The four-membered ring adduct **24a** decomposed extensively during distillation. In the case of the seven-membered ring lactone (**23d**), a mixture of products resulted (eq 8). From NMR and IR data it appears that the mixture consists of the desired adduct **24d** as well as **25** and **26**. The ketone **25** perhaps arises from fluoride-mediated ring opening of **24d**. However, **25** has a very reactive keto group. So, it reacts further with **1a** to give the bis-trifluoromethylated product **26**. These results show that a lactone carbonyl is sufficiently reactive to afford synthetically useful yields of interesting trifluoromethylated compounds, at least in the case of 5- and 6-membered ring systems. However, simple ester carbonyls did not react with **1a** even when a stoichiometric amount (with respect to **1a**) of TBAF was used. However, an activated ester, e.g., *n*-hexyl trifluoroacetate, reacted with **1a** in the presence of 1 molar equiv of TBAF to the extent of about 35% (^{19}F NMR) to give the silylated hemiketal **27** (eq 9).[28] Much of the silane **1a** was converted to undesired trifluoromethane due to rapid quenching of the incipient trifluoromethide species by protic impurities



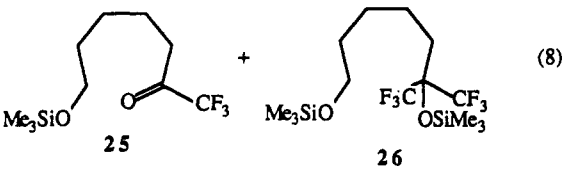
23a: n=2
23b: n=3
23c: n=4
23d: n=5

24a: n=2
24b: n=3
24c: n=4
24d: n=5

(7)



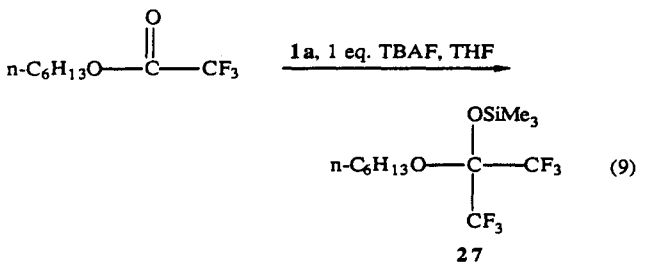
24d



25 **26**

(8)

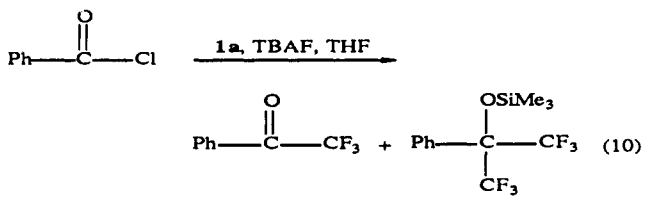
in the reaction mixture. Other activated esters, such as



27

(9)

oxalates, also are reactive toward **1a** under fluoride catalysis as reported recently in the case of di-*tert*-butyl oxalate.[27] Acid halides, such as benzoyl chloride, also reacted with **1a** to give a mixture of products (eq 10).[28] The reaction requires more than 1 molar equivalent of TBAF.



(10)

Summary

(Trifluoromethyl)trimethylsilane (**1a**), in the presence of a fluoride or oxyanion initiator, acts as a versatile and convenient equivalent for the exceedingly unstable trifluoromethyl carbanion. Perfluoroalkylation of aldehydes and ketones using the silanes **1** constitutes a general method for the preparation of a wide variety of perfluoroalkylated alcohols. An attractive feature of this reaction is the absence of enolization when aldehydes and ketones with α-hydrogens are used. Reactions of **1** with lactones leads to trifluoromethylated hemiketals.

Experimental Section

Proton, carbon-13, fluorine-19, and silicon-29 magnetic resonance spectra were obtained at 200, 50, 188, and 39.7 MHz, respectively, in $CDCl_3$ solution. IR spectra were obtained either as a KBr pellet or as neat films on KBr plates. Boiling points and melting points are uncorrected. Bromotrifluoromethane was supplied by E. I. DuPont de Nemours & Co. Anhydrous benzonitrile was obtained by drying the commercial sample over $MgSO_4$ followed by distillation from P_2O_5. Dry THF was obtained

(28) All of the exploratory reactions were conducted using 0.5–1.0 mmol of the substrate in THF and 1.2 equiv of **1a** either with catalytic or equivalent amount of TBAF. ^{19}F, ^{13}C, and ^1H NMR spectroscopy was used to deduce the formation of the product.

