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A Facile Stereoselective Synthesis of (*E*)-1-Aryl-1,2,3,3,3-pentafluoropropenes and (*E*)-1-Aryl-2-chloro-1,3,3,3-tetrafluoropropenes

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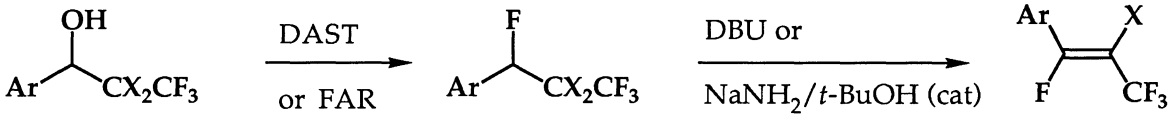
Arenecarbaldehydes ArCHO were allowed to react with a carbenoid reagent CF_3CX_2MtI (X = Cl, MtI = ZnCl; X = F, MtI = Li) to give adducts $ArCH(OH)CX_2CF_3$ whose hydroxyl group was substituted by fluorine. Dehydrohalogenation of the resultant $ArCHFCX_2CF_3$ (X = Cl or F) with DBU or $NaNH_2$/*t*-BuOH (cat) gave with excellent selectivity the title (*E*)-propenes.

Polyhalo-olefins including polyfluoro-olefins are versatile synthetic building blocks[1] and therefore employed for the synthesis of biologically active target molecules such as 1-aryl-2,2-dichloroethenes and 1-aryl-2-chloro-3,3,3-trifluoropropenes which respectively exhibit potent nematocidal and insecticidal activities.[2] Discussions on intensifying the biological activities led us to design perhalo-olefins of well-defined geometry.[3] In addition, synthesis of polyfluorinated (*E*)- and/or (*Z*)-olefins under high stereocontrol should allow us to study the stereochemical aspects of the synthetic, kinetic, and biological study of fluorine-containing compounds. For example, Dmowski[4a] and Wakselman[4b] independently demonstrated that the geometry of the olefins affected the regiochemistry of the nucleophilic reaction of polyfluorinated propenes. To our surprise, less attention has been paid to the selective synthesis of each stereoisomer due probably to the limited number of synthetic methods.[5] We report herein a facile stereoselective synthesis of (*E*)-1-aryl-2-chloro-1,3,3,3-tetrafluoropropenes (**1**) and (*E*)-1-aryl-1,2,3,3,3-pentafluoropropenes (**2**).



3 (X = Cl)
4 (X = F)

5 (X = Cl)
6 (X = F)

1 (X = Cl)
2 (X = F)

Organometallic reagents of type $MtlCX_2CF_3$ (MtI = ZnCl, X = Cl[6] or MtI = Li, X = F[7]) were reacted with arenecarbaldehydes to give adducts **3** or **4** respectively in good yields. The hydroxyl group of **3** and **4** was fluorinated with (diethylamino)sulfur trifluoride (DAST)[8] or the Ishikawa reagent hexafluoropropene-diethylamine (FAR)[9] to give fluorides **5** and **6** in good to excellent yields without any formation of dibenzyl ether byproducts.[10] Typical results are summarized in Table 1. Fluorination of alkanal-CX_2CF_3 adducts corresponding to **3** and **4** resulted in the recovery of the starting alcohols and/or formation of dehydration

products. Probably the intermediate cationic species or the transition state must be well stabilized by the Ar substituent for the success of the fluorination.

Subsequent dehydrohalogenation was carried out by using a base. When **5** was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane at room temperature, olefin **1** was obtained in good yield with high *E*-selectivity (Table 1). The *E*/*Z* ratios[11] determined by capillary gas chromatography fall within the range of 20-40 : 1. Metal alkoxides did not give high selectivity: Treatment of **5e** with potassium *t*-butoxide afforded **1e** in 76% yield with a 6 : 1 *E*/*Z* ratio in benzene; the reaction in tetrahydrofuran (THF) gave rise to 1-*t*-butoxy-2-chloro-3,3,3-trifluoro-1-(4-methoxyphenyl)propene in 46% yield with no trace of **1e**. Ortho-substituted substrate **5f** did not undergo the dehydrochlorination with DBU.

Dehydrofluorination of **6**, in contrast, could not be achieved with DBU. An electronegative fluorine might have prevented the attack of DBU to the geminal methine proton and, thus, a different type of base was needed. After screening a number of bases, we found that the combination of sodium amide and a catalytic amount of 2-methyl-2-propanol in THF at room temperature gave the best results as shown in Table 1. Sodium amide alone did not afford the desired olefin **1** effectively. It is noteworthy that the $NaNH_2$/*t*-BuOH (cat) system was not stereoselective enough for **1e**: *E* : *Z* = 5 : 1.