(29) Nakamura, E.; Murofushi, T.; Shimizu, M.; Kuwajima, I. *J. Am. Chem. Soc.* **1976**, *98*, 2346.

by distillation from lithium aluminum hydride. Hexaethylphosphorous triamide was prepared by the literature procedure.[31]

Preparation of (Trifluoromethyl)trimethylsilane (1a). Into a 2-L three-necked flask fitted with an efficient dry ice–acetone cold finger and a mechanical stirrer was placed 102 mL (87.3 g, 0.83 mol) of chlorotrimethylsilane dissolved in 100 mL of benzonitrile. Stirring was started, and the solution was cooled to ca. −30 °C. Bromotrifluoromethane (261 g, 1.75 mol) was precondensed in a flask and then allowed to evaporate into the reaction flask. The bath was cooled progressively until it was −60 °C. To the resulting slurry was added a solution of 216 g (0.876 mol) of hexaethylphosphorus triamide[30] in 175 mL of benzonitrile over a period of 2 h. After an additional hour at −60 °C, the bath and cold finger were allowed to warm up to room temperature, and the reaction mixture was stirred overnight. The reaction flask was then connected to a dry–acetone-cooled trap and subjected to aspirator vacuum (20 mm) with mild warming (45 °C) to drive out all volatile material. The liquid in the trap was washed rapidly with ice-cold water (3 × 75 mL), the product (top) layer was separated and dried ($MgSO_4$), and the dry liquid was decanted into a 100-mL flask. Fractional distillation using a 15-cm column packed with glass helices afforded 77.1 g (65% of theoretical yield, based on Me_3SiCl) of **1a** as a colorless liquid: bp 55–55.5 °C (lit.[18] bp 45 °C). GC and NMR analyses showed the product to be ca. 98% pure: ^1H NMR δ 0.25 (s); ^{13}C NMR δ 131.7 (q, $^1J(^{13}C-^{19}F)$ = 321.9 Hz), −5.2; ^{19}F NMR δ −66.1; ^{29}Si NMR δ +4.7 (q, $^2J(^{29}Si-^{19}F)$ = 37.9 Hz).

(Pentafluoroethyl)trimethylsilane (1b) and (heptafluoropropyl)trimethylsilane (1c) were similarly prepared following Ruppert's procedure. However, distilled **1b** and **1c** contained ca. 5% and 40%, respectively, of hexamethyldisiloxane as the impurity (formed during workup). The siloxane, however, was an innocuous impurity in subsequent reactions employing **1b** and **1c**.

(Pentafluoroethyl)trimethylsilane (1b): 50% yield; bp 69–70 °C; ^1H NMR δ 0.27 (s); ^{13}C NMR δ −5.0, 112.5–131.0 (CF_3CF_2); ^{19}F NMR δ −82.6 (br s, 3 F, CF_3), −132.1 (br s, 2 F, CF_2); MS (m/z) 169 (C_3F_7), 150, 131, 112, 93, 73 ($SiMe_3$), 69 (CF_3).

(Heptafluoropropyl)trimethylsilane (1c): 68% yield; bp 87–89 °C; ^1H NMR δ 0.12 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR δ −4.5, 105–132.0 ($CF_3CF_2CF_2$); ^{19}F NMR δ −80.8 (br s, 3 F, CF_3), −124.1 (br s, 2 F, CF_2), −129.7 (CF_2); MS (m/z) 119 (C_2F_5), 100, 81, 73 ($SiMe_3$), 69 (CF_3).

Trifluoromethylation of Aldehydes and Ketones. General Procedure To Prepare Trifluoromethylated Alcohols. A mixture of carbonyl compound (10 mmol) and **1a** (12 mmol) in 10 mL of THF cooled to 0 °C was treated with a catalytic amount (ca. 20 mg) of TBAF. Instantaneously, a yellow color developed with the initial evolution of fluorotrimethylsilane, and the reaction mixture was brought to ambient temperature and stirred. The mixture was periodically analyzed by GC for the completion of the reaction. The resulting siloxy compounds were then hydrolyzed with aqueous HCl. After the reaction, the mixture was extracted with ether (75 mL), and the ether extracts were washed with water (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated. The residue was either distilled or crystallized from a suitable solvent to give the products. The siloxy derivative **10** resulting from the reaction of benzophenone with **1a** was extremely resistant to hydrolysis (1 N HCl, 15 h, room temperature; 3 N HCl, 45–50 °C, 5 h). To prepare the carbinol **16**, 2.4 equiv of **1a** and 2 equiv of TBAF were used. Isolated yields and spectral data for all the prepared compounds are given below.

1-Phenyl-2,2,2-trifluoroethanol (4): 85% yield; colorless oil; bp 64–65 °C (5.0 mm); ^1H NMR δ 2.99 (br s, 1 H, OH), 4.89 (q, 1 H, J = 6.8 Hz), *H*COH), 7.34 (m, 5 H, Ph); ^{13}C NMR δ 72.8 (q, $^2J_{C-F}$ = 31.9 Hz), 124.3 (q, $^1J_{C-F}$ = 282.0 Hz, CF_3), 127.4, 128.6, 129.5, 134.0; ^{19}F NMR δ −79.2 (d, $^3J_{F-H}$ = 7.1 Hz); IR (film) 3405 (s), 1267 (s), 1172 (s) cm^{-1}. Anal. Calcd for $C_8H_7F_3O$: C, 54.55; H, 4.01. Found: C, 54.39; H, 4.18.

1-(Trifluoromethyl)-1-cyclohexanol (5): 77% yield; colorless oil, solidifies in receiver during distillation; bp 72–73 °C (40 mm); mp 59–61 °C; ^1H NMR δ 1.00–1.19 (m, 10 H), 1.93 (br s, 1 H, OH); ^{13}C NMR δ 20.2, 25.1, 29.8, 72.6 (q, $^2J_{C-F}$ = 28.2 Hz), 126.4 (q, $^1J_{C-F}$ = 284.4 Hz, CF_3); ^{19}F NMR δ −86.0; IR (KBr) 3364 (s), 1255 (s), 1146 (s) cm^{-1}. Anal. Calcd for $C_7H_{11}F_3O$: C, 50.00; H, 6.59. Found: C, 49.69; H, 6.51.

1-Cyclohexyl-2,2,2-trifluoroethanol (6): 80% yield; colorless oil; bp 60–61 °C (5.0 mm); ^1H NMR δ 1.00–2.20 (m, 11 H), 2.46 (br s, 1 H, OH), 3.69 (m, 1 H, C*H*OH); ^{13}C NMR δ 25.7, 26.0, 26.0, 26.8, 29.3, 38.3, 74.4 (q, $^2J_{C-F}$ = 28.9 Hz), 125.4 (q, $^1J_{C-F}$ = 283.4 Hz, CF_3); ^{19}F NMR δ −76.6 (d, $^3J_{C-F}$ = 7.6 Hz); IR (film) 3388 (s), 1276 (s), 1165 (s) cm^{-1}. Anal. Calcd for $C_8H_{13}F_3O$: C, 52.74; H, 7.19. Found: C, 52.06; H, 7.19.

1-Methyl-1-phenyl-2,2,2-trifluoroethanol (7): 74% yield; colorless oil; bp 69–70 °C (4.6 mm); ^1H NMR δ 1.78 (s, 3 H, CH_3), 2.59 (br s, 1 H, OH), 7.20–7.80 (m, 5 H, Ph); ^{13}C NMR δ 23.7, 74.9 (q, $^2J_{C-F}$ = 28.9 Hz), 125.6 (q, $^1J_{C-F}$ = 285.2 Hz, CF_3), 126.0, 128.3, 128.6, 138.5; ^{19}F NMR δ −81.8; IR (film) 3460 (s), 1287 (s), 1164–1074 (s) cm^{-1}. Anal. Calcd for $C_9H_9F_3O$: C, 56.84; H, 4.77. Found: C, 56.42; H, 4.84.