The high *E*-selectivity observed in the dehydrohalogenation of **5** and **6** may be ascribed to an anti-elimination of HX through a conformer like **A**, in which the net steric interactions are smaller than those in an alternative conformer **B**.[12] On the other hand, when **5** or **6** was treated with metal alkoxide, a chelate intermediate **C** wherein M^+ is Na^+ or K^+ might have been involved to some extent. This pathway leading to (*Z*)-olefins seems to be particularly remarkable in the convertion of **6e** into **2e** by means of *t*-BuOK in benzene. The fact that the same reaction carried out in THF gave (*E*)-**2e** predominantly may by ascribed to competitive coordiantion of THF to potassium ion to prevent such F-K^+ interaction. As a result, a pathway going through an intermediate **A** predominated to give rise to (*E*)-isomer.

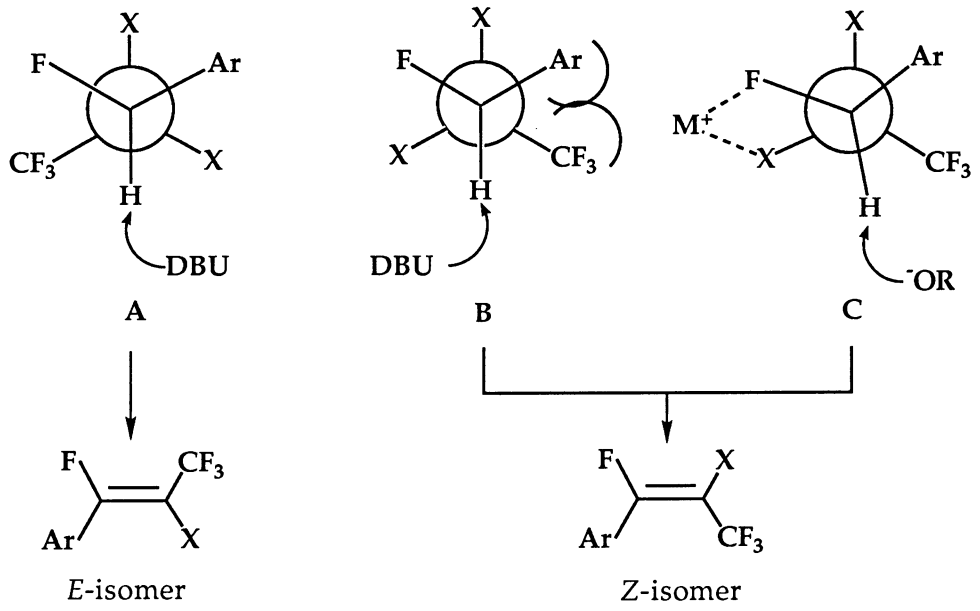
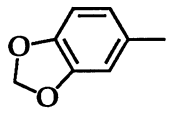


Table 1. Preparation of Polyfluorinated Propenes **1** and **2**

Ar	X		Fluorination reagent[a]	Product	% Yield[b]	Dehydrohalogenation base[c]	Product	% Yield[b]	$E:Z$[d]
Ph-	Cl	(3a)	FAR	**5a**	80	DBU	**1a**	75	24 : 1
			DAST	**5a**	83				
1-Naph-	Cl	(3b)	FAR	**5b**	85	DBU	**1b**	96	20 : 1
			DAST	**5b**	95				
4-Cl-C_6H_4-	Cl	(3c)	FAR	**5c**	92	DBU	**1c**	92	37 : 1
3,4-Cl_2-C_6H_3-	Cl	(3d)	FAR	**5d**	64	DBU	**1d**	88	40 : 1
			DAST	**5e**	98				
4-MeO-C_6H_4-	Cl	(3e)	FAR		99	DBU	**1e**	88	23 : 1
						t-BuOK[e]	**1e**	0[f]	
						t-BuOK[g]	**1e**	71	6 : 1
						$NaNH_2$/*t*-BuOH[e]	**1e**	94	5 : 1
2-MeO-C_6H_4-	Cl	(3f)	FAR	**5f**	91	DBU	**1f**	0[h]	
						$NaNH_2$/*t*-BuOH[e]	**1f**	98	2 : 1
	Cl	(3g)	FAR	**5g**	93	DBU	**1g**	93	25 : 1
Ph-	F	(4a)	FAR	**6a**	82	$NaNH_2$/*t*-BuOH[e]	**2a**	78	31 : 1
4-Cl-C_6H_4-	F	(4c)	FAR	**6c**	77	$NaNH_2$/*t*-BuOH[e]	**2c**	75	19 : 1
4-MeO-C_6H_4-	F	(4e)	FAR	**6e**	86	DBU	**2e**	0[h]	
						t-BuOK[e]	**2e**	66[i]	25 : 1
						t-BuOK[g]	**2e**	96	1 : 1.2
						$NaNH_2$/*t*-BuOH[e]	**2e**	89	13 : 1
						t-BuOLi[j]	**2e**	0[h]	
2-MeO-C_6H_4-	F	(4f)	DAST	**6f**	30[k]	$NaNH_2$/*t*-BuOH[e]	**2f**	85	25 : 1