2-(Trifluoromethyl)-2-adamantanol (8): 72% yield; white crystals, sublimed; mp 117–118 °C; ^1H NMR δ 1.50–2.60 (m, 15 H); ^{13}C NMR δ 26.2, 26.9, 32.5, 33.2, 33.3, 38.3, 76.0 (q, $^2J_{C-F}$ = 26.4 Hz), 127.1 (q, $^1J_{C-F}$ = 286.8 Hz, CF_3); ^{19}F NMR δ −76.6; IR (KBr) 3408 (s), 1164–1049 (s) cm^{-1}. Anal. Calcd for $C_{11}H_{15}F_3O$: C, 59.99; H, 6.87. Found: C, 59.48; H, 6.69.

1-Cyclopropyl-1-phenyl-2,2,2-trifluoroethanol (9): 81% yield; colorless oil; bp 82–84 °C (3.0 mm); ^1H NMR δ 0.20–0.76 (m, 4 H), 1.51–1.64 (m, 1 H), 2.20 (br s, 1 H, OH), 7.20–7.80 (m, 5 H, Ph); ^{13}C NMR δ 0.10, 1.60, 15.6, 75.5 (q, $^2J_{C-F}$ = 27.8 Hz), 125.9 (q, $^1J_{C-F}$ = 286.9 Hz, CF_3), 126.4, 128.2, 128.6, 138.1; ^{19}F NMR δ −79.5; IR (film) 3485 (m), 1273 (m), 1152 (s) cm^{-1}. Anal. Calcd for $C_{11}H_{11}F_3O$: C, 61.11; H, 5.13. Found: C, 60.85; H, 4.96.

1,1-Diphenyl-1-((trimethylsilyl)oxy)-2,2,2-trifluoroethane (10): 88% yield; colorless oil; bp 104–106 °C (1.1 mm); ^1H NMR δ −0.06 (s, 9 H, $Si(CH_3)_3$), 7.10–7.50 (m, 10 H, 2 Ph); ^{13}C NMR δ 1.3 ($Si(CH_3)_3$), 82.1 (q, $^2J_{C-F}$ = 28.2 Hz), 125.2 (q, $^1J_{C-F}$ = 287.3 Hz, CF_3), 127.7, 127.8, 128.3, 141.0; ^{19}F NMR δ −73.5; IR (film) 1125–1255 (s) cm^{-1}. Anal. Calcd for $C_{17}H_{19}F_3OSi$: C, 62.95; H, 5.90. Found: C, 62.54; H, 5.75.

2-(Trifluoromethyl)bicyclo[2.2.1]heptan-2-ol (11): 92% yield; colorless oil; bp 47–49 °C (4.5 mm); ^1H NMR δ 1.10–1.46 (m, 4 H), 1.48–2.04 (m, 4 H), 2.26 (br s, 1 H, OH), 2.48 (m, 2 H); ^{13}C NMR δ 22.4, 27.3, 36.3, 39.0, 41.0, 42.9, 79.5 (q, $^2J_{C-F}$ = 28.3 Hz), 126.7 (q, $^1J_{C-F}$ = 283.4 Hz, CF_3); ^{19}F NMR δ −81.4; IR (film) 3397 (s), 1149 (s) cm^{-1}. Anal. Calcd for $C_8H_{11}F_3O$: C, 53.33; H, 6.15. Found: C, 52.88; H. 6.33.

5-(Trifluoromethyl)-5-nonanol (12): 87% yield; colorless oil; bp 65–66 °C (3.3 mm); ^1H NMR δ 0.90 (m, 6 H, 2 CH_3), 1.10–1.80 (m, 12 H), 2.04 (br s, 1 H, OH); ^{13}C NMR δ 13.8, 23.1, 24.8, 33.2, 75.5 (q, $^2J_{C-F}$ = 27.4 Hz), 126.8 (q, $^1J_{C-F}$ = 286.5 Hz, CF_3); ^{19}F NMR δ −80.7; IR (film) 3428 (m), 1167–1130 (s) cm^{-1}. Anal. Calcd for $C_{10}H_{19}F_3O$: C, 56.59; H, 9.02. Found: C, 56.57; H, 8.98.

3-(Trifluoromethyl)-5α-cholestan-3-ol (13): 83% yield; white crystals (from methanol); mp 127–128 °C; ^1H NMR δ 0.50–2.20 (m, 47 H); ^{13}C NMR δ 11.2, 11.7, 18.3, 20.8, 22.2, 22.4, 23.5, 23.8, 27.6, 27.8, 28.1, 28.6, 31.3, 34.6, 35.0, 35.1, 35.4, 35.8, 39.1, 39.5, 41.3, 42.2, 53.6, 55.9, 56.0, 72.1 (q, $^2J_{C-F}$ = 27.3 Hz), 126.6 (q, $^1J_{C-F}$ = 286.1 Hz, CF_3); ^{19}F NMR δ −79.6; IR (KBr) 3394 (s), 1152–1170 (s) cm^{-1}. Anal. Calcd for $C_{28}H_{47}F_3O$: C, 73.64; H, 10.37. Found: C, 73.08; H, 10.22.

1-(Trifluoromethyl)-2-cyclohexen-1-ol (14) and 3-(trifluoromethyl)cyclohexanone (15): 60% yield; mixture (ca. 90/10) of **14** and **15**, respectively; colorless oil, bp 67.5–68.5 °C (20 mm). Spectral data for major isomer (**14**): ^1H NMR δ 1.50–2.65 (m, 6 H), 2.93 (br s, 1 H, OH), 5.66 (br d, 1 H), 6.10 (m, 1 H); ^{13}C NMR δ 17.1, 24.7, 28.9, 70.5 (q, $^2J_{C-F}$ = 28.9 Hz), 122.8, 126.0 (q, $^1J_{C-F}$ = 284.0 Hz, CF_3), 136.1; ^{19}F NMR δ −83.4; IR (film) 3396 (m), 1656 (m, C=C), 1152 (s) cm^{-1}. Minor isomer (**15**): IR (film) 1712 (m, C=O) cm^{-1}; ^{19}F NMR δ −75.5 (d, $^3J_{F-H}$ = 7.1 Hz). Anal. Calcd for $C_7H_9F_3O$: C, 50.60; H, 5.46. Found: C, 50.04; H, 5.51.

3-Methoxy-17-(trifluoromethyl)estra-1,3,5(10)-trien-17-ol (16): 62% yield of 90/10 mixture of **16** and estrone methyl ether, respectively. Pure **16** was obtained by recrystallizing thrice from cold (−10 °C) methanol: white powder; mp 95–97 °C; ^1H NMR

(30) Alkyl halides have been trifluoromethylated in moderate yields with trifluoromethylcopper. See: Kobayashi, Y.; Yamamoto, K.; Kumadaki, I. *Tetrahedron Lett.* **1979**, *42*, 4071.

(31) Stuebe, C.; Lankelma, H. P. *J. Am. Chem. Soc.* **1956**, *78*, 976.

δ 1.03 (s, 3 H, CH_3), 1.20–2.65 (m, 14 H), 2.90 (m, 2 H), 3.83 (s, 3 H, OCH_3), 6.73 (m, 2 H), 7.24 (m, 1 H); ^{13}C NMR δ 14.7, 23.7, 26.3, 27.5, 29.7, 32.5, 33.5, 39.3, 43.2, 47.1, 50.4, 55.2, 84.6 (q, $^2J_{C-F}$ = 26.0 Hz), 111.5, 113.8, 126.2, 127.1 (q, $^1J_{C-F}$ = 285.9 Hz, CF_3), 132.3, 137.8, 157.5; ^{19}F NMR δ -76.0; IR (KBr) 3442 (s), 1033–1254 (s) cm^{-1}. Anal. Calcd for $C_{20}H_{25}F_3O_5$: C, 68.27; H, 7.64. Found: C, 67.92; H, 7.26.

Preparation of Pentafluoroethyl- and Heptafluoropropyl-Substituted Alcohols (17–22). General Procedure. The same procedure as that described above to prepare the trifluoromethylated siloxy derivatives was employed here. However, the cleavage of the siloxy derivatives to the corresponding alcohols was effected by tetrabutylammonium fluoride (1 M solution in THF) as follows. To the cooled (0 °C) reaction mixture was added dropwise with stirring 10 mL of 1 M TBAF (10 mmol) in THF. After the addition the ice bath was removed, and the solution was stirred at room temperature for 5 h. Subsequent workup procedure was identical with that described above to isolate the trifluoromethylated alcohols.