a) The reaction was carried out in dichloromethane at 0 °C (with FAR) or at -78 °C (with DAST) using the fluorinating reagent (1.1 equiv.). b) Isolated yield. c) The amount of the base was following: DBU (1.2 equiv.), *t*-BuOK (3 equiv.), $NaNH_2$ (5 equiv.)/*t*-BuOH (cat), *t*-BuOLi (3 equiv.). The reaction was carried out in dichloromethane at room temperature unless otherwise noted. d) The *E*/*Z* ratio was determined by capillary gas chromatography (OV-1, 50 m). e) THF was used as the solvent. f) A 3 : 1 stereoisomeric mixture of 1-*t*-butoxy-2-chloro-3,3,3-trifluoro-1-(4-methoxyphenyl)propene was obtained in 46% yield. g) Benzene was used as the solvent. h) No reaction. i) A mixture of 1-*t*-butoxy-2,3,3,3-tetrafluoro-1-(4-methoxyphenyl)propene and 2-*t*-butoxy-1,3,3,3-tetrafluoro-1-(4-methoxyphenyl)propene was obtained as byproducts (14%).
j) 2-Methyl-2-propanol was used as the solvent. k) A dimeric product tentatively assigned as 1,1,1,2,2,3-hexafluoro-3-[2-methoxy-3-{2,2,3,3,3-pentafluoro-1-(2-methoxyphenyl)propyl}phenyl]propane was obtained as a byproduct (27%).

The (*Z*)-isomers of **5** and **6** were accessible by photochemical isomerization[14] using a high pressure Hg lamp at 20 °C to give a photostationary 1 : 2 mixture of (*E*)- and (*Z*)-propenes within 30 min. These two isomers were readily separated by chromatography. Thus, both (*E*)- and (*Z*)-isomers of **1** and **2**, available by the synthetic method presented herein, allows us to study the stereochemical aspects of stereospecificity and stereoselectivity of fluorine-substituted olefins as well as the biological assay of each stereoisomer.

References

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10) Fluorination of benzyl alcohols with FAR gives a fair amount of dibenzyl ethers in addition to the fluorination products. See Ref. 9.
11) The stereochemistry of the propene was assigned on the basis of the coupling constants observed in ^{13}C- and ^{19}F-NMR spectra: $^{4}J_{F\text{-}F}$ = 24.6 Hz (*E*) and 9.9 Hz (*Z*), and $^{3}J_{C\text{-}F}$ = 2.2 Hz (*E*) and 10.4 Hz (*Z*) for **1e**; $^{3}J_{F\text{-}F}$ = 130.7 Hz (*E*) and 9.0 Hz (*Z*) for **2e**.
12) Steric requirements of a CF_3 group are known to be greater than those for a chlorine or fluorine atom. H. Oberhammer, *J. Fluorine Chem.*, **23**, 147 (1983).
13) Recently, some kinds of metal ions are suggested to interact with fluorine(s) of fluorinated organic compounds. See C. A. Mirkin, K.-L. Lu, G. L. Geoffroy, and A. L. Rheingold, *J. Am. Chem. Soc.*, **112**, 461 (1990); Y. Morizawa, A. Yasuda, and K. Uchida, *Tetrahedron Lett.*, **27**, 1833 (1986); H. L. Carrell, J. P. Glusker, E. A. Piercy, W. C. Stallings, D. E. Zacharias, R. L. Davis, C. Astbury, and C. H. L. Kennard, *J. Am. Chem. Soc.*, **109**, 8067 (1987); P. Murray-Rust, W. C. Stallings, C. T. Monti, R. K. Preston, and J. P. Glusker, *ibid.*, **105**, 3206 (1983).
14) The isomerization did not occur below 200 °C.

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