2-Phenyl-3,3,4,4,4-pentafluorobutan-2-ol (17): 81% yield; colorless oil; bp 69–70 °C (3.6 mm); ^1H NMR δ 1.77 (s, 3 H, CH_3), 2.66 (s, 1 H, OH), 7.30–7.57 (m, 5 H, Ph); ^{13}C NMR δ 24.3, 75.1 (t, $^2J_{C-F}$ = 24.0 Hz), 108.9–123.0 (m, CF_2CF_3), 126.1, 128.2, 128.5, 138.6; ^{19}F NMR δ -78.4 (s, 3 F, CF_3), -121.7 (d, 1 F, J_{gem} = 277.4 Hz, C*F*(F)), -123.7 (d, 1 F, Jg_{em} = 277.4 Hz, CF(*F*)). Anal. Calcd for $C_{10}H_9FO$: C, 50.00; H, 3.78. Found: C, 50.38; H, 3.42.

1-(Pentafluoroethyl)-1-cyclohexanol (18): 82% yield; colorless oil; bp 63–64 °C (20 mm); ^1H NMR δ 1.66 (m, 10 H), 2.19 (s, 1 H, OH); ^{13}C NMR δ 20.2, 24.9, 29.7, 73.4 (t, $^2J_{C-F}$ = 22.7 Hz), 108.7–129.0 (m, CF_3CF_2); ^{19}F NMR δ -78.9 (3 F, CF_3), -127.7 (2 F, CF_2). Anal. Calcd for $C_8H_{11}F_5O$: C, 44.04; H, 5.08. Found: C, 44.06; H, 5.05.

1-Phenyl-2,2,3,3,3-pentafluoropropanol (19): 86% yield; colorless oil; bp 73–74 °C (4.2 mm); ^1H NMR δ 3.03 (br s, 1 H, OH), 4.97 (dd, 1 *H*, J_{H-F} = 16.4, 7.8 Hz, C*H*OH), 7.36 (br s, 5 H, Ph); ^{13}C NMR δ 72.0 (dd, J_{C-F} = 27.6, 22.9 Hz), 106.9–122.7 (m, CF_3CF_2), 127.9, 128.6, 129.7, 133.8; ^{19}F NMR δ -81.9 (3 F, CF_3), -122.8 (m, 1 F, $CF_3CF(F)$), -129.3 (m, 1 F, $CF_3C(F)F$). Anal. Calcd for $C_9H_7F_5O$: C, 47.80; H, 3.12. Found: C, 47.98; H. 3.14.

2-Phenyl-3,3,4,4,5,5,5-heptafluoropentan-2-ol (20): 78% yield; colorless oil; bp 63–64 °C (1.7 mm); ^1H NMR δ 1.80 (s, 3 H, CH_3), 2.66 (br s, 1 H, OH), 7.34–7.95 (m, 5 H, Ph); ^{13}C NMR δ 24.8, 76.4 (m), 104.0–121.7 (m, $CF_2CF_2CF_3$), 126.2, 128.2, 128.5, 138.7; ^{19}F NMR δ -81.5 (t, 3 F, $^3J_{F-F}$ = 10.7 Hz, CF_3), -117.1 to -120.8 (m, 2 F, CF_2), -121.5 to -125.2 (m, 2 F, CF_2). Anal. Calcd for $C_{11}H_9F_7O$: C, 45.53; H, 3.13. Found: C, 46.05; H, 3.11.

1-(Heptafluoropropyl)-1-cyclohexanol (21): 81% yield; colorless oil; bp 77–78 °C (20 mm); ^1H NMR δ 1.67 (m, 10 H), 2.63 (br s, 1 H, OH); ^{13}C NMR δ 20.3, 25.0, 29.8, 74.9 (t, $^2J_{C-F}$ = 22 Hz), 104.0–132.2 (m, $CF_2CF_2CF_3$); ^{19}F NMR δ -81.7 (t, 3 F, $^3J_{F-F}$ = 10.6 Hz, CF_3), -123.9 to -124.2 (m, 4 F, CF_2CF_2). Anal. Calcd for $C_9H_{11}F_7O$: C, 40.31; H, 4.13. Found: C, 40.36; H, 4.25.

1-Phenyl-2,2,3,3,4,4,4-heptafluorobutan-1-ol (22): 66% yield; colorless oil; bp 75–76 °C (3 mm); ^1H NMR δ 3.37 (br s, 1 H, OH), 5.00–5.12 (m, 1 H, *H*COH), 7.36 (m, 5 H, Ph); ^{13}C NMR δ 72.0 (dd, J_{C-F} = 28.2, 22 Hz), 103.0–121.4 (m, $CF_2CF_2CF_3$), 128.1, 128.6, 129.7, 134.0; ^{19}F NMR δ -81.6 (t, 3 F, $^3J_{F-F}$ = 10.2 Hz), -118.5 to -120.2 (m, 1 F, C*F*(F)CF_2), -126.0 to -128.1 (m, 3 F, CF(*F*)CF_2). Anal. Calcd for $C_{10}H_7F_7O$: C, 43.49; H, 2.55. Found: C, 43.06; H, 2.46.

General Procedure for Reaction of Lactones with 1a. Preparation of Compounds 24b and 24c. The stoichiometry and reaction conditions employed here were the same as that used to prepare the siloxy derivatives of the trifluoromethyl-substituted alcohols (see above). Thus 10 mmol of the lactone **23** and 12 mmol of **1a** in 10 mL of THF were treated with catalytic amount of TBAF (20 mg) at 0 °C. The ice bath was removed, and the reaction mixture was allowed to warm up to room temperature. After 1 h the solvent was removed with a rotary evaporator. Distillation of the residue afforded pure products. In the case of β-propiolactone (**23a**), the adduct **24a** was stable in solution. However, it decomposed extensively during attempted distillation under reduced pressure. ε-Caprolactone (**23d**) gave a mixture of products (see text) which was not separated. The product identities of **24d**, **25**, and **26** were carried out by GC–MS analysis and ^{13}C and ^{19}F NMR spectroscopy (three peaks at δ -80.3, -76.2, and -81.4 for **24d**, **25**, and **26**, respectively).

2-(Trifluoromethyl)-2-((trimethylsilyl)oxy)tetrahydrofuran (24b): 70% yield; colorless oil; bp 78–80 °C (40 mm); ^1H NMR δ 0.13 (s, 9 H, $Si(CH_3)_3$), 1.95–2.30 (m, 4 H), 3.90 (br q, 1 H, J = 7.2 Hz), 4.13 (m, 1 H); ^{13}C NMR δ 1.1, 24.4, 35.4, 70.7, 104.0 (q, $^2J_{C-F}$ = 32.8 Hz, $(CH_3)_3SiO(C)CF_3$), 123.1 (q, $^1J_{C-F}$ = 285.7 Hz, CF_3); ^{19}F NMR δ -84.5. Anal. Calcd for $C_8H_{15}F_3O_2Si$: C, 42.11; H, 6.63. Found: C, 42.50; H. 6.73.

2-(Trifluoromethyl)-2-((trimethylsilyl)oxy)tetrahydropyran (24c): 75% yield; colorless oil; bp 96–98 °C (38 mm); ^1H NMR δ 0.18 (s, 9 H, $Si(CH_3)_3$), 1.69 (m, 6 H), 3.75 (m, 2 H); ^{13}C NMR δ -1.35, 15.8, 22.7, 28.0, 60.1, 92.4 (q, $^2J_{C-F}$ = 31.7 Hz, $(CH_3)_3SiO(C)CF_3$), 121.3 (q, $^1J_{C-F}$ = 286.7 Hz, CR_3); ^{19}F NMR δ -81.2. Anal. Calcd for $C_9H_{17}F_3O_2Si$: C, 44.63; H. 7.07. Found: C, 44.35; H, 7.49.

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A Photoannulation Route to Naphthalenes from Cyclic Ketones

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A three-step naphthalene annulation of cyclic ketones has been developed. Aldol condensation with an aromatic aldehyde followed by Wittig olefination produces a 1,3-diene, which undergoes oxidative photocyclization to produce a naphthalene derivative. Ketone ring sizes of C_5 to C_8 were annulated successfully. The sequence was also applied successfully to three methyl-substituted derivatives and one polycyclic case.

Introduction

The photochemical electrocyclization of six π electron systems is one of the most general and useful organic photochemical transformations. The oxidative photocyclization of stilbenes to phenanthrenes, for example, has been widely studied and regularly reviewed.[1] A potentially useful example of a six π electron photocyclization is the conversion of a 1-aryl-1,3-butadiene to a naphthalene derivative. This reaction has been reported for several substituted examples[2] but the reaction fails for the parent hydrocarbon, 1-phenyl-1,3-butadiene; a variety of photoaddition and four π electron cyclization reactions are observed instead.[3] We initially felt that the failure of the

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